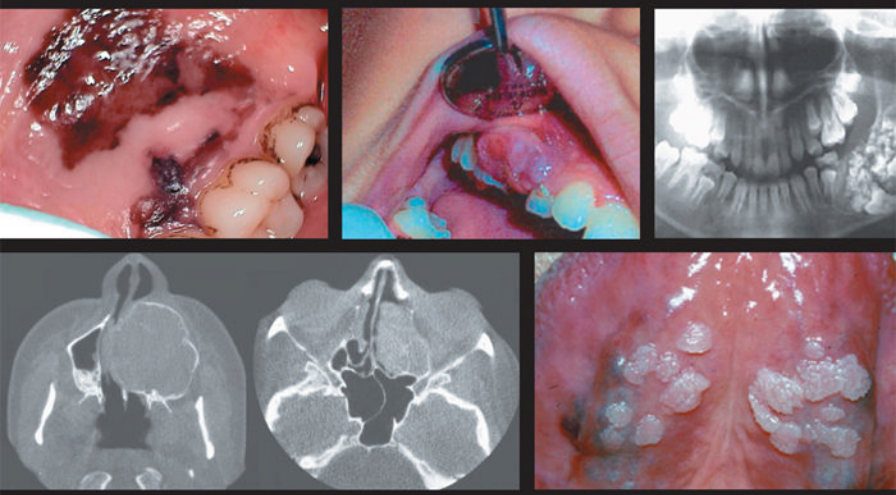
Fourth Edition

CLINICAL OUTLINE OF ORAL PATHOLOGY



• LEWIS R. EVERSOLE •

CLINICAL OUTLINE OF ORAL PATHOLOGY: DIAGNOSIS AND TREATMENT

FOURTH EDITION

CLINICAL OUTLINE OF ORAL PATHOLOGY: DIAGNOSIS AND TREATMENT

Fourth Edition

Lewis R. Eversole

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Contents

The Diagnostic Process

1

The diagnostic process involves four sequential steps: (1) obtainment of a comprehensive overview of the patient's past and current health status, referred to as the historical data base; (2) evaluation of all the findings to correlate the chief sign or symptoms with the current history, other physical findings, and the medical history; (3) formulation of a differential diagnosis to include all disease processes that could conceivably account for the collective findings; and (4) arrival at a definitive diagnosis on the basis of interrogation and specific clinical and laboratory tests that exclude specific diseases and point to a definite disease process. Once the diagnostic process is consummated, a plan for treatment can be generated with establishment of a follow-up assessment program.

Thorough and open communication between doctor and patient is a prerequisite to the diagnostic process. Because the ultimate goal is the definitive diagnosis, the doctor is charged with the duty of sleuth par excellence, meaning he or she must develop the communication skills to become an eminent interrogator. The questioning process is as important as having a large knowledge base regarding disease processes and the skills necessary to recognize tissue changes. The process of interrogation helps to exclude diseases that, on the basis of physical appearance or symptoms alone, would have been included as initial possibilities. What questions does one ask? First, the clinician must have a reasonable comprehensive knowledge of the possible disease entities he or she may encounter. Without this knowledge base, the appropriate line of questioning may not be obvious. Alternatively, the examiner who is aware of the various diseases sharing common symptoms or physical signs can ask appropriate questions to begin the process of elimination (i.e., limiting the differential diagnosis). As we proceed through the sequential steps of the diagnostic process, emphasis is placed on the development of a logical approach to interrogation.

Procurement of the Data Base

CHIEF COMPLAINT AND HISTORY OF THE PRESENT ILLNESS

The initial contact with the patient should be met with concern conveying a desire to be of assistance. Patients are often upset, fearful, annoyed, or short-tempered when they feel they are ill or have something wrong with them, particularly when pain is the primary complaint or when they have sought help from other health practitioners who were unable to arrive at a diagnosis. Nonverbal communication such as a hand on the shoulder, a look of kindness, or a comment expressing concern and determination to help will open the doors to trust and communication. Once these subtle gestures have helped to establish rapport, an assessment of the patient's problem or chief complaint can be explored. The chief complaint usually emerges as a symptom, a sign, or both.

Symptoms are subjective, representing a definite problem expressed by the patient. Common symptoms of oral and maxillofacial disease processes include the following:

Discomfort: Pain, ache, numbness (hypesthesia), tingling (paresthesia), itching (pruritus), burning, rawness, tenderness, and clicking/popping of temporomandibular joint (TMJ).
Textural changes: Roughness, dryness (xerostomia, xerophthalmia), and swelling (growth, enlargement).
Functional changes: Difficulty with swallowing, opening, or chewing: altered bite, taste, or hearing; difficulty with speech: tooth clenching or grinding: joint sounds; loose teeth and bleeding from mouth, gingiva, or nose.

Once the chief symptom is recorded, questioning helps to define the problem

more accurately. Interrogation revolving around the chief complaint should explore the nature of the problem, the duration, the periodicity, the location, and association with factors known to the patient. For example, if a patient complains of pain, the examiner should explore its nature (i.e., sharp, dull, throbbing, etc.). How long has the symptom been a problem? Has it persisted for a few hours, a few days, or for weeks, or months? What is the periodicity of the pain? Is it constant, intermittent, only at night, only at mealtime? Where is the pain located? It is localized or does it radiate? Can it be associated with hot liquids, cold liquids, spicy foods, citrus fruits, sugar, pressure, percussion? A similar line of questioning can be pursued for other subjective complaints or symptoms.

Signs are objective changes that can be observed or detected by palpation, percussion, auscultation, or analysis of laboratory data. Common signs of oral and maxillofacial disease processes include the following:

Soft-tissue changes: White, red, or pigmented spots or patches; ulcerations; blisters; multiple small nodules (papules); nodules; papillary growths; localized swellings; and diffuse swellings.
Hard-tissue changes (Clinical): Dental changes in number, shape, or structure; localized or diffuse osseous swellings; and facial asymmetry.
Hard-tissue changes (Radiographic): Dental changes, radiolucent or radiopaque lesions, and mixed radiolucent/radiopaque lesions.
Neuromuscular functional changes: Paralysis or flaccidness, muscle spasm or hypertrophy, sensory deficits, and alteration in salivation.

Not all patients relate a specific symptom. Often, they observe a change in the tissues. Objective signs can be noticeable tissue changes that the patient observes or changes that may be unknown to the patient but have been detected during the course of the physical examination. Signs should be characterized in detail by exploring their features and history. When a patient states that he or she discovered a tissue change, the clinician should attempt to uncover, through questioning, the nature of the disease from the patient's perspective, the duration, the location, and any associated factors. For example, a patient may state that while looking in the mirror he or she discovered a white patch on the tongue. The examiner will want to know how the patient perceives the change. Is it sore? Can you feel its presence? How long ago did you first notice it? Is that the only place in your mouth you've noticed a change? Do you recall biting your tongue or burning it?

MEDICAL AND DENTAL HISTORY

The recording of the problem—be it a symptom, a sign, or both—along with the history of the illness should have allowed the examiner to contemplate a partial list of suspected disease processes. At this point, the chief complaint is put aside until other aspects of the data base are procured. The next step in the diagnostic process is to evaluate the patient's history of illness. The patient's general health status is reviewed by determining how the patient feels. Does he or she feel weak or febrile? Any significant weight loss or loss of appetite? A history of past illness according to the body's organ systems is reviewed; the examiner knows that certain medical problems require dental treatment precautions. Furthermore, many systemic diseases manifest observable oral and facial lesions. Habits and medications can also affect the tissues of the head and neck. Previous hospitalizations and any complications from

past medical treatment can have a bearing on the oral and maxillofacial tissues. Finally, the dental history might have some influence with regard to the presenting problem.

PHYSICAL EXAMINATION

Provided the patient has no significant medical problems that would militate against proceeding with the physical examination, the examiner should begin a systematic evaluation of the tissues. In medicine, physical diagnosis involves examination of the organ systems. In dentistry, the primary emphasis is examination of the head and neck. Usually, prior to a detailed evaluation of these tissues, the vital signs, including blood pressure, pulse, respiration, and temperature are assessed. Subsequently, physical examination should include the external structures of the scalp, face, exposed skin, and hands; the oral, nasal, and laryngeal cavities; the tympanic membrane; the salivary glands and neck; the TMJ; and the dentition and periodontium. During the physical examination, deviations from normal are recorded.

Once the physical examination has been completed, the examiner should recall the chief complaint and focus attention on physical changes associated with the presenting signs and symptoms. Once a lesion has been uncovered and clinically characterized, the examiner should proceed by ordering adjunctive diagnostic tests. Many tests are available, and they should be used discriminantly to avoid excessive cost to the patient. In general, a differential diagnosis is established once the data base from the history and physical examination has been completed. When signs and symptoms point to a disease process in bone, however, radiographs are usually obtained prior to formulation of a differential diagnosis.

RADIOGRAPHIC EXAMINATION

When the patient's history and physical examination suggest pain of dental or osseous origin, salivary occlusion, asymmetry, or osseous enlargement, appropriate radiographs are obtained to characterize dental or intraosseous disease processes. In general, periapical and panoramic films are used initially. The location of the suspected problem dictates the use of specific types of radiographs (Table 1.1). New technology is emerging rapidly in radiology; detailed tissue imaging is possible with the use of three-dimensional computerized tomography, radioisotopic scanning, xeroradiography, and nuclear magnetic resonance imaging techniques. Many of these techniques are costly, yet may be extremely valuable diagnostically as well as for determining extent of disease. In most cases, routine radiographs and tomograms are obtained initially, and special radiographs are obtained as needed or when indicated. Cone beam CT has become an extremely valuable tool for dental diagnostics.

The ability of the radiologist or the clinician to describe the radiomorphology and list diseases known to exhibit specific patterns is of major importance. Radiographic interpretation alone is rarely diagnostic.

CLINICAL LABORATORY TESTS

Clinical findings may indicate the need for diagnostic clinical tests conducted by the pathology laboratory. These tests are used to evaluate blood chemistries, immunologic reactivity (serology), hematologic functions, urinalysis, microbiology, and genomic assays. Specific oral signs and symptoms may suggest a metabolic disease such as hyperparathyroidism whereby testing for serum calcium, phosphate, and

TABLE 1.1 Radiographs in Oral and Maxillofacial Medicine

Area of Investigation	*Radiography*
Dental caries	Bitewing
Infections of dental origin	Periapicals
Impactions	Panoramic, cone beam CT
Jaw lesions	Panoramic, cone beam CT
Salivary stones (submandibular)	Mandibular occlusal, sonograms, cone beam CT
Salivary stones (parotid)	Panoramic, sonograms, cone beam CT
Salivary occlusion, inflammation, tumors	Sialogram, radioisotope scan
Sinus lesions	Water's sinus, Caldwell sinus, sinus tomograms, cone beam CT
Other paranasal sinuses	Paranasal sinus tomograms, CT scans
Facial deformities	CT scans, cephalometric survey
Temporomandibular joints	TMJ tomograms, arthrograms, CT scans, nuclear magnetic resonance images, cone beam CT
Facial fractures	Many different radiographs are available to visualize specific sites, cone beam CT
Jaw and facial tumors	Panoramic, CT scans, radioisotope scans, nuclear magnetic resonance images, PET scans
Vascular jaw lesions	Angiography
Dental implant sites	Cone beam CT

parathormone levels support or confirm a clinical impression; serologic testing for antinuclear antibodies may confirm an autoimmune process; a blood count in a patient with swollen, inflamed gingiva may disclose leukemia; a urine sample may show protein indicative of renal disease; a culture may be obtained to identify a suspected fungal infection; a gene rearrangement study may confirm lymphoma. The tests performed in the clinical laboratory may, therefore, be the means to a definitive diagnosis.

Assessment of the Findings

Once all the preliminary data, including initial radiographs, is secured, the clinician must return to the chief complaint and physical findings. All these data must be placed in perspective by focusing on the problems and correlating them with the overall findings. During this process, new lines of interrogation may emerge. The problems and findings represent a mosaic that must achieve the best fit in order to arrive at a diagnosis. Provided the examiner's knowledge base is comprehensive, the pieces of the puzzle usually fall into place readily. Occasionally, however, some of these puzzles are quite complex and require more sophisticated diagnostic procedures. After all the data have been reviewed, collated, and correlated, the clinician should be able to list possible disease entities that could be responsible for the findings. This list of entities represents the differential diagnosis.

Formulating a Differential Diagnosis

The list of entities subsumed under the designation "differential diagnosis" can be quite staggering, particularly when only the presenting signs or symptoms are taken into account. To the astute clinician, the interrogative process along with the review of all findings should have eliminated many entities from the differential diagnosis list. In this regard, the "differential" has already been limited in scope. Perhaps only two or three disease processes remain worthy of consideration.

So far, the discussion has revolved around principles and generalities. A specific example may help to clarify some of these general considerations. Suppose a 40-year-old woman comes to you with a chief complaint of painful sores in her mouth. This is a presenting symptom. If you were to develop a differential diagnosis including all lesions that manifest mouth sores, you would probably use up an entire notebook. This task might be a terrific academic exercise, but the patient is waiting for help. At this point, you would want to obtain more history. She states that they appeared 2 weeks ago, she never had anything like this before, and they are getting worse. Despite all this, she does not feel tired or feverish. Review of her medical history is noncontributory, meaning she has a clean bill of health. Furthermore, she is not taking any medication. At this point, the long list in your differential diagnosis may be somewhat shortened.

You conduct the physical examination and find multiple oral lesions that are red, ulcerated, and sloughing. Furthermore, you discover a few large intact blisters. Being a sharp clinician, you conclude that this patient suffers from one of the bullous disorders. You have now considerably shortened the list because less than a dozen bullous diseases affect the oral tissues. Also, during your examination, you failed to note any conjunctival, nasal, or skin lesions. What you have is a limited, working differential diagnosis. Furthermore, based on her age, sex, and distribution of the oral lesions, you can eliminate some of the entities in the bullous disease category.

This example, then, helps to clarify the process of limitation of the differential diagnosis. The final step in the diagnostic phase of the approach to the patient involves devising a plan to secure a definitive diagnosis.

Securing a Definitive Diagnosis

Once a reasonable limited differential diagnosis is formulated, specific tests are conducted. These tests can further limit the differential by excluding some diseases (i.e., the rule out process). It is more advisable, however, to rule in probable disease processes. In oral medicine, the most useful diagnostic tool is biopsy. In most, yet not all instances, the pathologist can provide a definitive diagnosis based on histologic evaluation of the diseased tissue. Some diseases exhibit ambiguous or nonspecific histologic changes, and clinical or laboratory findings are more germane to the process of inclusion or exclusion.

Another important concept is the principle of "cause and effect." Just because two factors occur simultaneously (i.e., they are correlated) doesn't mean one causes the other. For example, an ulcer may occur on the tongue adjacent to a fractured tooth cusp. Before concluding a cause-and-effect relationship, the dentist should restore the tooth to normal contour and allow 2 weeks to pass. If the lesion persists, the initial observation ascribing an irritational causative role can no longer be substantiated. A biopsy should then be performed, and it may reveal an early cancerous lesion. Therefore, a cause should be sought in all cases, and if found, documentation is pursued to determine whether or not the observation was indeed causative or merely correlative.

In most instances, a definitive diagnosis can be secured on a clinical, histologic, radiologic, and/or laboratory basis. Occasionally, a final diagnosis cannot be made because all definitive tests and criteria are ambiguous. Under these circumstances, therapeutic trials may be in order. Perhaps the diagnosis is limited to two or three possibilities; if so, the most likely disease is selected and treated accordingly. If the treatment succeeds, then

one can usually conclude, on the basis of response to treatment, that the probable diagnosis was correct.

Formulating a Treatment Plan

Once a definitive diagnosis is made, the most efficacious treatment must be selected. Depending on the disease, the following management strategies are considered: (1) no treatment, (2) surgical removal, (3) pharmacologic agents, (4) palliative treatment, (5) behavioral or functional treatment, and (6) psychiatric therapy. Referral to a medical or dental specialist may be required. One should realize that many diseases cannot be cured, and treatment is aimed at control and alleviation of symptoms. Some diseases resolve of their own accord, some require a single curative treatment, and others require prolonged or indefinite treatment.

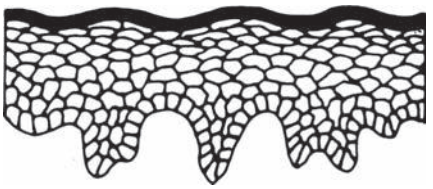
After a management strategy has been formulated and implemented, a plan for prevention of recurrence should be devised. For example, a patient with leukoplakia showing microscopic evidence of premalignant change (i.e., dysplasia) may have been successfully treated surgically. Failure to eliminate important etiologic factors such as continued alcohol and tobacco use could result in a recurrence of the disease in the same site or in a new location. The clinician should advise the patient about these potentially harmful habits and help the patient to curtail them.

The final consideration, and one of paramount importance, is patient follow-up and assessment. Patients with a disease that has a potential for recurrence should be placed on periodic recall. The length and periodicity are determined by the behavior and natural history of the disease process. Some diseases never recur, and initial therapy is conclusive and complete; therefore, short-term follow-up and assessment are adequate. Alternatively, neoplastic diseases and chronic illnesses may require frequent recall assessment and retreatment.

The diagnostic process must be thorough and include history procurement, physical examination, and radiologic examination when indicated. All patient findings are integrated to synthesize a differential diagnosis. The differential diagnosis is pared down with selective interrogation and specific diagnostic procedures, such as biopsy and clinical laboratory tests. With establishment of a definitive diagnosis, a management plan can be devised; results of therapy should be evaluated by follow-up assessment, and preventive measures, when applicable, should be instituted.

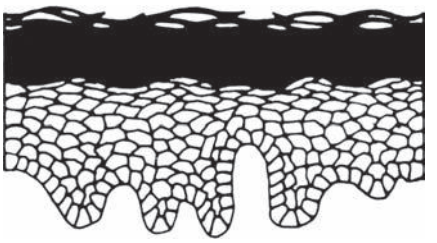
The remainder of this text is designed to aid the clinician in the attainment of a definitive diagnosis; each disease is described so that the examiner can evaluate efficiently the signs and symptoms to arrive at a definitive diagnosis. Most chapters are arranged according to physical findings; the final chapter, dealing with facial pain, being subjective, is outlined according to presenting symptoms. The recommended therapy is mentioned briefly, and the reader may find more detail regarding management by referring to the current references listed for each disease.

a



Normal mucosa

b



Hyperkeratosis

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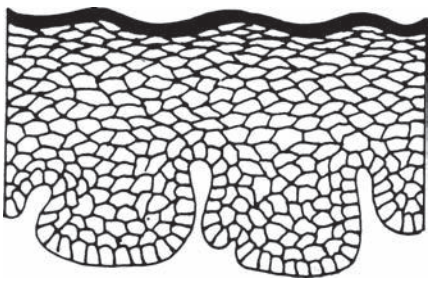

Acanthosis

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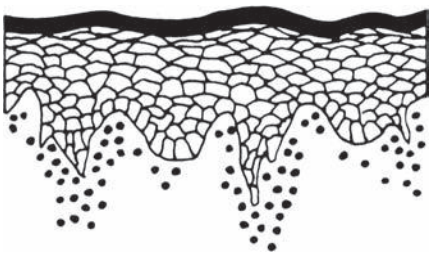

Lymphocytic infiltration

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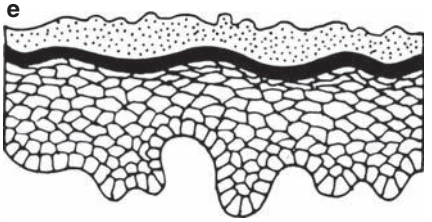

Extrinsic coating

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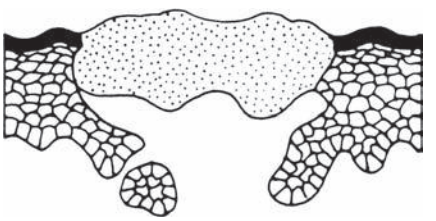

Ulcerative pseudomembrane

White Lesions

White Lesions

2

White lesions of oral mucous membranes appear thus because one or more of the epithelial layers is thickened or an extrinsic or intrinsic pseudomembrane is adherent to the surface mucosa. The white lesions encountered in practice may be subdivided into groups on the basis of pathogenesis or etiologic factors. Developmental white lesions are generally bilateral. Patients relate that a familial pattern exists, because most of the developmental white lesions are genetically inherited (genokeratosis).

As a gardener's hands become calloused from hours of friction from the hoe, so may the oral epithelium become calloused or thickened in response to chronic trauma. Tobacco in its many forms is also considered a local irritant and indeed is associated with carcinomatous transformation in white lesions of the oral mucosa. The white lesions associated with physical or tobacco-product irritation are grouped under the heading leukoplakias, as are other white lesions of undetermined origin. Because tobacco-associated and idiopathic white lesions may show microscopic evidence of malignancy, biopsy must be performed when (1) a cause cannot be detected or (2) the suspected traumatic agent is eliminated yet the lesion fails to involute or regress. Leukoplakia of the lateral tongue may be indicative of human immunodeficiency virus (HIV) seropositivity, particularly among patients who fall into AIDS-risk categories.

White lesions of nonhereditary diseases may coexist with skin lesions. These keratotic dermatoses may, however, occur as oral lesions with skin involvement. As no etiologic agent can be discerned in oral keratotic dermatoses, biopsy must be undertaken to confirm the diagnostic impression when classic clinical features of these disorders are lacking.

Inflammatory lesions that may produce thickened epithelium and/or a surface pseudomembrane appear white; in these instances, the surface coating may be rubbed away with gauze. The diagnosis of inflammatory white lesions can be secured by obtaining a thorough history, including questions regarding use of drugs, sexual habits or promiscuity, recent contact with persons manifesting similar illness, or contact with injurious chemicals.

This chapter illustrates and enumerates the features of white lesions in the context of clinical features as outlined earlier. The differential diagnosis for a given white lesion depends on obtaining a history, with primary considerations of (1) a familial pattern; (2) presence or absence of a causative agent with notations on oral habits, particularly tobacco use; (3) presence or absence of associated skin lesions; (4) questions relating to contact with individuals showing similar lesions; (5) AIDS-risk status; (6) presence or absence of fever; and (7) exploration of the nature of the white patch as to tenacity to underlying structures and ease of removal by rubbing. Based on responses and findings regarding these considerations, a ranking of entities in the differential diagnosis may ensue and, ultimately, biopsy—or in certain instances serology and blood count—must be performed to obtain a definitive diagnosis.

The white lesions encountered most frequently are (1) friction, idiopathic or tobacco-associated leukoplakias, (2) lichen planus, (3) candidiasis, and (4) Fordyce's granules.

White lesions associated with a potentially lethal outcome include (1) premalignant leukoplakias, (2) hairy leukoplakia, and (3) lupus erythematosus.

Flat Plaques, Solitary

FRICTIONAL BENIGN KERATOSES

Figure 2-1

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Frictional keratoses represent callus formation from chronic trauma with resultant thickening of one of the epithelial cell layers. The white lesions are therefore associated with various etiologic agents, including ill-fitting dental prostheses, chronic irritational habits such as cheek- or lip-biting, overzealous tooth brushing, and white calluses formed from occluding on edentulous ridges or the retromolar pads, a condition termed oral lichen simplex chronicus. The individual lesions may be smooth or irregular in texture, and their location and configuration coincide with the corresponding location of the causative agent. Frictional keratoses may also be multifocal.

MICROSCOPIC FEATURES

Frictional irritation may cause thickening of any layer or combination of layers of the epithelium with hyperorthokeratosis, hyperparakeratosis, and/or acanthosis. Depending on the degree of irritation, the underlying submucosa may show an inflammatory cell infiltrate, which is usually chronic.

DIFFERENTIAL DIAGNOSIS

White lesions arising from chronic irritation may be diagnosed as such when a causative agent presents itself. Providing the cause can be eliminated or reduced (e.g., leaving ill-fitting dentures out of the mouth for 2 weeks, smoothing irritating tooth cusps, avoiding habits), and the white lesion regresses or resolves; a cause-and-effect relationship can be substantiated. Failure of a white lesion to regress subsequent to elimination of the causative agent(s) should arouse suspicion with regard to precancerous leukoplakia, and biopsy is then indicated. In addition, other diseases manifesting white lesions may coincidentally correspond to denture-

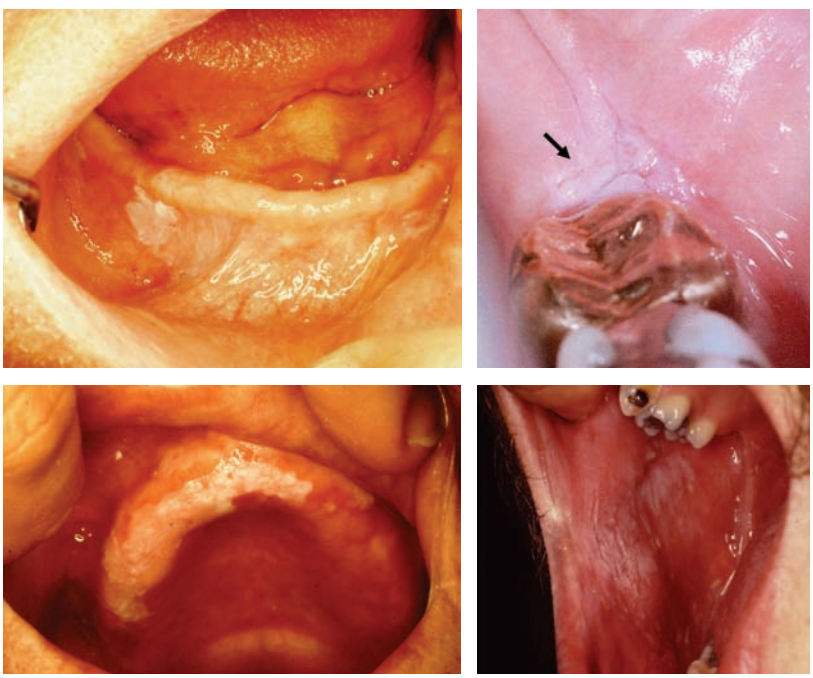

FIGURE 2-1
Frictional keratosis due to irritation.

bearing zones; however, diseases such as lichen planus, moniliasis, or the genokeratoses are typically located in regions beyond the confines of a potential irritant.

TREATMENT

Elimination of the causative agent is indicated. White lesions attributed to a chronic irritant probably have a limited tendency to undergo malignant change. Should the lesions fail to resolve after removal of the irritant, however, a biopsy should be performed to rule out atypical cell changes that occur independently.

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LEUKOPLAKIA

Figure 2-2

IDIOPATHIC/SMOKED TOBACCO-ASSOCIATED LEUKOPLAKIA

Homogeneous Leukoplakia

Age: Middle-aged and elderly adults
Sex: Males predominantly

Clinical features

White plaques of unknown etiology or those encountered in smokers and tobacco chewers are a common malady that may occur on any oral mucosal surface yet are more often seen on the buccal mucosa, mucobuccal fold, and oral floor. These leukoplakias may be smooth, ridged, rough, delineated, or diffuse. The smooth form or planar type fails to exhibit surface irregularity, being homogeneously white without a verrucous texture, yet others may have a ridged or verrucous appearance. The term leukoplakia is strictly clinical and has no implications with regard to microscopy. These lesions are usually benign yet may show microscopic evidence of premalignant cellular change. Whereas leukoplakias as a collective group display microscopic evidence of dysplasia, carcinoma in situ, or squamous cell carcinoma in approximately 20% of the cases, evidence suggests that the atypical cell changes are less prevalent in the smooth planar form compared with the verrucous appearing lesions. Leukoplakias of the oral floor manifest the highest incidence of atypical cell change; approximately 40% harbor atypical cells.

Microscopic features

The clinical extent does not necessarily predict the microscopic features. Idiopathic or tobacco-induced leukoplakias may merely show hyperorthokeratosis, hyperparakeratosis, acanthosis, or a combination. Alternatively, and most important, cellular atypia, dysplasia, carcinoma in situ, or frank superficially invasive squamous cell carcinoma may be encountered microscopically.

Differential diagnosis

Idiopathic and tobacco-associated leukoplakia must be differentiated from frictional leukoplakia on the basis of history. Lichen planus, lupus erythematosus, the genokeratoses, and inflammatory white lesions must also be eliminated from consideration on the bases of history and biopsy findings.

Treatment

Biopsy should be performed in all instances of idiopathic or tobacco-associated leuko-

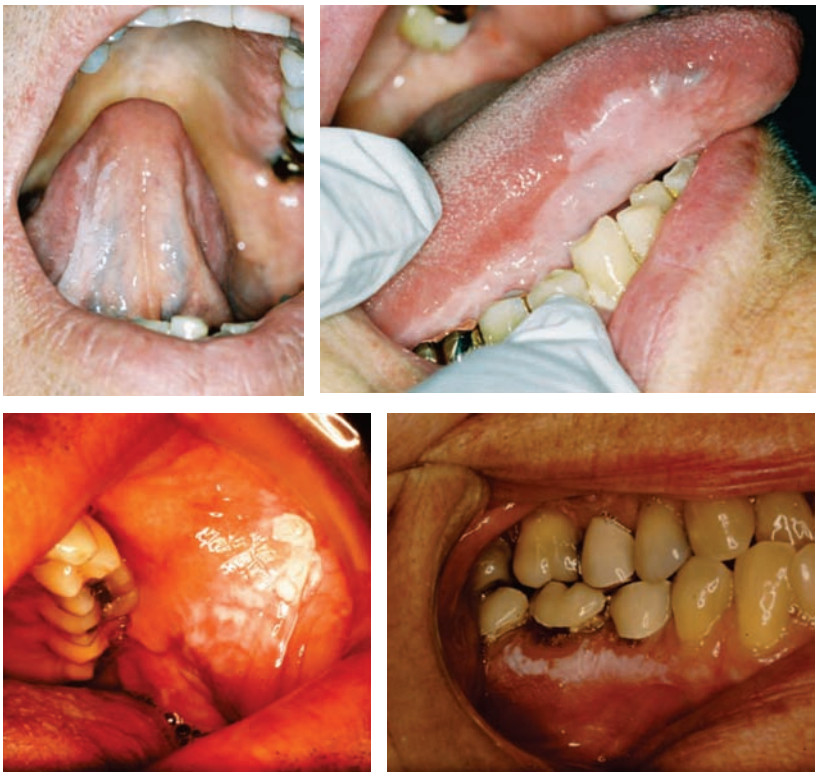

FIGURE 2-2
Thickened, diffuse white lesions representing idiopathic leukoplakia.

plakia to ascertain whether or not premalignant cell changes exist. Benign cellular features do not preclude future malignant change in the same location or in a new site. About 2% to 3% of benign leukoplakias may progress to carcinoma, whereas 17.5% of all oral leukoplakias, including cases with and without dysplastic change, progress to carcinoma over a mean follow-up period of 7½ years. Most dysplasias fail to progress to carcinoma and many spontaneously regress. Recent studies have disclosed that benign leukoplakias may progress to carcinoma over time in almost comparable numbers to those that are dysplastic. For these reasons, patients should be subjected to periodic follow-up with rebiopsy, particularly when a change in the clinical character of a lesion evolves. Lesions with a microscopic diagnosis of dysplasia or carcinoma in situ should be surgically stripped or removed in toto by standard surgery, cryosurgery, or laser surgery. Invasive carcinoma is usually managed by combined radiotherapy and surgery.

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ACTINIC CHEILITIS

Figure 2-3

Age: Middle-aged and elderly adults
Sex: Males predominate

CLINICAL FEATURES

Solar or ultraviolet light exposure may predispose the vermilion border to keratotic change, and certain individuals whose occupations or hobbies provide continuous exposure to sun are most prone to develop actinic cheilitis. The lower lip is more prominent and, therefore, more prone to actinic change than the upper. The lesion is white and usually smooth and diffuse. The borders may be sharply delineated from uninvolved vermilion, or the transition may be gradual. Ulcerations or focal zones of highly thickened keratin plaque may indicate early carcinomatous transformation.

MICROSCOPIC FEATURES

Solar cheilitis reflects a spectrum of microscopic changes similar to leukoplakia. The early limited changes are restricted to the keratin layer, which manifests thickening, and the subjacent connective tissue zones, which characteristically show clumping, fragmentation, and granulation of elastic fibers known as solar or senile elastosis. Progression to cytologic atypia, dysplasia, and frank invasive carcinoma can develop in actinic cheilitis. The earliest premalignant atypicality is represented by atrophy of the spinous cell layer, fragmentation of the basement membrane, and mild hyperchromatism and/or pleomorphism of the basal cells.

DIFFERENTIAL DIAGNOSIS

Habitual lip chewing must be differentiated from actinic cheilitis. Tobacco irritants (cigars, pipe stems, and reverse smoking) may induce hyperkeratotic lesions of the lips.

TREATMENT

A biopsy should be performed to determine whether or not dysplasia is present. A lack of premalignant cellular changes in actinic cheilitis does not preclude future evolvement. Protection from the sun with solar protective cream containing *p*-aminobenzoic acid (PABA) is recommended. Histologically, atypical change should be managed by lip stripping with incontinuity wedge resection if a zone of superficial carcinomatous invasion is coexistent.

If no foci of carcinoma exist, topical application of 1% 5-fluorouracil cream twice daily for 2 weeks will remove dysplastic epithelium, allowing for regeneration of normal epithelium. Other effective treatments include 5% imiquimod cream and photodynamic therapy with methyl aminolevulinic acid as the photosensitizer and red light at 630 nm.

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SMOKELESS TOBACCO KERATOSES

Figure 2-4

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

White lesions caused by snuff and chewing tobacco usage are located under the area in

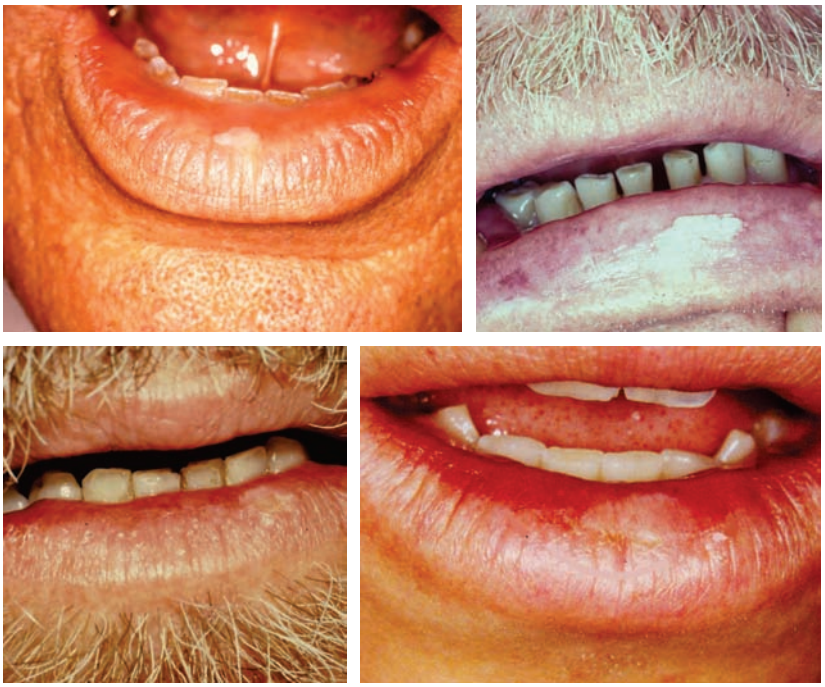

FIGURE 2-3
Actinic cheilitis of the lip.

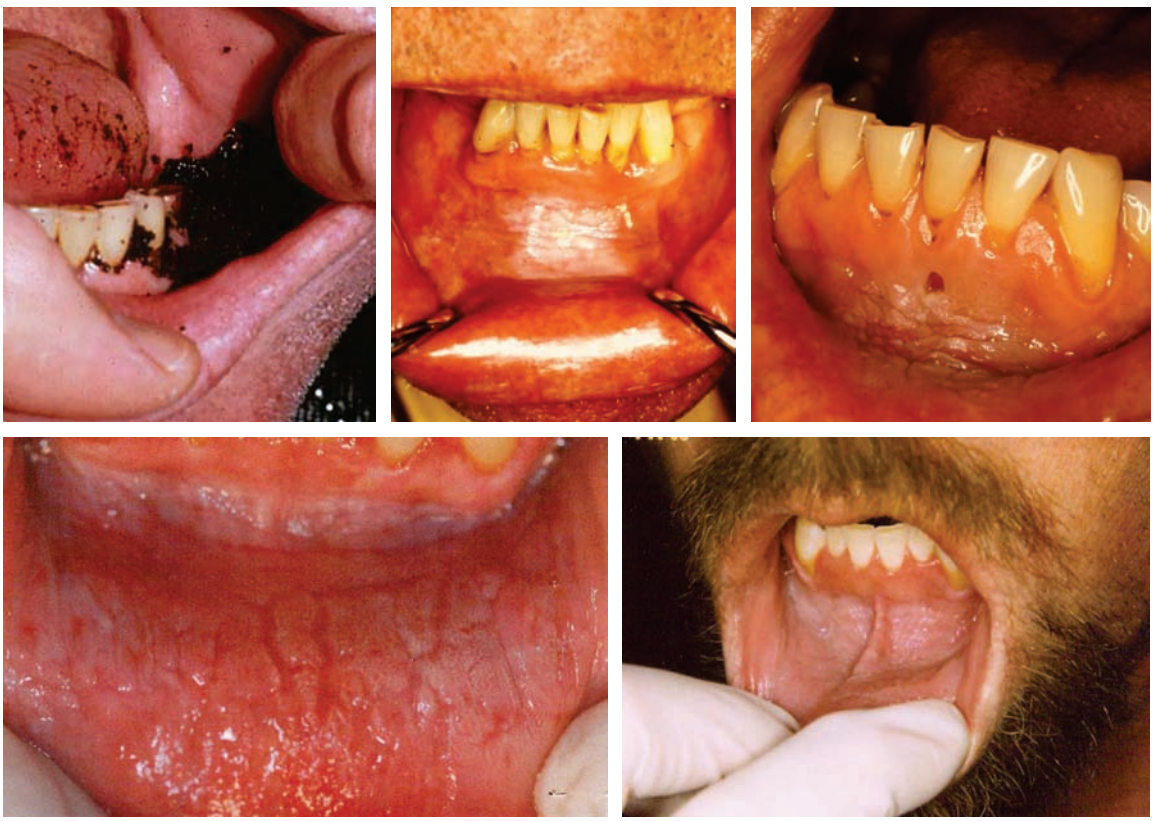

FIGURE 2-4
Corrugated white plaques attributed to smokeless tobacco (snuff dipper's keratosis).

which these agents are habitually placed; they are therefore encountered in the mucobuccal fold region. The lesion is somewhat rough and may manifest an undulating or wrinkled surface. The white areas are relatively well circumscribed and localized to the area of snuff placement. During the 1980s and currently, the incidence of smokeless tobacco use by teenagers has increased.

MICROSCOPIC FEATURES

As with other forms of tobacco-induced leukokeratosis, snuff keratosis may show a thickening of one of the epithelial layers (i.e., hyperorthokeratosis, hyperparakeratosis, acanthosis), with a tendency for "chevron"-shaped projections in the cornified layer. Cytologic atypia is rarely seen, and progression to invasive carcinoma is rare among moist snuff users yet is significantly more carcinogenic when dry snuff is used or when snuff is mixed with slaked lime, a common additive in India and the Middle East.

DIFFERENTIAL DIAGNOSIS

A white lesion in the mucobuccal fold may represent frictional keratosis or leukoplakia related to tobacco products. A thorough history will indicate whether or not the lesion is smokeless tobacco related. The "ebbing tide" effect on the white surface implicates snuff usage.

TREATMENT

All smokeless tobacco-associated white lesions must be examined microscopically to rule out premalignancy. If atypical cytologic changes are present in high risk populations, complete excision is recommended. Absence of cellular premalignant changes does not preclude future evolution to cancer; therefore, the habit should be curtailed. Tobacco-specific nitrosamines are thought to be the chief carcinogens in chewing tobacco and snuff.

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SANGUINARIA-INDUCED KERATOSES

Figure 2-5

Age: no predilection
Sex: no predilection

CLINICAL FEATURES

Sanguinaria (blood root) is a chemical that has been shown to be antimicrobial and was placed in dentifrice as well as in a mouth rinse preparation to reduce microbial plaque on tooth biofilms. A spurious find among chronic and heavy users of these Sanguinaria products was the appearance of leukoplakias, particularly on the maxillary anterior gingival and mucobuccal fold. This localization has been attributed to the physiology of mouth rinsing whereby the rinse is forcefully extended into the labial compartment of pursed lips.

MICROSCOPIC FEATURES

Most biopsies from Sanguinaria-induced leukoplakias exhibit benign keratosis without dysplasia. DNA ploidy studies, however, have disclosed abnormal DNA content in some of these lesions and, therefore, both rinse and dentifrice have been withdrawn from the market.

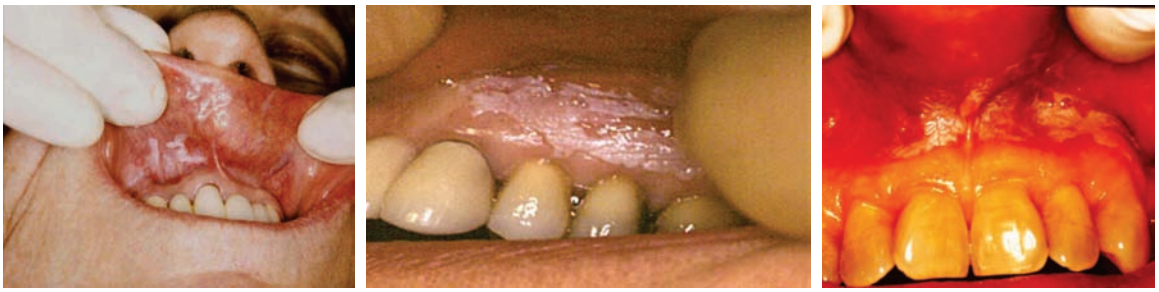

FIGURE 2-5
Sanguinaria-induced keratoses of the anterior maxillary gingival and vestibule.

DIFFERENTIAL DIAGNOSIS

Sanguinaria leukoplakia may simulate idiopathic leukoplakias and plaque-form lichen planus.

TREATMENT

Discontinuing the use of the product is required, and many months may elapse before the lesions resolve.

Additional Reading

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DYSKERATOSIS CONGENITA

Figure 2-6

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Dyskeratosis congenita (Zinsser-Engman-Cole syndrome) is inherited as either an autosomal recessive, X-linked or autosomal dominant disorder with telomere shortening mediated by mutations in six genes that encode either components of the telomerase complex (*DKC1, TERC, TERT, NOP10, NHP2*) or shelterin (*TINF2*). The syndrome is characterized by atrophic nail changes, telangiectatic pigmented reticular lesions of skin, pancytopenia, and oral white lesions associated with dorsal tongue depapillation and atrophy. Premature aging is also featured. Forty percent of oral lesions progress to squamous cell carcinoma before the age of 50.

MICROSCOPIC FEATURES

A nonspecific thickening of the parakeratin and spinous cell layer is seen. Dysplastic changes, absent in pachyonychia, evolve and progress to squamous cell carcinoma in dyskeratosis congenita.

DIFFERENTIAL DIAGNOSIS

The mucosal white lesions and constellation of other clinical findings of dyskeratosis congenita may be confused with pachyonychia congenita. Fanconi's anemia is a significant syndrome to consider in the differential diagnosis since it presents with bone marrow suppression and oral white lesions that can progress to carcinoma. Other keratoses such as white sponge nevus, HBID, and lichen planus should also be considered.

TREATMENT

Close clinical follow-up of oral lesions is mandatory since malignant transformation will occur later in life.

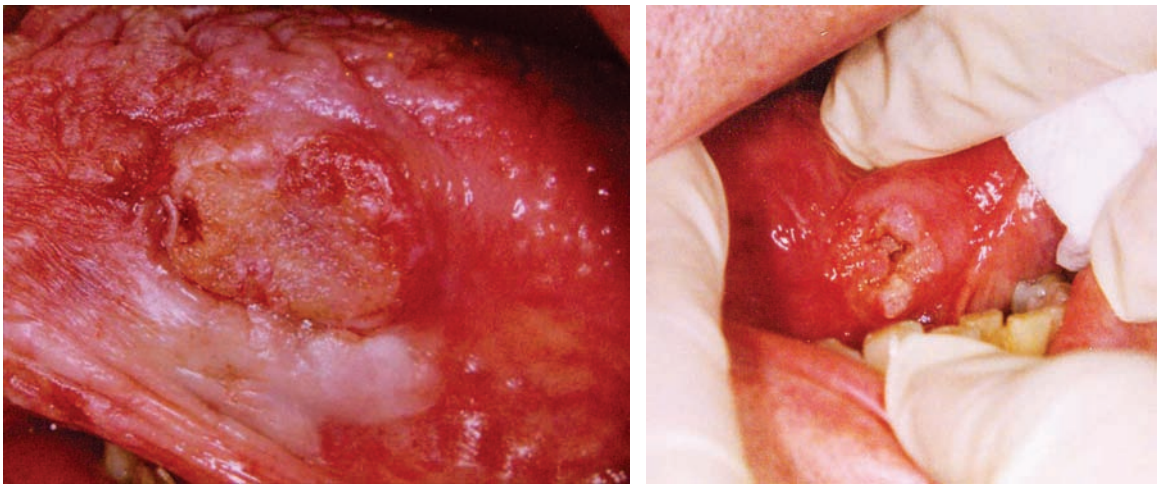

FIGURE 2-6
Dyskeratosis congenita. White lesions that progress to carcinoma.

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FANCONI'S ANEMIA

Figure 2-7

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Fanconi's anemia is an autosomal recessive genetic disorder involving as many as 13 genes of which mutations occur. If both parents are carriers, there is a 25% risk of having an affected child. Affected children develop bone marrow suppression with erythrocyte macrocytosis, and many will progress to acute myelogenous leukemia. Digital anomalies are characterized by anatomically deformed thumbs or agenesis. Pancytopenia occurs with thrombocytopenia and neutropenia. These events occur due to mutations in a group of core protein complexes (the FA genes) whose function involves DNA repair and antioxidant synthesis. These patients may develop leukoplakias located on the tongue or floor of the mouth that can later transform to carcinoma.

MICROSCOPIC FEATURES

The keratotic lesions in Fanconi's anemia exhibit the same histology as those found in idiopathic leukoplakias (i.e., benign keratosis, dysplasia, carcinoma).

DIFFERENTIAL DIAGNOSIS

The white lesions are similar to other leukoplakias being flat plaques. The unique constellation of syndromic characteristics usually allow for a straightforward diagnosis.

TREATMENT

The pancytopenia and leukemia can be managed by chemotherapy with greatest response being seen after bone marrow transplantation. Importantly, many head

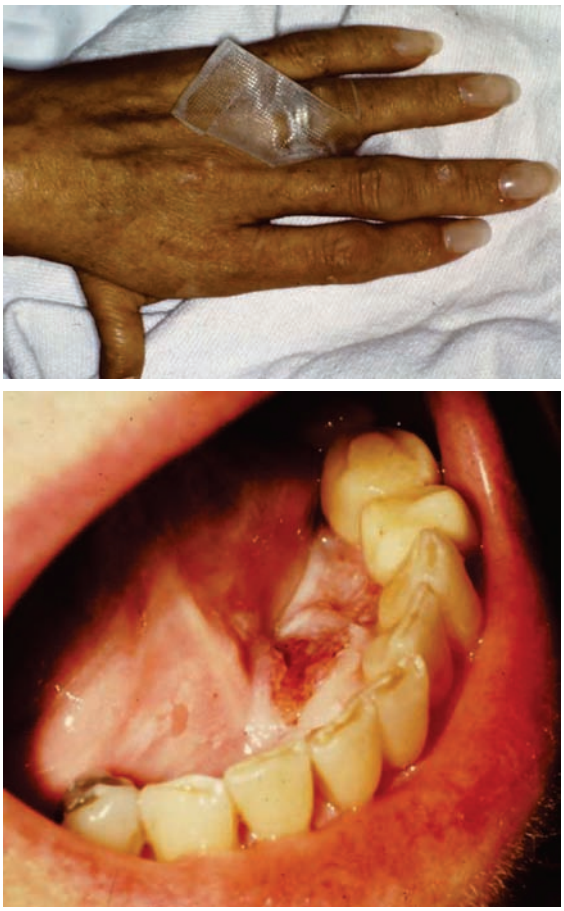

FIGURE 2-7
Fanconi's anemia. Thumb anomaly, oral carcinoma.

and neck cancers have evolved in Fanconi patients after marrow transplantation.

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DYSPLASIA, CARCINOMA IN SITU, SQUAMOUS CELL CARCINOMA, AND VERRUCOUS CARCINOMA

Figure 2-8

Age: Elderly adults
Sex: Males predominate

CLINICAL FEATURES

Early cancerous change within the oral epithelium may initially manifest as a white lesion or may arise in a preexisting leukoplakic area. Depending on the extent of the tumor, the white lesion may be relatively macular or plaque-like or, in larger lesions, associated with tumefaction and induration. Whereas oral cancer is generally localized, it may, on occasion, be multifocal with numerous isolated separate white lesions manifesting microscopic evidence of neoplastic transformation. Location is highly significant when considering the possibility of malignancy; although malignant change may be seen on any surface, the most common locations are oral floor, alveolar ridge and vestibule, and lateral posterior tongue.

The most important contributing etiologic factors regarding carcinogenesis of oral epithelium are use of tobacco and a high intake of alcohol. Patients with untreated syphilis and the Plummer-Vinson syndrome are also prone to develop oral or oropharyngeal cancer. Recent research indicates that a subpopulation of patients have tumors associated with, and probably caused by, human papillomavirus (HPV) type 16. In this subset, the tumors are found at the base of the tongue and the tonsillar pillar. As emphasized under the section on leukoplakias associated with tobacco, the apparent clinical innocence of white patches can be misleading; the most innocuous lesion may be cytologically malignant. One exception to clinical predictability regarding suspicion of potential malignancy may be encountered in the white lesion associated

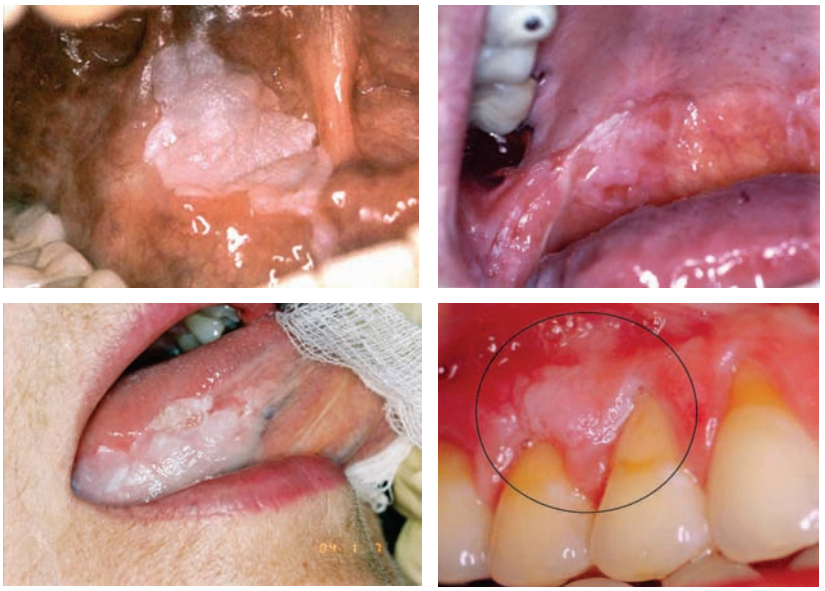

FIGURE 2-8
Dysplastic and neoplastic white lesions. All showed microscopic evidence of dysplasia or carcinoma.

with zones of erythema, so-called speckled leukoplakia. Isolated mixed red and white lesions should be considered malignant until proven otherwise (i.e., by biopsy).

A variant form of oral squamous cell carcinoma that is classically a warty-appearing keratotic white lesion is verrucous carcinoma (see Chapter 6).

MICROSCOPIC FEATURES

Epithelial dysplasia, carcinoma in situ, and invasive squamous cell carcinoma are, respectively, progressively advanced stages of malignancy. When they are characterized clinically as white lesions, they manifest a thickening of the keratin or parakeratin layer. The earliest changes, termed *dysplasia*, begin in the dividing cells of the basilar and parabasilar layers. Initial changes include nuclear hyperchromatism, pleomorphism, and an increase in mitotic figures. By definition, all layers, top to bottom, must evince atypical cell changes in carcinoma in situ; however, the basement membrane remains intact without evidence of invasion into the subjacent connective tissue. Violations of the basement membrane integrity results in superficially invasive carcinoma, which then progresses to frank squamous cell carcinoma.

Invasive squamous cell carcinoma may contain islands and nests of tumor cells that retain the characteristics of oral epithelium by manufacturing the chief protective products of that organ, albeit disorganized, keratin and parakeratin. These differentiated tissues are often arranged in laminated whorls termed *keratin pearls*. Tumors with this histologic morphology are termed *well-differentiated carcinomas* and are associated with a slower course, lower metastatic potential, and thus a better prognosis. A lack of, or a diminution in, keratin formation connotes a more rapidly progressing lesion with a poor prognosis and is termed *poorly differentiated carcinoma*. A moderately differentiated lesion logically falls between these two extremes both morphologically and behaviorally. Those tumors associated with HPV 16 tend to show features that are differentiated

along the lines of tonsillar crypt epithelium; they tend to have a better prognosis than non-HPV carcinomas of the head and neck. P16 is an immunohistochemical surrogate marker for HPV 16.

DIFFERENTIAL DIAGNOSIS

White lesions associated with tumefaction and induration present no problem in the clinical diagnosis, yet biopsy is indicated to determine the grade of malignancy (i.e., differentiation of tumor cells) prior to planning therapy. Early malignant change manifesting a plaque-like white lesion must be differentiated primarily from frictional leukoplakias, benign leukoplakias, and lichen planus. When a causative agent cannot be identified or eliminated, an adequate history and biopsy are necessary.

TREATMENT

Dysplasia or carcinoma in situ, if localized, can be managed by wide local excision, obtaining margins free from atypical changes; margins 1 cm away from clinically involved tissue should be adequate, yet microscopic confirmation is mandatory. Diffuse or multifocal dysplasia or carcinoma in situ may be treated by surgery or radiation therapy. Invasive carcinoma requires a complete work-up with evaluation of the neck, chest radiographs, and the presence of other symptoms. As treatment may include a variety of therapeutic methods either alone or in combination, including surgery, laser surgery, radiation, and chemotherapy, invasive squamous cell carcinoma should be evaluated and managed by a physician experienced in head and neck oncology.

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LICHEN PLANUS (HYPERTROPHIC TYPE)

Figure 2-9

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Lichen planus is described in greater detail later. The disease is a delayed hypersensitivity reaction in which an identifiable antigenic stimulus is usually not evident. The hypertrophic form is typically located on the dorsal tongue that is pavemented in confluent thick white plaques. These plaque-like lesions may also occur on the palate and the buccal mucosa. There may be some areas with a lacey reticulated pattern, but oftentimes these typical lichenoid figures are not present.

MICROSCOPIC FEATURES

A chronic interface mucositis is present, characterized by a patchy or band-like lymphocytic infiltrate in juxtaposition to the basal cell layer of the overlying epithelium. The cells are a mixture of CD4 and CD8 T lymphocytes. The infiltrated basal cell layer shows cytoplasmic fragmentation or liquefaction. Tongue cancer occurs in 0.5% to 1.0% of cases, and when dysplasia is evident

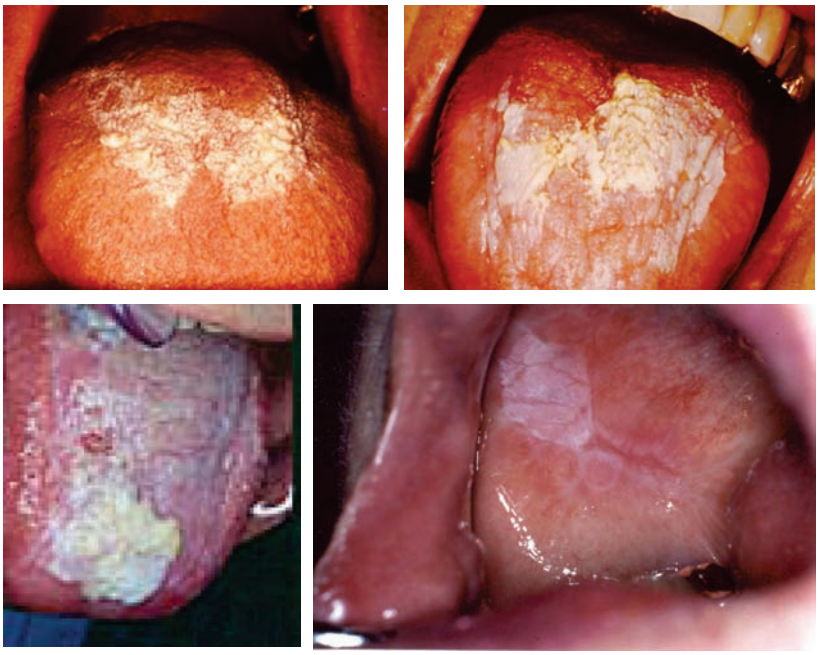

FIGURE 2-9
Dorsal tongue and buccal mucosa with plaque-form (hypertrophic) lichen planus.

along with lichen planus features, the term lichenoid dysplasia has been used.

DIFFERENTIAL DIAGNOSIS

The hypertrophic or plaque form of lichen planus is easily confused with various forms of leukoplakia.

TREATMENT

Close periodic follow-up is recommended and any zones of ulceration, redness, or positive toluidine blue uptake should be biopsied.

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MUCOUS PATCHES (SECONDARY SYPHILIS)

Figure 2-10

MUCOUS PATCHES OF SYPHILIS

Age: Adults
Sex: No predilection

Clinical Features

Mucous patches are smooth-surfaced plaques that manifest a glistening, opalescent character and are seen 6 to 8 weeks after formation of the chancre. In addition to the mucosal patches, split papules at the commissure and a maculopapular rash may be present. A history of promiscuous sexual activity can usually be obtained, although some patients may deny such activities. The lesions persist for 1 to 3 weeks, after which they resolve. The lesions in this stage are infectious.

Microscopic Features

Parakeratosis and fibrinous exudate over both intact and focally ulcerated epithelium

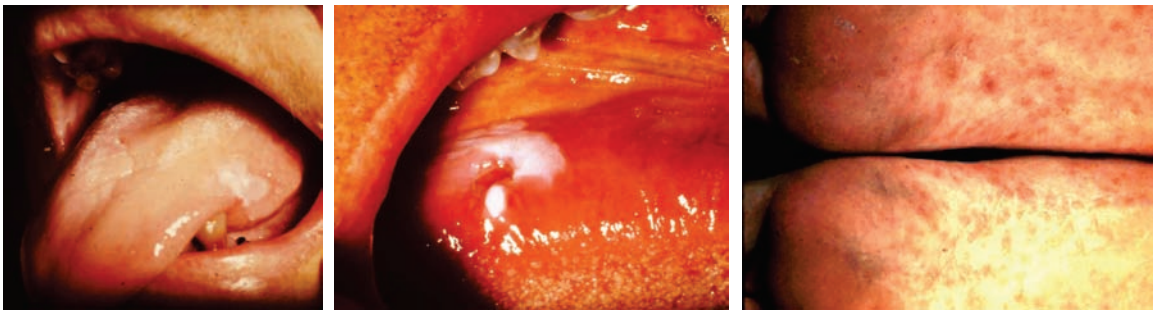

FIGURE 2-10
Secondary syphilis, mucous patches, maculopapular rash, soles of feet.

can be seen. The submucosa contains an avid plasma cell infiltrate. The spirochete is not visible on routine staining; a Warthin-Starry silver stain will demonstrate the microorganism in tissue sections.

Differential Diagnosis

Mucous patches may resemble a variety of white lesions of the oral cavity; because they are highly infectious, the clinician should always be aware of the fact that oral white lesions may be luetic. The primary considerations in the clinical differential diagnosis include moniliasis, plaque-form lichen planus, or leukoplakia of one type or another. An adequate history should elicit suspicion of syphilis, and the diagnosis may be confirmed by fluorescent treponemal antibody test or Venereal Disease Research Laboratory test. A smear with dark-field microscopy will demonstrate motile spirochetes.

Treatment

Treatment for syphilis is penicillin. The patient can be referred to a dermatologist or general physician for treatment.

Additional Reading

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Flat Plaques, Bilateral or Multifocal

LEUKOEDEMA

Figure 2-11

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Leukoedema occurs in blacks and dark-skinned whites and is encountered so frequently that it should be considered a normal variation in these individuals. The lesion is bilateral and diffuse, involving the buccal mucosa, and shows a filmy, mother-of-pearl appearance, often with delicate overlapping curtain-like mucosal folds. When the mucosa is stretched, the white appearance is diminished.

MICROSCOPIC FEATURES

The epithelium displays acanthosis, parakeratosis, and spongiosis.

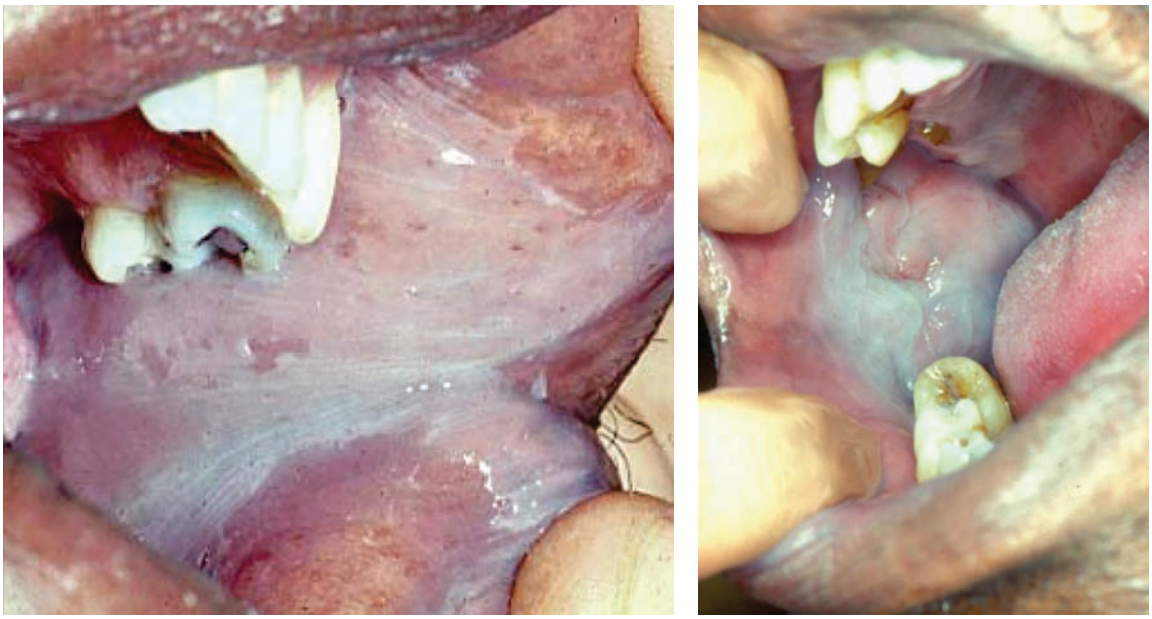

FIGURE 2-11
Leukoedema covering entire buccal mucosa.

DIFFERENTIAL DIAGNOSIS

The diffuse delicate mother-of-pearl sheen and the propensity to affect blacks are characteristics that permit differentiation from other hereditary white lesions of the genokeratosis group. The primary entities in the differential diagnosis include white sponge nevus and hereditary benign intraepithelial dyskeratosis (HBID), both of which are thicker, plaque-like, and show specific microscopic features.

TREATMENT

No treatment is necessary.

Additional Reading

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GENOKERATOSES

WHITE SPONGE NEVUS

Figure 2-12

Age: Childhood onset
Sex: No predilection

Clinical Features

White sponge nevus, inherited as an autosomal dominant trait, appears, from ultrastructural observations, to represent a defect in epithelial maturation involving tonofilament formation with impaired normal desquamation of the superficial strata of cells. Mutations have been identified in the genes coding for keratin 4 and 13. The condition is characterized by diffuse and, sometimes, patchy white lesions of the buccal mucosa, bilaterally, with involvement of the tongue and occasionally other oral mucosal sites. In severely

affected individuals, the buccal mucosal lesions are creased and exhibit corrugated vertical folds. The conjunctivas are spared; however, vaginal, esophageal, and anal mucous membranes may harbor white lesions similar to those of the oral tissues.

Microscopic Features

The epithelium shows parakeratosis and acanthosis with spongiosis. Parallel striae of condensed parakeratin traverse the surface layers in oblique planes. Individual cell keratinization may be seen in the spinous cell layer. Ultrastructurally, some spinous layer cells differentiate early, becoming enriched with tonofilaments that are compacted in disarray.

Differential Diagnosis

Other white lesions do not tend to be as thick and diffuse as white sponge nevus; however, HBID, lichen planus, and candidiasis should be considered in the differential diagnosis. Biopsy will disclose characteristic features.

Treatment

No treatment is necessary.

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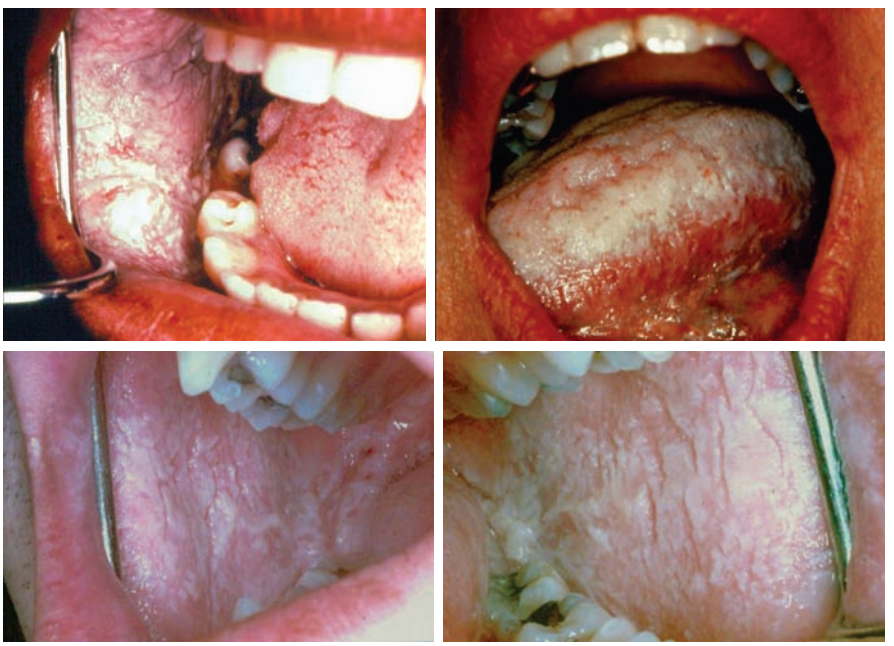

FIGURE 2-12
White sponge nevus. Thick bilateral plaques that cover most of the buccal mucosa and lateral tongue.

HEREDITARY BENIGN INTRAEPITHELIAL DYSKERATOSIS

Figure 2-13

Age: Childhood onset
Sex: No predilection

Clinical Features

HBID is inherited as an autosomal dominant trait, and electron microscopic studies have disclosed a defect in keratinization characterized by cytoplasmic accumulation of tonofilaments with loss of cellular interdigitation and desmosomes. A duplication in chromosome 4q35 is associated with HBID. As with the other genokeratoses, HBID manifests diffuse white plaques of the buccal mucosa and tongue, and secondary candidiasis is commonly encountered. In addition to the oral signs are coexistent conjunctival telangiectasias and occasionally thickened plaques of the bulbar conjunctiva, which may eventuate in blindness. The disease was originally described in a racial isolate group in the Carolina states.

Microscopic Features

Acanthosis with both hyperorthokeratosis and hyperparakeratosis is present within the epithelium. The pathognomonic features are benign dyskeratotic changes consisting of the cell-within-a-cell phenomenon and individual cell keratinization, similar to those features encountered in Darier-White's disease; however, no intraepithelial cleavage occurs. Periodic acid-Schiff (PAS) staining may disclose the presence of *Candida* mycelia in the cornified layer.

Differential Diagnosis

The oral white lesions must be differentiated from those in white sponge nevus, pachyonychia congenita, and lichen planus. The combination of eye and oral lesions in this disease should not be confused with the muco-oculocutaneous syndromes in which the oral lesions are either ulcerative, bullous, or erythematous.

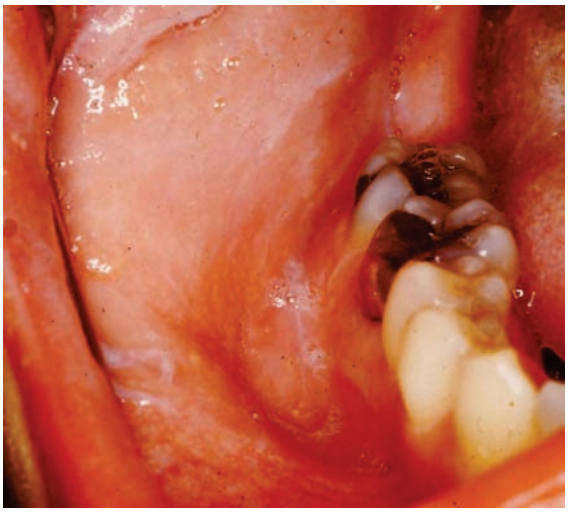

FIGURE 2-13
Hereditary benign intraepithelial dyskeratosis presents with oral white lesions.

Treatment

No treatment is necessary. Because of the potential for blindness, genetic counseling may be in order.

Additional Reading

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KERATOSIS FOLLICULARIS (DARIER-WHITE'S DISEASE)

Figure 2-14

Age: Generally adult onset
Sex: No predilection

Clinical Features

Keratosis follicularis is a dermatologic disorder manifesting orange-yellow papular and white keratotic lesions of skin. It is inherited as an autosomal dominant trait that affects cell-to-cell adhesion and keratinization resulting from numerous mutations in adenosine triphosphate (ATP) calcium transport proteins (ATP2A2). A coexistent defect in cell-mediated immunity has also been uncovered. Oral lesions are not seen in all patients, yet when present, they are papular and usually keratotic. Buccal mucosa, lips, palate, and tongue are the favored oral locations. Other mucous membranes including vulva, vagina, and anus may be involved.

Microscopic Features

Surface hyperkeratosis is present. Within the spinous cell layer are dyskeratotic changes represented by the cell-within-a-cell phenomenon known as *corps ronds* and pyknotic elongated nuclei termed *grains*. A suprabasilar cleavage is present with acantholysis; formation of wandering rete ridges manifesting cleft-like spaces produces a villous pattern. The microscopic appearance may be confused with pemphigus vulgaris and familial pemphigus (Hailey-Hailey disease). Ultrastructural evidence of defective cell maturation involving the tonofilament/desmosomal apparatus is extant.

Differential Diagnosis

The multipapular or cobblestone appearance and characteristic skin lesions differentiate Darier-White's disease from the other genokeratoses that generally manifest oral white lesions in a more diffuse or plaque-like pattern. This white papular eruption may be confused with other oral lesions showing multiple polyps or papules, including pyostomatitis vegetans, verrucous carcinoma, and denture papillomatosis. Biopsy affords a definitive diagnosis.

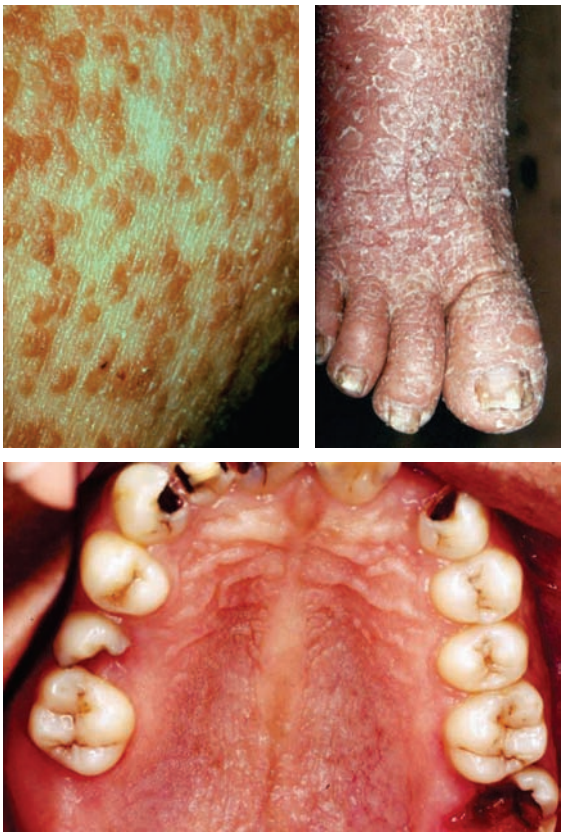

FIGURE 2-14
Keratosis follicularis. Orange papular lesions and keratoses of skin with confluent white plaques. (Courtesy of Dr. Dwight Weathers.)

Treatment

Retinoids have been used in high doses, the rationale being an attempt to eliminate the degree of skin keratinization. This treatment is of limited value.

Additional Reading

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PACHYONYCHIA CONGENITA

Figure 2-15

Age: Childhood onset
Sex: No predilection

Clinical Features

Pachyonychia congenita (Jadassohn-Lewandowsky syndrome) is an autosomal dominant disorder manifesting oral white lesions and laminated thickening of the finger- and toenails. This genokeratosis involves mutations in keratins K6a, K16, and K17. The oral white lesions are bilateral on the buccal mucosa, tongue, and other sites, and are usually limited in terms of the extent of mucosal tissues affected.

Microscopic Features

A nonspecific thickening of the parakeratin and spinous cell layer is seen. Dysplastic changes are absent in pachyonychia and do not evolve and progress to squamous cell carcinoma

Differential Diagnosis

The bilateral mucosal white lesions of pachyonychia congenita may be confused with white sponge nevus, HBID, and lichen planus; however, the fingernail changes, when considered in conjunction with the oral lesions, provide the diagnostic clinical features of the disease. Candidiasis of the oral mucosa with fingernail involvement should be considered in the differential diagnosis and can be ruled out by obtaining an oral cytologic smear that can be stained for hyphae.

Treatment

No treatment is necessary.

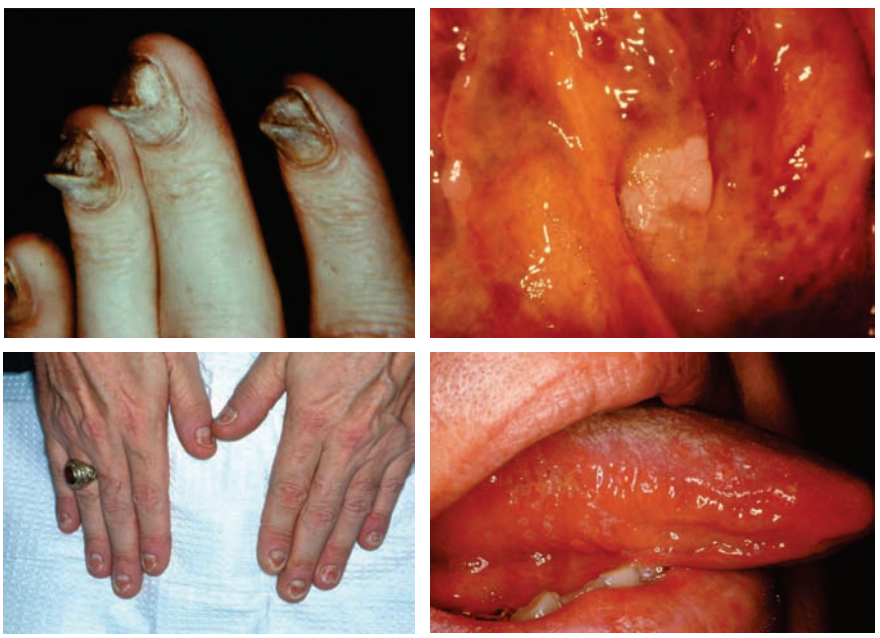

FIGURE 2-15
Pachyonychia congenita showing thickened nails (upper left) and surgically removed nail beds (lower left) with white lesions of oral mucosa.

Additional Reading

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INCONTINENTIA PIGMENTI

Figure 2-16

Age: Begins during infancy
Sex: Females

Clinical Features

Incontinentia pigmenti is inherited as a dominant trait, is lethal in males, and manifests both skin and dental defects. The disease is caused by deletions in chromosome Xq28 IP. The skin lesions vary from reticulated slate-gray pigmentations to vesicles and verrucous keratoses. Oral mucosal white lesions may occur on the buccal mucosa, yielding a patchy plaque or verrucous appearance. Partial anodontia, strabismus with nystagmus, and epilepsy may also be seen.

Microscopic Features

Skin lesions in the vesicular stage show intraepithelial vesicle formation with numerous eosinophils. Pigmented zones display incontinence of melanin granules from the basal cells with accumulation in dermal or submucosal macrophages. White lesions are characterized by hyperorthokeratosis, hyperparakeratosis, and acanthosis. Individual cell keratinization may be present.

Differential Diagnosis

The white lesions encountered intraorally may resemble those seen in other genokeratoses yet are generally focal and patchy. The other components of this disorder, including skin discoloration and keratosis as well as partial anodontia, separate this entity from other genetic diseases manifesting oral white lesions.

Treatment

There is no treatment.

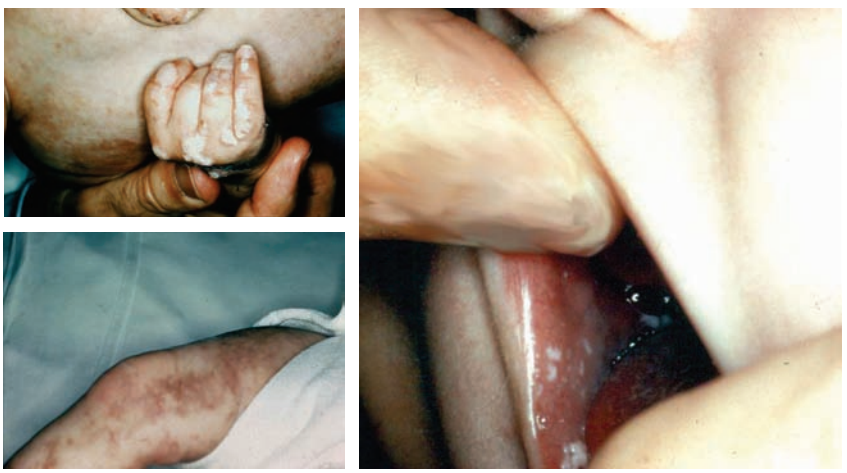

FIGURE 2-16
Oral lesions on buccal mucosa in an infant with incontinentia pigmenti along with keratoses and focal pigmentations of skin. (Courtesy of Dr. Sheldon Rovin.)

Additional Reading

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PLAQUE-FORM LICHEN PLANUS (SEE ABOVE)

Figure 2-17

CHEEK/TONGUE BITE KERATOSIS

Figure 2-18

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Chronic cheek and tongue biting is a form of frictional benign keratosis yet is clinically distinct. It evolves from a habit much like nail biting. The lesions are white and often shaggy and have been termed *morsicatio mucosae oris*. Despite this shaggy appearance, the keratinized surface is tenacious. These white lesions are oriented linearly from anterior to posterior, following the plane of dental occlusion. With appropriate questioning and observation, the habit is usually revealed.

MICROSCOPIC FEATURES

Severe parakeratosis is seen along with acanthosis. The parakeratotic layer is often edematous and the surface may be colonized by basophilic bacterial organisms. There is no carcinomatous tendency.

DIFFERENTIAL DIAGNOSIS

The lesions should be differentiated from other leukoplakias, hairy leukoplakia in particular. Cheek- and tongue-bite keratoses do not harbor Epstein-Barr virus (EBV) DNA.

TREATMENT

The lesions resolve when the habit is eliminated, and cessation may be facilitated by fabrication of a bite splint.

Additional Reading

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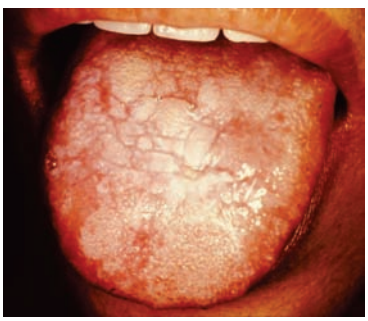

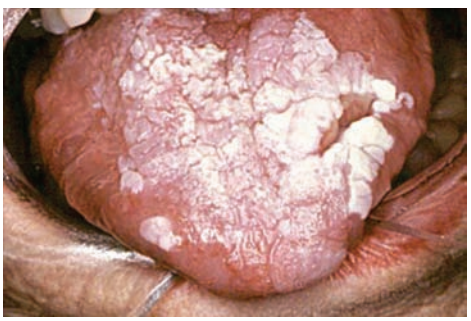

FIGURE 2-17
Multiple pavement like keratotic plaques in hypertrophic form of lichen planus.

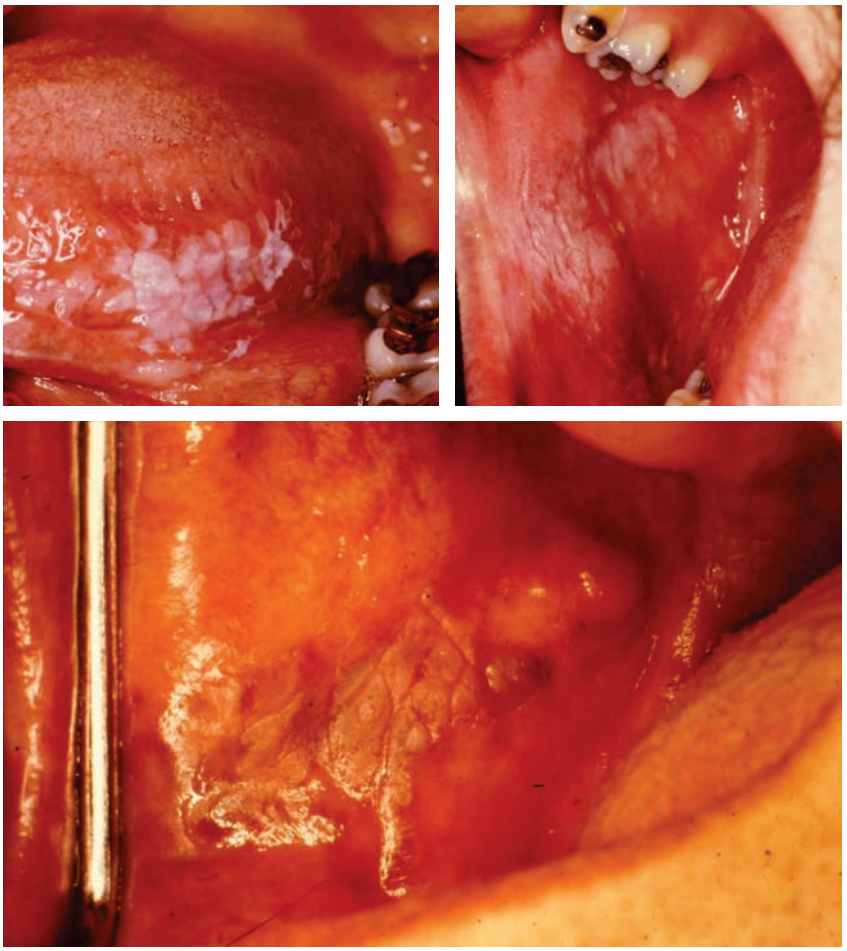

FIGURE 2-18
Cheek- and tongue-biting frictional keratoses along the occlusal plane.

Verrucous/Rippled Plaques

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA

Figure 2-19

Age: Elderly
Sex: Females predominate

CLINICAL FEATURES

Proliferative verrucous leukoplakia (PVL) is a clinically, rather than histologically, defined entity characterized by a diffuse warty or papillary white appearance. Most often, the lesions arise on the gingival, mandibular alveolar ridge and vestibular regions and over time spread laterally, becoming extensive. On long-term follow-up, many of these lesions progress to verrucous carcinoma or squamous cell carcinoma. Some of these lesions have been shown to harbor HPV DNA. Elderly females, most of whom do not use tobacco, contract this condition and, despite excision, recurrence is probable.

MICROSCOPIC FEATURES

There is a spectrum of histologic changes that are seen in PVL. The disease represents a continuum that progresses from benign warty change to invasive carcinoma, the progression often taking 10 to 20 years to evolve. In the early benign phase of PVL, the epithelium exhibits a verrucous pattern

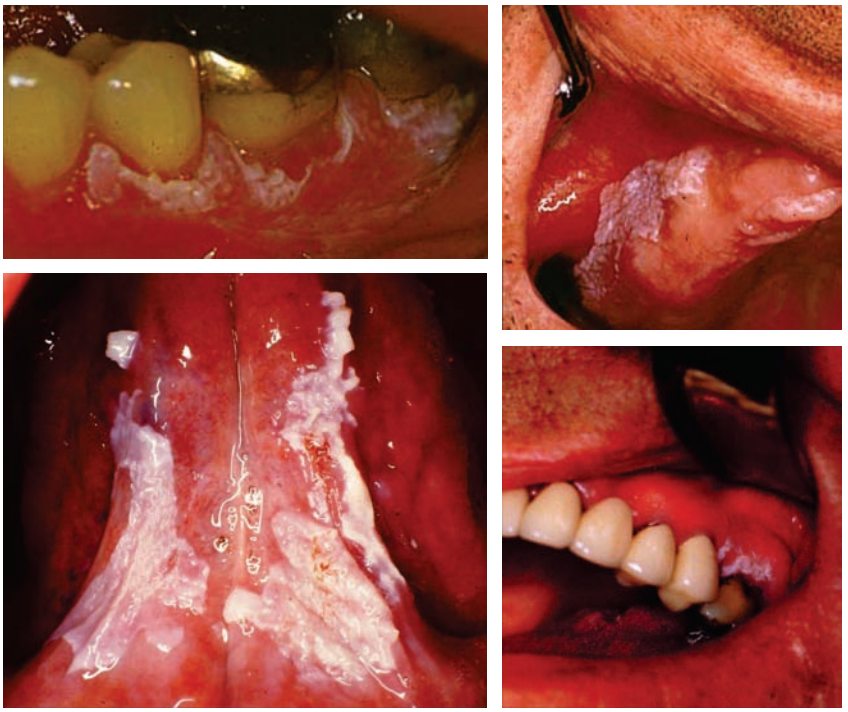

FIGURE 2-19
Proliferative verrucous leukoplakia with lesions representing a variety of histologies varying from atypical verrucous hyperplasia to verrucous carcinoma to invasive squamous cell carcinoma.

with alternating cryptic invaginations and polypoid or acroform projections. The cornified layer as represented by either parakeratin or orthokeratin is thickened, often substantially. The spinous cell layer is generally acanthotic, and in the early stages, cytologic atypia is lacking. The subjacent fibrous tissue is usually infiltrated by lymphocytes. Temporally, the lesion can evolve into verrucous lesions exhibiting marked acanthosis without cytologic atypia, and such changes are often designated atypical verrucous hyperplasia (AVH) showing the typical thickened verrucous pattern with parakeratin crypt formation. Over time, a classic verrucous carcinoma may evolve. Alternatively, some of these lesions develop dysplastic cellular changes and progress to either exophytic papillary or frankly invasive squamous cell carcinoma.

DIFFERENTIAL DIAGNOSIS

Verrucous leukoplakia cannot be differentiated clinically from verrucous carcinoma or an exophytic papillary form of squamous cancer. Biopsy is required.

TREATMENT

Verrucous leukoplakia is notorious for recurrence subsequent to surgical excision. Indeed, even when the margins appear normal, this disease recurs. Some patients have had lesions totally excised as many as six times. Verrucous leukoplakia is, therefore, a chronic, persistent disease and all instances should be considered premalignant. Radiation therapy is contraindicated owing to the potential to initiate dysplastic changes. Rather, each recurrence should be treated by conventional or laser surgery or cryosurgery.

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VERRUCOUS CARCINOMA

Figure 2-20

Age: Elderly
Sex: No predilection

CLINICAL FEATURES

Verrucous carcinoma is not a true cancer because it does not metastasize unless is undergoes anaplastic transformation. It is a proliferative lesion that often evolves from a preexisting verrucous leukoplakia or atypical verrucous leukoplakia. The lesion grows and spreads laterally without true invasion of the underlying connective tissue. Clinically verrucous carcinoma is exophytic with a warty, shaggy white surface. While some patients use smoked or smokeless tobacco, many affected patients have no history of a tobacco habit. The lesions are most frequently encountered on the alveolar ridge, gingiva, and mucobuccal fold.

MICROSCOPIC FEATURES

Surface stratified squamous epithelium exhibits a warty verrucous pattern with a markedly thickened parakeratin layer. Marked elongation and thickening of rete pegs is observed and parakeratin crypts descend into the acanthotic rete ridges, appearing as "elephant feet." The individual cells fail to display atypia, although basilar crowding and mild basal/parabasilar hyperchromatism are seen. The lesion is superficial and exophytic without invasion of the submucosa.

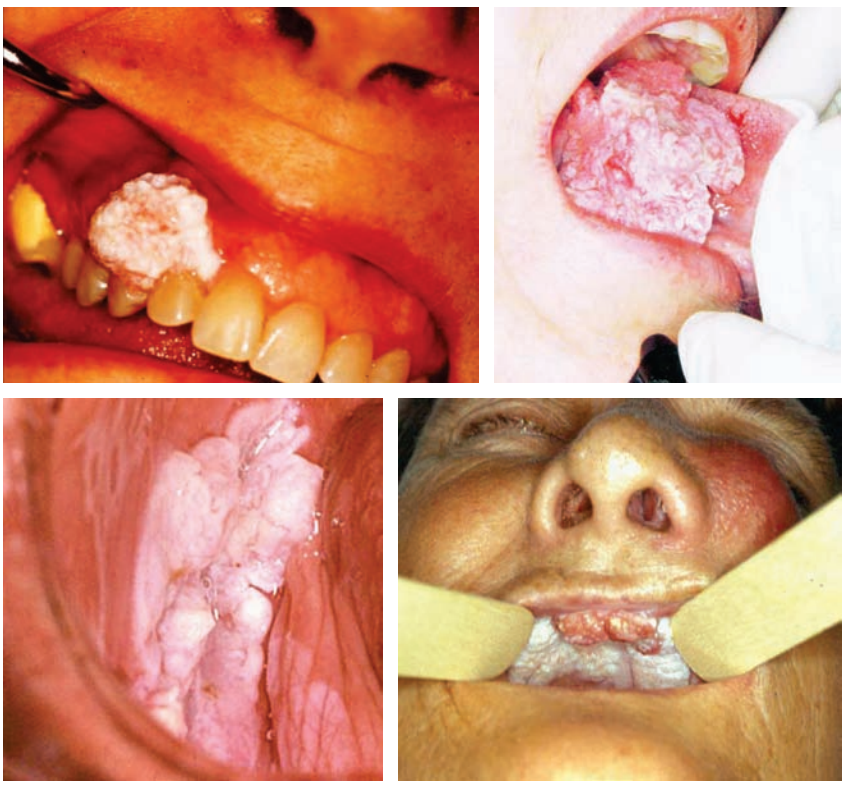

FIGURE 2-20
Verrucous carcinoma, warty thick white lesions.

DIFFERENTIAL DIAGNOSIS

Clinically, condylomata and papillary variant of squamous cell carcinoma are considered in the differential. Similarly, the microscopic features must be differentiated from papillary squamous cell carcinoma, a lesion with significant dysplastic changes. On the opposite end of the microscopic spectrum, AVH must be included in the differential diagnosis.

TREATMENT

Wide local excision with 1 cm margins is recommended. Anaplastic change with progression to invasive carcinoma has been known to occur following radiation therapy.

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Lacey White Lesions

LICHEN PLANUS

Figure 2-21

Age: Adults
Sex: Females affected slightly more often

CLINICAL FEATURES

Lichen planus is a dermatologic disorder, yet oral lesions without skin involvement are a common presentation of the disease. Whereas the etiology is unknown, lichen planus–like lesions are occasionally associated with systemic medications (see Lichenoid Reactions). The classic appearance is one of reticulated interconnected, white thread-like lesions, striae of Wickham, located bilaterally on the buccal mucosa and vestibule. Other areas such as ventral tongue and gingiva may also be involved; indeed, virtually any oral mucosal tissue may evince manifestations of lichen planus. Whereas the aforementioned features are most common, oral lichen planus may have protean clinical signs. The plaque form resembles leukoplakia with a multifocal distribution. Plaque-like lichen planus is usually a smooth and slightly irregularly surfaced white lesion found primarily on dorsal tongue mucosa. A circinate variety can be encountered. Circinate, oval, and target-appearing white lesions of lichen planus are seen most often on buccal mucosa. A pigmented form shows a mixture of stria on a slate-gray base.

Skin lesions, when present, are scaly keratoses overlying an erythematous or violaceous base and are seen most frequently on the extensor surfaces of the extremities.

Multifocal white lesions with an erythematous component are seen in the erosive and bullous forms of lichen planus, which are considered separately elsewhere. Malignant transformation is uncommon, being more often encountered among patients with erosive or plaque forms of the disease.

MICROSCOPIC FEATURES

Hyperkeratosis or parakeratosis may or may not be present. The basal cell layer is disrupted with loss of polarity; lymphocytes may be interposed between basal cells. If rete ridges are present, they taper off into the underlying connective tissue, imperceptibly blending into a subepithelial lymphocytic

infiltrate below, yielding a sawtooth pattern. The basement membrane is irregular and thickened. The juxtaposed lymphocytic infiltrate is zonal, localized only in the submucosa without involvement of the deeper connective tissue, representing a chronic interface mucositis. Phenotyping has disclosed that the lymphocytes are T cells with a preponderence of the CD4 subset.

DIFFERENTIAL DIAGNOSIS

The reticulated form is separated easily from other oral white lesions. Plaque forms may be confused with leukoplakias or premalignant conditions, moniliasis, or the genokeratoses. As mentioned, evidence is emerging that some instances of lichen planus are associated with malignant transformation. Whether or not these cases represent true lichen planus undergoing malignant change or leukoplakias and mucositis with a strong resemblance to oral lichen planus microscopically is unknown. Regardless, the plaque form may mimic other oral white lesions, and biopsy is often necessary to render a definitive diagnosis.

TREATMENT

Topical and systemic retinoid preparations have been used with limited improvement; however, the nonerosive, nonbullous forms of lichen planus are generally asymptomatic, requiring no treatment.

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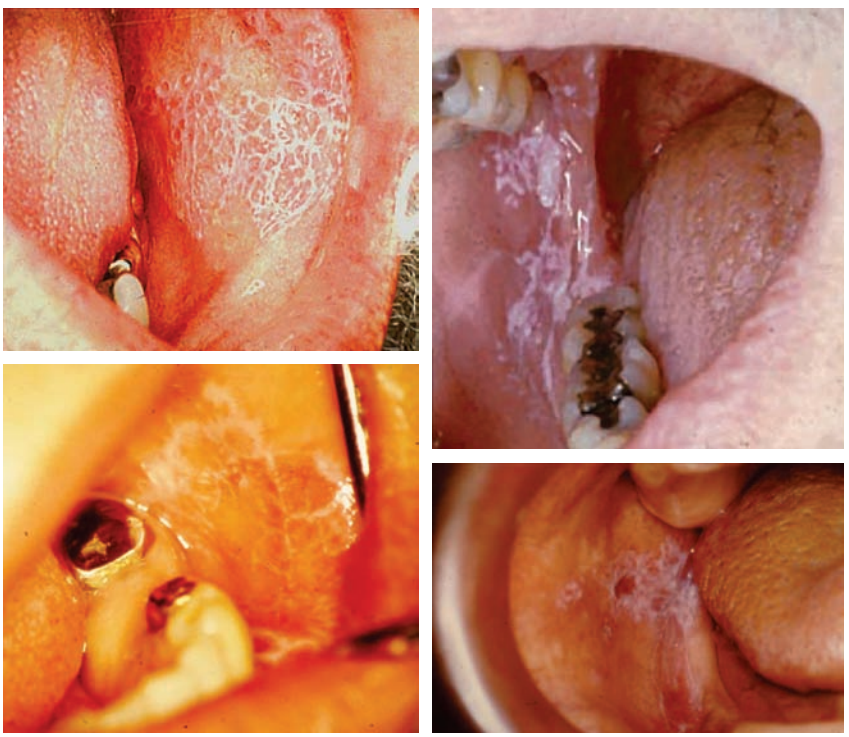

FIGURE 2-21
Reticulated lichen planus, stria of Wickham.

LICHENOID REACTIONS

Figure 2-22

Age: Adults
Sex: Slight female predilection

CLINICAL FEATURES

White lesions that lack classic features of lichen planus or appear without stria yet show a chronic interface histology may be referred to as "lichenoid reactions." Also included are lichen planus–like lesions that can be attributed to allergenic chemicals including both topical and systemic drugs (lichenoid drug eruption). The chief allergens under scrutiny are (1) contact dental restorative metals, chiefly mercury, that may leach out of old corroding amalgam restorations and trace metals from cast gold alloys, (2) a host of systemic medications, and (3) food stuff antigens such as cinnamon found in a variety of breakfast food and even used to flavor smokeless tobacco. Clinically, there is often a symptom of mucosal pain and burning. The lesions are usually white with erythema resembling erosive lichen planus. In lichenoid drug eruptions, cutaneous lichenoid lesions are also commonly encountered.

MICROSCOPIC FEATURES

A chronic interface mucositis is present with lymphocytic infiltration similar or identical to conventional lichen planus. In cinnamon allergies, the infiltrate is mixed with perivascular lymphoid aggregates in the submucosa. In lichen sclerosis et atrophicus, subepithelilal fibrosis is featured.

DIFFERENTIAL DIAGNOSIS

Conventional lichen planus, leukoerythroplakia, and other white lesions included here must be considered in the differential diagnosis. Questioning patients about

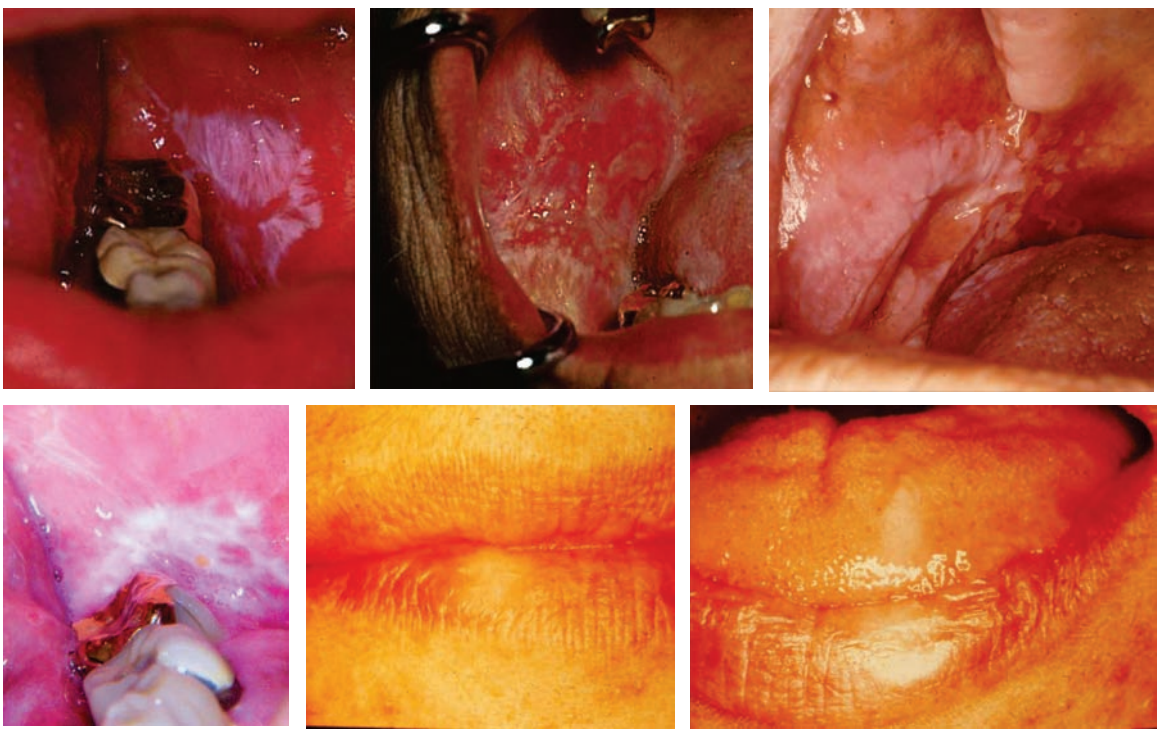

FIGURE 2-22
Lichenoid reactions: contact lesions, cinnamon reaction, drug eruption, lichen sclerosis et atrophicus of lip.

drug intake, cinnamon consumption, and other dietary potential allergens will help reveal the true diagnosis. So-called contact lesions adjacent to metal restorations should be managed by removal of the probable antigen.

TREATMENT

Removal of the antigenic source is essential, accompanied by topical steroid, tacrolimus, and/or cyclosporine and soothing mouth rinses for pain relief.

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LUPUS ERYTHEMATOSUS

Figure 2-23

Age: Young adults
Sex: Females

CLINICAL FEATURES

Lupus erythematosus, the discoid type, is a disorder manifesting erythematous dermatologic scaly lesions of skin. A more serious form, the systematic type, evinces lesions in the kidney and other visceral organs as well as on skin, being one of the collagen-vascular immunopathic diseases. Oral lesions are sometimes seen with lupus erythematosus, particularly the systemic type. The lesions are white and plaque-like, resembling lichen planus, and occasionally an erythematous component accompanies the white lesions. Disc and circinate patterns are common, and lesions often involve the vermilion border. The facial butterfly pattern—a plaque of erythema over the nasal bridge with bilateral flaring on the skin of the malar eminence region—is a classic feature of lupus erythematosus.

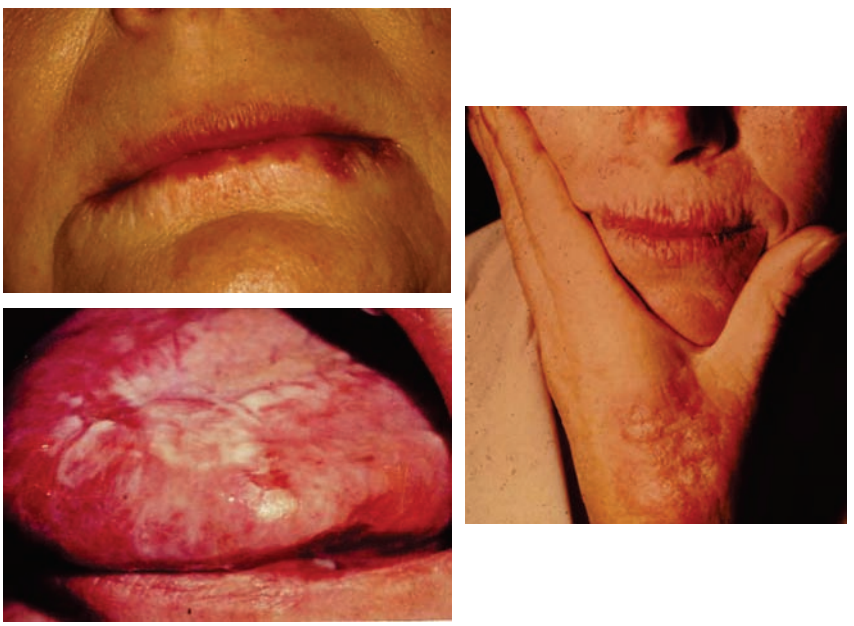

FIGURE 2-23
Discoid and lichenoid lesions of lupus erythematosus.

MICROSCOPIC FEATURES

The microscopic features are most characteristic when a biopsy is obtained from skin. Hyperkeratosis is accompanied by some disruption of the basal cell layer. The basement membrane is thickened with fibrinoid change. A lymphocytic infiltrate prevails, is patchy in distribution, and typically is localized in the vicinity of pilosebaceous structures. Oral lesions manifest microscopic features reminiscent of those of lichen planus, yet deeper zones of perivascular lymphocytic infiltration can be noted and the spinous layer is hyperplastic. Direct immunofluorescence on oral biopsies discloses IgG or IgM deposition along the basement membrane.

DIFFERENTIAL DIAGNOSIS

White lesions of lupus erythematosus must be differentiated from lichen planus, the genokeratoses, and leukoplakias. The characteristic skin lesions and butterfly pattern, when present, are important diagnostic signs. Lupus erythematosus may also be associated with erythematous and erosive oral lesions, usually admixed with a white component. Antinuclear factor, anti-DNA antibodies, immunofluorescence microscopic tests, and the lupus erythematosus preparation (LE prep) are usually positive in lupus, and elevated IgG may be seen. On direct immunofluorescence of patient lesional material, basement membrane IgM immunoreactants are usually deposited (lupus band test).

TREATMENT

Patients with lupus erythematosus may manifest systemic complications, particularly in the kidney. Prolonged systemic use of steroids or other immunosuppressive drugs is the treatment of choice, and these patients should be under the care of a physician, usually a dermatologist or rheumatologist.

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HIV-ASSOCIATED HAIRY LEUKOPLAKIA

Figure 2-24

Age: Young adults
Sex: Males

CLINICAL FEATURES

Oral hairy leukoplakia is an HIV-associated disease that involves the lateroventral tongue, although other oral sites are sometimes involved. Clinically, the lesion is relatively distinct in that parallel, fringe, or hair-like white lesions are vertically oriented along the lateral border of the tongue. In some instances, the lesion consists of a diffuse white plaque with only occasional hairy striae; other cases are almost exclusively striated. The disease is asymptomatic and may be bilateral. When hairy leukoplakia involves mucosal sites other than the tongue, it is smooth and homogeneous without striated margins. Most cases are colonized by *Candida albicans*; however, the etiology is viral. The EBV is associated with the disease and is, in all probability, causative, representing an opportunistic infection. Importantly, hairy leukoplakia

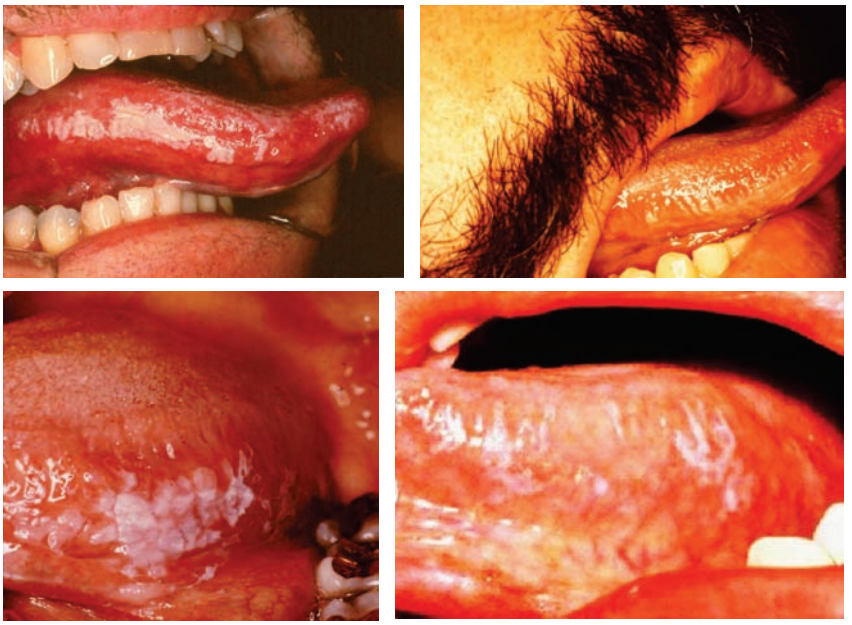

FIGURE 2-24
Hairy leukoplakia in HIV-infected males.

should be considered an AIDS prodrome as it is highly predictive for progression from asymptomatic HIV seropositivity to the full-blown syndrome.

MICROSCOPIC FEATURES

The parakeratin layer is thickened and is usually colonized by *Candida* hyphae. Characteristically, a subcorneal, upper spinous layer zone of cytopathically altered keratinocytes is evident. These subcorneal cells show cytoplasmic clearing and nuclear vesiculation with chromatin margination. The spinous layer is of moderate thickness and the submucosa is generally devoid of inflammation. Using DNA in situ hybridization with an EBV molecular probe on processed tissue sections or on cytospin preparations, upper spinous layer cells stain positively.

DIFFERENTIAL DIAGNOSIS

Ordinary leukoplakia associated with a tongue-chewing habit should be considered in the differential diagnosis along with lichen planus. These patients are HIV seropositive and fit into an AIDS-risk population group (homosexual male, intravenous drug abuser, transfusion recipient, etc). If the diagnosis is in doubt, DNA in situ hybridization should be undertaken. This lesion is extremely uncommon among other forms of immunosuppression.

TREATMENT

Generally, no treatment is required because the lesions are not painful or otherwise bothersome. Resolution follows acyclovir therapy; however, the lesions recur once the medication is withdrawn. Patients receiving triple drug therapy for the treatment of AIDS frequently manifest regression of the tongue lesions. Because hairy leukoplakia is most often seen as a pre-AIDS condition, it is important to refer affected patients to a physician who cares for such individuals.

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Papular Lesions

KOPLIK SPOTS OF MEASLES

Figure 2-25

Age: Children
Sex: No predilection

CLINICAL FEATURES

During the prodromal stages of rubeola infection when fever and malaise are waxing, focal white spots less than 1 cm in diameter may be encountered on the buccal mucosa. Patients may have only one lesion or as many as 50 on each side of the mouth. The lesions are plaque- or dome-like and are oval to round. When the maculopapular skin rash appears, Koplik spots begin to disappear.

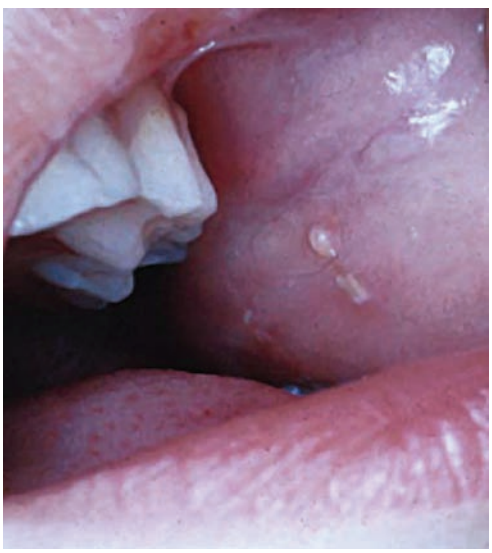

FIGURE 2-25
Prodromal measles Koplik spots.

MICROSCOPIC FEATURES

The epithelium shows superficial necrosis with an avid neutrophilic inflammatory cell infiltrate in the subjacent submucosa.

DIFFERENTIAL DIAGNOSIS

Koplik spots are usually not difficult to separate from other white lesions because they are focal and seen most often in children. Large Fordyce's granules and cheek-biting keratosis should be considered in the differential diagnosis. A diagnosis of Koplik spots is confirmed upon appearance of the classic rubeola maculopapular rash.

TREATMENT

Supportive care, including high fluid intake and the use of salicylates to control fever, with bed rest is recommended treatment. The child's physician should be notified; complications, although uncommon, may occur in measles.

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FORDYCE'S GRANULES

Figure 2-26

Age: All ages
Sex: No predilection

CLINICAL FEATURES

Fordyce's granules or ectopic sebaceous glands are present in 90% of the population. They are multifocal, less than 2 mm in diameter, and actually more yellow than white. They are located on the mucosal surfaces of the lips and buccal mucosa.

HISTOLOGIC FEATURES

Submucosal clusters of sebaceous acini are present and communicate with the oral epithelium by way of ducts.

DIFFERENTIAL DIAGNOSIS

The small size, multiplicity, and yellow color are characteristic and are unlikely to be confused with other mucosal diseases.

TREATMENT

No treatment is necessary.

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DENTAL LAMINA CYSTS, BOHN'S NODULES, EPSTEIN'S PEARLS

Figure 2-27

Age: Infants
Sex: No predilection

CLINICAL FEATURES

Focal white nodules seen on the alveolar ridges, palatal raphe area, or lateral palatal mucosa represent dental lamina cysts, Bohn's nodules, and Epstein's pearls, respectively. These nodules are encountered in neonates and represent keratin cysts that are remnants of embryonic processes of dental or minor salivary gland origin or, in the case of midpalatal Bohn's nodules, small cystic remnants of palatal process fusion.

MICROSCOPIC FEATURES

Microscopically, all three entities are identical. They are characterized by submucosal epithelial cysts that contain no true lumen

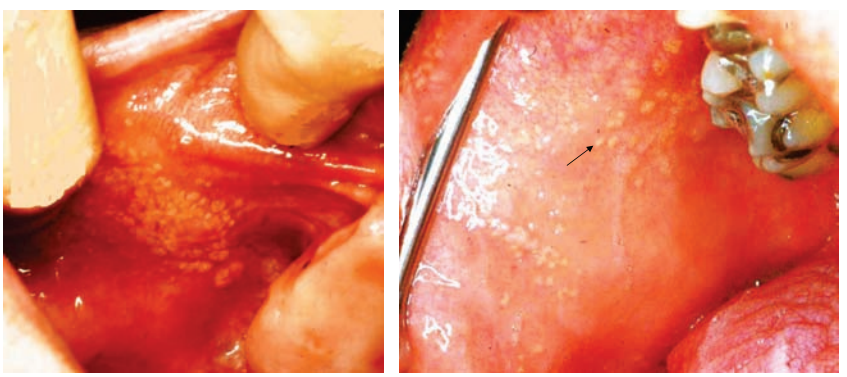

FIGURE 2-26
Yellowish white Fordyce's granules are multiple and clustered.

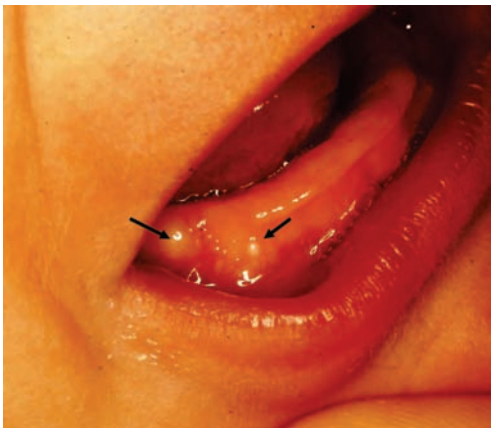

FIGURE 2-27
Congenital cysts of newborns.

but, instead, are filled with concentric swirls of keratin.

DIFFERENTIAL DIAGNOSIS

Neonatal alveolar ridge nodules may be confused with natal teeth, but closer scrutiny discloses the true nature of the spots as submucosal nodules and not prematurely erupting teeth.

TREATMENT

No treatment is necessary, as these small cysts spontaneously regress within 1 to 3 months.

Additional Reading

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STOMATITIS NICOTINA

Figure 2-28

Age: Middle-aged and elderly adults
Sex: Males predominate

CLINICAL FEATURES

Inveterate pipe and cigar smokers may manifest multiple focal keratotic papules restricted to the palatal mucosa, generally the posterior hard palate and anterior soft palate. The center of each papule in stomatitis nicotina evidences a pinpoint erythematous depression with an umbilicated appearance.

MICROSCOPIC FEATURES

The epithelium surrounding the palatal minor salivary gland duct orifice is thickened, with involvement of both keratin and spinous cell layers. The excretory salivary duct is acanthotic and may show mucous cell metaplasia. A periductal inflammatory cell infiltrate composed of lymphocytes and plasma cells accompanies capillary proliferation and dilatation in this zone.

DIFFERENTIAL DIAGNOSIS

The restriction of umbilicated papules to the palate in pipe smokers is characteristic for stomatitis nicotina. Oral keratotic papules may also be seen in keratosis follicularis (Darier-White's disease). Stomatitis nicotina differs from papillomatosis (papillary hyperplasia) in that the papules of the former are generally focal with clinically normal-appearing intervening mucous membrane; in addition, papillary hyperplasia is not keratotic and does not show a centrally depressed area.

TREATMENT

The presence of stomatitis nicotina is an indication that the patient is utilizing tobacco to a level that is toxic to mucosa. Although malignancy is not associated with this mucosal change, the patient may

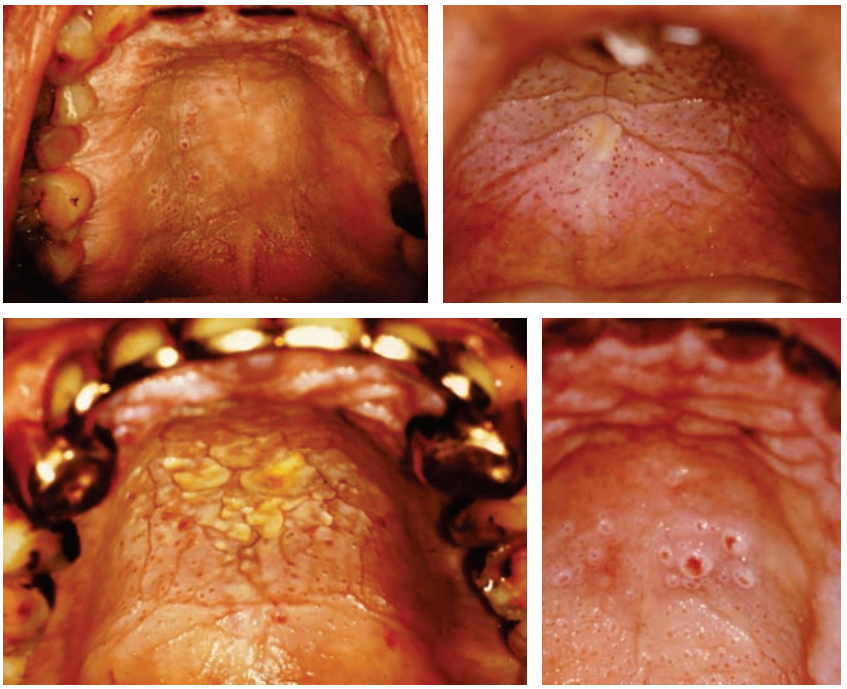

FIGURE 2-28
Stomatitis nicotina of the palate, umbilicated papules surrounded by keratosis.

nevertheless manifest leukoplakia plaques in other mucosal locations. The habit should be eliminated or severely limited.

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SPECKLED LEUKOPLAKIA

Figure 2–29

Age: Middle-aged and elderly adults
Sex: Males predominantly

CLINICAL FEATURES

Whereas the prevalence of atypical and malignant change in leukoplakia is approximately 20% (somewhat less prevalent among planar forms, more prevalent among the verruciform type), speckled leukoplakias are the most ominous in this regard. Clinically, speckled leukoplakia is a velvety red patch with multiple white papular foci. Therefore, it represents a combined leukoplakia-erythroplakia. Speckled leukoplakia is usually encountered on the oral floor, ventrolateral tongue, and soft palate.

MICROSCOPIC FEATURES

Foci of hyperkeratosis, parakeratosis, and acanthosis alternate with zones of epithelial atrophy devoid of a cornified layer. The atrophied foci correspond to those regions that appear red clinically, and usually the cells occupying the attenuated spinous layer show pleomorphism, hyperchromatism, and increased mitotic activity. The keratinized or parakeratinized regions representing the clinically evident white plaques may also harbor atypical cells and *Candida* hyphae may colonize the surface.

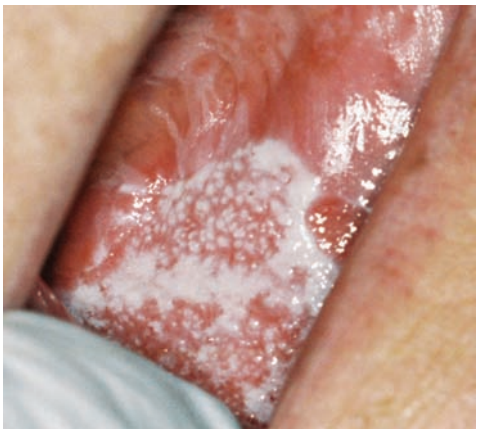
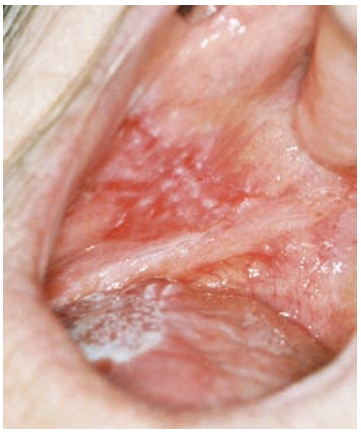

FIGURE 2-29
Velvety red lesions with white punctate papules in dysplastic speckled leukoplakia.

DIFFERENTIAL DIAGNOSIS

Speckled leukoplakia, with its mixed red and white appearance, may be confused clinically with erosive lichen planus and candidiasis. Whereas these two entities are usually multifocal, speckled leukoplakia is usually, yet not invariably, an isolated lesion. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Speckled forms of leukoplakia are usually found to harbor atypical cells. Dysplastic or carcinoma-in-situ lesions require surgical stripping, cryosurgery, or laser surgery with liberal margins of normal mucosa. Invasive cancer is managed by surgery and/or radiation therapy.

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Pseudomembranous Lesions

CHEMICAL BURNS

Figure 2-30

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Burns caused by caustic chemical agents produce coagulation necrosis of the epithelium with subsequent inflammation. The necrotic tissue loses its translucency and appears white. The white areas correspond to the areas of contact with the caustic agent and show a tendency to slough; initially, however, they may be adherent to the mucosa so that scraping with an instrument may not result in desquamation. The chief incriminating agents include aspirin, phenol, acids, and alkalies. The contactants may be introduced on a factitial or iatrogenic basis.

MICROSCOPIC FEATURES

Chemical burns cause coagulation necrosis of the epithelium so that, microscopically, the upper layers show a homogeneous appearance with loss of structure and a

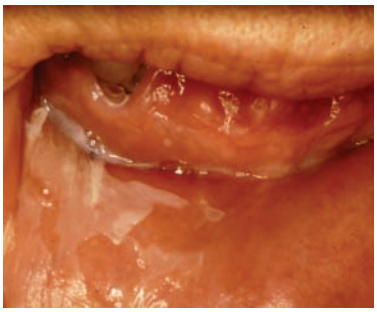
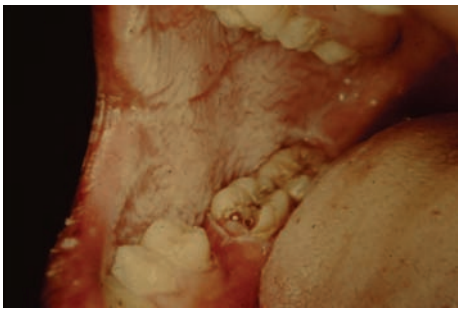

FIGURE 2-30
Aspirin burns, yellowish silver nitrate burn.

failure of nuclei to take stains. Desquamation occurs, and an inflammatory cell infiltrate within the underlying connective tissue can be seen.

DIFFERENTIAL DIAGNOSIS

The white necrotic surface is smooth with regional fissuring; this shiny surface, seen clinically, usually differentiates the necrotic surface from the keratotic lesions. Candidiasis should also be included in the differential diagnosis; however, the presence of pain and procurement of an adequate history will provide evidence for a diagnosis of mucosal burn.

TREATMENT

Treatment is supportive, with a consideration of eliminating pain until healing occurs. Orabase gel may provide relief, or palliation may result from the anesthetic effects of an antihistaminic mouth rinse in combination with Kaopectate (Upjohn; Kalamazoo, MI).

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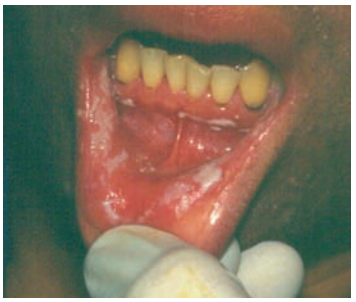
CANDIDIASIS (MONILIASIS, THRUSH)

Figure 2-31

Age: Infants and adults
Sex: No predilection in oral form

CLINICAL FEATURES

C. albicans is a superficial fungus that infects the mucous membranes of infants whose mothers display vaginal infestation at the time of parturition and of adults who have experienced an upset in their oral microflora from the use of conventional antibiotics. In addition, oral candidiasis may be associated with other systemic alterations, including diabetes mellitus, hypoparathyroidism, and immunodeficiency diseases. Instances are also commonly seen in the absence of preexisting or intercurrent systemic disease. The oral lesions consist of either multifocal or diffuse white velvety-appearing surfaces resulting from matted mycelia and parakeratotic cells. The lesions may be wiped away with gauze; however, often they are tenacious and resist such treatment. In elderly patients, moniliasis has been found occasionally to coexist with dysplastic or carcinomatous change. A cocarcinogenic effect has been suggested



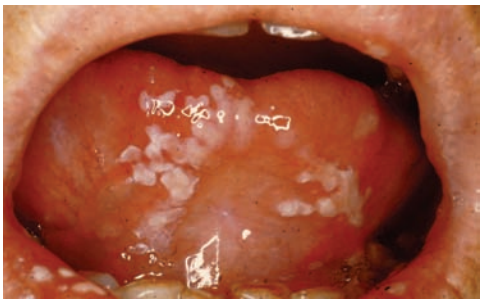


FIGURE 2-31
Candidiasis, pseudomembranous type.

for *Candida* in these instances, yet no cause-and-effect relationship has been proven. While *Candida* is generally characterized by white lesions, an erythematous component may accompany the white areas. Deep or systemic and granulomatous infection by *Candida* may occur in severely debilitated states, such as uncontrolled diabetes or severe immunodeficiency diseases. Indeed, chronic oral candidiasis is a common finding in AIDS patients, and it is commonly encountered in HIV-seropositive individuals who do not suffer from the full syndrome.

MICROSCOPIC FEATURES

Superficial infection is microscopically represented by surface parakeratosis with infiltration of the parakeratin and upper to middle spinous cell layers by PAS-positive mycelia and yeast forms. The submucosa may be free from inflammation or may contain a chronic inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The velvety surface is unique, yet the lesions of candidiasis may resemble white lesions of plaque-form lichen planus, leukoplakias, or even one of the genokeratoses, particularly since familial candidiasis has been described. A complete history, particularly questions relating to the recent use of antibiotics, will significantly limit the differential diagnosis. A cytologic smear with PAS staining for mycelium will confirm the diagnosis. On culture, not all instances are caused by the *Calbicans* species; other *Candida* species or *Geotrichium* may be responsible. Instances of *Candida* infection without any predisposing factors should arouse suspicion of underlying systemic disease. Appropriate laboratory tests for diabetes, hypoparathyroidism, and immunodeficiency states—fasting blood glucose and glucose tolerance tests, serum calcium, and immunoglobulin complement and lymphocyte blast transformation studies, respectively—should then be obtained. Lastly, it should be recalled that candidiasis is the most common oral marker for HIV seropositivity.

Candida infection in older age groups may coexist with precancerous or carcinomatous change. Biopsy is then indicated.

TREATMENT

Referral to a physician for control of any systemic derangement is mandatory. Management of the local infection involves the use of antifungal agents: nystatin oral pastilles or clotrimazole troches (4 times daily for 10-14 days) or ketoconazole (200-mg tablets once daily for 10 days), provided the patient is free of any liver disease.

Additional Reading

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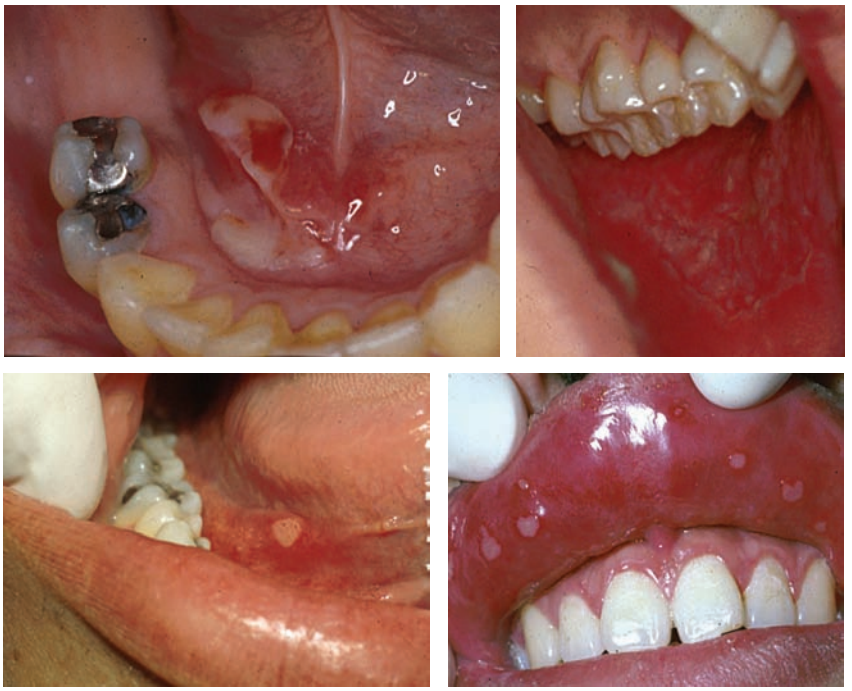

FIGURE 2-32
Grayish white fibrinous exudates in vesiculobullous-ulcerative diseases.

four cases. *Oral Surg Oral Med Oral Pathol.* 1964;18:27.
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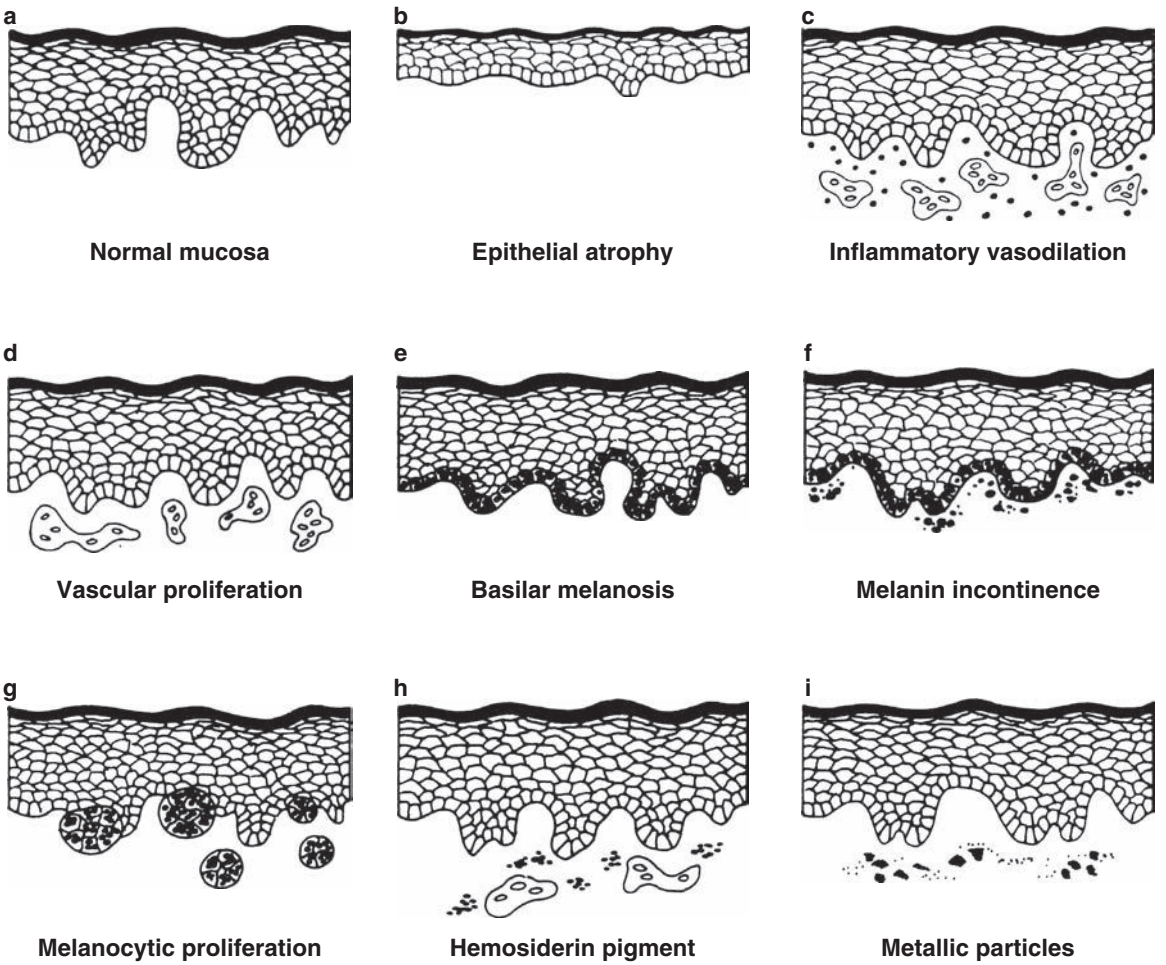
VESICULO-BULLOUS-ULCERATIVE DISEASES

Figure 2-32

Age: Varies according to disease entity
Sex: Vareis according to disease entity

CLINICAL FEATURES

A variety of diseases result in loss of the surface epithelium, and the underlying tissues become surfaced with fibrin, yielding a white-gray pseudomembrane. The specific entities are more appropriately categorized as vesiculobullous, desquamative, and ulcerative diseases covered in Chapters 4 and 5.



Red and Pigmented Lesions

Red and Pigmented Lesions

3

*See other listings in this chapter

Redness of the gingiva is the hallmark of plaque-related inflammatory disease, gingivitis, and periodontitis. These two entities have been intentionally omitted because they are dealt with extensively in dental practice and need no consideration here. When dental plaque cannot be incriminated as a source of inflammation, the clinician is obliged to pursue other causes. Diffuse gingivitis, often exhibiting pronounced erythema, may be encountered in association with systemic alterations (e.g., diabetes, pregnancy). In these instances, gingival enlargement accompanies the erythema; systemically associated gingivitis is discussed in the chapter dealing with intraoral tumefactions.

Red lesions or erythemas of the oral mucosa, including the gingiva, generally present to the assessing eye of the clinician a promulgation of inflammation. This generality should not, however, be made to the point of excluding other disease processes, particularly malignant neoplasia. Intense erythema represents increased vascularity as an expression of the inflammatory response, yet early oral cancer frequently heralds its own presence by accompanying inflammatory changes that often coexist.

In this section, red lesions are classified according to the degree of involvement with regard to surface area and the size of the isolated erythematous zone (i.e., focal erythemas, diffuse and multifocal erythemas, petechiae, and focal telangiectasia). When considering a grouping of disease entities as collective components of the differential diagnosis, one must be constantly cognizant of the fact that ulcerative and vesiculobullous lesions usually manifest a circumlesional erythematous halo. The primary character of the early lesion is of utmost relevance in the development of a differential diagnosis. Lesions that evince an erythematous component yet are primarily ulcerative or vesiculobullous-desquamative are considered in a separate chapter.

A previously mentioned concept warrants reemphasis: Most individual diseases encompassed within the erythematous group are inflammatory idiopathic disorders. Some represent a response to physical and chemical irritants; others are a manifestation of hypersensitivity to various allergens including foods and drugs. Importantly, premalignancy or incipient carcinomatous change may appear red clinically. As with other oral diseases, thorough history procurement relative to both the present illness and medical history is imperative when attempting to limit the differential diagnosis. Observation of the distribution, longevity, and temporal relationship of lesions to suspected causative agents will, in conjunction with the case history, lead to a tentative diagnosis. These features are detailed for each disease entity included in this discussion.

Pigmentations other than red lesions are considered in this section; they may be black, brown, or blue. The discolorations may result from the accumulation of either intrinsic or extrinsic chemicals in the mucosal tissues. The primary intrinsic pigmentations of the oral mucosa include the melanins and hemoglobin or hemosiderin. Extrinsic pigments responsible for discolorations are usually heavy metal particles introduced either locally or systemically. Pigmented areas that blanch when pressed represent vascular lesions. The differential diagnosis is based on extent; multiple pigmentations are associated with certain disorders, whereas focal, isolated pigmentations encompass a different group of diseases.

Common focal erythemas are nonspecific mucositis and erythroplakia (premalignant and malignant). Erythroplakia is potentially lethal.

The most common multifocal red lesions are geographic tongue, erosive lichen planus, and moniliasis. Multifocal red lesions associated with a potential lethal outcome include field cancerization, lupus erythematosus, and ecchymosis from clotting factor deficiencies.

The most common petechial lesions usually found on the palate are suction petechiae. Petechiae connoting a potentially lethal course are associated with leukemia and primary thrombocyte disorders.

The most common focal pigmentations are amalgam or graphite tattoo and melanotic macule. Melanoma is a potentially lethal, pigmented lesion that may be focal during the incipient phase, yet usually appears diffuse. All diffuse pigmentations, with the exception of racial melanosis, are rare.

Focal Erythemas

NONSPECIFIC (IRRITATIONAL) MUCOSITIS

Figure 3-1

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Localized zones of redness are often related to a physical agent that has irritated the mucosa. Ill-fitting dental prostheses or factitial injuries from chronic habitual irritation are the chief contributing factors. The zone of erythema corresponds to the source of irritation. Chemical burns may also produce a nonspecific erythematous mucositis. Incriminating chemical agents include acids, alkalies, caustic organic compounds, and volatile oils.

MICROSCOPIC FEATURES

The epithelium may be atrophic with regions bordering on ulceration. The submucosa displays capillary proliferation with dilation and a mixed inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

In older individuals, precancerous erythroplakia must be ruled out, particularly when an immediate cause is indeterminate or when removal of the suspected causative agent fails to mitigate or limit the extent of the lesion.

TREATMENT

Elimination of the irritating agent is necessary. If the area is painful, Orabase gel or an oral bandage may alleviate or palliate the symptoms until healing takes place.

Additional Reading

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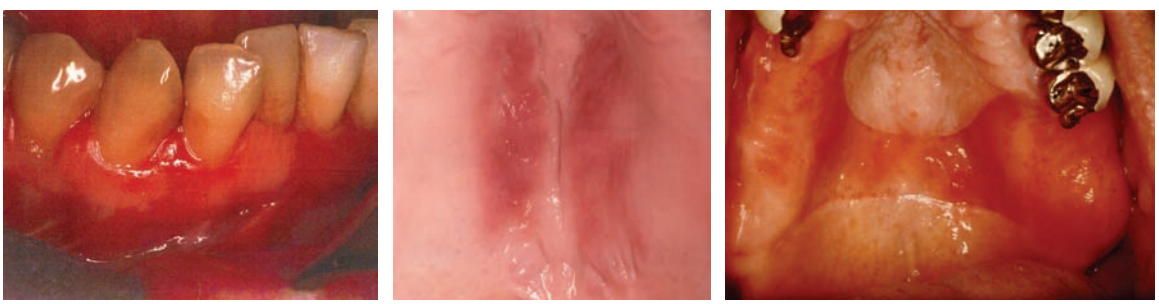

FIGURE 3-1
Tooth pic injury (left); Pizza burn of palate (center); Linear focal erythema corresponding to a partial denture gold connector that had mechanically irritated the palatal mucosa (right).

MEDIAN RHOMBOID GLOSSITIS

Figure 3-2

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The lingual papillae on the posterior midline dorsum of the tongue undergo atrophy leaving a smooth flat, or oftentimes somewhat bosselated, surface that is red. The lesion was thought to represent failure of the tuberculum impar to retract during embryogenesis; however, this theory is not considered likely because median rhomboid glossitis is only encountered in adults and therefore cannot represent a developmental defect. The surface is typically colonized by *Candida* organisms, yet not to the extent that a white pseudomembrane occurs.

MICROSCOPIC FEATURES

Epithelial hyperplasia is evident with transmigration of leukocytes into the epithelial layer. Periodic acid-Schiff (PAS) staining reveals the presence of *Candida* hyphae. The submucosa is infiltrated by lymphocytes and a hyalinized band of collagen representing the midline raphe of the tongue is frequently identified.

DIFFERENTIAL DIAGNOSIS

Very few diseases enter into the differential diagnosis. If notable swelling is encountered, a mesenchymal tumor such as granular cell tumor should be considered.

TREATMENT

Antifungal medication should be prescribed either systemically or as an oral lozenge.

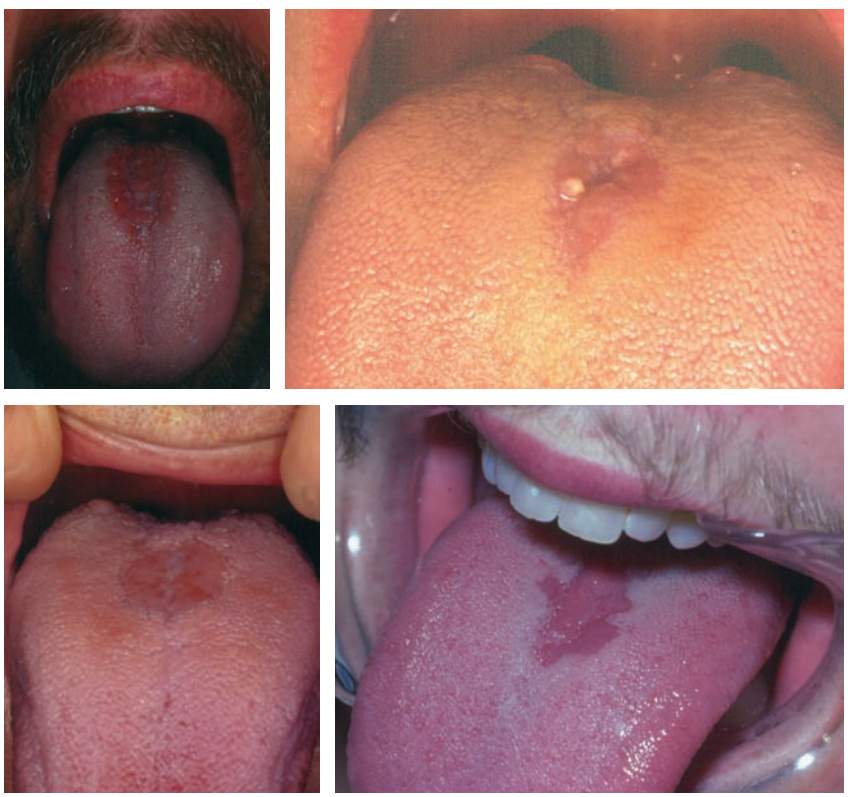

FIGURE 3-2
Median rhomboid glossitis, posterior dorsum.

Additional Reading

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HEMANGIOMA

Figure 3-3

Age: Congenital or childhood onset
Sex: Female predilection

CLINICAL FEATURES

Macular hemangiomas of the facial skin have been termed port-wine stains or nevus flammeus. They tend to follow the vascular components of neurovascular tracts of the trigeminal nerve pathways. The Sturge-Weber syndrome, encephalotrigeminal angiomatosis, manifests nevus flammeus of the facial skin with accompanying vascular hamartomas of the cerebrum and radiographically demonstrable serpentine calcifications. Ocular involvement may be present. Patients with this syndrome often suffer from epilepsy, contralateral hemiplegia, and visual disturbances. The angiomatous component may extend as a macular or tumorous lesion of the oral mucosa. Focal macular hemangiomas without evidence of skin involvement or central nervous system manifestations are also encountered in the oral cavity, although they are somewhat rare. The tumorous palpable type is more common.

MICROSCOPIC FEATURES

The submucosal or dermal connective tissue underlying the surface epithelium displays randomly dispersed small-caliber vessels, which are usually engorged with erythrocytes.

DIFFERENTIAL DIAGNOSIS

Nevus flammeus of the facial skin, when considered in conjunction with a history of long duration, poses no problem in the differential diagnosis. A diagnosis of Sturge-Weber syndrome requires radiographic demonstration of intracranial calcifications

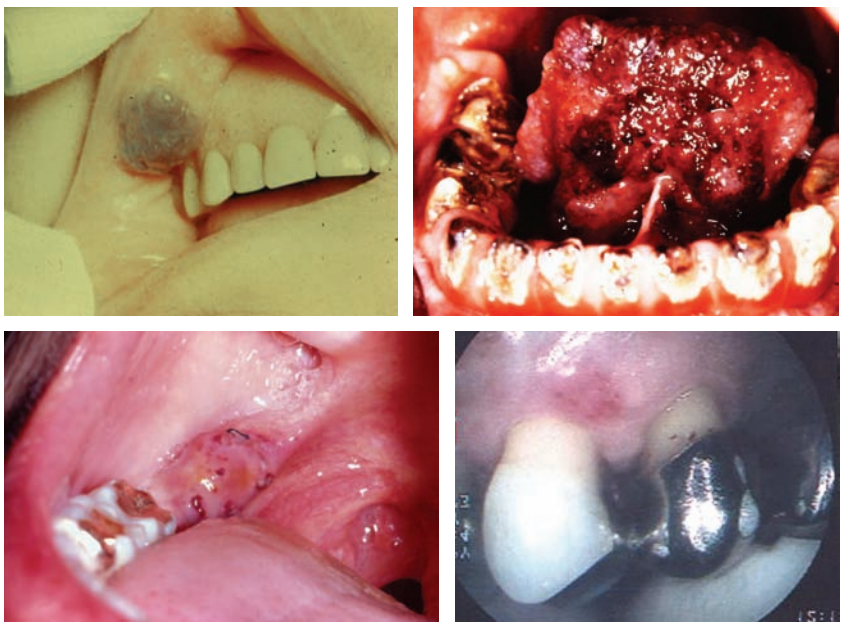

FIGURE 3-3
Hemangiomas range from purple to red. Upper right, treated with radiation therapy inducing severe gross decay.

and onset of the characteristic symptomatology. Focal mucosal hemangiomas may be confused with erythroplakia, mucositis, or chemical burns; however, history of onset and duration provides helpful clues as to the nature of the red lesion. Blanching on pressure may be evoked, and biopsy will confirm the diagnosis.

TREATMENT

Patients with Sturge-Weber syndrome should seek the care of a physician for control of epilepsy. Cosmetic surgery and tattooing may be indicated for the concerned patient with nevus flammeus. Oral macular hemangiomas may spontaneously regress after puberty. Once the diagnosis is established, no treatment is necessary for focal mucosa macular hemangiomas.

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VARIX

Figure 3-4

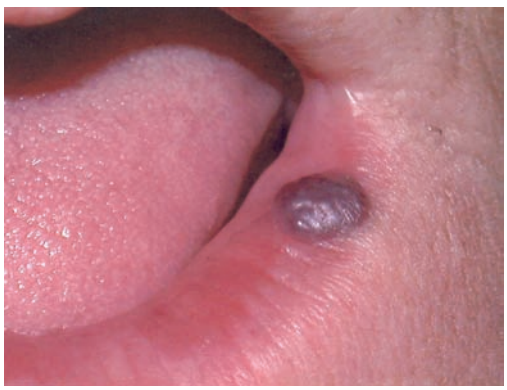
Age: Middle-aged and elderly adults
Sex: No predilection

CLINICAL FEATURES

Varices are often seen as multiple confluent blue/purple lesions bilaterally on the ventral tongue among elderly patients. The focal varix is typically seen on the lower lip yet may also occur in the vestibule and buccal mucosa. The lesions are blue, red, or purple and are typically raised nodules that are round or oval. They blanch under pressure (diascopy) unless a thrombus has formed within the vascular lumen. There is often a precedent trauma such as biting.

MICROSCOPIC FEATURES

A varix is simply a dilated vein that pursues a tortuous course throughout the connective tissue. Being a venule, the vascular channels lack a muscular coat. Often, an intraluminal thrombus develops and may undergo organization by granulation tissue.



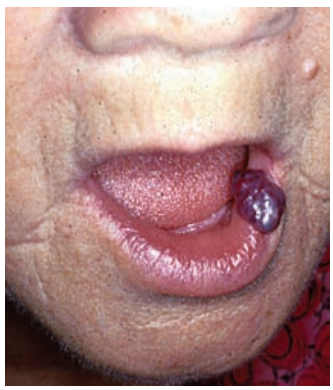


FIGURE 3-4
Focal nodular reddish purple lesions representing a varix.

DIFFERENTIAL DIAGNOSIS

The other vascular lesions included here should be considered. Failure to blanch could indicate the presence of a thrombus.

TREATMENT

Simple excision with cautery or laser is recommended.

Additional Reading

Corrêa PH, Nunes LC, Johann AC, Aguiar MC, Gomez RS, Mesquita RA. Prevalence of oral hemangioma, vascular malformation and varix in a Brazilian population. *Braz Oral Res.* 2007;21:40-45.

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ERYTHROPLAKIA

Figure 3-5

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Erythroplakia is the red counterpart to leukoplakia and should be used strictly in the clinical sense meaning, simply, red patch. Erythroplakia may therefore be represented by any of the focal erythemas listed in this chapter. Premalignant or malignant erythroplakia was originally described as a penile cancerous lesion termed *erythroplasia.* The oral mucosal counterpart is clinically similar in that a focal zone of redness may exist alone or be accompanied by leukoplakic zones. When multifocal keratotic white patches are superimposed on an erythematous base, the lesion is descriptively termed *speckled leukoplakia* or erythroplakia. A focal red lesion with no identifiable cause is a prime suspect for premalignant erythroplakia. Precancerous erythroplakia is most prevalent in the oral floor, on the soft palate, buccal mucosa, and ventral tongue.

MICROSCOPIC FEATURES

The epithelium may or may not possess a cornified layer. The spinous cell layer is atrophic, and rete ridge formation is either absent or shows bulbous projections. The spinous layer contains cells displaying atypia, hyperchromatism, pleomorphism, and increased numbers of mitotic figures. The underlying connective tissue is generally infiltrated by mononuclear inflammatory cells.

DIFFERENTIAL DIAGNOSIS

Focal erythemas representing precancerous erythroplakia can be clinically confused

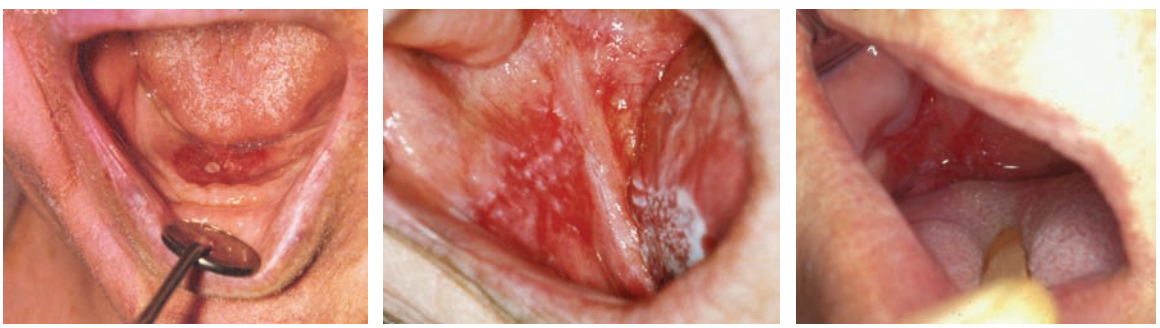

FIGURE 3-5
Erythoplakia and speckled erythroplakia histologically confirmed as carcinoma in situ.

with irritational mucositis, macular hemangioma, or chemical burn. Absence of any identifiable irritants warrants biopsy.

TREATMENT

Wide local excision of focal lesions, including 1 cm of clinically normal tissue, is recommended. The specimen should be evaluated microscopically for dysplastic-free margins.

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Diffuse and Multifocal Red Lesions

GEOGRAPHIC TONGUE (MIGRATORY GLOSSITIS)

Figure 3-6

Age: Onset in childhood or early adult life
Sex: Slight female predilection

CLINICAL FEATURES

Multifocal circinate and irregular zones of surface erosion characterized by loss of the filiform papillae are seen on the dorsum and lateral margins of the tongue. The fungiform papillae remain intact and may show mild swelling with variable degrees of erythema. The eroded zones are rimmed by keratotic white circumlesional hypertrophic filiform papillae. Whereas most cases are asymptomatic, some patients complain of glossodynia. The disease has been stated

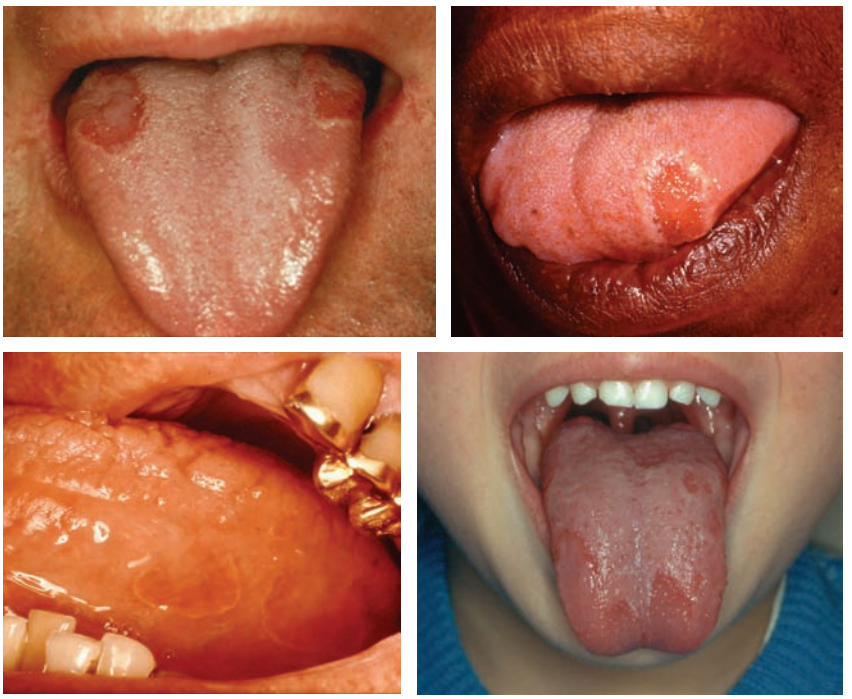

FIGURE 3-6
Circinate red macules with surrounding white halo in geographic tongue.

to occur in 1% to 2% of the population. The term *geographic tongue* is descriptive in that the foci of desquamation appear as islands and continents in a sea of normal-appearing glossal mucosa. The lesions wax and wane with periods of remission. During recurrent episodes, lesions appear in a different location.

MICROSCOPIC FEATURES

The epithelium evinces loss of filiform papillae with spongiotic abscesses similar to those encountered in psoriasis with migration of neutrophils into the spinous cell layer. The submucosa generally displays a mild chronic inflammatory cell infiltrate with variable degrees of capillary proliferation.

DIFFERENTIAL DIAGNOSIS

The clinical features, age, and history of chronicity with a tendency of the lesions to migrate are characteristic. Other diffuse erythemas that may mimic geographic tongue include moniliasis and erosive lichen planus, both of which manifest lesions in extraglossal mucosa. Geographic tongue shows microscopic features similar to psoriasis yet is not, in fact, an oral manifestation of psoriasis.

TREATMENT

No treatment is necessary. The patient should be reassured as to the benignity of the condition.

Additional Reading

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ERYTHEMA MIGRANS (MIGRATORY STOMATITIS)

Figure 3-7

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Erythema migrans is probably the extraglossal counterpart to geographic tongue. The lesions may actually accompany those of geographic tongue, or they may be independent. They are found on the buccal mucosa, lips, soft palate, oral floor, and ventral tongue mucosa. Multifocal erythematous patches are rimmed by a keratotic white margin and have a circinate pattern. As with

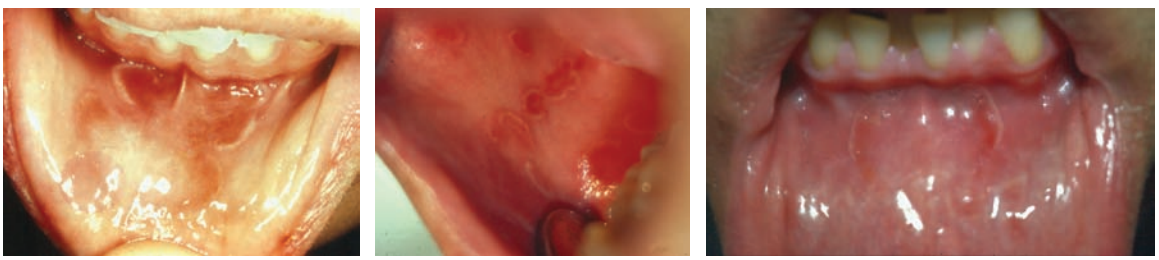

FIGURE 3-7
Circinate red macules with white border in erythema migrans.

geographic tongue, a history of migration is elicited. The erythematous regions are usually asymptomatic; however, stomatodynia may be a complaint in rare instances.

MICROSCOPIC FEATURES

The epithelium displays psoriasiform patterns; spongiosis with neutrophilic infiltration is seen in the spinous cell layer. The epithelium may be atrophic or may manifest elongated rete ridges with superficially oriented submucosal papillae.

DIFFERENTIAL DIAGNOSIS

A history of migration, lack of pain, and a circinate appearance are characteristic. Erythematous moniliasis, erosive lichen planus, lupus erythyematosus, and field cancerization should be considered in the clinical diagnosis; biopsy should be performed to rule out these diseases.

TREATMENT

The cause is unknown and no treatment is necessary. Assurance as to the benignity of the condition is indicated, particularly if the patient is cancerophobic.

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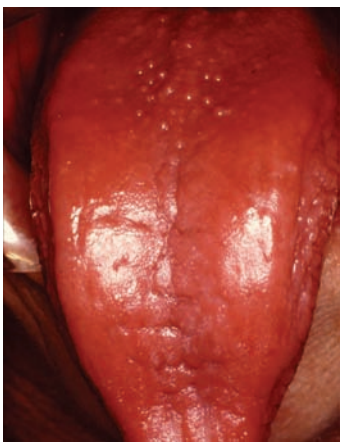
ATROPHIC GLOSSITIS

Figure 3-8

Age: Children and elderly adults
Sex: No predilection

CLINICAL FEATURES

Vitamin deficiencies are endemic in some regions of the world; in western populations, they are usually restricted to alcoholics suffering from malnutrition. Deficiency of the B vitamins such as riboflavin, niacin, and cyanocobalamine (B_{12}) with pernicious anemia, as well as folic acid deficiency and sprue resulting from an intolerance to gluten, may be accompanied by atrophic glossitis. Atrophic glossitis accompanying pernicious anemia has been termed *Hunter's* or *Moeller's glossitis.* The tongue is smooth, devoid of papillae, and shows diffuse erythema. Bald tongue has also been reported to occur in patients



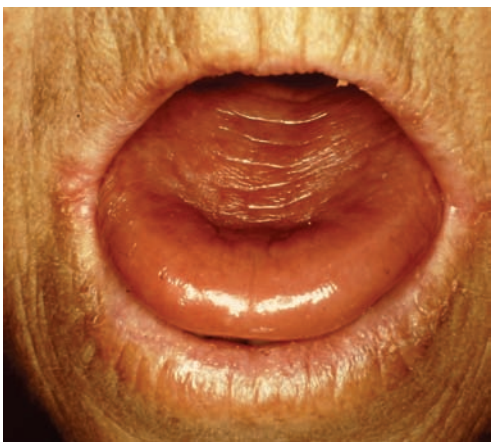


FIGURE 3-8
Bald tongue generally reddened in pernicious anemia or B-complex deficiency.

with xerostomia. The condition is reversible with adequate therapy.

MICROSCOPIC FEATURES

Tongue papillae are absent; there is a flattened epithelial layer. The submucosa shows mild chronic inflammatory cell infiltration.

DIFFERENTIAL DIAGNOSIS

Atrophic erythematous glossitis, when diffuse, is usually indicative of vitamin-B complex, or B_{12}, deficiency. Luetic glossitis should be considered in the differential diagnosis, yet usually lacks an erythematous component. Hematogram, bone marrow aspiration, and gastric analysis disclose the presence of pernicious anemia. Similar blood studies and stool analysis for steatorrhea are necessary when sprue is suspected.

TREATMENT

The nutritional deficiency should be rectified by proper diet and multiple vitamin tablets. Pernicious anemia should be managed by a physician and can be treated by vitamin B_{12} injections. Tropical sprue is managed by a nutritional diet, whereas nontropical sprue may be controlled by a gluten-free diet.

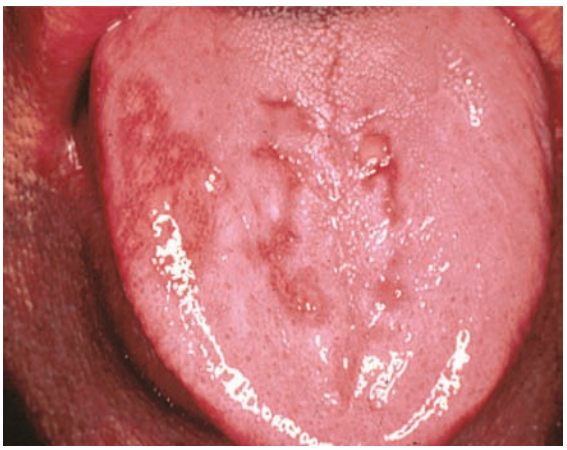


FIGURE 3-9
A pale red lesions on tongue with similar lesions in the oropharynx in a patient who received radiation for a carcinoma of the tongue.

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RADIATION MUCOSITIS

Figure 3-9

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Patients who have received external radiation therapy to the oral mucosa in excess of 3500 to 4000 rad for the treatment of oral, pharyngeal, or salivary malignant neoplasms often evince a painful diffuse erythema with telangiectasia of the mucosa. The red zones may initially be associated with a white pseudomembrane and are located in the zone of maximal radiation. *Candida* colonization is commonly present in association with these lesions.

MICROSCOPIC FEATURES

The surface epithelium may show ulceration or atrophy; depending on whether the area examined was involved with neoplastic change, residual cytologic atypia can be observed. Later changes show an inflammatory cell infiltrate in the submucosa with an attenuated spinous cell layer. Telangiectasia with nuclear pleomorphism of endothelial cells is often encountered; intimal

thickening and even thrombosis may be observed. Atypical cytologic features are no longer observed 6 weeks after radiation unless recurrence has developed. Cytologic smears stained with PAS help to determine whether candidiasis is superimposed.

DIFFERENTIAL DIAGNOSIS

A history of radiation therapy to the head and neck area points to a diagnosis of radiation mucositis. Persistence of the red lesion or increase in size should arouse suspicion that an erythroplakia connoting recurrence of carcinoma is evolving.

TREATMENT

Radiation mucositis regresses with time. Persistence or an increase in topographic extent may herald recurrence of carcinoma. Cytologic smears are the method of choice for monitoring postradiation mucositis. Unnecessary tissue breakdown, often evoked by surgical biopsy, can be avoided by this procedure. A bland dentifrice is recommended along with a soft diet. A soothing mouth rinse such as an antihistaminic with Kaopectate will offer pain relief. When *Candida* hyphae are demonstrable, 1.2% chlorhexidine rinses, nystatin pastilles, or clotrimazole troches should be prescribed.

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XEROSTOMIC MUCOSITIS

Figure 3-10

Age: Adults
Sex: Female predilection

CLINICAL FEATURES

Diffuse erythema from lack of salivary secretion is painful, with dry mucous membranes, and is severe on the gingiva. The diagnosis of xerostomic mucositis is realized on manual palpation of the major salivary glands with resultant failure to elicit flow from Wharton's and Stensen's ducts. Objectively, salivary flow rates can be assessed as can lacrimal flow with Schirmer strips. Xerostomic mucositis may result from (1) radiation fields in the region of the major salivary glands, (2) immunopathologic sialadenitis as seen with collagen diseases, Sjögren's syndrome, or Mikulicz's disease, or (3) prolonged use of antihistamines or antisialogogues. Rampant dental caries may accompany xerostomia, particularly when associated with radiation injury or long-standing Sjögren's syndrome. Notably, xerostomia may occur in the absence of any mucosal alterations. Secondary candidiasis of the

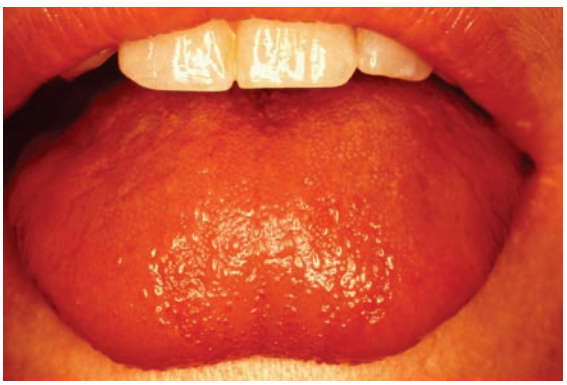

FIGURE 3-10
Generalized erythema of the oral mucous membranes occurring in severe xerostomia associated with Sjögren's syndrome.

erythematous foci is frequently identifiable by cytologic smear.

MICROSCOPIC FEATURES

Xerostomic mucositis shows a nonspecific chronic inflammatory cell infiltrate with capillary dilation in the submucosa.

DIFFERENTIAL DIAGNOSIS

Diffuse erythema of xerostomic mucositis must be differentiated from primary mucosal damage by direct irradiation (radiation mucositis). Failure to elicit salivary flow on palpation, symptoms of dry mouth, history of radiation to salivary gland regions, and bilateral parotid enlargement are all indicative of oral erythema from xerostomia. A definitive diagnosis can be made only by uncovering the cause of the condition.

TREATMENT

Management of xerostomic mucositis due to antisialogogues requires elimination or limitation of the drug. Treatment of dry mouth and mucositis due to compromised salivary function as a result of organic disease is problematic. Frequent rinsing with water or a saliva substitute and use of softline denture bases with Orabase may afford some degree of comfort. Use of sialogogues is of some benefit, yet may cause gastrointestinal irritability because of their cholinergic properties. Salivary flow may be increased by administration of pilocarpine. Daily fluoride application and meticulous oral hygiene will diminish the caries incidence. When *Candida* infection is present, antifungal medication should be given, and chlorhexidine rinses may be beneficial for some patients.

Additional Reading

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LUPUS ERYTHEMATOSUS

Figure 3-11

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

The oral lesions seen in lupus erythematosus may be red, white, or bullous. Often, red and white zones are present bilaterally on buccal mucosa with diffuse or multifocal involvement. The characteristic lesion resembles that seen in erosive lichen planus. A discoid erythematous plaque is observed and is enveloped by a white halo with radiating fringe-like striae. The dermatologic features are invariably present, and the "butterfly rash" over the nasal bridge and malar eminence region bilaterally is diagnostic when other skin lesions coexist. The systemic form more frequently manifests oral lesions. Antinuclear antibodies are typically present, being demonstrated more often in the systemic than in the discoid form of the disease. The presence of circulating antibodies to DNA is of more diagnostic significance.

MICROSCOPIC FEATURES

The oral mucosal changes in lupus erythematosus may resemble those in lichen planus. The basal lamina is thickened with subepithelial and perivascular lymphocytic infiltrates. Epithelial hyperplasia

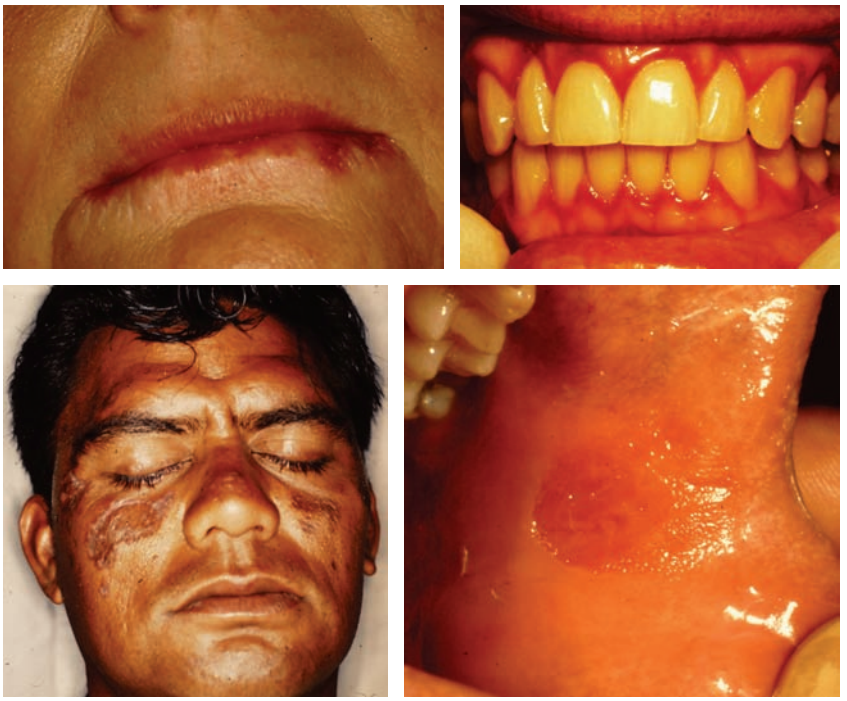

FIGURE 3-11
Diffuse red lesions of the mucosa in lupus erythematosus.

is a prominent finding with enlarged rete ridges that appear to break away from the surface epithelium. Immunofluorescence microscopy reveals the presence of granular in vitro tissue-bound immunoglobulins in the basal lamina.

DIFFERENTIAL DIAGNOSIS

The red and mixed red and white lesions of lupus erythematosus resemble those seen in erosive lichen planus. Candidiasis, allergic mucositis, erythema migrans, and multifocal precancerous erythroplakia must also be considered in the differential diagnosis. Antinuclear antibody, anti-DNA antibody, lupus erythematosus preparation (LE Prep), and renal function tests, with a consideration of the dermatologic condition, limit the differential diagnosis. Direct immunofluorescence on unfixed sections is a useful adjunctive test as well.

TREATMENT

Lupus erythematosus is treated by systemic immunosuppressant therapy and should be managed by a physician.

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ALLERGIC MUCOSITIS, FOREIGN BODY GINGIVITIS

Figure 3-12

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Inflammatory oral red lesions from immediate systemic hypersensitivity to drugs (stomatitis medicamentosa) or contact allergy (stomatitis venenata) may occur at any site on oral mucosa. Immediate antibody-mediated hypersensitivity may be seen with any parenteral medication, but is most commonly associated with antibiotics, sulfa drugs, iodine, and barbiturates. Diffuse and multifocal red lesions are usually accompanied by a pseudomembrane, desquamation, or, occasionally, bullae. Contact allergy can be seen in the region in direct continuity with the incriminating allergen, which may be any dental material including heavy metals, topical medications, or dental preparations such as toothpastes and mouth rinses. The lips and face may show erythematous lesions when cosmetics are the cause of allergy. A specific form of contact mucositis related to an allergen in chewing gum has been observed and is characterized by severe diffuse gingival erythema with ulceration of the lips and commissure. This condition has been termed *plasmacytosis gingivae*, so named because of the profuse infiltration of plasma cells into the submucosa of the gingiva. In both immediate and contact allergic reactions, pruritus or burning may be a primary symptom. Some instances of lichen planus represent allergies to drugs or to specific metals. *Foreign body gingivitis* is a nonimmunologic foreign body reaction to dental abrasives causing localized marginal gingival erythema.

MICROSCOPIC FEATURES

The submucosa in immediate hypersensitivity evinces capillary dilation and nonspecific infiltration of the inflammatory cells.

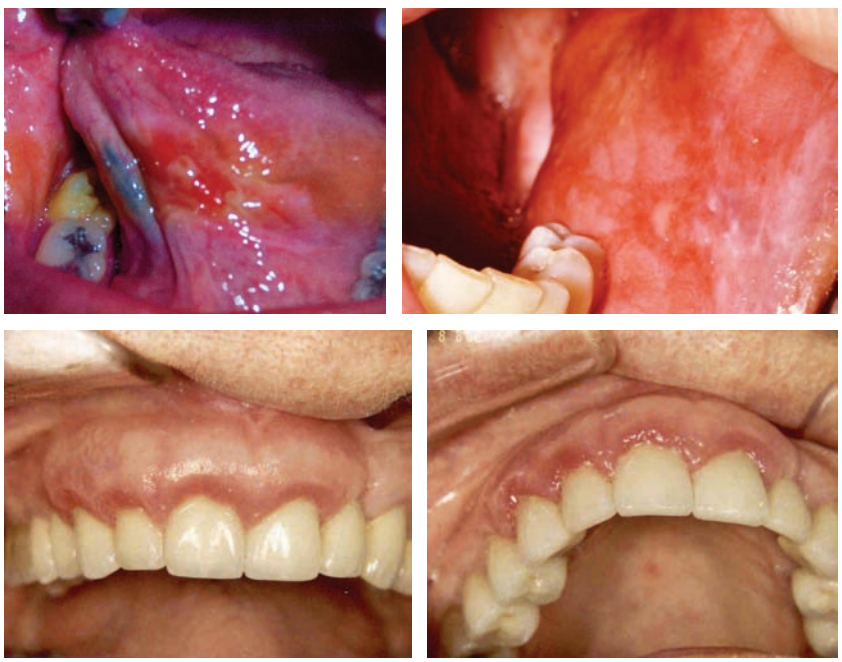

FIGURE 3-12
Allergy to cinnamon showing diffuse erythema (top) and reaction to dental finishing abrasive particles from crown margin finishing (foreign body gingivitis) (bottom).

Eosinophils are present in variable numbers yet are not usually a prominent feature. In plasmacytosis gingivae, an avid plasma cell infiltrate prevails, producing myeloma-like features microscopically. Delayed reactions are T-cell mediated and exhibit a lymphocytic submucosal infiltrate with scattered plasma cells and chronic epidermitis; the histologic features may be similar to lichen planus. In foreign body gingivitis, small refractile particles can be identified under polarized light.

DIFFERENTIAL DIAGNOSIS

Hypersensitivity-related oral red lesions may clinically mimic erosive lichen planus, lupus erythematosus, erythema migrans, or any of the other diffuse red lesions outlined in this section. The differential diagnosis may be limited by procuring a history of drug ingestion or occurrence of lesions after use of a suspected allergenic substance. Biopsy shows nonspecific features. Epimucous patch testing may be accomplished by applying the suspected allergen on dried mucosa overlaid with an oral bandage. Provided the material is not naturally caustic, a zone of erythema 24 to 48 hours later generally denotes allergy if the procedure can be reduplicated. Alternatively, most allergens causing mucositis evoke a positive cutaneous patch test, which is easier to perform. Patch testing is reserved for delayed contact reactions. If immediate hypersensitivity is suspected, scratch tests with suspected allergens can be performed or in vitro radioallergosorbant assays can be used diagnostically.

TREATMENT

Elimination of the allergen is necessary to provide cure. Acute reactions and symptoms can be minimized by prescribing antihistamines for systemic reactions or topical fluorinated steroids for contact allergy.

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BULLOUS/EROSIVE DISEASES

Figure 3-13

Age: Variable
Sex: Variable

CLINICAL FEATURES

The bullous/desquamative diseases are detailed in Chapter 5. Suffice it to mention here that most of these lesions show erythematous mucosal changes that occur in conjunction with the desquamative component. Thus, pemphigus vulgaris, benign mucous membrane pemphigoid, erythema multiforme, epidermolysis bullosa, and erosive lichen planus can all appear as red lesions; nevertheless, unlike the other erythematous lesions listed in this chapter, sloughing of the mucosa is evident. The reader is referred to the aforementioned chapter for detailed description of this group of disorders. Of all the bullous/erosive diseases, benign mucous membrane pemphigoid, erosive lichen planus, and erythema multiforme are more often represented by diffuse foci of erythema. In pemphigoid, the red lesions are primarily localized to the attached gingiva; erosive and atrophic lichen planus involve the gingiva, vestibule, and buccal mucosa, and the hemorrhagic sloughing lesions in erythema multiforme are most prominent on the lips.

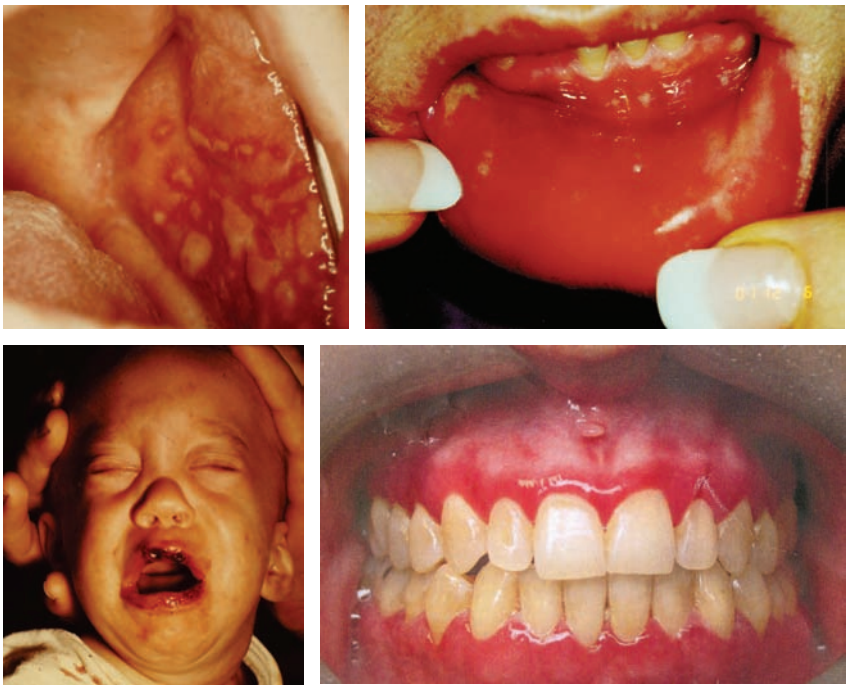

FIGURE 3-13
Bullous and desquamative diseases with erythema.

MICROSCOPIC FEATURES

The bullous diseases involve defects in cell-cell attachment or adhesion to the basement membrane. The specific histopathologic features for each of these conditions are given in Chapter 5.

TREATMENT

Because most of these diseases involve immunopathologic mechanisms and many are believed to be autoimmune, immunosuppressive therapy is used in their management. In most patients, topically applied steroid preparations suffice, whereas more severe instances may require systemic steroid therapy.

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CANDIDIASIS

Figure 3-14

Age: Infants and adults
Sex: No predilection

CLINICAL FEATURES

The classic pseudomembranous white lesions of *Candida albicans* infection may occasionally be supplanted or obscured by diffuse and multifocal red patches. A common clinical manifestation of erythematous candidiasis has been termed *denture sore mouth.* The red lesions are confined to denture-bearing mucosa, usually on the palate, and exhibit a patchy distribution often associated with speckled curd-like white

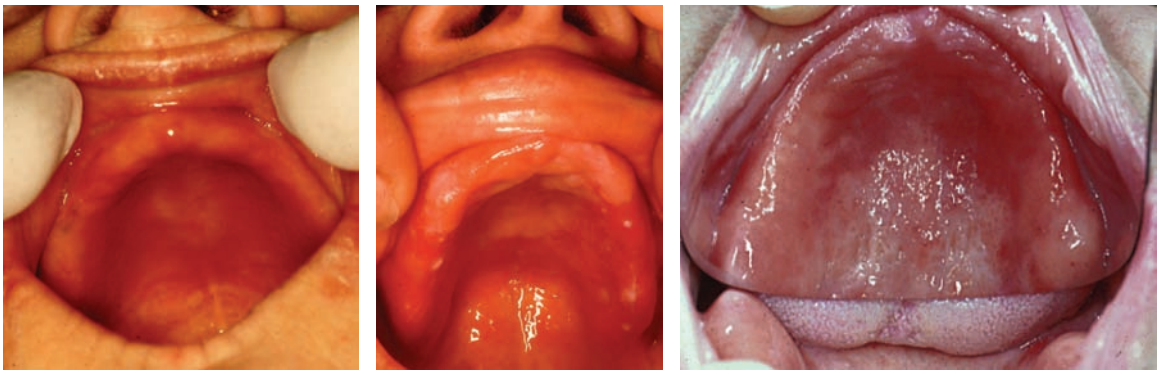

FIGURE 3-14
Multifocal red lesions of candidiasis underlying an ill-fitting maxillary dental prosthesis.

lesions, which are generally easily displaced by rubbing. Angular cheilitis often accompanies such changes. In addition to candidal-induced red lesions under dentures, erythematous candidiasis occasionally involves mucous membranes devoid of any overlying dental prosthesis. The red patches may be strictly erythematous or speckled as seen in denture sore mouth. The erythematous component in this form of candidiasis is a reflection of inflammation and may represent hypersensitivity to the organism. Although rare, this mycosis may become systemic with a granulomatous response, is potentially lethal, and usually heralds the presence of an immunodeficiency disorder.

MICROSCOPIC FEATURES

The epithelium is attenuated, and PAS staining exhibits superficially oriented mycelia. The underlying submucosa evinces a mild to avid chronic or subacute inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Denture sore mouth candidiasis must be distinguished from a true allergic reaction to denture-base resin (an extremely rare condition). Nondenture-related erythematous candidiasis may be confused with erythema migrans, radiation change, lupus erythematosus, erosive lichen planus, dermatitis herpetiformis, or malignancy. Indeed, candidal infection may coexist with carcinoma. A cytologic smear with PAS stain will disclose mycelia, or culture may be performed. Failure to respond to antifungal therapy should be followed by biopsy and consideration of other possible diseases in the differential diagnosis.

TREATMENT

Nystatin cream or ointment may be applied to the denture base for rapid resolution of erythema followed by reconstruction or relining. Erythematous candidiasis not related to ill-fitting dentures can be managed by nystatin pastilles used 4 times per day for 7 to 10 days or oral clotrimazole troches to be used 4 times daily. Alternatively, ketoconazole (a single 200-mg tablet per day for 10 days) is generally effective provided the patient does not suffer from liver disease.

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LYMPHONODULAR PHARYNGITIS

Figure 3-15

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Multifocal nodules with a pronounced erythematous base localized primarily to the soft palate and oropharynx are seen in lymphonodular pharyngitis, a coxsackie virus type A infection. Patients complain of sore throat and general malaise, are febrile, and manifest regional nodal lymphadenitis. The nodules are multifocal and approximately 0.5 cm in diameter with a wide erythematous base. Similar lesions may occasionally be seen anterior to the oropharynx. The disease resolves spontaneously in 5 to 7 days.

MICROSCOPIC FEATURES

The epithelium displays both intracytoplasmic and intranuclear inclusions with transmigration of neutrophils. The submucosa is infiltrated with nodular accumulations of lymphocytes that distend the overlying epithelium.

DIFFERENTIAL DIAGNOSIS

The lesions differ from those of other oral viral infections in that they are erythematous and nodular rather than vesicular. The coexistence of palatal and oropharyngeal lesions with fever allows segregation from other elements in the differential diagnosis, yet allergic mucositis and erythema multiforme should be considered. In these diseases, temperature is not elevated over 37.8°C, whereas in lymphonodular pharyngitis, it usually exceeds 38.4°C. Definitive diagnosis can be achieved by procuring a stool culture for isolation of coxsackie virus.

TREATMENT

Treatment of lymphonodular pharyngitis is palliative. The symptoms may be mitigated by prescribing a soothing oral rinse such as an antihistaminic expectorant mixed with equal parts of Kaopectate, with subsequent swallowing for sedative affects.

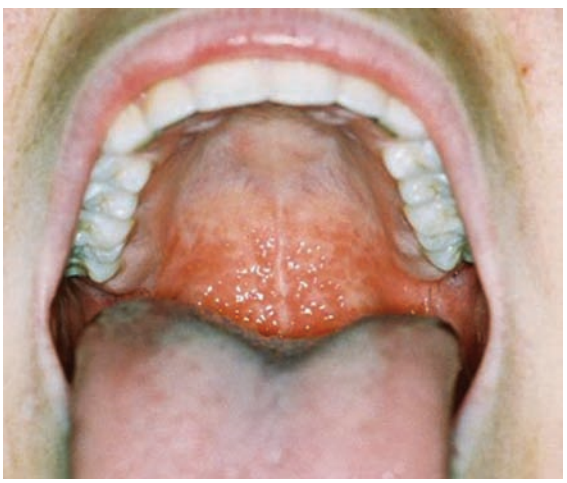

FIGURE 3-15
Multiple red papules of the soft palate and oropharynx characteristic of lymphonodular pharyngitis, a coxsackie virus infection.

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SCARLET FEVER

Figure 3-16

Age: Children
Sex: No predilection

CLINICAL FEATURES

Scarlet fever is caused by β-hemolytic streptococci, which generate an erythrogenic toxin. The toxin induces vascular dilation

and damage with an erythematous macular rash on the skin. A fiery red pharyngitis is accompanied by cervical lymphadenopathy. The tongue similarly becomes overtly erythematous with hypertrophy of the fungiform papillae, termed *strawberry tongue.* Constitutional signs of infectious disease are epitomized by fever and malaise. Potential complications include rheumatic fever, otitis media, and pharyngeal abscess. The disease was often fatal before antibiotic treatment became available.

MICROSCOPIC FEATURES

The pharyngeal mucosa may display superficial necrosis, a pseudomembranous exudate, and microbial colonies. The submucosa evinces an acute or subacute inflammatory cell infiltrate. The tongue is generally devoid of ulceration yet shows vasodilation with inflammatory cell infiltration, being a nonspecific mucositis.

DIFFERENTIAL DIAGNOSIS

The clinical tetrad of erythematous macules, pharyngitis, lymphadenopathy, and so-called strawberry tongue constitutes the hallmark of the disease. The tongue lesion may simulate a chemical burn. Atrophic glossitis seen in vitamin deficiency and pernicious anemia is usually mild and not nearly as bright red in appearance. Swab cultures of the oropharynx disclose the presence of hemolytic streptococci, and antistreptolysin-O titers are elevated.

TREATMENT

Penicillin is preferred if no allergy to the drug exists. Intramuscular injection of 1,000,000 units is followed by oral penicillin daily. As dangerous complications occasionally occur, the patient should be referred to his or her physician.

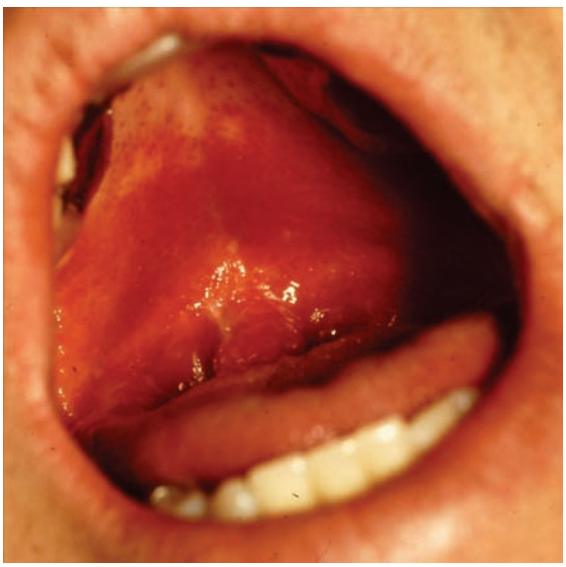

FIGURE 3-16
Acute erythematous pharyngitis, a feature of streptococcal sore throat.

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ATROPHIC LICHEN PLANUS

Figure 3-17

Age: Middle-aged adults
Sex: Predilection for females

CLINICAL FEATURES

When erythema, superficial ulceration, and desquamation accompany the white component, the term *erosive lichen planus* is used or atrophic lichen planus when only red lesions are extant. The buccal mucosa and mucobuccal fold are favored locations, yet other sites are generally involved as well. Reticulated white lines or striae are often, but not invariably, present and are superimposed over a red base. The lesions are patchy, with or without an overt slough.

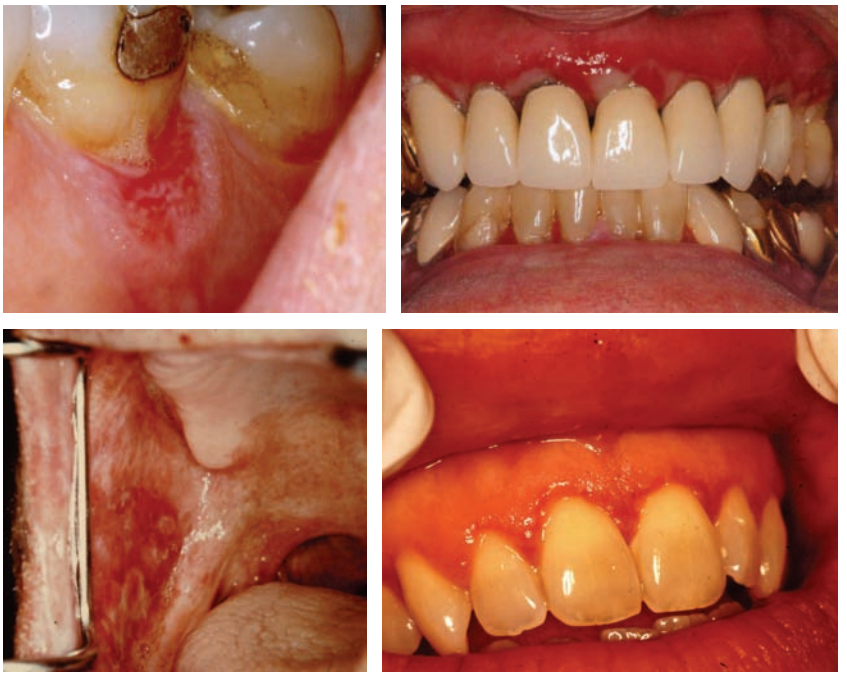

FIGURE 3-17
Atrophic lichen planus showing multifocal erythematous erosions.

Bullae may sometimes be seen with a predominantly erosive form of lichen planus. Pain and burning are frequently encountered. Skin lesions are infrequently associated with oral erosive lichen planus. Most patients are tense or anxiety prone, and the lesions wax and wane corresponding to periods of emotional stress. The erosive form of lichen planus has been associated in rare instances with oral carcinoma.

MICROSCOPIC FEATURES

The epithelium is generally attenuated and the basal cell layer is disorganized, with diffuse zones of degeneration. Transmigration of lymphocytes into the basal and parabasilar cell regions is a prominant feature, and the basement membrane is eosinophilic and thickened. A junctional separation at the level of the basement membrane is generally noted in multiple areas to the extent that the epithelial layer may be completely detached or missing. The immediate subjacent connective tissue evinces a zonal lymphocytic band. Immunofluorescence staining fails to demonstrate precipitation of immunoglobulins. Rather, fibrinogen globular deposits are demonstrated along the epidermal-submucosal interface corresponding to the zones of desquamation and basal lamina thickening.

DIFFERENTIAL DIAGNOSIS

When a white component with reticulated striae accompanies the red lesions, a clinical diagnosis of erosive lichen planus should be the foremost consideration. Radiation mucositis, allergic mucositis, lupus erythematosus, and erythroplakic precancerous lesions show similar clinical features. Oral red lesions with clinical and microscopic features of atrophic lichen planus may disclose foci of cytologic atypia with potential for carcinomatous transformation; such lesions have been termed *lichenoid dysplasia.* If bullous lesions accompany the red lesions, other bullous dermatoses should be considered in the differential diagnosis. Biopsy is indicated to secure a definitive diagnosis.

TREATMENT

A topical fluorinated steroid application (0.05% fluocinonide gel four to five times daily) is the treatment of choice and results in a clearing of the painful erythematous component. As erosive lichen planus is a paroxysmal chronic disease, this medication can be used periodically during the more severe episodes. Because of the occasional occurrence of carcinoma in this form of lichen planus, patients should be subjected to periodic follow-up. Biopsy of areas that are refractory to treatment should be performed.

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ECCHYMOSIS AND CLOTTING FACTOR DEFICIENCIES

Figure 3-18

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Red lesions caused by extravasation of blood will appear clinically as a submucosal erythema or a diffuse slightly elevated smooth-surfaced bruise. The color will range from red to brown to bluish black, depending on the duration. Ecchymosis from trauma is common, yet when no traumatic incident can be recalled or when the presence of ecchymosis far outweighs the degree of trauma experienced by the patient, a defective clotting mechanism should be suspected. Without exhaustive explanation, the following causes should be considered in the pathogenesis: (1) hereditary clotting factor deficiencies (e.g., hemophilia, Christmas disease), (2) use of medications with anticoagulant activity (e.g., coumarin), and (3) primary liver disease. Gingival hemorrhage and uncontrolled bleeding are also features associated with clotting factor deficiencies. Purpura is encountered in various platelet disorders and leukemia as well.

MICROSCOPIC FEATURES

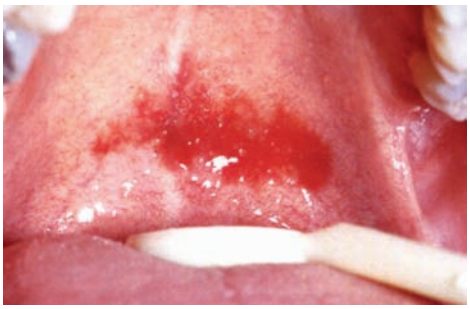
Ecchymosis is characterized by submucosal extravasation of erythrocytes with varying amounts of hemosiderin pigment and organization by fibrovascular and inflammatory cell elements.

DIFFERENTIAL DIAGNOSIS

Ecchymosis of the oral mucosa associated with clotting factor disorders is, in general, complicated by cutaneous manifestations or hemarthrosis. The oral lesions often appear as blood-filled diffuse bullae and, therefore, are not readily confused with other diffuse or multifocal red lesions. Defective thrombocyte deficiencies are generally heralded by petechial rather than ecchymotic hemorrhages; nevertheless, severe platelet anomalies manifest ecchymotic lesions. Patients with ecchymosis with no history of undue trauma should be initially subjected to a coagulation panel evaluation, including partial thromboplastin time, prothrombin time, thrombocyte count, thrombocyte aggregation assay, bleeding and clotting time, and a tourniquet test.

TREATMENT

Detection of an abnormal value in any of these tests warrants referral to an internist or hematologist. Oral surgical procedures should be deferred until the coagulation defect has been corrected or purified factor infusions can be administered just before initiation of any surgical procedures.



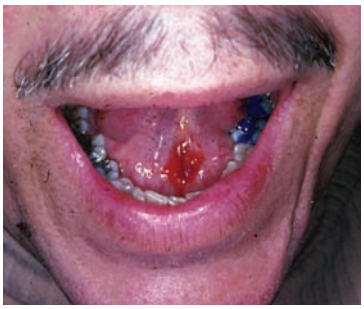


FIGURE 3-18
Multiple reddish brown ecchymotic pigmentations observed in hemorrhagic diatheses associated with clotting factor deficiencies.

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FIELD CANCERIZATION

Figure 3-19

Age: Middle-aged and elderly adults
Sex: Male predilection

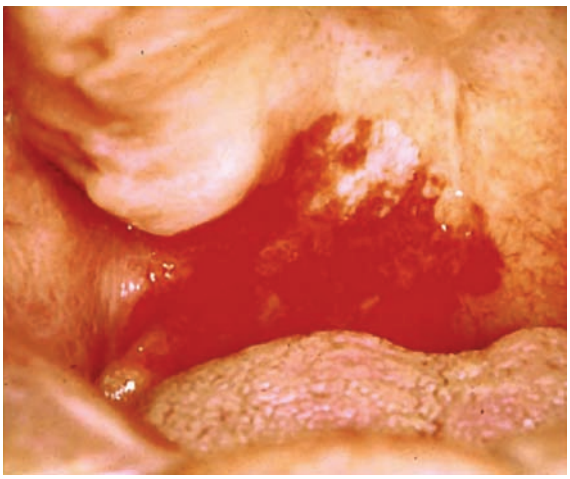

FIGURE 3-19
Erythroplakia with occasional leukoplakic foci are representative of widespread carcinoma in situ.

CLINICAL FEATURES

Multifocal erythroplakias show the same features as focal precancerous erythroplakia: velvety-red macules often accompanied by a patchy or speckled leukoplakia component. As with leukoplakia, most patients use tobacco and are heavy consumers of alcoholic beverages. Importantly, patients with a history of oral cancer are at risk for developing not merely a recurrence in the previous site of involvement but multifocal oral carcinomas. The larynx may also be the site for other primary carcinomas.

MICROSCOPIC FEATURES

The epithelium is invariably attenuated, with foci of hyperorthokeratosis or parakeratosis. The individual epithelial cells may evince changes ranging from atypia to frank invasive carcinoma. The submucosa is traversed by dilated capillaries with an accompanying dense diffuse inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Multifocal red lesions in elderly patients, particularly those with tobacco and alcohol habits, should arouse suspicion of malignancy. Biopsy is indicated immediately if no cause is discernible, even when other diseases are considered likely components of the differential diagnosis. Field cancerization made manifest by multifocal erythroplasia may mimic erythema migrans,

radiation mucositis, lupus erythematosus, allergic mucositis, erythema multiforme, erythematous candidiasis, or erosive lichen planus.

TREATMENT

Field cancerization is an extremely difficult management problem and is particularly enigmatic when a preexisting carcinoma was present and was managed by radiation therapy. Surgical stripping of carcinoma in situ and radiation therapy remain the treatment methods of choice. Complete examination with work-up for other primary lesions in the oropharynx and larynx is indicated, with management by an experienced oncologist.

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KAPOSI'S SARCOMA

Figure 3-20

Age: Young adults
Sex: Males

CLINICAL FEATURES

Kaposi's sarcoma was rarely seen during the pre-AIDS years, but afterward, oral and cutaneous Kaposi's sarcoma became common findings among human immunodeficiency

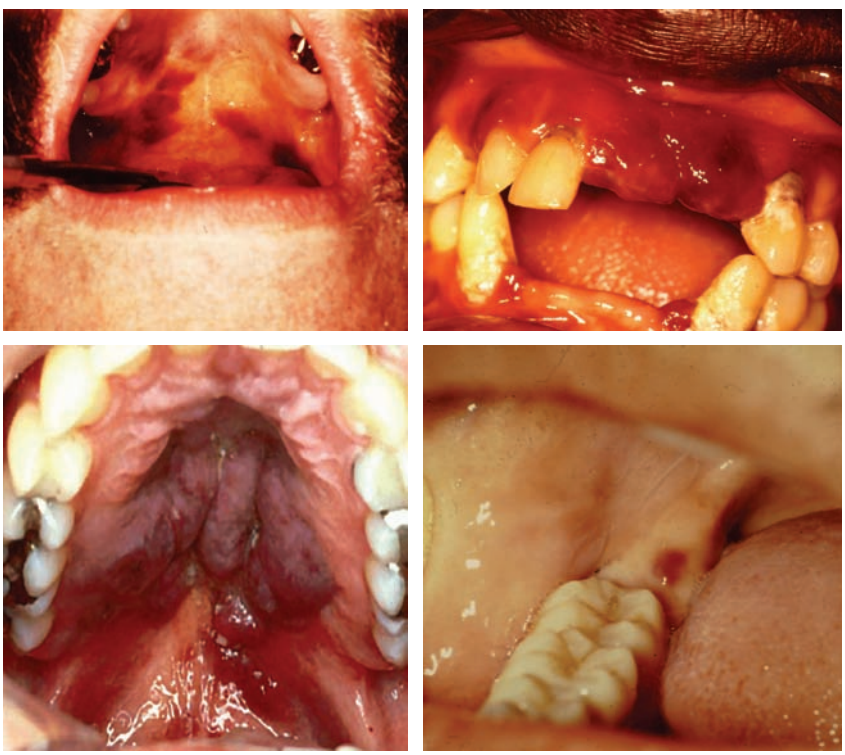

FIGURE 3-20
Red and purple macules and tumefactions in HIV-associated Kaposi's sarcoma.

virus (HIV)-infected males, predominantly homosexuals. The lesions are vascular, angiomatous neoplasms that begin as a red macule and progress to large tumefactive red and purple lesions. This neoplastic condition is an opportunistic infection caused by herpes virus type 8. Oral lesions may be multifocal and are typically seen on the palate and gingiva.

MICROSCOPIC FEATURES

Underlying surface epithelium is a spindle cell proliferation with many of the tumor cells found adjacent to sinusoidal spaces. The spindle cell nuclei show mild pleomorphism and cells lining vascular channels show a hobnail appearance. Hemosiderin pigment granules are found throughout the tumor.

DIFFERENTIAL DIAGNOSIS

Pyogenic granuloma, giant cell granuloma, and other angiomatous lesions are considered in the differential diagnosis.

TREATMENT

Lesions tend to resolve or are prevented when triple AIDS therapy is instituted. Unsightly lesions can be removed by injecting sclerosing agents, cauterization, or laser ablation.

Additional Reading

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Petechiae

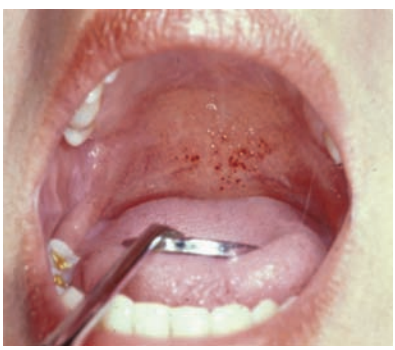
SUCTION PETECHIAE

Figure 3-21

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Petechiae are characterized by pinpoint-sized red spots 1 to 3 mm in diameter, are multifocal, and may show confluency. Suction petechiae are located either beneath a denture with a relief zone or on the soft palate in patients complaining of pruritus in that region. They may begin as a prodromal sign for sore throat, influenza, or the common cold. Onset of "itchiness" in the soft palate may induce the patient to suck or click the area for relief, with resultant microvascular rupture. Soft-palate petechiae are also the result of orogenital sexual activity.



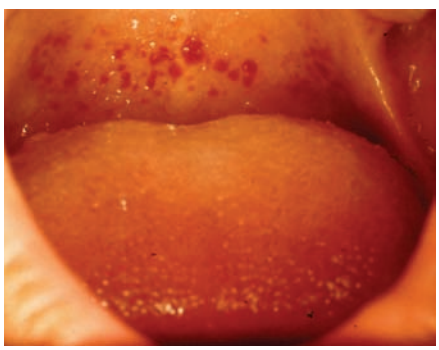


FIGURE 3-21
Petechial hemorrhages evolving as the result of negative pressure on the oral tissues.

MICROSCOPIC FEATURES

Damaged vascular walls of small vessels in the submucosa manifest a juxtaposed zone of erythrocyte extravasation.

DIFFERENTIAL DIAGNOSIS

Infectious mononucleosis may be present with palatal petechiae, yet other clinical and laboratory features provide data that eliminate consideration in the differential diagnosis. If the patient does not recall clicking his or her soft palate and if other mucocutaneous petechiae are observed, thrombocyte deficiencies or leukemia should be ruled out by instituting appropriate laboratory studies. Hereditary hemorrhagic telangiectasia shows other characteristics essential for the diagnosis. Scurvy may include petechiae as a component of vitamin C deficiency, but this disease is encountered with extreme rarity in this day and age.

TREATMENT

No treatment is necessary for nondenture-related suction petechiae. Those lesions related to a denture relief zone resolve after relining or rebasing the prosthesis.

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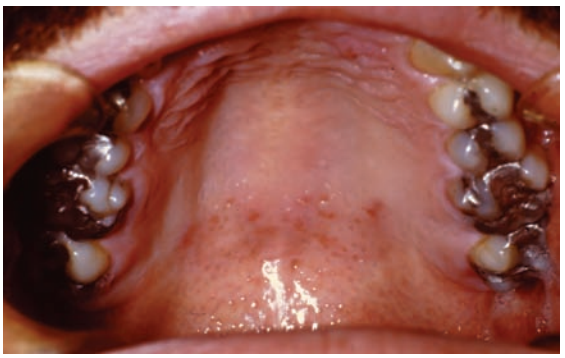

FIGURE 3-22
Soft-palate petechiae in infectious mononucleosis.

INFECTIOUS MONONUCLEOSIS

Figure 3-22

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Palatal petechiae are commonly seen in infectious mononucleosis, located on the soft palate. The petechiae are probably engendered by suction on a pruritic soft palate by the tongue as outlined for suction petechiae; however, other hemorrhagic manifestations such as epistaxis have been reported. A generalized stomatitis with erythema and ulceration may also be evident. Other clinical features implicating onset of infectious mononucleosis, a herpes virus infection (Epstein-Barr virus), include extreme malaise with lethargy, lymphadenopathy, hepatosplenomegaly, sore throat, and fever.

MICROSCOPIC FEATURES

Damaged vascular walls of small vessels in the submucosa manifest a juxtaposed zone of erythrocyte extravasation.

DIFFERENTIAL DIAGNOSIS

Palatal petechiae are seen in sore throat independent from infectious mononucleosis, in platelet disorders, and in hereditary hemorrhagic telangiectasia. The diagnosis of infectious mononucleosis may be confirmed when the heterophil antibody titer exceeds 1:28. The monospot screening serologic test, although not as accurate as the heterophil antibody titration, is rapidly performed and is usually adequate

diagnostically. The appearance of atypical lymphocytes (Downey cells) on the differential blood count is also a diagnostic finding.

TREATMENT

Treatment for infectious mononucleosis is supportive, with bed rest and high liquid intake. A mild analgesic and antipyretic are recommended.

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THROMBOCYTE DISORDERS

Figure 3-23

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Petechiae resulting from platelet deficiency or malfunction may be present on oral mucosa, yet lesions are encountered on skin surfaces as well. Various diseases may inhibit platelet formation. Myelophthisic anemia with thrombocytopenia can occur with leukemia, lymphoma, metastatic carcinoma to bone, and marble bone disease. Primary thrombocytopenic purpura, pancytopenia, and bone marrow depression from cytotoxic drugs result in lack of platelets. Malfunctioning platelets may be responsible for petechial hemorrhages in thrombocytopathic purpura, thrombasthenia, or secondary to overuse of salicylates. In addition to these bleeding disorders, a variety of nonthrombocytopenic purpuras exist, including anaphylactoid purpura, snake venom purpura, and certain infectious diseases. In all thrombocyte disorders, petechiae may be accompanied by gingival hemorrhage or prolonged bleeding after extraction.

MICROSCOPIC FEATURES

Damaged vascular walls of small vessels in the submucosa manifest a juxtaposed zone of erythrocyte extravasation.

DIFFERENTIAL DIAGNOSIS

Thrombocyte disorders may be differentiated clinically from other petechia-producing diseases in that the lesions are not confined to the palate yet may be ubiquitous with lesions on the skin of the extremities

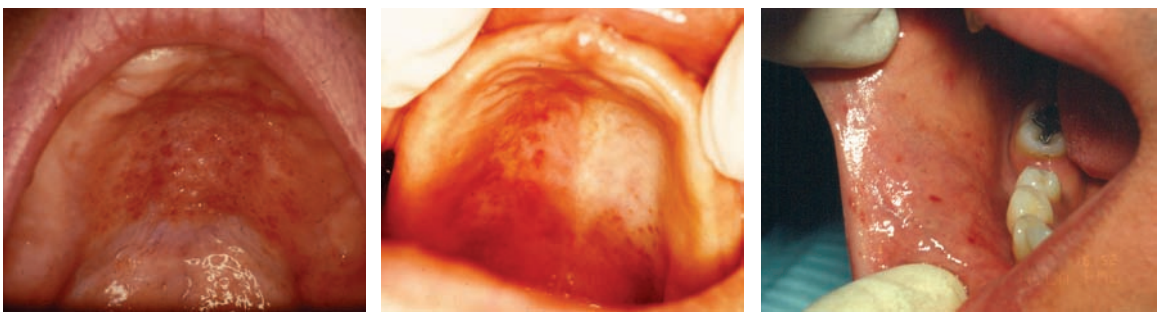

FIGURE 3-23
Petechial hemorrhages in leukemic patients with secondary thrombocytopenia.

and trunk. The tourniquet test is positive. A work-up for the underlying cause includes complete blood count and platelet count and other clinical and laboratory tests specific for the diseases enumerated under clinical features. A history of drug use is of utmost significance when considering causes of petechiae. Because evaluation of disease entities producing petechiae involves manifold considerations and complex relationships, the patient should be referred to a hematologist for definitive diagnosis and treatment.

TREATMENT

Management of platelet disorders is governed by the underlying cause. Definitive diagnosis and treatment should be determined by a physician.

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HEREDITARY HEMORRHAGIC TELANGIECTASIA

Figure 3-24

Age: Begins in infancy
Sex: No predilection

CLINICAL FEATURES

Hereditary hemorrhagic telangiectasia is inherited as a dominant trait and is characterized by the appearance of spider telangiectasias of skin, primarily on the face and neck with petechia-like lesions of the oral mucosa. Epistaxis is a prominent clinical sign. Bleeding from the gingiva is also a feature. Platelet and clotting factor functions are normal. Perivascular supportive tissue appears to be defective.

MICROSCOPIC FEATURES

Submucosal dilated vessels are present and evince leakage of the vascular contents with fibrin deposition in the perivascular region.

DIFFERENTIAL DIAGNOSIS

The resemblance to petechial disease is striking; however, close scrutiny of the skin lesions discloses the spider-like angiomas rather than true petechial macules, and a hereditary history will generally lead to a diagnosis of hereditary hemorrhagic telangiectasia. Bleeding and clotting times

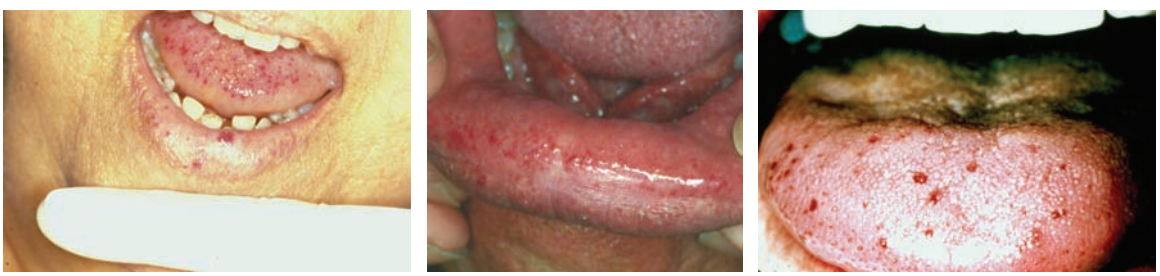

FIGURE 3-24
Red papules in hereditary hemorrhagic telangiectasia.

are normal. Platelets and clotting factors are within normal limits unless profuse hemorrhage has resulted in a blood-loss anemia with thrombocytopenia.

TREATMENT

Genetic counseling is recommended. A normal life span can be expected; however, death from epistaxis may occur. Hemorrhage can generally be controlled by placement of pressure packs.

Additional Reading

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Focal Pigmentations

AMALGAM AND GRAPHITE TATTOO

Figure 3-25

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Tattoos caused either by traumatic implantation of dental amalgam or by graphite from a lead pencil produce a gray to black pigment in the mucosa. The borders are generally somewhat diffuse, and the pigment does not blanch on pressure. Amalgam tattoos are usually located on the gingiva, alveolar ridge, or buccal mucosa, whereas graphite tattoos are more often seen on the palate where a pencil wound was self-inflicted. Large amalgam tattoos can be demonstrated radiographically. Amalgam tattoos are usually solitary but occasionally may be multiple.

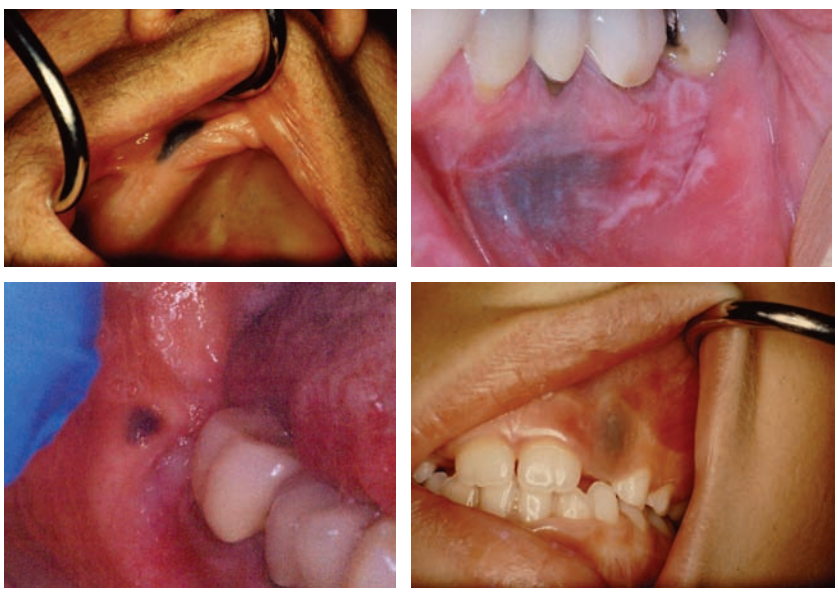

FIGURE 3-25
Dark areas representing amalgam tattoos.

MICROSCOPIC FEATURES

Brown or black foreign material is present yet fails to elicit a giant cell response. Stippling of collagen, reticulin, and perivascular connective tissues with particulate granules is a prominent feature, and inflammatory cells are present in limited number.

DIFFERENTIAL DIAGNOSIS

Amalgam tattoos must be differentiated from nevi and superficial melanoma. Pressure without blanching differentiates amalgam tattoos from vascular lesions.

TREATMENT

Failure to demonstrate radiopaque particles on radiographs for suspected amalgam tattoo necessitates biopsy to rule out nevus or melanoma. No treatment is necessary for those lesions that are radiographically demonstrable.

Additional Reading

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MUCOCELE

Figure 3-26

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Mucoceles may appear as focal reddish blue elevations if hemorrhage has occurred. As with the conventionally appearing fluid-filled mucous retention phenomena, hemorrhagic mucoceles follow trauma with rupture or severance of a minor salivary duct with pooling of mucus within the submucosa; they are most frequently encountered on the lips, buccal mucosa, and ventral tongue.

MICROSCOPIC FEATURES

The epithelium is distended by an underlying zone of pooled mucin encompassed by a granulation tissue pseudocystic membrane. Extravasated erythrocytes and fibrin are admixed with mucin and inflammatory cells.

DIFFERENTIAL DIAGNOSIS

Hemorrhagic mucoceles may be indistinguishable clinically from hemangioma,

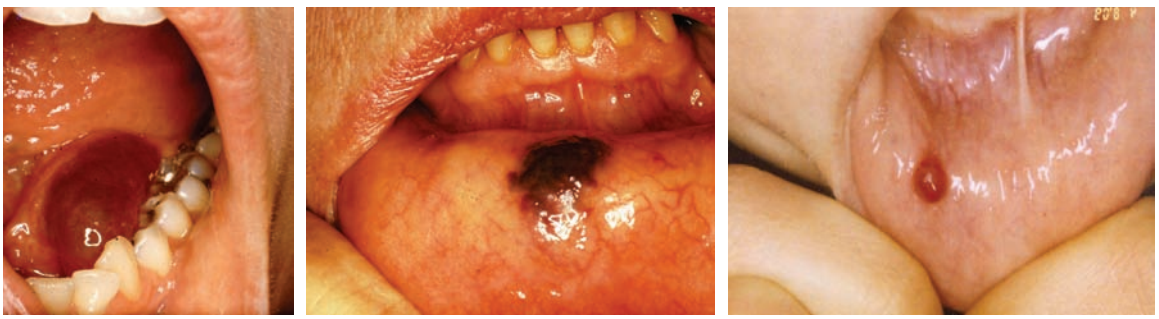

FIGURE 3-26
Mucocele containing extravasated blood and appearing as brown pigmented masses.

varix, hematoma, nevus, or even melanoma. A history of antecedent trauma can usually be elicited.

TREATMENT

Local excision with extirpation of the underlying minor salivary lobules is recommended. Failure to remove the glandular tissue may contribute to recurrence.

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HEMATOMA

Figure 3-27

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Mucosal hematomas or bruises result from vascular severance resulting from trauma. They are brown or blue and may be macular or swollen. Because the blood is not intraluminal but extravasated, hematomas do not blanch on pressure.

MICROSCOPIC FEATURES

The submucosa evinces profuse erythrocyte extravasation with fibrin deposition. Variable degrees of fibrovascular organization with inflammation are present.

DIFFERENTIAL DIAGNOSIS

Hematomas are the result of trauma yet may be confused clinically with hemorrhagic mucocele, tattoo, hemangioma or varix, nevus, and melanoma. Ecchymosis is identical, yet in blood dyscrasias, trauma is minor and the lesions are usually multifocal.

TREATMENT

A suspected hematoma should be observed over a 2-week period. Failure to resolve indicates the clinical impression was incorrect and biopsy should be performed. Any hematoma observed without significant provocation or trauma should arouse suspicion of associated with a blood dyscrasia.

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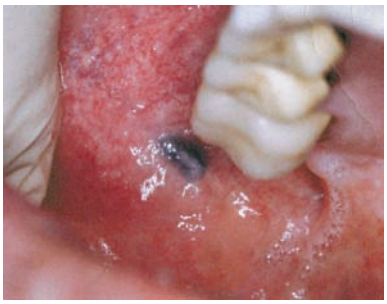

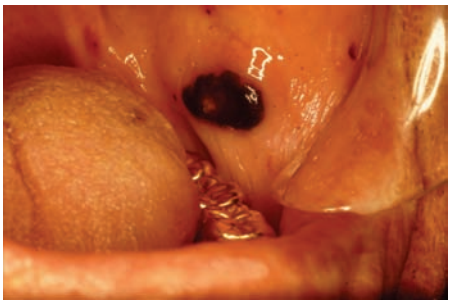

FIGURE 3-27
Hematoma of the buccal mucosa.

NEVUS

Figure 3-28

Age: No predilection
Sex: Female predilection

CLINICAL FEATURES

Oral nevi are rare and are characterized by a plaque- or dome-shaped sessile nodule with blue or black pigmentation. Occasionally, nonpigmented forms occur intraorally. They may be seen at any age, but are likely to have been present since childhood. Pigmented nevi do not blanch on pressure and are most frequently encountered on the palate, gingiva, buccal mucosa, and lips. They generally reach a given size, and the growth becomes static. Various types exist, including junctional, compound, intramucosal, blue nevus, and spindle cell nevus.

MICROSCOPIC FEATURES

The histology of nevi is variable. Nevocellular nevi are composed of oval epithelioid cells arranged in clumps or theques; junctional nevi maintain continuity with the epithelium, whereas intramucosal types are confined to the underlying connective tissue. Spindle cell nevi contain elongated spindle cells with a junctional (intraepithelial) component. Melanocytic or blue nevi are confined to the submucosa and are composed of fibroblast-like spindle cells with fasciculation. Melanin granules may be seen in all forms and may be sparse or pervasive.

DIFFERENTIAL DIAGNOSIS

Nevi do not blanch under pressure and may clinically be indistinguishable from a tattoo, hematoma, or superficial melanoma. An ephelis is flat, lacking any tumefaction yet is often indistinguishable clinically from junctional nevi and tattoos.

TREATMENT

Junctional nevi in adults may evolve into malignant melanoma. For this reason, all

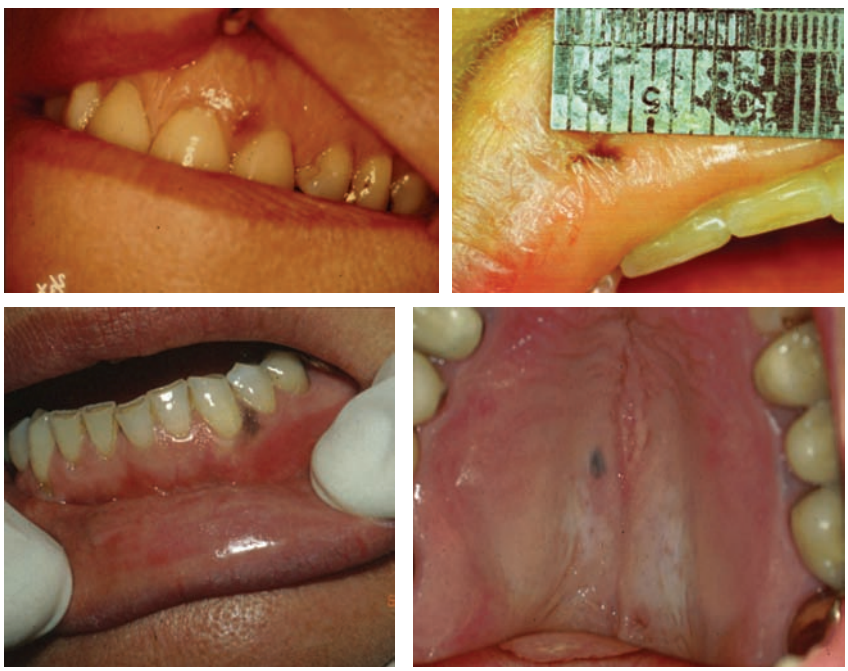

FIGURE 3-28
Pigmented nevi appear brown, black, or blue and may be papular or macular.

pigmented lesions in the mouth in which nevus is a consideration in the differential diagnosis should be excised and submitted for microscopic examination.

Additional Reading

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EPHELIS, ORAL MELANOTIC MACULE

Figure 3-29

Age: No predilection
Sex: Female predilection

CLINICAL FEATURES

Ephelis, or freckle, occurs on sun-exposed skin and is common on the face, yet unusual on the vermilion border. The lesion is brown or brownish black and macular; in most cases, it is less than one half of 1 cm. The melanotic macule occurs on oral mucosa and therefore is not related to actinic radiation. Oral melanotic macules are focal brown, blue, or black spots that are most frequently observed on the gingiva and buccal mucosa.

MICROSCOPIC FEATURES

Melanotic macules do not evolve from proliferation of melanocytes; rather, the

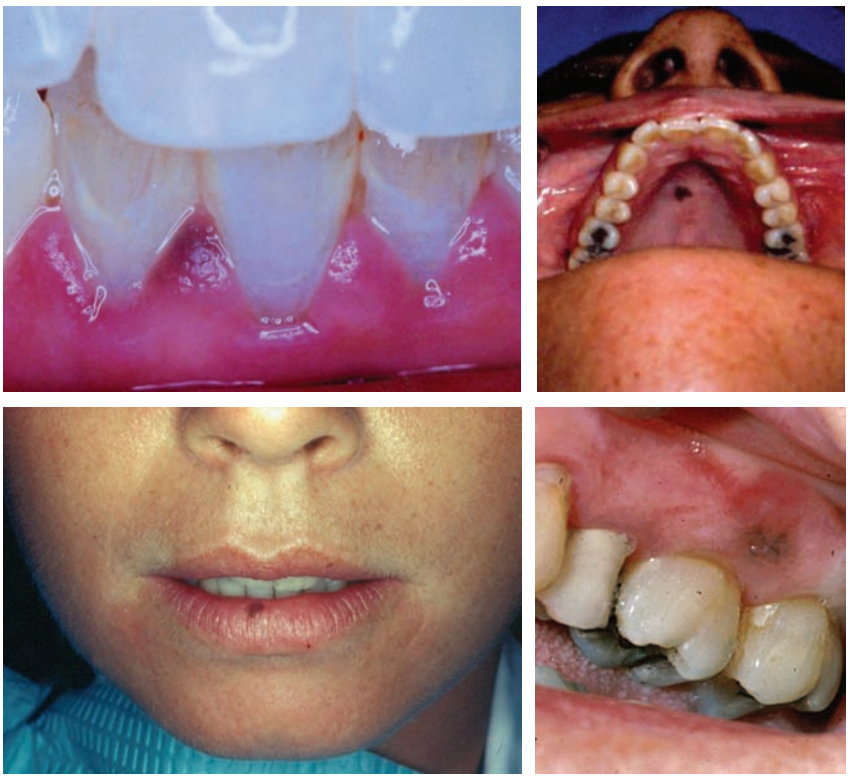

FIGURE 3-29
Oral melanotic macule.

epithelium is unremarkable, and the basal cells exhibit diffuse deposition of melanin pigment. Occasionally, melanin incontinence is observed with pigment granules identifiable in subepithelial melanophages.

DIFFERENTIAL DIAGNOSIS

The focal macular appearance of ephelis of the lip or melanotic macule of oral mucosa may be identical to amalgam tattoo, junctional nevus, or early superficial spreading melanoma. Pigmented lesions of this nature cannot be diagnosed without microscopic evaluation.

TREATMENT

Excision is the treatment of choice.

Additional Reading

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Diffuse and Multifocal Pigmentations

MALIGNANT MELANOMA

Figure 3-30

Age: Middle age and above
Sex: Male predilection

CLINICAL FEATURES

Oral melanomas exhibit a striking predilection for the palatal mucosa, chiefly anterior palate and maxillary alveolar ridge or gingiva. Most are pigmented, either bluish black or dark brown. They begin as macular focal lesions but may rapidly grow to fungating diffuse tumefactions. Ulceration

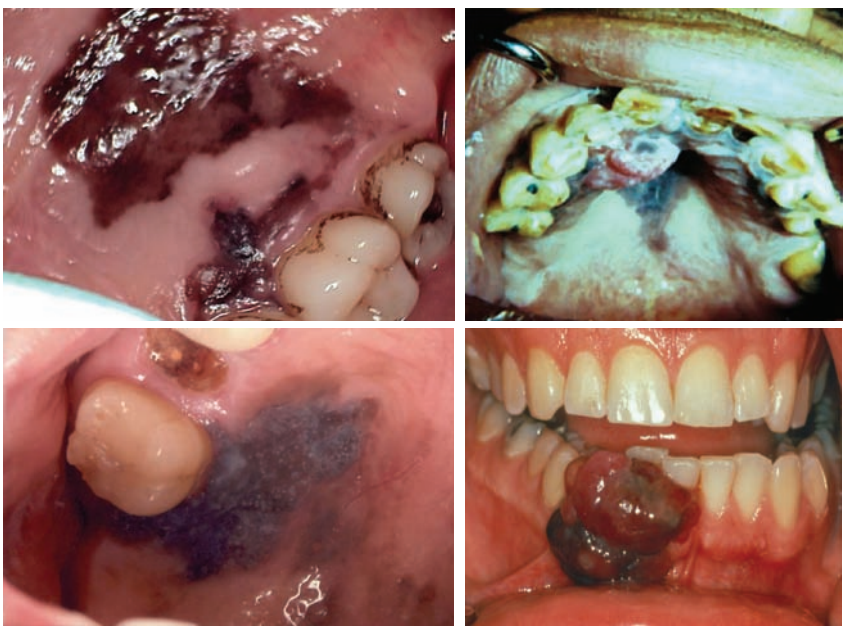

FIGURE 3-30
Malignant melanoma of the oral cavity, usually seen on the anterior maxillary or palatal mucosa. It begins as a brown-black or blue pigmentation with irregular borders and becomes progressively more diffuse.

is a common finding. As proliferation ensues, satellite lesions or streaking of pigment can be noted at the lateral margins. The tumor may or may not be indurated. Survival rates for oral and cutaneous melanomas are extremely low; less than 5% live for 5 years. Widespread dissemination to both nodes and distant sites is common. A superficial form known as malignant freckle of Hutchinson has a more favorable prognosis; although usually located on facial skin, oral cases have been reported. Malignant freckle is macular with minimal tumefaction. Nonpigmented varieties of melanoma occur and may be confused clinically with inflammatory and other neoplastic swellings. There is a genetic predilection for oral melanoma on certain islands in Japan.

MICROSCOPIC FEATURES

Three specific microscopic patterns are observed in melanoma. The Hutchinson's freckle variety is a slowly growing lesion usually seen on the malar skin characterized by proliferation of pleomorphic, palisaded melanocytes distributed along the epidermal/dermal junction with a horizontal or lateral direction of proliferation. These atypical cells fail to invade the upper epithelial layers. The second variety also proliferates along the epidermal/dermal junction and is termed the superficial spreading type. This type exhibits a pagetoid appearance with ovoid tumor cell nests showing a propensity for invasion of the upper epithelial layers. The third variety is invasive melanoma. This form may arise de novo or evolve from either of the aforementioned lesions. The invasive type is usually nodular and exhibits a vertical growth pattern that invades the underlying connective tissues. The cells are spindle, ovoid, or polygonal and are pleomorphic with variable amounts of melanin pigment. Invasive melanomas are graded depending on their depth of growth: lesions confined to the papillary dermis are "thin" melanomas whereas those with deep invasion are "thick" melanomas.

DIFFERENTIAL DIAGNOSIS

Early oral melanoma may be confused with other focal pigmentations. Because melanin does not blanch, differentiation from a vascular lesion can be made clinically. Because melanoma must be detected at its earliest stage to achieve cure, biopsies from all oral focal pigmentations are recommended.

TREATMENT

Radical surgery is indicated and should be performed by a cancer surgeon. Prophylactic neck dissection in the absence of clinically palpable nodes probably does not improve the prognosis.

Additional Reading

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RACIAL PIGMENTATION

Figure 3-31

Age: Present at birth
Sex: No predilection

CLINICAL FEATURES

The oral mucosa of blacks and many dark-skinned whites is often stippled with

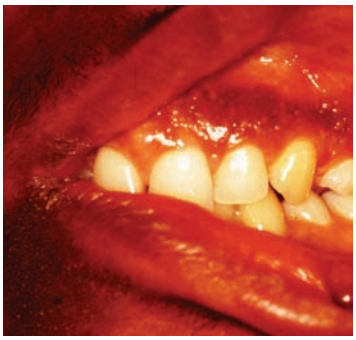
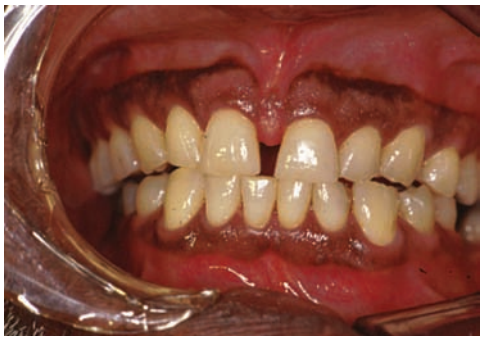

FIGURE 3-31
Racial melanosis can be seen anywhere in the mouth but is identified more commonly on the gingiva of blacks or dark-skinned whites.

multifocal and diffuse macular pigmentations, generally dark brown. These zones may occur anywhere in the mouth and are more often encountered on the gingiva. They are innocuous manifestations of racial or ethnic origin and have no premalignant potential.

MICROSCOPIC FEATURES

Melanin granules are densely accumulated in the basal cell layer.

DIFFERENTIAL DIAGNOSIS

When the patient's skin is heavily pigmented, oral pigmentation can be considered normal. In whites, other diseases must be considered, for example, Addison's disease, neurofibromatosis, or heavy metal ingestion.

TREATMENT

No treatment is necessary.

Additional Reading

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PIGMENTED LICHEN PLANUS

Figure 3-32

Age: Adults
Sex: Females more often affected

CLINICAL FEATURES

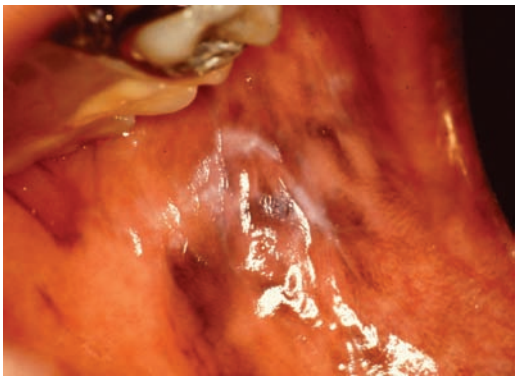
Whereas lichen planus is usually characterized by either white striated lesions or mixed red and white lesions in the erosive form, a pigmented variety is occasionally encountered. The pigmented zones are macular with a black, brown, or slate-gray appearance and are most prevalent on the buccal mucosa. Invariably, the pigmented mucosa is surrounded by a zone of white, and reticulated striae can be discerned.

MICROSCOPIC FEATURES

The surface keratin is thickened, and transmigration of lymphocytes into the basilar and parabasilar zones occurs. The basal cell layer contains melanin granules, and this layer is disrupted with melanin incontinence. The submucosa is occupied by a band-like lymphocytic infiltrate with interposed free melanin granules and melanophages.

DIFFERENTIAL DIAGNOSIS

The pigmented zones of this form of lichen planus may be confused with other diffuse pigmented lesions included here; however, one is usually able to detect the presence of



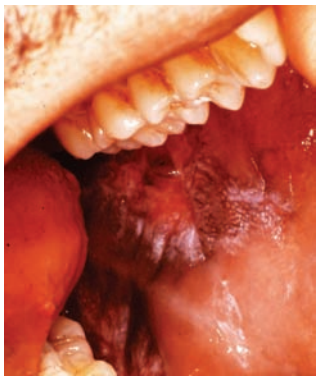
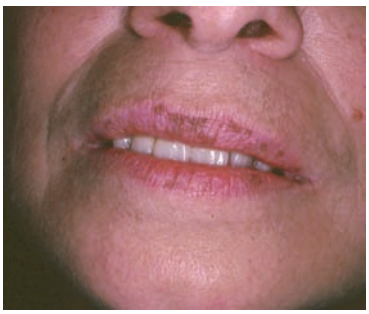
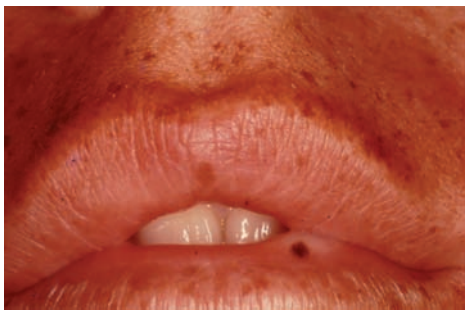
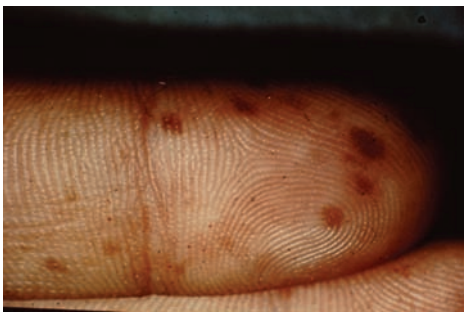


FIGURE 3-32
Gray melanin deposition associated with white stria in pigmented lichen planus.







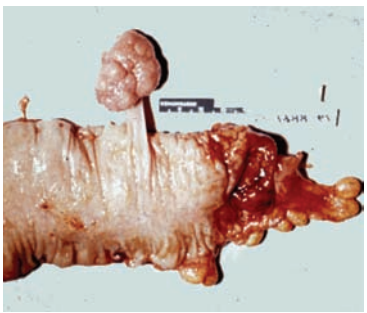


FIGURE 3-33
Peutz-Jeghers syndrome: melanotic macules of the lips, melanotic macules of the fingers, and benign intestinal polyps.

accompanying white striae. A biopsy will confirm the diagnosis.

TREATMENT

Provided an erosive component is lacking, no treatment is necessary.

Additional Reading

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PEUTZ-JEGHERS SYNDROME

Figure 3-33

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Peutz-Jeghers syndrome is inherited as an autosomal dominant trait and is characterized by multifocal macular melanin pigmentation in perioral locations. These macules or freckles stipple the vermilion and may extend into the facial skin as well as the oral mucosa. Intestinal polyposis with no tendency for malignant change

may contribute to colic pain in affected individuals. In addition to perioral lesions, the extremities may show dermal foci of pigmentation.

MICROSCOPIC FEATURES

The basal cell layer contains a profusion of melanin granules.

DIFFERENTIAL DIAGNOSIS

The perioral location is unique and diagnostic. Intestinal radiographic studies disclose the presence of polyps primarily in the small intestine.

TREATMENT

Provided an erosive component is lacking, no treatment is necessary. Patients can be advised of the genetic character of the disease. Referral to a gastroenterologist is recommended.

Additional Reading

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MULTIPLE NEUROFIBROMATOSIS

Figure 3-34

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

An inheritable disease characterized by multiple neurofibromatous nodules, von Recklinghausen's disease of skin also manifests pigmented macules of skin termed *café-au-lait spots.* The pigment is light brown and the macules vary considerably in size, displaying smooth demarcated borders. The neurofibromas exist in

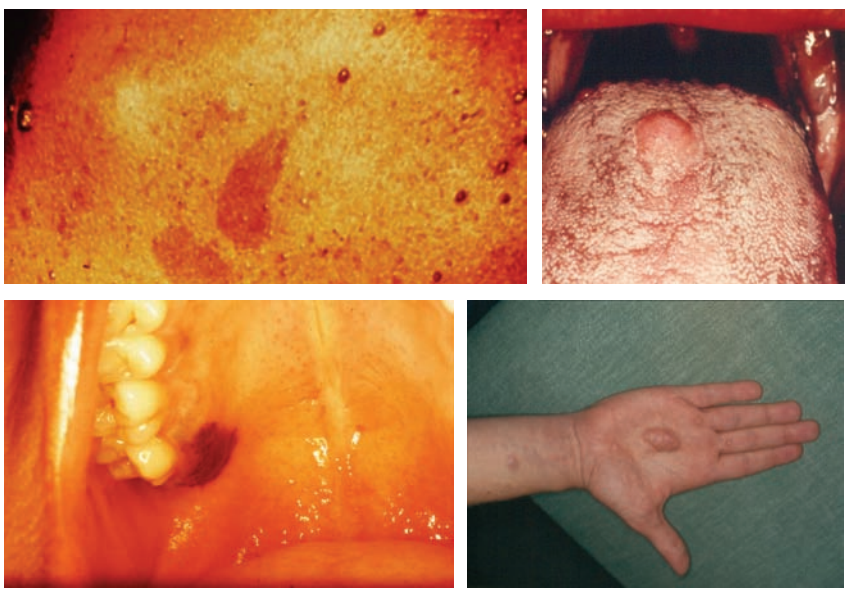

FIGURE 3-34
Café-au-lait pigmentations and tumor nodules in neurofibromatosis.

two forms: nodular, with a putty-like feel on palpation, or flabby pendulous folds. The neurofibromas and macular pigmentations may involve the oral mucous membranes as well as the skin. The *NF1* gene is mutated in this disease. Similar mucocutaneous pigmentation is seen in the McCune-Albright syndrome consisting of polyostotic fibrous dysplasia, endocrinopathy, and skin pigmentations.

MICROSCOPIC FEATURES

Café-au-lait pigmentation is represented by diffuse deposition of melanin granules within the basal cell layer.

DIFFERENTIAL DIAGNOSIS

Oral pigmentations of neurofibromatosis are similar to those of Peutz-Jeghers syndrome, racial pigmentation, and Addison's disease. The accompanying neurofibromatous tumefactions on skin differentiate von Recklinghausen's disease from the aforementioned entities.

TREATMENT

When function is compromised, the neurofibromas can be excised. The pigmented areas have no malignant potential; however, sarcomatous change in preexisting benign neurofibromas of von Recklinghausen's disease has been reported to occur in as many as 5% of the population with the disease.

Additional Reading

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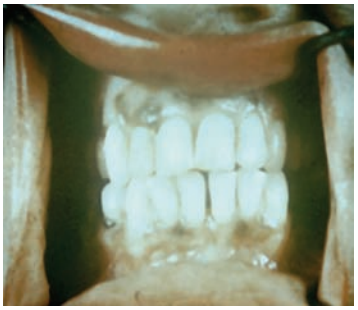
ADDISON'S DISEASE

Figure 3-35

Age: Middle-aged adults
Sex: Slight female predilection

CLINICAL FEATURES

Addison's disease is caused by adrenal cortical insufficiency of idiopathic origin or by cortical replacement as seen in granulomatous infection by tuberculosis or the deep mycoses. Decreased steroid levels stimulate pituitary corticotropin hormone (ACTH) output with increased levels of a melanocyte-stimulating factor. The skin becomes bronzed or shows brown pigmentation in



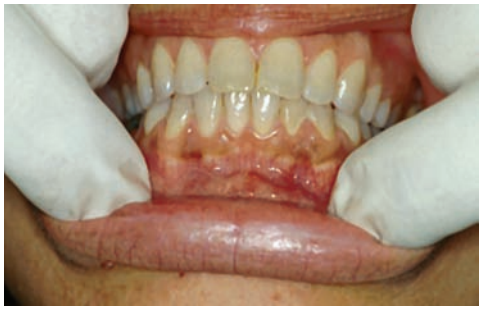


FIGURE 3-35
Progressive diffuse pigmentation of the mucosa in regions previously devoid of such change is suggestive of Addison's disease.

skin folds or over joints. Oral pigmentation is multifocal or diffuse and macular. Other symptoms of the disease include weakness, hypotension, and cold intolerance. Anorexia, vomiting, and diarrhea are also common symptoms. Cushing's syndrome associated with pituitary hyperfunction may also be associated with pigmentation on mucocutaneous surfaces.

MICROSCOPIC FEATURES

Pigmentation in Addison's disease is a manifestation of increased melanin production represented by diffuse melanin granule deposition in the basal cell layer.

DIFFERENTIAL DIAGNOSIS

Addisonian pigmentation in the mouth simulates that of racial pigmentation, Peutz-Jeghers disease, and von Recklinghausen's disease. The skin coloration particularly in pressure areas, lack of lesions seen in other diseases with oral pigmentations, history of recent onset with progressive deepening of the pigment, and the other clinical manifestations require work-up for adrenal cortical insufficiency.

TREATMENT

Addison's disease is managed by the physician. Any underlying cause must be treated, and maintenance levels of steroid therapy are required.

Additional Reading

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HEMOCHROMATOSIS

Figure 3-36

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

Characterized by excessive deposition of iron pigment within tissues, hemochromatosis represents a primary heritable disease with a pronounced male predilection or evolves as a secondary acquired defect accompanying cirrhosis, chronic anemia, porphyria, excessive dietary iron intake, or a postcaval shunt for portal hypertension. Classic clinical signs include hepatomegaly, diabetes, and bronze skin. Pigmentation of the palate and, less frequently, the gingiva is encountered. The pigmentation is slate-gray to brown with diffuse macular appearance. Oral and skin pigmentations are attributable to iron deposition

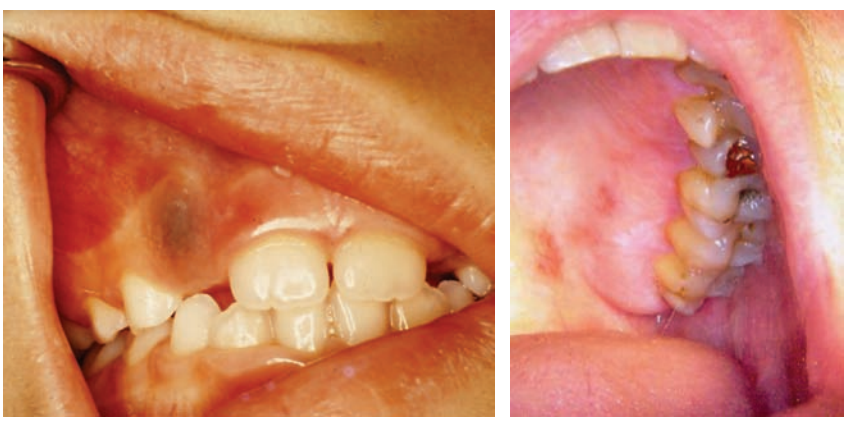

FIGURE 3-36
Blood pigment deposition in hemochromatosis.

as well as melanosis, probably secondary to adrenal cortical insufficiency related to pathologic deposition of iron in the adrenal cortex with subsequent elevations in melanogenic ACTH secretion. Involvement of the major and minor salivary glands has been reported, yet no symptoms or signs referable to glands are extant.

MICROSCOPIC FEATURES

A biopsy of oral mucosa may disclose basilar melanosis with deposition of brown granular hemosiderin or ferritin pigment within connective tissue and underlying salivary acini. A Prussian blue iron stain is especially useful for demonstrating the nature of the pigment. An inflammatory reaction is usually not present.

DIFFERENTIAL DIAGNOSIS

The macular diffuse slate-gray pigmentation observed in hemochromatosis may resemble early laterally spreading melanoma, diffuse tattoo, Addisonian pigmentation, and heavy metal ingestion. A history or documentation of cirrhosis with concomitant diabetes and bronzing of the skin should arouse suspicion of hemochromatosis. A biopsy with demonstration of diffuse iron deposition, in conjunction with the clinical findings and an elevated serum iron level allows for a definitive diagnosis.

TREATMENT

Hemochromatosis is a metabolic medical problem with many causes and should be managed by a physician.

Additional Reading

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HIV-ASSOCIATED ORAL PIGMENTATION

Figure 3-37

Age: Young adults
Sex: Male predilection

CLINICAL FEATURES

Progressive pigmentation of the skin and nails is seen among HIV-positive patients with opportunistic infections of the adrenal cortex culminating in Addison's disease. In addition, cutaneous pigmentation has been attributed to zidovudine therapy. Alternatively, oral pigmentation may occur in HIV-seropositive individuals who show no alterations in serum steroid or ACTH levels; furthermore, a drug-related etiology can be ruled out, because pigmentation of this type has been reported among individuals who are not taking any medications. The lesions are diffuse, grey or brown, and generally multifocal. The buccal mucosa, gingiva, palate, and tongue are the sites more often affected.

MICROSCOPIC FEATURES

Melanin granules are identifiable in the basal cell layer along with melanin incontinence. Melanophages are present in the immediate subjacent lamina propria. No melanocytic proliferation is evident.

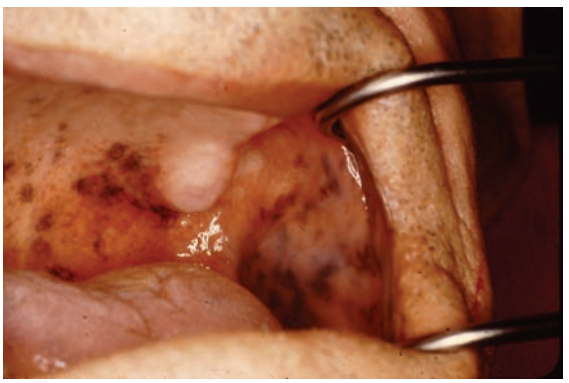

FIGURE 3-37
Diffuse gray pigmentation of the mucosa in an HIV-seropositive patient.

DIFFERENTIAL DIAGNOSIS

HIV-associated pigmentation may closely resemble the other forms of diffuse pigmentation enumerated in this chapter. The diagnosis can be confirmed only after a thorough work-up for AIDS and HIV infection has been undertaken. Among AIDS patients taking zidovudine, the pigmentation may be attributable to the medication.

TREATMENT

The lesions are asymptomatic and there is no specific treatment for the pigmentation in HIV-positive patients.

Additional Reading

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HEAVY METAL INGESTION

Figure 3-38

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Various heavy metals including lead, mercury, and bismuth may be ingested for medicinal reasons or as an occupational hazard. (Bismuth, lead, and mercury are the more common metals causing oral pigmentation.) The metal becomes deposited diffusely along the free gingival margin that scallops around the cervix of the teeth. The metallic line is gray. Occasionally, other mucosal sites show macular pigmentation. Systemic symptoms are often encountered, particularly in lead poisoning. These include abdominal pain, vomiting, anorexia, tremor, headaches, and mania.

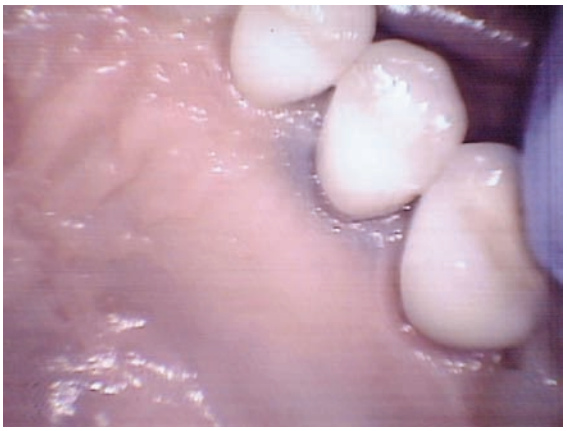

FIGURE 3-38
Heavy metal deposits in the marginal gingiva.

MICROSCOPIC FEATURES

Metallic crystals are located within the submucosal fibrous connective tissue immediately subjacent to the oral epithelium.

DIFFERENTIAL DIAGNOSIS

The limitation of pigment to the gingival margin is characteristic of heavy metal pigmentation. History of metal ingestion confirms the visual clinical impression.

TREATMENT

No treatment is necessary for the pigmented lesions. Once a metallic line has formed, the patient should be considered in a state of metal poisoning and exposure should be immediately terminated. Advanced periodontal disease may accompany mercury poisoning.

Additional Reading

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DRUG-INDUCED PIGMENTATION

Figure 3-39

Age: No predilection
Sex: Females

CLINICAL FEATURES

The antimalarial drugs are used for a variety of diseases owing to their anti-inflammatory actions. Many of these drugs are known to cause cutaneous, nail bed, and mucosal pigmentation. Quinoline, hydroxyquinoline, and amodiaquine have been used to manage autoimmune diseases, and oral pigmentation may occur in 10% of patients taking the drug on a long-term basis. The pigmentation is gray to blue and is usually located on the hard palate as a diffuse macule. The broad-spectrum antibiotic minocycline used in the treatment of acne vulgaris is also known to induce foci of pigmentation of the skin, bone, and thyroid. Oral involvement is most often encountered on the palate and facial gingiva. Birth control pills can be associated with brown pigmentation of the facial skin and perioral region (Malasma, Chloasma). Other drugs that may cause pigmentation are tranquilizers, phenolphthalein, and estrogens.

MICROSCOPIC FEATURES

Although not all instances of drug-induced oral pigmentations have been evaluated microscopically, some have, and the typical finding is basilar melanosis with melanin incontinence characterized by free melanin in the connective tissue and pigment within melanophages.

DIFFERENTIAL DIAGNOSIS

The diffuse distribution of pigment in drug-induced lesions is similar to that seen in Addison's disease and, in the palate, to early superficial spreading melanoma. The

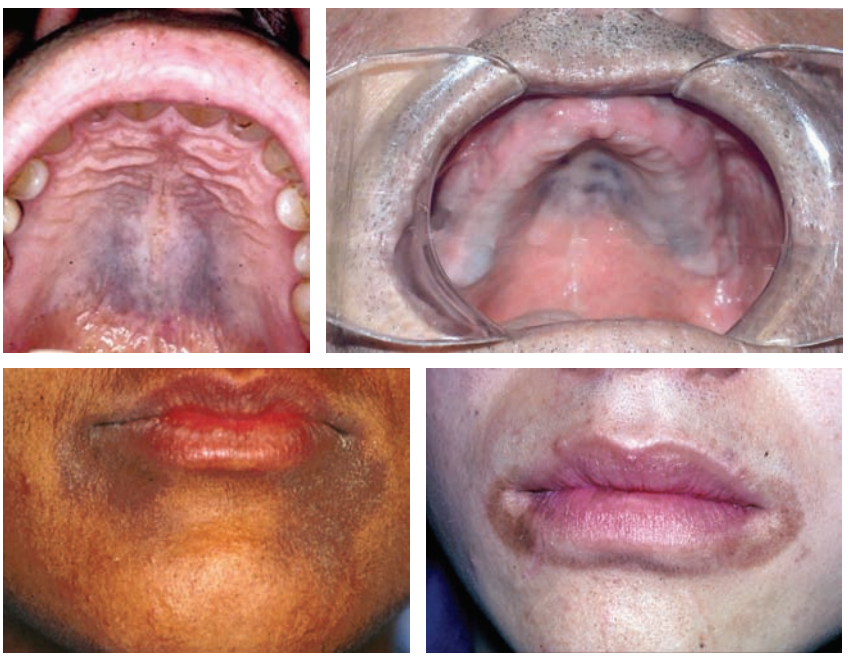

FIGURE 3-39
Minocycline pigmentations in the palate (top), Chloasma, the mask of pregnancy, may also be seen with patients taking birth control medication.

history is, of course, of prime importance, and biopsy is recommended.

TREATMENT

Withdrawal of the medication is recommended, although the pigmentation may persist for as long as 1 year after cessation of medication.

Additional Reading

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HAIRY TONGUE

Figure 3-40

Age: Middle-aged adults
Sex: More common in males

CLINICAL FEATURES

Diffuse brown or black pigment of the dorsal surface of the tongue accompanied by elongate hair-like projections of the filiform papillae is termed hairy tongue. The pigment is extensive and probably represents a combination of food products, tobacco stain, and chromogenic bacteria. A host of causative agents have been considered; however, the etiology remains obscure.

MICROSCOPIC FEATURES

The filiform papillae are elongated, with voluminous amounts of stratified parakeratin. Food and microbial debris are impacted between papillae.

DIFFERENTIAL DIAGNOSIS

Pigmentation localized to the dorsum of the tongue accompanied by elongated papillae is pathognomonic. Hairy tongue should not be confused with oral hairy leukoplakia, a white lesion of the lateral margin among HIV-seropositive individuals.

TREATMENT

Podophyllum resin has been used successfully, painted over the affected area as 1% solution. After application, the tongue is rinsed thoroughly and the rinse is expectorated, as ingested podophyllum can produce dangerous side effects. Three to five daily treatments are satisfactory. Many patients respond to brushing of the tongue with a hard-bristle toothbrush. This treatment

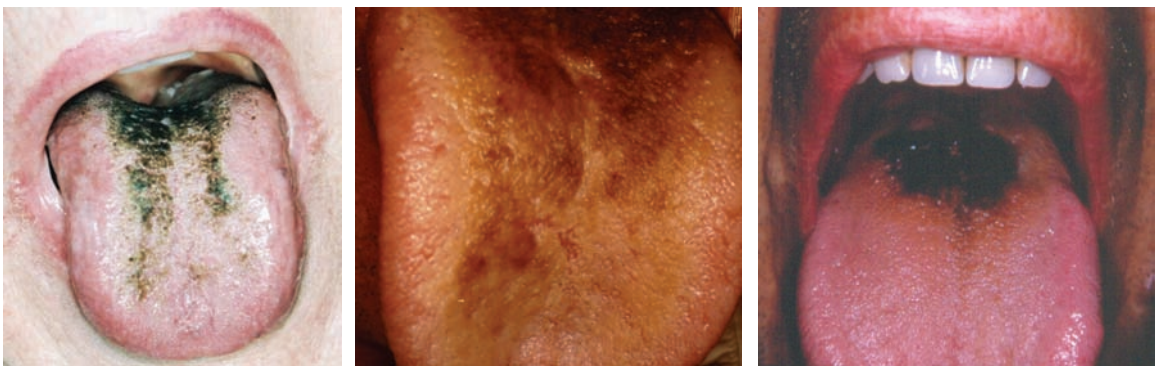

FIGURE 3-40
Hairy tongue characterized by elongation of the filiform papillae, which appear matted and pigmented, brown or black coloration being most common.

is preferable initially, with podophyllum reserved for cases that fail to resolve with mechanical abrasion.

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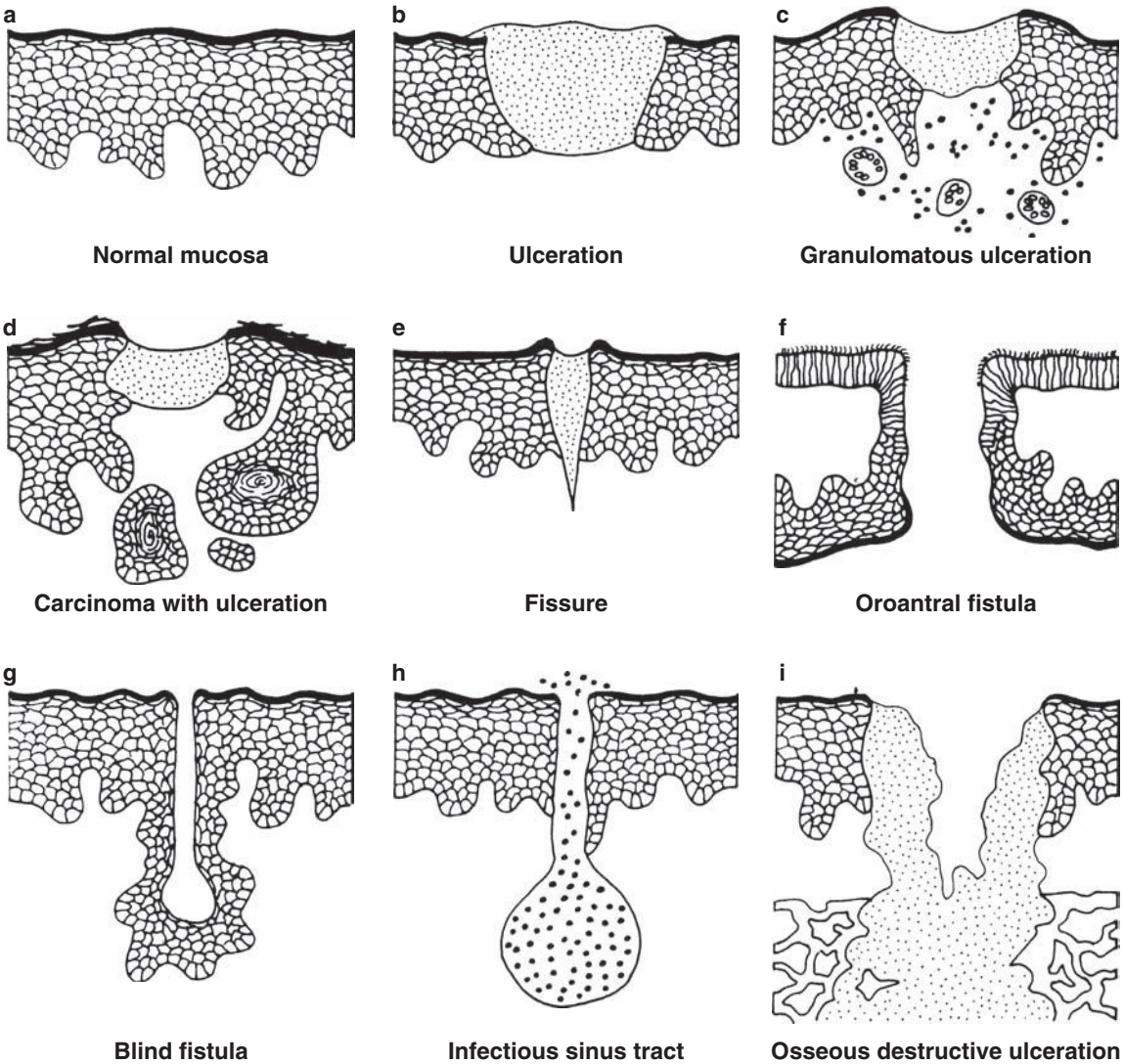

Ulcers, Fistulae, and Sinuses

Oral Ulcerations and Fistulae

4

Ulcerative lesions of the oral cavity are common. Assessment of the nature of oral ulcers requires a thorough history of the present illness. Certain ulcerations occur in multiples, and many are recurrent. Signs and symptoms relative to general health with review of organ systems will point to a diagnosis of certain systematic problems that can manifest oral ulceration. The nature of the ulcer itself is vitally important when a definitive diagnosis is pursued. One should always remember that oral vesiculobullous diseases are subject to trauma, with loss of the characteristic vesicular nature of the lesions clinically. For this reason, the patient should be questioned concerning the nature of the lesions at their outset, and attempts should be made to search for an intact vesicle. If the ulcerations prove to be, or to have been, vesiculobullous, refer to the next chapter for discussion of vesiculobullous diseases. In this section, only diseases that begin as ulcers are considered.

Draining tracts or fistulae are included in this chapter because, clinically, they may appear as areas of ulceration. By definition, a fistula represents an epithelial-lined tract connecting two body cavities, whereas a sinus is a drainage tract associated with an infection. Many clinicians do not make this distinction and refer to all tracts as fistulae. This is the context in which the term fistula is used here. Palpation of the underlying tissues usually elicits flow of purulent exudate from an area of tissue breakdown suspected to represent a fistula. Insertion of a probe or gutta-percha point will also aid in detecting a tract. The exudate may be subjected to culture and sensitivity tests to identify specific infectious agents.

The most common recurring oral ulcerations are aphthae, whereas the most frequently encountered nonrecurring multifocal ulcerative disease is acute necrotizing ulcerative gingivitis (ANUG). Potentially lethal diseases with multifocal ulcerations are agranulocytosis and uremia.

The traumatic ulcer from biting or denture irritation is the most common focal oral ulceration. Carcinoma, tuberculous, and mycotic ulcers are potentially lethal diseases.

Common perioral ulcerations include angular cheilitis and cancer, the latter being most serious.

Parulis of pulpal or periodontal origin is the most common form of oral fistula. All necrotic and osseous destructive lesions with drainage are serious disorders.

Recurrent and Multiple Ulcerations

APHTHOUS STOMATITIS

Figure 4-1

Age: Teenagers and young adults
Sex: No predilection

CLINICAL FEATURES

Aphthous ulcers may occur singly or in crops. The lesions are shallow and flat with a central white fibrinous pseudomembrane surrounded by an erythematous halo. Commonly known as canker sores, these lesions are prone to appear during times of stress; frequency of recurrence and multiplicity are extremely varied. They are quite painful, remain for 10 to 14 days, and then spontaneously regress. They occur most often on the oral soft tissues that are not bound to bone, yet occasionally the gingiva is involved. Aphthae can be small, punctate, and present in great numbers; lesions of this nature have been referred to as herpetiform ulcers, despite the fact that they are not caused by herpesvirus. Aphthous ulcers are occasionally a concomitant of chronic inflammatory bowel disease, including both ulcerative colitis and regional enteritis. L-form streptococci have been isolated from the lesions, and cell-mediated immune responses to oral epithelium have been demonstrated, whereas others have found evidence for an immunoregulatory

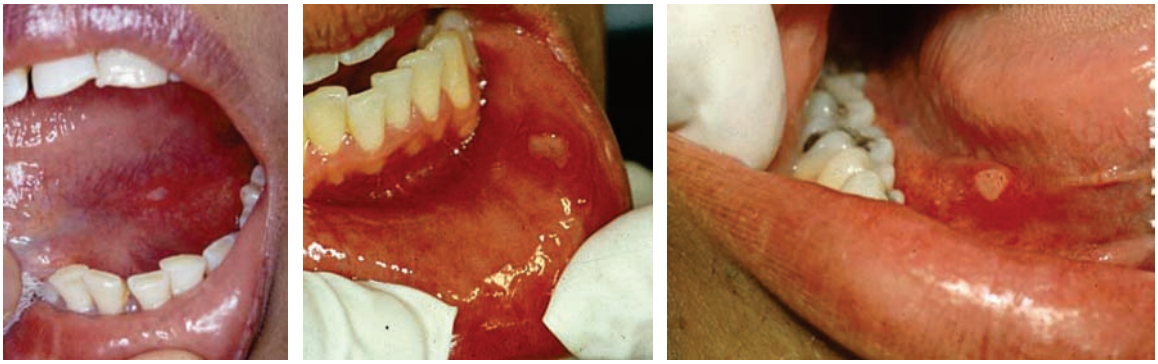

FIGURE 4-1
Aphthous ulcers of the oral mucosa—oval, shallow, and displaying an erythematous halo.

defect among T lymphocytes. Although a specific etiology has not been definitively identified, food allergens may be responsible in some instances.

MICROSCOPIC FEATURES

The epithelium is ulcerated, with an eosinophilic fibrinous coagulum on the surface. The connective tissue is infiltrated with mononuclear cells, chiefly lymphocytes, and the reaction is superficial.

DIFFERENTIAL DIAGNOSIS

Recurrent aphthous stomatitis must be differentiated from cyclic neutropenia by obtaining periodic blood counts when the recurrence of lesions is periodic and regular. Behçet's syndrome should be investigated because oral lesions in that disease are indistinguishable from aphthae.

Viral infection can be ruled out if no history of vesicle formation can be obtained. With the exception of palatal secondary herpesvirus infection, herpes of the oral soft tissues does not occur on a recurrent basis as do aphthae. Also, herpesvirus-induced lesions tend to cluster in geographic groups; aphthae show no such tendency, being randomly distributed.

TREATMENT

Single lesions or instances in which only a few ulcers appear can be treated by applying a wet applicator impregnated with silver nitrate for a few seconds, cauterizing the central core of the ulcer. Tetracycline oral suspension may invoke early involution. Selective elimination of suspected foods can be attempted.

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MAJOR SCARRING APHTHOUS STOMATITIS

Figure 4-2

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Major aphthae, also known as periadenitis mucosae necrotica recurrens or Sutton's

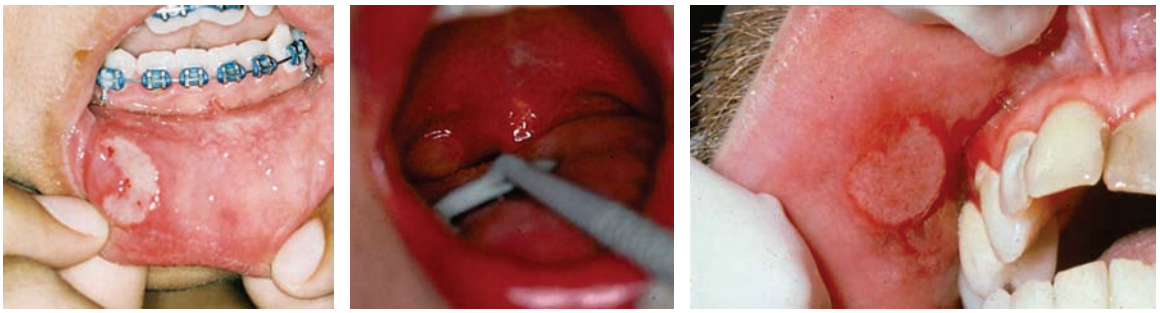

FIGURE 4-2
Major aphthous ulcers—extensive, often showing irregular margins, and with inflamed surrounding mucosa. They leave depressed scars after healing.

disease, are similar in appearance to minor aphthae. The ulcers, however, are more deep-seated, exceed 0.5 cm (indeed, they may be 1-2 centimeters in diameter), and like minor aphthae, soft tissues not bound to bone are predisposed to them. The faucial pillars and oropharynx are often the initial sites of ulceration. After resolution, which may require 1 to 4 weeks, healing with scar formation is seen. Remissions are short, with a new crop of ulcers appearing shortly after the older lesions resolve. Most patients are tense and anxious, and the lesions are extremely painful. The cause is unknown, but mounting evidence points to an immune defect. Both immunoglobulin and cell-mediated responses to oral epithelium have been demonstrated.

MICROSCOPIC FEATURES

The epithelium is ulcerated with an eosinophilic fibrin surface. A mononuclear inflammatory cell infiltrate composed predominantly of lymphocytes extends deeply into the submucosa.

DIFFERENTIAL DIAGNOSIS

Major aphthae are differentiated from minor aphthous stomatitis on the basis of size and tendency to heal with scarring. Cyclic neutropenia and agranulocytosis may be ruled out by obtaining a leukocyte and differential count.

TREATMENT

Initial attempts to control the severity and distress of major aphthae include the use of gauze compresses soaked in tetracycline oral suspension and applied three times daily. A palliative mouth rinse such as an antihistamine oral suspension mixed with equal parts of Kaopectate often minimizes pain. If tetracycline is ineffective, prednisone (40 mg daily in divided doses for 10 days) usually induces regression of ulcerations. These treatment regimens must be repeated when new lesions periodically appear.

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BEHÇET'S SYNDROME

Figure 4-3

Age: Young and middle-aged adults
Sex: Significant male predilection

CLINICAL FEATURES

One of the muco-oculocutaneous syndromes, Behçet's disease represents an immunopathic disorder characterized by oral aphthous ulcerations, uveoconjunctivitis, and genital ulceration. The disease is more often encountered in the Middle East, most patients being HLA-B51 and HLA-DRw52 antigen positive. L-form bacteria have been implicated in its pathogenesis; yet recent studies have detected circulating immune complexes with herpesvirus specificity. Not all components of the syndrome triad are present at any given time. The oral ulcerations are small with a white pseudomembrane and erythematous halo, indistinguishable from ordinary aphthae. The eye lesions consist of recurrent conjunctivitis, ulceration, uveitis, and hypopyon, with visual damage being a common sequela. In males, the genital lesions are located on the penis and scrotum; in females, the vulva is frequently affected. Gastrointestinal complaints such as diarrhea and pain are frequently encountered, as are joint pain and discomfort. Cutaneous macular, papular, and plaque lesions are also encountered in some patients.

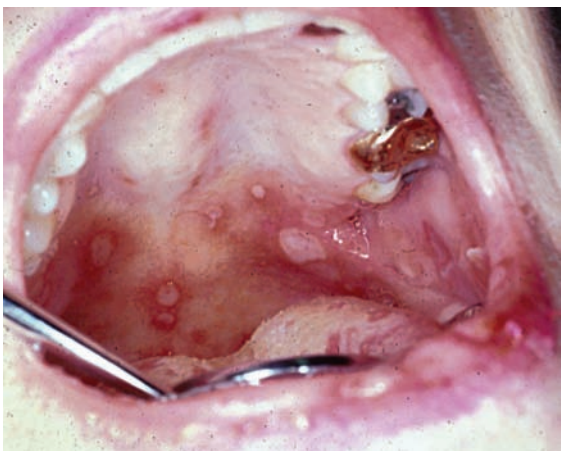

FIGURE 4-3
Oral ulcerations in Behçet's syndrome, resembling aphthae.

MICROSCOPIC FEATURES

The epithelium shows ulceration, being replaced by an eosinophilic coagulum. The connective tissue is infiltrated with mononuclear cells, chiefly lymphocytes.

DIFFERENTIAL DIAGNOSIS

The extraoral signs are sufficient to differentiate Behçet's syndrome from simple aphthae. When the dominant features are arthritis, dermatitis of the palms and soles, conjunctivitis, and genital ulceration, the disease is more correctly termed Reiter's syndrome. Both Behçet's and Reiter's syndromes are probably variants of the same immunopathologic process.

TREATMENT

Systemic steroids are required for control. Because of the multiplicity of defects, these patients should be managed by a general physician or dermatologist.

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GLUTEN ENTEROPATHY

Figure 4-4

Age: Young adults, adolescents
Sex: No predilection

CLINICAL FEATURES

Gluten enteropathy is one of the intestinal malabsorption syndromes whereby lipids are not readily absorbed to transport molecules resulting, therefore, in steatorrhea. Malabsorption of the fat-soluble vitamins may occur with mild symptoms of hypovitaminosis A, D, and K, the latter of which may predispose such patients to a hemorrhagic diathesis. Some patients complain of mouth sores and, clinically, the lesions resemble those encountered in recurrent aphthous ulcerations. These patients have circulating antigliadin antibodies. The recurring ulcerations subside once the patient follows a gluten-free diet.

MICROSCOPIC FEATURES

The histologic changes are essentially identical to those of aphthous stomatitis.

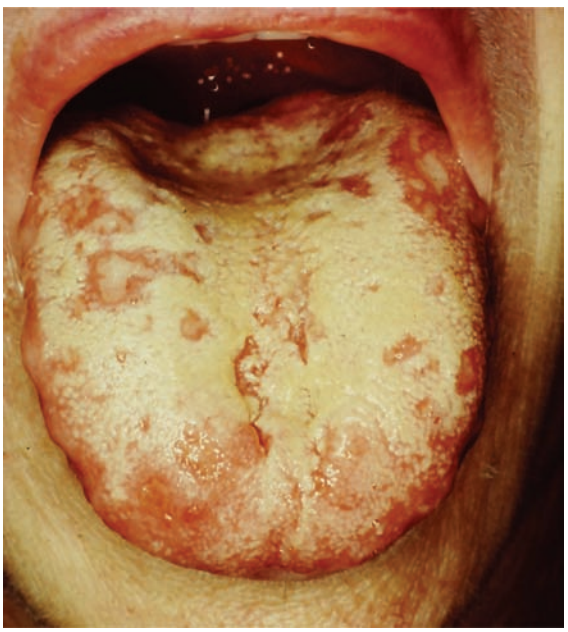

FIGURE 4-4
Aphthous-like lesions in a patient with gluten sensitivity.

DIFFERENTIAL DIAGNOSIS

Because the lesions are essentially identical to those of recurrent aphthae, a consideration of celiac disease should be explored in those patients with pale buoyant stools and episodic upset bowel symptoms.

TREATMENT

A gliadin-free diet should be instituted.

Additional Reading

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AGRANULOCYTOSIS AND IMMUNOSUPPRESSION

Figure 4-5

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

A deficiency in circulating blood granulocytes may represent a primary idiopathic disorder or may be secondary to bone marrow suppression by certain drugs that are cytotoxic for hematopoietic tissue. Cancer patients receiving antitumor chemotherapy are most often affected: however, organ transplantation recipients receiving immunosuppressive medications may also develop oral ulcerations. Because the granulocytic series are vital to defense against infection, patients with agranulocytosis are extremely prone to develop infections, pulmonary bacterial infections in particular. Death from uncontrollable infection is

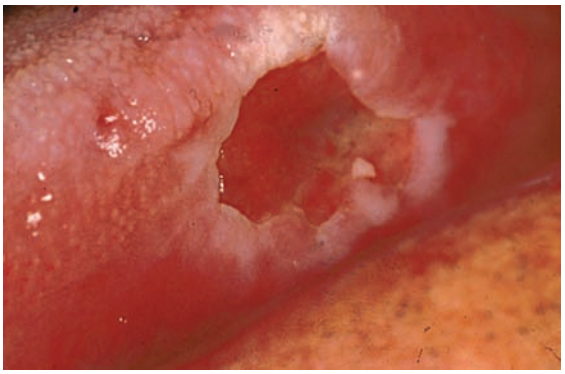

FIGURE 4-5
Agranulocytic ulcers, flat with a necrotic center.

common. The leukocyte count is usually under 2500/mm^3, and the differential count shows severely depressed numbers of neutrophilic granulocytes. The oral ulcers are oval and variable in size. In addition, gingivitis or periodontitis is a frequent finding with ulcerations located on the attached gingivae. Pain is a feature of these lesions.

MICROSCOPIC FEATURES

The microscopic changes are pathognomonic. The epithelium is lacking, and there is an eosinophilic fibrin surface. Underlying the pseudomembrane and imperceptibly merging with it is a zone of amorphous necrotic tissue, which is strikingly devoid of neutrophils. Indeed, other inflammatory cells, including round cells, are present in only limited numbers, probably because the lesions are detected and taken for biopsy early in their course.

DIFFERENTIAL DIAGNOSIS

Agranulocytic ulcers may appear identical to aphthae, major aphthae, and cyclic neutropenia. Differentiation from these entities requires biopsy and a complete blood count when the patient reports no history of cytotoxic drug intake.

TREATMENT

Oral ulceration in agranulocytosis is an ominous sign denoting severe depression of cellular defense mechanisms. If drug induced, it is a sign of dangerous toxicity levels and the dose of medication should be decreased immediately; otherwise, the patient is open to rapidly progressive infection. If no cause can be determined, the disease is of the idiopathic primary type, and referral to a hematologist is essential.

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CYCLIC NEUTROPENIA

Figure 4-6

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Oral ulcerations that are multifocal, are located primarily on movable mucosa, appear every 20 to 25 days, persist for 5 to 8 days, and reappear on a periodic basis probably represent oral manifestations of cyclic neutropenia. The ulcers are shallow, may show an erythematous halo, and vary in size. Coexistent severe premature periodontal lesions are common. The gingival papillae are erythematous and edematous, and may be ulcerated. Vertical alveolar bone loss with pocket formation is encountered in many regions throughout both dental arches. Otitis media, joint pain, and headache are often present during the neutropenic phase. The leukocyte count is depressed, as are the

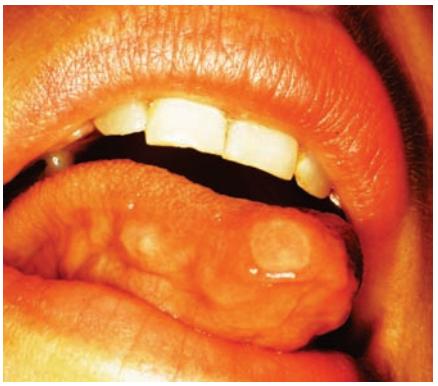
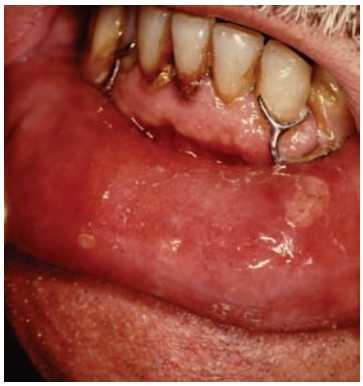

FIGURE 4-6
Cyclic neutropenia, characterized by premature periodontitis and focal ulcerations that appear every 20 or 25 days.

neutrophilic granulocytes during the period of ulceration. Throughout the course of the 20-day remission, the hemogram is within normal limits. During the agranulocytic phase, susceptibility to infection is a complication. The cause of this mysterious paroxysmal hematologic disorder is unknown but is related to a maturation arrest in the bone marrow with mutations in *ELA2*, gene that encodes neutrophil granule protease, neutrophil elastase.

MICROSCOPIC FEATURES

The ulcers are typically agranulocytic. The epithelium is lacking, and there is an eosinophilic necrotic zone. The submucosa is characterized by a paucity of inflammatory cells in general and a complete lack of neutrophils.

DIFFERENTIAL DIAGNOSIS

The ulcers of cyclic neutropenia are indistinguishable from aphthae, major aphthae, agranulocytosis, and Behçet's syndrome. The consistent cyclic nature of the lesions is highly suggestive of cyclic neutropenia; however, recurrent aphthae often show this pattern in the absence of an altered hemogram. The presence of premature periodontal lesions is another factor in favor of a diagnosis of cyclic neutropenia. The diagnosis can be established by obtaining leukocyte and differential blood counts every 3 days during periods of affliction and regression.

TREATMENT

Patients with cyclic neutropenia require management by a hematologist. Although the periodontal prognosis is poor, periodontal therapy is required for its own sake as well as to eliminate a focus of infection.

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UREMIC STOMATITIS

Figure 4-7

Age: Young and middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Patients suffering end-stage renal disease with elevated creatinine or blood urea nitrogen and electrolyte derangements

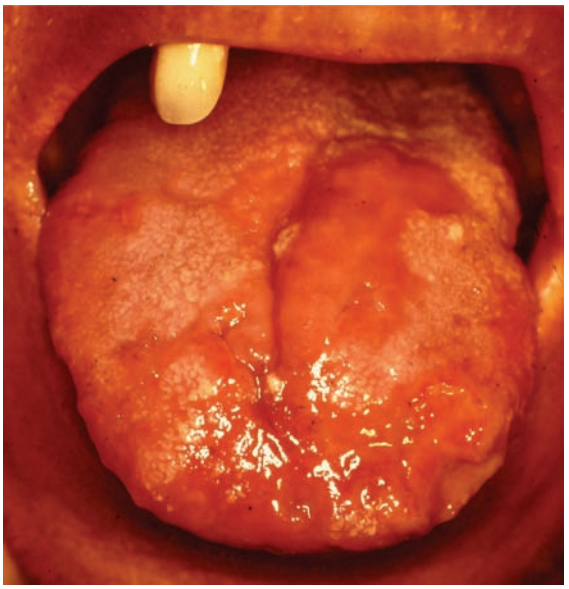

FIGURE 4-7
Diffuse stomatitis with zones of ulceration manifested in renal failure.

occasionally develop oral ulcerations. Uremic oral ulcers vary in size, are irregular in shape, and are usually shallow. They connote a poor prognosis, with death being imminent unless renal dialysis or kidney transplant is performed. The cause for ulceration is unknown, yet one suggestion is that it is the consequence of strongly alkaline saliva, a result of ammonia formation from retained urea secreted in the saliva. In other patients, the use of orally administered alkaline solutions used to alleviate metabolic acidosis may cause ulceration.

MICROSCOPIC FEATURES

The epithelium is lacking, having been replaced by an eosinophilic coagulum with a subjacent inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Patients with uremic ulcers manifest the clinical signs of the uremic syndrome: an ammonia odor on the breath, weight loss, anemia, cardiac arrhythmias, and, in many instances, secondary hyperparathyroidism. The oral ulcers are chronic rather than recurrent and may clinically simulate agranulocytic ulcers. Similar appearing ulcers may be encountered among renal transplant recipients (as well as other organ transplantations); these lesions are generally attributable to immunosuppressive drug therapy.

TREATMENT

Uremia may be secondary to pyelonephritis, glomerulonephritis, diabetic glomerulosclerosis, or lupus erythematosus. Management lies with a physician.

The oral ulcers, if painful, may be treated by prescribing a palliative oral rinse such as an antihistaminic oral suspension 50:50 with Kaopectate.

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VIRAL VESICULAR STOMATITIS

Figure 4-8

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Viral infections that manifest oral ulcerations do so secondarily, in that the early lesion is vesicular and, under masticatory trauma, the vesicles rupture and yield areas of ulceration. Herpes virus, varicella-zoster virus, and coxsackie viruses are the common infectious agents. The specific features encountered in oral viral infections are enumerated in the section on vesiculobullous

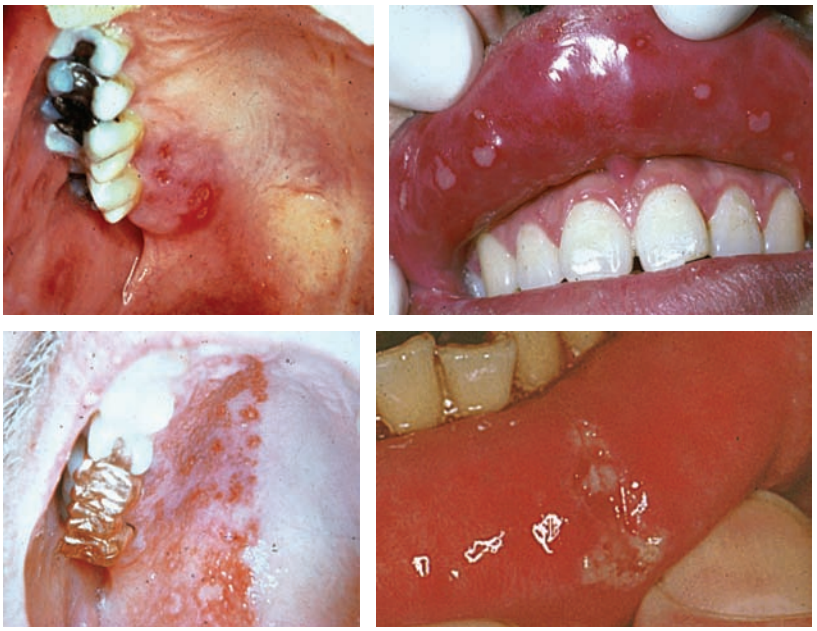

FIGURE 4-8
Viral stomatitides. Vesicles form and rupture within 24 hours, yielding shallow ulcers as seen in these examples recurrent intraoral herpes, primary herpetic gingivostomatitis, shingles, and cytomegalovirus.

and desquamative lesions. In general terms, oral ulcers that develop from viral infection are shallow, small, multifocal, and painful. A constant finding is elevation in temperature during primary infection.

MICROSCOPIC FEATURES

The classic cytologic changes unique to oral vesicular eruptions are usually not apparent after the vesicles rupture to leave ulcers. The ulcerated zones may show ballooning degeneration of spinous cells in the marginal epithelium. Usually only an area of ulceration with a subacute inflammatory cell infiltrate is seen, with evidence of regenerating epithelium on the surface.

DIFFERENTIAL DIAGNOSIS

Viral ulcerations are most frequently confused with aphthous stomatitis. If the oral ulcers are recurrent, then viral ulceration can be eliminated as a possibility; the viruses causing oral infection do so only as a primary disease and do not manifest intraoral recurrent infections.

Exceptions to this maxim are recurrent herpes labialis, which is not intraoral, and recurrent palatal herpes, which is unilaterally localized to the palatal gingiva as microvesicles that ulcerate, leaving tiny pinpoint ulcerative foci.

TREATMENT

Acyclovir analogues may result in early resolution of herpetic lesions. Soft diet, liquids, analgesic/antipyretic drugs, and a soothing oral rinse consisting of an antihistaminic oral suspension with equal parts of Kaopectate are recommended.

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ACUTE NECROTIZING ULCERATIVE GINGIVITIS

Figure 4-9

Age: Teenagers and young adults
Sex: Male predilection

CLINICAL FEATURES

ANUG, Vincent's disease, manifests multifocal pseudomembranous ulcerations localized primarily to the gingival interdental papillae. The papillae are blunted, with necrotic craters showing a marginal zone of erythema. Pain is a chief complaint, and halitosis is a constant feature. Uncommonly, ulcerations extend beyond the gingiva to include the palate and mucobuccal fold, where they may be extensive. The infectious microorganisms associated with ANUG are anaerobic fusiform and spirochetal bacteria that are saprophytic members of normal oral flora. They proliferate and may be considered pathogenic when the patient is under undue stress. In this context, it is not surprising that the disease often occurs among college students during final examination periods. It is also encountered in malnutrition.

MICROSCOPIC FEATURES

Smears and dark-field scrapings disclose the presence of fusiform and mobile spirochete bacterial forms. Tissue sections show nonspecific ulceration with superficial necrosis and a subacute inflammatory cell infiltrate. Bacterial colonies populate the necrotic surface.

DIFFERENTIAL DIAGNOSIS

Localization to gingival papillae and presence of a foul odor are essentially diagnostic. These features differentiate this disease from the other ulcerative disorders outlined in this section.

TREATMENT

In severe cases, systemic antibiotics (e.g., penicillin 250 mg 4 times daily for 1 week) are recommended. Less severe forms can be managed by 3% hydrogen peroxide rinses. Two to 3 days after therapy is instituted, dental prophylaxis should be performed.

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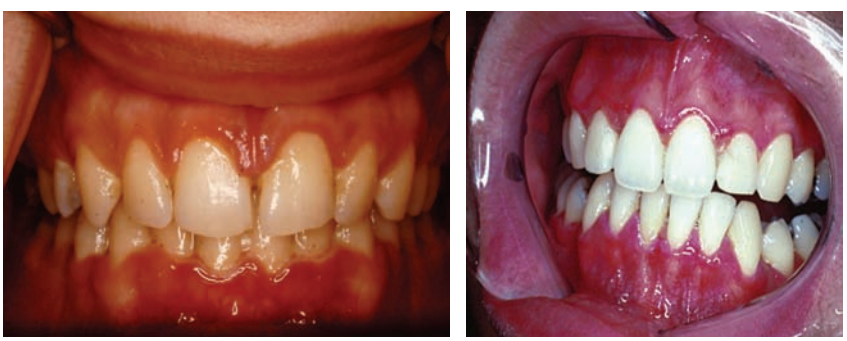

FIGURE 4-9
Gingivitis accompanied by crateriform ulcers with blunting of the papillae. The multifocal ulcers of acute necrotizing ulcerative gingivitis are generally confined to the interdental papillae.

ACUTE STREPTOCOCCAL/ STAPHYLOCOCCAL STOMATITIS

Figure 4-10

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Acute streptococcal or staphylococcal stomatitis is a rare disease characterized by gingival, oral mucosal, and tonsillar inflammation associated with cervical lymphadenopathy and occurring in the context of immunosuppression. The disease often represents a secondary bacterial infection following primary herpetic gingivostomatitis. There is an increased risk for streptococcal septicemia among patients with post–bone marrow transplant myelosuppression and oral mucositis implying that streptococci are harbored by the oral lesions. The lesions are ulcerative with an erythematous base and involve both fixed and movable mucosa. The gingiva is boggy with diffuse erythema; the ulcers do not confine themselves to the intradental papilla, nor are they restricted only to marginal gingiva. Fetid odor is not a feature. β-Hemolytic streptococci can be cultured, and antistreptolysin O titers are elevated during the convalescent period. The white blood cell count is elevated with a neutrophilic leukocytosis.

MICROSCOPIC FEATURES

The mucosa is ulcerated with a pseudomembranous fibrin surface. The ulcer bed is represented by granulation tissue exhibiting a nonspecific subacute inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Viral vesicular stomatitis, particularly primary herpetic gingivostomatitis, exhibits almost identical clinical features. Whereas primary herpes typically manifests a marginal gingivitis in addition to oral ulcers, streptococcal gingivitis fails to show this feature. Most of the other ulcerative diseases are not accompanied by fever and lymphadenopathy. Definitive diagnosis rests with a positive culture for β-hemolytic streptococci with elevated antistreptolysin O titers in the convalescent period.

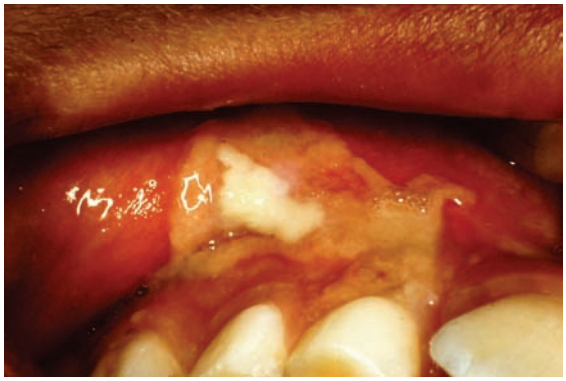

FIGURE 4-10
Child with diffuse ulcer and pseudomembrane in acute streptococcal stomatitis. (Courtesy of Dr. D. Adams.)

TREATMENT

Acute streptococcal stomatitis is managed by prescribing penicillin or synthetic penicillin analogs 250 mg every 6 hours for 2 weeks. A palliative oral mouth rinse or tetracycline oral suspension is also recommended.

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CHRONIC ULCERATIVE STOMATITIS

Figure 4-11

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Chronic ulcerative stomatitis is a rare lichenoid disease of oral mucosa that is characterized by the presence of antinuclear antibodies reactive with stratified squamous epithelial nuclei. Clinically, the lesions are painful white, red, ulcerative, and desquamative, appearing primarily on the tongue and buccal mucosa.

MICROSCOPIC FEATURES

A chronic lymphocytic interface mucositis is evident, resembling ordinary lichen planus. On immunoflourescent testing, fibrinogen may be localized along the basement membrane, but the singular feature is the presence of IgG and/or IgM antinuclear keratinocyte antibodies identified in the lower strata keratinocytes.

DIFFERENTIAL DIAGNOSIS

Lichen planus and lichenoid eruptions are the primary considerations in the differential diagnosis.

TREATMENT

The significance of the antinuclear antibodies is unknown and not related to lupus erythematosus. The condition is often recalcitrant to topical steroids. Short-term systemic corticosteroid therapy may or may not be effective. Hydroxychloroquine therapy may be prescribed.

Additional Reading

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GONOCOCCAL STOMATITIS

Figure 4-12

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Whereas gonorrhea is a common urethral infection, localization in the oral cavity and oropharynx is rare. When the oral mucosa is infected, irregular ulcerations ranging from 0.5 to 2.0 cm are observed and are accompanied by a perilesional zone of erythema. Tonsillar and pharyngeal involvement is characterized

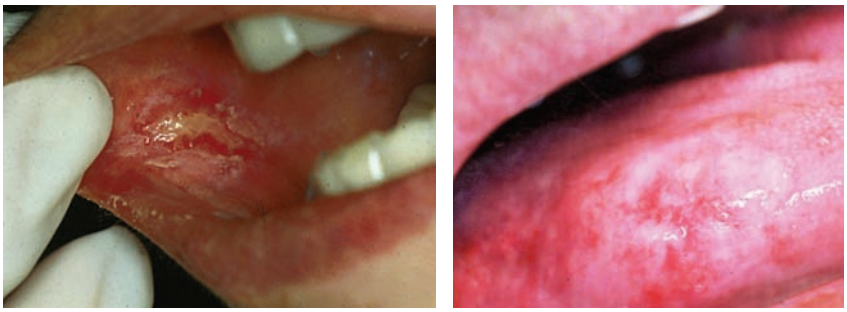

FIGURE 4-11
Red and ulcerative lesions in chronic ulcerative stomatitis associated with stratified epithelial specific antinuclear antibodies.

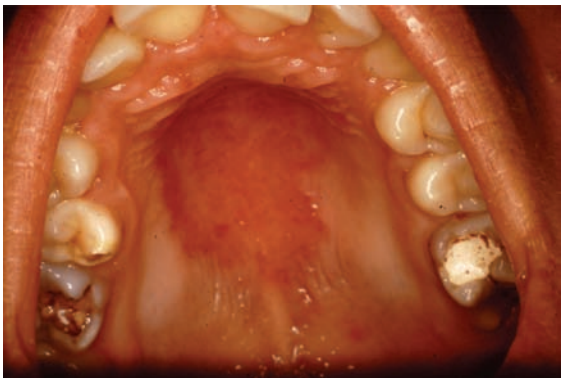

FIGURE 4-12
Irregularly outlined ulcer in gonococcal stomatitis.

by a pseudomembranous reaction with tonsillar enlargement accompanied by an erythematous pharyngitis. Lymphadenopathy and fever are also observed.

MICROSCOPIC FEATURES

The mucosa may be intact or ulcerated with a fibrinous pseudomembrane. The submucosa displays a nonspecific subacute inflammatory cell infiltrate. Cytologic smears prepared with a Gram stain disclose free and intraepithelial gram-negative diplococci.

DIFFERENTIAL DIAGNOSIS

The ulcerations of gonococcal stomatitis may simulate other diseases included here as ulcerative diseases. The variation in size and configuration and elevated temperature should arouse suspicion of gonorrhea along with a history of contact with a known carrier of the disease. A smear often, yet not invariably, discloses the presence of gram-negative diplococci. A culture is required to secure a definitive diagnosis.

TREATMENT

Penicillin is the treatment of choice. One gram of probenecid followed 30 minutes later by 4.8 million units of intramuscular procaine penicillin is recommended. Alternatively, 500 mg oral penicillin every 6 hours for 10 days generally eliminates the infection. Penicillin-resistant cases should be evaluated by culture and sensitivity testing.

Additional Reading

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HIV PERIODONTITIS AND ORAL ULCERATIONS

Figure 4-13

Age: Young adults
Sex: Male predilection

CLINICAL FEATURES

Although any human immunodeficiency virus (HIV)–infected individual may develop periodontal disease, HIV periodontitis is a specific form of periodontal breakdown resembling a fulminant, rapidly progressing ANUG. Although most instances have been seen in homosexual HIV-positive males, other infected individuals may be affected. Early marginal gingivitis is characterized by a band-like zone of erythema along the attached gingiva. Subsequently, the interdental papillae as well as the free marginal gingiva ulcerate, with appearance of a gray-white pseudomembrane. The unique change in this disease is the rapidly evolving periodontal stripping. Within a few weeks, both soft and supportive hard tissues undergo necrosis, culminating in exposure of root cementum. Indeed, in some patients, the ulcerations progressively extend onto the palate or adjacent vestibular soft tissues, resembling noma. The cultivatable microbiota includes gram-positive and -negative anaerobic rods, gram-positive

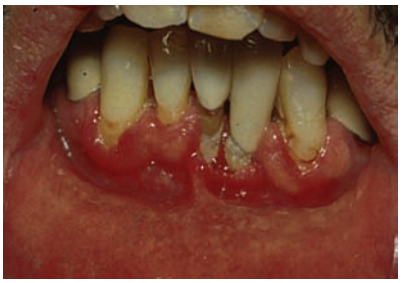
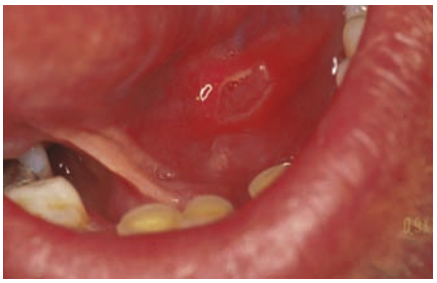

FIGURE 4-13
Left: multifocal gingival ulcerations with stripping of attached gingival and necrotic bone in HIV periodontitis. Right: aphthous-like ulceration in HIV patient.

cocci, and uniquely, *Candida* species. Patients presenting with HIV periodontitis may or may not harbor other opportunistic infections or neoplastic lesions characteristic of AIDS. Another form of ulceration in HIV patients is the focal ulcers that appear identical to aphthous ulcers and may in fact represent simple aphthae unrelated to HIV.

MICROSCOPIC FEATURES

The histologic findings are nonspecific. Ulceration with exposed fibrin, entrapped leukocytes, and underlying granulation tissue are observed. The inflammatory cell infiltrate is not particularly intense. Small osseous sequestra may be identifiable, and numerous polymorphic microbial colonies adhere to the necrotic ulcerated regions representing the sulcus. The aphthous-like ulcerations are nonspecific ulcers with underlying chronic inflammation.

DIFFERENTIAL DIAGNOSIS

The early changes are not particularly unique, resembling ordinary gingivitis. Early ulcerative changes are easily confused with ANUG. Once rapidly progressive necrosis with exposure of cementum occurs, HIV serologic testing should be considered. The oral aphthae must be differentiated from infectious ulcers with such opportunistic pathogens as mycobacteria, invasive fungi, and protozoal parasites.

TREATMENT

Periodontal debridement with povidone-iodine irrigation is recommended followed by home care brushing, flossing, and importantly, topical 1.2% chlorhexidine rinses. Severe disease warrants systemic antibiotics, either tetracycline or metronidazole, for a 10-day period in addition to topical treatment techniques.

Additional Reading

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Focal Ulcerations

TRAUMATIC ULCER

Figure 4-14

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

The traumatic ulcer is by far the most common type of focal ulceration. It may occur in response to a variety of traumatic insults

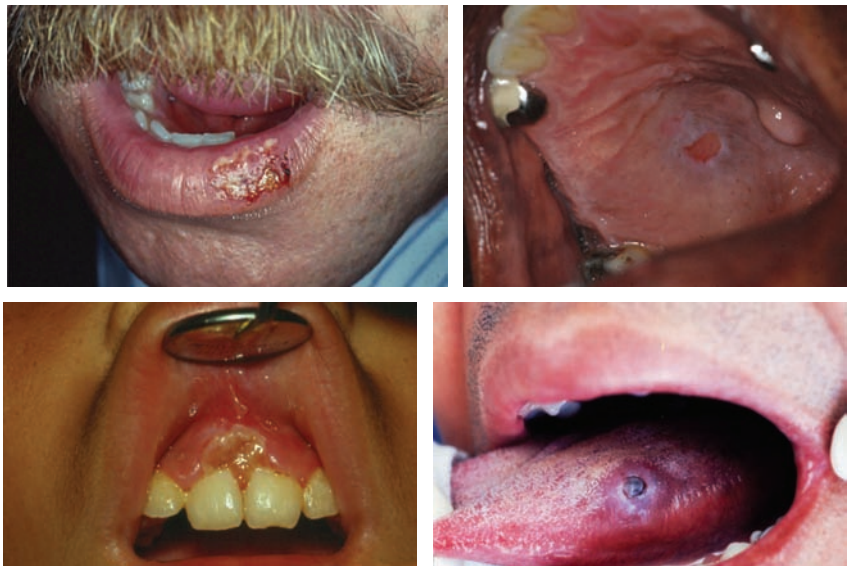

FIGURE 4-14
Traumatic ulcers are focal.

including denture irritation, cheek- or tongue-biting, pizza burn, or other forms of self-inflicted trauma or iatrogenic injury occurring in the dental office. The cause is usually readily determined by examining for flange overextension on dentures using pressure-indicating paste, or by checking for jagged or malposed cusps and restorations. The ulcer is generally shallow, yet may show rolled borders as a result of granulation tissue response. Marginal erythema is usually, yet not invariably, present. Traumatic ulcers of the soft palate in the region of the pterygoid hamulus in infants have been referred to as Bednar's aphthae. A traumatic ulcer of the lips in children with erupting teeth has been termed Riga-Fede disease. Deep traumatic ulcers of the tongue associated with a granulomatous tumefaction and a pronounced eosinophilic myositis have been termed traumatic ulcerative granuloma with stromal eosinophilia.

MICROSCOPIC FEATURES

The epithelium is lacking, exposing bare connective tissue with an eosinophilic surface coagulum. The superficial layer is infiltrated with neutrophils, and the deeper and marginal connective tissues evince a round cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Traumatic ulcers may be extensive and associated with tumefaction. In these patients, carcinoma, specific granulomatous inflammation, traumatic granuloma, and atypical histiocytic granuloma must be ruled out by biopsy.

TREATMENT

If a history of trauma is present or irritational factors are identified, they should be removed and 10 days should be allowed for healing. Failure to resolve necessitates a biopsy.

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TRAUMATIC GRANULOMA WITH STROMAL EOSINOPHILIA

Figure 4-15

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Traumatic granuloma is a large ulcerative lesion, often showing rolled margins, with a predilection for the lateral of the tongue. The ulcerated surface exceeds 1 cm and is gray-white, and the margins fail to show a prominent erythematous halo. The lesion may feel indurated owing to the extension of inflammation into the underlying skeletal muscle layer. Although the lesion is referred to as a "traumatic" granuloma, a history of trauma may be lacking, thereby obscuring the etiology of this histopathologically defined lesion. After an incisional biopsy, most of these lesions involute, resolving within 4 to 5 weeks.

A similar large ulcer with rolled margins can appear on the tongue, lips, or vestibule in elderly patients. The lesions are clinically ominous and, histologically, they resemble lymphoma. The unusual histologic findings account for the term *atypical histiocytic granuloma*. The lesion is probably a variant of the traumatic granuloma of the tongue as its behavior is comparable. Similar lesions may occur episodically in other intraoral sites. Regardless, they eventually resolve spontaneously and any provocation for their pathogenesis remains undetermined.

MICROSCOPIC FEATURES

The traumatic granuloma of the tongue shows loss of surface epithelium with underlying deeply infiltrative sheets of histiocytes and scattered eosinophils. This infiltrate extends into the intrinsic muscle fibers of the tongue and, although not related, closely resembles the infiltrates seen in histiocytosis X. Atypical histiocytic granuloma also shows surface ulceration and a histiocytic infiltrate; however, the histiocytes are cytologically pleomorphic and numerous mitotic figures are encountered. The histologic findings closely resemble those of lymphoma, and therefore, a medical work-up to rule out systemic lymphoma should be undertaken before a definitive diagnosis of

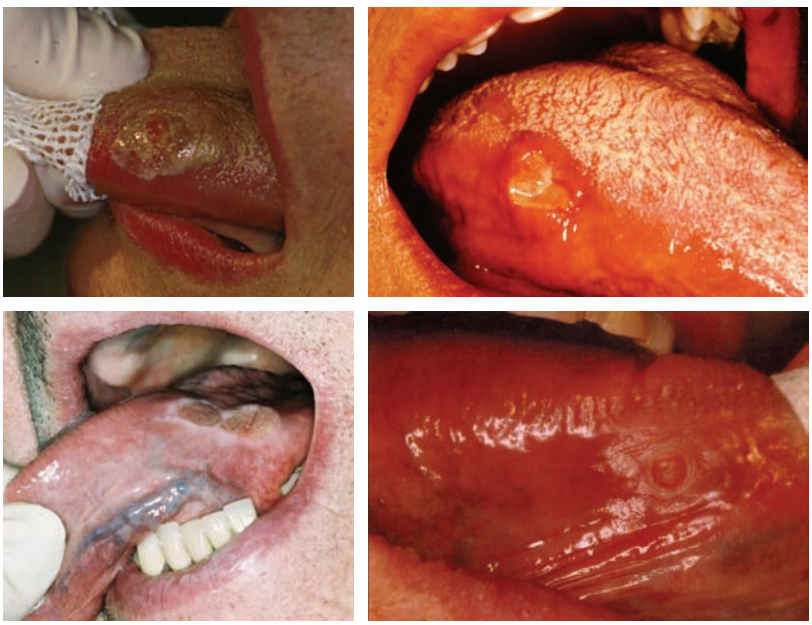

FIGURE 4-15
Traumatic ulcerative granuloma with stromal eosinophilia.

atypical histiocytic granuloma can be rendered. Immunocytochemical marker studies on fresh tissue samples help to rule out lymphoma because the atypical cells stain with histiocyte rather than lymphoid cell surface and cytoplasmic markers.

DIFFERENTIAL DIAGNOSIS

Clinically, both traumatic and atypical histiocytic granulomas appear identical to squamous cell carcinoma or specific granulomatous inflammatory ulcerations. Biopsy is therefore essential to determining the diagnosis.

TREATMENT

Once an incisional biopsy has been procured and the diagnosis is established, no further treatment is required. The lesions resolve in 4 to 5 weeks.

Additional Reading

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ATYPICAL HISTIOCYTIC GRANULOMA

Figure 4-16

Age: Elderly
Sex: No predilection

CLINICAL FEATURES

Some pathologists consider atypical histiocytic granuloma to be a variant of traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) since the two lesions share similar clinical and microscopic features. Atypical histiocytic granulomas are large with irregular margins occurring on the lips, vestibule, alveolar ridge, and rarely on the tongue, and microscopically, the cellular infiltrate is far more anaplastic than TUGSE, mimicking a lymphoma (Hodgkin's disease, and lymphomatoid papulosis in particular). These angry appearing ulcerations lack rolled borders and spontaneously resolve of their own accord. Some instances recur, only to resolve again. They are only mildly painful. No infectious agent has been associated with these ulcers.

MICROSCOPIC FEATURES

A loss of epithelium is evident and the ulcer bed exhibits a diffuse, often deep inflammatory cell infiltrate predominated by histiocytes with large nuclei and prominent

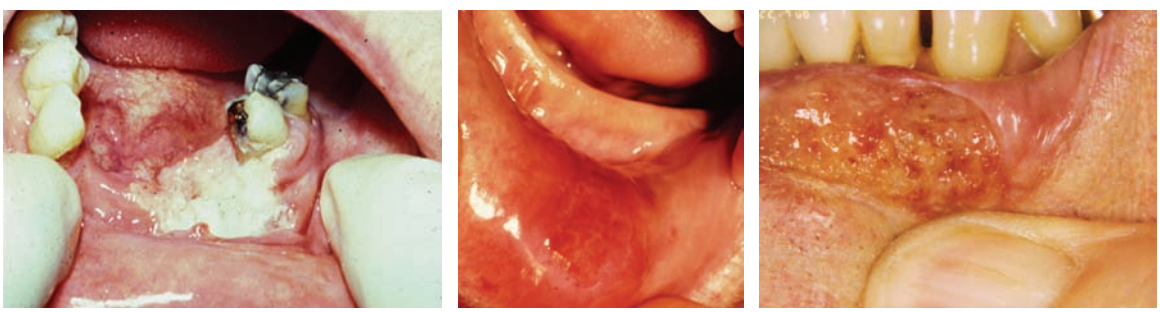

FIGURE 4-16
Atypical histiocytic granuloma appearing as large ulcers that eventually resolve.

nucleoli resembling Reed-Sternberg cells of Hodgkin's lymphoma. Plasma cells, lymphocytes, and eosinophils are also included in the infiltrate, yet show normal, benign features. Clinically, atypical histiocytic granuloma resembles squamous cell carcinoma and invasive fungal granulomas.

DIFFERENTIAL DIAGNOSIS

Some of these lesions show T-cell rearrangement with CD30 positivity using immunohistochemistry and should be considered as T-cell lymphomas. Molecular analysis is required to make the differentiation.

TREATMENT

Following biopsy, these ulcers tend to heal within 3 to 4 weeks. Recurrence may occur, yet these recurrences also spontaneously involute.

Additional Reading

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NECROTIZING SIALOMETAPLASIA

Figure 4-17

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The hard and soft palates show focal deep-seated ulceration, occasionally bilateral. Occasionally, other mucosal sites bearing minor salivary glands are affected. The ulcers are large, lack induration, and fail to show rolled margins; the necrotic center possesses a pebbly surfaced, gray membrane. Despite their extensiveness, they are generally painless. After biopsy, the lesions generally heal spontaneously within 2 months. The etiology is unknown, but vascular occlusion of the arterioles supplying the palate and associated minor salivary glands has been suggested.

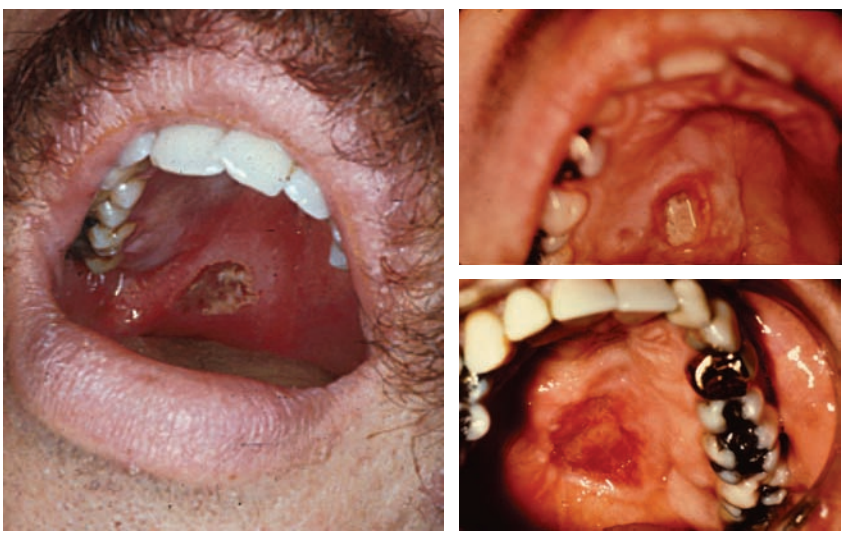

FIGURE 4-17
Necrotizing sialometaplasia, characterized by relatively deep-seated necrotic ulcers of the palatal mucosa.

MICROSCOPIC FEATURES

The ulcer bed is composed of necrotic debris and eosinophilic fibrinous material. The underlying salivary tissue is necrotic, with maintenance of cellular outlines reminiscent of ischemic necrosis. The salivary epithelium adjacent to the necrotic zone displays squamous metaplasia with loss of normal acinar morphologic characteristics. The metaplastic islands are oval or linear with rounded margins. Lesions should not be confused with mucoepidermoid or epidermoid carcinoma.

DIFFERENTIAL DIAGNOSIS

Clinically, necrotizing sialometaplasia may be confused with carcinoma, adenocarcinoma, granulomatous ulcer, or traumatic ulcer. Lack of induration and rolled margins should divert suspicion of malignancy. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Once a definitive diagnosis is secured, no treatment is required. The lesions spontaneously regress in 6 to 8 weeks. Palliation is not necessary because pain is generally not a problem.

Additional Reading

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SPECIFIC GRANULOMATOUS ULCER

Figure 4-18

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Specific granulomatous responses elicited by microorganisms are all primary pulmonary infections that involve oral mucous membranes secondarily by extrapulmonary dissemination; *Mycobacterium tuberculosis* and the deep fungi are specifically implicated. Of the fungal infections, histoplasmosis,

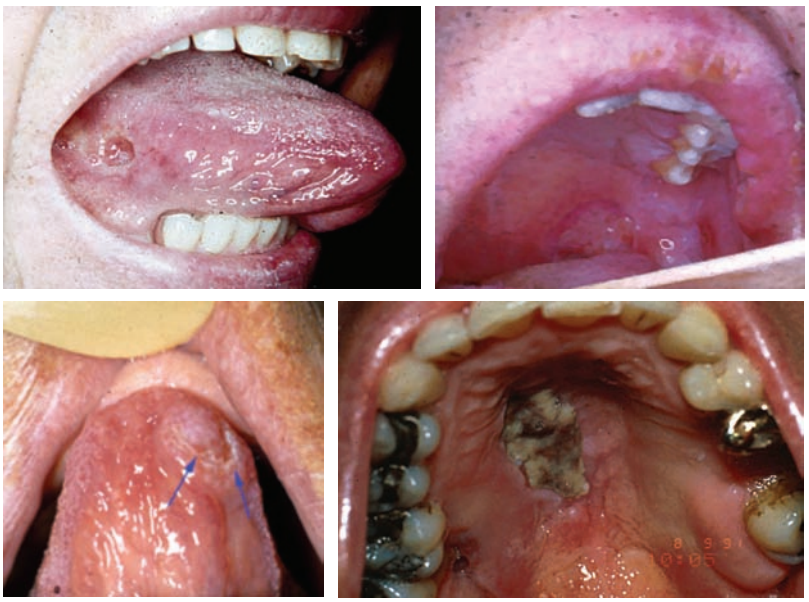

FIGURE 4-18
Granulomatous ulcers caused by mycobacteria or invasive fungi (histoplasmosis, blastomycosis).

blastomycosis, cryptococcosis, and coccidiodomycosis are most common. The ulcers are always associated with a granulomatous, firm swelling that characteristically evinces a papillary or cobblestone surface pattern with patchy erythema. Although any site may be affected, the tongue and buccal mucosa are favored. Often, more than one lesion is present. Because pulmonary infection is the dominant feature, chronic cough is noted. Transmission of infection by physical contact with the lesions is remote but possible.

Atypical mycobacteria, particularly *Mycobacterium avium intracellulare* and deep fungal infections manifesting as granulomatous ulcers of the oral mucous membranes may herald the onset of pre-AIDS or AIDS. Such opportunistic infections occur in the oral cavity subsequent to HIV infection, and serologic testing for the virus is warranted in high-risk patients.

MICROSCOPIC FEATURES

Subjacent to the ulcerated zones are focal condensations of chronically inflamed granulation tissue with epithelioid cells and multinucleated giant cells showing a horseshoe or wreath-like nuclear arrangement. Caseous necrosis is often, yet not always, seen in tuberculous granulomas. The deep fungal granulomas are noncaseating. Acid-fast stains disclose the presence of mycobacteria. Periodic acid-Schiff (PAS) or methenamine silver stain fungal cell walls.

DIFFERENTIAL DIAGNOSIS

Specific granulomatous ulcers may simulate carcinoma or traumatic ulcers. When predominantly papillary in appearance, they may be difficult to differentiate from papillary hyperplasia or verrucous carcinoma. Biopsy reveals the characteristic features of granulomatous infection. Skin tests may also be indicated to demonstrate delayed hypersensitivity to a specific microorganism.

TREATMENT

Because oral granulomatous lesions are associated with pulmonary disease, referral to an internist is indicated. Tuberculosis is treated with long-term isoniazid therapy. Deep fungi are managed with amphotericin B. HIV-associated granulomatous infections require administration of appropriate antibiotics in addition to antiretroviral drugs.

Additional Reading

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CHANCRE (PRIMARY SYPHILIS)

Figure 4-19

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Primary syphilitic chancre of the oral mucosa arises subsequent to venereal contact as a consequence of orogenital sexual relationships. The lesion is most frequently seen on the lips or tongue and is typically a painless fungating tumefaction with central ulceration, firm to palpation. The examiner should wear gloves as the primary lesion is teeming with *Treponema pallidum*, the causative spirochetal microorganism. Chancres appear 5 to 6 weeks after sexual contact. The Venereal Disease Research Laboratory test (VDRL), fluorescence treponemal antibody test, or treponemal immobilization assay usually are negative or only slightly reactive during the early stages of the disease and

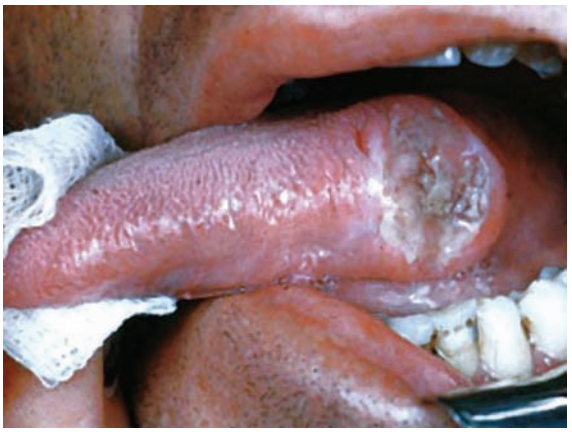

FIGURE 4-19
Chancre of primary syphilis. A central zone of ulceration is surrounded by indurated, rolled, or swollen margins.

therefore assays should be performed 1 to 2 weeks after appearance of the primary lesion.

MICROSCOPIC FEATURES

The epithelium is lacking over the clinically ulcerated surface. Granulation tissue, which evinces an intense plasma cell infiltrate with a tendency for perivascular orientation, constitutes the bulk of the tumefaction. A Warthin-Starry spirochete stain is required to visualize the microorganism. A smear with dark-field illumination discloses the presence of mobile spirochetes.

DIFFERENTIAL DIAGNOSIS

The granulomatous ulcer may resemble carcinoma, specific granulomatous ulcer of tuberculosis or the deep mycoses, and traumatic ulcer. A history of venereal transmission with rapid onset and growth should arouse suspicion of primary syphilis. VDRL, fluorescence treponemal antibody, or treponemal immobilization tests are positive 1 to 2 weeks after appearance of the chancre.

TREATMENT

Four million units of penicillin intramuscularly followed by 250 mg penicillin orally 4 times daily for 2 weeks is usually curative. Most states require that venereal disease cases be reported to the state board of health.

Additional Reading

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SQUAMOUS CELL CARCINOMA

Figure 4-20

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

The most common presenting sign of oral cancer is the focal ulceration with indurated margins. Any oral ulcer without a readily apparent cause should be considered carcinoma until proven otherwise, particularly if the lesion has persisted longer than 2 weeks. Carcinomatous ulcers may arise in preexisting leukoplakia or erythroplasia, but there may be no history of a precedent precancerous lesion. The patients usually give a history of smoking and show a proclivity for overimbibing alcoholic beverages. The lateral border of the tongue, floor of the mouth, alveolar ridge, and lower lip are the sites of predilection; however, oral cancer can develop in any location. The ulcer is often, yet not always, painless. The growth rate is variable but usually progresses relatively rapidly. The larger the tumefactive ulceration, the more likely the chance for nodal metastasis. Oral cancer spreads first to the submandibular and cervical lymph nodes. Regional metastatic disease in the neck, like the primary lesion, is indurated and fixed to adjacent tissues.

MICROSCOPIC FEATURES

Subjacent and lateral to the zone of ulceration are invasive islands, cords, and nests of malignant epithelial cells that demonstrate

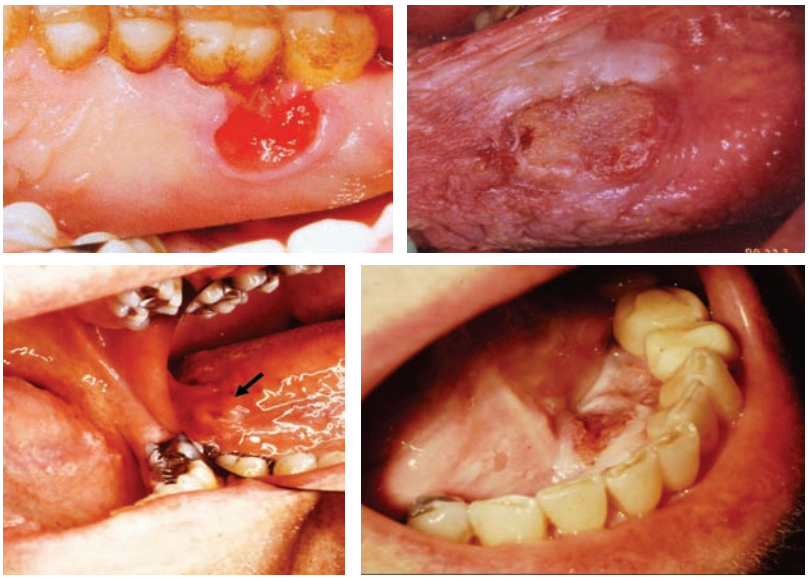

FIGURE 4-20
Squamous cell carcinoma beginning as a focal ulceration with rolled borders.

varying degrees of pleomorphism, hyperchromatism, and increased mitoses, many of which are bizarre. Keratin and parakeratin pearls are often present.

DIFFERENTIAL DIAGNOSIS

Carcinoma appearing as an oral ulcer may be clinically indistinguishable from traumatic ulcer, chancre, or one of the specific granulomatous infections. Biopsy provides a definitive diagnosis. Certainly, any ulcer without a cause, or one that fails to heal when a suspected cause is removed, requires microscopic examination.

TREATMENT

Cancer should be managed by an oncologist. Surgery, radiotherapy, or a combination of the two are the treatment methods of choice.

Additional Reading

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Perioral and Commissural Ulcerations and Fistulae

COMMISSURAL PITS

Figure 4-21

Age: From infancy
Sex: No predilection

CLINICAL FEATURES

Blind fistulae or pits located at the commissure of the lips are 1 to 2 mm in diameter and reach a depth of similar dimension. They may be unilateral or bilateral, show a familial tendency, and are more frequent among blacks than whites. Their incidence has been reported to vary from 1% to 20% of the population.

MICROSCOPIC FEATURES

Not applicable.

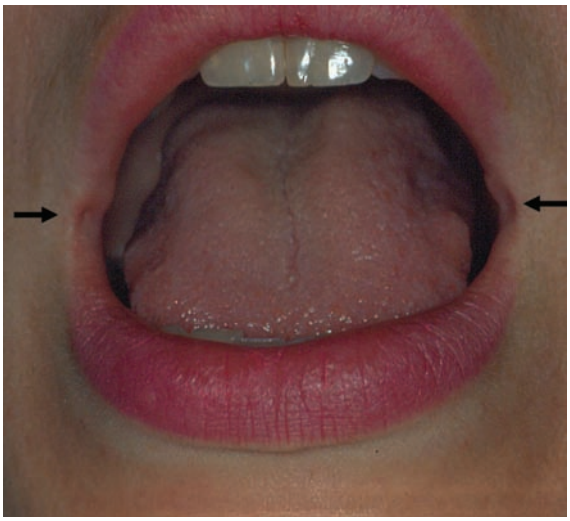

FIGURE 4-21
Commissural pits: bilateral blind fistulae devoid of tumefactive margins.

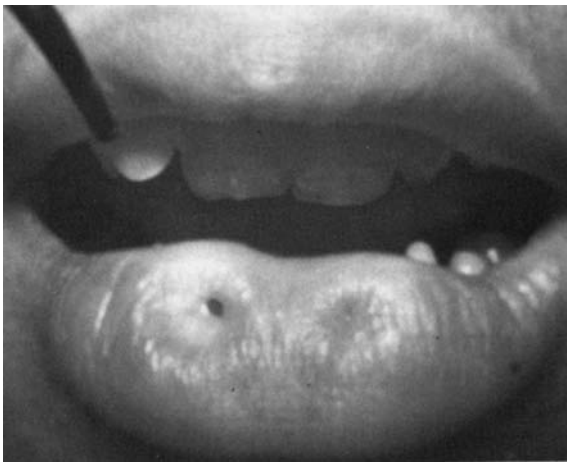

FIGURE 4-22
Congenital lip pits. These may be bilateral blind ducts or they may communicate with salivary conduits. (Courtesy of Dr. Caesar Lopez.)

DIFFERENTIAL DIAGNOSIS

Commissural pits are clean, uninflamed depressions that can be easily differentiated from inflammatory or neoplastic lesions involving the angles of the mouth.

TREATMENT

No treatment is necessary.

Additional Reading

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CONGENITAL LIP PITS

Figure 4-22

Age: From infancy
Sex: Slight female predilection

CLINICAL FEATURES

Developmental pits of the lower lip are blind fistulae located bilaterally on either side of the midline on the vermilion border. The fistulae may extend as deep as 2 cm and communicate with minor salivary ducts. The surrounding submucosa may be somewhat hyperplastic, producing a soft elevation of tissue around the broad sinuses. Although lip pits may be an isolated finding, they are more often associated with cleft palate-cleft lip. This syndrome is inherited as an autosomal dominant trait. Developmental pits have also occurred in the buccal mucosa.

MICROSCOPIC FEATURES

Not applicable.

DIFFERENTIAL DIAGNOSIS

Lip pits lack ulceration and inflammation, allowing for easy recognition as a developmental anomaly, particularly in light of their bilaterality and association with other developmental anomalies.

TREATMENT

Surgical removal may be undertaken for cosmetic purposes.

Additional Reading

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ANGULAR CHEILITIS

Figure 4-23

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Located bilaterally at the commissures of the lips, angular cheilitis is characterized by weeping focal ulcerations showing cracking, keratosis, and mild erythema. In most instances, the disease is caused by, or secondarily infected with, *Candida albicans*. Predisposing factors are commonly encountered: decreased vertical intermaxillary dimension, pronounced angular skin folds, vitamin B complex deficiency, pernicious anemia, and HIV infection.

MICROSCOPIC FEATURES

The surface epithelium shows zones of ulceration alternating with focal hyperkeratosis. Candida hyphae are aggregated in the superficial layers. The subjacent fibrous connective tissue displays a subacute or chronic inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The bilateral, weeping inflamed lesions devoid of tumefaction are characteristic. Underlying predisposing factors must be sought. A complete blood count and gastric analysis should be performed when pernicious anemia is suspected. Patients with pernicious anemia usually manifest atrophic glossitis in addition to angular cheilitis.

TREATMENT

The predisposing factors, be they local or systemic, must be eliminated or controlled. Topical application of nystatin cream or ointment three times daily eliminates complicating candidal infection.

Additional Reading

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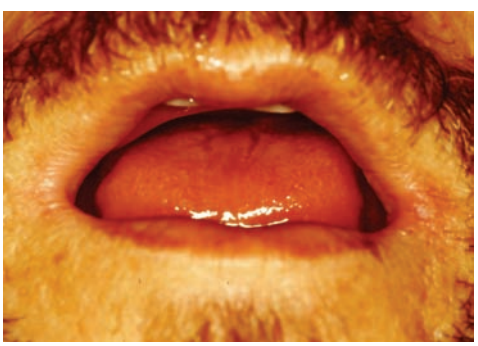

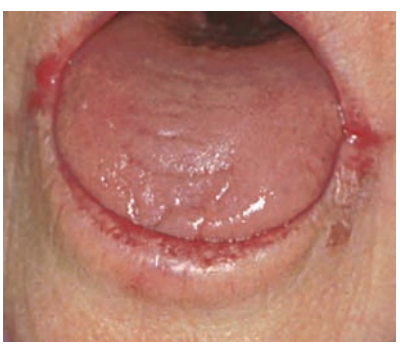

FIGURE 4-23
Angular cheilitis characterized by commissural fissuring with keratotic, weeping lesions.

Oral Fistulae

PERIAPICAL ABSCESS AND OSTEOMYELITIS

Figure 4-24

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Drainage tracts resulting from infection of odontogenic and periodontal origin are the most frequent forms of oral fistulae. They are most often encountered on the gingiva in close proximity to the tooth, acting as the source of infection or adjacent to a focus of destructive or sclerosing osteomyelitis as evidenced radiographically. When a carious or traumatized noncarious tooth is present, it will test nonvital with a vitalometer. The fistula contains a draining center from which a purulent exudate can often be expressed. Patients usually complain of a foul or metallic taste. Occasionally, the fistula is associated with a parulis.

MICROSCOPIC FEATURES

The drainage tract is lined by subacutely inflamed granulation tissue and occasionally may evince a squamous epithelial lining. In either case, communication with inflamed granulation tissue in bone is observed.

DIFFERENTIAL DIAGNOSIS

A draining fistula may be clinically confused with traumatic ulcer, aphthous ulcer, or, rarely, carcinoma. Searching for an infectious source and probing the lesion with a periodontal probe or gutta-percha point will aid in obtaining a diagnosis.

When radiographic evidence of osteomyelitis exists, culture and sensitivity of the exudate, particularly for actinomycetes, should be pursued. When teeth are missing, search for a retained root tip is advisable.

TREATMENT

Infected teeth must be treated endodontically or, if nonrestorable, extracted. When osteomyelitis is present, antibiotic treatment should be instituted and either maintained or altered depending on results of culture and sensitivity testing. When the patient is febrile with malaise and cellulitis is present, hospitalization and intravenous antibiotic treatment may be indicated.

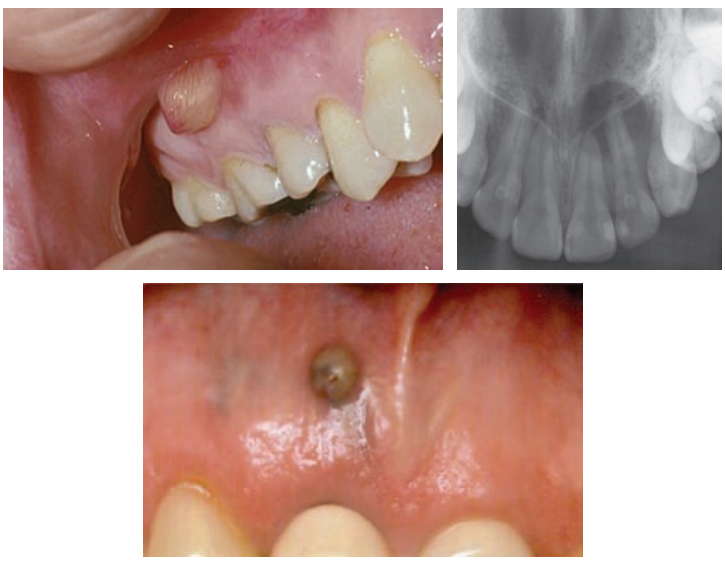

FIGURE 4-24
Oral fistula associated with a periapical abscess.

Additional Reading

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PERIODONTAL ABSCESS

Figure 4-25

Age: Adults
Sex: No predilection

CLINICAL FEATURES

An acute reaction to dental plaque irritants and bacteria may develop in periodontal pockets and in furcation areas. Whereas many periodontal abscesses drain via the sulcular pocket, others may spread through gingival tissues and perforate to form a fistula. The periodontally involved tooth may or may not be sensitive to percussion, and pain may be dull or severe. Constitutional signs of infection, including fever, malaise, and lymphadenopathy, may exist. Placing a probe into the periodontal pocket with mild manipulation often elicits drainage of exudate through the fistulous tract. When the pocket is deep and the abscess lies adjacent to lateral accessory root canals, retrograde pulpitis may ensue. Recurrent or multiple periodontal abscesses may be encountered in uncontrolled diabetics.

MICROSCOPIC FEATURES

The zone of abscess formation shows infiltration by neutrophils and macrophages. Capillaries course through the abscess, and both necrotic debris and microbial colonies may be present. The fistula contains an acute inflammatory cell infiltrate and is usually lined by granulation tissue; however, epithelialization may develop.

DIFFERENTIAL DIAGNOSIS

Fistulae of periapical origin must be ruled out on a radiographic and clinical basis utilizing methods to ascertain pulp viability. Occasionally, a periodontal abscess may coexist with, or indeed cause, pulp necrosis. Specific infection by actinomycetes may be present and can be diagnosed by microbial anaerobic culture or biopsy.

TREATMENT

Periodontal curettage or flap surgery with elimination of the abscess is required. Root planing and periodontal therapy in general should be undertaken. If periodontal abscess exists in conjunction with pulp necrosis, either endodontic treatment or extraction is indicated.

Additional Reading

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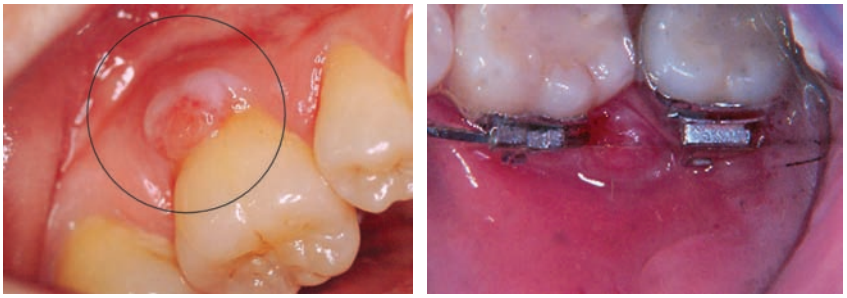

FIGURE 4-25
Oral fistula associated with a periodontal abscess.

ACTINOMYCOSIS

Figure 4-26

Age: Young adults
Sex: Male predilection

CLINICAL FEATURES

Either oral or extraoral fistulae may develop in an area of infection by *Actinomyces israelii.* The disease is most frequently encountered in the head and neck area and is acquired subsequent to tooth extraction or trauma. It usually manifests as an osteomyelitis with formation of granulation tissue and abscess in the submandibular region, producing so-called lumpy jaw. The infection may localize in periapical periodontal foci of inflammation. The organisms may be expressed through the fistulae and appear as small yellow flecks termed sulfur granules. Anaerobic methods are required to culture the organism.

MICROSCOPIC FEATURES

The granulation tissue in bone, or underlying the fistulae, shows foci of epithelioid histiocytes or localized abscesses. The microbial colonies are clove shaped, display a peripheral fringe, and are PAS positive. They lie in the center of a sea of neutrophilic granulocytes.

DIFFERENTIAL DIAGNOSIS

Actinomycosis manifesting oral fistulae cannot be differentiated from nonspecific infection of pulpal or periodontal origin. Culture and biopsy disclose the presence of actinomycotic microorganisms.

TREATMENT

The granulation tissue bed in bone should be curetted and the patient should receive antibiotic therapy. Penicillin (1 million units intramuscularly, followed by 500 mg for 10 days) is the drug of choice. In patients allergic to penicillin, erythromycin may be prescribed. If the disease fails to respond, massive intravenous doses of antibiotic may be required to achieve cure.

Additional Reading

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Weir JC, Buck WH. Periapical actinomycosis: Report of a case and review of the literature. *Oral Surg Oral Med Oral Pathol.* 1982;54:336.

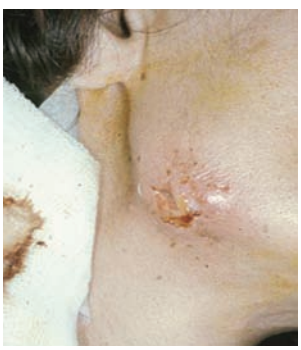
OROANTRAL FISTULA

Figure 4-27

Age: Adults
Sex: No predilection

CLINICAL FEATURES

A fistula that traverses the maxillary alveolus, causing an oral-antral communication, may arise subsequent to tooth extraction in which a perforation of the antral floor



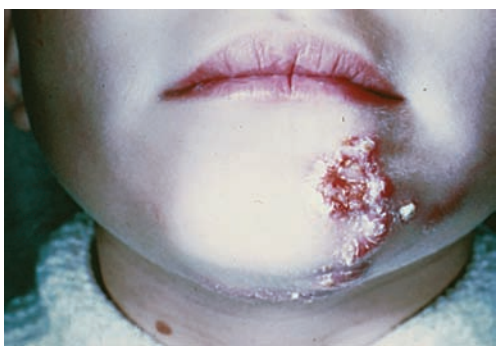


FIGURE 4-26
Drainage tracts, which develop either extraorally or intraorally in actinomycotic infection.

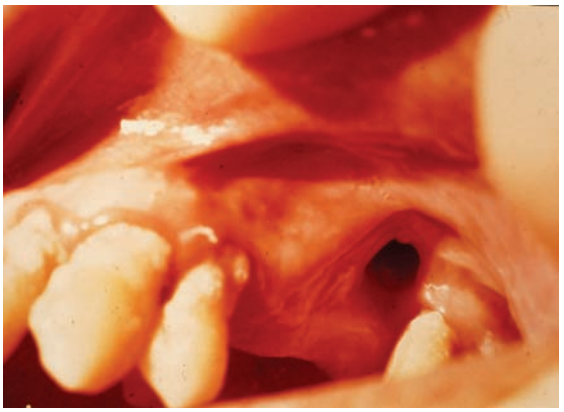


FIGURE 4-27
Oroantral fistula representing a through-and-through communication between the oral cavity and antrum.

developed. The fistula usually opens on the crest of the maxillary alveolar ridge, yet may exit in the mucobuccal fold area. The opening may be narrow or large and is usually devoid of erythema and purulent drainage. If residual inflammation exists in the maxilla or antral cavity, an exudate may be present. Occasionally, antral polyps herniate through the fistula as a fluctuant bulbous tumefaction.

MICROSCOPIC FEATURES

The fistula is lined by stratified squamous and often respiratory epithelium. The surrounding fibrous connective tissue evinces an inflammatory cell infiltrate of variable intensity.

DIFFERENTIAL DIAGNOSIS

Oroantral fistulae must be differentiated from fistulae developing from underlying osteomyelitis or actinomycosis. The location on the maxillary alveolus, history of extraction, and ability to probe through the defect into the antrum usually provide sufficient evidence to make the diagnosis. The presence of associated swelling or necrotic tissue could be indicative of a more serious disorder, such as maxillary sinus carcinoma or mucormycosis. A biopsy should then be performed.

TREATMENT

The fistula should be curetted to disrupt the epithelialized communication, and a palatal flap can be rotated over the defect for primary closure. Gold or platinum foil may be employed during surgery to occlude the opening and facilitate tissue closure.

Additional Reading

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Goldman EH, Stratigos GT, Arthur AL. Treatment of oroantral fistula by gold foil closure: Report of a case. *J Oral Maxillofac Surg.* 1969;27:875.

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SOFT TISSUE ABSCESS

Figure 4-28

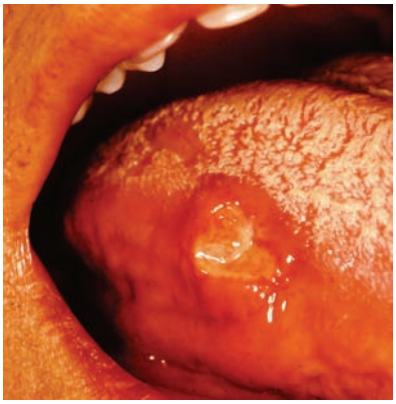
Age: No predilection
Sex: No predilection

CLINICAL FEATURES

An abscess may develop in the submucosal connective tissues subsequent to a penetrating wound or introduction of a foreign body. Rarely, *Actinomyces* may cause a soft tissue abscess. Any tissue site may be involved; however, the tongue and buccal mucosa are most frequently affected. A tumefaction is usually palpable or visible subjacent to the site of drainage. Pain is often present, and compression of the area elicits exudation through the fistula.

MICROSCOPIC FEATURES

Granulation tissue with foci of neutrophilic infiltration is observed. When a foreign body is present, it is usually identifiable under ordinary or polarized light. Giant



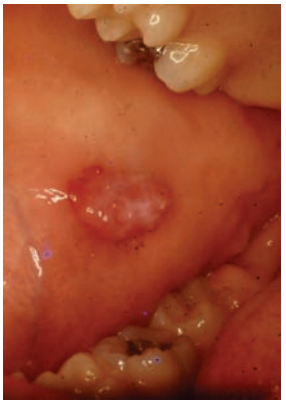
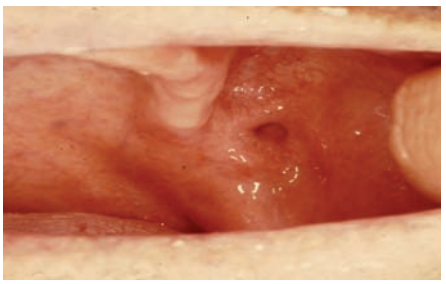


FIGURE 4-28
Soft tissue abscess formation showing swelling with a focus of drainage.



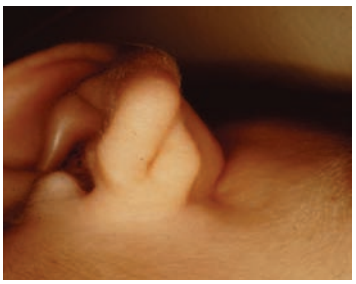


FIGURE 4-29
Left: Developmental sinus lateral to the pterygomandibular raphe. Right: Blind sinus in external ear.

cells surround the foreign material. The fistulous tract is lined by granulation tissue.

DIFFERENTIAL DIAGNOSIS

A draining fistula in the soft tissues, because it is often associated with tumefaction, must be differentiated from specific granulomatous diseases and neoplasms that have become inflamed.

TREATMENT

Incision with curettage and drainage should be performed and the tissue should be submitted for microscopic examination to confirm the clinical impression.

If fever is present and the abscess is large, the patient should receive antibiotic therapy while culture and sensitivity are obtained.

Additional Reading

Archer WH. *Oral and Maxillofacial Surgery*. 5th ed. Philadelphia, PA: W. B. Saunders; 1975:490, 492.

Tov YS et al. Facial cutaneous fistula due to a foreign body in Wharton's duct. *J Laryngol Otol.* 1988;102:370.

DEVELOPMENTAL ORAL SINUSES

Figure 4-29

Age: From infancy
Sex: No predilection

CLINICAL FEATURES

A variety of developmental fistulae and sinuses occur within the oral cavity. Some of these pits and fistulae fail to communicate with underlying structures or embryonic remnants, whereas others do communicate. Included in this group of developmental defects are (1) fistula of the nasopalatine duct, (2) tonsillar faucial fistulae, (3) pits of the pterygomandibular fold, and (4) lingual thyroglossal sinus of the foramen cecum area. Most of these sinuses are blind and are devoid of inflammatory changes. Occasionally, oral pits and sinuses

are associated with preauricular pits and deafness.

MICROSCOPIC FEATURES

Not applicable.

DIFFERENTIAL DIAGNOSIS

The bilateral nature, location, and healthy tissue appearance allow for easy identification.

TREATMENT

No treatment is necessary.

Additional Reading

Campbell EH. Perforation of the faucial pillars. *Arch Otolaryngol Head Neck Surg.* 1925;1:503.

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Leider AS, Lucas JW, Eversole, LR. Sebaceous choristoma of the thyroglossal duct. *Oral Surg Oral Med Oral Pathol.* 1977;44:261.

FISSURED (SCROTAL) TONGUE

Figure 4-30

Age: All ages
Sex: Slight male predilection

CLINICAL FEATURES

Cracks and fissures may cover the surface of the tongue, representing a developmental innocuous, and rather common, condition. In some instances a central linear fissure is seen with small contributories fanning laterally. The fissures may be up to 8 mm deep and can entrap food, causing irritation and discomfort.

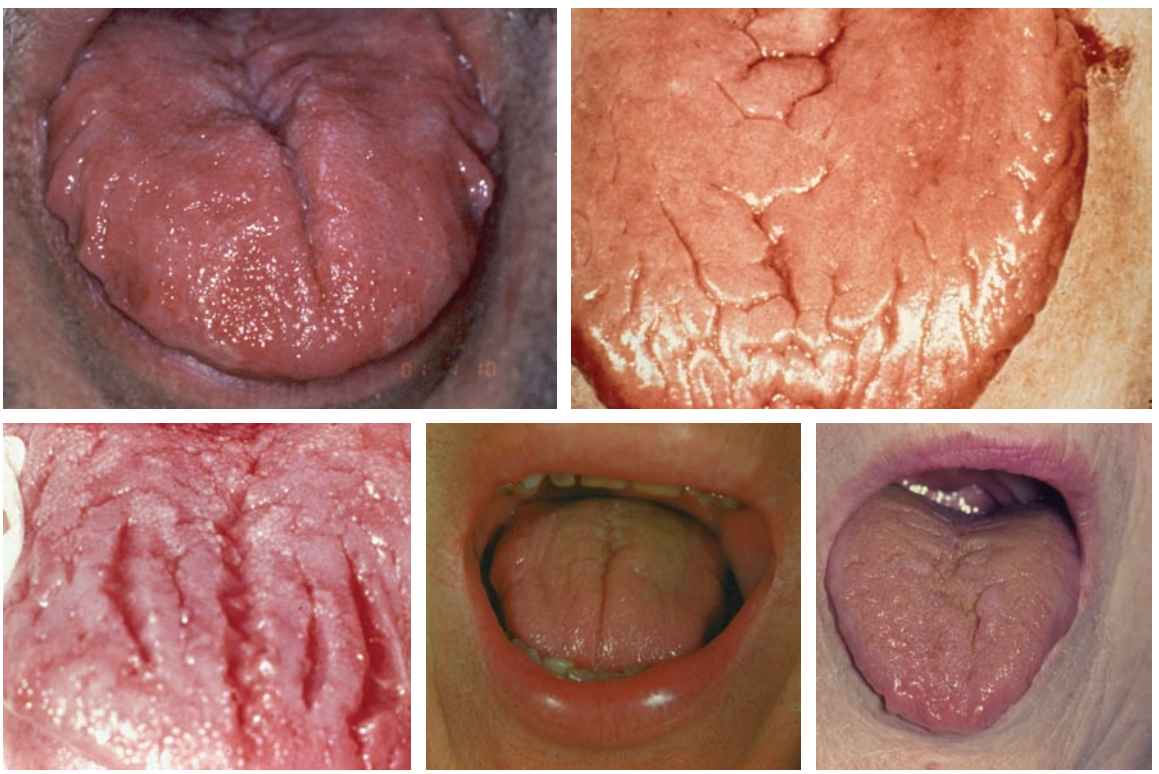

FIGURE 4-30
Fissures on dorsum (scrotal tongue).

MICROSCOPIC FEATURES

The fissures are lined by normal appearing stratified squamous epithelium and are in fact not truly ulcerated.

DIFFERENTIAL DIAGNOSIS

The clinical presentation is classic and not confused with other oral ulcerations. Fissured tongue is a component of the Melkerson-Rosenthall syndrome, a component of oro-facial granulomatosis in which the lips are enlarged with granulomatous inflammation and patients develop facial nerve palsy.

TREATMENT

None. If irritation occurs, the fissures can be brushed out with a soft bristle brush.

Additional Reading

Binmadi NO, Jham BC, Meiller TF, Scheper MA. A case of a deeply fissured tongue. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2010;109:659-63.

Hoexter DL. Melkerson Rosenthal syndrome. *N Y State Dent J.* 2007;73:30-32.

Yarom N, Cantony U, Gorsky M. Prevalence of fissured tongue, geographic tongue and median rhomboid glossitis among Israeli adults of different ethnic origins. *Dermatology.* 2004;209:88-94.

Zargari O. The prevalence and significance of fissured tongue and geographical tongue in psoriatic patients. *Clin Exp Dermatol.* 2006;31:192-195.

Necrotic and Osseous Destructive Lesions

FACTITIAL INJURY AND TRAUMA

Figure 4-31

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Self-inflicted wounds, chronic irritation, and postsurgical defects may result in osseous or soft tissue perforations of the palate. Occasionally, the palate breaks down, leaving a defect after cleft palate repair. A large rhinolith may irritate the palatal roof, causing palatal perforation. Habitual cocaine use may cause nasal osseous necrosis with extension through the palate. The defects are usually clean with little evidence of erythema, granulation tissue, or necrosis. Patients may experience altered speech and difficulty in eating.

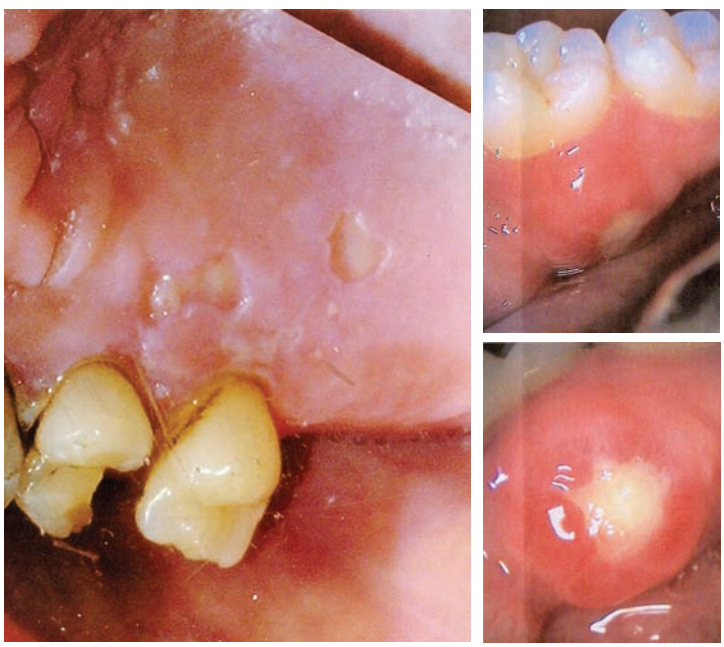

FIGURE 4-31
Osseous destruction due to trauma. Ulcer on right caused by irritation during intubation.

MICROSCOPIC FEATURES

Not applicable.

DIFFERENTIAL DIAGNOSIS

Palatal perforations resulting from factitial injury as a result of trauma or as sequelae to surgical intervention may simulate other osseous destructive lesions included in this section. The clean noninflamed character and a thorough history usually provide information sufficient to secure the diagnosis. A biopsy rules out other entities of a more serious nature.

TREATMENT

The defect may be occluded with a dental prosthesis or may be closed surgically with the aid of a palatal flap.

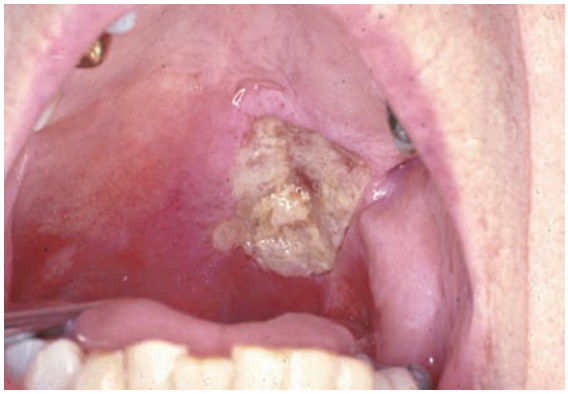

FIGURE 4-32
Palatal perforation from nasal lesions in Wegener's granulomatosis. (Courtesy of Dr. T. Daniels.)

Additional Reading

Archer WH. *Oral and Maxillofacial Surgery*. 5th ed. Philadelphia, PA: W. B. Saunders; 1975:1616, 1621.

Silvestre FJ, Perez-Herbera A, Puente-Sandoval A, Bagán JV. Hard palate perforation in cocaine abusers: a systematic review. *Clin Oral Investig*. 2010.

WEGENER'S GRANULOMATOSIS

Figure 4-32

Age: Adults
Sex: Female predilection

CLINICAL FEATURES

Midline lethal granuloma is a clinically defined entity in which midfacial osseous resorption and necrosis are seen, often with palatal perforation and loss of the nasal septum. Both Wegener's granulomatosis and extranodal natural killer (NK)/T-cell lymphoma (polymorphic reticulosis), a form of non-Hodgkin's lymphoma, will present with this clinical profile. With time, the entire midface may be destroyed with involvement of the orbits. Wegener's granulomatosis is a systemic collagen disease that can manifest these destructive and ulcerative lesions of the face and oral cavity. In addition, erythematous granular tumefactions may be encountered on the gingiva and other mucosal sites. Widespread manifestations are present with granulomatous and destructive lesions of the kidneys and lungs. Patients with Wegener's are positive for a serum autoantibody known as antineutrophil cytoplasmic antibodies (ANCA).

MICROSCOPIC FEATURES

The granulomatous tissue surrounding the defects is infiltrated with mononuclear cells and a foreign-body type of multinucleated giant cell. Scattered eosinophils are occasionally observed. The sine qua non of the histomorphologic findings is the presence of necrotizing vasculitis. Special stains fail to disclose the presence of specific bacterial or fungal microorganisms.

DIFFERENTIAL DIAGNOSIS

The palatal perforation and midfacial destructive lesions of these granulomatous inflammations must be differentiated microscopically from malignant reticulosis, gummatous necrosis, mucormycosis, and antral carcinoma.

TREATMENT

Wegener's granulomatosis is potentially lethal if left untreated. It is treated with immunosuppressive drugs such as high-dose steroids, azathioprine, and cyclophosphamide and should be managed by a physician.

Additional Reading

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Edwards MB, Buckerfield JP. Wegener's granulomatosis: a case with primary mucocutaneous lesions. *Oral Surg Oral Med Oral Pathol.* 1978;46:53.

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EXTRANODAL NK/T-CELL LYMPHOMA

Figure 4-33

Age: Young adults
Sex: Males

CLINICAL FEATURES

Midline lethal granuloma is a midface osseous destructive process that can be seen in Wegener's granulomatosis and polymorphic reticulosis, now termed extranodal NK/T-cell lymphoma, nasal type. In the latter, the disease is more often seen in Asia, Mexico, and Central America. The malignancy causes nasal obstruction and epistaxis and evolves into a destructive lesion that erodes the midface structures as invasion and extension into the nasopharynx, paranasal sinuses, orbit, and oral cavity. Distant metastases ultimately evolve, and additional symptoms appear such as fever, malaise, and weight loss.

MICROSCOPIC FEATURES

The lymphomatous infiltrate tends to be angiocentric and angiodestructive. The cells are small yet admixed with large and oftentimes anaplastic lymphoblasts. The nuclei are granular without prominent nucleoli. In many cases, the malignant infiltrate is joined by normal inflammatory cells. The immunohistochemical profile shows positivity for CD56, CD2, and granzyme B.

DIFFERENTIAL DIAGNOSIS

Wegener's is the chief entity in the differential diagnosis, yet trauma, cocaine abuse, other malignancies, and invasive fungi are also considerations.

TREATMENT

Extranodal NK/T-cell lymphomas are managed by radiation therapy and chemotherapy combined. Prognosis is variable with potential for wide dissemination.

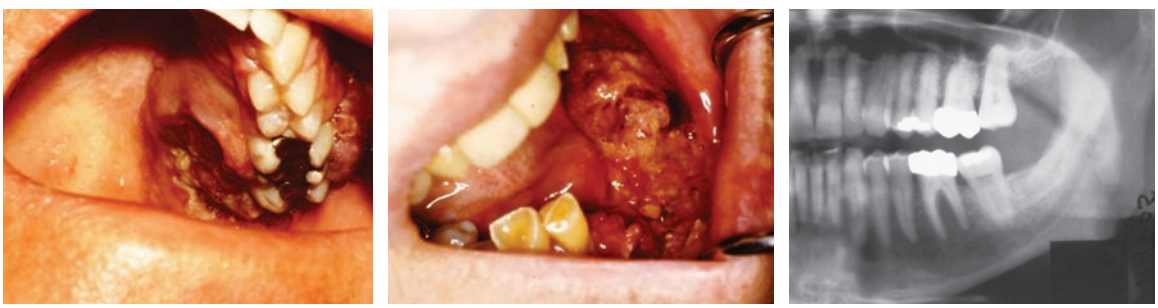

FIGURE 4-33
Osseous destructive ulcers in lymphoma (NK/T cell nasal type, large B cell lymphoma, central lymphoma of bone).

Additional Reading

Avilés A, Díaz NR, Neri N, Cleto S, Talavera A. Angiocentric nasal T/natural killer cell lymphoma: a single centre study of prognostic factors in 108 patients. *Clin Lab Haematol.* 2000;22:215-220.

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Harabuchi Y, Takahara M, Kishibe K, Moriai S, Nagato T, Ishii H. Nasal natural killer (NK)/T-cell lymphoma: clinical, histological, virological, and genetic features. *Int J Clin Oncol.* 2009;14:181-190.

Kim J, Kim EY, Lee SK, et al. Extranodal nasal-type NK/T-cell lymphoma: computed tomography findings of head and neck involvement. *Acta Radiol.* 2010;51:164-169.

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TERTIARY SYPHILIS

Figure 4-34

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Gummatous necrosis of the oral tissues frequently involves the palate. The gumma is rubbery with necrotic rolled margins and often sloughs, leaving a relatively clean, vacant perforation of the palate. After a course of antibiotic therapy, large masses of necrotic tissue may be lost (Herxheimer's reaction). Other signs of tertiary syphilis are encountered: psychotic behavior with delusions of grandeur, luetic glossitis, other foci of gummatous necrosis, aortic aneurysm, peripheral neuropathy, and tabes dorsalis. The VDRL is positive at this late stage; however, the lesions are essentially noninfective.

MICROSCOPIC FEATURES

The tissue adjacent to the zone of palatal perforation shows foci of eosinophilic necrotic aggregates, and the surrounding granulation tissue evinces a mononuclear inflammatory cell infiltrate. Treponemal organisms are usually not demonstrable.

DIFFERENTIAL DIAGNOSIS

Palatal perforation by syphilitic gumma may be confused clinically with Wegener's granulomatosis, midline lethal granuloma, malignant reticulosis, mucormycosis, and antral carcinoma. Other clinical signs and symptoms that aid in arriving at a diagnosis of syphilis are usually present. A VDRL serologic evaluation should be obtained.

TREATMENT

Tertiary syphilis should be managed by a physician because many of its ramifications involve various organ systems.

Additional Reading

Bains MK, Hosseini-Ardehali M. Palatal perforations: past and present. Two case reports and a literature review. *Br Dent J.* 2005;199:267-269.

Gaikwad AV et al. Syphilitic palatal perforation and rehabilitation denture. *J Indian Dent Assoc.* 1986;58:461.

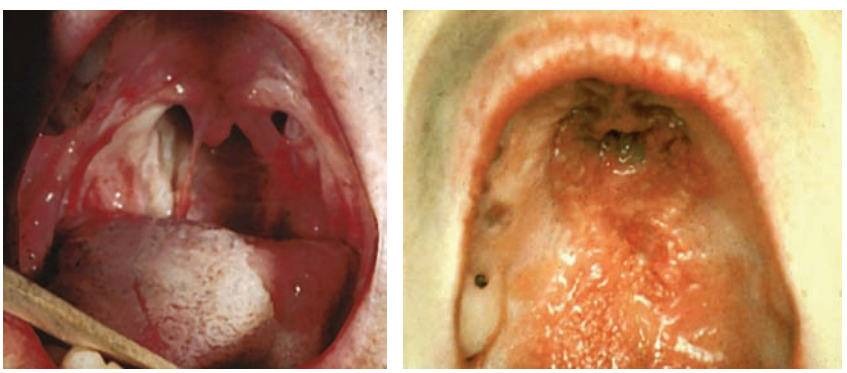


FIGURE 4-34
Gummatous necrosis in tertiary syphilis.

Huebsch RF. Gumma of the hard palate with perforation. *Oral Surg Oral Med Oral Pathol.* 1955;8:690.
Meyer I, Shklar G. The oral manifestations of acquired syphilis. *Oral Surg Oral Med Oral Pathol.* 1967;23:45.
Penneau M et al. Syphilitic necrosis of the incisive bone. *Rev Stomatol Chir Maxillofac.* 1980;81:392.

OSTEORADIONECROSIS

Figure 4-35

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Patients who have received cancericidal radiation to the jaws experience a vascular derangement in the osseous tissues that severely compromises the inflammatory defense of the tissue to the onslaught of infection. Odontogenic or periodontal infection may become rampant and spread quickly through the bone. The mandible is more susceptible than the maxilla. Oral fistulae develop in the involved area, with sequestration of large fragments of necrotic bone. Indeed, the entire alveolar ridge may show ulceration and drainage with exposure of nearly one half the mandible. Lesions are usually exudative with a foul odor. Pain is invariably present. Radiographically, moth-eaten radiolucencies with opaque sequestra are observed. The risk of developing osteoradionecrosis is less with newer supravoltage radiation sources such as the linear accelerator, betatron, and cobalt-60 machines.

MICROSCOPIC FEATURES

The soft tissues display necrosis with an acute or subacute inflammatory cell infiltrate. The osseous tissue lacks lacunar osteocytes; the marrow spaces contain necrotic debris, microbial colonies, and a neutrophilic infiltrate not unlike nonspecific acute osteomyelitis.

DIFFERENTIAL DIAGNOSIS

Because osteoradionecrosis is located chiefly in the mandible, it is not likely to be confused with the other osseous destructive draining lesions included in this section. At any rate, a history of radiation therapy in excess of 6000 rad confirms a diagnosis of osteoradionecrosis. Recurrent tumor in the area must be ruled out by biopsy when tumefaction surrounds or infiltrates the involved osseous tissue.

TREATMENT

Sequestra should be carefully removed and the area debrided. When extensive areas of necrosis are present, surgical intervention

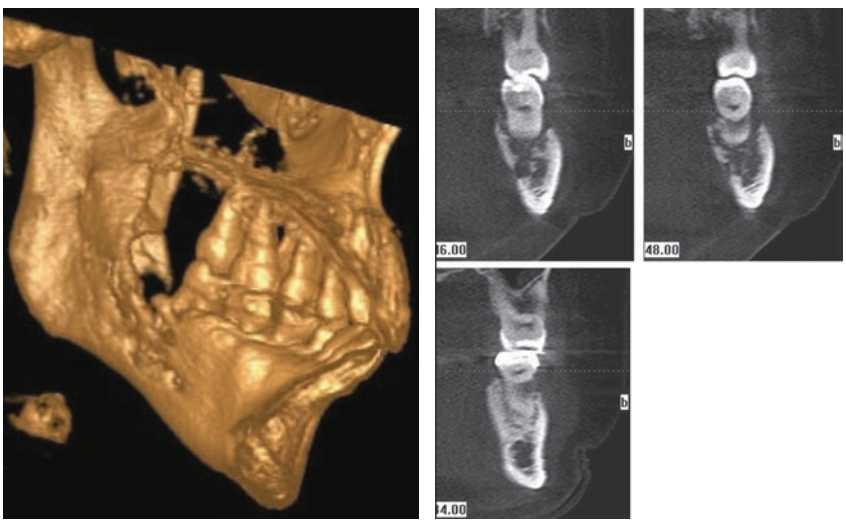


FIGURE 4-35
Osseous sequestrum in a patient who received radiation for a mandibular alveolar ridge squamous cell carcinoma.

should be delayed. The patient requires hospitalization with supportive care and intravenous antibiotic therapy. Hyperbaric oxygen therapy has been shown to be effective in facilitating healing in some cases. Prevention is the key to management. All pulpally or periodontally infected teeth should be extracted or treated before radiation; posttherapeutically, a strict oral hygiene program should be instituted with inclusion of daily topical application of fluoride gels to the remaining dentition.

Additional Reading

Cook HP. Tooth extraction and radiation therapy of the mouth. *Br Dent J.* 1966;120:372.
Hart GB, Mainous EG. The treatment of radiation necrosis with hyperbaric oxygen (OHP). *Cancer.* 1976;37:2580.
Jacobson AS, Buchbinder D, Urken ML. Reconstruction of bilateral osteoradionecrosis of the mandible using a single fibular free flap. *Laryngoscope.* 2010;120:273-275.
Motila E, Westerholm N. Osteoradionecrosis of the jaw. *Odontol Tidskr.* 1965;73:239.
Silverman S, Jr. Radiation effects. *Oral Cancer.* New York, The American Cancer Society; 1981:66.

MUCORMYCOSIS

Figure 4-36

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

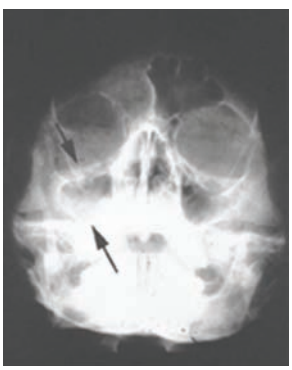
Mucormycosis is an infection caused by one of the phycomycetes and is not pathogenic unless the patient is suffering from debilitating illness. Patients with diabetes or widespread lymphoma and those receiving antitumor chemotherapeutic agents are the most frequent sufferers. The antrum is usually the site of origin of the infection. As the antrum becomes progressively eroded by necrotic and granulation tissues, perforation ensues with osseous destruction and oroantral fistula formation. Anesthesia or paresthesia of the second division of the trigeminal nerve frequently occurs. The infected antrum is opacified on panoramic or Water's sinus radiographs, and evidence of bony erosion of the antral walls can be visualized, especially on tomograms. Aspergillosis may manifest features identical to those of mucormycosis when the antrum is involved.

MICROSCOPIC FEATURES

The granulation and necrotic tissues contain colonies of large hyalinized basophilic hyphae that are devoid of septae. Inflammatory cells, chiefly neutrophils and eosinophils, prevail in the granulation tissue that is located peripheral to widespread zones of necrosis. Vascular invasion by the microorganism is common and results in ischemic necrosis with infarction.

DIFFERENTIAL DIAGNOSIS

Palatal osseous destructive lesions of mucormycosis may simulate nonspecific oroantral fistula, midline lethal granuloma,



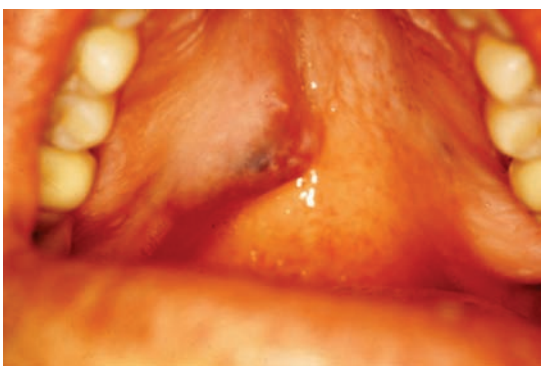


FIGURE 4-36
Necrotic osseous destruction of the palate in antral mucormycosis.

Wegener's granulomatosis, and malignant disease. A history of diabetes should arouse suspicion of mucormycosis. Biopsy discloses the presence of the infectious agent.

TREATMENT

Because mucormycosis is a secondary invader, the underlying medical illness must be treated concurrently with the infection. Intravenous administration of amphotericin B is the treatment of choice.

Additional Reading

Blitzer A et al. Patient survival factors in paranasal sinus mucormycosis. *Laryngoscope.* 1980;90:635.

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Rapidis AD. Orbitomaxillary mucormycosis (zygomycosis) and the surgical approach to treatment: perspectives from a maxillofacial surgeon. *Clin Microbiol Infect.* 2009;15(suppl 5):98-102.

Savetsky L, Waltner J. Aspergillosis of the maxillary antrum. *Arch Otolaryngol Head Neck Surg.* 1961;74:695.

Taylor CG et al. Mucormycosis (polycomycosis) involving the maxilla. *Oral Surg Oral Med Oral Pathol.* 1969;27:806.

ANTRAL CARCINOMA

Figure 4-37

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Cancer of the maxillary sinus develops insidiously and is extensive when perforation of bone occurs. The carcinoma may extend and perforate through any of the antral walls. The palate is a frequent site, with formation of osseous destructive zones rimmed by necrotic tissue. Tumefaction may herniate through the perforation; however, the oroantral communication is more often a simple ulcerated perforation. The malar skin often shows erythema with facial swelling. Displacement of the nasal septum and globe is also frequently encountered. Second-division anesthesia or paresthesia is a frequent symptom. Water's sinus, panographic, and antral tomograms show opacification and osseous destruction of the sinus walls.

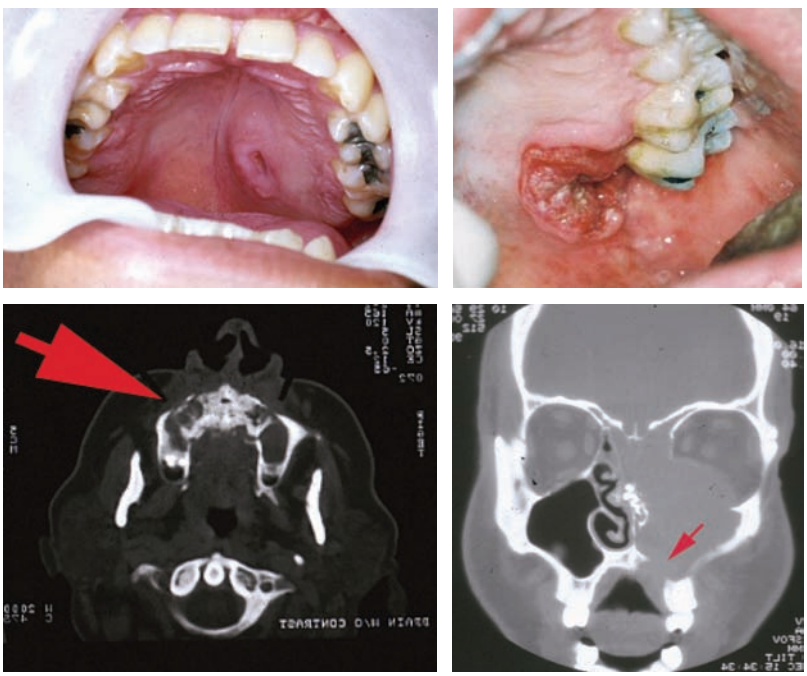

FIGURE 4-37
Ulceration and palatal destruction in antral carcinoma.

MICROSCOPIC FEATURES

Tissue removed from around the site of perforation shows infiltrating islands, cords, and nests of tumor cells. Their morphologic characteristics vary from squamous to adenomatous differentiation. Metastatic tumors and sarcomas may also arise in the antrum and invade the palate.

DIFFERENTIAL DIAGNOSIS

When antral carcinoma extends into the oral cavity with palatal perforation, other osseous destructive lesions including midline lethal granuloma, syphilitic gumma, and mucormycosis must be considered in the differential diagnosis.

TREATMENT

Antral carcinoma carries an extremely poor prognosis. It is treated surgically, radiotherapeutically, or with a combination of the two, and should be managed by an oncologist.

Additional Reading

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Huang JS, Kok SH, Lee JJ, Hsu WY, Chiang CP, Kuo YS. Extensive maxillary sequestration resulting from mucormycosis. *Br J Oral Maxillofac Surg.* 2005;43: 532-534.

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Merrick RE, Rhone DP, Chilis TJ. Malignant fibrous histiocytoma of the maxillary sinus. *Arch Otolaryngol Head Neck Surg.* 1980;106:365.

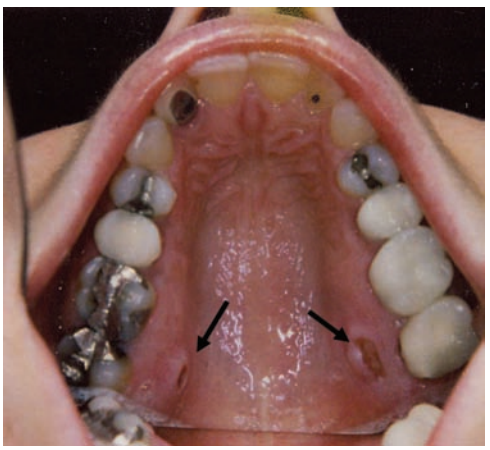
BISPHOSPHONATE-RELATED OSTEONECROSIS OF THE JAWS

Figure 4-38

Age: Elderly
Sex: No predilection

CLINICAL FEATURES

Patients with metastatic bone disease, melanoma, and generalized osteoporosis are often treated with intravenous bisphophonates such as zoledronate and pamidronate in order to increase bone mass. A subpopulation of these subjects develop osteonecrosis of the jaws. Recently, patients taking oral preparations of bisphosphonates have also developed sequestrating lesions, usually in the mandible, yet also in the palate and maxillary alveolus. Prior trauma or extractions are reported in many of these patients, yet a significant proportion develop the condition without any provocation. The lesions are painful and ulcerative without significant tumefaction, and at the time of examination, sequestra can be seen in the base of the ulcers. Radiographs disclose



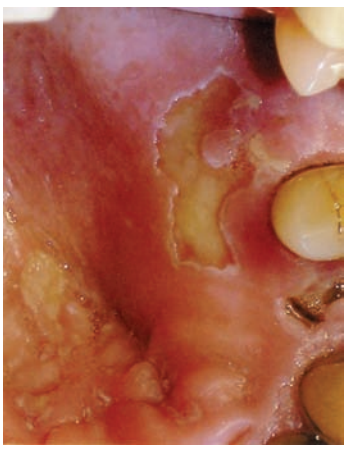


FIGURE 4-38
Ulceration and exposure of underlying bone in bisphosphonate-related osteonecrosis of the jaws.

irregular, ragged opacities usually surrounded by a resorptive radiolucency. The risk for developing osteonecrosis while taking bisphosphonates can be quite reliably predicted by ordering serum C-terminal telopeptide (CTX). High levels are indicative of decreased risk for jaw necrosis (150 pgm/ml).

MICROSCOPIC FEATURES

Nonvital trabeculae show lacunae devoid of osteocyte nuclei with adherent microbial colonies. Many of the colonies are PAS positive with a peripheral fringe and peripheral neutrophils typical for actinomycotic organisms.

DIFFERENTIAL DIAGNOSIS

Sequestra of other etiologies must be considered in the differential diagnosis, including odontogenic osteomyelitis, trauma, intubation, if lesions are located on the posteriorlingual mandibular mucosa and postradiation osteonecrosis to mention a few.

TREATMENT

Systemic antibiotics, sequestrectomy with gentle nonaggressive debridement, and betadine rinses are recommended along with bisphosphonate withdrawal.

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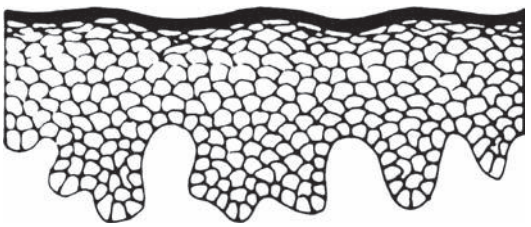
a



Normal mucosa

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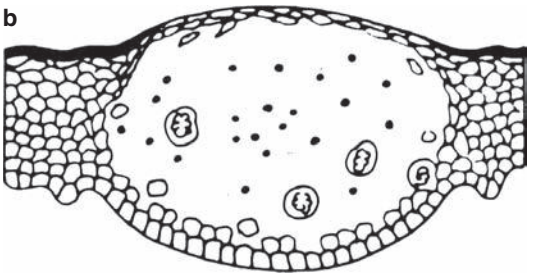

Intraepithelial viral vesicle

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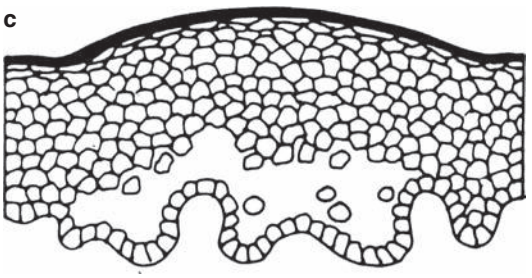

Suprabasilar bulla

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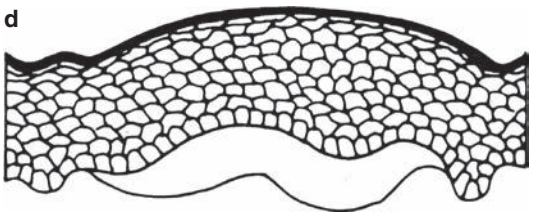

Sub-basilar bulla

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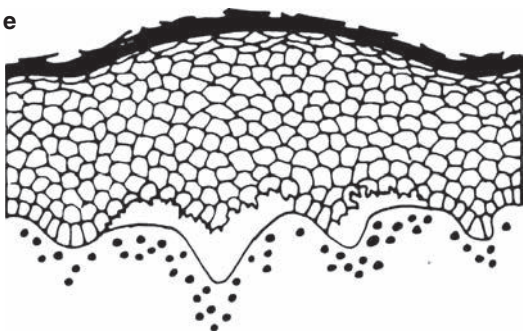
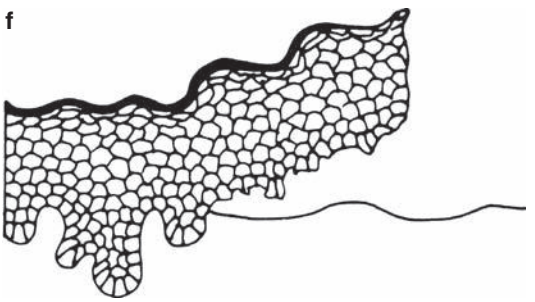


Intrabasilar bulla

f



Erosion desquamation

Vesiculobullous Lesions

Vesiculobullous and Desquamative Lesions

5

Vesicles are fluid-filled blisters measuring less than 5 mm; bullae are blisters in excess of 5 mm. On skin, vesicles and bullae are bleb-like and tense. In the oral cavity, both vesicles and bullae are more flattened, with a smooth gelatinous surface. Because of chronic masticatory forces and a less rigid epithelial surface, oral vesicles and bullae are prone to rupture, leaving ulcerative and desquamative lesions later in the course of disease. When ulcers, erosions, and desquamations are observed in the mouth, a search should be made to detect intact fluid-filled surface lesions; the history should be investigated for indications that the early lesions were blister-like from onset.

When attempting to differentiate between a disease that is primarily vesicular and one that is bullous, the size of the individual lesions is the key to diagnosis. One must, however, be cognizant of the fact that vesicles often cluster together and may appear bullous. Furthermore, a tendency for clustering of vesicles in a localized area is most suggestive of herpesvirus infection.

The vesicular diseases are primarily infectious and, specifically, most are the result of assault by viral organisms that propagate in epithelial cells and are harbored as dormant virus in sensory nerve ganglion nuclei. Of utmost importance in arriving at a definitive diagnosis is evaluation of the patient's temperature. For this reason, vesicular eruptions of the mouth have been divided into those associated with elevated temperature and those in which the patient is afebrile. The latter group may occasionally manifest mild elevation in temperature; if detected, it is invariably less than 100°F. When viral infections are suspected, a cytologic smear of intact vesicular contents often reveals the presence of viral-specific nuclear ballooning degeneration or inclusion bodies. The specific diagnosis of viral vesicular eruptions is obtained by observing the pattern of distribution of the lesions. These features are enumerated for each entity.

The bullous dermatoses are skin diseases characterized by bulla formation. All of the diseases included here manifest precedent or coexistent oral bullae. One disease, benign mucous membrane pemphigoid (BMMP), is limited to the mucous membranes. The bullous lesions themselves may appear identical from one disease to the next. Biopsy is mandatory to arrive at a definitive diagnosis in most patients. Some of the entities in this group show specific site distributions or are accompanied by skin manifestations that evince a diagnostic pattern or configuration. These features are detailed in the text. An immunopathogenesis underlies the mechanism of bulla formation in most of these disorders. Some of these diseases are T–cell–mediated, whereas others are antibody-mediated autoimmune processes.

A final group of disorders in this chapter include those in which large areas of epithelial detachment occur. Bullae do not form; rather, diffuse zones of sloughing or desquamation ensue and are often accompanied by intense erythema.

The most common vesicular diseases are primary herpetic gingivostomatitis and secondary herpes labialis. Frequent recurrences of shingles may accompany underlying malignant lymphoma.

Most of the bullous dermatoses are rare. Erythema multiforme is the most common disease in this group. Pemphigus vulgaris and certain forms of epidermolysis bullosa are potentially lethal.

All three diseases included with the desquamative group are relatively common, erosive lichen planus being most prevalent. None is lethal.

Febrile-Associated Vesicular Eruptions

HERPETIC GINGIVOSTOMATITIS

Figure 5-1

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Primary infection with herpesvirus hominis type 1 of the oral cavity is characterized by multiple vesicular eruptions located on the attached gingiva and movable musosa, chiefly the lips and buccal mucosa. Type 2 herpesvirus can also cause primary herpetic gingivostomatitis, being transmitted by either oral-oral or genito-oral routes. Regardless of the genotypic forms of herpes simplex, the clinical manifestations are identical. The vesicles rapidly rupture, leaving a raw or white pseudomembranous erosion. Erythema surrounds the vesicular and ulcerative zones. The oropharynx is involved only occasionally. The lesions are painful, and eating is a significant problem. The temperature is elevated and may approach 103 to 104°F. Constitutional symptoms of inflammatory disease, including malaise and cervical lymphadenopathy, are present. The disease is contagious; however, most individuals exposed to it are either already immune or suffer only subclinical manifestations, such as transient fever. During the course of infection, antiherpes antibody titer is elevated. The disease runs its course in 10 to 14 days, and healing develops without scar formation. Rarely, complications develop, particularly in debilitated children and infants. The Pospischill-Feyrter syndrome and Kaposi's varicelliform eruption are disseminated herpes infections that are

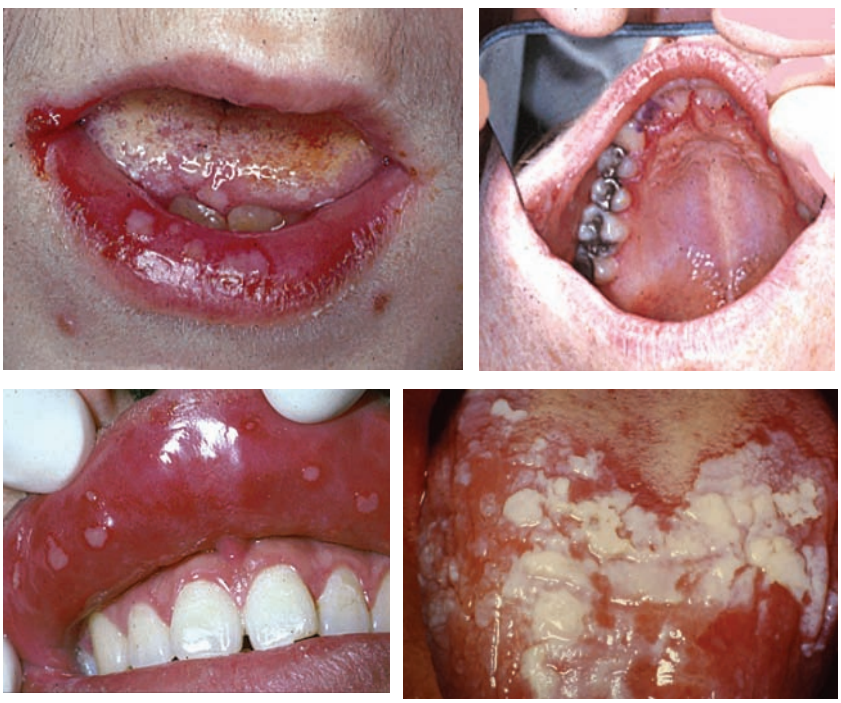


FIGURE 5-1
Marginal gingivitis with ulceration accompanied by small vesicles with erythematous halos that rapidly desquamate to yield ulcers in primary herpetic gingivostomatitis.

potentially lethal. Herpesvirus infections may also occur on the facial skin and conjunctiva. Contact with infected patients by dentists and oral health auxiliary personnel who have never been exposed to the disease may result in herpetic whitlow, a viral dermatitis of the finger.

MICROSCOPIC FEATURES

Intraepithelial vesicle formation is seen with necrotic exudate and a neutrophilic infiltrate. Eosinophilic inclusion bodies (Lipschütz bodies) in the vesicular space are accompanied by epithelial cells showing nuclear ballooning degeneration. Immunoperoxidase staining with type-specific antisera helps to differentiate types 1 and 2, provided the lesion is sampled before day 4 of the infection. These viral infection-specific changes are not obvious in ulcerated vesicles.

DIFFERENTIAL DIAGNOSIS

The vesiculoulcerative lesions of herpes are often confused with recurrent aphthae. Aphthae are not associated with a highly elevated temperature, and there is a history of recurrent episodes. Herpetic gingivostomatitis does not recur intraorally, with the exception of recurrent herpetic stomatitis, which usually manifests microvesicles localized unilaterally on the palatal gingiva. Primary herpes can be differentiated from coxsackievirus infections on the basis of lesional distribution, the latter being localized to the oropharynx. Shingles, seen in older individuals and with unilateral lesions, can be ruled out on the basis of age and distribution. The gingival lesions of primary herpes can be confused with acute necrotizing ulcerative gingivitis; however, the latter fails to show vesicles on nongingival mucosa.

TREATMENT

Supportive care consists of prescribing a soft diet: milkshakes, baby foods, and liquids. Aspirin reduces fever and pain. A soothing mouth rinse composed of equal parts of an antihistamine elixir with Kaopectate is useful in adults. One percent viscous lidocaine is recommended for children. Acyclovir therapy shortens the duration of disease. Severe orofacial herpes infections may develop in immunocompromised patients; in such instances, treatment with acyclovir is recommended. Although this antiviral medication is beneficial, an acyclovir-resistant mutant organism that escapes treatment may evolve. Preliminary animal studies indicate that chlorhexidine rinses may be virocidal.

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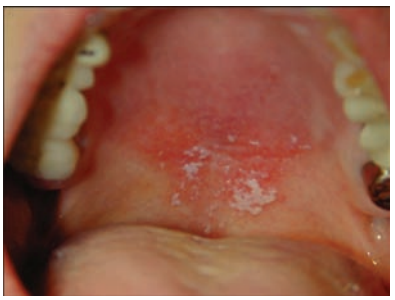
HERPANGINA

Figure 5-2

Age: Children
Sex: No predilection

CLINICAL FEATURES

Infection with Group A coxsackieviruses and enterovirus 71 (EV-71) may produce herpangina. The disease is limited to the oropharynx with vesicles located primarily on the soft palate and faucial pillars. Extension anteriorly is rare. The lesions are pain-



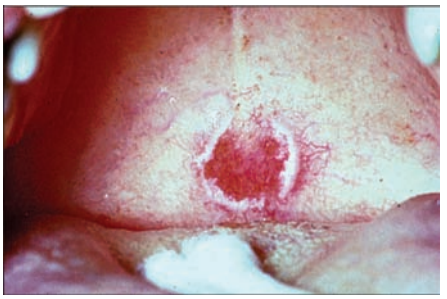


FIGURE 5-2
Multiple erythematous vesicles limited to the soft palate and oropharynx in herpangina, a coxsackievirus infection.

ful and are accompanied by generalized oropharyngitis evidenced by erythema of the throat. The vesicles tend to cluster and become ulcerated 3 to 4 days after onset. Fever, malaise, lymphadenitis, headache, and sore throat develop. The disease shows an incubation period of 1 week or less and runs its course in the same amount of time. Meningitis is a complication but is usually self-limited. The disease is contagious, and outbreaks among school-age children are common. EV-71, more often encountered in Asian countries, may also cause severe neurologic damage when it infects the CNS.

MICROSCOPIC FEATURES

Intraepithelial vesicles contain an eosinophilic exudate, and nuclear ballooning degeneration of epithelial cells is a feature.

DIFFERENTIAL DIAGNOSIS

Herpangina must be differentiated from infection by herpesvirus and varicella-zoster virus and, when ulceration predominates, from aphthae. The limitation of lesions to the soft palate/faucial region is essentially diagnostic. Virus may be retrieved from stool specimens by tissue culture techniques.

TREATMENT

A palliative oral rinse, such as an antihistamine elixir mixed 50:50 with Kaopectate, is advised. Soft diet and antipyretics are recommended as well.

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HAND-FOOT-AND-MOUTH DISEASE

Figure 5-3

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Group A coxsackieviruses and enterovirus 71 are responsible for the vesicular eruption of hand-foot-and-mouth disease with EV-71 more often encountered in Asia. The disease is more often seen in spring and summer in preschool and school children and is mildly contagious. The distribution of lesions is pathognomonic in that, after a short incubation period, vesicles with an erythematous halo appear in the oral cavity, on the hands, and on the feet. The oral lesions are located primarily on the lips and buccal mucosa,

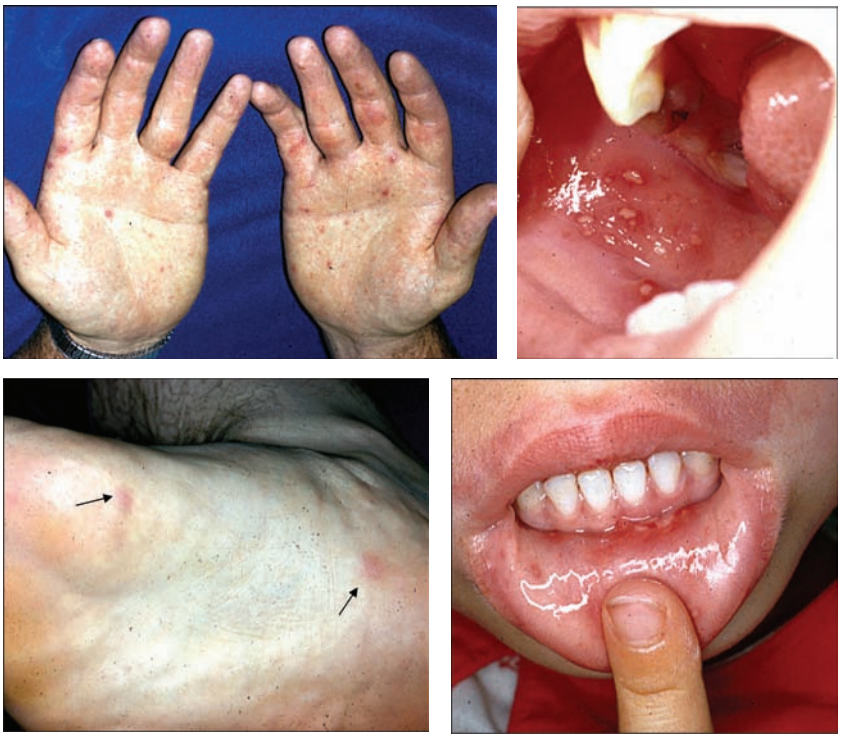

FIGURE 5-3
Hand-foot-and-mouth disease, caused by a coxsackievirus and showing vesiculoulcerative lesions of the oral mucous membranes accompanied by a vesicular eruption of the hands and feet.

sparing the oropharynx. Within 24 to 48 hours, the oral vesicles rupture, leaving erosions or ulcerations with a white or grey pseudomembrane. The extremity lesions are limited to the skin below the knees and elbows, are vesicular with circumferential erythema, and are located on both dorsal and ventral surfaces of the hands and feet. All lesions are painful, and constitutional signs of infection include elevated temperature, malaise, and lymphadenopathy. EV-17 may also cause encephalitis.

MICROSCOPIC FEATURES

Intraepithelial vesicles are seen in the early stages with intracytoplasmic eosinophilic inclusion bodies. Later stages are characterized by shallow ulcerations and erosions with regeneration of the marginal epithelium. A superficial inflammatory cell infiltrate is present in the submucosa.

DIFFERENTIAL DIAGNOSIS

The oral vesiculoulcerative lesions are similar to those encountered in herpetic gingivostomatitis, herpangina, varicella, and aphthous stomatitis. The distribution of lesions in hand-foot-and-mouth disease is diagnostic and eliminates these other entities from consideration. Coxsackie virus can be cultured from stool specimens.

TREATMENT

Antipyretic-analgesics, soft or liquid diet, fluids, and a soothing oral rinse such as an antihistamine elixir mixed 50:50 with Kaopectate are recommended. Viscous lidocaine may be used in small children.

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PRIMARY VARICELLA-ZOSTER (CHICKENPOX)

Figure 5-4

Age: Children
Sex: No predilection

CLINICAL FEATURES

Chickenpox is a dermal vesicular exanthem caused by the varicella-zoster virus. The incubation period lasts 2 to 3 weeks. The lesions are located primarily on the trunk and face, are vesicular with an erythematous boundary, and are extremely pruritic. Fever, malaise, and mild generalized lymphadenopathy are present. Oral manifestations are common, with early onset of vesicles that rapidly rupture and leave erosions with a surface pseudomembrane. These lesions are limited in extent. The palatal mucosa is the predominant oral location. The lesions resolve within 5 to 8 days. Most childhood vaccines include varicella-zoster such that the disease is rarely encountered now in developed countries. Nevertheless, many adults who contracted chickenpox during childhood harbor latent VZV in ganglia and may develop shingles.

MICROSCOPIC FEATURES

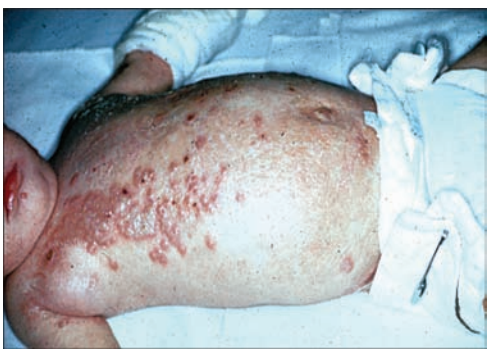
Superficial intraepithelial vesicle formation is present. The vesicular contents contain eosinophilic exudate, inflammatory cells, and epithelial cells. Nuclear ballooning degeneration is a feature. A superficial submucosal inflammatory cell infiltrate is discernible.

DIFFERENTIAL DIAGNOSIS

Oral vesiculoulcerative lesions of chickenpox resemble those of herpes, the coxsackieviruses, and aphthae. The skin lesions predominate and must be differentiated from smallpox and Kaposi's varicelliform eruption, the latter caused by dermatotrophic herpevirus. Antibody titers to varicella-zoster are elevated.

TREATMENT

Although complications are rare, it is nevertheless recommended that children with chickenpox be under the care of a pediatrician. Oral lesions may be treated palliatively with viscous lidocaine.



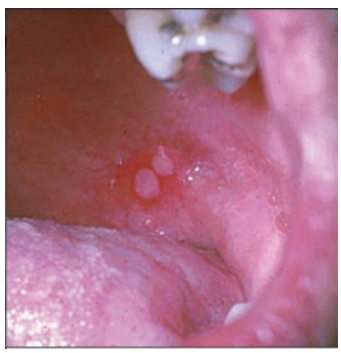


FIGURE 5-4
Focal vesicles seen in the mouth, usually the soft palate area in children with the typical dermal vesicular exanthem of chickenpox.

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SECONDARY VARICELLA-ZOSTER (SHINGLES)

Figure 5-5

Age: Adults and elderly people
Sex: Slight male predilection

CLINICAL FEATURES

Shingles is caused by reactivation of varicella-zoster virus and may be conceptualized as a recurrent form of chickenpox. In the secondary or recurrent form, it is neurodermatropic. The virus propagates within ganglia, and the vesicular eruption follows the distribution of sensory nerves, being segmental and unilateral. Prodromal neuralgia is followed by clustered vesicular eruptions. Although the thoracic and abdominal nerves are most frequently involved, the mucosa supplied by the second or third division of the trigeminal nerve may be the site of infection if the virus is harbored and propagated within the Gasserian ganglion. The vesicles are unilaterally distributed, stop at the midline, and are extremely painful. Patients experiencing multiple recurrent episodes of shingles have been shown to be at risk for lymphoma, leukemia, and carcinomatosis; a single episode does not connote any increased risk for malignancy. After healing of shingles, postherpetic neuralgia may develop. The disease has a 1- to 3-week incubation period, and the vesicular stage may persist for 1 to 5 weeks. Constitutional signs of infectious disease, including elevated temperature, malaise, and lymphadenitis, are apparent.

When trigeminal shingles occurs in young males, underlying human immunodeficiency virus (HIV) infection should be suspected. Indeed, any individual considered to be at risk for AIDS showing classic clinical features for shingles should be evaluated serologically for HIV infection.

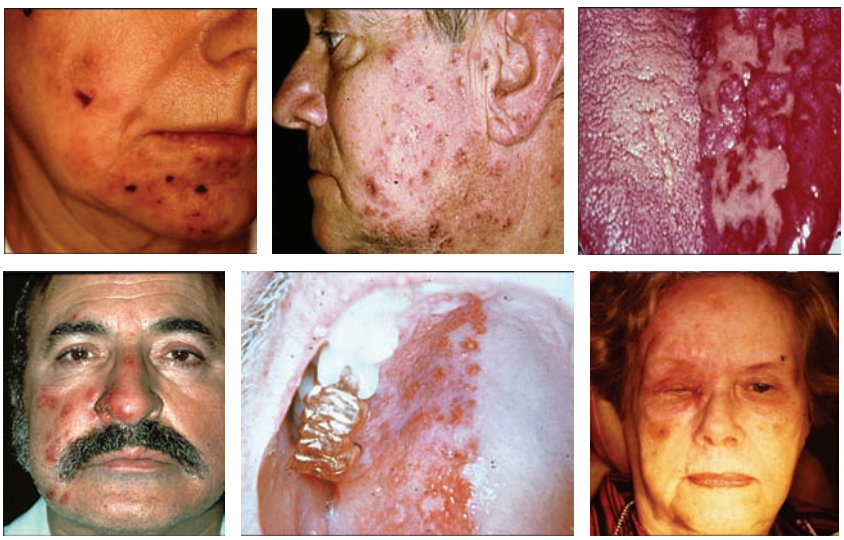

FIGURE 5-5
Reactivation by the varicella-zoster virus, which causes shingles. The lesions begin as small vesicles that are unilateral, with a tendency to follow the sensory nerve pathways.

MICROSCOPIC FEATURES

The epithelium manifests intraepithelial vesicles with epithelial nuclear ballooning degeneration. The subjacent submucosa contains a mononuclear inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Oral vesiculoulcerative eruptions of shingles mimic those observed in herpesvirus, coxsackievirus, and aphthous stomatitis. Unilateral segmental distribution, prevalence in adults, and severe pain are features that allow for clinical differentiation. Antibody titers to varicella-zoster virus are elevated. Systemic malignancy should be ruled out.

TREATMENT

Varicella-zoster virus infections in the form of shingles restricted to the oral mucosa can be treated by prescribing soft or liquid diet, analgesic-antipyretic medication, and a palliative oral rinse such as an antihistamine elixir mixed with equal parts of Kaopectate. Definitive antiviral therapy with 1000 mg acyclovir should be initiated at the onset of the eruption. Should multiple recurrent episodes occur, referral to a physician or dermatologist is recommended; search for underlying lymphoma, leukemia, widespread cancer, or HIV infection must be undertaken.

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Nonfebrile-Associated Vesicular Eruptions

RECURRENT HERPES STOMATITIS

Figure 5-6

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Recurrent infection of the oral mucosa by herpesvirus hominis type 1 is uncommon. When it occurs, it is usually restricted to the palatal gingiva unilaterally and is characterized by the formation of microvesicles that rapidly rupture to leave small punctate ulcerations with a tendency to cluster. Even less common is the appearance of vesicles of the buccal mandibular gingiva in the vicinity of the mental foramen or the buccal maxillary gingiva and adjacent buccal mucosa. The lesions are slightly painful and persist for only 5 to 7 days. Fever and malaise are usually not present.

Importantly, HIV-infected patients are subject to recurrent orofacial herpetic infection, and such infections, although vesicular, do not always show the usual patterns.

MICROSCOPIC FEATURES

The epithelium contains small vesicles with epithelial nuclear ballooning degeneration. The submucosa displays a mild mononuclear inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Recurrent oral herpetic vesicular eruptions are distributed unilaterally and must be differentiated from the lesions of shingles. Because pain is not severe and resolution is rapid, the distinction can usually be

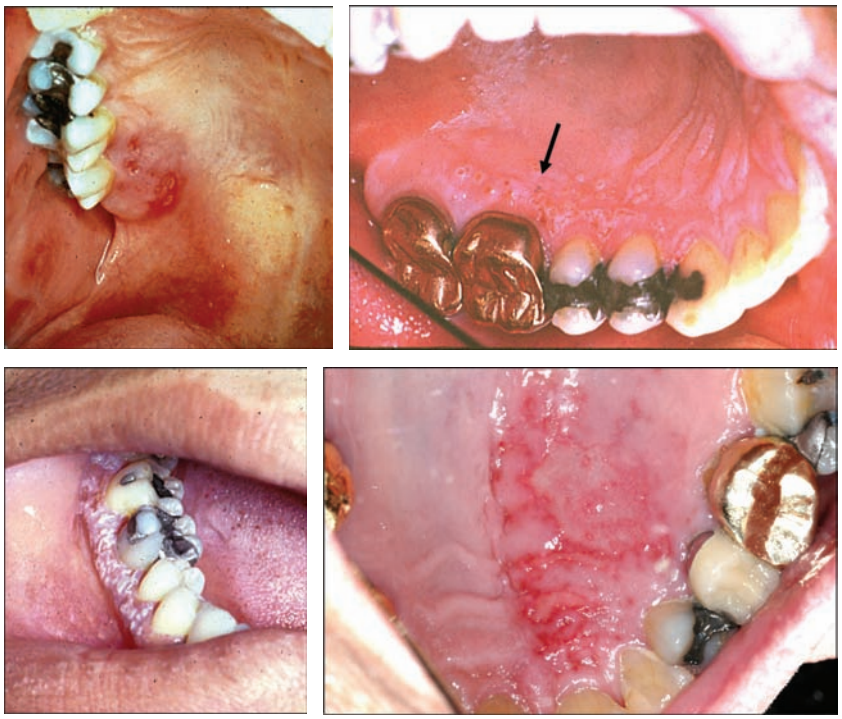

FIGURE 5-6
Clustered painful microvesicles, which quickly rupture in intraoral herpes. Most cases are located on the palatal gingiva but may also follow the distribution of the long buccal nerve.

made. Recall that the sine qua non for herpes simplex recurrent infection is clustering of vesicles, confined to a limited area of the mucosa. Antiherpes antibody titers are elevated during the course of infection. Differentiation from recurrent aphthae is not difficult; intraoral recurrent herpes lesions are microvesicles or tiny clustering punctate ulcerations of attached mucosa, whereas aphthae do not tend to involve mucosa fixed to bone. Herpetic lesions that fail to resolve within 4 weeks are highly suspected for HIV infection. Indeed, orofacial herpes persisting more than 30 days with HIV positivity fulfills the criteria for a diagnosis of AIDS.

TREATMENT

No treatment is necessary. Elective palliative mouth rinses may be employed. Alternatively, persistant herpes associated with AIDS should be treated with oral or intravenously administered acyclovir. In some patients, the lesions are nonresponsive and may require therapy with other antiviral agents.

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RECURRENT HERPES LABIALIS

Figure 5-7

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Recurrent infection of the lips by herpesvirus hominis type 1 is herpes labialis. Vesicles

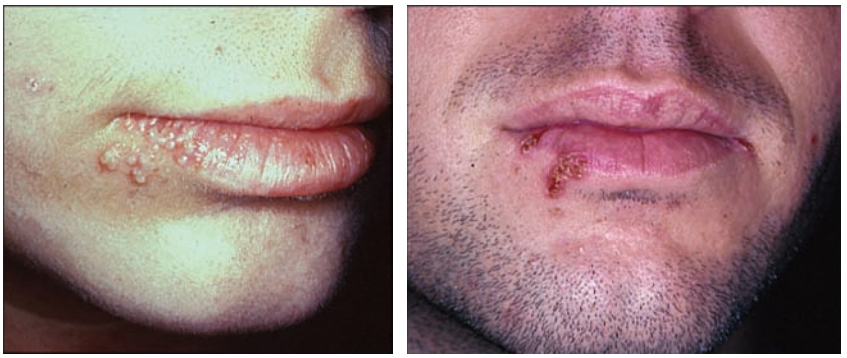

FIGURE 5-7
Vesicular eruptions of the lips with erythema and edema typically encountered in recurrent herpes labialis (cold sores). Early lesions (left), crust stage (right).

occur in clusters on the vermilion border and adjacent perioral skin of the lips. Edema, which may be severe, and erythema underlie the vesicles. The patient is usually afebrile. The vesicles are associated with pain. Because of their location, they are unsightly. The oral cavity is free of disease. Various factors trigger the infection, including trauma and sunlight (ultraviolet light) exposure, even though the patients possess antiherpes antibody. Evidence implicates a latent property to the virus, which may remain sequestered from the immune system by residing in ganglia. During latent periods, no symptoms or lesions are encountered.

As noted previously with regard to recurrent intraoral herpetic stomatitis, persistent herpes labialis may be indicative of an immunocompromised status, including HIV infection. In such instances, lesional involvement may be extensive.

MICROSCOPIC FEATURES

Cytologic smears of nonruptured vesicles disclose the presence of nuclear ballooning degeneration. Microscopic sections are represented by the presence of intraepithelial vesicles with the same cytologic changes already specified for primary herpes. The submucosa or dermis evinces an inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Recurrent herpes labialis shows vesicles that may be confused with impetigo or contact dermatitis. Focal clustering of lesions, history of trauma or sun exposure, tendency to occur in young adults, lack of linear streaking, and inability to correlate onset with contact by a potential allergen aid in eliminating these latter diseases from consideration. A cytologic smear of vesicular contents discloses the presence of viral-specific cytologic alterations.

TREATMENT

Photoactivated dye treatments are contraindicated in light of studies implicating carcinogenic transformation. Topical antiviral agents, including acyclovir and its analogues are marginally effective in clearing vesicles early. Alternatively, systemically administered acyclovir 400 mg taken daily will prevent the occurrence of the infection among patients who initially present with severe and frequent recurrences. Subsequent to rupture of the vesicles, a topical steroid cream with antibiotic can be applied. Steroid-antibiotic preparations can be combined with 1% anesthetics to achieve pain control. Caution should be taken not to prescribe steroid creams during the early infective stage of the disease (i.e., the first 3 to 4 days). Oral or intravenous acyclovir therapy is indicated in immunocompromised patients; even so, some individuals harbor thymidine kinase-resistant strains and may require other antiviral medications to control the disease. Prophylactic use of antiviral agents is recommended for

severely compromised patients (200 mg, 4 times daily taken orally).

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CONTACT VESICULAR STOMATITIS

Figure 5-8

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

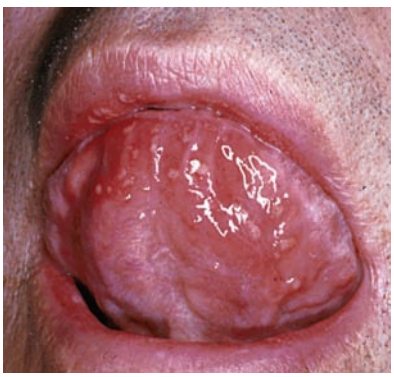
Immediate or humorally mediated immune reactions to allergens contacting the oral mucous membranes may manifest vesicle formation. The vesicles do not tend to cluster and are superimposed on a broad matted erythematous base. Pain or burning, rather than pruritus, is present. Vesicles arise in areas of allergenic contact and therefore are on perioral skin if cosmetics are the offending substances. Intraorally, various substances may elicit hypersensitivity responses in patients who are allergic. Specifically, mouthwashes, dentifrices, acrylic, topical antibiotics, and foods can be incriminated. Perhaps more frequently, oral allergic eruptions of the immediate type arise subsequent to a systemically introduced allergen such as shellfish, berries, or drugs. Allergic stomatitis is less common than atopic dermatitis. The lesions regress within 3 to 5 days, providing repeated contact with allergen is avoided.

MICROSCOPIC FEATURES

Intraepithelial vesicles are present. The vesicular contents are composed of an eosinophilic exudate and an acute inflammatory cell infiltrate composed of both neutrophils and eosinophils. The submucosa is traversed by dilated capillaries and is infiltrated with leukocytes.

DIFFERENTIAL DIAGNOSIS

The vesicular eruption of allergic mucositis may resemble primary herpes, hand-foot-and-mouth disease, and erythema multiforme. Because the patient is afebrile, this feature tends to eliminate the aforementioned diseases from the differential diagnosis. Questioning the patient with regard



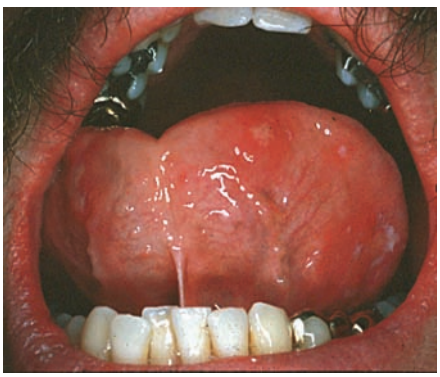


FIGURE 5-8
Multiple vesicles and small ulcers appearing as a manifestation of allergy to various mouth rinses, dentifrices, dental materials, foods, and drugs.

to the use of newly contacted materials or chemicals usually provides the necessary clue to the nature of the allergen. Those substances suspected of being allergenic may be applied to the mucosa for epimucous patch testing. This testing is accomplished by mixing suspected allergens with Orabase and applying to the mucosa. A positive reaction may be seen in 24 to 48 hours.

TREATMENT

Suspected contact allergens should be discontinued. Antihistamines, 50 mg diphenhydramine hydrochloride (Benadryl), or 12.5 mg promethazine hydrochloride (Phenergan), twice daily will effect an early resolution of vesicles and associated discomfort.

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IMPETIGO

Figure 5-9

Age: Children
Sex: No predilection

CLINICAL FEATURES

Impetigo is a vesicular eruption on the perioral skin and vermilion border. Oral mucosa is not affected. The lesions are caused by staphylococci or a mixed staphylococcal-streptococcal infection. They are painful and pruritic and, because the patient scratches the lesions, they are excoriated and eroded. Scratching causes implantation of organisms, so that a linear or serpentine configuration of vesicles occurs. The disease is contagious.

MICROSCOPIC FEATURES

Intraepithelial vesicles are engorged with neutrophils. The submucosa evinces a subacute inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Perioral vesicles of impetigo must be differentiated from those seen in recurrent herpes labialis and contact dermatitis. Involvement is usually more widespread with impetigo than with herpes, and the presence of linear tracks of vesicles is highly suggestive of impetigo. A cytologic smear of an intact vesicle rules out virus-specific cytologic changes.

TREATMENT

Topical application of bacitracin, neomycin, and polymyxin is recommended. Systemically administered penicillin (500 mg 4 times daily for 10 days) is recommended if lymphadenopathy or fever is present.

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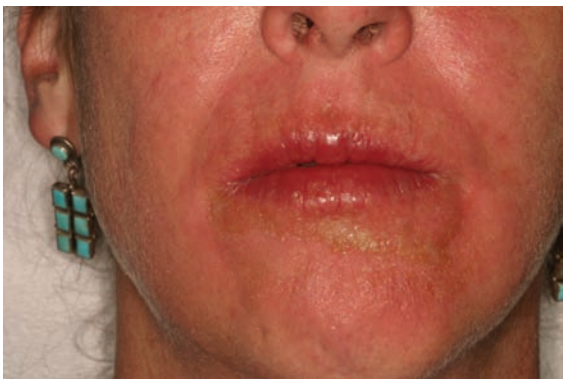

FIGURE 5-9
Excoriated clustering vesicles occurring in crops and linear streaks on the perioral skin in impetigo.

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Bullous Diseases

PEMPHIGUS VULGARIS

Figure 5-10

Age: Middle-aged and elderly adults
Sex: No predilection

CLINICAL FEATURES

Pemphigus vulgaris is an immunopathologic dermatologic disease characterized by bulla formation. Affected patients develop autoantibodies to a normal protein associated with cell-cell adhesion between keratinocytes. This antigen has been characterized electrophoretically. Oral lesions are invariably present at some time in the course of the disease and may actually precede the development of skin lesions in as many as 50% of the affected population. The oral bullae begin as bleb-like blisters or diffuse gelatinous plaques. Rupture of the bullae occurs within a few days, leaving broad areas of desquamation with associated erythema. The lesions are usually painful. Generalized desquamative lesions of the attached gingiva are commonly encountered. Rubbing uninvolved skin or mucosa may elicit the formation of a bullous lesion (Nikolsky's sign). Instances of pemphigus-like lesions have been reported to evolve subsequent to administration of certain drugs, particularly penicillamine. If left untreated, the disease may be fatal. Patients die of dehydration and septicemia through exposed denuded bullae of the skin.

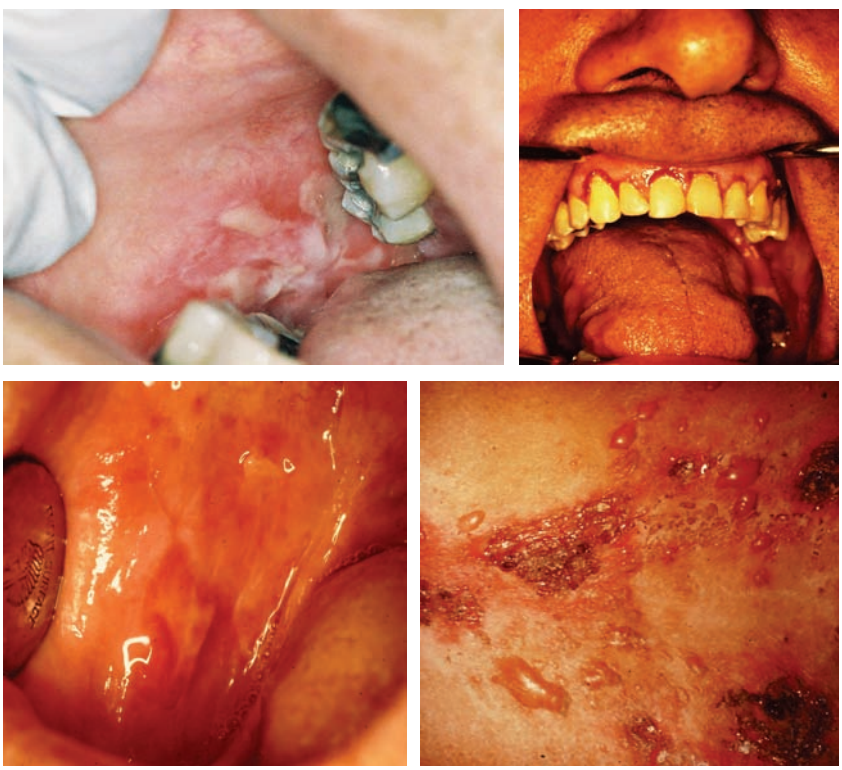

FIGURE 5-10
Bullous lesions accompanied by a desquamative gingivitis in pemphigus vulgaris.

MICROSCOPIC FEATURES

Biopsy should be performed on intact bullae when possible. The epithelium displays a suprabasilar cleft with round, smooth epithelial cells (acantholytic, Tzanck cells), found suspended in the bullous cavity. In vivo, bound immunoglobulins can be detected in the intercellular cement regions, and patients with active disease have circulating antibodies and complement directed to the desmosomal adhesion protein desmoglein 3. Direct immunofluorescence shows perikeratinocyte staining with IgG, IgM, and complement fraction 3 yielding a "fish net" pattern.

DIFFERENTIAL DIAGNOSIS

When only oral bullae are present, perphigus may be indistinguishable from the other bullous dermatoses listed in this section. A biopsy is required to confirm the diagnosis. Occasionally, pemphigus lesions are confined to the gingiva. If this is the case, gingivosis should be considered in the differential diagnosis.

TREATMENT

Pemphigus vulgaris should be treated by a general physician or dermatologist; high-dose, long-term systemic steroid therapy is required for control of the disease. With severe dermal involvement, fluid/electrolyte balance must be controlled and septicemia must be prevented. Levamisole in conjunction with prednisone allows for lower steroid dosage. Azathioprine with prednisone may be effective as well.

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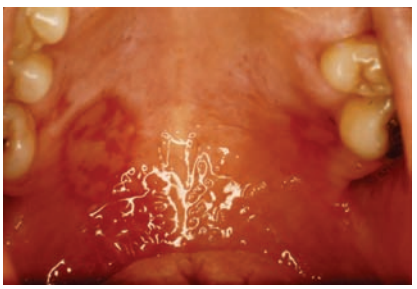
BULLOUS PEMPHIGOID

Figure 5-11

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Bullous pemphigoid is an immunopathologic bullous dermatosis characterized by bulla formation of skin. The antigen in bullous pemphigoid has been characterized and is a normal protein constituent of the hemidesmosome-basement membrane complex. Lesions are located primarily in the axillary and inguinal and abdominal regions. They begin as erythematous and eczematous plaques that ultimately prog-



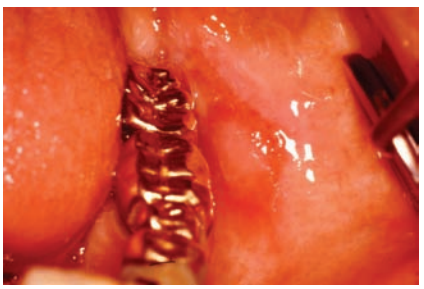


FIGURE 5-11
Bullous pemphigoid, a bullous dermatosis of skin occasionally accompanied by oral bullae.

ress to bullae. Occasionally, but not invariably, the oral mucosa is affected. The bullae are tense blebs or broad gelatinous plaques. As in the other oral bullous disorders, rupture with desquamation takes place shortly after the lesions appear. The disease is annoying yet not usually fatal; nevertheless, septicemia may be a complication. There is some evidence that patients with bullous pemphigoid accompanied by oral lesions are more likely to develop malignancies elsewhere in the body.

MICROSCOPIC FEATURES

The bullae are subepithelial. The bulluos roof in an early lesion possesses well-aligned and polarized basal cells, whereas the connective tissue floor is devoid of or shows only mild infiltration by mononuclear cells. Patients with active disease show high antibody titers of immunoglobulins that specifically bind to lamina lucida basement membrane proteins BP230 and BP180. Direct immunofluorescence discloses a linear pattern along the course of the basement membrane with IgG, IgM, and complement fraction 3.

DIFFERENTIAL DIAGNOSIS

Bullous pemphigoid must be differentiated from the other bullous dermatoses listed in this section. The restriction of lesions to the axillary and inguinal intertriginous zones is typical for pemphigoid. Biopsy is required to arrive at a definitive diagnosis. Immunofluorescence antibody testing to detect antibasement membrane antibodies may be useful in the diagnosis.

TREATMENT

Bullous pemphigoid is treated by systemic steroids. Dapsone has also been shown to be effective in the management of the disease; however, red cell suppression may be a complication. The disease, being a primary cutaneous disorder, should be managed by a dermatologist.

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BENIGN MUCOUS MEMBRANE PEMPHIGOID

Figure 5-12

Age: Middle-aged and elderly adults
Sex: Female predilection

CLINICAL FEATURES

BMMP is a bullous disorder that resembles bullous pemphigoid, yet the bullae have a predilection for mucous membranes. The oral cavity and conjunctivas are favored sites, although pharyngeal, anal, and vaginal lesions are present in one half of the patients. The BMMP antigen is unique and differs from that of the bullous pemphigoid antigen. Bullae of the facial neck, and genital skin are also occasionally present. The oral bullae develop slowly and vary in size. They are tense or gelatinous plaques. Desquamation of the gingiva is also a frequent finding. The eye lesions are found on both palpebral and bulbar conjunctivas and tend to heal with scarring. Fibrous bands extend from the lid to the sclera and are termed symblepharon. This finding, in conjunction with oral bullae, is essentially diag-

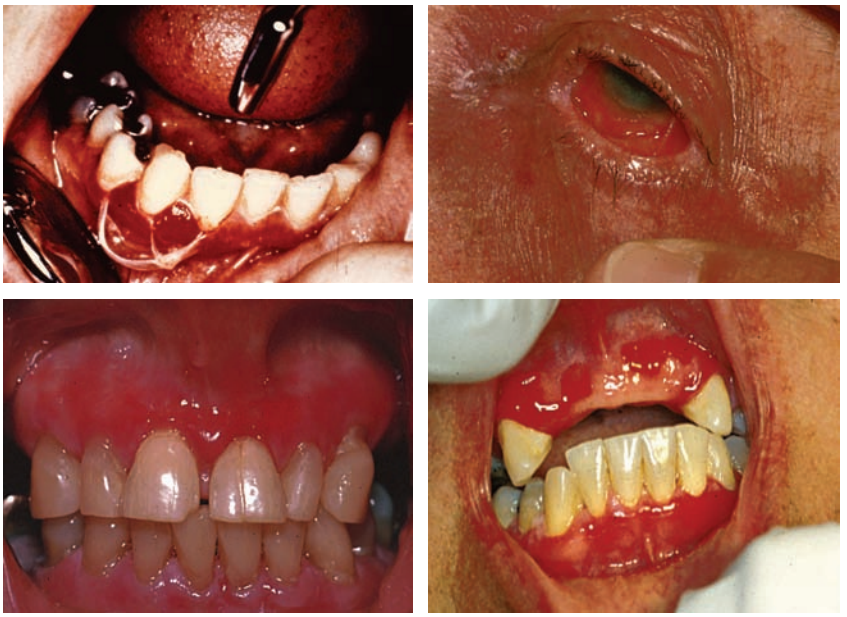

FIGURE 5-12
Benign mucous membrane pemphigoid, a bullous disorder showing extensive oral bullae on an erythematous base. Symblepharon is seen traversing palpebral and bulbar conjunctivae.

nostic for BMMP. The disease is not lethal and follows a protracted course. The major complication is entropion with blindness.

MICROSCOPIC FEATURES

The bullous lesions are subepithelial with an intact basal cell layer on the roof. The submucosa in early lesions shows minimal inflammation. These features are identical to those encountered in bullous pemphigoid. Antibasement membrane antibodies in serum can be detected, yet are present in very low titers. The target antigen in mucous membrane pemphigoid (MMP) is heterogeneous and usually localized to the lamina lucida (laminin 5, collagen VII, and other nonlaminin basement adhesion molecules). Direct immunofluorescence shows basement membrane linear distribution of IgG, complement fraction 3, and IgA (linear IgA disease).

DIFFERENTIAL DIAGNOSIS

The oral lesions of BMMP are similar in appearance to those of the other bullous dermatoses, but they develop more slowly and tend to be smaller and less extensive. The eye lesions are characteristic, and when oral biopsy discloses subepithelial bullae, a clinicopathologic diagnosis can be obtained.

TREATMENT

Systemic steroid therapy, consisting of 40 mg of prednisone in divided doses daily, can be used until control of lesions is achieved, after which medication is withdrawn until new lesions develop. Dapsone has also been found to be effective. Topical 0.05% fluocinonide (Lidex) or tacrolimus ointment can be applied 4 to 6 times daily to oral bullous and desquamative lesions.

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BULLOUS LICHEN PLANUS

Figure 5-13

Age: Middle-aged adults
Sex: Slight female predilection

CLINICAL FEATURES

Although lichen planus is typically a white lesion, erosive and bullous variants occur. The latter is very rare, most cases being desquamative without intact bullae. The oral bullae are most often encountered on the buccal mucosa and appear as flattened gelatinous bullous plaques surrounded by zones of erythema. Often, but not invariably, white lesions or striae can be found adjacent to bullae or in other intraoral locations. Burning discomfort or mild pain may be a complaint. Skin lesions are present in some instances. The disease is benign and chronic. A familial form affects the extremities, appears in early childhood and teenage years, and is inherited as an autosomal dominant trait.

Rarely, both lichen planus, a T cell-mediated disease process, and bullous pemphigoid, a humoral-mediated process, may occur simultaneously, affecting both skin and mucosa. This condition is referred to as *lichen planus pemphigoides.*

MICROSCOPIC FEATURES

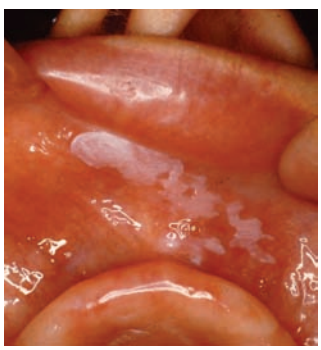
The diagnostic features of bullous lichen planus are most obvious on the margin of the lesion. A subepithelial separation is present. The roof of the bulla is composed of disoriented fragmented basal cells lacking polarization. The floor shows fragmented basal cells overlying fibrous tissue with a zonal superficial infiltrate of lymphocytes. The margin of the bulla blends with mucosa showing the microscopic features typical of the conventional type of lichen planus. On direct immunofluorescence, fibrinogen is consistently identified along the basal lamina with a fringe pattern. In lichen planus pemphigoides, antibasement membrane IgG is also demonstrated.

DIFFERENTIAL DIAGNOSIS

When white striae are present in conjunction with bullae, providing the microscopic features are typical, and the diagnosis is easily determined. When only bullae are present, bullous lichen planus may be clinically indistinguishable from other bullous dermatoses. Biopsy is then required for a definitive diagnosis.

TREATMENT

Topical application of 0.05% fluocinonide ointment (Lidex) or 0.05% clobetasol propri-



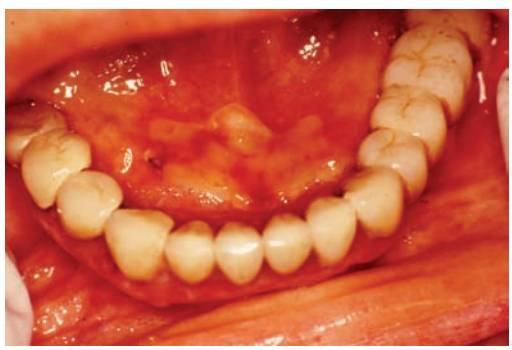


FIGURE 5-13
Bullous lesions in lichen planus, a rare presentation that proceeds to erosions.

onate (Temovate) is useful in controlling the bullous and erythematous component of the disease but will not eliminate the white lesions that may be present.

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ERYTHEMA MULTIFORME

Figure 5-14

Age: Young adults
Sex: Male predilection

CLINICAL FEATURES

Erythema multiforme is a dermatologic disorder that is often but not invariably precipitated by allergens such as sulfa drugs. Precedent herpes infection is a common finding in many instances in which no allergen can be identified. Postherpetic erythema multiforme has been shown to evolve as a consequence of perivascular immune complex deposition of immunoglobulin, herpes virus antigen, and complement. The disease manifests a variety of lesions of skin and mucosa including bullae, macules, erosions, and, on skin, an erythematous circular wheal with a circumferential halo, the so-called target or iris lesion. The oral cavity is usually involved. Bullae develop and rapidly burst, leaving raw erosions with desquamation and underlying erythema. Although any oral tissue can be involved, the lips are almost constantly affected, with painful exudative erythematous erosions. Occasionally, oral lesions are seen without dermatologic manifestations. A slightly elevated temperature is commonly detected. The disease runs its course in 2 to 5 weeks.

MICROSCOPIC FEATURES

The bullae or desquamating regions generally manifest a junctional separation. This feature is not consistent throughout; zones of irregular intraepithelial separation are usually encountered. The upper spinous and parakeratin layers often contain vesicular pools of eosinophilic coagulum (mucopolysaccharide-keratin dystrophy). The subjacent fibrous connective tissue evinces a subacute inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The bullous lesions of erythema multiforme are clinically similar to those of the other bullous dermatoses. Severe involvement of the lips, target lesions of skin, and slight elevation of temperature are indicative of erythema multiforme. Biopsy should be performed to rule out the other bullous dermatoses. Localization of lesions on the oral, conjunctival, and genital mucous membranes are typical for Stevens-Johnson syndrome, a variant of erythema multiforme.

TREATMENT

Systemically administered antihistamines, antipyretics, and a palliative oral rinse such as antihistamine oral expectorant mixed 50:50 with Kaopectate are recommended. In more severe cases, 20 mg of prednisone in divided doses may be required. Fluid intake should be maintained and the patient should be placed on a soft diet. Among patients with precedent herpesvirus infection, acyclovir (400 mg daily) prevents recurrences of both herpetic lesions and the associated erythema multiforme eruptions in most patients.

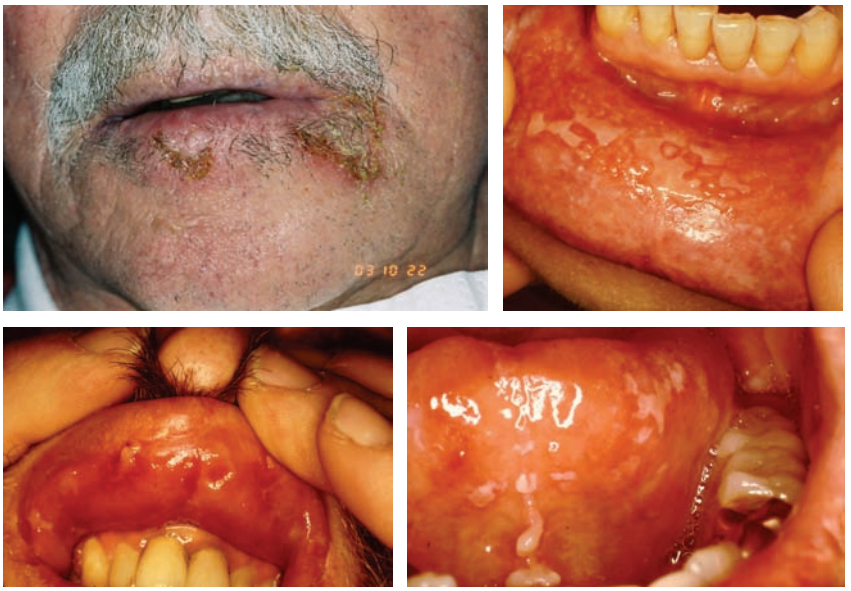

FIGURE 5-14
Erythema multiforme with vesiculobullous lesions having a tendency to hemorrhage are seen throughout the oral mucosa, with predilection for the lips and vermilion border.

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STEVENS-JOHNSON SYNDROME

Figure 5-15

Age: Young adults
Sex: Male predilection

CLINICAL FEATURES

Stevens-Johnson syndrome is a form of erythema multiforme often termed erythema multiforme major, in which bullous and erosive erythematous lesions are found in the oral cavity, on the bulbar and palpebral conjunctivas, and on the external genitalia (glans penis, vulva). Typical iris or target skin erythematous wheals are often present as well. The oral manifestations of Stevens-Johnson syndrome may be confused with other bullous dermatoses. The oral lesions invariably involve the lips as a diffuse hemorrhagic exudative bullous eruption. Sulfa drugs are often found to precipitate this syndrome, which may be fatal if no treatment is rendered. As in erythema multiforme of the minor type, this major syndrome may follow herpes infection.

MICROSCOPIC FEATURES

See Erythema Multiforme.

DIFFERENTIAL DIAGNOSIS

The bullous and erosive lesions of Stevens-Johnson syndrome may be confused with other bullous dermatoses. The triad of oral, eye, and genital involvement is classic for Stevens-Johnson syndrome. This distribution should not present a problem when differentiating this disease from the muco-

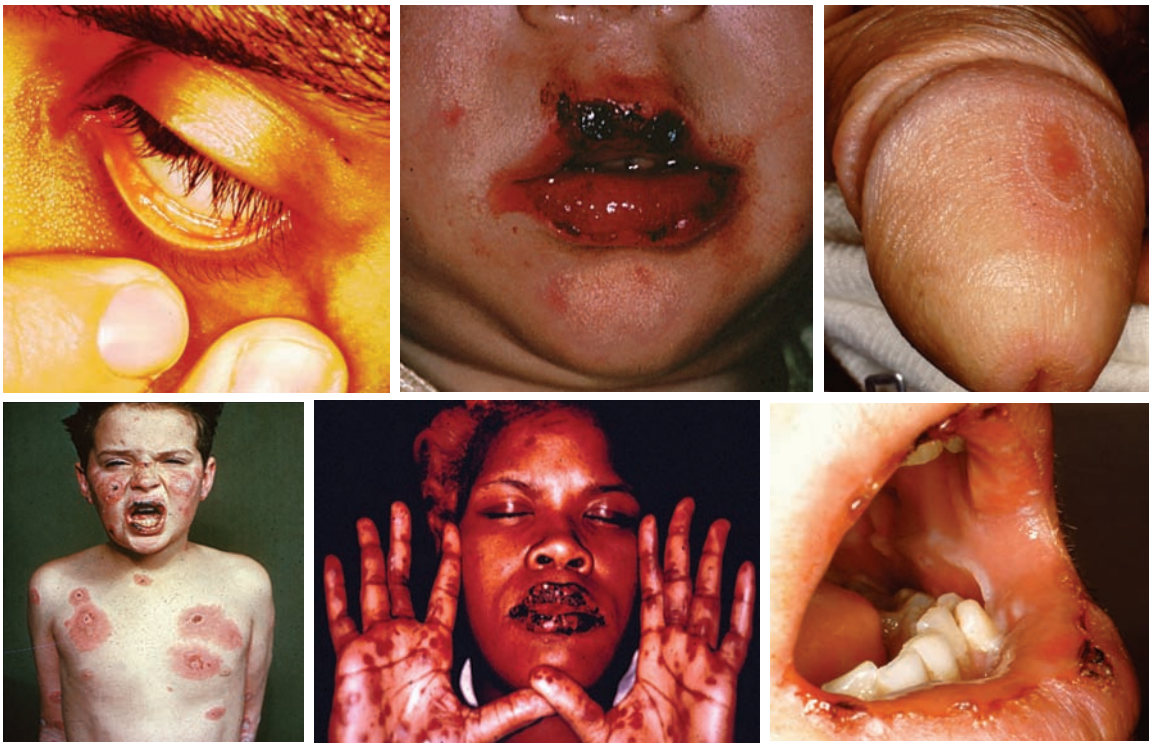

FIGURE 5-15
The Stevens-Johnson syndrome, representing a specific form of erythema multiforme in which the oral mucosa, conjunctiva, and genital mucosa manifest a vesiculobullous eruption.

oculocutaneous lesions of Behcet's syndrome and Reiter's disease because these latter two disorders manifest aphthous-like ulcerations rather than desquamating bullae of the oral cavity.

TREATMENT

Any allergenic drug or food should be withdrawn. The disease is then managed as outlined for erythema multiforme. Systemic steroids should be prescribed in severe cases, because fatalities in Stevens-Johnson syndrome associated with sulfa drugs have been recorded.

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PARANEOPLASTIC PEMPHIGUS

Figure 5-16

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Paraneoplastic pemphigus is an oral/cutaneous condition that occurs as a consequence of autoantibodies directed to desmoplakin proteins in keratinocytes. The

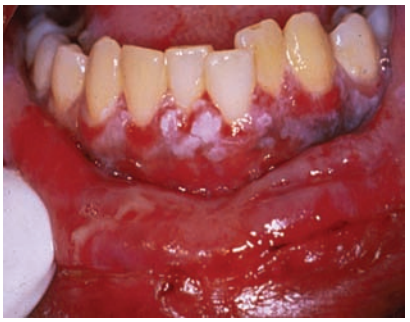
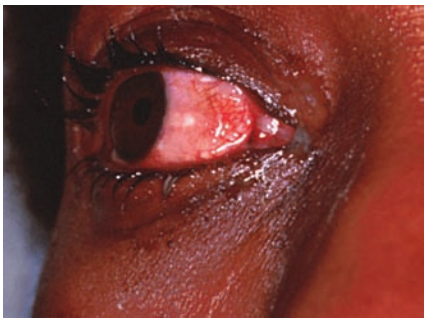

FIGURE 5-16
Oral and ocular lesions of paraneoplastic pemphigus in a patient with Castleman's disease.

autoantibodies were generated in response to a malignant lesion located viscerally. More than 85% of cases have an associated B cell lymphoma or Castleman's disease. The oral lesions are bullous, desquamative, and ulcerated involving the lips, oral mucosa, and conjunctiva. Patients complain of oral burning pain.

MICROSCOPIC FEATURES

The erosive/desquamative lesions of paraneoplastic pemphigus do not parallel those of pemphigus vulgaris; rather they are more often lichenoid with a lymphocytic chronic interface mucositis, or they may appear as a nonspecific chronic mucositis. On direct immunofluorescence, a pericellular distribution is identified along with demonstration of basement membrane immunoreactants reflecting the location of desmoplakins in both desmosomes and hemidesmosomes.

DIFFERENTIAL DIAGNOSIS

Paraneoplastic pemphigus often presents with ocular lesions, being confused with mucous membrane pemphigoid. In some instances the patient is already aware of a cancerous process, in yet others the oral and/or ocular lesions may be the initial presentation and an oncologic workup should be initiated.

TREATMENT

Topical steroids will lessen the inflammatory process with its accompaniment of burning and pain. Most importantly, a clandestine neoplastic process needs to be uncovered with institution of appropriate therapy.

Additional Reading

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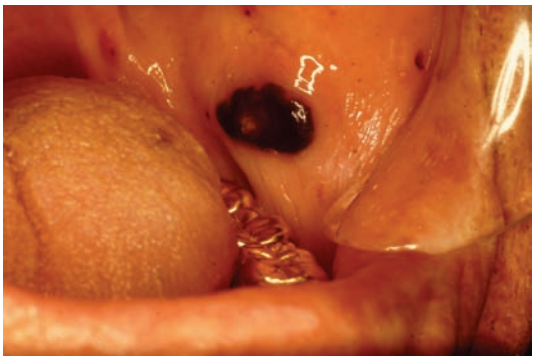
ANGINA BULLOSA HEMORRHAGICA

Figure 5-17

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Hemorrhagic bullae are believed to evolve as a consequence of trauma and are commonly encountered on the hard or soft palate. There may only be a single bullae or multiple lesions can be seen and they are often painful in the early stage. They are tense bullae that are ruby red or deep pur-



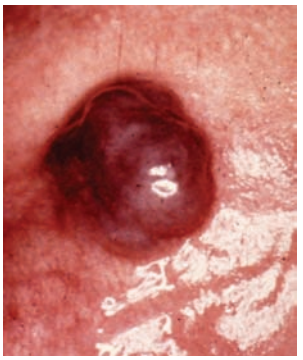


FIGURE 5-17
Blood blisters in angina bullosa haemorrhagica.

ple that, shortly after their formation, burst to leave a broad erosion that heals over in 7 to 10 days.

MICROSCOPIC FEATURES

Unknown

DIFFERENTIAL DIAGNOSIS

Other bullous diseases must be included in the differential diagnosis because any blister can be hemorrhagic. A blood-filled mucocele should also be a consideration.

TREATMENT

The erosions left after the bullae burst resolve of their own accord. Soothing mouth rinses such as an antihistamine/Kaopectate syrup will attenuate pain.

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EPIDERMOLYSIS BULLOSA

Figure 5-18

Age: Infants (hereditary variants)
Sex: Varies with mode of inheritance

CLINICAL FEATURES

There are many forms of epidermolyis bullosa (EB), most being inherited. This group of diseases has been subdivided on the basis of inheritance patterns, severity of disease, and histopathologic features of blister formation. The "simplex" form is present at birth and improves with ensuing years. The disorder primarily affects the feet, hands, and neck, with nail changes being variable; scarring is nonexistent. Oral bullae are mild and the teeth are not affected. In the "generalisata gravis" form, an autosomal recessive disease, blisters appear at the nail beds shortly after birth and the nails are then shed. Involvement of the trunk, umbilicus, face, scalp, and extremities follow, and some patients die as a consequence of septicemia. Many patients survive and show fragile, hemorrhagic oral bullae, particularly of the palate. Hypoplastic, pitted enamel involving the molar teeth is a feature and, characteristically, perioral and perinasal granular hemorrhagic crusted lesions evolve. The dystrophic or hypertrophic form is inherited as a dominant trait and the flattened bullae appear on the hands, elbows, ankles, knees, and feet before the first year of life

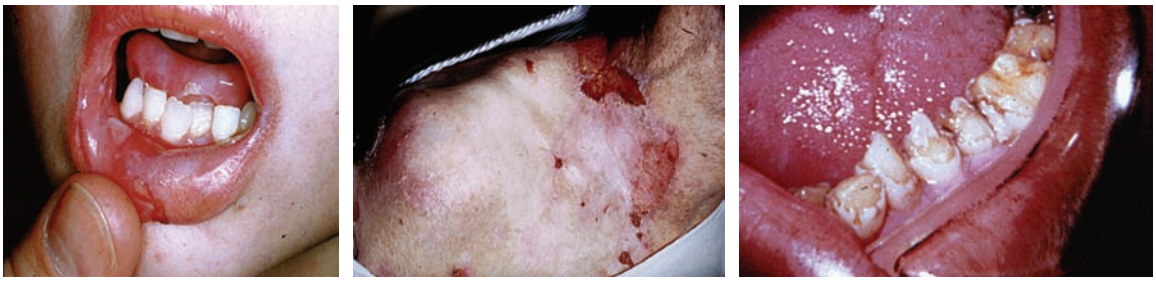

FIGURE 5-18
Oral lesions accompanying bullous, scarring lesions located on skin over joints, a manifestation of epidermolysis bullosa (Courtesy of Dr. J. Mink).

with improvement after puberty. Oral bullae are occasionally seen.

The "scarring" variety is subdivided into four autosomal recessive disease forms, all of which occur in infants. The occipital and scapular skin is blistered, as is that on the elbows, fingers, buttocks, and feet. Scarring with pigmentation and depigmentation are featured and the hands become claw-like. Bullae arise in the larynx and esophagus leading to hoarseness/aphonia and dysphagia, respectively. Oral bullae are also generally present along with scarring and mucosal atrophy; the teeth show hypoplastic enamel. The nonhereditary acquisita form of the disease shows antibodies to type VII collagen; however, oral lesions are rarely encountered. Other varieties of the disease are not associated with oral or dental manifestations.

MICROSCOPIC FEATURES

The histologic classification of EB does not necessarily correlate with the clinical forms and includes four specific subgroups. This classification is based on the microscopic focus of bulla formation: type I, the split is intraepithelial; type II, junctional cleavage at the level of the basal lamina; type III, dermal separation associated with atrophy and scarring; type IV, the nonhereditary form, also with junctional separation. The simplex and generalisata gravis varieties involve an intrabasilar split owing to hemidesmosome hypoplasia without significant submucosal inflammation. In the scarring form, the level of cleavage is below the basal lamina.

DIFFERENTIAL DIAGNOSIS

Most of the other bullous diseases included in this section occur in adults. Blistering diseases of childhood that should be considered in the differential diagnosis include bullous impetigo, porphyria, and dermatitis herpetiformis. Although biopsy is helpful, the distribution of lesions and degree of scarring are important features in the establishment of a definitive diagnosis. Referral to a dermatologist or pediatrician is recommended.

TREATMENT

Prevention of septicemia is of paramount importance in severely affected patients. Those forms of EB with dental hypoplasia are associated with severe caries and the affected teeth should be restored with full crowns.

Additional Reading

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DERMATITIS HERPETIFORMIS (GLUTEN ENTEROPATHY)

Figure 5-19

Age: Middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

Dermatitis herpetiformis is an immunopathologic vesiculobullous disease of skin rarely showing oral manifestations. The condition represents the cutaneous expression of gluten enteropathy (gliadin sensitivity). The skin lesions are pruritic and are located primarily on the extremities and buttocks. They are vesicular with a tendency to rupture and desquamate. Oral bullae may be encountered and many patients present with aphthous like ulcers. The disease is chronic, lasting for many years, yet is not life threatening.

MICROSCOPIC FEATURES

The epithelium displays a sub-basilar separation with a subacute inflammatory infiltrate located in the dermal or submucosal papilla zones. The predominant cell type is the eosinophil. Lumps of IgA can be demonstrated in the dermal papilla area with immunofluorescence staining.

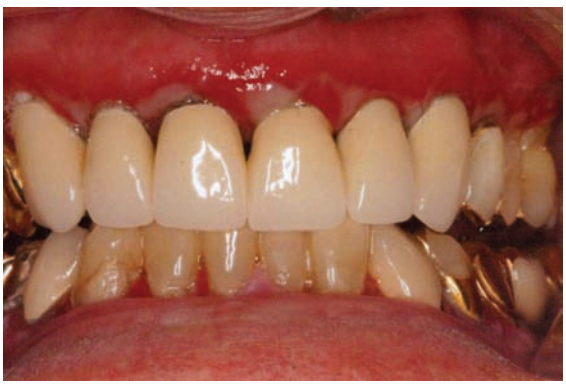

FIGURE 5-19
Oral lesions in gluten enteropathy with cutaneous dermatitis herpetiformis.

DIFFERENTIAL DIAGNOSIS

The oral lesions of dermatitis herpetiformis are similar in appearance to those of the other bullous dermatoses. The clustered vesicles with pigmented base on the skin are highly suggestive but not pathognomonic for the disease. Biopsy discloses characteristic features.

TREATMENT

Because the disease is primarily a dermatologic disorder, referral to a dermatologist is recommended. Dermatitis herpetiformis responds to sulfapyridine therapy; steroids are not particularly useful.

Additional Reading

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Desquamative Lesions

GINGIVOSIS (DESQUAMATIVE GINGIVITIS)

Figure 5-20

Age: Middle-aged adults
Sex: Exclusive female predilection

CLINICAL FEATURES

Gingivosis was, at one time, considered a specific desquamative disease occurring

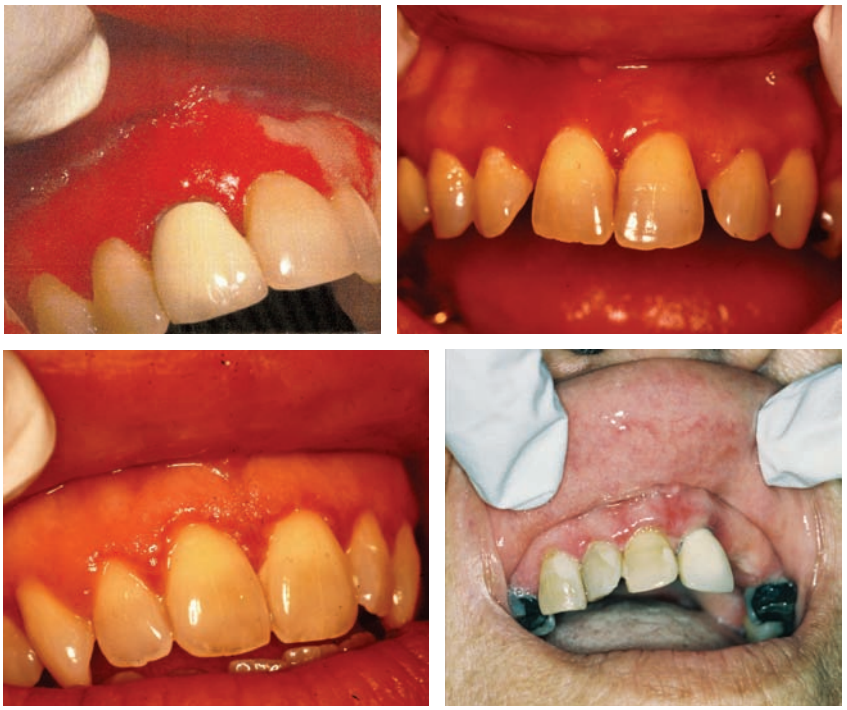

FIGURE 5-20
Gingivosis characterized by an erythematous gingivitis accompanied by desquamation. These lesions are seen in pemphigoid (top), erosive lichen planus (bottom left), and pemphigus vulgaris (bottom right).

after menopause and confined to the attached gingiva. Because the clinical and microscopic features of the disease are similar to those encountered in BMMP, most investigators and clinicians have suggested that gingivosis is a form of BMMP that is merely confined to gingiva. Many of the diseases classified previously as bullous disorders can manifest desquamative lesions of the gingiva. Therefore, *desquamative gingivitis* is a clinical term and is not specific for any given disease; nevertheless, gingival desquamation is most commonly seen in patients with BMMP.

MICROSCOPIC FEATURES

In BMMP, a junctional separation occurs, with maintenance of an intact basal cell layer adherent to the desquamated tissue. The underlying submucosa manifests an intense chronic inflammatory cell infiltrate with numerous dilated capillaries. The histology for other bullous diseases is detailed elsewhere in this chapter.

DIFFERENTIAL DIAGNOSIS

The desquamation of the gingiva as seen in BMMP may also occur in many of the bullous dermatoses, including pemphigus vulgaris. Erosive lichen planus and toothpaste idiosyncrasy reactions may show features similar to gingivosis; however, the former usually shows extragingival lesions and the latter lacks an erythematous component.

TREATMENT

The patient should avoid spicy or acidic foods. A palliative mouth rinse may be used and topically applied 0.05% fluocinonide (Lidex) ointment is beneficial in minimizing the inflammatory component.

Additional Reading

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EROSIVE LICHEN PLANUS

Figure 5-21

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

The erosive form of lichen planus is as common as the nonerosive type. The lesions are most frequently located on the gingiva, mucobuccal fold, and buccal mucosa. The erosions and zones of desquamation are accompanied by erythema. Peripheral to the erosive lesions are white plaques or typical reticulated striae. Mild to moderate pain or burning is a common complaint. This form of lichen planus is also often associated with diabetes mellitus and hypertension, a triad known as Grinspan's syndrome. Instances of carcinomatous transformation in erosive lichen planus have been infrequently reported; the incidence is higher than that seen in the nonaffected population. The disease runs a protracted course and may or may not be associated with skin manifestations. The oral lesions partially resolve in one region only to reappear at some new site. Many patients are prone to anxiety. Oral and cutaneous lesions identical to lichen planus are occasionally encountered in patients receiving gold therapy and other drugs such as antimalarials and penicillamine. Bone marrow graft recipients may also develop lichenoid mucocutaneous lesions.

MICROSCOPIC FEATURES

At the margin of the erosions, the histomorphologic features typical of lichen planus (chronic lymphocytic interface mucosistis) are encountered. Transition is seen,

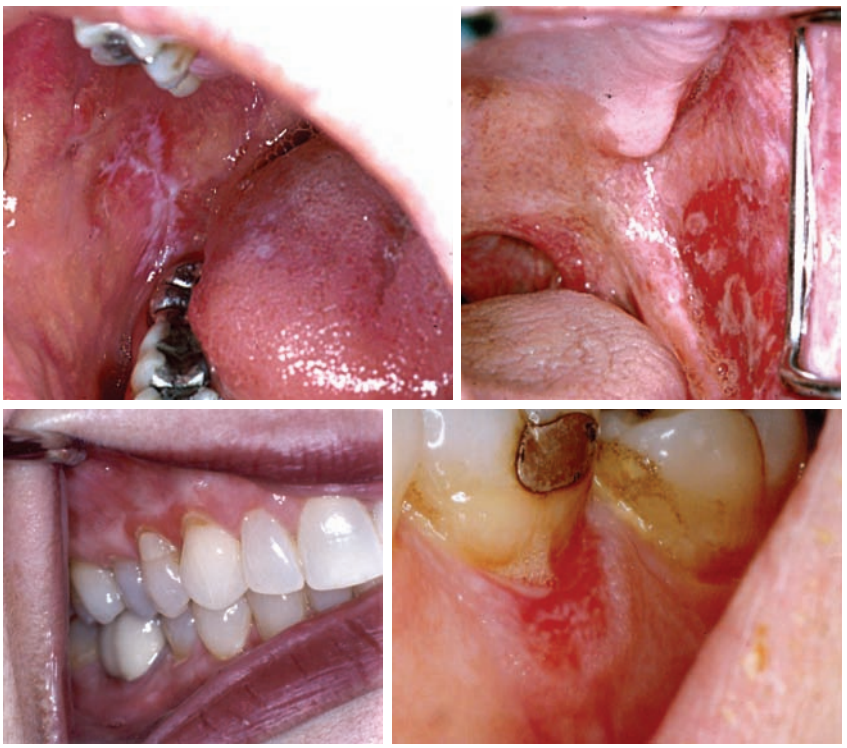

FIGURE 5-21
The erosive form of lichen planus showing white striae accompanied by intense redness with superficial sloughing of the mucosa.

whereby the epithelium becomes detached from the underlying chronically inflamed submucosa. Damage with disorientation of the basal cell layer is an important diagnostic feature.

DIFFERENTIAL DIAGNOSIS

When confined to gingiva, erosive lichen planus may simulate gingivosis. Erosive lichen planus is usually, however, multifocal and not localized to gingiva. Careful examination usually discloses the presence of white striae. A biopsy should be performed; the microscopic features are pathognomonic.

TREATMENT

Topical application of 0.05% fluocinonide (Lidex) or 0.05% clobetasol (Temovate) ointment should be applied to lesional tissue 4 to 6 times each day. Maximal effects are observed if contact can be maintained overnight. Decadron oral rinses are also effective. When erosive lichen planus is severe, a regimen of 40 mg prednisone for 1 week with tapering doses for the ensuing 5 to 7 days may be initiated, followed thereafter with topical steroids for control of lesions. The white component is not controlled with topical steroids.

Additional Reading

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LICHENOID CONTACT STOMATITIS

Figure 5-22

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Lichenoid reactions show clinical and microscopic features of classic, idiopathic lichen planus yet often lack the reticular pattern with stria. In general, they represent delayed type hypersensitivity reactions to contactants or represent lichenoid drug eruptions that are triggered by specific pharmacologic agents. More than 60 drugs have been shown to serve as allergens in susceptible subjects. The lesions are typically mixed red and white, often showing erosions and ulcerations. When the allergen is a metallic hapten, the metals become chelated to host proteins making them immunogenic for certain people. Lichenoid lesions that contact dental amalgams are termed "contact lesions" and can usually be attributed to mercury sensitivity although other metals may be allergenic. Cinnamon is a commonly consumed spice that can induce lichenoid oral lesions. Malignant transformation to squamous cancer occurs in 2% of lichen planus patients and there is evidence supporting the notion that lichenoid reactions may be more at risk than classic lichen planus.

MICROSCOPIC FEATURES

A chronic interface lymphocytic mucositis is seen, identical to conventional lichen planus and direct immunofluorescence demonstrates basement membrane fibrinogen deposition, thereby excluding the efficacy of this test when attempting to differentiate conventional lichen planus from a lichenoid reaction. Therefore, the diagnosis is based on clinical findings of a potential antigen. A singular histology is seen in cinnamon lichenoid reactions in that the chronic interface mucositis is mixed with lymphocytes,

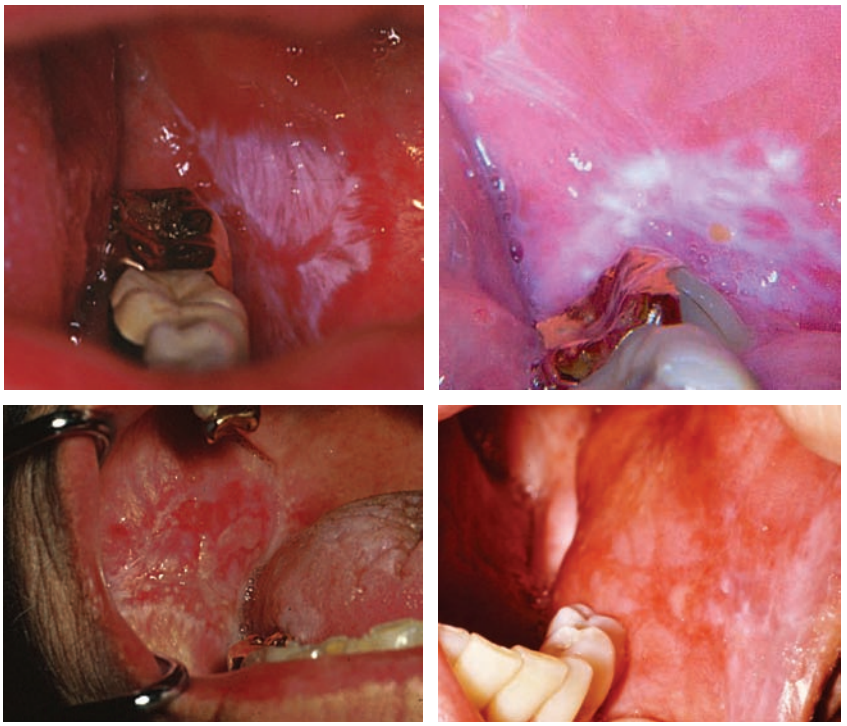

FIGURE 5-22
Erosive lesions in lichenoid reactions that represent local contact allergy (note proximity to dental restorative metals(top), or to systemic drug eruptions).

plasma cells, and histiocytes and is accompanied by submucosal perivascular lymphoid aggregates. Some of these aggregates show germinal center formation.

DIFFERENTIAL DIAGNOSIS

The chief entity in the differential diagnosis is conventional lichen planus. Chronic ulcerative stomatitis, lupus erythematosis, and erythroleukoplakia are also included in the differential diagnosis.

TREATMENT

Withdrawal of the putative allergenic material or pharmacologic agent should result in resolution. Topical steroid gels and mouthrinses may facilitate clearance.

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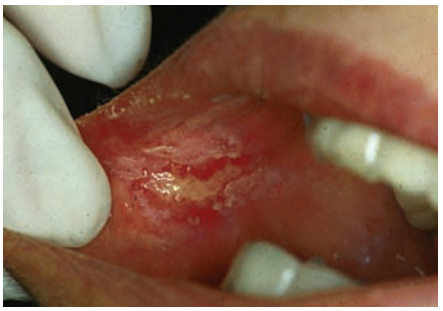
CHRONIC ULCERATIVE STOMATITIS

Figure 5-23

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Chronic ulcerative stomatitis is a rare lichenoid disease of oral mucosa that is



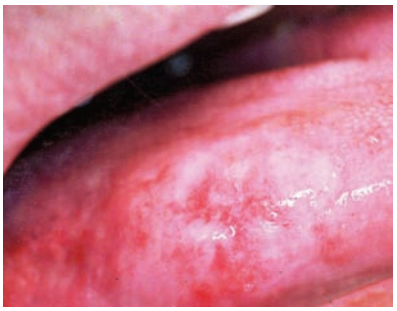


FIGURE 5-23
Ulceration and desquamation in chronic ulcerative stomatitis with antinuclear stratified squamous epithelial antibodies.

characterized by the presence of antinuclear antibodies reactive with stratified squamous epithelial nuclei. Clinically, the lesions are painful white, red, ulcerative, and desquamative, appearing primarily on the tongue and buccal mucosa.

MICROSCOPIC FEATURES

A chronic lymphocytic interface mucositis is evident, resembling ordinary lichen planus. On immunoflourescent testing, fibrinogen may be localized along the basement membrane, but the singular feature is the presence of IgG and/or IgM antinuclear keratinocyte antibodies identified in the lower strata keratinocytes.

DIFFERENTIAL DIAGNOSIS

Lichen planus and lichenoid eruptions are the primary considerations in the differential diagnosis.

TREATMENT

The significance of the antinuclear antibodies is unknown and not related to lupus erythematosus. The condition is often recalcitrant to topical steroids. Short-term systemic corticosteroid therapy may or may not be effective. Hydroxychloroquine therapy may be prescribed.

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PYOSTOMATITIS VEGETANS

Figure 5-24

Age: Adults
Sex: No Predilection

CLINICAL FEATURES

A subset of patients with ulcerative colitis and regional enteritis (Crohn's disease) may manifest cutaneous or mucosal lesions that share a common histology. On the skin, the condition is known as pyodermatitis vegetans, in which multifocal white verrucous patches may develop. In oral mucosa, the lesions of pyostomatitis vegetans are yellowish shallow erosions that appear as willowy serpentine tracts, like the trail left behind by a mollusk on the ocean floor. These lesions are painful and burning. Why only a small minority of patients with inflammatory bowel disease manifest this complication is unknown.

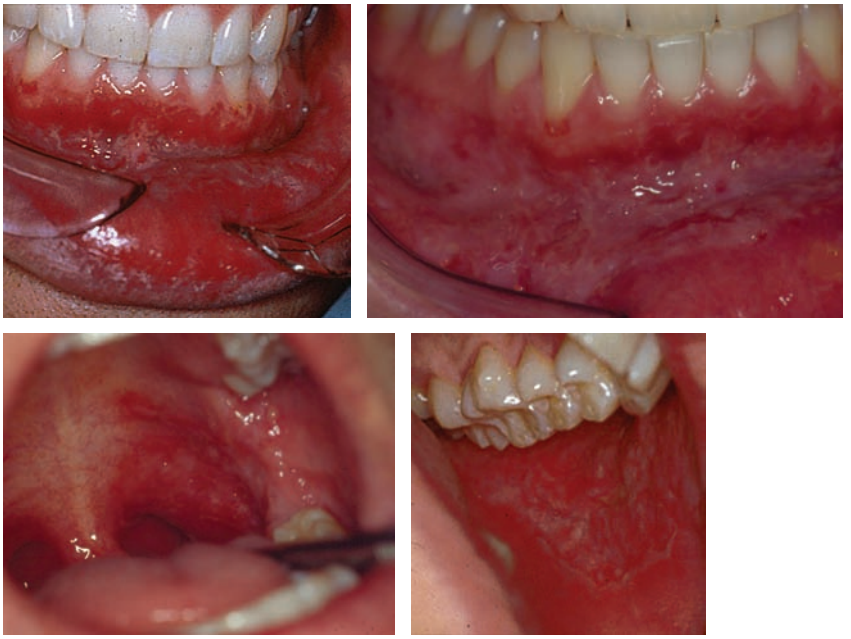

FIGURE 5-24
Erosions in pyostomatitis vegetans, an oral manifestation of ulcerative colitis.

MICROSCOPIC FEATURES

There are alternating zones of thickening and atrophy of the epithelial layer with spinous layer edema and transmigration of leukocytes. The submucosa also shows nonspecific inflammation. The hallmark of pyostomatitis vegetans is the appearance of eosinophilic abscesses located within the spinous layer of the epithelium. Direct immunofluorescence is negative. A similar condition both clinically and microscopically is ***Neuman type pemphigus vegetans***. This is a pemphigus vulgaris variant that may show oral lesions, yet there is no association with inflammatory bowel disease. Furthermore, autoantibodies to desmoglein 3 are present with a pemphigus-like direct immunofluorescence pattern.

DIFFERENTIAL DIAGNOSIS

Other bullous diseases included here must be considered in the differential. When there is a history of inflammatory bowel disease or frequent complaints of gastrointestinal cramping, pyostomatitis should be the chief consideration; biopsy will confirm the clinical impression.

TREATMENT

Systemic corticosteroids (e.g., 50 mg of prednisone daily) will usually allow for clearance of lesions within 7 to 10 days. Topical fluorinated steroid gels and high potency rinses can then be used at the earliest onset of recurrences.

Additional Reading

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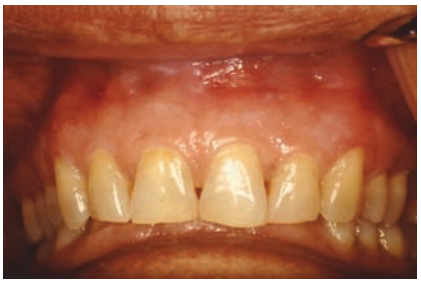

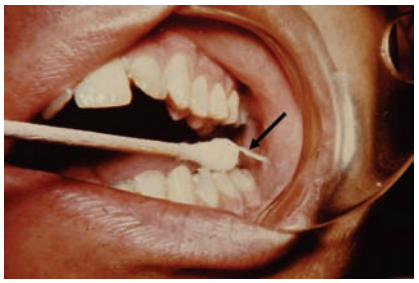

FIGURE 5-25
Pale mucosal tissues that show a superficial slough of the mucosal cornified layer in response to specific dentifrices.

TOOTHPASTE IDIOSYNCRATIC LESIONS

Figure 5-25

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Certain dentifrices, usually those containing fluoride salts, cause a superficial desquamation or slough of the cornified layer in susceptible patients. The reaction does not appear to represent a true form of allergy, but is more consistent with a mild irritant reaction; it is rather uncommon. The buccal mucosa and mucosal surfaces of the lips show a thin, white membrane that is easily dislodged by rubbing with gauze. Pain and erythema are lacking. The disease resolves when the causative agent is withdrawn.

MICROSCOPIC FEATURES

Biopsy at the margin of the zonal slough reveals a separation beneath the stratum corneum without vesicle formation, and transmigration of leukocytes into epithelium and submucosa is not a feature.

DIFFERENTIAL DIAGNOSIS

Erosive lichen planus and gingivosis must be considered in the differential diagnosis. Absence of white striae, erythema, and pain or burning should limit the diagnosis to toothpaste idiosyncrasy reaction. The clinical diagnosis can be confirmed if the desquamation resolves after withdrawal of the suspected causative dentifrice.

TREATMENT

The patient should abstain from the use of toothpaste for 1 week, after which a bland nonfluoride dentifrice should be prescribed.

Additional Reading

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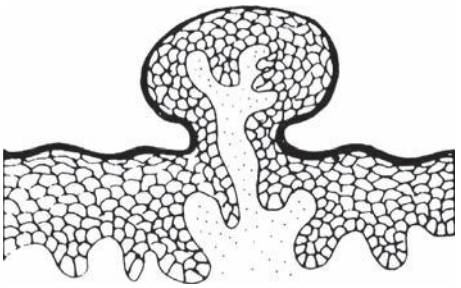
a



Pendunculated swelling

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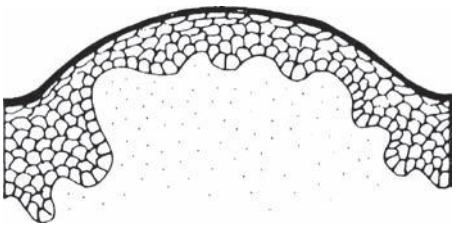

Sessile swelling

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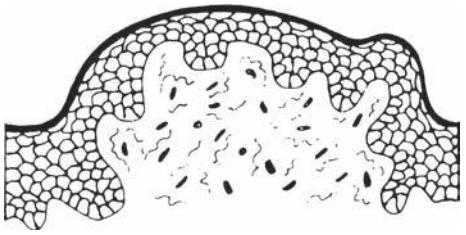

Hyperplasia, reactive

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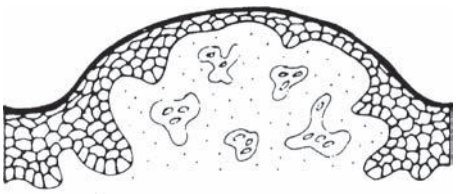

Vascular proliferation

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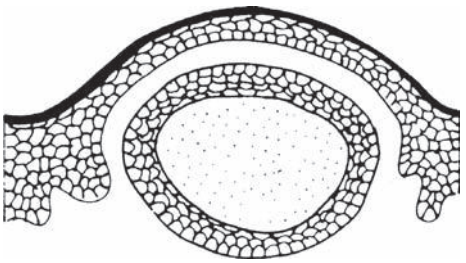

Cyst

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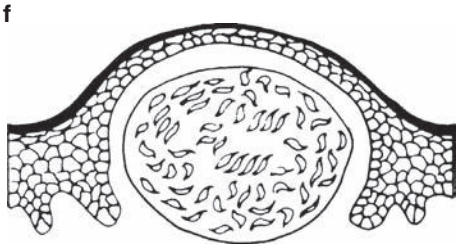
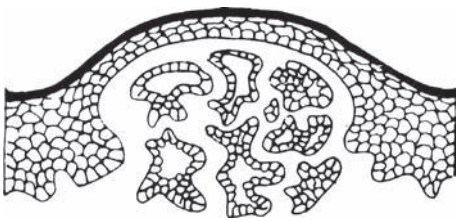


Mesenchymal neoplasm

g



Glandular neoplasm

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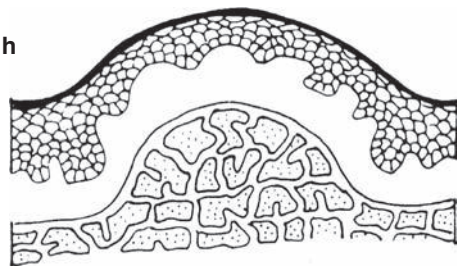

Osseous enlargement

Soft Tissue Swellings

Intraoral Soft Tissue Swellings

6

Tongue Swellings 232

Palatal Swellings 250

*Discussed under Gingival Masses
**Discussed elsewhere in this chapter

Both epithelial and mesenchymal lesions can produce tumefaction in soft tissues. The swellings may be of developmental, inflammatory, or neoplastic origin, or they may reflect an oral representation of a generalized systemic disorder. When the clinician develops a differential diagnosis for a given lump in the oral cavity, three parameters are of paramount importance in the limitation of the differential: location, consistency, and the presence or absence of pain. In this section, diseases that appear as tumefactions are categorized according to location. Although a disease is listed for a given topographic locale, that lesion is not limited exclusively to that region. To eliminate redundancies, the grouping of lesions according to location is based on prevalence or a tendency for that lesion to occur in a given site.

When developing a differential diagnosis, one must be aware both of the tendency for a lesion to arise in a given locale and of the tissues normally present in a given region. For example, a swelling in the palate should suggest a diagnosis of salivary tumor, because the palate is replete with minor salivary glands. Nevertheless, salivary tissue is, with few exceptions, ubiquitous in oral mucous membranes. For this reason, a swelling in any of the oral tissues could represent a salivary neoplasm. When a disease entity is restricted exclusively to a given location, this condition is specified in the text.

The consistency of a swelling is of utmost importance when one considers diagnostic probabilities, determines procedures for securing a definitive diagnosis, and provides treatment. Tumefactions that are movable and firm, yet not indurated, are most consistent with benign neoplasms; tumefactions that are fixed, indurated, and ulcerated are more likely to be malignant neoplasms. Swellings that are tender or painful and may manifest fistulation are, in all probability, inflammatory conditions.

The most common tumefactions of the gingiva or alveolar ridge are the parulis of pulpal or periodontal origin, the pyogenic and peripheral giant cell granuloma, the peripheral fibroma, and the ossifying fibroma. Recall that a central jaw lesion may perforate bone and manifest as a gingival growth or epulis.

The common swellings of the oral floor are the ranula, the dermoid cyst, and the lymphoepithelial cyst. The common swellings of the lips are mucoceles (lower lip) and benign salivary tumors (upper lip).

Commonly encountered swellings of the tongue include mesenchymal tumors, chiefly benign hemangiomas or lymphangiomas, neural sheath tumors, and granular cell tumor. Lethal lesions include carcinoma and sarcoma. Systemic diseases that may cause death and produce tongue swellings include amyloidosis and specific granulomatous diseases, such as tuberculosis and histoplasmosis.

The more common palatal swellings are tori, palatal abscesses, and benign or malignant salivary tumors, the latter of which are potentially lethal.

Common swellings in the cheek include benign mesenchymal tumors, fibrous hyperplasia, and salivary tumors. Malignant salivary tumors may cause death. Retromolar swellings include primarily dentigerous cysts from underlying impacted third molars, pericoronitis, and, importantly, mucoepidermoid carcinoma.

Localized Gingival Tumefactions

PARULIS

Figure 6-1

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Inflammation of pulpal or periodontal origin may drain peripherally, producing a

fistula with submucosal abscess formation in the gingival tissues. The swelling is fluctuant and may be sore or painless. A parulis of odontogenic origin is associated with a necrotic pulp, and periapical pathosis is radiographically demonstrable. A parulis of periodontal origin is found adjacent to a deep periodontal pocket.

MICROSCOPIC FEATURES

Abscess formation, composed of loose connective tissue, eosinophilic exudate, and neutrophils, may be accompanied by necrotic debris and scattered chronic inflammatory cells, chiefly macrophages.

DIFFERENTIAL DIAGNOSIS

Parulis can be differentiated from other gingival epulides by locating the source of infection. Periapical radiographs, pulp tests, and pocket probing are useful in this respect. A gutta-percha point may be inserted through the fistula feeding the parulis and radiographed to disclose the incriminating tooth when other clinical findings are equivocal.

TREATMENT

Elimination of the source of inflammation is curative; if pulpal, then endodontics or extraction is required. If the source is periodontal, curettage or surgery with debridement of calculus and granulation tissue is indicated.

Additional Reading

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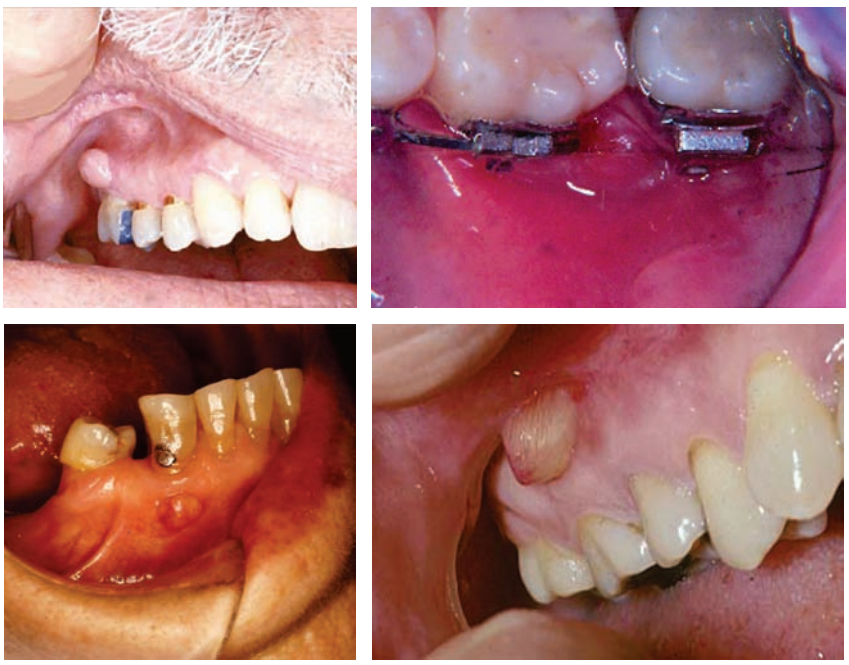

FIGURE 6-1
Gingival abscess or parulis (gum boil) represents drainage from an endodontic infection.

PYOGENIC GRANULOMA

Figure 6-2

Age: Teenagers and young adults
Sex: Female predilection

CLINICAL FEATURES

The pyogenic granuloma is a reactive, exuberant overgrowth of granulation tissue resulting from irritation. It may occur anywhere on the mucocutaneous surfaces but is most common on the gingiva. The lesion is smooth or bosselated, usually ulcerated, hemorrhagic, and compressible. Pyogenic granulomas often reach large proportions yet generally emanate from a stalk originating at a gingival papilla. This lesion is common among gravid females, hence the term *pregnancy tumor*. It has been suggested that the hormonal imbalance coincident with pregnancy heightens the organism's response to irritation.

MICROSCOPIC FEATURES

The surface is usually ulcerated, and the tumor mass is composed of erythrocyte-engorged dilated vascular spaces. The intervening fibrous stroma is infiltrated with inflammatory cells.

DIFFERENTIAL DIAGNOSIS

Unlike parulis, the pyogenic granuloma does not contain a purulent exudate nor is there an inflammatory source of infection from dental origin. The lesion must be differentiated from other reactive gingival swellings and hemangioma.

TREATMENT

Pyogenic granuloma is managed by excision and thorough scaling and curettage of the adjacent teeth and root surfaces. In the gravid patient, recurrence is likely and treatment, to be successful, should await parturition.

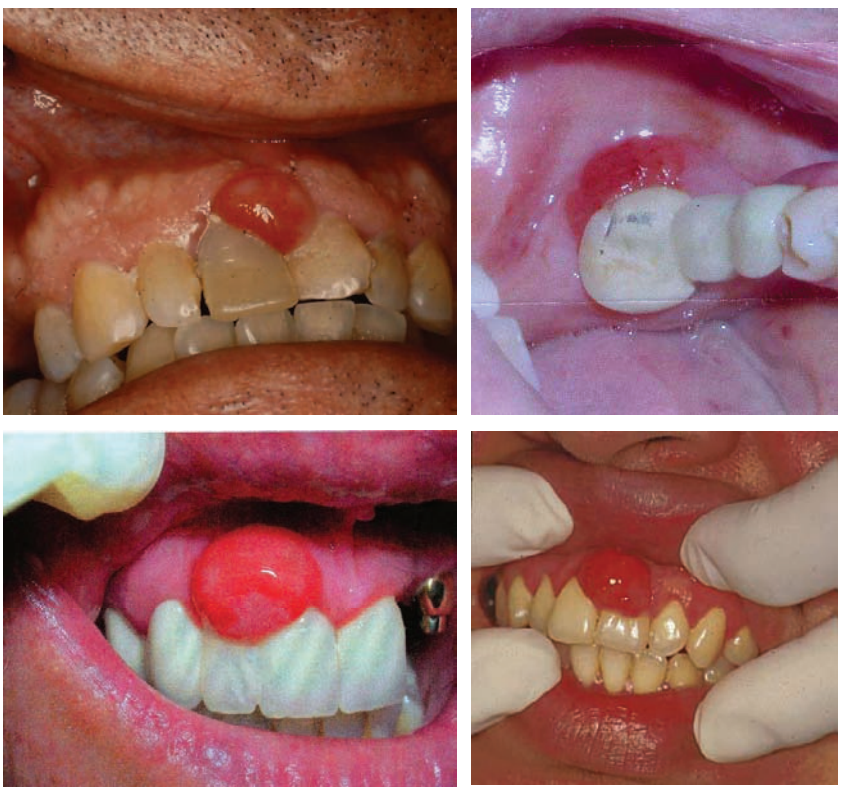

FIGURE 6-2
Pyogenic granuloma of maxillary gingiva are erythematous and not related to pulp disease.

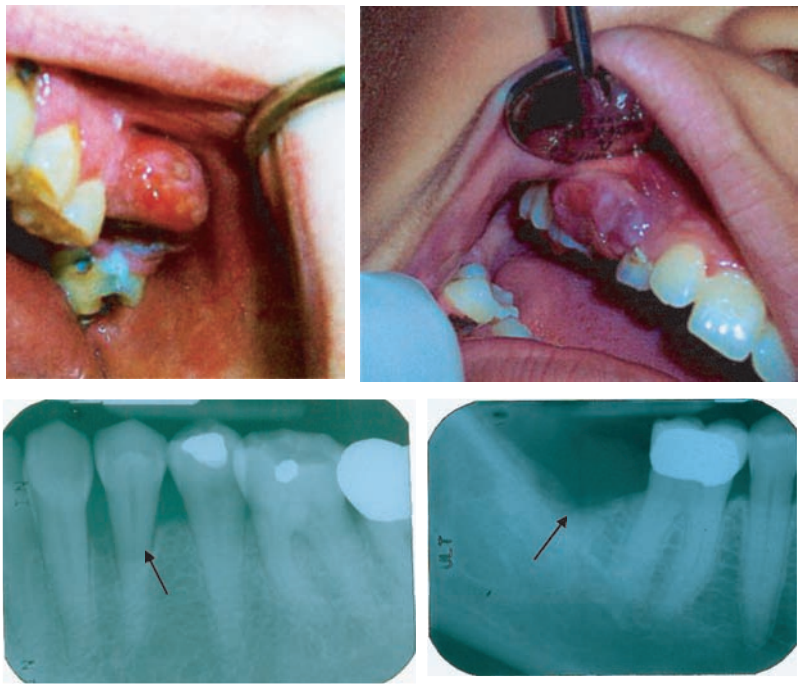

FIGURE 6-3
Peripheral giant cell granulomas are reddish purple reactive masses and may erode the underlying alveolar bone.

Additional Reading

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PERIPHERAL GIANT CELL GRANULOMA

Figure 6-3

Age: No predilection
Sex: Female predilection

CLINICAL FEATURES

Peripheral giant cell granuloma may arise on both dentulous and edentulous alveolar ridges and is restricted in location only to these regions of the mouth. The lesion may reach a large size and may have a sessile base. The surface is either smooth or granular, often with a blue or purple tinge. It is somewhat firm to palpation. Giant cell granuloma is aggressive and has the potential to erode into underlying alveolar bone. Like other reactive gingival growths, it is common in pregnant women and has a tendency to recur after excision.

MICROSCOPIC FEATURES

A hypercellular fibrovascular stroma prevails; numerous giant cells are present, many of which line vascular spaces. The multinucleated cells show a random distribution of nuclei within the cytoplasm. The lesion is often lobulated with heavy deposits of hemosiderin granules located about the periphery. Osteoid is also a common feature, elaborated within the granulomatous stroma.

DIFFERENTIAL DIAGNOSIS

Peripheral giant cell granuloma can clinically resemble any of the other gingival tumefac-

tions, including reactive and neoplastic conditions. An infectious source is lacking.

TREATMENT

Giant cell granulomas originate from gingival tissues (i.e., periosteum) and require excision extending to bone. Recurrence can be anticipated if the lesion is not excised in its entirety. The adjacent teeth should be scaled to remove any irritants associated with plaque.

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PERIPHERAL FIBROMA

Figure 6-4

Age: Young adults
Sex: Female predilection

CLINICAL FEATURES

Peripheral fibroma is merely a focal fibrous hyperplasia of the marginal gingiva and is analogous to the fibroma or inflammatory hyperplasia occurring elsewhere in the mouth. Peripheral fibroma may evolve as such or may represent a late sclerosing stage of a pyogenic granuloma. It is usually smooth, nonulcerated, firm, and lacking discoloration. Although peripheral fibromas may become quite large, they usually emanate from a slender stalk originating on a single gingival papilla.

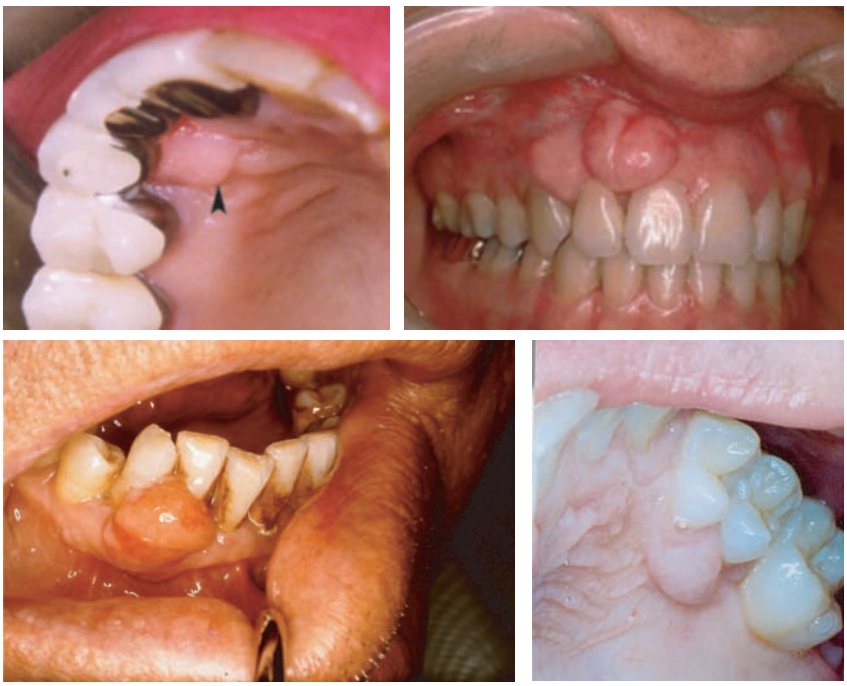

FIGURE 6-4
Peripheral fibroma manifesting as a firm, normal-colored tumefaction.

MICROSCOPIC FEATURES

Surface epithelium is distended by a mass of dense fibrous connective tissue that may contain mild diffuse inflammatory cell infiltrates or may be devoid of inflammation. Occasionally, multinucleated fibroblasts are encountered, the so-called *giant cell fibroma*.

DIFFERENTIAL DIAGNOSIS

The normal mucosal color and firm consistency help to differentiate the peripheral fibroma from pyogenic or peripheral giant cell granuloma. The clinical appearance may be identical to that of ossifying fibroma, gingival cysts, or peripheral odontogenic tumors.

TREATMENT

Excision with root scaling of adjacent teeth is recommended.

Additional Reading

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GIANT CELL FIBROMA

Figure 6-5

Age: Teenagers and young adults
Sex: No predilection

CLINICAL FEATURES

The giant cell fibroma is basically a fibrous proliferation with distinctive microscopic features and may represent a reactive or benign neoplastic process. It is smooth or papillary and usually pedunculated. Most lesions are small and normal in color. One half of these lesions are located on the gingiva, with mandibular lesions occurring more frequently than maxillary growths. They also arise on the tongue, palate, buccal mucosa, and lips. Similar lesions can be found on the skin and genitalia.

MICROSCOPIC FEATURES

The mass may be papillary or smooth and is covered by a thin layer of stratified squamous epithelium. The bulk of the specimen is represented by irregular swirls of collagen fibers with interspersed plump stelate and spindle-shaped fibroblasts. Many of these cells exhibit a "manta ray" appearance and possess 2 to 5 oval nuclei.

DIFFERENTIAL DIAGNOSIS

Papillary appearing lesions are clinically indistinguishable from papilloma, condyloma, and other focal papillary lesions described in the next chapter. Dome-shaped lesions may be confused with the other localized gingival swellings listed in this chapter. Most giant cell fibromas arise on attached gingiva away from the interdental papilla and are normal in color, thereby eliminating most of the reactive proliferations from consideration. A biopsy is required to obtain a diagnosis.

TREATMENT

Most giant cell fibromas are pedunculated, and simple surgical excision is the treatment of choice. Recurrence is rare.

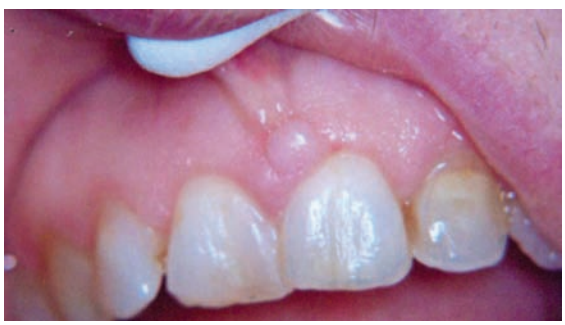

FIGURE 6-5
Small gingival nodule representing a giant cell fibroma.

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PERIPHERAL OSSIFYING FIBROMA

Figure 6-6

Age: Young adults
Sex: Female predilection

CLINICAL FEATURES

Peripheral ossifying fibroma is located exclusively on the gingiva and is rarely seen on edentulous ridges. Like other reactive proliferations of the gingivae, female predilection and association with pregnancy are encountered. The lesion is firm, usually not discolored. The surface is smooth, yet may occasionally be ulcerated. It emanates from one gingival papilla. It frequently recurs after excision.

MICROSCOPIC FEATURES

Surface epithelium may be ulcerated, and the bulk of the tissue mass is composed of collagenous fibers with hypercellular plump fibroblasts. Osteoid or oval cementum-like deposits are randomly oriented within the fibrous element.

DIFFERENTIAL DIAGNOSIS

Peripheral ossifying fibroma resembles the other focal swellings included here; however, unlike pyogenic granuloma and peripheral giant cell granuloma, it usually has a normal coloration. Microscopic examination is required for a definitive diagnosis.

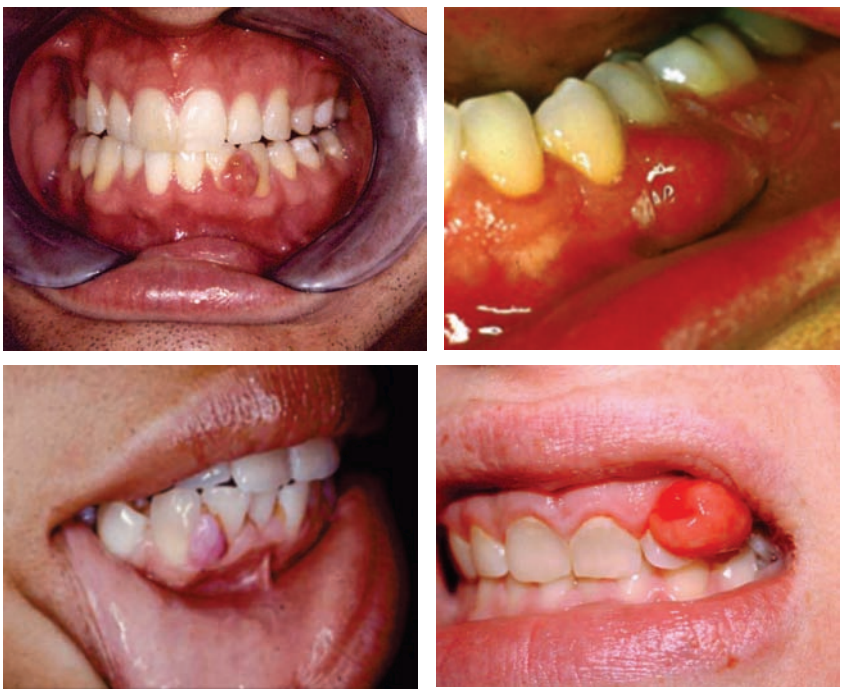

FIGURE 6-6
Peripheral ossifying fibroma, which is a firm, usually normal-colored growth of the marginal gingiva.

TREATMENT

Because the lesion probably arises in the periodontal ligament, the excision should be deep, including periosteum and ligament, and thorough root scaling of adjacent teeth should be performed.

Additional Reading

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JUVENILE SPONGIOTIC GINGIVAL HYPERPLASIA

Figure 6-7

Age: Children
Sex: Female predilection

CLINICAL FEATURES

Papillary hyperplastic lesions occur on the gingiva among children and appear "pasted on" to the gingival mucosa. Many of these lesions occur in children with braces. The lesions show a granular red surface with a strawberry appearance, which may be ulcerated and often emanate from the interdental papillae. These lesions may be reactive in nature with clinical features of an inflamed papillary pyogenic granuloma.

MICROSCOPIC FEATURES

Epithelial hyperplasia is seen with spongiotic acanthosis characterized by anastomosing rete pegs. The supportive connective tissue fronds are represented by areolar, hypervascular connecitve tissue showing a mixed leukocytic infiltrate.

DIFFERENTIAL DIAGNOSIS

Inflamed papilloma and pyogenic granuloma are the chief entities to be considered in the differential diagnosis. Microscopic examination is required for the final diagnosis.

TREATMENT

Focal gingivectomy (local excision) is the treatment of choice.

Additional Reading

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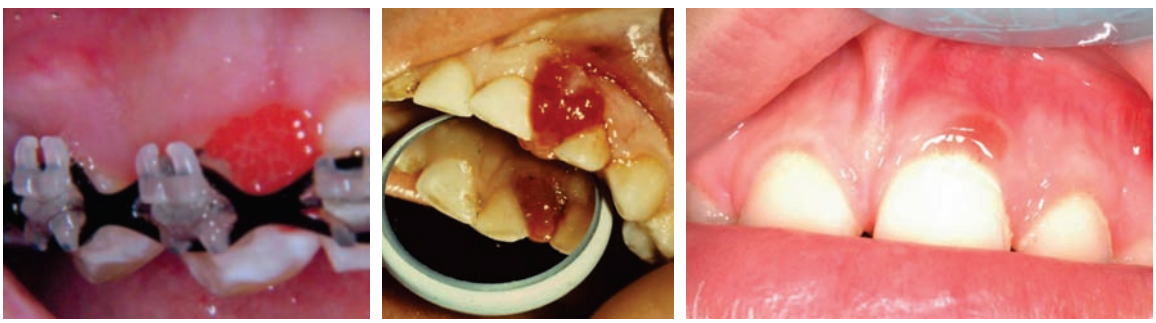

FIGURE 6-7
Juvenile spongiotic gingival hyperplasia.

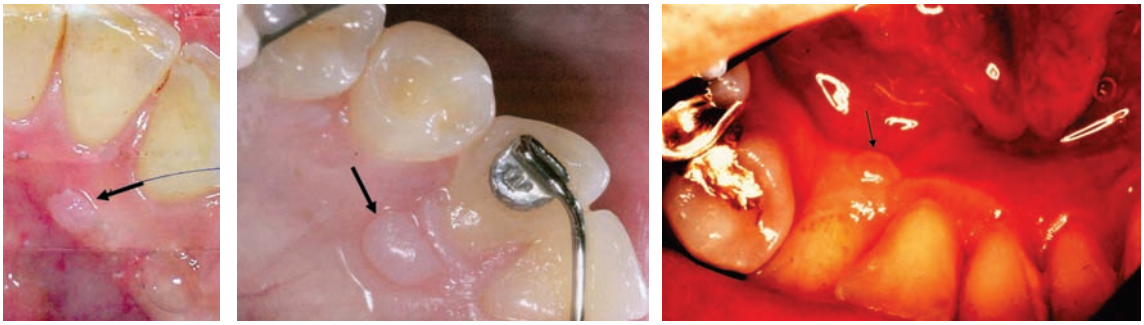

FIGURE 6-8
The retrocuspid papilla, a developmental papule located on the lingual gingiva adjacent to mandibular cuspids.

RETROCUSPID PAPILLAE

Figure 6-8

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Retrocuspid papillae are 2- to 4-mm papules located bilaterally on the lingually attached gingiva immediately posterior to the mandibular cuspids. They are soft, of normal color, and not associated with any causative factor. They probably represent developmental anomalies and may merely represent a variant of giant cell fibroma.

MICROSCOPIC FEATURES

An epithelium-covered papule is composed of fibrous connective tissue. Fibroblasts may contain 2 or 3 nuclei being stellate or spindle in shape.

DIFFERENTIAL DIAGNOSIS

The small papules may resemble a parulis or fistula; however, lack of an infectious source and bilateral location generally allow for a clinical diagnosis.

TREATMENT

No treatment is necessary.

Additional Reading

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TORUS MANDIBULARIS AND EXOSTOSES

Figure 6-9

Age: Adults
Sex: Slightly more common among females

CLINICAL FEATURES

Whereas tori and exostoses are hard tissue lesions, they are included with the soft tissue swellings because of their clinical resemblance to other gingival swellings. Mandibular tori are located bilaterally on the lingual mandibular gingiva in the cuspid-premolar region. Being bosselated and extremely hard, they represent bony excrescences. Unilateral instances occur less

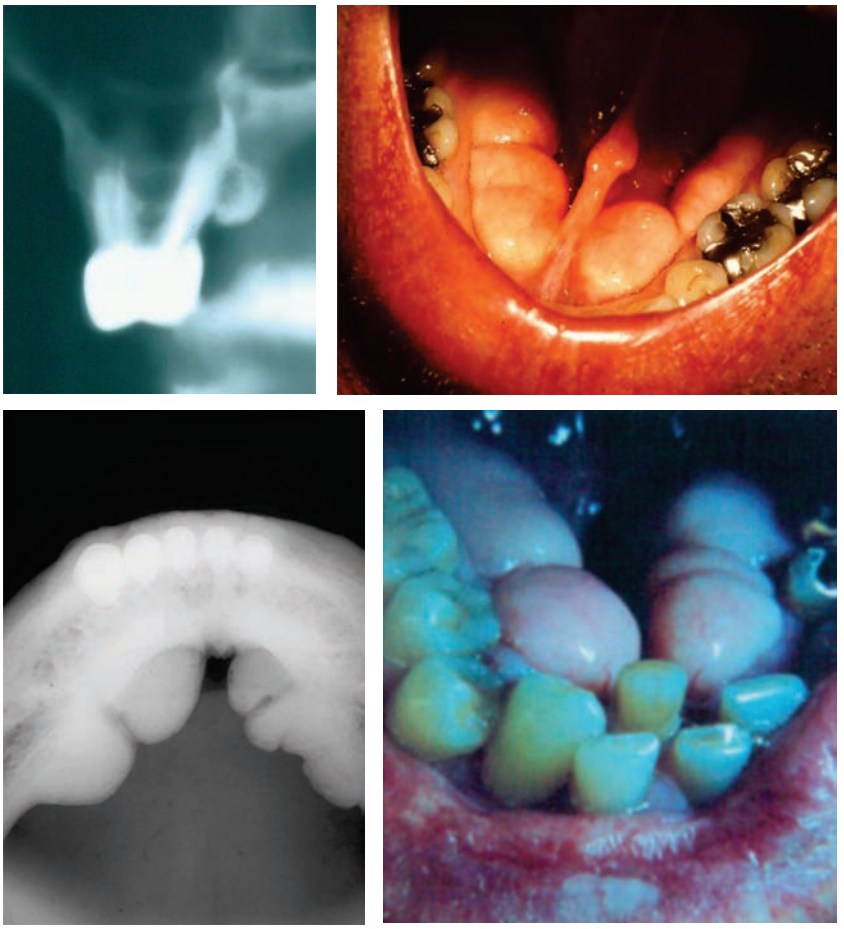

FIGURE 6-9
Lingual tori. These are usually small, yet may reach the large proportions seen here.

frequently. They are rather common among all races and are encountered in one third of the Eskimo population. Tori are inherited as an autosomal dominant trait. Progressive slow growth occurs throughout adulthood. Exostoses are multiple similar lesions located on the buccal aspect of the maxillary and mandibular alveolus. Both may show oval radiopacities on dental radiographs.

MICROSCOPIC FEATURES

Mature osseous trabeculae emanate from an outer cortex and are admixed with fibrous or adipose marrow.

DIFFERENTIAL DIAGNOSIS

The bony, hard consistency and bilaterality of tori are features sufficiently unique to allow for a clinical diagnosis.

TREATMENT

No treatment is required. Tori can be removed by chisel or burr should they interfere with fabrication of a dental prosthesis.

Additional Reading

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GINGIVAL CYST

Figure 6-10

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Submucosal cysts of the gingiva appear as firm or compressible smooth-surfaced nodules with a blanched appearance. The mandibular gingiva adjacent to the premolars is the most common location. The pathogenesis is variable; they may arise from rests of Serres or epithelial implantation, or they may be the peripheral counterpart of the central lateral periodontal cyst. Others may not be clinically obvious, but are discernible as microcysts in routine gingival surgical specimens. Regardless of their origin, all gingival cysts are relatively self-limited in terms of their growth potential. They are located in attached gingiva removed from the free gingival margin.

MICROSCOPIC FEATURES

The cystic lining resembles that of nonkeratinizing lateral periodontal cyst. The microscopic features are unique. The lining epithelium is cuboidal and pursues a tortuous course with a multicystic pattern. Focal acanthotic excrescences are seen and are composed of clear cells. The multiple cystic cavities probably interconnect at various levels and are separated by dense fibrous tissue devoid of inflammation. Some gingival cysts show ameloblastic differentiation with ghost cells, keratinization, and calcification. Lesions of this nature represent peripheral calcifying and keratinizing (Gorlin) cysts.

DIFFERENTIAL DIAGNOSIS

Reactive proliferations generally arise in the gingival papilla area, whereas cysts are oriented away from the gingival margin. Parulis and peripheral odontogenic tumors may show identical clinical fea-

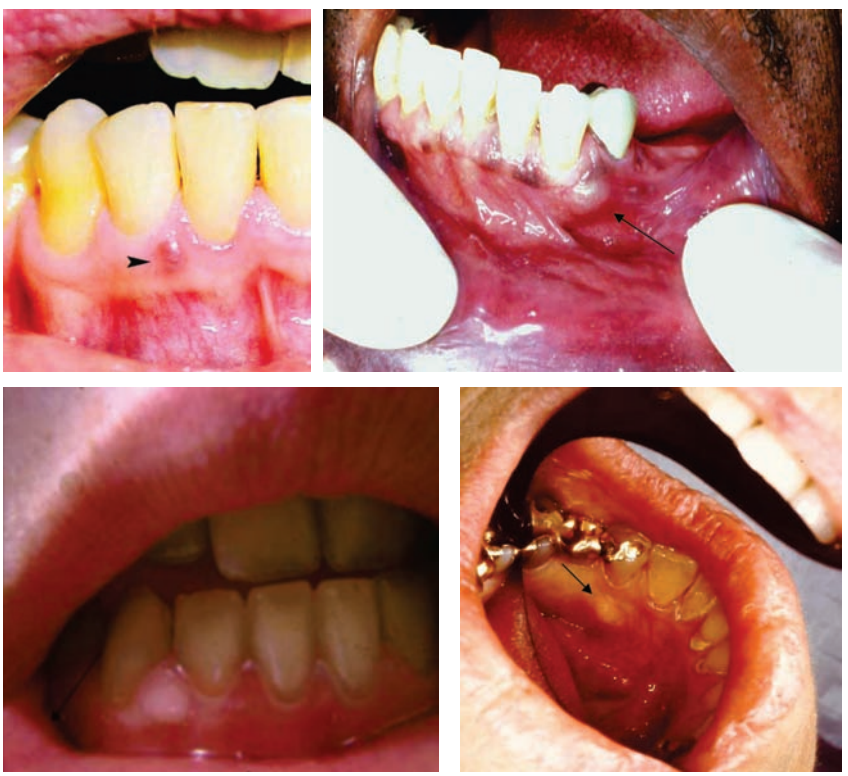

FIGURE 6-10
Gingival cysts arising from the dental lamina or rests of Serres are either firm or fluctuant.

tures; the former can usually be eliminated from consideration by ruling out a source of inflammation.

TREATMENT

Gingival cysts can be excised or enucleated.

Additional Reading

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ERUPTION CYST

Figure 6-11

Age: Children
Sex: No predilection

CLINICAL FEATURES

The eruption cyst is a soft tissue dentigerous cyst arising from the reduced enamel epithelium and follicle of an erupting deciduous or permanent tooth. Therefore, it is seen directly overlying the alveolus at the site of eruption. It may be dark red when it is blood filled.

MICROSCOPIC FEATURES

Lining stratified squamous or columnar epithelium is present, and the follicular wall evinces an avid inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The clinical features are diagnostic. Neoplasia has not been reported to arise from the lining of eruption cysts.

TREATMENT

The soft tissue cap can be excised to uncover the erupting tooth.

Additional Reading

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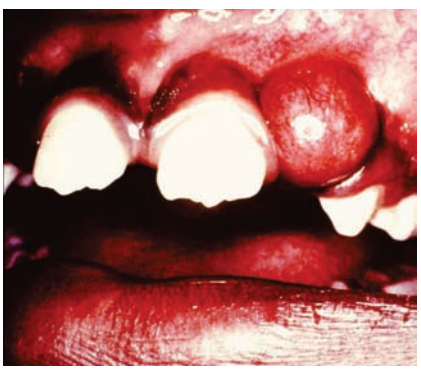

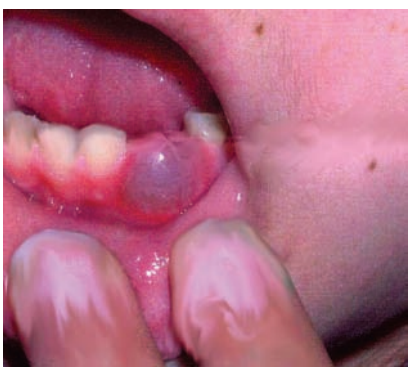

FIGURE 6-11
An eruption cyst appearing as an inflamed mass of the gingiva overlying an erupting tooth.

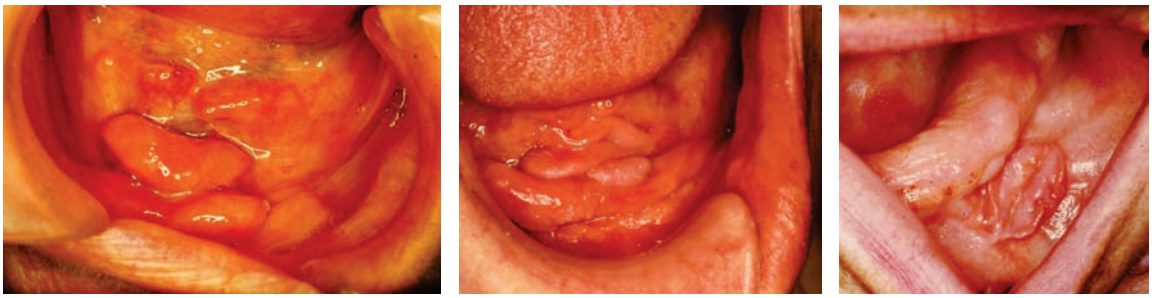

FIGURE 6-12
Redundant tissue folds underlying a denture flange, representing fibrous hyperplasia secondary to irritation.

EPULIS FISSURATA

Figure 6-12

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Flabby, redundant soft tissue masses, which are often fissured or bosselated, emanate from the base of the alveolar ridge and extend into the mucobuccal fold, as hyperplastic responses to ill-fitting dental prostheses. The hyperplastic tissue is located at the contact area of the denture flange and generally has a broad base of attachment. Epulis fissurata is usually of normal color, yet may show foci of inflammation with ulceration. It is soft to palpation.

MICROSCOPIC FEATURES

Surface epithelium overlies masses of dense fibrous connective tissue that contains variable amounts of inflammatory cells. Focal myxomatous zones and cartilaginous rests may be seen when the lesion is located on the interior maxillary alveolus and mucobuccal fold.

DIFFERENTIAL DIAGNOSIS

Redundant hyperplastic tissue must be differentiated from the other gingival tumefactions, including carcinoma. Its soft movability and broad base are usually sufficient to make this lesion clinically recognizable.

TREATMENT

The tissue should be excised and examined microscopically. A new set of dentures or a relining is required to prevent reestablishment of the hyperplastic response.

Additional Reading

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CONGENITAL EPULIS

Figure 6-13

Age: Present at birth
Sex: Female predilection

CLINICAL FEATURES

The congenital epulis is a neoplasm of unknown origin found exclusively on the alveolar ridge. A large polypoid soft swelling, which may reach a diameter of several centimeters, emanates from a constricted stalk that attaches the tumor to the

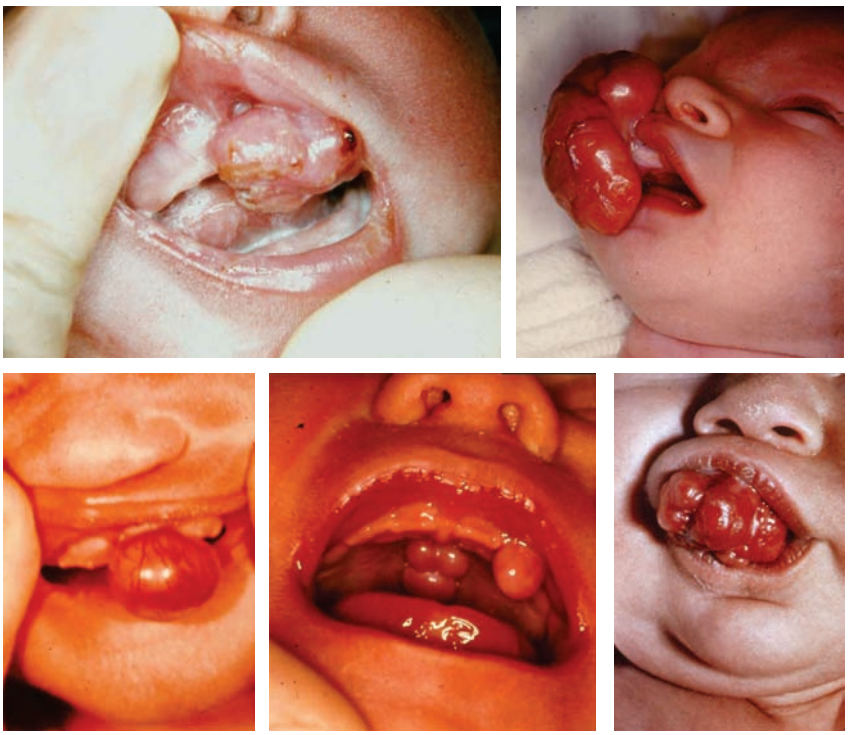

FIGURE 6-13
Firm or rubbery gingival masses emanating from a constricted stalk in congenital epulis of the newborn.

edentulous alveolus of newborns. Congenital epulis is more common on the maxillary anterior alveolar ridge. The tumor is somewhat firm yet may be compressible.

MICROSCOPIC FEATURES

The overlying epithelium is intact and unremarkable. The tumor is composed of large swollen granular or foamy cells with a round pyknotic nucleus. The fibrous stroma is scant; only small vascular channels are seen. The cellular architecture is extremely monomorphic with no cytologic atypia, and organoid configurations are not featured. Recent evidence based on electron microscopic findings supports a pericyte origin for this lesion.

DIFFERENTIAL DIAGNOSIS

Congenital epulis is infrequently found. A pedunculated mass in the newborn on the gingiva may occur in congenital sarcoma or teratoma, both of which are extremely rare.

TREATMENT

Excision with inclusion of the stalk or base may be accomplished without danger of recurrence.

Additional Reading

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MESENCHYMAL TUMORS

Figure 6-14

Age: No predilection
Sex: Depends on tumor type

CLINICAL FEATURES

A variety of soft tissue tumors may arise on the gingival and alveolar ridges. The more common entities are hemangioma, nerve sheath tumors, leiomyomas and solitary fibrous tumor. These lesions are far less commonly encountered than the reactive lesions of fibrovascular and periodontal fibrous origin. As a group, they present as dome shaped, sometimes multinodular, submucosal tumefactions with normal coloration except for angiomatous lesions, which are red or purple. They are firm yet not indurated and are usually fixed to the underlying periosteum.

MICROSCOPIC FEATURES

The mesenchymal tumors show microscopic features that differentiate into patterns that resemble their cells of origin. Hemangiomas may show cavernous or cellular capillary structures that are engorged with red cells. Angioleiomyomas show central vascular lumens surrounded by concentric layers of smooth muscle cells and collagenous tissues, the former positive for smooth muscle actin. Nerve sheath tumors include neurilemmom and neurofibroma, the former with Antoni A tissue and verrocay bodies, the latter with delicate haphazardly arranged fibrous tissue showing S-100 nuclear and cytoplasmic localization. Leiomyomas are spindle cell benign proliferations populated by spindle nuclei with blunt ends and stain with smooth muscle actin. Solitary fibrous tumors are patternless spindle cell proliferations with wavy collagen and stain for CD34.

DIFFERENTIAL DIAGNOSIS

The soft tissue tumors are clinically similar to reactive gingival lesions yet biopsy will disclose their mesenchymal differentiation depending on the tissues they resemble. Neurofibromas may be multiple with accompanying skin tumors and café-au-lait pigmentations in von Recklinghausen's neurofibromatosis.

TREATMENT

Simple local excision with clear margins is the treatment of choice.

Additional Reading

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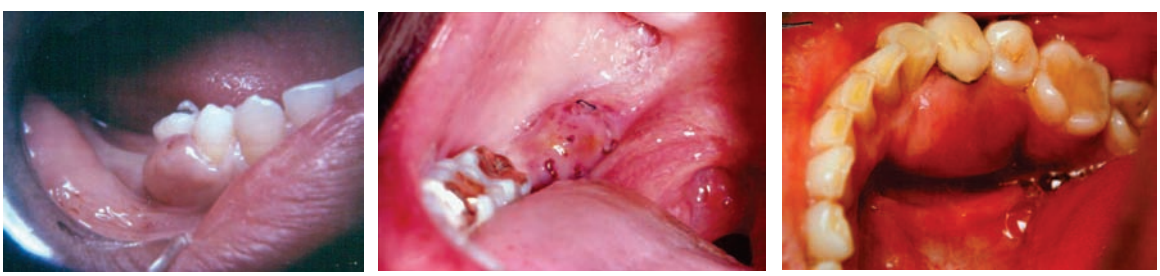

FIGURE 6-14
Mesenchymal gingival tumors (nerve sheath tumor, hemangioma, leiomyoma) are firm submucosal masses.

PERIPHERAL ODONTOGENIC TUMORS

Figure 6-15

Age: Young adults
Sex: Depends on tumor type

CLINICAL FEATURES

Tumors that arise from the odontogenic apparatus or remnants of the tooth germ are, as a rule, intraosseous. Occasionally, they arise in the extraosseous tissues of the alveolus. Clinically, they are nodular smooth-surfaced tumefactions of the gingiva that are firm to palpation. Soft tissue ossification may be detectable in radiographs in some of these tumors. The odontogenic tumors that can originate in the gingiva are the Gorlin cyst, Pindborg tumor, odontogenic adenomatoid tumor, ameloblastoma, peripheral odontogenic hamartoma, peripheral odontogenic fibroma, and ameloblastic fibrodentinoma.

MICROSCOPIC FEATURES

The tumor cells may or may not be encapsulated and vary, depending on the type of tumor seen (see chapters dealing with radiolucencies and radiopacities). Two odontogenic tumors are characteristically extraosseous. The peripheral odontogenic hamartoma is composed of fibrous tissue with linear epithelial cords and is synonymous with peripheral odontogenic fibroma. The other gingival tumor, ameloblastic fibrodentinoma, occurs in children and is represented by dental lamina-like epithelial cell rests, some of which show stellate reticulum. These cell rests are dispersed throughout a mesenchymal stroma that is poorly endowed with collagen. An eosinophilic dentin-like amorphous product is found in juxtaposition to the epithelial cell component.

DIFFERENTIAL DIAGNOSIS

Extraosseous odontogenic tumors show clinical features in common with the reactive proliferations and gingival cysts.

TREATMENT

Simple excision is the treatment of choice. Peripheral forms of odontogenic tumors,

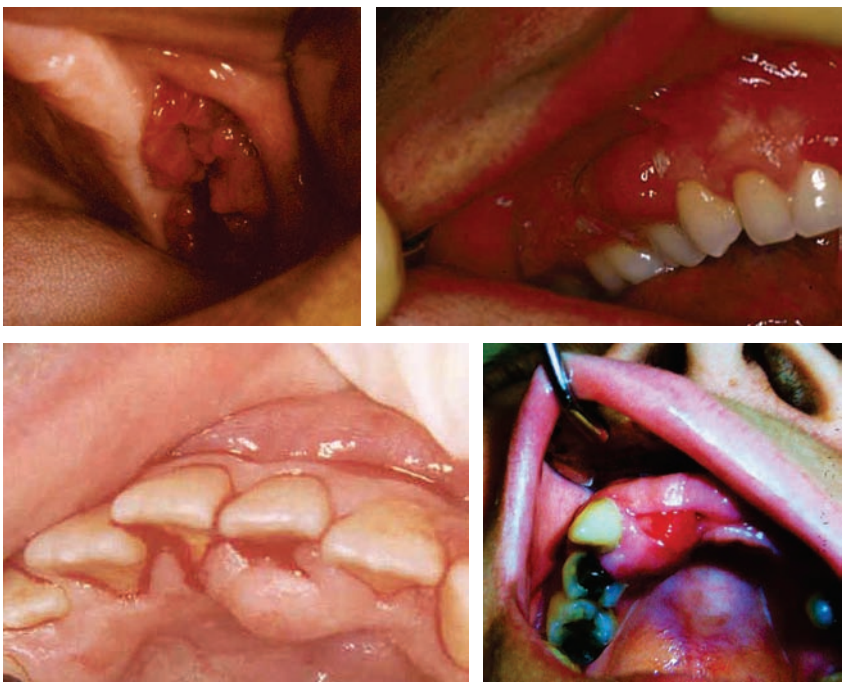

FIGURE 6-15
Peripheral odontogenic tumors (calcifying odontogenic cyst, ameloblastic fibroma, calcifying epithelial odontogenic tumor, ameloblastoma).

considered aggressive when located centrally, behave nonaggressively, with little tendency for recurrence.

Additional Reading

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SQUAMOUS CELL CARCINOMA

Figure 6-16

Age: Elderly
Sex: Male predilection

CLINICAL FEATURES

Squamous cancer of the gingiva and alveolar ridge represents about 15% of all oral squamous cell carcinomas. The swelling is either red or keratotic and may appear granular or ulcerated. The lesion frequently extends into the mucobuccal fold or oral floor and is most prevalent on the mandibular arch. In addition, the marginal tissue is frequently leukoplakic or erythroplakic. The swelling is usually indurated. Palpation of the submandibular and cervical regions is essential in order to detect any clinical evidence of regional metastasis; a thorough medical work-up should be pursued along with a chest radiograph to evaluate for distant metastases. All squamous cell carcinomas in this location should be assessed for bone invasion of the alveolus by procuring panoramic and periapical radiographs.

MICROSCOPIC FEATURES

Invasive nests and islands of squamous epithelium are encountered, and most tumors evince parakeratin pearls or squamous eddies. The individual cells show varying degrees of pleomorphism, hyperchromatism, and mitoses. The fibrous stroma is frequently infiltrated by mononuclear cells.

DIFFERENTIAL DIAGNOSIS

Swellings of the gingiva or edentulous ridge representing carcinoma may be confused with reactive proliferations included in this section on gingival tumefactions. Usually the patient's age, when considered along with lesional induration, ulceration, and/or keratosis, supports a clinical impression of cancer. An incisional biopsy is essential to a definitive diagnosis.

TREATMENT

Squamous cell carcinoma must be treated aggressively to achieve a cure. Radiotherapy and surgery are generally combined, along with regional node dissection in the presence of palpable nodes. Prophylactic neck dissection or radiation therapy is usually indicated in the absence of palpable nodes. The prognosis is based on tumor size (T), the presence or absence of nodal metastasis (N), and the presence or absence of distant metastasis (M). The 5-year survival for patients with lesions less than 3 cm is about 80%. Invasion of underlying bone along with periosteal lymphatic invasion worsen the prognosis; bone scanning may provide additional information regarding extent of disease before planning surgical intervention.

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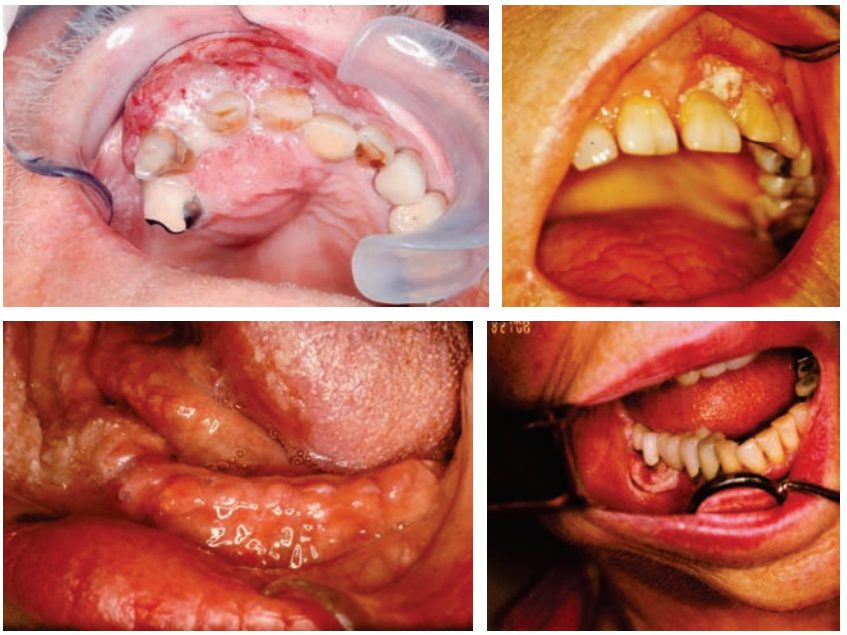

FIGURE 6-16
Squamous cell carcinoma of the gingiva.

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SARCOMAS

Figure 6-17

Age: Young adults
Sex: Depends on tumor type

CLINICAL FEATURES

Like benign mesenchymal tumors, sarcomas differ according to their differentiation. These malignancies are very rare in the oral cavity and may occur in any location. The more common are fibrosarcoma, malignant fibrous histiocytoma, angiosarcoma in human immunodeficiency virus (HIV) patients, neurogenic sarcoma, and leiomyosarcoma. As a group, they are rapidly growing, often ulcerated and indurated masses, and many are friable and hemorrhagic. Myelogenous leukemia may form extravascular infiltrates of the soft tissues accompanied by leukocytosis and bone marrow infiltrates (granulocytic sarcoma).

MICROSCOPIC FEATURES

As mentioned earlier, the sarcoma nosology is based on patterns of differentiation. Immunohistochemical markers are of value in refining or corroborating the histopathologic features. As a group, most are spindle cell proliferations that exhibit hypercellularity, nuclear pleomorphism, and mitotic figures, many of which are atypical. Most sarcomas stain positively for vimentin, a connective tissue protein. Other markers are also assessed for aiding the diagnosis such as muscle (desmin, actin), nerve sheath (S-100 protein), and hematologic (various CD cell surface proteins). Granulocytic sarcoma is characterized by a round cell infil-

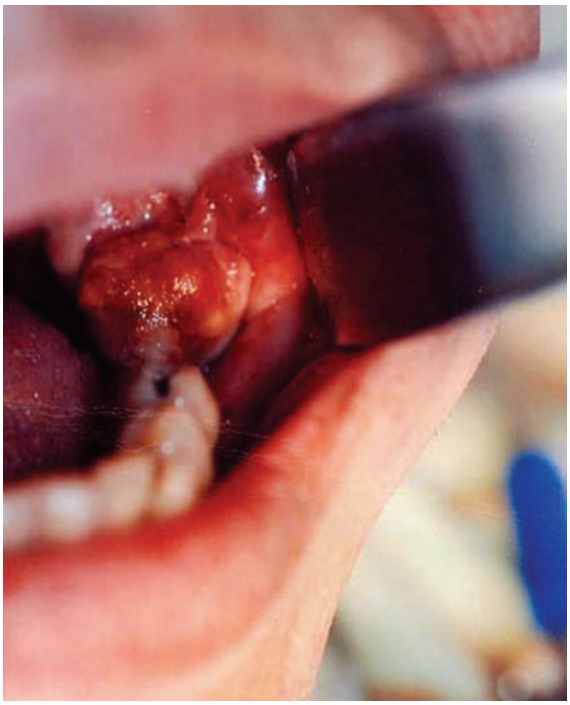

FIGURE 6-17
Fibrosarcoma of the gingiva.

trate, positive with myeloid markers and chloracetate esterase.

DIFFERENTIAL DIAGNOSIS

The rapid growth, size, and induration seen with sarcomas are also seen in primary squamous cell carcinomas, lymphomas, and metastatic tumors. The use of the aforementioned markers will assist the pathologist in determining what cell the tumor is attempting to mimic.

TREATMENT

Radical surgery is usually required along with resection of the jaws. Some types respond to radiation therapy and adjunct chemotherapy. The specific type of sarcoma dictates the treatment.

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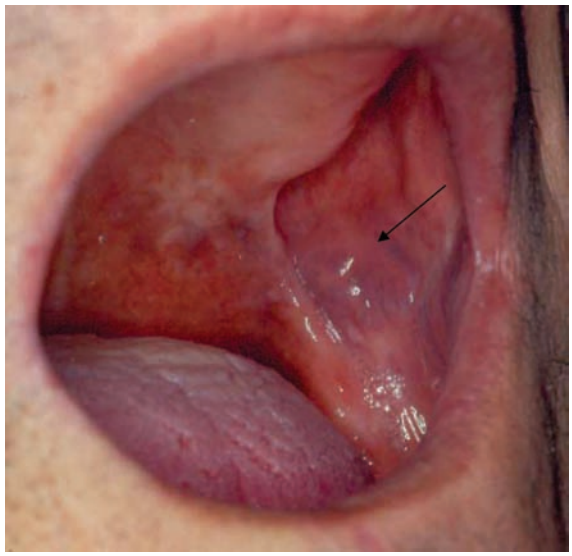

FIGURE 6-18
Mucoepidermoid carcinoma, often observed as a swelling in the retromolar pad area.

MUCOEPIDERMOID CARCINOMA

Figure 6-18

Age: Teenagers and adults
Sex: No predilection

CLINICAL FEATURES

Mucoepidermoid carcinoma is included with gingival tumefactions because of the propensity of this tumor to arise at the posterior confines of the mandibular alveolus, the retromolar pad. It arises from salivary glands normally present in this location and may be indurated or fluctuant and cystic, resembling a mucocele. The surface mucosa is generally intact. Occasionally, cystic, mucin-filled spaces occur superficially, giving the tumor a vesicular or bleb-like appearance.

MICROSCOPIC FEATURES

Neoplastic ductal, cuboidal, and squamous epithelia are present, as are mucous cells. The neoplastic islands may be solid or cystic with large dilated mucin-filled spaces.

DIFFERENTIAL DIAGNOSIS

The other tumefactions of the gingiva included in this section tend to occur anteriorly. Retromolar swellings, which appear clinically similar, include mucocele, eruption cyst from an impacted third molar, and mesenchymal neoplasms.

TREATMENT

Low-grade tumors are treated by wide local excision. High-grade malignancy requires wide excision and block resection of the underlying mandibular bone. Careful evaluation of the neck is necessary because nodal involvement requires in-continuity neck dissection or, at least, supraomohyoid dissection when submandibular nodes are palpable.

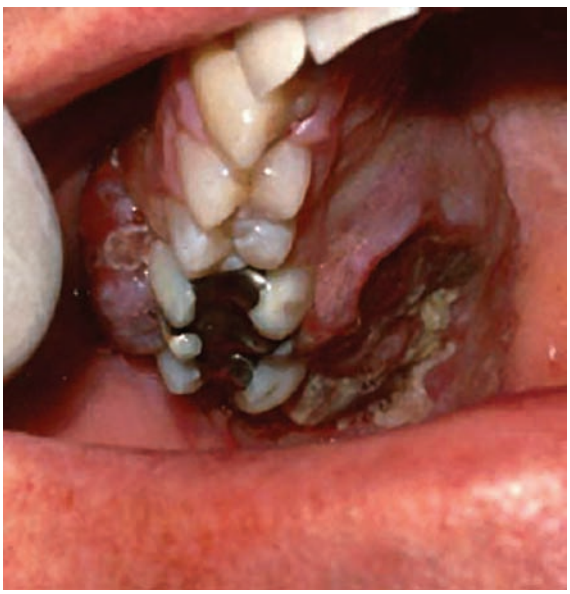

FIGURE 6-19
Gingival mass representing HIV-associated extranodal lymphoma.

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NON-HODGKIN'S LYMPHOMA

Figure 6-19

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

Lymphomas in the oral cavity are extranodal and rare. When they occur, one should be suspicious of HIV infection. Clinically, HIV-associated lymphomas of the oral cavity are most often encountered on the gingiva, particularly the palatal gingiva. The lesions are indurated, ulcerated, and erythematous and manifest extremely rapid growth. Pain and paresthesia are uncommon symptoms. Gingival lesions may induce saucerization of the underlying bone. Oral non-Hodgkin's lymphomas among non-HIV subjects often arise centrally in the jaws. T-cell lymphomas associated with human lymphotropic virus are endemic on certain islands in Japan, yet the head and neck lesions tend to arise in Waldeyer's ring rather than in the oral cavity proper.

MICROSCOPIC FEATURES

As with nodal lymphomas, non-Hodgkin's lymphomas of the oral regions are usually of B-lymphocyte origin and can exhibit a

variety of cytologic patterns depending on the degree of differentiation. Therefore, some lesions consist of large cleaved and noncleaved lymphoblasts, whereas others are represented by small lymphoblasts or lymphocytes. A nodular pattern is not usually observed in these extranodal lesions, and the periphery of the infiltrate is commonly represented by stringy, elongated degenerative lymphocytes. A Burkitt's lymphoma-like histologic pattern (starry-sky pattern) is frequently noted, particularly in HIV-associated oral lymphomas. Some lesions contain Epstein-Barr virus genomic DNA.

DIFFERENTIAL DIAGNOSIS

Reactive gingival tumefactions, including pyogenic granuloma and giant cell granuloma, must be considered in the clinical diagnosis, because they too can display an extremely rapid growth rate. Most of the lesions appearing as localized tumefactions of the gingiva do not spread laterally and diffusely as does lymphoma.

TREATMENT

Extranodal non-Hodgkin's lymphomas in the oral cavity convey variable prognoses depending on the specific type. Often the patient has disseminated disease, and it is imperative to subject patients to a complete work-up for lesions in other areas once a histologic diagnosis has been established. Radiation therapy is recommended for localized oral lesions; disseminated disease requires multiregimen chemotherapy.

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METASTATIC CARCINOMA

Figure 6-20

Age: Adults and elderly
Sex: Depends on tumor type

CLINICAL FEATURES

Metastatic tumors may be seen central in bone as well as in the soft tissues of the

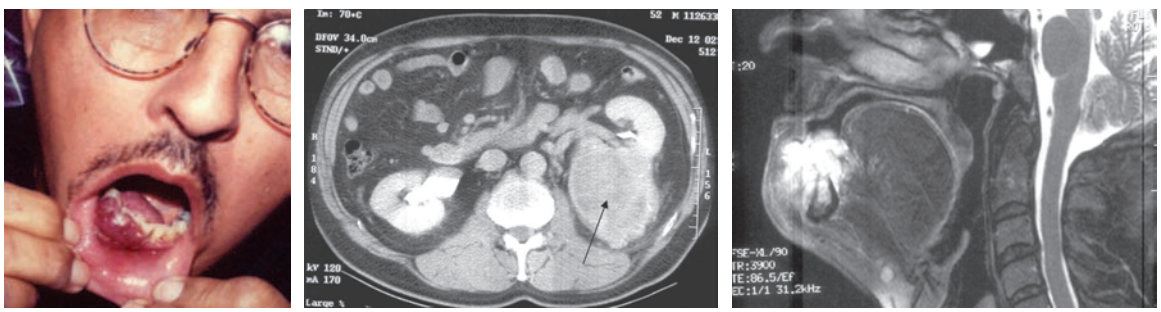

FIGURE 6-20
Metastatic renal cell carcinoma, magnetic resonance imaging showing metastatic tumor infiltration of mandible and abdominal images of primary tumor (arrow) involving kidney.

gingiva. The most common primary sites are breast, lung, colon, prostate, and kidney. They appear as multinodular, often hemorrhagic ulcerated masses with rapid growth. Oftentimes, at the time of biopsy, the primary site is unknown, and a metastatic work-up is required.

MICROSCOPIC FEATURES

The microscopic features are unique to the patterns seen in the primary organs of origin. The tumors usually comprise cytologically atypical cells that can represent undifferentiated tumors, clear cell tumors, adenocarcinomas, and squamous cell carcinomas. Immunohistochemistry (IHC) markers are valuable in defining the organs of origin including breast markers such as progesterone and estrogen receptors as well as Her-2-Nu, prostate specific antigen, carcinoembryonic antigen, and cytokeratins to name but a few.

DIFFERENTIAL DIAGNOSIS

Metastatic tumors clinically resemble primary malignancies such as squamous cell carcinoma, salivary malignancies, lymphomas, and sarcomas. When assessed microscopically and the tumor is thought to represent a metastasis, a metastatic clinical, imaging, and laboratory work-up is required in order to locate the primary focus.

TREATMENT

Therapy is varied depending upon site of origin and degree of dissemination usually requiring various combinations of surgery, radiation, and chemotherapy.

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LANGERHANS CELL HISTIOCYTOSIS

Figure 6-21

Age: Children
Sex: No predilection

CLINICAL FEATURES

The Langerhans cell is a specialized macrophage that resides in the epithelium of skin and mucous membranes and functions as an antigen-presenting cell in the context of the afferent limb of the immune response. Clonal proliferation of Langerhans cells may be focal or multifocal. Acute disseminated Langerhans cell histiocytosis (LCH) occurs in infants and toddlers presenting with multiorgan involvement, typically liver and spleen along with a cutaneous papular

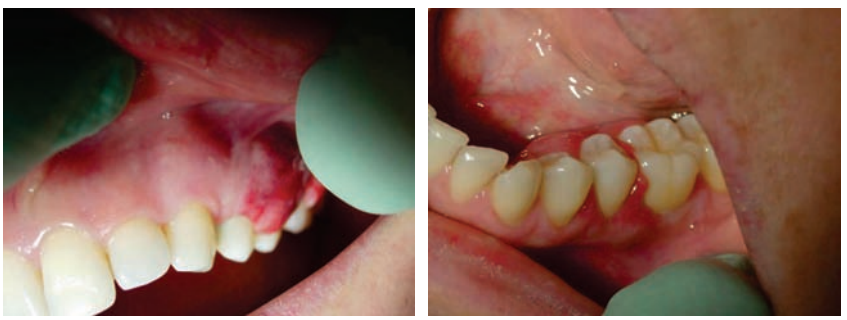

FIGURE 6-21
Langerhans histiocytosis is primarily a bone lesion in the jaws yet may extend into the gingiva.

rash. Chronic disseminated LCH occurs in children and teens in which infiltrates of Langerhans cells may result in intraosseous lesions including radiolucencies of the skull and jaws, retro-orbital infiltrates causing exophthalmos and posterior pituitary lesions with resultant diabetes insipidis. In young adults, localized LCH may present with a single focus of tumor cells, often seen in the lungs or the jaws. Jaw lesions of LCH may appear as periradicular periodontal radiolucenies yielding a "tooth floating in space" appearance, and the overlying gingiva is red, enlarged, and often ulcerated.

MICROSCOPIC FEATURES

The Langerhans cell is dentrocytic when seen in the epithelium; however in LCH, large mononuclear cells are seen and possess oval clear nuclei with surrounding eosinophilic cytoplasms and an accompaniment of scattered eosinophils. Langerhans cells stain for CD1a and S-100 protein and on election microscopy Birbeck organelles, shaped like small tennis rackets, are encountered.

DIFFERENTIAL DIAGNOSIS

LCH may be confused with an inflammatory reaction or Hodgkin's lymphoma. IHC staining of S-100 and/or CD1a are useful markers for the diagnosis of LCH.

TREATMENT

Surgical intervention and tooth extraction may be required for oral and jaw lesions. Disseminated disease is successfully managed by chemotherapy, usually Vinca alkaloids (vincristin, vinblastin).

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Generalized Gingival Swellings

FIBROMATOSIS GINGIVAE

Figure 6-22

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Transmitted as an autosomal dominant trait, hereditary fibromatosis gingivae becomes obvious soon after eruption of the primary teeth. The gingiva shows multinodular enlargement, most prominent in the interdental papillar regions. The tissue is firm and of normal color, and the hyperplasia may be so extensive that the entire

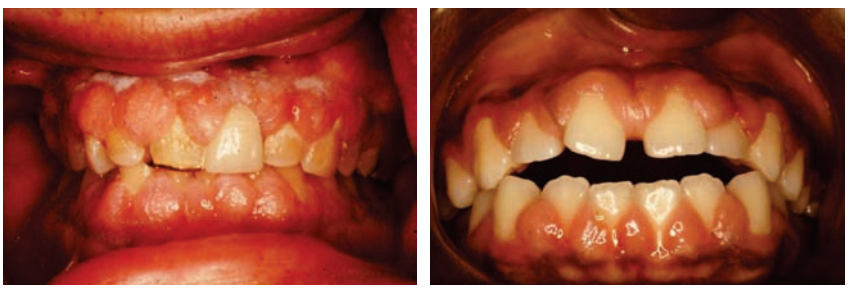

FIGURE 6-22
Generalized fibrotic enlargement of the gingival tissues, a feature of hereditary fibromatosis gingivae.

coronal portion of the teeth is obliterated. Elimination of dental plaque does not significantly lessen the severity. The disorder has been linked to 2p21. Gingival fibromatosis may be accompanied by other disorders, including splenomegaly, enlarged nasal and external ear soft tissues, shortened terminal phalanges, hyperflexia of joints, and hypoplasia of the nails, the so-called Laband syndrome.

MICROSCOPIC FEATURES

Gingival epithelium is distended by massive accumulations of mature, dense collagenous tissue. Inflammation is minimal.

DIFFERENTIAL DIAGNOSIS

Dilantin (phenytoin sodium) hyperplasia, hyperplastic gingivitis, and leukemic infiltration of the gingiva may show signs clinically indistinguishable from fibromatosis gingivae. A history of familial involvement is of paramount importance in making the diagnosis.

TREATMENT

Periodic gingivectomy with placement of a gingival acrylic splint or prosthesis can be done for both cosmetic and functional reasons. Recurrence to some degree should be anticipated.

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DRUG INDUCED HYPERPLASIA

Figure 6-23

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Gingival hyperplasia is encountered among patients receiving hydantoin, nifedipine, and cyclosporin A. Gingival enlargement occurring in seizure patients receiving sodium diphenylhydantoin is generalized. The gingiva shows bulbous fibrotic firm nodules emanating from the papillar regions and may be severe enough to obscure the crowns of the teeth. The condition is worsened when oral hygiene is poor and dental plaque accumulates. Hyperplastic tissue on edentulous ridge areas is extremely rare, yet has been reported to occur in edentulous patients. In general, cyclosporin- and nifedipine-induced hyperplasia are less severe and a pebbly surface is often encountered. Recent research indicates that specific subpopulations of fibroblasts in the gingiva respond to these drugs with increased proliferation and fibrillogenesis.

MICROSCOPIC FEATURES

Surface epithelium is distended by dense collagenous fibrous tissue. Long, slender so-called test-tube rete ridges extend deeply into the subjacent fibrous tissue. Inflammatory cell infiltration is not a prominent or consistent finding.

DIFFERENTIAL DIAGNOSIS

A history of epilepsy controlled by diphenylhydantoin is necessary for the diagnosis. This drug-related gingival enlargement may be indistinguishable from fibromatosis gingivae and may resemble that seen in leu-

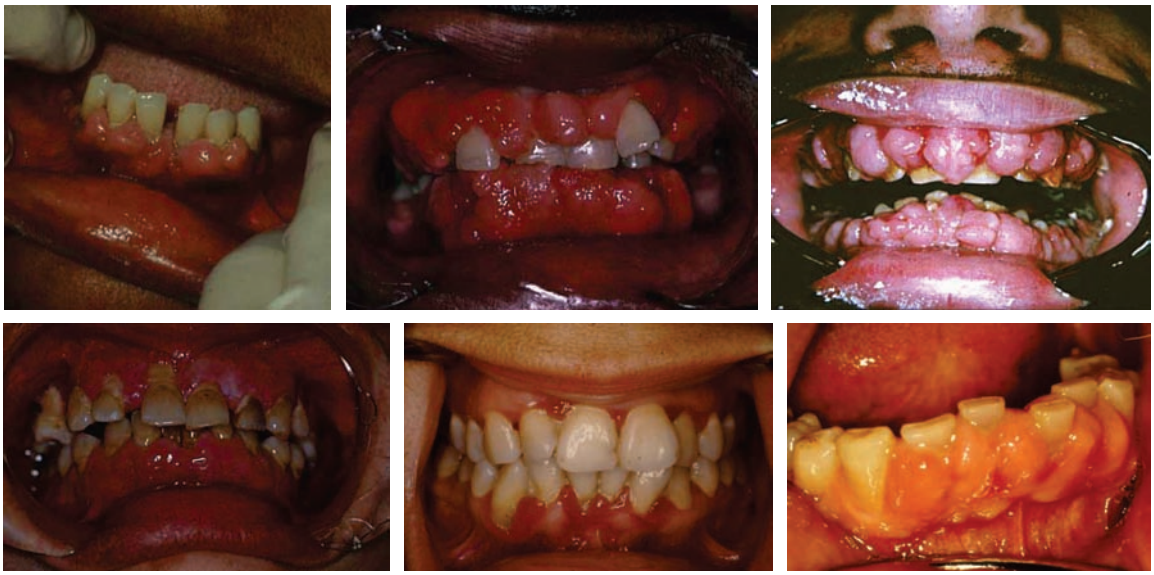

FIGURE 6-23
Generalized enlargement of the gingiva as a consequence of medications (hydantoin, cyclosporine, calcium channel blockers).

kemia and nonspecific hyperplastic gingivitis. Nifedipine is a calcium channel blocker used in therapy for coronary artery disease, whereas cyclosporin is an immunosuppressive agent prescribed for organ transplant patients.

TREATMENT

Cosmesis and function may be restored by gingivectomy followed by thorough prophylaxis and institution of a conscientious oral hygiene home care program. Recurrence is common, yet the degree of enlargement can be lessened provided appropriate periodontal maintenance therapy is followed.

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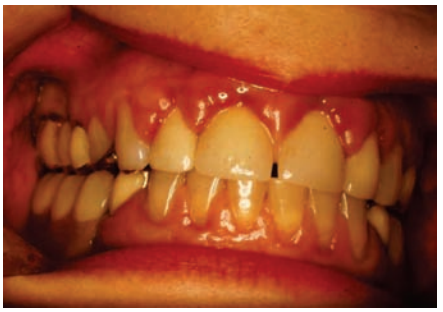
NONSPECIFIC HYPERPLASTIC GINGIVITIS

Figure 6-24

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Whereas most forms of nonspecific gingivitis result in mild edema with erythema, an occasional response is one of swelling from edema, fibroplasia, and inflammatory cell infiltration. This hyperplastic form of gingivitis is characterized by generalized enlargement, particularly interdentally; the tissues are boggy, and ulceration is not frequent. Erythema is generally present. Dental plaque is accumulated and periodontal disease with pocket formation is often present as well. The hyperplastic form may be



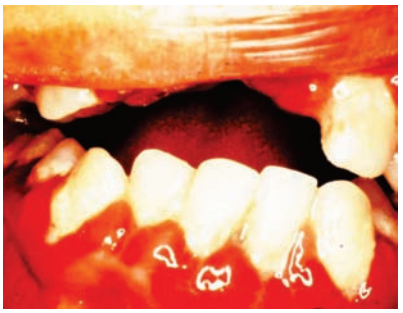


FIGURE 6-24
Nonspecific inflammatory enlargement of the gingiva.

uncomplicated by systemic disease; however, underlying medical problems such as uncontrolled diabetes mellitus or cyclic neutropenia must be ruled out. This form of gingivitis is frequently seen in gravid women.

MICROSCOPIC FEATURES

Surface epithelium may be unremarkable, whereas the crevicular epithelium evinces anastomosing elongated rete ridges. The underlying tissues are fibrovascular with nonspecific inflammatory cell infiltrates. Fragments of calculus and microbial colonies are often found adherent to crevicular epithelium.

DIFFERENTIAL DIAGNOSIS

Leukemic infiltrates may show indistinguishable features. Fibromatosis gingivae and Dilantin hyperplasia can mimic hyperplastic gingivitis, yet the former two lesions are usually not boggy or erythematous. A blood count, fasting blood sugar, or, preferably, a glucose tolerance test can be obtained to rule out leukemia, cyclic neutropenia, and diabetes.

On rare occasions, granulomatous inflammations such as Wegener's granulomatosis or tuberculosis can manifest generalized gingival enlargement. In these instances, the surface is pebbly or granular and ulceration is present. A biopsy differentiates nonspecific hyperplastic gingivitis from these lesions and from leukemia.

TREATMENT

Dental prophylaxis with scaling and periodontal curettage causes the hyperplastic tissue to subside. If the problem is complicated by systemic disease, systemic as well as local factors must be controlled.

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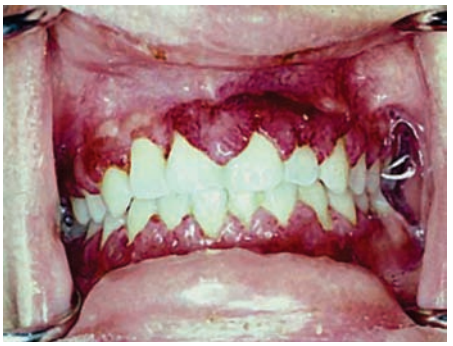
WEGENER'S GRANULOMATOSIS

Figure 6-25

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Wegener's granulomatosis is a rare disorder with pathogenic features akin to many of the collagen diseases. The pathologic manifestations include destructive granulomas



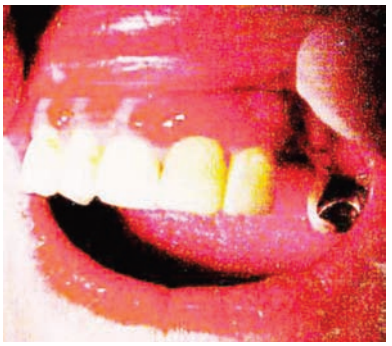


FIGURE 6-25
Diffuse granular gingival enlargement in Wegener's granulomatosis (strawberry gums).

of both upper and lower respiratory tract, necrotizing angiitis, and glomerulonephritis signaled by sinusitis and rhinitis, cough with hemoptysis, and uremia. Other tissues that may be involved include the middle ear, urethra, skin, and salivary glands. Whereas osseous destructive lesions are sometimes observed in the nose, sinuses, and palate, the gingival changes are unique and may, in fact, be pathognomonic of the disease. A generalized hyperplastic gingivitis is seen with a characteristic granular or pebbly telangiectatic appearance. Antineutrophil cytoplasmic antibodies (ANCA) are classically present in serum.

MICROSCOPIC FEATURES

A gingival biopsy discloses granulomatous inflammation with a mononuclear infiltrate. Multinucleated giant cells are present and in some patients the granulomas are infiltrated by numerous eosinophils. The sine qua non on a microscopic basis is the presence of necrotizing vasculitis.

DIFFERENTIAL DIAGNOSIS

Although the other entities included here as diffuse gingival enlargements may be considered, the granular telangiectatic appearance is classic for Wegener's granulomatosis. Other symptoms of the disease may be present, and altered laboratory findings include an elevated sedimentation rate and an elevated creatinine level. Chest radiographs disclose pulmonary involvement.

TREATMENT

Chemotherapy is the treatment of choice. Combined cyclophosphamide and prednisone therapy achieves resolution of lesions with remission in a few months. Some patients enjoy fairly long-term remission even after cessation of treatment.

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TYPE I DIABETES MELLITUS

Figure 6-26

Age: Children
Sex: No predilection

CLINICAL FEATURES

The most severe form of diabetes (juvenile, type I) is most apt to be associated with gingival enlargement although periodontal lesions may also be encountered among

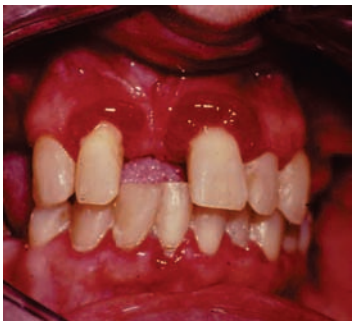
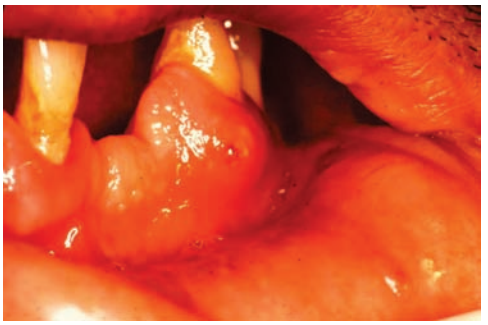

FIGURE 6-26
Hyperplastic gingivitis with abscess formation in type I diabetes.

adult onset cases that are severe. The juvenile form is an autoimmune disease with an immune response being generated to islets of Langerhans cells and resultant insulin depletion. Patients develop hyperglycemia, glycosuria, and ketoacidosis as well as microangiopathic vascular lesions and large vessel atherosclerotic disease. The gingival enlargement may be diffuse or multifocal with hyperplastic changes and striking erythema. In addition, periodontal abscesses may occur and pus may be compressed from periodontal pockets.

MICROSCOPIC FEATURES

There are no diabetes-specific changes as a rule. Diffuse chronic inflammation is encountered along with focal abscess formation. Small vessels may show microangiopathy with thickened vascular walls exhibiting hyaline change.

DIFFERENTIAL DIAGNOSIS

Clinical laboratory tests will confirm diabetes. When gingival enlargement is encountered along with periodontal abscesses, diabetes is usually overt. Fasting blood glucose will be over 150 mg % (hyperglycemia) and sugar will be found in the urine (glycosuria). Prolonged glucose elevation is monitored by assay of glycosylated hemoglobin.

TREATMENT

Antibiotic therapy and periodontal debridement or surgery are usually necessary, and referral to the patient's primary care physician should be undertaken, attempting to achieve improved metabolic control of their disease.

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PUBERTY/PREGNANCY GINGIVITIS

Figure 6-27

Age: Teens, pregnant women
Sex: Females

CLINICAL FEATURES

During puberty and pregnancy, female hormonal changes are taking place and these metabolic events, in a subset of girls and expectant mothers, manifest generalized or multifocal gingival enlargement. The endocrinologic mechanism for gingival lesions is unknown. Why some females develop inflammatory gingival enlargement and others do not has not been determined. The gingival tissues are boggy, swollen, and fiery red. They tend to bleed freely upon gingival probing.

MICROSCOPIC FEATURES

The epithelium is hyperplastic with elongated anastomosing rete ridges. The underlying connective tissue is highly vascularized and an intense, diffuse, and nonspecific chronic inflammatory infiltrate prevails.

DIFFERENTIAL DIAGNOSIS

Other forms of gingival enlargement must be considered, and when warranted, biopsy will help to rule out ominous disease such as Kaposi's sarcoma, angiosarcoma, and leukemia.

TREATMENT

Periodontal therapy is the treatment of choice, and antibiotics may be administered should any clinical evidence of abscess formation be encountered.

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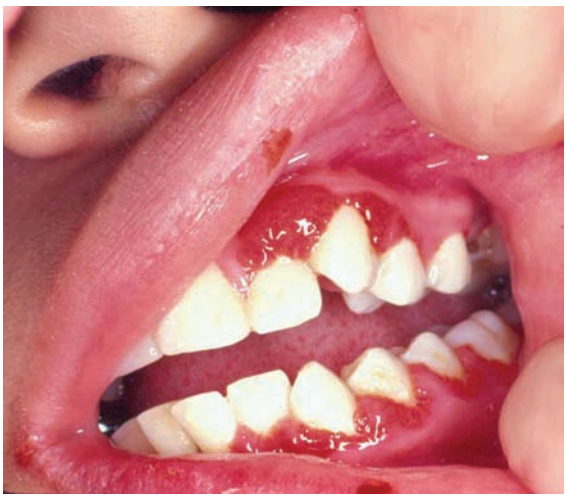

FIGURE 6-27
Pregnancy gingivitis. Similar lesions may be seen during transition to puberty.

LEUKEMIA

Figure 6-28

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Infiltration of leukemic cells into the gingiva occurs in approximately one half of patients suffering from acute leukemia, particularly acute monocytic leukemia. The interdental papillae are enlarged, red or bluish, and usually boggy, although they may occasionally feel firm to palpation. Ulceration with pseudomembrane is often seen. Other signs may accompany gingival enlargement: pallor of the skin and remaining mucosa, gingival hemorrhage, formation of petechiae and ecchymoses, joint swelling related to hemarthrosis, and general malaise.

MICROSCOPIC FEATURES

The fibrous tissue underlying surface and sulcular epithelium displays a monomorphic, monotonous infiltrate of leukemia cells. In monocytic leukemia, the cells are oval or round with vesicular nucleoplasm and prominent nucleoli.

DIFFERENTIAL DIAGNOSIS

Nonspecific hyperplastic gingivitis may show identical features. Fibromatosis gingivae and phenytoin sodium (Dilantin) hyperplasia, although usually not associated with inflamed tissue, should nevertheless be considered in the differential diagnosis. Other generalized signs and symptoms will arouse suspicion of leukemia. A biopsy and complete blood count should be obtained.

TREATMENT

Leukemia should be managed by a hematologist. Oral signs diminish or resolve with successful treatment of the disease, usually with chemotherapeutic drugs.

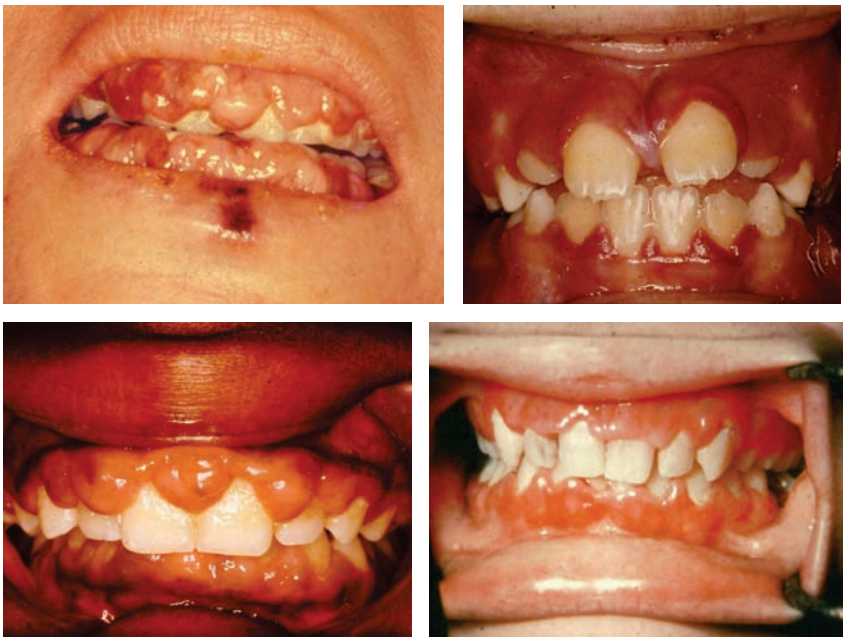

FIGURE 6-28
Leukemic cell infiltration of the gingiva, producing generalized enlargement.

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Swellings of the Oral Floor

RANULA AND SIALOCYSTS

Figure 6-29

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

A ranula is a mucin-filled cystic or pseudocystic cavity in the floor of the mouth. Because the mucin accumulation is superficial, the swelling appears fluid filled and has a bluish cast; the thin membranous surface is traversed by obvious capillary markings. It is compressible and usually located unilaterally in the vicinity of one of the submandibular ducts. Salivary flow on the affected side cannot be elicited by milking the gland when a major duct is involved. When minor glands in the floor of the mouth are affected, salivary flow may be normal. Many of the smaller cystic lesions are true sialocysts.

MICROSCOPIC FEATURES

Most ranulas are fluid (mucin)-filled spaces lined by a granulation tissue wall representing a large mucocele. Less frequently, they may be lined by cuboidal ductal epithelium with areas of oncocytic metaplasia representing sialocysts.

DIFFERENTIAL DIAGNOSIS

The ranula may be differentiated clinically from other oral floor swellings by virtue of its compressible cystic nature, location lat-

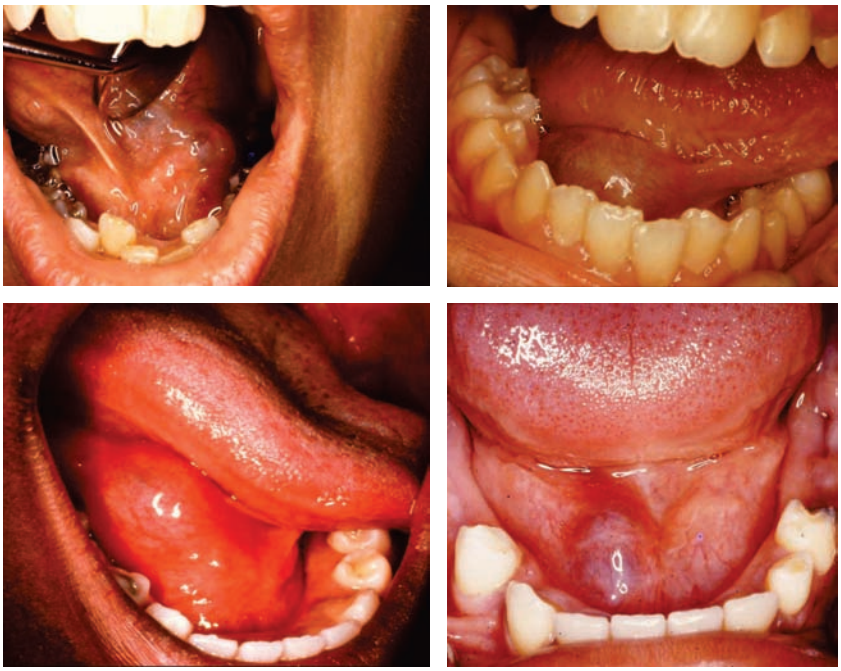

FIGURE 6-29
Ranula, a mucocele of the oral floor, soft and fluctuant.

eral to the midline, and bluish, fluid-filled character. It is conceivable that a low-grade cystic mucoepidermoid carcinoma in the floor of the mouth could resemble ranula in clinical appearance.

TREATMENT

Ranula is conventionally managed by marsupialization.

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DISONTOGENIC CYSTS

Figure 6-30

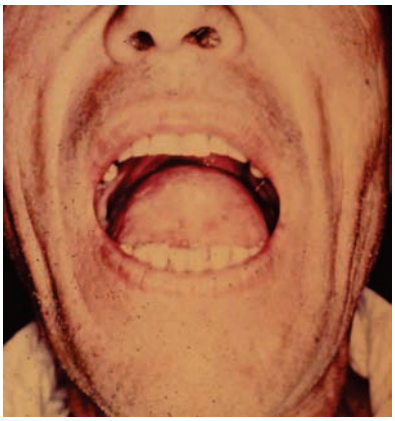
Age: Adults
Sex: No predilection

CLINICAL FEATURES

The disontogenic cyst includes epidermoid cyst, dermoid cyst, and teratoid cyst. They have been suggested to be derived from entrapped epithelium remaining from fusion of the embryonic processes forming the oral floor. These cysts are located in the midline of the anterior floor of the mouth as a dome-shaped mass. They protrude orally when localized above the mylohyoid muscle, submentally when arising below this muscle. Because disontogenic cysts are filled with semisolid keratin and sebum, they are doughy on palpation.

MICROSCOPIC FEATURES

The cyst lining is keratinizing stratified squamous epithelium in the epidermoid



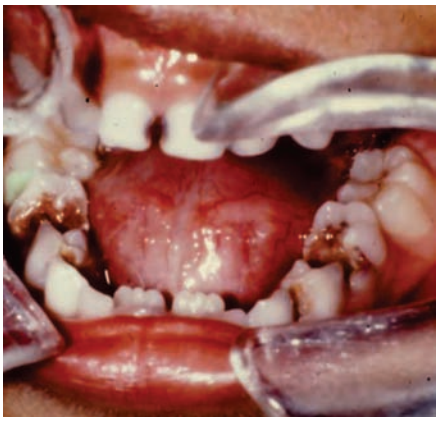


FIGURE 6-30
Dermoid cysts arising from the oral floor in the midline—firm, rubbery tumefactions that elevate the tongue.

cyst, and the lumen may contain keratin. The dermoid cyst shows histologic patterns from the ectodermal and mesodermal germ layers. The luminal contents are eosinophilic, amorphous, and caseous. Respiratory epithelium is occasionally present. Within the fibrous wall are skin adnexal structures such as sebaceous glands, sweat glands, and hair follicles. Minor salivary tissue may be present as well. When other connective tissues and neural elements are encountered, the cyst is classified as a teratoid cyst.

DIFFERENTIAL DIAGNOSIS

Most of the other lesions listed in this section as oral floor swellings arise lateral to the midline. The central location, doughy consistency, and tendency to elevate the tongue are classic signs of a disontogenic cyst. As the cyst contents are semisolid, little or no fluid can be obtained on aspiration.

TREATMENT

The cyst can be delivered surgically by simple enucleation. When it is superior to the mylohyoid, an intraoral approach is preferred. Submylohyoid dermoids are removed by an extraoral approach.

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LYMPHOEPITHELIAL CYST

Figure 6-31

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The lymphoepithelial cyst arising in the oral floor is histologically analogous to its extraoral counterpart, the branchial cleft cyst of the neck. The intraoral variety is generally small, located in the anterior oral floor, ventral tongue, or lingual frenum and is a doughy, well-circumscribed nodule. Because of the involved lymphoid tissue, it may have a yellowish cast. The origin is obscure but may arise from confinement of salivary duct epithelium in a small lymph node. Alternatively, oral lymphoepithelial cysts have been suggested to represent tonsillar tissue with keratin-plugged cystic crypts.

MICROSCOPIC FEATURES

Stratified squamous or, rarely, respiratory epithelium lines the cyst. When squamous

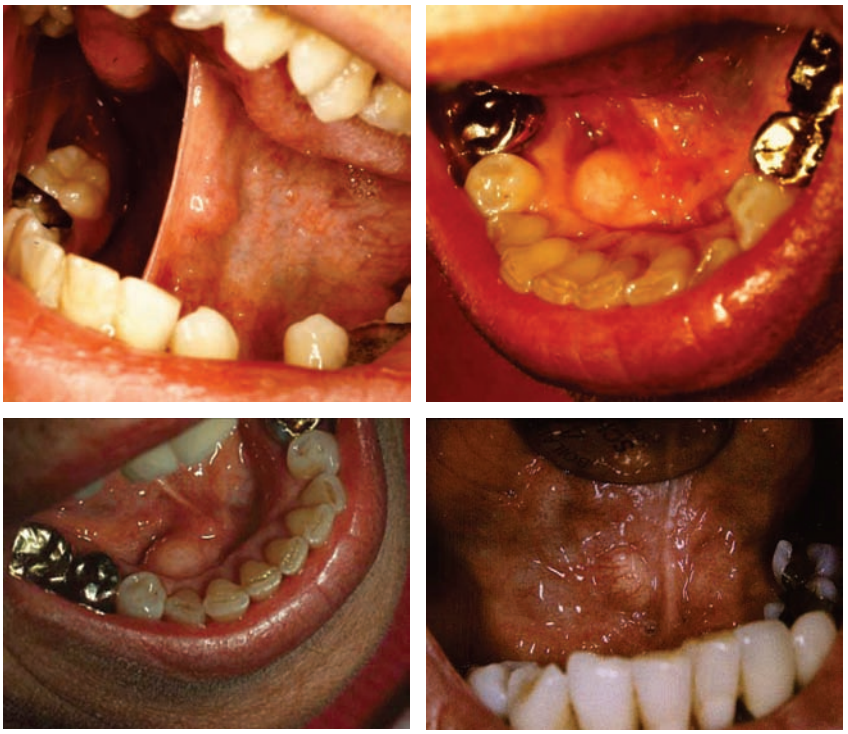

FIGURE 6-31
Benign lymphoepithelial cysts, yellow modules with a smooth surface usually located in the oral floor or ventral tongue.

epithelium is present, keratin fills the lumen. The wall of the cyst contains sheets of lymphocytes with germinal centers. Some examples show a microscopic communication with the oral epithelium.

DIFFERENTIAL DIAGNOSIS

The small nodule of lymphoepithelial cyst must be differentiated from salivary tumors, benign mesenchymal neoplasms, mucocele, and salivary stones.

TREATMENT

The nodule should be excised because a clinical diagnosis cannot unequivocably be made.

Additional Reading

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SIALOLITHIASIS WITH SIALADENITIS

Figure 6-32

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

More than 90% of all sialoliths occur within the submandibular duct. When they arise in the distal aspect, they do so as oral floor swellings. Duct occlusion produces swelling and fibrosis of the affected gland. The duct is usually painless; however, pain on the affected side is elicited when eating. Salivary flow from the sublingual orifice cannot be initiated on milking of the gland.

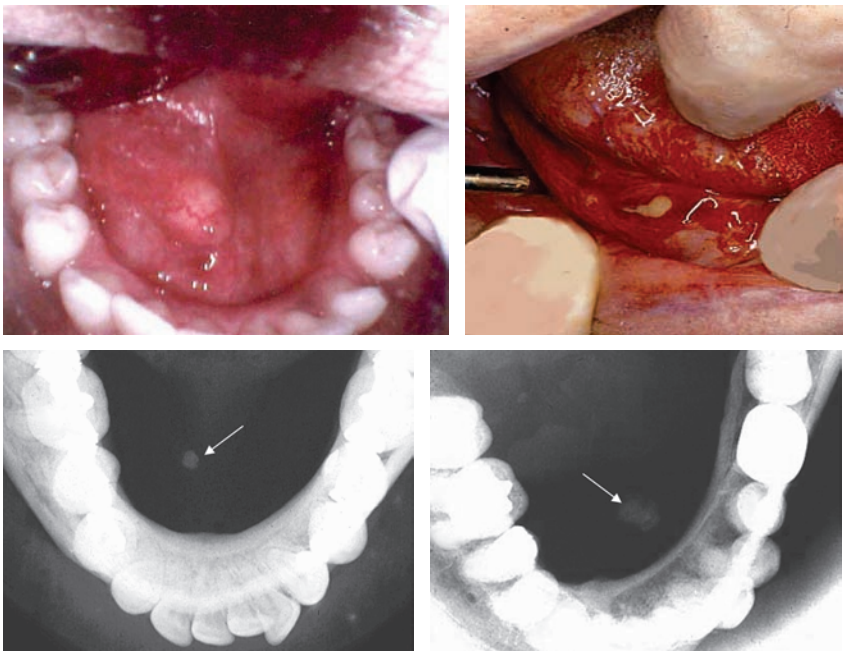

FIGURE 6-32
Salivary stones causing swelling in the oral floor with distension of the submandibular salivary duct, visible with occlusal radiographs.

The dilated duct containing the stone is a rock-hard nodule. Occasionally, an occluded gland becomes subject to secondary pathogenic bacteria with development of acute sialadenitis. The affected gland and duct enlarge and are acutely tender to palpation. In addition, an exudate can often be milked from the Wharton's duct.

MICROSCOPIC FEATURES

The decalcified specimen shows a stone with concentric laminations. The ductal lining shows metaplasia within the epithelium so that stratified squamous, mucous cell formation, or oncocytic change may be discerned. Respiratory epithelium may be present.

DIFFERENTIAL DIAGNOSIS

The oral floor swelling may mimic neoplasm or cyst; however, the symptoms and indurated calcific nature of sialolithiasis are usually present, providing the information necessary to make a clinical diagnosis. An occlusal radiograph discloses the presence of a radiopacity in the floor of the mouth.

TREATMENT

Small stones may be delivered through the duct orifice by manual manipulation. When they are large, surgical removal is indicated. Removal of the involved gland may be necessary, particularly if fibrosis and secondary infection exist. The use of lithotriptor destruction of salivary stones has proven successful.

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SALIVARY GLAND TUMORS

Figure 6-33

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

Salivary neoplasms, benign or malignant, may on rare occasions arise within the major or minor sublingual glands in the floor of the mouth. Salivary tumors of the oral floor are more commonly seen in the submandibular gland with evidence of a mass in the lateroposterior region. Submandibular tumors may not be visually noticeable intraorally but become obvious on bimanual palpation. If the tumor is benign, it will be firm but encapsulated and movable. The most common tumor is the pleomorphic adenoma; however, both submandibular and sublingual gland neoplasms are more apt to represent malignancies than are parotid tumors. Adenocarcinomas may be of any type, yet adenoid cystic carcinoma or cylindroma and mucoepidermoid carcinoma are the tumors more frequently encountered. Malignant salivary tumors are nonencapsulated, indurated, and may or may not evince fixation.

MICROSCOPIC FEATURES

The microscopic features vary, depending on the type of tumor present. The major forms are discussed under palatal swellings.

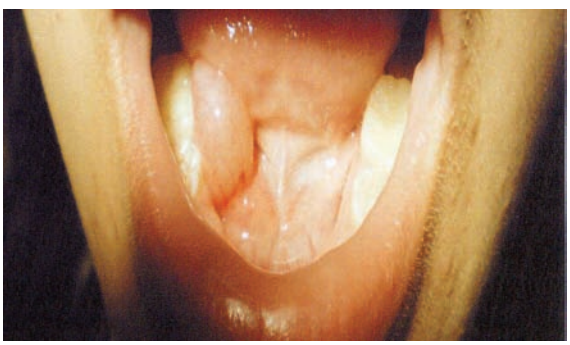

FIGURE 6-33
Salivary neoplasms of the submandibular and sublingual glands can manifest as unilateral oral floor swellings.

DIFFERENTIAL DIAGNOSIS

Benign salivary tumors must be differentiated from mesenchymal neoplasms and sclerosing sialadenitis. Indurated swellings suspected of being salivary adenocarcinomas must be differentiated from submandibular lymph node metastasis from a primary oral carcinoma and from primary sarcomas.

TREATMENT

Benign tumors are treated by sialectomy. Malignant salivary neoplasms require resection with radical neck dissection when cervical or supraomohyoid nodes are palpable.

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ADENOMATOID HYPERPLASIA

Figure 6-34

Age: Teens, adults
Sex: No Predilection

CLINICAL FEATURES

Adenomatous or adenomatoid hyperplasia of minor salivary glands occurs unilaterally in the posterior hard palate and soft palate. Clinically, the lesion is soft to palpation and

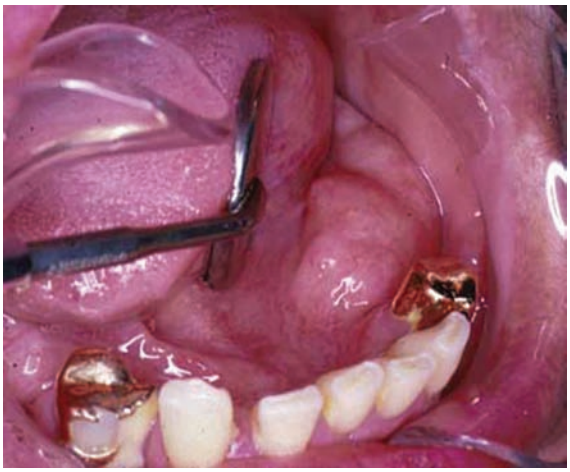

FIGURE 6-34
Adenomatous hyperplasia of the submandibular gland.

asymptomatic appearing as a submucosal nodule. Similarly, glandular hyperplasia of the sublingual or submandibular gland may cause lobular swellings in the floor of the mouth. This lesion is frequently mistaken for a salivary gland tumor. In fact, adenomatoid hyperplasia is a non-neoplastic overgrowth of normal salivary glands. *Sclerosing polycystic adenosis* may also arise in the submandibular gland although it is more common in the parotid. There is disagreement as to whether this lesion is hyperplastic or neoplastic, yet some develop dysplasia.

MICROSCOPIC FEATURES

These hyperplasias show histologic features identical to that of the normal resident salivary glands. Seromucous acini with serous demilunes typical for submandibular gland are seen along with ductal elements. Sclerosing polycystic adenosis is characterized by multiple cystic spaces lined by columnar and cuboidal cells, often with apocrine differentiation.

DIFFERENTIAL DIAGNOSIS

Clinically, salivary tumors are the primary concern.

TREATMENT

Once the diagnosis has been secured by biopsy, no further treatment is required.

Additional Reading

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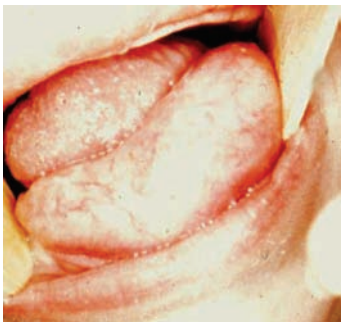
MESENCHYMAL NEOPLASMS

Figure 6-35

Age: More frequent in adults
Sex: Slight male predilection

CLINICAL FEATURES

Benign or malignant connective tissue tumors may arise in any location. Although mesenchymal neoplasms are more frequently seen in the tongue and buccal mucosa, they nevertheless arise in the oral floor and appear as smooth-surfaced elevations. Reactive tumor-like proliferations, the fibromatoses, may also be located in the floor of the mouth. Benign mesenchymal tumors are encapsulated or well delineated, soft or firm, and movable. The more common entities include lipoma, fibroma, hemangioma, and neural sheath tumors. A special form of lymphangioma, the cystic hygroma, occurs in this location and usually bulges extraorally. The sarcomas are multinodular, indurated, and usually fixed. Although all sarcomas are rare in this



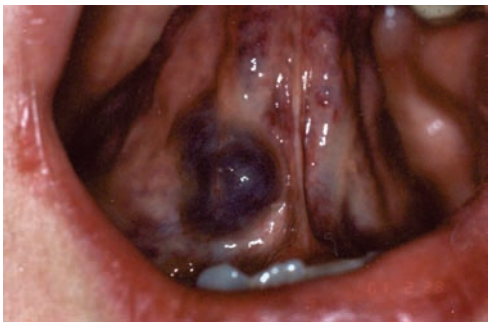


FIGURE 6-35
Mesenchymal neoplasms in the oral floor (neurofibroma, hemangioma).

region, the entities most likely to be present include fibrosarcoma and lymphoma.

MICROSCOPIC FEATURES

The histologic patterns found in mesenchymal neoplasms are extremely varied, depending on the type of tumor and cell of origin. Some are described in the section on tongue swellings.

DIFFERENTIAL DIAGNOSIS

Oral floor swellings representing mesenchymal tumors are firm or indurated and must be differentiated from salivary tumors, sclerosing sialadenitis, and metastatic lymphadenopathy. Those of vascular origin may be less encapsulated, particularly lymphangiomas, and therefore require wide excision. Sarcomas require radical excision. A diagnosis of lymphoma requires further work-up to detect dissemination; the disease is managed by radiation and chemotherapeutic methods.

TREATMENT

Well-localized nodules representing benign mesenchymal neoplasms are treated by simple surgical excision.

Additional Reading

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LUDWIG'S ANGINA

Figure 6-36

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Odontogenic infection with drainage into the fascial spaces of the oral floor produces swelling. When bilateral involvement of the submandibular and sublingual spaces occurs in conjunction with cellulitis of the mylohyoid and tongue musculature, a diffuse boardhard swelling evolves and is obvious both extraorally and intraorally. The patient is febrile, with malaise. Pain is severe. Death may ensue from encroachment of edema and cellulitis on the airway or spread of infection into the paravertebral space and mediastinum.

MICROSCOPIC FEATURES

The tissues are avidly and diffusely infiltrated with neutrophils and scattered histiocytes.

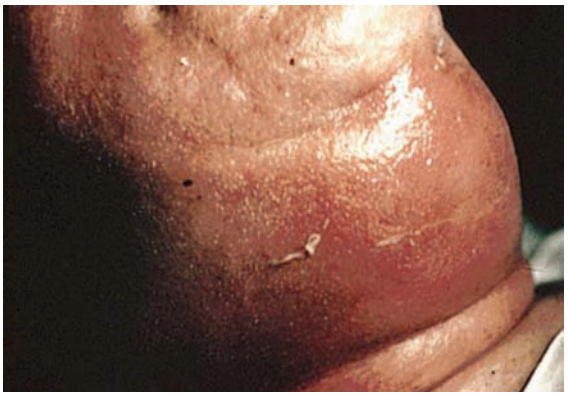

FIGURE 6-36
Ludwig's angina with diffuse swelling of the submandibular area, also showing elevation of the oral floor.

DIFFERENTIAL DIAGNOSIS

The only other disease that can extend into all regions of the oral floor as an indurated swelling resembling Ludwig's angina is infiltrating carcinoma or sarcoma. In these instances, fever is not a dominant sign and conspicuous odontogenic infection with a carious or nonvital tooth is not featured, unless it occurs as a coincidental finding. Whereas streptococci are usually cultured from the tissue, anaerobic organisms may be responsible, either as concomitants or as primary agents.

TREATMENT

Antibiotic therapy with multiple incisions for drainage is required to prevent respiratory embarrassment. Intravenous antibiotic therapy with hospitalization and supportive care for infection are necessary.

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SQUAMOUS CELL CARCINOMA

Figure 6-37

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Squamous cancer of the oral floor may appear red, white, mixed red and white, ulcerated, or tumefactive; the floor of the mouth represents the most common site for oral cancer. Invasive tumefactive lesions are indurated and usually ulcerated. They are most frequently located anteriorly, overlying Wharton's duct. They may infiltrate laterally to involve the alveolar ridge or ventral tongue. About one half of patients present with nodal involvement of the submandibular or cervical region.

MICROSCOPIC FEATURES

Oral floor squamous cell carcinoma is characterized by invasive cords, nests, and islands comprising squamous cells showing varying degrees of hyperchromatism, pleomorphism, and increased mitotic activity. Parakeratin pearl formation can usually be identified. Many oral floor tumors, particularly smaller lesions, maintain carcinoma in-situ changes along the lateral margins. These changes frequently extend along salivary excretory ducts.

DIFFERENTIAL DIAGNOSIS

Most noncancerous oral floor swellings are soft and exhibit an intact mucosal surface. Any lesion that is indurated and ulcerated should be considered, in all probability, a carcinoma; immediate biopsy is indicated.

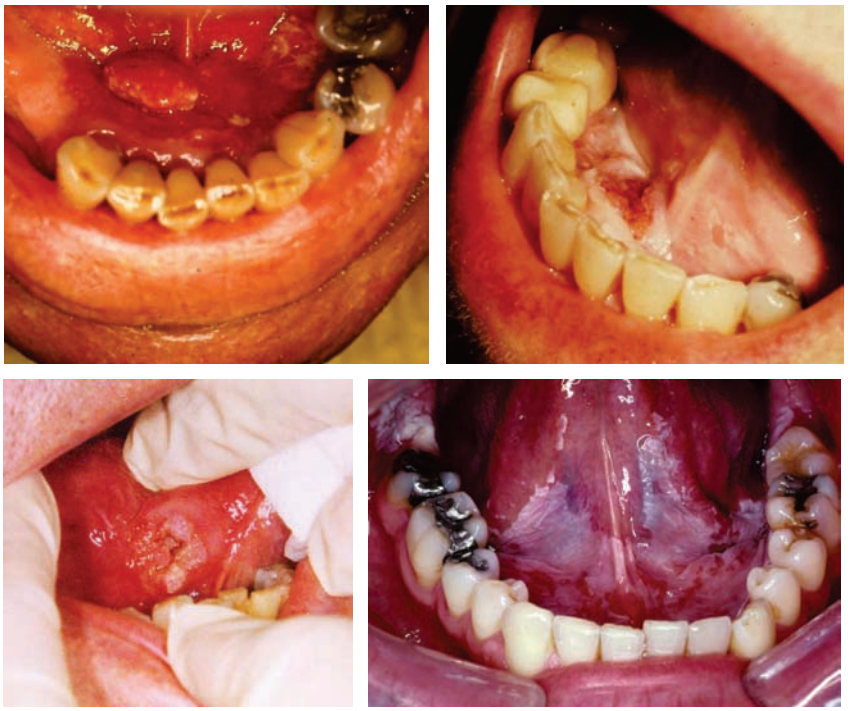

FIGURE 6-37
Squamous cell carcinomas of the oral floor showing keratotic and ulcerated tumefaction.

TREATMENT

Combined radiation therapy and surgery are preferable over a single method. Lymph node dissection is advocated when palpable nodes are present and is usually advisable in the absence of palpable nodes. Survival depends on extent of disease. Resection of the adjacent mandible is often necessary owing to periosteal extension of tumor. Overall 5-year survival for this site is about 50%.

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Swellings of the Lips and Buccal Mucosa

MUCOUS RETENTION (EXTRAVASATION) PHENOMENON (MUCOCELE)

Figure 6-38

Age: Young adults
Sex: Slight male predilection

CLINICAL FEATURES

The mucocele is the most common swelling of the lower lip and arises secondary to traumatic severance of a minor salivary duct with pooling of extraductal mucin in the submucosa. It may be seen on the buccal mucosa as well. It is a dome-shaped elevation, which, if superficial, has a

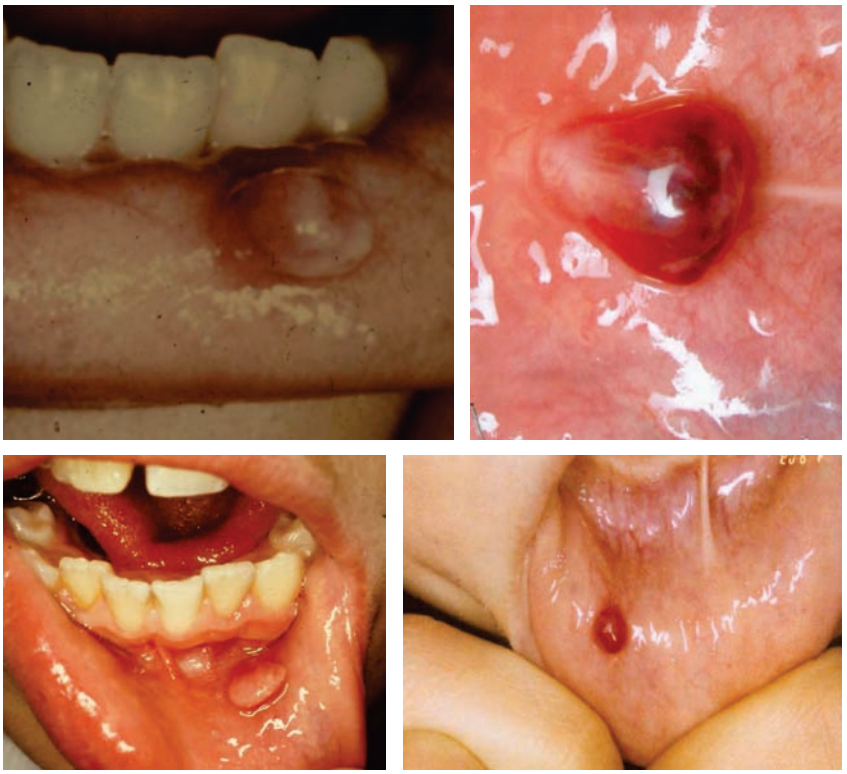

FIGURE 6-38
Mucocele, generally seen on the lower lip as fluctuant fluid-filled blebs.

bluish fluid-filled appearance. If situated deep, it may be of normal color. A history of paroxysmal swelling and collapse is common.

MICROSCOPIC FEATURES

The epithelium is distended by a pseudocystic space filled with mucin infiltrated with neutrophils and foamy histiocytes. The wall is composed of granulation tissue.

DIFFERENTIAL DIAGNOSIS

When mucoceles are superficial, they may resemble bullae. The remaining oral tissues, conjunctivas, and skin must be examined to rule out bullous dermatoses. Mucoepidermoid carcinoma may clinically resemble mucocele yet is extremely rare in the lip. Deeply situated mucoceles may appear identical to fibrous hyperplasia or mesenchymal neoplasms. Occasionally, blood enters the cystic cavity of a mucocele, giving the appearance of hemangioma or varix.

TREATMENT

Mucoceles cannot be unroofed and be expected to resolve. Excision with inclusion of the underlying salivary tissue helps to minimize the chance for recurrence.

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SIALOCYST

Figure 6-39

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Sialocysts are fluid filled, well-localized swellings of the submucosa. Whereas the floor of the mouth is the favored site for most sialocysts, the lips and buccal mucosa are also frequent locations, especially in elderly patients who have oncocytic cells in their lining. Whether or not sialocysts are true blind cysts or merely represent aneurysmal-like dilatation of an obstructed duct is not conclusive. The latter is more probable because many patients report fluctuations in the size of the lesions with episodic release of the fluid contents. Therefore, some sialocysts may arise from partial duct blockage by mucous plugs. Clinically, the lesions are fluctuant, nonulcerated, and movable submucosal nodules. Although most are clearly visualized, deeper lesions may only be detectable by palpation. Some patients have multiple lesions.

MICROSCOPIC FEATURES

Sialocysts occur in three variations: simple mucous retention cysts lined by cuboidal epithelium, reactive oncocytoid cysts lined by columnar ductal cells with foci of oncocytic metaplasia, and mucopapillary cysts that are multilocated and tortuous, and contain papillary configurations with lining columnar and mucous-secreting cells. Some

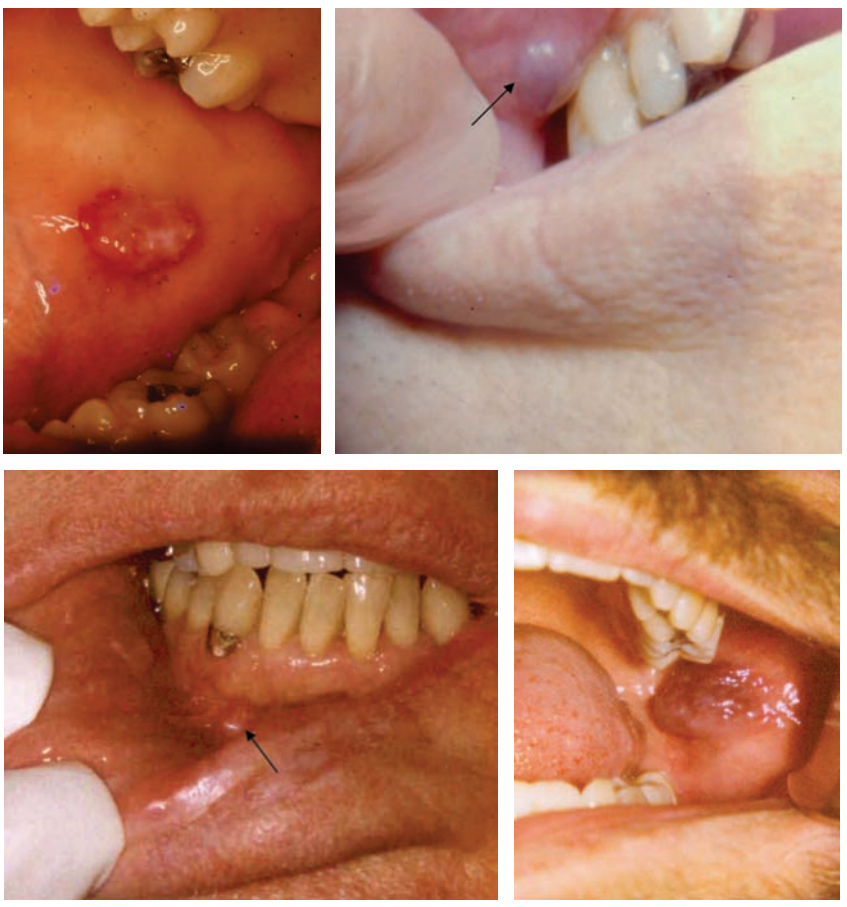

FIGURE 6-39
Sialocyst of the buccal mucosa.

pathologists think that the mucopapillary cysts are true benign neoplasms and prefer to label them as papillary cystadenomas.

DIFFERENTIAL DIAGNOSIS

Sialocysts are clinically indistinguishable from mucoceles owing to their compressible, fluctuant nature; fluctuation in size is also a common feature. Low-grade mucoepidermoid carcinoma should be considered in the differential diagnosis. Indeed, microscopically, the mucopapillary cyst closely resembles low-grade mucoepidermoid carcinoma.

TREATMENT

Complete excision is the treatment of choice. Most sialocysts are easily enucleated. The mucopapillary cyst is more tortuous and requires wider excision. Recurrences are extremely rare.

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MINOR GLAND SIALOLITHIASIS

Figure 6-40

Age: Middle-aged adults
Sex: Slightly more common in males

CLINICAL FEATURES

Salivary stones occasionally form within the ducts of minor glands, being most frequently detected in the buccal mucosa and upper lip. They are not always visible yet are easily detected by palpation. Larger stones may produce a nodular bulge; in all cases, the lesion is hard and may give the impression of a foreign body such as a beebee or shot. They are usually asymptomatic.

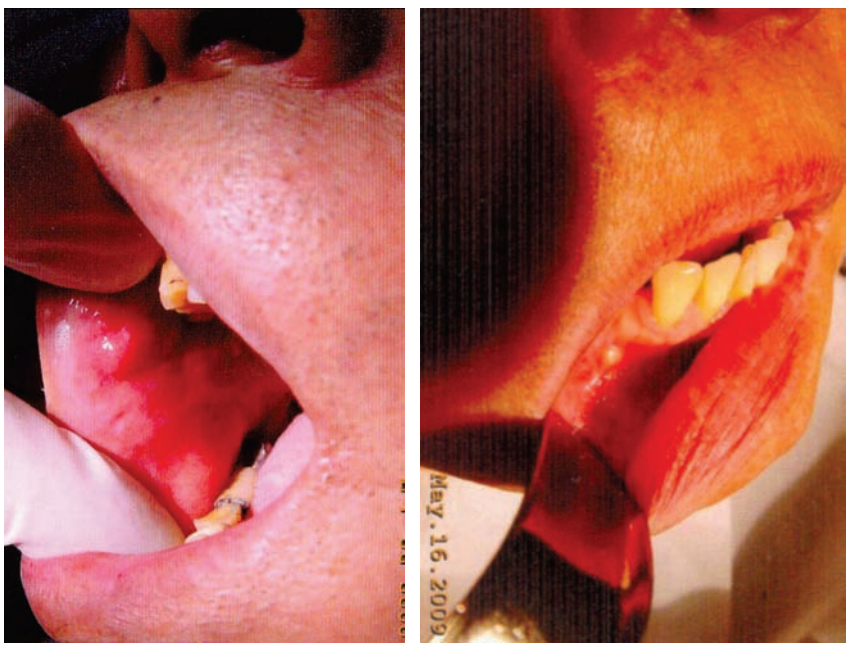

FIGURE 6-40
Small hard palpable nodules representing minor gland sialoliths.

MICROSCOPIC FEATURES

Minor gland sialoliths are situated within a dilated duct that shows mucous, respiratory, or squamous metaplasia. The stone is composed of concentric acellular laminations of basophilic amorphous material in decalcified specimens. Adjacent acini exhibit degenerative changes with fibrous and inflammatory changes.

DIFFERENTIAL DIAGNOSIS

These lesions are clinically typical in that a hard movable nodule can be palpated. They may, however, be confused with a foreign body.

TREATMENT

Surgical excision is the treatment of choice.

Additional Reading

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NASOALVEOLAR (KLESTADT) CYST

Figure 6-41

Age: Adults
Sex: Female predilection

CLINICAL FEATURES

The nasoalveolar cyst is restricted in location to the submucosal tissues between, and superior to, the roots of the maxillary lateral incisor and cuspid lying above the mucobuccal fold. It is soft and fluctuant or tense and often extends superiorly into the anterior nasal floor, producing a bulge below, and anterior to, the inferior turbinate. Bilateral cases have been reported. On aspiration, a mucous fluid is obtained, and injection of radiopaque dye clearly demonstrates its cystic nature radiographically. This cyst is believed to derive from entrapped embryonic epithelium.

MICROSCOPIC FEATURES

The cyst is lined by pseudostratified columnar epithelium. Cilia are demonstrable in most cases. Mucous metaplasia is frequently encountered. The fibrous wall usually lacks inflammatory cell infiltration.

DIFFERENTIAL DIAGNOSIS

A clinically cystic lesion in the location of the maxillary cuspid is almost invariably a nasoalveolar cyst. Nevertheless, it must be differentiated from a salivary or mesenchymal neoplasm and an abscess (parulis) related to drainage from odontogenic infection.

TREATMENT

Simple excision by enucleation generally is not followed by recurrence.

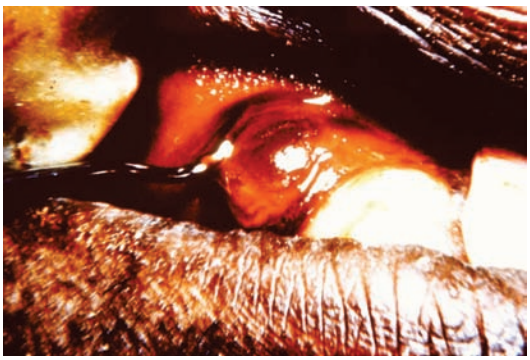

FIGURE 6-41
Swelling with elevation of the ala of the nose in a nasolabial cyst. (Courtesy of Charles Tomich.)

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CHEILITIS GRANULOMATOSA

Figure 6-42

Age: Young adults
Sex: Females

CLINICAL FEATURES

Either upper, lower, or both lips show a diffuse nodular enlargement that involves not just a portion but the entire lip from one commissure to the other. The lip is firm to palpation but devoid of any superficial inflammation or discoloration. Cheilitis granulomatosa accompanied by fissured tongue and facial paralysis constitutes the *Melkersson-Rosenthal syndrome*, a form of *orofacial granulomatosis*. The fissured tongue may also show nodular or papillary tumefactions. In actuality, a spectrum of changes may be encountered in patients with cheilitis granulomatosa. Twenty percent of patients exhibit facial paralysis and 40% have fissured tongue; other oral sites, primarily the buccal mucosa and palate, are affected by multinodular lesions or erythematous or bluish edematous plaques. Cheilitis granulomatosa is of unknown origin but has been suggested to represent a regional form of sarcoidosis or an atypical granulomatous disease, possibly allergic in origin.

MICROSCOPIC FEATURES

The swelling is accounted for by the presence of granulomatous inflammation with infiltration and replacement of the minor salivary glands. The granulomas are multinodular, composed of swirled collagen fascicles with interspersed multinucleated giant cells.

DIFFERENTIAL DIAGNOSIS

The appearance is similar to that of angioneurotic edema or edema and cellulitis of odontogenic infectious origin. These two lesions are diffuse and soft to palpation, whereas cheilitis granulomatosa is firm and multinodular.

TREATMENT

Intralesional injection of triamcinolone or another steroid on 6 to 10 weekly occasions

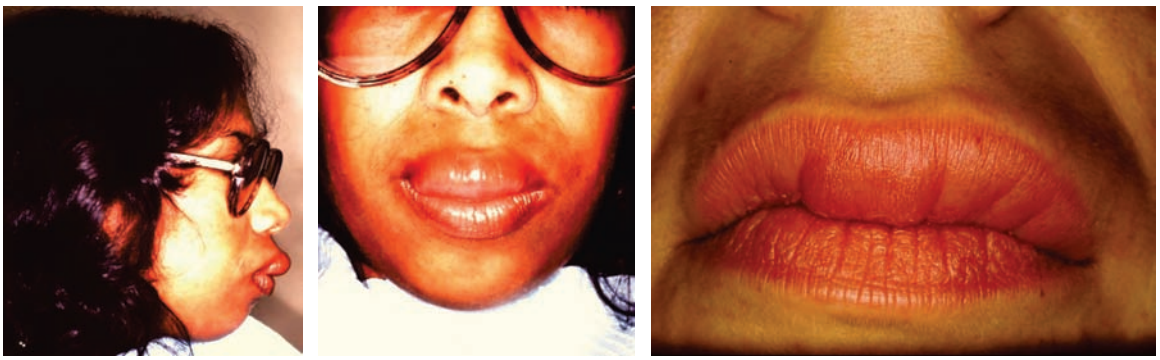

FIGURE 6-42
Diffuse, firm enlargement of the upper lip seen in cheilitis granulomatosa: a lesion associated with orofacial granulomatosis and the Melkersson-Rosenthal syndrome.

may result in significant diminution in the size of the lip. Intralesional steroids are not always effective, and surgical excision of lip granulomas may be followed by recurrence. Surprisingly, elimination of odontogenic and periodontal sources of infection often coincide with a diminution in signs and symptoms.

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CHEILITIS GLANDULARIS

Figure 6-43

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Cheilitis glandularis is a disease of unknown etiology that represents both a superficial and deep (salivary) inflammatory disorder. Overexposure to sun with superimposed infection has been suggested to give rise to this uncommon condition. The vermilion border and mucosa may be of normal color, or diffuse keratosis with scaling may be featured. The lower lip is affected and a multinodular enlargement is seen. Multiple pits or fistulae representing dilated minor salivary ducts stipple the lip surface, and exudate may be expressed from these openings in some but not all instances. Carcinoma of the lip has been reported to complicate a number of cases.

MICROSCOPIC FEATURES

The surface epithelium may be unremarkable; more often, hyperkeratosis and actinic changes are observed. The underlying salivary gland lobules show hypertrophy and sialadenitis, often of an acute nature.

DIFFERENTIAL DIAGNOSIS

Cheilitis glandularis may simulate the clinical features seen in cheilitis granulomatosa; however, the multiple dilated duct orifices along with multinodular enlargement are classic clinical findings. Actinic prurigo is also a major consideration, yet tends to occur in Amerindians. Biopsy should be performed, particularly in patients with foci of keratotic thickening or ulceration.

TREATMENT

Excision of the involved area can generally be accomplished without extending the

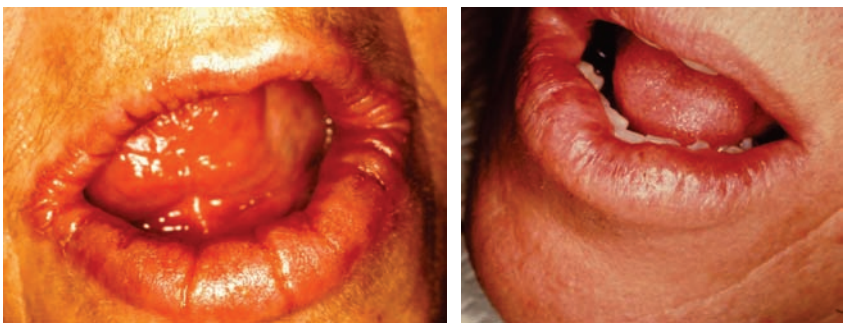

FIGURE 6-43
Cheilitis glandularis characterized by enlargement of the lower lip accompanied by accentuation of the salivary excretory duct pores. (Courtesy of Dr. H. Cherrick.)

surgical margin onto the vermilion, thereby avoiding cosmetic deformity.

Additional Reading

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ANGIONEUROTIC EDEMA

Figure 6-44

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Angioneurotic edema represents a histamine-mediated immediate hypersensitivity reaction to some allergenic substance, usually a food or drug. An intraoral vesiculoerythematous reaction may accompany the edematous episode, which consists of diffuse, often massive swelling of the upper lip and face. The swelling, resulting from accumulation of edema fluid, is soft. Often the periorbital skin is involved and the swelling may be such that the eyes cannot open. A hereditary form exists and is usually accompanied by generalized skin urticaria. The inherited variety shows a biochemical defect in the complement fixation pathway with a deficiency of C'1 esterase inhibitor.

MICROSCOPIC FEATURES

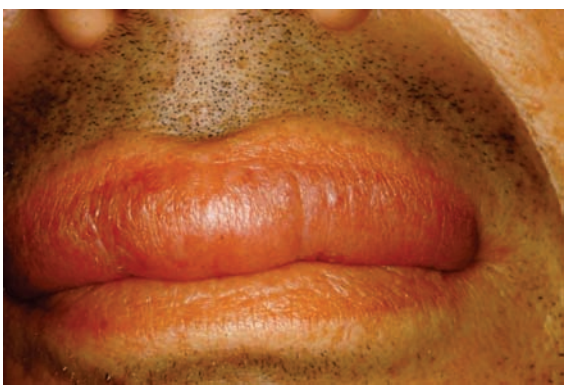
Not applicable.

DIFFERENTIAL DIAGNOSIS

The rapid onset of swelling often preceded by pruritus is unique. The only other disease that may mimic angioneurotic edema is diffuse cellulitis with edema resulting from odontogenic infection in an anterior maxillary tooth. The hereditary form follows an autosomal dominant pattern with both skin and visceral manifestations.

TREATMENT

Any suspected allergens should be withdrawn. Systemically administered antihistamines cause resolution within hours. Repeated exposure to the allergen can result in Quincke's edema and progress to anaphylactic shock. Patients with hereditary angioneurotic edema should be referred to an allergist. Three daily 200-mg doses of danazol on a maintenance schedule



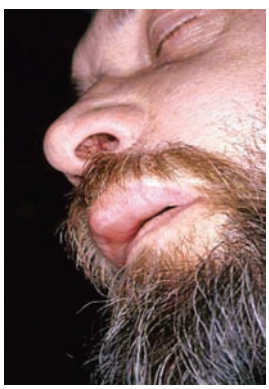


FIGURE 6-44
Angioneurotic edema, an allergic reaction, results in soft edematous enlargement of the upper lip and face.

are effective in the hereditary form of the disease.

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ACTINIC PRURIGO

Figure 6-45

Age: Teens, adults
Sex: No predilection

CLINICAL FEATURES

Actinic prurigo, also termed *familial polymorphous light eruption of American Indians*, is more often seen in Central America and Asia than in North America and Europe, typically among individuals living at high altitude. Sun exposure is probably a major etiologic factor. The lower lip becomes enlarged and tender without keratotic changes and cutaneous plaques, and nodules appear commonly on the face, arms, and legs.

MICROSCOPIC FEATURES

The lip is edematous with a diffuse mononuclear infiltrate in the submucosa and may show perivascular CD4 lymphoid aggregates. It may be that UV-irradiated keratinocytes develop neoantigens causing an autoimmune reaction.

DIFFERENTIAL DIAGNOSIS

Cheilitis glandularis, cheilitis granulomatosa and actinic cheilitis are the chief entities to consider. Biopsy will exclude these processes.

TREATMENT

Topical steroid ointments and gels are effective, and sun screen should be used once the inflammation and swelling resolve.

Additional Reading

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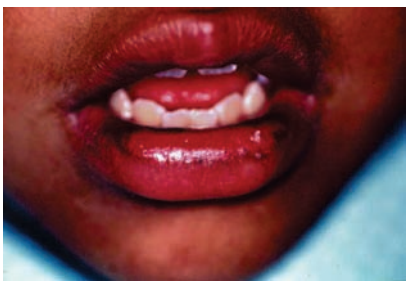

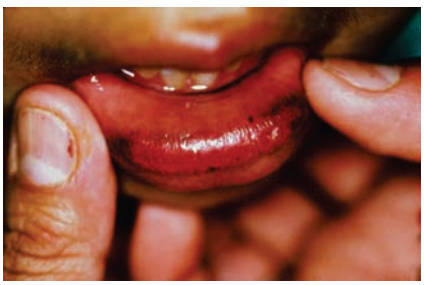

FIGURE 6-45
Diffuse lip swelling in actinic prurigo. *Source:* Moundsdon T, Kratochvil F, Auclair P, Neal J, Lee L. Actinic prurigo of the lower lip. *Oral Surg Oral Med Oral Pathol.* 1988;65:327-332.

INFLAMMATORY FIBROUS HYPERPLASIA

Figure 6-46

Age: Adults, elderly
Sex: No predilection

CLINICAL FEATURES

Ill-fitting dentures evolve over time as the alveolar ridges slowly atrophy. The consequences of this atrophy are overextension of the denture flanges into the vestibule, serving as a chronic irritant. The host responds by attempting to lay down a fibrous connective tissue "pillow" that clinically is a bosselated multinodular hyperplastic soft growth in the vestibular area. These reactive proliferations are soft and can become ulcerated. They are often referred to as *epulis fissuratum*.

MICROSCOPIC FEATURES

The surface epithelium is typically hyperplastic with elongated thick rete ridges. The surface is often lobulated, and underlying the epithelial is normal-appearing collagenous connective tissue. Minor salivary gland lobules are commonly seen along the base, exhibiting chronic sialadenitis.

DIFFERENTIAL DIAGNOSIS

Any of the swellings listed here are in the differential; however, the association with an ill-fitting denture and localization to the vestibule are features favoring inflammatory fibrous hyperplasia.

TREATMENT

Surgical excision is the treatment of choice followed by fabrication of a new denture.

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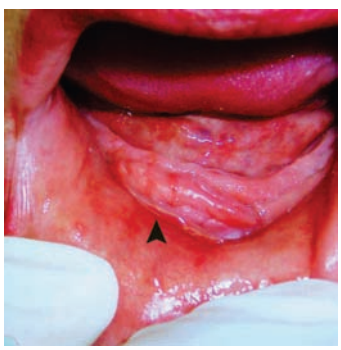
FOREIGN BODY GRANULOMA

Figure 6-47

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

A variety of foreign bodies may be introduced into the oral submucosal tissues. Most foreign bodies are iatrogenic, whereby a substance becomes implanted during an extraction or oral surgical procedure. Not all foreign agents and chemicals elicit a granulomatous response. Common reac-



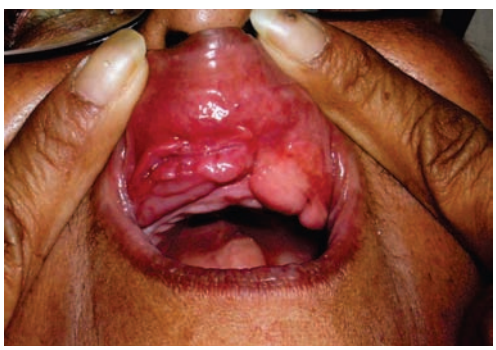


FIGURE 6-46
Inflammatory fibrous hyperplasia appears as redundant soft tissue folds associated with ill-fitting dentures.

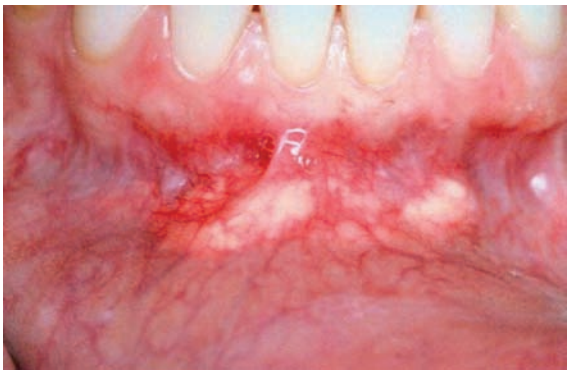


FIGURE 6-47
Lip augmentation hyaluronate foreign body granuloma that, after injection, migrated into sulcus forming a pale mass.

tions of this nature occur with handpiece oil (oil granuloma), vegetable matter (pulse granuloma), and dental cements. The true nature of the foreign agent often cannot be ascertained. The mucobuccal fold is probably the most common location; the lesions are soft or firm and either dome shaped or multinodular.

MICROSCOPIC FEATURES

The submucosa is fibrotic with chronically inflamed granulation tissue evincing a mild inflammatory cell infiltrate. Multinucleated giant cells are observed and usually phagocytosis of the foreign material can be seen. Oil granulomas appear as large vacant vacuoles. Pulse granulomas exhibit compartmentalized spaces with enveloping giant cells. When a foreign material is not readily identifiable, polarized lenses may be used to detect refractile materials.

DIFFERENTIAL DIAGNOSIS

Foreign body granulomas are dome-shaped nodules that cannot usually be differentiated clinically from benign mesenchymal neoplasms, salivary neoplasms, or other granulomatous lesions. Whereas a history of trauma to, or previous surgery in, the area would certainly arouse suspicion of a foreign body reaction, biopsy is required to obtain a definitive diagnosis.

TREATMENT

Local excisional biopsy is the treatment of choice.

Additional Reading

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CROHN'S DISEASE

Figure 6-48

Age: Teenagers and adults
Sex: No predilection

CLINICAL FEATURES

Crohn's disease, also termed regional enteritis, is a segmental transluminal inflammatory bowel disease that most frequently affects the distal ileum and colon. Patients generally complain of subumbilical or lower right quadrant abdominal pain with diarrhea. Other complications include chronic fever, general malaise, malabsorption, joint pain, and growth failure. Characteristic segmental changes are observed in radiographic gastrointestinal series. Extracolonic manifestations are common and include arthritis, skin, ocular and oral lesions, and hepatic involvement. Whereas oral ulcerations may occur, particularly in youngsters, adults more often manifest tumefactive lesions of the buccal mucosa

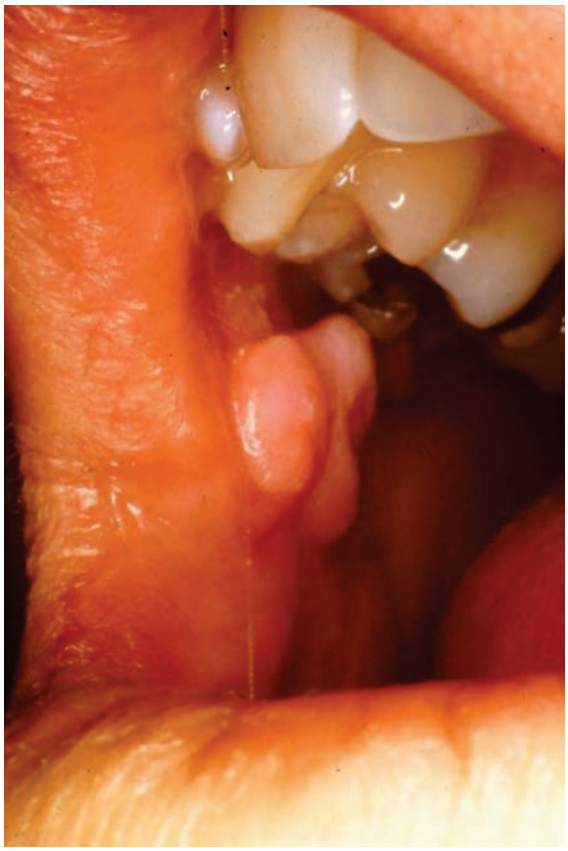

FIGURE 6-48
Multinodular mass of the submucosa representing noncaseating granulomas of Crohn's disease.

and vestibule. The lesions may be multinodular or fissured or possess a cobblestone surface pattern. Certain periodontopathic bacteria (*Wolinella*) have been implicated as potential pathogens.

MICROSCOPIC FEATURES

The nodular lesions show a chronic inflammatory cell infiltrate with formation of noncaseating granulomas characterized by oval aggregates of epithelioid histiocytes surrounded by a halo of mature lymphocytes and histiocytes. No caseation necrosis is evident in the center of the granulomas.

DIFFERENTIAL DIAGNOSIS

The nodular lesions are most often confused with simple fibrous hyperplasia or epulis fissuratum, although many other inflammatory or even submucosal neoplastic processes may show similar features. In a patient with bowel symptoms, malaise, and arthritis, the clinician should certainly suspect Crohn's disease. Biopsy is not diagnostic; however, the presence of noncaseating granulomas without an infectious etiology should arouse suspicion of regional enteritis, and a medical work-up for bowel disease is then indicated.

TREATMENT

The patient with suspected Crohn's disease should be referred to a gastroenterologist. Most patients respond to systemic prednisone, sulfasalazine, and metronidazole therapy.

Additional Reading

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TRAUMATIC FIBROMA

Figure 6-49

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

The traumatic fibroma may arise in any oral location. It represents the most common swelling of the buccal mucosa and is

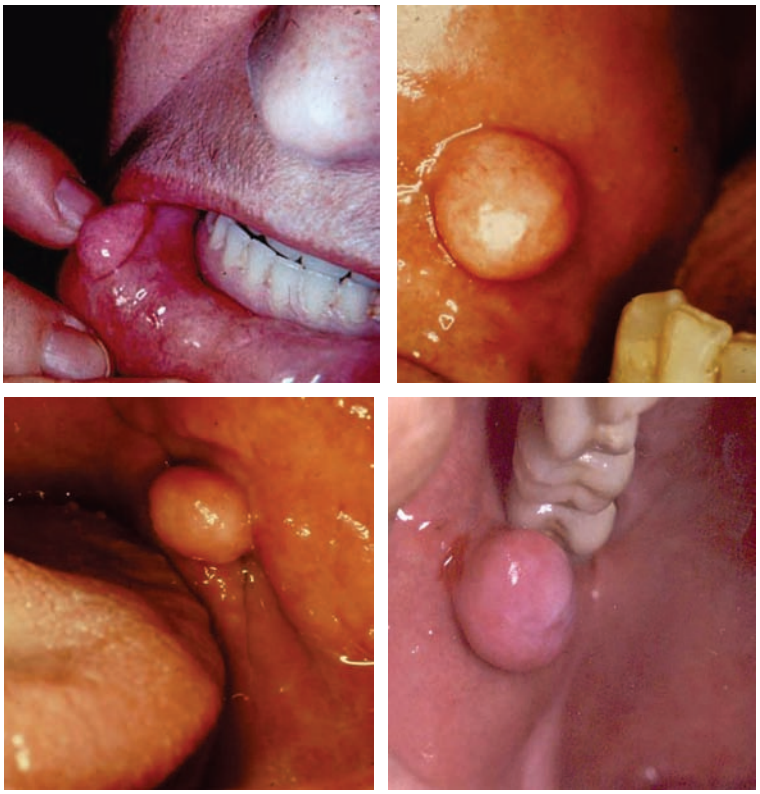

FIGURE 6-49
Traumatic fibromas are very common in the buccal mucosa and lips.

also extremely common on the mucosal surface of the lips. Traumatic fibroma represents reactive fibrous hyperplasia owing to trauma and is not a true neoplasm. It is a sessile, dome-shaped soft nodule, usually of normal color, and may be ulcerated from trauma as in cheek biting.

MICROSCOPIC FEATURES

The epithelium is distended by a mass of dense collagenous tissue with interspersed fibroblasts. Capillaries traverse the tissue, and few if any inflammatory cells are evident. When stellate multinucleated cells are seen, the lesion represents a giant cell fibroma.

DIFFERENTIAL DIAGNOSIS

Traumatic fibroma may be clinically indistinguishable from true mesenchymal neoplasms, benign salivary tumor, a deeply situated mucocele, or an epidermoid cyst.

TREATMENT

Excisional biopsy is recommended to rule out the presence of a true neoplasm.

Additional Reading

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TRAUMATIC (AMPUTATION) NEUROMA

Figure 6-50

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

An amputation neuroma evolves subsequent to severance of a nerve, whereby the distal segment undergoes Wallerian degeneration and the proximal segment attempts in vain to reunite with the distal nerve sheath. When the severed segments are displaced, the proximal portion proliferates, pursuing a tortuous course, resulting in tumefaction. The swelling is most frequently encountered in the mucobuccal fold adjacent to the mental foramen. The nodule is firm yet usually movable. Pain is often elicited when pressure is applied: however, some patients suffer from spontaneous facial pain. Most amputation neuromas measure less than 0.5 cm in diameter.

MICROSCOPIC FEATURES

A tortuous array of axis cylinders accompanied by neurilemma sheath and enveloping perineurium is encountered, resembling an overabundance of normal nerve tissue.

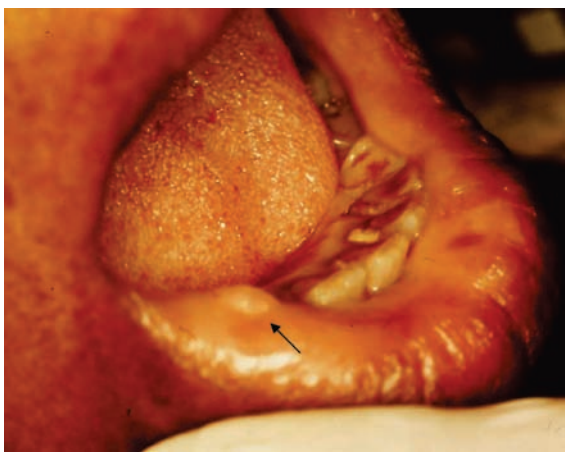

FIGURE 6-50
Traumatic neuroma, a small nodule that arose on the lip after trauma.

A variant form is *palisaded encapsulated neuroma* characterized by palisaded spindle-shaped cells invested by a descrete capsule. S-100 protein is positive.

DIFFERENTIAL DIAGNOSIS

The swelling observed with amputation neuroma is identical to that seen in mesenchymal neoplasms, salivary tumors, or foreign body granulomas. A parulis may be considered in the differential diagnosis when the lesion lies directly below the attached gingiva. Firmness with pain on palpation should arouse clinical suspicion of neuroma. When multiple neuromas are identified, the neuropolyendocrine syndrome should be ruled out.

TREATMENT

Simple surgical excision is rarely followed by recurrence.

Additional Reading

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MESENCHYMAL NEOPLASMS

Figure 6-51

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Various neoplasms of mesenchymal origin may arise in the buccal mucosa and lips.

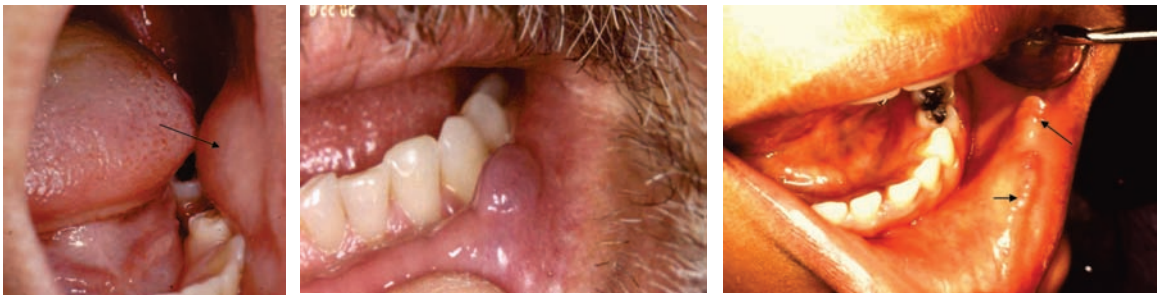

FIGURE 6-51
Benign mesenchymal neoplasms such as lipoma, neurofibroma, and neurilemmoma are common tumefactions of the cheek.

Because of its prevalence, hemangioma is considered separately. The most common mesenchymal tumors in this location are neurofibroma, neurilemmoma, and lipoma. Less frequently encountered benign neoplasms or neoplastic-like swellings of connective tissue origin include leiomyoma, fibrous histiocytoma, and oral focal mucinosis. As a group, they vary considerably in size, may be soft or firm, movable, and well demarcated or encapsulated. Ulceration of the surface mucosa is unusual. In the cheek, a diffuse swelling composed of adipose tissue usually represents herniation of the buccal fat pad rather than a true lipoma. Sarcomas and lymphomas are rarely encountered; ulceration and induration usually are present when the mass represents a mesenchymal malignancy.

MICROSCOPIC FEATURES

The microscopic patterns vary with the tissue of origin. Neural sheath tumors are described under tongue swellings.

DIFFERENTIAL DIAGNOSIS

Swellings of the cheek and lips in mesenchymal tumors are identical to those of salivary neoplasm, traumatic fibroma, or deep mucocele. Indurated and ulcerated sarcomatous tumors may clinically resemble squamous cell carcinoma or malignant salivary neoplasms.

TREATMENT

Enucleation and excision are the treatments of choice for benign mesenchymal tumors. Sarcomas require radical wide excision.

Additional Reading

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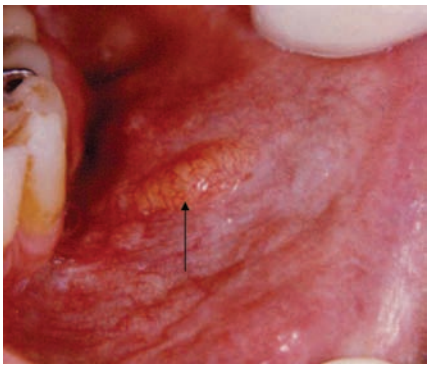
HERNIATED BUCCAL FAT PAD

Figure 6-52

Age: Middle-aged and elderly adults
Sex: No predilection

CLINICAL FEATURES

The buccal fat pad lies external to the buccinator muscle. Trauma to this thin muscle from cheek biting or surgery may weaken or separate the muscle fibers, allowing adipose tissue to herniate orally. Herniated fat pads are soft to palpation and may appear



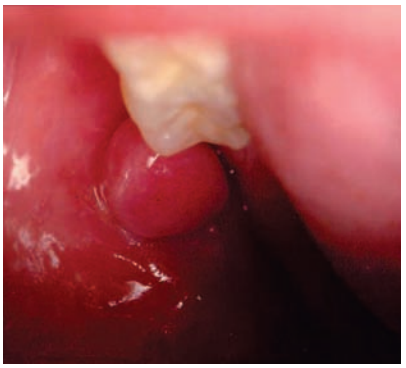


FIGURE 6-52
Soft masses, sometimes yellow, in posterior aspect of buccal mucosa are composed of adipose tissue that has herniated through the buccinator muscle following trauma or a cheek-biting episode.

faintly yellow. They either are dome-shaped tumefactions or exhibit surface lobulation.

MICROSCOPIC FEATURES

The lesion is composed of normal-appearing adipose tissue traversed by capillary septae. They cannot usually be differentiated histologically from lipoma; however, scattered isolated muscle fibers are occasionally admixed with the adipose tissue, a feature not encountered in lipoma.

DIFFERENTIAL DIAGNOSIS

The buccal mucosal mass representing a herniated fat pad may clinically resemble the other mesenchymal and reactive lesions included in this section. The consistency and gross appearance do not allow for differentiation from lipoma. A history of trauma aids in arriving at a diagnosis in conjunction with biopsy.

TREATMENT

The excess fatty tissue should be excised; if the zone of buccinator perforation can be located, the fibers should be juxtaposed and sutured.

Additional Reading

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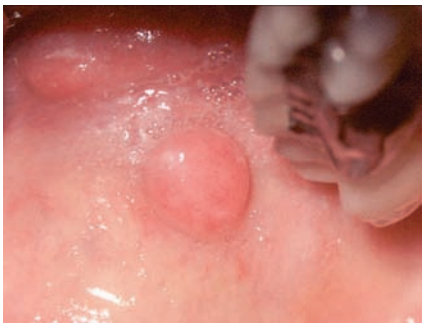
REACTIVE LYMPHOID HYPERPLASIA

Figure 6-53

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Facial nodes located adjacent to the facial vein and buccinator muscle are present in about 20% of the population. The nodes are usually not palpable unless stimulated to undergo reactive hyperplasia. Lymphoid hyperplasia of the buccal nodes may not be visible; yet the enlarged node is firm, palpable, and movable, being located near Stensen's duct. The etiology is not always apparent yet may accompany generalized lymphadenopathy in viral infections or represent local adenopathy secondary to oral or facial skin infections. Occasionally, an enlarged buccal node represents a specific infection, such as latent acquired toxoplasmosis. Handling of contaminated cat litter is usually the route of transmission; in gravid



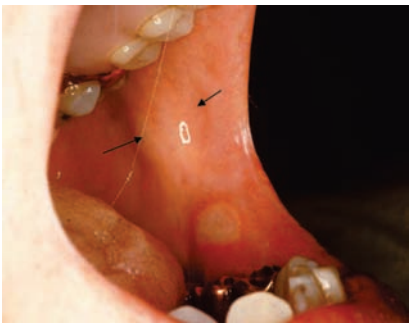


FIGURE 6-53
Buccal lymph nodes will undergo enlargement when an antigenic challenge occurs.

females, this could significantly endanger the developing fetus. Malignant lymphoma is extremely rare in this location.

MICROSCOPIC FEATURES

The node is enlarged and encapsulated. Hyperplastic germinal centers are impacted with active large immunoblasts. The paracortical region may continue to possess a mature lymphocytic mantle; however, large blast cells may occupy this region. The medullary zone is often congested; in addition to mature lymphocytes, histiocytes showing phagocytosis and plasma cells may be present. Toxoplasma lymphadenitis is characterized by extrafollicular pale epithelioid histiocytes.

DIFFERENTIAL DIAGNOSIS

Reactive lymphoid hyperplasia is indistinguishable clinically from mesenchymal neoplasms, benign salivary tumors, and focal granulomas. For this reason, a biopsy is required to arrive at a definitive diagnosis.

TREATMENT

Provided no infectious source can be uncovered, further treatment, even for toxoplasma lymphadenitis, is not required. Generalized or systemic disease should be treated according to the nature of the process. Rarely, lymphoma may arise in a buccal node.

Additional Reading

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HEMANGIOMA AND VARIX

Figure 6-54

Age: Hemangiomas—children; Varix—adults
Sex: No predilection

CLINICAL FEATURES

Vascular lesions are commonly located on the lips and buccal mucosa. In children, they represent hamartomatous proliferation of vascular channels (hemangiomas). Intramuscular hemangiomas may attain considerable dimensions; being situated in deeper tissues, they do not necessarily impart a red or bluish appearance to the distended overlying mucosa. In older patients, the clinical features are nearly identical but vascular growths generally represent aneurysma-like dilations of venules known as varices. A localized varix may appear subsequent to trauma. Both hemangiomas and varices

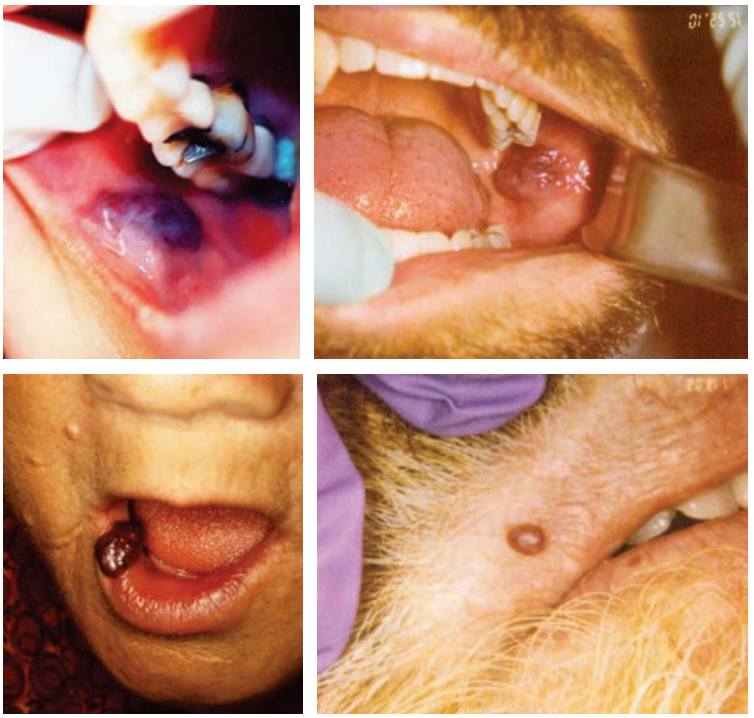

FIGURE 6-54
Hemangioma and varix of the lip and buccal mucosa. These benign vascular red and blue lesions blanch under pressure.

appear as smooth or slightly nodular, red to purple soft swellings that blanch on pressure. Hemangiomas of the oral mucosa may accompany facial skin angiomatoses or port-wine stain and can be a component of the Sturge-Weber syndrome. Angiomas or varices of long duration may contain radiographically demonstrable phleboliths. Aggressive, or even malignant, hemangioendotheliomas or hemangiopericytomas are rare, have a rapid growth rate, and are usually indurated. The *caliber persistant labial artery* is another vascular lesion found on the lip and simply represents a superficially placed arteriole in the submucosa.

MICROSCOPIC FEATURES

Hemangiomas may be capillary in type, with numerous small-caliber vascular channels, or they may be cavernous with large dilated vessels. A varix may represent a single dilated tortuous venule, which, on microscopic section, shows numerous dilated channels similar to cavernous hemangiomas. Thrombi are frequently seen within the dilated vascular lumina.

Hemangioendotheliomas are cellular with only slit-like vascular channels and sheets of plump endothelial cells. Likewise, hemangiopericytomas are hypercellular, yet reticulum stains disclose that the neoplastic cells proliferate beyond the confines of periendothelial reticulum. In addition, the vascular spaces are irregular, evincing a "stag-horn" pattern.

DIFFERENTIAL DIAGNOSIS

Other swellings of the lips and cheek are not pigmented; however, deeply situated vascular lesions may not show a red color and therefore must be differentiated from mucocele, other mesenchymal neoplasms, salivary neoplasms, and inflammatory hyperplasia.

TREATMENT

Local excision is the treatment of choice for small lesions; excessive hemorrhage is

generally not encountered. Large diffuse hemangiomas may be excised or sclerosed. If they do not interfere with function or are not a cosmetic problem, they may be left untreated. Hemangiomas in children may show spontaneous regression before or during pubescence. Wide excision with liberal margins is in order for hemangioendothelioma and hemangiopericytoma. When these tumors are encountered, a thorough medical work-up is necessary, as they occasionally metastasize.

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SQUAMOUS CELL CARCINOMA

Figure 6-55

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Early squamous cell carcinoma may appear as a focal ulcer on the lower lip and often shows actinic cheilosis. As tumefaction ensues, the surface may remain ulcerated or be encrusted with keratin. Usually, but not invariably, the mass is indurated and fixed to the adjacent soft tissues. Metastatic deposits may be detected in the submental, submandibular, or cervical nodes. Squamous cell carcinoma in the buccal mucosa is similarly ulcerated and indurated. Not uncommonly, it may show a white keratinized surface.

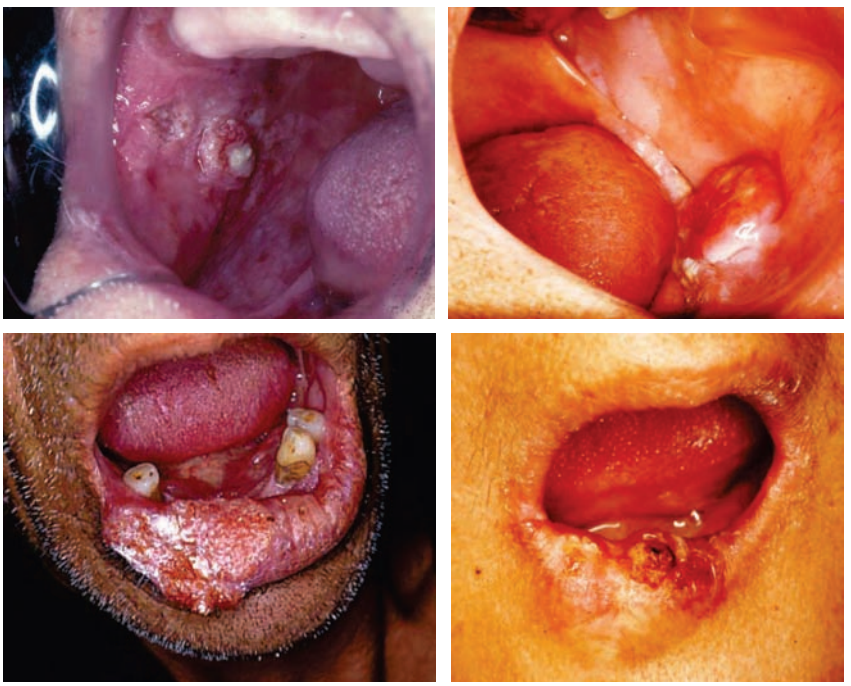

FIGURE 6-55
Squamous cell carcinoma of the lower lip has a good prognosis after complete excision.

MICROSCOPIC FEATURES

The neoplastic epithelium is well differentiated when it involves the lip, showing minimal hyperchromatism or pleomorphism. Tumor islands display central parakeratin or keratin pearls. Two specific forms of squamous cancer occur on the lip and show unique histomorphologic features. Adenoid squamous cell carcinoma is characterized by acantholysis of cells, producing clefting within tumor islands. This change imparts an adenoid appearance. Spindle cell carcinoma is another variant of squamous cell carcinoma. Microscopically, the cells appear sarcomatoid with streams of invasive spindle cells that are usually in continuity with, and emanate from, the basal layer. Buccal mucosa carcinomas may not necessarily be well differentiated.

DIFFERENTIAL DIAGNOSIS

Small squamous cell carcinomas may be well localized and clinically appear identical to keratoacanthoma. Larger lesions are usually fungating and may resemble granulomatous lesions. Specific granulomatous infections of the lips and buccal mucosa are rare. Crusted or ulcerated lesions of the upper lip are more likely to represent basal cell carcinomas. Because they usually originate on the skin rather than on the vermilion border, basal cell carcinomas are dealt with in the section on soft tissue swellings of the neck and face. Ulcerated and indurated carcinoma of the buccal mucosa must be distinguished from malignant salivary or mesenchymal neoplasms.

TREATMENT

Biopsy must be performed to ensure a diagnosis of squamous cell carcinoma. Lip cancer is preferably treated with surgical excision and lip shave. Buccal mucosal carcinoma should be managed by a cancer specialist and may require both irradiation and surgery.

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MONOMORPHIC ADENOMA

Figure 6-56

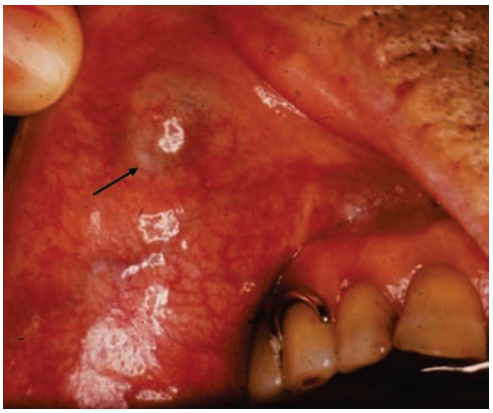
Age: Middle-aged and elderly adults
Sex: Female predilection

CLINICAL FEATURES

A variety of histologically distinct salivary neoplasms including canalicular adenoma, basal cell adenoma, and membranous adenoma are collectively grouped as monomorphic adenomas. These tumors arise most frequently in the minor glands of the upper lip, where they appear as movable nodules with either a fluctuant or soft consistency. Although usually solitary, this type of adenoma can be multifocal. This finding would support a hamartomatous pathogenetic nature.

MICROSCOPIC FEATURES

Three primary variations are encountered. The canalicular adenoma is characterized by anastomosing cords of basaloid cuboidal cells with an intervening delicate mucoid vascular stroma. Multicentric foci are frequently observed, and an intralobular origin can be documented in some cases. The basal cell adenoma is represented by cords and islands of basaloid cells showing duct formation. The stroma is fibrovascular without chondroid, adipose, or myxoid differentiation. The membranous adenoma is



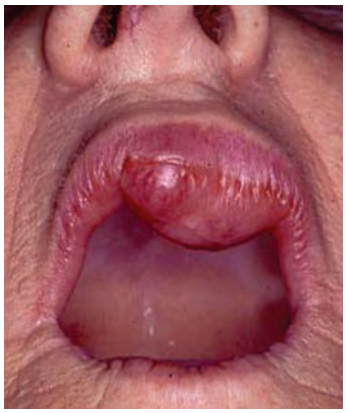


FIGURE 6-56
A basal cell adenoma (left) and a canalicular (monomorphic) adenoma arising from minor salivary glands.

histologically similar to the basal cell type; however, the stroma is hyalinized. Interestingly, all three patterns may be identified within a single specimen.

DIFFERENTIAL DIAGNOSIS

Clinically, monomorphic adenoma is indistinguishable from other salivary neoplasms or encapsulated mesenchymal tumors. A movable mass in the upper lip, however, usually represents monomorphic adenoma.

TREATMENT

Excision of the tumor with an attempt to remove some of the adjacent marginal tissue is recommended.

Additional Reading

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OTHER SALIVARY NEOPLASMS

Figure 6-57

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Salivary tumors are frequently seen in the cheek and upper lip; the lower lip is rarely the site of origin. The pleomorphic adenoma, which is most common, is a well-demarcated, encapsulated, soft-to-firm movable mass. Malignant salivary tumors infrequently arise in labial glands, but are often located in the buccal mucosa. They are firm or indurated and may or may not show ulceration. Specific tumors include polymorphous low-grade adenocarcinoma, adenoid cystic carcinoma, and mucoepidermoid carcinoma. Acinic cell carcinoma is seen most often in the parotid; when it arises from oral minor glands, the buccal mucosa and lip are the more prevalent sites.

MICROSCOPIC FEATURES

The histologic findings vary depending on the specific type of tumor. These features are separately enumerated in the section on palatal swellings.

DIFFERENTIAL DIAGNOSIS

Salivary neoplasms appearing as upper lip or buccal mucosal swellings resem-

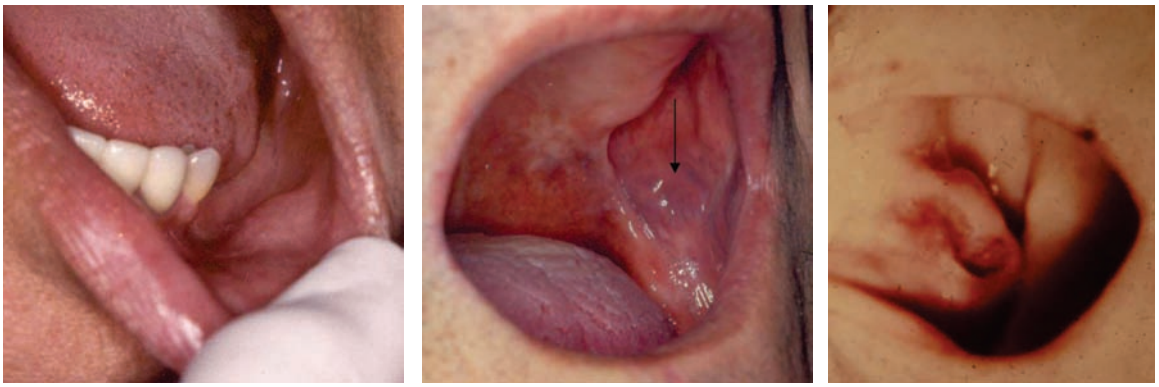

FIGURE 6-57
Benign or malignant salivary neoplasms of the buccal mucosa present as submucosal swellings, some of which have a bluish cast due to mucin production in the tumor.

ble mucocele (which rarely occurs in the upper lip), mesenchymal neoplasm, or inflammatory hyperplasia. Ulcerated and indurated adenocarcinomas must be differentiated from squamous cell carcinoma and sarcomas.

TREATMENT

Benign salivary tumors should be excised rather than merely enucleated, because the latter procedure often results in recurrence. Wide and often radical excision is necessary to eradicate malignant salivary tumors. Depending on the histologic designation, neck dissection may be indicated.

Additional Reading

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Tongue Swellings

MEDIAN RHOMBOID GLOSSITIS

Figure 6-58

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

A smooth-surfaced, slightly nodular pink elevation that is devoid of papillae and is located immediately anterior to the foramen caecum and circumvallate papillae in the midline characterizes median rhomboid glossitis. This anomaly could represent a developmental defect: persistence of the tuberculum impar with failure to retrude during embryogenesis. This theory is equivocal in light of evidence that suggests the lesion is not congenital but arises later in life. *Candida* organisms are associated with this lesion, and although some investigators think they play a causative role, this theory has not been documented in all instances. It is innocuous, painless, and rarely warrants removal.

MICROSCOPIC FEATURES

The surface epithelium is devoid of papillae and shows rete ridge extension into the

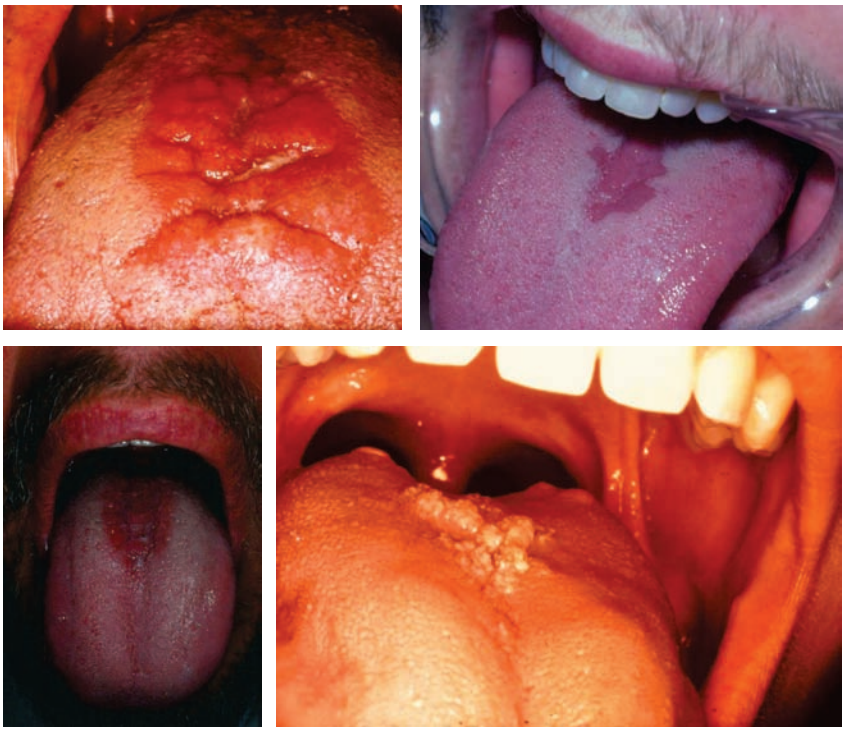

FIGURE 6-58
Median rhomboid glossitis, characterized by a midline swelling located on the dorsum of the tongue.

submucosa. Candidal organisms are often present within the parakeratin layer. The subjacent fibrous tissue is mildly infiltrated with leukocytes.

DIFFERENTIAL DIAGNOSIS

Median rhomboid glossitis may clinically resemble mesenchymal neoplasms, lingual cyst, and glossal-oriented thyroglossal duct cyst. Generally, a clinical diagnosis is easily rendered by virtue of its configuration, lack of growth potential, and midline location.

TREATMENT

If the tumefaction is large, a biopsy is indicated to rule out neoplasia or cyst. When it is of limited size, periodic recall should be instituted to determine that no growth is taking place.

Additional Reading

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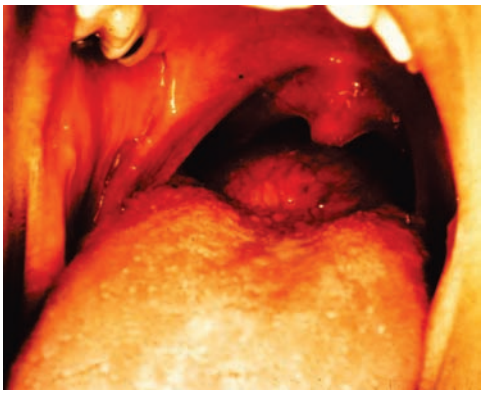
ECTOPIC LINGUAL THYROID

Figure 6-59

Age: Early adulthood
Sex: Female predilection

CLINICAL FEATURES

Ectopic thyroid tissue appears as a smooth, nodular, or occasionally cystic swelling posterior to the foramen caecum. Dysphagia may be a feature. In most patients, no thyroid tissue can be detected in the usual location. For this reason, excision could result in postsurgical hypothyroidism. An ^{131}I radioisotope scan is useful in the diagnosis of



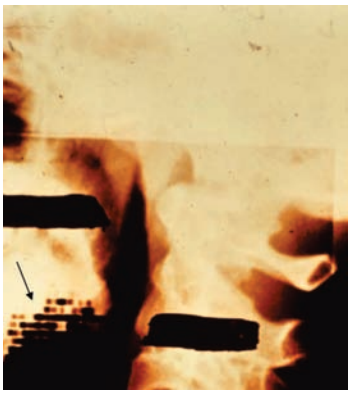


FIGURE 6-59
Lingual thyroid nodule at base of tongue. Radioactive iodine uptake is seen in base of tongue rather than in the normal region of the anterior neck.

suspected lingual thyroid and serves as an indication as to whether or not any thyroid tissue is present in the usual location. The ectopic location reflects the failure of normal developmental migration of the thyroglossal tract and gland primordium. Both adenoma and adenocarcinoma have been reported to arise in lingual thyroid nodules.

MICROSCOPIC FEATURES

The oral epithelium is distended by mature thyroid follicles filled with colloid and lined by cuboidal epithelium.

DIFFERENTIAL DIAGNOSIS

The lingual thyroid nodule must be differentiated from thyroglossal duct cyst, a large superiorly displaced vallecular cyst, and mesenchymal neoplasm. An ^{131}I scan can outline the extent of the lesion and identify any normally located thyroid tissue.

TREATMENT

Incisional biopsy may be performed to aid in diagnosis; however, the entire mass should not be removed if normally located thyroid tissue cannot be demonstrated. Should the lesion show a history of recent growth, biopsy is indicated to rule out thyroid neoplasia.

Additional Reading

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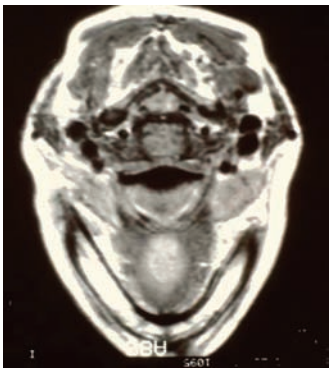
THYROGLOSSAL DUCT CYST

Figure 6-60

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Thyroglossal cysts arise from remnants of the thyroid anlage and are generally seen above the thyroid in the vicinity of the hyoid bone in the midline of the neck. They may, however, arise in the substance of the tongue below the foramen caecum. They are compressible and yield a yellow fluid on aspiration. Dysphagia may develop. Carcinoma has been reported to arise from the cyst lining.



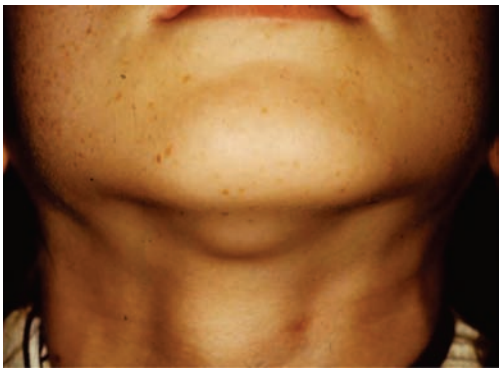


FIGURE 6-60
Thyroglossal cyst in the tongue. *Source:* Macdonald DM. Thyroglossal cysts and fistulae. *Int J Oral Maxillofac Surg.* 1974;3:342.

MICROSCOPIC FEATURES

The cyst is lined by columnar, respiratory, or stratified squamous epithelium. Follicles of thyroid glandular epithelium are frequently located in juxtaposition to the cyst lining.

DIFFERENTIAL DIAGNOSIS

Lingually localized thyroglossal duct cyst has features similar to lingual thyroid nodule, mesenchymal neoplasms, and even a posteriorly located median rhomboid glossitis.

TREATMENT

The cyst should be surgically excised or enucleated.

Additional Reading

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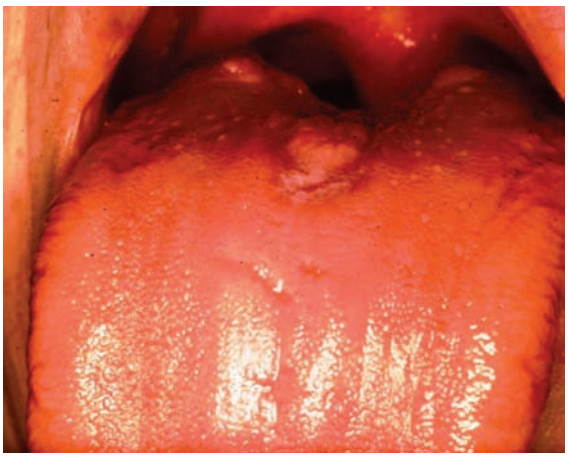

FIGURE 6-61
Lingual developmental gastric cyst in the area of the foramen ceacum.

LINGUAL CYST (ENTEROCYSTOMA, GASTRIC CYST)

Figure 6-61

Age: Insufficient data to determine
Sex: Insufficient data to determine

CLINICAL FEATURES

The lingual cyst is rare and is located in the anterior midline of the tongue. It is movable and compressible. Few cases have been reported. It has been suggested to arise as a result of epithelial entrapment during

fissural closure of the lateral lingual processes during development. Many of these lesions harbor gastric primordial epithelium; hence, the term *enterocystoma*.

MICROSCOPIC FEATURES

Most lingual cysts are lined by aberrant gastric epithelium and are referred to as gastric cysts or enterocystoma. Some lesions are simply lined by columnar, respiratory, or stratified squamous epithelium.

DIFFERENTIAL DIAGNOSIS

The smooth nodular swelling protrudes dorsally so that confusion with dermoid cyst or ranula should be no problem. A lingual abscess or mesenchymal neoplasm may clinically resemble a lingual cyst.

TREATMENT

Surgical excision is recommended.

Additional Reading

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HYPERPLASTIC LINGUAL TONSIL

Figure 6-62

Age: Adults
Sex: No predilection

CLINICAL FEATURES

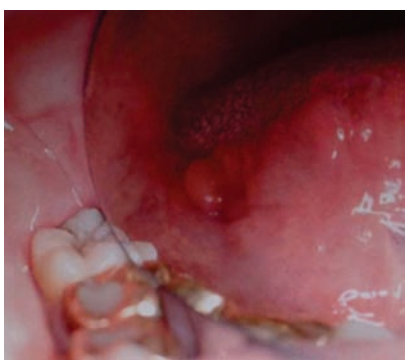
The foliate papillae located at the posterolateral tongue base represent lingual tonsils with epithelial lined crypts surrounded by lymphoid tissue that may produce germinal centers. These tonsillar tissues become enlarged during upper respiratory infections or from trauma. The hyperplastic tissue is smooth, reddish yellow, and nonulcerated. They are usually painless, yet in some patients discomfort is a complaint.

MICROSCOPIC FEATURES

Surface stratified squamous epithelium is hyperplastic and is distended by sheets of lymphocytes with germinal centers that are also hyperplastic. The epithelial lined tonsillar crypts blend imperceptibly with the surrounding lymphocytes.

DIFFERENTIAL DIAGNOSIS

Hyperplastic lingual tonsils are common and occur in the same site as squamous cell carcinoma of the posterolateral tongue. Unlike carcinoma, hyperplastic tissues are not indurated, being soft to palpation. Biopsy should be performed for patients who smoke just to be certain.



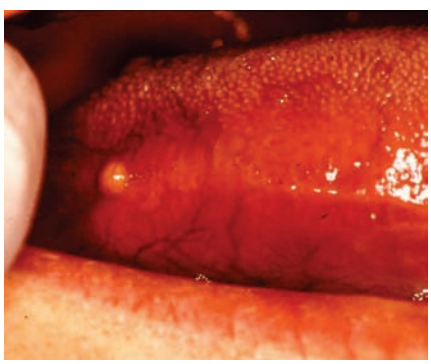


FIGURE 6-62
Hyperplastic lymphoid tissue is nodular, located at the lateral tongue base (foliate papillae).

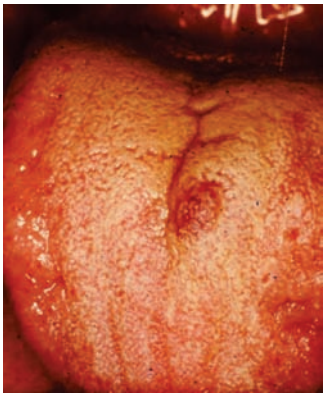
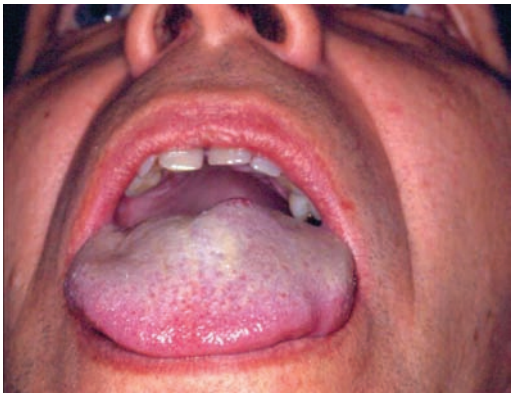



FIGURE 6-63
Submucosal abscesses are firm and tender. Many occur after trauma or a piercing by a small fishbone.

TREATMENT

Short-term follow-up is recommended. The hyperplastic tissues tend to regress over time.

Additional Reading

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Parham K, Newman R. Recurrent lingual tonsil hyperplasia. *Arch Otolaryngol Head Neck Surg.* 2003;129: 1010-1012.

LINGUAL ABSCESS

Figure 6-63

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Trauma from a tongue bite or introduction of a foreign object such as a fish bone can leave a laceration that can fester, becoming infected with pyogenic bacteria such as staphylococci or streptococci. Clinically, the tongue becomes swollen, is exquisitely painful to touch, and often has a fistula.

MICROSCOPIC FEATURES

A foreign object may be seen microscopically and when none is found, reexamination under polarized light may reveal refractile particles. Muscle necrosis and degeneration are evident with a suppurative infiltrate of leukocytes.

DIFFERENTIAL DIAGNOSIS

Pain signals an acute infection in a tongue mass. Other reactive and neoplastic lesions should be considered.

TREATMENT

Excision with debridement should be undertaken. Antibiotic therapy is reserved for patients with fever.

Additional Reading

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REACTIVE LESIONS (FIBROMA, PYOGENIC GRANULOMA)

Figure 6-64

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The most common swelling of the tongue is the traumatic fibroma. It appears as a dome-shaped submucosal mass that shows normal mucosal coloration and is rarely ulcerated. They can be located anywhere on the tongue. Fibromas evolve secondary to trauma, usually a tongue bite incident.

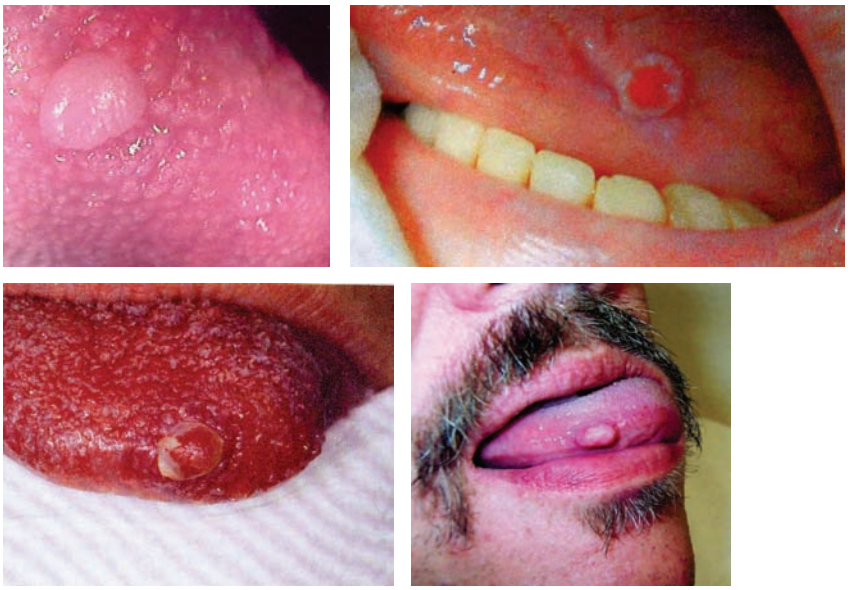

FIGURE 6-64
Reactive lesions of the tongue include pyogenic granulomas that are red or purple and traumatic fibromas, usually of normal coral pink coloration.

Pyogenic granulomas are similarly reactive proliferations that also appear as dome-shaped masses. They are typically red and usually show a whitish surface secondary to ulceration. Pyogenic granulomas usually proliferate rapidly, alarming patients that they may have cancer.

MICROSCOPIC FEATURES

Fibromas show a layer of surface epithelium that may manifest hyperkeratosis and acanthosis. Comprising the bulk of the specimen is mature fibrous connective tissue that is traversed by capillaries. Scattered leukocytes are sometimes present. *Giant cell fibromas* contain multinucleated fibroblasts with a splayed "manta ray" cytoplasm. Pyogenic granulomas are often ulcerated with a fibrinous surface membrane. The specimen comprises granulation tissue, prominently vascularized, and the vessels are often arranged in a lobular pattern of growth.

DIFFERENTIAL DIAGNOSIS

Other mesenchymal tumors are easily mistaken clinically for reactive growths. Biopsy is required to secure a definitive diagnosis.

TREATMENT

Excision is the treatment of choice. Fibromas do not tend to recure whereas pyogenic granulomas sometimes do.

Additional Reading

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Kuo RC, Wang YP, Chen HM, Sun A, Liu BY, Kuo YS. Clinicopathological study of oral giant cell fibromas. *J Formos Med Assoc.* 2009;108(9):725-729.

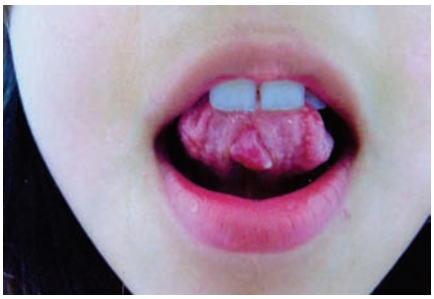
MUCOCELE

Figure 6-65

Age: Children
Sex: No predilection

CLINICAL FEATURES

Most mucoceles occur on the lower lip and once excised, the recurrence rate is low provided the underlying feeder glands are enucleated during surgical excision. Mucocels that arise from the glands of Blandin-Nuhn



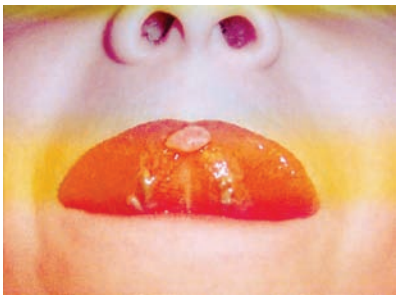


FIGURE 6-65
Mucoceles in the region of the minor salivary glands of Blandin-Nuhn tend to recur following excision.

behave differently. They appear as unifocal nodules on the ventral anterior tongue and may be translucent or blue. They are fluctuant to palpation and evolve subsequent to trauma such as tongue biting or ventral tongue lacerations. Since the minor glands of Blandin-Nuhn reside within the intrinsic muscle layers, they are often left behind during treatment, providing saliva leakage that predispose to a recurrence.

MICROSCOPIC FEATURES

The epithelium is distended by pooled mucin undergoing varying degrees of organization by granulation tissue. Minor glands may be seen interposed between muscle fibers.

DIFFERENTIAL DIAGNOSIS

The clinical appearance is quite classic, although in sclerosing lesions, a fibroma or mesenchymal tumor may be expected.

TREATMENT

Excision of the mucocele, making sure to dissect out the intramuscular glands, is essential to avoid recurrence.

Additional Reading

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HEMANGIOMA AND LYMPHANGIOMA

Figure 6-66

Age: Children
Sex: No predilection

CLINICAL FEATURES

Vascular tumors often arise within the tongue and manifest a swelling of the midline or lateral margins. When superficial, which is often the case, racemose nodules are present; in hemangioma, they are red and blanch on pressure. Lymphangiomas do not impart a color change to the mucosa. The entire tongue or only a portion of it may be occupied by neoplastic vessels. Calcified thrombi or phleboliths are often present in hemangiomas of long standing; the calcified nodules are demonstrable as soft tissue radiopacities radiographically. The more aggressive vascular tumors, hemangioendothelioma and hemangiopericytoma, are more firm to palpation, have a rapid growth rate, and have metastatic potential.

MICROSCOPIC FEATURES

Hemangioma and lymphangioma have similar microscopic characteristics. Dilated

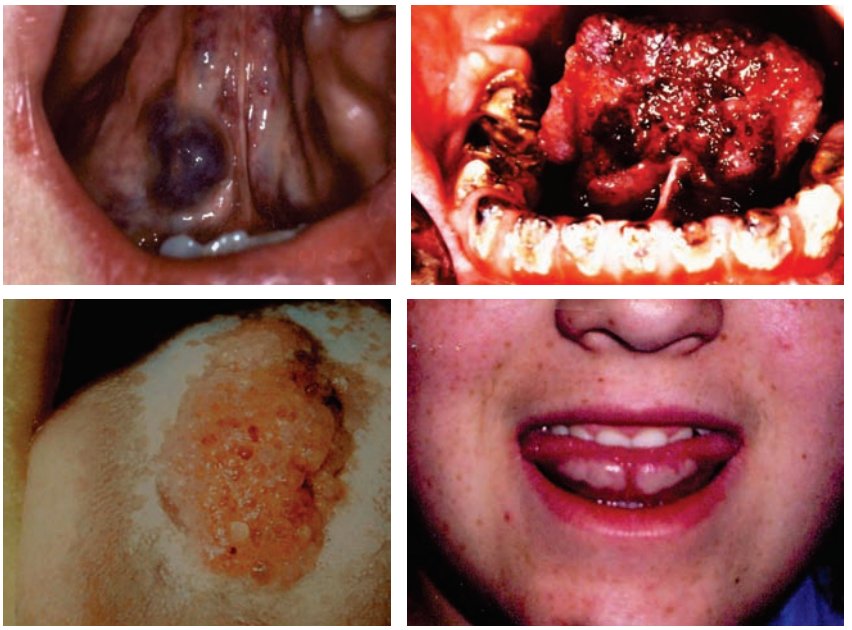

FIGURE 6-66
Hemangiomas are common in the tongue, appearing at infancy or childhood. The hemangioma in the upper right was radiated, causing advanced radiation caries in the dentition. Case in lower right is creamy white being a lymphangioma.

endothelium-lined channels course throughout the tongue stroma and are often intramuscular. When superficially oriented, exophytic extensions composed of vessels distend the surface epithelium. The vascular channels of hemangioma contain erythrocytes and occasionally thrombi. When the lesions are primarily cellular, they are designated as *cellular hemangioma* or *benign hemangioendothelioma.* These lesions behave benignly, similar to simple hemangiomas. Lymphangiomas contain lymph, an eosinophilic coagulum. The aggressive hemangioendothelioma is highly cellular, composed of monomorphic, plump elongated nuclei with little pleomorphism. These cells line vacant clefts resembling stag horns. Hemangiopericytomas are composed of similar cells but are arranged in swirls around a small lumen.

DIFFERENTIAL DIAGNOSIS

Most vascular lesions are extensive so that confusion with focal midline tongue lesions such as median rhomboid glossitis, lingual thyroid, or cystic lesions is not probable. A racemose surface pattern is invariably a feature of vascular neoplasm. Deeply situated angiomas may be confused with other mesenchymal neoplasms.

TREATMENT

When the lesions are small, local excision is recommended. Lingual hemangiomas may bleed profusely. Extensive lesions, once diagnosed by biopsy, may be left untreated if asymptomatic. The aggressive angiomas (hemangioendothelioma, hemangiopericytoma) require wide local excision with periodic follow-up. Metastasis may develop late but metastatic predictability is difficult if not impossible for aggressive angiomas based on microscopic evaluation.

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NEURAL SHEATH TUMORS

Figure 6-67

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Benign neoplasms of cells that ensheath nerves include those derived from the neurilemma, neurilemmomas, and those derived by perineuronal fibroblasts, neurofibromas. Both types may arise anywhere in the mouth, but are encountered most frequently in the tongue, where they appear as smooth-surfaced firm or rubbery painless nodules. Neurilemmomas are encapsulated yet may be multinodular. Neurofibromas are well defined, yet lack true encapsulation. When multiple oral neurofibromas are associated with similar lesions of skin and café-au-lait pigmentations, they represent a component of von Recklinghausen's neurofibromatosis. Oral neurofibromas are, however, most frequently solitary. Neural tumors occurring as multiple small nodules may be a component of the Sipple syndrome (see papillary and multiple polypoid swellings).

MICROSCOPIC FEATURES

Neurilemmoma shows a fibrous capsule; the tumor cells are arranged in parallel rows, demonstrating palisading of nuclei, Antoni type A tissue. Palisaded nuclei are separated by a dense acellular fibrillar zone. Organoid swirls of Antoni A tissue constitute Verocay bodies. Antoni B tissue is composed of loosely arranged collagen with interfibrillar vacuolated foci. Neurofibromas are composed of elongated nuclei randomly dispersed in a fibrous background. The cellular pattern is winding, giving the appearance of intercoiled spaghetti noodles. Rare

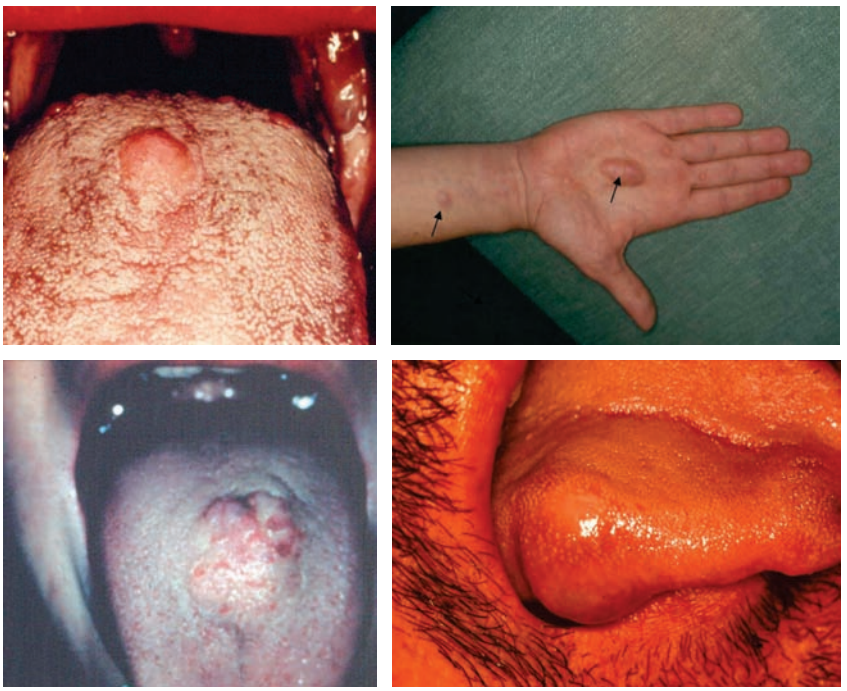

FIGURE 6-67
Nerve sheath tumors of the tongue. Most neurofibromas are solitary; the patient on the upper left has neurofibromatosis. Lower left: neurilemmoma (Schwannoma).

nerve sheath tumors include benign nerve sheath myxoma, palisaded encapsulated neuroma, and ancient neurilemmoma.

DIFFERENTIAL DIAGNOSIS

Neural sheath neoplasms tend to locate in the anterior one third of the tongue, and the swelling must be differentiated from other mesenchymal neoplasms, lingual cysts, and salivary tumors, which occasionally arise from minor glands of the tongue.

TREATMENT

Simple excision is rarely complicated by recurrence.

Additional Reading

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GRANULAR CELL TUMOR

Figure 6-68

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Granular cell tumors are derived from cells that ensheath other cells such as neurilemma (Schwann) cells or sarcolemma. The term *granular cell myoblastoma* was used in the past because most of these lesions in the mouth are associated with muscle fibers. Nevertheless, many are clearly derived from nerve sheath cells. The lesions appear as small elevated nodules on the dorsum

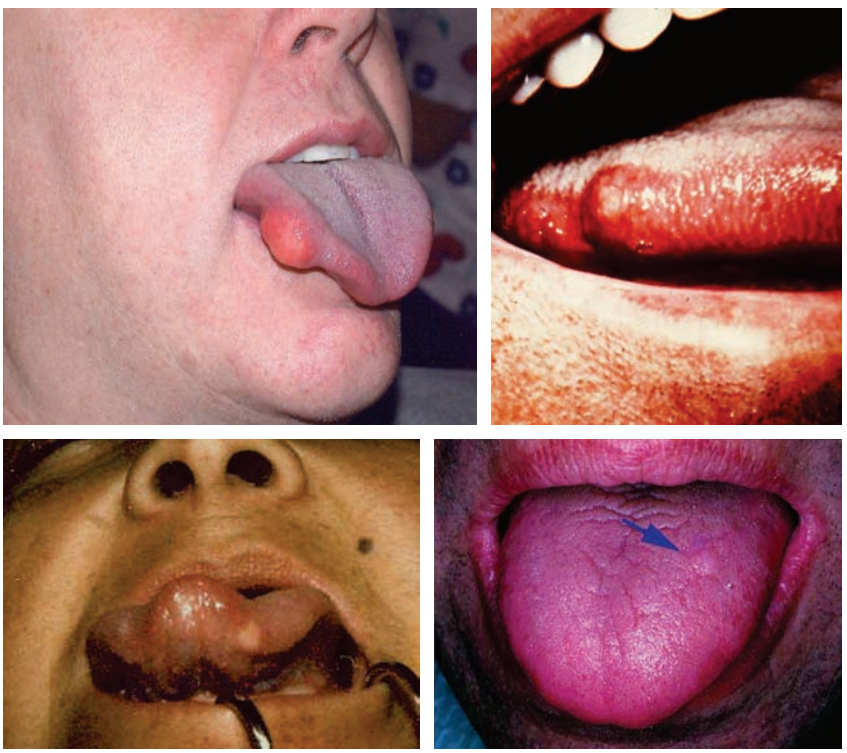

FIGURE 6-68
Granular cell tumors of the tongue, generally presenting as a smooth nodule with a sessile base.

or lateral border of the tongue. They are painless and soft to palpation. The *rhabdomyoma,* a rare tumor of muscle origin, also arises in the tongue. These tumors are encapsulated and have limited growth potential.

MICROSCOPIC FEATURES

Oval eosinophilic granular cells have pyknotic nuclei and are separated from one another by scant stroma. When superficial, the epithelium may show extensive pseudoepitheliomatous hyperplasia. The granular cells may emanate from either muscle fibers or neural sheath. Rhabdomyomas are composed of large oval or elongated cells with eosinophilic granular cytoplasm showing evidence of cross-striations. The nuclei are eccentric.

DIFFERENTIAL DIAGNOSIS

Granular sheath cell lesions and rhabdomyoma may be clinically similar to median rhomboid glossitis or other mesenchymal neoplasms.

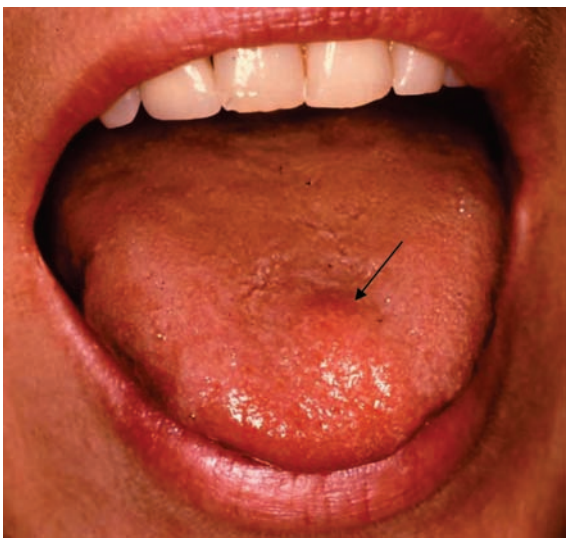

FIGURE 6-69
Leiomyoma. These are rare in the mouth; when they occur, the tongue is the favored site.

TREATMENT

Simple excision is recommended. Recurrence is almost nonexistent.

Additional Reading

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LEIOMYOMA

Figure 6-69

Age: Middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

Leiomyomas are smooth-surfaced tumefactions that may arise in any location. In the mouth, they are most frequently encountered on the tongue. The tumor is encapsulated, painless, firm, and may be multinodular.

MICROSCOPIC FEATURES

The tumor cells possess elongated, blunt-ended nuclei with a vesicular nucleoplasm. The cells course in streams and fascicles, often evolving from vessels showing perivascular concentric laminations of spindle cells. The fibrillar background may be distinguished from collagen with a trichrome stain and smooth muscle actin IHC.

DIFFERENTIAL DIAGNOSIS

Leiomyoma may be clinically indistinguishable from other mesenchymal neoplasms.

TREATMENT

Simple surgical excision is recommended. Recurrence is unlikely after complete excision.

Additional Reading

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OSTEOCARTILAGINOUS CHORISTOMA

Figure 6-70

Age: Young adults
Sex: Female predilection

CLINICAL FEATURES

Discrete nodules of osseous or osteocartilaginous tissue may form in the substance of the tongue. Whereas most are asymptomatic, some cause dysphagia. They may be located in the anterior, mid, or posterior regions and are more often visualized or palpable on the dorsal aspect. They are firm or hard, sessile or pedunculated, and freely movable. Because no osteoprogenitor cells are within the tongue, their origin is obscure; hence, they represent choristomas. Their potential for growth is probably self-limited.

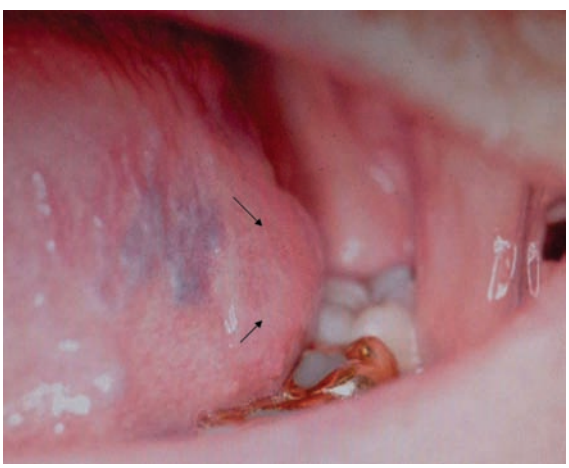

FIGURE 6-70
Cartilaginous choristoma appearing as blanched nodule of ventral tongue.

MICROSCOPIC FEATURES

Some lesions are entirely dense lamellar osseous tissue with a paucity of fibrous marrow or stroma. Others exhibit enclaved foci of chondroid tissue.

DIFFERENTIAL DIAGNOSIS

Clinically, osseous or osteocartilaginous choristomas may resemble traumatic fibromas or other mesenchymal neoplasms. On palpation, however, a movable rock-hard nodule should arouse suspicion of osseous choristoma. An occlusal radiograph will show a radiopaque mass within the soft tissue of the tongue.

TREATMENT

Osseous and osteocartilaginous choristomas are easily enucleated from adjacent soft tissues. Pedunculated varieties can simply be excised at the base of the stalk.

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ECTOMESENCHYMAL CHONDROMYXOID TUMOR

Figure 6-71

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The ectomesenchymal chondromyxoid tumor (ECT) is a rare neoplasm found almost exclusively on the tongue. It is most commonly seen on the dorsum and is usually less than 2 cm in size. ECT appears as a submucosal nodule that is soft and movable with a nonulcerated intact surface mucosa.

MICROSCOPIC FEATURES

Surface epithelium is intact and overlies a well-demarcated submucosal mass with a variety of tissue patterns including epithelial-like strands with eosinophilic cytoplasm and monomorphic nuclei. A myxoid element is prominent with immature chondromyxoid tissue. Hypercellularity is not a feature, and mitotic figures are absent.

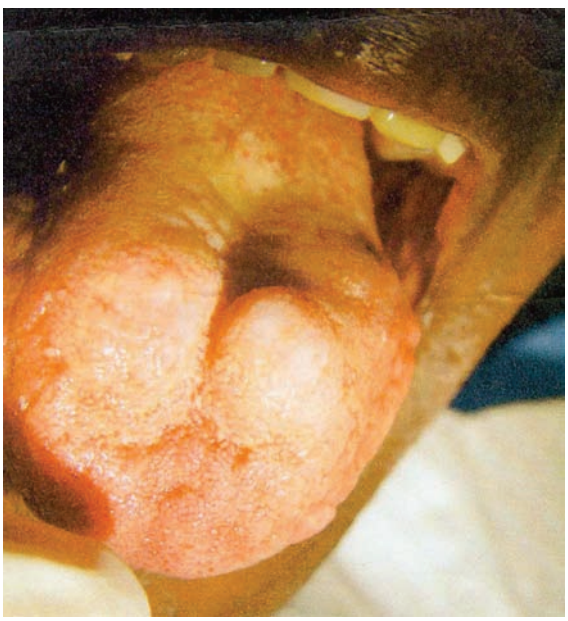

FIGURE 6-71
Ectomesenchymal chondromyxoid tumors are rare and limited to the tongue. They appear as movable soft-to-firm submucosal nodules.

Immunohistochemical markers that stain positively include cytokeratins, glial fibrillary acidic protein, S-100, and CD-57.

DIFFERENTIAL DIAGNOSIS

Clinically, the other mesenchymal tumors listed here are in the differential, and the consistency being soft resembles lipoma or soft tissue myxoma.

TREATMENT

Local excision is the standard treatment with recurrence being rare.

Additional Reading

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SARCOMAS

Figure 6-72

Age: Varies with tumor type
Sex: No predilection

CLINICAL FEATURES

Sarcomas of the oral cavity are rare. They may arise in any locality, including the tongue. The more frequently encountered types include rhabdomyosarcoma and fibrosarcoma. All sarcomas show a rapid growth

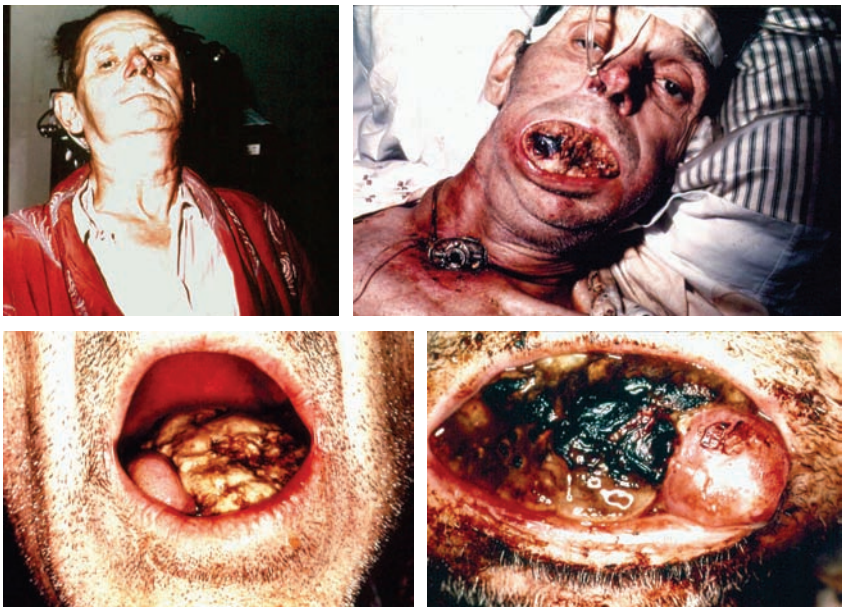

FIGURE 6-72
Rhabdomyosarcoma of the tongue. Upper left represents initial presentation. Lower right is just prior to death, just 1 month later.

rate, are indurated and fixed, and have a tendency toward ulceration. Hematogenous metastasis is the most frequent route of spread from sarcomas leading to pulmonary and widespread metastatic foci.

MICROSCOPIC FEATURES

Histologic findings vary, depending on differentiation of the tumor. Most sarcomas are composed of spindle, pleomorphic, and anaplastic cells with multiple and bizarre mitotic figures. Invasion of adjacent tissues is a constant feature. Microscopically, sarcomas must be differentiated from cellular fibromatoses and pseudosarcomas.

DIFFERENTIAL DIAGNOSIS

Indurated fixed swellings in the tongue must be differentiated from carcinoma and salivary adenocarcinoma.

TREATMENT

Radical excision or glossectomy is required. Despite radical treatment, the prognosis is poor.

Additional Reading

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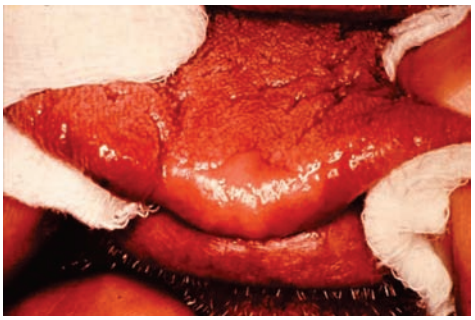
AMYLOID NODULES

Figure 6-73

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Amyloidosis is a metabolic disorder characterized by deposition of a starch-like protein in the tissues. Solitary nodules may be deposited in the tongue, or widespread



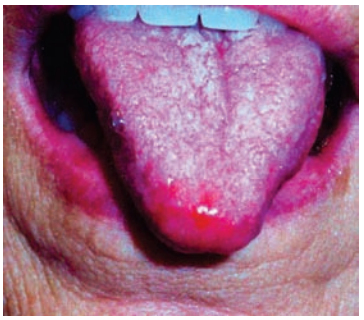


FIGURE 6-73
Amyloid nodules of the tongue. (Courtesy of Drs. S. Silverman and T. Daniels.)

multifocal organ involvement may evolve. It may be primary, secondary to chronic infection such as tuberculosis or osteomyelitis, or associated with multiple myeloma. A unique form of amyloid, β2-microglobulin amyloidosis, is encountered in patients undergoing long-term hemodialysis. The tongue is the most common oral location for the accumulation of amyloid, and the areas of deposition appear as focal or multiple nodular elevations that are normal in color, nonulcerated, and painless. Diffuse involvement of the tongue musculature culminates in macroglossia with stiffness and lack of mobility.

MICROSCOPIC FEATURES

Normal connective tissue is displaced by accumulations of amorphous eosinophilic deposits. The amyloid material stains with Congo red and exhibits dichroism with green birefringence under polarized light. Frequently, the deposits are in perivascular distribution.

DIFFERENTIAL DIAGNOSIS

Solitary amyloid nodules may resemble inflammatory hyperplasia or mesenchymal neoplasm. Multiple nodules may be confused with those encountered in the Sipple syndrome or neurofibromatoses.

TREATMENT

Secondary amyloidosis and amyloidosis associated with myeloma must be managed by control of the primary disease process. All forms should be managed by a physician.

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SPECIFIC GRANULOMA

Figure 6-74

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Specific granulomatous infection is primary in the lungs and appears orally as a secondary manifestation of miliary spread. In the United States, the infections most often encountered include tuberculosis, histoplasmosis, and cryptococcosis. Less frequently, blastomycosis and coccidioidomycosis have oral manifestations. The lesions may develop anywhere in the mouth and are frequently seen on the tongue. They are characterized

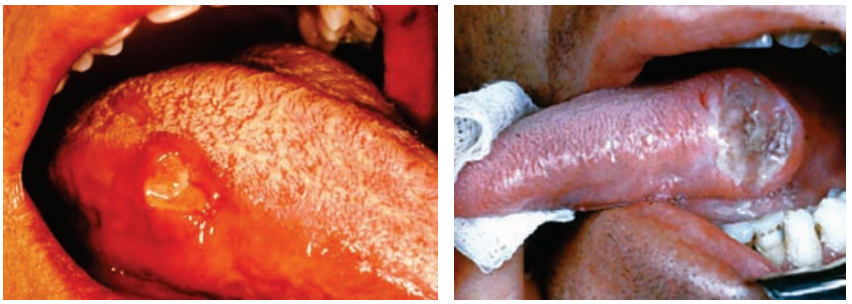

FIGURE 6-74
Ulcerated nodules representing primary syphilis (right) and histoplasmosis (left), granulomatous infections.

by elevated nodular swellings with rolled margins and an ulcerated central region, or they are pebbly granular swellings. Pain is usually not a feature. Primary syphilitic chancre also occurs on the tongue, showing the same clinical features as the secondary granulomatous infections. Histoplasmosis of the oral mucosa in an HIV-positive patient represents a sentinel of disseminated disease and is diagnostic for AIDS.

MICROSCOPIC FEATURES

Granulation and fibrous tissues are admixed with macrophages and multinucleated giant cells. Fungi can usually be found free and within giant cells with routine stains. Acid-fast preparations are required for identification of tubercle bacilli, and periodic acid-Schiff or methenamine silver readily discloses the presence of mycotic microorganisms. A dense plasma cell infiltrate is suggestive of syphilis; however, a Warthin-Starry stain is required to demonstrate spirochetes.

DIFFERENTIAL DIAGNOSIS

The ulcerated granulomas of tuberculosis or the deep mycoses may clinically resemble carcinoma or even sarcoma. Biopsy is required to establish a definitive diagnosis. When tuberculosis or deep mycotic infection is discovered, it should be recalled that the oral lesions represent secondary infection with primary pulmonary disease. Syphilitic chancre is not accompanied by positive serologic findings; serologic testing should be performed 2 to 3 weeks after the appearance of the primary lesion. A darkfield smear discloses the presence of spirochetes.

TREATMENT

Once a diagnosis of granulomatous infection is confirmed, a work-up for pulmonary disease is in order and the patient should be placed under the care of a physician for management and therapy. Syphilis can be treated by penicillin therapy.

Additional Reading

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SQUAMOUS CELL CARCINOMA

Figure 6-75

Age: Elderly adults
Sex: Predominantly males

CLINICAL FEATURES

The tongue is the second most common site for squamous cancer in the mouth, exceeded

only by floor of the mouth. The posterior lateral border is the most common location; however, carcinoma may also affect the mobile and ventral regions. The dorsum is rarely involved; when it is, syphilitic glossitis is usually preexistent. Lesions showing poor differentiation in the base of the tongue, and tonsillar pillars are associated with, and may be caused by, human papilloma virus (HPV), especially HPV 16, the same oncogenic virus implicated in uterine cervix carcinoma. The neoplasm may be red, white, mixed red and white, ulcerated, or tumefactive. Even tumefactive lesions are usually ulcerated and often have coexistent leukoplakia and/or erythroplakia on the margins. The mass is fixed and indurated and may have involved the oral floor or tonsillar pillar. These tumors are staged according to extent. Submandibular or cervical lymphadenopathy is frequently observed, particularly in association with larger tumors.

MICROSCOPIC FEATURES

Invasive islands and cords of neoplastic cells extend into the underlying submucosa and muscle. Keratin pearl formation is usually present, and the individual cells exhibit pleomorphism, hyperchromatism, and increased mitotic activity. The stroma is infiltrated by plasma cells and lymphocytes. The IHC marker p16 is a surrogate marker for HPV infection. The presence of HPV is associated with a more favorable treatment outcome.

DIFFERENTIAL DIAGNOSIS

Tongue swellings located on the lateral margin with ulceration and induration rarely represent benign lesions. Immediate biopsy is indicated.

TREATMENT

Combined radiation therapy and radical surgery, along with neck dissection and/or radiation to the neck, are indicated for large tumors. Indeed, bilateral neck dissection should be undertaken as contralateral metastases are frequently found. Small stage I tumors are usually curable with either wide local excision or radiation therapy.

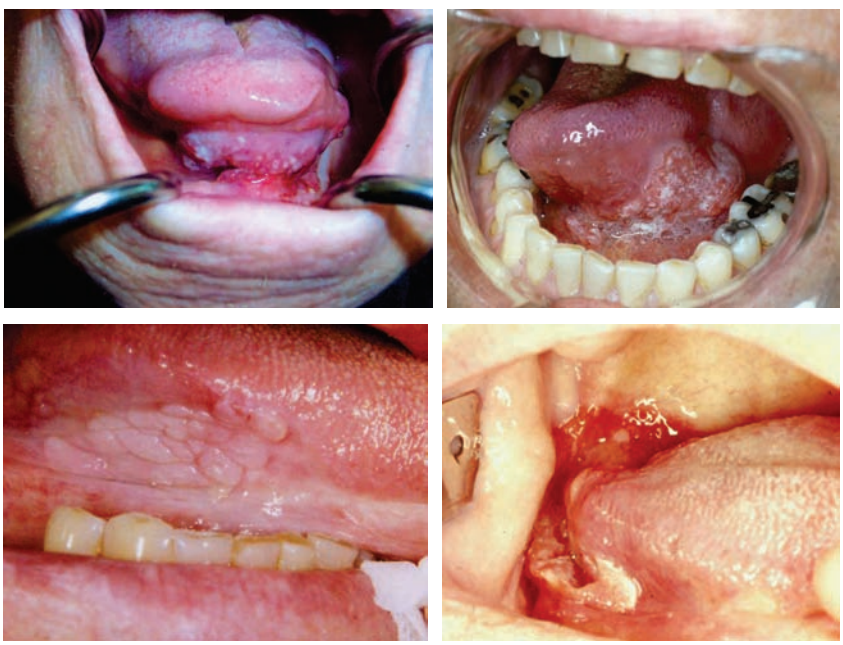

FIGURE 6-75
Squamous cell carcinoma of the tongue, indurated ulcerated masses.

Additional Reading

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Palatal Swellings

TORUS PALATINUS

Figure 6-76

Age: Young adults
Sex: Female predilection

CLINICAL FEATURES

Palatal torus is a bone-hard excrescence that develops after puberty in the midline of the palatal vault. It represents a developmental hereditary overgrowth of bone and is extremely hard to palpation. The surface mucosa is generally intact and often shows lobulation. Tori vary considerably in size and are common, occurring in 20% of the population. Orientals show a greater incidence than whites and blacks. The palatal torus may be quite small, or it may grow to fill the entire palatal vault.

MICROSCOPIC FEATURES

The excrescence is composed of an outer cortical plate with a central cancellous zone. The osseous tissues show normal histologic features.

DIFFERENTIAL DIAGNOSIS

The midline location, slow growth, and bone-hard nature of palatal tori allow for differentiation from palatal abscess or salivary tumors, which are softer and usually located somewhat lateral to the palatal raphe.

TREATMENT

Tori may be left untreated. When a torus interferes with fabrication of a maxillary dental prosthesis, it may be excised.

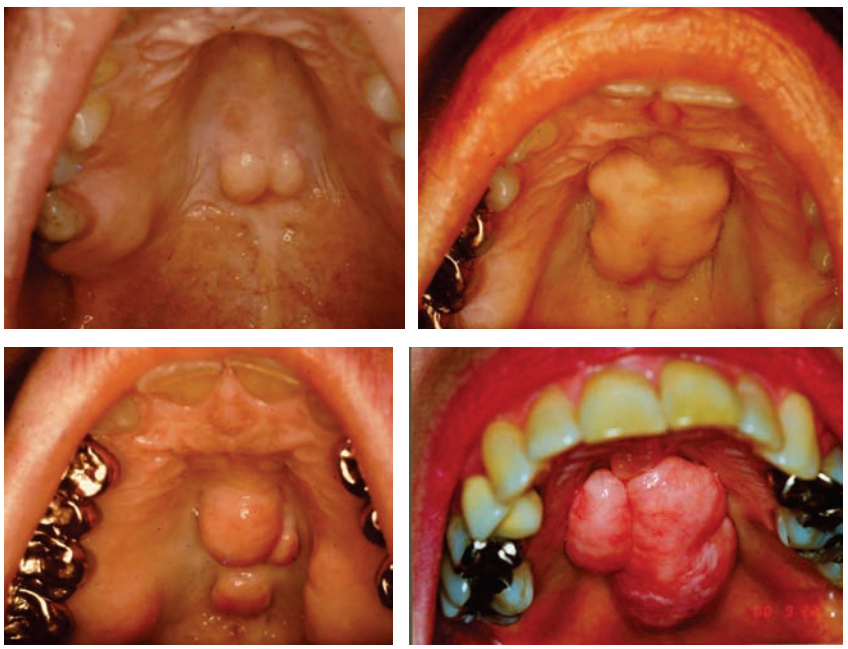
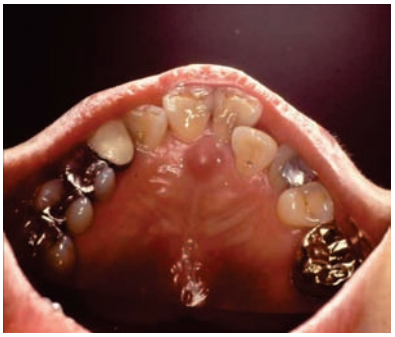


FIGURE 6-76
Torus palatinus, a bone-hard bosselated swelling located in the palatal vault.



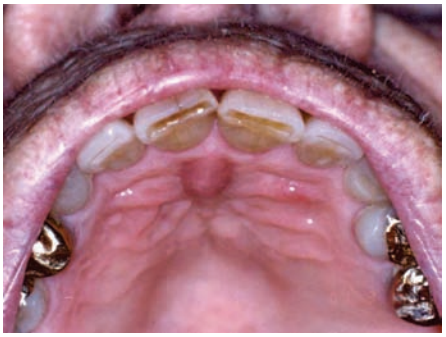


FIGURE 6-77
Anterior palatal midline swelling representing a cyst of the incisive papilla. (Courtesy of Dr. A. Leider.)

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CYST OF THE INCISIVE PAPILLA

Figure 6-77

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

When epithelial remnants of the nasopalatine duct or incisive canal reside immediately subjacent to the incisive papilla and undergo proliferation with cystic change, they are termed *cysts of the incisive papilla.* They therefore represent the oral soft tissue counterpart of the incisive canal cyst. The cysts are usually small, soft, or fluctuant on palpation and may develop a draining fistula.

MICROSCOPIC FEATURES

The cyst lining is stratified squamous epithelium, although on rare occasion, respiratory epithelium is coexistent. The fibrous wall is rich in neurovascular elements, and an inflammatory cell infiltrate is not uncommon.

DIFFERENTIAL DIAGNOSIS

The location is characteristic; however, cysts of the incisive papilla must be differentiated from a central incisive canal cyst with draining fistula and palatal abscess arising from odontogenic infection.

TREATMENT

Simple excision is recommended.

Additional Reading

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PALATAL ABSCESS

Figure 6-78

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Palatal abscess is seen in the premolar-molar region lateral to the midline and is a tense yet compressible swelling. It represents palatally directed drainage of infection of

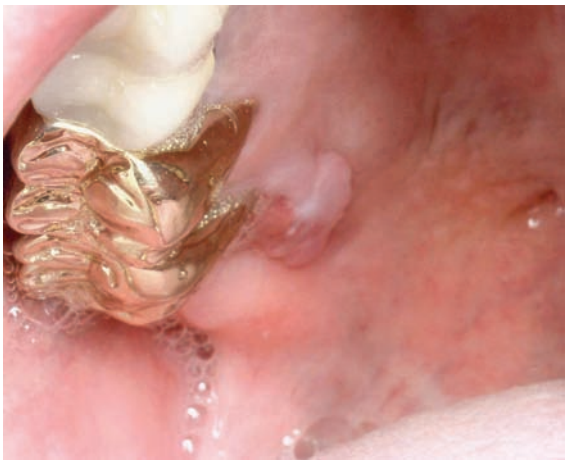

FIGURE 6-78
Firm palatal swelling adjacent to a carious molar, representing a subperiosteal abscess of odontogenic infectious origin.

odontogenic or periodontal origin. A palatal molar root is the most common source. Pain is a frequent finding. A purulent exudate may be aspirated from the swelling.

MICROSCOPIC FEATURES

The palatal abscess is composed of necrotic debris, exudate, and infiltration of neutrophils and histiocytes. The abscess is usually enveloped by a granulation tissue wall.

DIFFERENTIAL DIAGNOSIS

Palatal abscess can be differentiated clinically from salivary neoplasms by noting the presence of pain and identifying an odontogenic infectious source by vitalometer testing or a periapical lesion by radiographs.

TREATMENT

The source of infection must be identified and arrested by either extraction or pulpectomy. The abscess may be incised and drained to relieve pain.

Additional Reading

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REACTIVE LESIONS OF PALATAL GINGIVAL

Figure 6-79

See gingival tumefactions

ADENOMATOUS HYPERPLASIA

Figure 6-80

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

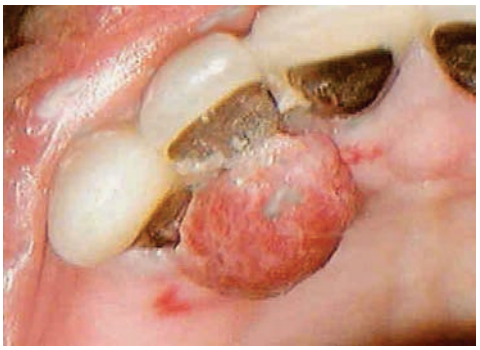
Occasionally, a sessile mass on either the soft or hard palate, appearing to represent a neoplasm, is found to consist of normal-appearing mucous acini and accompanying ducts. These lesions are soft to palpation and usually do not exceed 2 cm. They are covered by normal-appearing mucosa and may represent a developmental anomaly or a focal glandular hyperplasia.

MICROSCOPIC FEATURES

Lobules of normal-appearing palatal minor mucous acini and associated ductal elements lie within the connective tissue under normal surface epithelium.

DIFFERENTIAL DIAGNOSIS

Benign salivary neoplasms and atypical lymphoproliferative disease should be considered in the differential diagnosis. A palatal abscess can be ruled out by virtue of location (adenomatous hyperplasia is usually not confluent with palatal gingiva) and absence of an odontogenic source of infection.



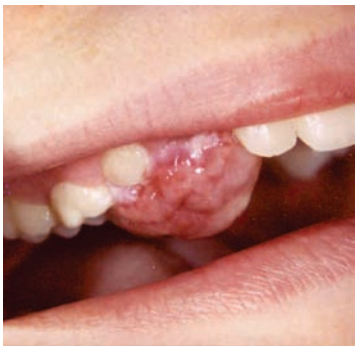
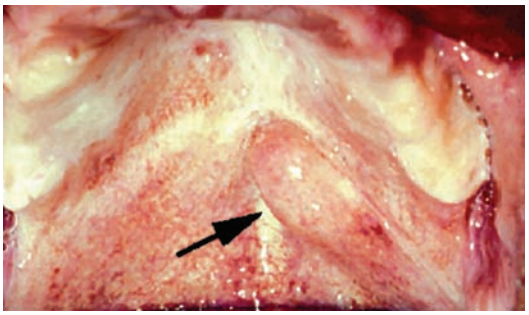


FIGURE 6-79
Fleshy growths represent pyogenic granulomas.



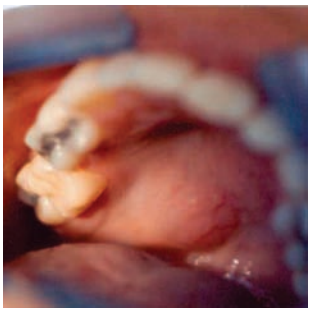


FIGURE 6-80
Adenomatous hyperplasia at hard-soft palate junction.

TREATMENT

Biopsy of masses of this nature should be performed to rule out tumor. Once a diagnosis of adenomatous or glandular hyperplasia is made, no further treatment is required.

Additional Reading

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PLEOMORPHIC ADENOMA

Figure 6-81

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Pleomorphic adenomas may arise in any of the major or minor salivary glands. When intraoral, the palate is the site of predilection. The tumor is located lateral to the midline in the hard or soft palate, is firm to palpation, and as a rule lacks surface ulceration.

MICROSCOPIC FEATURES

Pleomorphic adenoma possesses a circumferential capsule. The tumor is composed of nests and sheets of cuboidal epithelium with ductal formations. Interspersed throughout are various mesenchymal tissues, which include fat, cartilage, and bone. Myxoid tissue is common and may be accompanied by proliferation of spindle-

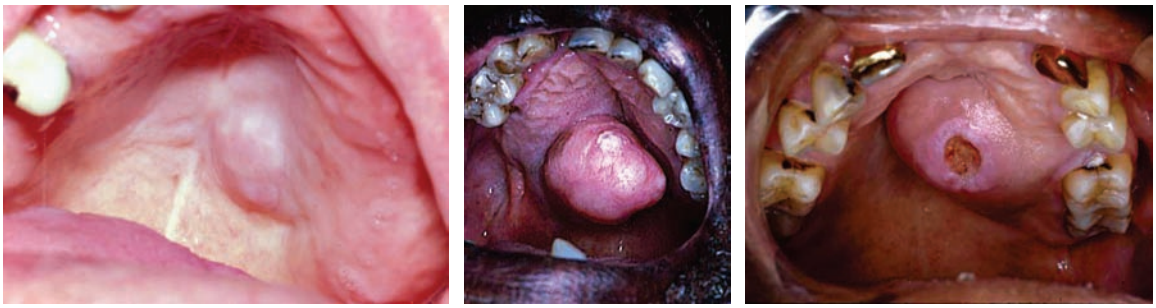

FIGURE 6-81
Pleomorphic adenoma located in the lateral hard palate. Ulceration is not often seen.

shaped myoepithelial cells. Histologic variants are encountered, including those with "plasmacytoid" hyaline cells and tumors with tyrosine crystals.

DIFFERENTIAL DIAGNOSIS

Pleomorphic adenoma can be differentiated from palatal abscess by failure to locate an infectious source; pain is not a feature. Clinically, it may simulate a malignant salivary tumor or a mesenchymal neoplasm; the latter is relatively uncommon in this location.

TREATMENT

Because tumor islands may actually perforate the capsule, simple enucleation may result in recurrence. Excision of the tumor and adjacent tissue is recommended. In the hard palate, the capsule may fuse with periosteum, necessitating subperiosteal dissection with excision.

Additional Reading

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POLYMORPHOUS LOW-GRADE ADENOCARCINOMA

Figure 6-82

Age: Elderly
Sex: Female predilection

CLINICAL FEATURES

As with most minor salivary tumors of the oral cavity, the palate is the favored site for polymorphous low-grade adenocarcinoma, the most common of the minor salivary gland malignancies. Tumors also frequently arise in the buccal mucosa and are less commonly seen in the retromolar region, lips, and base of the tongue. The typical lesion of the palate is asymptomatic, fixed and firm without ulceration, arising off the midline. Surface ulceration or telangiectasia are not commonly seen with this low-grade malignancy.

MICROSCOPIC FEATURES

The polymorphous low-grade adenocarcinoma manifests two distinct microscopic patterns: infiltrating cords and lobular islands. In all tumors, the cells possess relatively monomorphic oval or prolate nuclei without significant hyperchromatism. The

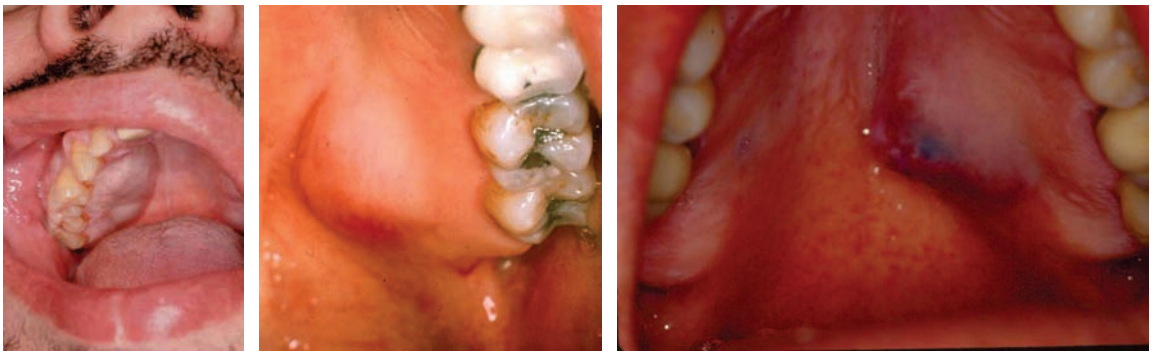

FIGURE 6-82
Submucosal mass at hard-soft palate junction representing polymorphous low-grade adenocarcinoma.

lobular formations usually occupy the central region of the tumor (the term lobular carcinoma has been applied to this lesion) and may exhibit cribriform foci. The peripheral aspects comprise tubular, duct-like cords of cells with some tendency for streaming and spindling of nuclei. The tumor is well circumscribed yet nonencapsulated. A somewhat distinctive immunohistochemical staining pattern is identifiable, cells being S-100 protein positive with weak actin labeling.

DIFFERENTIAL DIAGNOSIS

As with all palatal masses, palatal abscess and other salivary tumors should be considered in the clinical differential diagnosis. Biopsy is required to arrive at a definitive diagnosis, and the histologic characteristics may be confused with those of adenoid cystic carcinoma.

TREATMENT

Wide local excision is the treatment of choice, and local recurrence varies from 10% to 15%. Metastasis is uncommon; when it occurs, spread is generally to regional lymph nodes in the neck. Long-term follow-up is advisable; recurrences have been known to occur 10 years postoperatively.

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MISCELLANEOUS ADENOCARCINOMAS

Figure 6-83

Age: Adults
Sex: No predilection

CLINICAL FEATURES

A variety of salivary tumors occur in the oral cavity that are rare or uncommon compared to the other more commonly encountered forms of adenocarcinoma. These variants are malignancies that differ from one another in

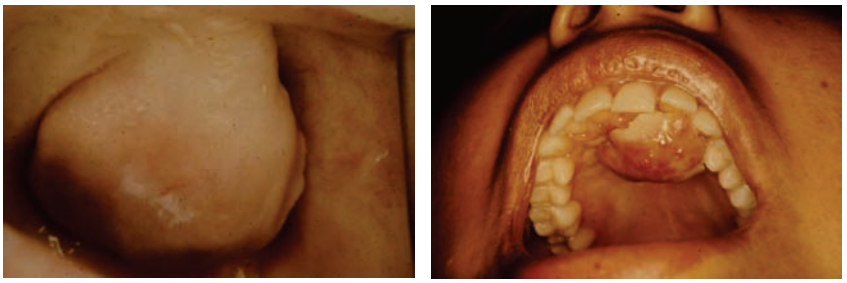

FIGURE 6-83
Miscellaneous rare adenomas (left) and adenocarcinomas (right) also tend to arise in the palatal glands.

terms of metastatic potential, local aggressiveness, and prognosis. Lower-grade tumors include cystadenocarcinoma, papillary cystadenocarcinoma, epithelial/myoepithelial carcinoma of intercalated ducts, clear cell carcinoma, minor gland acinic cell carcinoma, and basal cell adenocarcinoma. High-grade tumors include salivary duct carcinoma, squamous cell carcinoma of salivary origin, mucinous carcinoma, invasive carcinoma ex mixed tumor, and anaplastic small and large cell carcinomas. Most of these variants are more often seen in the major glands.

MICROSCOPIC FEATURES

Each specific variety of salivary carcinomas exhibit unique, characteristic, and diagnostic features. Outlining the microscopy for each of these lesions is beyond the scope of this clinical atlas. Suffice it to say that these tumors, with exception of squamous cell carcinoma and the anaplastic lesions, show various patterns with salivary ductal and acinar cell types.

DIFFERENTIAL DIAGNOSIS

The rare adenocarcinoma variants clinically resemble other salivary neoplasms being submucosal nodules in the palate or other oral sites where minor salivary glands occur. Some are ulcerated. Biopsy is required to arrive at a definitive diagnosis.

TREATMENT

The low-grade tumors are treated by surgical excision with wide margins and because some may metastasize, neck node clinical and magnetic resonance imaging evaluation should be performed. High-grade tumors require surgical resection with neck dissection when positive nodes are present and some respond to adjunct radiation and/or chemotherapy. Since some of these tumors are capable of distant metastases, a chest film should be ordered.

Additional Reading

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ADENOID CYSTIC CARCINOMA

Figure 6-84

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Adenoid cystic carcinoma or cylindroma is a common intraoral malignant salivary

neoplasm and is most often seen in the hard palate. It appears as an indurated swelling lateral to the midline and frequently shows ulceration or surface telangiectasia. Pain is not uncommon. Despite this malignant behavior, it may show a lengthy growth progression. Metastasis is common late in the course of the disease and may not be detected for many years after initial therapy. It has an equal tendency for both regional and hematogenous spread.

MICROSCOPIC FEATURES

The tumor lacks encapsulation and tends to invade adjacent hard and soft tissues. Tumor cells characteristically invade perineural lymphatics and may progress for extended distances along nerve sheaths. The classic pattern shows hyperchromatic, monomorphic cuboidal cells arranged in islands forming multicystic cribriform patterns resembling Swiss cheese. The cystic lumina often contain a basophilic hyaline substance, and the stroma may display eosinophilic hyalinization. When solid basaloid islands predominate, the tumor has a worse prognosis.

DIFFERENTIAL DIAGNOSIS

Cylindroma may be clinically identical to other benign or malignant salivary tumors, sarcomas, or antral carcinoma with palatal invasion.

TREATMENT

Wide excision with partial maxillectomy is necessary. Neck dissection is indicated when nodes are palpable. When they are not palpable, node dissection may not be warranted as the tumor has great tendency to spread to distant sites. All patients with cylindroma should be evaluated with radiographs of the chest. Adenoid cystic carcinoma pursues a slow rate of growth, and many years elapse before recurrence and distant metastases become detectable. The 5-year survival for palatal lesions is less than 35%; 10-year survival rate drops to about 15%.

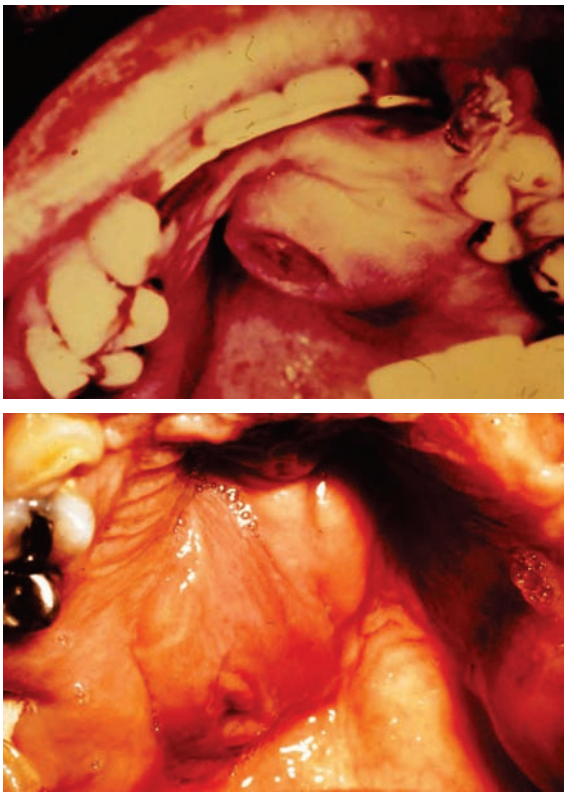

FIGURE 6-84
Adenoid cystic carcinoma with tumefaction showing surface ulceration.

Additional Reading

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MUCOEPIDERMOID CARCINOMA

Figure 6-85

Age: Young and middle-aged adults
Sex: No predilection

CLINICAL FEATURES

When minor glands give rise to mucoepidermoid carcinoma, the palate is the most frequent location. The tumor may be cystic or indurated to palpation and usually fails to show ulceration. Telangiectasia is frequently noted. The growth rate is often slow, and behavior is correlated with histologic grade of malignancy. Despite gradations, all mucoepidermoid carcinomas have metastatic potential. Recent studies appear to indicate that low-grade tumors in the oral cavity do not metastasize; however, this theory has not been completely documented. The higher grade tumors spread by way of lymphatics; however, hematogenous metastasis often occurs in addition to, or in lieu of, nodal metastasis.

MICROSCOPIC FEATURES

Tumor islands may be solid or may show large, dilated cystic formations. A capsule is lacking. The individual tumor cells show a biphasic differentiation with both an epidermoid and a mucous cell component. When the tumor is less cystic and epidermoid cells predominate, the prognosis is worse and the tumor is classified as high grade. Low-grade tumors are cystic with a preponderance of mucous and columnar cells.

DIFFERENTIAL DIAGNOSIS

Palatal abscess, other benign and malignant salivary tumors, antral cancer, and mesenchymal neoplasms are clinically similar in appearance to palatal mucoepidermoid carcinoma.

TREATMENT

Low-grade tumors can be treated successfully by wide local excision, making sure margins are free of tumor microscopically. High-grade lesions require more radical surgery. Maxillectomy is recommended for palatal tumors. Chest radiographs should be obtained to rule out lung metastasis.

Additional Reading

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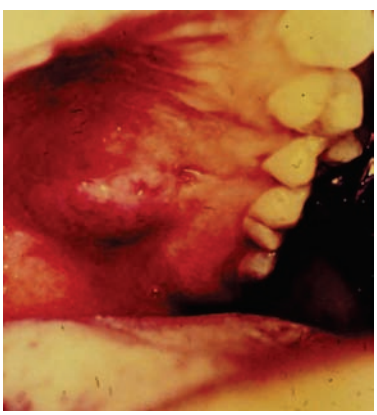

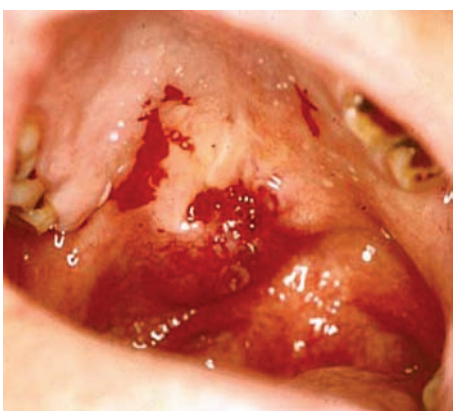

FIGURE 6-85
Sessile palatal masses representing mucoepidermoid carcinoma.

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ADENOCARCINOMA, NOS

Figure 6-86

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Adenocarcinomas, not otherwise specified (NOS), are malignant salivary gland tumors; they do not show microscopic features that allow specific classification into one of the recognized salivary tumor taxonomic categories. They appear as indurated, often ulcerated swellings lateral to the midline. Surface telangiectasia is common. These tumors behave aggressively and may metastasize regionally or distantly. Their behavior is similar to that of adenoid cystic carcinoma.

MICROSCOPIC FEATURES

There is no capsule. Tumor cells show invasion and are arranged in sheets and cords showing ductal formations. Some are monomorphic whereas others evince anaplasia and pleomorphism. Rarely, a benign pleomorphic adenoma undergoes adenocarcinomatous transformation; these lesions are referred to as carcinoma ex mixed tumor.

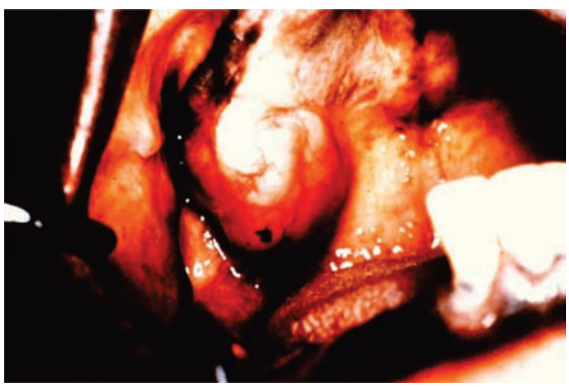

FIGURE 6-86
Adenocarcinoma NOS (not otherwise specified. This heterogeneous group of tumors fail to show microscopic features that would place them in a specific category.

DIFFERENTIAL DIAGNOSIS

Adenocarcinomas clinically resemble other salivary neoplasms, mesenchymal tumors, antral carcinoma, or a palatal abscess.

TREATMENT

Wide surgical excision with resection of underlying bone is recommended. Radiographs of the chest should be obtained to rule out metastasis to lungs.

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ATYPICAL LYMPHOPROLIFERATIVE DISEASE

Figure 6-87

Age: Elderly adults
Sex: No predilection

CLINICAL FEATURES

Lymphoid infiltration of salivary glands is generally a feature of autoimmune sialadenitis such as Sjögren's syndrome or Mikulicz's disease, when the major salivary glands are involved. When the palatal salivary glands manifest diffuse lymphoid

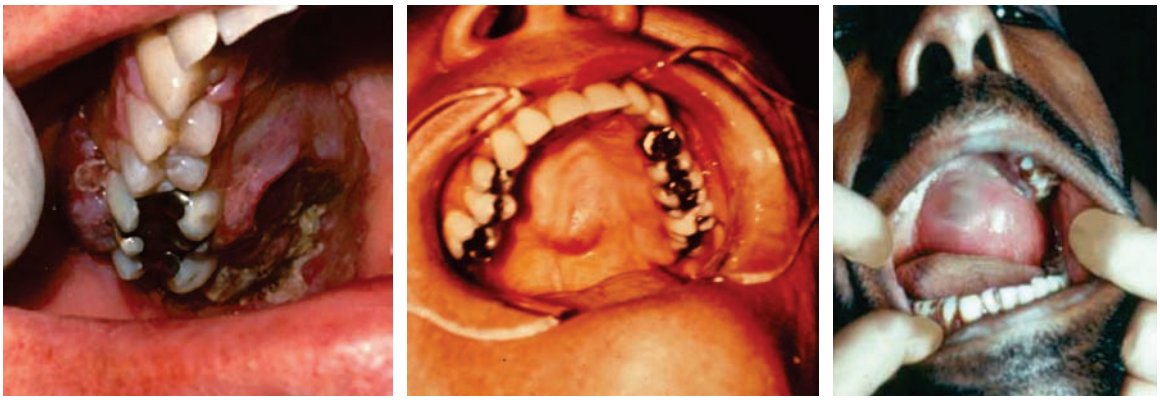

FIGURE 6-87
Diffuse soft swelling of hard palate representing lymphoproliferative disease. Most are low-grade non-Hodgkin's lymphomas.

infiltration, however, the disease process in most instances represents non-Hodgkin's lymphoma. Atypical lymphoproliferative disease of the palate is a unique entity because the microscopic features often suggest a benign lesion. The disease is characterized by diffuse soft tissue enlargement located unilaterally in the hard palate. Occasionally, the lesion extends into the soft palate area and may cross the midline with bilateral swelling. The lesion is soft or spongy on palpation, and the mucosa either maintains normal coloration or manifests a bluish hue without evidence of ulceration or telangiectasia. Accompanying cervical lymphadenopathy is generally not noted at the time of diagnosis. Once the diagnosis is secured, work-up for malignant lymphoma is mandatory. Many patients show evidence of lymphoma in other locations at the time that the palatal mass is detected; others may be free from disease in other sites yet develop generalized lymphoma at a later date. In still other patients, the lesion remains static and progression to disseminated disease does not ensue, suggesting the palatal mass may represent pseudolymphoma. Insufficient long-term follow-up information exists in this latter group of patients to determine whether or not malignant lymphoma will eventually develop, given sufficient time. Non-Hodgkin's lymphomas among AIDS patients are rare in the oral cavity, yet when they arise, the palate and gingiva are the favored sites.

MICROSCOPIC FEATURES

The palatal salivary glands are infiltrated by lymphocytes that may be monomorphic and well differentiated or mildly pleomorphic and poorly differentiated. Interspersed thread-like basophilic strands with a tendency for compaction are common and probably represent degenerating lymphocytes. Reed-Sternberg cells are not encountered. The overall pattern of the infiltrate may be diffuse or nodular. The salivary tissue shows acinar replacement; however, ducts are often intact, embedded in a sea of lymphocytes. These residual ducts often show pronounced periductal hyalinization. Epimyoepithelial islands encountered in benign lymphoepithelial lesions are rarely encountered in lymphoproliferative disease of the palate. Mucosa-associated lymphatic tissue (MALT) lymphomas show features similar to autoimmune sialadenitis, yet the malignant lymphoid cells are monoclonal plasmacytoid and monocytoid in appear-

ance. Classic extranodal non-Hodgkin's lymphomas are also encountered in the palate. Cell surface proteins termed CD antigens are present in specific types of lymphomas and can be identified with IHC stains. The chief ones are CD3 for T cells, CD20 for B cells and CD 56 for natural killer cells. AIDS-related lymphomas are clearly malignant histologically, being represented by large lymphoblasts. Plasmablastic lymphoma is AIDS specific in the oral cavity and resembles myeloma histologically.

DIFFERENTIAL DIAGNOSIS

A soft, spongy swelling of the hard palate that is diffuse and sessile should arouse suspicion of atypical lymphoproliferative disease, especially in elderly patients. Malignant salivary neoplasms are generally localized and indurated. Pleomorphic adenoma and palatal abscess have clinical features in common with lymphoproliferative disease; palatal abscess can be eliminated from consideration when an infectious source is lacking.

TREATMENT

Once a diagnosis of atypical lymphoproliferative disease is established, the patient should be referred for complete evaluation to uncover evidence of malignant lymphoma in other reticuloendothelial tissues. Should the results prove negative, the patient should be subjected to periodic follow-up and reexamination semiannually in anticipation of probable dissemination of disease. The palatal lesion has been shown to respond favorably to radiation therapy; 8 to 10 Gy is generally adequate to cause resolution. This treatment alone may not necessarily prevent the occurrence of lesions in other anatomic sites. Other bona fide lymphomas are treated with chemotherapeutic agents specific to a given histologic type combined with radiation therapy.

Additional Reading

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SQUAMOUS CELL CARCINOMA

Figure 6-88

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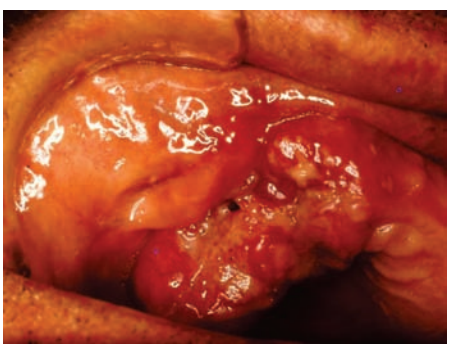

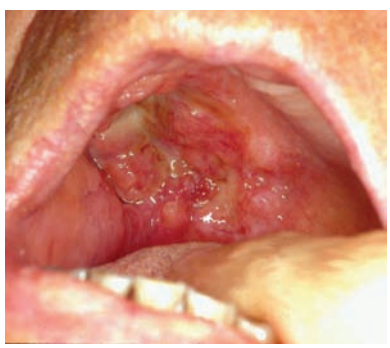

FIGURE 6-88
Palatal squamous cell carcinomas are uncommon.

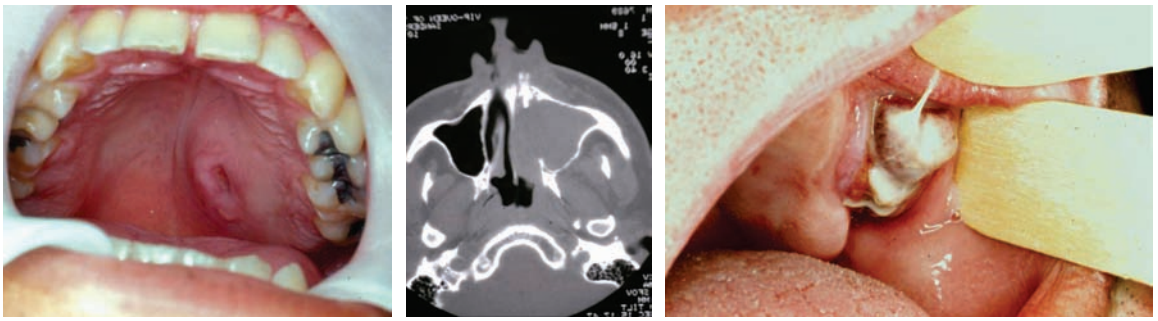

FIGURE 6-89
Carcinoma of the antral mucosa invading the antral floor and producing a palatal swelling with ulceration.

CARCINOMA OF THE ANTRUM

Figure 6-89

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Cancer arising in the antrum generally becomes advanced before signs or symptoms occur. The tumor may erode any of the antral bony walls including the orbital floor, the lateral or medial wall, or often the palate. When the palate becomes eroded, a mass protrudes and is invariably ulcerated. A perforation or oroantral fistula is frequently encountered. Toothache, maxillary division paresthesia, nasal obstruction, and loosening of teeth are common clinical symptoms. Radiographically, antral clouding and evidence of osseous erosion can be demonstrated on Water's views or laminography.

MICROSCOPIC FEATURES

Antral cancer is either typical squamous cell carcinoma or demonstrates glandular differentiation as an adenocarcinoma. Occasionally, one of the salivary tumors arises from antral submucosal glands.

DIFFERENTIAL DIAGNOSIS

Antral carcinoma resembles the other malignant palatal swellings included here, necessitating biopsy with microscopic confirmation. Sinus radiographs are of diagnostic importance, and tomograms or computed tomographic scans help to determine the extent of the disease.

TREATMENT

Radiation therapy to the antrum and neck may be coupled with maxillectomy. When nodes contain tumor, any treatment should be considered palliative, as cures at this stage are almost nonexistent.

Additional Reading

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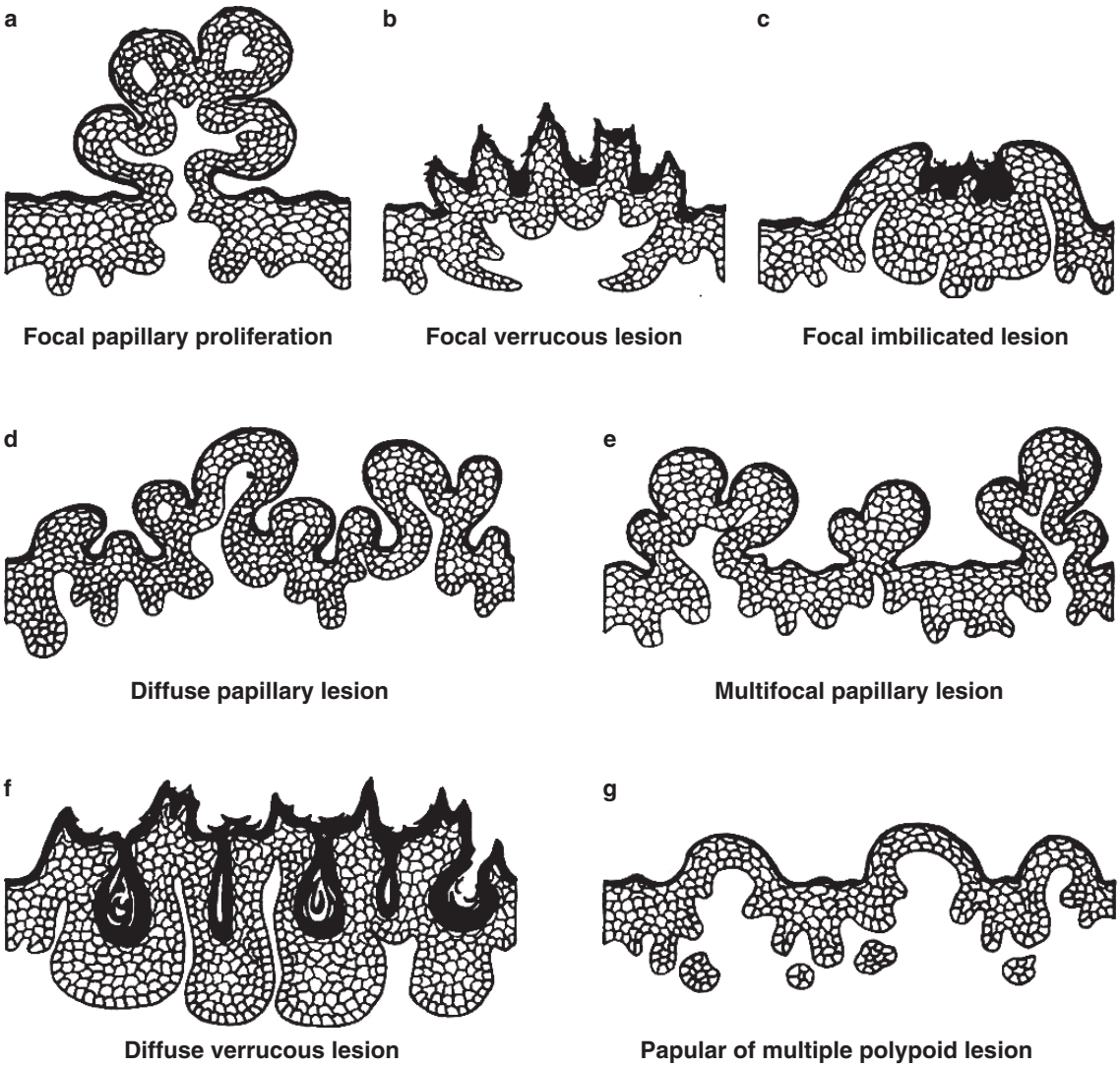

Papillary, Papular, and Multiple Polypoid Lesions

Papillary, Papular, and Multiple Polypoid Lesions

7

Papillary lesions represent swellings with finger-like projections imparting a cauliflower appearance; these microprojections are rounded and blunt like the fungiform papillae of the tongue. Verrucous lesions are similar, yet possess a more irregular surface. Indeed, differentiation between papillary and verrucous lesions is based more on microscopic features rather than on the clinical appearance. Umbilicated nodules are oval dome-shaped lesions with rolled margins and a central pit, which may be plugged with keratin. Papules are small, usually less than 0.5 cm, elevations that tend to occur in multiples or in crops. Polypoid lesions are similar in appearance to papules; however, they usually exceed 1.0 cm and, in the mouth, tend to be multifocal.

Most of the lesions discussed in this chapter represent proliferations of the surface epithelium. Alternatively, some are the result of pathologic changes occurring in the lamina propria with secondary elevation of the epithelium. Although most papillary and focal umbilicated lesions are primary diseases of oral mucosa, some, particularly diffuse papular and polypoid lesions, represent oral markers of a systemic disorder. Biopsy is usually indicated to secure a definitive diagnosis; because some of these lesions herald the presence of an internal illness, the pathologist should be provided with data from the medical history.

Papilloma and giant cell fibroma are the most common focal papillary lesions. All lesions listed as focal umbilicated papules, extremely rare in the oral cavity, are more frequently encountered on skin.

Most of the diseases included as diffuse and multifocal papillary lesions are rare with condyloma acuminatum or venereal wart being the exception. Such lesions are noted frequently in homosexual males.

Papillary hyperplasia, also termed denture papillomatosis, is the most common entity observed as a diffuse papular lesion; stomatitis nicotina is also fairly common.

Most of the other diseases in this group are rare and are associated with either cutaneous or internal organ involvement.

Focal Papillary Lesions

PAPILLOMA

Figure 7-1

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Oral squamous papillomas are either pedunculated or sessile, show a cauliflower surface with finger-like projections, and may be white and keratotic or normal in color. These small epithelial neoplasms are most often encountered on the palate, uvula, tongue, and lip; they tend to reach a certain size, after which the growth essentially becomes arrested. Papillomavirus types 6 and 11 are identifiable in some, yet not all, common squamous papillomas. A variant form of papilloma, *juvenile spongiotic hyperplasia*, is found in children on the gingival and presents with a brightly erythematous papillary appearance.

MICROSCOPIC FEATURES

The epithelium shows a thickened parakeratin layer and a papillary corrugated pattern. The epithelial projections are supported by fibrovascular cores, and inflammatory cells may be discernible.

DIFFERENTIAL DIAGNOSIS

A focal papilloma, by virtue of its papillary cauliflower surface, is readily recognized. Larger lesions must be differentiated from verrucous carcinoma. On the lips, papilloma may be indistinguishable from verruca vulgaris. Multiple confluent papillomas must be differentiated from condyloma acuminatum.

TREATMENT

Simple excision is recommended. Recurrence is extremely rare.

Additional Reading

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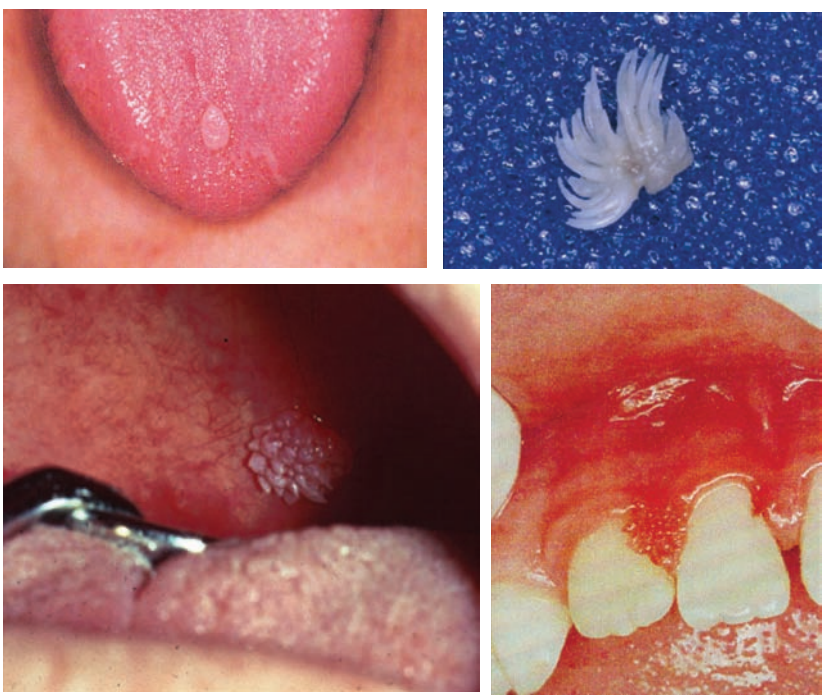

FIGURE 7-1
Squamous papillomas showing a papillary cauliflower-like surface. Juvenile spongiotic hyperplasia is papillomatous (lower right).

cell papillomas. *Oral Surg Oral Med Oral Pathol.* 1980;49:419.
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VERRUCA VULGARIS

Figure 7-2

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Verruca vulgaris, the common wart, is a virus-induced neoplasm of the skin caused by human papillomavirus. It may be seen on the vermilion border; lesions showing microscopic features indistinguishable from those of skin verrucae have been identified in the mouth. The lesion is white, with a keratotic surface and a well-delineated border. A stalk is not discernible. The papillary excrescences are composed of finger-like projections with a sharply angulated surface. Human papillomavirus types 2 and 4 are consistently identifiable in labial verruca; yet viral genomes of these types are rarely seen in intraoral examples.

MICROSCOPIC FEATURES

The epithelium possesses surface projections superficial to the normal tissue surface and showing no invagination. The projections are acute, pointed angles rather than bulbous or rounded, as with papillomas. Thickened keratin is a feature. Viral inclusion bodies are usually discernible in the upper spinous layer.

DIFFERENTIAL DIAGNOSIS

Verruca vulgaris is distinctive on vermilion border or skin, yet intraorally, it may be clinically identical to papilloma.

TREATMENT

Simple local excision is recommended.

Additional Reading

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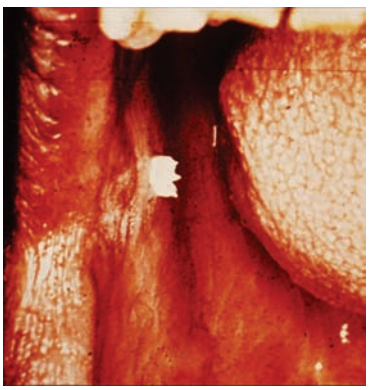

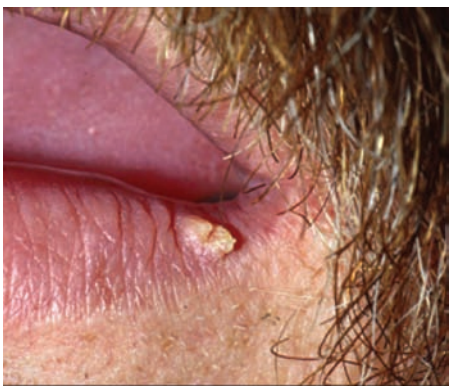

FIGURE 7-2
Verruca vulgaris, rarely occurring on oral mucosa yet not particularly uncommon on the lip. The lesion is raised with a verrucous surface, which is white due to hyperkeratosis.

Green TL, Eversole LR, Leider AS. Oral and labial verruca vulgaris. *Oral Surg Oral Med Oral Pathol.* 1986;62:410.
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CONDYLOMA ACUMINATUM

Figure 7-3

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Condyloma acuminatum is a verrucous papillary lesion caused by human papillomavirus types 6 and 11. The lesions are generally confined to the anogenital intertriginous regions. They are autoinoculable and may also be transmitted as a venereal disease, accounting for the term *venereal warts.* Oral condylomata are similar in appearance to anogenital condylomata. The resemblance to the common oral papilloma is striking; however, condyloma tends to appear more racemose and also shows a tendency for multiplicity with clustering. A history of sexual contact as a source of transmission can usually be obtained, and lesions are most often encountered among prison inmates and homosexual males. More than 85% of oral condylomata harbor human papillomavirus types 6, 11, or both. HIV-seropositive homosexual males are commonly affected and their lesions may harbor genotypes not ordinarily associated with venereal warts (e.g., type 7).

MICROSCOPIC FEATURES

Surface-stratified squamous epithelium displays a papillary pattern with rounded finger-like projections. A prominent parakeratin layer is present, and acanthosis is striking. Numerous mitotic figures can be encountered in the basal and parabasilar strata. Viral inclusion bodies are usually discernible in the upper spinous layer. The subjacent fibrous connective tissue is traversed by dilated vascular channels. HPV DNA can be demonstrated by *in situ* hybridization.

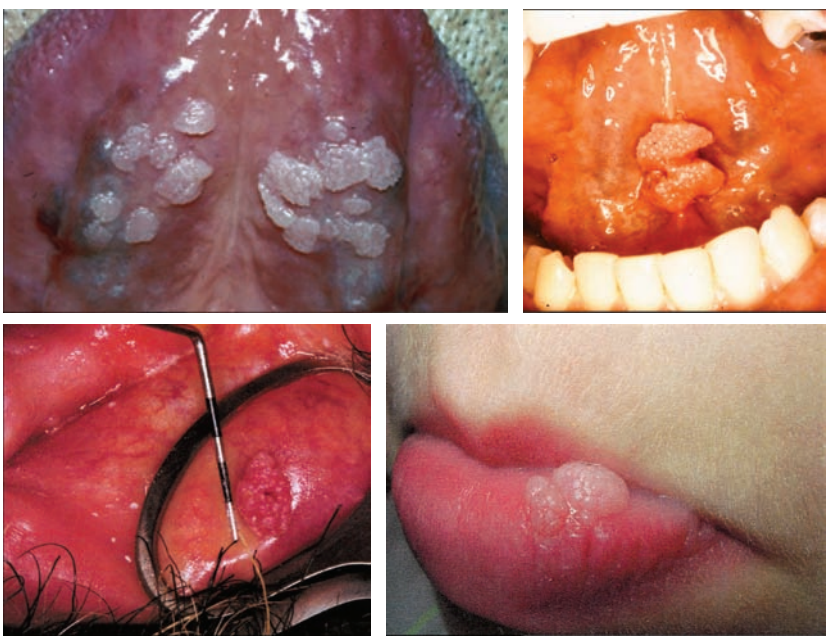

FIGURE 7-3
Condyloma acuminatum. Large and multifocal cauliflower appearance.

DIFFERENTIAL DIAGNOSIS

Condyloma acuminatum is most often confused with the common squamous papilloma. Differentiation can usually be made clinically by a history of sexual transmission. Multiplicity with clustering of lesions is also a feature in favor of a diagnosis of condyloma. In florid papillomatoses, the entire oral cavity is involved; in the Goltz syndrome, the dermal manifestations are characteristic.

TREATMENT

Biopsy is necessary to obtain a definitive diagnosis. Once the diagnosis is secured, excision or cryotherapy with cotton applicators soaked in liquid nitrogen effectively removes the lesions. Recurrence is common, and the lesions are contagious.

Additional Reading

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VERRUCIFORM XANTHOMA

Figure 7-4

Age: Adults
Sex: Female predilection

CLINICAL FEATURES

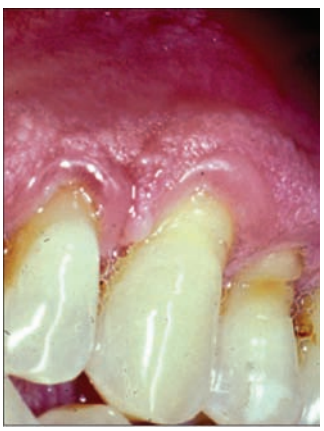
Verruciform xanthoma is most often encountered on the alveolar ridge and buccal mucosa yet has also been reported in extraoral mucosal sites. It is keratotic yet may show a normal-colored pebbly surface. The lesion is well circumscribed, may be pedunculated, but more often is sessile and is less than 1.5 cm in diameter. There is no known relationship between the occurrence of this lesion and irritation, tobacco habits, or hyperlipidemia.

MICROSCOPIC FEATURES

The surface epithelium is hypercornified and corrugated with small surface projections. The submucosal papillae extending between elongated rete ridges are diffusely infiltrated with foam cell histiocytes.

DIFFERENTIAL DIAGNOSIS

Clinically, verruciform xanthoma cannot be distinguished from verruciform hyperkera-



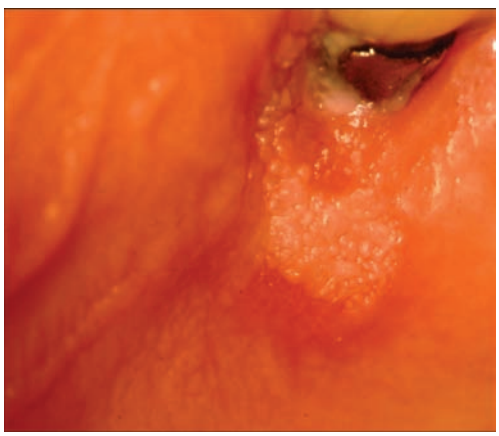


FIGURE 7-4
Verruciform xanthoma. Flat, sessile papillary lesions.

tosis. The lesion must also be differentiated from verrucous carcinoma; however, age differences are helpful in this case. A sessile papilloma may be grossly identical.

TREATMENT

Verruciform xanthoma can be locally excised. There is no known relationship between this type of xanthoma and the hyperlipoproteinemias.

Additional Reading

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SIALADENOMA PAPILLIFERUM

Figure 7-5

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

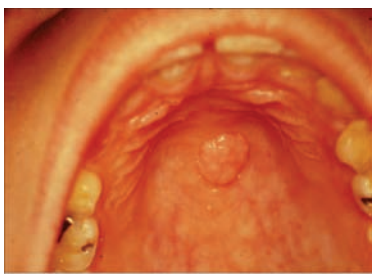
Sialadenoma papilliferum is a benign salivary tumor that presumably arises from the excretory duct system close to the surface mucosa when origin is from oral minor glands. Clinically, the lesion represents a well-localized sessile or pedunculated papillary growth, usually located on the hard palate. This tumor has also been observed to arise from the parotid gland and buccal mucosa minor glands. Because the proliferation extends down into the gland, the underlying base of the lesion is usually firm or indurated.

MICROSCOPIC FEATURES

The papillary surface is usually represented by stratified squamous epithelium. These papillary folds extend into the deeper tissues undermining the surface. In this location, cystic channels are witnessed and the papillary projections protruding into the lumina are lined by ductal pseudostratified columnar epithelium. The individual cells are oncocytic with foci of mucous metaplasia. The base of the tumor lies directly over normal-appearing acinar tissue. There are sporadic reports describing dysplastic changes in the ductal components of the tumor.

DIFFERENTIAL DIAGNOSIS

Sialadenoma papilliferum appears clinically similar to most of the other focal papillary lesions included in this discussion. Localization to the palate along with palpation of a firm submucosal base are findings that would support the clinical diagnosis. Nevertheless, biopsy is required to secure the diagnosis.



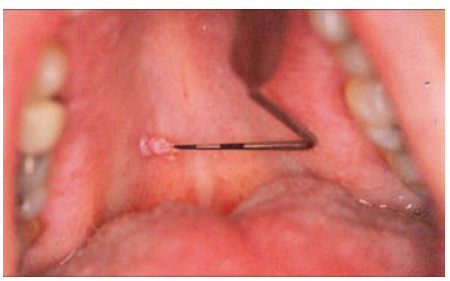


FIGURE 7-5
Sialadenoma papilliferum is an exophytic papilloma arising within a salivary excretory duct.

TREATMENT

Because the lesion extends submucosally into salivary ducts, superficial excision is inadequate. Once the diagnosis is provided histologically, a deeper wedge resection to include underlying glandular tissue is advisable.

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GIANT CELL FIBROMA

Figure 7-6

Age: Teenagers and young adults
Sex: No predilection

CLINICAL FEATURES

Although most oral traumatic fibromas are smooth-surfaced nodules, giant cell fibromas are usually multinodular or papillary. They may be pedunculated or sessile and are most frequently encountered on the gingiva, tongue, and palate.

MICROSCOPIC FEATURES

The surface is multinodular and is covered by a thin layer of stratified squamous epithelium, which is distended by swirls of dense collagen fibers. The intervening fibroblasts are spindle or stellate, and many have copious basophilic cytoplasm with 2 to 5 oval nuclei.

DIFFERENTIAL DIAGNOSIS

Papillary giant cell fibromas may be confused clinically with papillomas, verrucae, or condylomata. Biopsy is required to make the diagnosis.

TREATMENT

Complete surgical excision is the treatment of choice.

Additional Reading

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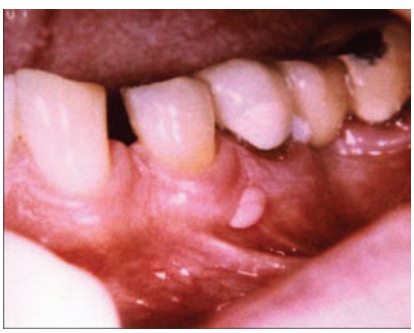

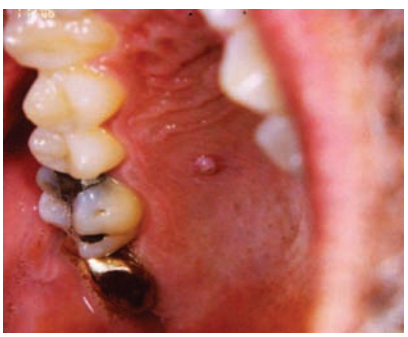

FIGURE 7-6
Giant cell fibromas are small and often have a papillary, corrugated surface.

Weathers DR, Callihan MD. Giant-cell fibroma. *Oral Surg Oral Med Oral Pathol.* 1974;37:374.

SQUAMOUS ACANTHOMA

Figure 7-7

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Squamous acanthomas are small focal white lesions that often show a rough, corrugated surface. They are commonly found on the gingiva and palate appearing as flat warts. Although the etiology is unknown and HPV association has not been found, they are probably a hyperplastic response to local mild trauma. Unlike leukoplakia, squamous acanthoma is innocuous without premalignant potential.

MICROSCOPIC FEATURES

Focal hyperkeratosis is minimal whereas a localized acanthosis is prominent. The surface may be somewhat verrucous. There are no dysplastic changes.

DIFFERENTIAL DIAGNOSIS

Verruca vulgaris flat wart appears clinically identical.

TREATMENT

Local excision is the treatment of choice.

Additional Reading

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Focal and Umbilicated Papules

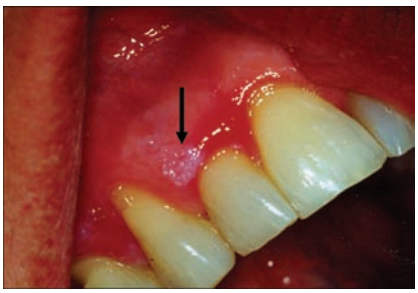
KERATOACANTHOMA

Figure 7-8

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

The facial skin and lower lip, sun-exposed areas, are the common sites for keratoacanthoma, which rarely evolves from mucous membranes. Keratoacanthoma is a benign focal proliferation of surface epithelium that is classically dome shaped with a crateriform appearance. The lesion is round with rolled margins and possesses a central pit or core filled with a keratin plug that is frequently discolored, yellowish brown. Oral examples usually possess a white core. Occasionally, the keratin plug exhibits a verrucous surface.



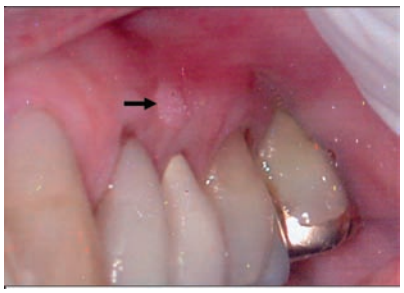


FIGURE 7-7
Squamous acanthoma is a focal, localized benign keratosis.

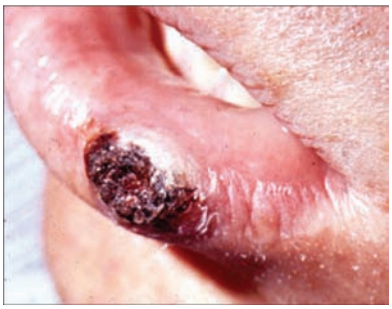
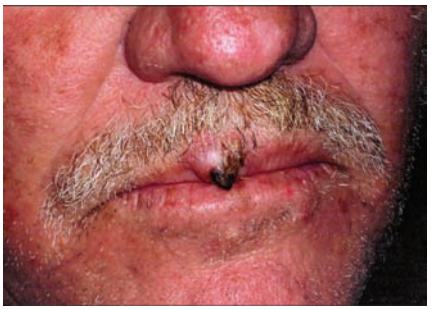



FIGURE 7-8
Oral keratoacanthoma of the lip present as focal keratotic lesions with rolled borders.

MICROSCOPIC FEATURES

Keratoacanthoma is characterized by an abrupt marginal change with acanthosis and hyperparakeratosis or hyperorthokeratosis. The surface is verrucous. On low power, the lesion has a flask-shaped configuration with a superficial collarette and a bulbous expanded base. The individual cells are unremarkable, with one exception: the parabasilar cells may be hyperchromatic. Rarely, cytologic atypia may be a prominent feature, so-called squamous cell carcinoma with keratoacanthoma features.

DIFFERENTIAL DIAGNOSIS

Squamous cancer may show similar clinical features; however, cancerous lesions usually fail to exhibit a smooth round regularity. Warty dyskeratoma and molluscum have gross features in common with keratoacanthoma; yet, they are usually small (less than 0.5 cm) and keratoacanthoma can attain dimensions of 1.0 to 2.0 cm.

TREATMENT

The lesion usually regresses spontaneously within 1 or 2 years. Despite this fact, it cannot be definitively diagnosed clinically, is unsightly, and if allowed to regress, often leaves a depressed scar. Surgical excision is the treatment of choice.

Additional Reading

Eversole LR, Leider AS, Alexander G. Intraoral and labial keratoacanthoma. *Oral Surg Oral Med Oral Pathol.* 1982;54:663.

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WARTY DYSKERATOMA

Figure 7-9

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Warty dyskeratoma, a localized lesion of skin, is occasionally encountered in the mouth. The oral lesion is usually found on the palate or alveolar ridge and appears as a small papule with a depressed central pit or as focal verrucous nodules. A variant, termed focal acantholytic dyskeratosis, manifests a similar appearance with two or three discrete lesions arising adjacent to one another.

MICROSCOPIC FEATURES

Both warty dyskeratoma and focal acantholytic dyskeratosis display microscopic features that are nearly identical to those observed in keratosis follicularis. These two focal lesions have a keratinized surface with an invaginated central depres-

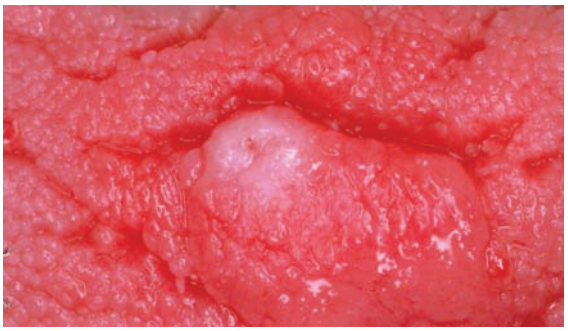

FIGURE 7-9
Warty dyskeratoma appearing as crateriform lesion on the tongue.

sion. The spinous layer is thickened and contains individually keratinized cells. The pathognomonic change is observed inferiorly where villous rete ridges pervade and exhibit acantholysis.

DIFFERENTIAL DIAGNOSIS

Other umbilicated or crateriform lesions listed here resemble, or are clinically identical to, warty dyskeratoma. When a pitted papule fails to show tumefaction, a traumatic lesion may be suspected clinically; therefore, the diagnosis requires a biopsy.

TREATMENT

Surgical excision of these small lesions is usually accomplished during biopsy.

Additional Reading

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Szymanski FJ. Warty dyskeratoma, a benign cutaneous tumor resembling Darier's disease microscopically. *Arch Dermatol.* 1957;75:567.

Tomich CE, Burkes EJ. Warty dyskeratoma (isolated dyskeratosis follicularis) of the oral mucosa. *Oral Surg Oral Med Oral Pathol.* 1971;31:798.

MOLLUSCUM CONTAGIOSUM

Figure 7-10

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Molluscum contagiosum represents a unique type of viral wart, resulting from infection by a member of the poxvirus family. The disease is usually encountered on the skin of children or in the anogenital region in adults. It appears as a dome-shaped nodule that is usually, yet not invariably, characterized by a central pit or depressed core. The lesion is rare on the lips or in the mouth and when it does occur it is usually in an immunocompromised host.

MICROSCOPIC FEATURES

The histologic findings are unique and diagnostic. The epithelium exhibits an abrupt zone of acanthosis with a central parakeratinized invagination. Large prominent eosinophilic globules, referred to as molluscum bodies, are located as conglomerates in the upper and middle spinous layers. Coalescing bulbous rete ridges are present, and the underlying connective tissue is often chronically inflamed.

DIFFERENTIAL DIAGNOSIS

Molluscum may clinically resemble a fistula or parulis, keratoacanthoma, or warty dyskeratoma when it occurs on lips or mucosa. Biopsy is required to make the diagnosis.

TREATMENT

Excisional biopsy is the treatment of choice.

Additional Reading

Barsh LI. Molluscum contagiosum of the oral mucosa. *Oral Surg Oral Med Oral Pathol.* 1966;22:42.

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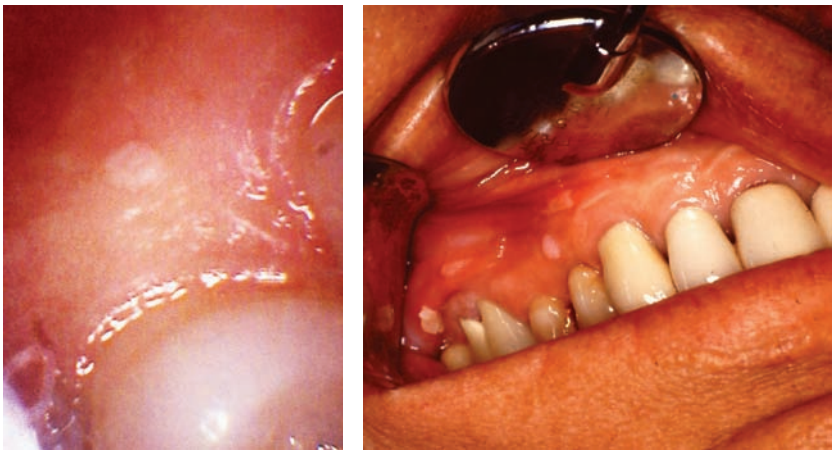

FIGURE 7-10
Multiple lesions of molluscum contagiosum in HIV-infected patients.

Lynch PJ, Minkin W. Molluscum contagiosum of the adult. *Arch Dermatol.* 1968;98:141.
Nelson JF, Tsaknis PJ. Molluscum contagiosum of the lower lip: report of a case. *J Oral Pathol Med.* 1980;35:62.
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Diffuse and Multifocal Papillary Lesions

FOCAL DERMAL HYPOPLASIA (GOLTZ SYNDROME)

Figure 7-11

Age: Children
Sex: No predilection

CLINICAL FEATURES

Many defects accompany the skin lesions of the Goltz syndrome, including multiple papillomas of the lips and oral mucosa. The oral lesions consist of exophytic papillary outgrowths that are identical to the ordinary oral squamous papilloma, yet are prone to be multiple with tendency for confluency. The skin lesions located on the extremities are rubbery nodules with wrinkled pigmented surfaces and represent herniation of the subcutaneous tissues through a genetically deficient dermal layer. Other features of the syndrome include mental retardation, strabismus, syndactyly, and colobomas of the iris.

MICROSCOPIC FEATURES

The oral papillomas of the Goltz syndrome show histomorphologic features indistinguishable from the ordinary squamous papilloma.

DIFFERENTIAL DIAGNOSIS

The various components of the syndrome allow differentiation from other diseases manifesting oral papillary or polypoid lesions.

TREATMENT

The papillomas should be excised, as they can be traumatized by mastication and thus hemorrhage.

Additional Reading

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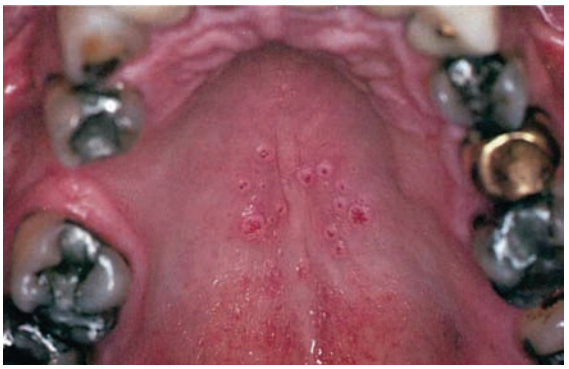

FIGURE 7-11
Orolabial papillomas in focal dermal hypoplasia syndrome. (Courtesy of Dr. Juan Seoane.)

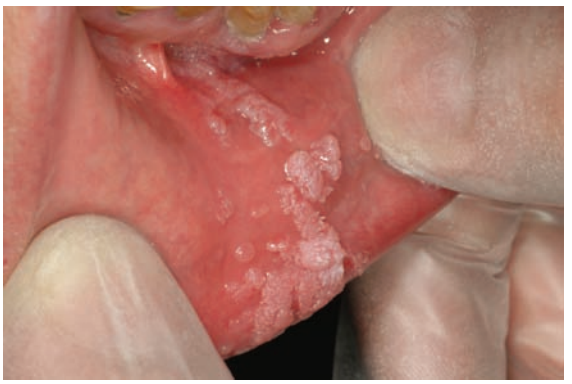

FIGURE 7-12
Unilateral extensive papillary proliferations involving oral mucosa in nevus unius lateris. (Courtesy of Dr. Giuseppe Ficarra.)

Seoane J, Gibson RL, Almagro M, Pintos E. Oral manifestations associated with focal dermal hypoplasia. *Dermatology.* 2009;219:368-370.

NEVUS UNIUS LATERIS

Figure 7-12

Age: Children
Sex: No predilection

CLINICAL FEATURES

A developmental verrucous lesion of skin, nevus unius lateris (also termed the epidermal nevus syndrome) usually occurs on the arm as a keratotic washboard-rough lesion that conforms to a narrow linear configuration. When the face is involved, extension into the oral cavity may occur. The lesion continues its linear orientation, yet its appearance assumes a pebbly papillary pattern identical to papilloma.

MICROSCOPIC FEATURES

The skin lesion demonstrates acutely angulated verrucous epithelial hyperkeratotic projections not unlike those of verruca vulgaris. The oral lesion is microscopically indistinguishable from simple papilloma.

DIFFERENTIAL DIAGNOSIS

Nevus unius lateris must be differentiated from verrucous carcinoma, pyostomatitis vegetans, and florid papillomatosis. The linear configuration, extension onto facial skin, and development during childhood allow for differentiation from these entities.

TREATMENT

After microscopic confirmation of the diagnosis, the lesion may be removed surgically or with electrocautery in stages. The facial lesions should be managed by a plastic surgeon.

Additional Reading

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Kelly JE, Hibbard ED, Giansanti JS. Epidermal nevus syndrome; report of a case with unusual oral

manifestations. *Oral Surg Oral Med Oral Pathol.* 1972;34:774.
Muller JT, Pickett AB, Frederick FD. Facial hemihypertrophy associated with nevus unius lateris syndrome. *Oral Surg Oral Med Oral Pathol.* 1980;50:226.

ACANTHOSIS NIGRICANS

Figure 7-13

Age: Adults, maligna form older adults
Sex: No predilection

CLINICAL FEATURES

Acanthosis nigricans is a localized large papillary lesion with variable amounts of pigmentation. It exists in two forms: benign and malignant. These two forms are clinically indistinguishable being broad-based velvety papillary lesions that occur on the skin, lips, or mucous membranes and are usually solitary. They do not progress to carcinoma. The benign form may be associated with various endocrinopathies including hypo- or hyperthyroidism, acromegaly, insulin-dependent diabetes, and Cushing's syndrome. The malignant form represents a paraneoplastic syndrome whereby affected patients will suffer from an internal malignancy, most frequently of the stomach (adenocarcinomas).

MICROSCOPIC FEATURES

A diffuse papillary pattern is observed with parakeratosis and acanthosis. There are melanin pigment granules in the basal cell layer with incontinence into the submucosa. Dysplastic changes are not encountered.

DIFFERENTIAL DIAGNOSIS

On skin the pigmented velvety papillary appearance is clinically distinct. In the mucous membrane, these lesions may resemble other papillary lesions discussed here, however, any papillary lesion with brown pigmentation should be suspect.

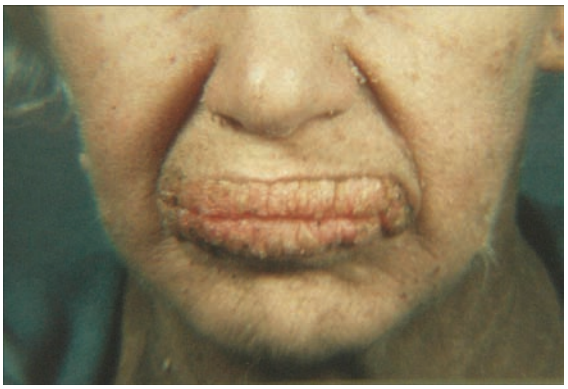

FIGURE 7-13
Acanthosis nigricans of the lips. (Courtesy of Dr. Heddie Sedano.)

TREATMENT

The lesion may be excised or removed by laser if cosmetically problematic. Systemic work-up for diabetes, other endocrinopathies, and internal malignancy should be undertaken.

Additional Reading

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ATYPICAL VERRUCOUS LEUKOPLAKIA

Figure 7-14

Age: Middle-aged and elderly adults
Sex: Female predilection

CLINICAL FEATURES

Verrucous leukoplakia, also referred to as verrucous hyperplasia or verruciform leukoplakia, is a precancerous lesion that represents the benign end of the Prolferative Verrucous Leukoplakia spectrum and may

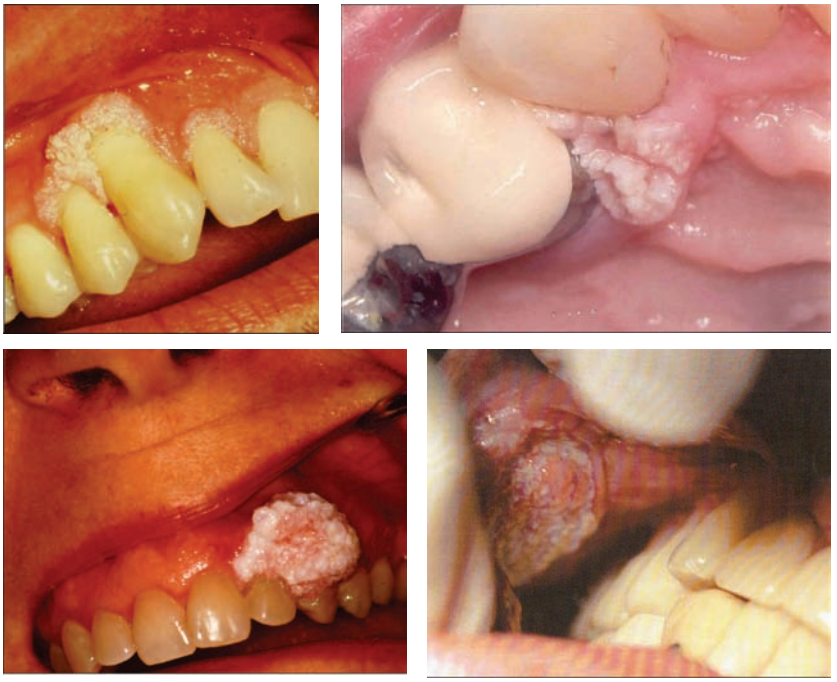

FIGURE 7-14
Atypical verrucous leukoplakia, a histologic variant of proliferative verrucous leukoplakia.

progress to carcinoma. Clinically, the lesion is a localized yet often diffuse verrucous or papillary lesion found most often on the gingiva, alveolar ridge, or mucobuccal fold. It may be white, pink, or speckled. Planar leukoplakia is frequently observed in association with the verrucous lesion, either in continuity or in separate locations. Some patients give a history of smokeless tobacco usage, although others deny any tobacco habits whatsoever. Some lesions harbor human papillomavirus DNA; however, most are devoid of any known genotypes.

MICROSCOPIC FEATURES

Some examples exhibit sharp verrucous projections (acrokeratotic) or blunt rounded projections (polypoid and cryptic). The surface is frequently hyperortho- or hyperparakeratotic, and acanthosis is usually observed. There is a high incidence of dysplastic cytologic change, and many of these lesions lie adjacent to zones of verrucous carcinoma or invasive squamous cell carcinoma.

DIFFERENTIAL DIAGNOSIS

The clinical appearance of verrucous leukoplakia is similar, if not identical, to verrucous carcinoma, particularly when a white keratotic surface is present. Furthermore, occurrence in the elderly differentiates this lesion from other diffuse papillary lesions that occur in children.

TREATMENT

Once the diagnosis is made, biopsy of other areas of a large lesion should be performed, with examination for the presence of carcinoma. Wide local excision is recommended with periodic follow-up. If coexistent carcinoma is detected, the treatment must be more aggressive. This disease is extremely difficult to eradicate and recurrence is the rule rather than the exception.

Additional Reading

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Yeh CJ. Treatment of verrucous hyperplasia and verrucous carcinoma by shave excision and simple cryosurgery. *Int J Oral Maxillofac Surg.* 2003;32: 280-283.

VERRUCOUS CARCINOMA

Figure 7-15

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Verrucous carcinoma is a nonmetastasizing, laterally spreading epithelial tumor, sometimes associated with tobacco chewing or snuff dipping. The lesion is typically fungating with a white verrucoid keratotic surface that has a shaggy appearance. It is most often encountered in the mucobuccal fold and buccal mucosa. In the later stages of disease, extensive lateral spread becomes manifest. Human papillomavirus type 2 DNA has been demonstrated in a minority of cases.

MICROSCOPIC FEATURES

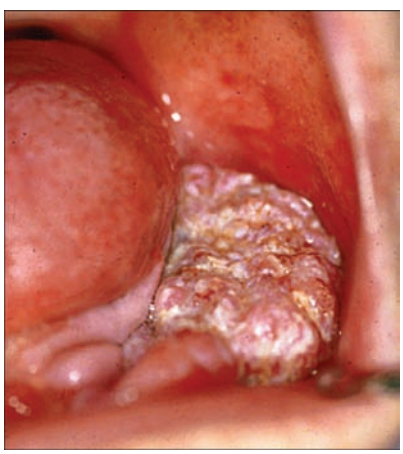
The histomorphologic characteristics are distinctive. Massively enlarged bulbous acanthotic rete ridges invaginate into the connective tissue, yet extensions from the basal cell layer showing invasion do not exist. Apart from basilar and parabasilar hyperchromatism, cytologic atypia is not featured; rather, a normal maturation of epithelium exists. Deep crypts, filled with parakeratin, extend downward from the surface into the center of the bulbous rete ridge invaginations.

DIFFERENTIAL DIAGNOSIS

Verrucous carcinoma may clinically simulate papillary hyperplasia, pyostomatitis vegetans, and, importantly, squamous cell carcinoma that may be clinically verrucous in appearance. Only biopsy can differentiate between true verrucous carcinoma and a clinically verrucoid-appearing squamous cell carcinoma.

TREATMENT

Wide surgical excision is recommended; recurrence is common. In the past, radiation therapy was contraindicated in verrucous carcinoma because anaplastic transformation occurred after such treatment. The higher energy radiation sources used today minimize this complication; inoperable lesions have shown resolution with radiation therapy.



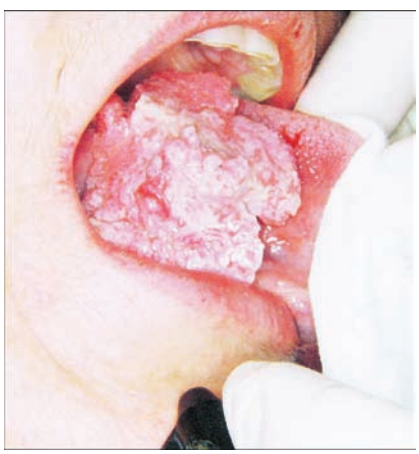


FIGURE 7-15
Verrucous carcinoma, a nonmetastasizing neoplasm of oral mucosa that shows a shaggy, verrucous keratotic surface, an end stage of proliferative verrucous leukoplakia.

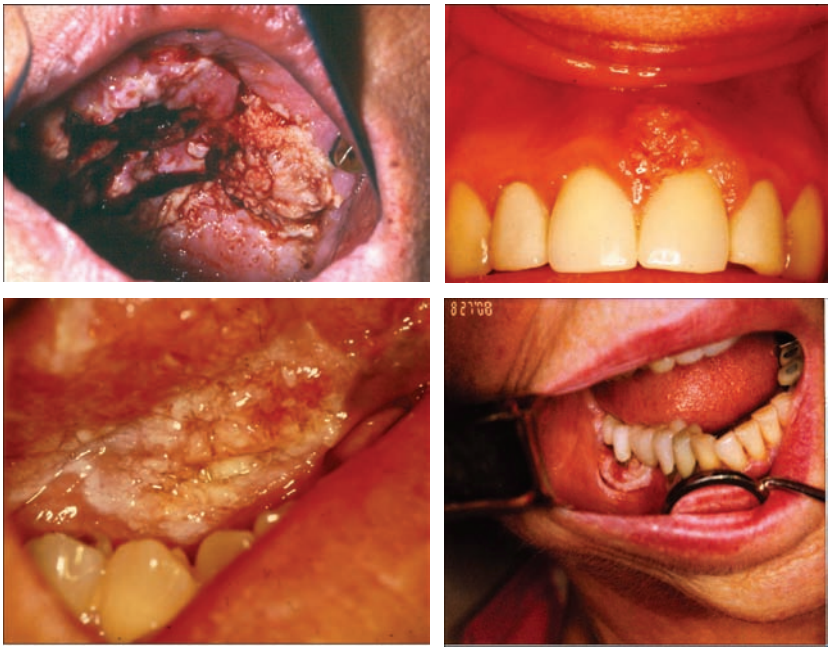


FIGURE 7-16
Papillary exophytic squamous cell carcinoma, may also be an end-stage lesion of proliferative verrucous leukoplakia.

Additional Reading

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Perez CA, Kraus FT, Evans JC, Powers WE. Anaplastic transformation in verrucous carcinoma of the oral cavity after radiation therapy. *Radiology.* 1966;86:108.

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PAPILLARY SQUAMOUS CELL CARCINOMA

Figure 7-16

Age: Elderly
Sex: Slight female predilection

CLINICAL FEATURES

Papillary squamous cell carcinoma is a unique tumor that tends to be exophytic without extensive invasion. The lesions are diffuse and may be red, pink, or speckled with white keratoses. They show polypoid extensions across the surface. The tumor evolves slowly, proliferating superficially, and may reach 3 cm or more before foci of invasion into the submucosal connective tissue occurs. Only late stage lesions of T4 size and long duration may metastasize locally.

MICROSCOPIC FEATURES

Stratified squamous epithelium shows an exophytic papillary growth pattern with elongated wide rete pegs. Cytologically, dysplastic changes are seen, particularly in lower strata keratinocytes. In larger lesions of longer duration, invasive foci of carcinoma may be encountered in the connective tissue.

DIFFERENTIAL DIAGNOSIS

The papillary appearance in this specific form of carcinoma may be quite similar to the other benign entities in this chapter. They mirror verrucous carcinoma and atypical verrucous hyperplasia; however, papillary squamous cancer tends to be less keratotic.

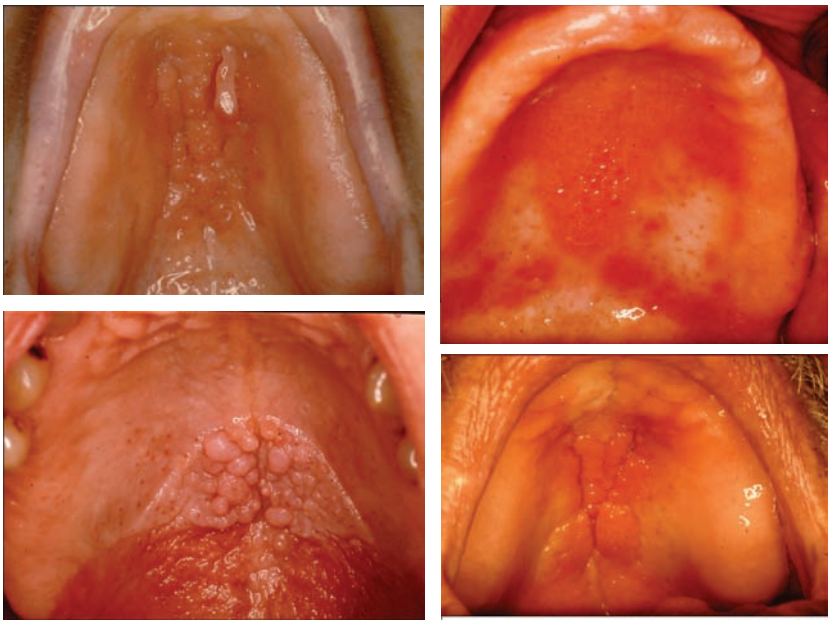

FIGURE 7-17
Papillomatosis in the vault is found under ill-fitting maxillary dentures.

TREATMENT

Tumors in stage T1 and T2 rarely metastasize whereas nodal spread is common among T3 and T4 stage tumors. Wide local excision is the treatment of choice and neck radiation or dissection is recommended when nodes are detected clinically or by magnetic resonance imaging.

Additional Reading

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Diffuse Papular and Polypoid Lesions

PAPILLARY HYPERPLASIA

Figure 7-17

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Confined to the palatal vault, papillary hyperplasia or papillomatosis is most often associated with a maxillary denture. Occasionally, it occurs in dentulous mouths in association with a partial denture. The lesion displays a cobblestone appearance and is either normal in color or erythematous. When the papillary lesions are reddened, secondary infection with *Candida* is common. The cause is unknown but is probably related to trauma and may arise in response to negative pressure placed on the palatal tissues. The lesion is not premalignant.

MICROSCOPIC FEATURES

The epithelium manifests multiple dome-shaped papules with elongated rete ridges

and pseudoepitheliomatous hyperplasia. The submucosa contains a diffuse chronic inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The combination of dental prosthesis and palatal vault papillary outgrowth allows for a clinical diagnosis. If the lesion extends onto the alveolar ridge, it must be differentiated from verrucous carcinoma or a specific granulomatous infection.

TREATMENT

The hyperplastic tissue may resolve after removal of the old denture. If not, surgical removal is recommended before fabrication of a new prosthesis.

Additional Reading

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STOMATITIS NICOTINA

Figure 7-18

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Pipe and cigar smokers occasionally develop multiple white keratotic papules with red depressed centers that represent dilated, inflamed minor salivary ducts on the hard and soft palate. The papules do not coalesce and are separated by intervening normal-appearing mucosa. It is not known whether these multifocal keratotic papules arise as a consequence of heat or tobacco tars. The lesion is rarely seen in cigarette smokers; evidence does not support a premalignant potential.

MICROSCOPIC FEATURES

The surface epithelium is hyperkeratotic and usually acanthotic. The salivary excretory ducts are dilated and evince a periductal mononuclear inflammatory infiltrate.

DIFFERENTIAL DIAGNOSIS

White papules with a red center located on the palate of a pipe or cigar smoker are usually sufficient findings to permit establishment of the diagnosis on a clinical basis. Other papular lesions fail to show this combination of findings.

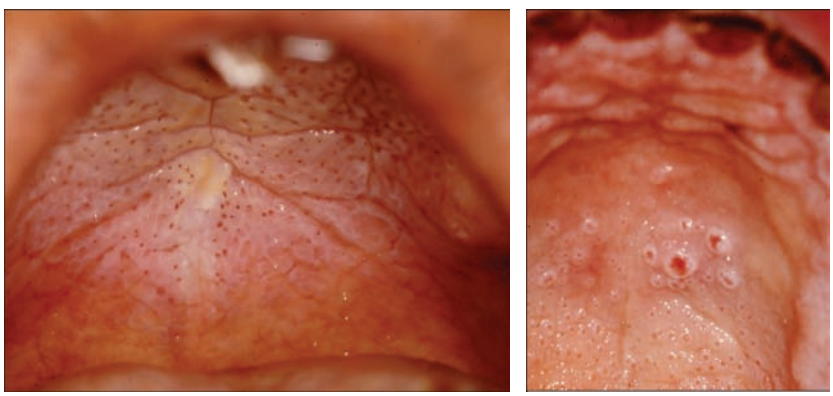

FIGURE 7-18
Stomatitis nicotina, multiple crateriform papules.

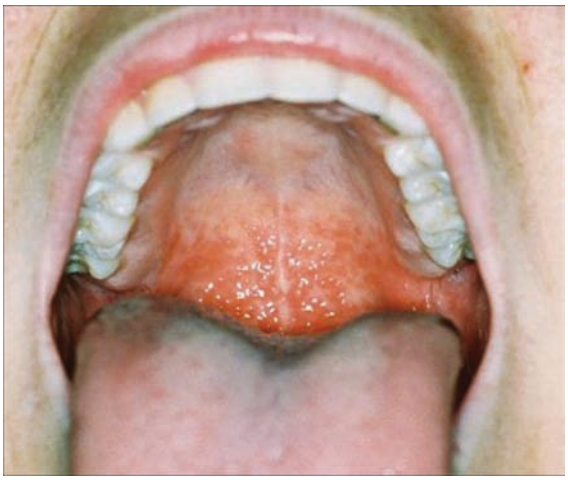

FIGURE 7-19
Multiple red papules of the soft palate and oropharynx characteristic of lymphonodular pharyngitis, a coxsackie virus infection.

TREATMENT

Abating the tobacco habit allows resolution. The oral cavity should be examined thoroughly to detect leukoplakic or erythroplakic foci, which may coexist.

Additional Reading

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ACUTE LYMPHONODULAR PHARYNGITIS

Figure 7-19

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Coxsackie virus infections manifest a variety of clinical presentations. Lymphonodular pharyngitis is unique and is usually diagnosed clinically, based on morphologic characteristics and location of the lesion. Multiple yellowish pink papules are distributed over the soft palate, tonsillar fauces, and oropharynx. The patient fails to show a cutaneous exanthem. Fever, lymphadenopathy, and sore throat are the typical symptoms. Epidemics among school children are common.

MICROSCOPIC FEATURES

Surface epithelium is distended by focal aggregates of lymphocytes, and attempts at germinal center formation can be observed in some of these lymphoid papules.

DIFFERENTIAL DIAGNOSIS

None of the other entities listed as papular or multiple polypoid lesions are restricted to the oropharynx, nor are they associated with constitutional symptoms of infectious disease. A clinical diagnosis can be made. If confirmation is required, a stool culture for coxsackie virus can be ordered.

TREATMENT

The disease is self-limited and resolves in 7 to 10 days. Antipyretic medication may be used along with a palliative mouth rinse or gargle.

Additional Reading

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KERATOSIS FOLLICULARIS

Figure 7-20

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

A primary disease of skin, keratosis follicularis or Darier-White's disease frequently

affects the oral mucous membranes. This autosomal dominantly inherited disorder affects epithelial maturation and keratinization and is associated with mutations in the *ATP2A2* gene that encodes calcium pump proteins. Orange-brown keratotic papules appear on the skin and often keratinize progressively, resulting in diffuse white verrucoid plaques. The oral lesions may be white or may exhibit normal coloration; they diffusely affect the buccal mucosa and palate, thus appearing as multiple confluent papules with a cobblestone pattern.

MICROSCOPIC FEATURES

Hyperkeratosis occurs, and the spinous cell layer contains individually keratinized cells, many of which are enveloped by spinous layer cells (corps ronds). The rete ridges assume a villous pattern with suprabasilar acantholytic cleavage.

DIFFERENTIAL DIAGNOSIS

The cobblestone pattern resembles that seen in Cowden's disease, papillary hyperplasia, and pyostomatitis vegetans. The occurrence of papular and keratotic cutaneous lesions suggests keratosis follicularis clinically, and the microscopic features confirm this impression.

TREATMENT

Retinoids have been employed with moderate success for the cutaneous lesions. No effective treatment exists for the oral lesions.

Additional Reading

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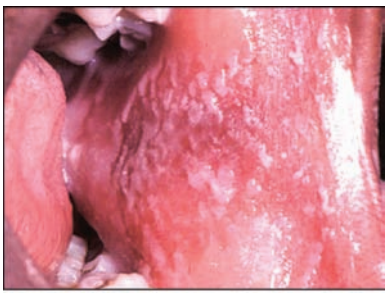
FOCAL EPITHELIAL HYPERPLASIA (HECK'S DISEASE)

Figure 7-21

Age: Children
Sex: No predilection

CLINICAL FEATURES

Focal polypoid nodules that appear primarily on the lips and buccal mucosa during the prepubescent period are characteristic of Heck's disease. These peculiar lesions occur in clusters and in isolated crops, which eventually spontaneously regress. They are pale to normal in color and show a flattened surface. American Indians and other ethnic groups of Athapaskan descent are often afflicted, but this disorder has also been reported in other ethnic groups, including Europeans. Similar-appearing lesions may be encountered among HIV-seropositive homosexual males. Focal epithelial hyperplasia is caused by human papillomavirus types 13 and 32.



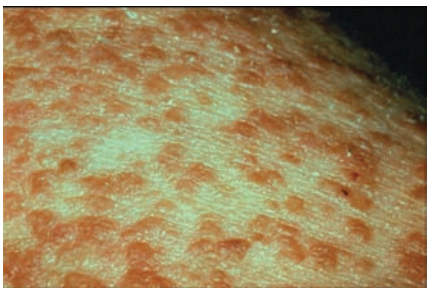


FIGURE 7-20
Keratosis follicularis. Oral papular lesions and cutaneous scaly papules.

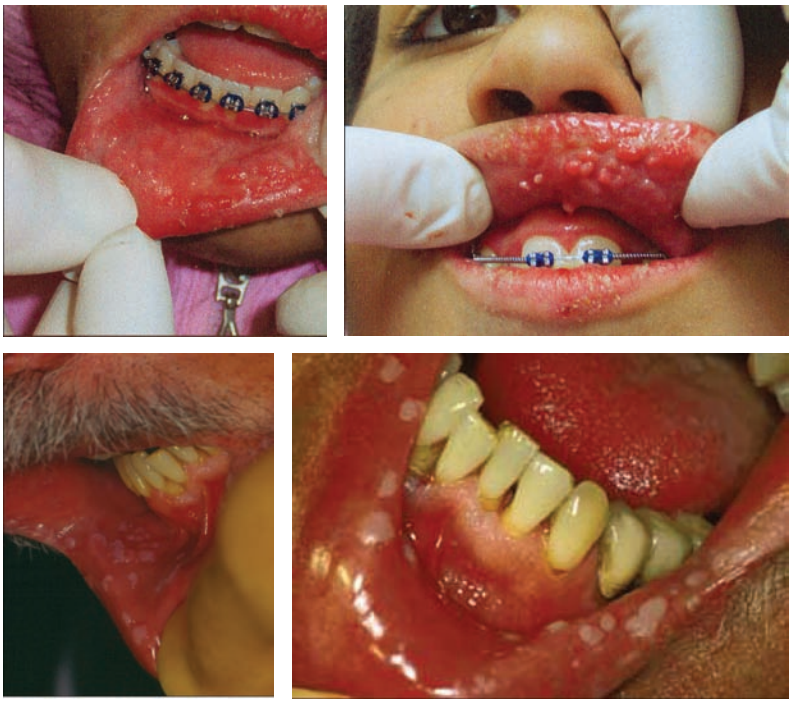


FIGURE 7-21
Multiple sessile papules of the lips and buccal mucosa characteristic of focal epithelial hyperplasia.

MICROSCOPIC FEATURES

The epithelium displays an exophytic nodular surface with thickened parakeratin. The major portion of the outgrowth is accounted for by epithelial hyperplasia with acanthosis and elongated anastomosing rete ridges. Inclusion bodies may be seen in cells occupying the spinous cell layer.

DIFFERENTIAL DIAGNOSIS

The appearance of multifocal polypoid lesions on the lips of Indian children is characteristic. Lack of total confluency aids in differentiating Heck's disease from the other lesions included in this section.

TREATMENT

No treatment is required; spontaneous regression occurs.

Additional Reading

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MULTIPLE HAMARTOMA (COWDEN) SYNDROME

Figure 7-22

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Also known as Cowden's disease, the multiple hamartoma syndrome represents an autosomal dominant hereditary disease with mutations in a candidate tumor suppressor

gene, *PTEN*. It is characterized by widespread hamartomas and neoplasms of skin, mucosa, and internal organs. The oral lesions are found on the attached gingiva. Multiple papular nodules yield a cobblestone pebbly surface. Cutaneous papulonodular lesions are seen around the nares, lip commissures, and palmar surface of the hands. Patients with Cowden's disease also develop goiter or thyroid adenomas and fibrocystic disease of the breast, which may progress to malignancy. Other organs may also be involved.

MICROSCOPIC FEATURES

The oral papules exhibit microscopic features of fibroepithelial polyps. The epithelium is somewhat hyperplastic with acanthosis and elongated, anastomosing rete ridges. Supporting this epithelium is a mature fibrous connective tissue core.

DIFFERENTIAL DIAGNOSIS

The cobblestone lesions of multiple hamartoma syndrome may appear similar to the papular lesions observed in Sipple syndrome, pyostomatitis vegetans, keratosis follicularis, and focal epithelial hyperplasia. Localization to the gingiva, observed papules on the facial skin, and a history of thyroid or breast disease in conjunction with familial involvement lead to the diagnosis.

TREATMENT

No treatment is necessary for the oral lesions. A complete medical work-up for organ-system involvement is recommended.

Additional Reading

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Weary PE, Gorlin RJ, Gentry WC Jr, Comer JE, Greer KE. Multiple hamartoma syndrome (Cowden's disease). *Arch Dermatol.* 1972;106:682.

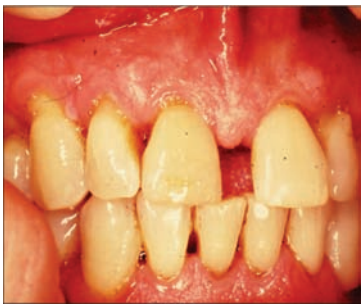
PYOSTOMATITIS VEGETANS

Figure 7-23

Age: Middle-aged adults
Sex: Slight female predilection

CLINICAL FEATURES

Pyostomatitis vegetans is a vegetating disease of oral mucosa characterized by both erosive and multifocal polypoid lesions of the lips and buccal mucosa. Although it may occur in the absence of systemic disease, it is more often associated with either ulcerative colitis or regional enteritis, thereby representing the oral mucosal counterpart to the skin disease *pyodermatitis vegetans of Hallopeau*. The individual polyps vary in size and are usually inflamed. Pain is a prominent feature when erosions are present.



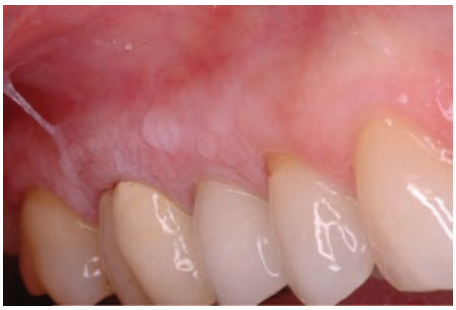


FIGURE 7-22
Gingival papules in Cowden syndrome.

MICROSCOPIC FEATURES

The surface epithelium is acanthotic with polypoid extensions of submucosal connective tissue. A subacute inflammatory cell infiltrate prevails, with foci of eosinophilic abscesses located in the papillae and at the epithelial connective tissue junction.

DIFFERENTIAL DIAGNOSIS

The lesion must be differentiated from verrucous carcinoma, oral florid papillomatosis, mycotic granuloma, and focal epithelial hyperplasia (Heck's disease). Biopsy with identification of eosinophilic abscesses and medical work-up for ulcerative colitis are recommended to aid in arriving at a definitive diagnosis.

TREATMENT

Treatment is empiric. Systemic steroids (25-30 mg prednisone daily) with standard care for ulcerative colitis usually results in diminution of the oral lesions. Ulcerative colitis is managed by a general physician or gastroenterologist.

Additional Reading

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CROHN'S DISEASE

Figure 7-24

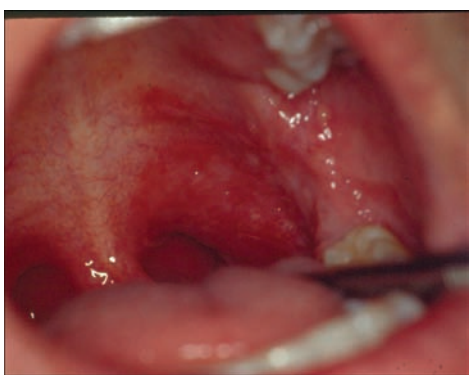
Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Regional enteritis or Crohn's disease is a segmental granulomatous disease of the ileum and ascending colon. Oral lesions are occasionally present and consist of bosselated multiple polyps usually located in the buccal mucosa or mucobuccal fold. They are firm, usually normal in color, and painless. Gingival swellings and erythematous pebbly lesions may also be encountered. Patients complain of gastrointestinal irregularity, mild chronic diarrhea, and abdominal discomfort.

MICROSCOPIC FEATURES

The epithelium is distended by an underlying mass of organized granulation tis-



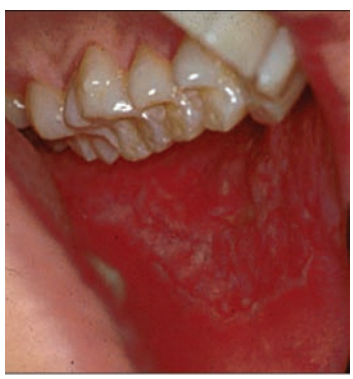


FIGURE 7-23
Multiple papules and erosions in pyostomatitis vegetans associated with ulcerative colitis.

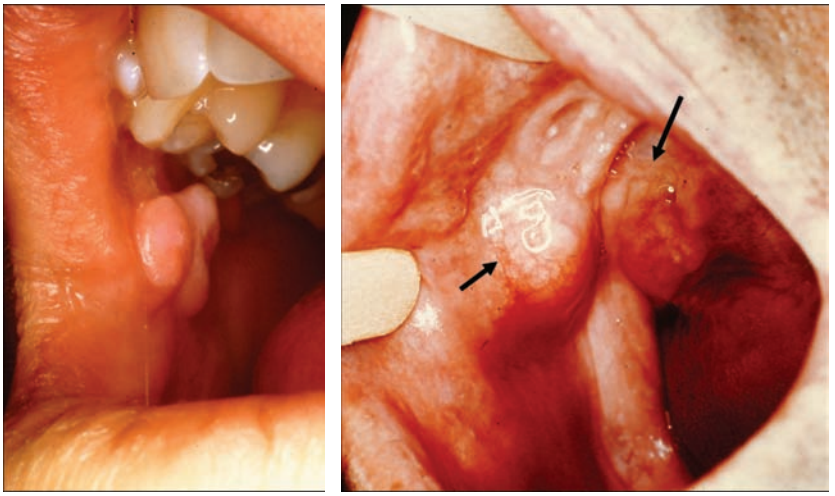


FIGURE 7-24
Multiple polypoid tumefactions of the buccal mucosa and mucobuccal fold are oral manifestations of Crohn's disease.

sue with lymphoid infiltration, epithelioid histiocytes, and giant cells yielding a noncaseating specific granulomatous reaction. Special stains fail to disclose the presence of microorganisms.

DIFFERENTIAL DIAGNOSIS

The polypoid masses in Crohn's disease are broader and, overall, larger than most of the other polypoid or papillary lesions included in this section. They must be differentiated from denture hyperplasia, pyostomatitis vegetans, and mycotic granuloma.

TREATMENT

The oral lesions may be excised. Crohn's disease is managed by a general physician or gastroenterologist.

Additional Reading

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SPECIFIC GRANULOMATOUS INFECTIONS

Figure 7-25

Age: Adults
Sex: Equal distribution

CLINICAL FEATURES

Infectious and noninfectious granulomatous inflammatory lesions of the oral mucous membranes are usually localized and exhibit a granular or papillary surface. The lesions are usually raised and firm and may appear somewhat erythematous. Most of them are infectious, representing hematogenous spread from a primary pulmonary focus. The deep fungal diseases such as histoplasmosis and blastomycosis are more apt to show pebbly granular lesions. The inherited disorder known as chronic granulomatous disease may manifest similar lesions. This disorder is characterized by ineffective phagocytolysis by leukocytes with recurrent and persistent infections accompanied by granulomatous inflammation. Oral lesions of sarcoidosis may also present in similar fashion clinically. Granulomatous

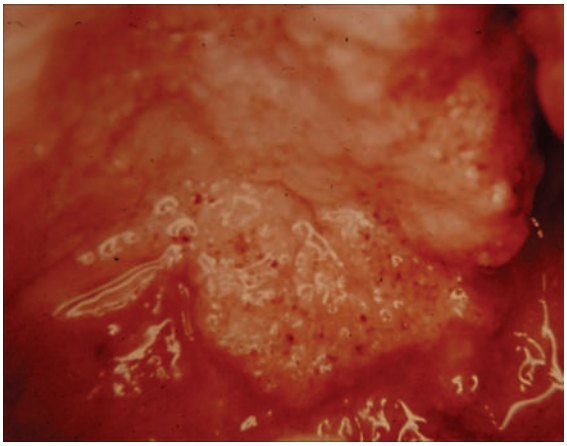

FIGURE 7-25
Granulomatous inflammation due to blastomycosis with cobblestone appearance.

infections with *Mycobacterium avium intracellulare*, *Histoplasma capsulatum*, and other parasites occur in the submucosa among human immunodeficiency virus (HIV)-seropositive patients, many of whom have no pulmonary involvement with the specific organism in question.

MICROSCOPIC FEATURES

The epithelium may exhibit pseudoepitheliomatous hyperplasia; foci of granulomatous inflammation are located within the underlying connective tissue. Epithelioid histiocytes predominate, and multinucleated giant cells can be identified. Specific histochemical stains such as acid-fast, *periodic acid-Schiff* (PAS), and methenamine silver demonstrate the presence of microorganisms in the infectious granulomas.

DIFFERENTIAL DIAGNOSIS

Most of the focal papillary lesions included here are small and fail to evince surface erythema. Granulomatous lesions are often large and invariably sessile. A history of pulmonary disease or persistent cough and dyspnea should arouse suspicion of systemic granulomatous inflammatory disease. HIV infection should be suspected in those patients presenting with a history of risk factors.

TREATMENT

Depending on the organism identified, if any, the treatment is medical. Fungal infections are generally treated with amphotericin B or ketoconazole.

Additional Reading

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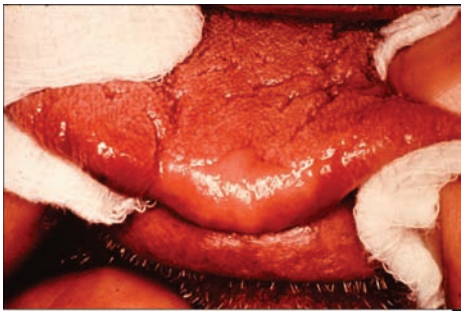
AMYLOIDOSIS

Figure 7-26

Age: Middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

Amyloidosis is a systemic disease in which a heterologous group of glycoproteins accumulates within the connective tissues and around vascular walls. The disease may be primary or secondary. Secondary forms are more common and arise in conjunction with multiple myeloma or, occasionally, in association with a chronic granulomatous disease. The tongue is the most common intraoral site, yet deposits of amyloid protein may also be identified in the lips and buccal mucosa. The lesions are usually multifocal and appear as sessile, deep nodules that are indurated. Amyloid A, deposited in senile and familial amyloidosis, is a protein derived from prealbumin, whereas amyloid



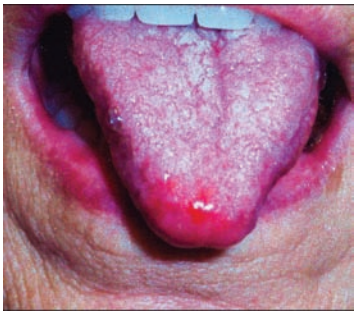


FIGURE 7-26
Multiple tongue nodules in amyloidosis.

L, seen in myeloma, originates from immunoglobulin light chains. A third type, AB2M derived from β2-microglobulin, is encountered in patients undergoing long-term hemodialysis.

MICROSCOPIC FEATURES

Globular aggregates of acellular eosinophilic proteinaceous material distend the surface epithelium and are deposited within the underlying connective tissues. Amyloid with β-pleated structure shows Congo red staining with polarization microscopy resulting in green birefringence.

DIFFERENTIAL DIAGNOSIS

Large nodular deposits causing macroglossia are usually observed, and these features do not closely parallel those seen in the other papular or multiple polypoid lesions listed here. Microscopically, amyloidosis resembles hyalinosis cutis et mucosae. A biopsy along with Congo red staining provide a definitive diagnosis.

TREATMENT

Once amyloidosis is diagnosed, a thorough medical work-up is indicated to uncover myeloma or granulomatous disease. In the former, cytologic chemotherapeutic drugs are prescribed. Large amyloid nodules interfering with speech or deglutition can be removed surgically.

Additional Reading

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HYALINOSIS CUTIS ET MUCOSAE (LIPOID PROTEINOSIS)

Figure 7-27

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Also known as lipoid proteinosis or the Urbach-Wiethe syndrome, hyalinosis cutis et mucosae represents a rare autosomal recessive disorder involving many organ systems. It is caused by a mutation in the *ECM1* gene (extracellular matrix). Diffuse deposits of hyaline glycoprotein and acid as well as neutral glycosaminoglycans occur in the mucosal tissues, skin, and vessel walls. Deposits are also found in the brain with

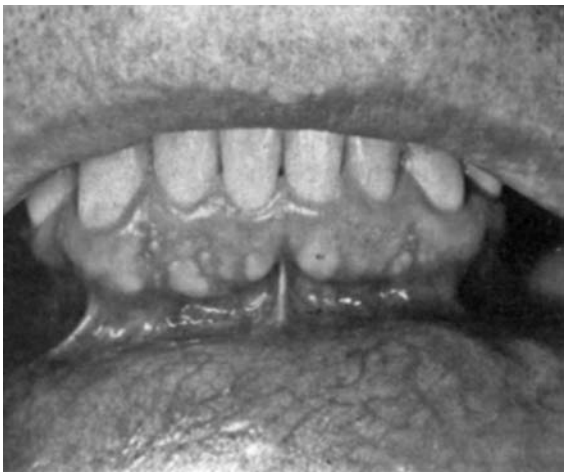

FIGURE 7-27
Multiple gingival papules in hyalinosis cutis et mucosae.

calcifications of the dorsum sellae. The oral tissues show infiltrated plaques, papules, and nodules that are yellowish white and are distributed in multiple array over the lips, tongue, buccal mucosa, and pharynx with occasional gingival involvement. The larynx is frequently involved as well. Cutaneous lesions may commence as vesicles; on healing, acneform scars develop. Subsequently, pale yellow nodules may form. The face, neck, and eyelids are most often involved. Hypodontia involving the maxillary lateral incisors and premolars is also a feature of the syndrome.

MICROSCOPIC FEATURES

A biopsy of one of the mucosal nodules shows diffuse connective tissue hyalinization with prominent hyaline perivascular cuffing. These deposits are PAS positive and show equivocal reactions for amyloid.

DIFFERENTIAL DIAGNOSIS

Neuropolyendocrine syndrome, focal epithelial hyperplasia, Cowden syndrome, and amyloidosis may show similar clinical features. A dermatologic examination should be performed. The clinical findings in conjunction with microscopic and histochemical findings provide a definitive diagnosis.

TREATMENT

There is no known treatment for this syndrome. Most patients enjoy normal longevity of life. Gingivectomy is recommended when diffuse hyperplastic-appearing gingival infiltration is present.

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HEMANGIOMA/ LYMPHANGIOMA

Figure 7-28

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Both blood and lymph vessel hamartomas may appear as diffuse polypoid masses yielding a grape cluster configuration. These lesions are most often observed on the tongue and buccal mucosa. Hemangiomas are red, blue, or purple, whereas lymphangiomas often mimic a mass of clustered vesicles. Most vascular hamartomas are present from early childhood; however, some lesions do not begin to proliferate until the patient is in the second decade of life.

MICROSCOPIC FEATURES

Racemose exophytic papules are covered by a thin layer of stratified squamous epithelium, which is distended by dilated, endothelium-lined vascular channels. These channels usually extend into the deeper connective tissues and may course between skeletal muscle fibers. In hemangioma, the vascular channels are filled with erythrocytes, whereas lymphangiomas are represented by ectatic vessels filled with an eosinophilic coagulum.

DIFFERENTIAL DIAGNOSIS

Most of the vascular hamartomas are distinctive and are not often confused clinically with other diffuse papular and polypoid lesions. The clustered grape pattern and localization are typical features. Nevertheless, a biopsy should be procured to confirm the clinical impression.

TREATMENT

Hemangiomas and lymphangiomas may be treated by injection of sodium morrhuate as a sclerosing agent or excised by scalpel or electrocautery. The surgeon should bear in mind the tendency for these lesions to extend into underlying muscle.

Additional Reading

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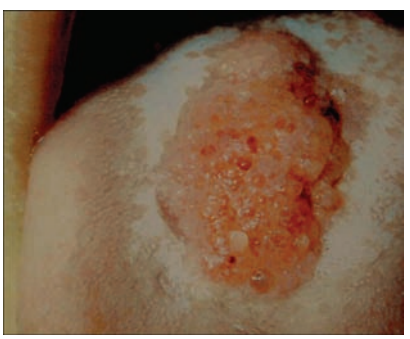
MULTIPLE ENDOCRINE NEOPLASIA, TYPE IIB

Figure 7-29

Age: Teenagers and young adults
Sex: No predilection

CLINICAL FEATURES

Inherited as an autosomal dominant trait, the neuropolyendocrine syndrome or multiple endocrine neoplasia, type IIb represents one of the phakomatoses in that the lesions do not evolve until the second decade or late childhood. There is a mutation in the *RET* gene. Numerous forms of multiple endocrine neoplasia (MEN) are known; type IIb shows oral lesions. The oral manifestations are multiple isolated polyps or nodules on the lips, tongue, and eyelids that represent plexiform neuromatous hamartomas. These neural tumors are also seen on the eyelids. A Marfanoid facies is present. The importance of uncovering this syndrome lies with the more serious manifestations that coexist, including malignant tumors of various



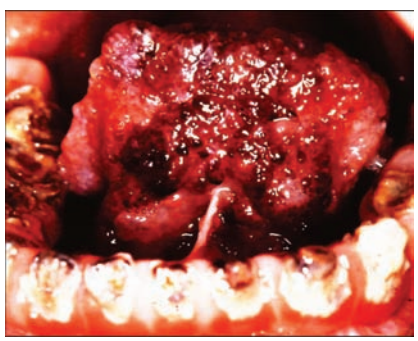
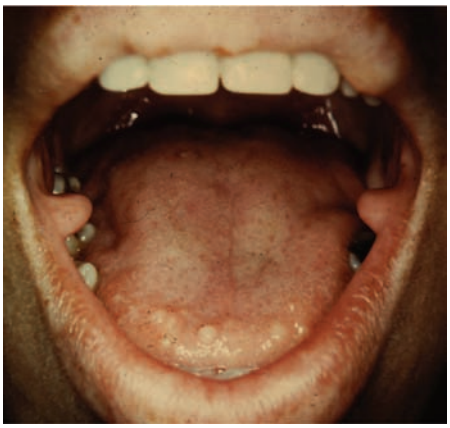


FIGURE 7-28
Lymphangioma with pebbly surface (left), hemangioma showing grape-like clustered papules (right).



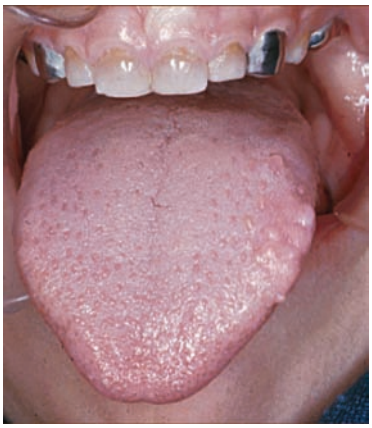


FIGURE 7-29
Multiple papular neuromas of the tongue accompanied by medullary carcinoma of the thyroid and adrenal pheochromocytoma.

endocrine glands. Adrenal pheochromocytoma and medullary carcinoma of the thyroid are the most frequently encountered cancers.

MICROSCOPIC FEATURES

The oral neuromas are characterized by an organoid, plexiform arrangement of nerve and nerve sheath elements similar to those of traumatic neuroma. The neural elements are enveloped by perineurium and are separated from one another by intervening fibrous stroma.

DIFFERENTIAL DIAGNOSIS

Multiple mucosal neuromas of the Sipple syndrome may clinically simulate focal epithelial hyperplasia and Crohn's disease. Biopsy discloses their true nature.

TREATMENT

The oral lesions may be excised or left untreated once a diagnosis is obtained. Referral to an internist is recommended to detect or anticipate the occurrence of endocrine malignancies.

Additional Reading

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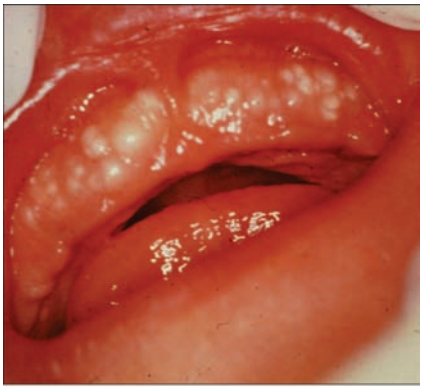
DENTAL LAMINA CYSTS

Figure 7-30

Age: Infancy
Sex: No predilection

CLINICAL FEATURES

Developmental soft tissue cysts arise in various locations of the oral mucosa and ultimately involute or are shed within 6 months. They appear as small white pearly nodules measuring less than 2 to 4 mm and tend to be multiple. When on the alveolar mucosa prior to tooth eruption they are referred to as dental lamina cysts where they are thought to originate from epithelial rests of



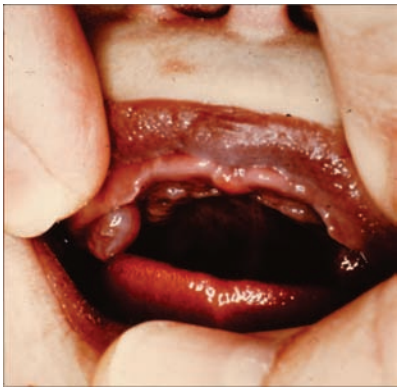


FIGURE 7-30
Multiple alveolar ridge papules in a neonate representing dental lamina cysts.

the nascent tooth germ, the dental lamina. Epstein's pearls are multiple and are located in the midline of the palate whereas Bohn's nodules are similar yet reside in the palate off the midline.

MICROSCOPIC FEATURES

These tiny cysts are represented by multiple nodules of stratified squamous epithelium with lumens filled with keratin.

DIFFERENTIAL DIAGNOSIS

MENIIb may be considered as may focal epithelial hyperplasia. Nevertheless the confinement to the alveolus, small size, and occurrence at birth allow for easy recognition.

TREATMENT

None necessary

Additional Reading

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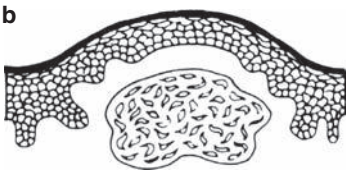
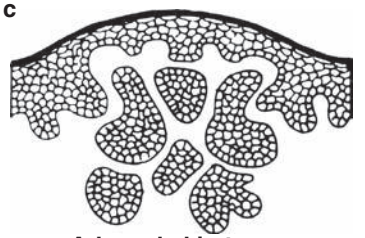
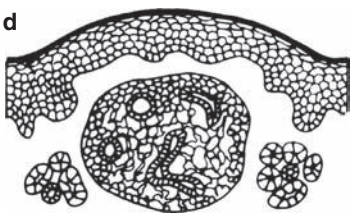
a Cyst



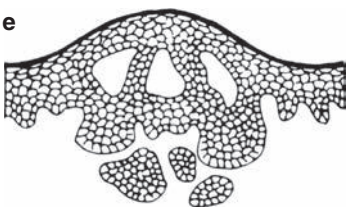
b Mesenchymal neoplasm



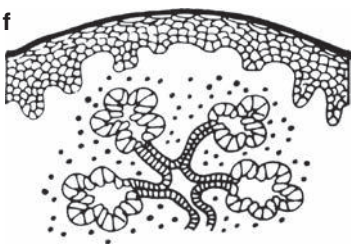
c Adnexal skin tumor



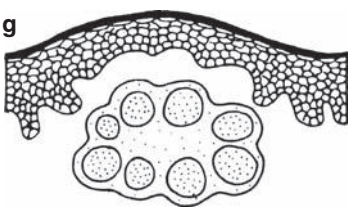
d Glandular neoplasm



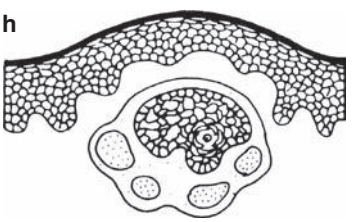
e Epithelial neoplasm



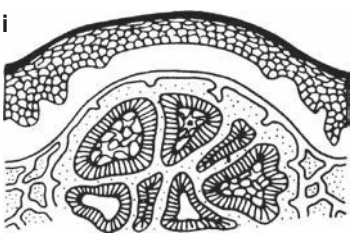
f Sialadenitis



g Lymphadenitis



h Lymph node metastasis



i Expansile osseous neoplasm

Extraoral Swellings

Soft Tissue Swellings of the Neck and Face

8

As with swellings located anywhere in the body and particularly in the subcutaneous tissues, neck and facial swellings may represent neoplasms, inflammatory disorders, hyperplastic reactions, or developmental defects. If the mass is painful or tender, soft and movable, and associated with fever, the process is probably inflammatory. If the mass is painless, well circumscribed, soft or firm yet not indurated, and can be grasped and moved freely, a benign neoplastic or reactive process should be foremost in the mind of the examiner. Indurated fixed swellings with a history of progressive enlargement are prime suspects for malignancy.

Anatomic localization of the tumefaction is perhaps the most germane consideration when attempting to diagnose masses in the head and neck region. In this chapter, the nosology of extraoral swellings is approached in this fashion. The rationale for grouping lesions according to site rests with regional anatomic considerations. For example, the lateral neck is riddled with lymph nodes; most swellings in the lateral neck, located along the course of the sternomastoid muscle, include developmental cysts, specific infectious diseases of lymphoid tissue, and various mesenchymal and lymphoid neoplasms. Midline neck swellings are more likely to represent thyroid disease. Swellings located at the mandibular angle or just anterior to the ear in the parotid region are usually salivary neoplasms or inflammatory diseases of the parotid gland. When a swelling of the parotid region is detected and the mass is clinically consistent with neoplasia, fine-needle aspiration cytology should be considered. If the cytologic findings are equivocal, the preferred approach is to perform a partial lobectomy and obtain frozen sections at the time of the operation. Depending on the diagnosis, this procedure may be adequate or further surgery may be indicated.

Localized swellings on the facial skin often represent skin adnexal or dermal neoplasms. Diffuse facial swellings produce asymmetry and may be caused by soft tissue enlargement or expansion of the underlying osseous tissue of the maxilla or mandible.

When extraoral swellings are encountered, a source of disease should be sought. Infections of the upper air passages or odontogenic infection are the most common causes of lymphadenopathy in the neck. The work-up should consist of physical evaluation of the mass itself, noting its location, consistency, relationship to adjacent tissues, and whether or not it is tender. The patient's temperature should be obtained. A complete oral soft tissue examination should be performed; if it yields negative results, the larynx, nasopharynx, and nasal cavity should be inspected. The dentition should be evaluated for necrotic teeth and periodontal abscesses. Radiographs of the jaw and, if all else proves negative or if symptoms warrant, sinus radiographs and tomograms may be ordered. If no source of disease can be found and the mass fails to resolve in 2 weeks, the patient should be referred to an appropriate specialist for biopsy.

The most frequently encountered lateral neck swellings are lymphadenitis of dental origin, infectious mononucleosis, lipoma, metastatic tumor, and lymphoma. The latter two, as well as sarcoma and tuberculosis, are potentially lethal.

The most common midline neck swellings are goiter and thyroglossal tract cyst. Thyroid carcinoma is potentially lethal. Common parotid region swellings include obstructive sialadenitis, pleomorphic adenoma, and adenocarcinoma, the latter being potentially life-threatening. Localized facial swellings generally represent nevi, sebaceous cyst, seborrheic keratosis, or basal cell carcinoma. The latter may be lethal if left untreated. The most common diffuse facial swellings are cellulitis and underlying expansile bone lesions such as fibrous dysplasia or benign intraosseous neoplasms.

Lateral Neck Swellings

BRANCHIAL CLEFT CYST

Figure 8-1

Age: Onset in childhood or early adulthood
Sex: No predilection

CLINICAL FEATURES

The lymphoepithelial or branchial cleft cyst is believed to be derived from epithelial remnants of the embryonic branchial clefts that become entrapped within cervical lymph nodes. An alternative theory implicates intranodal entrapment of salivary epithelial elements. The cyst may reach impressive proportions and can be located anywhere along the anterior surface of the sternomastoid muscle within the subcutaneous tissues. It is doughy or firm and movable on palpation. Rarely, cysts similar to the branchial cleft cyst, yet derived from cervically migrating thymus or parathyroid anlagen, localize in the lateral neck.

MICROSCOPIC FEATURES

The cyst lining consists of either stratified squamous or respiratory epithelium or alternating zones of both. The cyst wall is composed of lymphoid tissue, which often contains germinal centers. Carcinomatous change (so-called branchiogenic carcinoma) has been reported to occur from the lining of such cysts; however, the probability that the carcinoma represents metastatic disease to nodal tissue from an upper respiratory or facial skin primary tumor must be considered.

DIFFERENTIAL DIAGNOSIS

The compressible, movable mass of branchial cleft cyst must be differentiated from benign mesenchymal neoplasms, specific infectious lymphadenitis, and carotid body tumors. Lymphomas may also, albeit rarely, show clinical features of a benign lesion. Biopsy affords a definitive diagnosis.

TREATMENT

The lesion may be excised.

Additional Reading

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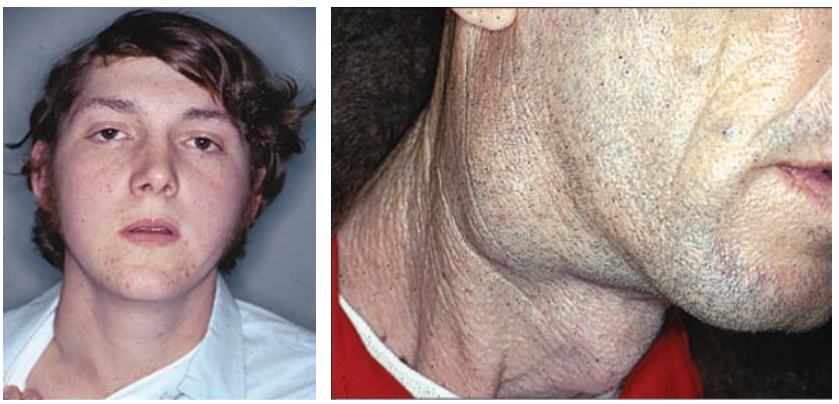

FIGURE 8-1
Branchial cleft cyst, a compressible, movable mass overlying the sternomastoid.

CERVICAL RIB AND TRANSVERSE PROCESS

Figure 8-2

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Although rare, an extension of the transverse process of a cervical vertebra may appear as an anomalous rib. Clinically, a bone-hard swelling can be palpated directly behind the sternomastoid muscle or in the parotid region. To the unwary examiner, the lump has all the features of malignant or metastatic disease. An anteroposterior radiograph through the neck discloses the presence of the elongated transverse process. Occasionally, symptoms may accompany this anomaly as a result of neurovascular compression in the region of the branchial plexus and subclavian vessels. Neural compression may result in neuralgia, paresthesia, and paralysis of the skin in the areas supplied by the eighth cervical and first thoracic nerves. These latter symptoms are usually seen with a cervical rib from C7, which is not palpable.

MICROSCOPIC FEATURES

Not applicable.

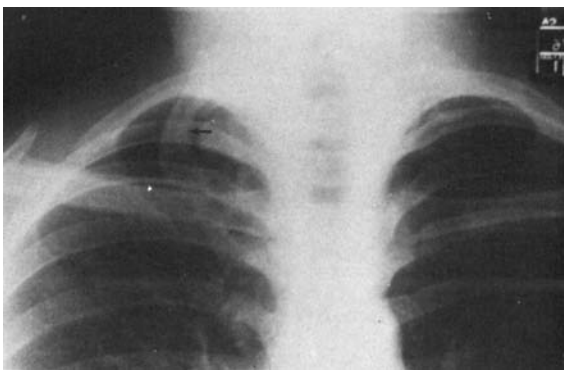

FIGURE 8-2
Cervical rib emanating from lower cervical vertebra. Similar anomalies on the upper cervical vertebrae are palpable.

DIFFERENTIAL DIAGNOSIS

The rock-hard character of a cervical rib may allow for easy confusion with lymphoma, primary sarcoma, or metastatic carcinoma. A radiograph of the neck quickly eliminates these from consideration.

TREATMENT

No treatment is necessary.

Additional Reading

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NONSPECIFIC LYMPHADENITIS

Figure 8-3

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Tender soft-to-firm swellings of the lateral neck are usually indicative of regional lymphadenopathy subsequent to upper respiratory or odontogenic infection. The swellings are often bilateral when upper respiratory inflammation occurs and are generally unilateral in the face of acute odontogenic or periodontal inflammation. The upper cervical nodes located just inferior to the angle of the mandible are most frequently affected by this reactive hyperplastic swelling. The patient is usually slightly or moderately febrile. A search should be made for inflammatory change

in the pharynx or oropharynx; tonsillar enlargement is often present. A variety of specific viral or bacterial infectious diseases may be responsible. In the absence of upper respiratory infection, the dentition should be evaluated clinically and radiographically to disclose the presence of pulpal or periodontal inflammatory disease. Two specific diseases with cervical lymphadenitis and fever are Kikuchi-Fujimoto disease, a lesion with specific histology that is probably viral in origin and can persist for many months, and Kawasaki disease. Both of these conditions are probably viral induced and tend to occur in Asian children. Kawasaki disease is associated with potentially fatal coronary aneurysms and thrombosis; erythematous oral and lip lesions may be seen as well (mucocutaneous lymph node syndrome).

MICROSCOPIC FEATURES

The lymph node is grossly enlarged and shows enlargement of the germinal centers. The reticulum cells may show evidence of mitosis, and a prominent lymphoid mantle is obvious. The medullary sinusoids are impacted with small and large lymphocytes. In Kikuchi-Fujimoto disease, areas of necrosis are seen along with histiocytic infiltration of the node. In Kawasaki disease, sinus histiocytosis is observed along with necrotizing arteritis.

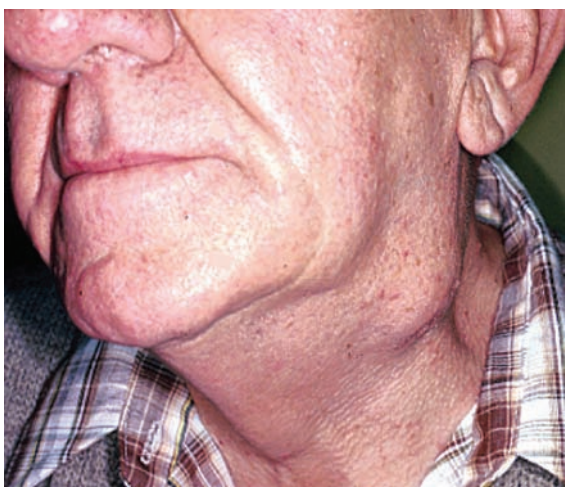

FIGURE 8-3
Nonspecific lymphadenitis associated with a necrotic mandibular molar.

DIFFERENTIAL DIAGNOSIS

Soft tender swellings, typical of cervical lymphadenopathy, must be differentiated from specific inflammatory lymphadenitides such as infectious mononucleosis, cat-scratch fever, actinomycosis, and tuberculous lymphadenitis. The latter two diseases are often accompanied by fistulous tracts onto the skin surface. Failure of the neck swellings to subside after conventional treatment for cervical lymphadenopathy (i.e., control of upper respiratory infection or odontogenic infection) warrants further work-up to rule out the aforementioned entities. Fine-needle aspiration cytology is a less invasive diagnostic method than open biopsy and has proven to be efficacious.

TREATMENT

Cervical lymphadenitis is a secondary reactive manifestation of infectious disease elsewhere. Throat infections should be managed by an otolaryngologist or general physician. Periodontal infection should be managed by surgery and/or curettage, whereas pulpal infection can be treated by therapeutic pulp canal exposure with subsequent endodontics or extraction. If fever is present, the patient should receive antibiotics, preferably penicillin (250 mg 4 times daily for 7 days), and local control of the infection should be instituted.

Additional Reading

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INFECTIOUS MONONUCLEOSIS

Figure 8-4

Age: Teenagers and young adults
Sex: No predilection

CLINICAL FEATURES

Caused by the Epstein-Barr virus, a form of herpesvirus, infectious mononucleosis is a relatively common infectious disease that is transmitted by oral droplet contamination and frequently develops after kissing. It is not as contagious as many of the childhood exanthems. The disease is characterized by extreme malaise, intense painful pharyngitis, and moderate-to-severe lymphadenopathy. The submandibular, upper cervical, and occipital lymph nodes may be enlarged, are painful, and are usually soft or rubbery. Tonsillar enlargement and pharyngeal ulceration with formation of a pseudomembrane are evident. Petechial lesions of the soft palate are present in nearly one half of the instances. The patients are febrile. The disease persists from 2 to 5 weeks.

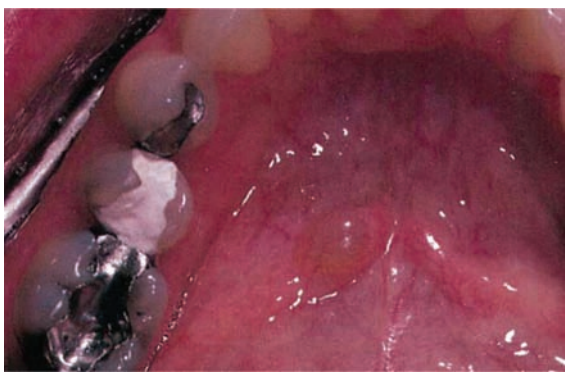

FIGURE 8-4
Lymphadenitis in a patient with infectious mononucleosis.

Persistent adenopathy and malaise, lasting for months or years, has been termed the "chronic fatigue syndrome," and although Epstein-Barr virus has been implicated as a causal agent, a retrovirus has recently become a suspect.

MICROSCOPIC FEATURES

Lymph nodes show hypertrophy with hyperplasia of the germinal centers. Both the germinal centers and medullary sinusoids contain epithelioid-appearing atypical lymphocytes.

DIFFERENTIAL DIAGNOSIS

The enlarged nodes in infectious mononucleosis are usually bilateral. The presence of lymphadenopathy in conjunction with intense pharyngitis and malaise must be differentiated from streptococcal sore throat, scarlet fever, diphtheria, and lymphoma. A swab culture may be obtained to rule out bacterial infection. The peripheral blood in infectious mononucleosis shows atypical "Downey" lymphocytes, and the Paul-Bunnell or heterophil antibody titer is positive by the second or third week of the disease. EBER is detectable by DNA in situ hybridization and confirms the diagnosis.

TREATMENT

Bed rest and supportive care with fluids, soft diet, an anesthetic gargle, an analgesic-antipyretic, and systemic antibiotics to control secondary bacterial pharyngitis are recommended.

Additional Reading

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Minagawa K, Okada T. Primary Epstein-Barr virus infection and cervical lymphadenopathy in childhood. *Josai Shika Daigaku Kiyo.* 1986;15:450.
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TUBERCULOUS LYMPHADENITIS (SCROFULA)

Figure 8-5

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

The lateral neck is the most common location for tuberculous inflammation of lymph nodes. As opposed to other mucocutaneous manifestations of tuberculosis that are secondary to pulmonary disease, cervical node tuberculosis or scrofula is often primary and may be associated with a portal of entry in the throat. It may be contracted by ingestion of contaminated milk. Although *Mycobacterium tuberculosis* is usually responsible, atypical tuberculosis may be acquired by infection with less common strains of mycobacteria. The lesion is located in the submandibular or cervical nodes, is usually unilateral, and eventually manifests exudative drainage via a fistula. The swelling is initially painless and on palpation is firm, generally movable, and of normal temperature, hence the designation *cold abscess*. Mycobacteria can be cultured from the exudate.

MICROSCOPIC FEATURES

The lymph node is replaced by focal granulomas evincing epithelioid cells and Langhan's giant cells. Caseation necrosis with neutrophil infiltration is seen in fistulating lesions. Acid-fast bacilli are detected with the appropriate special stains.

DIFFERENTIAL DIAGNOSIS

The isolated swelling with fistula must be differentiated from actinomycosis. When a fistula is not present, scrofula may simulate other specific granulomatous lymphadenitides or benign neoplasms. The exudate can be smeared and stained for acid-fast organisms, and definitive identification can be obtained by culture. A complete work-up to define the systemic extent of the disease is warranted.

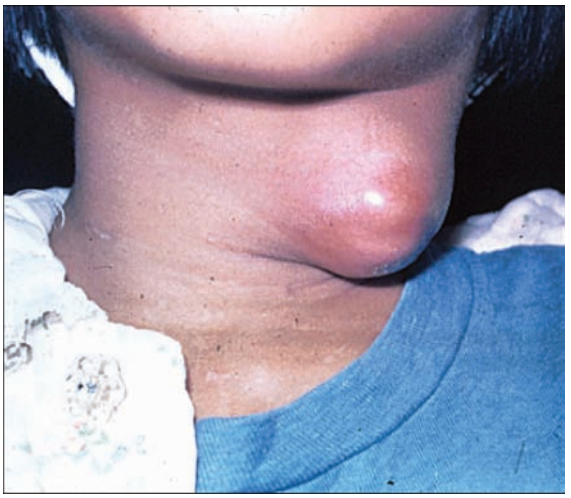

FIGURE 8-5
Tuberculous lymphadenopathy of cervical nodes.

TREATMENT

The caseating granuloma can be excised; however, this does not necessarily remove all infectious microorganisms. The patient requires conventional isoniazid therapy and the care of a physician.

Additional Reading

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CAT-SCRATCH FEVER

Figure 8-6

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

As the term implies, the disease is contracted after scratch by a cat. Many patients do not report a scratch, yet have been in contact with cats. The causative agent is *Bartonella henselea,* a cell-wall–defective gram-negative bacillus. A papule develops in the zone of contact, with subsequent lymph node swelling in the region draining the scratch site; other nodes may enlarge as well. In the head and neck area, the submandibular, cervical, or occipital nodes are involved. The nodes are sore, somewhat firm, and movable. Occasionally, a fistula is encountered. Fever, malaise, headache, and nausea become manifest early in the course of the disease.

MICROSCOPIC FEATURES

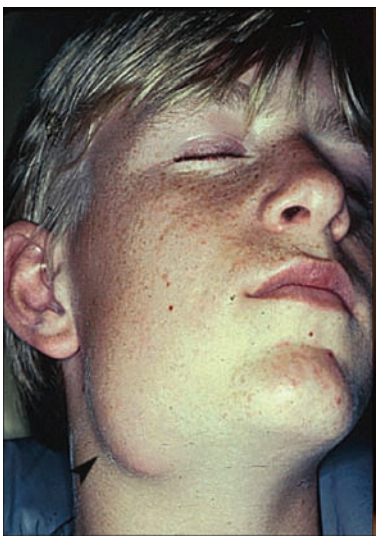
The involved node or nodes are replaced by focal granulomas that are characterized by epithelioid histiocyte infiltration and multinucleated giant cells that surround central zones of granular eosinophilic necrotic material. The organism may be demonstrable with a Wharthin-Starry or Giemsa's stain.

DIFFERENTIAL DIAGNOSIS

The cervical swelling of cat-scratch fever must be differentiated from actinomycosis, scrofula, and other rare granulomatous lymphadenitides such as tularemia, lymphogranuloma venereum, atypical tuberculosis, and neoplasms. A history of scratch or contact with a cat is, of course, helpful in making the diagnosis. A definitive diagnosis is obtained by noting a positive intracutaneous reaction with Mollaret's antigen or a positive complement-fixation test.

TREATMENT

The disease does not always respond to antibiotics, although some patients may benefit from gentamicin or cefoxitin. Supportive care with fluids, good diet, bed rest, and administration of antipyretics are recommended. Extremely tender nodes may require incision with drainage.



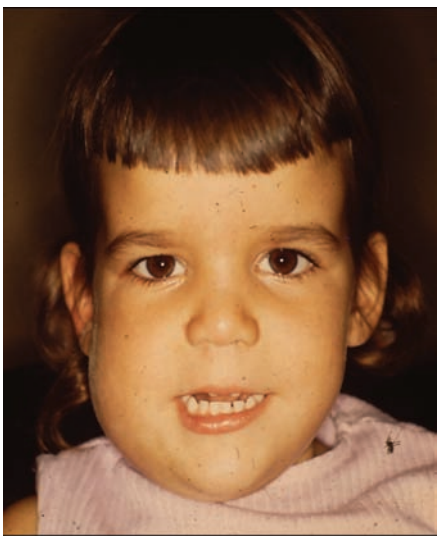


FIGURE 8-6
Cervical lymphadenopathy in cat-scratch fever.

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ACTINOMYCOSIS

Figure 8-7

Age: Young adults
Sex: Male predilection

CLINICAL FEATURES

The submandibular and lateral neck regions are the most commonly involved areas in cervical-facial actinomycosis. Caused by infection with *Actinomyces israelii*, actinomycosis is characterized by a firm, often indurated multinodular tumefaction that has a tendency to develop drainage. The exudate contains clumped colonies of the microorganisms that appear crystalline and yellow, hence the term *sulfur granules.* The mass usually develops after trauma or tooth extraction, which apparently provides a portal of entry for the fungus-like bacillus. The lesion develops within a few weeks to months with slow progressive enlargement. It is more frequently encountered among rural than urban inhabitants.

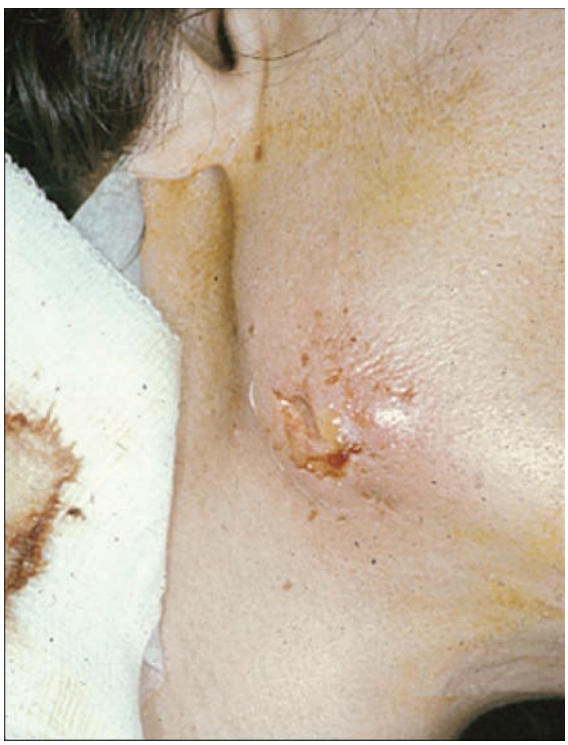

FIGURE 8-7
Swollen cervical fistula in actinomycosis.

MICROSCOPIC FEATURES

The focus of inflammation is characterized by surrounding fibroplasia with extensive vascular proliferation. Focal abscesses are distributed throughout and are characterized by sheets of neutrophils that surround amphophilic club-shaped colonies that manifest a peripheral fringe. These colonies are positively stained with the periodic acid-Schiff technique. In the early stages, microbial colonies may elicit a granulomatous response with epithelioid histiocytes and multinucleated giant cells.

DIFFERENTIAL DIAGNOSIS

The indurated swelling of the neck seen in actinomycosis is often "woody" and must be differentiated from a neoplasm by biopsy. Once a fistula has developed, suspicion of actinomycosis is high. Nevertheless, other lateral neck swellings with drainage, such as scrofula or less common granulomatous infections, must be considered as possibilities. Identification of tiny yellow sulfur granules (usually measuring less than 2 mm) from the exudate or curettage of the lesion is of diagnostic aid. Anaerobic methods of culture provide a definitive diagnosis.

TREATMENT

Actinomyces infection responds to penicillin therapy. High-dose therapy—10 to 20 million units intravenously for 5 to 6 weeks—is required in many instances. Erythromycin may be prescribed for patients with allergy to penicillin.

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REACTIVE PROLIFERATIONS

Figure 8-8

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Various fibroproliferative lesions such as fibromatosis, myofibromatosis, pseudosarcomatous fasciitis, and dermatofibrosarcoma protuberans, collectively grouped as the fibrous histiocytomas, often arise within the subcutaneous tissues of the lateral neck. These swellings are multinodular and firm but are usually somewhat movable within the surrounding tissues. They often grow rapidly and may become large if not removed. Clinically, they appear to represent neoplasms, yet are more likely to evolve as a reaction to injury.

MICROSCOPIC FEATURES

All of the fibroproliferative reactions are similar in their histomorphologic characteristics. Spindle cells are grouped into fascicles or form pinwheel-like swirls (storiform pattern) with variable amounts of collagen. Epithelioid or foam cell histiocytes are often present but are usually sparse and randomly distributed among fibroblastic cells. Many of these tumors are cellular and, under these circumstances, may closely mimic sarcoma.

DIFFERENTIAL DIAGNOSIS

Reactive proliferations are clinically indistinguishable from a variety of mesenchymal neoplasms, actinomycosis, or specific granulomatous enlargements. They may be indurated and suggest lymphoma, sarcoma, or metastatic disease. Multinodularity is suggestive of a reactive proliferation. A biopsy is required for a definitive diagnosis.

TREATMENT

Although encapsulation is common, a merging with adjacent fascia or connective tissue is also frequently encountered. For

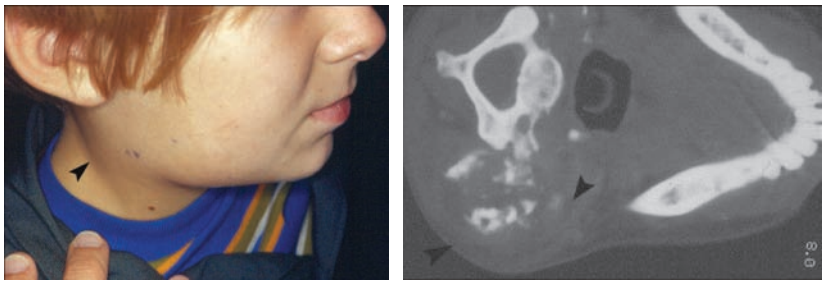

FIGURE 8-8
Fibrous histiocytoma of the lateral neck (left), fibromatosis with calcification (right radiograph).

this reason, wide local excision is generally required to eradicate the disease and circumvent recurrence. Combination radiation and chemotherapy has been successful in patients with extensive disease.

Additional Reading

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SINUS HISTIOCYTOSIS

Figure 8-9

Age: Children
Sex: No predilection

CLINICAL FEATURES

Sinus histiocytosis with massive lymphadenopathy is a childhood disease that occurs more frequently among Blacks than among Whites. The affected children show enlargement of the cervical and submandibular nodes, usually bilaterally, and these nodal swellings often reach massive proportions. The neck is distended by bosselated, nodular confluent masses that are firm, painless, and may become fixed to adjacent tissues. Other node groups (axillary, inguinal, hilar, and retroperitoneal lymph nodes) often show enlargement; however, the size is not comparable to that of the cervical adenopathies. Cutaneous nodules and lytic lesions of long bones occur in 30% to 40% of affected individuals and gallium scanning often discloses skeletal lesions. Fever is a constant finding; however, other constitutional signs of infectious disease, such as anorexia and malaise, are not present. Neutrophilic leukocytosis, elevated erythrocyte sedimentation rate, normocytic anemia, and hypergammaglobulinemia are present.

The disease persists for months or even years, shows no tendency for malignant change, and eventually undergoes spontaneous resolution. Elevated antibodies to the Epstein-Barr virus have been demonstrated in this disease, yet a cause-and-effect relationship has not been proven.

MICROSCOPIC FEATURES

Capsular fibrosis is a constant finding. The lymph node architecture is obliterated by dilated sinusoids lined by oval histiocytes with abundant granular or foamy cytoplasm; multinucleated forms are common. A hallmark of the disease is a tendency for phagocytosis of both lymphocytes and erythrocytes.

DIFFERENTIAL DIAGNOSIS

Bilateral multinodular lymphoid swelling seen in sinus histiocytosis must be differentiated from similar changes encountered

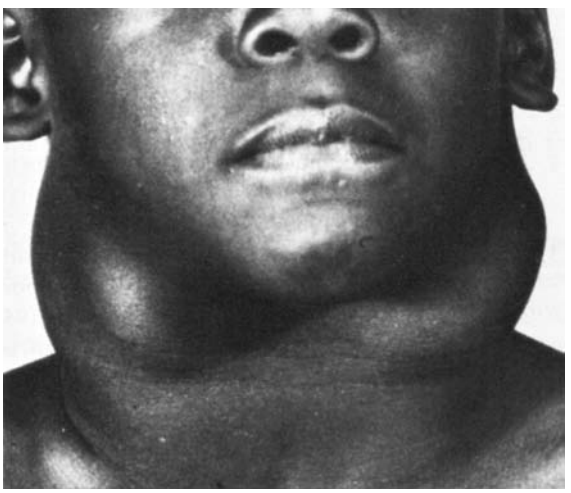

FIGURE 8-9
Sinus histiocytosis with massive lymphadenopathy of the cervical lymph nodes. *Source:* Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy: a pseudolymphomatous benign disorder. Analysis of 34 cases. *Cancer.* 1972;30:1174.

in other infectious lymphadenitides such as tuberculosis or cat-scratch fever, malignant lymphoma, and metastatic carcinoma. The absence of positive skin tests for specific microorganisms, presence of fever without malaise, and laboratory data as designated earlier point to a diagnosis of sinus histiocytosis. Biopsy discloses the characteristic features.

TREATMENT

Neither antibiotics nor steroids show any therapeutic value. Radiation therapy likewise is of no benefit in reducing the size of the tumefactions. Because the etiology is essentially unknown, no treatment can be rendered. The lesions eventually regress, even though the disease persists for many months or even years.

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BENIGN MESENCHYMAL TUMORS

Figure 8-10

Age: Adults
Sex: Depends on specific histologic type

CLINICAL FEATURES

A variety of connective tissue tumors arise in the lateral neck region. The more common forms are lipoma, neurilemmoma, neurofibroma, and lymphangioma (cystic hygroma). Plexiform neurofibromas and schwannomas may present in the context of neurofibromatosis type 1. The mass is either soft or firm, yet not indurated, and is movable on palpation. The neoplasms are slow growing and are usually painless. If left untreated, they may become quite large. Ulceration, surface telangiectasia, and fistulization of the overlying skin are extremely rare with benign mesenchymal neoplasms. Computed tomography (CT), magnetic

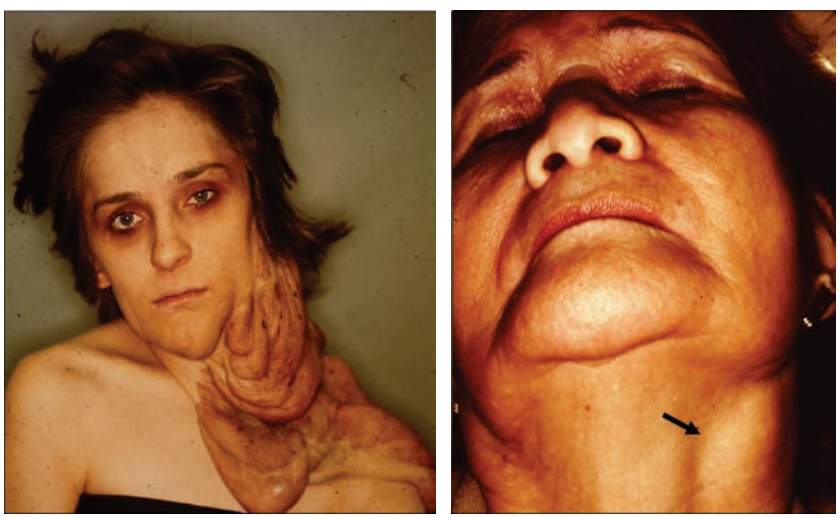

FIGURE 8-10
Neurofibroma in NF1 appearing as a lateral neck mass (left); lipoma (right).

resonance imaging (MRI), and sonography are useful diagnostic tools for determining location and extent of disease.

MICROSCOPIC FEATURES

The histomorphologic features vary depending on the tissue cell of origin. Nearly all are well differentiated and have well-defined margins or are encapsulated. Lipomas are tumor masses composed of normal adipose tissue, whereas the neural sheath neoplasms are composed of benign-appearing spindle cells associated with varying amounts of collagen.

DIFFERENTIAL DIAGNOSIS

The firm or soft movable nonulcerated mass representing a benign mesenchymal neoplasm must be differentiated from branchial cleft cyst, carotid body tumor, and nonfistulating granulomatous inflammations of lymph nodes. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Practically all benign mesenchymal neoplasms of the neck can be treated by conservative surgical excision. For most, recurrence rates after simple excision are low.

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CYSTIC HYGROMA (LYMPHANGIOMA)

Figure 8-11

Age: Infancy and childhood
Sex: No predilection

CLINICAL FEATURES

Cystic hygroma is considered separately from the other benign mesenchymal neoplasms because of its propensity to arise in the soft tissues of the neck in children. The tumor mass may be present at birth or develop during the early childhood years. It may reach large proportions, becoming pendulous. The mass is soft and pliable on palpation. The neoplastic lymphatic channels may infiltrate between muscle and the contiguous soft tissues, thus making it difficult to determine the extent of the condition; however, CT, MRI, and lymphatic scintigraphy are useful in the determination of extent of disease. Patients with Down's and Turner syndromes have a predilection for cystic hygroma of the neck.

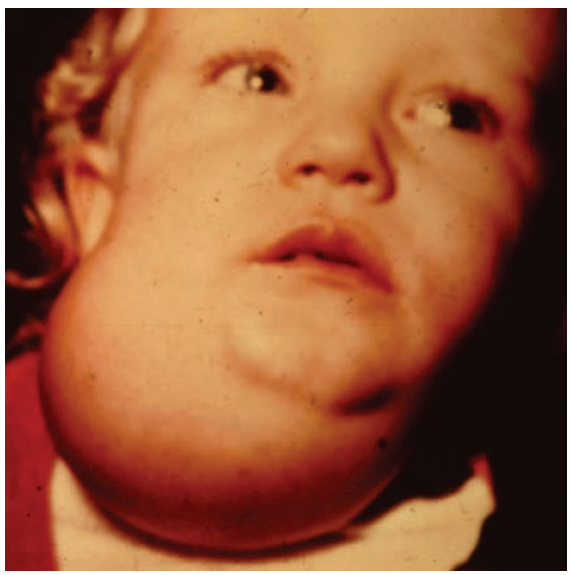

FIGURE 8-11
Lymphangioma (cystic hygroma) of the neck in an infant.

MICROSCOPIC FEATURES

Cystic hygroma is composed of dilated endothelium-lined lymphatic channels. The channels lie in juxtaposition to one another with little intervening fibrous stroma. Infiltration of adjacent tissues is common; however, the endothelial cells show no signs of cellularity, pleomorphism, or hyperchromatism.

DIFFERENTIAL DIAGNOSIS

Cystic hygroma must be differentiated from branchial cleft cyst, sinus histiocytosis, and lipoma. When the mass is small, it may simulate one of the specific granulomatous inflammations such as tuberculosis. When a large, soft, pliable mass is detected in the lateral neck in a child, the foremost diagnostic consideration is cystic hygroma. Biopsy is required for a definitive diagnosis.

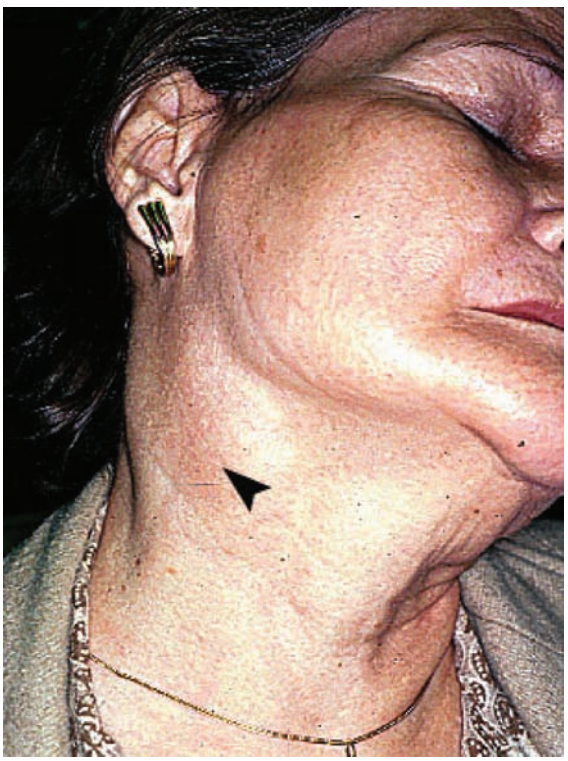

FIGURE 8-12
Carotid body tumor causing large tumefaction overlying carotid bifurcation.

TREATMENT

The mass requires surgical excision with careful dissection from surrounding tissues, which it may infiltrate. Intralesional injection with OK-432 sclerosing agent has shown favorable results.

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CAROTID BODY TUMOR (CHEMODECTOMA)

Figure 8-12

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Neoplasms originating in the carotid body are rarely malignant. Tumors are located in the upper lateral neck adjacent to the angle of the mandible. They are firm and movable anteroposteriorly, yet cannot be manipulated in a superoinferior direction because of their attachment to the carotid bifurcation. The tumors are generally asymptomatic, yet a bruit may be detected, the overlying skin may be warm, and medial growth may constrict the airway. Rarely, paralysis of cranial nerves X or XII may be observed. Occasionally, chemodectomas arise more

inferiorly from other chemoreceptors located along the carotid and aortic arteries. The mass may be somewhat tender, yet is usually asymptomatic.

MICROSCOPIC FEATURES

Carotid body tumors typically mimic, morphologically, the normal carotid body with organoid nests of polygonal cells. Two cell types are seen: the more prevalent vesicular with similarly vesicular oval nuclei, the other pyknotic and hyperchromatic. The organoid nests are separated from one another by a prominent vascular network. Synaptophysin and chromogranin IHC are positive.

DIFFERENTIAL DIAGNOSIS

Carotid body tumors, by virtue of their location, must be differentiated from lymphadenopathy, other mesenchymal tumors, and lymphoma. Their unique clinical features with regard to limited movement in a vertical plane with movability in the horizontal plane, although not pathognomonic, are certainly highly suggestive. Angiography discloses a well-circumscribed vascular "blush" in the carotid bifurcation area.

TREATMENT

Surgical excision is recommended. The tumor must be removed with great care to avoid carotid perforation and, therefore, should be managed by an experienced head and neck surgeon. Recent evidence indicates that radiation therapy may be effective for these tumors. Embolization of head and neck paragangliomas with n-butyl cyanoacrylate or onyx shows favorable results.

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METASTATIC CARCINOMA

Figure 8-13

Age: Teenagers (nasopharyngeal) and elderly adults (squamous cell carcinoma)
Sex: Male predilection

CLINICAL FEATURES

The first depot of metastatic carcinoma from primary lesions of the upper respiratory tract and face is the regional cervical and submandibular group of lymph nodes. Although usually unilateral, malignant disease with more longevity may manifest bilateral metastases. The mass is usually, yet not invariably, fixed to the adjacent fascia or sternomastoid muscle and is almost always indurated. Nasopharyngeal carcinomas occur more frequently in teenagers than in adults. The neck metastases may be the first sign of disease, as they may be considerably larger than the primary tumor itself. When an indurated swelling is detected in the lateral neck, a diligent search for a primary tumor in the oral cavity, nose, throat, nasopharynx, and paranasal sinuses is mandatory. Carcinomas of the skin of the face and scalp may also metastasize to cervical lymph nodes. When nodal metastases are encountered, the prognosis is considerably worsened. It should be noted that primary adenocarcinomas of salivary origin and melanoma of the head and neck frequently manifest cervical metastasis. CT and MRI detect metastatic disease that may not be evident clinically.

MICROSCOPIC FEATURES

The metastatic tumor is essentially identical microscopically to the primary lesion. Tumor cells tend to localize first in the subcapsular

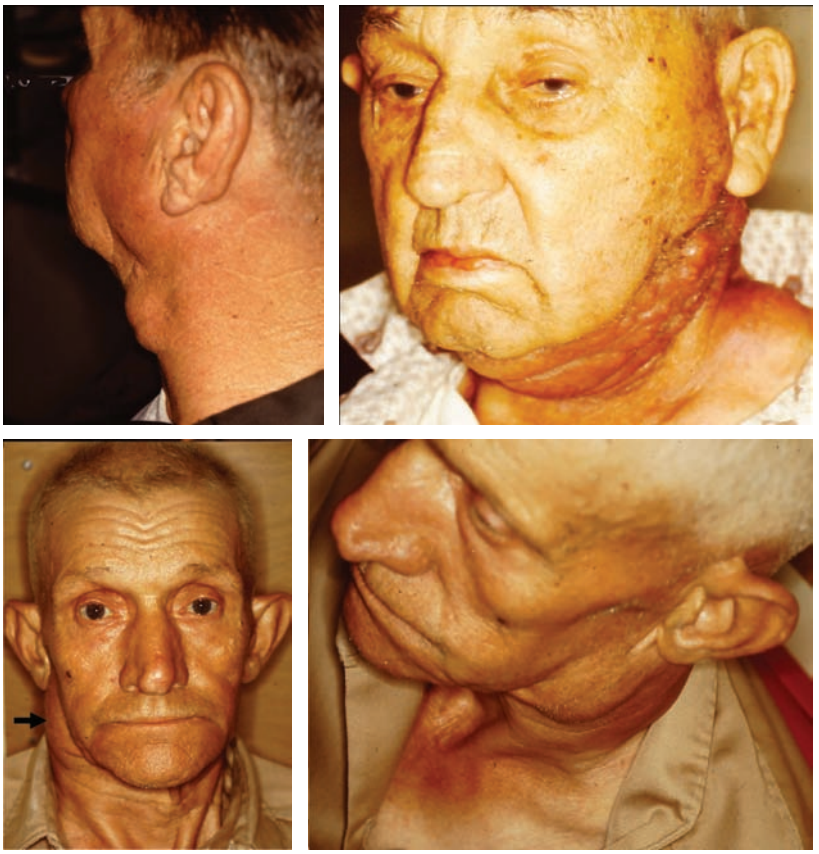

FIGURE 8-13
Metastatic cancer in cervical nodes from a primary carcinoma of the oral cavity.

region and later replace the entire node. Infiltration into the adjacent tissues ensues.

DIFFERENTIAL DIAGNOSIS

The indurated fixed node containing metastatic cancer must be differentiated from malignant lymphoma, primary sarcoma, and certain inflammatory diseases such as actinomycosis and scrofula, which may also be hard and immovable. Detection of a primary tumor in the head and neck region determines the diagnosis. Occasionally, no primary tumor can be found when intranodal carcinoma is discovered on biopsy. Most lesions of this nature arise in the nasopharynx, which must again be examined with scrutiny.

TREATMENT

The primary tumor may be treated surgically or with radiation therapy. Metastatic disease to nodes may be treated by cervical node dissection, often in continuity with the primary lesion, or may be radiated. These treatment methods must be selected carefully for each case by the oncologist or head and neck team.

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SARCOMAS

Figure 8-14

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Primary sarcomas of the head and neck region are rare, yet when they occur, the orbit and lateral neck are the most frequently affected sites. In the neck, the most frequently encountered tumors are fibrosarcoma, malignant fibrous histiocytoma, rhabdomyosarcoma, and synovial sarcoma. The swellings are firm or indurated and fixed to adjacent tissues. They may or may not be painful. When large, telangiectasia and erythema of the overlying skin may be seen. Growth is progressive and often rapid.

MICROSCOPIC FEATURES

The histomorphology varies depending on the cell of origin. The mesenchymal malignancies are, as a group, spindle cell neoplasms with significant cellularity, pleomorphism, and nuclear hyperchromatism or vesiculation. Encapsulation is lacking, and invasion of muscle and fascia is an almost constant feature.

DIFFERENTIAL DIAGNOSIS

Primary sarcomas of the neck, being fixed and indurated, must be differentiated from lymphoma, metastatic carcinoma, some of the reactive proliferations, and specific granulomatous inflammations, which are occasionally hard to palpation. Biopsy is required to determine the diagnosis and ascertain the tissue of origin.

TREATMENT

Wide radical excision is required and should be undertaken by an oncologic surgeon. Even with radical surgery, recurrences may ensue and the prognosis is generally poor.

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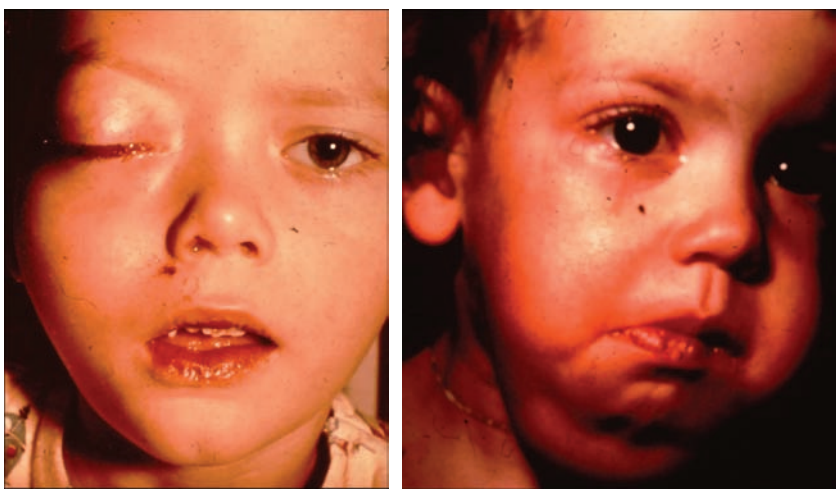

FIGURE 8-14
Periorbital indurated neck mass is rhabdomyosarcoma (left); fibrosarcoma (right).

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MALIGNANT LYMPHOMA

Figure 8-15

Age: Young and middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

Two basic types of lymphoid malignancy, Hodgkin's disease and non-Hodgkin's lymphoma, involve the cervical lymph nodes. Indeed, the cervical nodes are one of the most frequently involved node groups in the entire body. The swelling is occasionally unilateral, but is more often bilateral. The tumor masses may be multinodular and are, as a rule, fixed and indurated. Growth is progressive and may be rapid. The two forms of lymphoma manifest similar clinical features, yet differ in prognosis; Hodgkin's lymphomas, as a group, progress more slowly, and longevity is greatly increased over the non-Hodgkin's group. As the disease progresses, more extensive node involvement occurs with axillary and inguinal enlargement. Hilar node enlargement becomes apparent radiographically. Hepatosplenomegaly eventually occurs, and extranodal involvement with visceral, central nervous system, and osseous tumor is seen in the terminal stages. Low-grade fever, malaise, weight loss, frequent night sweats, and pruritus are common symptoms. Shingles is a frequent complication. Lymphoma is the second most common malignancy seen in human immunodeficiency virus (HIV) infection.

MICROSCOPIC FEATURES

The microscopic changes in the lymph nodes are highly variable. The sine qua non for Hodgkin's disease is the presence of a binucleated large histiocyte with prominent

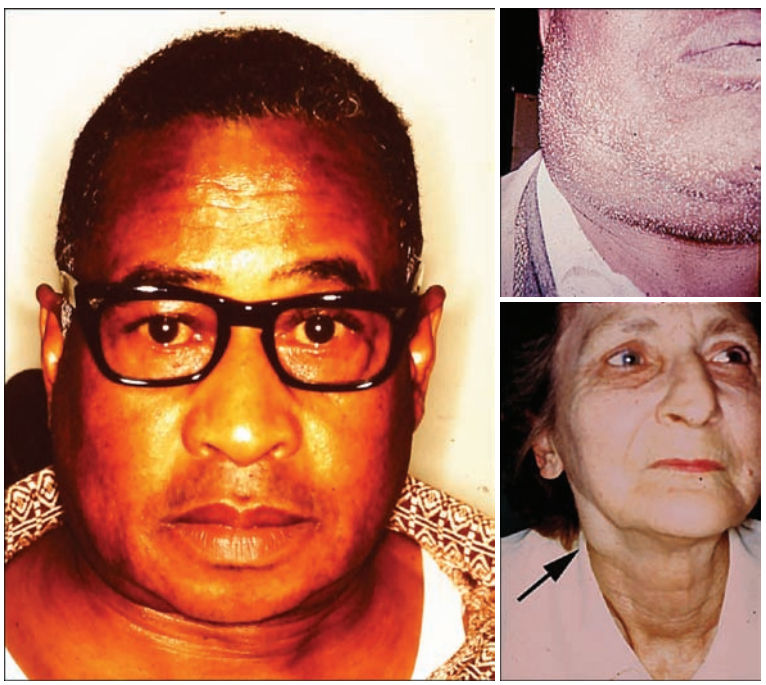

FIGURE 8-15
Cervical masses in malignant lymphoma.

central nucleoli known as the Reed-Sternberg cell. The non-Hodgkin's lymphomas show either well- or poorly differentiated lymphocytes arranged in follicular patterns or in monotonous cell sheets. The various subtypes in both groups have different natural histories and prognoses. In the head and neck area, large B-cell lymphoma is the most common type. Immunohistochemical markers and gene rearrangement studies for B- and T-cell lineages are crucial for typing these tumors and determining appropriate chemotherapy.

DIFFERENTIAL DIAGNOSIS

Unilateral neck node enlargement in lymphoma must be differentiated from sarcoma, metastatic carcinoma, and certain inflammatory enlargements such as scrofula and actinomycosis. Bilateral enlargements must be differentiated from sinus histiocytosis, metastatic carcinoma, and nonspecific lymphadenopathy. A complete physical examination, which includes hematologic studies, chest radiographs, and lymphangiography, is required to determine the extent of the disease.

TREATMENT

Lymphomas should be treated by a hematologist, oncologic chemotherapist, and/or radiotherapist. The disease is managed by radiotherapy in combination with multiphasic antitumor chemotherapy.

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Unilateral Parotid and Submandibular Swellings

ACUTE SIALADENITIS (SURGICAL MUMPS)

Figure 8-16

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Acute inflammatory disease of the major salivary glands most commonly affects the parotid. Unilateral involvement is more

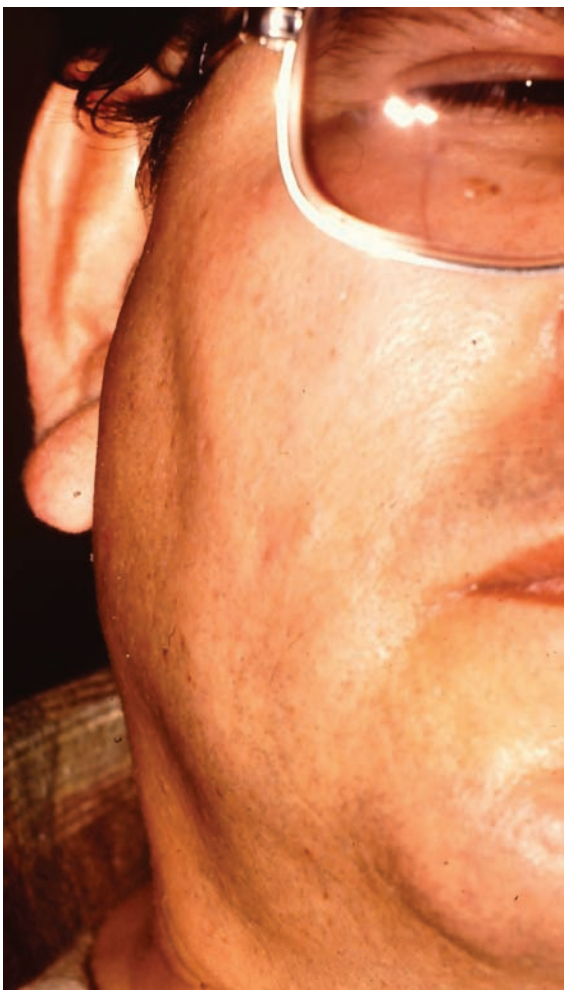

FIGURE 8-16
Parotitis developing shortly after abdominal surgery.

frequent than bilateral. Staphylococci and streptococci are the causative organisms. The disease is uncommon; when present, it is seen primarily in debilitated patients and those who are recovering from major surgery. It has also been reported to occur in patients with xerostomia complicating the use of phenothiazine drugs. The patients are febrile, the swelling is painful, and a purulent exudate can be milked from the salivary ducts.

MICROSCOPIC FEATURES

The acinar parenchyma shows degeneration and necrosis with diffuse infiltration by neutrophils. The ducts display ectasia and are impacted with necrotic debris and neutrophils.

DIFFERENTIAL DIAGNOSIS

Acute parotitis of bacterial origin must be differentiated from endemic parotitis and duct occlusion phenomenon (sialolithiasis). Pain and swelling are common to all three disorders. Purulent drainage from the duct orifice is more common in acute parotitis; bacteria can be cultured from this exudate and, in addition, a history of recent surgery or a predisposing debilitating condition can be obtained.

TREATMENT

Fluid and electrolyte balance should be maintained in postsurgical patients. Efforts to control any debilitating disease should be made in consultation with the patient's physician. The parotitis is treated with penicillin therapy in nonallergic patients while waiting for results from culture and sensitivity testing.

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SIALOLITHIASIS AND OBSTRUCTIVE SIALADENITIS

Figure 8-17

Age: Middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

The formation of salivary calculi within the ducts of the major salivary glands is overwhelmingly more common in the submandibular ducts. The stone develops on some sort of nidus, perhaps a mucous plug, and calcium salts become deposited in a concentric fashion. When the stone reaches sufficient size, the duct becomes occluded, mucin is retained, and the gland develops sclerosing sialadenitis. Clinically, the gland becomes enlarged and firm but is still movable. Pain is often severe or stabbing during mealtime, when salivation is stimulated. The stone can often be palpated within the duct or demonstrated radiographically. The parotid duct is only occasionally involved. Rarely, the intraoral minor glands develop a calculus. Occasionally, developmental or posttraumatic strictures develop in the duct system. The clinical signs and symptoms simulate sialolithiasis, and sialography aids in identifying the stricture. Ultrasonography can be a useful diagnostic approach to the diagnosis of sialolithiasis.

MICROSCOPIC FEATURES

The stone, when decalcified, is composed of concentric laminations of amorphous basophilic matrix. The occluded gland shows acinar degeneration with replace-

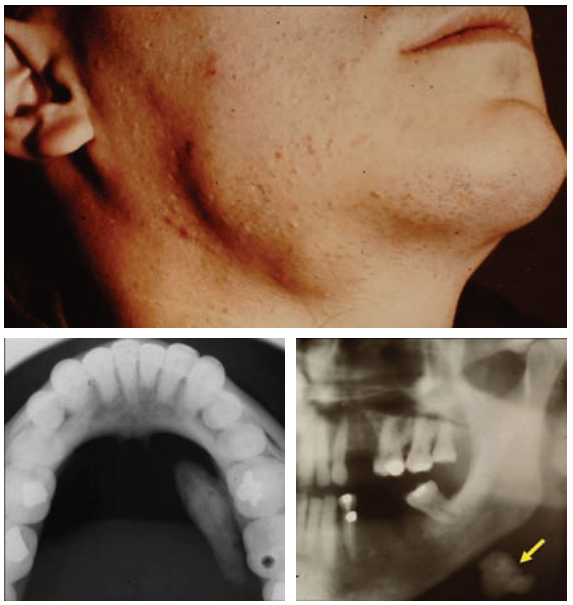

FIGURE 8-17
Submandibular swelling in sialadenitis secondary to duct blockage by a sialolith.

ment by fibrous tissue and mononuclear cells. Ducts are dilated, contain impacted mucin, and show oncocytic, mucous, and squamous metaplasia.

DIFFERENTIAL DIAGNOSIS

Sclerosing sialadenitis associated with sialolithiasis may show features that can be confused with endemic parotitis, salivary neoplasm, or mesenchymal neoplasm. Presence of pain that is increased at mealtime, failure to obtain flow when milking the gland, and presence of a palpable indurated mass in the complementary duct lead to a diagnosis of sialolithiasis. Submandibular duct stones are visualized with mandibular occlusal radiographs; parotid duct stones can be detected on panographic jaw radiographs. In addition, endoscopy can be performed to detect strictures and mucous plugs as well as stones.

TREATMENT

The stone can often be digitally manipulated out of the duct orifice. If this cannot be achieved, surgical removal is indicated. If pain, induration, and lack of function persist, particularly in cases of long-standing occlusion, sialectomy is indicated. Lithotripsy may prove to be a valuable method for managing large stones.

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CHRONIC SIALADENITIS

Figure 8-18

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Chronic sialadenitis is caused by retrograde infection with bacteria up the salivary duct tree. Infections of this nature are usually the consequence of duct blockage from ductal atresia, stricture, a mucous plug, or a stone. The gland enlarges and is usually tender to palpation as salivary flow becomes blocked and accumulates in the ductal system. Exudate and inflammatory cells within acinar lobules also account for the swelling. If the infectious flora changes, the inflammation may become acute with elevated temperature and leakage of a purulent exudates from the ductal opening.

MICROSCOPIC FEATURES

A chronic sclerosing sialadenitis is observed with loss of acini, mononuclear infiltration,

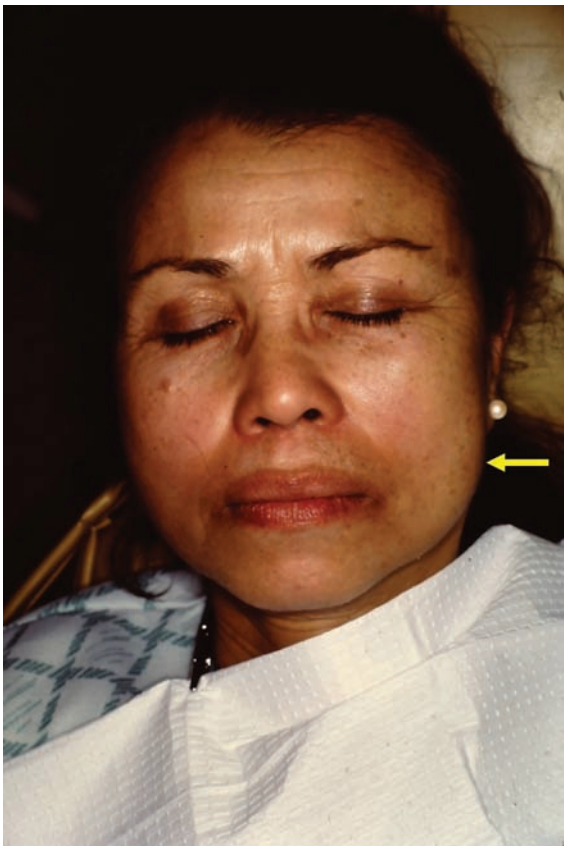

FIGURE 8-18
Chronic parotitis, duct blockage with bacterial infection.

and interstitial fibrosis. In acute lesions, abscess pockets may occur both within ducts and in the parenchyma.

DIFFERENTIAL DIAGNOSIS

Neoplastic lesions should be considered. Milking the ducts may elicit the flow of pus from the orifice indicating the infectious nature of the process during an acute phase. Ultrasound imaging is also useful in arriving at a definitive diagnosis.

TREATMENT

If possible, saliva should be milked from the gland and subjected to culture and sensitivity in order to select the appropriate antibiotic. A search must be made to uncover any possibility of duct blockage.

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INTRAPAROTID MESENCHYMAL TUMORS

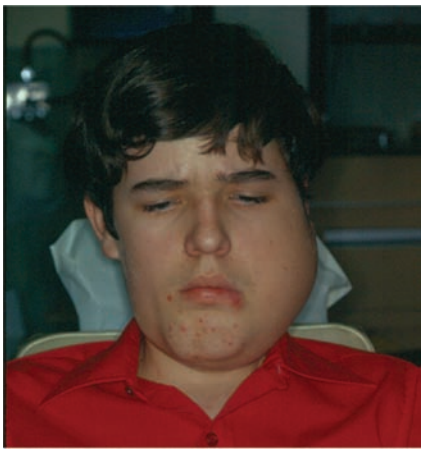
Figure 8-19

Age: Infants and children
Sex: Female predilection

CLINICAL FEATURES

Neoplasms arising from the supportive stroma of the salivary glands are less common than parenchymal tumors. When they do occur, they are primarily seen in children. Vascular tumors are the most frequently encountered mesenchymal tumors. Juvenile nevoxanthogranulomas and neurilemmomas also arise from salivary stromal progenitor cells. Sarcomas in major glands are extremely rare. The benign tumor(s) may be present at birth or develop slowly during childhood. The gland substance is unilaterally affected and may evince a soft-to-firm diffuse swelling, or the neoplasm may be well localized and encapsulated. The masses are painless, and no erythema or skin surface changes are found. Spontaneous regression of cutaneous vascular tumors by puberty is a frequent occurrence; however, intraparotid lesions do not tend to involute.

Venous aneurysms, although not neoplastic, represent other mesenchymal lesions occurring within parotid tissue. They are nonpulsatile soft swellings that appear when the head is lowered below the level of the heart. The swelling resolves in 2 to 3 minutes after the patient elevates the head.



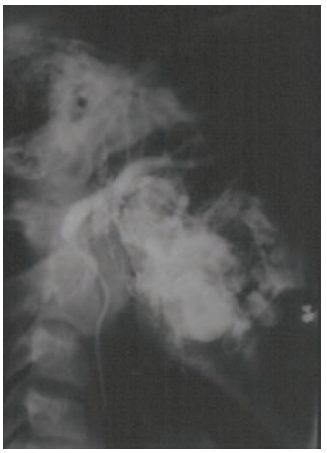


FIGURE 8-19
Intraparotid hemangioma, arteriogram.

MICROSCOPIC FEATURES

Intraparotid hemangiomas and lymphangiomas are characterized by infiltrative endothelium-lined channels of variable cellularity that tend to course between lobules and acini. Neurilemmomas are typically encapsulated and are composed of spindle-shaped nuclei and condensed collagen with foci of microcyst formation (Antoni B) and nuclear palisading (Antoni A) zones.

DIFFERENTIAL DIAGNOSIS

The slowly enlarging tumor mass seen with mesenchymal neoplasms must be differentiated from tuberculosis and unilateral mumps. The latter has an acute course with pain and fever. Primary parenchymal salivary tumors, particularly benign lesions, show identical clinical features, but are rarely seen in children. Biopsy is required to provide a definitive diagnosis.

TREATMENT

Vascular tumors, being infiltrative, lack encapsulation and, therefore, require lobectomy or parotidectomy, depending on the extent. Treatment should be deferred until after puberty, as regression may occur; however, parotid vascular tumors are less prone to involute spontaneously than are angiomas of skin. Neurilemmomas may be locally excised.

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LYMPHOMA

Figure 8-20

Age: Middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

Whereas lymphomas generally make their initial appearance in the cervical nodes of the lateral neck, intraparotid nodes may also

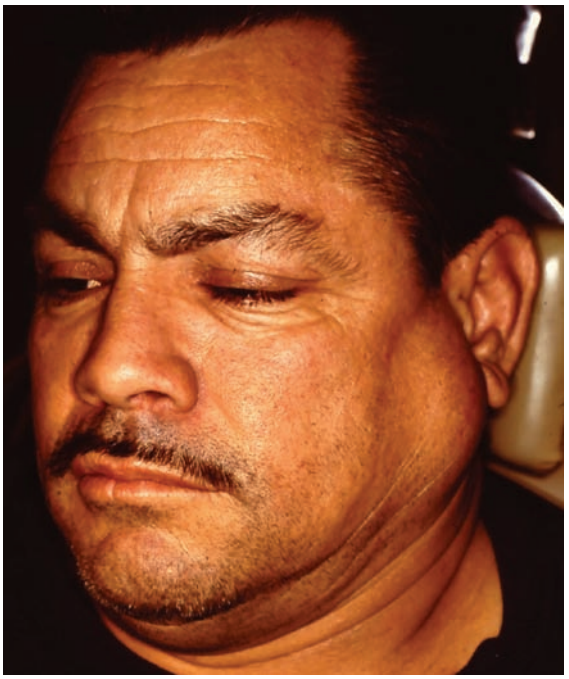

FIGURE 8-20
Intraparotid MALT type malignant lymphoma.

be the site of original tumefaction, producing enlargements anterior to the ears and over the mandibular angle. They are indurated and may be bilateral. Salivary flow is usually not affected and can be milked from the ducts. Pain is uncommon. When both parotids are enlarged in conjunction with lymphomatous swelling of the lacrimal glands, the disease is said to represent Mikulicz's syndrome (not to be confused with Mikulicz's disease, which is one of the benign lymphoepithelial lesions). Most instances of intraparotid lymphoma are of the non-Hodgkin's type and many are MALT lymphomas. Patients with Sjögren's syndrome are prone to develop lymphoma, both in the affected parotid and other body sites.

MICROSCOPIC FEATURES

In lymphoma both acini and ducts within salivary lobules are replaced by diffuse sheets of lymphocytes. Epimyoepithelial islands as seen in benign autoimmune sialadenitis are also identifiable in MALT lymphomas. Other types of lymphomas are diagnosed on the basis of pattern, lymphocyte morphology, and immunohistochemical markers.

DIFFERENTIAL DIAGNOSIS

Bilateral parotid swellings seen in acute sialadenitis and endemic parotitis may be differentiated from lymphoma on the basis of high fever, pain, lack of induration, and rapid onset. Lymphoma may be confused clinically with Sjögren's syndrome, Mikulicz's disease, Heerfordt's syndrome, and tuberculosis. In these disorders, however, the glandular swellings are soft or only moderately firm and lack fixation. Biopsy is required to obtain a definitive diagnosis. Once a diagnosis of malignant lymphoma is established, thorough physical examination, laboratory evaluation, and radiologic survey are required to determine the extent of disease.

TREATMENT

The patient should be under the care of an oncologist, a hematologist, and a radiotherapist. Combination chemotherapy and radiotherapy are used in treatment.

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PLEOMORPHIC ADENOMA

Figure 8-21

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

The pleomorphic adenoma or mixed tumor is the most common neoplasm of the major salivary glands. Over 80% arise in the parotid, and most of the remaining 20% involve submandibular gland and minor salivary glands. The tumor is generally located superficially overlying the angle of the mandible. It is firm or soft, movable, slow growing, and usually free from pain, even on palpation. It has a great growth potential in that long-standing tumors may become so enormous that they hang to the shoulders. Malignant transformation is uncommon but does occur.

MICROSCOPIC FEATURES

The term *pleomorphic* refers to the stromal element of the tumor and is the paramount pathologic feature. Monomorphic basophilic epithelial cells grow in diffuse sheets or are grouped into clusters showing duct formation. A spindle cell element is seen to proliferate in juxtaposition to the epithelial cell component and may actually be the predominant cell type. These myoepithelial spindle cell proliferations merge with stromal components that differentiate into myxomatous, cartilaginous, osseous, or adipose tissues. Some tumors contain myoepithelial hyaline cells with a plasmacytoid appearance, and occasionally, tyrosine crystals are encountered. Encapsulation is a constant finding; however, multiple extracapsular satellite cell nests or a multinodular pattern are frequently noted.

DIFFERENTIAL DIAGNOSIS

Pleomorphic adenoma must be differentiated from papillary cystadenoma lymphomatosum, oncocytoma, mesenchymal neoplasms, and adenocarcinomas, all of which may appear well circumscribed. Although the clinical features may appear to be typical for pleomorphic adenoma,

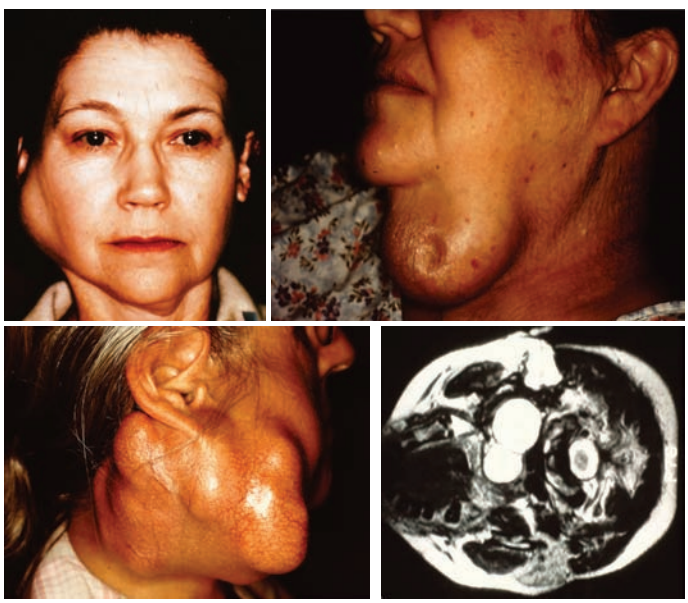

FIGURE 8-21
Pleomorphic adenoma of the parotid gland.

biopsy is required to rule out these other entities. Aspiration cytology is less invasive and is often diagnostic; however, cellular mixed tumors may be confused with adenocarcinomas.

TREATMENT

Simple excision is contraindicated, as recurrence is a common complication. Lobectomy or in-continuity gland extirpation is the treatment of choice. Facial nerve palsy and the auriculotemporal syndrome are common complications subsequent to parotid gland surgery.

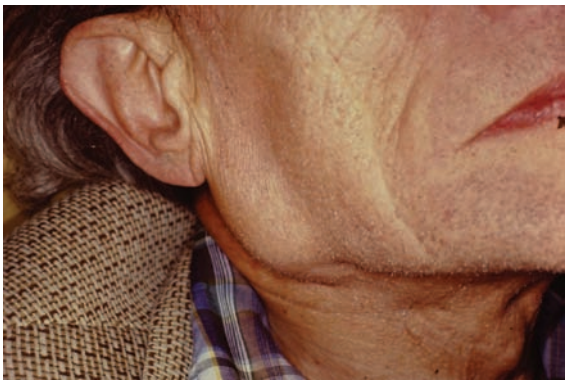

FIGURE 8-22
Parotid nodule representing papillary cystadenoma lymphomatosum.

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PAPILLARY CYSTADENOMA LYMPHOMATOSUM

Figure 8-22

Age: Middle-aged and elderly adults
Sex: Significant male predilection

CLINICAL FEATURES

Papillary cystadenoma lymphomatosum or Warthin's tumor is a benign tumor of salivary origin that probably represents a hamartomatous enlargement rather than a true neoplasm. Credence is given to this concept on the basis of the clinical features of the lesion. It is slow growing and self-limited. Once it reaches 2 to 4 cm, growth ceases in most cases. Another feature supporting the concept of a hamartomatous lesion is its frequent bilateral occurrence. The tumor is restricted to the parotid gland(s) and is not found in other major or minor glands. It tends to be superficial, well circumscribed, and movable, and classically feels doughy and compressible on palpation.

MICROSCOPIC FEATURES

The lesion is well encapsulated and shows cystic spaces lined by papillary projections of columnar oncocytes with a double row of nuclei. The stroma is composed of lymphocytes with scattered germinal centers. A variant contains nests of squamous epithelial islands showing cyst formation and sebaceous acinar differentiation. The variant is termed *sebaceous lymphadenoma.* Although extremely rare, adenocarcinoma and squamous cell carcinoma have been reported to arise in papillary cystadenoma lymphomatosum.

DIFFERENTIAL DIAGNOSIS

Warthin's tumor must be differentiated from other benign salivary neoplasms of parenchymal and stromal origin and enlarged parotid lymph nodes. Occurrence in males, doughy compressible consistency, and indolent growth are typical features. Bilateral swellings with these characteristics

are almost invariably Warthin's tumors; nevertheless, biopsy should be performed to confirm the clinical diagnosis.

TREATMENT

Simple local excision is recommended.

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ONCOCYTOMA

Figure 8-23

Age: Elderly adults
Sex: Female predilection

CLINICAL FEATURES

Oncocytoma or oxyphilic adenoma is a rare benign salivary tumor that rarely occurs before the age of 60 years. It arises most frequently in the parotid gland but may be located in the submandibular region as well. The mass is firm, well demarcated, and movable. It has a slow growth rate.

MICROSCOPIC FEATURES

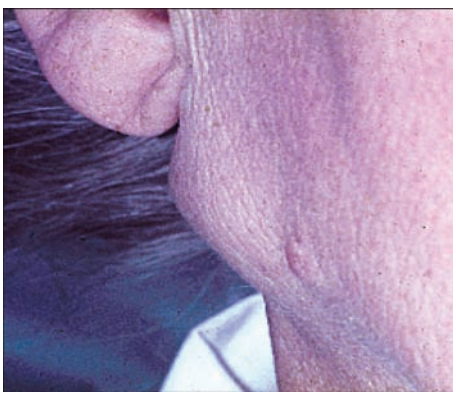
Solid sheets or trabecular cords of rectangular cells show voluminous amounts of granular eosinophilic cytoplasm with pyknotic or small nuclei containing a central nucleolus. Cystic spaces or duct formations may be encountered, yet rarely predominate. Oncocytic metaplasia in ductal cells is common in both major and minor salivary glands with ensuing age; however, this represents reactive rather than neoplastic change. A rare variant with clear cells admixed with oncocytes has been described.

DIFFERENTIAL DIAGNOSIS

The well-localized movable swelling of oncocytoma must be differentiated from Warthin's tumor, pleomorphic adenoma, mesenchymal neoplasm, and enlarged parotid lymph node. Age is highly significant, and a swelling of this nature in an elderly patient is strongly suggestive of oncocytoma. Microscopic examination is required to make the diagnosis.

TREATMENT

Simple local excision is recommended.



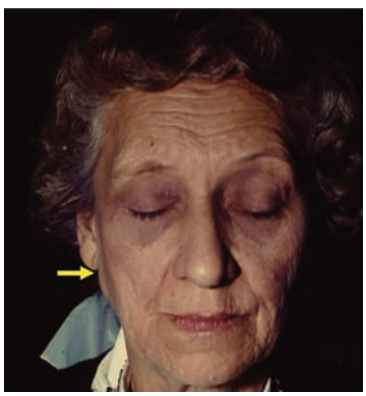


FIGURE 8-23
Oncocytoma of the parotid in an elderly female.

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MISCELLANEOUS ADENOMAS

Figure 8-24

Age: Adults
Sex: Female predilection

CLINICAL FEATURES

A variety of histologically distinct benign glandular tumors, other than the more common types included in this chapter, arise within the major salivary glands, usually the parotid. Most of them are rare. Included in this group are basal cell adenoma, membranous adenoma, sialadenoma papilliferum, myoepithelioma, sebaceous lymphadenoma, and papillary cystadenoma. Generally located within the superficial parotid, they appear as movable soft or somewhat firm nodules. Facial nerve compression resulting in paralysis is rare. Sialadenoma papilliferum may extend through skin with an overlying cutaneous cauliflower-like papillomatous mass.

MICROSCOPIC FEATURES

Each tumor exhibits characteristic histomorphologic patterns. Basal cell adenomas are composed of tumor islands, which comprise polygonal monomorphic cells with oval or round nuclei. Ductal elements are often encountered. Membranous adenomas appear similar to basal cell adenomas with zones of hyalinization encompassing individual nests or islands of monomorphic-appearing cells; such lesions are often associated with cutaneous tumors and are referred to as dermal analogue tumors. Sialadenoma papilliferum shows cystic areas lined by papillary interconnecting projections lined by oncocytic columnar cells. When surface skin is involved, the ductal-appearing cells merge with papillary projections covered with stratified squamous epithelium. Myoepitheliomas are characterized by diffuse sheets of spindle cells resembling mesenchymal cells; thorough search of the specimen reveals streaming of spindle cells around small ducts. Sebaceous lymphadenomas, a variant of Warthin's tumor, show ducts, sebaceous acini, and lymphoid stroma. Papillary cystadenomas are cystic with papillary projections into the lumina.

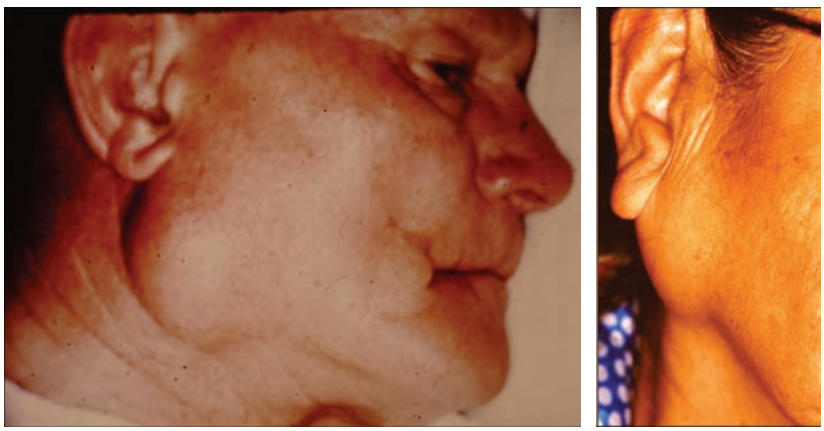

FIGURE 8-24
Basal cell adenoma of the parotid gland.

DIFFERENTIAL DIAGNOSIS

These miscellaneous adenomas are soft or firm movable masses that are clinically indistinguishable from the other benign adenomas included here.

TREATMENT

The recurrence rate after excision is not known for most of these less commonly encountered tumors. It would probably be advisable to perform excision with in-continuity lobectomy.

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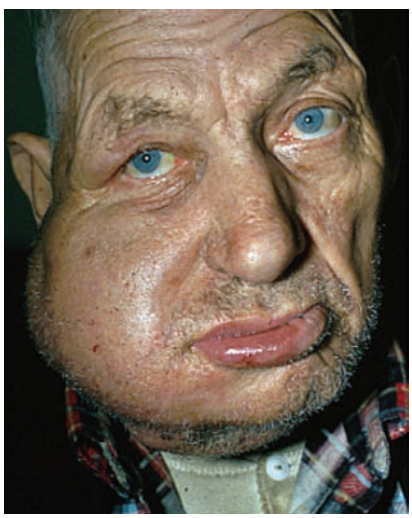
ADENOID CYSTIC CARCINOMA

Figure 8-25

Age: Middle-aged adults
Sex: Slight female predilection

CLINICAL FEATURES

Adenoid cystic carcinoma or cylindroma occurs more frequently in adults than in children. Unlike other malignant tumors of the salivary glands, it is just as likely to be encountered in the submandibular as in the parotid gland. The tumor mass is firm or indurated, often fixed, and does not necessarily grow rapidly. Unlike benign tumors, pain is often a symptom. In the parotid gland, facial nerve paralysis is encountered in nearly one third of the patients. When the tumor lies in close proximity to the overlying skin, erythema, telangiectasia, and ulceration may be seen. The tumor metastasizes to regional cervical nodes and distantly by hematogenous spread with about equal frequency. A feature typical of adenoid cystic carcinoma is its slow rate of metastasis. Many tumors have been known to manifest metastatic foci 10 or 15 years after treatment.



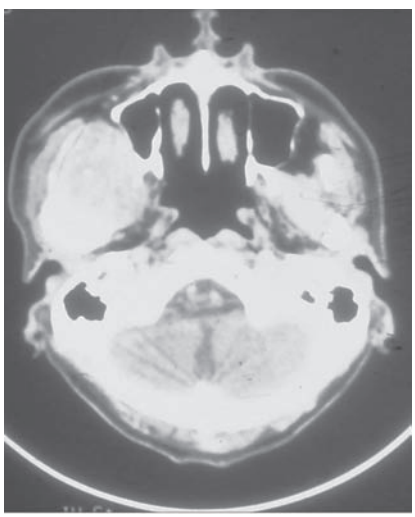


FIGURE 8-25
Adenoid cystic carcinoma of the parotid gland appearing as an indurated erythematous mass below the ear lobe.

MICROSCOPIC FEATURES

The tumor cells are cuboidal, uniform, and hyperchromatic. Pleomorphism is uncommon. The cells are arranged in cords, solid sheets, or, typically, a multicystic honeycombed or cribriform pattern. The cystic areas contain a basophilic secretion product; the outer margin of the tumor islands, in the basal lamina region, evince a thickened hyaline rim. Tumor cells show a tendency for invasion of perineural lymphatic vessels. The leading margins lack encapsulation, and invasion of contiguous tissues is a constant finding. Histologic grading has been undertaken whereby the typical cribriform pattern is grade I, cribriform with admixed solid sheets is grade II, and basaloid or anaplastic predominance is grade III.

DIFFERENTIAL DIAGNOSIS

Because cylindromas are not always solidly fixed, they may simulate benign salivary neoplasms and mesenchymal tumors. When indurated and fixed, they must be differentiated from other malignant salivary tumors such as mucoepidermoid carcinoma, acinic cell carcinoma, and adenocarcinoma. Microscopic examination is required to make the diagnosis.

TREATMENT

Depending on location, total parotidectomy or excision of the entire submandibular gland is mandatory. If the gland capsule is invaded, inclusion of adjacent tissues is necessary. Postoperative radiation therapy is recommended. In-continuity neck dissection should be performed when nodes are palpable; because hematogenous spread is frequent, chest radiographs must be obtained. Twenty percent of patients with major gland tumors exhibit nodal metastasis, whereas 50% present with, or eventually develop, distant metastases. The recurrence rate is high (over 50%) when wide excision (not gland extirpation) is performed. The determinate 5-year survival is about 30%; 10-year survival, 20%; and 15-year survival, 10%. Histologic grading is not highly correlated with prognosis. Recurrent disease is usually managed by radiation therapy in conjunction with hyperthermia.

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MUCOEPIDERMOID CARCINOMA

Figure 8-26

Age: Middle-aged adults
Sex: Slight female predilection

CLINICAL FEATURES

Mucoepidermoid carcinoma is most common in adults; however, a significant number of cases involve children. The parotid gland is by far the most frequent site of origin. The tumors are divided microscopically into low- and high-grade varieties. Low-grade tumors are cystic and may be soft and compressible on palpation, whereas the more cellular high-grade lesions are often fixed and indurated. The skin overlying a superficially oriented tumor may be ulcerated, erythematous, and telangiectatic. Low-grade tumors

have metastatic potential if left untreated, yet as a group the prognosis is good when treatment is adequate. High-grade tumors show a more rapid growth rate and metastasize by both lymphatic and hematogenous routes. It should be noted that nearly 15% of patients have other salivary primaries or cancer of other organs.

MICROSCOPIC FEATURES

Low-grade tumors show a tendency for demarcation but lack a capsule. The tumor nests show large cystic spaces lined by stratified squamous epithelium, columnar ductal cells, and mucus-secreting cells. Pleomorphism is not a feature. High-grade tumors contain a preponderance of epidermoid cells with a low population of mucous cells. Cyst formation is less frequent, with a tendency for tumor cells to grow in sheets. Clear cells are commonly seen admixed with the epidermoid component. In fact, some tumors are predominantly clear cell tumors and closely resemble renal cell carcinoma. Cytophotometric analysis can differentiate diploid from atypical chromatin, the latter predicting an unfavorable course. Rarely, a pure epidermoid carcinoma arises from salivary epithelium.

DIFFERENTIAL DIAGNOSIS

Cystic or low-grade mucoepidermoid carcinomas are soft, compressible, and often demarcated and movable. In these instances, clinical differentiation from pleomorphic adenoma and other benign tumors is impossible. Indurated fixed carcinomas are clinically identical to other salivary adenocarcinomas. Biopsy is necessary to obtain a definitive diagnosis.

TREATMENT

Surgical removal of the entire gland with the tumor is required for both low- and high-grade tumors. Nearly one third of both varieties recur after simple excision. Nodal metastases are observed at admission in 30% of patients with parotid tumors and over 50% when the tumor arises in the submandibular gland. According to

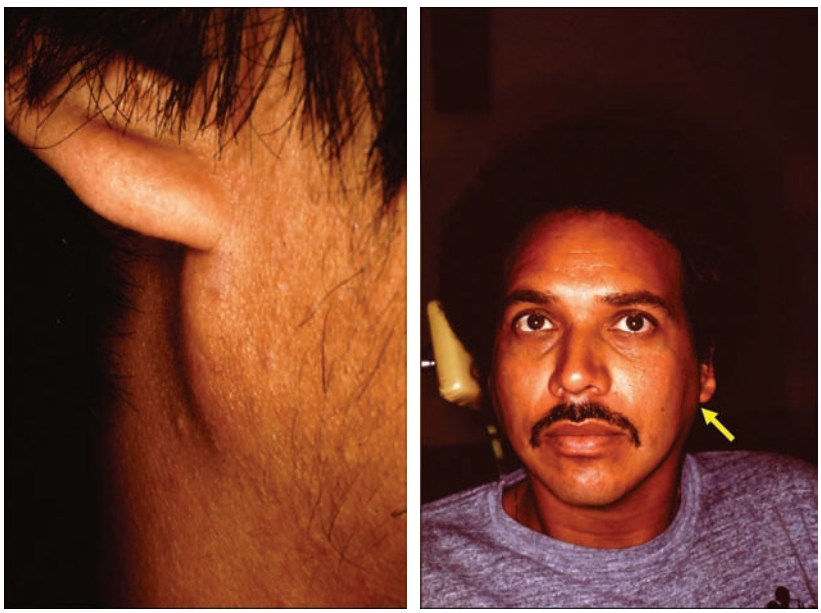

FIGURE 8-26
Nodular mass of parotid representing a mucoepidermoid carcinoma.

histologic grade, less than 10% with low-grade tumors present with positive nodes, whereas almost 60% of patients with high-grade tumors exhibit positive palpable nodes. If palpable nodes are present, a neck dissection should be performed. Radiation therapy is not as effective as surgery in obtaining a cure. Five-year survival for low-grade tumors is good, exceeding 90%. Five-year survival for high-grade tumors is less than 50%. Ten-year survival rates are lower, but the precipitous decrease seen in other salivary malignancies is not a feature of mucoepidermoid carcinoma.

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ACINIC CELL CARCINOMA

Figure 8-27

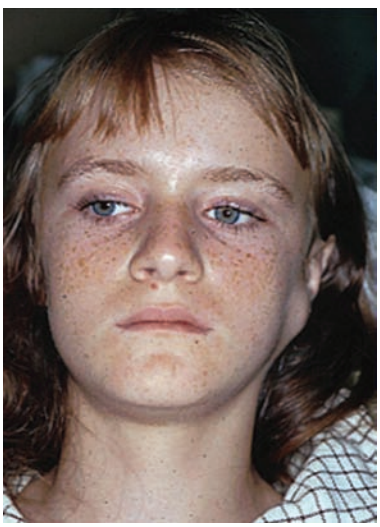
Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Acinic cell carcinoma occurs primarily in the substance of the parotid gland, appearing as a firm nodule, which may be fixed or somewhat movable. Vague pain is often a symptom, as is some degree of facial muscle weakness on the affected side. The duration is often long, with a history of slow progressive enlargement. Despite its early indolent course, the tumor is prone to recur after simple excision and is capable of both nodal and distant metastases.

MICROSCOPIC FEATURES

Neoplastic tumor cells are arranged in acinus-like clusters, and cystic spaces are often a prominent feature. When present, these cystic cavities are lined by cells that are not ductal cell types, but have a cobblestone



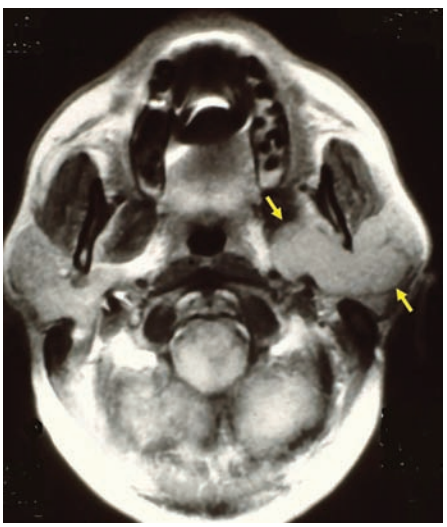


FIGURE 8-27
Acinic cell carcinoma of the parotid.

pattern and resemble those cells arranged in the acinar organoid groupings. The individual cells contain copious amounts of clear or finely granular cytoplasm or may be filled with zymogen granules. Whereas the tumor margins are often well defined, neoplastic islands extend beyond the body of the tumor mass.

DIFFERENTIAL DIAGNOSIS

Because of its slow growth potential, acinic cell carcinoma may mimic the clinical features of benign salivary neoplasms, stromal tumors, and enlarged lymph nodes. When a firm, slowly enlarging mass in the parotid is accompanied by pain and facial weakness, acinic cell carcinoma should be the primary consideration. Biopsy must be performed to secure a definitive diagnosis.

TREATMENT

Local excision, or even superficial parotidectomy, results in recurrence in over 50% of the cases, whereas total parotidectomy significantly lowers the propensity for recurrence. Overall 5-year survival exceeds 75%.

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ADENOCARCINOMA NOS AND MISCELLANEOUS MALIGNANCIES

Figure 8-28

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Adenocarcinomas not otherwise specified (NOS) do not show microscopic features that allow classification with the other salivary tumors included here. Their frequency of occurrence is on a parity with adenoid cystic carcinoma with a predilection for the parotid gland. They are indurated and fixed to adjacent tissue, may be associated with erythema and telangiecta-

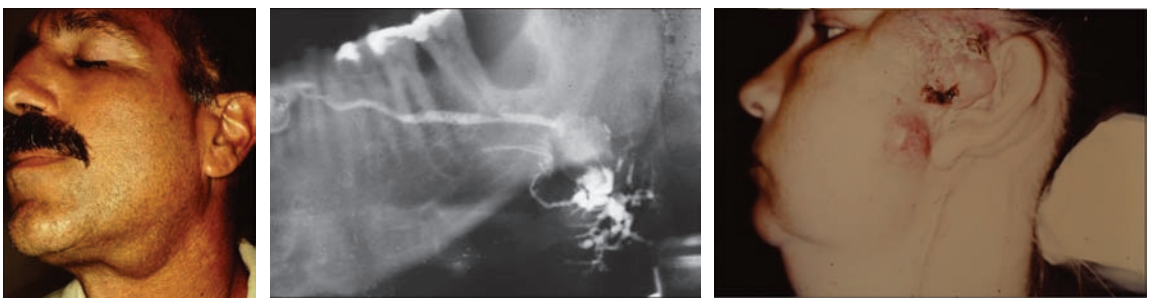

FIGURE 8-28
Adenocarcinoma, not otherwise specified (NOS). Submandibular mass, sialogram showing ductal compression and sialectasia (left and center); extension on to skin (right).

sia of the overlying facial skin, and may compress the facial nerve, thus causing paralysis. Approximately 2% of pleomorphic adenomas develop adenocarcinomatous transformation (carcinoma ex pleomorphic adenoma), are malignant from onset, or metastasize despite a benign histologic appearance. Among the adenocarcinomas not associated with mixed tumors are histologically distinct subcategories, which have been more clearly defined during the last decade. They include primary squamous cell carcinoma of salivary origin, small (oat) cell carcinoma, clear cell myoepithelioma of intercalated ducts, and papillary cystadenocarcinoma. Other malignant tumors arising in salivary glands are quite rare. Primary melanomas and sarcomas of stromal origin are included among these rarities. These uncommon salivary neoplasms all show rapid growth, fixation, and induration.

MICROSCOPIC FEATURES

Adenocarcinoma NOS is infiltrative, lacking a capsule. The histomorphology is protean. Tumor cells may be arranged in trabecular cords, sheets, or ductal formations. The cytologic features are also variable, some tumors showing hyperchromatic monomorphic cells, others being pleomorphic or anaplastic. Malignant mixed tumors (carcinoma ex pleomorphic adenoma) show the classic features of benign pleomorphic adenoma with foci of malignant transformation displaying the aforementioned characteristics. Salivary squamous cell carcinomas exhibit similar features to those of surface mucosa origin. Small (oat) cell carcinomas are characterized by solid islands of small pleomorphic hyperchromatic nuclei without overt evidence of ductal differentiation. Clear cell myoepitheliomas fail to show pleomorphism; rather, they manifest small ducts lined by eosinophilic cuboidal cells enveloped by sheets of clear cells. Papillary cystadenocarcinomas are cystic with papillary proliferations of columnar cells displaying pleomorphism, hyperchromatism, and mitotic figures.

DIFFERENTIAL DIAGNOSIS

Adenocarcinoma and the other rare salivary malignancies (epidermoid carcinoma, melanoma, and sarcoma) are indurated and fixed. They must be differentiated from the other specific malignant salivary neoplasms and malignant lymphoma by microscopic evaluation.

TREATMENT

Wide surgical excision including the entire gland is required. Neck dissection should be performed in continuity when palpable nodes are detected clinically. Adenocarcinoma NOS is moderately radiosensitive, so combined radiation therapy and surgery may be considered in the treatment plan. Chest radiographs should be procured, as adenocarcinoma shows a tendency for both regional and distant metastasis. The survival figures for most adenocarcinomas NOS are similar to those for adenoid cystic carcinoma.

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Bilateral Parotid and Submandibular Swellings

ENDEMIC PAROTITIS (MUMPS)

Figure 8-29

Age: Children
Sex: No predilection

CLINICAL FEATURES

Mumps virus, a paramyxovirus, has an incubation period of 2 to 3 weeks. The initial parotid swelling is usually unilateral; enlargement of the opposite gland follows shortly thereafter. Frequently, only one gland remains involved. The swelling is diffuse and soft and causes elevation of the ear lobe. Submandibular involvement is also common. The swelling is accompanied by moderate-to-severe pain. An exudate may be expressed from the parotid duct in some cases, but not always. Sour foods are intolerable, eliciting severe pain. Patients manifest other signs of infectious disease, including malaise, headache, and fever. The virus is not limited to salivary tissue; pancreatitis and meningitis are complications, and orchitis may lead to sterility in males. Orchitis develops within 3 to 5 days after parotid swelling if spread to the testes occurs.

FIGURE 8-29
Endemic parotitis showing diffuse parotid enlargement in a febrile child.

MICROSCOPIC FEATURES

The parotid ducts are dilated and contain secretion products with inflammatory cells. The acini manifest degenerative changes such as degranulation and vacuolization with a mononuclear inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Mumps must be differentiated from bacterial or occlusive salivary inflammatory disease, the benign lymphoepithelial lesions (Sjögren's syndrome, Mikulicz's disease), Heerfordt's syndrome, and parotid lymphoma. Most of these entities occur in adults, whereas mumps is more common in childhood. Serum amylase levels are elevated early in mumps, and leukopenia is a common finding.

TREATMENT

The patient is infectious and should be confined to bed. A bland diet with added liquids and prescription of antipyretics and analgesics are recommended. Because of the possibility of orchitis and meningitis, the patient's physician should be consulted.

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SJÖGREN'S SYNDROME

Figure 8-30

Age: Middle-aged adults
Sex: Significant female predilection

CLINICAL FEATURES

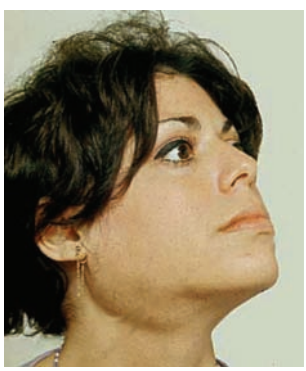
Sjögren's syndrome is a collagen disease of the rheumatoid group of immunopathologic disorders. The syndrome triad consists of xerostomia, xerophthalmia, and rheumatic joint disease. The parotid glands show slight to moderate enlargement bilaterally, and milking the glands fails to elicit flow from the ducts. Pain is occasionally a symptom. The mouth feels dry, the oral mucosa is often erythematous, and eventually cervical dental decay develops. The conjunctivas are also dry because of the lacrimal gland involvement with cessation of secretion, producing keratoconjunctivitis sicca. Classic signs of rheumatoid arthritis, including joint pain and swelling, are present in most patients. All three components of the syndrome are not necessarily coexistent in any one patient. Sjögren's syndrome may accompany other collagen-immune diseases such as lupus erythematosus, polyarteritis nodosa, and scleroderma, such instances being referred to as secondary Sjögren's syndrome. Malignant lymphoma is more common among patients with Sjögren's syndrome, and the lymphoid malignancies are usually found within the gland and in extrasalivary locations.

MICROSCOPIC FEATURES

The acini are replaced by diffuse infiltrative sheets of well-differentiated small and large lymphocytes. Ductal elements are not destroyed but manifest cellular proliferation in the form of epimyoepithelial islands. This histology is referred to as *autoimmune lymphoepithelial sialadenitis*. Fluorescence antibody studies show immunofluorescence of ductal epithelium. Intraoral minor salivary glands show multifocal lymphoid aggregates dispersed throughout the gland lobules and in periductal arrangement. These infiltrates are quantitatively graded from 0 to 4+, whereby 1+ is suspected and 2+ or above is typical for the syndrome.

DIFFERENTIAL DIAGNOSIS

Diffuse enlargement of the parotid glands in Sjögren's syndrome is clinically similar to that seen in Mikulicz's disease, Heerfordt's syndrome, parotid lymphoma, and metabolic sialadenosis. The occurrence in females and existence of other components of the syndrome are essentially classic features of



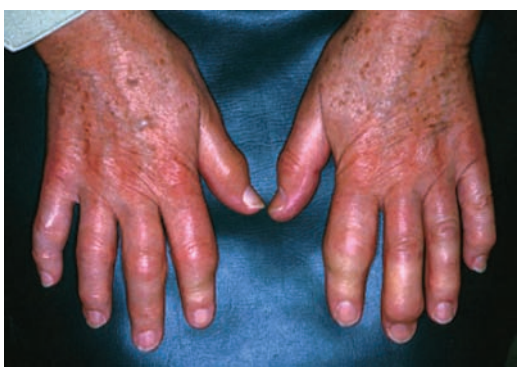


FIGURE 8-30
Bilateral parotid enlargement associated with xerostomia, xerophthalmia, and rheumatoid arthritis characterizing Sjögren's syndrome.

Sjögren's syndrome. The disease may be confirmed by evaluation of parotid flow rates, use of the Shirmer lacrimation test, and evaluation of serum for the presence of rheumatoid (RA) factor as well as specific autoantibodies (anti-Ro, anti-La). Sialograms reveal multifocal microsialectasia with a "birdshot" appearance of contrast medium retention. Labial gland biopsy is also useful in diagnosis.

TREATMENT

Patients with Sjögren's syndrome should be thoroughly evaluated for the presence of malignant lymphoma and other collagen diseases. Their care should be managed by a physician. The disease is treated with steroids or other immunosuppressive therapeutic agents. Rituximab immunotherapy offers some degree of control particularly when some exocrine function is still present.

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MIKULICZ'S DISEASE

Figure 8-31

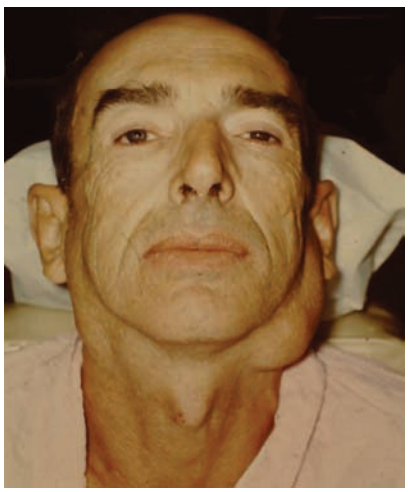
Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Mikulicz's disease is a benign lymphoepithelial lesion of the parotid and lacrimal glands that occurs in males and is probably a localized form of Sjögren's syndrome. The disease in males is not associated with rheumatoid arthritis. The parotid swellings are soft, movable, and painless. Xerostomia is present, yet is rarely as severe as in women with Sjögren's syndrome. The term Mikulicz's disease is synonymous with localized benign lymphoepithelial lesion and should not be confused with *Mikulicz's syndrome,* which refers to parotid and lacrimal enlargement due to malignant lymphoma.

MICROSCOPIC FEATURES

The microscopic changes in Mikulicz's disease are identical to those encountered in Sjögren's syndrome with the addition of



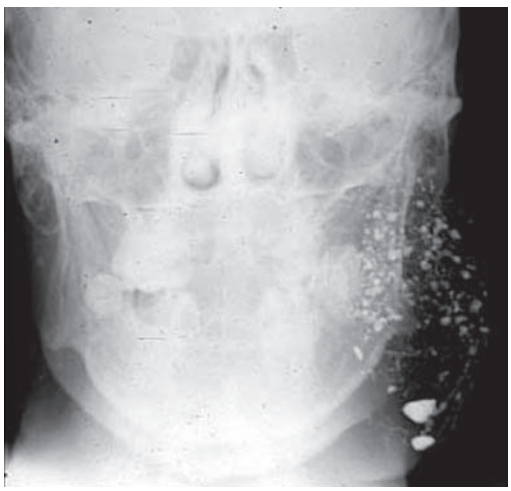


FIGURE 8-31
Bilateral benign lymphoepithelial lesions of the parotid in Mikulicz's disease; sialogram showing a lack of ductal arborization in Mikulicz's disease.

IgG4+ plasma cells and elevated IgG4 levels in serum.

DIFFERENTIAL DIAGNOSIS

Mikulicz's disease is differentiated from Sjögren's syndrome on the basis of gender and limitation of extent, rheumatoid disease and systemic autoimmune conditions being absent. In all probability, both diseases are merely variations of the same process. Other disorders that must be considered in the differential diagnosis are malignant lymphoma, Heerfordt's syndrome, disseminated tuberculosis, and metabolic sialadenosis. Parotid biopsy discloses the classic benign lymphoepithelial morphology. Sialographic changes are identical to those seen in Sjögren's syndrome.

TREATMENT

Moderate doses of steroids (e.g., 20-30 mg prednisone daily) may help control the immune process. The patient may require the use of a water bottle periodically to relieve xerostomia.

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SARCOID SIALADENITIS AND HEERFORDT'S SYNDROME

Figure 8-32

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Sarcoidosis of the salivary glands occurs in less than 5% of patients suffering from

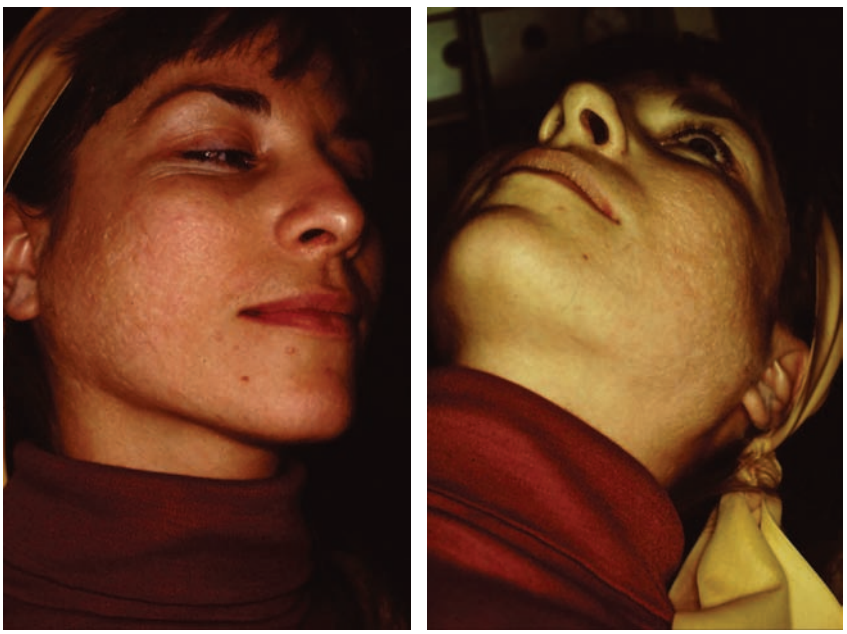

FIGURE 8-32
Parotid swelling in sarcoidosis.

the generalized form of the disease. When the sarcoid granulomas are present within the salivary tissue, parotid and lacrimal enlargement and induration are the primary signs. The enlarged glands are firm to palpation and free from pain, and the patients are often slightly febrile. The enlargement evolves slowly, requiring many months to manifest clinically obvious signs. It is usually bilateral but rarely symmetric. Diminished flow of saliva from the involved glands is a common finding, and if the granulomatous infiltration is extensive, xerostomia with widespread cervical caries may be seen. Sialography discloses pathologic findings with deficient secondary and tertiary ducts and dye pooling, which yields a clouded pattern that represents terminal ectasia. Extensive lacrimal infiltration leads to xerophthalmia and conjunctivitis. Other manifestations of generalized sarcoidosis, such as hilar node enlargement on chest radiographic examination, are frequently identifiable. The cause for this tuberculoid granulomatous disease is unknown. It is most commonly encountered in middle European countries.

MICROSCOPIC FEATURES

Sarcoid sialadenitis is characterized by multifocal granulomatous infiltration of the gland. The epithelioid histiocytes are admixed with multinucleated giant cells, and the former are arranged in fasciculated whorls. The granulomas are devoid of caseation necrosis.

DIFFERENTIAL DIAGNOSIS

The enlargement seen in Heerfordt's syndrome may clinically resemble that seen in Sjögren's syndrome, Mikulicz's disease, tuberculosis, or lymphoma. A search for other signs of generalized sarcoidosis should be pursued. Serum calcium levels are often elevated. Biopsy reveals the features of noncaseating granulomas. The Kveim test uses specific antigen to detect delayed hypersensitivity and is positive in most cases. Fine-needle aspiration can yield diagnostic findings.

TREATMENT

Because generalized sarcoidosis is often present, a thorough physical examination is required. The disease is treated with steroids or other immunosuppressive agents and should be managed by an internist or general physician.

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TUBERCULOSIS

Figure 8-33

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Both the parotid and submandibular glands may show involvement with *Mycobacterium tuberculosis*. Diffuse enlargement occurs in conjunction with disseminated or miliary tuberculosis, along with extensive pulmonary disease. The enlargement may be unilateral or bilateral and is more common in the parotid gland. Pain and fistula formation are unusual findings. As in the case of cervical node scrofula, primary tuberculosis in the absence of pulmonary infection may develop in parotid lymph nodes. In this form of the disease,

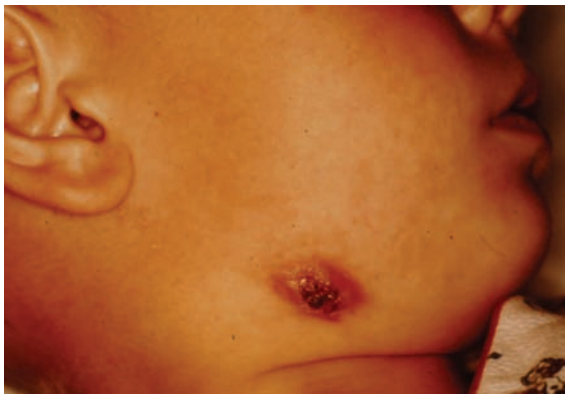

FIGURE 8-33
Tuberculous granulomas in parotid lymph nodes and cutaneous fistula.

the enlargement is unilateral and manifests as a firm circumscribed tumefaction. A drainage tract may appear on the skin. The tonsil or pharynx is the probable portal of entry in this form.

MICROSCOPIC FEATURES

Tuberculosis granulomas with epithelioid histiocytes and Langhans giant cells are present. Zones of caseous necrosis are often but not invariably present. Focal abscess formation with neutrophilic infiltrates is often present, particularly in the localized primary form.

DIFFERENTIAL DIAGNOSIS

The firm parotid swelling of disseminated tuberculosis must be differentiated from Mikulicz's disease, Sjögren's syndrome, Heerfordt's syndrome, and malignant lymphoma. Sialography reveals lakes of pooled contrast medium and foci of ductal stenosis. Tuberculin skin tests and chest radiographs are required to obtain a definitive diagnosis and determine the extent of disease. The localized form of intrasalivary tuberculosis must be differentiated from salivary tumor, mesenchymal neoplasms, or sclerosing sialadenitis. Biopsy discloses specific granulomatous inflammation. Acid-fast stains demonstrate the bacilli.

TREATMENT

Isoniazid therapy is the treatment of choice for typical tubercular lesions.

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HIV SALIVARY DISEASE (DIFFUSE INFILTRATIVE LYMPHOCYTOSIS SYNDROME)

Figure 8-34

Age: Children, young adults
Sex: No predilection

CLINICAL FEATURES

Bilateral salivary enlargement has been noted in 10% to 15% of children with AIDS. Although most children contract the HIV infection perinatally, some have acquired the infection from contaminated blood products. Adults can also manifest HIV salivary disease. In both children and adults, the swellings are bilateral and somewhat firm to palpation; induration is not generally a feature. The overlying skin is of normal color without ulceration, and pain is not a common complaint. Some patients present with a Sjögren's-like disease in which the parotid swellings are associated with xerostomia. When the glands are evaluated with CT or MRI scanning, soft tissue enlargements are seen in the gland proper and are riddled with multicystic radiolucent foci.

HISTOLOGIC FEATURES

The microscopic changes accompanying HIV-associated salivary disease are protean and are not well defined, particularly in children. In adult patients who have been examined, diffuse lymphocytic infiltration by CD8 lymphocytes is seen along with follicular hyperplasia and epithelially lined cystic spaces, the latter two features being different than those seen in benign lymphoepithelial lesion. Some patients with salivary enlargement, however, particularly adults, suffer from non-Hodgkin's lymphoma.

DIFFERENTIAL DIAGNOSIS

The enlargement seen in HIV infection simulates the other bilateral salivary enlargements listed here. Certainly, suspicion should be heightened among individuals that constitute HIV-risk groups. CT or MRI may be useful owing to the unique multicystic nature of the enlargement. Lower lip minor gland biopsy may show lymphocytic infiltrates akin to those seen in Sjögren's syndrome. Biopsy should be performed in adult patients because lymphoma does occur in AIDS-risk patients.

TREATMENT

There is no treatment for HIV salivary disease. In some cases, the enlargement diminishes once patients are placed on antiretroviral medications. Unsightly, large swellings may be surgically excised. When dry mouth is extant, prevention of dental caries is essential with institution of a topical fluoride regimen.

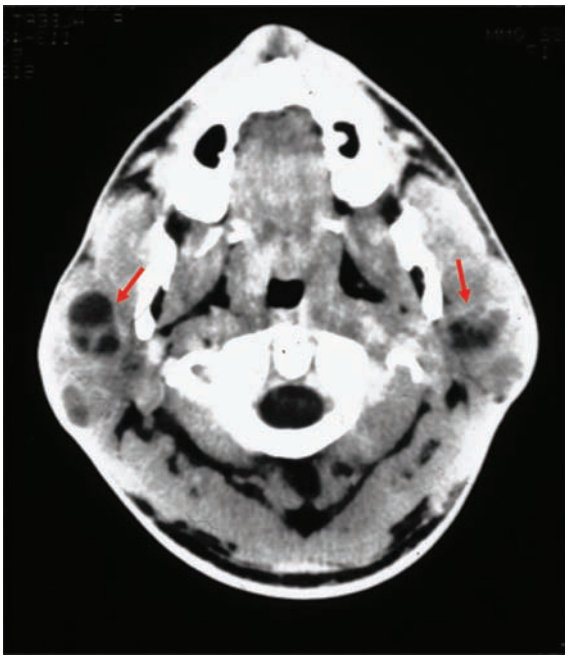

FIGURE 8-34
Cystic parotid swelling in HIV sialadenitis.

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DYSGENETIC CYSTS OF THE PAROTID

Figure 8-35

Age: Children
Sex: Females

CLINICAL FEATURES

Dysgenetic cysts are developmental cysts that arise from salivary duct epithelium. They appear as bilateral soft fluctuant parotid swellings, although occasional

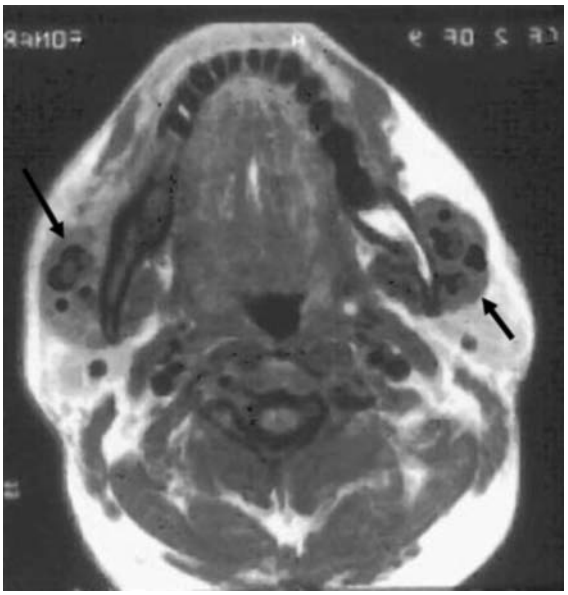

FIGURE 8-35
Bilateral dysgenetic cysts of the parotid in an adult.

unilateral instances have occurred. On sialograms pockets of dye are retained and on MRI a polycystic pattern is seen within the parotid parenchyma.

MICROSCOPIC FEATURES

Multiple dilated cysts are seen and are lined by cuboidal cells that are reminiscent of intercalated ducts of normal glands. There is no inflammatory element present.

DIFFERENTIAL DIAGNOSIS

HIV salivary disease is included in the differential diagnosis. Otherwise, there are very few disorders that cause bilateral parotid swellings in children.

TREATMENT

No treatment is necessary unless a bacterial sialadenitis occurs for which antibiotics and ductal dilation are recommended.

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METABOLIC SIALADENOSIS

Figure 8-36

Age: Middle-aged and elderly adults
Sex: Female predilection

CLINICAL FEATURES

Metabolic sialadenosis is not a single specific disorder but, rather, an alteration both clinically and functionally of the salivary glands that accompanies a variety of generalized metabolic disorders. The most common of these diseases are hormonal imbalances (including changes evolving in conjunction with menopause, pregnancy, and menarche), alcoholism, and a salivary manifestation of diabetes mellitus. Similar changes may also be seen in hypothyroidism, cirrhosis, and uremia. In all of these disorders, the parotid is the salivary gland most often affected. Preauricular soft movable swellings are seen bilaterally in sex hormonal sialadenosis, whereas the swellings are more prominent below and behind the mandibular angle in diabetic sialadenosis. Salivary flow is diminished, there is no pain, and the patients are afebrile.

MICROSCOPIC FEATURES

Both acinar and ductal cells appear edematous with cloudy swelling. Degranulation of zymogen secretory granules is a prominent

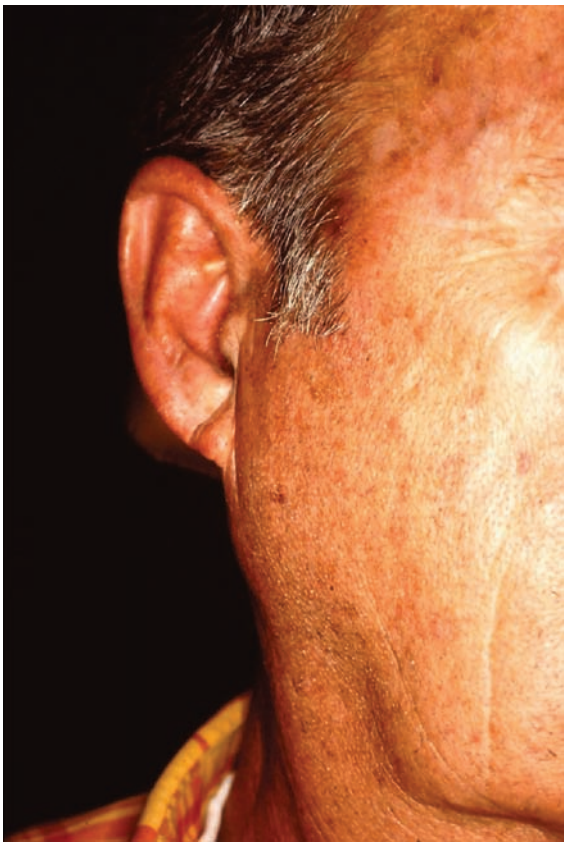

FIGURE 8-36
Metabolic sialadenosis associated with diabetes.

feature, and extensive fatty infiltration of the stroma is observed.

DIFFERENTIAL DIAGNOSIS

The slow-growing soft enlargement seen in metabolic diseases with salivary involvement is unusual; however, the disease must be differentiated from other chronic sialadenopathies manifesting bilateral enlargement such as Sjögren's syndrome, Mikulicz's disease, Heerfordt's syndrome, tuberculosis, and lymphoma. Sialograms may appear normal; however, close scrutiny usually discloses a filamentous, fine network of ducts. Analysis of parotid electrolytes is helpful, as potassium levels are elevated and sodium values are decreased in sialadenosis. A thorough history and physical evaluation are required to uncover the underlying, coexisting metabolic disorder.

TREATMENT

Treatment consists of correcting the underlying metabolic disturbance and should be managed by a physician.

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Midline Neck Swellings

THYROGLOSSAL TRACT CYST

Figure 8-37

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Derived from epithelium that coursed through the neck during thyroid organogenesis, the thyroglossal tract cyst may be localized anywhere between the foramen caecum at the base of the tongue and the mature thyroid gland in the lower midline of the neck. The cyst is firm or soft and compressible, freely movable (unless entwined with the hyoid bone), and frequently develops a fistula. Most are located below the hyoid bone. If localized in the tongue or hyoid region, dysphagia may be a symptom. Rarely, thyroid carcinoma may arise from remnants of the tract.

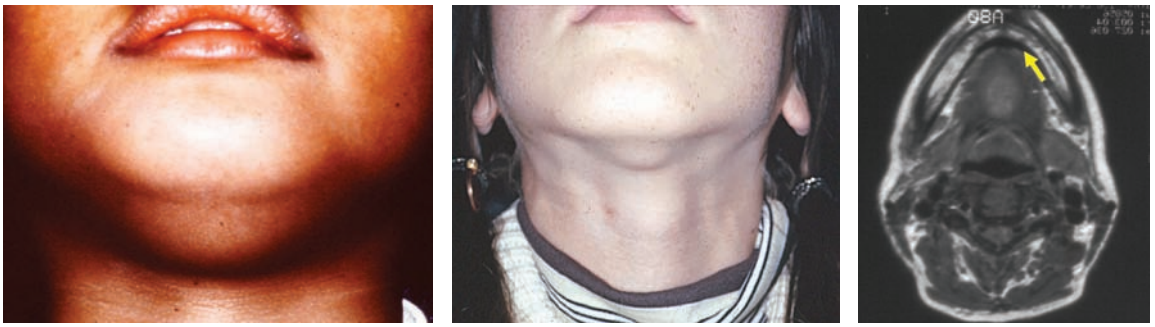

FIGURE 8-37
Thyroglossal tract cysts appearing as a small nodule in the flexure of the midline of the neck.

MICROSCOPIC FEATURES

The cyst is lined by stratified squamous or respiratory epithelium. The fibrous wall may evince a mild mononuclear inflammatory cell infiltrate, and both mucous glands and thyroid follicles can be observed.

DIFFERENTIAL DIAGNOSIS

Cysts located high in the midline of the neck must be differentiated from the dermoid cyst; if they are located low in the neck, goiter and thyroid neoplasms must be considered in the differential diagnosis.

TREATMENT

Simple excision is the treatment of choice. When the cyst is intimately associated with the hyoid bone, it may be necessary to remove a portion of the bone to ensure complete excision and avoid recurrence.

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GOITER

Figure 8-38

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Goiter refers to benign thyroid enlargement. Many forms exist, including iodine deficiency goiter, adenomatous goiter, and hyperthyroidism with exophthalmos (Graves' disease). When hypothyroidism accompanies goiter, the patients are dull and lethargic, and if the condition is severe, they show diffuse myxedema of the soft tissues. The enlargement, located below the thyroid cartilage in the midline, is firm or compressible, movable, and in adenomatous goiter, multinodular. In Graves' disease, the metabolic rate is elevated, the patients are nervous and tense, and the goitrous swelling lacks nodularity, being diffuse. Large goiters in elderly patients may cause airway obstruction.

MICROSCOPIC FEATURES

The histologic findings vary depending on the type of goiter. In iodine deficiency and adenomatous goiter, the thyroid follicles are

enlarged and impacted with thyroglobulin. In Graves' disease, the follicular epithelium shows hyperplasia.

DIFFERENTIAL DIAGNOSIS

The goitrous conditions must be differentiated from one another on the basis of clinical signs and symptoms. Metabolic studies evaluating ^{131}iodine uptake and radioactive thyroid scans are useful, as is evaluation of serum T_3 and T_4 levels. The diffuse nature of the swelling usually allows differentiation from tumor; however, when the swelling is small or located just lateral to the midline, neoplasia in the thyroid gland must be considered.

TREATMENT

Some goiters can be treated surgically, others medically. Referral to an internist or endocrinologist is recommended.

Additional Reading

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THYROID NEOPLASIA

Figure 8-39

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Thyroid neoplasms may be benign adenomas or malignant adenocarcinomas. They are classified according to their histomorphology. The benign adenomas arise in one pole of the gland so that they are located slightly lateral to the laryngeal cartilage. The tumors are generally small and may not be visually obvious; rather, they are often detected by palpation. They are soft or slightly firm and movable. Adenocarcinomas manifest a similar localization, but tend to be firm or indurated and fixed to adjacent tissues. They, too, may be small

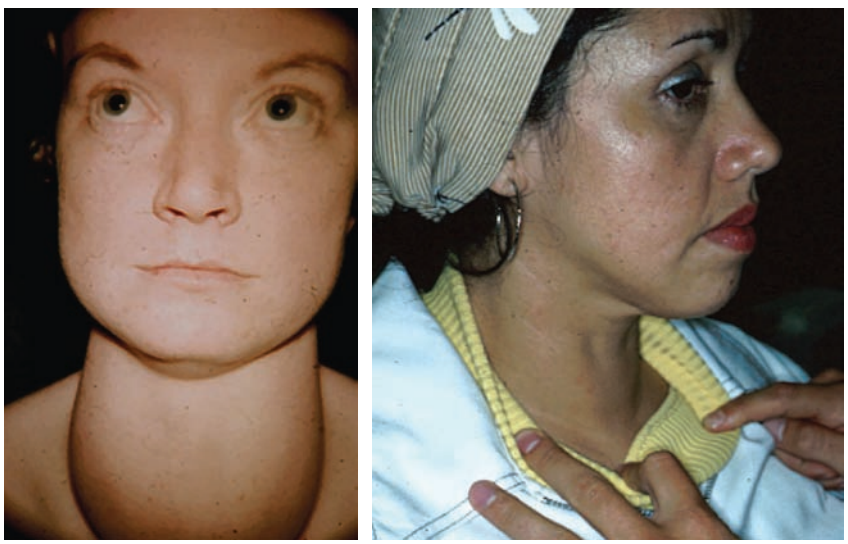

FIGURE 8-38
Diffuse swelling in the thyroid area representing nontoxic goiter (right) and Graves' disease with exophthalmos (left).

when first detected. Indeed, cervical node metastasis may be detected before a noticeable thyroid enlargement presents itself.

MICROSCOPIC FEATURES

It is beyond the scope of this book to outline the microscopic features of thyroid tumors. The more common benign neoplasms are fetal and follicular adenomas. Papillary carcinoma is the most common form of thyroid cancer. Medullary carcinoma may arise in conjunction with oral neuromas and other endocrine neoplasms as a component of the neuropolyendocrine syndrome.

DIFFERENTIAL DIAGNOSIS

Neoplastic swellings in the thyroid region must be differentiated from one another by microscopic evaluation. Rarely, they must be differentiated from goiter.

TREATMENT

Most thyroid tumors are treated surgically. Those that take up iodine may be treated with ^{131}iodine radiotherapy. An oncologic surgeon or otolaryngologist should manage the care of patients with thyroid neoplasms.

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DERMOID CYST

Figure 8-40

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The dermoid cyst is usually encountered in the oral floor. When it arises inferior to the mylohyoid muscle, it protrudes inferiorly, as an extraoral swelling in the upper midline of the neck in the submental flex-

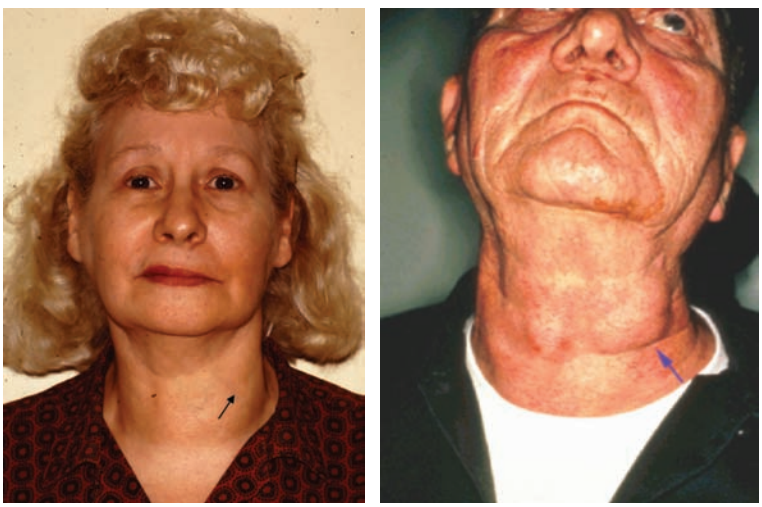

FIGURE 8-39
Thyroid adenoma (left); papillary carcinoma (right).

ure area. The mass is movable and has a doughy consistency on palpation.

MICROSCOPIC FEATURES

The cyst is lined by keratinizing stratified squamous epithelium. Skin adnexal tissues such as sebaceous glands, sweat glands, and hair follicles are present within the fibrous wall. When all three germ layers can be demonstrated, the lesions are termed *teratoid cysts.*

DIFFERENTIAL DIAGNOSIS

A superiorly located thyroglossal tract cyst may simulate the dermoid cyst. Sebaceous cysts should also be considered in the differential diagnosis.

TREATMENT

Simple excision using an extraoral approach is recommended for dermoid cysts located below the mylohyoid muscle.

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Growths and Swellings of the Facial Skin

NEVI

Figure 8-41

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Moles or nevi are the most common swellings of the facial skin. They are usually less than 1 cm in diameter, may be multiple, and are either brown, blue, or nonpigmented. Most importantly, benign nevi are symmetrically round or oval with smooth nonjagged borders. Once they reach a certain size, they stop growing.

MICROSCOPIC FEATURES

Nevi may be junctional, compound, or intradermal. The nevus cells contain variable amounts of melanin pigment if clinically pigmented. Nonpigmented nevi are composed of sheets and theques of polygonal epithelioid cells devoid of melanin granules. A unique lesion, common on the face, is the deep penetrating nevus, which shows

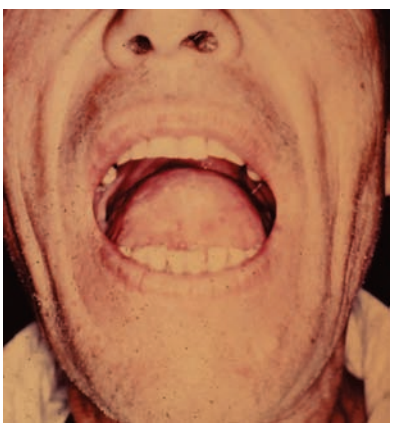

FIGURE 8-40
Midline swelling of neck and submandibular region representing a dermoid cyst; contrast media showing cystic wall.

melanoma-like cells that extend deeply into the dermis.

DIFFERENTIAL DIAGNOSIS

Pigmented nevi are differentiated from melanoma on the basis of history and clinical appearance. A long duration with arrested growth and lack of ulceration are indicators of a benign lesion. Should a pigmented lesion continue to grow or ulcerate, a biopsy is indicated. Nonpigmented nevi must be differentiated from basal cell carcinoma, adnexal skin tumors, and sebaceous cysts. Basal cell carcinomas show progressive growth and often ulcerate. If they are not ulcerated, they usually show surface telangiectasia.

TREATMENT

Skin nodules that are pigmented or nonpigmented and lack ulceration or telangiectasia, if they have persisted unchanged for many years, are probably nevi. No treatment is required. Excisional biopsy is recommended if recent growth has occurred, if the lesion is ulcerated, or if surface telangiectasia is encountered.

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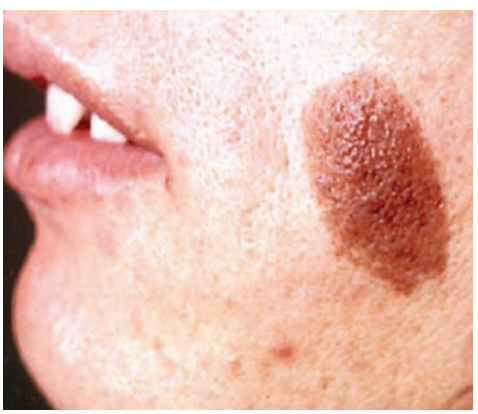
SEBACEOUS CYST

Figure 8-42

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Sebaceous and epidermoid cysts are derived from the pilosebaceous apparatus. Similar cysts result from implantation of surface epithelium after a cut or laceration. The cysts are often quite superficial and small; however, they can exceed 2 to 3 cm in diameter. When superficial, they have a pearly, blanched quality. Larger cysts are fixed to the dermis yet can be moved about over the subcutaneous tissues and are compressible; they have a doughy consistency. When multiple sebaceous cysts are encountered, work-up for Gardner's syndrome should be undertaken.



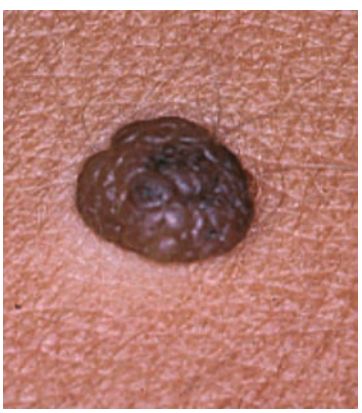


FIGURE 8-41
Benign nevi with smooth borders.

MICROSCOPIC FEATURES

The lumen is filled with an eosinophilic caseous material, and shredded keratin fibers desquamate from the keratinizing stratified squamous epithelium. The wall is often ruptured with keratin and epithelial cells embedded within the fibrous wall. A foreign-body reaction with multinucleated giant cells is seen under these circumstances. A specific type of cyst is derived from the hair follicle, which contains basophilic epithelial cells and luminally oriented ghost cells (eosinophilic epidermal cells with vacuolated spaces in place of nuclei). This specific type of pilar cyst is known as the calcifying epithelioma of Malherbe.

DIFFERENTIAL DIAGNOSIS

Sebaceous and epidermoid cysts, particularly when superficial, resemble basal cell carcinoma, adnexal skin tumors, or benign mesenchymal tumors.

TREATMENT

Surgical enucleation of the cyst is the treatment of choice, although a minimal-incision technique has proven successful.

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SEBORRHEIC KERATOSIS

Figure 8-43

Age: Middle-aged and elderly adults
Sex: No predilection

CLINICAL FEATURES

Seborrheic keratoses usually occur in multiples. They are focal papular or nodular lesions with a brown waxy character, so superficial that they appear to have been "stuck on" to the skin. They are not encountered in young individuals, but become more numerous with advancing age. Etiology is unknown.

MICROSCOPIC FEATURES

The epithelium evinces acanthosis that is exophytic, with a smooth surface. Invagination of epidermal cells into the dermis is not a feature. The acanthotic epithelium may contain keratin pearls and cysts or may evince a retiform pattern with accompanying dermal connective tissue papillae. Acantholysis is typically observed.

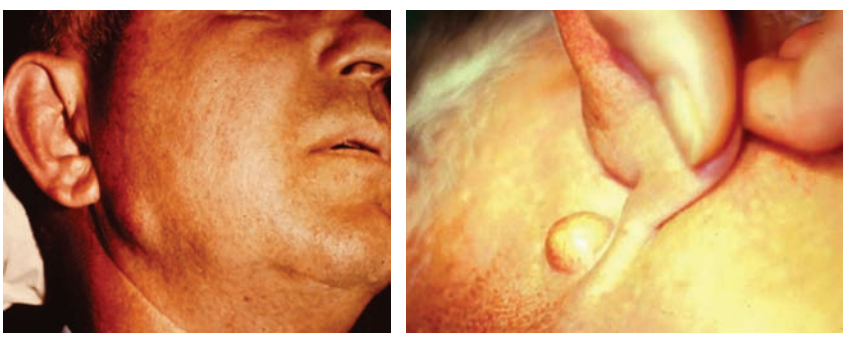

FIGURE 8-42
Sebaceous cyst of the skin.

DIFFERENTIAL DIAGNOSIS

Because of their pigmentation, seborrheic keratoses may be confused with nevi. Nevi are not as superficial, lack the waxy or oily character of seborrheic keratosis, and do not become prevalent with advancing age.

TREATMENT

No treatment is necessary. If cosmesis is a problem, the keratosis can be shaved superficially or cauterized.

Additional Reading

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ADNEXAL SKIN TUMORS

Figure 8-44

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Tumors of skin that are derived from, or differentiate along, the lines of the skin appendages commonly arise on the face. Hair follicle tumors (trichoepithelioma), sebaceous cell adenomas, and sweat gland adenomas (eccrine acrospiroma, hidradenoma) are all benign neoplasms. Malignant

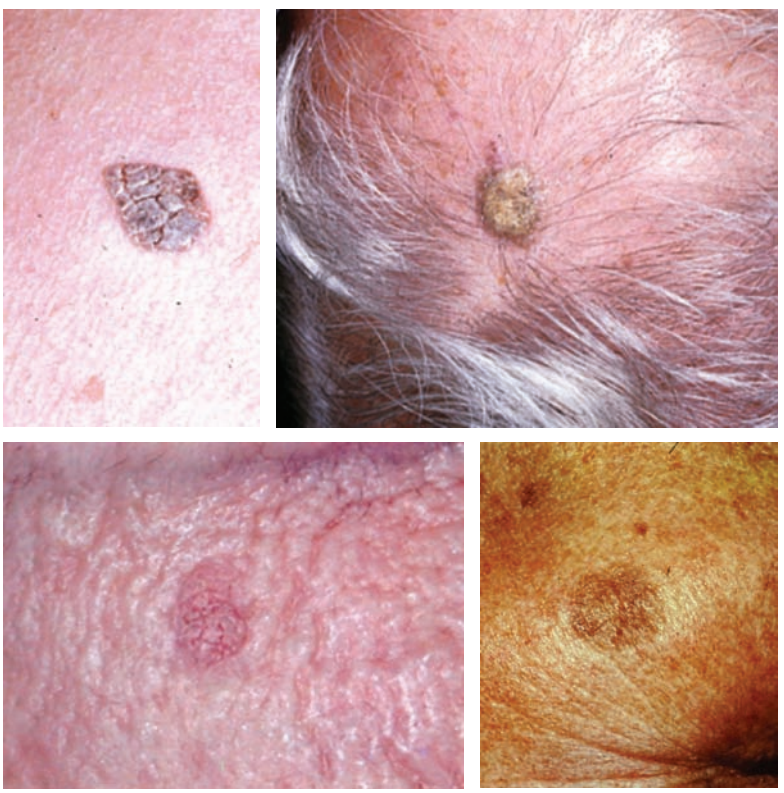

FIGURE 8-43
Scaly nodule of scalp in an elderly male representing seborrheic keratosis.

counterparts occur but are rare. The adnexal skin tumors as a group may be either uninodular or multinodular. Most are firm, painless, and nonulcerated; however, malignant varieties are often ulcerated with surface telangiectasia.

MICROSCOPIC FEATURES

The adnexal skin tumors vary considerably in their histomorphologic characteristics. They are composed of epithelial cells that differentiate along pilar, sebaceous, or adenomatoid lines.

DIFFERENTIAL DIAGNOSIS

The nodular swellings of adnexal skin tumors must be differentiated microscopically from one another. Clinically, they have features in common with basal cell carcinomas, mesenchymal dermal neoplasms, and sebaceous cysts.

TREATMENT

Surgical excision is the treatment of choice.

Additional Reading

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BASAL CELL CARCINOMA

Figure 8-45

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

The basal cell carcinoma is an aggressive yet nonmetastasizing neoplasm of the skin; rare instances of metastasis have been reported. Over 90% of all basal cell carcinomas are encountered on the skin of the upper face and forehead. The tumor may be solitary or multiple; it tends to occur in patients with fair complexions and in those who are constantly exposed to solar radiation. The early tumor may be a smooth-surfaced nodule with telangiectasia, a focal ulcer, or a nodule with central keratosis. Large lesions are ulcerative with rolled, indurated margins. Multiple basal cell tumors that show a slow growth rate or reach a given size and become static may be seen in children and

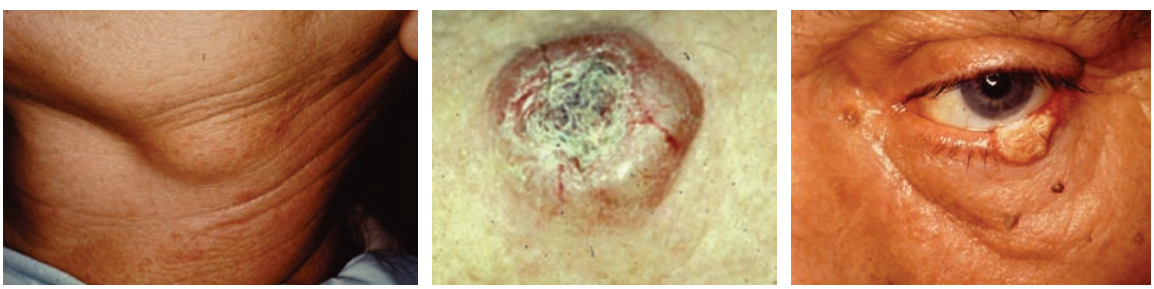

FIGURE 8-44
Adnexal skin tumors. Syringoma (top), microcystic adenocarcinoma (bottom left), sebaceous cell carcinoma (bottom right).

young adults suffering from odontogenic keratocysts of the jaws and a bifid rib. This triad, in conjunction with other anomalies, constitutes the nevoid basal cell carcinoma syndrome.

MICROSCOPIC FEATURES

Surface epithelium shows a transition, whereby neoplastic cords and islands of hyperchromatic monomorphic basaloid-appearing epithelial cells demonstrate invasion into the dermis. The center of the neoplastic cell nests may contain keratin pearls; however, acanthotic squamous cells mimicking the normal spinous cell layer are not typically present. Adenoid forms with tubular rete-ridge cords and ductal patterns are occasionally encountered. The morphea type shows extensive desmoplasia.

DIFFERENTIAL DIAGNOSIS

Early basal cell carcinomas lacking ulceration must be differentiated from nonpigmented nevi, adnexal skin tumors, mesenchymal dermal tumors, and sebaceous cysts. Surface telangiectasia is strongly indicative of basal cell carcinoma. Larger lesions with ulceration and rolled margins must be differentiated from squamous cell carcinoma, which is significantly less prevalent on the face. Specific granulomatous infection must also be considered in the differential diagnosis. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Basal cell carcinoma requires excision with a 1-cm margin from the clinically obvious tumor. This is necessary to avoid recurrence, because the neoplasm commonly displays microscopic invasion or multicentricity that is often not visually detectable clinically. Mohs surgical technique is used to obtain clear margins.

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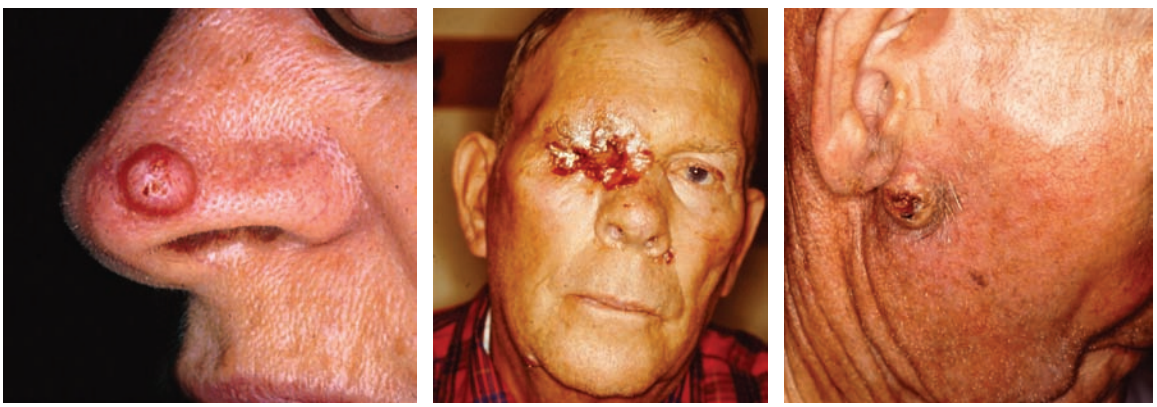

FIGURE 8-45
Basal cell carcinoma of the face showing rolled margins with central ulceration.

SQUAMOUS CELL CARCINOMA

Figure 8-46

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Squamous cancers of the face usually occur above the level of the lower lip; many arise from a preexisting actinic keratosis that has undergone dysplastic changes. The lesions are tumefactive and indurated with surface ulceration and telangiectasia. As with basal cell carcinoma, actinic radiation is a primary carcinogenic factor. Unlike basal cell carcinoma, cutaneous squamous cell carcinomas have metastatic potential, spreading regionally to the intraparotid and cervical lymph nodes. Perineural invasion may occur and lesions on the lip may spread to the mental and inferior alveolar nerve presenting with a numb lip.

MICROSCOPIC FEATURES

Surface stratified squamous epithelium shows dysplastic changes, and islands of neoplastic squamous epithelium invade the underlying dermis. Keratin pearl formation is usually seen and individual cells show hyperchromatism, pleomorphism, and mitotic activity. *Spindle cell variants* may occur and there are lesions that show acantholytic change termed *pseudoglanular* squamous cell carcinoma.

DIFFERENTIAL DIAGNOSIS

Included in the differential are basal cell carcinoma, metastatic carcinoma, adnexal carcinomas, and amelanotic melanoma. Biopsy is required for a definitive diagnosis.

TREATMENT

Wide excision is required with 1.5-cm margins, or Moh's surgery can be performed, ensuring that margins are clear. The regional nodes should be assessed clinically and by MR or positron emission tomography imaging.

Additional Reading

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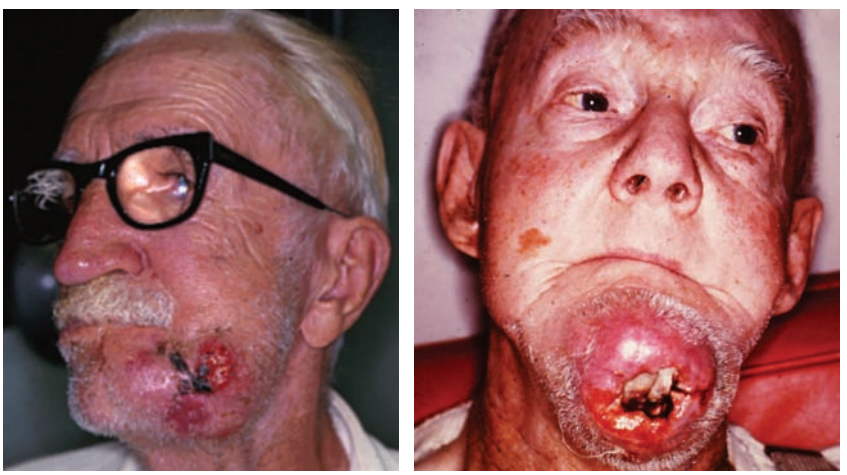

FIGURE 8-46
Squamous cell carcinoma of facial skin.

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KERATOACANTHOMA

Figure 8-47

Age: Middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

Keratoacanthoma is a benign tumor of epithelial origin. It may be solitary or multifocal. Multiple keratoacanthoma is a dominantly inherited disorder. The tumor is characterized by an elevation with rolled margins and a central keratotic core; the margins are sharply delineated. The lesion may occur anywhere, but is most frequently seen on the extremities and the face. The tumor proliferates rapidly, becomes static with regard to growth, and within 6 to 12 months spontaneously involutes, leaving a depressed scar.

MICROSCOPIC FEATURES

The histologic features are similar to those of a well-differentiated squamous cell carcinoma. A central zone composed of voluminous strata of keratin and parakeratin is observed. The spinous cell layer is thickened and rete-ridge formation is present, yet invasion of the dermis is not observed. Pathognomonic features of this tumor are identifiable at the lateral margins. The acanthotic central core shows lipping at the margins, and at this point, an abrupt transition into normal epithelium is observed.

DIFFERENTIAL DIAGNOSIS

The umbilicated nodule with a keratin plug, typical for keratoacanthoma, may also be encountered with basal and squamous cell carcinomas and with some adnexal tumors of skin.

TREATMENT

Excision is the treatment of choice. Waiting for spontaneous involution is not advisable for two reasons: (1) one cannot be assured clinically that the lesion does indeed represent keratoacanthoma rather than cancer,

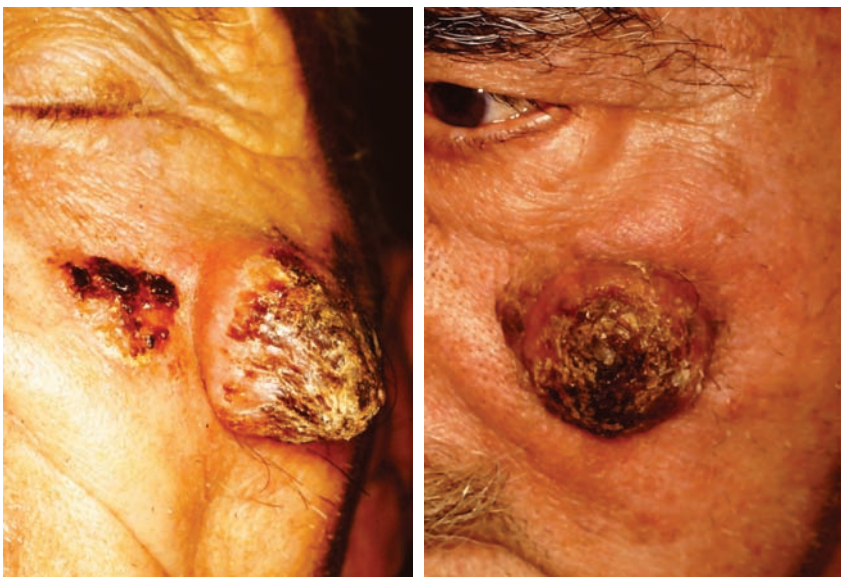

FIGURE 8-47
Keratoacanthoma of facial skin showing rolled borders with a central keratotic plug.

and (2) the scar remaining after surgery is often more cosmetic than that which develops after spontaneous regression.

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MESENCHYMAL TUMORS

Figure 8-48

Age: Young and middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Mesenchymal neoplasms arising in the dermal and subcutaneous connective tissues of the face are uncommon. The superficial dermatofibroma shows a smooth or slightly keratotic surface and is pale brown or pink, which may blanch on pressure. Hemangiomas are also seen on the face, may be flat or tumefactive, are reddish purple, and blanch on pressure. Lipomas and neural sheath neoplasms arise on the facial skin. The former are quite soft, compressible, and movable. The latter are uninodular or multinodular, firm, and movable. Multiple neurofibromatous nodules and brown café-au-lait macules are encountered in von Recklinghausen's disease of skin. Other mesenchymal tumors also arise here, but are rare.

MICROSCOPIC FEATURES

The benign connective tissue tumors are encapsulated or well localized and fail to show pleomorphism. Their differentiation depends on the tissue cells of origin.

DIFFERENTIAL DIAGNOSIS

Benign mesenchymal tumors have a smooth surface and are soft or firm. These features may be seen with sebaceous cysts, nonpigmented nevi, and adnexal tumors of skin. Microscopic examination is required to determine the cell of origin.

TREATMENT

Local excision is the treatment of choice. Recurrence rate for most mesenchymal neoplasms of the skin is quite low.

Additional Reading

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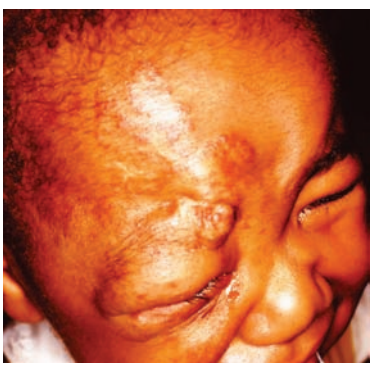

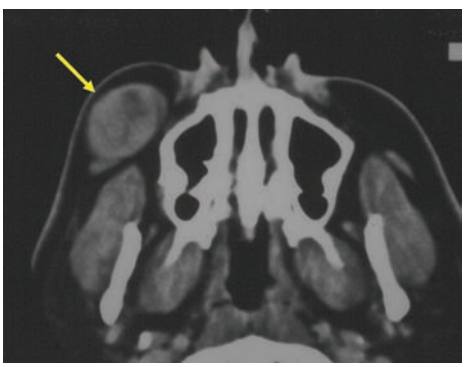

FIGURE 8-48
Mesenchymal tumors (left), hemangioma (right), CT scan, dermatofibrosaracoma protuberans.

Mandal RV, Duncan LM, Austen WG, Jr, Nielsen GP. Infiltrating intramuscular spindle cell lipoma of the face. *J Cutan Pathol.* 2009;36(suppl 1):70-73.
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MALIGNANT MELANOMA

Figure 8-49

Age: Elderly
Sex: No predilection

CLINICAL FEATURES

Melanocyte malignancy in the facial region, typically the malar region, most often begins as superficial spreading melanoma characterized by a variegated coloration of black, blue, brown, and white with irregular margins. Ultimately, nodules may evolve indicating progression to invasive disease. Some melanomas of facial skin are amelanotic, showing no clinical evidence of pigmentation. Melanomas have a marked tendency for both regional lymph node metastasis and distant hematogenous spread. The prognosis is based on depth of invasion as assessed microscopically.

MICROSCOPIC FEATURES

Melanomas show a variety of histomorphologic features. In superficial spreading melanoma the malignant melanocytes proliferate along the basal layer of the epithelium, spreading laterally. The cells show nuclear atypia, a feature that differentiates them from junctional nevi. As lesions progress, they invade into the papillary dermis and later into the reticular dermis. In skin, the Breslow method of invasion depth is used as a prognosticator among other factors. The invasive lesions may comprise spindle cells, round cells, or pleomorphic cells and most, yet not all, show melanin pigment granules. The early invasive lesions are considered as thin melanomas whereas the late, more extensive, tumors are referred to as thick melanomas. The immunohistochemical markers positive in melanoma are HMB45, S-100, Vimentin, and Melan A.

DIFFERENTIAL DIAGNOSIS

Early melanomas may resemble pigmented nevi or basal cell carcinomas when nonpig-

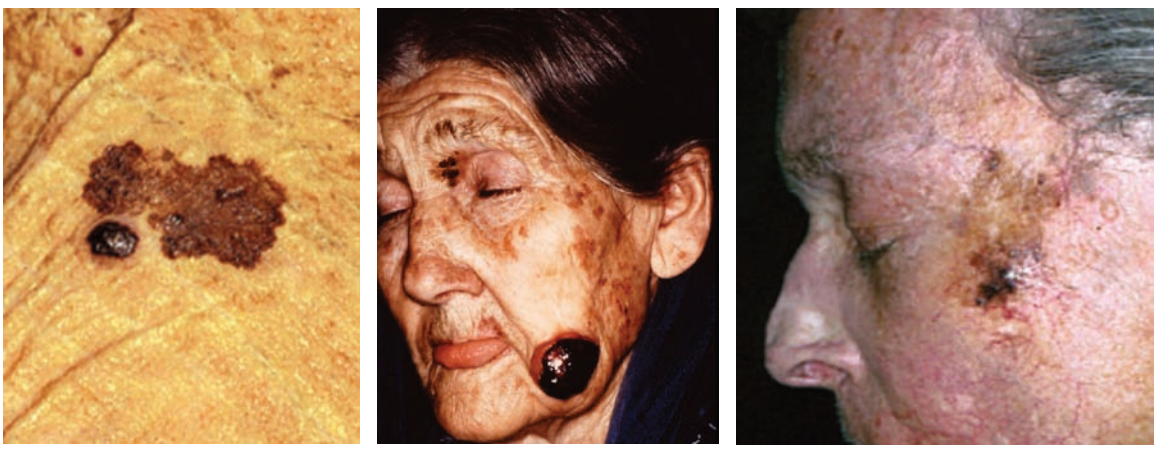

FIGURE 8-49
Malignant melanoma, flat macular superficial spreading lesions; nodular invasive lesions.

mented types occur. Most benign nevi have smooth borders with homogeneous coloration while melanomas are multicolored and manifest irregular margins. There are also cases reported of squamous cell and basal cell carcinomas that synthesize melanin pigment.

TREATMENT

Wide local excision with 3- to 4-cm margins is recommended and a work-up for metastatic spread should be performed. Thin melanomas have a much more favorable prognosis than thick melanomas. Melanoma of the scalp and neck carries a 10-year survival (60%). Melanomas of the ear, face, and eyelid have 10-year survival rates of 70%, 80%, and 90%, respectively.

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Diffuse Facial Swellings

CELLULITIS AND SPACE INFECTIONS

Figure 8-50

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Cellulitis of the facial tissues usually arises subsequent to spread of odontogenic infection. The swelling is diffuse, firm, or indurated and warm. The overlying skin may display erythema. Moderate-to-severe pain is present. The patient is febrile and complains of malaise, and cervical lymphadenopathy is a frequent finding. Examination of the teeth or dental radiographs discloses a carious tooth and periapical radiolucency. Cellulitis localizes in the soft tissue adjacent to the infected tooth. When a question exists with regard to the incriminating tooth, vitalometer testing is in order. Anterior maxillary teeth may drain into the soft tissues of the upper face and orbit; posterior maxillary and mandibular teeth are associated with cellulitis in the masseter region. The soft tissue inflammation may ultimately point and drain, or may progress through fascial planes and spaces. If the mediastinum becomes involved, the process may be lethal.

MICROSCOPIC FEATURES

Muscle and fascial connective tissue fibers are diffusely infiltrated with neutrophils and scattered histiocytes. Tissue edema is not prominent.

DIFFERENTIAL DIAGNOSIS

Because of its induration, cellulitis may simulate malignant neoplasm or underlying bone disease. Fever, constitutional signs of infectious disease, and localization of infectious sources, either in the dentition or periodontium, allow for a clinical diagnosis of cellulitis.

TREATMENT

The patient should be placed on a regimen of analgesics and antipyretics. Penicillin is the drug of choice, provided the patient is not allergic to it. The source of infection should be eliminated either by pulp exposure or extraction. Hot packs can be applied to the swelling in an attempt to localize the infection, after which incision and drainage can be performed. Failure of the processes to show resolution in 48 hours requires routine and anaerobic culture and sensitiv-

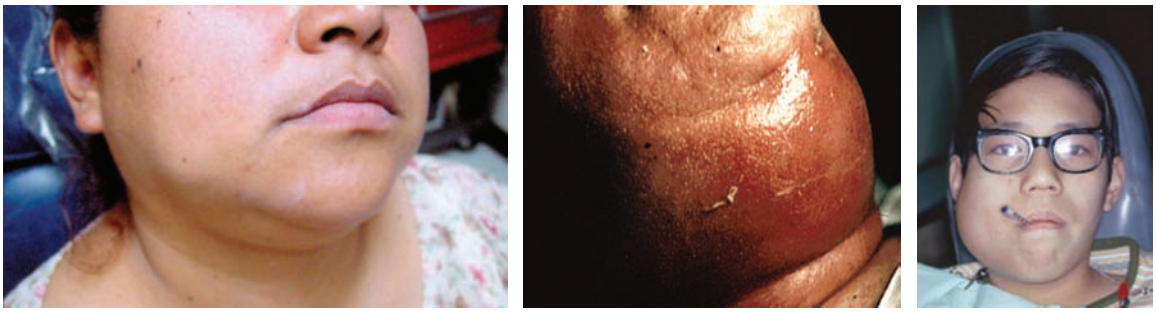

FIGURE 8-50
Diffused soft tissue swellings of face subsequent to spread of odontogenic infection represents space infection (left), Ludwig's angina (center) and cellulites (right).

ity tests of an aspirate from the inflamed tissues.

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EMPHYSEMA

Figure 8-51

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Emphysema of the oral and facial soft tissues arises as the result of entrapment of air introduced into tissue or fascial spaces. This phenomenon is usually iatrogenic, following some dental or surgical procedure rendered in conjunction with application of positive-pressure air introduction into a wound, periodontal pocket, surgical flap, or root canal. As the air becomes trapped within tissues, it causes diffuse swelling, which yields a bubbly sensation with soft crepitus when palpated. Pain is often a complaint.

MICROSCOPIC FEATURES

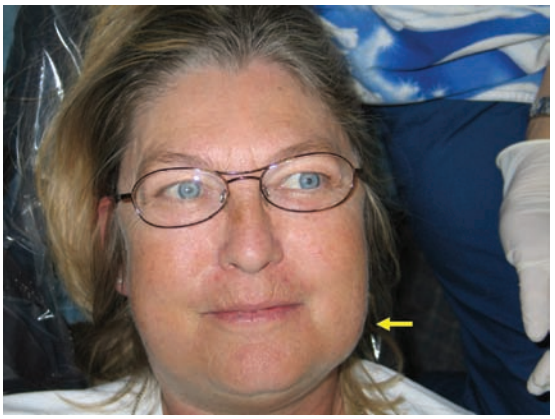
Not applicable.

DIFFERENTIAL DIAGNOSIS

Soft tissue emphysema is easily differentiated from other diffuse facial swellings on the basis of the bubbly consistency detected on palpation. Occasionally, emphysema may be confused with the soft swellings seen in edema, particularly angioneurotic edema. A complete history with consideration of potential etiologic factors allows differentiation on a clinical basis.

TREATMENT

Soft tissue emphysema may be complicated by venous air embolism, which is often fatal, or by soft tissue abscess; in the latter, antibiotic therapy is indicated. Emphysema generally resolves in 4 to 7 days with no treatment. If the swelling is significant, negative-pressure needle aspiration may aid in resolution.



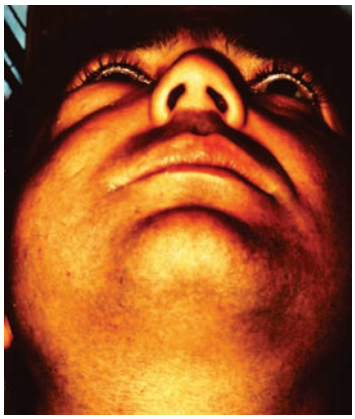


FIGURE 8-51
Diffuse soft swelling of the cheek due to air entrapment in the facial tissues.

Additional Reading

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ANGIONEUROTIC EDEMA

Figure 8-52

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Patients allergic to certain foods or drugs exhibit urticaria in most instances; however, for unknown reasons, the allergic manifestations may be localized to the facial area. The facial swelling may also be accompanied by urticaria. The facial swelling of angioneurotic edema is the result of histamine-mediated profuse capillary permeability with a resultant diffuse, often massive, edematous swelling of the upper lip, face, and periorbital area. The tissue is soft, pliable, and usually pruritic. The reaction is a manifestation of immediate immunoglobulin-mediated hypersensitivity that takes place within 1 or 2 hours after antigenic challenge, which is usually venom from a localized spider bite or bee sting to the face. Ingestion of food allergens may also result in angioneurotic edema. A hereditary form of angioneurotic edema occurs. Patients with this form are genetically deficient in an enzyme that inhibits an esterase responsible for a certain reaction in the complement-fixation process.

MICROSCOPIC FEATURES

Not applicable.

DIFFERENTIAL DIAGNOSIS

The diffuse swelling of angioneurotic edema must be differentiated from emphysema and facial cellulitis associated with spread of odontogenic infection. Cellulitis may show an early edematous phase prior to cellular infiltration with induration. Infection of dental origin should be ruled out with appropriate radiologic and clinical evaluation. Diligent questioning is required to uncover the suspected allergen, and reexposure to the suspected agent may be necessary to confirm the etiology.

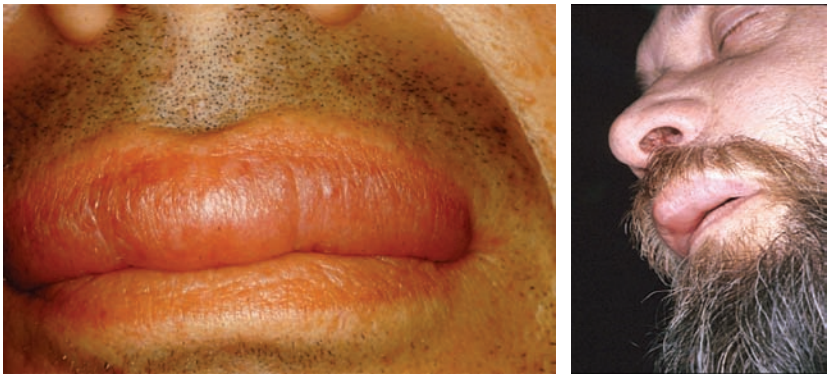

FIGURE 8-52
Diffuse soft swelling of the lips in angioneurotic edema.

TREATMENT

The suspected allergen should be withdrawn and avoided in the future. The disease can be treated by prescribing 50 mg of diphenhydramine or 12.5 mg of promethazine 4 times daily for 3 days. Progression to anaphylactic shock may develop but is not a frequent complication. In hereditary angioedema, subcutaneous icatibant, a bradykinin receptor antagonist, is the treatment of choice

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CUSHING'S SYNDROME

Figure 8-53

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Cushing's syndrome is characterized by bilateral edematous swelling of the face, upper torso adiposity (buffalo hump), abdominal stria, hypertension, and hyperglycemia. These signs and symptoms are the result of adrenal hypercorticism. The disease may be associated with an adrenal cortical adenoma or hyperplasia, pituitary adenoma, or steroid-secreting malignancies of other organs. The most common cause is prolonged steroid drug therapy, producing the so-called moon facies or cushingoid facies. The soft tissues of the cheeks are bilaterally puffy and edematous, yielding a round face.

MICROSCOPIC FEATURES

Not applicable.

DIFFERENTIAL DIAGNOSIS

The soft bilateral swellings of slow onset are quite characteristic. A history of steroid therapy confirms the impression. Cushing's syndrome occurring in patients who are not taking steroid medication requires a complete medical work-up with laboratory studies to determine the cause of elevated steroid levels. Obtaining a high blood pressure reading (secondary to mineralocorticoids) and fasting sugar (elevated because of glucocorticoids) represents the initial phase of the work-up.

TREATMENT

The cause of the disease must be determined initially; treatment rests with medical and/or surgical intervention.

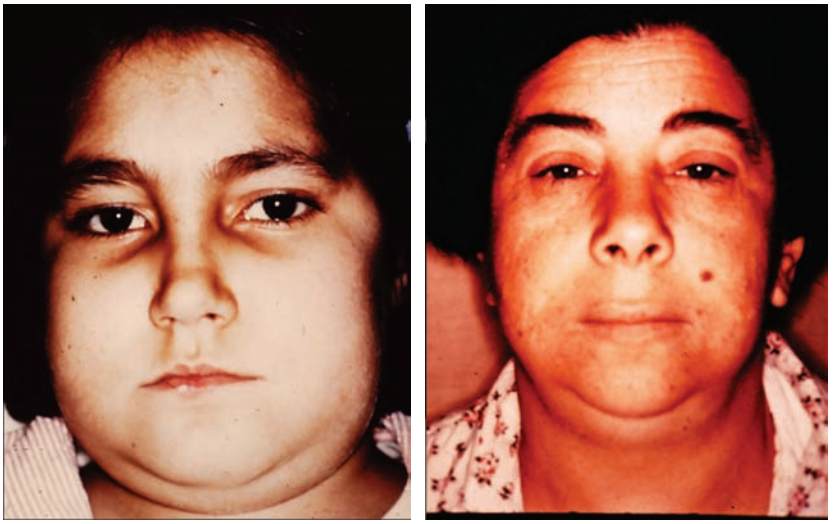

FIGURE 8-53
Cushing's syndrome with diffuse facial edema.

Additional Reading

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FACIAL HEMIHYPERTROPHY

Figure 8-54

Age: Childhood onset
Sex: Male predilection

CLINICAL FEATURES

Hypertrophy of the facial tissues is a developmental defect of unknown origin, which has been suggested to be related to an anomalous vascular supply. The disease is unilateral, with enlargement of both osseous and soft tissues. The opposite side of the face is normal, whereas the affected side shows enlargement of the facial bones and mandible. The eye is laterally displaced. One half of the tongue is enlarged, and the cheek tissues are thickened. The enlarged osseous tissues do not show an alteration of trabeculation on radiographs. Teeth on the affected side may be larger than those on the normal side. In nearly one half of patients with this peculiar syndrome, the remainder of the body shows a similar unilateral involvement. Syndactyly and polydactyly are present in some instances, and one fifth of the patients with hemihypertrophy are retarded. A familial or genetic trend is not encountered.

MICROSCOPIC FEATURES

The affected tissues do not show any histopathologic changes.

DIFFERENTIAL DIAGNOSIS

The history of long-standing facial asymmetry helps to limit the differential diagnosis. Facial hemihypertrophy must be differentiated from fibrous dysplasia and other osseous enlargements. This can be accomplished by obtaining radiographs, because no radiologic changes in osseous trabeculation occur in facial hemihypertrophy. In neurofibromatosis (NF1), facial plexiform neurofibromas may cause facial asymmetry that can be confused with congenital facial hemihypertrophy.

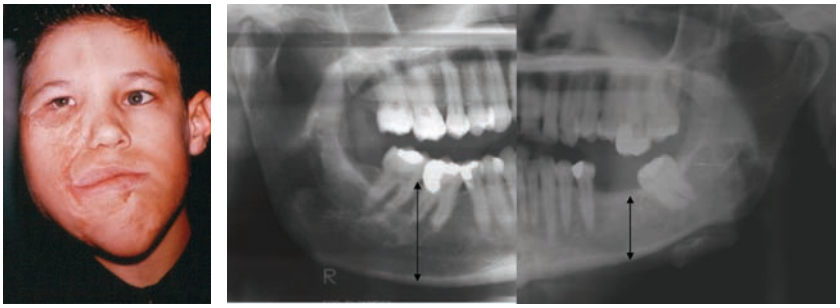

FIGURE 8-54
Facial hemihypertrophy. *A:* Unilateral enlargement of the maxilla and mandible. *B:* Panorex shows osseous asymmetry.

TREATMENT

The disease is self-limiting but is certainly a cosmetic dilemma. Cosmetic surgical osseous contouring may be performed, with plastic surgical correction for the soft tissue enlargement.

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FIBROUS DYSPLASIA AND OTHER BONE LESIONS

Figure 8-55

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Diffuse facial swellings not related to soft tissue enlargement are included here for the sake of differential diagnosis because their clinical appearance may simulate the other entities included in this section. Any central lesion of the jaws that induces cortical expansion can distort the facial contour, producing enlargement and asymmetry. Fibrous dysplasia of bone is one of the more frequent diseases to appear in such a fashion. The maxilla is more often affected than the mandible. The swelling is usually obvious over the malar eminence, zygoma, or lateroinferior orbital rim. The other features of fibrous dysplasia are discussed in the chapter on radiopaque lesions of the jaws. Neoplasms of mesenchymal or odontogenic origin often cause bony expansion and facial enlargement. These specific neoplasms are also described in detail in subsequent chapters, which categorize lesions on the basis of radiographic characteristics.

MICROSCOPIC FEATURES

The microscopic features vary according to the specific disease actually represented. Refer to the chapters on radiolucent and radiopaque lesions in which descriptions of fibro-osseous lesions and central jaw neoplasms are presented.

DIFFERENTIAL DIAGNOSIS

Osseous enlargements are differentiated from one another on the basis of clinical, radiologic, and microscopic features. Osseous enlargements may simulate other diffuse facial swellings included here. By merely palpating the area, the clinician can determine the osseous nature of

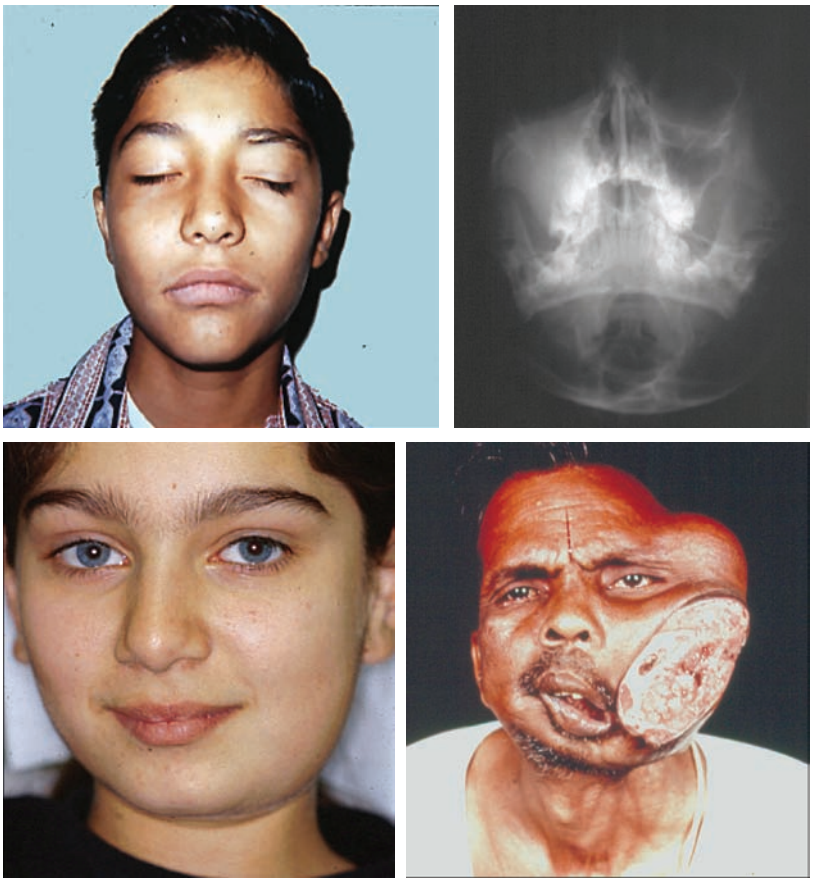

FIGURE 8-55
Enlargement of the jaws due to underlying bone lesions. Fibrous dysplasia (top), Garré osteomyelitis (bottom left), ameloblastoma (bottom right).

the enlargement and essentially rule out enlargements of soft tissue origin.

TREATMENT

The treatment varies considerably, based on the final diagnosis.

Additional Reading

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MASSETERIC HYPERTROPHY

Figure 8-56

Age: Onset in young adulthood
Sex: No predilection

CLINICAL FEATURES

Bilateral swellings located over the ascending ramus of the mandible characterize benign muscular hypertrophy of the masseters. The enlargement may be confused with parotid disease; however, if the patient is asked to clench his teeth, the enlargements increase in size and become firm as the result of muscular contraction.

Pain is not a feature. The cause for this condition is not always apparent. Some instances appear to represent congenital disease, whereas others may be related to physiologic hypertrophy of muscle fibers from overuse of the jaws, as in bruxism.

MICROSCOPIC FEATURES

Normal skeletal muscle fibers are present; some may show enlarged diameters.

DIFFERENTIAL DIAGNOSIS

The bilateral distribution differentiates masseteric hypertrophy from other facial swellings such as cellulitis, emphysema, or facial hemihypertrophy. Because the location is such that parotid disease may be confused with this entity, such disorders as Sjögren's syndrome, Mikulicz's disease, and Heerfordt's syndrome should be considered in the differential diagnosis. These can generally be eliminated on the basis of other clinical findings (a lack of xerostomia and increase in induration on clenching), which are features of masseteric hypertrophy.

TREATMENT

Botulinum toxin type A injection directly into affected muscles reduces their size in 3 months.

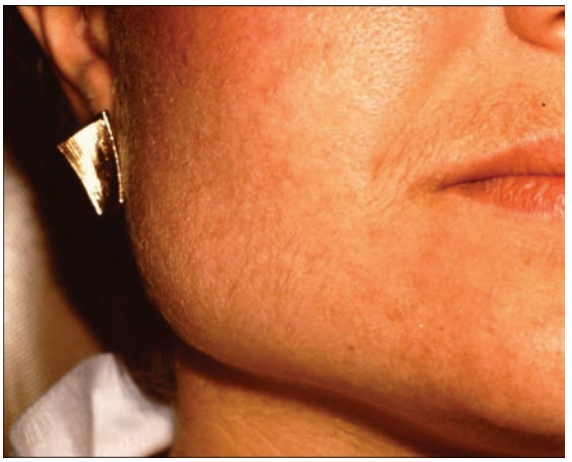

FIGURE 8-56
Masseteric hypertrophy.

Additional Reading

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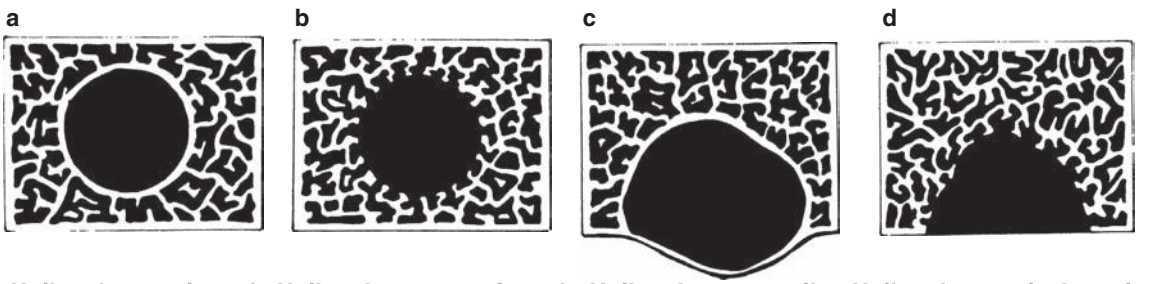

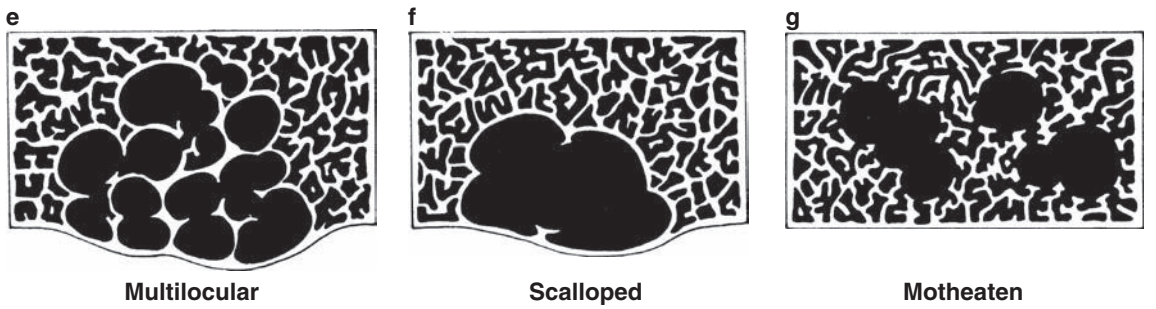

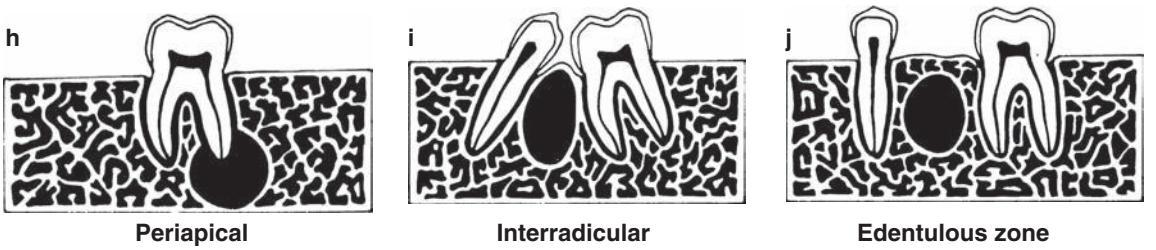

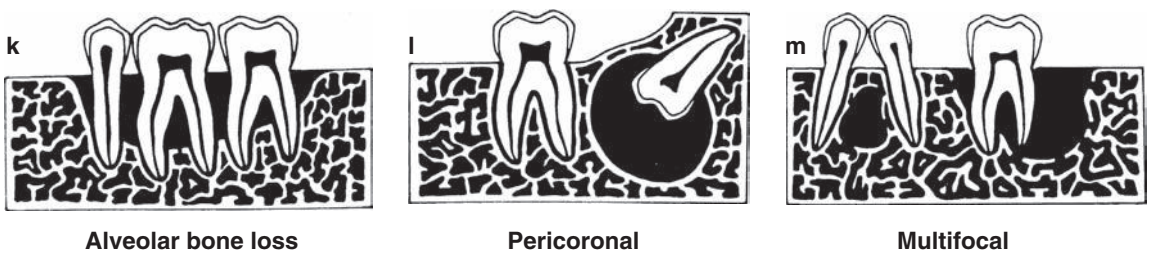

Radiolucent Lesions

Radiolucent Lesions of the Jaws

9

*See Pericoronal Radiolucencies
**See Generalized Osteoporotic Lesions
†See Multilocular Radiolucencies
‡See Periapical Radiolucencies
§See Interradicular Radiolucencies

The diseases that affect the osseous marrow and cortex of the jaw bones are included both in this chapter and in the succeeding chapter dealing with radiopaque lesions. Central lesions of the jaws may manifest signs and symptoms such as pain, discomfort, paresthesia, and swelling, or they may be discovered serendipitously when full-mouth radiographs or panographic surveys are procured.

It should be stressed from the onset that a definitive diagnosis can rarely be secured on the basis of radiologic features alone; a thorough case history and a bone biopsy are required in most instances. The radiolucent lesions are grouped according to location and configuration. It is axiomatic that this categorization is not all-inclusive; the entities listed in a given category are not always represented by the radiographic headings under which they are listed. Rather, the diseases have been placed under a given pattern heading because it is that particular configuration that the disease most often assumes.

Some generalizations can be put forward with regard to radiolucent lesions of the jaws. A unilocular radiolucency with well-demarcated boundaries or cortication is usually indicative of a benign, slow-growing process. Radiolucencies with ill-defined or irregular margins may be either benign or malignant.

Radiolucencies surrounding the crown of a tooth are, as a rule, cystic or neoplastic lesions of odontogenic origin. Multilocular radiolucencies with well-defined margins frequently show cortical expansion. Lesions with this configuration are generally benign yet aggressive reactive or neoplastic disorders. When evaluating unilocular radiolucencies, one should remember that those diseases categorized as *multilocular radiolucencies* must initially appear as unilocular lesions, with or without expansion depending on the size of the growth.

Because arteriovenous malformations are radiolucent, surgical biopsy should not be performed on radiolucent lesions of the jaws before needle aspiration of the defect is attempted.

The most common periapical radiolucency is apical periodontitis secondary to pulp necrosis. Periapical cemental dysplasia and traumatic cyst are less common yet are by no means rare. The lateral periodontal cyst and odontogenic keratocyst are the most common interradicular radiolucent lesions.

Alveolar bone loss is the hallmark of periodontal disease and is seen in nearly one half of the adult population. Nevertheless, the clinician should be aware of the fact that many life-threatening diseases (diabetes, histiocytosis X, leukemia, and malignant neoplasms) can manifest identical radiographic features.

The most common multilocular radiolucencies are the odontogenic keratocyst, central giant cell granuloma, and ameloblastoma. Central arteriovenous malformations are potentially lethal if traumatized or tampered with surgically. Osteomyelitis is the most common disease showing a moth-eaten pattern. A variety of sarcomas and metastatic carcinomas show similar radiologic features; however, these malignancies, as opposed to osteomyelitis, are represented by expansion of the cortical plates.

The most common multifocal radiolucency is periapical cemental dysplasia; this is included among the periapical radiolucencies. The acute disseminated form of histiocytosis X and multiple myeloma, both manifesting multiple radiolucent lesions, are potentially lethal diseases. Generalized rarefaction or osteoporotic lesions involving the entire skeleton usually exhibit jawbone changes. Senile osteoporosis is the most common condition, whereas the genetic hemolytic anemias are potentially, yet rarely, lethal.

Periapical Radiolucencies

APICAL PERIODONTITIS (ABSCESS, GRANULOMA, AND CYST)

Figure 9-1

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Inflammatory lesions of bone resulting from apical progression of dental pulp inflammation evolve subsequent to dental caries or trauma to the teeth. Radiographically, the lesions are usually well circumscribed and are located directly below the apex of the involved teeth. If the source of infection emanates from an accessory root canal, the radiolucency may be laterally displaced. Any tooth with a carious pulp exposure can develop periapical disease; however, incisors and first molars are most frequently involved. Radiographically, abscesses, granulomas, or cysts have the same features and cannot be differentiated without microscopic examination. Acute periapical abscess is accompanied by severe pain that often interferes with sleep. Pain on percussion is a feature. Granulomas and cysts may be asymptomatic or associated with a dull ache or, occasionally, severe pain. If the periapical lesion resolves with

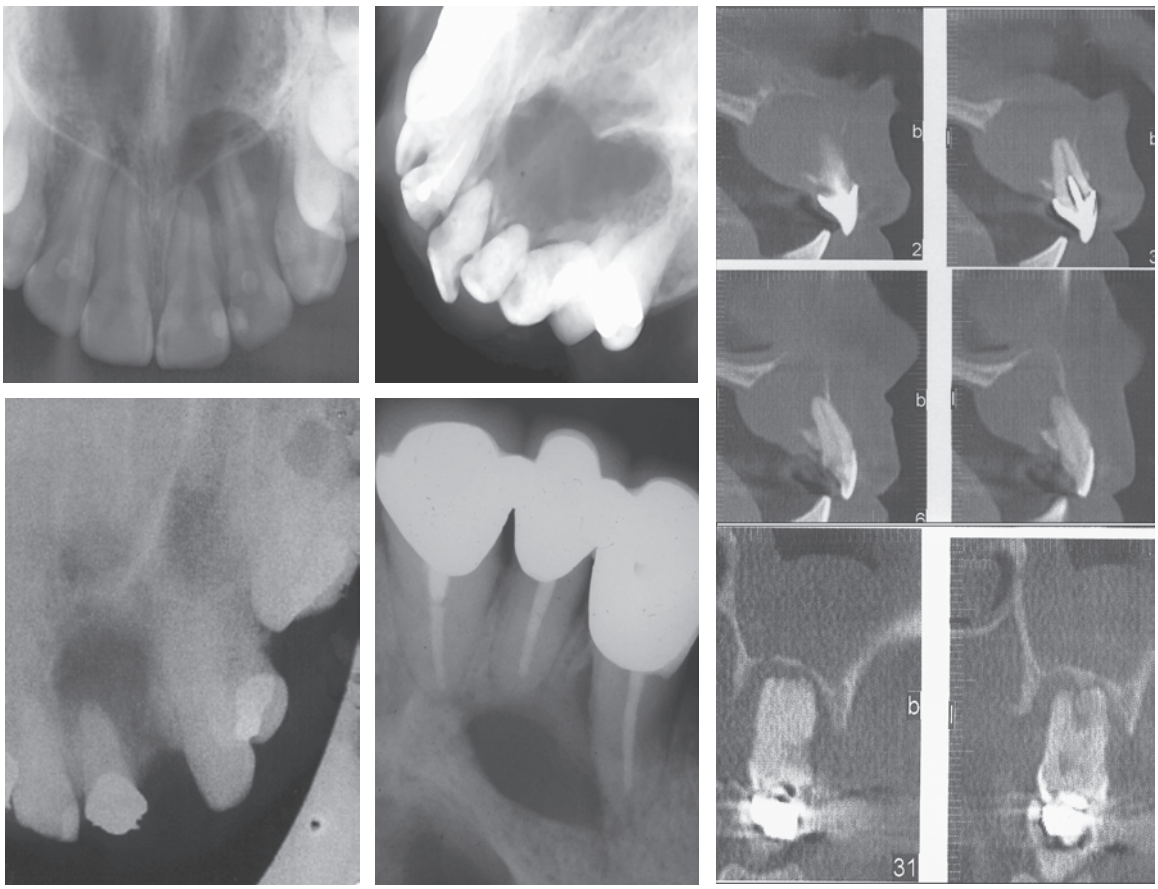

FIGURE 9-1
Apical periodontal cysts and granulomas associated with nonvital teeth. Cone beam computed tomographic sections on the right.

treatment yet is not replaced by bone, a residual periapical fibrous scar may persist. Even after extraction of the necrotic tooth, a through-and-through fibrous defect may persist and be radiographically demonstrable as an ill-defined radiolucency. Infection may spread, with intraoral fistulation and parulis formation. Infected maxillary teeth may drain into the maxillary sinus, into tissues of the face, producing a cellulitis, or, rarely, inflammation may spread via the facial veins and progress to cavernous sinus thrombosis. Mandibular teeth may drain buccally, causing space infections or Ludwig's angina, which, if left untreated, may progress into the parapharyngeal spaces and ultimately into the mediastinum. This in turn may be fatal, because constriction is caused by edema of the airway. *Treponema denticola* and *Enterococcus faecalis* are cultivated from periapical lesions with previous pain, while *Porphyromonas gingivalis* is associated with tenderness to percussion in both deciduous and permanent teeth.

MICROSCOPIC FEATURES

Periapical abscess shows loose areolar granulation tissue and diffuse sheets of neutrophils with scattered macrophages. Granulomas are composed of fibrous and granulation tissue with a diffuse or patchy subacute or chronic inflammatory cell infiltrate. The apical periodontal cyst is lined by nonkeratinizing squamous epithelium, often fragmented and with elongated anastomosing rete ridges. Hyaline bodies are often present within the spinous layer. Transmigration of neutrophils into the spinous cell layer is common. The fibrous and granulation tissue wall is infiltrated with inflammatory cells and often contains cholesterol clefts.

DIFFERENTIAL DIAGNOSIS

Apical periodontitis may be radiographically identical to immature periapical cemental dysplasia, focal condensing osteitis, benign cementoblastoma, and traumatic cyst. The presence of deep carious lesions or a history of a traumatic episode implicates an infectious or inflammatory lesion of pulpal origin. The diagnosis is confirmed by a negative response to vitalometer testing. Many other primary cysts and tumors of the jaws often lie in juxtaposition to tooth roots; however, the teeth are vital.

TREATMENT

Teeth with periapical inflammation are nonvital and require endodontic therapy or extraction. Should the periapical radiolucency fail to resolve within 6 to 12 months, apical curettage with apicoectomy is indicated.

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PERIAPICAL CEMENTAL DYSPLASIA

Figure 9-2

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

More common among blacks than whites, periapical cemental dysplasia or cemen-

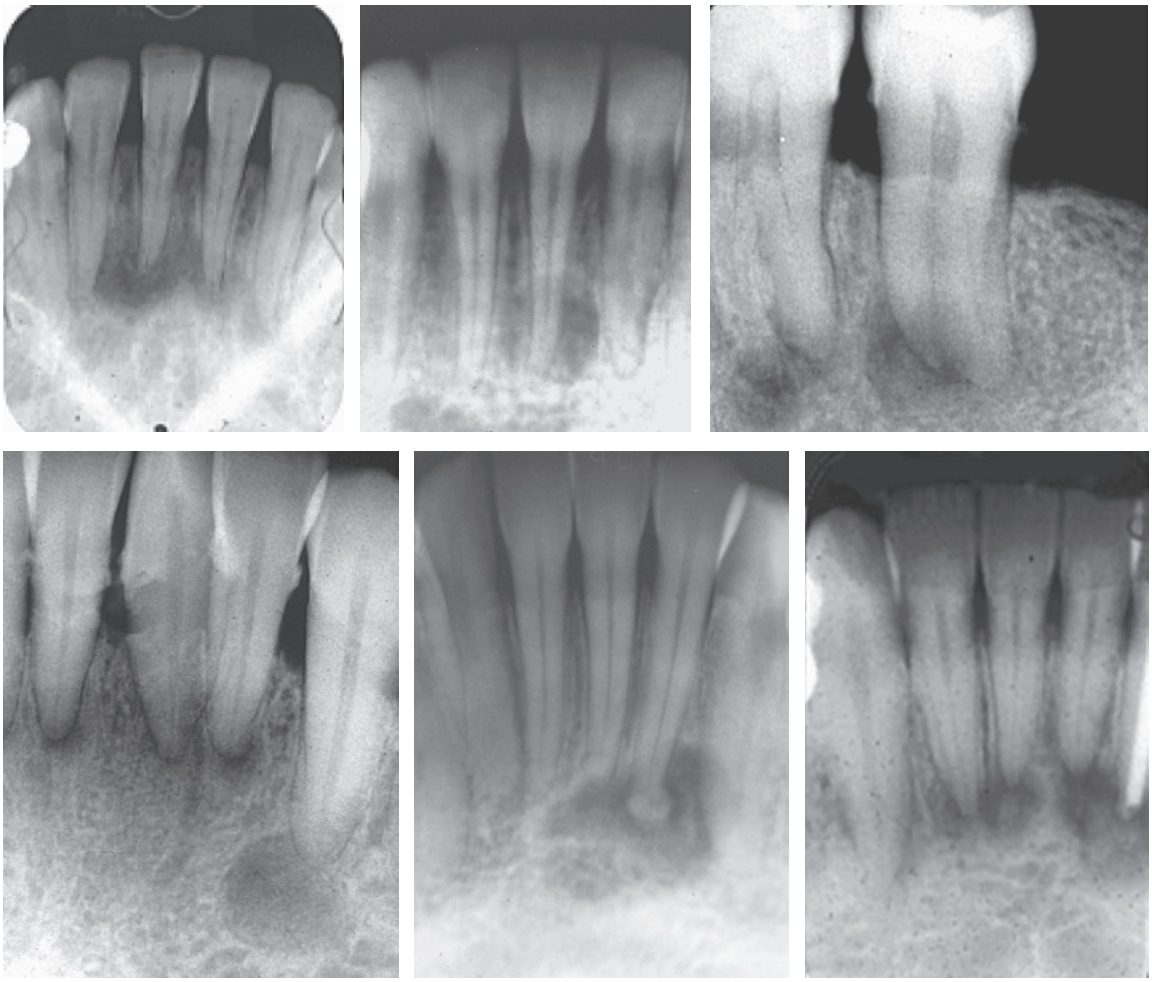

FIGURE 9-2
Multiple apical radiolucencies underlying vital teeth represent periapical cemental dysplasia. Some show early calcifications in the center of a radiolucent halo.

toma appears radiographically as a non-expansile radiolucency in its early or immature stage. The lesion may be single or multiple and is considerably more common in the anterior mandible. Incisors and premolars are more often associated with the periapical radiolucencies, and periapical cemental dysplasia does not involve molar teeth unless multiple lesions are present. Periapical cemental dysplasia and focal cemento-osseous dysplasia probably represent the same pathologic process, the latter found in the posterior mandibular quadrants. The radiolucency is usually, but not invariably, circumscribed and located subjacent to an intact apical periodontal ligament space. The overlying teeth are vital, clinical evidence of expansion is lacking, and pain is not a feature. The etiology is unknown.

MICROSCOPIC FEATURES

The early stage of periapical cemental dysplasia is characterized by the presence of hypercellular fibrous tissue with irregular, small osseous trabeculae or curvilinear cemental trabeculae. Droplet calcifications are frequently observed.

DIFFERENTIAL DIAGNOSIS

Periapical cemental dysplasia can be differentiated from apical periodontitis on the basis of vitalometer testing, as the pulp is vital in the former disease. Focal condensing osteitis and cementoblastoma are usually associated with molars rather than with anterior teeth.

TREATMENT

Nonexpansile periapical radiolucencies associated with vital anterior teeth are clinically considered to represent periapical cemental dysplasia. No treatment is required. The patient should be recalled for periodic radiographic evaluation, to assure that the lesion follows the usual progression into mature stages with opacification. If the lesion progressively enlarges or causes expansion, it probably represents another disease and biopsy is indicated.

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FOCAL CEMENTO-OSSEOUS DYSPLASIA

Figure 9-3

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Focal cemento-osseous dysplasia is a fibro-osseous hamartoma that begins central in bone as a radiolucency. Over time the lesion

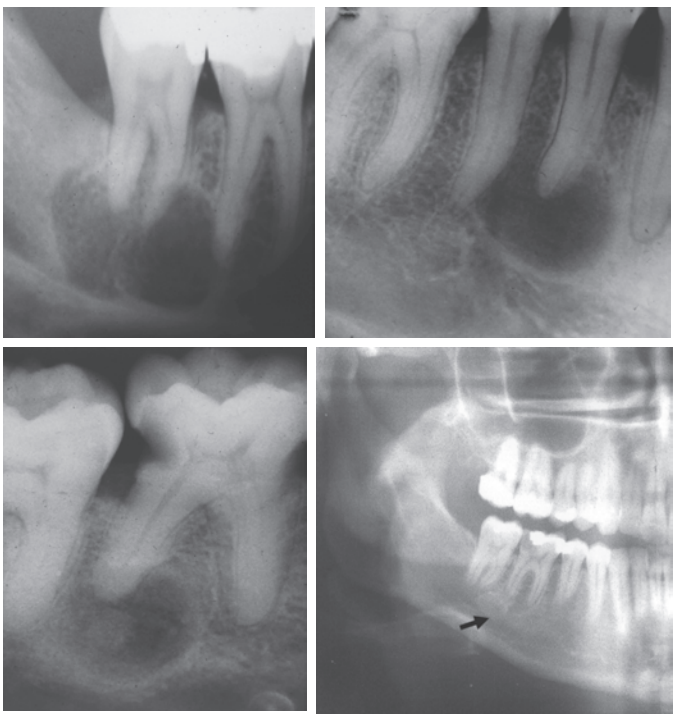

FIGURE 9-3
Focal cemento-osseous dysplasia beginning as apical radiolucent lesions in early stages.

undergoes ossification, becoming a radiolucency with a central opacity. These lesions are commonly seen in the molar areas. They grow to a given size without expansion of bone and become quiescent. The pathogenesis is therefore very similar to their anterior jaw counterpart, periapical cemental dysplasia. Importantly, in both lesions, the overlying teeth are vital.

MICROSCOPIC FEATURES

The lesion is typically curetted away from a bony crypt and appears as multiple small lobules. A fibro-osseous pattern is observed with a hypercellular monomorphic fibroblastic proliferation throughout which lie irregular trabeculae. Cemental-like oval calcifications are also present.

DIFFERENTIAL DIAGNOSIS

Ossifying fibroma should be considered and can be ruled out when osseous expansion is abscent. Focal sclerosing osteomyelitis can be eliminated when an odontogenic source of infection (i.e., caries, nonvital teeth, large restorations) is identifiable.

TREATMENT

No treatment after biopsy is required.

Additional Reading

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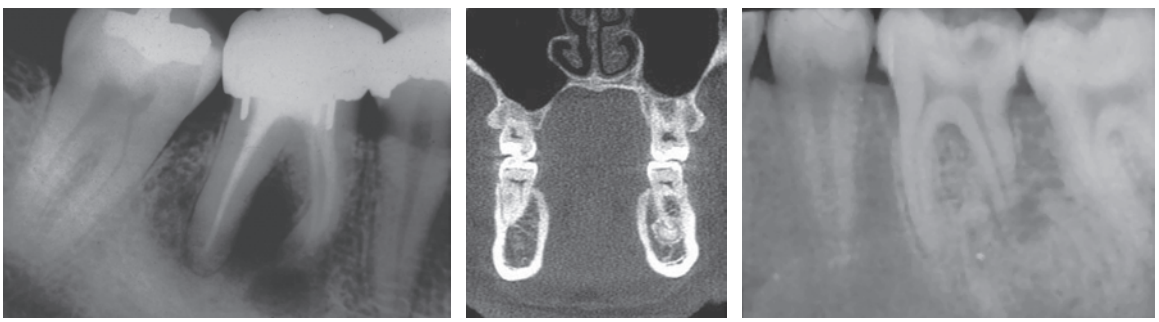

FIGURE 9-4
Focal sclerosing osteomyelitis showing early lucent stage compared with later stages with opacification. Teeth manifest pulpitis from caries and are usually vital.

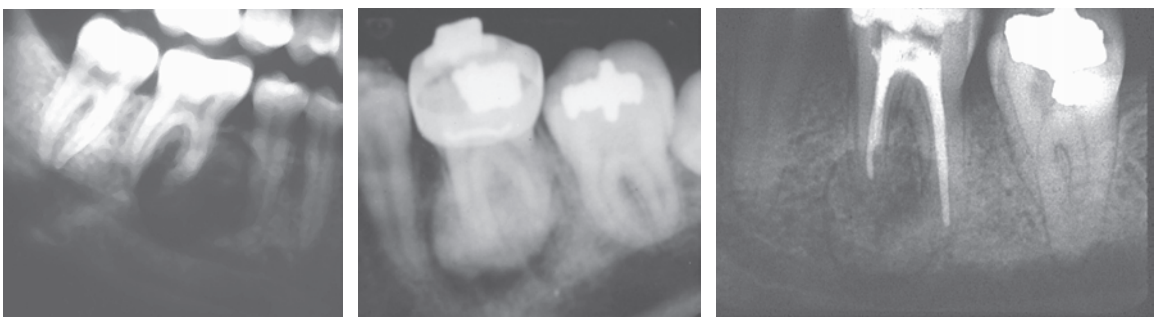

FIGURE 9-5
Benign cementoblastoma in the early immature radiolucent stage and late calcified stage.

Su L, Weathers DR, Waldron CA. Distinguishing features of focal cemento-osseous dysplasia and cemento-ossifying fibromas. II. A clinical and radiologic spectrum of 316 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1997;84:540-549.

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FOCAL SCLEROSING OSTEOMYELITIS

Figure 9-4

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Whereas focal sclerosing osteomyelitis is most often observed as a radiopaque lesion, it may evolve from a radiolucent stage, which becomes progressively opacified. This rare form is characterized by a well-circumscribed periapical radiolucency in association with a carious mandibular molar. The caries are usually deep, and the crown may appear gutted. The pulp from the overlying tooth is vital with a chronic inflammatory cell infiltrate (i.e., chronic pulpitis). The area may be asymptomatic or a dull ache may be present. Response to vitalometer testing is often altered; however, the overlying tooth rarely tests nonvital because the pulp is inflamed rather than necrotic.

MICROSCOPIC FEATURES

Hypercellular or moderately cellular fibrous connective tissue is stippled with small, irregular osseous trabeculae that are usually rimmed by osteoblasts. Curvilinear cemental trabeculae and ovoid calcifications may also be seen. The pulp from the overlying tooth is vital, with a chronic inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

Focal osteitis is most frequently confused with periapical cemental dysplasia. The two can be differentiated on clinical grounds. Focal osteitis arises in association with posterior teeth with a large carious lesion, whereas periapical cemental dysplasia involves noncarious vital anterior teeth. Benign cementoblastoma may show similar features in the radiolucent stage. This lesion is not associated with caries and pulpitis. In addition, cortical expansion is a feature of cementoblastoma but is rarely seen in focal osteitis. The microscopic appearance may be indistinguishable from that of other fibro-osseous lesions of the jaws, so that the diagnosis depends on clinical features.

TREATMENT

Because the pulp is inflamed and may progress into an acute phase, with ultimate necrosis, endodontic therapy is indicated.

Additional Reading

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BENIGN CEMENTOBLASTOMA

Figure 9-5

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

A true neoplasm of cementoblastic origin, the benign cementoblastoma, is seen to arise

in association with tooth roots. Molar teeth, particularly the mandibular first molar, are the predominant sites for this lesion, usually encountered in a radiopaque stage. Early lesions may be radiolucent. They are well circumscribed and envelop one or both roots, usually extending midway up the root surface. They are well demarcated and may be totally lucent or contain calcific flecks. Expansion of the buccal and/or lingual cortical plates occurs and, if of significant magnitude, may be demonstrated on occlusal radiographs. The tooth tests vital, pain is not a feature, and a dull, ankylosed sound is produced when the tooth is percussed.

MICROSCOPIC FEATURES

Linear-radiating trabeculae of osseous tissue are dispersed throughout a fibrous marrow and are intimately associated with, and fused to, the root cementum. These trabeculae generally show polarization patterns more consistent with osseous tissue than with cementum; rimming by osteoblasts is a prominent feature.

DIFFERENTIAL DIAGNOSIS

Cementoblastoma in its immature radiolucent stage must be differentiated from focal sclerosing osteomyelitis, apical periodontitis, and periapical cemental dysplasia. These latter entities do not produce an ankylosed sound when percussed and fail to expand the cortical plates. Periapical cemental dysplasia involves anterior teeth, whereas cementoblastoma arises from the root area of posterior teeth.

TREATMENT

A vital posterior tooth with an expansive periapical radiolucency probably represents cementoblastoma in its early stage. Surgical exploration with biopsy is advisable. If a gritty or cartilage-like tissue is encountered during surgery and appears to be fused to the root surface, the tooth and accompanying fused tumor mass should be excised in toto. If left untreated, the lesion may progressively enlarge and expand the encasing bone.

Additional Reading

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INCISIVE CANAL CYST

Figure 9-6

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The incisive canal cyst is a developmental nonodontogenic cyst derived from embryonic epithelial remnants of the nasopalatine duct or incisive canal. It is a well-delineated oval or heart-shaped radiolucency located between, and apical to, the two maxillary central incisors directly in the midline. It rarely causes facial expansion, yet palatal swelling is common. Occasionally, the incisors evince root resorption. The cyst is asymptomatic and the teeth test vital. It is sometimes difficult to ascertain radiographically whether the radiolucency is truly pathologic or merely represents a large incisive foramen. Cystic unilocular lesions of the palatal midline (median pala-

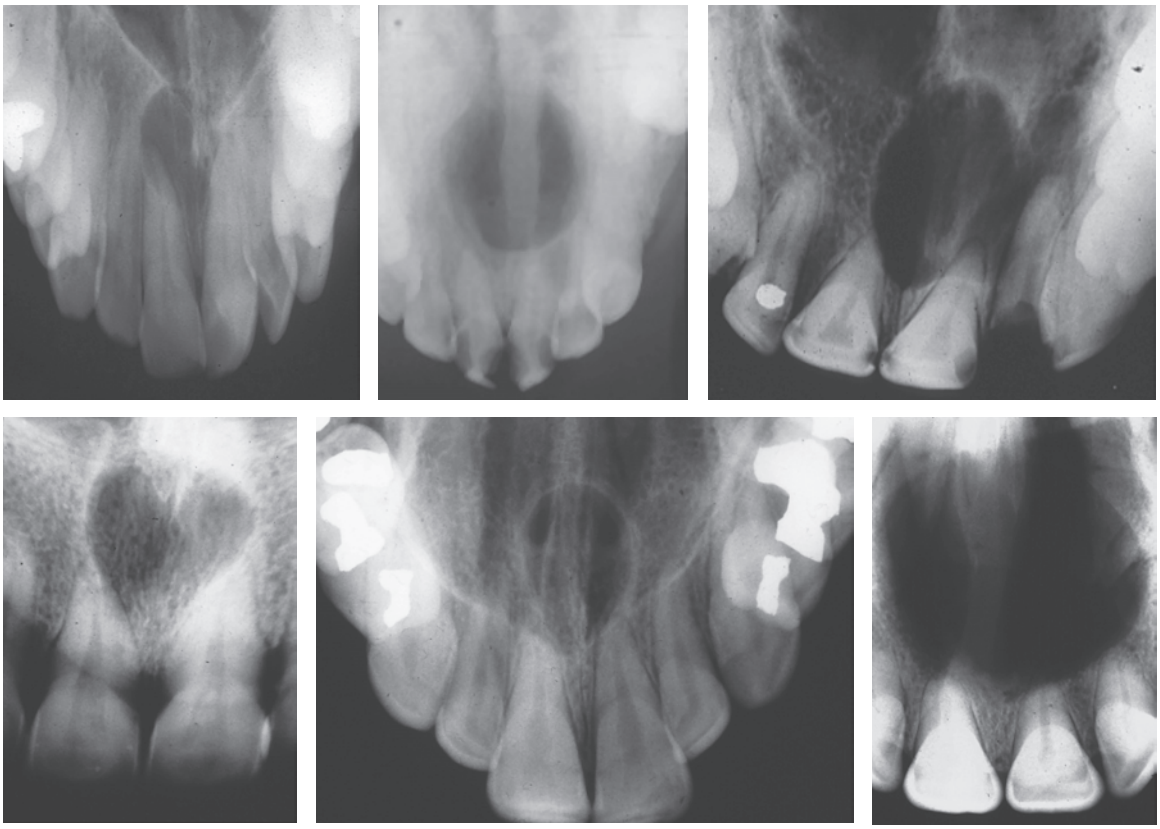

FIGURE 9-6
Incisive canal cysts are prolate or heart-shaped midline radiolucencies that may cause root divergence.

tal cyst) may represent true fissural cysts from epithelial entrapment of the fusing secondary palatal processes. Alternatively, these lesions may represent posterior extension of an incisive canal cyst.

MICROSCOPIC FEATURES

The cyst may be lined by stratified squamous epithelium, respiratory epithelium, or both. When respiratory epithelium is present, mucous goblet cells may be seen.

The fibrous wall characteristically is traversed by large neurovascular bundles.

DIFFERENTIAL DIAGNOSIS

A midline radiolucency of the maxilla almost invariably represents incisive canal cyst. Rarely, lateral periodontal cysts, primordial cysts, and odontogenic keratocysts arise in this location.

TREATMENT

When a radiologic diagnosis of incisive canal cyst is made, treatment may consist of surgical enucleation or periodic radiographic follow-up. Progressive enlargement warrants surgical intervention.

Additional Reading

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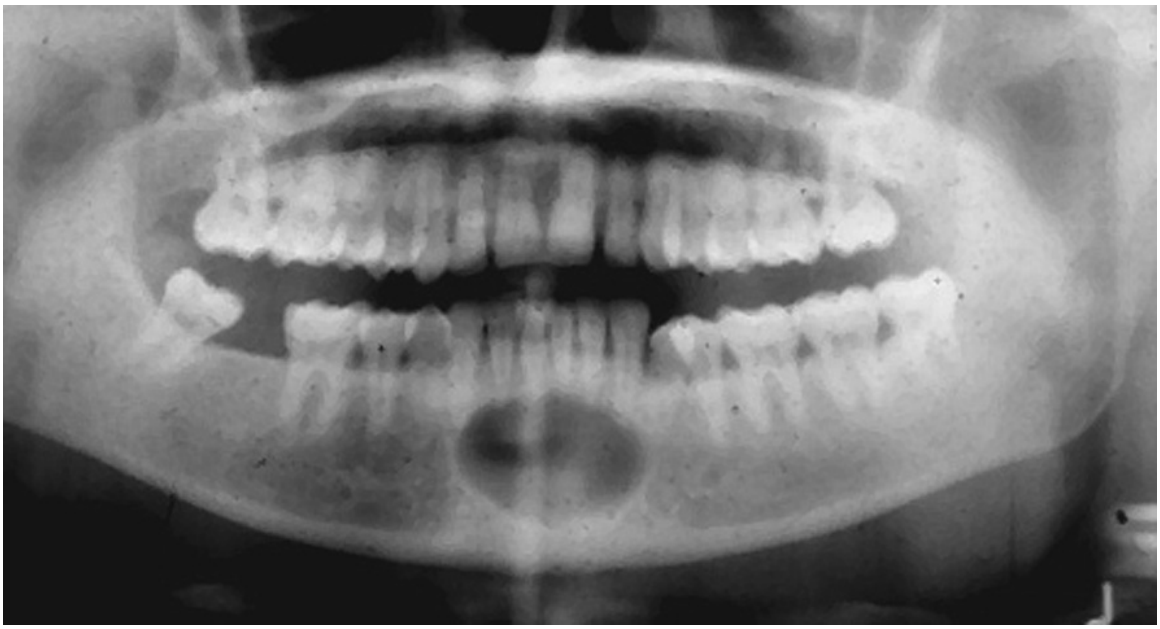

FIGURE 9-7
Median mandibular cyst underlying vital teeth.

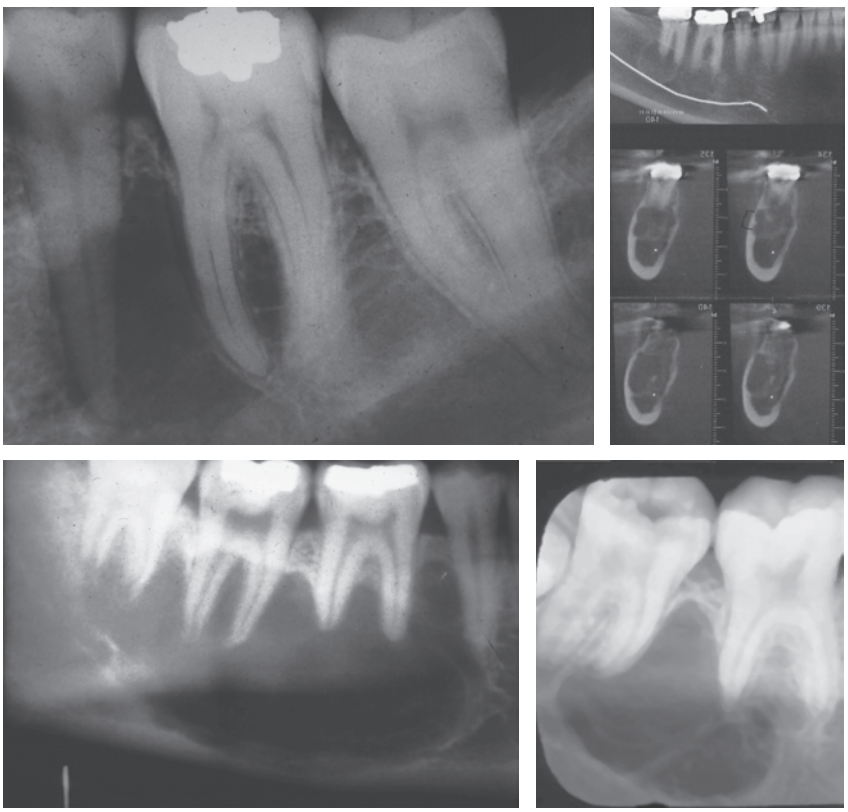

FIGURE 9-8
Traumatic or hemorrhagic bone cyst appears as a nonexpansile periapical radiolucency. The overlying molars test vital. The lesion tends to scallop into the furcation region and between contiguous teeth.

MEDIAN MANDIBULAR CYST

Figure 9-7

Age: Adults
Sex: No known predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The median mandibular cyst is theoretically a fissural cyst that evolves from entrapped epithelial remnants enclaved in the mandibular symphysis region subsequent to fusion of the mandibular processes. Some authors dispute this theory and ascribe the cystic lesion to various other pathogenetic derivations from odontogenic sources (i.e., primordial cyst from a supernumerary bud, lateral periodontal cyst, odontogenic keratocyst). It appears as a unilocular, often expansile, radiolucency underlying vital mandibular incisors.

MICROSCOPIC FEATURES

Some cases represent odontogenic keratocyst. Others are lined by nonkeratinizing stratified squamous epithelium, whereas others have been reported with a respiratory lining. This feature does not necessarily support a fissural origin, since other odontogenic cysts may exhibit respiratory metaplasia. Furthermore, this region does not typically harbor respiratory epithelium during the embryonic morphogenetic period.

DIFFERENTIAL DIAGNOSIS

Traumatic cyst may occur in this location, yet rarely expands bone. Likewise, the sublingual salivary gland depression, also nonexpansile, is characterized by a radiolucency in the anterior mandible. Apical cysts and granulomas can be ruled out when pulpal necrosis is documented.

TREATMENT

Surgical enucleation or curettage is the treatment of choice.

Additional Reading

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TRAUMATIC (HEMORRHAGIC) CYST

Figure 9-8

Age: Young adults
Sex: Slight male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The traumatic cyst does not represent a true epithelial cyst; rather, it is an empty or fluid-filled cavity of bone lined with a fibrous or granulation tissue membrane. The term *traumatic* was used to implicate trauma as a causative factor; however, less than half of the instances are associated with any significant trauma to the jaw. The etiology remains unknown. Clinically, pain and expansion are unusual. The lesion is located most often in the body or anterior portion of the mandible, and radiographically, it is radiolucent. A classic feature is its tendency to scallop between the tooth roots. Portions of the cystic lesion are well demarcated from the neighboring bone, whereas in other areas the margins are ill defined. The teeth that overlie the lesion test vital.

MICROSCOPIC FEATURES

When biopsy is attempted, an empty space in the medullary bone is encountered. A thin membrane may line the cavity and is characterized microscopically by the presence

of fibrous granulation tissue that usually shows mild-to-moderate inflammation.

DIFFERENTIAL DIAGNOSIS

Traumatic cysts must be differentiated from apical periodontitis on the basis of vitality testing. The teeth overlying traumatic cysts are vital. Because these lesions may be extensive and show peripheral scalloping, they could be mistaken for one of the lesions included as multilocular radiolucencies, for example, keratocyst, central giant cell granuloma, and certain odontogenic tumors. These lesions are usually expansile, whereas traumatic cysts generally do not expand the cortex. Aspiration of a traumatic cyst may be negative or yield a blood-tinged fluid.

TREATMENT

After aspiration, the area should be entered surgically. A portion of the lining membrane should be made to induce hemorrhage into the bone cavity. The clot organizes, ossifies, and remodels within 6 to 12 months. Although evidence has been forwarded that traumatic cysts may resolve spontaneously, surgical exploration is recommended for diagnostic confirmation.

Additional Reading

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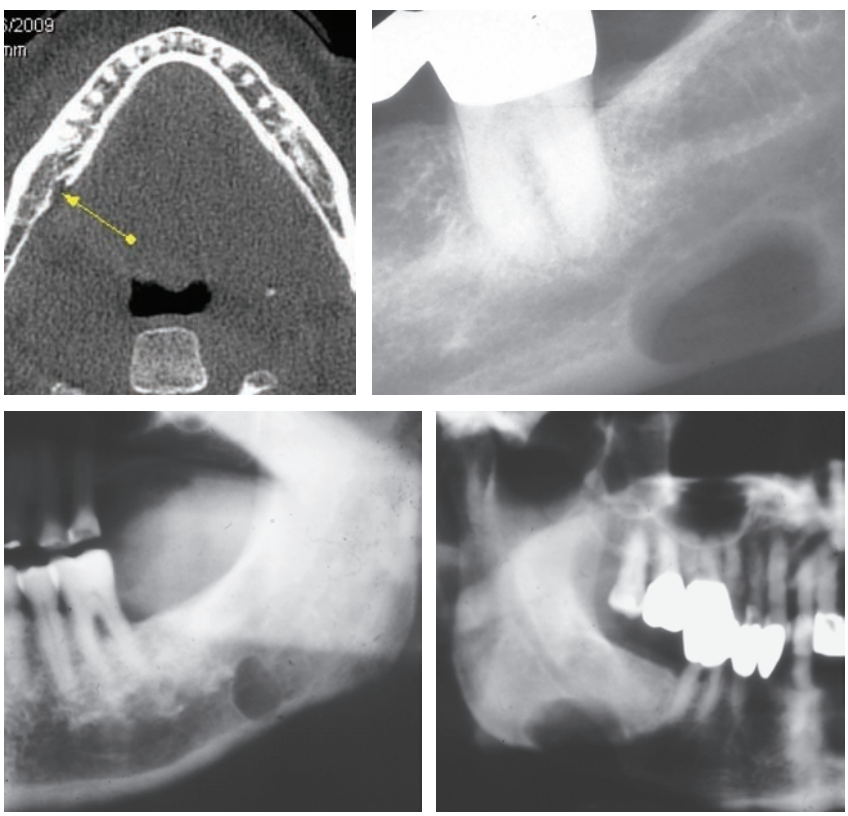

FIGURE 9-9
Unilocular, well-circumscribed radiolucency lying below the inferior alveolar canal represents a submandibular gland depression on the lingual aspect of the mandible.

Sapp JP, Stark ML. Self-healing traumatic bone cysts. *Oral Surg Oral Med Oral Pathol.* 1990;69:597.

STATIC BONE CYST (SUBMANDIBULAR GLAND DEPRESSION)

Figure 9-9

Age: Onset in childhood
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The static bone cyst or submandibular salivary gland depression is usually discovered coincidentally on dental radiographs because no symptoms are associated with this benign developmental process. The lesion is a well-circumscribed corticated oval radiolucency situated periapical to the second or third mandibular molar. The defect is not in continuity with root tips; rather, it is located below the inferior alveolar canal. It is often bilateral. The lesion reflects a lingual depression of the cortical plate in which normal salivary gland tissue rests. A sialogram may be obtained and discloses the presence of ductal elements converging in the region of the radiolucent defect. Similar lesions of the mandibular ramus may encase parotid tissue.

MICROSCOPIC FEATURES

The contents of salivary depressions consist of normal submandibular salivary tissue, depending on the site of involvement.

DIFFERENTIAL DIAGNOSIS

The localization of submandibular gland depressions below the alveolar canal in the absence of expansion or pain is characteristic, allowing for a radiologic diagnosis.

TREATMENT

No treatment is required. Periodic radiographic follow-up is recommended to ensure that no growth is taking place.

Additional Reading

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SUBLINGUAL GLAND DEPRESSION

Figure 9-10

Age: Onset in childhood
Sex: No known predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The sublingual glands may reside within a lingual bone depression, similar to the static bone cyst in relation to the submandibular glands. The lesion lies apical to the anterior mandibular teeth and is a well-circumscribed unilocular radiolucency. Bilateral defects may be witnessed. The lucent foci may show progressive enlargement, which arrests in the teenage years. There is no evidence of cortical expansion.

MICROSCOPIC FEATURES

A biopsy discloses the presence of normal-appearing sublingual gland tissue.

DIFFERENTIAL DIAGNOSIS

The teeth are vital, and periapical cemental dysplasia may be considered. Usually the radiolucent area encompasses the apical one third of the root. There is no racial predilection. Because the disease is rare, an exploratory biopsy is usually performed to

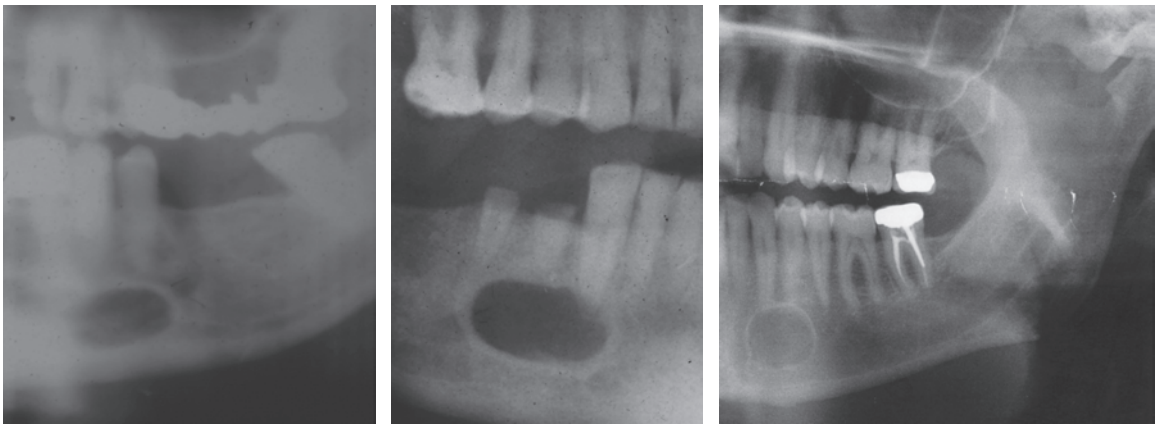

FIGURE 9-10
Periapical radiolucency underlying mandibular cuspid and premolars representing sublingual gland depression.

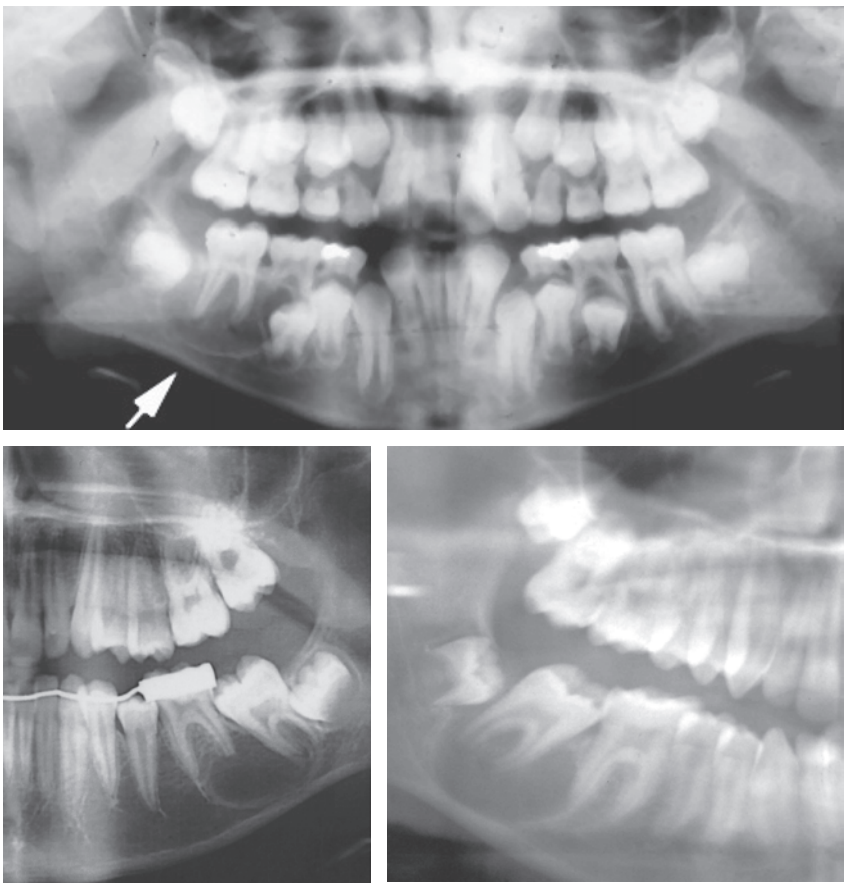

FIGURE 9-11
The paradental cyst lies buccal to vital tooth roots being superimposed over the roots. These cysts are often expansile.

rule out some other disease process that may coincide in this location. In a youngster with no clinical evidence of expansion, sublingual gland depression should be considered; a lingual surgical approach can be used for exploratory purposes.

TREATMENT

Once a definitive diagnosis is obtained by exploration and/or biopsy, no treatment is necessary.

Additional Reading

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Stene T, Pedersen KN. Aberrant salivary gland tissue in the anterior mandible. *Oral Surg Oral Med Oral Pathol*. 1977;44:72.

PARADENTAL (BUCCAL INFECTED) CYST

Figure 9-11

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The paradental or buccal cyst is an odontogenic cyst located buccal to an erupted to partially erupted vital molar tooth, or according to some others, it can appear interradicularly or distal to a tooth. Many pathologists are of the belief that the paradental cyst is merely a variant of dentigerous cyst in which the lesion became laterally displaced during tooth eruption. These cysts are by far most commonly encountered in the mandibular molar region and often show clinical, as well as radiographic, evidence of buccal expansion. The radiolucency is unilocular and well marginated, often superimposed over the affected tooth roots, yet many times the lesion projects between contiguous teeth. Many paradental cysts communicate with the gingival sulcus and develop a pericoronitis. Pain and purulent discharge are common complaints.

MICROSCOPIC FEATURES

The paradental cyst is an inflammatory lesion and shares histologic features with other odontogenic cysts; as mentioned previously, it probably originates from a laterally displaced follicle, thereby being an inflamed dentigerous cyst. The lesion is lined by nonkeratinizing stratified squamous epithelium that is hyperplastic with anastomosing, elongated rete ridges. The cyst wall is thickened, exhibiting a diffuse mononuclear inflammatory cell infiltrate, and foci of acute inflammation may be seen.

DIFFERENTIAL DIAGNOSIS

Radiographically, paradental cyst differs from most of the other interradicular lesions listed here in that the radiolucency is frequently superimposed over the tooth rather than being solely interposed between the roots. Biopsy is required to rule out other more serious lesions.

TREATMENT

Enucleation and curettage can be undertaken without sacrificing the adjacent teeth. Recurrence is not problematic.

Additional Reading

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CENTRAL GIANT CELL GRANULOMA

Figure 9-12

Age: Young adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Central giant cell granuloma is a neoplastic-like reactive proliferation of the jaws that usually exhibits a multilocular pattern as observed radiographically. Early smaller lesions are usually unilocular and frequently lie apical to vital teeth. The lesion is more common in the mandible than in the maxilla underlying anterior or premolar teeth. Buccal or lingual cortical expansion can often be detected both clinically and radiographically; expansile lesions can cause root divergence or resorption.

MICROSCOPIC FEATURES

Multinucleated giant cells, dispersed throughout a hypercellular fibrovascular stroma, possess randomly arranged nuclei that are either pyknotic and hyperchromatic or oval and stippled with prominent nucleoli. Erythrocyte engorgement of vessels and extravascular hemosiderin pigment are frequently observed as are occasional osseous trabeculae.

DIFFERENTIAL DIAGNOSIS

The overlying teeth are generally vital, a feature that eliminates apical periodontitis. When expansion is present, most of the other lesions listed here can be eliminated, with the exception of cementoblastoma, which is rarely encountered in the incisor-premolar region. Other neoplastic processes and keratocysts can coincidentally arise in periapical locations and expand bone. Biopsy is required to make the diagnosis.

TREATMENT

Thorough curettage is the treatment of choice. When the diagnosis has been established, appropriate laboratory tests should be performed to rule out brown tumor of hyperparathyroidism.

Additional Reading

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MALIGNANCIES

Figure 9-13

Age: Adults
Sex: Depends on primary tumor location and diagnosis

CLINICAL AND RADIOGRAPHIC FEATURES

The most common malignant tumor of the jaws is metastatic carcinoma. Metastatis to the jaws may arise from primary tumors of the breast, colon, lungs, kidney, prostate, and other organs less frequently. The mets tend to localize to the posterior mandible and ramus, often causing mental nerve paresthesia. They are usually radiolucent but may induce osteogenesis and are typically found adjacent to the roots of posterior teeth. Although most metastatic carcinomas manifest moth-eaten margins, some may appear to be well delineated yet punched out. Primary malignancies of bone can also present as apical radiolucencies and include both sarcomas and carcinomas that arise from odontogenic

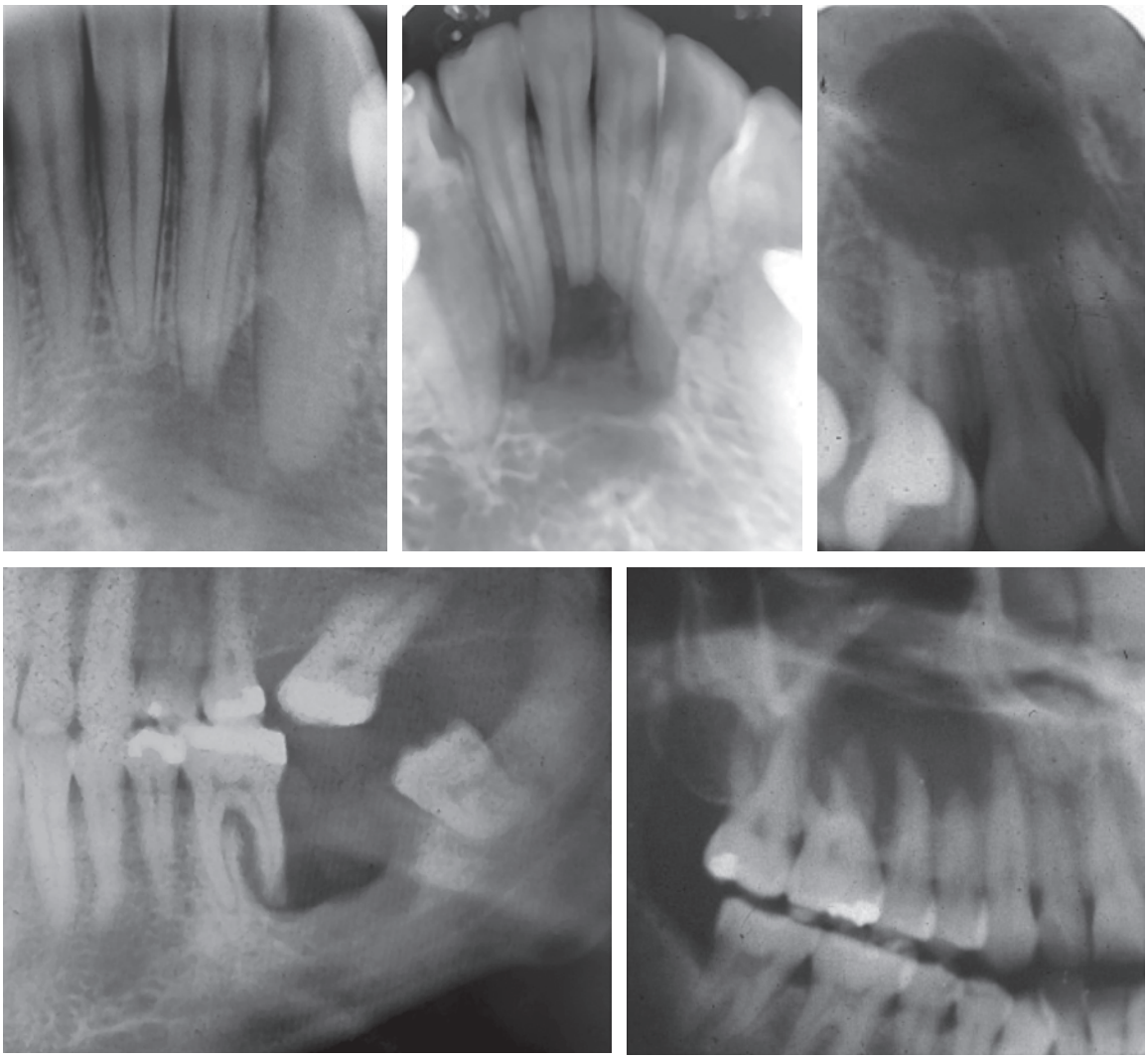

FIGURE 9-12
Central giant cell granuloma appearing as periapical radiolucencies with root resorption.

epithelium. They are discussed elsewhere in this chapter.

MICROSCOPIC FEATURES

Most metastatic tumors are adenocarcinomas and will show ductal differentiation, or the individual tumor cells will be cuboidal or columnar. When metastasis is suspected, immunohistochemical markers can be employed to assist in finding the primary site of the tumor (e.g., prostate-specific antigen for prostate cancer; estrogen, progesterone, and Her2Nu for breast cancer; carcinoembryonic antigen and specific cytokeratins for colon cancer; and S-100 protein for melanoma to mention but a few).

DIFFERENTIAL DIAGNOSIS

The other lesions listed here as apical radiolucencies should be considered; metastatic tumors typically occur in association with vital teeth, and lip paresthesia is a telling symptom for malignancy.

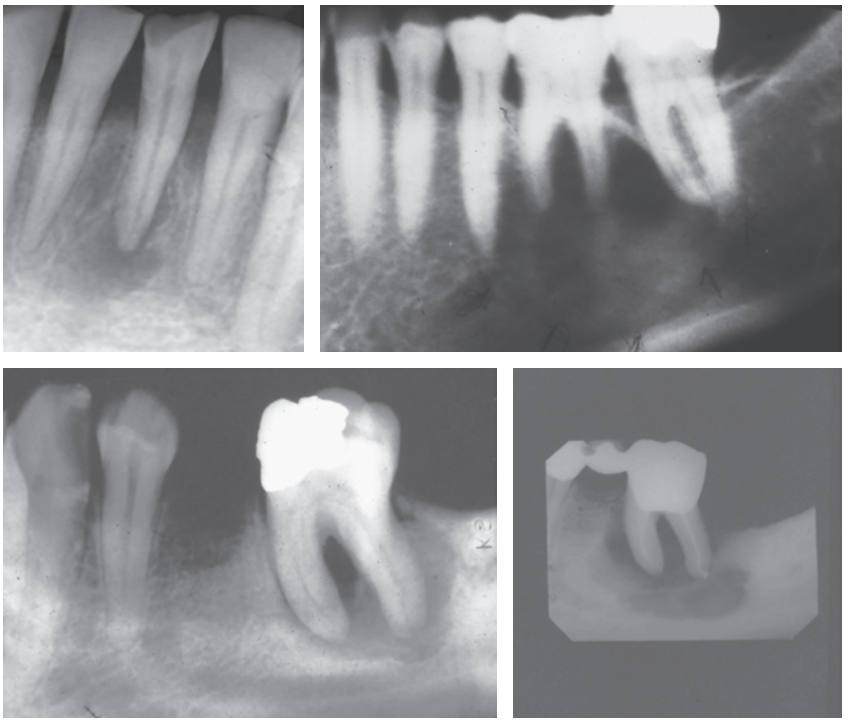

FIGURE 9-13
Malignant lesions: metastatic carcinoma of the breast (upper left), multiple myeloma (upper right), primary intra-alveolar carcinoma (lower).

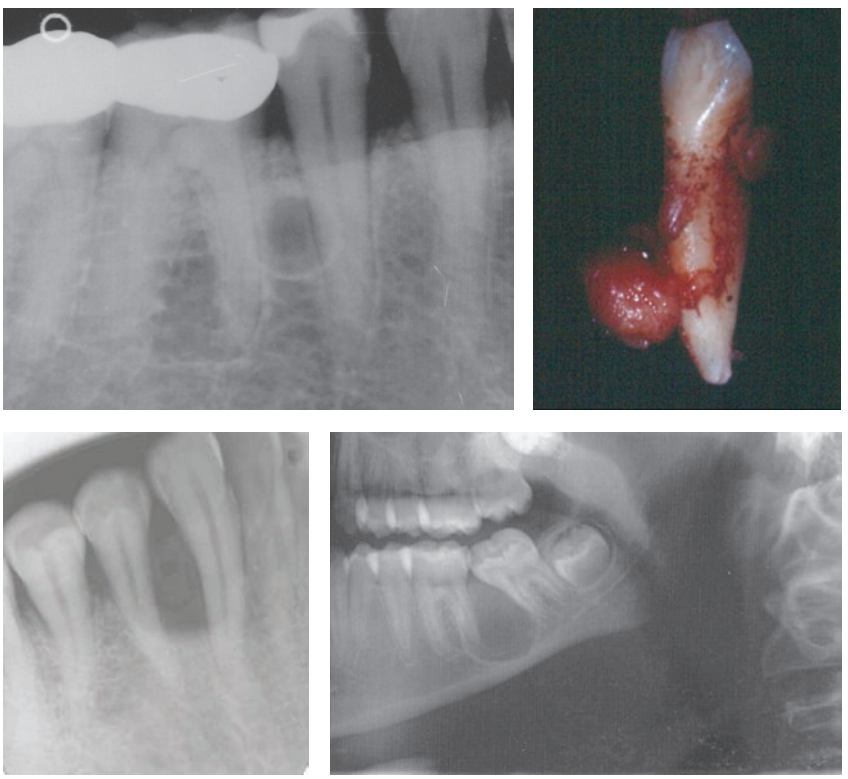

FIGURE 9-14
Lateral periodontal cyst interposed between two vital mandibular teeth.

TREATMENT

First and foremost is the detection of the primary tumor in cases of metastasis. Chemotherapy is usually required and most cases have a poor prognosis.

Additional Reading

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Interradicular Radiolucencies

LATERAL PERIODONTAL CYST

Figure 9-14

Age: Adults
Sex: Slight female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The lateral periodontal cyst may arise from epithelial rests in the periodontal ligament or may represent a primordial cyst originating from a supernumerary tooth bud. The fact that this cyst is most frequently encountered in the mandibular premolar region, a common location for supernumerary teeth, lends credence to this latter hypothesis. Radiographically, the lateral periodontal cyst is an interradicular radiolucency with well-defined or corticated margins. The adjacent teeth usually show some degree of root divergence, and they are vital when evaluated with an electric pulp tester. The buccal cortical plate may or may not show moderate bulging when examined clinically. Pain is not a feature.

MICROSCOPIC FEATURES

The cyst lining is either nonkeratinizing stratified squamous, or stratified cuboidal, epithelium that shows a tendency for convolution and irregularity. The fibrous wall manifests minimal inflammation.

DIFFERENTIAL DIAGNOSIS

Lateral periodontal cyst may be differentiated from a laterally displaced apical periodontal cyst on the basis of vitalometer testing because the former arise developmentally, having no relationship to pulpal disease. The radiographic features may be identical to those of keratocyst, primordial cyst, globulomaxillary cyst, incisive canal cyst, and calcifying epithelial odontogenic (Gorlin) cyst. Biopsy is required to differentiate among most of these entities.

TREATMENT

Surgical enucleation or curettage with preservation of adjoining teeth is the treatment of choice.

Additional Reading

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LATERALLY DISPLACED APICAL PERIODONTAL CYST OR GRANULOMA

Figure 9-15

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Apical or radicular cysts are usually located directly distal to the tooth root apex as a consequence of endodontic infection. When teeth harbor accessory root canals that are oriented from the pulp chamber to the lateral aspect of the root or when an infected root fracture is present, the spread of infection can progress laterally and occur as far as midway up the root. Pain may be a feature, or in low virulence infections the tooth may be asymptomatic.

MICROSCOPIC FEATURES

Apical periodontal cysts show a nonkeratinized, often hyperplastic, stratified squamous epithelial lining along with a fibrous cyst wall that is infiltrated by leukocytes; many also contain cholesterol clefts. Apical granulomas comprise inflamed granulation tissue and may have foreign material from endodontic sealers in previously treated teeth.

DIFFERENTIAL DIAGNOSIS

The most common considerations in the differential are lateral periodontal cyst and odontogenic keratocyst. The globulomaxillary cyst was at one time considered to be a fissural cyst located between a divergent maxillary lateral incisor and cuspid. Most of these are apical cysts from endodontic infection, others are lateral periodontal cysts or keratocysts. Vitality testing should be undertaken.

TREATMENT

If the incriminated tooth is nonvital, endodontic therapy along with cystectomy is the treatment of choice.

Additional Reading

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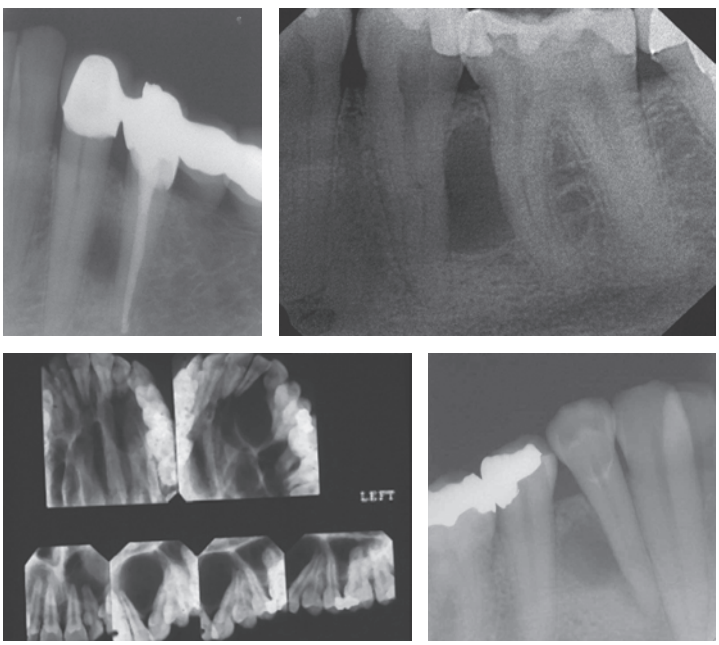

FIGURE 9-15
Laterally displaced endodontic infections are found when infection spreads through a lateral root fracture or accessory canal.

Lim AA, Peck RH. Bilateral mandibular cyst: lateral radicular cyst, paradental cyst, or mandibular infected buccal cyst? Report of a case. *J Oral Maxillofac Surg.* 2002;60:825-827.

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Steiner DR. A lesion of endodontic origin misdiagnosed as a globulomaxillary cyst.
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RESIDUAL CYST

Figure 9-16

Age: Adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

A residual cyst is any type of odontogenic cyst that persists in bone after the tooth with which it was associated has been removed. Therefore, a residual cyst may represent an apical periodontal cyst if a necrotic tooth overlying the lesion was extracted, or it may represent a dentigerous cyst if an impacted tooth was removed; whereas most are asymptomatic, some are associated with pain. Radiographically, the lesion is a well-circumscribed, often corticated, radiolucency located in an edentulous region once occupied by a tooth.

MICROSCOPIC FEATURES

Residual cysts are lined by noncornified stratified squamous epithelium that may contain hyaline bodies within the spinous cell layer. The fibrous wall generally shows an inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The residual cyst is easily confused radiographically with primordial cyst. The latter arises in lieu of a tooth, whereas the former arises in relation to an extracted tooth. Residual cyst may also be confused radiographically with keratocyst, lateral periodontal cyst, and calcifying epithelial odontogenic cyst. Biopsy is required to arrive at a definitive diagnosis.

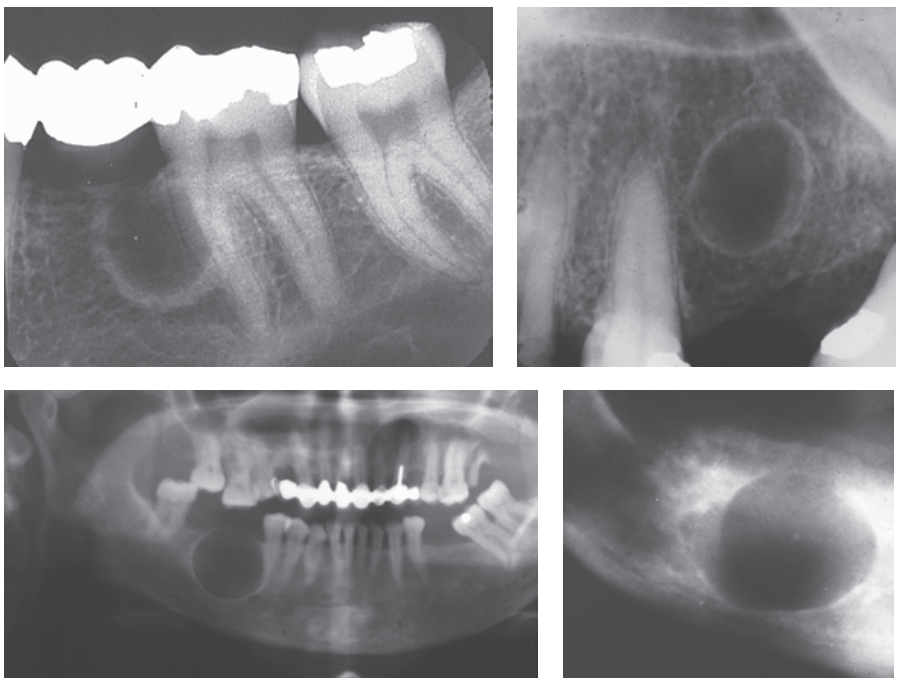

FIGURE 9-16
Residual periapical cysts are located in a site previously occupied by a carious nonvital tooth.

TREATMENT

Surgical enucleation or curettage is the treatment of choice.

Additional Reading

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ODONTOGENIC KERATOCYST

Figure 9-17

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The odontogenic keratocyst is a specific form of odontogenic cyst that is microscopically distinct. It may assume the character of any of the odontogenic cysts and therefore may represent a keratinizing variant of the lateral periodontal cyst. Radiographically, when interradicular, it is a well-marginated radiolucency with a propensity for root divergence and cortical expansion. It is not found in relation to nonvital teeth; pain is not a symptom. When multiple keratocysts of the jaws are observed, the nevoid basal cell carcinoma syndrome should be investigated.

MICROSCOPIC FEATURES

The lumen is often filled with desquamated keratin. The lining, stratified squamous epithelium, possesses a corrugated parakeratin layer, an attenuated spinous cell layer, and a polarized basal cell layer. In general, the fibrous wall is free from inflammation.

DIFFERENTIAL DIAGNOSIS

Lateral odontogenic keratocyst must be differentiated by biopsy from lateral periodontal cyst, primordial cyst, residual cyst, incisive canal cyst, and calcifying epithelial odontogenic cyst. In addition, the odontogenic adenomatoid tumor and any of those lesions classified with the multilocular radiolucencies may begin as unilocular radiolucencies in an interradicular location.

TREATMENT

Surgical enucleation is indicated. At surgery, the keratocyst is represented by a thin delicate membrane. Small cysts have a low recurrence rate, probably less than 20%, whereas large expansile lesions commonly recur following curettage.

Additional Reading

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PRIMORDIAL CYST

Figure 9-18

Age: Onset in young adulthood
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Primordial cysts arise from a developing tooth that fails to differentiate; rather, the

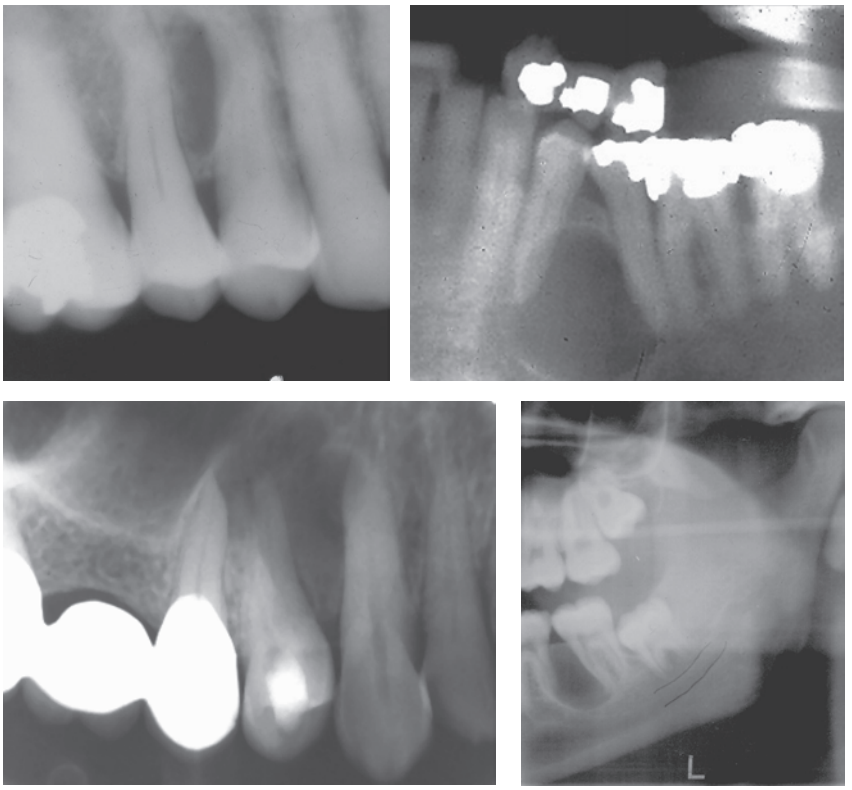

FIGURE 9-17
Interradicular radiolucencies with mild root divergence represent odontogenic keratocysts.

odontogenic epithelium becomes cystic prior to the formation of dental hard tissues. Radiographically, the primordial cyst is unilocular, radiolucent, and well demarcated. The lesion is interradicular or adjacent to teeth and is always present in an area where a tooth would normally have developed. The most common locations are third molar regions and the midline of the maxilla, apparently from the tooth germ of a mesiodens. Despite the aforementioned features, many oral pathologists disclaim the existence of primordial cyst as defined here. Other pathologists in Africa and Europe define primordial cysts as keratocysts.

MICROSCOPIC FEATURES

Primordial cysts are lined by stratified squamous epithelium, and most of them represent keratocysts. The fibrous wall usually lacks an inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The primordial cyst may be radiographically differentiated from the residual cyst because the former arises in lieu of a tooth, whereas the latter is seen after tooth extraction. The primordial cyst must also be differentiated from lateral periodontal cyst and calcifying epithelial odontogenic cyst.

TREATMENT

Surgical enucleation is the treatment of choice.

Additional Reading

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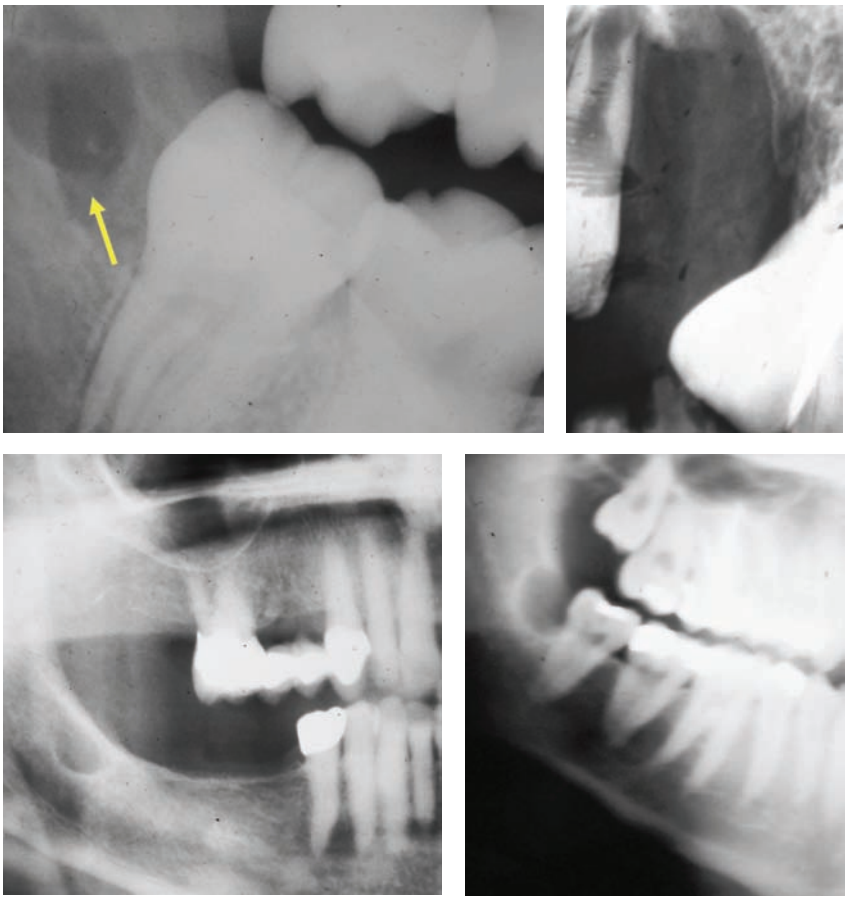

FIGURE 9-18
Unilocular radiolucencies arising in lieu of a tooth representing primordial cysts.

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CALCIFYING CYSTIC ODONTOGENIC TUMOR

Figure 9-19

Age: No predilection
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The calcifying odontogenic cyst, or Gorlin cyst, arises most often in the premolar region of the mandible, appearing as a well-demarcated unilocular radiolucency located interproximally. The lesion may be entirely radiolucent or may contain radiopaque calcific flecks. Divergence of the juxtaposed roots is a common finding. After this lesion was first recognized, it was discovered that there are solid tumor forms, also benign in their behavior. Nearly one fourth of these cysts are located peripheral to bone on the attached gingiva. The teeth test vital, and pain is not a feature.

MICROSCOPIC FEATURES

The lining epithelium shows distinct pathognomonic features. The basal cell layer is polarized, assuming the posture of ameloblasts. The spinous cell layer resembles that of stratified squamous epithelium or may acquire the features of stellate reticulum. Melanin pigment has been reported to occur in these lesions. The spinous cells undergo keratinization toward the luminal surface; large eosinophilic cells with vacuoles replacing nuclei are apparent, termed *ghost cells.* An eosinophilic dentinoid material is often

found within the fibrous wall in juxtaposition to the basal cells. Occasionally, the epithelium proliferates along the differentiated lines just enumerated yet fails to form a true cyst. Many Gorlin cysts are therefore benign neoplastic proliferations rather than true cysts. The features of this cyst on occasion are found in association with odontomas or even in other types of odontogenic tumors. Two variants include the *dentinogenic ghost cell tumor* and the *malignant ghost cell tumor*. The former shows sheets of odontogenic epithelium with focal aggregates of ghost cells and deposition of induced dentine; the latter is similar histologically yet is highly cellular with mitotic figures.

DIFFERENTIAL DIAGNOSIS

Calcifying cystic odontogenic cysts and tumors in the entirely radiolucent stage may be confused radiographically with lateral periodontal cyst, odontogenic keratocyst, primordial cyst, residual cyst, or one of the nonodontogenic developmental cysts if located in specific areas in which confusion may occur. Apical periodontal cysts arising from a necrotic lateral pulp canal can be ruled out on the basis of vitalometry.

TREATMENT

Surgical excision or curettage is the treatment of choice. Recurrence is rare, although the aggressive malignant ghost cell tumor may require resection.

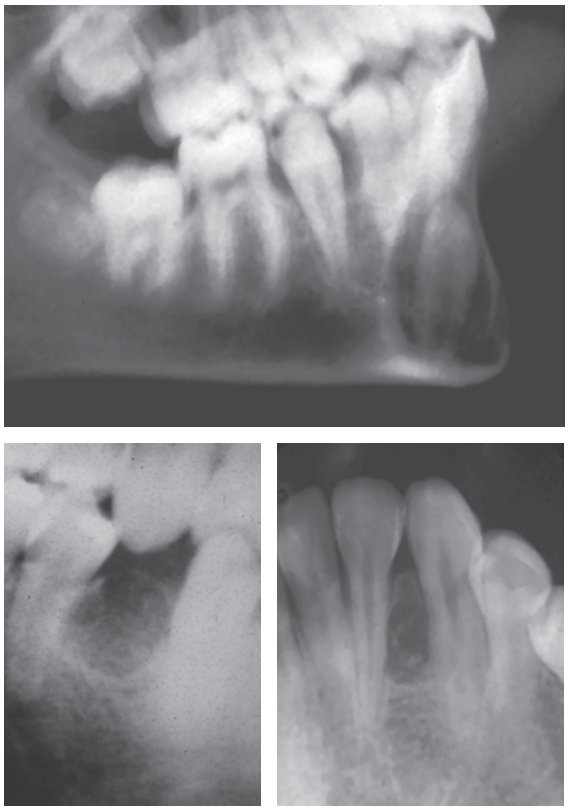

FIGURE 9-19
The calcifying cystic odontogenic tumor may be predominantly cystic or it may be a solid tumor. It is usually a well-circumscribed radiolucency located in the anterior segments.

Additional Reading

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Gorlin RJ, Pindborg JJ, Clausen FP, Vickers RA. The calcifying odontogenic cyst—a possible analogue of the cutaneous calcifying epithelioma of Malherbe. *Oral Surg Oral Med Oral Pathol.* 1962;15:1235.

Ledesma-Montes C, Gorlin RJ, Shear M, et al. International collaborative study on ghost cell odontogenic tumours: calcifying cystic odontogenic tumour, dentinogenic ghost cell tumour and ghost cell odontogenic carcinoma. *J Oral Pathol Med.* 2008;37:302-308.

Soames JV. A pigmented calcifying odontogenic cyst. *Oral Surg Oral Med Oral Pathol.* 1982;53:395.

SQUAMOUS ODONTOGENIC TUMOR

Figure 9-20

Age: Young adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Squamous odontogenic tumor is a hamartomatous proliferation of odontogenic epithelium, probably arising from the rests

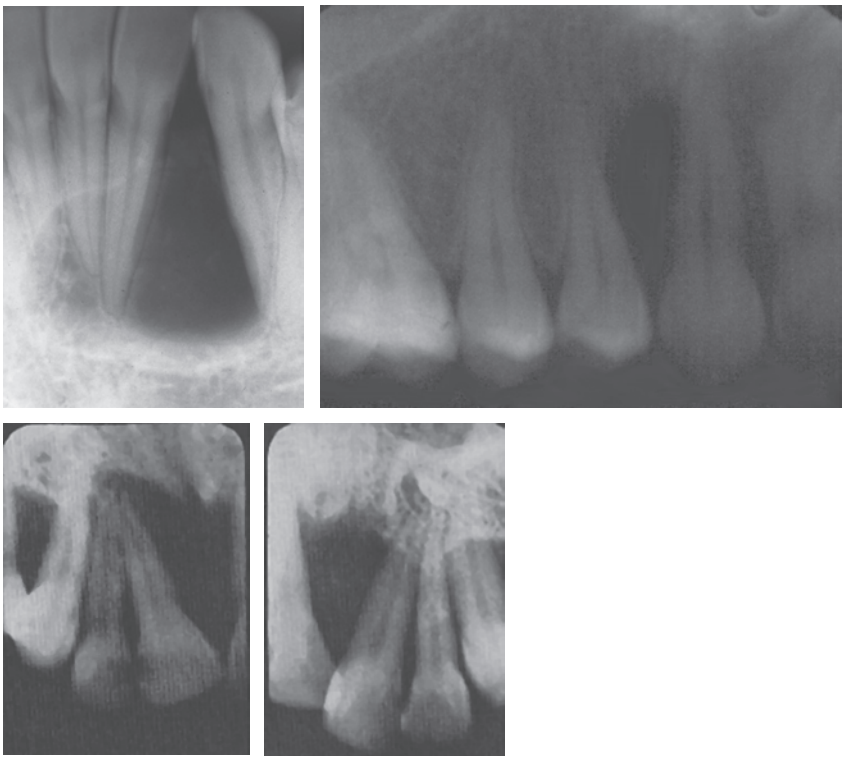

FIGURE 9-20
Interradicular defect in squamous odontogenic tumor. (Courtesy of Dr. A. Jonker.)

of Malassez. The maxillary incisor-canine area and mandibular molar area are the primary sites of involvement. Most cases are unifocal with well demarcated margins and shaped like a wine flask. Tooth mobility is the chief presenting sign; radiographically, a localized radiolucency interposed between contiguous teeth appears as a well-circumscribed periodontal defect. Most cases are either triangular or semicircular in configuration. Some lesions exhibit an intact overlying alveolar crest; most, however, extend coronally with loss of crestal bone. Although usually a solitary lesion, familial multifocal lesions have been reported.

MICROSCOPIC FEATURES

Oval, round, and curvilinear nests of squamous epithelial cells are dispersed throughout a mature collagenous stroma. The basilar stratum fails to show polarization. Cystic degeneration is commonly seen, and some of the squamous nests exhibit ovoid crystalloid structures.

DIFFERENTIAL DIAGNOSIS

The radiographic features simulate a localized periodontal defect enveloping roots. Langerhans disease should also be considered in the differential diagnosis.

TREATMENT

Most cases fail to recur after extraction of the involved tooth and thorough curettage of the lesional tissue. Maxillary lesions may be more extensive, involving the sinus; resection may be required to prevent recurrence.

Additional Reading

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SURGICAL CILIATED CYST

Figure 9-21

Age: Adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

After a Caldwell-Luc operation, fragments of sinus epithelial lining may become entrapped in the maxillary surgical site. If this epithelium undergoes benign cystic proliferation, a unilocular well-delineated radiolucency becomes discernible in the maxilla. The lesion lies within the alveolar bone subjacent to the antral floor and is generally confined to an edentulous or interradicular area in the posterior maxilla. Pain or discomfort may be present.

MICROSCOPIC FEATURES

The cyst is lined by pseudostratified columnar ciliated epithelium. The connective tissue wall may display an inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

By virtue of its location, the surgical ciliated cyst may radiographically resemble an apical periodontal cyst, residual odontogenic cyst, or low sinus extension. Indeed, loculations of the maxillary sinus are common. A history of previous sinus surgery coupled with biopsy allows for a definitive diagnosis.

TREATMENT

Surgical enucleation is the treatment of choice.

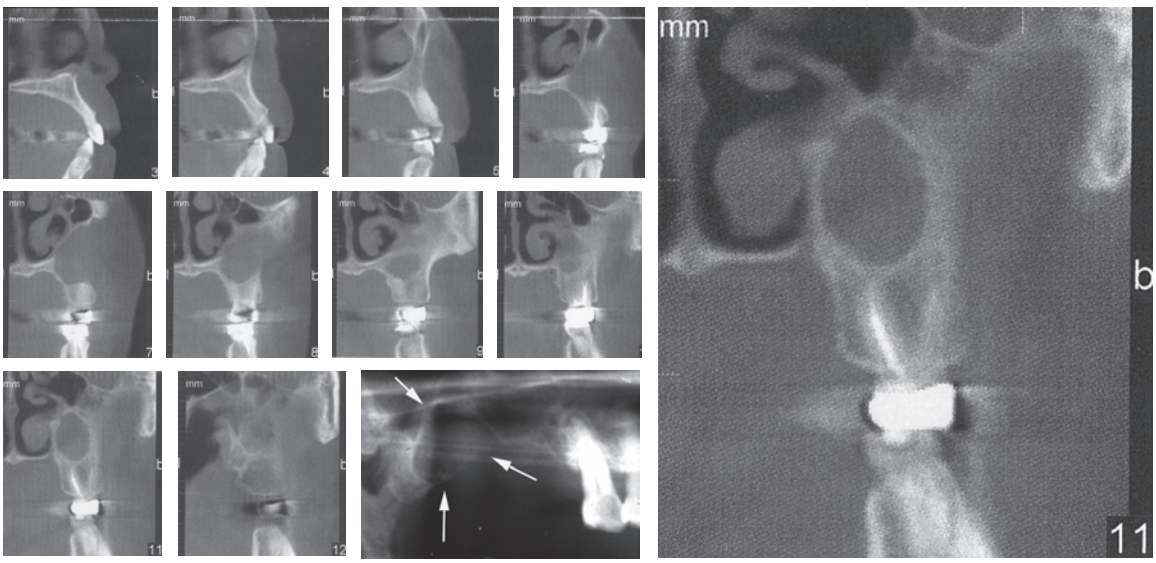

FIGURE 9-21
Well-circumscribed radiolucency in the posterior maxilla subsequent to a Caldwell-Luc procedure or a postosteotomy is typical for surgical ciliated cysts.

Additional Reading

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OSTEOPOROTIC BONE MARROW DEFECT

Figure 9-22

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

After tooth extraction, the socket may heal by formation of hematopoietic marrow rather than cancellous bone. This results in a radiolucency located in the edentulous region previously occupied by a tooth. The radiolucency characteristically shows ill-defined ragged margins that blend into the normal adjacent cancellous bone. Cortical expansion does not occur, and pain is not a feature.

MICROSCOPIC FEATURES

Adipose tissue is seen with multiple foci of hematopoietic blast cells of myeloid, erythroid, lymphoid, and megakaryocytic cell lines. Thin osseous trabeculae are also encountered.

DIFFERENTIAL DIAGNOSIS

A nonexpansile poorly marginated radiolucency in an edentulous or interproximal area is probably an osteoporotic bone marrow defect. The other interradicular radiolucencies listed in this chapter show well-defined borders. Other nonexpansile poorly demarcated radiolucencies include multiple myeloma, histiocytosis X, and metastatic cancer. For this reason, even though suspicion is high for bone marrow defect, a biopsy should be performed.

TREATMENT

Once the diagnosis is confirmed by biopsy, no further treatment is needed.

Additional Reading

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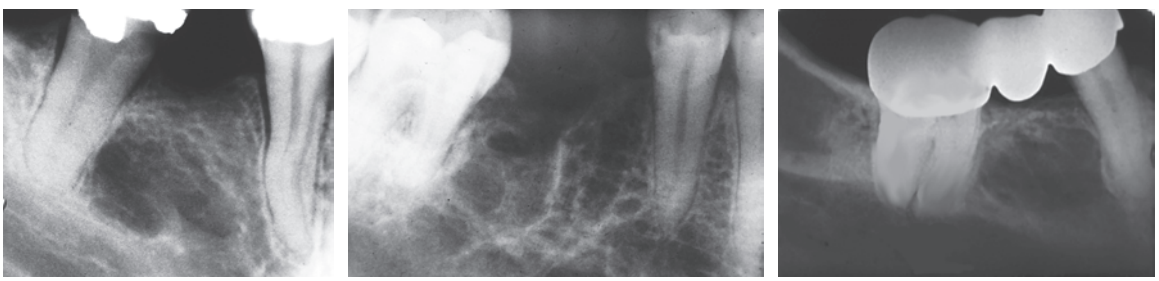

FIGURE 9-22
Radiolucency in previous extraction site representing an osteoporotic bone marrow defect.

Standish SM, Shafer WG. Focal osteoporotic bone marrow defects of the jaws. *J Oral Maxillofac Surg.* 1962;20:123.

CENTRAL OSSIFYING (CEMENTIFYING) FIBROMA

Figure 9-23

Age: Children and young adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Ossifying fibroma of bone is a neoplasm representing one of the benign fibro-osseous lesions of the jaws. When the tumor synthesizes cementum rather than osteoid, the lesion is referred to as a cementifying fibroma. Clinically, the lesion manifests as a painless enlargement with cortical expansion, and the mandible is affected far more frequently than the maxilla. Radiographically, the lesion is unilocular, although multilocular patterns are also encountered. Expansion with clearly demarcated borders is typical: in the mandible, a smooth bowing expansion of the inferior border is commonly observed. The lesion usually extends between teeth and causes root divergence. In the early growth stage, the lesion may appear entirely radiolucent; with time, the center becomes progressively radiopaque as more calcified product is elaborated. If left untreated, the tumor may reach massive proportions and result in significant facial disfigurement. Ossifying fibromas are found in hyperparathyroidism among patients with a mutation in the *HRPT2* gene: the *hyperparathyroidism-jaw tumor syndrome.*

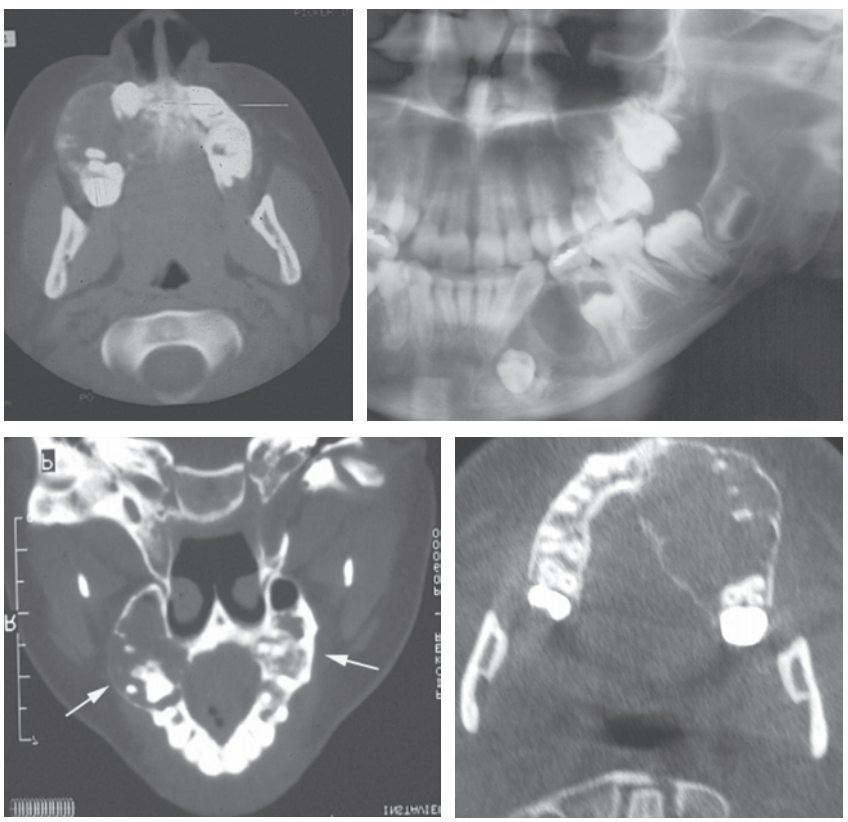

FIGURE 9-23
Radiolucencies with expansion extending between molar roots represent central ossifying fibromas. One instance shows two separate lesions, a rare finding.

MICROSCOPIC FEATURES

A highly cellular fibroblastic stroma prevails, with the presence of delicate collagen fibers. Capillaries course throughout this stroma, and foci of osteoid trabeculae are observed. In radiolucent lesions, the fibrous element is predominant and the osteoid matrix is poorly calcified. When ovoid or curvilinear trabeculae prevail and show polarization patterns consistent with cementum, then the lesion is differentiating along periodontal ligament progenitor cell lines. These cementifying patterns are more often seen in black than in white patients.

DIFFERENTIAL DIAGNOSIS

Ossifying and cementifying fibromas in the early radiolucent stage must be differentiated from various cysts appearing as interradicular radiolucencies and from other fibro-osseous and central neoplasms included in the section on multilocular radiolucencies, because any of those lesions may begin as a unilocular radiolucency. Differentiation from fibrous dysplasia is not difficult when microscopic and radiologic features are considered together. Fibrous dysplasia evinces poorly demarcated borders radiographically, whereas ossifying and cementifying fibromas show well-marginated borders.

TREATMENT

Surgical enucleation is rarely followed by recurrence. Nevertheless, aggressive behavior is encountered, and some cases manifest multiple recurrences. In these instances, en bloc resection may be required to eradicate the disease.

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ODONTOGENIC ADENOMATOID TUMOR

Figure 9-24

Age: Teenagers
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Although the odontogenic adenomatoid tumor typically arises in association with the crown of an impacted tooth, 25% are located laterally. The maxilla is more often affected, with radiolucency interposed between contiguous teeth. They typically localize to the premolar or anterior regions. The radiolucency often contains radiopaque flecks because portions of the tumor can calcify. It is almost invariably unilocular and is well demarcated or corticated. Painless cortical expansion is often the presenting sign.

MICROSCOPIC FEATURES

The tumor is surrounded by a dense fibrous capsule. The epithelial neoplastic tissue often assumes the appearance of a cyst with luminal proliferation. The epithelial cells are elongated and arrange themselves in swirls. This growth pattern yields a granuloma-like configuration. Admixed with the spindle cell component are oval nests of columnar epithelial cells

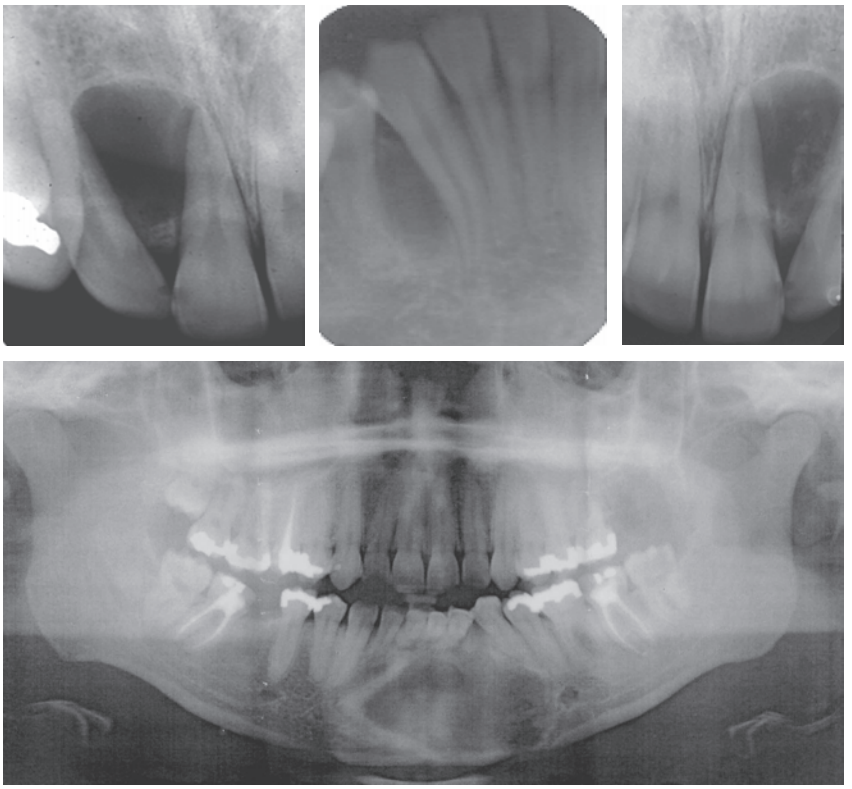

FIGURE 9-24
Interradicular odontogenic adenomatoid tumors are radiolucent and over time develop calcifications.

with ameloblastic cytologic features. These cells are oriented about an eosinophilic secretion product and in classic examples assume ductal patterns with a central lumen. Hyaline eosinophilic elements are also present, and in many areas, these cell products undergo a dystrophic type of calcification. Rarely, melanin pigment may be present. Other coexistent odontogenic tumor histologic patterns are occasionally encountered.

DIFFERENTIAL DIAGNOSIS

Odontogenic adenomatoid tumors seen as interradicular radiolucencies must be differentiated from other lesions that arise between teeth. The young age, anterior location, and tendency for the calcifications to occur are highly suggestive of odontogenic adenomatoid tumor. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Simple enucleation of the neoplasm is adequate treatment. Sometimes one or both of the adjacent teeth will require extraction. The tumor rarely recurs.

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ODONTOGENIC FIBROMA

Figure 9-25

Age: Wide range
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The odontogenic fibroma is classified as a mesenchymal odontogenic tumor. It is typically interradicular and may be located anywhere in the jaws. As the tumor enlarges it can resorb the roots of adjacent teeth. In maxilla tumors, a dimple may be seen on the palate adjacent to where the tumor is located. The lesion is usually asymptomatic. This tumor also occurs peripherally on the gingiva. Odontogenic fibromas may also occur around the crowns of impacted teeth and are multiple and associated with hypoplastic enamel in the *odontogenic fibroma/hamartoma enamel hypoplasia syndrome* (see pericoronal radiolucencies).

MICROSCOPIC FEATURES

A mature collagenous proliferation is present with monomorphic-appearing fibroblasts and a small vessel network. The lesion is relatively hypocellular. Dispersed throughout are small oval and linear odontogenic epithelial islands with prominent eosinophilic, or sometimes clear, cytoplasm. Some cases may show amyloid deposits, and the epithelial islands are wrapped with dentritic cells positive for CD1a. Some cases of odontogenic fibroma were found

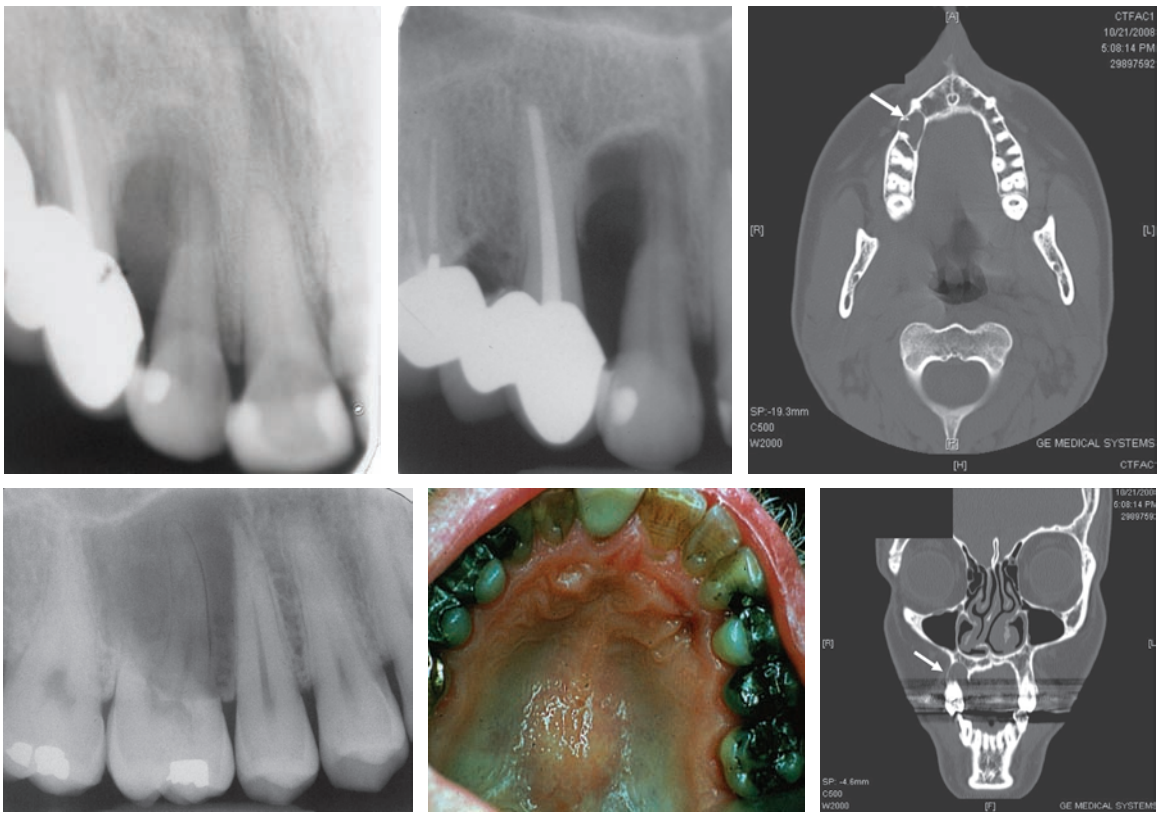

FIGURE 9-25
Odontogenic fibromas often cause root resorption. A palatal "dimple" may also occur adjacent to the tumor.

to contain granular cells both in the epithelium and the stroma. This variant has been reclassified as *granular cell odontogenic tumor*. Another variation is the coexistence of odontogenic fibroma with central giant cell granuloma.

DIFFERENTIAL DIAGNOSIS

The presence of root resorption and palatal dimpling are highly suggestive of odontogenic fibroma. Other entities included here must be considered.

TREATMENT

Curettage is the treatment of choice. Teeth exhibiting resorption will usually require extraction.

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CENTRAL GIANT CELL GRANULOMA

Figure 9-26

Age: Young adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Central giant cell granuloma is a neoplastic-like reactive proliferation of the jaws that usually exhibits a multilocular pattern as observed radiographically. Early smaller lesions are usually unilocular and frequently lie adjacent to vital teeth. The lesion is more common in the mandible than in the maxilla underlying anterior or premolar teeth. Buccal or lingual cortical expansion can often be detected both clinically and radiographically; expansile lesions can cause root divergence or resorption.

MICROSCOPIC FEATURES

Multinucleated giant cells, dispersed throughout a hypercellular fibrovascular stroma, possess randomly arranged nuclei that are either pyknotic and hyperchromatic or oval and stippled with prominent nucleoli. Erythrocyte engorgement of vessels and extravascular hemosiderin pigment are frequently observed as are occasional osseous trabeculae.

DIFFERENTIAL DIAGNOSIS

The adjacent teeth are generally vital, a feature that eliminates an endodontic infection. When expansion is present, other lesions listed here must be considered. Other neoplastic processes and keratocysts can coincidentally arise in interradicular locations and expand bone. Biopsy is required to make the diagnosis.

TREATMENT

Thorough curettage is the treatment of choice. When the diagnosis has been established, appropriate laboratory tests should be performed to rule out brown tumor of hyperparathyroidism.

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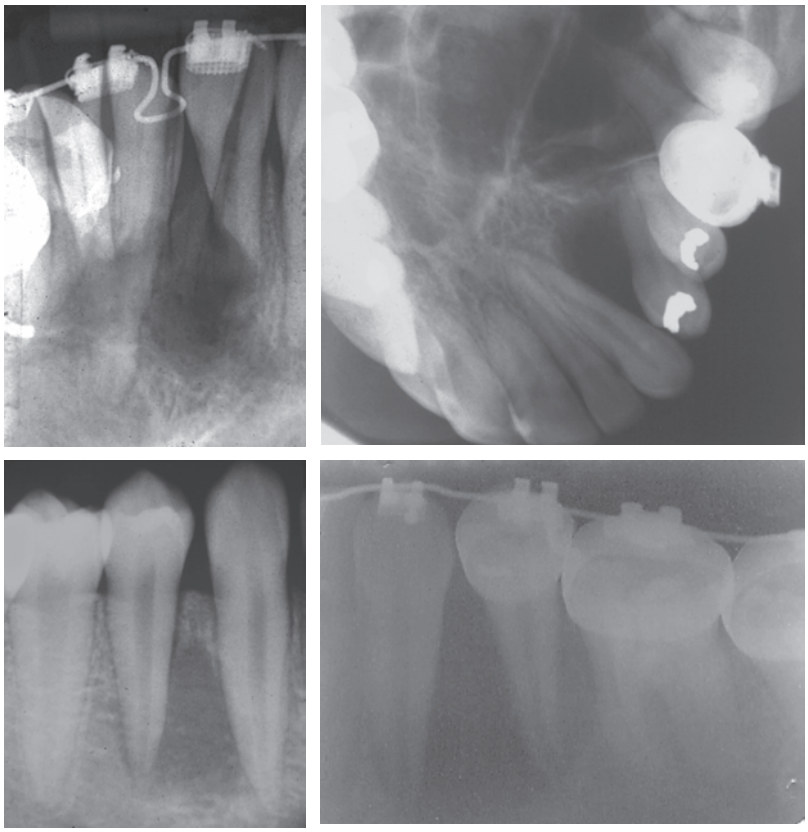

FIGURE 9-26
Root divergence is common with central giant cell granulomas.

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Periodontal (Alveolar) Bone Loss

CHRONIC PERIODONTITIS

Figure 9-27

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The most common cause of alveolar bone loss, as evidenced radiographically, is chronic periodontitis. Indeed, it is the most common oral disease of adulthood. Whereas overt manifestations are encountered during middle age, early features of the disease are often apparent in teenagers and young adults. Periodontal pockets in excess of 3 mm are indicative of early periodontitis. Radiographically, the alveolar bone evinces either a uniform apical migration (horizontal bone loss) or multifocal sharply demarcated trenching (vertical bone loss). The earliest stage is a V-shaped wedge seen on the alveolar process in the interproximal region. The gingiva may be edematous and hyperemic. Itching is often a symptom; however, the disease may become severe without any symptoms of pain. The precise etiology is unknown, but the severity of inflammation and bone loss is proportional to the amount of accumulated plaque and calculus.

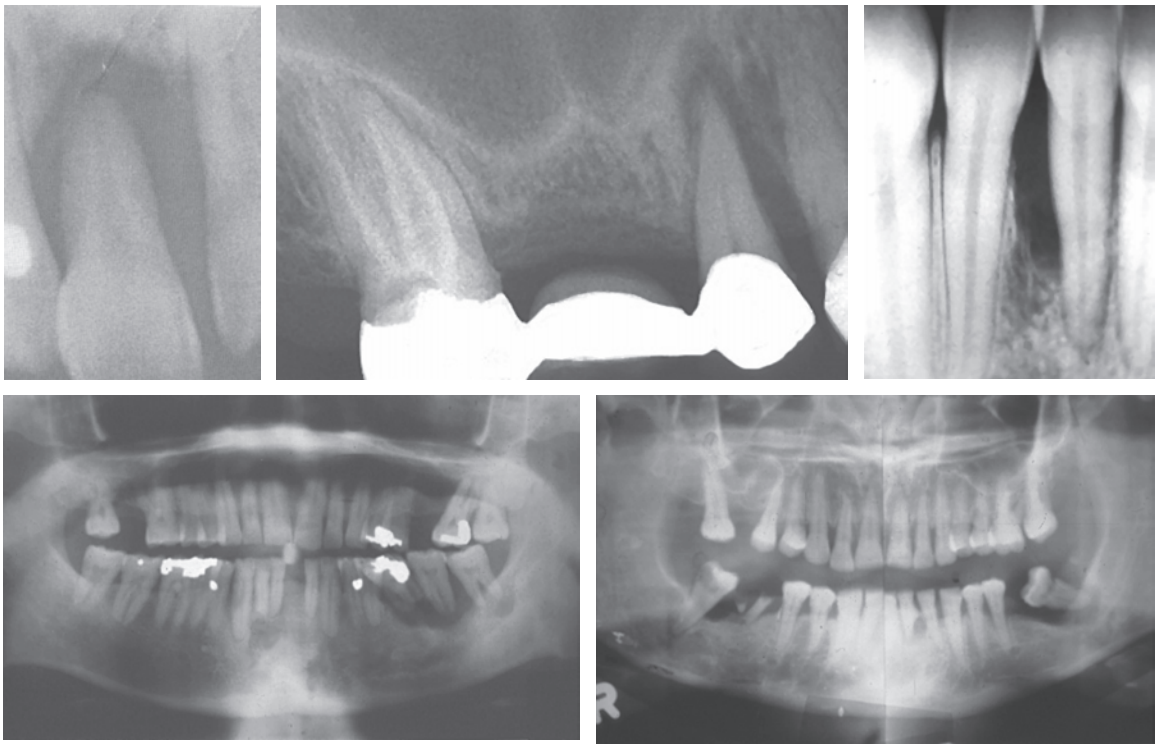

FIGURE 9-27
Alveolar bone loss in chronic periodontitis.

MICROSCOPIC FEATURES

The crevicular epithelium lacks a cornified layer and shows elongation of rete ridges with transmigration of neutrophils into the spinous layer. The subjacent fibrous and granulation tissues are avidly infiltrated with plasma cells and lymphocytes.

DIFFERENTIAL DIAGNOSIS

Rapid alveolar bone loss may occur in conjunction with juvenile diabetes, cyclic neutropenia, Langerhans disease, and leukemia. These diseases should be strongly considered in the differential diagnosis of alveolar bone loss in young adults and teenagers. Periodontosis must be included in the differential diagnosis yet shows a specific distribution of bone loss.

TREATMENT

Prevention is the key to control of periodontal disease. This is accomplished by instituting periodic dental prophylaxis in conjunction with daily toothbrushing and flossing. Diets low in refined sugar and carbohydrate also aid in minimizing plaque accumulation. Once alveolar bone loss with pocket formation develops, root planing, curettage, or periodontal surgery is indicated.

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DIABETIC PERIODONTITIS

Figure 9-28

Age: Young and middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Nonspecific chronic periodontitis develops at an early age in diabetics, particularly in those with hyperglycemia of childhood onset. As a result of microangiopathic lesions throughout the body, including the periodontium, in conjunction with deficient fibroblastic energy metabolism resulting from decreased intracellular glucose utilization, wound healing is impaired. Periodontal disease progresses rapidly with widespread horizontal or vertical alveolar bone loss. Multiple foci of periodontal abscess formation often accompany the chronic disease process. Diabetes accompanied by premature periodontal disease is usually overt, and patients show elevated fasting blood glucose and glycosuria.

MICROSCOPIC FEATURES

The microscopic features of diabetic periodontitis are the same as those described for uncomplicated chronic periodontitis. Occasionally, hyaline arteriolosclerosis can be demonstrated.

DIFFERENTIAL DIAGNOSIS

Premature alveolar bone loss is occasionally seen in uncomplicated periodontitis yet is also a feature of periodontosis, Langerhans disease, cyclic neutropenia, and leukemia. When severe or premature bone loss is encountered, a fasting blood glucose test and urinalysis should be performed. If the blood glucose is within normal limits, a 5-hour glucose tolerance test can be performed.

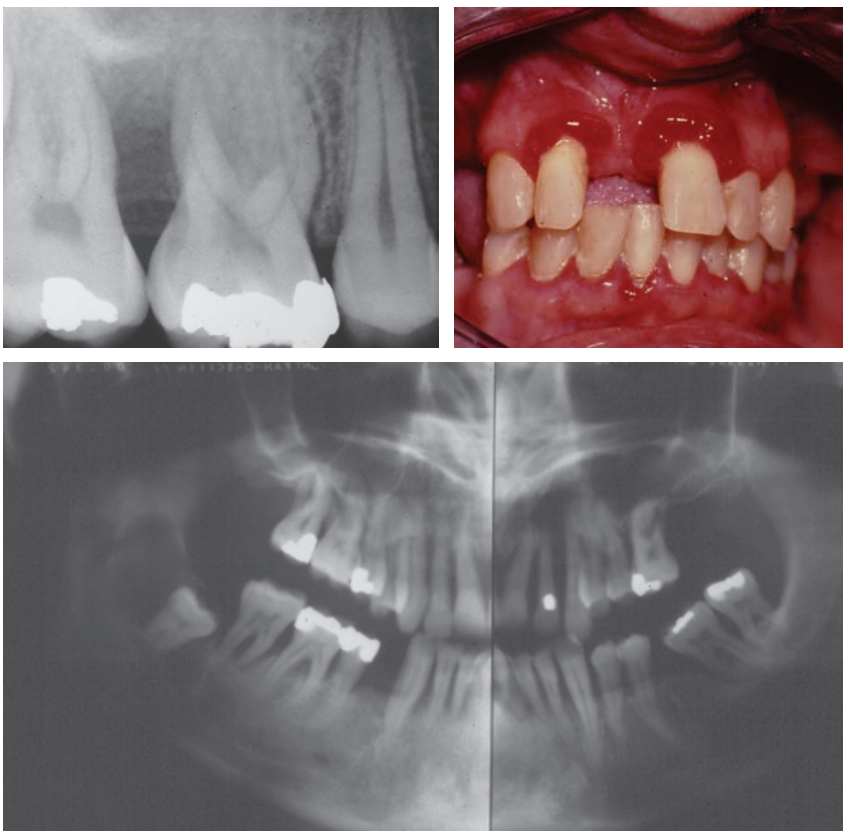

FIGURE 9-28
Premature horizontal and vertical bone loss in a diabetic. Also note coincidental dentigerous cyst around mandibular third molar.

TREATMENT

Once diabetes is diagnosed, the patient requires medication in the form of oral hypoglycemic drugs or parenteral insulin. Referral to a physician is indicated. The periodontal disease should be managed the same as that uncomplicated by diabetes; however, if arteriolar vascular disease is widespread, the prognosis for controlling or preventing continuation of the periodontal lesions is not particularly good.

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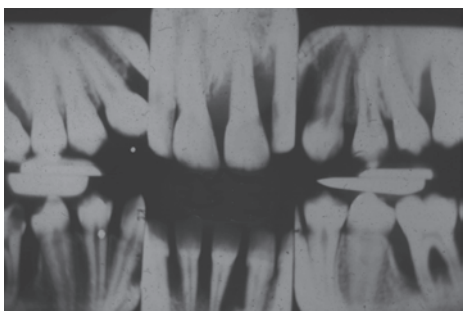
JUVENILE PERIODONTITIS AND PAPILLON-LEFEVRE SYNDROME

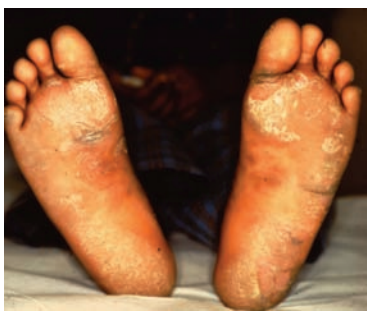
Figure 9-29

Age: Childhood onset
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

A disease of obscure etiology, periodontosis, or juvenile periodontitis represents an inflammatory lesion of the perodontium with the formation of periodontal pockets, loosening of teeth, and rapidly progressive alveolar bone loss. Local factors such as tooth-accumulated material and calculus are not significant etiologically. Immunopathic mechanisms, a granulocyte disorder, and anaerobic bacteria have been implicated as etiologic factors. In the generalized form, a leukocyte adhesion deficiency occurs; however, the localized form has no known association with a hematologic disorder. The subgingival gram-negative anaerobic flora is specific and unique to juvenile periodontosis and differs considerably from the flora isolated





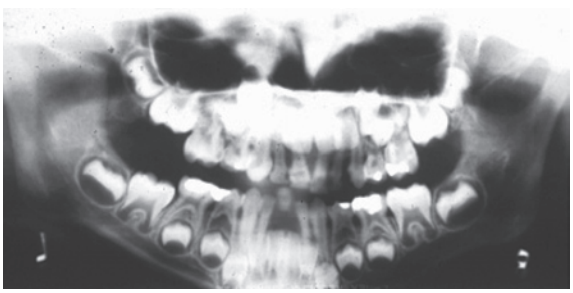


FIGURE 9-29
Alveolar bone loss confined to incisor and molar regions in juvenile periodontitis (Papillon-LeFevre). Bottom: nonsyndrome case of juvenile periodontitis.

from the pockets of adult chronic inflammatory periodontal disease—*Actinobacillus* and *Bacteroides* being predominant organisms. Whether these organisms are pathogens and play a causative role is unknown. Radiographically, a classic topography of alveolar osseous recession is encountered in the generalized form. The periodontal tissues around the molars and incisors are selectively lost and replaced by granulation tissue, whereas the cuspids and premolars are spared or involved only to a minimal degree. Not all instances of childhood-onset periodontal disease manifest this pattern. When this pattern of bone loss is accompanied by hyperkeratosis of the palms and soles, the condition is termed the Papillon-Lefevre syndrome. The disease has an autosomal recessive genetic pattern with a mutation in cathepsin C.

MICROSCOPIC FEATURES

Biopsy specimens of pocket tissue show granulation tissue with nonspecific chronic inflammation composed chiefly of lymphocytes and plasma cells.

DIFFERENTIAL DIAGNOSIS

Periodontitis, diabetic periodontitis, cyclic neutropenia, Langerhans cell histiocytosis, and leukemia must all be considered in the differential diagnosis. Onset at a young age and classic incisor-molar alveolar bone loss in conjunction with nonspecific chronic inflammation as evidenced microscopically lead to a diagnosis of periodontosis.

TREATMENT

The dental prognosis is poor. Teeth lose periodontal support despite efforts directed toward plaque control. The teeth involved in alveolar bone degeneration should be maintained without resorting to heroic surgical procedures; when they are no longer functional, extraction becomes necessary. Metronidazol helps to stop progression.

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VANISHING BONE DISEASE (MASSIVE OSTEOLYSIS)

Figure 9-30

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Vanishing bone disease (also known as massive osteolysis, phantom bone disease, and Gorham's disease) is one of the most enigmatic processes in medicine and dentistry. Entire bones, for no apparent reason, undergo massive resorption until the entire osseous membrane has completely disappeared radiographically, grossly, and histologically. Virtually any bone may be affected by this idiopathic resorptive process, including the jaws. Symptoms are lacking until resorption proceeds to the extent that pathologic fracture becomes a complication. Normal osseous tissues are replaced by fibrous connective tissue. The process pursues a protracted course, with disappearance of the affected bone after many years. Radiographically, the lesions begin as localized, ill-defined osteoporotic foci, which coalesce to yield massive zones of osteolysis with noncorticated borders. The

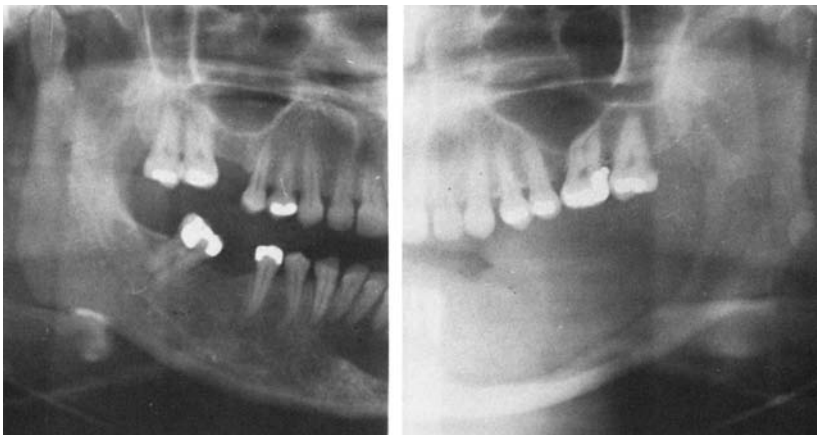

FIGURE 9-30
Widespread alveolar bone loss in the absence of tumor or any identifiable etiologic agent, representing massive osteolysis.

loss of bone may begin at the alveolar crest, with an appearance resembling progressive advanced periodontitis. Often, more than one jaw quadrant is involved. Eventually, the entire mandible, hemimandible, or maxilla may virtually disappear from view radiographically. Serum calcium and phosphorus levels are within normal limits.

MICROSCOPIC FEATURES

Normal osseous trabeculae are present and show foci of resorption. In the resorbed zones, fibrous tissue predominates with proliferation of capillaries. A chronic inflammatory cell infiltrate is often encountered. Pronounced osteoclastic activity is not a feature.

DIFFERENTIAL DIAGNOSIS

The radiographic appearance of massive osteolysis may resemble that seen in periodontitis, Langerhans disease, malignancy, and diabetes. The diagnosis is generally made when cultures are negative and the aforementioned entities are excluded on the basis of histologic examination. Thus, the diagnosis rests on the process of exclusion. Often, long-term follow-up is required before a definitive diagnosis can be rendered.

TREATMENT

Bone grafts are usually unsuccessful, as they too become involved in the resorptive process. Because the etiology remains unknown, no successful treatment has been realized.

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LANGERHANS CELL HISTIOCYTOSIS

Figure 9-31

Age: Children and teenagers
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Langerhans cell histiocytosis is a disease process with a wide spectrum of severity. The basic pathologic process is a neoplasia-

like disorder whereby normal tissues are infiltrated with Langerhans histiocytes, hence the synonymous term Langerhans cell granulomatosis. The younger the patient, the worse the prognosis. Infants show soft tissue histiocytic infiltrates of the skin, spleen, liver, and lymph nodes. This form, known as acute disseminated histiocytosis or Letterer-Siwe disease, is usually fatal. Older children develop the chronic disseminated form, also known as Hand-Schuller-Christian disease. Histiocytic infiltration of the pituitary and retro-orbital soft tissue leads to diabetes insipidus and exophthalmos, respectively. Intraosseous lesions and otitis media are also features of the chronic disseminated form. The chronic limited form is more common among teenagers and young adults, is restricted to bone, and is termed *eosinophilic granuloma of bone.* Pulmonary infiltration by histiocytes may occur in all three forms and can be detected radiographically. Radiographically, the lesions of histiocytosis appear as well-demarcated, yet noncorticated, radiolucencies. The lesions often simulate periodontal disease. Multifocal zones of vertical alveolar bone loss are encountered and may actually completely engulf the apices, giving the impression that the involved teeth are floating in space.

MICROSCOPIC FEATURES

Bone defects contain diffuse sheets of histiocytes that possess voluminous amphophilic cytoplasm with an oval or kidney-shaped vesicular nucleus. Being Langerhans cells, these histiocytes are positive for CD1 and S-100 protein markers. Multinucleated giant cells are often seen; in the chronic forms, foam cells may predominate, yielding a lipogranulomatous picture. Scattered or clustered eosinophils are more numerous in the chronic limited form (eosinophilic granuloma).

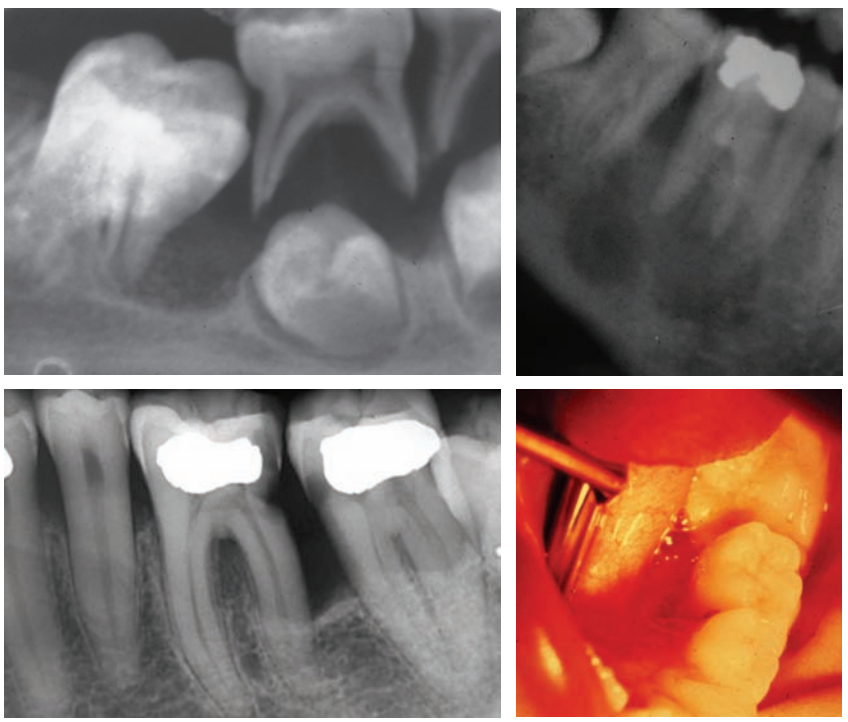

FIGURE 9-31
Localized vertical alveolar bone loss in Langerhans cell histiocytosis, some with "tooth floating in space" appearance.

DIFFERENTIAL DIAGNOSIS

When histiocytosis manifests multifocal zones of periodontal destruction, periodontitis, diabetic periodontitis, cyclic neutropenia, and leukemia must be considered. Signs and symptoms of extraosseous disease are encountered in the disseminated forms, and biopsy discloses the characteristic microscopy of histiocytosis. When the diagnosis is rendered, a skeletal survey and physical examination should be performed to determine the extent of disease.

TREATMENT

Teeth may be saved if the osseous lesions are not too extensive. When alveolar bone is resorbed significantly, it will not regenerate after treatment. Treatment of choice is curettage and Vinca alkaloid chemotherapy.

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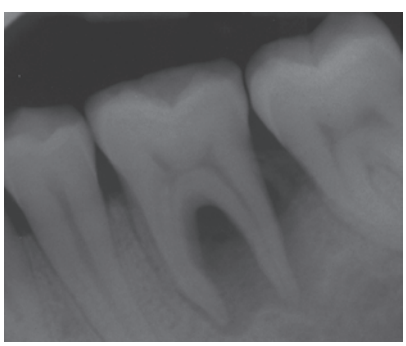
CYCLIC NEUTROPENIA

Figure 9-32

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Cyclic neutropenia is a blood dyscrasia in which a selective diminution in neutrophilic granulocytes develops on a predictably recurrent periodic basis. The neutrophils disappear from the circulation as a result of a bone marrow maturation defect of unknown etiology, although in one third of cases, it appears to be inherited as an autosomal dominant trait. The leukocyte count drops for 5 to 7 days at regular 21-day intervals. In the interim, the white and differential counts are virtually normal; however, neutrophils are rarely present in numbers exceeding 50% of the total leukocyte population. During neutropenia, ragged oral aphthous-like ulcerations appear; when the white count returns to normal, the ulcers heal. During the granulocytopenic phase, malaise, fever, and cervical lymphadenopathy occur. The other chief oral manifestation is premature, or precocious, alveolar bone



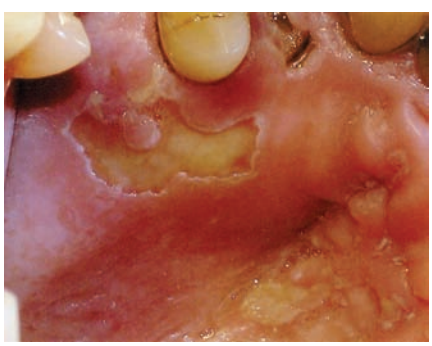


FIGURE 9-32
Horizontal alveolar bone loss in cyclic neutropenia.

loss with classic clinical manifestations of periodontitis.

MICROSCOPIC FEATURES

Curettage from periodontal pockets shows granulation tissue with a mononuclear inflammatory cell infiltrate. The oral ulcers are notably devoid of neutrophils.

DIFFERENTIAL DIAGNOSIS

Precocious periodontal bone loss may be seen in diabetic periodontitis, periodontosis, Langerhans disease, and leukemia as well as in cyclic neutropenia. Regularly recurring ulcerations of the mucosa should arouse suspicion. The diagnosis can be secured by obtaining complete blood counts every 4 days for a 3-week period in order to demonstrate the neutropenic phase.

TREATMENT

Efforts to control plaque, to institute home-care oral hygiene, and to palliate the oral ulcerations with an antihistamine/Kaopectate oral rinse should be made. The patient should be referred to a hematologist to manage the blood dyscrasia and watch for complications such as recurrent infection. Recombinant granulocyte stimulating factor may prove to be of therapeutic value.

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LEUKEMIA

Figure 9-33

Age: Childhood and adult forms
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Leukemias are classified according to the leukocyte blast cell of origin. The more common forms are myelogenous (granulocyte precursors) and lymphocytic. Furthermore, both acute and chronic forms exist. The former pursues a rapid, often fatal, course; however, cures can be achieved with combination drug chemotherapy. The chief clinical signs and symptoms include malaise, low-grade fever, pallor, and dyspnea. Gingival hemorrhage, petechiae, and ecchymoses develop when the platelet count drops subsequent to bone marrow replacement by malignant leukocytes. Gingival enlargement is a feature, with boggy erythematous swellings beginning in the interdental papilla area; these oral manifestations do not often occur, however. Nevertheless, it is important to recognize the fact that leukemic infiltration may involve the periodontium, producing a radiographic picture reminiscent of periodontal disease with vertical pocket formation.

MICROSCOPIC FEATURES

Curettage or an incisional biopsy discloses the presence of diffuse sheets of poorly differentiated leukocyte blast cells. Regardless of whether the leukemia is myeloid, erythroid, or lymphoid, the blast cells are mononuclear and usually monomorphic. Zones of necrosis may be encountered.

DIFFERENTIAL DIAGNOSIS

Radiographic evidence of alveolar bone loss in leukemia may be identical to that seen in nonspecific periodontitis, diabetic periodontitis, periodontosis, histiocytosis,

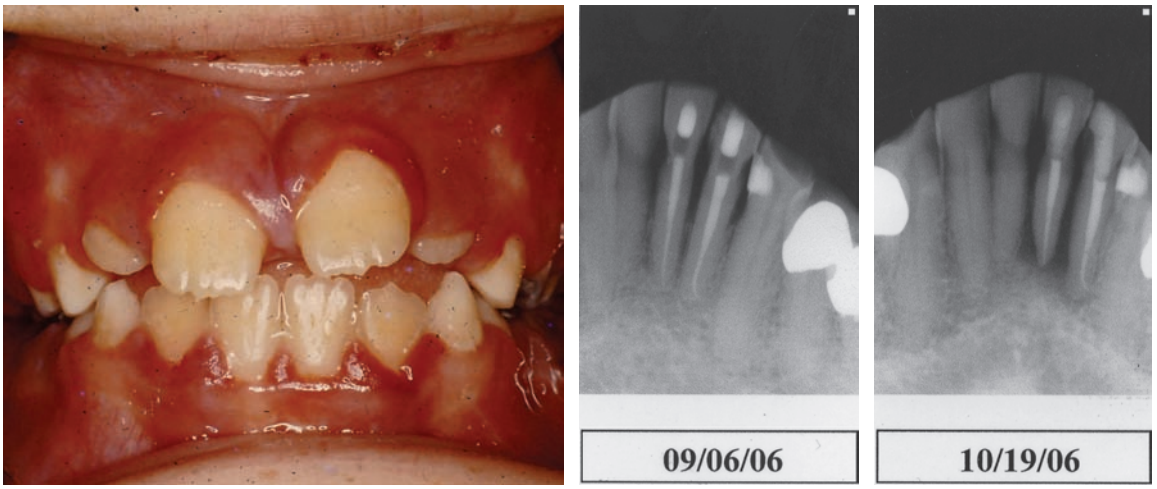

FIGURE 9-33
Leukemic infiltrate with advanced periodontal bone loss in the anterior mandible. Hyperplastic gingivitis is also a feature.

or cyclic neutropenia. Other symptoms, such as fatigue, malaise, petechia, ecchymosis, and gingival hemorrhage, warrant work-up for leukemia. A complete blood count should be obtained.

TREATMENT

Chemotherapeutic control should be instituted as soon as possible by an oncologist or hematologist. Oral lesions respond to systemic medications used for control of leukemia.

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Widened Periodontal Ligament Space

PERIODONTIC/ENDODONTIC INFLAMMATION

Figure 9-34

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Infection of periodontal origin may spread down the entire periodontal ligament, producing a localized widening of the periodontal ligament space. This may be circumradicular or localized to only the mesial or only the distal root region. The periodontal defect can be probed and often induces exudation through the gingival sulcus. The infection can progress through lateral acces-

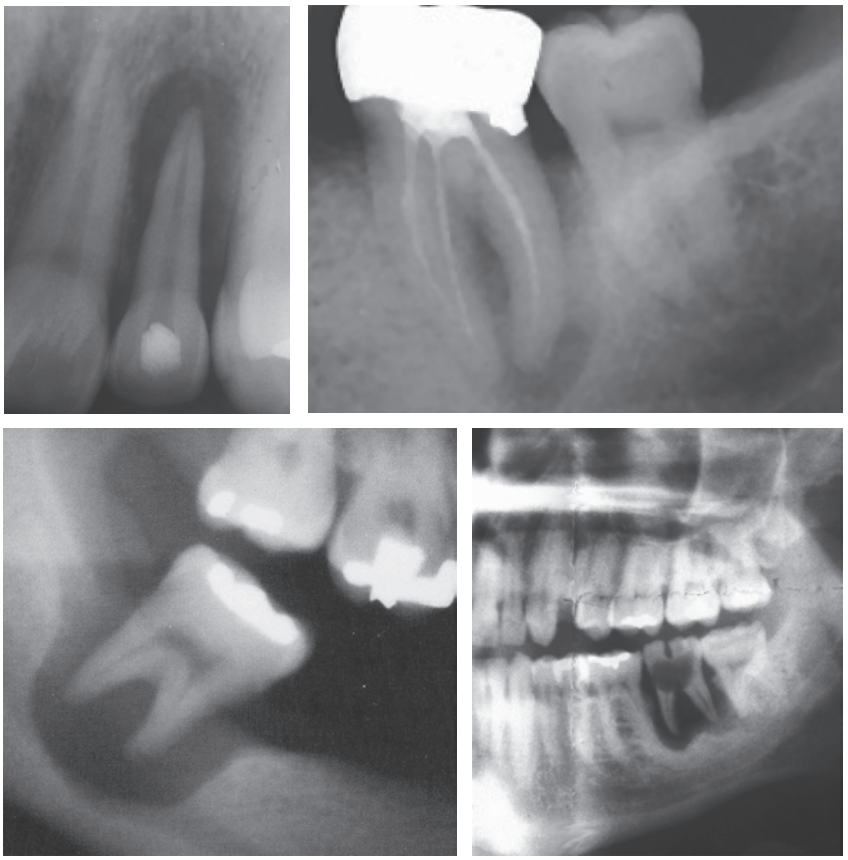

FIGURE 9-34
Widened periodontal ligament space involving nonvital lateral incisor representing combined periodontic-endodontic inflammation.

sory canals or proceed in retrograde fashion through the apical foramen to initiate pulp necrosis. Alternatively, pulpal infection may progress both apically and laterally via accessory canals to involve the lateral periodontal ligament, and the infection may spread coronally with sulcular drainage.

MICROSCOPIC FEATURES

Tissue removed from the widened periodontal ligament is granulation tissue, usually exhibiting a subacute inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

The localized widening of the periodontal ligament space in endodontic/periodontic infection may radiographically resemble incipient osteogenic sarcoma. Periodontal probing and pulp vitality testing usually allows for a clinical diagnosis. More advanced cases may radiographically resemble histiocytosis. When no exudate appears after probing or when the defect resists insertion of the periodontal probe, a biopsy should be procured.

TREATMENT

Advanced cases with pulp necrosis and excessive mobility usually require extraction. In some instances, endodontic therapy with splinting to adjacent teeth is successful, thus avoiding extraction.

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SCLERODERMA

Figure 9-35

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The systemic form of scleroderma is a collagen-immune disease affecting fibrous tissues of the dermis, submucosa of the gastrointestinal tract, and various internal organs. The skin becomes stiff and board-like, losing its flexibility. This change is most obvious on the face, which becomes wrinkle-free and expressionless. As the disease progresses, virtually all body surfaces become involved. The periodontium is affected in a limited number of instances. The crestal alveolar bone is not compromised; rather, a uniform generalized widening of the periodontal ligament space is observed. A pronounced notching of the inferior border of the mandible just anterior to the angle region is also a feature in scleroderma and resorption of the mandibular condyle has been reported to occur.

MICROSCOPIC FEATURES

The periodontal ligament contains dense collagen fibers similar to those seen in the normal ligament.

DIFFERENTIAL DIAGNOSIS

Uniform widening of the periodontal ligament space is seen when a tooth is in severe traumatic occlusion or partially avulsed or, rarely, in periodontitis. If the condition is localized to one or two teeth, early osteogenic sarcoma must be considered in the differential diagnosis. When uniform

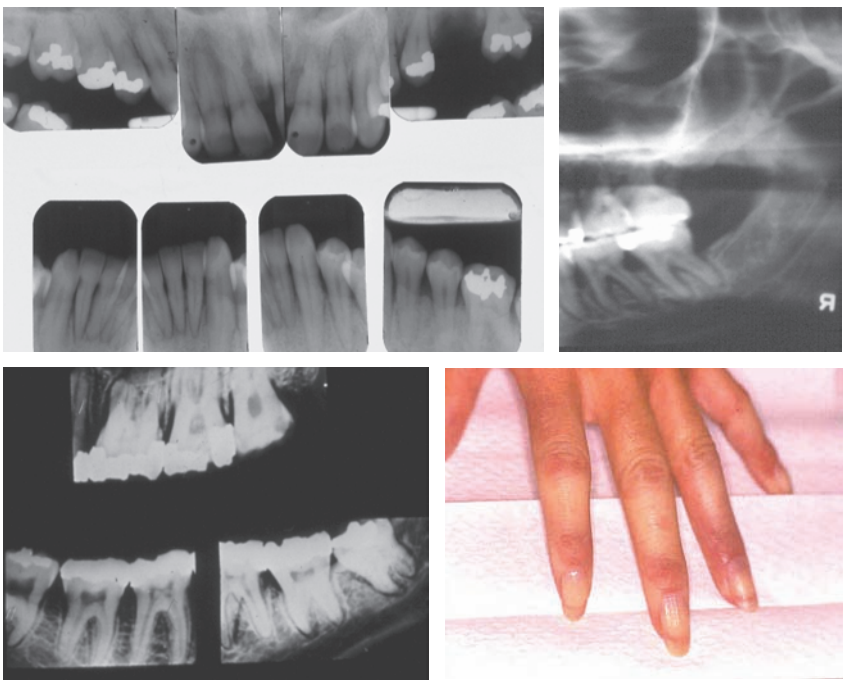

FIGURE 9-35
Generalized widening of periodontal ligament spaces in scleroderma. Raynaud vasoconstriction of fingers.

widening involves the entire dentition, the classic skin changes of scleroderma are invariably encountered.

TREATMENT

The involved teeth are generally secure and not prone to exfoliation. The disease is treated with steroids or immunosuppressive drugs and should be managed by a dermatologist.

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OSTEOGENIC SARCOMA

Figure 9-36

Age: Adults
Sex: Slight male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Primary osteogenic sarcoma of the jaws may manifest a variety of radiographic alterations ranging from radiolucent to radiopaque. It is included in this section because of its tendency to manifest localized symmetric widening of the periodontal ligament space when the lesion is incipient. At this stage, mild cortical expansion may be observed. The medullary bone adjacent to the widened ligament spaces may be normal or show a ragged moth-eaten pattern. Usually, patients do not complain of pain.

MICROSCOPIC FEATURES

Osteogenic sarcoma may be predominantly fibroblastic, chondroblastic, or osteoblastic. The cellular elements display hypercellularity, hyperchromatism, and pleomorphism. Osteoid is elaborated in irregular fashion and is profusely endowed with lacunar spaces containing pleomorphic nuclei. The trabeculae are similarly rimmed by angular malignant osteoblasts. When cartilage is present, lacunae are numerous and often encase multiple nuclei.

DIFFERENTIAL DIAGNOSIS

Localized widening of the periodontal ligament space should always arouse suspicion of osteogenic sarcoma. Similar changes are seen in localized traumatic occlusion and traumatically avulsed teeth. When clinical features of these latter two conditions are not apparent, biopsy is indicated.

TREATMENT

Osteogenic sarcoma requires resection of the jaw, hemimandibulectomy, or partial maxillectomy, and should be managed by a head and neck tumor surgeon. Metastases are usually hematogenous; nodal spread is uncommon. The 5-year survival is less than 35%.

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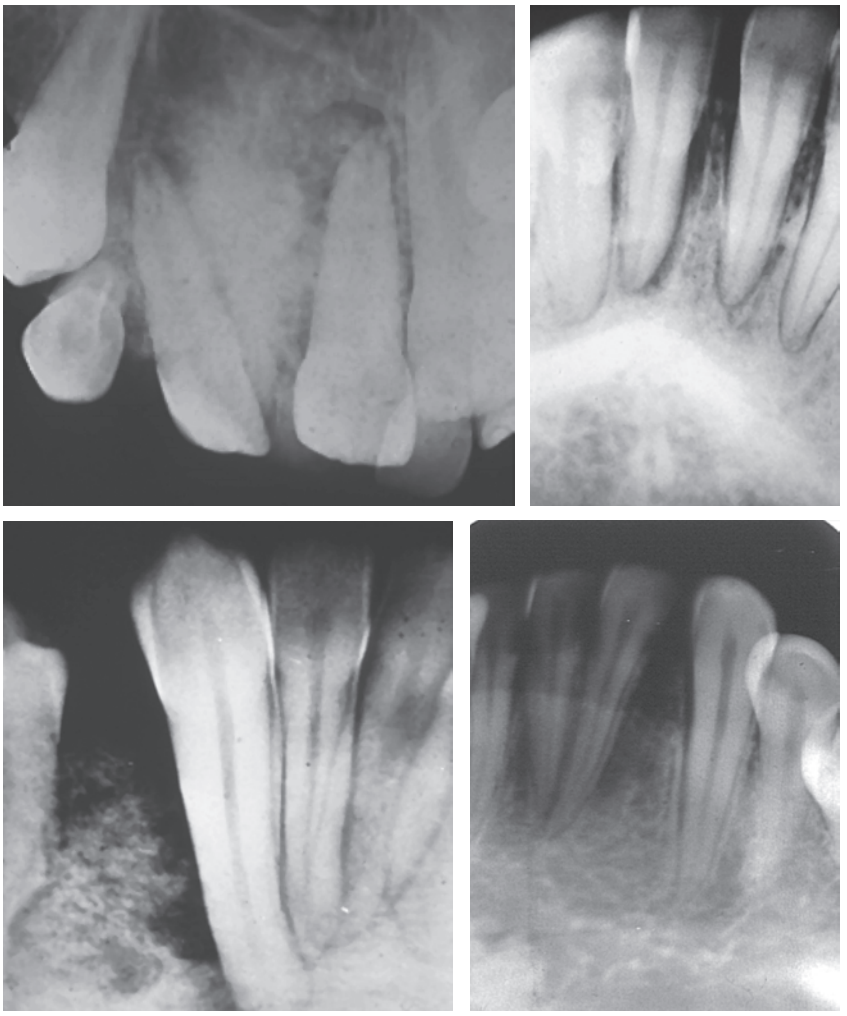

FIGURE 9-36
Localized symmetric widening of the periodontal ligament space in a patient with incipient osteogenic sarcoma.

Pericoronal Radiolucencies

DENTIGEROUS CYST

Figure 9-37

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The follicular or dentigerous cyst is the most common type of developmental odontogenic cyst. By definition, it is a cystic lesion derived from the reduced enamel epithelium encompassing the crown of an impacted tooth. The pericoronal radiolucency is typically well demarcated and may be extensive. The third molars and cuspids are most frequently involved. Cortical expansion and multilocularity may occasionally occur with simple dentigerous cysts; however, these features are more often indicative of neoplastic transformation or keratinizing metaplasia within the cyst lining.

MICROSCOPIC FEATURES

A lining composed of eosinophilic columnar (reduced enamel) epithelium is encoun-

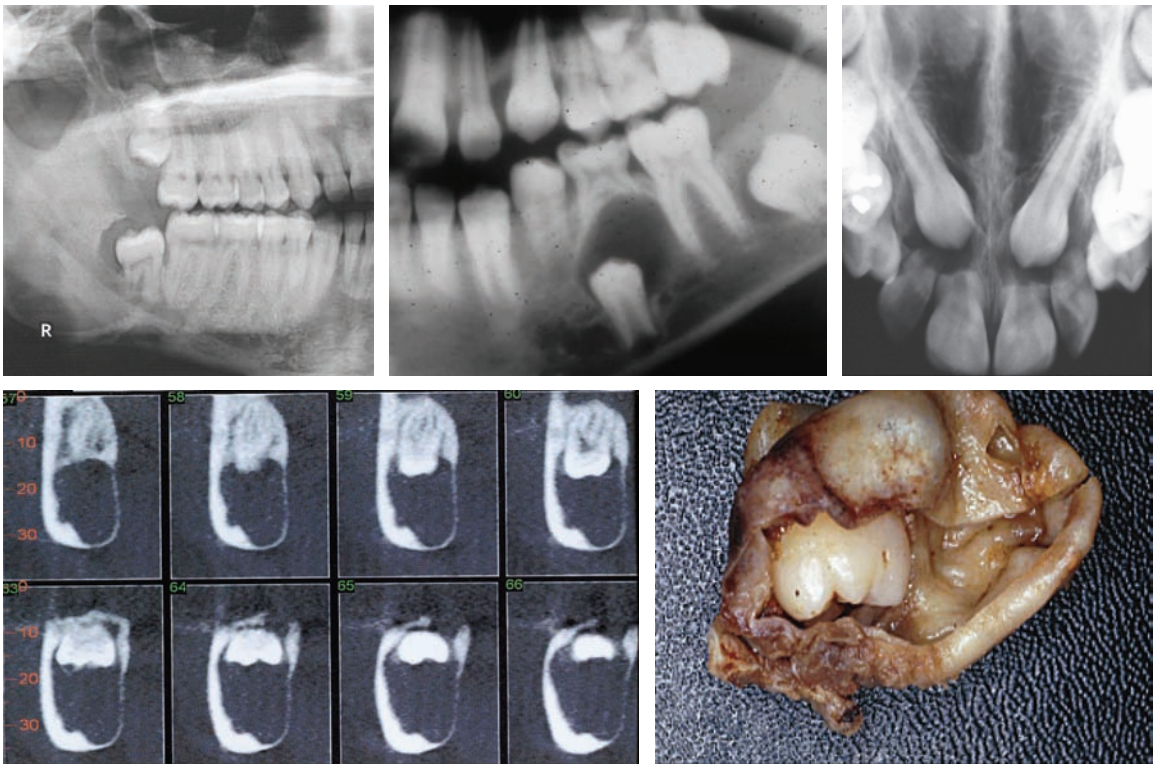

FIGURE 9-37
Dentigerous cysts.

tered in dentigerous cyst removed from younger patients. In older individuals, the lining is composed of stratified squamous epithelium, which is devoid of a cornified layer and fails to display significant rete-ridge formation. Mucous metaplasia, surface cilia, and hyaline bodies are often present within the lining epithelium. The fibrous wall may be devoid of inflammation or may possess a chronic inflammatory cell infiltrate. Varying numbers of oval or elongated odontogenic cell rests are usually seen, and cholesterol clefts may occupy focal regions of the fibrous wall.

DIFFERENTIAL DIAGNOSIS

A nonexpansile pericoronal radiolucency is usually a simple dentigerous cyst. Because many odontogenic tumors, keratocysts, and even malignant neoplasms can arise from the epithelial lining, all dentigerous cysts should be removed and examined microscopically.

TREATMENT

The impacted tooth should be removed if it cannot be orthodontically erupted, and the cyst should be thoroughly curetted.

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ODONTOGENIC KERATOCYST

Figure 9-38

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Because of its protean radiographic manifestations, the odontogenic keratocyst, also termed *keratocystic odontogenic tumor*, is included under many categories in this chapter. Perhaps its most common radiographic presentation is that of a pericoronal radiolucency. The cyst is often encountered when it has reached a size sufficient to produce cortical expansion with noticeable deformity. The impacted tooth is often displaced to the outer margin of the radiolucency, and root development is usually incomplete. The mandibular third molar area is the most common location. Large cysts tend to be multilocular. If multiple pericoronal radiolucencies are present and are microscopically keratinizing, the nevoid basal cell carcinoma syndrome should be considered. Odontogenic keratocysts both solitary and syndrome associated are associated with *PTCH1* gene mutations.

MICROSCOPIC FEATURES

The lining epithelium is attenuated, displaying a corrugated parakeratin or keratin surface, and the basal cell layer is polarized without manifestations of rete-ridge formation. The fibrous wall rarely contains significant inflammation. Epithelial cell rests are

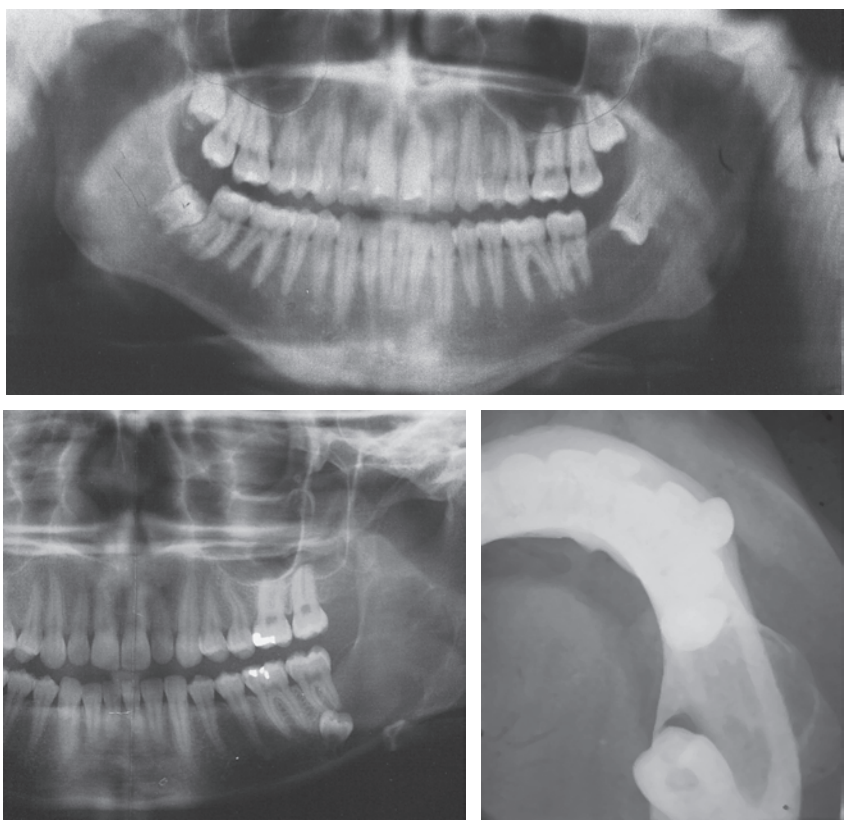

FIGURE 9-38
Odontogenic keratocyst appearing as a pericoronal radiolucency.

present within the fibrous wall, and satellite or daughter cysts are frequently observed.

DIFFERENTIAL DIAGNOSIS

Expansile or loculated pericoronal radiolucencies typical of keratocysts are also featured when neoplastic transformation develops in a dentigerous cyst. Biopsy is required to differentiate among the various lesions presenting this radiographic pattern.

TREATMENT

Thorough curettage should be instituted, along with extraction. Neighboring teeth may need to be sacrificed if significant root resorption has developed. Odontogenic keratocysts are aggressive lesions and may be difficult to eradicate. Recurrence rates in excess of 30% have been recorded. Recurrent lesions may require en bloc resection. Cysts that are characterized histologically by orthokeratin are termed *Orthokeratotic Odontogenic Cyst* and show a lower rate of recurrence.

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GLANDULAR ODONTOGENIC CYST

Figure 9-39

Discussed under Multilocular Radiolucencies

UNICYSTIC AMELOBLASTOMA

Figure 9-40

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Ameloblastomas may arise from any source of odontogenic epithelium. Approximately 20% are associated with the crown of an impacted tooth, usually a mandibular third molar. Although invasive ameloblastomas usually affect middle-aged adults, those that arise from the linings of dentigerous cysts are typically encountered during the second or third decades. Whereas the pericoronal radiolucency may be small, most cystogenic ameloblastomas exhibit a classic radiographic pattern characterized by a large unilocular radiolucency involving the entire ramus, extending to the coronoid process. They are most frequently associated with an impacted, displaced third molar showing incomplete root formation. Occasionally, these tumors are multilocular or evince scalloped margins. When expansion occurs, clinically observable deformity or facial asymmetry may be apparent. Pain and paresthesia are generally not evident.

MICROSCOPIC FEATURES

Most pericoronal ameloblastomas arise from the odontogenic epithelial lining of dentigerous cysts. The earliest evidence of transformation is characterized by polarization of basal cells, superior displacement of nuclei, hyperchromatism, and cytoplasmic vacuolization. Slender tube-like rete ridges extend into the fibrous wall, and the overlying spinous layer resembles stellate reticulum. When the bulk of the tumor protrudes luminally, the designation *luminal ameloblastoma* is used; when the majority of tumor cells invade the fibrous wall, *mural ameloblastoma* is the designation. The term *unicystic ameloblastoma* has been applied to

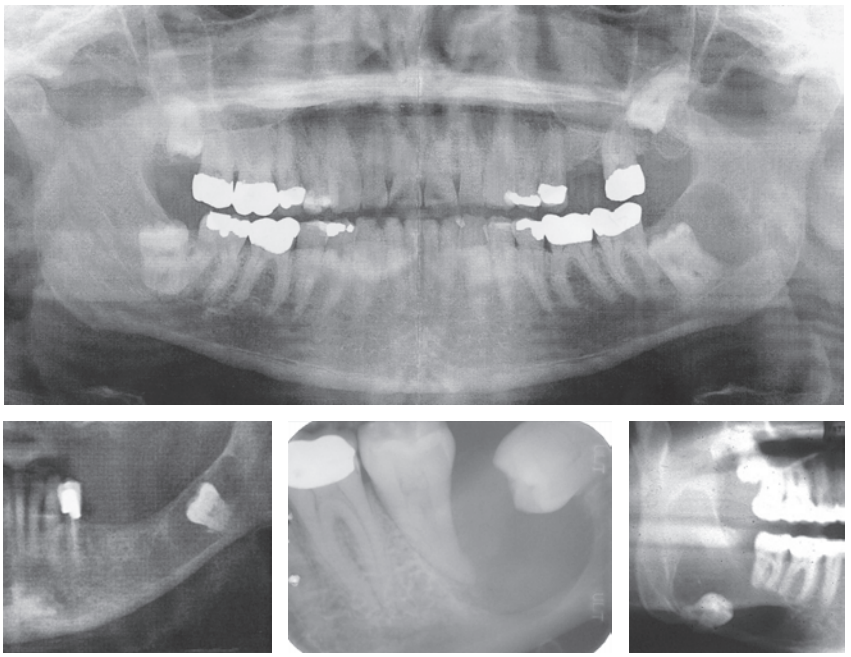

FIGURE 9-39
Pericoronal glandular odontogenic cysts.

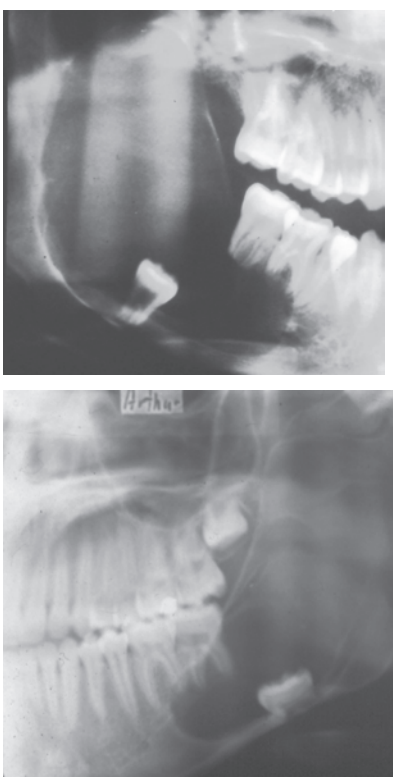

FIGURE 9-40
Unicystic ameloblastomas with inferiorly displaced molars.

those lesions in which ameloblasts line the entire cyst. The later stages of oncogenesis manifest typical histomorphologic features of ameloblastoma.

DIFFERENTIAL DIAGNOSIS

Ameloblastomas arising from dentigerous cysts are radiographically indistinguishable from odontogenic keratocysts, other odontogenic tumors included in this section, and carcinoma arising in a dentigerous cyst. Biopsy is required for a definitive diagnosis.

TREATMENT

Luminal ameloblastomas do not invade the encasing bony crypt. The initial therapy should be curettage when lesions arise in the mandible. Intramural spread of tumor will increase the odds for recurrence. Maxillary tumors that have perforated the antrum are extremely difficult to control with curettage. A partial maxillary resection is recommended in these instances.

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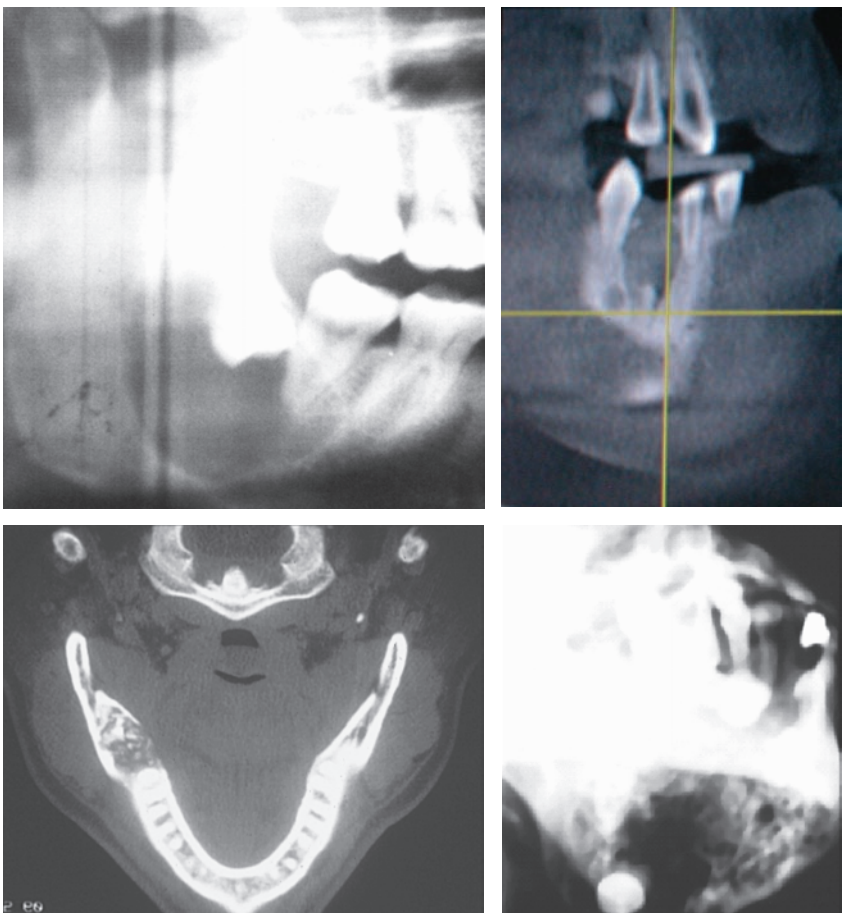

FIG 9-41
Calcifying epithelial odontogenic tumor.

CALCIFYING EPITHELIAL ODONTOGENIC TUMOR

Figure 9-41

Age: Young and middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The calcifying epithelial odontogenic (Pindborg) tumor is rare: when it occurs, it is usually found in association with an impacted tooth. Because the tumor contains foci of calcification, it may show radiopaque flecks, powder-like opacities, or irregular confluent calcific globules. Many tumors, however, are predominantly or entirely radiolucent. Cortical expansion is a regular feature, and the radiolucency may be traversed by thin opaque septae. The margins are generally well demarcated, although radiographic zones of poor margination are encountered in which lesion tends to blend imperceptibly into the adjacent normal medullary bone. As with odontogenic keratocysts, there are reports of *PTCH 1* gene mutations in CEOT.

MICROSCOPIC FEATURES

The neoplastic epithelial cells grow in a variety of patterns, ranging from diffuse sheet-like arrangements to islands and invasive cords. The individual cells bear little resemblance to components of the tooth germ. They are polygonal, eosinophilic, and contain large nuclei that are often hyperchromatic; significant pleomorphism may be present despite the benignity of the tumor. A clear-cell variant exists and is distinguished by sheets and islands of tumor cells that are devoid of stainable cytoplasm. Eosinophilic hyaline is associated with epithelium, and stains are positive for amyloid. Both dystrophic and concentrically laminated Leisegang calcifications are encountered. The radiolucent lesions contain less calcification than the tumors with opacities. Other odontogenic tumor elements such as adenomatoid odontogenic tumor may coexist.

DIFFERENTIAL DIAGNOSIS

Calcifying epithelial odontogenic tumors with irregular, poorly demarcated expansile borders may give the radiographic appearance of osteogenic and chondrogenic sarcoma or osteolytic metastatic tumor. Identification of an impacted tooth in association with such a lesion is more suggestive of odontogenic neoplasm. More clearly demarcated tumors must, by biopsy, be differentiated from keratocyst, ameloblastoma, mixed odontogenic tumor, and dentigerous cyst with carcinomatous transformation.

TREATMENT

The Pindborg tumor is aggressive and requires total or en bloc resection. Simple enucleation or curettage is generally inadequate, and the tumor recurs.

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ODONTOGENIC ADENOMATOID TUMOR

Figure 9-42

Age: Teenagers
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Although the odontogenic adenomatoid tumor may arise between teeth, more than

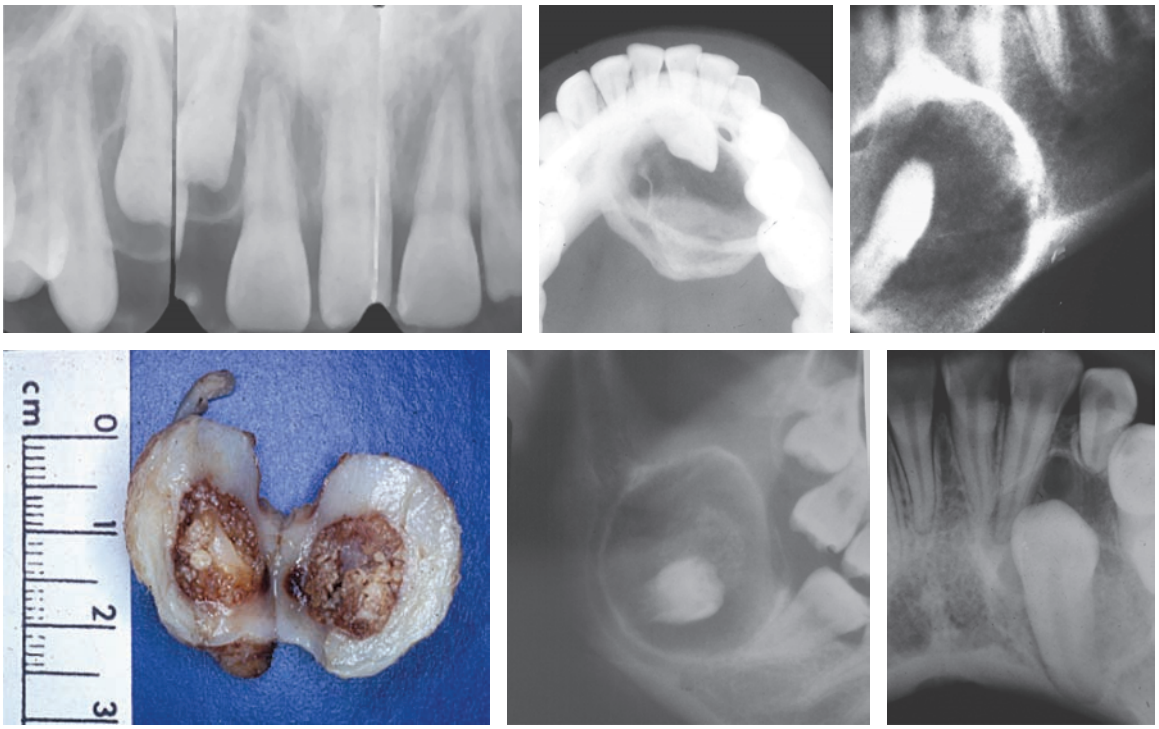

FIGURE 9-42
Impacted teeth with expansile well-circumscribed pericoronal radiolucencies, representing odontogenic adenomatoid tumor.

75% are associated with the crown of an impacted tooth. The maxilla is more often affected, with a pericoronal radiolucency enveloping the crown of a cuspid. The radiolucency often contains radiopaque flecks because portions of the tumor can calcify. Whereas simple dentigerous cysts emanate from the cervix of the tooth, the odontogenic adenomatoid tumor often manifest a pericoronal radiolucency that almost completely engulfs the entire tooth, including the root. It is almost invariably unilocular and is well demarcated or corticated. Painless cortical expansion is often the presenting sign.

MICROSCOPIC FEATURES

The tumor is surrounded by a dense fibrous capsule. The epithelial neoplastic tissue often assumes the appearance of a cyst with luminal proliferation. The epithelial cells are elongated and arrange themselves in swirls. This growth pattern yields a granuloma-like configuration. Admixed with the spindle cell component are oval nests of columnar epithelial cells with ameloblastic cytologic features. These cells are oriented about an eosinophilic secretion product and in classic examples assume ductal patterns with a central lumen. Hyaline eosinophilic elements are also present, and in many areas, these cell products undergo a dystrophic type of calcification. Rarely, melanin pigment may be present. Other coexistent odontogenic tumor histologic patterns are occasionally encountered.

DIFFERENTIAL DIAGNOSIS

Odontogenic adenomatoid tumors seen as pericoronal radiolucencies must be differentiated from ordinary dentigerous cysts, keratocysts, and other odontogenic tumors that may arise from cyst lining. The young age, anterior location, and tendency for the radiolucency to envelop the lower root region of

the impacted tooth are highly suggestive of odontogenic adenomatoid tumor. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Extraction with simple enucleation of the neoplasm is adequate treatment. The tumor rarely recurs.

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AMELOBLASTIC FIBROMA

Figure 9-43

Age: Children and teenagers
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The mixed odontogenic tumors include ameloblastic fibroma, ameloblastic fibrodentinoma, ameloblastic fibro-odontoma, and odontoma. Only ameloblastic fibroma is entirely radiolucent. Although all of the

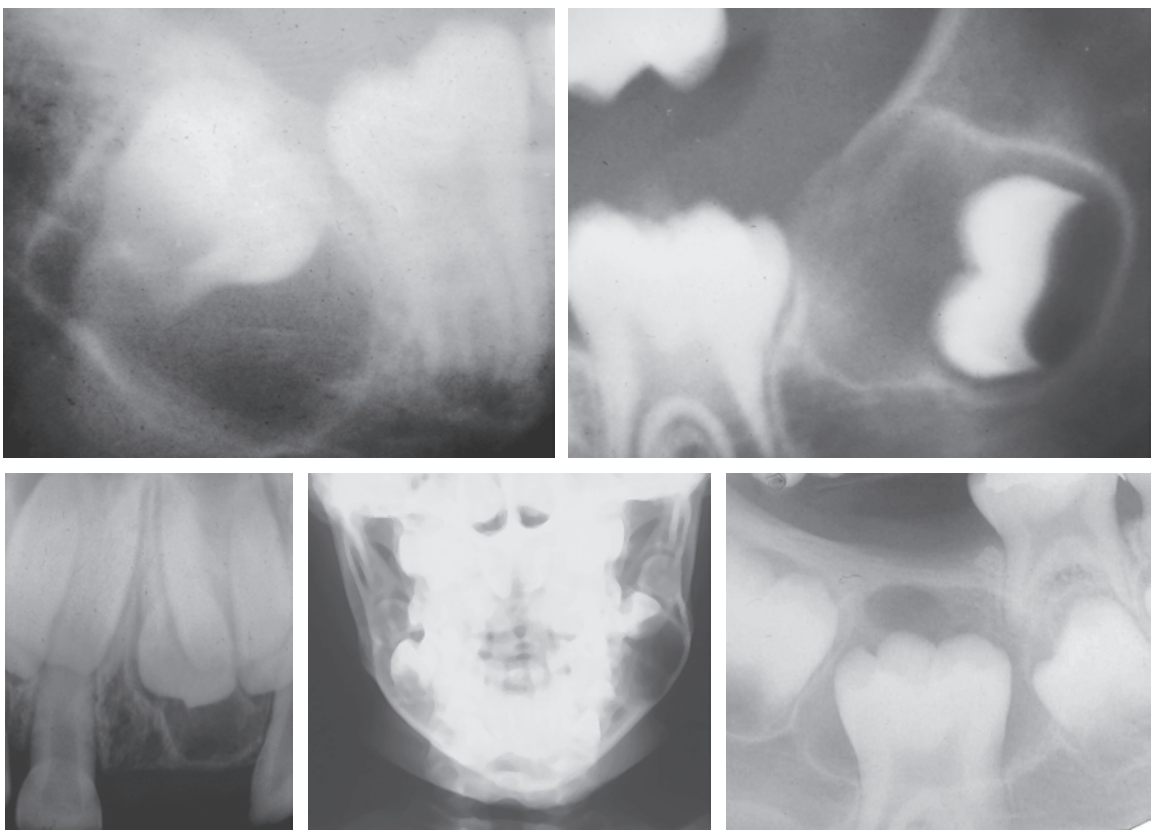

FIGURE 9-43
Ameloblastic fibroma, a mixed odontogenic tumor appearing as a pericoronal radiolucency surrounding the crowns of unerupted molars.

mixed odontogenic tumors may begin as radiolucent lesions, the remainder eventually develop radiopaque foci. Over 90% of ameloblastic fibromas are associated with an impacted tooth and therefore appear as pericoronal radiolucencies. They may be unilocular or multilocular, expansile or nonexpansile, and when initially detected, they may be large or small. The ameloblastic fibroma grows slowly, yet, if left untreated, it has a significant growth potential. A microscopically malignant, clinically aggressive mixed odontogenic tumor has been described as ameloblastic fibrosarcoma.

MICROSCOPIC FEATURES

The mixed odontogenic tumors possess both epithelial and mesenchymal tumor elements, and they mimic the histiogenic differentiation of the developing tooth germ. The least differentiated is the ameloblastic fibroma. It is composed of a diffuse mass of embryonic mesenchyme, which is traversed by elongated cords of cuboidal or columnar odontogenic epithelial cells that resemble the dental lamina. These cords terminate in bulbous projections that contain a central stellate reticulum. Ameloblastic fibrodentinomas are similar, yet a dense eosinophilic dentinoid material lies in juxtaposition to the epithelial element. Ameloblastic fibro-odontomas are further differentiated in that both dentin and enamel matrix are formed and are admixed with zones identical to simple ameloblastic fibroma. The odontoma contains all elements of the mature tooth germ yet does not evince a significant soft tissue cellular overgrowth.

Ameloblastic fibrosarcoma exhibits a sarcomatoid mesenchymal element that is hypercellular; the individual fibroblasts are pleomorphic and hyperchromatic with discernible mitotic figures.

DIFFERENTIAL DIAGNOSIS

Pericoronal radiolucencies representing ameloblastic fibroma may be radiographically identical to simple dentigerous cyst, odontogenic keratocyst, ameloblastoma, Pindborg tumor, or carcinoma arising from a dentigerous cyst. These latter lesions tend to arise in adults rather than in youngsters. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Enucleation with extraction of the impacted tooth is recommended. The ameloblastic fibroma has a limited tendency to recur. Whereas ameloblastic fibrosarcomas are apparently nonmetastasizing, they are aggressive and recurrence after curettage is commonplace; furthermore there is a 10 percent transformation rate from preexistant benign ameloblastic fibromas. These tumors should be treated by en bloc resection.

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ODONTOGENIC FIBROMA-LIKE HAMARTOMA/ENAMEL HYPOPLASIA

Figure 9-44

Age: Children
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Occurring primarily among South African black children, the odontogenic fibroma/

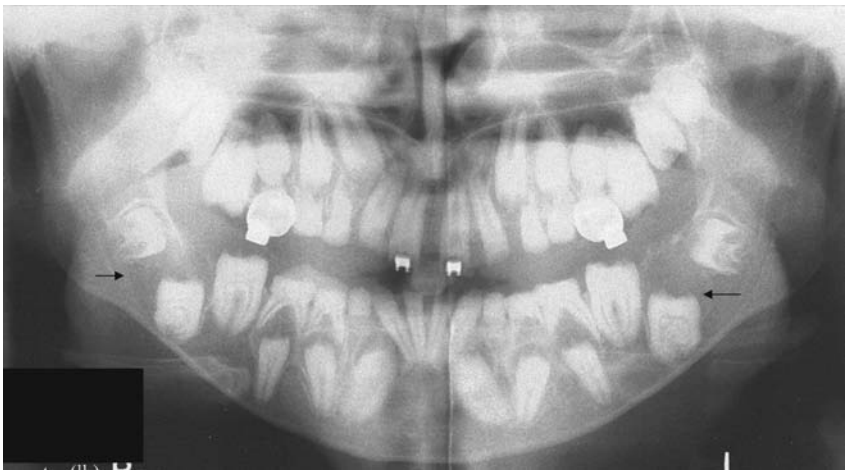

FIGURE 9-44
Pericoronal radiolucencies in the odontogenic fibroma/hamartoma syndrome.

hamartoma with enamel hypoplasia syndrome, also termed enamel dysplasia with hamartomatous atypical follicular hyperplasia, shows unerupted posterior teeth with peridental radiolucencies with bony expansion. Enamel hypoplasia resembles amelogenesis imperfecta and there is gingival hyperplasia, pulp calcifications, and hypodontia.

MICROSCOPIC FEATURES

The microscopic features of the enlarged peridental follicles mirror that of the solitary odontogenic fibroma with delicate yet mature collagen fibers and a moderately cellular monomorphic fibroblast population. Linear and oval odontogenic epithelial islands are dispersed throughout.

DIFFERENTIAL DIAGNOSIS

Enlarged follicles may also be seen in the mucopolysaccharidoses yet histologically excessive ground substance is present as glycosaminoglycans without resemblance to odontogenic fibroma.

TREATMENT

Extractions and curettage are sometimes necessary and restorative dental procedure are in order for enamel defective teeth.

Additional Reading

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CENTRAL MUCOEPIDERMOID CARCINOMA

Figure 9-45

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Mucoepidermoid carcinoma arising centrally in bone is rare. When it does, it is often, but not always, associated with an impacted tooth. Many instances have been reported in which the neoplasm could be demonstrated to arise from the epithelial lining of a dentigerous cyst. The pericoronal

radiolucency is well demarcated and tends to be multilocular. The posterior mandible is the most frequent location. Expansion is encountered. Pain is generally not a feature, but paresthesia may develop with large lesions. Squamous cell carcinoma has also been reported to arise from the lining of odontogenic cysts.

MICROSCOPIC FEATURES

Evidence of a dentigerous cyst lining may be encountered or the neoplastic tissue

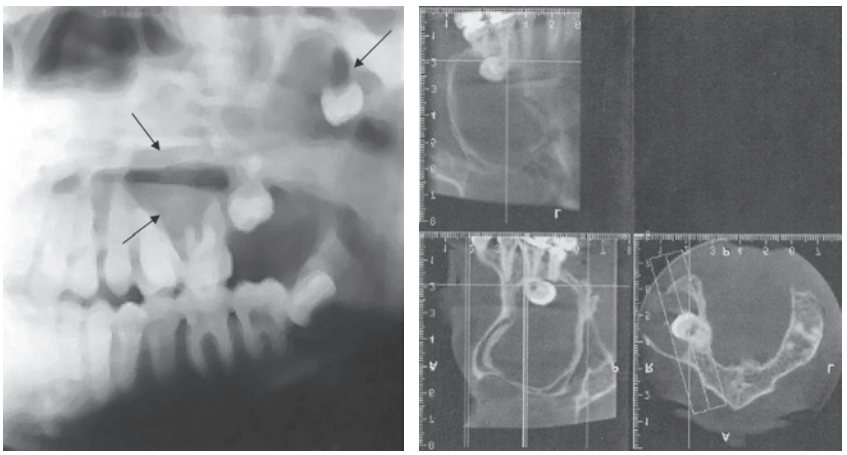

FIGURE 9-45
Impacted third molar with associated radiolucency filling the sinus, representing a central mucoepidermoid carcinoma arising from the lining of a dentigerous cyst. (Courtesy of Dr. H. Cherrick.)

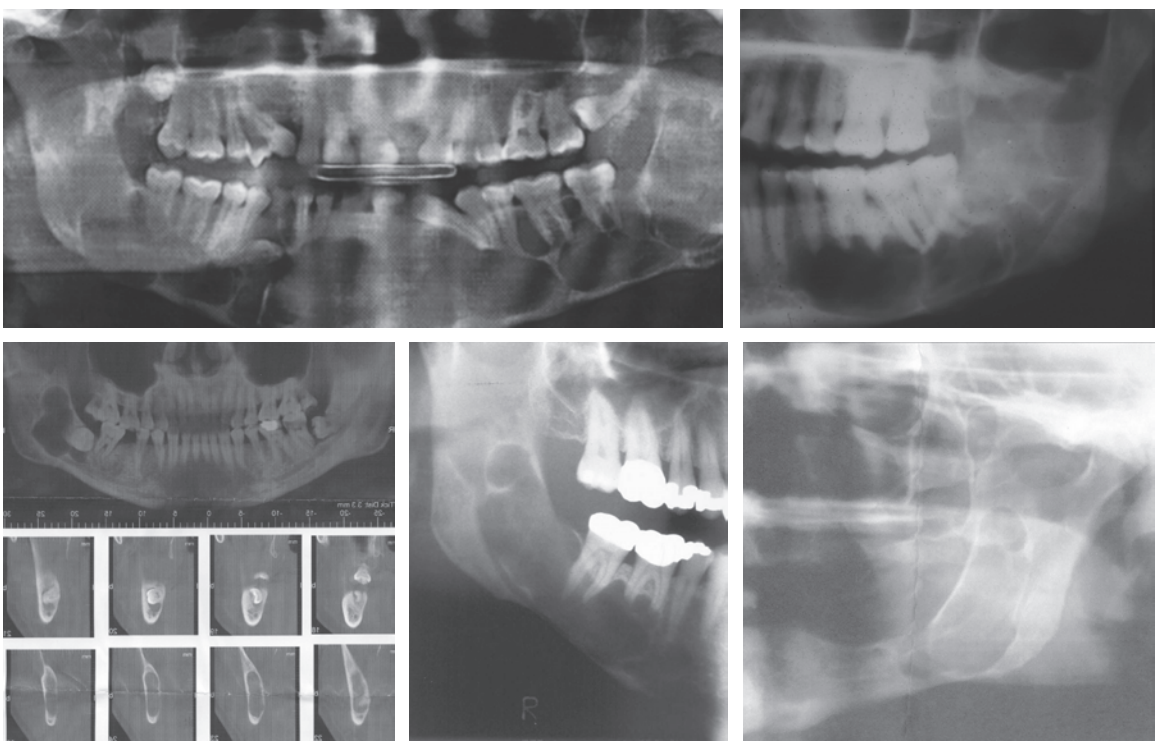

FIGURE 9-46
Multilocular keratocysts.

may be so dominant that demonstrable origin from a cyst is obscured. The tumors are usually low grade with cystic spaces lined by columnar and mucus-secreting cells admixed with epidermal spinous cells. Squamous cell carcinomas show the same features as those derived from surface mucosa.

DIFFERENTIAL DIAGNOSIS

Pericoronal radiolucencies representing central mucoepidermoid carcinoma may show radiographic features in common with dentigerous cysts, keratocysts, or odontogenic neoplasms. The true nature of the disease can be ascertained only after microscopic evaluation, although glandular odontogenic cyst must be considered in the differential diagnosis microscopically.

TREATMENT

Central mucoepidermoid carcinoma of the jaws is usually of the low-grade variety. High-grade tumors in this location are unusual. When the tumor is low grade, the disease can be cured by resection. Lymph node dissection should be performed when clinically palpable nodes are encountered.

Additional Reading

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Multilocular Radiolucencies

ODONTOGENIC KERATOCYST

Figure 9-46

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The odontogenic keratocyst is probably the most common lesion to produce an expansile multilocular radiolucency of the jaws. It has been included in the differential diagnosis of pericoronal and interradicular radiolucencies because it is commonly seen in those relationships as well. When the keratocyst is multilocular, it generally manifests clinically obvious expansion. The posterior body and ramus of the mandible are the most frequent areas of involvement. The lesion is aggressive and, if left untreated, it may destroy large areas of bone. Cortical expansion is usually seen; however, the cortex may actually be perforated. When multiple keratocysts are detected, examination of the skin for basal cell nevi and a radiograph of the chest or demonstration of a bifid rib should be undertaken. Odontogenic keratocysts, both solitary and multiple, involve mutations in the patch gene of the sonic hedgehog growth pathway. The *orthokeratoic odontogenic cyst* shows similar features as the odontogenic keratocyst yet is far less aggressive with lower recurrence rates.

MICROSCOPIC FEATURES

The cyst lumen is usually filled with keratin. The stratified squamous epithelial lining possesses a corrugated parakeratin layer, an attenuated spinous layer, and a polarized basal cell layer with no rete-ridge formation. Occasionally, however, bulbous epithelial extensions invaginate into the fibrous wall where they proliferate and give rise to satellite (daughter) cysts. The

orthokeratotic odontogenic cysts are lined by epithelium synthesizing orthokeratin with a granular cell layer.

DIFFERENTIAL DIAGNOSIS

A multilocular radiolucency representing keratocyst must be differentiated from all of the other lesions listed in this section. If an impacted tooth is present in association with the radiolucency, the lesion is odontogenic and the entities listed as pericoronal radiolucencies must be included in the differential diagnosis. Aspiration usually yields negative results with keratocysts because they are filled with caseous keratin rather than fluid.

TREATMENT

Initial therapy should consist of thorough enucleation and curettage. Recurrence rates for large multilocular keratocysts are more than 50%, whereas recurrence for lesions smaller than 2 cm is less than 30%. The orthokeratinized odontogenic cyst rarely recurs after curettage. Recurrent cysts can be recuretted or excised en bloc. Marsupialization, cryotherapy, and Carnoy solution lavage are also employed in treatment.

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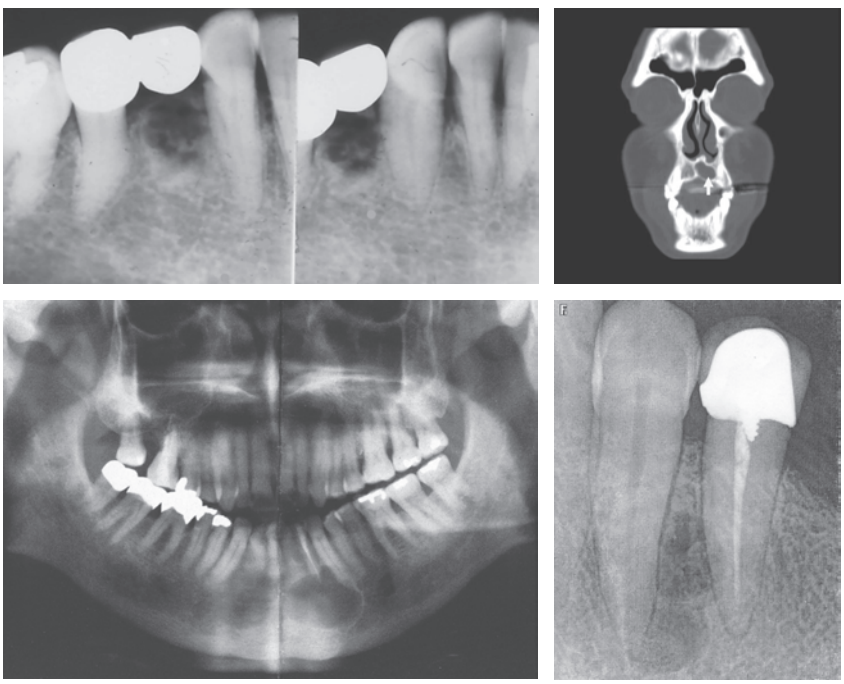

FIGURE 9-47
Botryoid odontogenic cysts can be multilocular or have a soap-bubble appearance.

BOTRYOID ODONTOGENIC CYST

Figure 9-47

Age: Predilection unknown
Sex: Predilection unknown

CLINICAL AND RADIOGRAPHIC FEATURES

The botryoid odontogenic cyst is a rare lesion that grossly resembles a cluster of grapes. It is found central in bone and may appear unilocular or multilocular radiographically. A soft tissue location for this lesion has been observed as well. Expansion is observed in central lesions. The origin of this cyst is unknown, yet it is probably odontogenic. Microscopically, it closely resembles gingival and lateral periodontal cysts.

MICROSCOPIC FEATURES

The lesion is multicystic, and each cystic cavity is separated from others by fibrous septae. The lining epithelium is low cuboidal or squamous, being only 1 or 2 cells thick. Focal acanthotic clear-cell clusters are randomly scattered along the lining, a finding identical to that of lateral periodontal cyst and not a pathognomonic feature for botryoid cyst.

DIFFERENTIAL DIAGNOSIS

This unusual cyst may radiographically resemble lateral periodontal cyst; when multilocular or scalloped, it cannot be differentiated from the other lesions listed in this section.

TREATMENT

Enucleation is the treatment of choice. Although not common, these cysts can recur.

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GLANDULAR ODONTOGENIC CYST

Figure 9-48

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The glandular or sialo-odontogenic cyst is a central jaw lesion derived from epithelial remnants of the odontogenic apparatus, yet capable of glandular differentiation. This cyst is developmental, although an apical periodontal cyst may rarely contain a few mucus-secreting cells in its lining. Like most other odontogenic cysts, those with glandular histologic features are asymptomatic and may present with a variety of radiologic patterns, ranging from unilocular to multilocular; all show a well-delineated, corticated border. Certainly, young lesions are probably unilocular only to become racemose with progressive growth. Some instances of glandular odontogenic cyst are pericoronal, although most are not. Growth is probably steady and slow, yet these cysts are capable of attaining large dimensions. The anterior aspect of the mandible appears to be the site of origin more often than the maxilla.

MICROSCOPIC FEATURES

The histologic findings of glandular differentiation are what distinguish this cyst from other odontogenic cysts. The lining is often tortuous and consists of nonkera-

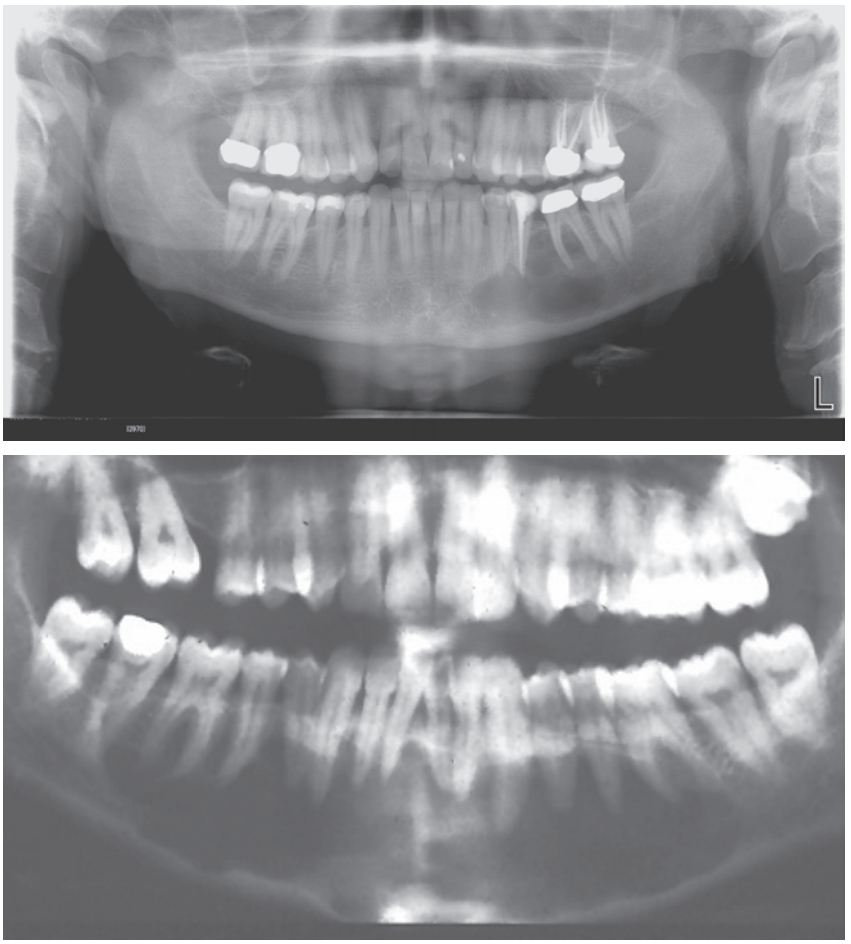

FIGURE 9-48
Expansile, loculated lucency representing glandular odontogenic cyst.

tinizing stratified squamous epithelium. Compartmentalization into multiple confluent cyst cavities is not uncommon. Characteristically, foci of mucous metaplasia are encountered within the cyst wall and organization into acinar-like clusters within the spinous layer is observed. These mucinous cells are readily stained with mucin stains. Some of the superficial cells confronting the lumen are cuboidal or columnar.

DIFFERENTIAL DIAGNOSIS

Radiographically, the glandular odontogenic cyst exhibits large loculations when multilocular and may therefore resemble keratocysts, ameloblastoma, aneurysmal bone cyst, and giant cell granuloma. Microscopically, a highly loculated cyst can be confused with central mucoepidermoid carcinoma of the jaws.

TREATMENT

Surgical curettage is the favored approach. The number of reported instances is too few to establish a rate of recurrence for these cysts.

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CHERUBISM (FAMILIAL FIBROUS DYSPLASIA)

Figure 9-49

Age: Childhood onset
Sex: Slight male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Cherubism is familial and there is evidence that it represents an autosomal dominant trait with variable expressivity. The gene maps to chromosome 4p16, site of the 3BP2 adapter protein involved in mast cell activation. The term is descriptive of the clinical appearance. The posterior mandible is expanded bilaterally, yielding a cherubic facies. Radiographically, extensive multilocular radiolucencies occupy the entire ramus and posterior body of the mandible on both sides. Delicate septae course throughout the radiolucent lesion, and the anterior limits are generally ill defined. The maxillary tuberosity regions often contain expansile multilocular radiolucencies as well. Premature exfoliation of deciduous teeth or impaction and displacement may be features. The progressive expansion begins in early childhood and eventually the growth becomes static, usually shortly after puberty. Recently, cherubism has been reported to occur in conjunction with the *Noonan syndrome*, which is characterized by congenital heart disease, chest deformity, mental retardation, short stature, facial bone anomalies, and cryptorchidism. It may also be found in the *Ramon syndrome* that consists of mental deficiency, epilepsy, gingival fibromatosis, hypertrichosis, and rheumatoid arthritis.

MICROSCOPIC FEATURES

Loose areolar fibrous connective tissue or even hypercellular fibrous tissue is pres-

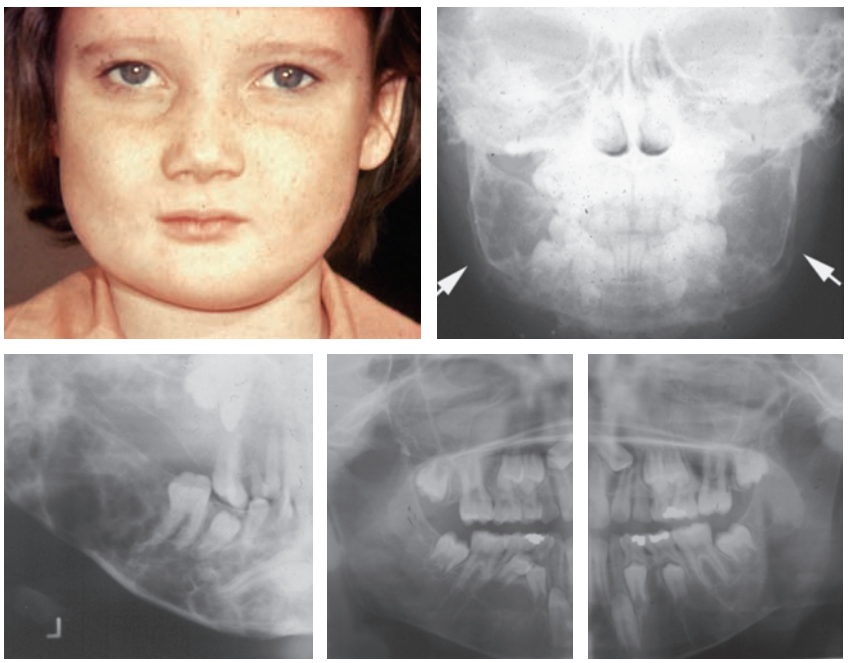

FIGURE 9-49
Bilateral multilocular radiolucencies of the posterior mandible in a patient with familial fibrous dysplasia.

ent and contains isolated, poorly formed osseous tissue and multinucleated giant cells. Vascular channels evince perivascular collagenous condensation or cuffing.

DIFFERENTIAL DIAGNOSIS

The clinicoradiologic features are pathognomonic when a familial tendency can be demonstrated. A biopsy should be performed because multiple keratocysts or brown tumors of hyperparathyroidism could show similar characteristics, particularly if no familial tendency can be ascertained.

TREATMENT

Surgical intervention during childhood is not recommended. The lesion recurs and may actually be activated by the procedure. When growth has ceased, cosmetic osseous contouring may be instituted.

Additional Reading

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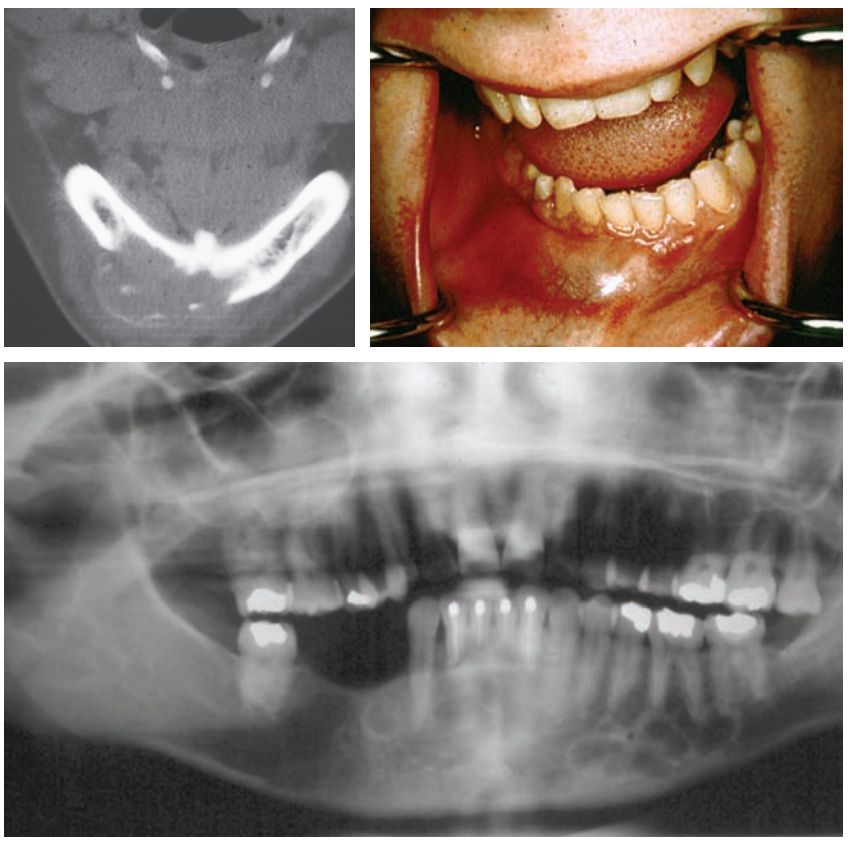

FIGURE 9-50
Expansile multilocular radiolucency of anterior mandible representing central giant cell granuloma.

CENTRAL GIANT CELL GRANULOMA

Figure 9-50

Age: Young adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The central giant cell granuloma is an aggressive reactive process of the jaw bones that arises most often in the mandible anterior to the first molars. Indeed, it is the most common anteriorly located multilocular expansile radiolucency. Smaller lesions may be unilocular, and most are detected when clinical expansion alerts the patient to the disease. When radiographs are obtained, a soap-bubble loculated radiolucency is encountered. Cortical expansion is seen radiographically, and the margins of the radiolucency are well demarcated. Root divergence and resorption are frequent findings. The overlying teeth remain vital, and pain or paresthesia is generally not present. The lesion is capable of rapid growth.

MICROSCOPIC FEATURES

A highly cellular fibrovascular stroma prevails. Dispersed throughout are multinucleated giant cells that tend to lie in juxtaposition to vascular channels. Osteoid or osseous trabeculae are present in most lesions, and hemosiderin granules may be deposited in profusion.

DIFFERENTIAL DIAGNOSIS

Brown tumor of hyperparathyroidism is clinically, radiographically, and microscopically indistinguishable from giant cell granuloma. A serum calcium determination should be obtained to check for parathyroid adenoma. Radiographically, giant cell granuloma may be confused with the other lesions listed in this section. Aspiration may be negative or, because of the vascularity of the lesion, small amounts of blood may be obtained.

TREATMENT

Surgical enucleation is the treatment of choice. Teeth may need to be sacrificed to eradicate the disease completely. If the lesion is not totally excised, it may recur. Intralesional steroid injection has been reported to cause resolution; however, a large series with follow-up documentation is lacking.

Additional Reading

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ANEURYSMAL BONE CYST

Figure 9-51

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The aneurysmal bone cyst is not a true cyst. It is closely related pathogenically to the giant cell granuloma, being an aggressive reactive process. Because the lesion is composed of large vascular sinusoids, blood can be aspirated with a syringe. The blood coursing through the lesion is under low pressure so that a bruit cannot be auscultated. The lesion has a great potential for growth and may produce significant expansion and deformity. The multilocular radiolucency is traversed by thin septae, and cortical expansion is radiographically demonstrable. The mandibular body is the most frequent site for this lesion and, when

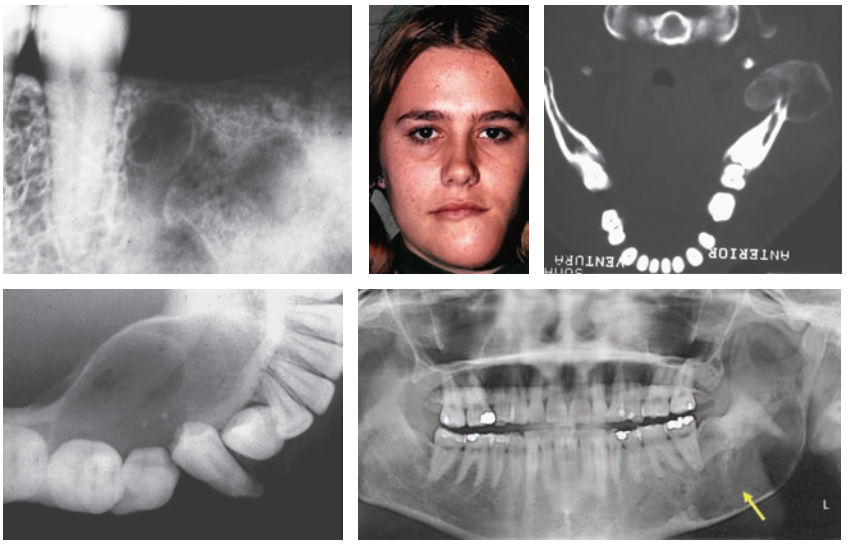

FIGURE 9-51
Multilocular radiolucencies with expansion represent aneurysmal bone cyst.

it is large, the inferior border shows a significant blowout expansile bulge. Aneurysmal bone cyst is occasionally encountered in association with other fibro-osseous lesions of the jaws such as giant cell granuloma and fibrous dysplasia.

MICROSCOPIC FEATURES

Large tortuous blood-filled sinusoidal channels are lined by a flat endothelial layer. The surrounding tissue is fibroblastic and hypercellular. Multinucleated giant cells lie adjacent to the sinusoids, and osteoid trabeculae tend to orient themselves in close proximity to the vascular spaces.

DIFFERENTIAL DIAGNOSIS

Radiographically, the aneurysmal bone cyst may demonstrate features indistinguishable from the other multilocular radiolucencies included in this section. Aspiration of blood allows for limitation of the differential diagnosis; however, central arteriovenous malformation or hemangioma of bone also yields a bloody aspirate. A bruit is usually present in the latter, but not in aneurysmal bone cyst. Carotid time-lapse angiography may be of aid when attempting to differentiate aneurysmal bone cyst from arteriovenous malformation, in that blood traverses the former slowly but progresses through the latter at a rapid rate.

TREATMENT

Despite the rapid growth and aggressiveness of the aneurysmal bone cyst, simple enucleation rarely results in recurrence. Intraoperatively, the lesion may hemorrhage profusely; however, the blood is not under a great degree of pressure.

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HYPERPARATHYROIDISM

Figure 9-52

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

A parathyroid adenoma secretes excessive amounts of parathormone, which mobilizes calcium into the serum and leads to osteoporosis with elevated serum calcium levels. The poorly mineralized bone is replaced by fibrous tissue, resulting in the condition known as *osteitis fibrosa cystica.* Calcium salts precipitate in the kidneys with urolithiasis, which in turn contributes to pyelonephritis. Secondary hyperparathyroidism may occur in association with renal disease in which calcium is lost in the urine, causing a compensatory parathyroid hyperplasia. In addition to parathyroid adenoma and renal secondary hyperparathyroidism, certain malignant neoplasms, such as oat cell carcinomas of the lung, secrete excess parathormone with the development of hyperparathyroidism. Late in the course of the disease, lesions may develop in any bone, including the jaws. These are giant cell tumors known as brown tumors. In the jaws, they appear as expansile multilocular radiolucencies. Ossifying fibromas may also occur in the jaws among genetically predisposed patients with hyperparathyroidism.

MICROSCOPIC FEATURES

The microscopic features of brown tumor are indistinguishable from those of central giant cell granuloma. Fibrovascular tissue is admixed with numerous multinucleated giant cells. Trabeculae of bone may be present.

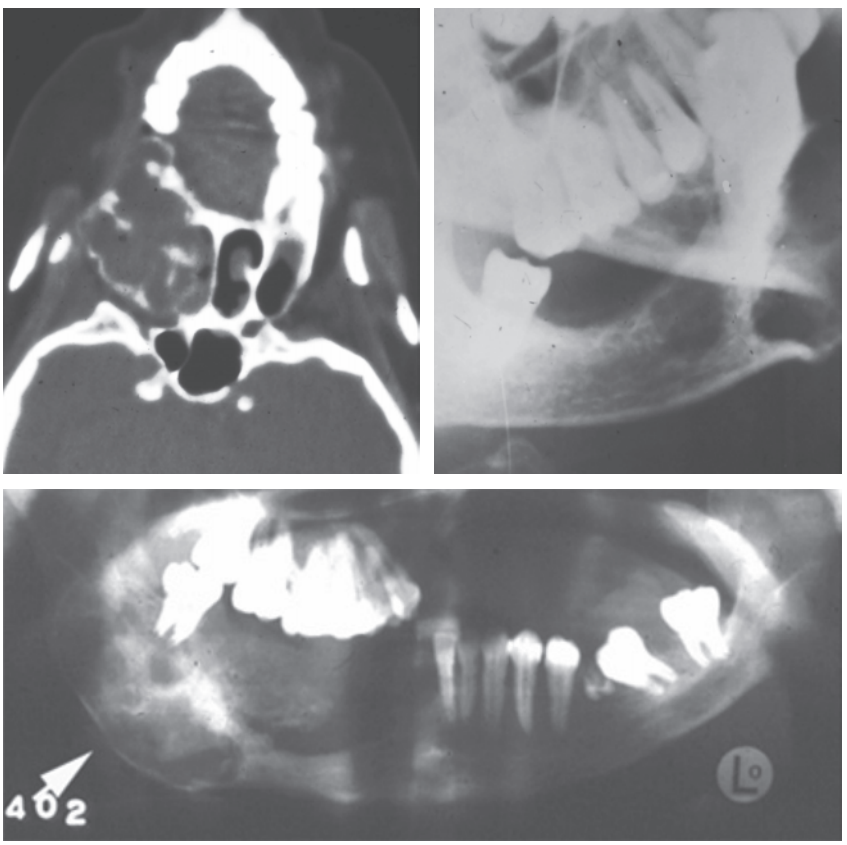

FIGURE 9-52
Multilocular radiolucencies are brown tumors of hyperparathyroidism.

DIFFERENTIAL DIAGNOSIS

The brown tumor of hyperparathyroidism is clinically, radiographically, and microscopically indistinguishable from central giant cell granuloma. For this reason, a bone chemistry panel must be evaluated. Testing reveals serum levels of calcium are elevated, phosphorus is low, and alkaline phosphatase is within normal limits. Radiographically, brown tumor may resemble the other radiolucencies included in this section.

TREATMENT

After the diagnosis has been established, the patient should be referred to a surgeon for excision of the parathyroid adenoma or for evaluation of renal function when secondary hyperparathyroidism is suspected. When this work-up is negative, an endocrine-secreting carcinoma should be ruled out. The jaw lesions resolve after treatment; however, expansion may be maintained. Elective cosmetic osseous contouring may then be performed.

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AMELOBLASTOMA

Figure 9-53

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The ameloblastoma is classically a multilocular radiolucency with a predilection for the posterior mandible. Radiographs show a well-circumscribed, expansile soap-bubble radiolucency with clearly demarcated borders. The neoplasm may arise from the lining of a dentigerous cyst but more often arises independent of any association with

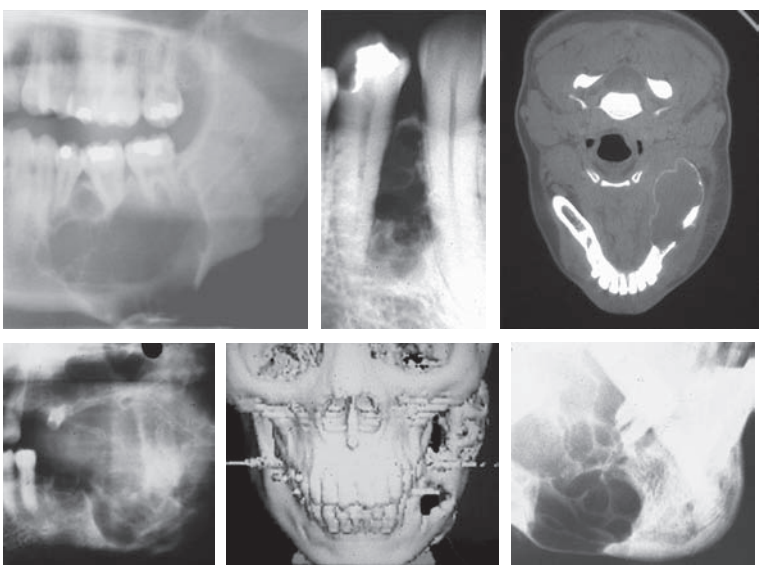

FIGURE 9-53
Multilocular radiolucency with root divergence and resorption in ameloblastoma.

impacted teeth. It shows a progressive moderate growth rate and, if left untreated, may reach enormous proportions. Expansion is seen clinically and radiographically. Pain is generally not a symptom. Maxillary tumors frequently perforate into the antrum and may grow freely, with extension into the nasal cavity, ethmoid sinuses, and cranial base. A small number of microscopically benign ameloblastomas have been reported to undergo distant metastases.

MICROSCOPIC FEATURES

Ameloblastomas show various growth patterns; however, none of these histomorphologic variations has any bearing on predicting growth potential, metastatic potential, or prognosis. The classic microscopic features of ameloblastoma are represented by sheets and islands of tumor cells showing an outer rim of columnar ameloblasts with nuclei polarized away from the basement membrane. The center of these nests is composed of stellate epithelial cells that mimic the stellate reticulum. Occasionally, these cells show squamous metaplasia or contain eosinophilic granular cells. Plexiform, cystic, and basaloid patterns are often dominant. Rarely, an ameloblastoma exhibits cytologic features of malignancy. Tumors of this nature maintain histologic resemblance to benign ameloblastoma with an outer columnar stratum and a central stellate reticulum zone with squamous differentiation. These tumors are diagnosed as ameloblastic carcinoma.

DIFFERENTIAL DIAGNOSIS

The expansile multilocular pattern of ameloblastoma is also encountered in other odontogenic and nonodontogenic lesions listed in this section. Aspiration is negative, and biopsy is required to obtain a definitive diagnosis.

TREATMENT

Curettage may be attempted for small mandibular ameloblastomas. Recurrence rates are high. Larger lesions, particularly those extending to the inferior border, require en bloc resection or hemimandibulectomy. Maxillary ameloblastomas require resection because they tend to invade the antrum; any attempt to eradicate tumor by curettage will fail and importantly, recurrences may not be controlled by subsequent surgical resection. Less than 1% of benign-appearing ameloblastomas metastasize to distant sites. These metastatic tumors are frequently the granular cell type.

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MYXOMA

Figure 9-54

Age: Young and middle-aged adults
Sex: No prediction

CLINICAL AND RADIOGRAPHIC FEATURES

The myxoma, because of its limitation to jaw bones, is included as an odontogenic neoplasm, which probably originates from the dental papilla or follicular mesenchyme. It is typically multilocular and expansile, and sometimes is associated with impacted teeth. The septae coursing through the radiolucency are extremely delicate and look like a finely reticulated spiderweb. The border may be clearly delineated, but occasionally, the marginal limits of the tumor are indis-

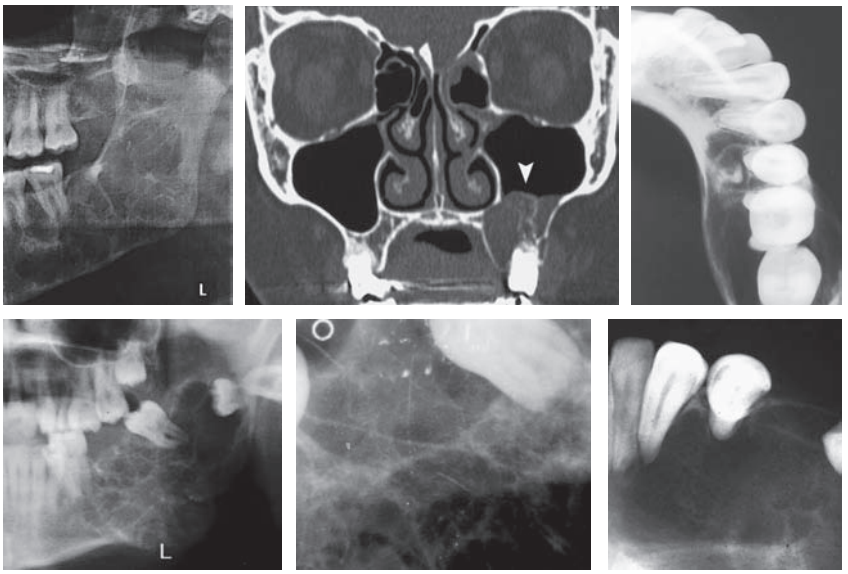

FIGURE 9-54
Finely reticulated septate pattern in odontogenic myxoma. (Courtesy of Dr. James Shemke.)

crete. Myxomas are slow growing but are aggressively invasive; if left untreated, they may become huge. The body of the mandible is the favored site. Maxillary myxomas may perforate and invade the antrum.

MICROSCOPIC FEATURES

The microscopic pattern is distinctive. Spindle and stellate fibroblasts are associated with basophilic ground substance and delicate immature collagen fibers representing myxomatous tissue. Oval odontogenic epithelial cell rests may or may not be present.

DIFFERENTIAL DIAGNOSIS

A delicate reticulated pattern of septae, as seen radiographically in a multilocular radiolucency, is highly suggestive of myxoma. Regardless, the other lesions in this section must be included in the differential radiographic diagnosis. Aspiration is negative, and biopsy is indicated.

TREATMENT

Myxomas are grossly gelatinous or mucoid; so curettage is untenable in most instances. Occasionally, myxomas are more fibrous and can be managed by curettage with less chance for recurrence than those with a mucoid consistency. En bloc resection should be performed, particularly in larger gelatinous lesions, to circumvent recurrence.

Additional Reading

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CENTRAL NEUROGENIC NEOPLASMS

Figure 9-55

Age: No predilection
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Neurilemmomas and neurofibromas arising from the sheath cells of the inferior alveolar

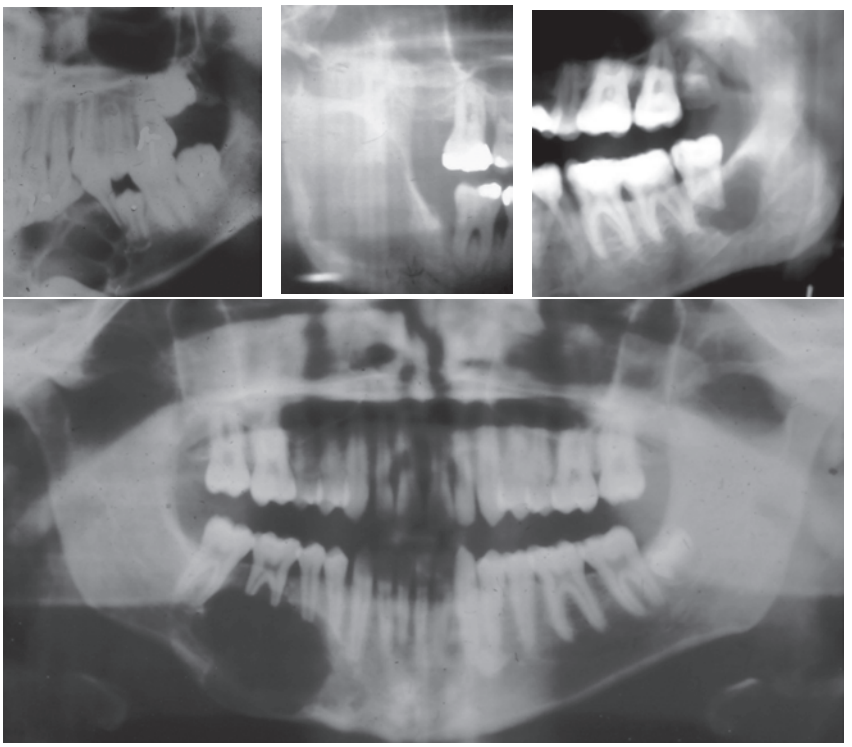

FIGURE 9-55
Multilocular radiolucency due to a central neural sheath neoplasm (upper left). *Source:* Sugimura M, Shirasuna K, Yoshimura Y, Fujimoto K, Nakajo Y. A case of neurilemmoma in the mandible. *Int J Oral Surg.* 1974;3:194.

nerve appear as unilocular or multilocular radiolucencies along the course of the nerve. Of all bones in the body, excluding the temporal bone, the mandible is the most common site for central nerve sheath neoplasms, probably because no other bone transports a nerve for such a distance. Expansion of the buccal plate is common, yet pain is not a feature. Paresthesia may or may not be present. Central neurofibromas are more likely to be solitary than to represent stigmata of von Recklinghausen's neurofibromatosis.

MICROSCOPIC FEATURES

Nerve sheath tumors of bone display the same microscopic features as their soft tissue counterparts. Neurilemmomas are composed of spindle cells arranged in palisading columns and swirls separated by finely fibrillar vacuolated connective tissue. Neurofibromas contain fibroblastic nuclei haphazardly arranged and admixed with wavy delicate collagen fibers with myxomatous regions. Plexiform or organoid patterns are commonly observed. Even rare instances of neurogenic sarcoma have been reported with nuclear pleomorphism and high mitotic rate. S-100 nuclear and cytoplasmic staining assist in the diagnosis of neural sheath tumors.

DIFFERENTIAL DIAGNOSIS

Multilocular central neural tumors must be differentiated from the other lesions included here. They often show widening of the inferior alveolar canal with scalloped margins that make radiographic distinction from the traumatic cyst impossible. Biopsy is required to arrive at a definitive diagnosis.

TREATMENT

Simple surgical enucleation is the treatment of choice. Recurrence is uncommon.

Additional Reading

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CENTRAL ARTERIOVENOUS MALFORMATION

Figure 9-56

Age: Children and teenagers
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

An arteriovenous (AV) malformation of the mandible is potentially lethal and extremely dangerous when teeth are surrounded by the lesion, because they will become loose and, if extracted, uncontrollable hemorrhage often results. Spontaneous gingival hemorrhage or seeping of blood from the gingival sulci is a common sign. The malformation develops from the central vessels of the mandible during early childhood. High arterial pressure is exerted within the vessels because of direct communication of arteries with veins (an interposed capillary bed fails to develop). This often causes compensatory expansion of the cortices, and a bruit can be heard on auscultation. The overlying skin may be warmer than that on the uninvolved side. Radiographically, AV malformations are microloculated. These tiny locules represent small arterial channels. Bright-red fresh blood is obtained on aspiration. Indeed, the plunger of the syringe may be forced out as a result of the pressure within the lesion. Feeder vessels are derived from the ipsilateral inferior alveolar artery; however, contralateral vascular communications are common. Unfortunately, vertebral vessels sometimes anastomose with the arterial channels of the jaw lesion. Angiography clearly demonstrates these anastomoses. Occasionally, central vascular anomalies are under low pressure. In these instances, they are perhaps more aptly termed *central hemangiomas.*

MICROSCOPIC FEATURES

Biopsy should not be performed when aspiration is positive and a bruit is detected. Resected mandibles show large-caliber muscular vascular channels, which course profusely throughout the medullary bone.

DIFFERENTIAL DIAGNOSIS

Central AV malformations show radiographic features in common with the other multilocular radiolucencies included here. A blood aspirate and detectable bruit allow for a clinical diagnosis. A central AV malformation may exist in the absence of a bruit or cortical expansion. In these cases, because aspiration is positive, differentiation from an aneurysmal bone cyst is critical. Time-lapse angiography is indicated as blood passes through an AV malformation rapidly, whereas the time phase of aneurysmal bone cysts is not much different from that of a normal arterial-capillary-venous clearance.

TREATMENT

Iatrogenic embolization with autologous muscle chips or other materials is contraindicated, as pulmonary embolism may occur (the vascular lumina may remain

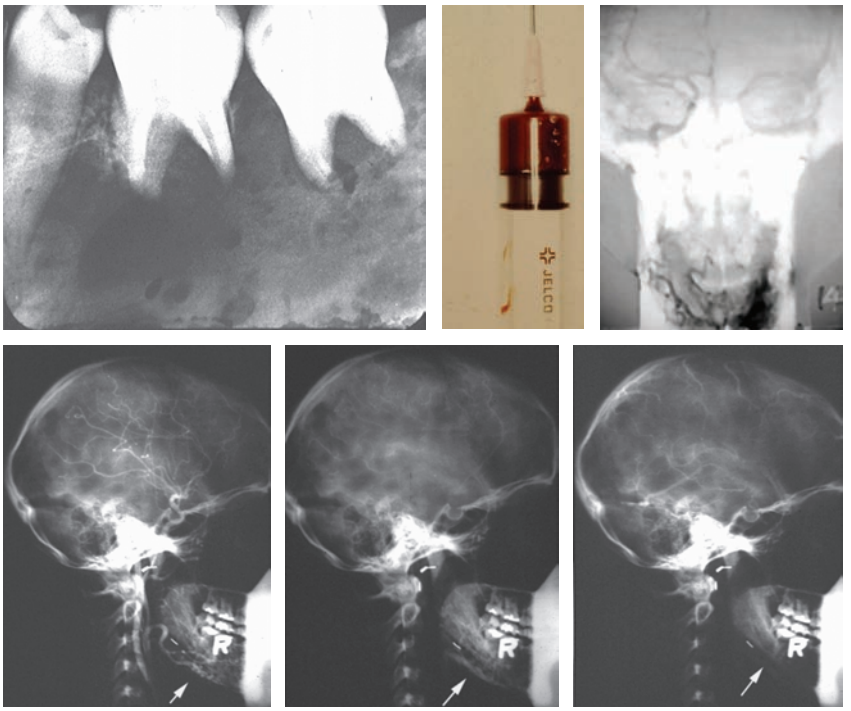

FIGURE 9-56
Upper: micro multilocular radiolucency (worm hole pattern) of mandible, an arteriovenous malformation, bloody aspirate. Lower: angiogram showing that blood clears the mandibular lesion before the meningeal vessels enter the venous phase of filling.

patent and equal in size through the course of the defect). The external carotids should be ligated bilaterally with resection of the involved portion of mandible. Even then, hemorrhage may be profuse. Ten units of donor blood should be available if needed.

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CENTRAL (LOW FLOW) HEMANGIOMA OF BONE

Figure 9-57

Age: Infants, children
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Whereas blood pressure is at arterial systolic levels in arteriovenous malformations, low flow intraosseous hemangiomas are at, or below, venous pressure. Low flow central hemangiomas of the mandible develop within the inferior alveolar canal and usually show a honeycomb or worm hole multilocular pattern with bony expansion of the cortical plates. There may also be a soft tissue component with erythema of overlying skin or mucosa. A bruit is not evident.

MICROSCOPIC FEATURES

Low flow hemangiomas and venous malformations comprise cavernous blood-filled

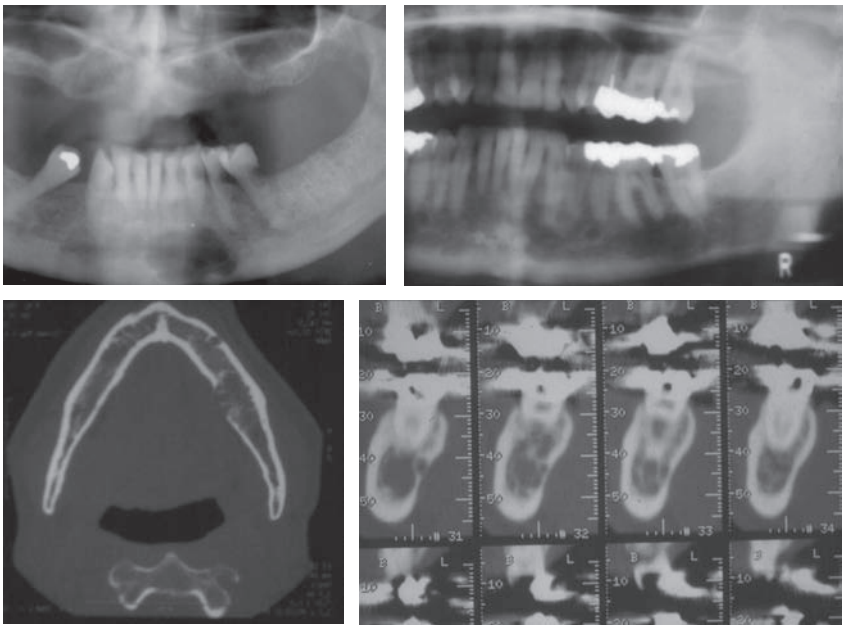

FIGURE 9-57
Low pressure central hemangiomas.

spaces that course among thin osseous trabeculae. These vessels lack muscular coats yet may show advential thickening. Small capillary clusters are often interposed.

DIFFERENTIAL DIAGNOSIS

Multilocular lesions should be aspirated before biopsy, and if blood fills the syringe, vascular imaging studies are in order. Ultrasound and time-lapse angiographic techniques can disclose flow levels aiding in the differentiation between hemangioma and AV malformation.

TREATMENT

Blood loss during surgery can be a significant complication, yet not the life-threatening event that could occur attempting to curette or resect an AV malformation. Feeder vessel ligation and embolization techniques are employed in addition to curettement or resection.

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CENTRAL LEIOMYOMA

Figure 9-58

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Smooth muscle tumors central in the mandible derive from the vascular smooth muscle along the inferior alveolar canal vasculature (vascular leiomyomas). They are asymptomatic and result in uni- or multilocular radiolucencies with well-defined margins. Cortical expansion is usually seen in these rare tumors.

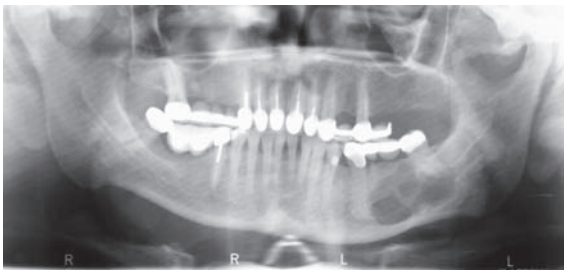

FIGURE 9-58
Intraosseous leiomyoma.

MICROSCOPIC FEATURES

Leiomyomas are benign spindle cell neoplasms with streaming and fasciculation of the cells that show elongated, cigar-shaped nuclei. Since most of these tumors arise from vessel wall smooth muscle, they show a tendency for perivascular, circumferential layering of tumor cells. Mitotic figures are not encountered. The cells are positive for muscle markers, smooth muscle actin in particular.

DIFFERENTIAL DIAGNOSIS

The clinical and radiographic features may simulate many of the other lesions listed here as multilocular. Microscopically, myofibroma is a consideration, and both myofibroma and leiomyoma are smooth muscle actin positive. Importantly, fine collagen is identified between spindle cells in myofibroma whereas leiomyoma is strictly smooth muscle as seen on trichrome staining.

TREATMENT

Thorough enucleation is required. The neurovascular bundle is sacrificed with resultant lip paresthesia, a symptom that may ultimately resolve.

Additional Reading

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PSEUDOTUMOR OF HEMOPHILIA

Figure 9-59

Age: Children
Sex: Males

CLINICAL AND RADIOGRAPHIC FEATURES

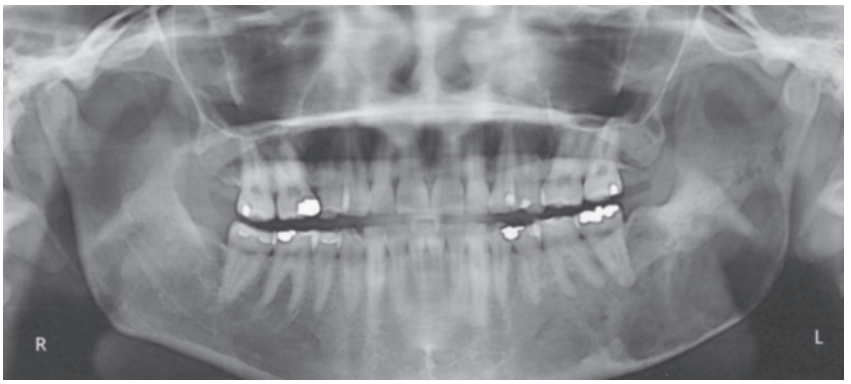
Hemophilia, an X-linked recessive disease, affects males primarily and results in a deficiency of coagulation factor VIII. Gingival bleeding, ecchymosis, and hemarthrosis are the major findings. Two percent of the patients experience subperiosteal hemorrhage after trauma. Patients with factor IX deficiency may experience similar problems. The subperiosteal focus of hemorrhage may progress to involve medullary bone. Clinically, a firm expansile mass is observed over the body and angle of the mandible. Radiographically, a multilocular radiolucency is observed and is expansile.

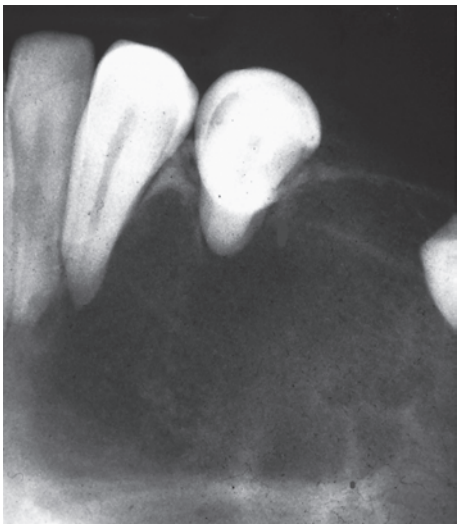
MICROSCOPIC FEATURES

The lesion shows foci of granulation tissue, fibrous tissue, hematoma with extravasated erythrocytes, and reactive new bone formation. Cystic spaces without an epithelial lining are also frequently encountered.

DIFFERENTIAL DIAGNOSIS

A multicystic expansile mass in the mandible of a patient with a genetic coagulation disorder and a history of trauma suggest the diagnosis of hemophilic pseudotumor. Alternatively, a hemophiliac could, of course, develop any of the other lesions included here. A biopsy is recommended for securing a definitive diagnosis.





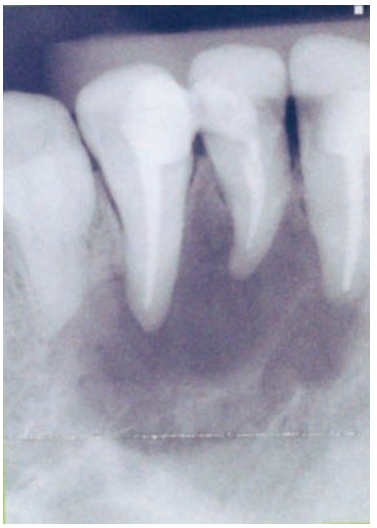


FIGURE 9-59
Hemophilic pseudotumor involving the mandible.

TREATMENT

Biopsy and definitive surgery must be performed after administration of the appropriate factor cryoprecipitate. Curettage is the treatment of choice. The mandible may heal yet remain expanded.

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MYOFIBROMATOSIS (DESMOPLASTIC FIBROMA OF BONE)

Figure 9-60

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Aggressive juvenile myofibromatosis is a reactive fibroblastic proliferation of the soft tissues. Rarely, histologically similar lesions

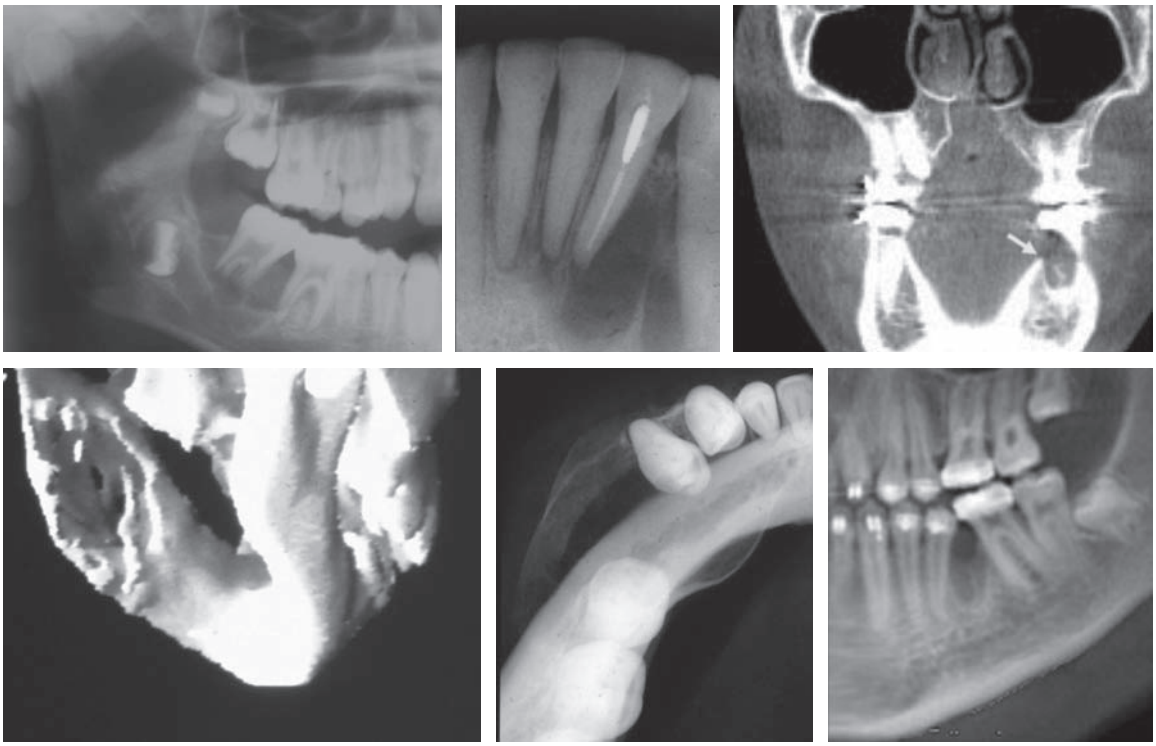

FIGURE 9-60
Intraosseous myofibromatosis.

arise centrally in the jawbones and are reminiscent of central desmoplastic fibromas that arise in the long bones. Rapid expansion with facial asymmetry is the usual presenting sign, and the mandible is more often the site of origin. Radiographically, a well-delineated multilocular or unilocular pattern is encountered with concomitant root resorption or divergence. Perforation of the cortex is by no means rare, and when large lesions occur it may be difficult to determine whether the lesion arose centrally with perforation or peripherally with bony invasion.

MICROSCOPIC FEATURES

The lesion is hypercellular, being composed of fibroblasts and varying amounts of collagen. The collagen fibers are usually thin and delicate with fasciculations and herringbone, chevron, or storiform configurations. In keeping with desmoplastic fibroma of long bones, some of these fibroblastic proliferations synthesize more mature, dense collagen bundles. Osseous trabeculae are either lacking or are a minor element. This myofibroblastic lesion is positive for smooth muscle actin and vimentin using immunohistochemistry staining.

DIFFERENTIAL DIAGNOSIS

Myofibromatosis central in bone cannot be differentiated with certainty from the other aggressive neoplasms included here. A history of rapid expansion and ability to clinically and radiographically detect cortical perforation in a teenage patient should arouse suspicion of fibromatosis.

TREATMENT

Myofibromatosis is aggressive with significant potential for growth despite its benignity. Indeed, some pathologists prefer

to refer to these lesions as nonmetastasizing fibrosarcomas. Small lesions with total osseous confinement may be successfully managed by thorough enucleation and curettage. Large or massive tumors with cortical perforation usually require marginal or en bloc resection.

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FIBROUS DYSPLASIA

Figure 9-61

Age: Teenagers
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

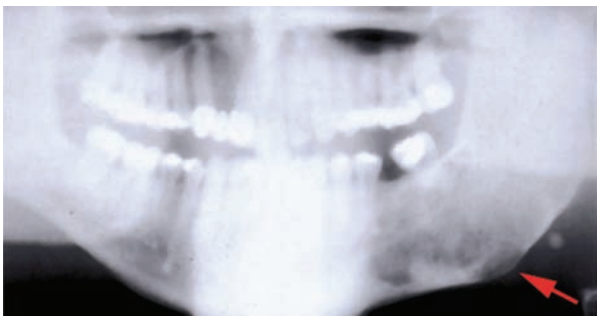
Whereas fibrous dysplasia of the jaws is more frequently encountered in the maxilla as a ground-glass radiopacity, when the mandible is involved, the lesion often assumes a multilocular radiolucent pattern. Characteristically, expansion is evident and the radiographic margins of the growth are indiscrete. The expansion develops insidiously during the early teenage years with progressive slow growth. The growth potential begins to wane as skeletal maturity ensues. In rare instances, fibrous dysplasia shows a rapid enlargement with an aggressive clinical course. Polyostotic lesions should be sought by means of skull radiographs and a skeletal survey.

MICROSCOPIC FEATURES

A hypercellular proliferative fibrous tissue element predominates the sections. Dispersed throughout are irregular, poorly formed osseous trabeculae that are usually, but not invariably, fetal or woven. These trabeculae are often devoid of any osteoblastic rimming.

DIFFERENTIAL DIAGNOSIS

When fibrous dysplasia appears as a multilocular radiolucency, it must be differentiated from the other diseases included here as multilocular lesions. The lack of definition at the lesional borders is highly suggestive of fibrous dysplasia, yet biopsy must be performed to confirm the clinicoradiologic impression.



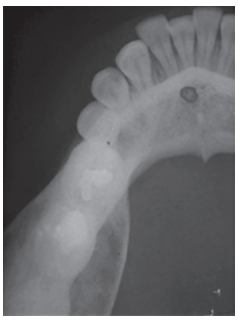


FIGURE 9-61
Diffuse, poorly marginated multicystic lesion of posterior mandible in monostotic fibrous dysplasia.

TREATMENT

Treatment should be postponed until growth of the lesion subsides. Surgical intervention before cessation of growth may actually result in activation of the lesion. In those lesions showing a rapidly proliferative course, close follow-up should be instituted. If the lesion begins to manifest massive growth potential, resection should be considered. In the ordinary, less aggressive and common form of the disease, cosmetic osseous contouring can be undertaken when growth ceases. Radiation therapy has been shown to predispose to postradiation sarcoma.

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INTRAOSSEOUS MUCOEPIDERMOID CARCINOMA

Figure 9-62

See description under Pericoronal Radiolucencies

THALASSEMIA MAJOR

See description under Generalized Osteoporotic Lesions

Moth-Eaten Radiolucencies

OSTEOMYELITIS

Figure 9-63

Age: No predilection
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Osteomyelitis of the jaws usually originates from odontogenic infection. It may be acute, subacute, or chronic, the first being most painful. The patient is usually only slightly febrile, and cervical lymphadenopathy is a frequent finding. Staphylococci and streptococci are the predominant causative organisms; however, actinomycetes and anaerobic gram-negative bacilli are cultured in many instances. Clinically, in acute and subacute stages, multiple fistulae with draining purulent exudate are encountered. Paresthesia and pain are associated with acute infections. Radiographically, the cortices rarely show expansion. The lesion may be multilocular or show approximating multifocal radiolucencies with ill-defined, moth-eaten margins. Radiopaque sequestrae are frequently seen to "float" within radiolucent crypts. Specific forms of chronic osteomyelitis (phosphorus poisoning, syphilis, and tuberculosis) may involve the jaws. Another specific osseous inflammation, osteoradionecrosis, develops in jaws of patients undergoing radiation therapy for oral carcinoma. Patients with Paget's disease of bone and osteopetrosis are prone to develop widespread osteomyelitis of the jaws from odontogenic infection.

MICROSCOPIC FEATURES

Osseous trabeculae and necrotic bone are surrounded by granulation tissue, necrotic debris, and inflammatory cells. The inflammatory cell infiltrate varies depending on whether the process is acute, subacute, or chronic. Syphilitic osteomyelitis may dis-

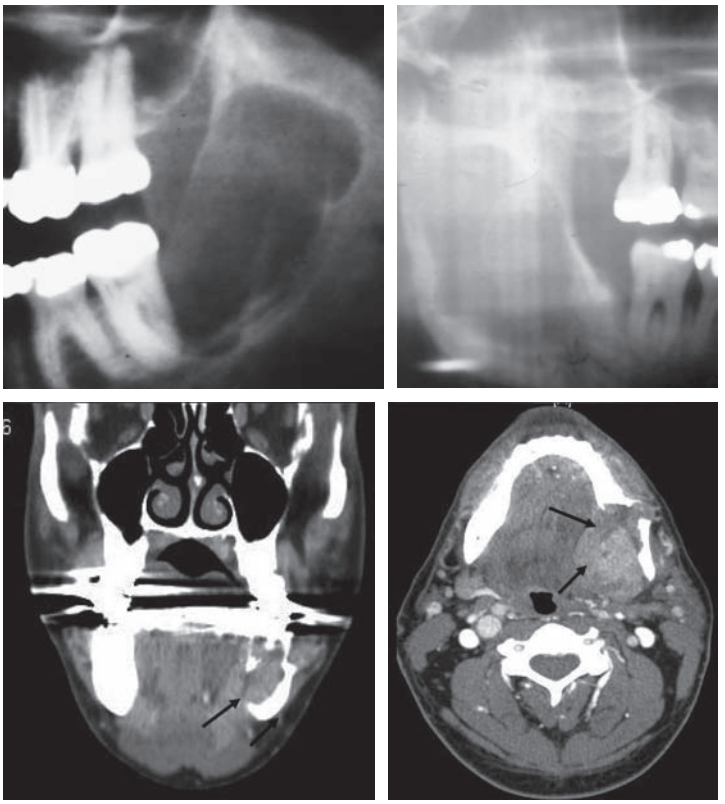

FIGURE 9-62
Intraosseous mucoepidermoid carcinoma.

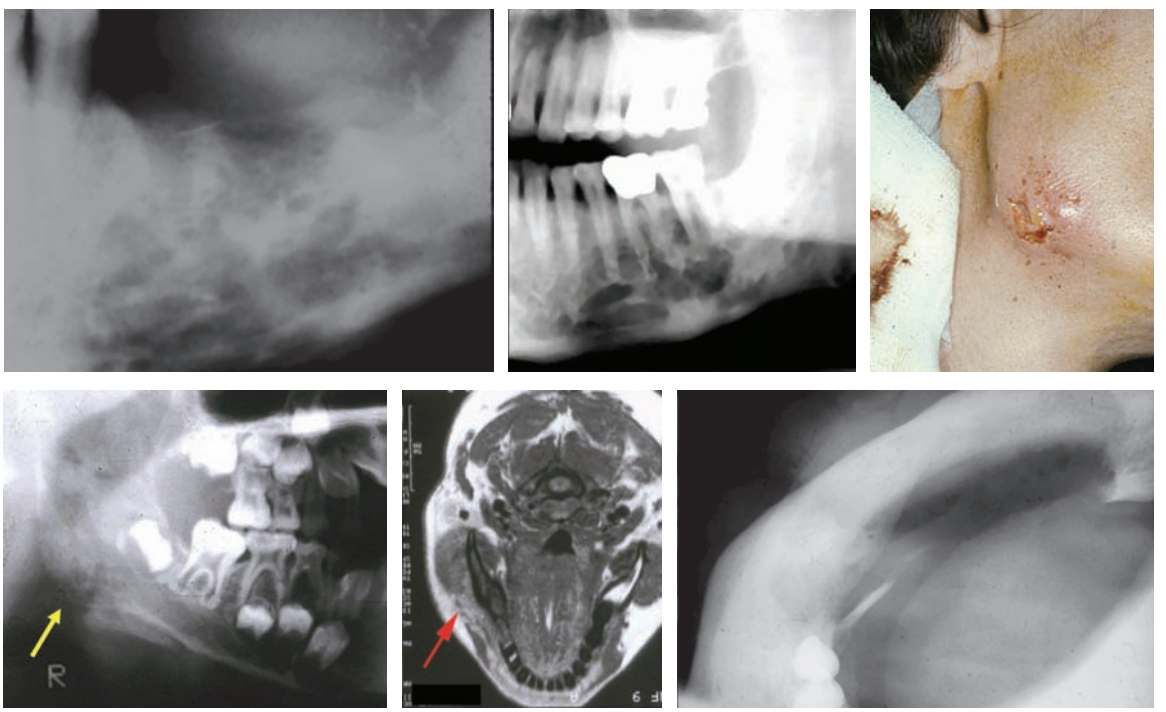

FIGURE 9-63
Osteomyelitis showing a diffuse moth-eaten radiolucent pattern.

play foci of gummatous necrosis. Tuberculous osteomyelitis is characterized by the presence of specific granulomatous inflammation with Langhans' giant cells.

DIFFERENTIAL DIAGNOSIS

When an offending necrotic tooth overlies the radiographic defect, when pain is present and the patient is febrile, a clinical diagnosis can usually be made. Nevertheless, moth-eaten radiolucencies occur in metastatic and primary epithelial and mesenchymal malignant neoplasms. Failure to respond within 2 weeks to therapeutic measures to control infection necessitates biopsy.

TREATMENT

Nonspecific osteomyelitis requires elimination of the source of infection (tooth extraction), incision and drainage if spaces are involved, and antibiotic therapy. Penicillin is the drug of choice. Before antibiotic therapy is instituted, a sterile aspirate should be obtained and submitted for both routine and anaerobic culture and sensitivity tests. In patients with high fever, space infection, or accompanying cellulitis, hospitalization with intravenous antibiotic therapy and supportive care may be required. Surgical debridement with removal of sequestra is indicated when widespread osseous involvement is seen.

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OSTEORADIONECROSIS

Figure 9-64

Age: Adults, elderly
Sex: Male predilection (oral cancer is more frequent in males)

CLINICAL AND RADIOLOGIC FEATURES

Patients receiving more than 20 gray of radiation to the jaws are subject to osteomyelitis secondary to odontogenic/endodontic infection. In most instances, the radiation dosage is higher when used as a radiotherapeutic regimen for treatment of oral and oropharyngeal squamous cancer or in some instances certain radiosensitive salivary gland malignancies. Radiographically, a moth-eaten pattern is seen and clinically alveolar ridge ulceration with bony sequestration may be identified. Bacterial infection spreads throughout the marrow spaces, and fistulae are usually present. Pain is often severe.

MICROSCOPIC FEATURES

Simply put, osteoradionecrosis is osteomyelitis of radiated bone and as such, is microscopically similar to subacute osteomyelitis with inflammatory infiltration of marrow spaces along with bony sequestra. The vasculature may show endothelial pleomorphism as a consequence of radiation-induced cellular change.

DIFFERENTIAL DIAGNOSIS

Clinically, osteoradionecrosis must be differentiated from recurrent carcinoma in bone by obtaining biopsies from the lesional tissue.

TREATMENT

Of utmost importance is prevention. Extraction or root canal therapy of infected teeth and elimination of periodontal sepsis must be undertaken prior to administration of radiation. Lead shields are used to prevent salivary damage and can be used over bony

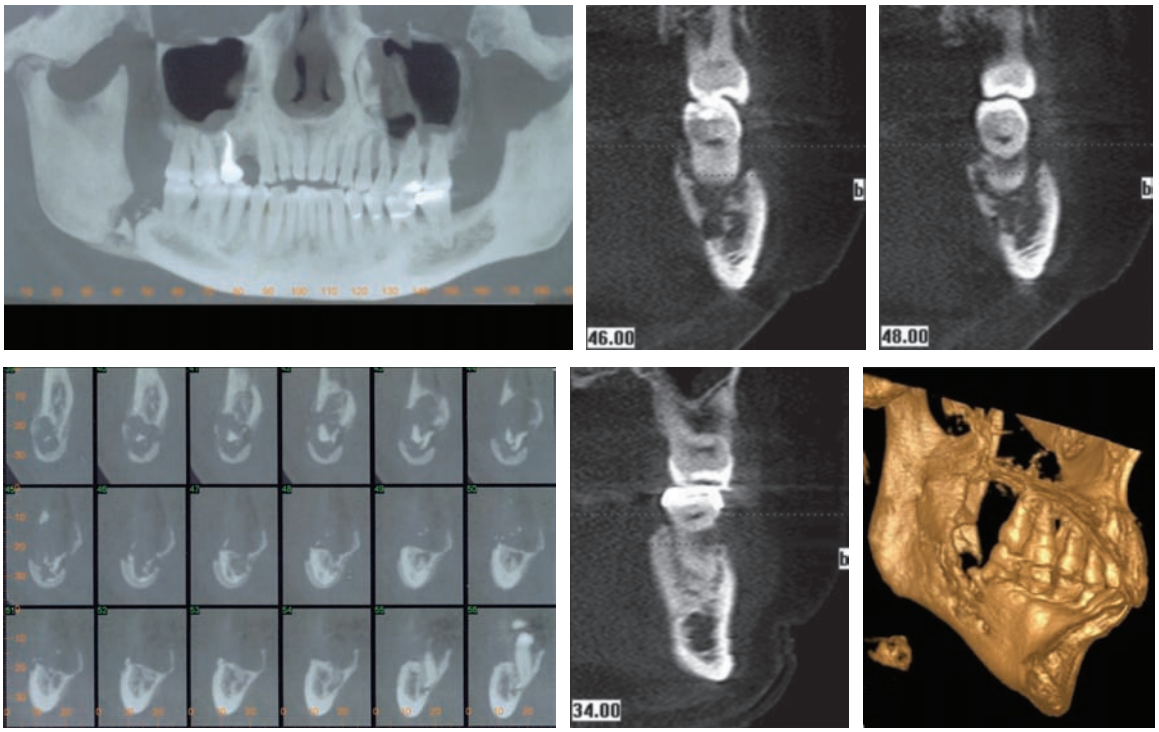

FIGURE 9-64
Postradiation osteoradionecrosis.

areas that are not involved with tumor. Otherwise for active disease, antibiotic therapy, debridement, and hyperbaric oxygen therapy are recommended.

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BISPHOSPHONATE-RELATED OSTEONECROSIS OF THE JAWS (BRONJ)

Figure 9-65

Age: Elderly
Sex: No predilection

CLINICAL AND RADIOLOGIC FEATURES

During the last century, people who worked in phosphorous mines were prone to develop osteomyelitis of their jaws and were said to suffer from "phossy jaw." Recently it was discovered that bisphosphonate salts could be useful in promoting osteogenesis among osteoporotic patients. Furthermore it was found that bone formation in patients with intraosseous malignancies such as multiple myeloma and metastatic cancer can be improved with bisphosphonate therapy. In a subgroup of patients taking bisphos-

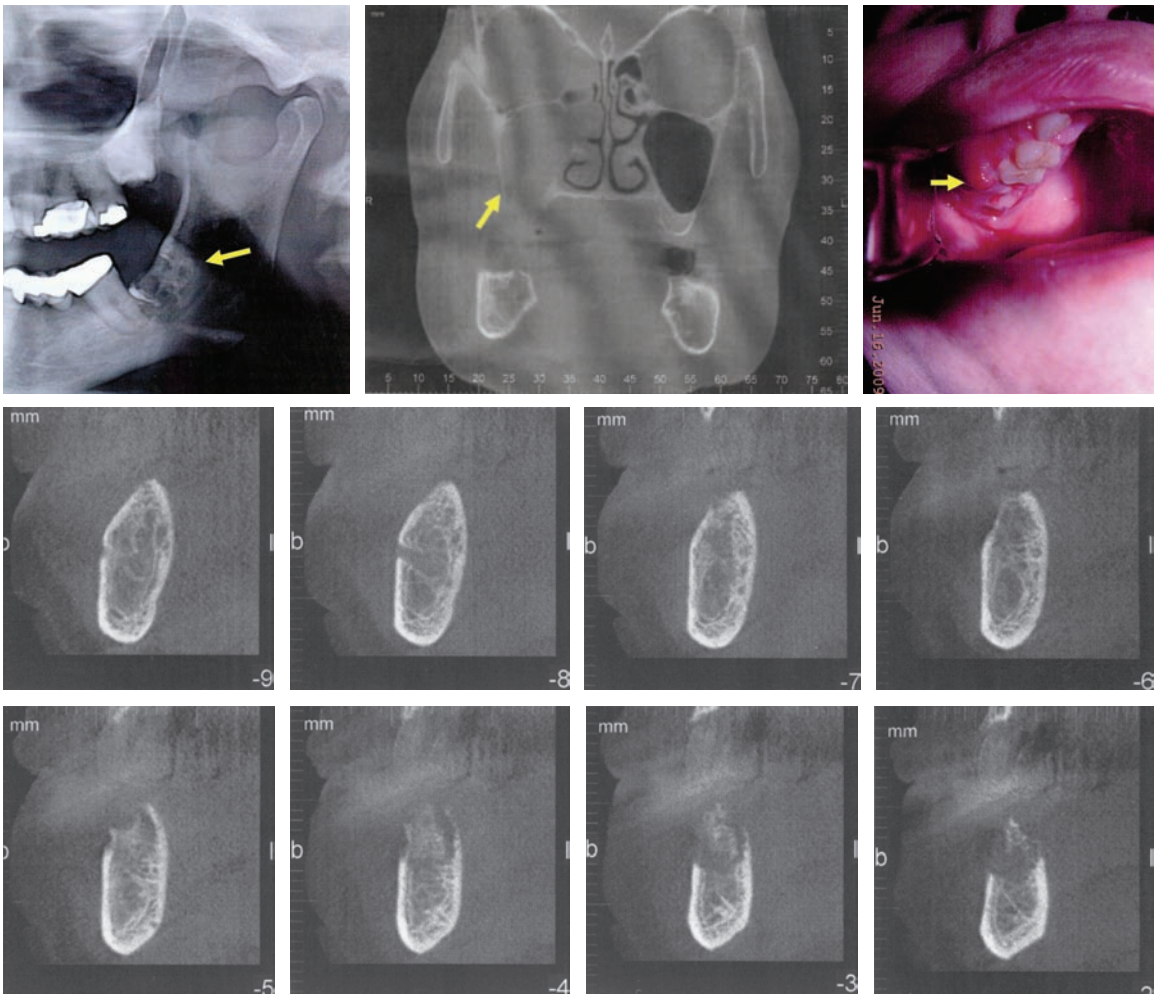

FIGURE 9-65
Bisphosphonate-related osteonecrosis of the jaws.

phonates intravenously, bone necrosis and sequestion were witnessed in the mandible and maxilla. Subsequently, cases were reported in patients taking bisphosphonates orally. There is usually pain, ulceration of the alveolus, and exposed bony sequestra that were spontaneously extruded. These osseous destructive lesions presented, often without any provocation, as radiolucent foci with moth-eaten ragged borders and floating sequestra. In many instances, actinomycetes are cultivatable. The risk for developing osteonecrosis while taking bisphosphonates can be quite reliably predicted by ordering serum C-terminal telopeptide (CTX). High levels are indicative of decreased risk for jaw necrosis (>150 pgm/ml).

MICROSCOPIC FEATURES

Necrotic bone characterized by lamellar sequestra showing lacunae devoid of osteocyte nuclei are identified and are surrounded by necrotic debris and microbial colonies. In many instances these colonies show a radial fringe consistent with actinomycetes. Viable soft tissues are often absent.

DIFFERENTIAL DIAGNOSIS

The features are similar to those of osteomyelitis and osteoradionecrosis. The fact

that the patients are being medicated for bone cancer or senile osteoporosis with bisphosphonates underlies the diagnosis.

TREATMENT

Careful, nonaggressive sequestrectomy is required along with antiseptic lavage and antibiotic therapy.

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PRIMARY INTRAOSSEOUS CARCINOMA

Figure 9-66

Age: Middle-aged adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Primary malignant epithelial tumors central in bone are extremely rare, but may arise from odontogenic epithelium enclosed within the periodontal ligament or other intraosseous locations. The chief clinical manifestations are the same as those for metastatic carcinomas of the jaws. Clinically demonstrable expansion, paresthesia, pain, and, occasionally, unexplained loosening of teeth occur. Radiographically, the lesion is

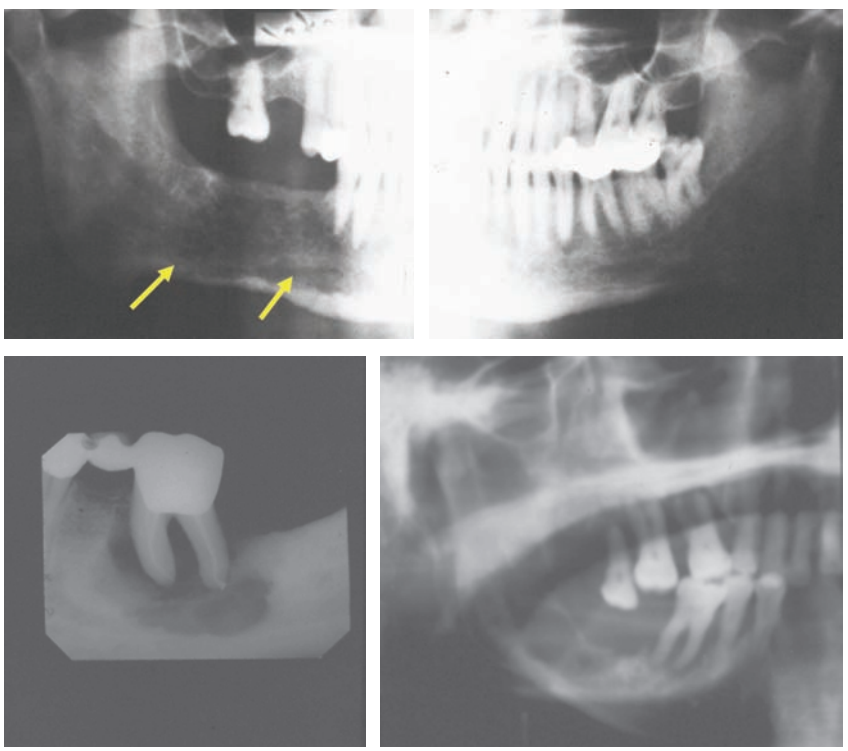

FIGURE 9-66
Nondiscrete diffuse radiolucencies of jaws in primary intraosseous carcinoma.

multilocular with poorly defined borders. Expansion or cortical perforation is encountered. Primary squamous cell carcinomas of the jaws may also arise from the linings of odontogenic cysts, usually residual cysts.

MICROSCOPIC FEATURES

Intraosseous carcinoma shows sheets and islands of neoplastic epithelium manifesting the cardinal signs of malignancy—hyperchromatism, pleomorphism, and mitoses. Acanthotic regions resembling pearl formation are occasionally present. Thus, the tumor closely resembles squamous cell carcinoma. A distinctive feature is the odontogenic nature of the tumor cells. An outer rim of ameloblastic cells occupies the position usually assumed by basal cells in an ordinary squamous cell carcinoma. Carcinomas arising from odontogenic cysts usually do not show odontogenic features; rather, they represent typical squamous cell carcinoma.

DIFFERENTIAL DIAGNOSIS

The moth-eaten radiolucent pattern of intraosseous carcinoma is similar to that of osteomyelitis; however, cortical expansion is not common in infectious processes. Primary malignant mesenchymal tumors must also be included in the differential diagnosis. Metastatic carcinoma must be ruled out, even after biopsy, by thorough physical examination and diagnostic radiologic surveys. Only then may the tumor be considered a primary carcinoma of the jaws.

TREATMENT

Resection of the involved segment with regional node dissection is recommended. Chest radiographs should be evaluated for distant spread. Survival rates are less than 30% for 5 years.

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CYSTOGENIC CARCINOMA

Figure 9-67

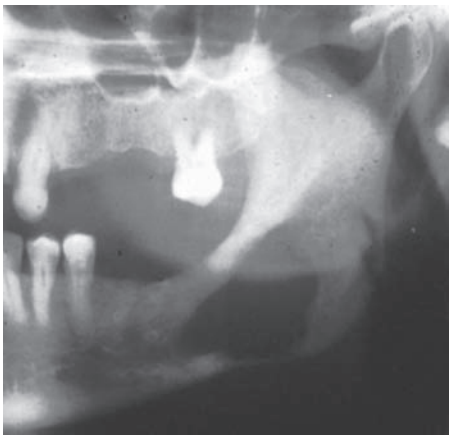
Age: Elderly
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Squamous cell carcinoma may, on rare occasions, arise from the lining of odontogenic cysts. Central mucoepidermoid carcinoma, a malignant salivary neoplasm, may also evolve from odontogenic cyst linings. Whereas squamous cancers are more often associated with residual cysts of the mandibular body, mucoepidermoid tumors are generally observed in the posterior mandible, and tumorigenesis from a dentigerous cyst can often be speculated or even documented. Maxillary cases have also been reported; however, documented origin from cyst lining is problematic when antral involvement exists. Clinically, paresthesia is a frequent, yet certainly not invariable, symptom. Radiographically, a poorly marginated unilocular or moth-eaten pattern is observed.

MICROSCOPIC FEATURES

Remnants of ordinary stratified squamous epithelial lining are seen with both mural and luminal proliferation of squamous cell carcinoma exhibiting nuclear hyperchromatism, pleomorphism, increased mitotic activity, and keratin pearl formation. Cys-



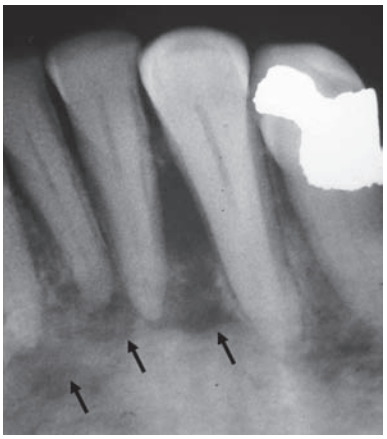


FIGURE 9-67
Residual and radicular cysts with carcinomatous transformation from the cyst lining.

togenic mucoepidermoid tumors are usually of the low-grade variety with solid and cystic islands consisting of mucous, epidermoid, and intermediate cells.

DIFFERENTIAL DIAGNOSIS

Cystogenic cancers, especially when paresthesia is present, radiographically and clinically, simulate other malignant bone tumors including metastatic carcinoma, intraosseous carcinoma, and primary sarcomas. Biopsy with documented evidence of typical cyst lining is required for the diagnosis.

TREATMENT

Complete block resection is required; should any palpable nodes be discovered, a neck dissection is indicated. Because of insufficient data on these lesions, the prognosis remains unknown.

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METASTATIC CARCINOMA

Figure 9-68

Age: Adult predilection
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Metastasis to the jaws from primary carcinoma located in visceral or parenchymal organs (usually the lung, breast, colon, or prostate) may reach the medullary bone by hematogenous spread via arterial dissemination from tumor foci located in the lungs or via retrograde migration of tumor emboli through Batson's paravertebral plexus, thereby bypassing the lungs. Metastatic cancer is the most common malignancy of the jawbones. Whereas most instances of osseous metastasis to the jaws appear as irregular moth-eaten expansile radiolucencies, some metastatic carcinomas may induce ossification so that areas of radiolucency are admixed with irregular radiopaque foci. Prostatic and thyroid

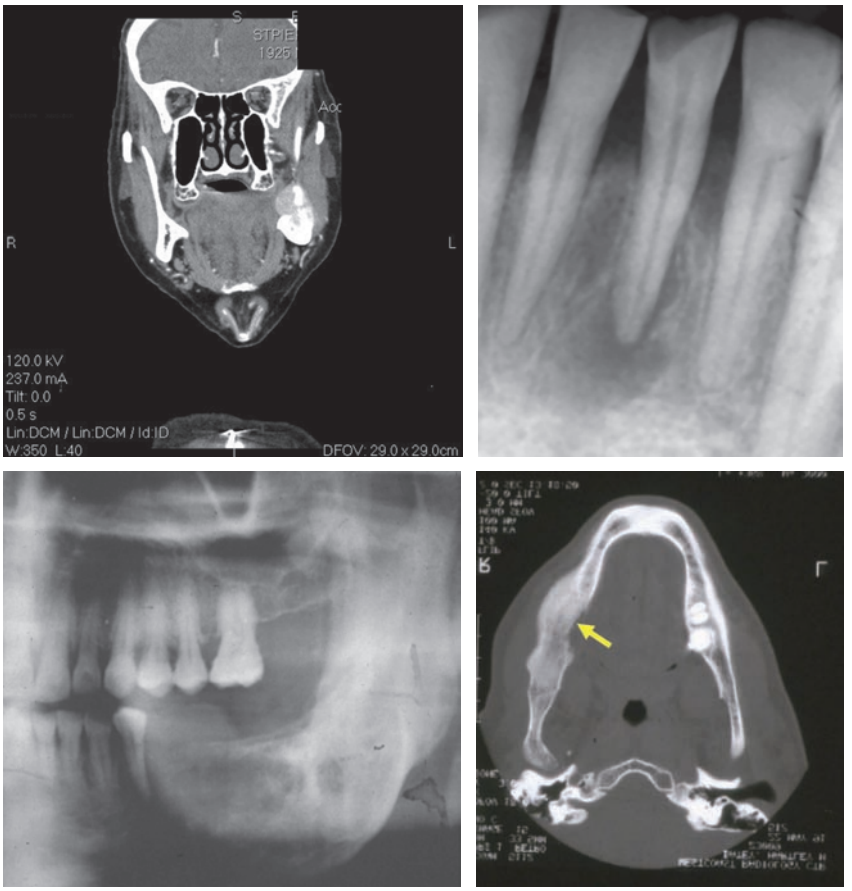

FIGURE 9-68
Diffuse irregular radiolucencies representing metastatic carcinomas. Some mets induce osteogenesis as seen in lower right.

tumors are more prone to demonstrate osteoblastic foci. Juxtaposed teeth may show root resorption; however, large areas of osseous destruction with no resorptive changes of the teeth are more common. The angle and body of the mandible are the favored sites of deposition, probably because of the rich intraosseous vascularity in these areas. The most important and consistent clinical findings include swelling, paresthesia of the lip, and deeply situated bone pain. Loosening of teeth is also a frequent finding.

MICROSCOPIC FEATURES

Nests, islands, and cords of neoplastic epithelium are supported by a fibrous stroma. In the case of osteoblastic metastasis, extensive osteoplasia may be demonstrated microscopically. The individual tumor cells may display keratinizing, adenoid, or anaplastic morphologic characteristics depending on the site of origin of the primary tumor.

DIFFERENTIAL DIAGNOSIS

The irregular poorly marginated expansile radiolucencies encountered in metastatic carcinoma may also be seen in other malignant tumors of the jaws: reticulum cell sarcoma; Ewing's sarcoma; Burkitt's lymphoma; and osteogenic, chondrogenic, or fibrogenic sarcomata. Osteomyelitis rarely shows expansion. A history of cancer elsewhere or the presence of paresthesia is highly suggestive of metastatic cancer. Primary intra-alveolar carcinoma shows microscopic features that are somewhat unusual; however, the diagnosis should be reserved for those patients in whom exhaustive examination procedures fail to disclose the presence of a primary carcinoma located elsewhere.

TREATMENT

The discovery of a metastatic deposit in the jaws carries an extremely poor prognosis. Once the diagnosis is rendered, a complete work-up is indicated to locate the primary tumor, as is a metastatic radiographic series to search for other sites of osseous metastasis. In most cases, the disease is treated palliatively, and radiation therapy may be indicated to relieve pain. Rarely, the jaw lesion may represent a single focus of metastasis and the disease may be treatable by surgical and/or radiation therapy to both the primary tumor and jaw metastasis.

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MALIGNANT ODONTOGENIC TUMORS

Figure 9-69

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Whereas primary intraosseous carcinoma and carcinoma ex odontogenic cyst derive from odontogenic epithelium, both retain the morphologic characteristics of squamous cell carcinoma. Other odontogenic tumors are extremely aggressive and some may be malignant with metastatic potential. Included in this group of odontogenic carcinomas are ameloblastic carcinoma, the clear-cell odontogenic tumor, and the malignant ghost cell tumor, all of which are distinguished on the basis of histologic features. The chief clinical finding is jaw enlargement without pain, although loosening of teeth in the affected area may be a complaint. Cortical expansion is clinically detected. Radiographically, the lesions are radiolucent, destructive, and poorly marginated. Teeth in the area of these tumors tend to be displaced, except for clear-cell lesions that rarely exhibit root resorption, and the teeth appear to be suspended within the lesion.

MICROSCOPIC FEATURES

Ameloblastic carcinomas retain the morphologic structure of ameloblastoma with a peripheral stratum of ameloblasts surrounding stellate reticulum. Of note is the presence of cytologic atypia and mitotic activity. Ameloblastomas without evidence of atypia have been reported to metastasize, and such lesions are referred to as malignant ameloblastomas as opposed to ameloblastic carcinoma, a term reserved for lesions exhibiting cytologic atypia. The malignant ghost cell tumor resembles the calcifying and keratinizing odontogenic cyst yet shows atypia. The clear-cell tumor is characterized by nests and islands of epithelial cells that tend to anastomose with one another. Most of these lesions are biphasic with nests of basiloid cells alternating with nests comprising exclusively clear cells. The basal or outermost stratum of cells are flattened without polarization. The basaloid cells contain slightly pleomorphic nuclei without mitotic figures. A mature fibrous stroma intervenes.

DIFFERENTIAL DIAGNOSIS

Radiographically, malignant odontogenic tumors resemble histiocytosis, metastatic disease, or other central jaw malignant tumors. Microscopically, when clear cells are extant, renal cell carcinoma is the chief consideration and a primary kidney tumor should be ruled

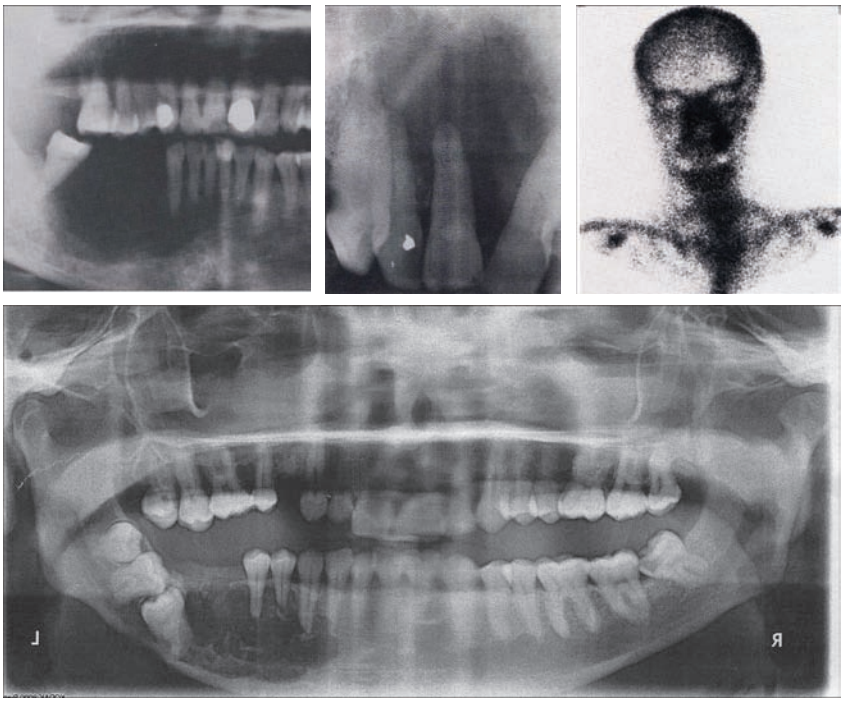

FIGURE 9-69
Poorly marginated lesion with root divergence representing clear-cell odontogenic tumor. Bone scan showing high activity in maxilla.

out by imaging studies before accepting clear-cell jaw tumors as primary disease.

TREATMENT

These poorly marginated aggressive tumors are generally managed by en bloc resection. These lesions are extremely rare and therefore no information is available on their susceptibility to radiation or chemotherapeutic agents.

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OSTEOSARCOMA AND CHONDROSARCOMA

Figure 9-70

Age: Adults
Sex: No predilection (female predilection in mandibular tumors)

CLINICAL AND RADIOGRAPHIC FEATURES

Whereas both osteogenic and chondrogenic sarcomas are capable of calcification, with resultant opacification on radiographs, many forms fail to show significant calcification and appear as irregular, poorly delineated, expansile radiolucencies. Both tumors are rare in the jaws; as opposed to osteosarcoma of other bones, jaw lesions tend to occur in older individuals as well as in teenagers. The mandible is affected more often than the maxilla. Both osteo- and chondrosarcomas are rapidly growing neoplasms with a propensity for distant rather than nodal metastasis. Expansion, pain, and paresthesia are common features.

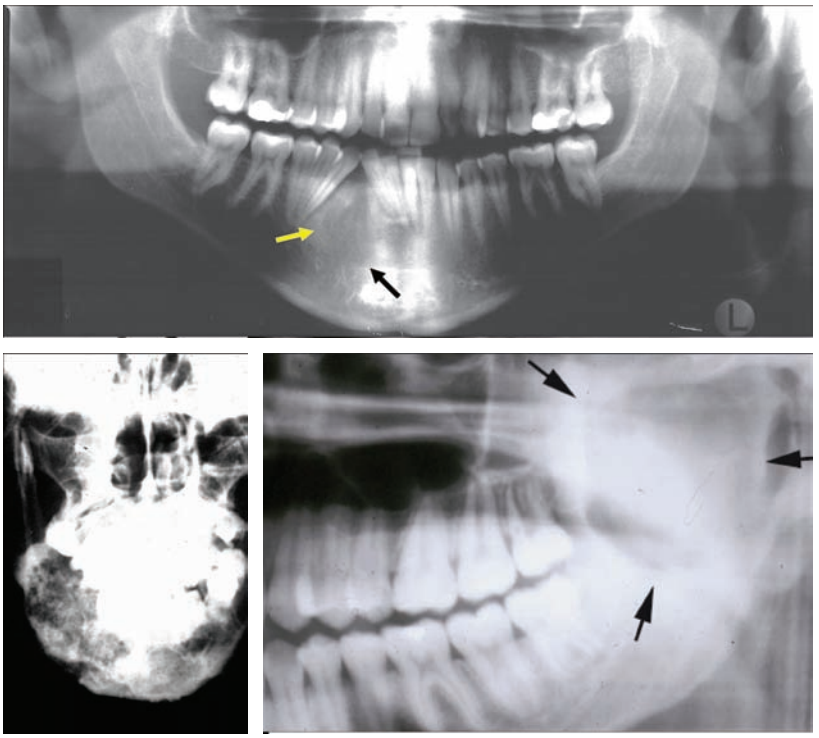

FIGURE 9-70
Poorly marginated radiolucencies of the mandible in osteogenic sarcoma.

MICROSCOPIC FEATURES

Osteogenic sarcoma exists in three histomorphologic variations: osteoblastic, chondroblastic, and fibroblastic. The latter is most often radiolucent. The histology cannot be correlated with prognostic predictability. Chondrosarcomas generally contain hyaline cartilage with pleomorphic chondroblasts. A specific histologic variant, the mesenchymal chondrosarcoma, has a predilection for the jaws. These tumors contain little identifiable hyaline cartilage, but are composed of immature hypercellular spindle and stellate cells with intervening basophilic ground substance. Focal areas are traversed by cleft-like channels reminiscent of hemangiopericytoma.

DIFFERENTIAL DIAGNOSIS

Osteo- and chondrosarcomas of moth-eaten radiolucent pattern resemble metastatic carcinoma, intra-alveolar carcinoma, and other mesenchymal malignancies such as reticulum cell sarcoma, Ewing's sarcoma, neurosarcoma, and fibrosarcoma of bone. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Hemimandibulectomy or maxillectomy is required. Radium needle implants, followed by resection, have also been employed. The 5-year survival for osteogenic sarcoma of the jaws is less than 50%. Mandibular tumors show a better prognosis than those arising in the maxilla. Because regional metastases are extremely rare, prophylactic neck dissection is not indicated.

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EWING'S SARCOMA

Figure 9-71

Age: Teenagers
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Ewing's sarcoma is a rare primary malignant mesenchymal neoplasm of bone. The true cell of origin is unknown, but it is probably an undifferentiated osseous mesenchymal cell. The disease is most frequently encountered in the long bones of the lower extremities, but may appear initially in the jaws, usually the mandible. Expansion with pain, paresthesia, or anesthesia usually constitutes the chief complaint. Unexplained loosening of teeth may also be a feature, and leukocytosis with elevated temperature is often encountered. Radiographically, the tumor is radiolucent with ill-defined margins. Expansion or erosion of the cortex is observed, and occasionally, an osteophyte reaction or cortical redundancy (onion skinning) is demonstrable. If left untreated, widespread metastasis to other bones and visceral organs ensues rapidly. In Ewing's, the (11;22)(q24;q12) chromosomal translocation that encodes the EWS/FLI oncoprotein is involved in most cases.

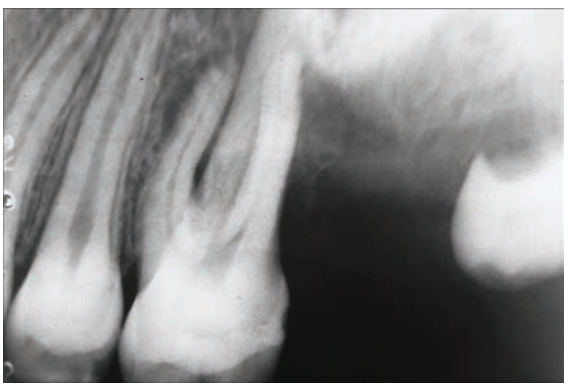

FIGURE 9-71
Moth-eaten radiolucent lesion of tuberosity in a child with Ewing's sarcoma.

MICROSCOPIC FEATURES

The tumor is composed of diffuse sheets of hyperchromatic round cells with virtually no fibrous stroma. Septae traverse the neoplastic element, and tumor cells tend to orient themselves about blood vessels. Multifocal zones of necrosis are commonly seen CD99 is positive.

DIFFERENTIAL DIAGNOSIS

Ewing's sarcoma may radiographically and clinically resemble osteomyelitis. Particularly when onion skinning is present, confusion with Garré's periostitis may arise. The moth-eaten expansile radiographic appearance may also be seen in a variety of bone malignancies, including metastatic carcinoma, lymphoma, and other bone sarcomas. Biopsy is required to provide a definitive diagnosis.

TREATMENT

Ewing's sarcoma is a highly malignant neoplasm with a 5-year survival of less than 10%. The disease is treated by multidrug chemotherapy and should be managed by an oncologist. Treatment is usually by radiation and chemotherapy. Surgical intervention is occasionally attempted. Teeth should be extracted before radiation therapy when they are embedded in tumor.

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PRIMARY LYMPHOMA OF BONE

Figure 9-72

Age: Young adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Primary lymphoma that originates from bone marrow lymphoid precursor cells is generally of the non-Hodgkin's variety, lymphocytic and/or histiocytic type. This form was, in the past, referred to as reticulum cell sarcoma of bone. The pelvis and long bones of the lower extremities are the usual sites of origin, yet the jaws may be involved initially or jaw lesions may accompany tumor in other osseous sites. The clinical features include expansion, pain or paresthesia, and unexplained loosening of teeth. Radiographically, the medullary bone shows significant osseous destruction or merely a loss of trabeculation with ill-defined margins. Cortical expansion or perforation is often demonstrable radiographically. In HIV-infected patients, central jaw lymphomas may resemble Burkitt's or may represent *plasmablastic lymphoma*, an AIDS-specific oral lymphoma.

MICROSCOPIC FEATURES

The biopsy specimen shows diffuse sheets of oval-to-round nucleated cells separated by scant or often undiscernible stroma. The nuclei are larger than those of mature lymphocytes, and the nucleoplasm is moderately stained with stippling. Most are classified as diffuse large B-cell lymphomas. Plasmablastic lymphoma shows microscopic features similar to anaplastic multiple myeloma.

DIFFERENTIAL DIAGNOSIS

Ill-defined moth-eaten radiolucencies with pain, typical of primary lymphoma of bone,

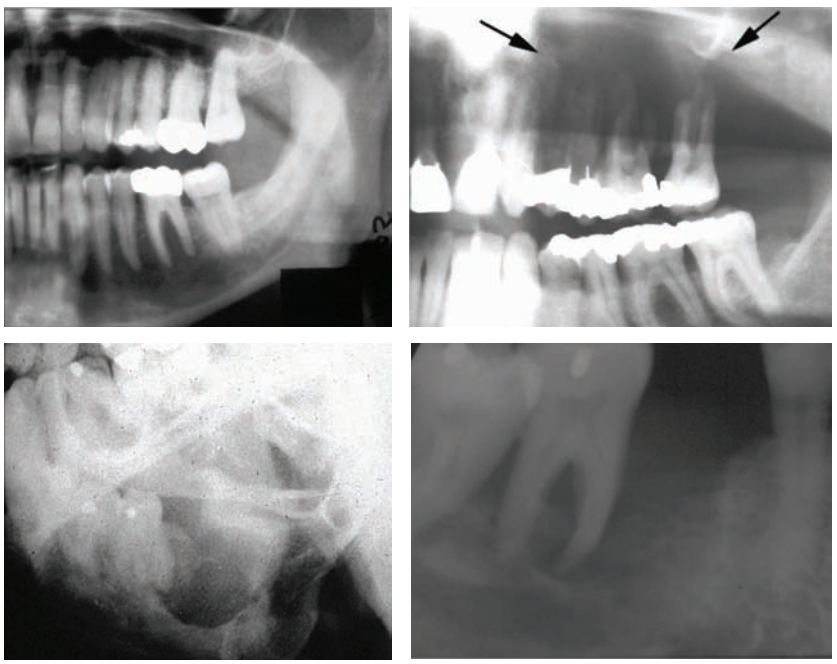

FIGURE 9-72
Irregular, poorly defined radiolucencies representing primary lymphoma of bone.

are also features of osteomyelitis. In the latter, an infectious source, usually odontogenic, is detectable; expansion of the cortex is unusual. These same radiographic features are seen with Ewing's sarcoma, other primary sarcomas of osteogenic mesenchymal tissue, and metastatic carcinoma. The diagnosis requires microscopic evaluation. Once the diagnosis has been secured, a complete blood count should be performed to rule out leukemia with infiltration into bone.

TREATMENT

Radiation therapy with or without chemotherapy is the treatment of choice and should be performed by an oncologist or radiation therapist. Teeth should be extracted from the radiation field before therapy. The prognosis is poor and even worse for plasmablastic lymphoma.

Additional Reading

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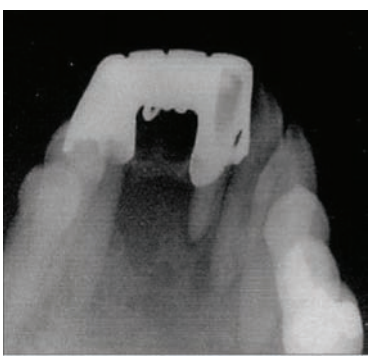
BURKITT'S LYMPHOMA

Figure 9-73

Age: Children
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Burkitt's (African) lymphoma is a unique form of lymphoma found primarily in Uganda and Kenya. Clinically similar cases have been discovered in the United States. The unique character of the disease rests with the predilection for tumor to involve certain organs and locations, namely the jaws, abdominal nodes, and ovaries. Other visceral tissues may be infiltrated as well. The disease occurs in a specific geographic locale and at specific ranges in altitude, implicating an insect vector of transmission. Accumulating evidence suggests that the Epstein-Barr virus may be causative (the same virus that causes the benign lymphoproliferative disorder infectious mononucleosis). Clinically, the tumor is capable of massive growth with significant expansion and facial disfigurement with loosening and displacement of teeth.



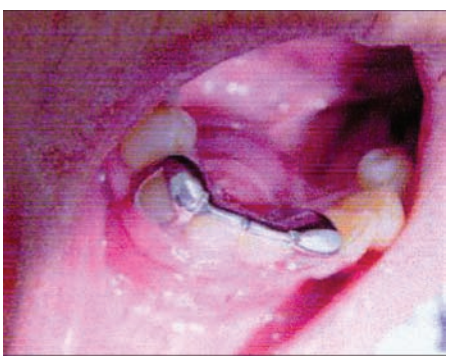


FIGURE 9-73
Diffuse, destructive lesion in Burkitt's lymphoma. (Courtesy of Dr. George Chew.)

Abdominal distention from node and visceral lesions is common. Radiographically, massive destruction of bone is observed with a moth-eaten, poorly marginated, pattern. The cortex shows expansion or erosion and perforation. Destruction of developing tooth buds is commonly seen. There is evidence that Epstein-Barr virus may induce a translocation of the *MYC* gene, forming a fusion protein with immunoglobulin promoter sequences.

MICROSCOPIC FEATURES

Diffuse sheets of mature lymphocytes are seen, and the tumor is essentially devoid of fibrous stroma. Reticulum stains show a profuse network of reticulum around tumor cells. The pathognomonic microscopic pattern of Burkitt's lymphoma, referred to as the "starry-sky" appearance, is characterized by multiple foci of large pale-staining histiocytic cells with vesicular nuclei and generous amounts of cytoplasm dispersed randomly within a sea of darker staining lymphoid cells.

DIFFERENTIAL DIAGNOSIS

The combination of jaw lesions with abdominal masses in an African child is classic for Burkitt's lymphoma. In other geographic areas, the moth-eaten expansile radiolucency of Burkitt's lymphoma must be differentiated from other lesions occurring with equal or greater frequency. Osteomyelitis may show similar features, but expansion is uncommon. Other sarcomas of bone as well as metastatic childhood tumors (e.g., neuroblastoma, nephroblastoma) must be included in the differential diagnosis. Biopsy discloses the characteristic histomorphologic features of Burkitt's lymphoma.

TREATMENT

This form of lymphoma is fatal, but chemotherapy effects remarkable tumor shrinkage and accounts for extended remissions. The care of the patient should be managed by a medical oncologist.

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FIBROGENIC AND NEUROGENIC SARCOMA

Figure 9-74

Age: Young and middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Sarcomas derived from fibroblasts or nerve sheath (Schwann cells, perineural fibroblasts) are occasionally encountered in bone. Indeed, central neurogenic sarcomas are encountered more frequently in the mandible than in any other bone, probably because of the unique anatomy by which the alveolar nerve traverses a long distance while encased in bone. The chief clinical findings include paresthesia, swelling, and loosening of teeth. Both fibrosarcomas and neurosarcomas manifest as ill-defined radiolucencies, which may cause root resorption or divergence. Expansion may be obvious; however, large areas of osseous destruction may evolve in the absence of any expansion. Neurosarcomas often produce a fusiform widening of the inferior alveolar canal, tending to grow along the course of the nerve as high as the Gasserian ganglion.

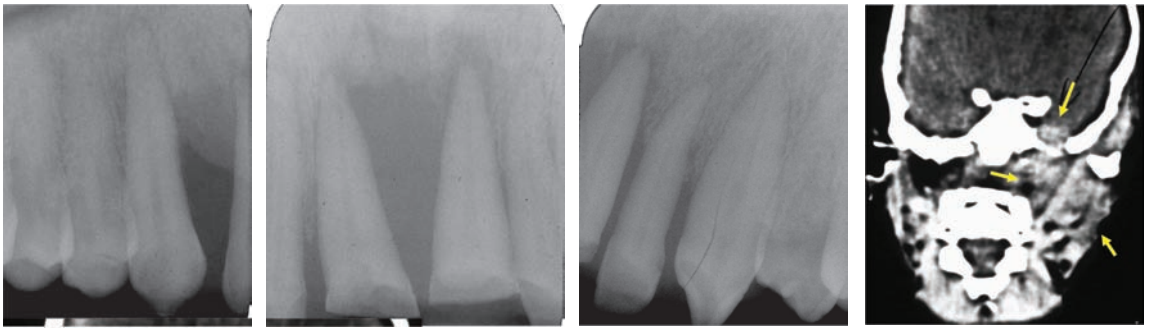

FIGURE 9-74
Ill-defined radiolucency in mandible representing a central fibrosarcoma. Computed tomography showing invasive myofibrosarcoma with skull base invasion.

MICROSCOPIC FEATURES

Both fibrogenic and neurogenic sarcomas are hypercellular spindle cell proliferations displaying little or only moderate pleomorphism. Mitotic figures are usually numerous. The tumor cells grow in parallel fascicles, and palisading may be a feature of neural sheath malignancies. This feature is not a constant, however, and proof of origin from nerve sheath requires the demonstration of continuity between an intact nerve and the circumneural tumor mass.

DIFFERENTIAL DIAGNOSIS

An ill-defined enlargement of the inferior alveolar canal in conjunction with paresthesia is highly suggestive of central neurogenic sarcoma. Because both fibrosarcoma and neurosarcoma may show an expansile moth-eaten radiolucency with or without resorption of adjacent teeth, other malignant tumors including metastatic cancer and primary sarcomas of bone must be included in the differential diagnosis. Microscopic evaluation is necessary to secure a definitive diagnosis.

TREATMENT

Surgical resection, hemimandibulectomy, or partial maxillectomy, including at least 3 cm of tumor-free margin, is the treatment of choice. In the case of neurosarcoma, dissection of the inferior alveolar nerve, sampling for microscopic evidence of tumor, is advisable. Central fibrosarcoma has a better prognosis in the jaws than it does in other bones. The 5-year survival exceeds 50%.

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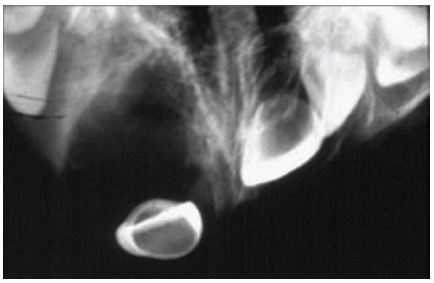
MELANOTIC NEUROECTODERMAL TUMOR OF INFANCY

Figure 9-75

Age: Infancy
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Melanotic neuroectodermal tumor of infancy is a benign neoplasm derived from neural



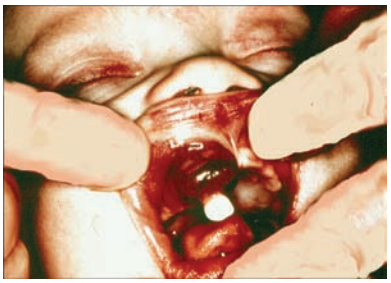


FIGURE 9-75
Displaced developing incisor with underlying, poorly marginated radiolucency in melanotic neuroectodermal tumor of infancy.

crest cells with a propensity to involve tooth-bearing regions in the maxilla. The precise origin is controversial. At one time, this neoplasm was classified with the odontogenic tumors; however, cases have been reported in the skull, shoulder region, testes, and uterus. Some cells within the dental papillae have been shown to derive from neural crest precursors, so the tumor may represent a neuroectodermal odontogenic lesion when it arises in the jaws. Early theories suggested origin from ectopic retinal tissues. These theories account for the various terms applied to this neoplasm (pigmented ameloblastoma, retinal anlage tumor, progonoma). The neoplasm is rarely encountered after 6 months of age and, as previously stated, is more often seen in the maxilla than the mandible. Clinically, the edentulous alveolus of the infant shows a smooth-surfaced bulging and is generally nonpigmented. Radiographically, the lesion is radiolucent with irregular, ill-defined margins. Developing teeth may lie within the radiolucent area or are significantly displaced by the neoplasm. As with other neoplasms of neuroblastic origin, vanillylmandelic acid may be detected in the urine. Apparently, some of these tumors, albeit few, are capable of metastasis.

MICROSCOPIC FEATURES

The tumor is composed of alveolar nests of cells oriented about cleft-like spaces, with a surrounding dense fibrous stroma. Two cell types are encountered: an epithelioid polygonal cell with an oval vesicular nucleus is seen to contain melanin granules, and the other cell type resembles a neuroblast, with a round hyperchromatic nucleus with sparse or unidentifiable cytoplasm. These two types coexist in the alveolar clusters.

DIFFERENTIAL DIAGNOSIS

The poorly marginated borders of melanotic neuroectodermal tumor would appear to support a radiologic diagnosis of malignancy. Similar features may, of course, be seen in any of the malignant bone tumors included among the moth-eaten radiolucencies; however, none of the malignant osseous neoplasms shows a tendency to arise in infants. Therefore, a maxillary aggressive-appearing radiolucent lesion in a neonate should arouse suspicion that one is dealing with neuroectodermal tumor. Because sarcomas do occasionally arise in early childhood, biopsy confirmation is mandatory.

TREATMENT

Local curettage is the treatment of choice for this benign neoplasm. Recurrences have been recorded; however, most lesions can be cured without resorting to en bloc resection. Because metastasis has occurred in a few cases, a complete radiologic evaluation should be performed, and close periodic follow-up is recommended.

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Multifocal Radiolucencies

BASAL CELL NEVUS SYNDROME

Figure 9-76

Age: Teenagers
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The basal cell nevus syndrome is an autosomal dominant genetic disease characterized by a primary triad with variable secondary anomalies. The chief features include nevoid basal cell carcinomas, one or more bifid ribs, and multiple odontogenic keratocysts of the jaws. The basal cell lesions have limited growth potential, arise during childhood or early adulthood, and appear in regions of the skin not necessarily exposed to solar radiation. The keratocysts are multiple; they may be interradicular or pericoronal well-delineated unilocular radiolucencies; some may be multilocular. Cortical expansion in larger cysts is obvious clinically as well as radiographically. Other anomalies seen in the syndrome include frontal bossing, hypertelorism, calcified falx cerebri, prognathism, and palmar-plantar hyperkeratosis. Individuals with this disorder are also prone to develop medulloblastomas, malignant posterior fossa brain tumors. Perturbations in the sonic hedgehog growth pathway involve mutations in the *PTCH* gene, molecular lesions that are found in both keratocysts and nevoid basal cell tumors.

MICROSCOPIC FEATURES

The keratocysts of the basal cell nevus syndrome do not differ from those seen as

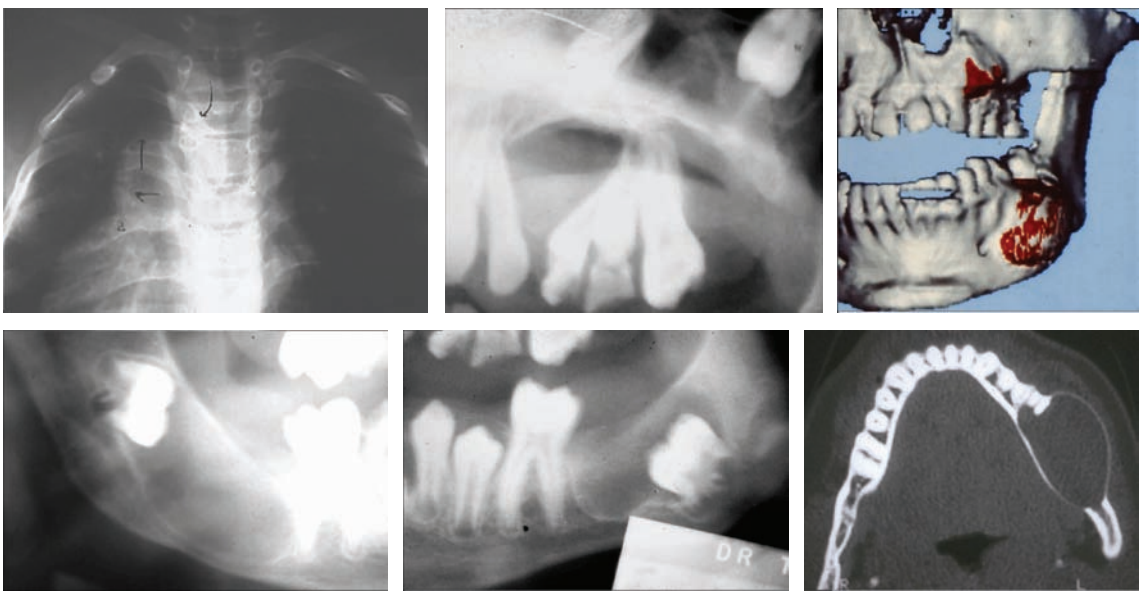

FIGURE 9-76
Basal cell nevus syndrome with bifid rib and multiple odontogenic keratocysts.

solitary lesions. The lumen contains laminations of keratin. The lining epithelium displays a corrugated surface, attenuated spinous layer, and polarized basal cell layer.

DIFFERENTIAL DIAGNOSIS

The multifocal radiolucencies, particularly when many of them are pericoronal, in conjunction with bifid ribs and basal cell tumors are classic for the basal cell nevus syndrome. From the radiographs of the jaw alone, the multifocal radiolucencies may resemble multiple keratocysts without other features of the syndrome, multiple dentigerous cysts, or even histiocytosis. The latter rarely shows expansion.

TREATMENT

Thorough curettage of the jaw cysts is required. Chemical cautery of the bony crypt may be performed. Recurrences are common and require repeated surgical intervention. The basal cell nevi may be too numerous to remove; however, they generally are not aggressive as are ordinary basal cell carcinomas. Most cases are sporadic yet hereditary linked cases are occasionally encountered. A thorough neurologic work-up with periodic examinations should be carried out to rule out medulloblastoma.

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LANGERHANS CELL HISTIOCYTOSIS

Figure 9-77

Age: Children and young adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Histiocytosis or Langerhans cell granulomatosis, a histiocytic proliferative disorder of the reticuloendothelial system and bone, exists in three forms: acute disseminated, chronic disseminated, and chronic limited variants. The latter two, previously termed Hand-Schuller-Christian disease and eosinophilic granuloma, respectively, are dealt with here because they are more apt to involve the jaws. Chronic disseminated histiocytosis manifests a classic triad of features: exophthalmos from retro-orbital infiltration, diabetes insipidus owing to posterior pituitary histiocytic infiltrates, and osseous lesions. Otitis media and lung infiltrations are also common. This form occurs in children and teenagers. Chronic limited histiocytosis is more often seen in young adults, is generally limited to bone with either solitary or multifocal osseous defects, and occasionally manifests pulmonary infiltrates. Jaw lesions in all forms of the disease show similar features. Pain and expansion are usually absent. Teeth may become loose for no apparent reason, and the gingiva may appear inflamed in involved areas. The lesions are more common in the mandible than maxilla and are often, yet not invariably, multifocal irregular radiolucencies lacking marginal cortication. When the alveolus is involved, the teeth may give the impression that they are floating in space, because they may be entirely encompassed by a radiolucent defect. The skull often contains punched-out radiolucencies.

MICROSCOPIC FEATURES

Diffuse sheets of histiocytes with pale nuclei and abundant cytoplasm prevail. These

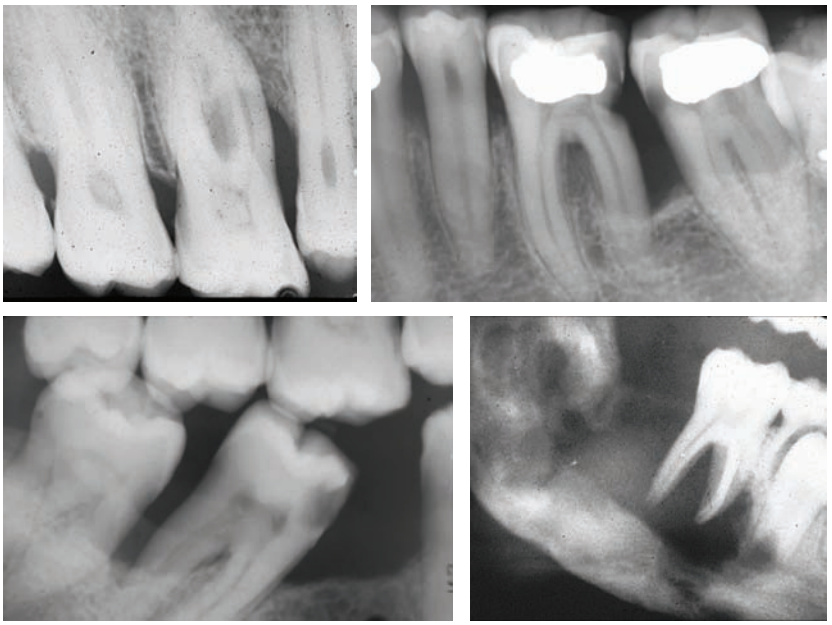

FIGURE 9-77
Radiolucent lesions in both jaws in a patient with Langerhans cell histiocytosis.

cells represent CD1a+ Langerhans cells. Occasionally, multinucleated histiocytes and foam cells are encountered. Multiple foci of eosinophilic abscesses are encountered. Fibrous stroma is scant.

DIFFERENTIAL DIAGNOSIS

Multifocal noncorticated radiolucencies of the jaws may occur in diseases other than the histiocytoses, including multiple myeloma, the basal cell nevus syndrome, and, occasionally, multifocal metastatic carcinoma and primary lymphoma of bone. Multiple early-stage periapical cemental dysplasia must be considered in the differential diagnosis when lesions are located at the apex of teeth. Biopsy is required for definitive diagnosis. A skeletal radiographic survey should be obtained to check for disease in other bones.

TREATMENT

Chronic disseminated histiocytosis has a guarded prognosis. The disease responds to chemotherapy, particularly the vinca alkaloids. The chronic limited form with jaw lesions can be treated by local curettage.

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MULTIPLE MYELOMA

Figure 9-78

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Multiple myeloma is a malignant osseous neoplastic disorder of immunoglobulin-secreting plasma cells. It probably represents a multicentric malignancy, as multiple osseous foci of disease may be detected simultane-

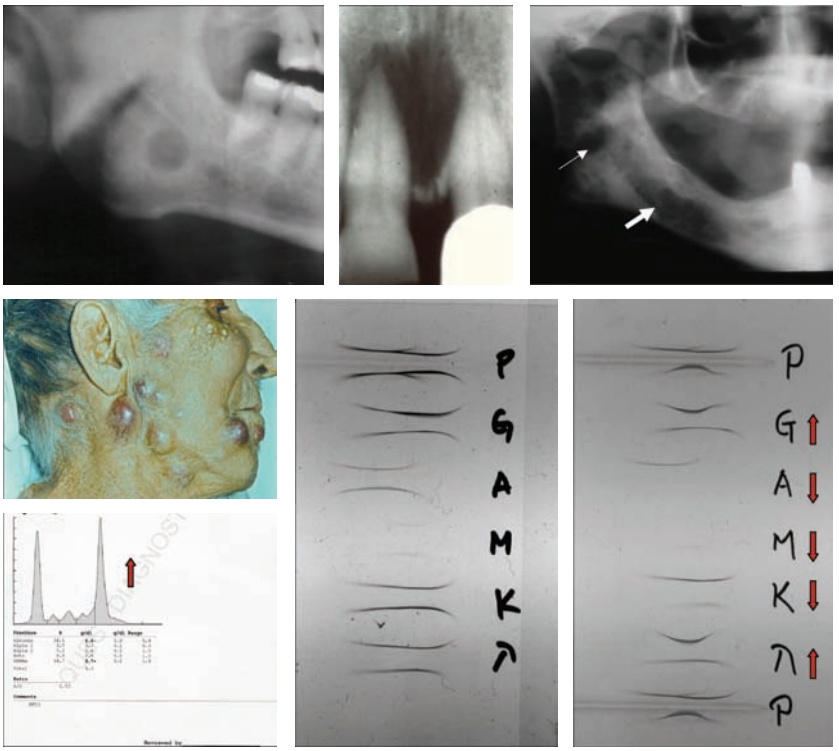

FIGURE 9-78
Multifocal punched-out lesions of the jaws, typically seen in multiple myeloma. A γ-spike is seen on electrophoresis and immunoelectrophoresis portrays light chain restriction for λ.

ously. The jaws, usually the mandible, are involved in over one fourth of the cases. Immunoglobulins, usually of a single class and allotype, are detected in serum. Bence-Jones protein, representing globulin fragments, is often detectable in the urine. When the jaw is involved, bone pain and paresthesia are common complaints. The tumor cells may perforate the cortex, causing a soft tissue bulge or antral invasion. Loosening of teeth may be observed. Radiographically, multiple oval well-demarcated, but noncorticated, radiolucencies are observed. Cortical expansion is rare, perforation being more common when the lesions extend to the periphery of bone. Root resorption may occur. A skeletal survey discloses similar lesions in other bones, particularly the skull.

MICROSCOPIC FEATURES

Monotonous sheets of relatively well-differentiated plasma cells prevail. Mitoses and multinucleated cells are frequent findings. As opposed to chronic inflammation with a predominance of plasma cells, myeloma infiltrates lack dense stroma or granulation tissue, and other inflammatory cells in virgin lesions are not encountered. Amyloid deposits are frequently present. Immunoperoxidase techniques can be performed on formalin-fixed sections; the demonstration of monotypic antibody employing techniques for class immunoglobulin heavy chains, a single type of light chain, or the presence of J-protein is specific for myeloma. Immunoglobulin gene rearrangement assays demonstrate the monoclonal nature of the malignancy.

DIFFERENTIAL DIAGNOSIS

The punched-out well-defined radiolucencies typical of myeloma may also occur in histiocytosis, disseminated metastatic carcinoma, and primary lymphoma of bone. Multiple keratocysts should be included in the radiographic differential diagnosis.

Microscopic examination is required for a definitive diagnosis.

TREATMENT

Multiple myeloma has a grave prognosis, with 5-year survival of less than 10%. The disease is treated by chemotherapy and should be managed by a medical oncologist.

Additional Reading

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Generalized Osteoporotic Lesions

OSTEOMALACIA

Figure 9-79

Age: Varies according to pathogenesis
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Osteomalacia represents a collective of disorders, whereby osteoid is not thoroughly mineralized. Genetic and acquired deficiencies in calcium absorption and incorporation into bone matrix are responsible. Dietary vitamin D deficiency, or rickets, occurs in children as does the hereditary form of rickets, whereby an enzyme deficiency precludes the normal activation of vitamin D (hypophosphatemic or vitamin D refractory rickets). In both cases, lack of active vitamin D results in deficient calcium absorption and incorporation into osteoid. Malabsorption syndromes such as biliary cirrhosis and various forms of steatorrhea encountered in adults are characterized by hypocalcemia. Renal osteodystrophy develops in late-stage glomerular disease as a consequence of renal calcium diuresis. Certain drugs, particularly anticonvulsants, interfere with enzymatic activation of vitamin D. *Oncogenic osteomalacia* is a rare paraneoplastic syndrome in which certain mesenchymal tumors secrete phosphaturic factors leading to hypophosphatemia. Regardless of the mechanism, osteomalacia is the result of hypocalcemia. Radiographically, diffuse rarefaction is observed in both the maxilla and the mandible. The density of trabeculae per unit area is diminished, and the lamina dura may be quite thin. These radiographic alterations are often subtle and are not always observed. Pathologic fractures may also complicate the condition.

MICROSCOPIC FEATURES

Routine histologic examination is not particularly revealing. During processing, decalcification occurs quickly. Otherwise, the histologic appearance of trabeculae in osteomalacia is usually unremarkable.

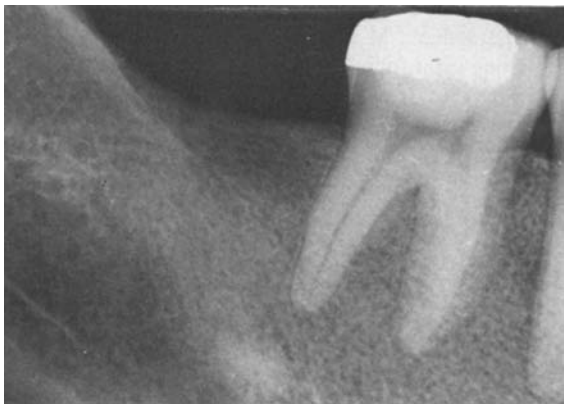

FIGURE 9-79
Diffuse granular trabeculation in osteomalacia secondary to advanced renal disease.

DIFFERENTIAL DIAGNOSIS

The diffuse rarefaction of osteomalacia is basically identical to that seen in osteoporosis and is similar to the changes observed in the other systemic diseases included here. Because many pathogenic mechanisms are involved, a complete medical evaluation is imperative. A biochemical bone panel to evaluate alkaline phosphatase, calcium, and phosphorus levels is necessary. The work-up usually includes renal function tests, a renal panel, urinalysis, a liver panel, and a skeletal survey.

TREATMENT

Referral to an internist is recommended. Treatment consists of establishing an appropriate calcium balance and is based on determining the underlying pathogenetic mechanism of the problem.

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SENILE OSTEOPOROSIS

Figure 9-80

Age: Elderly adults
Sex: Predominantly females

CLINICAL AND RADIOGRAPHIC FEATURES

Senile osteoporosis develops with ensuing age in conjunction with decreased anabolic hormones, particularly estrogen in postmenopausal women. Mineral content is not problematic as in osteomalacia; rather, the total bone matrix volume decreases. The axial skeleton is involved primarily, and a decrease in stature is evident. Back pain may be a feature; as the appendicular skeleton becomes progressively involved, a minor fall may result in fracture. Jaw radiographs in advanced cases show thinning of the cortices, being most obvious in the mandible with a generalized loss of defined trabeculation. This loss of trabecular definition may yield a somewhat ground-glass or granular pattern with an overall general radiolucent appearance. The biochemical bone panel generally is within normal limits. Studies comparing mandibular cortices on panoramic films fail to differentiate osteoporosis from normal bone densities.

MICROSCOPIC FEATURES

In osteoporosis, low-power assessment discloses a thinning of the cortical bone with a decreased ratio of trabeculae to marrow. The medullary trabeculae are thin and atrophic without evidence of osteoblastic rimming.

DIFFERENTIAL DIAGNOSIS

Senile or postmenopausal osteoporosis is radiographically indistinguishable, in the

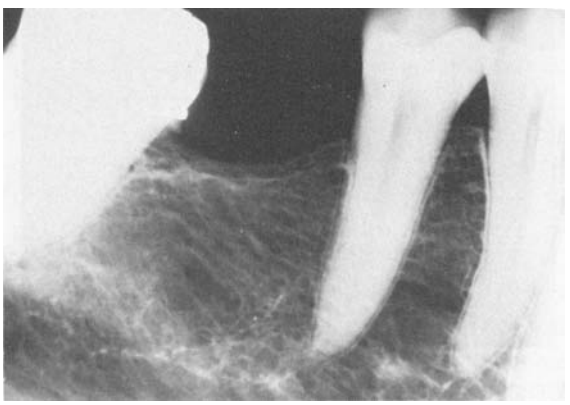

FIGURE 9-80
Senile osteoporosis with loss of cortical prominence and altered trabeculation.

jaws, from osteomalacia or steroid osteoporosis. The hemolytic anemias generally have a distinctive altered and unusual trabecular pattern.

TREATMENT

These elderly patients should limit their physical activities while maintaining proper and balanced nutrition. Referral to a physician is recommended.

Additional Reading

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STEROID OSTEOPOROSIS

Figure 9-81

Age: Varies according to pathogenesis
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Osteoporotic changes develop in patients with elevated blood corticosteroids. In Cushing's syndrome, either an adrenal cortical adenoma or a pituitary corticotropin-secreting tumor with adrenal cortical hyperplasia exists. Clinically, the facial tissues are edematous, yielding the so-called *moon facies*; other features include upper trunk adiposity, hypertension, and hyperglycemia. Elevated urine 17-ketosteroid and elevated serum cortisol levels can be detected. Treatment of immunopathic disorders such as lupus erythematosus, pemphigus, or mixed collagen diseases is usually effected by using steroid medication. High doses over a prolonged period result in cushingoid changes. Prolonged elevation of cortisone or steroid analogues result in generalized osteoporosis affecting both the axial and appendicular skeleton, including the skull and jaws. Radiographically, the changes mimic those seen in senile osteoporosis with thin cortices, attenuated lamina dura, and generalized granular rarefaction.

MICROSCOPIC FEATURES

The cortices are thin, and the medullary trabeculae are scant with abundant soft tissue marrow.

DIFFERENTIAL DIAGNOSIS

The diffuse rarefaction of steroid osteoporosis is essentially identical to that seen in senile osteoporosis. A history of systemic steroid medication or Cushing's syndrome establishes the diagnosis.

TREATMENT

Cushing's syndrome can be treated by surgical removal of the adrenal or pituitary tumor. Osteoporosis secondary to steroid administration can be minimized to some extent by prescribing the drug during early morning hours, which coincide with physiologic secretion peaks.

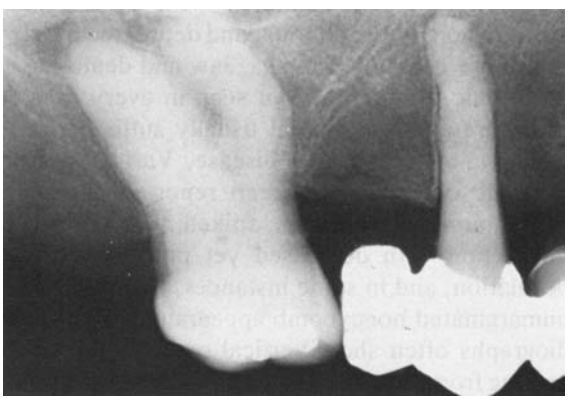

FIGURE 9-81
Cushing's syndrome with loss of trabecular markings.

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SICKLE CELL ANEMIA

Figure 9-82

Age: Childhood onset
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Sickle cell anemia is an autosomal recessive inherited disease that affects less than 1% of the black population, in which a defective hemoglobin molecule is synthesized. This abnormal hemoglobin (HgS) can be detected with the use of hemoglobin electrophoresis. Other abnormal hemoglobin molecules (e.g., HbC) may be encountered in sickle cell disease. Oxygen tension is low, and erythrocytes carrying this abnormal reduced hemoglobin assume altered morphology (sickled forms). During a crisis, sludging of cells occurs with formation of microthrombi. A severe crisis can be fatal. A compensatory bone marrow erythroblastic hyperplasia develops and leads to generalized osteoporotic changes radiographically. The clinical features include weakness, dyspnea, pallor, and generalized body pains. Jaw radiographs show a reduction in the number of trabeculae; those that remain are clearly defined and appear thickened. Some cases show a so-called *step-ladder* appearance with parallel horizontal trabeculation in the interradicular zone. The cortices are thin.

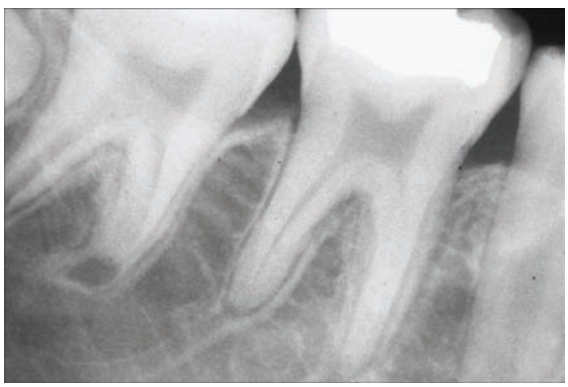

FIGURE 9-82
Step-ladder trabeculation in sickle cell anemia. (Courtesy of Dr. R. Sanger.)

MICROSCOPIC FEATURES

The microscopic features are not particularly diagnostic. Careful search for sickled erythrocytes within vessels should be undertaken.

DIFFERENTIAL DIAGNOSIS

The step-ladder effect and reduced trabeculation may be seen in normal patients. Similar radiographic changes may also be encountered in thalassemia. The other osteoporoses appear more granular on jaw radiographs. When the aforementioned radiographic features are encountered in black children, sickle cell anemia should be considered; a complete blood count, testing for sickle cell phenomenon, and hemoglobin electrophoresis should be ordered.

TREATMENT

There is no effective treatment. Parental genetic counseling is recommended.

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THALASSEMIA MAJOR

Figure 9-83

Age: Childhood onset
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

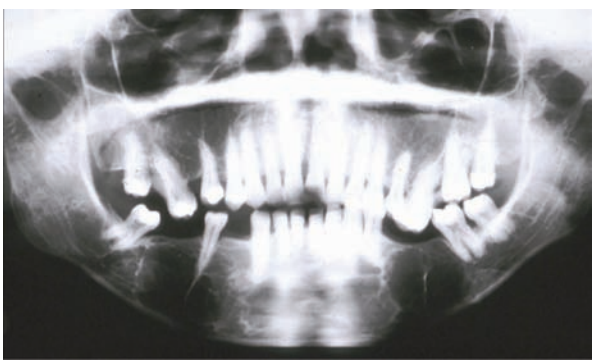
Thalassemia, found predominantly among Italians and Greeks, is a hemoglobinopathy with resultant hemolytic anemia that represents a heritable defect in either the α- or β-hemoglobin chain. Elevated fetal hemoglobin (HbF) level is present in erythrocytes and can be quantitated, using hemoglobin electrophoretic techniques. Major and minor β- (Cooley's anemia) and α-forms exist with full expression in the homozygous forms. Clinically, homozygotes are affected from birth or early childhood; pallor, malaise, and paroxysmal fever occur. Splenomegaly and appearance of mongoloid features with prominent malar region, incisor flaring, and depressed nasal bridge are common findings. Jaw and dental radiographic changes are not seen in every case; when present, the patient usually suffers from the β-major form of the disease. Various radiographic changes have been reported and include thinning of cortices, spiked roots, taurodonts, calcified inferior alveolar canal, diffuse rarefaction with decreased yet prominent trabeculation, and in some instances, a diffuse and unmarginated honeycomb appearance. Skull radiographs often show vertical osteophytes emanating from the inner table of the calvarium producing the hair-on-end effect.

MICROSCOPIC FEATURES

Biopsy that includes hematopoietic marrow or bone marrow aspiration smears discloses hypochromic microcytes with poikilocytosis and anisocytosis. Large numbers of immature erythroblastoid cells are present, indicating a maturation arrest.

DIFFERENTIAL DIAGNOSIS

The radiographic features simulate, to some extent, those changes observed in sickle cell anemia. Serum levels of unconjugated bilirubin are elevated, and hemoglobin electrophoresis discloses elevated amounts of HbF. The aforementioned bone marrow and peripheral blood changes are also of diagnostic importance.



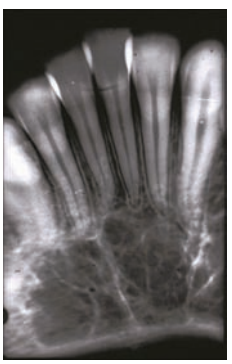


FIGURE 9-83
Multifocal honeycomb trabeculation in thalassemia major. (Courtesy of Dr. H.G. Poyton.)

TREATMENT

No effective treatment exists. Iron chelating agents are administered orally to remove excessive iron. Genetic counseling is recommended for parents.

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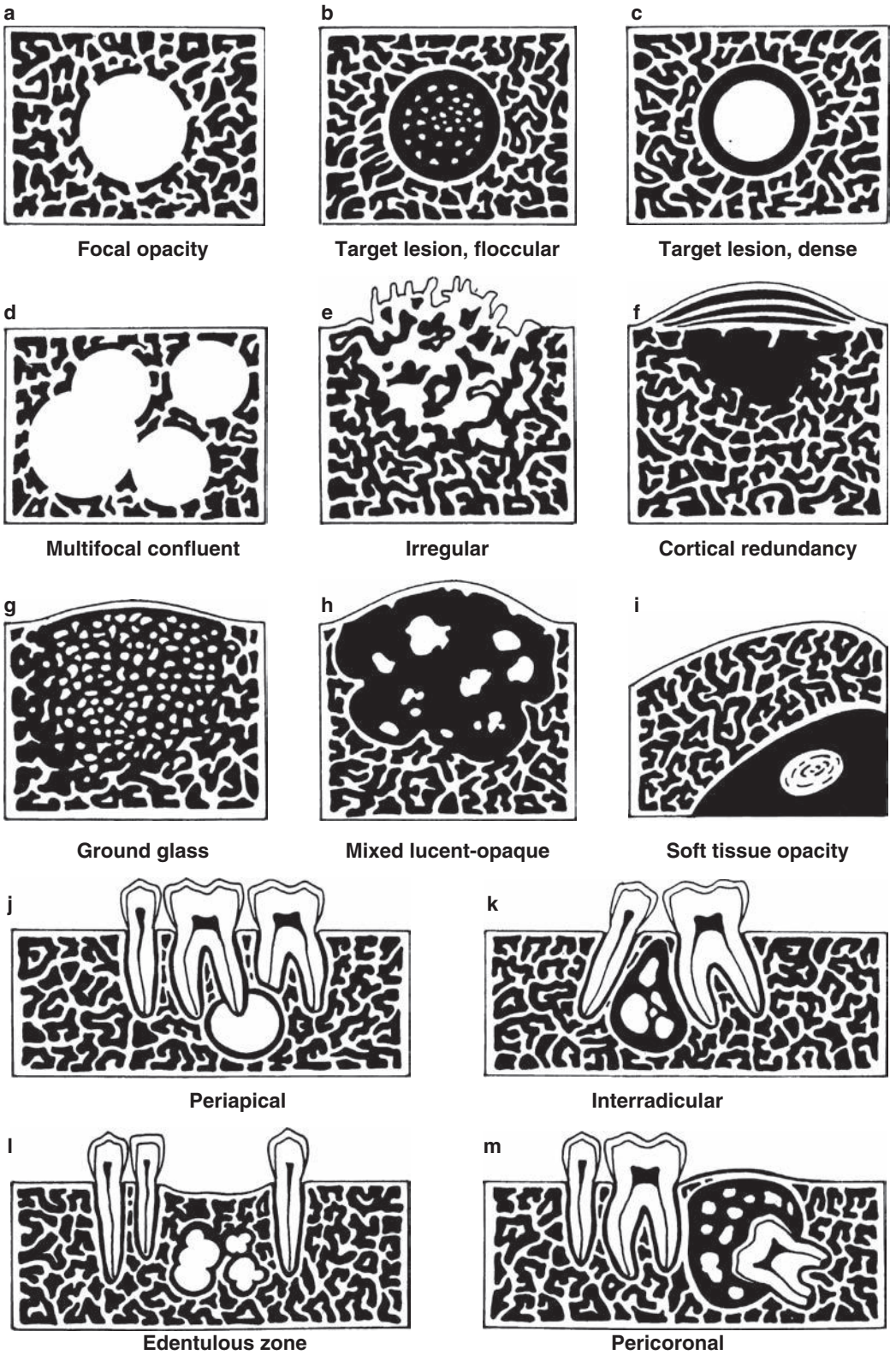

Radiopaque Lesions of the Jaws

Radiopaque Lesions of the Jaws

10

*Detailed descriptions of target lesions appear in the text under the other headings included in this chapter.
†See ground-glass radiopacities.
+++See antral opacities

Radiopacities portrayed on radiographs are a reflection of the potential for a disease to elaborate calcified products. They can also represent foreign objects lodged within bone or soft tissues superimposed on the normal osseous structures. The calcifiable matrices within the jaws include osseous tissue, cartilage, cementum, dentin, and enamel. Any lesions capable of forming these cell products may appear radiopaque. Because the matrix for calcification may be elaborated prior to any mineralization, many of the lesions with a radiopaque radiographic pattern may at an early stage in their development appear radiolucent. As mineralization of the matrices develops, the lesion becomes progressively opaque. For this reason, many calcifying tumors or diseases show a radiolucency with central opaque flecks or conglomerates. Many of the bone lesions presented in the previous chapter on radiolucencies are included here because the later stages, for reasons just mentioned, appear as radiopacities.

General radiologic considerations should be taken into account when one evaluates radiopaque lesions. Well-circumscribed corticated borders usually represent benign slow-growing diseases. Target lesions, opacities with a well-delineated radiolucent halo, are benign and are, as a rule, odontogenic. Likewise, opacities associated with the crown of an impacted tooth are invariably odontogenic.

Diffuse radiopacities with ill-defined borders are difficult to interpret because they represent a wide range of both benign and malignant conditions. Multifocal radiopacities or those involving multiple quadrants of the jaws are generally benign fibro-osseous disorders.

Opacification of the antrum is usually, yet not invariably, the result of a soft tissue proliferation or represents the presence of fluid accumulation.

In some instances, a radiographic diagnosis can be made; however, a bone biopsy is generally necessary for definitive diagnosis or confirmation of the clinical impression.

The most common periapical radiopacities are periapical cemental dysplasia, focal sclerosing osteomyelitis, and focal periapical osteopetrosis.

The most common inter-radicular radiopacities include osteopetrotic scar and odontoma. Odontoma and odontogenic adenomatoid tumor are the more frequently encountered pericoronal radiopacities.

Fibrous dysplasia is the most common disease to manifest a ground-glass pattern; tori and florid cemento-osseous dysplasia are the most common lesions yielding multifocal confluent radiopacities.

Garré's periostitis is the primary disease showing cortical layering. Potentially fatal diseases with an opaque radiographic appearance include the malignant bone neoplasms, Ewing's sarcoma, osteogenic and chondrogenic sarcomas, and metastatic carcinoma. Gardner's syndrome is accompanied by gastrointestinal tract malignancy.

Diffuse antral opacification is usually a radiographic sign of inflammatory allergic disease. Importantly, antral carcinoma causes the antrum to appear clouded; this is potentially fatal.

Periapical Radiopacities

PERIAPICAL CEMENTAL DYSPLASIA

Figure 10-1

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Periapical cemental dysplasia or cementoma is most commonly encountered

in blacks. Solitary lesions are limited to anterior teeth. Multiple lesions are also located anteriorly, usually in the mandible but sometimes extending to the apices of first molars. Pain and expansion are lacking, and the teeth are vital. The etiology is unknown. Radiographically, single or multiple opacities are encountered apical to the incisors, cuspids, or premolars. They may appear with a target pattern or merely as well-delineated opacities. The apical lamina dura is often intact. Occasionally, the lesion is larger than the usual 0.5 to 1 cm, yet expansion is not detectable. The lesion begins as a radiolucency; with ensuing time, calcification progresses so that a solid opaque mass becomes the dominant radiographic feature.

MICROSCOPIC FEATURES

Mature lesions are composed of compact lamellar bone, quilted cementum, lamellar cementum, or a combination of these,

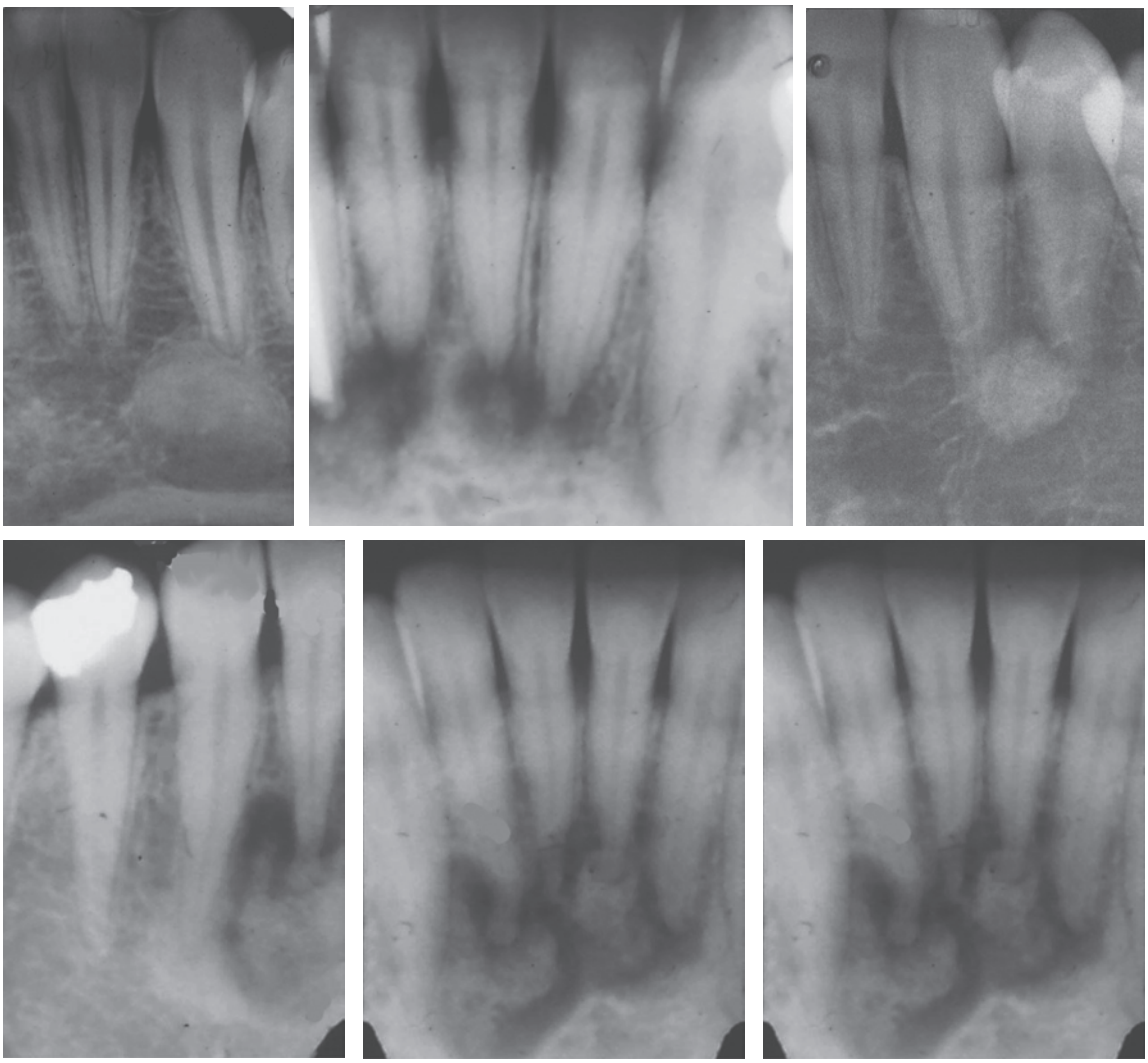

FIGURE 10-1
Periapical radiopacities underlying vital teeth representing periapical cemental dysplasia.

with little fibrous stroma. Those detected midway in development manifest a fibro-osseous pattern with a hypercellular fibrous element containing multiple ovoid or linear trabeculae of bone and cementum.

DIFFERENTIAL DIAGNOSIS

Periapical cemental dysplasia presents a radiopaque pattern similar to that encountered with focal condensing osteitis, focal periapical osteopetrosis, and benign cementoblastoma. All these conditions tend to involve posterior teeth. Focal osteitis is associated with a deep carious lesion or restoration, and cementoblastomas are expansile. In the absence of expansion, a well-circumscribed opacity apical to anterior mandibular teeth can be considered to represent PACD, and no biopsy is necessary.

TREATMENT

No treatment is necessary. When biopsy is deferred, the patient should be subjected to periodic radiographic follow-up to ensure that the lesion is not a proliferative one that coincidentally involves the periapical region. Biopsy is indicated if growth is observed.

Additional Reading

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FOCAL CEMENTO-OSSEOUS DYSPLASIA

Figure 10-2

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Focal cemento-osseous dysplasia (FCOD) is a benign dysplastic, nonpremalignant lesion of bone that represents the posterior jaw counterpart to periapical cemental dysplasia. Unlike periapical cemental dysplasia, FCOD is typically a single solitary lesion identified apical to or adjacent to the roots of the mandibular premolars, and first and second molars. This lesion is asymptomatic and nonexpansile being an endosseous pathologic process of unknown etiology. Some studies show a predilection for African descent subjects; however, the lesion can occur in any race. The classic appearance radiologically is that of a target lesion (radiolucent with opaque central foci).

MICROSCOPIC FEATURES

Multiple small curetted fragments are seen and demonstrate a fibro-osseous element and usually an accompanying osteosclerotic focus. The fibro-osseous component is typically hypercellular and the trabecular elements may be linear or ovoid and some confluent, yielding a "ginger-root" morphology.

DIFFERENTIAL DIAGNOSIS

The primary lesion to consider in the differential is ossifying fibroma, a neoplastic process that expands bone and, unlike FCOD, continues to enlarge.

TREATMENT

No treatment is necessary. Progressive clinical and imaging follow-up is recommended and if expansion evolves, excisional biopsy

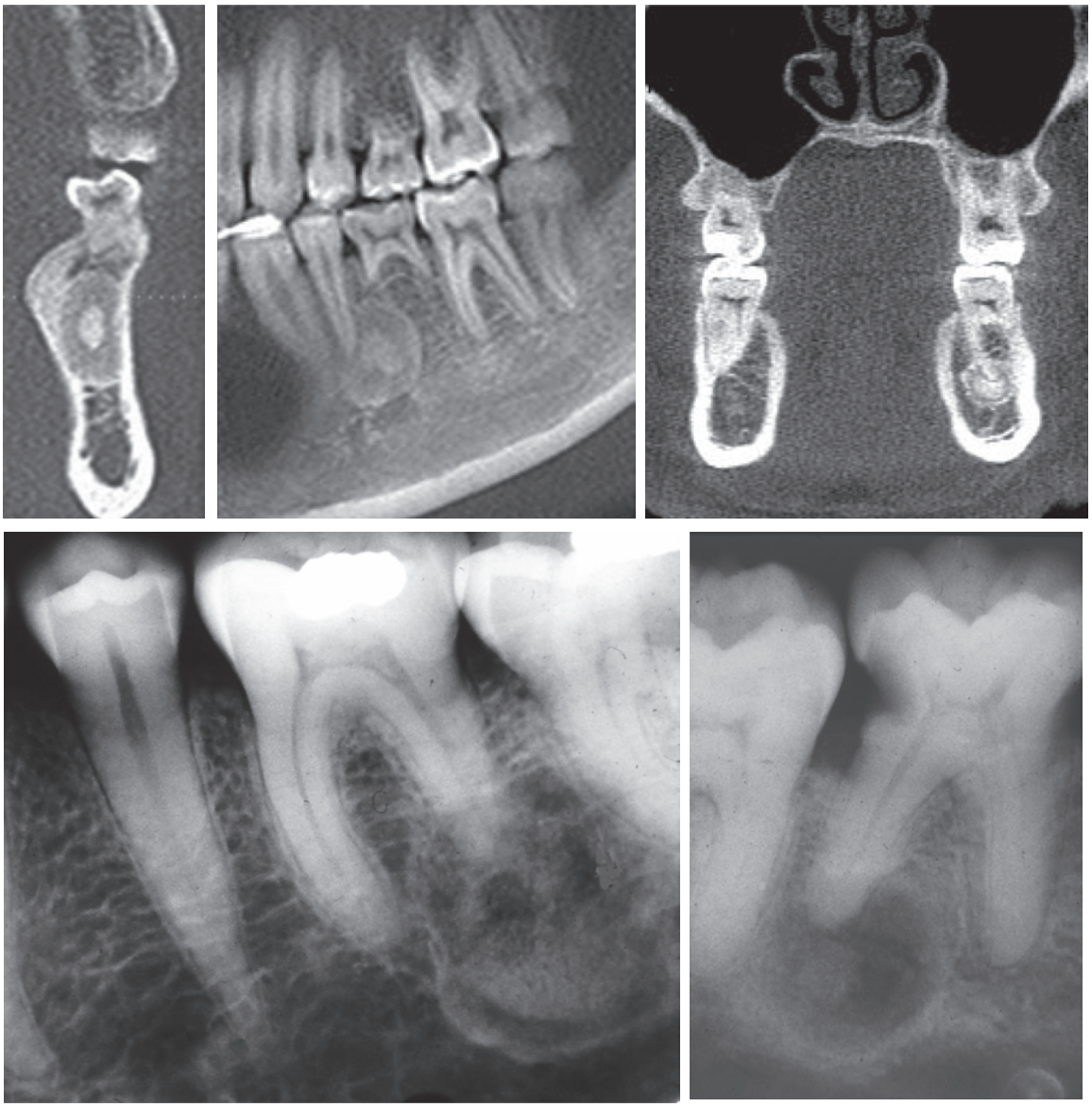

FIGURE 10-2
Focal cemento-osseous dysplasia. Juxtaradicular target lesions.

with a provisional diagnosis of ossifying fibroma should be considered.

Additional Reading

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FOCAL SCLEROSING OSTEOMYELITIS

Figure 10-3

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Low-grade pulpal inflammation, usually located in the first mandibular molar, induces a reactive osteosclerotic response at the apex. The tooth tests vital because pulp necrosis is not present; rather, the pulp is vital yet inflamed. There is generally no pain; however, the patient sometimes complains of a dull ache. The most obvious clinical feature is the presence of gross caries or a large restoration with a deep pulpal floor. Radiographically, a well-demarcated radiopacity is located below the root apices, and occasionally extends up the root for a limited distance. The opacity does not merge with root cementum, so that a periodontal ligament space is usually discernible. The opacity may or may not be enveloped by a radiolucent halo. Cortices do not expand.

MICROSCOPIC FEATURES

Depending on the degree of calcification, the tissue may be composed of compact bone or cementum with scant stroma. In less calcified specimens, a fibro-osseous pattern with a hypercellular stroma prevails. Oval, linear, or curved trabeculae are dispersed throughout this stroma. The pulp may appear histologically unremarkable, or a vital pulp exhibiting a mild mononuclear inflammatory infiltrate may be encountered. Occasionally, pulpal necrosis is observed in teeth with periapical sclerotic foci.

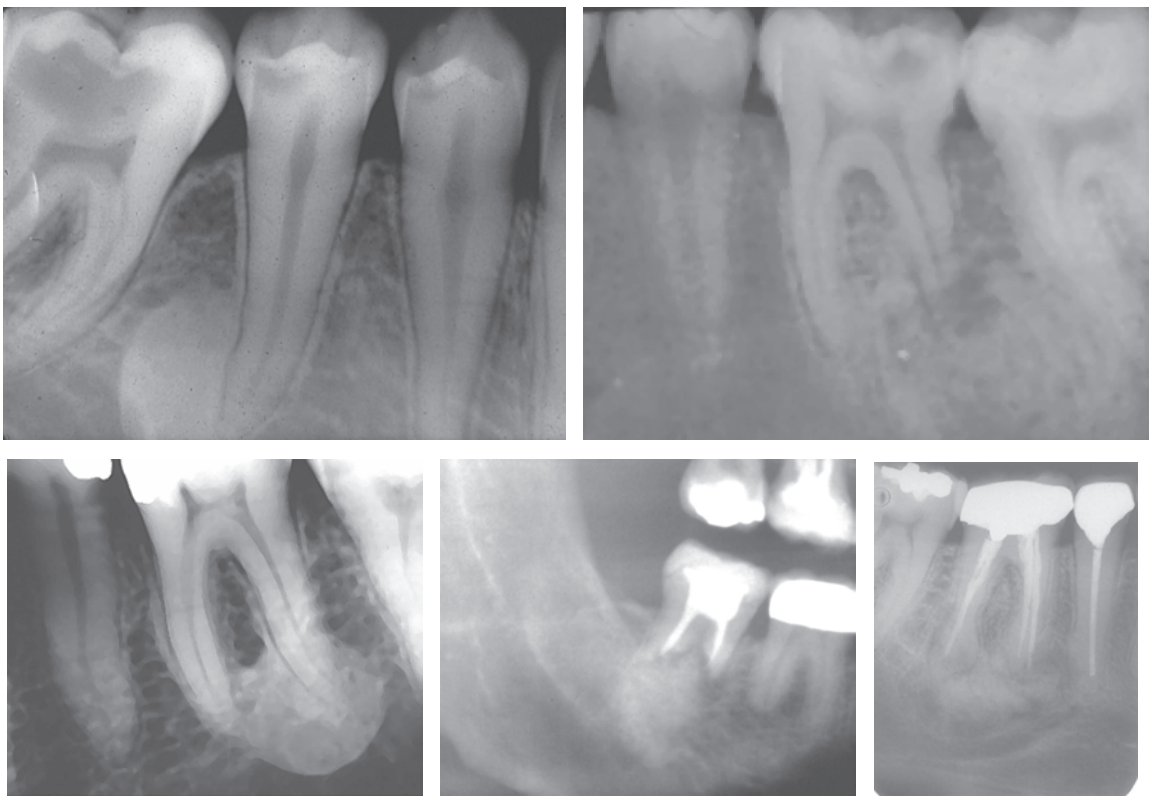

FIGURE 10-3
Focal sclerosing osteomyelitis. Apical radiodensities, pulpal inflammation.

DIFFERENTIAL DIAGNOSIS

The appearance of a well-circumscribed or target radiopacity at the apex of a first molar may be confused with periapical cemental dysplasia, focal periapical osteopetrosis, or benign cementoblastoma. Focal osteitis is the result of pulp disease with caries, whereas cementoma and focal osteopetrosis are not. Cementoblastoma shows fusion with the tooth root and expands bone, whereas neither of these features is encountered in focal sclerosing osteomyelitis.

TREATMENT

Pulp extirpation with endodontic therapy is recommended.

Additional Reading

Boyne PJ. Incidence of osteosclerotic areas in the mandible and maxilla. *J Oral Maxillofac Surg*. 1960;18:486.

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FOCAL PERIAPICAL OSTEOSCLEROSIS

Figure 10-4

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Well-localized radiopacities lying below the apices of vital, noncarious molar teeth represent focal osteopetrosis. The etiology is obscure because no pulp inflammation is present; the teeth are asymptomatic and test vital with a vitalometer. Many oral radiologists prefer to include lesions of this nature with focal sclerosing osteomyelitis; because no clinical or radiologic evidence of pulpal insult can be detected, they have been arbitrarily segregated as a separate entity. The lesion is usually detected with routine periapical or panographic views. The opacity generally lacks a radiolucent halo, yet is well demarcated with respect to the surrounding bone. Any of the three mandibular molars may overlie the opacity.

MICROSCOPIC FEATURES

Bone biopsy shows dense viable lamellar bone with fibrous marrow canals. Inflammatory cells are lacking.

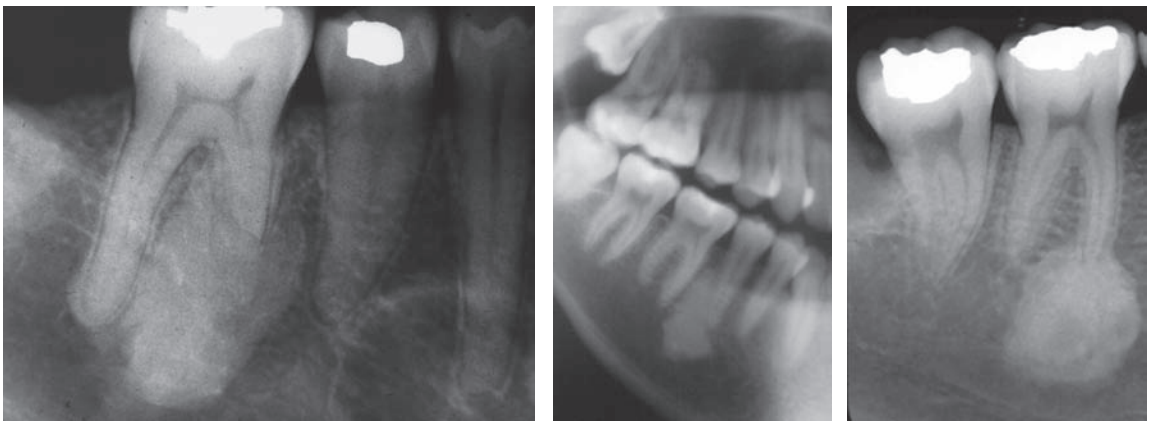

FIGURE 10-4
Focal periapical osteosclerosis. Idiopathic focal opacities without pulpal insult.

DIFFERENTIAL DIAGNOSIS

Periapical osteopetrosis can be distinguished from cementoma by virtue of its posterior location and lack of racial, sex, or age predilection. Cementoblastoma can be eliminated because no continuity with the root can be demonstrated radiographically or by means of percussion. Expansion is also lacking. Focal condensing osteitis must rank high in the differential diagnosis; however, neither deep caries, large restorations, nor other sources of pulp inflammation can be demonstrated.

TREATMENT

The diagnosis is clinicoradiologic, and no treatment is required.

Additional Reading

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Damm DD. Oral diagnosis. Mandibular radiopacities. Idiopathic osteosclerosis. *Gen Dent*. 2007;55:591-595.

Eversole LR, Stone CE, Strub D. Focal sclerosing osteomyelitis and focal periapical osteopetrosis: radiographic patterns. *Oral Surg Oral Med Oral Pathol*. 1984;58:456.

BENIGN CEMENTOBLASTOMA

Figure 10-5

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

A true neoplasm of cementoblasts, the benign cementoblastoma, arises most often on the first mandibular molars. Other molar teeth and premolars are involved less frequently. Clinically, there is no pain; the cortex is slightly expanded both buccally and lingually. The tooth is vital and usually noncarious. The involved tooth is ankylosed to the tumor mass; on percussion, an audible difference between affected and unaffected teeth can be discerned. Radiographically, the apical mass may be lucent with either central opacities or a solid opacity. A thin, radiolucent halo can be seen around densely calcified lesions. The tumor is expansile when visualized with occlusal radiographs, and on periapical views, the mass extends occlusally to encompass and become confluent with the lower third of the molar roots.

MICROSCOPIC FEATURES

Radially oriented trabeculae emanate from the attached root cementum. In most specimens, the trabeculae polarize like bone rather than cementum. Osteoblasts rim the trabeculae, often to the point of stratification. The marrow is fibrous.

DIFFERENTIAL DIAGNOSIS

Benign cementoblastoma must be differentiated from periapical cemental dysplasia, focal sclerosing osteomyelitis, and periapical osteopetrosis. Radiographic demonstration of confluency with tooth roots, the presence of expansion, a dull sound on percussion, and lack of pulp disease allow for a clinicoradiologic diagnosis.

TREATMENT

Because cementoblastomas are somewhat aggressive, they require excision. Removal cannot be achieved without sacrificing the ankylosed tooth.

Additional Reading

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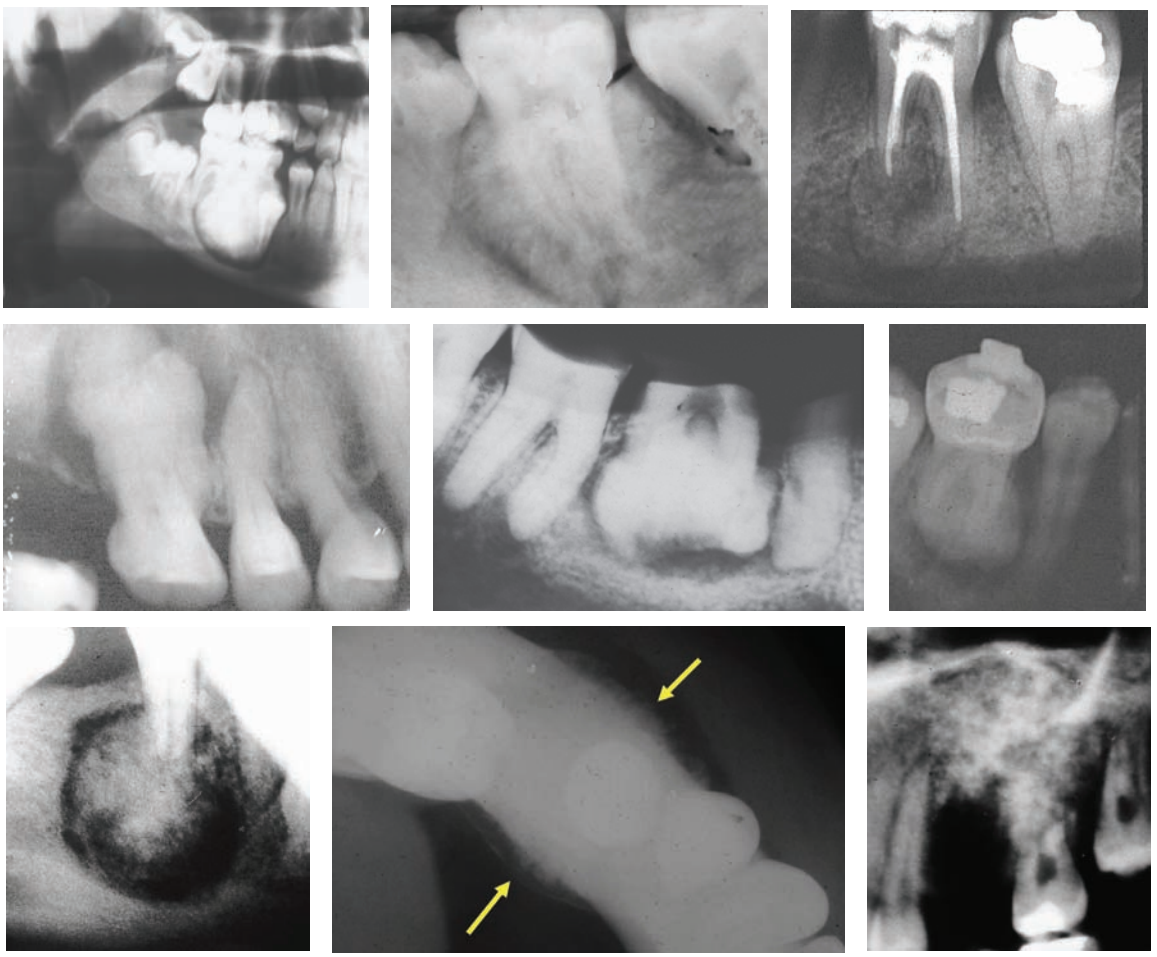

FIGURE 10-5
Benign cementoblastoma. Expansile lesions encompassing roots.

Inter-Radicular Radiopacities

RESIDUAL FOCAL OSTEITIS AND CEMENTOMA

Figure 10-6

Age: Adults
Sex: Osteitis—no predilection; cementoma—female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

When teeth overlying periapical cemental dysplasia (cementoma) or focal sclerosing osteomyelitis are extracted, the radiopaque mass often remains without undergoing resolution. As the alveolar bone resorbs, the lesion appears to lie in an inter-radicular location in the edentulous zone. Radiographically, anterior focal opacities retain their features of periapical cemental dysplasia, whereas posterior opacities represent focal osteitis. In both instances, pain and expansion are lacking, and the lesion is well delineated with or without a circumferential radiolucent rim. As the alveolar bone atrophies, both lesions may sequestrate.

MICROSCOPIC FEATURES

With both lesions, dense lamellar bone or cementum is seen, with scant intervening fibrous marrow. When sequestration

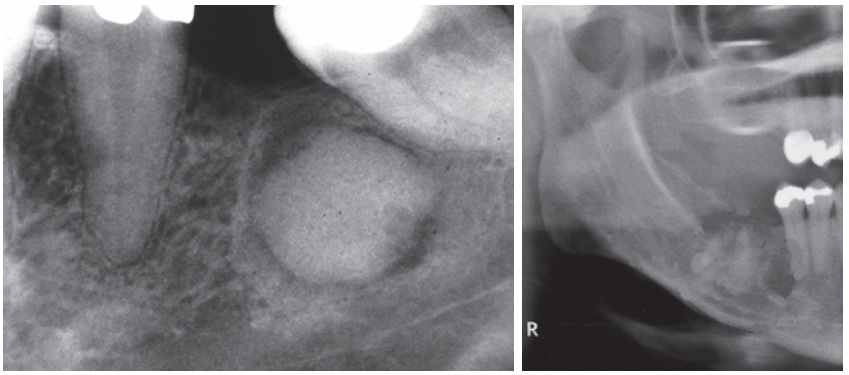

FIGURE 10-6
Opacities in edentulous areas following tooth extractions for teeth with periapical cemental dysplasia or focal cemento-osseous dysplasia.

ensues, the calcified tissue is accompanied by inflamed granulation tissue.

DIFFERENTIAL DIAGNOSIS

Residual osteitis or cementoma is more regular, round, or oval than postextraction osteopetrotic scar. When a radiolucent halo is present, the lesion cannot be differentiated radiographically from the calcifying odontogenic tumors included in this section. Biopsy is required to ascertain the true nature of the radiographically demonstrable process.

TREATMENT

Once the diagnosis has been established by trephinement or excisional bone biopsy, no further treatment is required.

Additional Reading

Boyne PJ. Incidence of osteosclerotic areas in the mandible and maxilla. *J Oral Maxillofac Surg*. 1969;18:486.

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IDIOPATHIC OSTEOSCLEROSIS

Figure 10-7

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

After tooth extraction or, occasionally, loss of deciduous teeth, the socket heals with excessive ossification. The result is a radiographically demonstrable opacity that lies within the edentulous space between contiguous teeth or is found in an interradicular location between permanent teeth when deciduous tooth loss elicited the reaction. The premolar and first molar regions are favored. Pain and expansion are lacking. Radiographically, the opaque lesion is elongated vertically or may assume an irregular yet well-delineated configuration.

MICROSCOPIC FEATURES

Dense viable lamellar bone with scant fibrous marrow spaces is seen.

DIFFERENTIAL DIAGNOSIS

In the absence of expansion or other symptoms, most lesions included in this section on inter-radicular radiopacities can be eliminated when the lesion assumes an elongated or irregular outline devoid of a radiolucent halo. If pain is present or if a fistula is observed, sequestration with osteomyelitis should be considered.

TREATMENT

In the absence of pain or expansion with an elongated or irregular inter-radicular opacity, a clinicoradiologic diagnosis can be rendered. No treatment is required other than periodic radiographic follow-up.

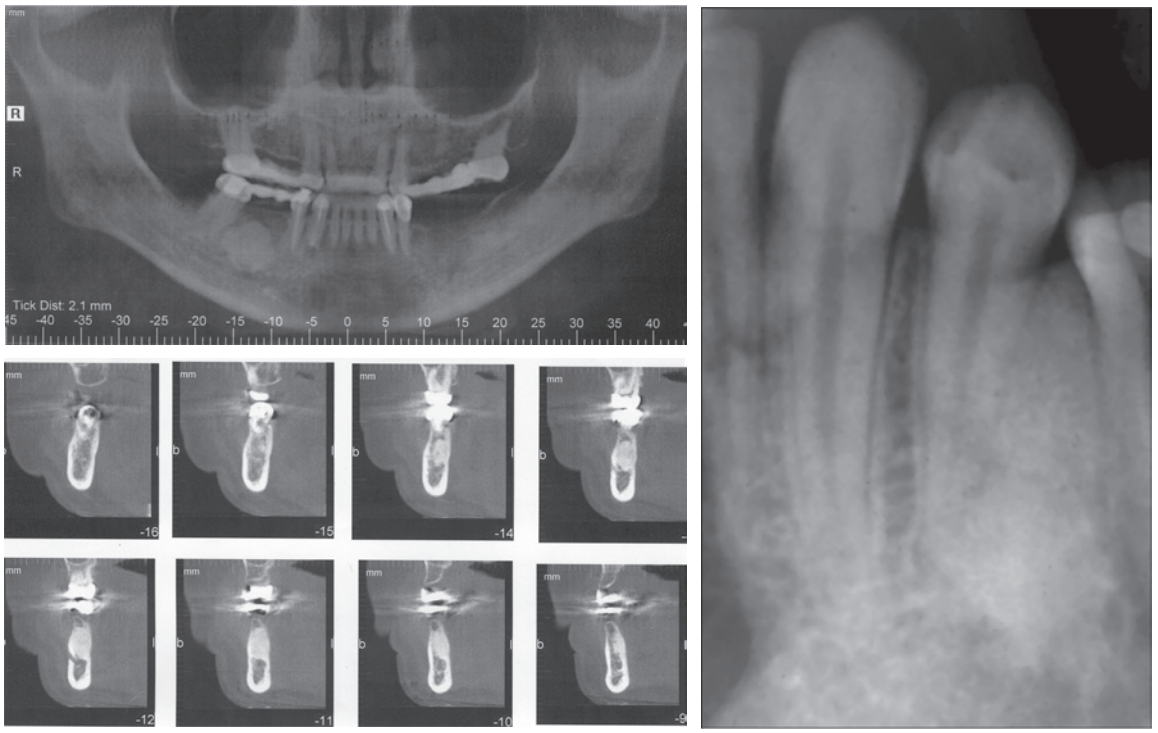

FIGURE 10-7
Idiopathic osteosclerosis. Nonexpansile opacities.

Additional Reading

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BISPHOSPHONATE-RELATED OSTEONECROSIS OF THE JAWS

Figure 10-8

Age: Elderly
Sex: No predilection

CLINICAL FEATURES

Patients with metastatic bone disease, melanoma, and generalized osteoporosis are often treated with intravenous bisphosphonates such as zoledronate and pamidronate to increase bone mass. A subpopulation of these subjects develop osteonecrosis of the jaws. Recently, patients taking oral preparations of bisphosphonates have also developed sequestrating lesions, usually in the mandible, yet also in the palate and maxillary alveolus. Prior trauma or extractions are reported in many of these patients, yet a significant proportion develop the condition without any provocation. The lesions are painful and ulcerative without significant tumefaction and at the time of examination, sequestra can be seen in the base of the ulcers. Radiographs disclose irregular, ragged opacities usually surrounded by a resorptive radiolucency. The risk for developing osteonecrosis while taking bisphosphonates can be quite reliably predicted by ordering serum C-terminal telopeptide (CTX). High levels are indicative of decreased risk for jaw necrosis (150 pg/mL).

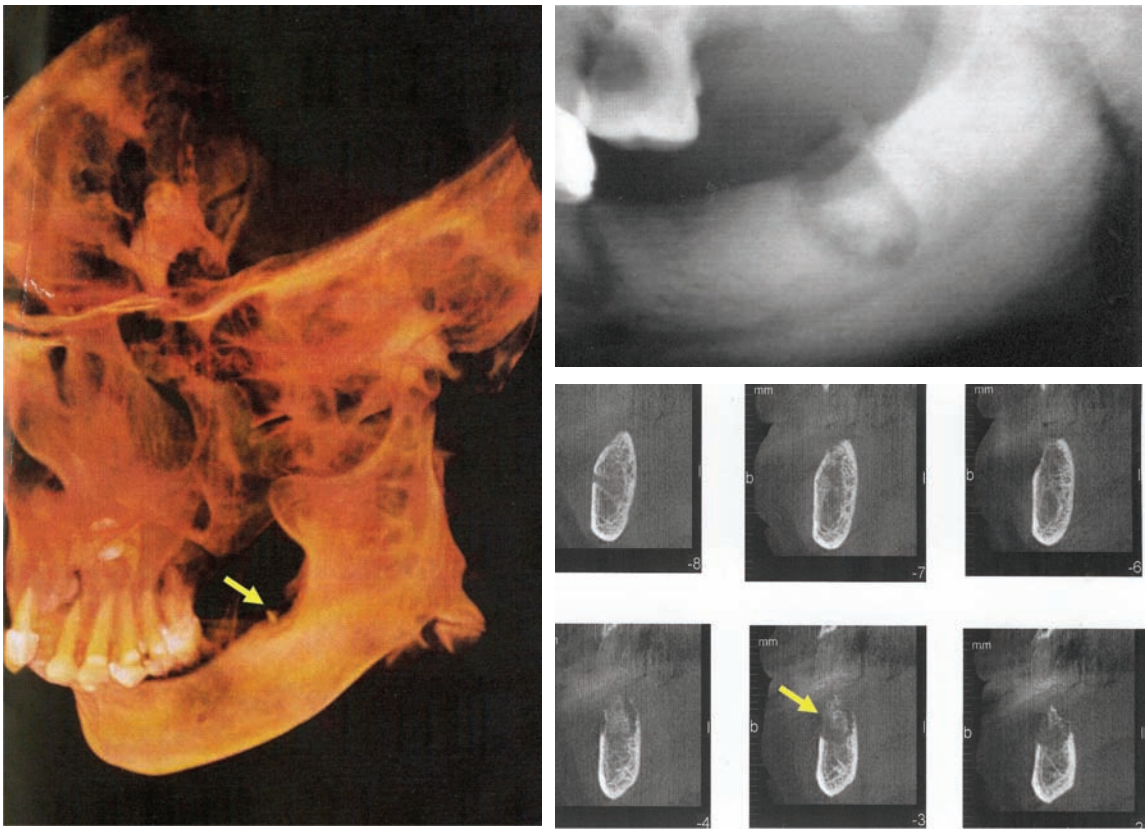

FIGURE 10-8
Sequestra and surrounding radiolucency in bisphosphonate-related osteonecrosis of the jaws.

MICROSCOPIC FEATURES

Nonvital trabeculae show lacunae devoid of osteocyte nuclei with adherent microbial colonies. Many of the colonies are periodic acid-Schiff (PAS) positive with a peripheral fringe and adherent neutrophils typical for actinomycotic organisms.

DIFFERENTIAL DIAGNOSIS

Sequestra of other etiologies must be considered in the differential diagnosis including odontogenic osteomyelitis, trauma, intubation if lesions are located on the posterior-lingual mandibular mucosa, and postradiation osteonecrosis to mention a few.

TREATMENT

Systemic antibiotics, sequestrectomy with gentle nonaggressive debridement and betadine rinses are recommended along with bisphosphonate withdrawal.

Additional Reading

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CALCIFYING AND KERATINIZING EPITHELIAL ODONTOGENIC CYST/TUMOR

Figure 10-9

Age: No predilection
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The calcifying and keratinizing epithelial odontogenic or Gorlin cyst is a tumor-like cyst found predominantly in the mandibular premolar region. Nearly one quarter of such cysts are peripheral, producing radiographically evident calcification above the underlying cortex and manifesting a gingival swelling. Intrabony lesions may cause expansion. The teeth are vital, and pain is not a feature. Radiographically, the lesion begins as a radiolucency and progressively calcifies, yielding a target lesion (opaque, with a circumferential lucent halo). Midstage cysts may be predominantly lucent with centrally located calcific opaque flecks. Root divergence is a common finding.

MICROSCOPIC FEATURES

The cyst lining is composed of stratified squamous epithelium with a rigidly polarized basal layer assuming ameloblastoid features. The spinous layer is often spongiotic, mimicking stellate reticulum. The luminal surface contains eosinophilic keratinized cells devoid of nuclei, so-called ghost cells. These cells undergo calcification. Melanin pigment may occasionally be encountered in these lesions. The fibrous wall often contains eosinophilic cell products resembling osteoid or dentinoid. When the cyst wall ruptures, an avid foreign-body reaction may ensue.

DIFFERENTIAL DIAGNOSIS

The intercellular target lesion seen with calcifying epithelial odontogenic cyst may be featured by other odontogenic tumors, including the odontogenic adenomatoid tumor, mixed odontogenic tumors, odontoma, and ossifying or cementifying fibroma. Microscopic evaluation is required to arrive at a definitive diagnosis.

TREATMENT

Enucleation with curettage is rarely complicated by recurrence.

Additional Reading

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ODONTOGENIC ADENOMATOID TUMOR

Figure 10-10

Age: Teenagers
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Although usually associated with the crown of an impacted anterior tooth, the odontogenic adenomatoid tumor may also arise between tooth roots. Painless expansion is often the chief complaint. The maxillary incisor-cuspid region is the site of predilection. Radiographically, the tumor is well delineated, expansile with root divergence, and radiolucent with calcific flecks (target appearance).

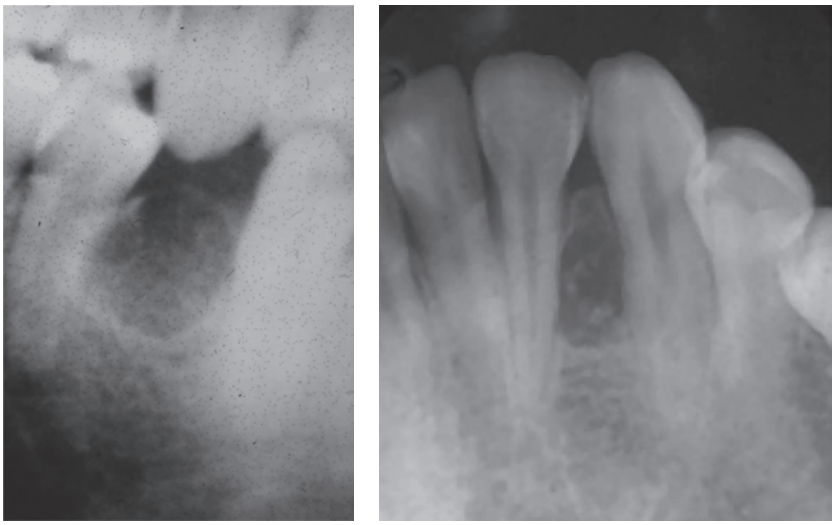

FIGURE 10-9
Calcifying and keratinizing odontogenic cyst/tumor involving inter-radicular area, typically occurring in premolar regions.

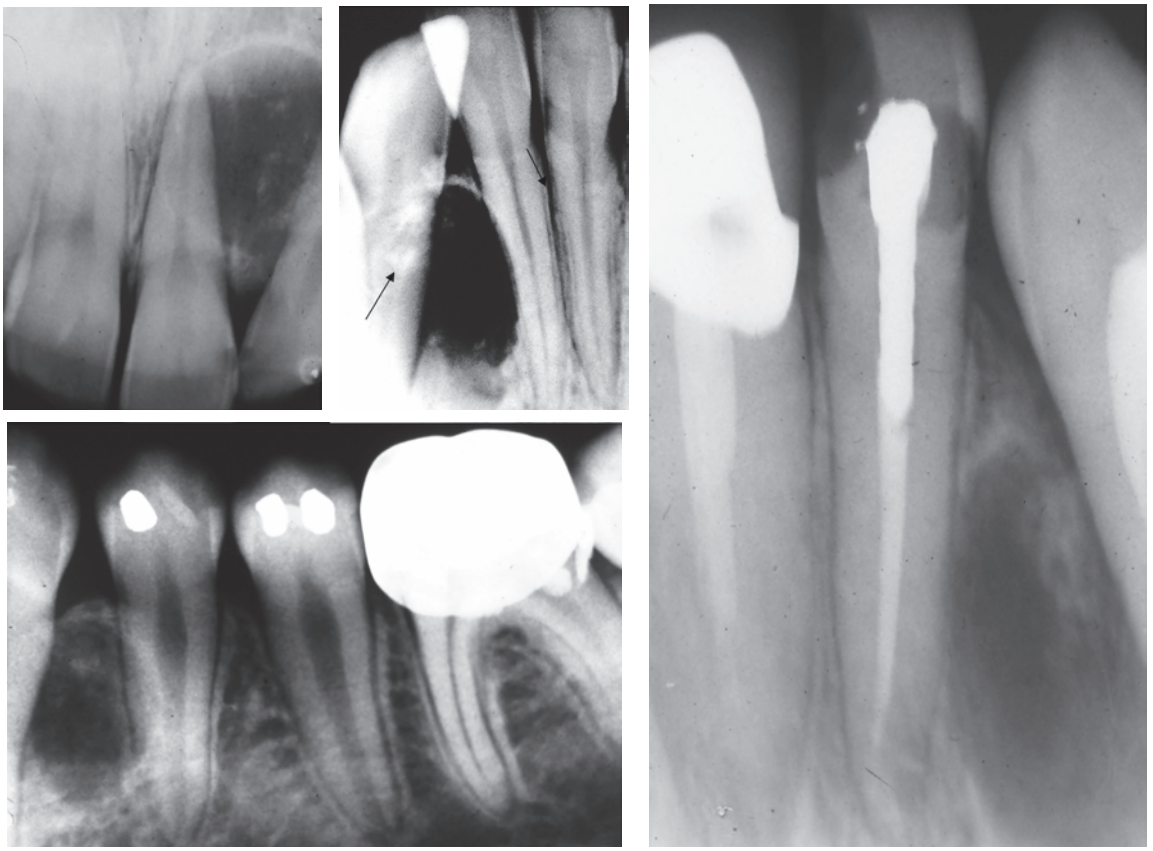

FIGURE 10-10
Radiolucency with opaque foci in odontogenic adenomatoid tumor.

MICROSCOPIC FEATURES

The odontogenic adenomatoid tumor displays a thick fibrous capsule with an inner epithelial neoplastic component composed of organoid clusters of spindle cells. Columnar cells are arranged in rosettes or ductal patterns dispersed throughout the organoid cell proliferation. Dystrophic calcifications are deposited throughout. Some of these tumors contain melanin pigment.

DIFFERENTIAL DIAGNOSIS

The expansile radiolucent lesion with central opacities or target appearance assumed by the odontogenic adenomatoid tumor is similar to or indistinguishable from that of the calcifying epithelial odontogenic cyst, other mixed odontogenic tumors, odontomas, and central ossifying or cementifying fibroma. The age, sex, and location favor a radiologic diagnosis of odontogenic adenomatoid tumor; however, microscopic confirmation is mandatory.

TREATMENT

Simple surgical enucleation is recommended. Recurrence is extremely rare.

Additional Reading

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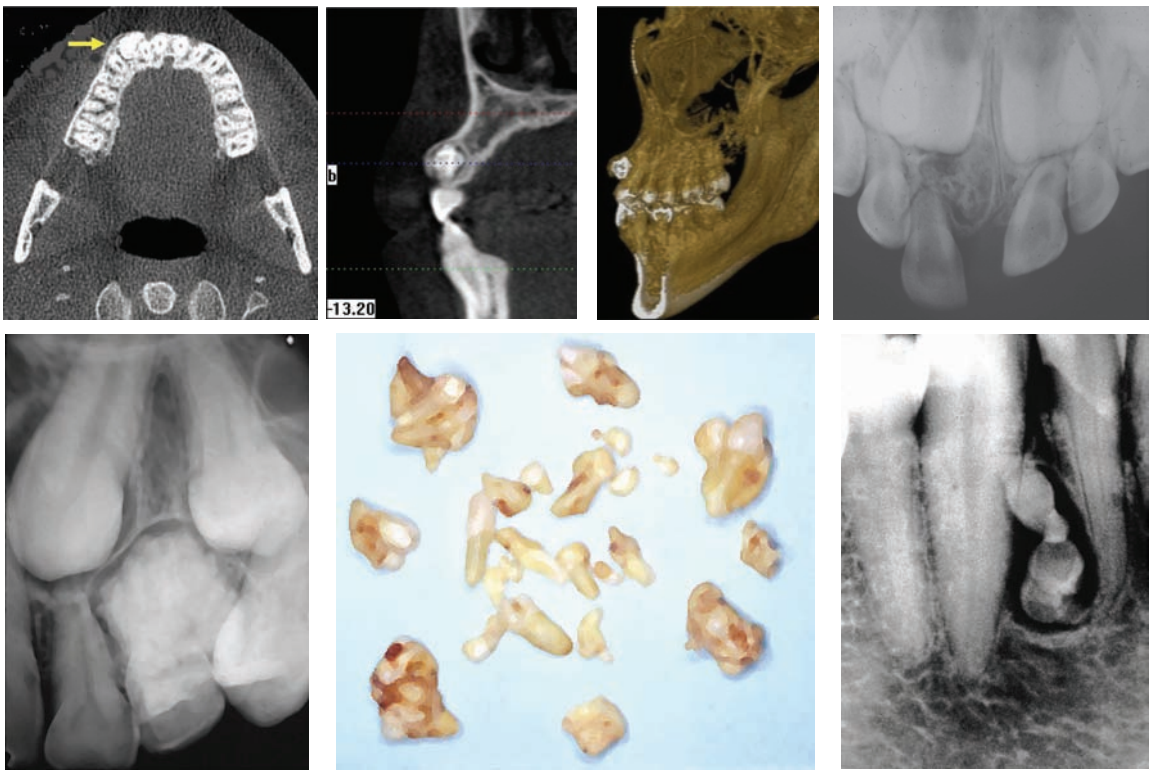

FIGURE 10-11
Odontomas.

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ODONTOMA

Figure 10-11

Age: Teenagers, young adults
Sex: Slight male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

A mixed odontogenic tumor emulating all the hard tissue products of a mature tooth germ, the odontoma is probably the most common type of odontogenic tumor or hamartoma. Although usually located pericoronal to an impacted tooth, the odontoma may also arise from odontogenic progenitor cells within the periodontal ligament and become located between tooth roots. There is no pain, and cortical expansion is either not discernible or present only to a limited degree. Radiographically, the lesion may present one of two patterns. When a target pattern with a lucent halo prevails, the central opacities assume tooth-form configurations. This variety has been called *compound composite odontoma* and is frequently interposed between anterior teeth. The *compound complex odontoma* is more common in the posterior region, is less commonly inter-radicular, and manifests a well-localized opacity with frayed margins, a "sunburst" pattern. On rare occasions, multiple odontomas may be encountered.

MICROSCOPIC FEATURES

Enamel matrix, dentin, cementum, and bone are arranged in tooth-germ-like configurations or admixed in haphazard fashion. Odontogenic epithelium, odontoblasts, and pulp mesenchyme are also present. The soft tissue components show no proliferative activity. Some odontomas exhibit a central radiolucent zone, being cystic (dilated odontome). Oftentimes, the features of a Gorlin cyst are present in addition to the odontoma.

DIFFERENTIAL DIAGNOSIS

The compound composite variety with tooth forms is easily recognized radiographically. The compound complex type may present radiologic features in common with the other odontogenic tumors included here, as well as residual osteitis and cementoma, ossifying or cementifying fibroma, and Gorlin cyst. Both types may develop a dentigerous cyst from the follicular wall.

TREATMENT

Odontomas are generally encapsulated by a fibrous lining and can be enucleated. Because dentigerous cysts and even other odontogenic neoplasms can arise from the odontogenic epithelial component of odontomas, they should be removed.

Additional Reading

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CENTRAL OSSIFYING OR CEMENTIFYING FIBROMA

Figures 10-12A & 10-12B

Age: Teenagers, young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The ossifying and cementifying fibromas are mesenchymal neoplasms of the jaws; they may differentiate along osseous, cemental, or both osseous and cemental

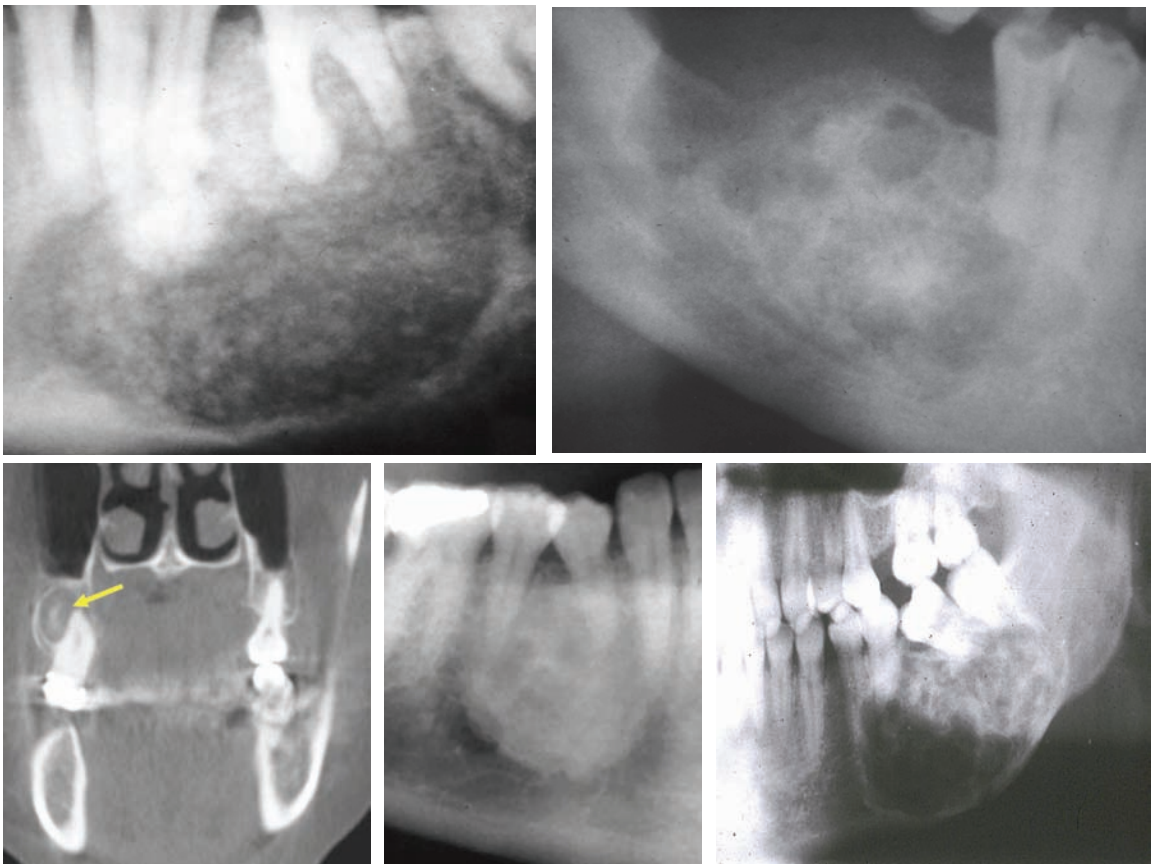

FIGURE 10-12A
Central ossifying fibromas often initiate root divergence or resorption.

lines. The neoplasm is usually located in the body or anterior region of the mandible or maxilla and classically produces expansion, usually in a buccal plane. Pain is not a feature; the overlying alveolar mucosa is generally intact, devoid of ulceration. Radiographically, expansion is usually demonstrable along the inferior border of the mandible; on occlusal films, the buccal plate is bulged. The tumor displays sharply delineated margins and is usually unilocular, although multilocular patterns are noted on occasion. The central zone contains opaque calcific flecks or a dense radiopaque conglomerate mass. Divergence of adjacent tooth roots is a common finding. Although most ossifying and cementifying fibromas are slow-growing lesions, occasionally these tumors are extremely aggressive with rapid growth, a tendency for expansion, and a potential for reaching massive proportions. This type of lesion has been referred to as *aggressive juvenile ossifying fibroma* for which there are two microscopic variants: *psammomatoid* and *trabecular* types both of which are aggressive and may grow rapidly. Psammomatoid ossifying fibroma is associated with a specific gene translocation, t(X;2)(q26;q38). There is a tendency for the psammomatoid type to arise in the facial/sinonasal bones. These tumors are expansile and radiolucent with central floccular calcifications and may reach 5 to 6 cm in diameter.

Ossifying fibromas may be multifocal and some are affiliated with familial hyper-

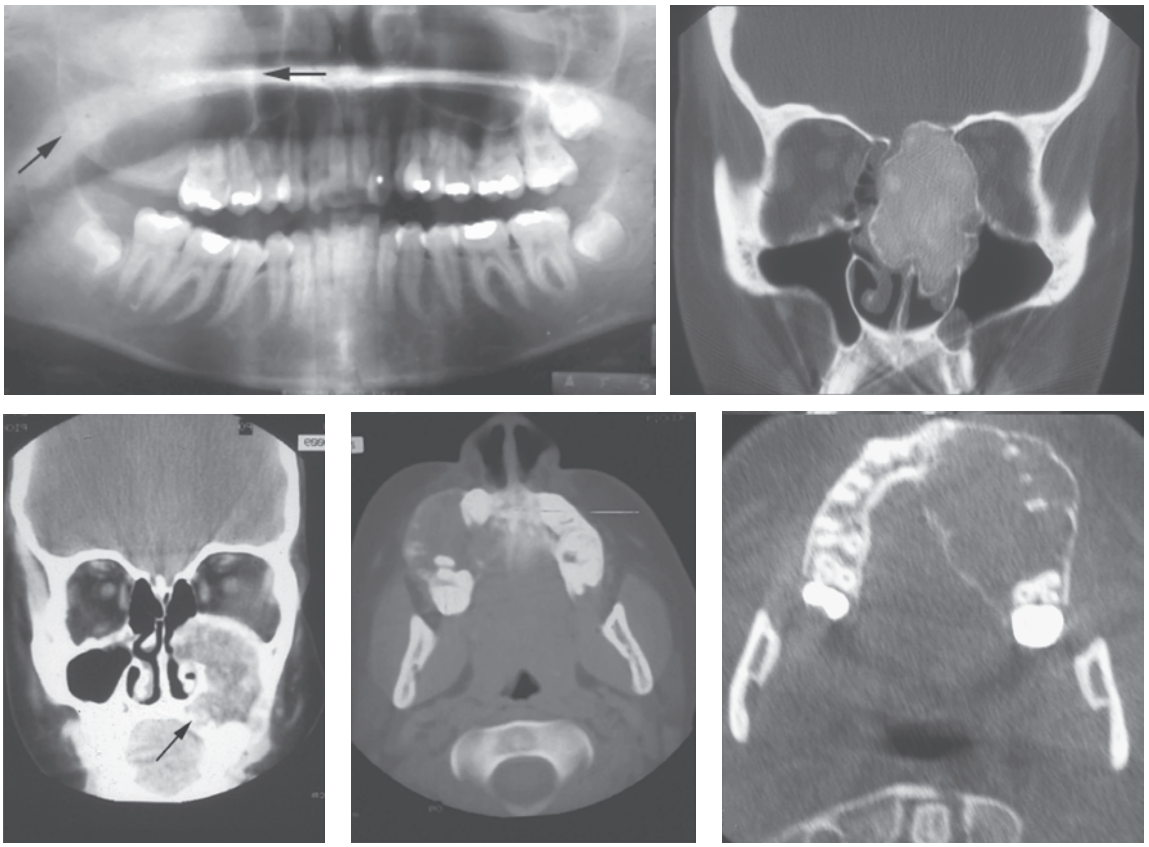

FIGURE 10-12B
Juvenile aggressive ossifying fibroma, expansile destructive lesions of psammomatoid, and trabecular types.

parathyroidism in which there is a mutation in the *HRPT2* tumor suppressor gene.

MICROSCOPIC FEATURES

A fibro-osseous microscopic pattern with a hypercellular fibroblastic stroma prevails. Ossifying fibroma contains irregular osteoid spicules or retiform trabeculae often rimmed by osteoblasts. Ovoid and curvilinear trabeculae that polarize with a microlamellar or quilted pattern are typical of cementifying fibromas. Alternatively, some lesions show both types of trabeculae. The active juvenile variant may not be readily segregated on the basis of histopathologic features. Although pronounced hypercellularity is an indication of rapid proliferation, it is not necessarily predictive of aggressive behavior. Aggressive juvenile ossifying fibromas exhibit a hypercellular fibroblastic element. The psammomatoid type shows ovoid psammoma bodies throughout, whereas the trabecular type shows sheets of fibroblastic regions with pockets of multinucleated giant cells similar to those of giant cell granuloma, and yet other regions of immature osteoid trabeculae.

DIFFERENTIAL DIAGNOSIS

The expansile target pattern typical of ossifying and cementifying fibromas may be seen with the calcifying epithelial odontogenic cyst, odontogenic adenomatoid tumor, and some of the mixed odontogenic tumors. Lesions at an early stage may not show dense opacities; rather, faint calcified flecks

float within an expanding radiolucency. In these cases, the differential diagnosis should include Pindborg tumor as well as the aforementioned entities. Biopsy discloses the characteristic histomorphologic features.

TREATMENT

Surgical enucleation is rarely followed by recurrence for relatively small lesions. Large expansile tumors with root divergence or resorption and thin cortical boundaries may require en bloc resection to prevent recurrence. The juvenile aggressive ossifying fibroma, as determined histologically and radiographically with clinical observation of rapid growth, should be resected.

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BENIGN OSTEOBLASTOMA

Figure 10-13

Age: Children and teenagers
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

A tumor that generally arises in the long bones and vertebrae, the osteoblastoma may occasionally arise in the maxillofacial complex. It is a benign neoplasm of osteoblastic origin with a rapid growth rate capable of expansion and facial deformity. Radiographically, it is relatively well circumscribed, although the tumor margins may be scalloped. Centrally, radiopaque foci are encountered. Adjacent teeth are displaced and root resorption is usually encountered. Although the disease is rare, there may be a predilection for the maxilla.

MICROSCOPIC FEATURES

Dispersed throughout an areolar fibrous marrow are irregular or retiform arrangements of thin osteoid trabeculae rimmed to the point of stratification by plump basophilic osteoblasts. Osteoclasts are also present, and the marrow is generally well vascularized.

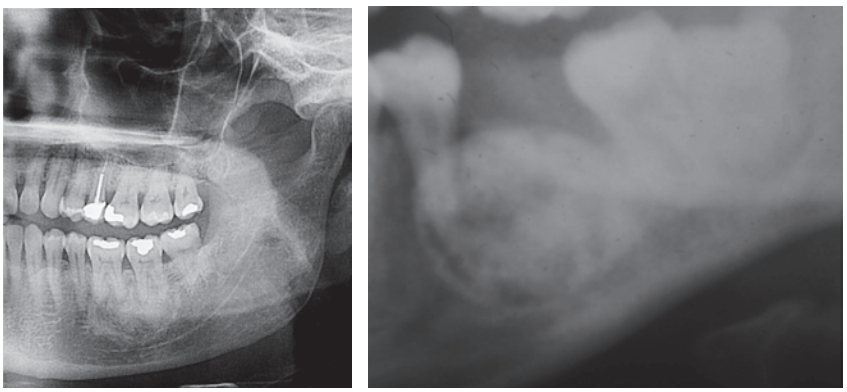

FIGURE 10-13
Benign osteoblastoma, well circumscribed mixed lucent/opaque pattern.

DIFFERENTIAL DIAGNOSIS

Expansile inter-radicular radiopacities as seen in benign osteoblastoma may be encountered in central ossifying or cementifying fibromas and certain mixed odontogenic tumors. Biopsy is required to achieve a definitive diagnosis.

TREATMENT

Benign osteoblastoma is an aggressive neoplasm; although enucleation may be attempted, recurrence is a distinct possibility. If the lesion recurs, en bloc resection is recommended to eradicate the disease.

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Pericoronal Radiopacities

ODONTOGENIC ADENOMATOID TUMOR

Figure 10-14

Age: Teenagers
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

More than three quarters of all odontogenic adenomatoid tumors arise from reduced enamel epithelium surrounding the crown of an impacted anterior tooth; some lesions have been extraosseous. The maxillary cuspid is the most commonly affected tooth. Clinically, expansion of the buccal and palatal or lingual plates is seen in the absence of pain. Radiographically, the lesion is usually a well-delineated, corticated radiolucency containing calcific flecks. The pericoronal lesion, as opposed to a simple dentigerous cyst, tends to originate low on the root rather than from the dentinoenamel junction. Occasionally, a classic target pattern is seen, whereby a circumferential halo envelops a dense, central, round radiodense mass.

MICROSCOPIC FEATURES

The tumor is composed of swirled spindle-shaped epithelial cell conglomerates with focal duct-like configurations lined by columnar cells. Dystrophic calcifications are distributed throughout. A dense fibrous wall confines the neoplastic element. Occasionally, other histologic patterns representing various other odontogenic tumors are coexistent.

DIFFERENTIAL DIAGNOSIS

A pericoronal radiolucency with an opaque center occurring in the anterior segment of the jaws in teenage females invariably represents odontogenic adenomatoid tumor. Nevertheless, the differential diagnosis must include other odontogenic tumors included in this section, because they may assume similar radiologic characteristics. Biopsy is necessary for a definitive diagnosis.

TREATMENT

Simple surgical excision is curative. Recurrence is almost nonexistent.

Additional Reading

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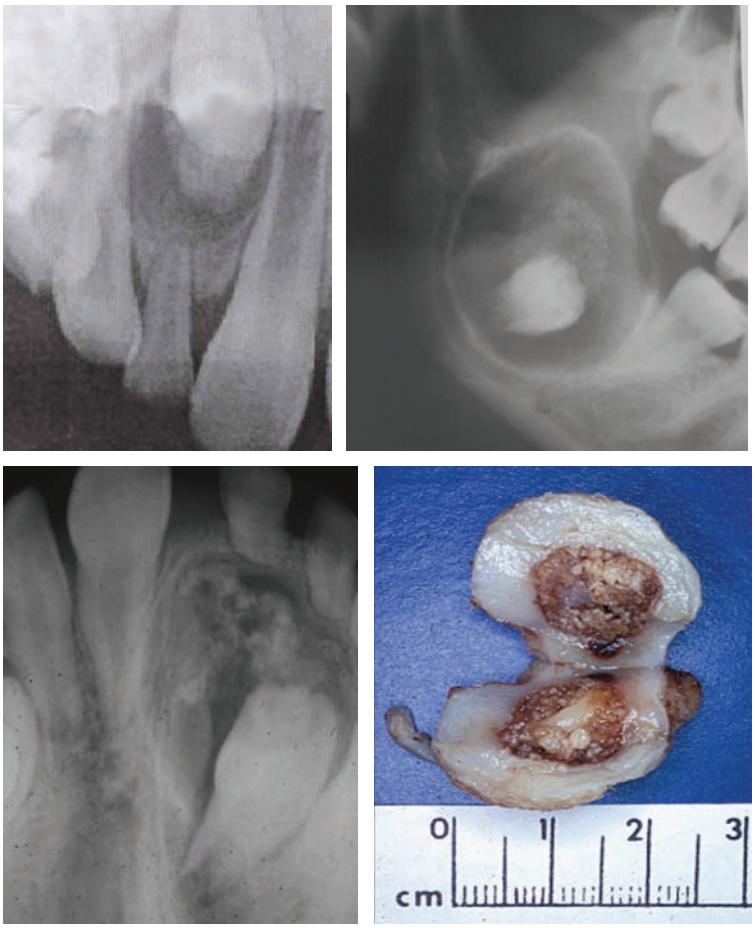

FIGURE 10-14
Odontogenic adenomatoid tumor tends to be a peridental lucency with central opaque flecks.

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CALCIFYING EPITHELIAL ODONTOGENIC TUMOR

Figure 10-15

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The calcifying epithelial odontogenic (Pindborg) tumor is an aggressive odontogenic neoplasm of epithelial derivation. Most lesions are associated with an impacted tooth, and the mandibular body or ramus is by far the most common site of origin. Pain is usually not a complaint. The chief sign is cortical expansion. Radiographically, expanded cortices can be visualized in buccal, lingual, and vertical dimensions. The lesion is usually radiolucent with poorly defined or, at the least, noncorticated borders. It may appear unilocular, multilocular, or moth-eaten. Multiple radiopaque foci can be detected within the radiolucent zone in the form of flecks, conglomerates, or diffuse opacities yielding a "driven-snow" appearance. Root divergence and resorption are common findings. The impacted tooth usually shows arrested root development and is often significantly displaced by

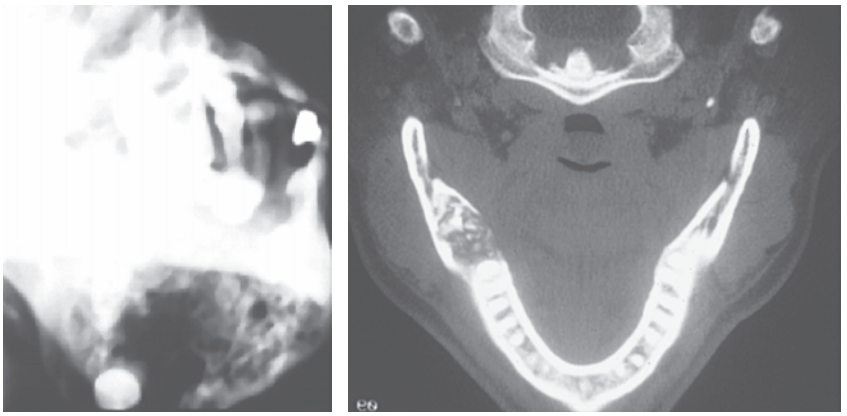

FIGURE 10-15
Calcifying epithelial odontogenic tumor (Pindborg tumor) is an aggressive expansile tumor.

the tumor. A mutation in the ameloblastin gene has been identified.

MICROSCOPIC FEATURES

Sheets, nests, and cords of eosinophilic epithelial cells prevail, bearing no resemblance to tooth germ primordia. Nuclear pleomorphism may be significant despite the benignity of the tumor. Neoplastic cells are oriented about amyloid droplets, conglomerates of odontogenic ameloblast-associated protein (ODAM). Concentrically laminated Leisegang calcifications similar to psammoma bodies are a classic finding. A variety of so-called *atypical variants* are encountered; the primary variant is a clear cell lesion that is composed of sheets and islands of cells with vacuolated cytoplasm and associated amyloid deposits with calcification.

DIFFERENTIAL DIAGNOSIS

The radiographic appearance of Pindborg tumor may simulate a variety of both benign and malignant lesions of the jaws. The more well-delineated tumors must be microscopically differentiated from the other benign odontogenic neoplasms included in this section. Lesions with expansile mixed radiolucent/radiopaque patterns lacking margination must be differentiated from osteogenic and chondrogenic sarcomas; however, these malignancies are rarely associated with an impacted tooth.

TREATMENT

Calcifying epithelial odontogenic tumors are aggressive and may reach large proportions. Their behavior is reminiscent of that of ameloblastoma. En bloc resection, hemimandibulectomy, or partial maxillectomy, depending on tumor size, are the treatment methods required to eradicate the disease.

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AMELOBLASTIC FIBRODENTINOMA

Figure 10-16

Age: Teenagers, young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

This rare mixed odontogenic tumor represents an ameloblastic fibroma that has differentiated to the extent that dentin is elaborated. Expansion is often present, but pain is not a feature. The lesion invariably arises in association with an impacted tooth; depending on the degree of dentinal calcification, it may appear radiolucent with central opaque flecks or may assume a target configuration. It may be unilocular or multilocular with well-defined margins. A variant form occurs in children and is located peripherally as a gingival swelling. Some pathologists believe that this lesion is simply an early phase in the development of an odontoma.

MICROSCOPIC FEATURES

Dispersed throughout an embryonic hypercellular hypocollagenous mesenchymal element are linear cords of cuboidal epithelium that tend to open, creating tooth germ configurations with a central stellate reticulum element. In juxtaposition to these epithelial nests are sheets of eosinophilic hyalinized material representing dentinoid. Occasionally, tubules are demonstrable. Cell nuclei may be entrapped within this product.

DIFFERENTIAL DIAGNOSIS

Pericoronal lucencies with central opacities as seen in ameloblastic fibrodentinoma are also typical of other odontogenic neoplasms included in the section. Biopsy is required to secure a definitive diagnosis.

TREATMENT

Simple surgical nucleation is the treatment of choice. Recurrence is uncommon.

Additional Reading

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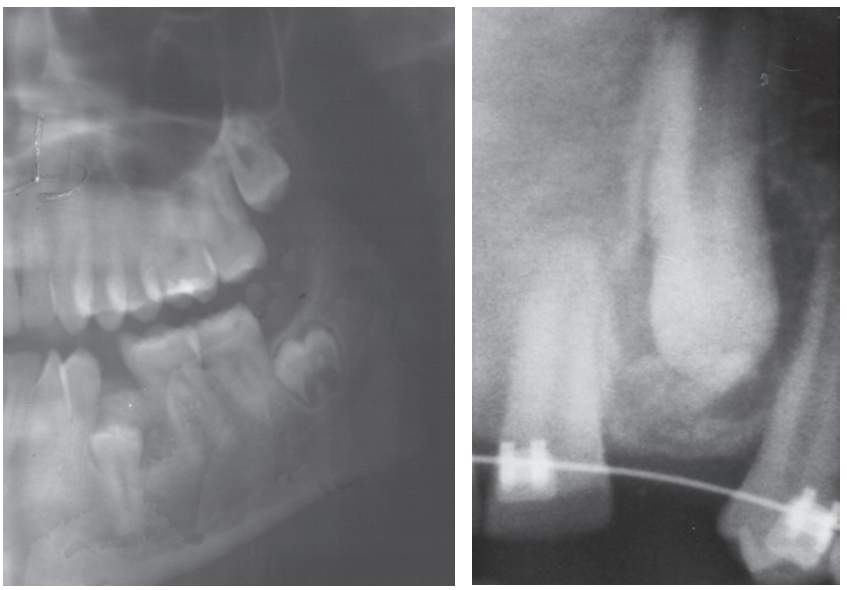

FIGURE 10-16
Ameloblastic fibrodentinoma, a nonaggressive tumor.

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AMELOBLASTIC FIBRO-ODONTOMA

Figure 10-17

Age: Teenagers
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The ameloblastic fibro-odontoma, referred to in the past simply as ameloblastic odontoma, is an aggressive mixed odontogenic neoplasm that is analogous to an ameloblastic fibroma capable of elaborating all of the hard tissues found in a mature tooth. Clinically, the mandibular body and ramus regions are the most frequent sites of origin, and expansion is the chief sign. Radiographically, most are associated with the crown of an impacted tooth. The lesion may reach large proportions yet is well demarcated. It may be unilocular or multilocular and contains multiple radiopaque foci with irregular configurations.

MICROSCOPIC FEATURES

Calcified and uncalcified matrices of dentin, enamel, and cementum prevail in haphazard arrangement. A significant portion of the tumor is composed of proliferating epithelial and mesenchymal soft tissue with features identical to those of ameloblastic fibroma. Inductive changes with dentinoid and a mantle of enamel matrix are interposed between the epithelial and mesenchymal tissues in focal regions.

DIFFERENTIAL DIAGNOSIS

Large, well-defined radiolucencies with multifocal central opacities in association with an impacted tooth, usually a molar, are typically seen with ameloblastic fibrodentinoma and odontoameloblastoma as well as with ameloblastic fibro-odontoma. Microscopic examination is therefore required.

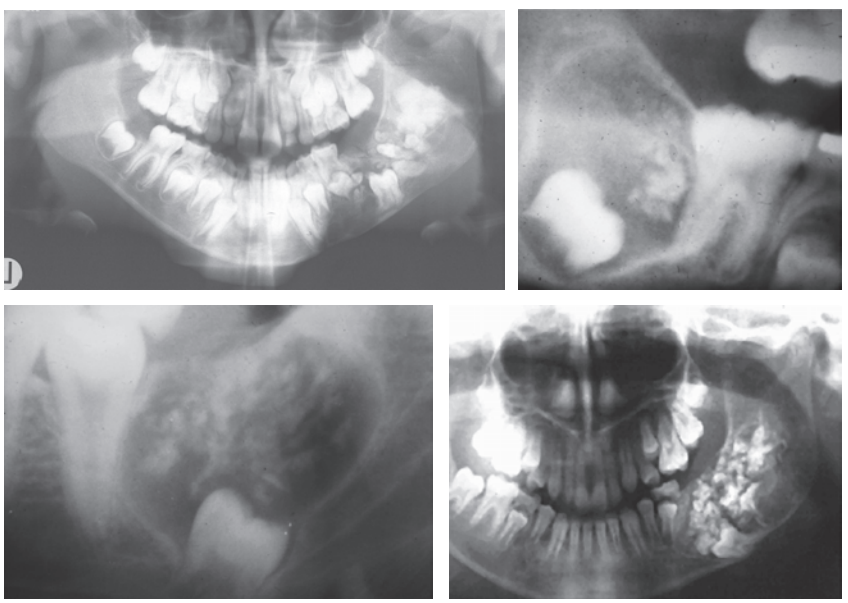

FIGURE 10-17
Ameloblastic fibro-odontoma showing expansile well-circumscribed radiolucency with multiple opaque tooth-like foci in association with an impacted molar. These tumors represent an ameloblastic fibroma proliferation in conjunction with an odontoma.

TREATMENT

Surgical enucleation is the treatment of choice. Recurrence may develop, but is uncommon.

Additional Reading

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ODONTOMA

Figure 10-18

Age: Teenagers, young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The odontoma, a mixed odontogenic tumor with the capability of elaborating all dental tissues found in a mature tooth, is self-limiting in its growth potential. It is the most common pericoronal radiopacity. Expansion, if present at all, is limited. Lesions located high in the alveolus may tend to erupt, with ulceration, fistulization, and inflammation. Radiographically, a pericoronal radiolucency with well-defined or corticated borders is seen. The center contains tooth-like calcified masses (composite type) or round, oval, or sunburst masses (complex type). When odontoma are associated with

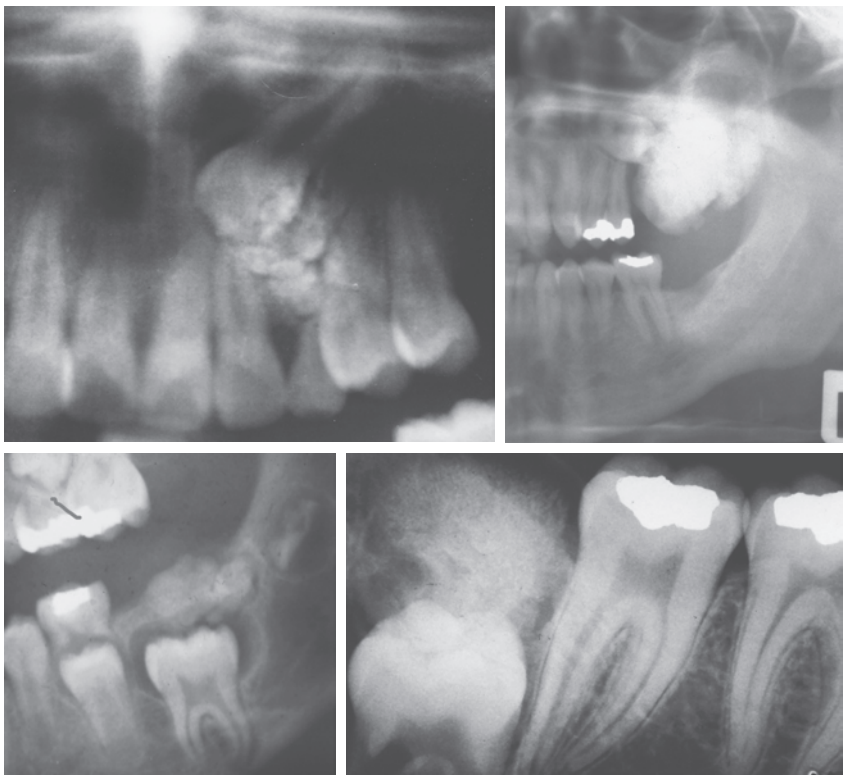

FIGURE 10-18
Odontomas frequently arise in dental follicles of impacted teeth.

impacted teeth, they are usually mandibular molars.

MICROSCOPIC FEATURES

Enamel matrix, tubular dentin, and cementum are associated with their complementary soft tissue elements, odontogenic epithelium, odontoblasts, and cementoblasts, respectively. The calcified components may or may not assume tooth-form configurations.

DIFFERENTIAL DIAGNOSIS

When tooth-like opacities are present within a unilocular radiolucency, a radiographic diagnosis can often be rendered. The complex varieties or larger pericoronal lesions must be microscopically differentiated from other odontogenic neoplasms such as Pindborg tumor, ameloblastic fibrodentinoma, ameloblastic fibro-odontoma, and odontoameloblastoma.

TREATMENT

Surgical enucleation is easily achieved because of encapsulation by follicular fibrous tissue. The lesion should be removed, because odontomas may prevent eruption, displace adjacent teeth, or develop dentigerous cysts.

Additional Reading

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ODONTOAMELOBLASTOMA

Figure 10-19

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

An extremely rare mixed odontogenic tumor, the odontoameloblastoma is an aggressive neoplasm capable of producing

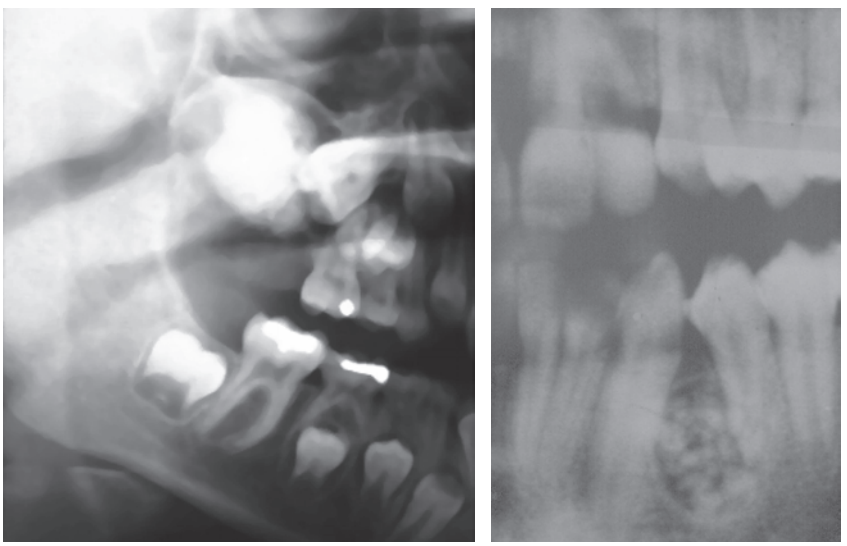

FIGURE 10-19
Odontoameloblastomas show radiologic features in common with ameloblastic fibro-odontomas and represent an odontoma with proliferating ameloblastoma.

significant expansion and facial asymmetry. The tumor is composed of all tissue components of a normal tooth and can be considered an aggressive variant of the odontoma. Radiographically, an impacted tooth with a well-circumscribed expansile radiolucency containing multifocal radiopaque foci is demonstrated. The central opacities often resemble malformed teeth. They may arise in either jaw with a tendency to locate in the body area in association with an impacted molar, which is usually displaced by the lesion. Root divergence or resorption may be discernible.

MICROSCOPIC FEATURES

Decalcified specimens show a diverse array of calcified tissue matrices: enamel, dentin, and cementum. These are often arranged in morphologic structures that resemble developing anomalous teeth. The hard tissues are admixed and associated with odontogenic epithelium, which in many regions is proliferative, displaying ameloblastoma-like histomorphologic structure. These ameloblastomatous islands are embedded in mature collagenous stroma.

DIFFERENTIAL DIAGNOSIS

Odontoma and odontogenic adenomatoid tumor are rarely as aggressive as odontoameloblastoma; nevertheless, they should be included in the differential radiographic diagnosis. Ameloblastic fibro-odontoma, ameloblastic fibrodentinoma, and calcifying epithelial odontogenic tumor may all appear radiographically indistinguishable from odontoameloblastoma.

TREATMENT

Because few cases of this tumor have been reported, a reliable prognostic index cannot be based on previous experiences. Reported cases often recur. Thorough enucleation is recommended and, if a recurrence develops, resection may be required.

Additional Reading

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Antral Opacities

MAXILLARY SINUSITIS

Figure 10-20

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Sinusitis is a common disease and is usually allergic. Many cases of acute sinusitis and some cases of chronic sinusitis are associated with or caused by infectious organisms; chief among these are *Hemophilus influenzae*, *Streptococcus pneumoniae*, and rhinovirus. Allergic sinusitis is generally secondary to rhinitis, in which the lateral nasal mucous membranes become edematous, leading to blockage of the ostium. The affected sinus fills with mucous secretion and if also infected, a purulent aspirate can be obtained. Repeated bouts of inflammation with periodic blockage and drainage can lead to a thickening of the sinus membrane. Fluid-filled sinuses appear as a diffuse opacification; transillumination of the sinuses reveals a dull or opaque appearance when a fiberoptic light source is placed against the palate in a darkened room. When the upper sinus is pneumatized while fluid occupies the lower region, a discrete fluid level can be identified on

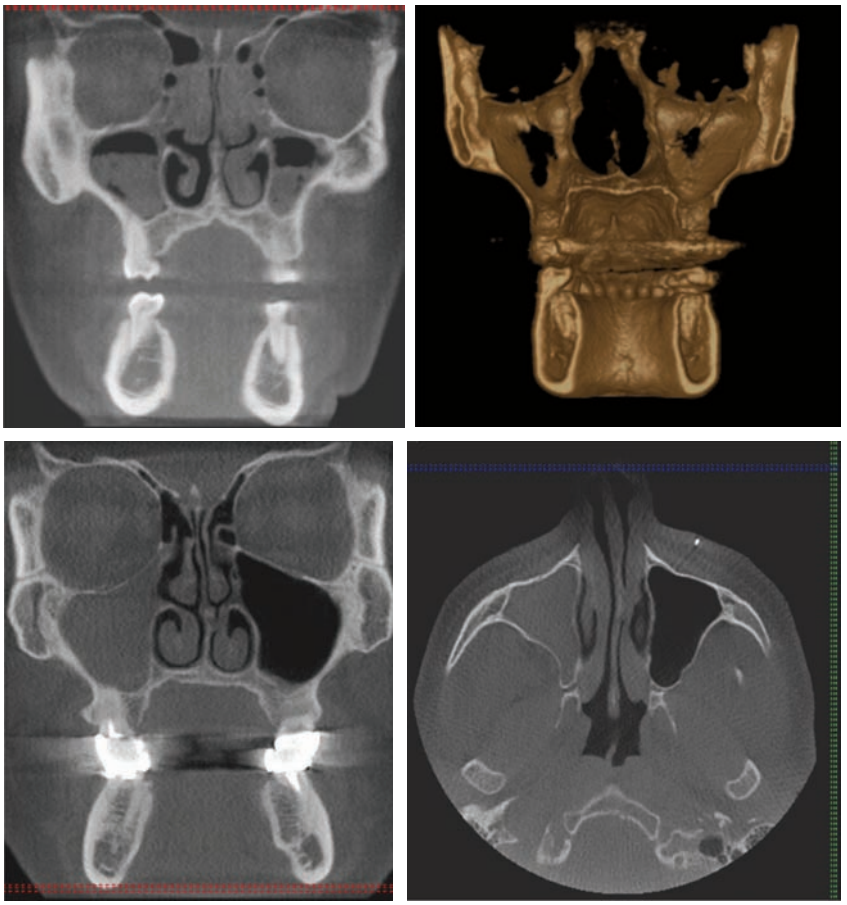

FIGURE 10-20
Maxillary sinusitis with air/fluid levels and complete clouding fail to cause bone erosion or expansion.

Water's projections. Chronic recurrent sinusitis often discloses patency with a thickened membrane. In general, a membrane thickening greater than 8 mm is associated with symptoms. Many asymptomatic patients exhibit mild to moderate thickening radiographically. The chief symptom of active chronic sinusitis is dull pain that is referred to all posterior maxillary teeth, which are sensitive to percussion. When the head is lowered, the pain intensifies. Acute infectious sinusitis is associated with moderate to severe maxillary pain and pressure, both of which occur spontaneously and on palpation.

MICROSCOPIC FEATURES

An aspirate in cases of acute infectious sinusitis shows neutrophils, whereas subacute or chronic infectious lesions contain a preponderance of mononuclear cells. The mucous membranes in chronic sinusitis are edematous with a leukocytic infiltrate containing many eosinophils. Polypoid excrescences are common and show similar histologic changes to hyperplastic mucosal thickening.

DIFFERENTIAL DIAGNOSIS

Osseous destruction is not usually a feature of chronic sinusitis. Nevertheless, neoplastic processes may cause diffuse homogeneous opacification; however, pain is not usually featured. Failure of the opacification to resolve after conventional therapy for sinusitis warrants exploration, sinoscopy, and biopsy. Dental sources of infection should be ruled out.

TREATMENT

A therapeutic trial with nasal decongestants and antihistamines should be initiated. Should the symptoms and radiographic opacification fail to resolve within 4 or 5 days, an aspirate should be obtained to evaluate the presence of leukocytes. Furthermore, a culture and sensitivity test should be performed to explore the possibility of an infectious etiology; appropriate antibiotic therapy, usually ampicillin or amoxicillin, should follow.

Additional Reading

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ANTRAL POLYP

Figure 10-21

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The so-called mucous retention cyst of the antrum represents an inflammatory polyp without an epithelial lining and is, therefore, not a true cyst. Furthermore, this lesion should not be confused with a true mucocele of the sinuses, which, unlike the mucosal polyp, exhibits aggressive behavior. The antral mucous retention cyst should be referred to as an inflammatory mucosal polyp. Usually no symptoms are present; however, there may be a history of nasal discharge, congestion, or other symptoms of chronic sinusitis. Radiographically, panoramic, Caldwell, and Water's views reveal a smooth-surfaced, dome-shaped homogenous opacity that emanates from the antral floor and in more advanced sinusitis, the polyps may be multinodular. On anterioposterior views, an air space usually separates the polyp from the lateral sinus bony wall. Neither bone erosion nor expansion is fea-

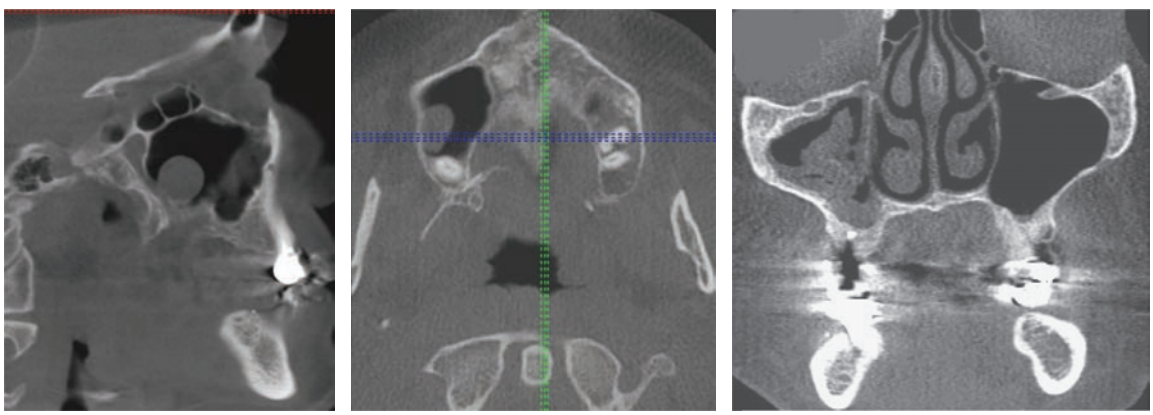

FIGURE 10-21
Inflammatory polyps are typically allergic and dome shaped.

tured. The maxillary teeth underlying the sinus lesion are vital. Antrochoanal polyp is a variant in which the polyp extends into the nasal cavity and posteriorly into the choanal region.

MICROSCOPIC FEATURES

The antral retention polyp lacks an epithelial lining. The sinus respiratory epithelium occupies the surface and is distended by an underlying mass of areolar and myxomatous fibrous or granulation tissue. Mucoid lakes are often observed and are compartmentalized by intervening delicate fibrovascular septa. Ductal ectasia of the tubuloacinar glands is common, and a mild inflammatory cell infiltrate composed of lymphocytes, plasma cells, neutrophils, and eosinophils prevails throughout.

DIFFERENTIAL DIAGNOSIS

Antral mucosal polyps appear identical to antral polyps associated with spread of odontogenic infection. Periapical cysts or granulomas with sinus extension can be ruled out by vitalometer testing. Most neoplasms fail to show a discrete dome-shaped opacity emanating from the sinus floor. Osteomas, antroliths, and odontomas are more discrete and are generally more opacified than antral mucosal polyps.

TREATMENT

Symptoms rarely exist; thus, no treatment is necessary. Periodic follow-up radiographs should be obtained; most lesions spontaneously resolve within 1 year.

Additional Reading

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SINUS MUCOCELE

Figure 10-22

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The sinus mucocele is usually located in the frontal or anterior ethmoidal sinus; occasionally, the antrum is involved. Rare cases of pansinus involvement have been reported. Although the etiology is unknown, the most plausible cause is blockage of the sinus openings with mucous retention. There is usually a history of surgery, trauma, or recurrent sinusitis. Frontoethmoidal lesions expand and displace the eye laterally and inferiorly. A crepitant bulge can usually be detected in the frontal region. Radiographically, diffuse opacification is seen along with effacement of the septate configuration. Erosion of the sinus walls may be preceded or accompanied by reactive osteosclerosis. Rarely, proliferative osteomyelitis is observed with dense opacification and obliteration of the sinus air spaces. An acute infection may also evolve (mucopyocele). When the antrum is involved, diffuse opacification is seen along with osseous destruction. Clinically, the teeth may loosen and the ipsilateral eye may exhibit proptosis. Computerized tomography is extremely useful for determining extent of disease.

MICROSCOPIC FEATURES

Although the sinus lining usually maintains a pseudostratified columnar ciliated appearance, foci of squamous metaplasia may be present. An inflammatory cell

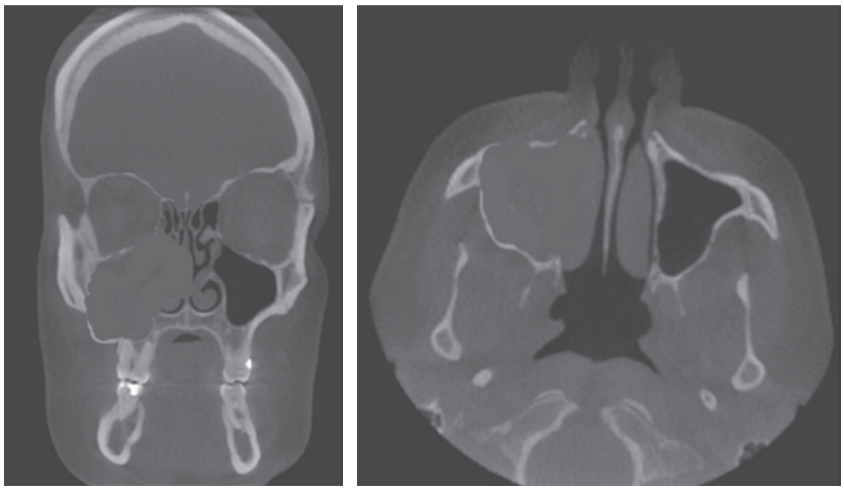

FIGURE 10-22
Sinus mucoceles are invasive expansile aggressive lesions that can erode sinus walls.

infiltrate is frequently encountered in the submucosa.

DIFFERENTIAL DIAGNOSIS

When a mucocele arises in the antrum, the diffuse opacification with erosion of the sinus walls cannot be reliably differentiated from tumor. Aspiration that reveals a mucoid secretion suggests mucocele. A Caldwell-Luc procedure with sinus exploration and biopsy should be performed.

TREATMENT

Frontal sinus and ethmoidal mucoceles may extend intracranially. A modified Lynch-Howarth surgical procedure is recommended, along with establishment of a wide and patent nasofrontal duct. Antral lesions should be treated in similar fashion, employing a Caldwell-Luc approach and maintaining a large and patent antronasal opening.

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PERIAPICAL INFECTION WITH ANTRAL POLYPS

Figure 10-23

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Because of the close proximity of the maxillary molar root apices to the antrum, periapical spread of infection often results in perforation. Acute pulpal infections may drain, causing an acute sinusitis. Radiographically, the entire antrum becomes opacified with intact bony margins. Apical granulomas and cysts may expand the antral floor cortex or erode and become confluent with the mucosal lining, thus creating an elevated dome-shaped soft tissue opacity. Radiographically, when cortices are expanded, a halo effect about the root apex is observed (apical radiolu-

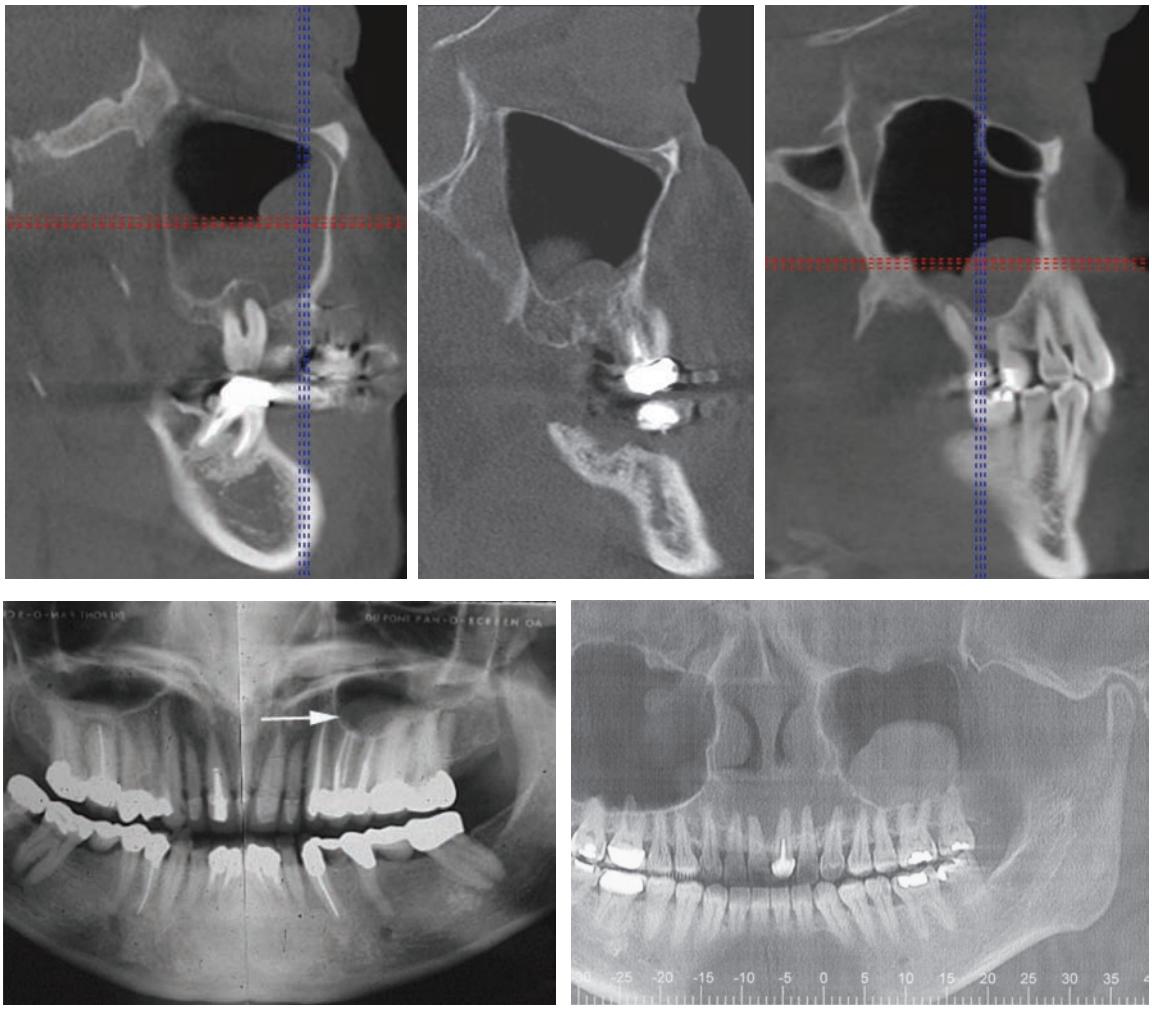

FIGURE 10-23
Endodontic infections may spread into the antrum with overlying polypoid configurations. The teeth test nonvital.

cency with an eggshell-like cap). When the inflammatory tissue perforates the cortex, a smooth-surfaced, dome-shaped homogenous opacity emanates from the antral floor.

MICROSCOPIC FEATURES

Antral polyps secondary to odontogenic infection are composed of extremely loose mucoid areolar granulation tissue exhibiting a leukocytic infiltrate. The surface is covered by respiratory epithelium. Apical periodontal cysts protruding into the antrum may fuse with sinus lining so that both stratified squamous and respiratory epithelial tissues constitute the cyst lining.

DIFFERENTIAL DIAGNOSIS

Antral polyps associated with necrotic teeth appear identical radiographically to antral mucosal cysts. Pulp vitality testing is essential to uncover the etiology. The apical periodontal ligament space is often, yet not invariably, widened in instances involving infected teeth. Because both of

these lesions appear as smooth-surfaced, dome-shaped opacities arising from the antral floor, confusion with the more generalized opacifications represented by other antral lesions should not be problematic.

TREATMENT

Once the incriminating tooth has been treated endodontically or extracted, the antral lesion resolves. Occasionally, however, an osseous protuberance evolves during healing.

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ANTRAL INVASIVE MYCOSES

Figure 10-24

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Fungal sinusitis generally affects only debilitated patients such as juvenile brittle diabetics and immunosuppressed individuals. The Phycomycetes and Aspergillus organisms may become opportunistic pathogens in the milieu of the immunologically compromised patient, particularly in mucormycosis. Maxillary enlargement with ocular displacement, loosening of maxillary teeth, and palatal perforation are later manifestations. Radiographically, the antral walls and orbital floor may exhibit bony erosion, and the entire antrum is faintly opacified. In aspergillosis, radiopaque concretions may be identified. It has been shown that overfilled root canals may predispose to maxillary sinus aspergillosis.

MICROSCOPIC FEATURES

The sinus membrane is infiltrated by mononuclear inflammatory cells, and the antral contents are represented by necrotic debris

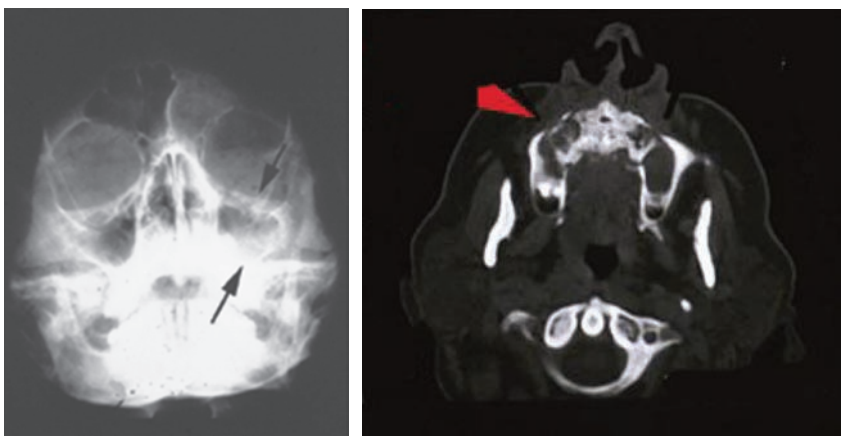

FIGURE 10-24
Mucormycosis with orbital floor erosion.

that is laced with hyphae. The organisms are readily identifiable with PAS staining. Spores are prominent in aspergillosis.

DIFFERENTIAL DIAGNOSIS

The opacification and osseous destruction observed in mucormycosis and aspergillosis are reminiscent of carcinoma. A history of advanced overt diabetes or systemic cancer in a patient receiving chemotherapy should arouse suspicion of antral mycosis. Biopsy is the most rapid method of diagnosis; however, culture of the sinus contents is recommended to specifically identify and differentiate the two organisms.

TREATMENT

Aggressive therapy is indicated because widespread mycotic osteomyelitis can result in massive sequestration of bone. The underlying systemic problem should be controlled if at all feasible, and systemic antifungal therapy with amphotericin B or ketokonazole should be administered. Both Aspergillus and Phycomycete infections should also be treated by surgical curettage.

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FUNGUS BALL (ASPERGILLUS MYCETOMA)

Figure 10-25

Age: Adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Aspergillus mycetoma or fungus ball of the paranasal sinuses is a relatively innocuous colonization of hyphae from *Aspergillus*

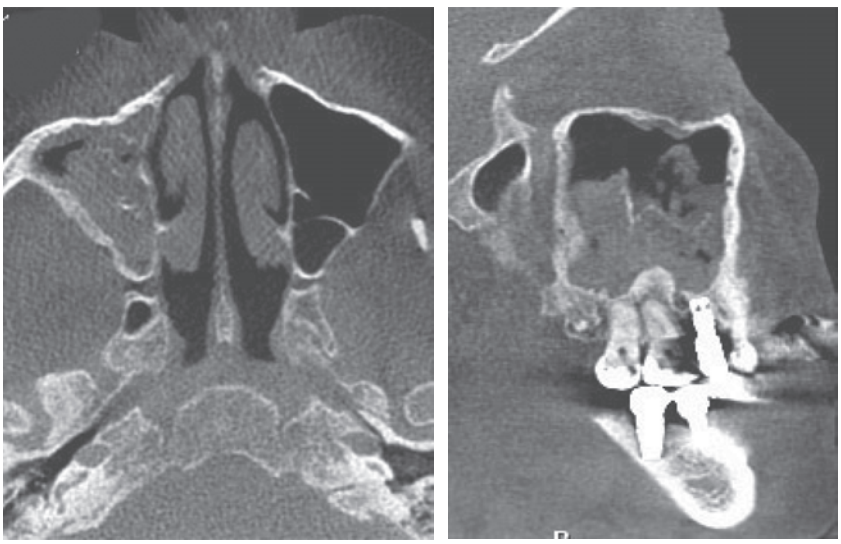

FIGURE 10-25
Polyps with calcification in localized aspergillosis (fungus ball).

species that forms within the sinus lumen, failing to invade the mucous membranes, submucosa, or bony wall. A well-demarcated radiopacity, usually round or oval, is identified within the antral cavity.

MICROSCOPIC FEATURES

Fungus ball is composed of matted colonies of hyphae without any host response other than a few adherent leukocytes. The branching hyphae are distinguishable from phycomycetes and bipolaris fungi and readily stain with PAS or Grocott's methenamine silver (GMS) fungal stains.

DIFFERENTIAL DIAGNOSIS

The opacity of fungus ball must be differentiated from foreign body, misplaced teeth, and odontomas and antrolith.

TREATMENT

Endoscopic surgery with removal of the fungal mass usually results in cure.

Additional Reading

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ALLERGIC FUNGAL SINUSITIS

Figure 10-26

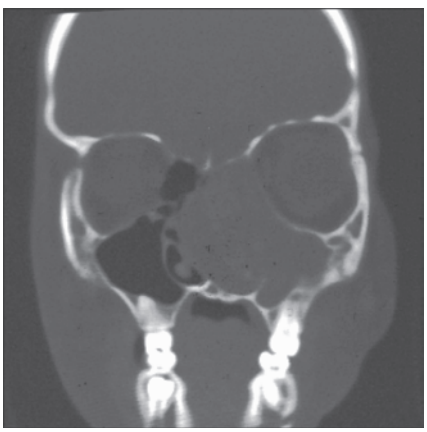
Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Inhalation of otherwise harmless soil fungi of the *Bipolaris* genus results, among susceptible patients, in a fulminant allergic reaction with pronounced tissue eosinophilia. The host response rather than the organism accounts for the symptoms of nasal stuffiness and blockage. Imaging studies of the maxillary sinus typically reveal unilateral involvement with opacification of the sinus and resorption, apposition, and erosion of the sinus wall.

MICROSCOPIC FEATURES

The material curetted from the sinus has the gross appearance of "peanut butter." Microscopically, necrosis and eosinophils are seen as layed smudge. Chacot-Leyden crystals are usually prominent and scat-



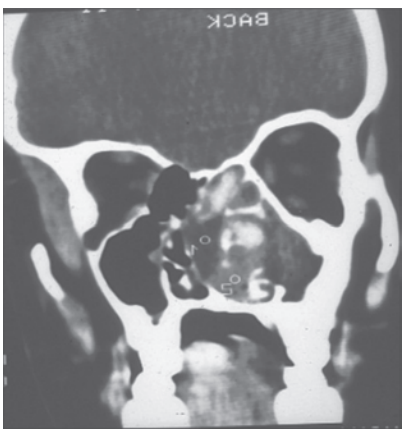


FIGURE 10-26
Allergic fungal sinusitis showing bony invasion and expansion is typically associated with noninvasive pleomorphic soil fungi.

tered colonies of large pleomorphic hyphae are evident and readily demonstrated with PAS or GMS fungal stains.

DIFFERENTIAL DIAGNOSIS

The expansile and osseous resorptive changes seen on imaging studies in allergic fungal sinusitis are ominous findings and malignancy must be included in the differential diagnosis.

TREATMENT

Thorough sinus lavage and curettage are indicated followed by a 12-week course of systemic corticosteroids.

Additional Reading

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DISPLACED TEETH, ROOTS, AND FOREIGN BODIES

Figure 10-27

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Teeth or root fragments within the sinus are usually readily identifiable by their morphologic features and radiologic identification of a pulp chamber or root canal shadow. They may radiographically appear in this location as a consequence of (1) traumatic displacement, (2) displace-

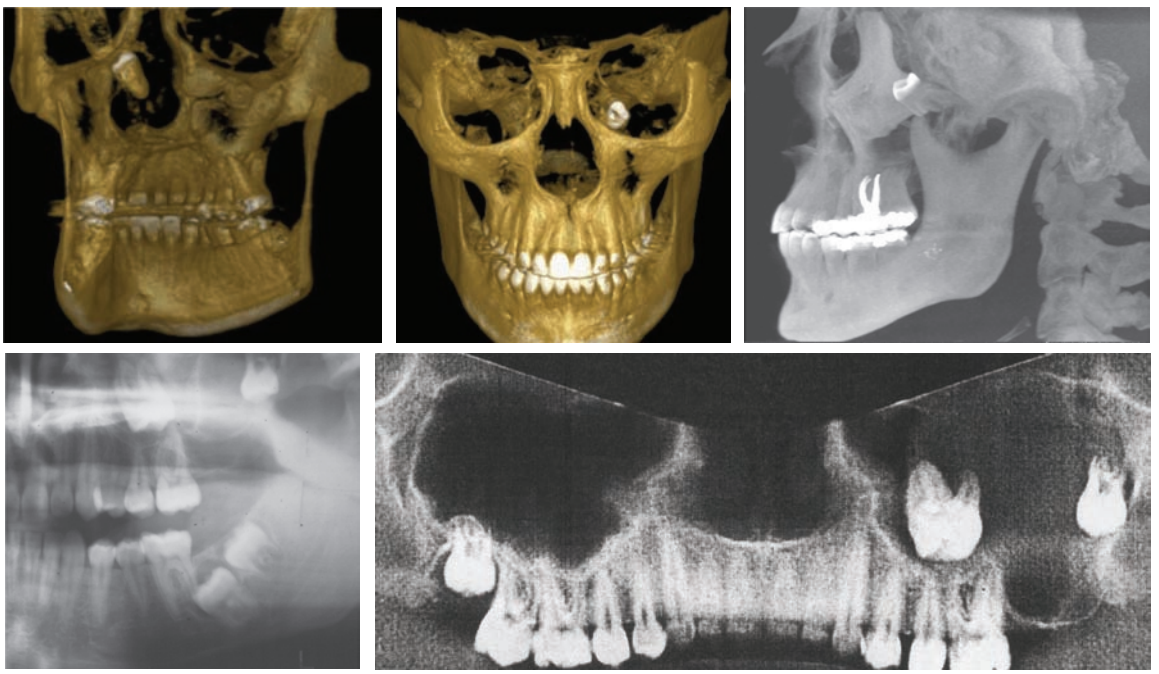

FIGURE 10-27
Displaced teeth in the sinuses.

ment of fractured root tips after exodontia, (3) developmental displacement, or (4) superior displacement by an enlarging dentigerous cyst. Water's views are not as efficacious as periapical, Caldwell, and lateral sinus views. When teeth or roots lie within the sinus cavity, they may change positions with head movement. More often, the tooth fragment is trapped between the antral bony floor and the lining membrane; in these instances, a change in head position will not alter the localization radiographically. Unerupted teeth appearing to lie within the sinus often are not, in actuality, within the sinus itself. Rather, they are encased in bone and show a periodontal ligament space with an eggshell-thin cortex interposed between tooth and sinus cavity. Last, it should be stressed that during surgery, a tooth may be displaced into the infratemporal space, or a root tip may become lodged between the periosteum and outer cortical table. A variety of radiographic projections and tomography help to pinpoint the precise location. Root tips lying free within the sinus may serve as an infectious source with resultant sinusitis and diffuse opacification. Rarely, other foreign bodies may reside within the sinus. Impression material forced through an oral-antral fistula and traumatically placed metals are more common.

MICROSCOPIC FEATURES

Not applicable.

DIFFERENTIAL DIAGNOSIS

Focal opacities representing teeth or roots may be confused radiographically with osteoma, exostosis, or antrolith. Usually, the opacity is recognizable by virtue of its morphology as tooth structure.

TREATMENT

Using a Caldwell-Luc approach, intrasinus teeth and/or root tips should be removed surgically. A longstanding asymptomatic displaced root fragment may be left in place and monitored on a regular basis.

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AUGMENTATION MATERIALS

Figure 10-28

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Sinus lift surgery is performed to create bone bulk in order to support dental metallic implants. The mucosal sinus floor is elevated and a variety of augmentation materials are placed between the sinus floor bone and the elevated membrane. Autogenous bone and synthetic calcific materials used to stimulate osteogenesis are placed. Radiographically, a floccular appearance is seen represented by multiple calcified particles. Most augmentations provide 8 to 10 mm of height.

MICROSCOPIC FEATURES

Inert calcified particles are observed or intact lamellar bone fragments are seen with surrounding mature collagenous connective tissue. Appositionally, neo-osteogenesis is seen and some of the nonviable materials are partially resorbed.

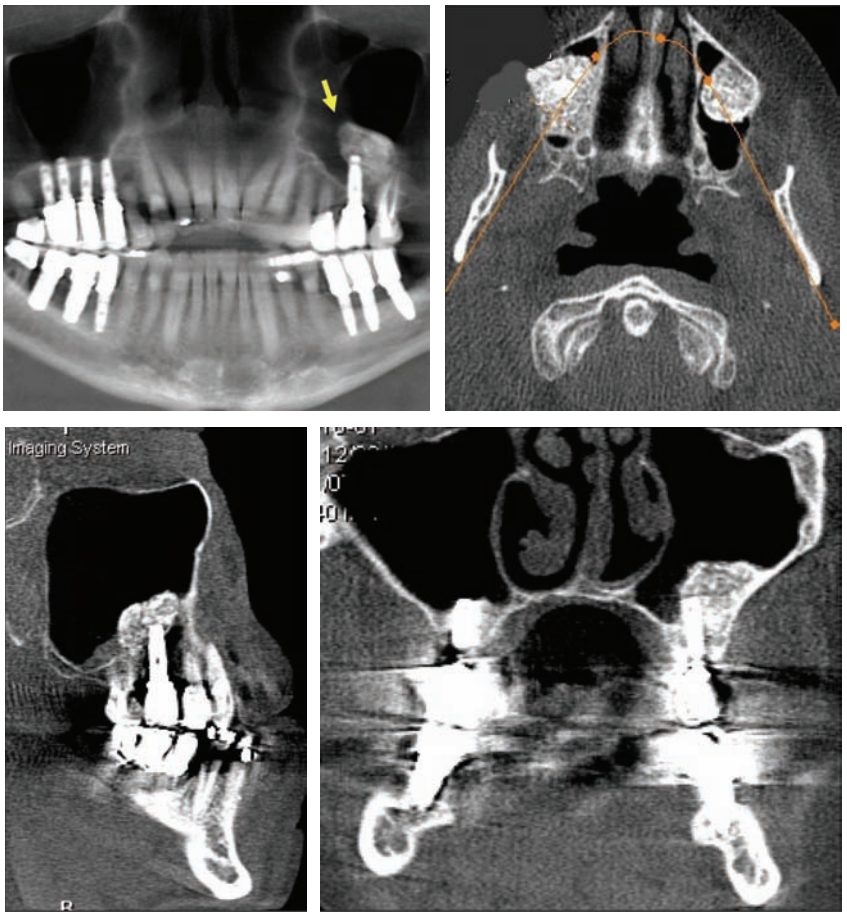

FIGURE 10-28
Powdered calcifications in sinus lift surgeries to augment bone support for integrated dental implants.

DIFFERENTIAL DIAGNOSIS

These augmentation sites must be differentiated from osteogenic and odontogenic tumors. Furthermore, the surgically placed materials lack encapsulation as seen in many benign cysts and tumors. Of course, history is the main revealing factor.

TREATMENT

No treatment.

Additional Reading

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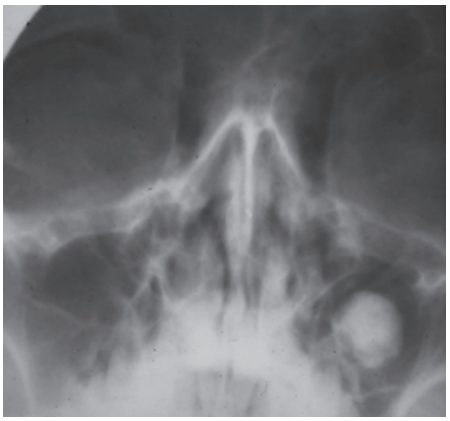
ANTROLITH/RHINOLITH

Figure 10-29

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Stones arising in the antral cavities are uncommon. They may develop around a nidus, which usually represents a foreign body such as a tooth root; on the other hand, no particular material may be identified as serving as the nidus for mineral-



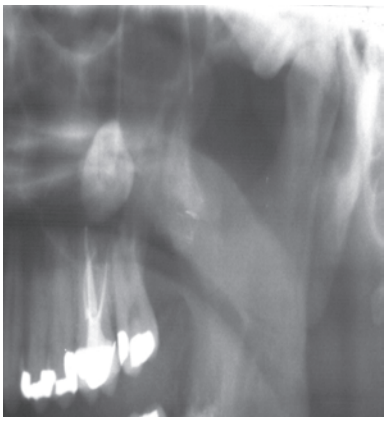


FIGURE 10-29
Antroliths represent dystrophic calcifications.

ization. Microbial colonies in bacterial and mycotic antral infections may serve as a matrix for calcification as well. The antrolith may be associated with dull pain or ache, mimicking sinusitis. Radiographically, a dense, irregular yet well-defined mass can be identified in the antrum, usually resting on the antral floor. Stones may develop within the nasal cavity; they are obvious on panoramic views, Water's radiographs, and tomograms.

MICROSCOPIC FEATURES

Decalcified specimens are composed of dystrophic calcified amorphous matrices. The adjacent antral membrane may be polypoid with a submucosal inflammatory cell infiltrate.

DIFFERENTIAL DIAGNOSIS

A radiopacity with well-defined margins located in the antrum can be differentiated from an antral retention cyst. A root fragment located in the antrum is perhaps more common. The osteomas in Gardner's syndrome often localize within the sinuses as well.

TREATMENT

Antroliths should be removed because they irritate the sinus lining and predispose to sinusitis.

Additional Reading

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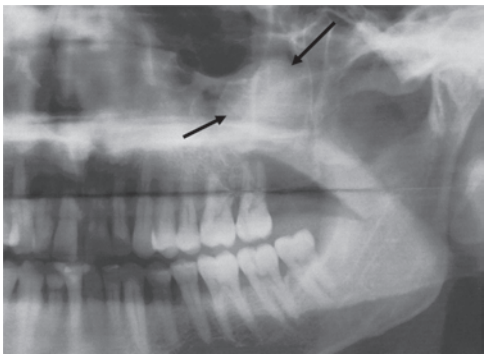
ODONTOGENIC TUMORS

Figure 10-30

Age: Teenagers and adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Occasionally, a maxillary odontoma develops in the maxillary bones of the sinus wall. Alternatively, some odontomas actually lie free within the sinus cavity without an enveloping osseous encasement. Free odontomas within the sinus often manifest symptoms of dull aching pain and nasal discharge and predispose to a chronic sinusitis. Radiographically, the opacity may be focal; more often, multifocal confluent opacities are clus-



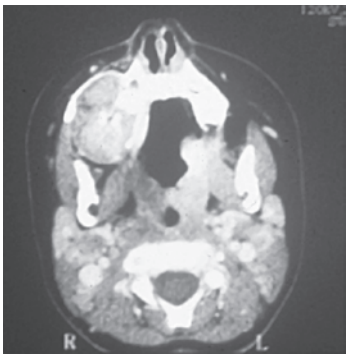


FIGURE 10-30
Odontogenic tumors in the maxilla may erode into the sinuses.

tered, and a fully formed unerupted tooth lies juxtaposed to the hamartomatous element. Free odontomas change position when the head is moved during procurement of various maxillary radiographs. If the odontoma is encased in bone or entrapped under the sinus membrane, no positional change occurs. Maxillary odontogenic tumors such as ameloblastoma, calcifying epithelial odontogenic tumor, and odontogenic myxoma among others may proliferate and perforate the antral floor where they may then grow freely in the sinus showing a soft tissue density in the sinus cavity. Alternatively, there are some instances that have evolved within the sinus, separate from the alveolus.

MICROSCOPIC FEATURES

Haphazardly arranged dental hard tissues, including enamel matrix, dentin, and cementum, are present and often histologically mimic miniature tooth buds. Dental pulp with an odontoblastic layer is usually identifiable, and odontogenic epithelium lies adjacent to enamel matrix. A fibrous follicle is also present. The microscopic features of other odontogenic tumors are described elsewhere in chapters 9 and 10.

DIFFERENTIAL DIAGNOSIS

Composite odontomas with multiple tooth-like configurations are easily recognized radiographically. Complex varieties may be confused radiographically with osteoma or antrolith; thus, a definitive diagnosis necessitates biopsy. Soft tissue densities from other types of odontogenic tumors will simulate the other sinuses lesions described here.

TREATMENT

A Caldwell-Luc approach with surgical removal is the treatment of choice. Any associated tooth should be removed in continuity. In addition, any polypoid lesions resulting from irritation by the tumor should be excised.

Additional Reading

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OSTEOMAS AND EXOSTOSES

Figure 10-31

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Ossified bodies (osteomas) and bony excrescences (exostoses) may be found within

the antrum, although they are more common in the frontal and ethmoidal sinuses. Antral cases are quite rare, and the etiology is obscure. Identification of an osteoma in the antrum should alert the clinician to the possibility of Gardner's syndrome, characterized by supernumerary teeth, osteomas of the jaws and sinuses, desmoid tumors of the skin, and premalignant adenomatous polyposis coli. Antral osteomas may predispose to sinusitis with symptoms of maxillary pain and nasal discharge. Radiographically, osteomas may be seen as single or multiple round or oval radiopacities. A concomitant sinusitis may show a fluid level or diffuse opacification of the affected sinus. Exostoses are firmly adherent and confluent with the sinus wall, usually the lateral wall.

MICROSCOPIC FEATURES

Both osteomas and exostoses are composed of mature lamellar bone. They are usually ovoid bodies with an outer cortical margin that encases a medullary trabecular zone. The marrow spaces are represented by areolar fibrous or adipose tissue. When multiple osteomas occur, the ossified bodies are usually discrete, separated from one another by mature fibrous tissue. Some sinus osteomas will demonstrate osteoblastoma-like histologic foci, a feature that does not portend a more aggressive potential.

DIFFERENTIAL DIAGNOSIS

Osteomas may be radiographically indistinguishable from antroliths or complex odontomas. Once biopsy has confirmed a diagnosis of osteoma, paranasal sinus radiographic series and jaw radiographs should be obtained to uncover osteomatous lesions. Should they be discovered, a work-up for Gardner's syndrome should be undertaken.

TREATMENT

The Caldwell-Luc approach should be used to remove the lesion along with hyperplastic sinus membrane or polyps. As mentioned previously, Gardner's syndrome should be ruled out by referral to an internist or gastroenterologist.

Additional Reading

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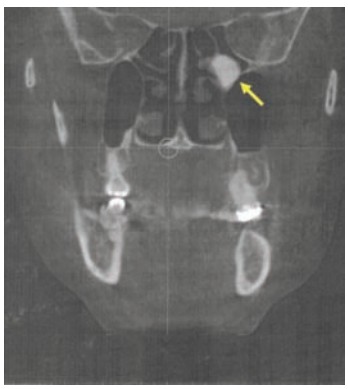

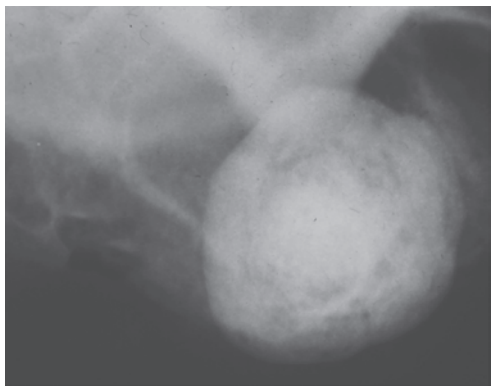

FIGURE 10-31
Osteomas of the antrum.

cases with emphasis on tumors with osteoblastoma-like features. *Arch Pathol Lab Med*. 2009;133:1587-1593.

BENIGN MESENCHYMAL NEOPLASMS

Figure 10-32

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Benign neoplasms of connective tissue origin arising in the antrum are rare. Vascular and nerve sheath neoplasms are more frequently encountered; these lesions arise primarily within the submucosa of the sinus membrane. Intraosseous neoplasms of the maxilla may expand and displace the lateral sinus wall medially; ossifying and cementifying fibromas as well as maxillary odontogenic tumors may behave in this fashion. Ameloblastomas of the maxilla can perforate into the antral space. Primary benign neoplasms grow to fill the sinus air space with symptoms of swelling and nasal congestion. Radiographically, diffuse opacification is observed; in larger neoplasms, the sinus walls may exhibit expansion with bowing in all dimensions, particularly obvious along the medial wall on sinus films. Osseous erosion and perforation can also occur with benign neoplasms.

MICROSCOPIC FEATURES

The histologic features vary depending on the cell of origin. The reader is referred to the chapter on oral soft tissue swellings for

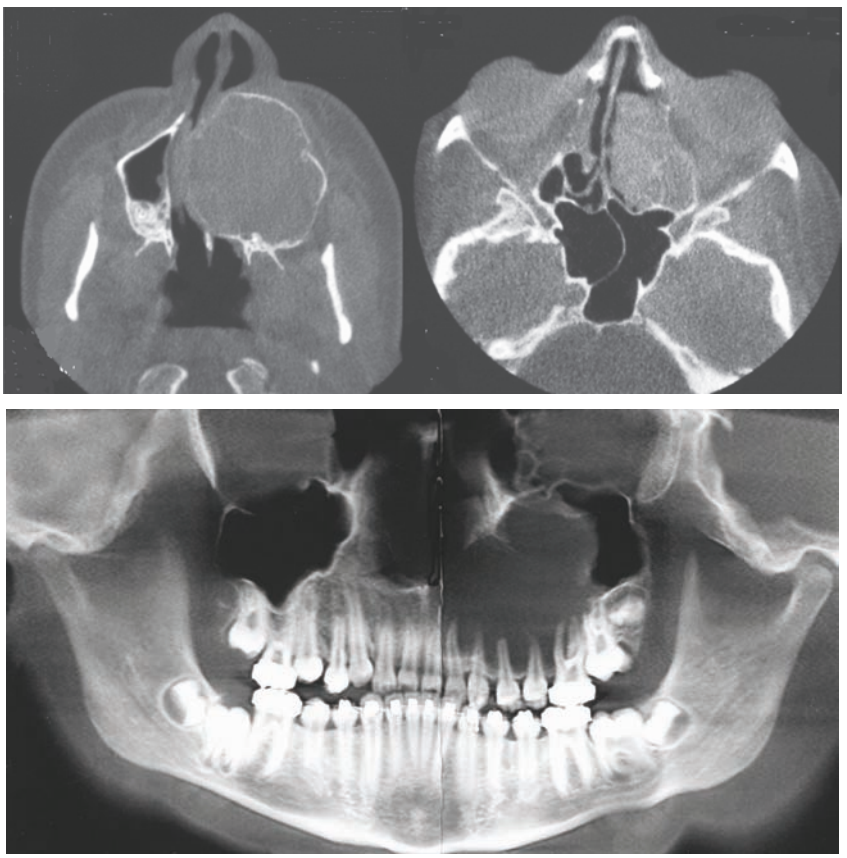

FIGURE 10-32
Benign mesenchymal tumors, a nerve sheath tumor (upper right), juvenile ossifying fibroma (upper left), anuerysmal bone cyst (below).

microscopic descriptions of vascular and neural sheath neoplasms.

DIFFERENTIAL DIAGNOSIS

The diffuse opacifications seen in benign mesenchymal neoplasms along with symptoms of congestion may be confused with sinusitis. When expansion and erosion are present, mycotic infections and malignant tumors must be considered, and immediate exploration with biopsy is recommended.

TREATMENT

Most benign neoplasms of connective tissue origin can be treated by curettage or excision. Osseous invasion or large destructive lesions may require hemimaxillectomy.

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INVERTING PAPILLOMA

Figure 10-33

Age: Middle-aged adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Unlike the common inflammatory nasal and antral polyp, the inverting or Schneiderian papilloma represents a true neoplastic process arising from the ectodermally derived epithelium. Human papillomaviruses are of etiologic importance in fungiform papillomas of the nasal cavity yet are rarely encountered in the inverting papilloma. It arises from the lateral nasal wall, either in the region of the middle turbinate or ethmoidal recess. The lesion invades the submucosa and frequently, either via the ostium or by bony erosion, extends into the antral or ethmoidal sinus. Clinically, the most common symptom is nasal obstruction. Radiographically, the affected sinus is opacified; maxillary tomograms often disclose destruction of the medial antral wall with opacification of the nasal cavity. Importantly, carcinoma is associated with inverting papilloma in 7%

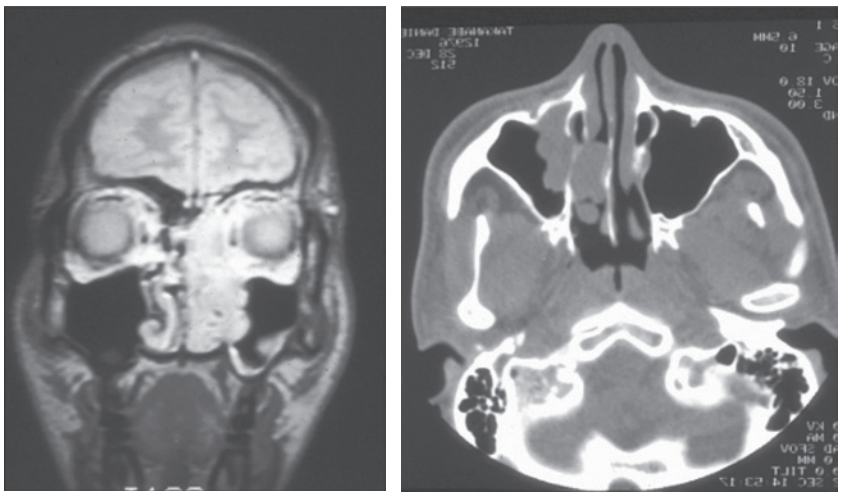

FIGURE 10-33
Aggressive inverting papillomas of the sinonasal tract may transform into carcinoma.

of the cases. The common fungiform papilloma is limited to the nasal septum and does not invade the maxillary sinus.

MICROSCOPIC FEATURES

Inverting papillomas, as the term implies, grow in inverted fashion into the subjacent sinus and nasal submucosa. Budding folds of stratified squamous epithelium are frequently covered by a single row of ciliated columnar cells. Microcysts with mucin are located throughout the spinous cell layer. A rare variant termed *cylindric cell (oncocytic) papilloma* may also invade the antrum. The inverted architecture prevails; however, the tumor element is represented by eosinophilic columnar cells, which may show surface cilia.

DIFFERENTIAL DIAGNOSIS

Complete antral opacification with inverting papilloma may be encountered in many other benign and malignant lesions of the maxillary sinus. A concurrent opaque mass in the ipsilateral nasal cavity suggests inverted papilloma; however, biopsy is required for a definitive diagnosis.

TREATMENT

Inverting papillomas are aggressive, and more than 60% recur after simple excision (polypectomy). Computed tomographic (CT) scans or paranasal sinus tomograms are recommended to determine the extent of disease. Lateral rhinotomy offers the greatest chance for cure. Interestingly, this lesion tends to recur more often in females. Carcinomatous transformation requires hemimaxillectomy with extended margins and radiation therapy.

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ANTRAL CARCINOMA

Figure 10-34

Age: Elderly adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Maxillary sinus carcinoma rarely manifests worrisome signs or symptoms in the early stages. Patients may complain of unilateral dull sinus pain along with nasal discharge, which masquerade as sinusitis. The majority of cases represent squamous cell carcinoma; transitional cell or anaplastic carcinoma and adenocarcinoma of lining cell origin are less common. Occasionally, adenocarcinomas of tubuloacinus origin occur in the antrum and show histopathologic features similar or identical to salivary tumors. As these malignant tumors proliferate, they fill the sinus cavity, and in later stages, they induce osseous destructive changes. Medial growth perforates the nasal cavity, superior growth may displace the eye with diplopia, posterior extension into the pterygopalatine and pterygomandibular spaces may cause trismus, and inferior extension causes loosening of maxillary teeth with palatal enlargement or perforation. Infraorbital paresthesia may be featured, and facial expansion can occur. Radiographically, opacification is observed; with conventional sinus radiographs, sinus tomograms, and CT scans, osseous destructive changes can be identified in advanced

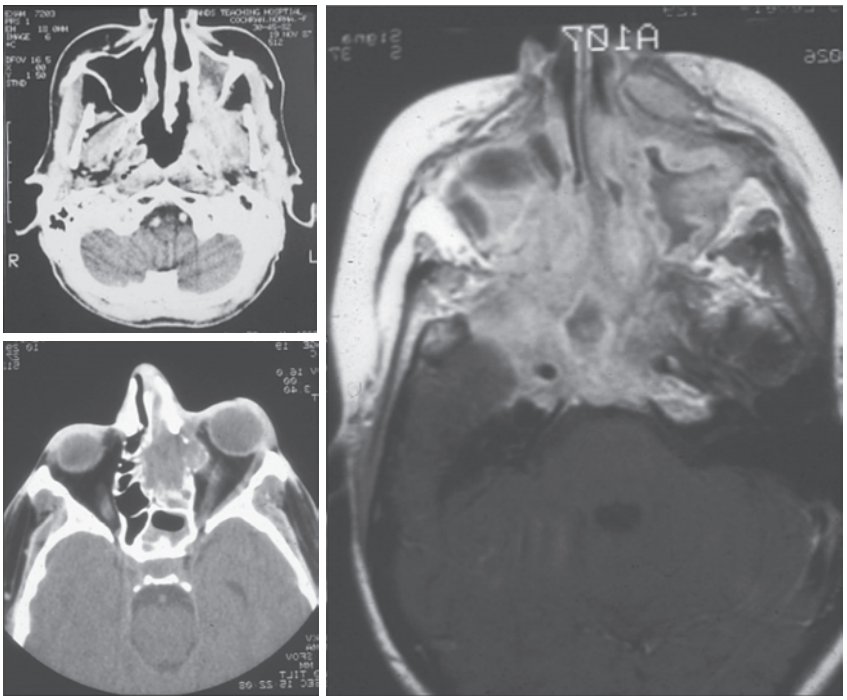

FIGURE 10-34
Squamous cell carcinoma and sinonasal undifferentiated carcinoma (SNUC, right) are osseous destructive, the latter being universally fatal.

cases. Extension into other sinuses and cranial base involvement may be extant at the time of admission. Despite the advanced stage and diffuse extent of disease, palpable nodes in the submandibular and upper neck regions are encountered in less than 20% of these patients.

Other carcinomas may arise within or invade the maxillary sinus including ameloblastic carcinoma, primary adenocarcinoma, salivary gland carcinomas, and metastatic carcinomas, renal cell carcinoma in particular.

MICROSCOPIC FEATURES

Squamous cell carcinoma, which is most common, shows proliferating islands and cords of epidermal cells with keratin formation that is generally not abundant. Occasionally, adjacent tissue represents inverted papilloma that has undergone carcinomatous transformation. Adenocarcinomas show tubular and ductal differentiation. Both adenoid cystic and mucoepidermoid carcinoma may be encountered.

DIFFERENTIAL DIAGNOSIS

Early tumors may exhibit opacification without destruction of the bony walls and may therefore simulate sinusitis. When osseous destruction is witnessed, sarcomas and mycotic infections must be included in the radiographic diagnosis. Persistent opacification following conventional therapy for sinusitis should be explored and biopsied.

TREATMENT

Most antral cancers are advanced (T3, T4) by the time they are discovered. Maxillectomy with exploration and surgical excision of tumor in contiguous sinus cavities followed by postoperative external radiation (7500 rad) offers the best chance for cure. Five-year survival for T3 and T4 lesions is about 75% and 35%, respectively.

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ANTRAL SARCOMA

Figure 10-35

Age: Adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Malignant lymphomas and extramedullary plasmacytomas are the most common malignant mesenchymal tumors found to arise in the maxillary sinus. Malignant fibrous histiocytoma, rhabdomyosarcoma, and fibrosarcoma may also occur; occasionally, metastatic neoplasms are located in the antrum. These malignant mesenchymal neoplasms share common clinical and radiographic findings that are similar to those observed in antral carcinoma. As the neoplasm proliferates with the sinus, expansion with facial swelling may be encountered along with extension of a mass into the nasal fossa, superior displacement of the eye, and palatal swelling with loosening of the maxillary teeth. Infraorbital paresthesia and epistaxis are common signs and symptoms, particularly with lymphoma and plasmacytoma. Radiographically, diffuse opacification is seen with expansion and sinus wall osseous destruction. Water's views and tomograms often show opacification of the ipsilateral nasal cavity, and CT scans aid in determining extent of disease.

MICROSCOPIC FEATURES

Lymphomas are characterized by sheets of neoplastic lymphoblasts and may be diffuse or nodular. Malignant reticulosis, which represents a specific form of lymphoma that affects the upper air passages, may also be encountered. Extramedullary plasmacytomas are composed of diffuse sheets of plasma cells with a scant vascular stroma. Many lesions of this nature are associated with or progress to multiple myeloma.

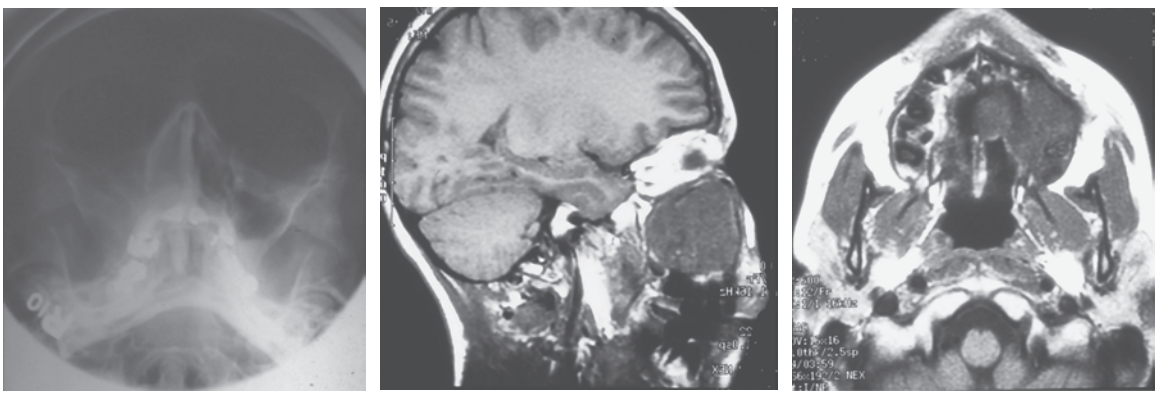

FIGURE 10-35
Sarcomas are destructive expansile lesions that rarely arise in the sinus. Malignant fibrous histiocytoma is the most common type to occur in the antrum.

Malignant spindle cells with bizarre nuclei are seen in fibrosarcoma, malignant fibrous histiocytoma, and rhabdomyosarcoma.

DIFFERENTIAL DIAGNOSIS

Clinical evidence of epistaxis in conjunction with antral disease represents an ominous finding. Radiographically, expansile and osseous destructive changes occurring in malignant mesenchymal sinus tumors cannot be differentiated from carcinoma. Biopsy is required for a definitive diagnosis.

TREATMENT

Lymphoma and plasmacytoma respond to 6000 rad of external beam radiation therapy. Spindle cell malignancies require radical maxillectomy. A thorough work-up for involvement of other organ systems and bones should be undertaken.

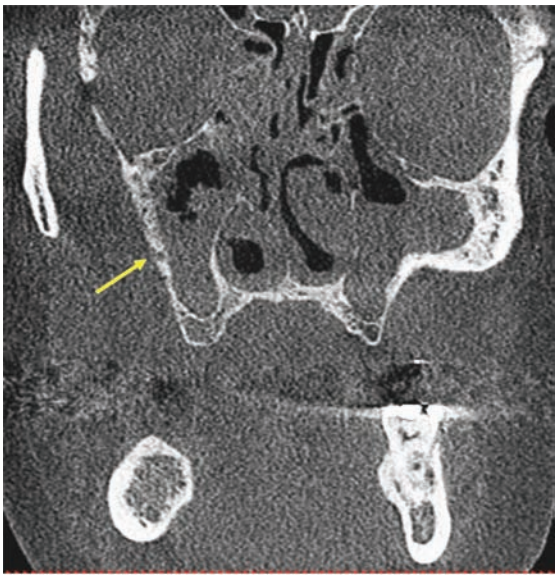

FIGURE 10-36
In the silent sinus syndrome, a unilateral collapse of the antrum is seen and in this instance, sinus polyps are evident.

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SILENT SINUS SYNDROME

Figure 10-36

Age: Teens, young adults
Sex: No predilection

CLINICAL AND RADIOLOGIC FEATURES

Silent sinus syndrome presents as a facial asymmetry secondary to unilateral atelectasis of the maxillary sinus. Enophthalmos and hypoglobus are secondary to thinning and inward curvature of the maxillary sinus roof. There are no symptoms of intrinsic sinonasal inflammatory disease. On imaging, the affected sinus is atrophied and opacified.

MICROSCOPIC FEATURES

The sinus is replaced by mature lamellar bone and fibrous marrow.

DIFFERENTIAL DIAGNOSIS

The condition can be distinguished from other sinus opacities based on the clinical finding of atrophy with progressive change that begins in teenage years.

TREATMENT

Surgical correction is indicated.

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Ground-Glass Radiopacities

FIBROUS DYSPLASIA (FIGURES 10-37A & 10-37B)

Age: Teenagers and young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Fibrous dysplasia is the most common disease of the jaws to manifest a ground-glass radiographic pattern. It is molecularly characterized by a mutation in the α-subunit of G protein that plays a role in coupling cAMP to hormone receptors. It may exist as a solitary lesion (the monostotic form), as multiple lesions involving many bones of the jaws and cranium (the craniofacial form), or throughout the skeleton (the polyostotic variety). The latter may be complicated by endocrine defects, including precocious puberty, goiter, and café-au-lait macular pigmentations of the skin. This form of polyostotic fibrous dysplasia is known as Albright's syndrome. When long bones are affected, deformed limbs and pathologic fractures are frequent findings. The monostotic variant is by far the most common type seen when the jaw is affected. The disease is a painless expansile dysplastic process of osteoprogenitor connective tissue. Slow growth is seen with progressive facial deformity. Pain and paresthesia are generally lacking. The maxilla is most often the site of involvement. When the mandible is affected, the radiographic pattern is more apt to be multicystic or mottled. The maxillary lesion

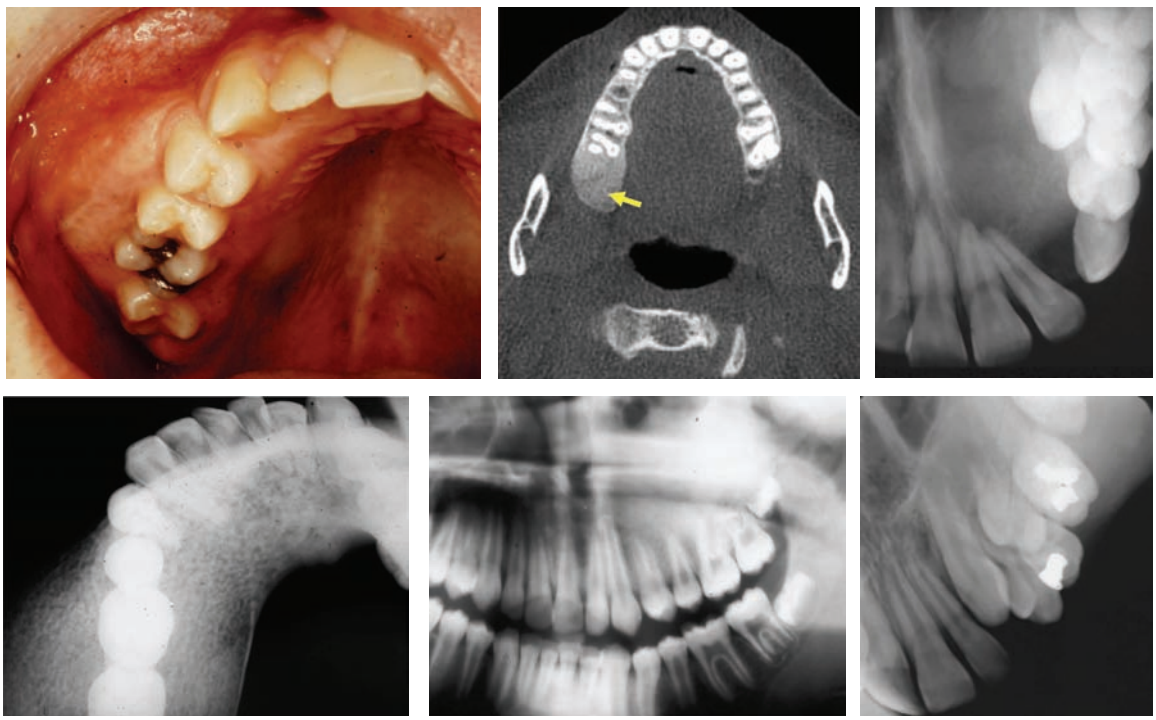

FIGURE 10-37A
Fibrous dysplasia showing ground-glass patterns.

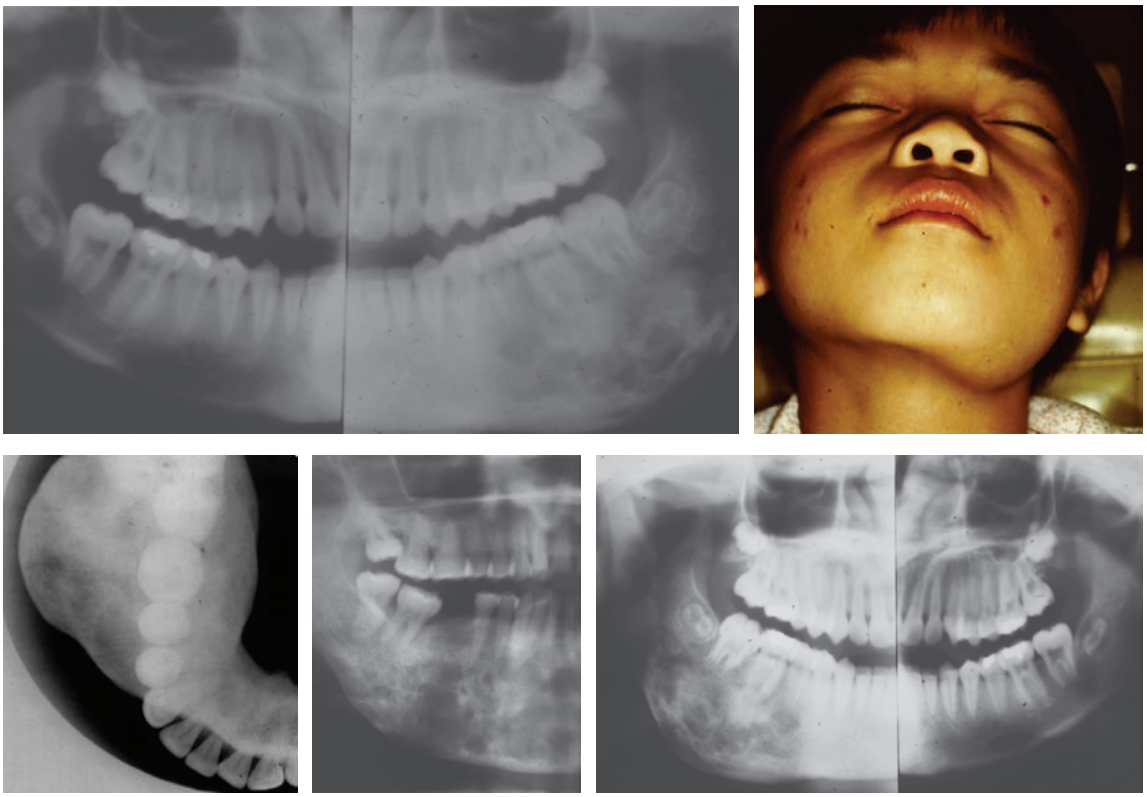

FIGURE 10-37B
Fibrous dysplasia showing mottled patterns.

is monotonously ground-glass or "orange-peel" in configuration, shows expansion, and characteristically lacks margination. Rather, the dysplastic process appears to blend subtly into the adjacent trabecular bone. The lesion does not cross the midline and shows a tendency to limit itself to one bone, crossing sutures only occasionally. The antrum is often obliterated, and involvement of the orbital floor may displace the globe.

MICROSCOPIC FEATURES

Dispersed throughout a hypercellular fibrous stroma are irregular, haphazardly arranged osseous trabeculae with no structural arrangement; however, a retiform pattern may be discerned in some cases. With polarized light, most of the trabeculae show a woven bone pattern, but the presence of lamellar trabeculae does not militate against a diagnosis of fibrous dysplasia.

DIFFERENTIAL DIAGNOSIS

The ground-glass pattern of fibrous dysplasia may be encountered in the early stages of osteitis deformans and in hyperparathyroidism. Osteitis deformans characteristically crosses the midline, is a disease of elderly people, and produces significantly elevated serum alkaline phosphatase levels. During early or active growth stages of fibrous dysplasia, serum alkaline phosphatase levels may be elevated as well. Hyperparathyroidism is more apt to manifest brown tumors of the jaws than ground-glass lesions. A skeletal survey should be taken to rule out polyostotic lesions.

TREATMENT

Treatment should be deferred, if possible, until skeletal maturity is reached. Attempts to intervene surgically during

the lesional growth phase may actually activate the process. Fibrous dysplasia tends to become arrested and static at the same time that the epiphyseal growth centers close. A rare aggressive form of the disease known as *active juvenile fibrous dysplasia* shows rapid aggressive growth, particularly in the maxilla, and may invade the cranial base. Extremely aggressive clinical behavior in the face of cellularly active disease requires partial maxillectomy to achieve control. Taking the aforementioned features into consideration, it is recommended that children with a diagnosis of fibrous dysplasia be followed quarterly with clinical, radiographic, and periodic study-model evaluation to determine whether accelerated or diminished growth is taking place.

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CHRONIC DIFFUSE SCLEROSING OSTEOMYELITIS

Figure 10-38

Age: Children, teens
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Occurring in youngsters, chronic diffuse osteomyelitis is a rare lesion with features that parallel those of fibrous dysplasia in many respects. Patients complain of episodic mandibular pain manifested as a mild nagging ache and clinical examination reveals cortical expansion. Radiographically, a diffuse ground-glass opacification is seen with indistinct margins. Usually, on axial CT of occlusal images, cortical redundancy (onion skinning) is identified (Garré's phenomenon). The etiology is unknown in many instances whereas in others a possible odontogenic source of infection is uncovered (caries, pulpal inflammation, tooth fracture). In some, yet not all, instances a trephine bone sample can be culture positive for anaerobic bacteria.

MICROSCOPIC FEATURES

A fibro-osseous pattern is seen with anastomosing trabeculae along with other fields of diffuse osteosclerosis. The fibrous element is not as cellular as seen in other fibro-osseous lesions. Paradoxically, a robust inflammatory infiltrate is lacking although a few small clusters of lymphocytes may be encountered.

DIFFERENTIAL DIAGNOSIS

The chief entity in the differential is fibrous dysplasia. Clinically, the occurrence of paroxysmal dull pain, Garré's phenomenon, a potential source of infection and the microscopic features of a more mature osteogenesis allow for establishment of a definitive diagnosis of chronic diffuse sclerosing osteomyelitis.

TREATMENT

Long-term or intravenous antibiotic therapy usually only provides temporary relief, yet results improve among some patients who also receive hyperbaric oxygen therapy. The use of bisphosphonates may be promising. Some patients will manifest osteomyelitis elsewhere in the skeleton warranting a bone scan.

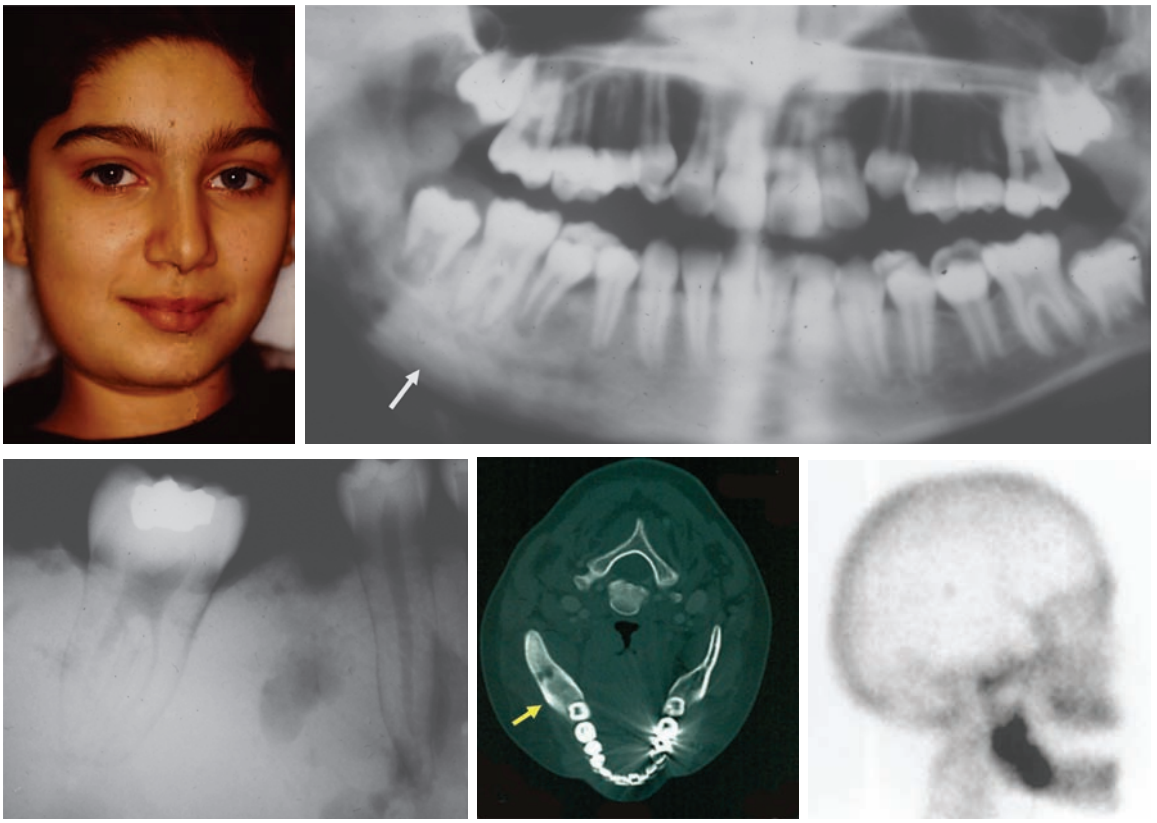

FIGURE 10-38
Diffuse sclerosing osteomyelitis with osseous expansion. Bone scan reveals activity in mandible.

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OSTEITIS DEFORMANS (PAGET'S DISEASE OF BONE)

Figure 10-39

Age: Elderly adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Osteitis deformans is a dysplastic bone disease that classically occurs in elderly people and involves replacement of normal bone by an irregular osseous growth, with an increase in osteoblastic activity. The molecular underpinnings involve mutations of the sequestosome gene and the tumor necrosis family gene *TNFRSF11A* (osteoprotegrin). The long bones, pelvis,

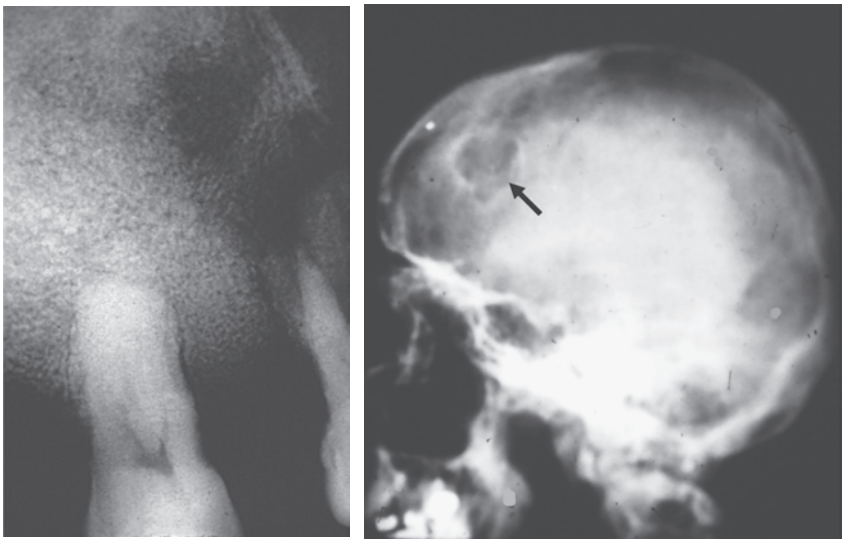

FIGURE 10-39
Ground-glass opacification of alveolar bone. Osteitis circumscripta in skull.

and cranium are predilected sites that show expansion and deformity. As skull lesions develop, foramina become constricted, leading to cranial nerve neuropathies such as blindness, deafness, and facial palsy. Skull lesions begin in early stages as focal radiolucencies, so-called osteitis circumscripta. Later, the cranium enlarges with fuzzy radiopaque conglomerates, producing the classic cotton-wool pattern. In the jaws, the maxilla is involved more often than the mandible, and the early stages show a uniform ground-glass appearance with faint, poorly demarcated periapical clearing (ill-defined radiolucencies). The teeth remain vital. The cotton-wool pattern eventually replaces the ground-glass appearance, and teeth may develop hypercementosis. The maxillary lesions cross the midline to involve both quadrants and clinically manifest progressive expansion, which in turn leads to diastema formation in dentulous patients. Giant cell tumors similar to giant cell granuloma are occasionally encountered in patients with Paget's disease, appearing as expansile multilocular radiolucencies. Osteomyelitis and an increased risk for development of sarcomas in bone are complications.

MICROSCOPIC FEATURES

A fibro-osseous microscopic pattern is seen in the early stages of osteitis deformans; a hypercellular fibrous stroma supports irregular osteoid trabeculae rimmed by osteoblasts on one side with resorbing osteoclasts on the opposite side. Vascularity is prominent, and osteoclastic giant cells are often encountered in fibrous areas removed from any osseous trabeculae. Mosaic bone is usually encountered even in the early stages, yet is far more prevalent in lesions of long standing.

DIFFERENTIAL DIAGNOSIS

A uniform bilateral maxillary ground-glass pattern with expansion and periapical clearing in an elderly patient is nearly diagnostic for Paget's disease. Alkaline phosphatase, calcium, and phosphorus levels should be obtained; bone biopsy is recommended. Alkaline phosphate is characteristically elevated, whereas calcium and phosphorus levels are within normal limits. Although fibrous dysplasia and hyperparathyroidism may show similar radiographic features, the former is seen in young persons and is restricted to one quadrant, and the latter

fails to expand bone and is characterized by an elevated serum calcium level.

TREATMENT

Calcitonin is effective only temporarily, yet intravenous administration of biphosphonates has shown promise. Patients developing periapical inflammation or requiring tooth extraction should receive antibiotics because widespread osteomyelitis, which is difficult to control, is a complication.

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HYPERPARATHYROIDISM

Figure 10-40

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The jaw manifestations of hyperparathyroidism are rare and, when present, are encountered only late in the course of the disease. The result of an adenoma of the parathyroid gland with increased output of parathormone, the characteristic laboratory finding is an elevation in serum calcium levels with a decreased level of phosphorus. Elevated calcium leads to precipitation of mineral in tissues (metastatic calcification), particularly in the bladder; this action leads to nephrocalcinosis and urolithiasis. Elevated calcium levels also cause muscular weakness and lethargy. Mobilization of calcium from bone results in osteitis fibrosa cystica, a generalized demineralization; subperiosteal resorption in the middle phalanges is a characteristic finding. When the jaw is involved, multilocular radiolucencies representing giant cell brown tumors may be seen, or a diffuse ground-glass nonexpansile pattern may be encountered. The lamina dura is missing, and the teeth become mobile. The same changes can be seen in secondary hyperparathyroidism, which evolves subsequent to renal insufficiency and in which excessive urinary loss of calcium evokes a compensatory parathyroid hyperplasia.

A rare subset of patients with secondary renal hyperparathyroidism develop massive facial bone and calvarial enlargement deformities designated in the past as *leontiasis ossea*, and more recently as big *head disease, uglyfying face syndrome, or Sagliker syndrome*. Also, as mentioned previously in this chapter, familial hyperparathyroidism may have jaw area ossifying fibromas as an accompaniment.

MICROSCOPIC FEATURES

A fibro-osseous pattern prevails in the ground-glass lesion whereby fibrous stroma replaces normal bone and is stippled with irregular osseous trabeculae showing excessive osteoclastic activity.

DIFFERENTIAL DIAGNOSIS

Although the ground-glass pattern of hyperparathyroidism may be similar to that seen in fibrous dysplasia and osteitis deformans, expansion is lacking. The loss of lamina dura in conjunction with the ground-glass appearance in an isolated jaw quadrant occasionally is seen in metastatic

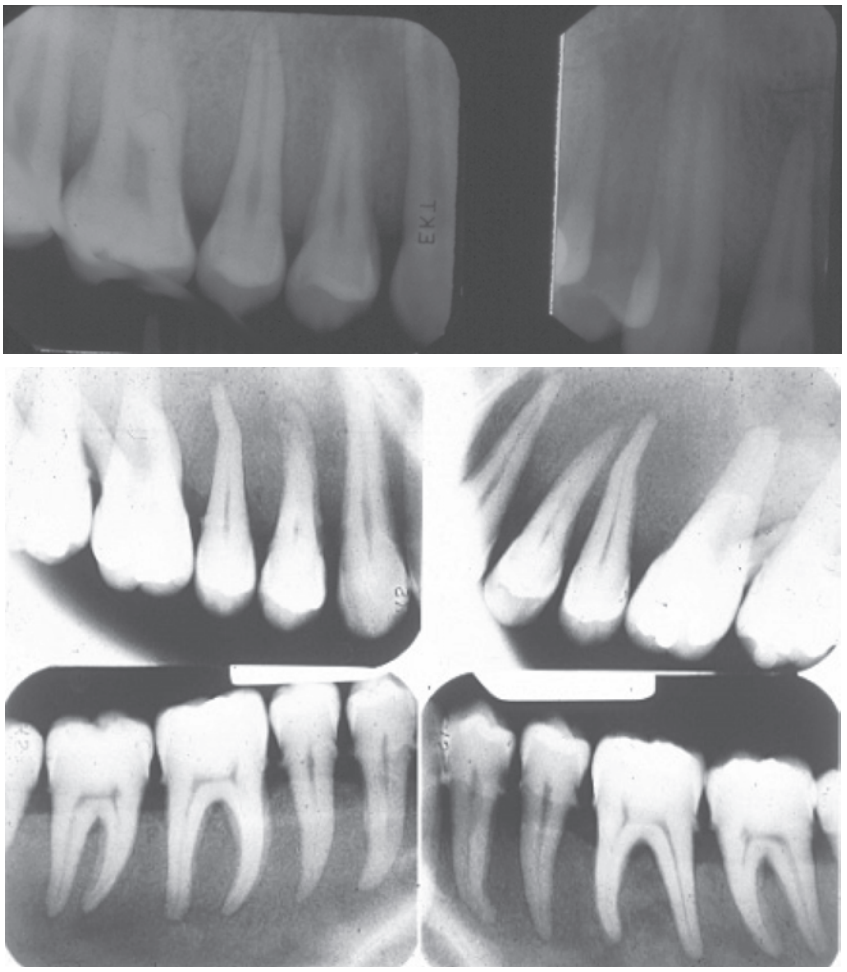

FIGURE 10-40
Secondary renal hyperparathyroidism with loss of lamina dura.

carcinoma or even primary sarcomas of the jaws. A bone chemistry profile, including calcium, phosphorus, and alkaline phosphatase levels, should be obtained, even when clinical symptomatology (urolithiasis, muscular weakness) points to a diagnosis of hyperparathyroidism.

TREATMENT

Once it has been determined that the cause for the ground-glass lesion is hyperparathyroidism (usually by an elevated serum calcium level), the patient should be referred to an internist to determine whether a primary neoplasm or renal disease is causative. Parathyroid adenomas are treated surgically. Even after elimination of the disease, the ground-glass pattern in the jaws may persist.

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SEGMENTAL ODONTOMAXILLARY DYSPLASIA

Figure 10-41

Age: Teens, adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

This anomaly is sporadic and is first noted during teenage years when routine dental or orthodontic radiographs are procured or when facial asymmetry becomes apparent. Unilateral asymmetry with maxillary enlargement is usually mild and may not be particularly noticeable. Radiographically, the area of alveolar enlargement shows a somewhat ground-glass appearance that is vertically streaked yielding a "falling rain or sleet" pattern. One or both premolar teeth are missing and retained deciduous teeth are morphologically anomalous.

MICROSCOPIC FEATURES

Pathologic changes in the affected maxillary bone are characterized by osteocytic hyperplasia (increased number of intralacunar osteocytes per unit area of bone), lacunar enlargement, and sheet-like arrangements of woven bone. Osteoblastic and osteoclastic activities appear decreased. The fibrous marrow element is hypocellular, mature, or myxoid. Affected teeth show variability in dentinal tubule diameter.

DIFFERENTIAL DIAGNOSIS

Fibrous dysplasia may be a consideration yet does not show anomalous or missing teeth.

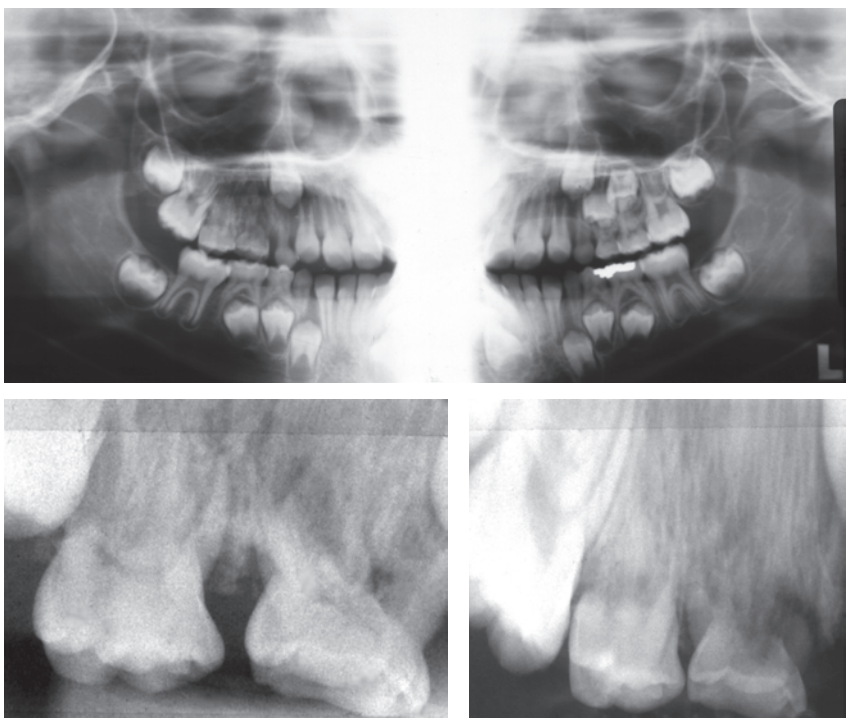

FIGURE 10-41
Segmental odontomaxillary dysplasia showing missing teeth and vertical sleet-like osseous changes.

TREATMENT

No treatment is necessary. Any unerupted teeth in the area of lesional bone should be extracted. If maxillary enlargement is a cosmetic concern, surgical contouring may be undertaken.

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OSTEOPETROSIS

Figure 10-42

Age: Childhood onset
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Osteopetrosis, also known as marble bone disease or Albers-Schönberg disease, is inherited as an autosomal dominant trait (benign form) or as an autosomal recessive trait (malignant form). The former may develop later in life; the severe recessive form is present from birth, and life expectancy rarely exceeds 20 years. The disease is apparently the result of defective osteoclastic activity, engendered by mutations in numerous genes (*CA-II*, *TCIRG1*, *ClCN7*, *OSTM1*, and *PLEKHM1*) that are all involved in the effector function of mature osteoclasts, being linked to acidification of the cell/bone interface. Unchecked osteoblastic activity leads to excessive osteogenesis. Radiographically, trabeculation is obscured by an extremely dense opacification of medullary bone. The bone may appear so dense that dental root morphology is obscured. Excessive endosteal bone formation results in a myelophthisic anemia and pancytopenia. Neural compression accounts for neurologic sensory and motor function deficits, and the long bones become brittle and are subject to fracture. Hepatosplenomegaly with extramedullary hematopoiesis, hydrocephalus, and mental retardation may be encountered.

MICROSCOPIC FEATURES

Medullary bone resembles cortex with thick anastomosing lamellar trabeculae obliterating soft tissue marrow.

DIFFERENTIAL DIAGNOSIS

The other entities included as ground-glass opacities are finely granular and should not be confused radiographically with osteopetrosis, which is strikingly radiodense. Familial historic genetic mapping may uncover affected relatives of the propositus.

TREATMENT

There is no effective treatment. Periapical infections may progress to severe osteomyelitis. Dental sepsis and extraction of teeth in affected individuals should be treated in conjunction with antibiotic therapy.

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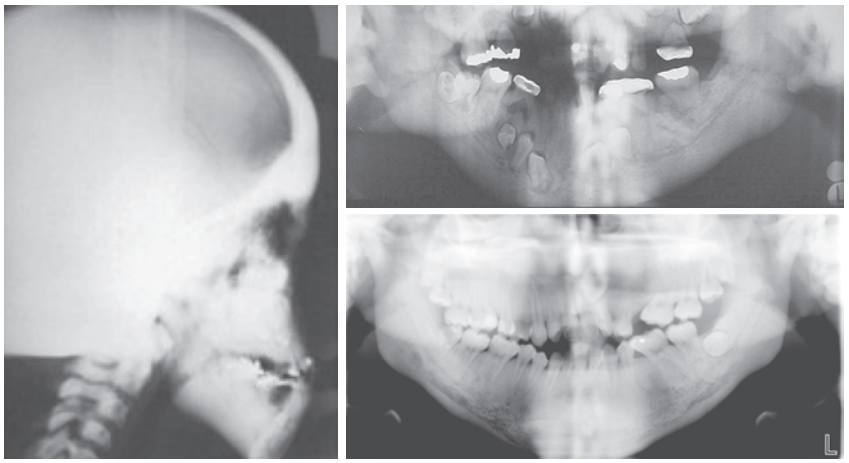

FIGURE 10-42
Osteopetrosis. Teeth are obscured by opacification.

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Multifocal Confluent (Cotton-Wool) Radiopacities

OSTEITIS DEFORMANS (PAGET'S DISEASE OF BONE)

Figure 10-43

Age: Elderly adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Osteitis deformans is a dysplastic bone disease of older people that is more severe in females than in males, yet affects males more frequently than females. The molecular underpinnings involve mutations in the sequestosome gene and the tumor necrosis family gene *TNFRSF11A* (osteoprotegrin). It is polyostotic; when the long bones and spine are severely involved, deformity and crippling results. The skull and maxilla are rarely spared, with expansile overgrowth that is uniformly symmetric. Osteoblastic hyperactivity prevails, with resultant excess secretion of osteoblastic alkaline phosphatase. The enzyme may be detected in elevated serum levels often approaching 10-fold elevations over normal amounts. As the craniofacial bones expand, the skull and upper face enlarge, with resulting increase in hat size, inability to wear dentures, or, if the patient is dentulous, diastema formation. Bone enlargement in the area of neural foramina results in bizarre nerve deficits such as hearing loss, blindness, and facial palsy. The early stages appear as ground-glass radiopacities; as the disease progresses, osteoblastic activity prevails, with the appearance of multifocal radiopacities in the maxilla, yielding a cotton-wool pattern. The process is generalized throughout the maxilla and calvarium, and is bilateral. Hypercementosis is a common finding. The jaws are susceptible to odontogenic infection; therefore, widespread osteomyelitis may develop. Patients with Paget's disease are at risk for malignant transformation to osteogenic sarcoma or fibrosarcoma central in bone.

MICROSCOPIC FEATURES

A fibro-osseous pattern predominates with irregular osseous trabeculae implanted in a hypercellular vascular marrow. Concomitant osteoblastic and osteoclastic rimming trabe-

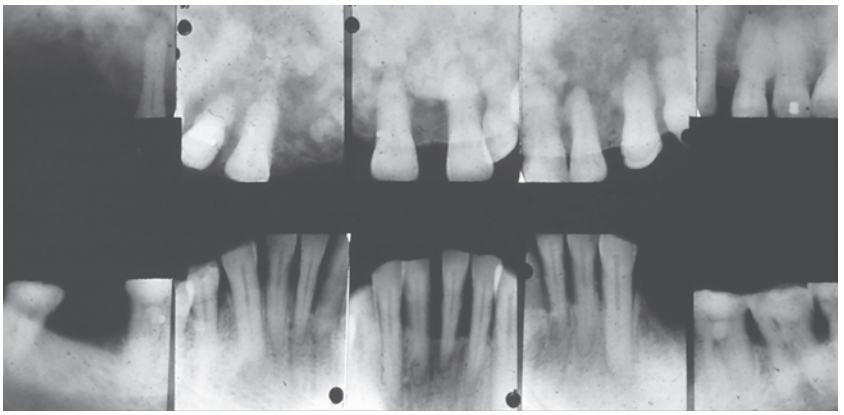

FIGURE 10-43
Osteitis deformans with ground-glass and confluent dense ossifications.

culae is a dominant feature. Large dense and compact trabeculae are riddled with basophilic resting and reversal lines, producing a jigsaw-puzzle arrangement. Occasionally, giant cell lesions accompany Paget's disease.

DIFFERENTIAL DIAGNOSIS

The cotton-wool, multifocal radiodense conglomerates seen in osteitis deformans may also be encountered in florid cemento-osseous dysplasia and Gardner's syndrome. The osseous lesions are restricted to the maxillofacial complex in these disorders, whereas in Paget's disease of bone, the skull, long bones, and vertebrae are also usually involved. The jaw lesions of Paget's are usually maxillary with only occasional involvement of the mandible, as opposed to florid cemento-osseous dysplasia, which is more common in the mandible. The presence of supernumerary teeth and other features of Gardner's syndrome are unique, allowing for differentiation on a clinicoradiologic basis. Alkaline phosphatase level elevations are a feature of Paget's disease; these values are not significantly elevated in other diseases considered in the differential diagnosis. In addition, the mosaic bone pattern observed microscopically is not featured in other diseases.

TREATMENT

Osteitis deformans is managed by administration of bisphophonates. When dental abscess occurs, necessitating extraction, antibiotic coverage should be provided to circumvent the complication of osteomyelitis. Follow-up both clinically and radiographically for sarcomatous change is indicated.

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FLORID OSSEOUS DYSPLASIA

Figure 10-44

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Florid cemento-osseous dysplasia occurs predominantly in middle-aged black women and has been postulated to represent a low-grade inflammatory lesion of

the jaws, resulting from pulpal or periapical infection; hence the term *diffuse sclerosing osteomyelitis.* Alternatively, an infectious source is usually not identifiable. For this reason, the condition has been suggested to represent a dysplastic process of periodontal ligament (cementoblastic) origin common in black females. Nevertheless, it is occasionally seen in members of other races. Radiographically, one or all four jaw quadrants can be affected, although there is a tendency to be limited to or more extensive in the mandible. The jaws possess multiple confluent radiopacities yielding a cotton-wool pattern. More often than not, the jaws are edentulous. Sequestrum formation with a surface nodularity may be demonstrable, but expansion of the cortices is lacking or present to a limited degree. The alkaline phosphatase level is usually within normal limits. The pathologic osseous tissue is susceptible to infection, with development of acute osteomyelitis with bony sequestration and fistula formation.

MICROSCOPIC FEATURES

A fibro-osseous histologic pattern prevails in areas devoid of acute inflammation. A hypercellular fibrous stroma supports curvilinear trabeculae that show the polarization microscopic features of cementum; however, some examples are composed predominantly of bone. Mononuclear inflammatory cells, if present at all, are sparse.

DIFFERENTIAL DIAGNOSIS

The cotton-wool radiographic appearance of florid osseous dysplasia is easily confused with that of osteitis deformans. The former is primarily mandibular, extragnathic osseous lesions are absent, and the alkaline phosphatase level is normal; in Paget's disease, the dysplastic osseous

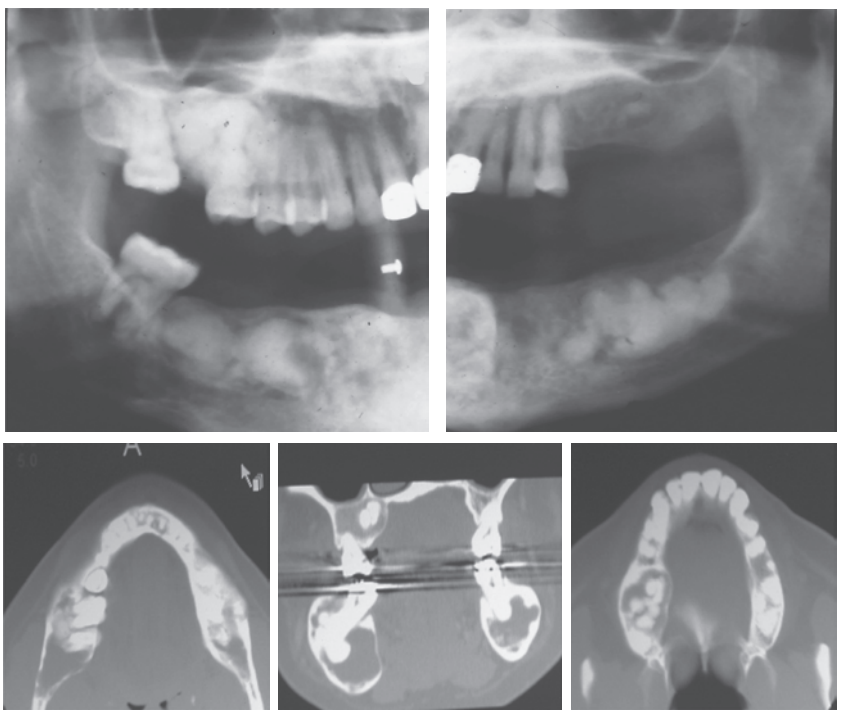

FIGURE 10-44
Florid osseous dysplasia. Lower panels show expansion, an uncommon finding, with lucent and opaque foci.

process is polyostotic, the alkaline phosphatase level is elevated, and the maxillary quadrants are affected exclusively or more extensively than those of the mandible. Gardner's syndrome must also be included in the differential diagnosis. The cotton-wool osteomas of this syndrome are rarely limited to the jaws, the sinuses being a common site of localization. In addition, the other manifestations of Gardner's syndrome are diagnostic.

TREATMENT

No treatment is required. Should osteomyelitis of an acute nature evolve, antibiotic therapy with surgical removal of sequestra and debridement is recommended.

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GARDNER'S SYNDROME

Figure 10-45

Age: Young adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Inherited as an autosomal dominant trait, Gardner's syndrome is characterized by multiple osteomas of the jaws and sinuses, supernumerary teeth, desmoid (fibrous) tumors of skin, epidermal inclusion cysts, and intestinal polyps with a predilection for malignant transformation into adenocarcinomas. A mutation in the *AP1* tumor suppressor gene (adenomatous/polyposis) is the underlying molecular lesion. The intestinal polyps are limited to colorectal mucosa and can be detected on gastrointestinal radiologic analysis and proctoscopic examination. The skin lesions are multiple and appear as nodular, smooth-surfaced lesions located primarily on the trunk and back. The manifestations include multiple supernumerary teeth and odontomas, most of which are impacted. The osteomas are demonstrable on jaw, panographic, and Water's sinus radiographs as multiple diffuse and confluent radiopacities that may involve all four jaw quadrants. The antra and frontal sinuses often contain similar irregular radiodensities. Because the osteomas may reside both centrally and in parosteal locations, clinically detectable indurated protuberances can be identified on palpation.

MICROSCOPIC FEATURES

The osteomas are composed of dense lamellar Haversian bone with scant fibrous stroma.

DIFFERENTIAL DIAGNOSIS

The multifocal cotton-wool radiodensities of Gardner's syndrome are similar radiologically to the lesions encountered in Paget's disease and florid osseous dysplasia. A tendency for localization of osteomas in the sinuses, the presence of supernumerary teeth, and the other features of the syndrome are sufficient to rule out these other entities.

TREATMENT

The osteomas may be removed if they interfere with function or present a cosmetic problem. Supernumerary teeth and odon-

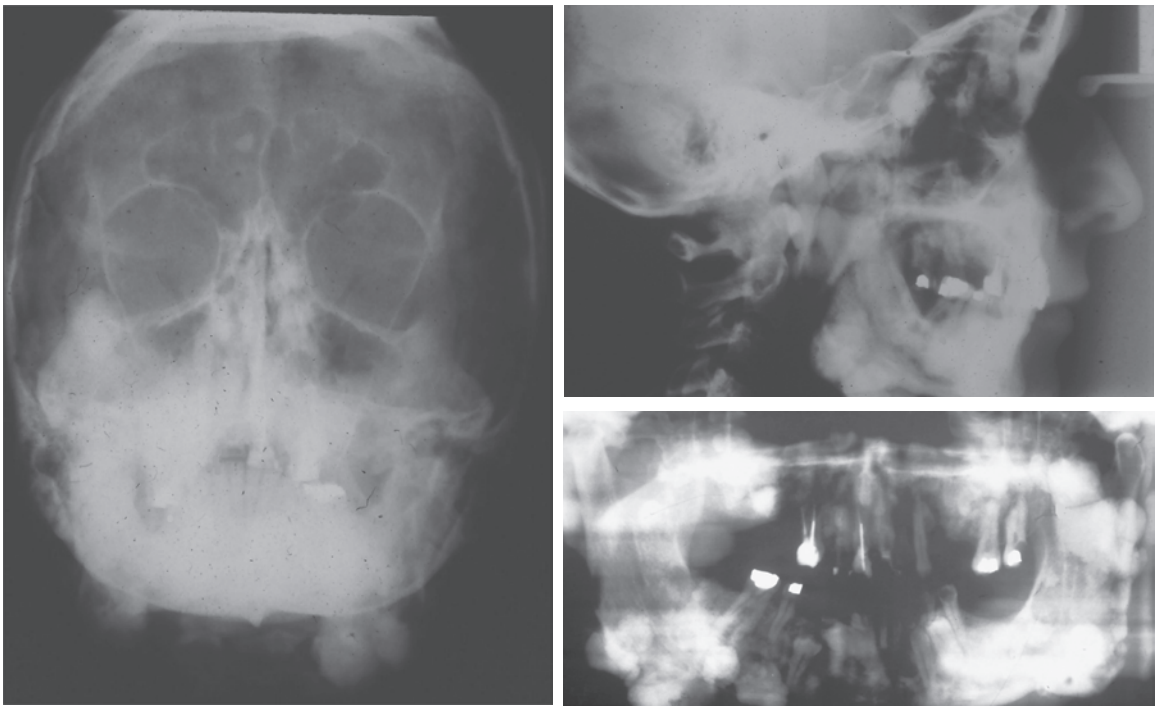

FIGURE 10-45
Gardner's syndrome. Multiple osteomas.

tomas should be removed. Patients should be referred to a gastroenterologist because intestinal adenocarcinoma is the most serious aspect of this syndrome.

Additional Reading

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FAMILIAL GIGANTIFORM CEMENTOMA

Figure 10-46

Age: Evolves during childhood
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The familial gigantiform cementoma is a rare disease in which only a few family pedigrees have been reported. Clinically, painless expansion of the jaws occurs. Although a single lesion may appear initially, multiple sites eventually become evident either clinically or radiographically. Although both upper and lower jaws may be involved, bilaterality is common as well. The radiographs disclose large, sometimes huge, expansile lesions that are generally fairly well delineated. The lesions are mixed radiolucent/radiopaque

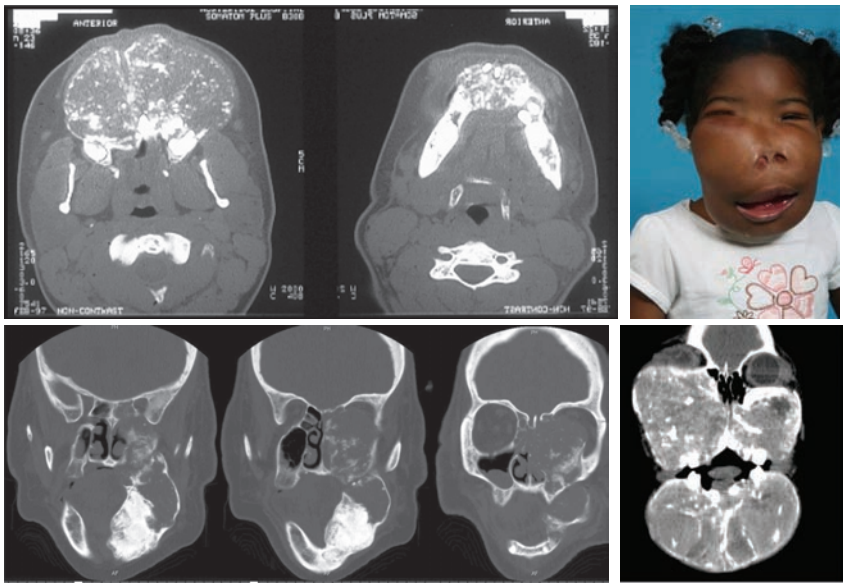

FIGURE 10-46
Gigantiform cementoma. Multifocal massive lesions with marked facial deformity. Courtesy of Dr. Samir ElMofty.

yet become more dense with ensuing years, and confluent opacities superimposed over dental roots may progress from one molar around to the next. The disease appears to be inherited as an autosomal dominant trait with considerable variability of expressivity, particularly with regard to the number and size of lesions. There are other instances of large, expansile ossifying fibromas that involve more than one quadrant in which no familial tendency has been documented.

MICROSCOPIC FEATURES

Typical fibro-osseous histologic characteristics are observed whereby the stroma is collagenous and somewhat cellular with monomorphic appearing fibroblasts. Irregular and haphazardly arranged osseous trabeculae are present and may form into confluent sclerotic masses. Small ovoid calcifications are also common.

DIFFERENTIAL DIAGNOSIS

Familial gigantiform cementoma has been erroneously confused with florid osseous dysplasia. Although both manifest radiographically demonstrable diffuse and confluent opacities of both jaws, only familial gigantiform cementoma has the potential for massive enlargement with a hereditary disposition. Paget's disease may show similar features, yet does not begin at an early age.

TREATMENT

The lesions are often huge and disfiguring requiring surgical intervention. Although recurrence may be anticipated in younger patients, once they reach adult life, surgical osseous recontouring, although not ablative, is usually successful; lesional tissue may persist, yet the potential for recurrent growth is often limited or nonexistent.

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Cortical Redundancies (Onion-Skin Patterns)

GARRÉ'S PERIOSTITIS

Figure 10-47

Age: Children and teenagers
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Garré's periostitis represents a reactive periosteal proliferative inflammatory response to infection or trauma. In the jaws, proliferative periostitis is typically associated with chronic diffuse sclerosing osteomyelitis and may or may not have an odontogenic microbial source. A soft tissue or parotid abscess overlying periosteum may also stimulate periosteal osteogenesis. As new bone is formed, expansion becomes evident; radiographically, a redundant cortical layering phenomenon is usually but not invariably encountered. A constant radiographic feature is preservation of the normal boundary of the cortex subjacent to the expanded region. The disease is essentially confined to the mandibular body when the jaws are affected. Toothache or dull bone pain may cause the patient to seek dental consultation.

MICROSCOPIC FEATURES

A fibro-osseous histologic pattern prevails, with a cellular fibroblastic stroma interposed between irregular or parallel trabeculae of woven or lamellar bone. Scattered mononuclear inflammatory cells are often observed.

DIFFERENTIAL DIAGNOSIS

The cortical layering with expansion seen in Garré's periostitis is also encountered

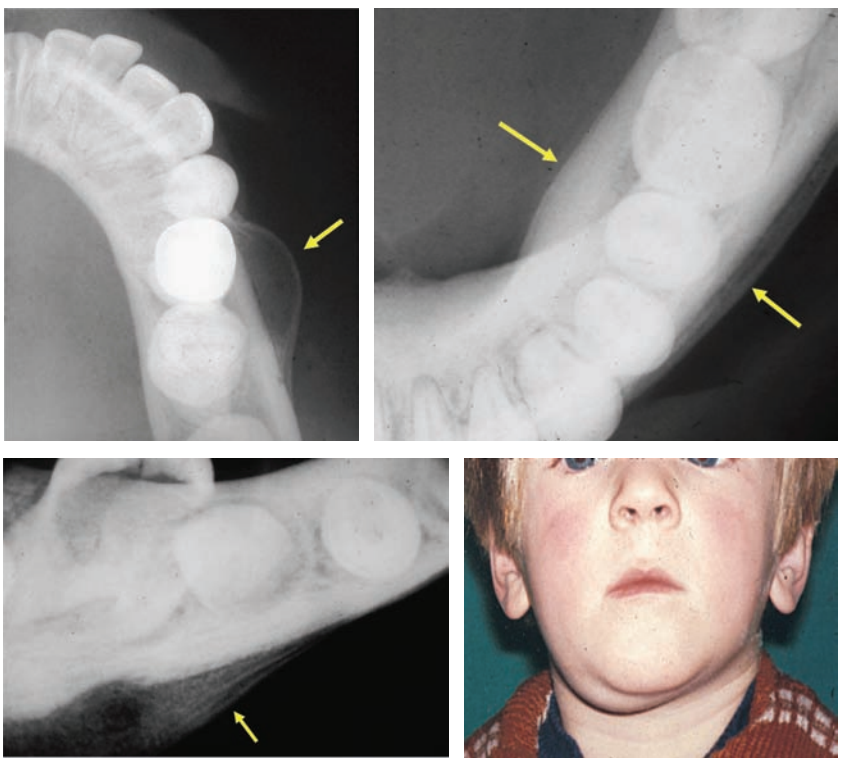

FIGURE 10-47
Diffuse sclerosing osteomyelitis with periosteal onion skinning (Garré's).

in Caffey's disease and Ewing's sarcoma. Because Garré's periostitis is an inflammatory disorder, an infectious source, usually a carious molar tooth with a periapical radiolucency, can be identified. Caffey's disease is seen in infants, is bilateral, and involves numerous bones of the appendicular skeleton. A biopsy is recommended to rule out Ewing's sarcoma.

TREATMENT

The periosteal proliferative response becomes arrested and remodels to normal contour once the infectious process responsible for its genesis has been eliminated.

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INFANTILE CORTICAL HYPEROSTOSIS

Figure 10-48

Age: Infants
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Inherited as an autosomal dominant trait, infantile cortical hyperostosis or Caffey-Silverman disease begins before 6 months of age as a polyostotic cortical hyperostosis. The thickened cortices reflect exaggerated periosteal osteogenesis, which has been suggested to evolve subsequent to tissue hypoxia resulting from genetically defective periosteal vessels. It has been proposed that all infants exhibit an accelerated appositional bone growth spurt, and periosteal redundancy is merely an exaggerated form of this growth phase, which is radiographically demonstrable in some infants. Clinically, the overlying soft tissues are tender, warm, and swollen. The swellings are bilateral and are particularly obvious about the mandible. Fever and leukocytosis are generally apparent. Radiographically, the body and ramus manifest expansion with onion-skin cortical redundancy. Within a few months, the generalized condition resolves spontaneously.

MICROSCOPIC FEATURES

The microscopic features of the osseous lesions have not been well delineated.

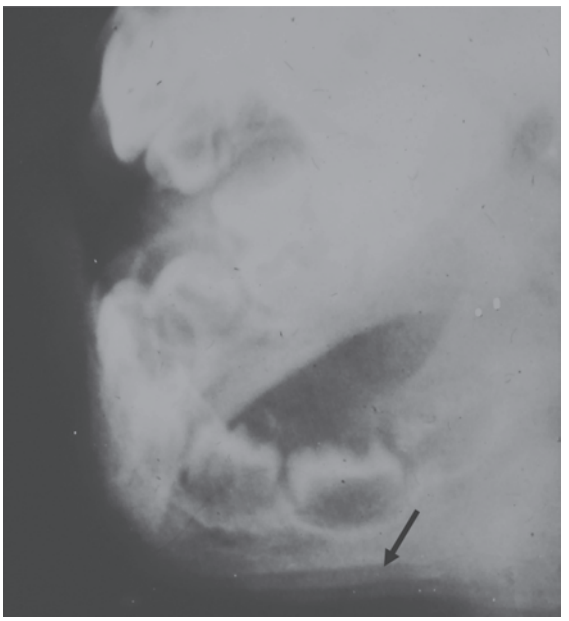

FIGURE 10-48
Infantile cortical hyperostosis with periosteal neoosteogenesis.

DIFFERENTIAL DIAGNOSIS

The polyostotic symmetric distribution of cortical redundancies of infancy permit differentiation from other diseases manifesting similar radiographic features. Familial fibrous dysplasia or cherubism shows bilateral mandibular expansion. Cortical redundancy is not a feature, however; the jaw lesions of cherubism are multilocular and expansile.

TREATMENT

No treatment is necessary because the disease spontaneously regresses. Despite this fact, some residual jaw deformity may predispose to malocclusion.

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GENERALIZED CORTICAL HYPEROSTOSIS

Figure 10-49

Age: Childhood onset
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Generalized cortical hyperostosis or Van Buchem's disease is inherited as an autosomal recessive trait that maps to chromosome 17q12-q21. The disease is characterized by generalized thickening of the cortical table throughout the skeleton, primarily the tubular bones, the calvaria, and the mandible. The hyperostotic changes become evident during the second decade of life. The jaw is squared and enlarged. Thickening of the cranial base may eventually lead to foramina narrowing with attending neurologic deficits, including facial paralysis, optic atrophy, and hearing loss. Serum alkaline phosphatase levels are elevated. Radiographically, the cortices show a two or threefold thickening. *Sclerostosis* is a variant form that favors the calvaria, mandible, and clavicles along with syndactyly. Typical facies are observed in infancy and include a long face with high forehead, hypertelorism, enlarged head, and mandibular prognathism.

MICROSCOPIC FEATURES

Grossly, the cortices are thickened with irregular grooving and osteophyte formation. The cortical Haversian bone is thickened yet histologically unremarkable.

DIFFERENTIAL DIAGNOSIS

Sclerostosis and Van Buchem's disease are similar, but they can be differentiated on the basis of the digital anomalies observed in sclerostosis. Osteopetrosis may manifest similar changes, yet the entire medullary bone is hyperostotic and yields a diffuse, rather than strictly cortical, opacification.

TREATMENT

There is no effective treatment. Cosmetic surgery of the mandible has been undertaken successfully.

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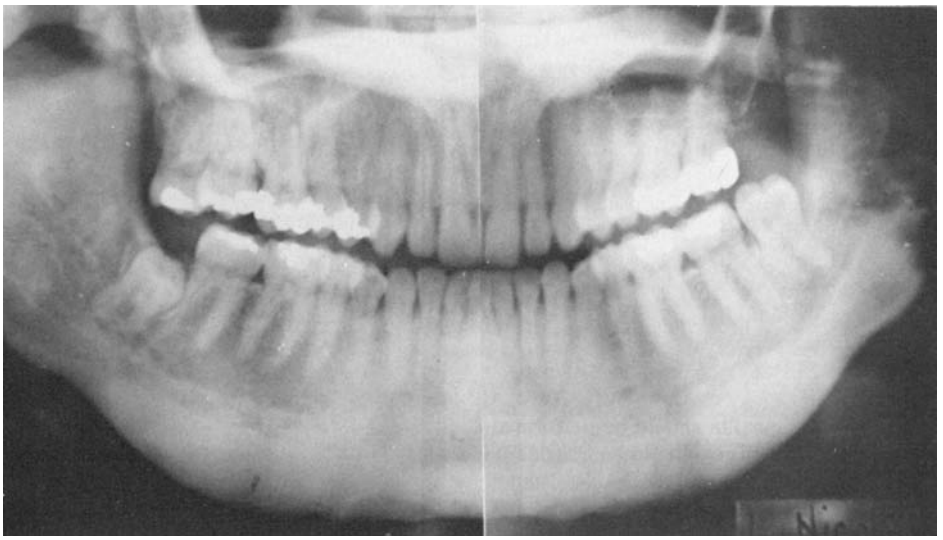

FIGURE 10-49
Sclerostosis is bilateral.

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JUXTACORTICAL OSTEOGENIC SARCOMA

Figure 10-50

Age: Adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Also termed *parosteal osteogenic sarcoma*, the juxtacortical neoplasm apparently arises from periosteal osteoblasts, and elaboration of tumor bone is peripheral. The mandible is affected more often than the maxilla, and the prognosis of this type of osteogenic sarcoma is much more favorable than that of its endosteal counterpart. Pain may be featured; however, the most common complaint is alveolar swelling with a history of rapid growth. Radiographically, a mottled appearance of opacification is observed on periapical films. Occlusal radiographs reveal the characteristic features. An onion-skin appearance is usually not apparent; instead, an irregular opacification is observed, and radially protruding osteophytic spicules can be identified. Cortical invasion with erosion may be featured. Occasionally, the periosteal new growth is clearly demarcated from cortex by an interposed radiolucent band. Such lesions are referred to as periosteal osteogenic sarcoma.

MICROSCOPIC FEATURES

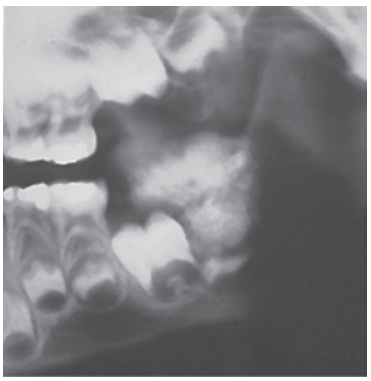
Most of these neoplasms are well differentiated; others are anaplastic. Pleomorphic osteoblasts and a hypercellular stroma are observed with formation of irregular trabeculae, which are also hypercellular. Chondroid foci are present in one half the cases.

DIFFERENTIAL DIAGNOSIS

Both proliferative periostitis and infantile cortical hyperostosis show onion-skin patterns as opposed to irregular osteophytic changes. Myositis ossificans and fasciitis ossificans should be considered in the radiographic diagnosis.

TREATMENT

Despite the peripheral orientation of the tumor, an en bloc resection of the underlying



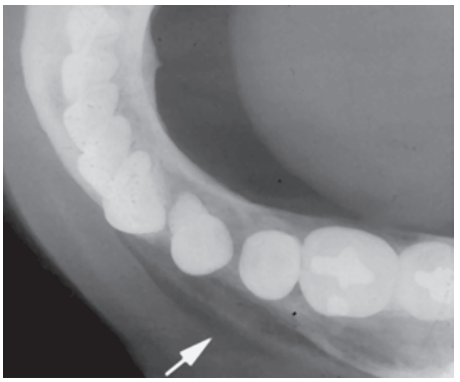
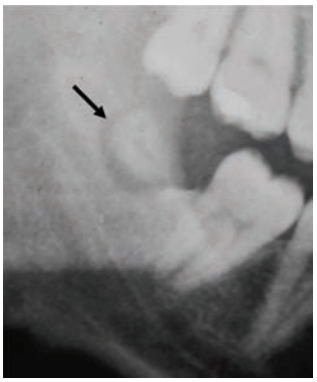


FIGURE 10-50
Osteogenic sarcoma, sunburst patter, and periosteal reaction.



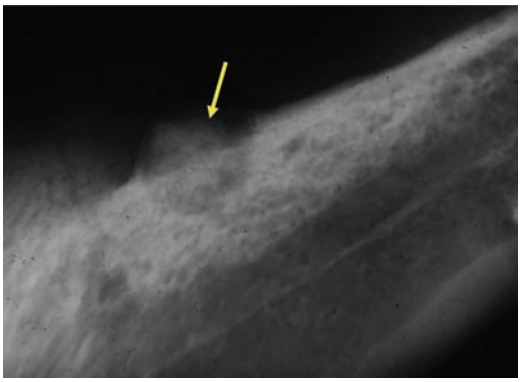


FIGURE 10-51
Osteoid osteoma over cortex.

mandible or maxilla should be performed. Adjunctive chemotherapy should be considered for those lesions with invasion of the endosteum. Anaplastic invasive tumors behave poorly, similar to those lesions arising centrally. Patients with well-differentiated peripheral tumors have shown a 75% 5-year survival.

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OSTEOID OSTEOMA

Figure 10-51

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Osteoid osteoma is a benign self-limited bone lesion that arises in the cortex. The lesion may be painful if compressed. It usually presents with a faint central radiolucency within a round radiopaque structure that is generally around 1 cm in diameter. An outer lucent halo yields a target appearance.

MICROSCOPIC FEATURES

A central nidus of formative osteoid is encountered with a fibro-osseous appear-

ance. The bone external to the nidus is more mature and lamellar with prominent osteoblastic rimming, becoming accentuated radially at the periphery.

DIFFERENTIAL DIAGNOSIS

Differentiation from cementoblastoma is based on the fact that osteoid osteoma is located on the cortex and not in continuity with tooth roots as is cementoblastoma. Within the nidus, the lesion shows histologic similarities to the aggressive tumor benign osteoblastoma.

TREATMENT

Surgical excision is the preferred treatment.

Additional Reading

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MANDIBULAR TORI AND EXOSTOSES

Figure 10-52

Age: Middle-aged adults
Sex: Female predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Mandibular tori are bony excrescences located in the premolar region on the lingual alveolus; exostoses are similar developmental osseous nodules found at the mucobuccal fold on the maxillary buccal alveolar ridge. Both, if large enough, are visible radiographically as multiple, usually bilateral, ovoid radiodensities superimposed over the premolar and molar roots. These lesions are quite common, occurring in nearly 8% of the population, and have a familial tendency. They may continue to grow slowly with advancing years.

MICROSCOPIC FEATURES

The osseous nodules are composed of a thickened outer cortical plate of Haversian bone. Medullary trabeculae extend internally and are admixed with an intervening fibroadipose marrow.

DIFFERENTIAL DIAGNOSIS

Exostoses and mandibular tori may radiographically simulate the jaw lesions of osteitis deformans, osteomyelitis, and Gardner's syndrome. Tori and exostoses, as opposed to these other diseases, manifest radiopacities located near the crest of the alveolus without extension below root apices. When the radiographic findings are compared with the clinical features, a definitive diagnosis is easily rendered.

TREATMENT

No treatment is required unless the bony nodules interfere with function or placement of a prosthetic appliance. In these instances, they may be removed surgically.

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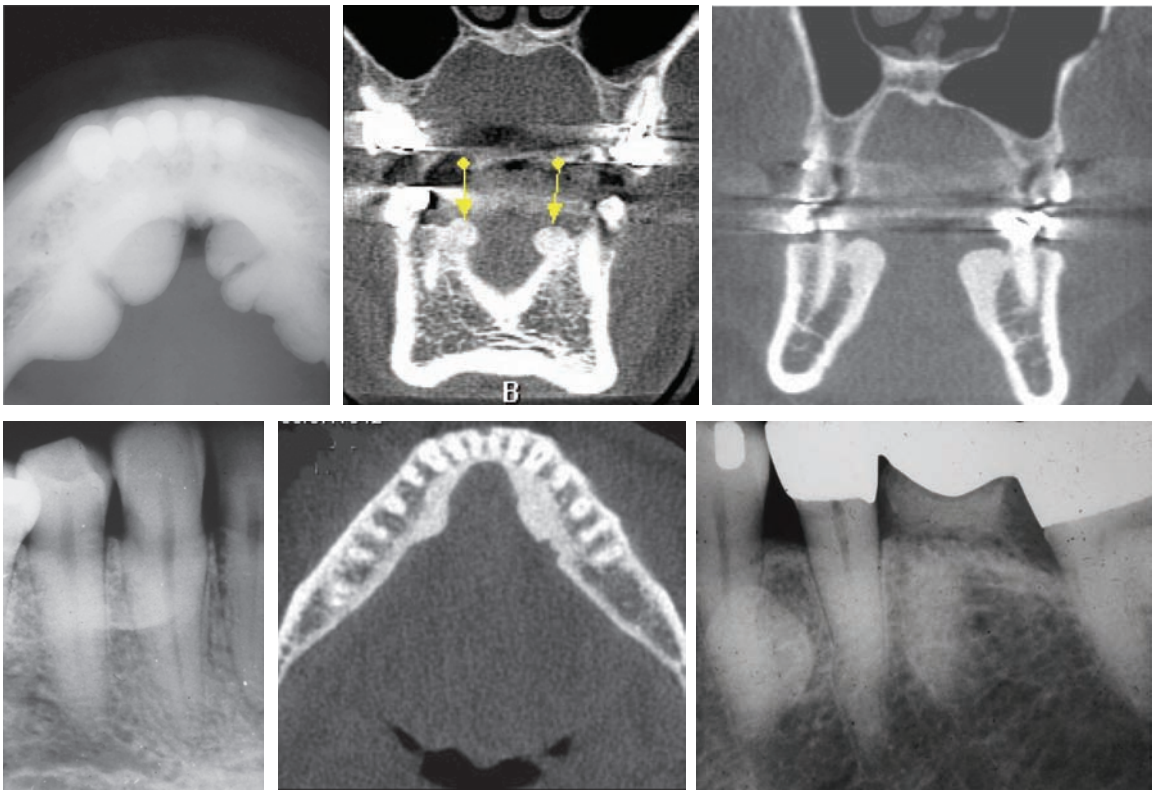

FIGURE 10-52
Tori and exostoses superimposed over teeth.

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Irregular, Ill-Defined Expansile Radiopacities

CALCIFYING EPITHELIAL ODONTOGENIC TUMOR

Figure 10-53

Age: Middle-aged adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The Pindborg or calcifying epithelial odontogenic tumor is a neoplasm of epithelial origin. Clinically, depending on the size and duration, cortical expansion or facial asymmetry heralds its presence. Radiographically, the tumor may manifest many patterns, one of the predominant ones being a mixed radiolucent-radiopaque expansile lesion with irregular configuration. The margins are poorly defined, and osteophytic spicules may project outward, yielding a sunray pattern. Most cases are associated with an impacted tooth, and the body or ramus regions of the mandible are favored sites.

MICROSCOPIC FEATURES

The neoplastic epithelial element exists in sheets or islands of eosinophilic or clear polygonal cells with vesicular nuclei. Often bizarre and pleomorphic nuclear elements are encountered, but this feature has no bearing on the prognosis. Within the stroma and often in intimate association with the

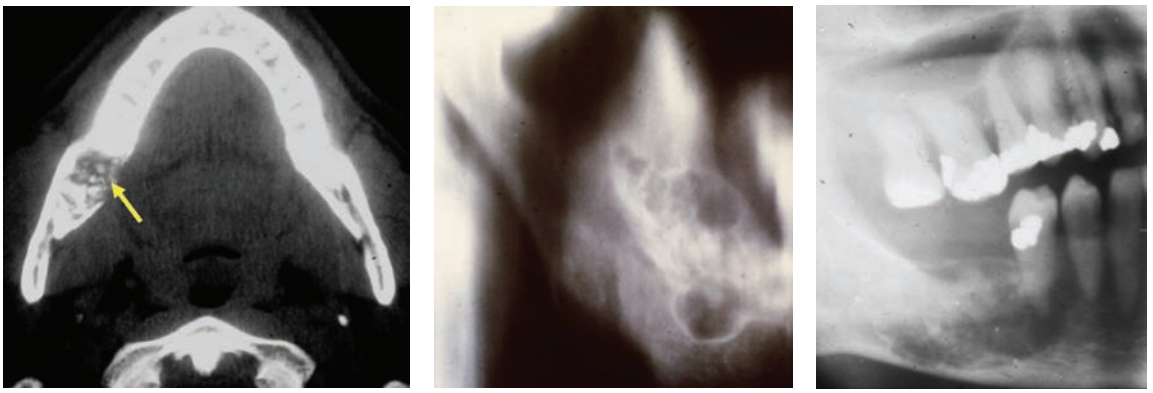

FIGURE 10-53
Calcifying epithelial odontogenic tumor with irregular calcifications and expansion.

epithelial islands are amorphous globules of amyloid material. Circular and ovoid laminated calcifications or Leisegang rings are seen in most tumors.

DIFFERENTIAL DIAGNOSIS

When the Pindborg tumor appears radiographically as an expansile ill-defined lesion with irregular radiodense conglomerates and spicules, malignant neoplasms of bone should be considered in the differential diagnosis. If an impacted tooth is encompassed by a lesion with the aforementioned features, Pindborg tumor should be the foremost consideration. Biopsy is required in any case.

TREATMENT

Pindborg tumor is aggressive and recurs if adequate therapy is not instituted. Large lesions require resection, hemimandibulectomy, or partial maxillectomy; smaller tumors may be cured by en bloc or marginal resection.

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DESMOPLASTIC AMELOBLASTOMA

Figure 10-54

Age: No predilection
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

The desmoplastic ameloblastoma is a variant of ameloblastoma that has been segregated owing to its unique radiographic and histologic features. Ameloblastomas are most frequently found in the posterior body and ramus of the mandible; however, the desmoplastic variant is found with equal frequency in the maxilla and mandible and has a tendency to arise in the anterior regions. Radiographically, many of these tumors are mistaken for fibro-osseous lesions owing to their mixed radiolucent-radiopaque appear-

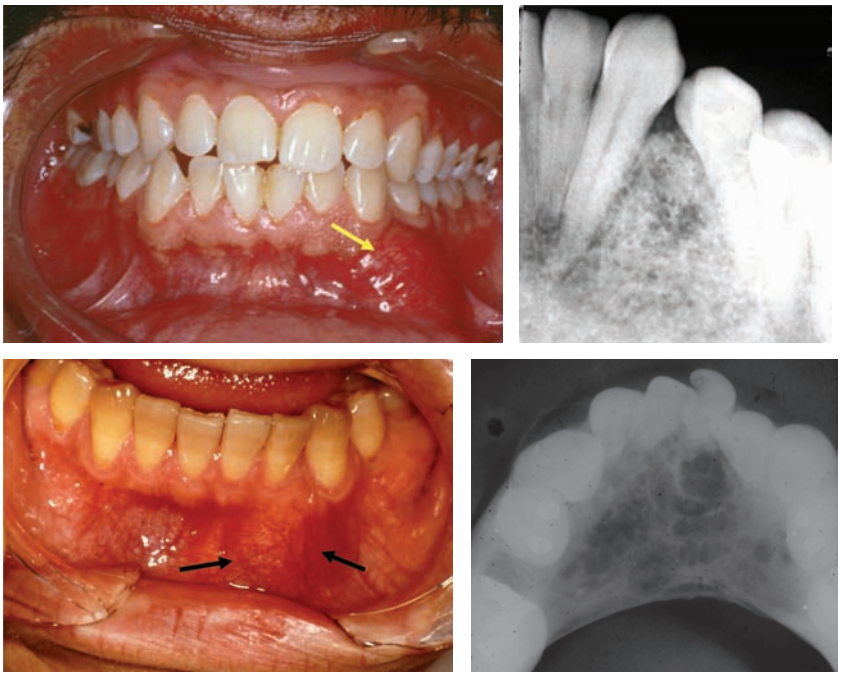

FIGURE 10-54
Desmoplastic ameloblastoma with a benign fibro-osseous-like pattern.

ance. Although some are well delineated, others show diffuse margins without any cortication. Clinically, painless expansion is the chief complaint, although in many instances, the patient is not aware of any signs or symptoms.

MICROSCOPIC FEATURES

Characteristically, the stroma dominates over the epithelial neoplastic component. Thin cords of hyperchromatic epithelial cells are seen and many islands fail to show distinct ameloblastic columnar cells, although careful perusal of the tissue generally reveals foci of stellate reticulum and some attempts at ameloblastic differentiation. Adenoid structures are commonly found. The stroma is densely collagenous and abundant.

DIFFERENTIAL DIAGNOSIS

Radiographically, as mentioned previously, these tumors are often mistaken for benign fibro-osseous lesions, especially fibrous dysplasia. The lack of margination may be suggestive of metastatic tumor or primary sarcoma. Biopsy is required to obtain a definitive diagnosis.

TREATMENT

Small lesions should be treated by surgical enucleation, whereas larger tumors with poorly defined margins are probably better managed by en bloc or marginal resection with reconstruction. Although data are limited, these tumors appear to behave in similar fashion to ordinary ameloblastoma.

Additional Reading

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OSTEOGENIC AND CHONDROGENIC SARCOMA

Figure 10-55

Age: Teenagers and young adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Both osteogenic and chondrogenic sarcomas of the jaws are rare. They show similar radiographic features, although sarcomas of chondroblastic origin tend to be more radiolucent. When the tumor cartilage or osteoid calcifies, both chondrosarcoma and osteosarcoma can manifest irregular, poorly marginated radiopaque foci. Osteogenic sarcomas show a sunray or sunburst pattern of osteophytic radiodense spicules in 25% of the cases. Expansion of the alveolar cortices is demonstrable both clinically and radiographically. The mandible is more often affected than the maxilla. Pain, paresthesia, and loosening of teeth in the region of tumor are common complaints. Both sarcomas tend to metastasize via hematogenous routes.

MICROSCOPIC FEATURES

Osteogenic sarcomas are histologically divided into three groups: osteoblastic, chondroblastic, and fibroblastic. This classification has no bearing on prognosis. The tumor may differentiate along all three cell lines; yet, regardless of the preponderance of fibrous and cartilaginous elements, the sine qua non of osteogenic sarcoma is the elaboration of neoplastic osteoid matrix. Tumor osteoid is found in all osteogenic sarcomas, including the chondroblastic variant. Chondrosarcomas fail to elaborate tumor osteoid. The cellular element is composed, in both instances, of pleomorphic angulated, polygonal, or spindle-shaped cells.

DIFFERENTIAL DIAGNOSIS

Irregular, poorly marginated radiopacities should always suggest a tentative diagnosis of osteogenic or chondrogenic sarcoma. Pindborg tumor, particularly if an impacted tooth is associated with the lesion, and metastatic carcinoma must be considered in the differential radiographic diagnosis. Biopsy is required to arrive at a definitive diagnosis.

TREATMENT

The prognosis for osteogenic sarcoma is better for mandibular (70% 5-year survival) than for maxillary tumor (50% 5-year survival). Information of this nature does not exist for chondrosarcoma of the jaws. The treatment consists of maxillectomy with preservation of the orbit if extent of disease allows. Mandibular tumors are treated with intraosseous radium needles with external radiation when soft tissues are involved (10,000 rad total dosage). After radiation, en bloc resection or hemimandibulectomy is performed.

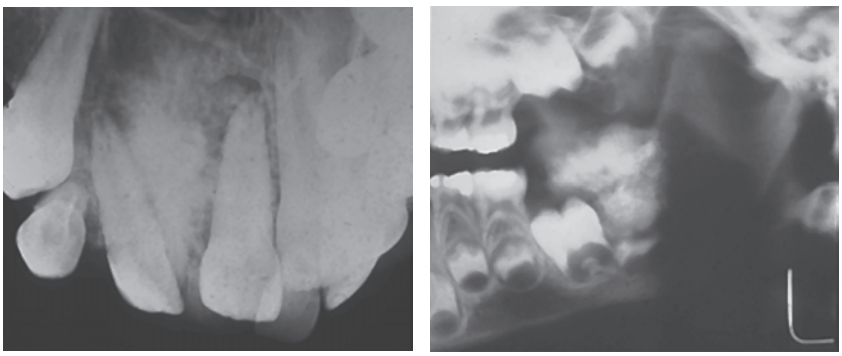

FIGURE 10-55
Osteogenic sarcoma.

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METASTATIC CARCINOMA

Figure 10-56

Age: Middle-aged and elderly adults
Sex: Depends on primary site

CLINICAL AND RADIOGRAPHIC FEATURES

Carcinoma arising in the lung, breast, thyroid, prostate, and colon tends to metastasize to bone. When the jaws become a metastatic depot, these malignancies may become deposited in marrow spaces and actually simulate osteoblastic activity. The body and ramus areas of the mandible are most frequently involved. The chief clinical finding is paresthesia of the lower lip. Radiographically, expansion is usually obvious, as are focal radiolucent zones admixed with irregular radiopaque foci. The margins of the metastatic lesion are poorly defined. Metastatic carcinoma is the most common malignant tumor of the jaws.

MICROSCOPIC FEATURES

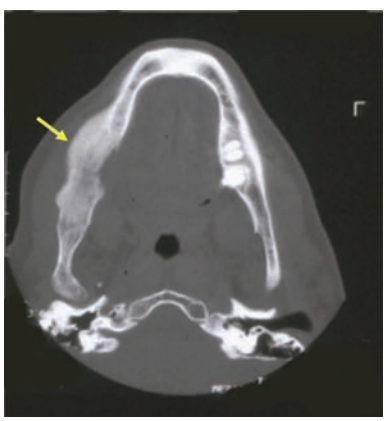
The microscopic features are variable, depending on the tissue site of origin. In general, nests, cords, or sheets of neoplastic epithelial cells show pleomorphism, anaplasia, and numerous mitotic figures. The tumor cells are dispersed within a fibrous stroma and lie in juxtaposition to dense and irregular osseous trabeculae.

DIFFERENTIAL DIAGNOSIS

The irregular, poorly marginated radiopacities as seen in osteoblastic metastatic carcinomas are also seen in Pindborg tumor, osteogenic sarcoma, and chondrosarcoma. A history of cancer elsewhere in the body helps to limit the differential diagnosis; however, microscopic confirmation is necessary. On the other hand, the jaw metastasis may be the first indication of a primary tumor of internal organs.

TREATMENT

The primary tumor must be identified, as well as other sites of metastasis; a skeletal



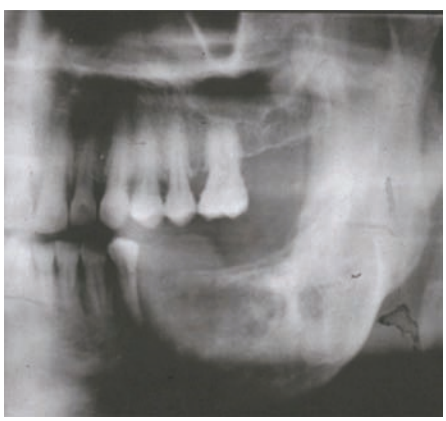


FIGURE 10-56
Osteogenic reaction in metastatic disease to the mandible.

survey is indicated to detect other osseous foci of disease. The prognosis is extremely poor. An oncologist should manage patient care.

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Superimposed Soft Tissue Radiopacities

SIALOLITHIASIS

Figure 10-57

Age: Middle-aged adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Salivary stones are calcium phosphate salts that crystallize about a central nidus

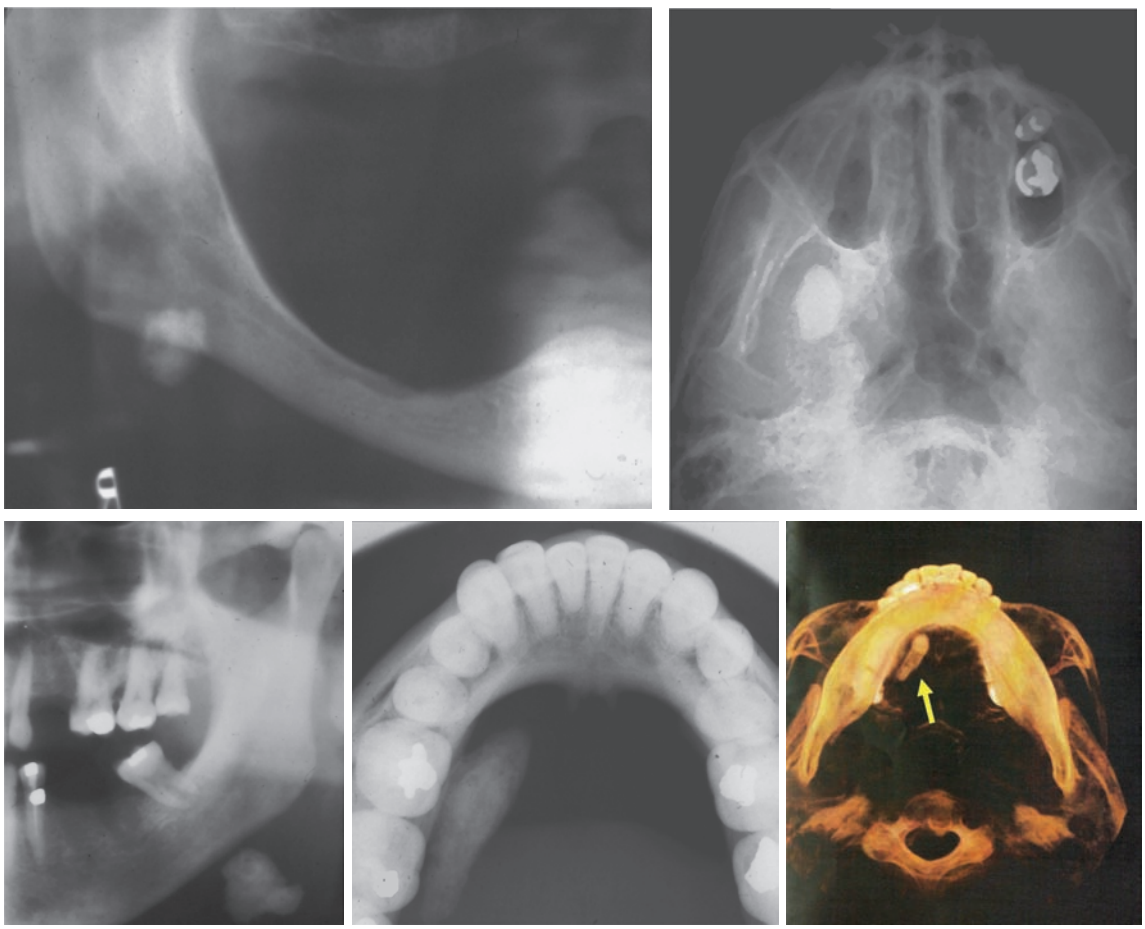

FIGURE 10-57
Sialoliths and calcified submandibular gland (lower left).

of gelled mucin, desquamated epithelial cells, or bacterial colonies. They are most frequently formed within the submandibular ducts, but may arise within the parotid gland or minor salivary gland ducts of the lips or buccal mucosa. When a major duct becomes occluded, swelling with sialadenitis ensues and pain while eating is a common complaint. Many patients may be asymptomatic. Milking the involved gland fails to elicit flow. When submandibular sialoliths become large, they produce a radiopacity that may become superimposed over the mandible on dental films. They are well circumscribed and oval or elongated; if the entire gland becomes filled with intraductal stones, they may show a cauliflower pattern radiographically. An occlusal radiograph helps to locate the stone in the soft tissue of the oral floor. No relationship exists between hyperparathyroidism and a tendency to form salivary calculi.

MICROSCOPIC FEATURES

The decalcified stone shows concentric laminations without viable cellular elements. The ducts show sialodochitis with squamous, mucous, or respiratory epithelial metaplasia. The gland displays acinar degeneration with fibrous and mononuclear leukocytic infiltration representing a chronic sclerosing sialadenitis.

DIFFERENTIAL DIAGNOSIS

When a stone is superimposed over the body of the mandible, a central lesion manifesting a radiopaque appearance must be included in the differential diagnosis. Occlusal and soft tissue films rule out the possibility of a central lesion. Other soft tissue lesions, which may manifest a superimposed radiopacity, must also be considered.

TREATMENT

Small stones may be manipulated manually through the duct orifice. Larger ones may require surgical extirpation, although the use of a lithotripter is a nonsurgical alternative form of therapy. If recurrent sialadenitis with a purulent discharge develops after removal, sialadenectomy is usually indicated.

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PHLEBOLITHIASIS

Figure 10-58

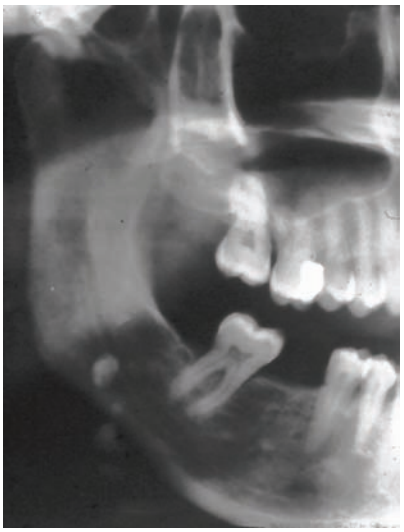
Age: No predilection
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Phleboliths are calcified thrombi that form within the lumina of dilated vascular channels. They are most frequently encountered in hemangiomas and varices. The vascular lesions can be visualized clinically and are generally palpable, particularly when phleboliths are present. When these lesions arise in tissues such as the cheek, lips, and tongue, the calcifications, which may be multiple, are demonstrable on dental radiographs. The stones appear as circular or oval, well-demarcated focal radiopaque foci.

MICROSCOPIC FEATURES

Vascular channels are dilated and intraluminal thrombi are present. Within these thrombosed regions, dystrophic and laminated calcific foci are observed.



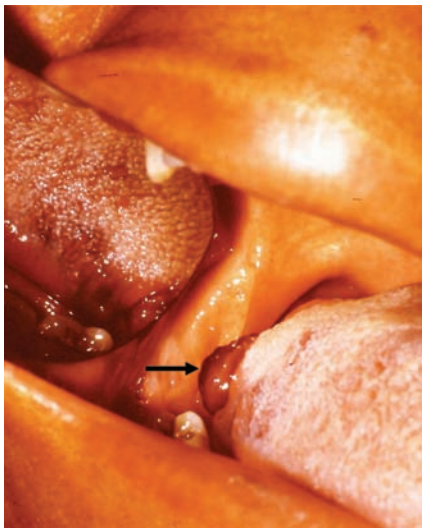


FIGURE 10-58
Pleboliths in a hemangioma at the base of the tongue.

DIFFERENTIAL DIAGNOSIS

Phleboliths with radiographically demonstrable calcifications must be differentiated from central osseous lesions. Occlusal and soft tissue radiographs rule out this possibility. Other soft tissue disorders manifesting radiopacities must be included in the differential radiographic diagnosis. Clinical examination discloses the presence of a vascular lesion unless it is deep seated; in these instances, biopsy is indicated.

TREATMENT

Because most hemangiomas show a cessation in growth potential, no treatment is required provided the diagnosis has been confirmed. Surgical removal may be indicated if function is compromised by the tumor or if cosmesis is a concern.

Additional Reading

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OSSEOUS/CARTILAGINOUS CHORISTOMA

Figure 10-59

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Benign nodular growths of cartilage or bone occasionally encountered in the oral mucosa are self-limited choristomas. Such lesions may occur in any submucosal location yet are most common in the tongue. Radiographically, depending on the view ordered, the calcified nature of the choristoma is evident as an opacity. In panoramic or periapical radiographs, a round or oval opacification may appear to overlie the mandible if the lesion is located in the tongue. Most of these calcified choristomas can be palpated and an occlusal film will disclose its soft tissue localization.

MICROSCOPIC FEATURES

These hard tissue choristomas may histologically consist of benign, mature bone, cartilage, or both. A fibrous capsule is generally observed and fibrous tissue marrow-like spaces may be seen.

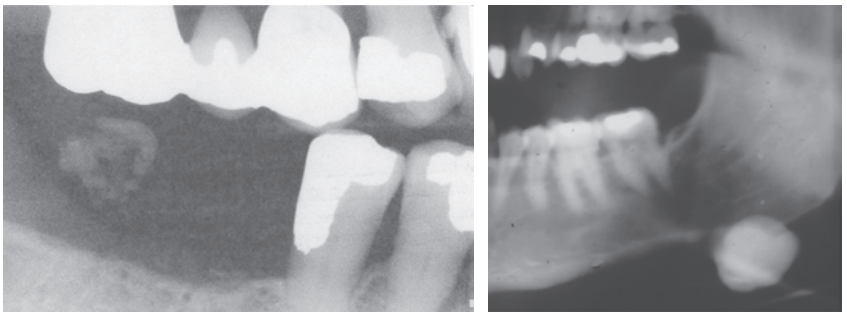

FIGURE 10-59
Osseous choristomas in the soft tissues.

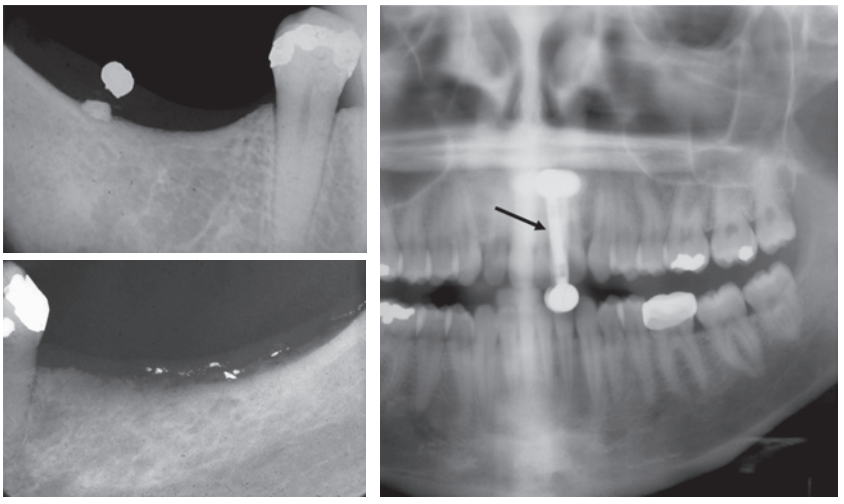

FIGURE 10-60
Foreign bodies: amalgam tattoos and tongue piercing (right).

DIFFERENTIAL DIAGNOSIS

Osteocartilaginous choristomas may be confused radiographically with sialoliths and phleboliths, both of which tend to be oval or round. Palpation of a mass in the tongue or other mucosal sites warrants a biopsy.

TREATMENT

Simple excision is recommended. Recurrence is extremely rare.

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FOREIGN BODIES

Figure 10-60

Age: No predilection
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Foreign objects are introduced into the oral soft tissues as a result of traumatic or iatrogenic injuries. Dental amalgam and metal fragments from automobile accidents or assault are the more frequently encountered foreign bodies that are demonstrable radio-

graphically. When these metallic objects become lodged within the buccal mucosa, lips, tongue, alveolar ridges, or gingiva, they appear as irregular ragged radiopacities superimposed over the maxilla or mandible. Many foreign bodies are easily visualized clinically as discolorations or swellings, or they may be palpable. Tongue, lip, and buccal mucosal piercings have made for some interesting radiographic artistry.

MICROSCOPIC FEATURES

Metallic foreign bodies cannot be processed for routine microscopy. The surrounding tissue may be fibrous, granulomatous with giant cells, or acutely inflamed, depending on the chemical and physical properties of the foreign object.

DIFFERENTIAL DIAGNOSIS

Foreign-body radiopacities superimposed over bone are usually readily identifiable because of irregular outline or configuration of the metal deposit. In addition, the opacity is generally more dense and homogeneous than that of calcific lesions. Soft tissue films and biopsy provide a definitive diagnosis.

TREATMENT

The foreign body should be excised, particularly if a fistula or swelling is present. Amalgam pigmentation seen clinically in conjunction with a radiopacity does not require treatment.

Additional Reading

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CALCIFIED LYMPH NODES

Figure 10-61

Age: Adults
Sex: No predilection

CLINICAL AND RADIOGRAPHIC FEATURES

In the head and neck area, submandibular, cervical, and digastric nodes are most often enlarged during infectious processes. Occasionally, a node or group of nodes with longstanding lymphadenopathy undergoes fibrosis and subsequently develops foci of dystrophic calcification. Scrofula, or tuberculous lymphadenitis, is probably the most prevalent disease process to eventuate in nodal calcification. Actinomycosis, cats-cratch fever, and other chronic infectious diseases may also eventually become quiescent with dystrophic calcification of sclerotic nodes. Radiographically, a single ovoid calcification or clustered calcifications may be encountered in regions in which groups of lymph nodes are typically found.

MICROSCOPIC FEATURES

The normal architecture of the lymph node is usually obliterated; however, the periphery may occasionally be represented by aggregates of lymphocytes and atrophic germinal centers. The central zone is occupied by dense collagenous connective tissue with confluent deposits of calcification.

DIFFERENTIAL DIAGNOSIS

Calcified lymph nodes radiographically resemble sialoliths, phleboliths, or foreign bodies. Sialography is often helpful in that the calcified node is not associated with the duct tree. A history of scrofula or other diseases associated with chronic lymphadenitis aids in arriving at a definitive diagnosis,

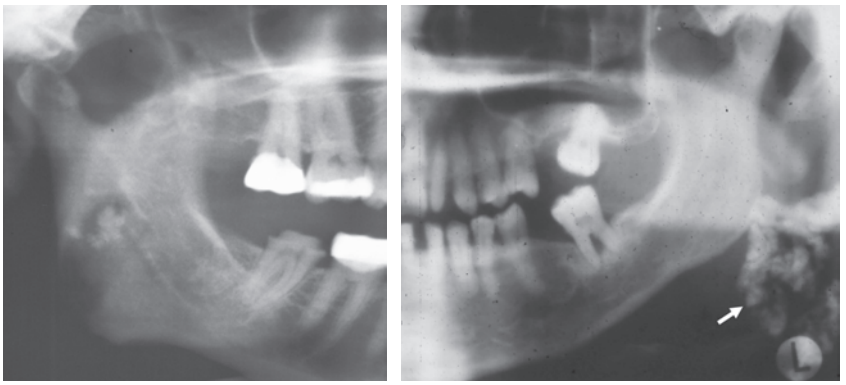

FIGURE 10-61
Calcified lymph nodes.

particularly when the radiopacities are located in an area known to be populated by lymph nodes.

TREATMENT

No treatment is required.

Additional Reading

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MYOSITIS OSSIFICANS

Figure 10-62

Age: Adults
Sex: Male predilection

CLINICAL AND RADIOGRAPHIC FEATURES

Ossification of muscle occurs in a generalized form that begins in childhood and becomes progressively more extensive with ensuing age. In this form, intestinal smooth muscle, skeletal muscle, and fascia undergo calcification. The facial muscles may be involved. The etiology is unknown. The second form, seen in a single muscle, is more often encountered in the perioral musculature and is secondary to trauma (traumatic myositis ossificans). The traumatic episode is thought to produce an intramuscular hematoma, which organizes and subsequently calcifies. The masseter, temporal, pterygoid, and geniohyoid muscles have been reported to be involved by this process. The affected muscle shows rapid enlargement subsequent to trauma and then becomes indurated. Motion may be limited. Radiographically, the muscle involved shows a radiopaque zone that may be discrete or show frayed margins. Myositis ossificans in the masseter, pterygoids, or muscles in the floor of the mouth manifest a radiopacity superimposed over the mandible.

MICROSCOPIC FEATURES

Osteoid trabeculae are rimmed by osteoblasts, and the intervening fibrous tissue is hypercellular. The overall picture is one of extremely active osteoplasia that has been mistaken for sarcoma. The ossified zone is surrounded by muscle fibers. Mononuclear inflammatory cells are occasionally present in limited number.

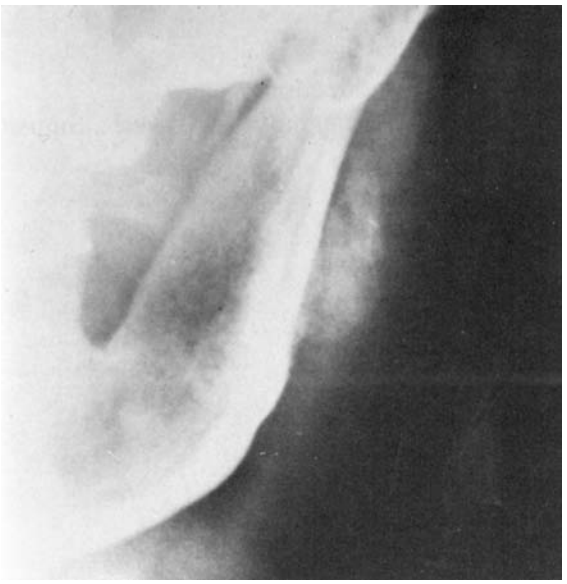

FIGURE 10-62
Myositis ossificans in masticatory muscles. (Right photo from Plezia RA, Mintz SM, Calligaro P. Myositis ossificans traumatica of the masseter muscle. *Oral Surg Oral Med Oral Pathol.* 1977;44:351.)

DIFFERENTIAL DIAGNOSIS

The history and clinical features usually indicate that the radiopaque mass is external to bone. Radiographic views from various angles usually locate the lesion in the soft tissues in the vicinity of muscle. Sialoliths can be eliminated from consideration on the basis of location and symptoms, particularly with the aid of occlusal radiographs. In addition, most sialoliths and phleboliths are focal, small calcific structures, whereas the opacity seen in myositis ossificans is generally large and diffuse.

TREATMENT

Once a tentative diagnosis is established, the muscle can be entered surgically and the calcified mass is excised; a portion of the adjacent normal-appearing muscle must also be obtained. A biopsy is needed to confirm the clinical diagnosis. Recurrence is uncommon.

Additional Reading

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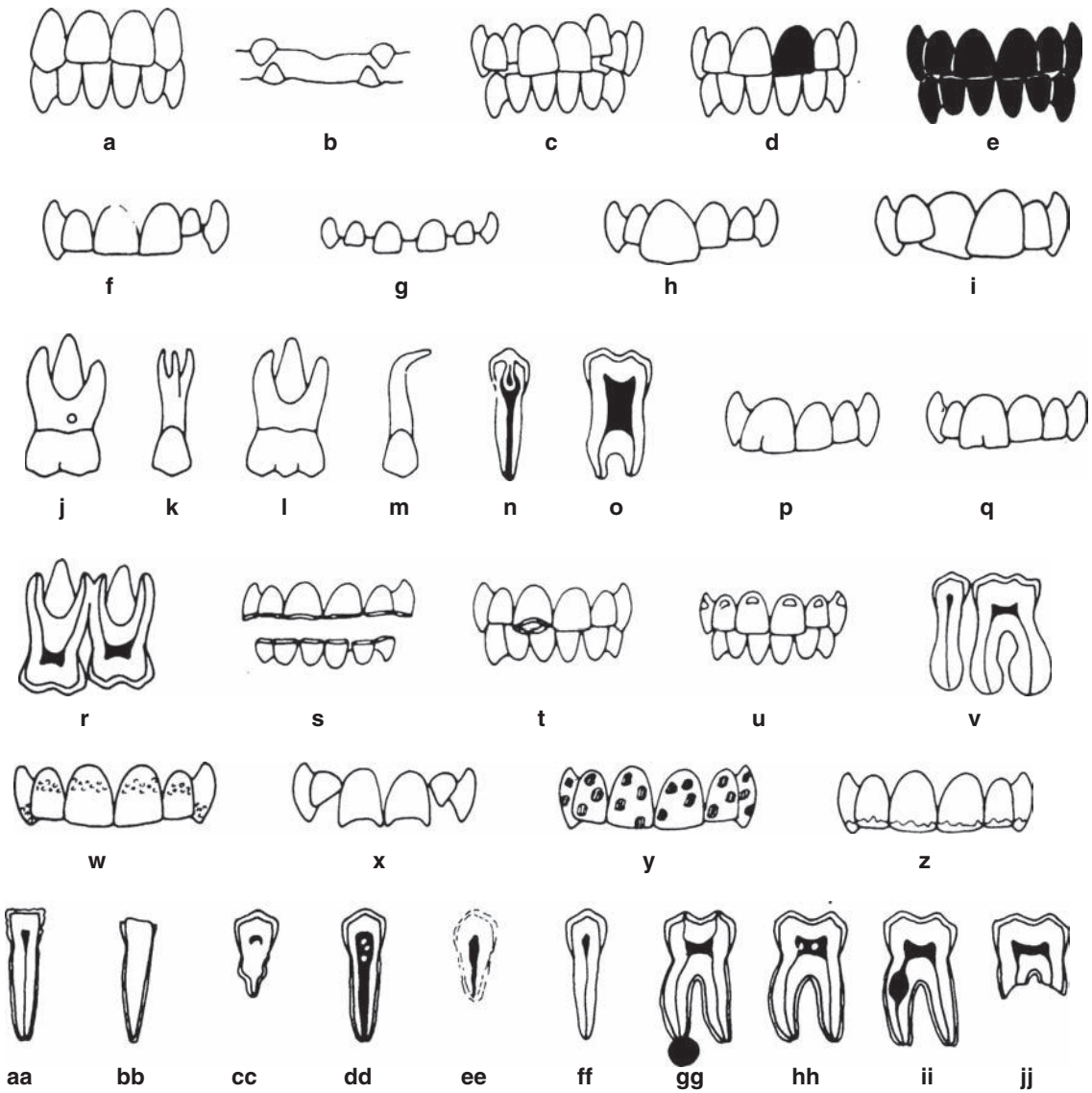

Dental Defects

a, Limited hypodontia; b, Severe hypodontia; c, Hyperdontia; d, Focal pigmentation; e, Generalized pigmentation; f, Localized microdontia; g, Generalized microdontia; h, Localized macrodontia; i, Generalized macrodontia; j, Enamel pearl; k, Accessory roots; I, Accessory cusps; m, Dilaceration; n, Dens-in-dente; o, Taurodontia; p, Fusion; q, Gemination; r, Concrescence; s, Attrition; t, Abrasion; u, Erosion; v, Hypercementosis; w, Enamel hypoplasia; x, Congenital syphilis; y, Fluorosis; z, Snowcapped teeth; aa, Amelogenesis imperfecta; bb, Dentinogenesis imperfecta; cc, Dentin dysplasia I; dd, Dentin dysplasia II; ee, Odontodysplasia; ff, Cemental agenesis (hypophosphatasia); gg, Vitamin D refractory rickets; hh, Pulp stones; ii, Internal resorption; jj, External resorption

Dental Defects 11

*Obliterated Pulp Chambers/ Root Canals**

Alterations in Eruption/ Exfoliation Times 601

Pigmentations 603

*Refer to other Headings in this Chapter for Detailed Description.

The anomalies of teeth have been categorized conventionally to include defects in number, morphology, and hard tissue structure. Most dental defects are strictly local; others are inheritable disorders associated with other anomalies of the jaws and/or other organ systems. Most of the dental defects outlined here are familial or follow definite Mendelian patterns of inheritance. Some are associated with life-threatening diseases.

Age predilection has been omitted for many of the entities included in this chapter. This omission is intentional, because it can be inferred that the defect makes its appearance at the time the dentition has completed development or the teeth have erupted, thereby being initially observable in children.

The most common disorders showing missing teeth are simple, uncomplicated cases of hypodontia. Missing teeth are seen in incontinentia pigmenti, a potentially fatal disease of females.

Supernumerary teeth are common. Gardner's syndrome is a potentially lethal disease associated with supernumerary and impacted teeth.

Common defects in size and morphology of teeth include accessory cusps, enamel pearl, dilaceration, and dens invaginatus.

The most common anomalies in dental structure are enamel hypoplasia, snowcapped teeth, and dental fluorosis. Hypophosphatasia, associated with premature exfoliation and cemental agenesis, is a potentially lethal metabolic bone disease.

Alterations in eruption and exfoliation processes are included in this chapter, as are diseases that cause the deposition of pigments either in or on dental hard tissues.

Alterations in Number: Missing Teeth

HYPODONTIA

Figure 11-1

Sex: No predilection

CLINICAL FEATURES

Hypodontia may involve both deciduous and permanent teeth but is far more often encountered in the latter. The third molars, any or all of them, are the most frequently observed congenitally missing teeth. The maxillary lateral incisors and second mandibular bicuspids are also frequently missing. Rarely does partial anodontia affect the mandibular lateral incisors and first molars. When deciduous teeth are involved, the maxillary lateral incisors are most often affected. When this occurs, the corresponding permanent succedaneous teeth are also usually missing. Hypodontia shows a definite familial tendency. Occasionally, numerous congenitally missing teeth are encountered in children who received radiation to the jaws as infants for therapeutic reasons. Tooth germs are quite sensitive to radiation and low doses may arrest or cause abortion of odontogenesis.

Two specific syndromes, both of which are rare, are associated with localized hypodontia. Böök's syndrome is characterized by premature whitening of the hair, hyperhidrosis of the palms and soles, and aplasia of the premolars and third molars. It is inherited as an autosomal dominant trait. Rieger's syndrome, also an autosomal dominant hereditary disorder, shows oligodontia and microdontia associated with iridial hypoplasia and anterior synechiae; occasionally, glaucoma is a complication. Missing teeth also occur in association with a variety of other rare syndromes.

TREATMENT

When teeth are congenitally missing, the occlusion is usually defective. Orthodontic therapy may be indicated.

Additional Reading

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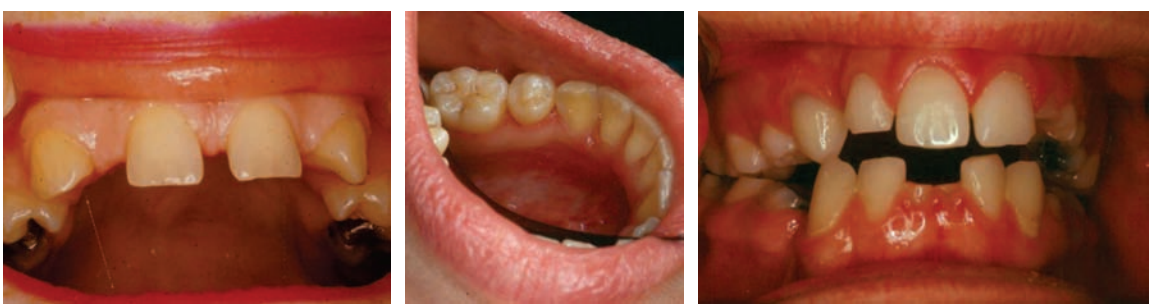

FIGURE 11-1
Partial anodontia.

INCONTINENTIA PIGMENTI

Figure 11-2

Sex: Exclusively in females

CLINICAL FEATURES

Incontinentia pigmenti is transmitted as an X-linked dominant trait and is lethal for males; only females with the disease survive infancy. Vesicular and erythematous skin lesions appear shortly after parturition, becoming keratotic. The characteristic lesions are diffuse, reticulated slate-gray macules that cover broad areas of the skin. Skeletal, ocular, and neurologic disorders accompany the disease. White lesions may be seen on the oral mucosa. Delayed eruption, conical crown forms, and oligodontia are the chief dental anomalies seen.

TREATMENT

The disease cannot be treated. The dental defects may be corrected with orthodontic and prosthetic therapy.

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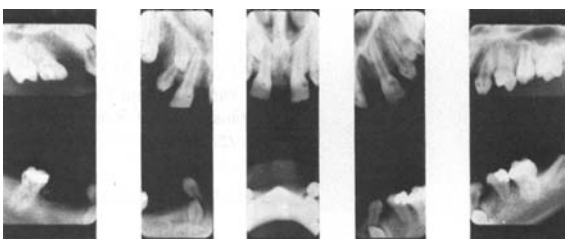

FIGURE 11-2
Hypodontia with coronal defects in incontinentia pigmenti. (Courtesy of Dr. R. Gorlin.)

HYALINOSIS CUTIS ET MUCOSAE

Figure 11-3

Sex: No predilection

CLINICAL FEATURES

Hyalinosis cutis et mucosae, also known as lipoid proteinosis and the Urbach-Wiethe syndrome, is inherited as an autosomal recessive disorder characterized by pathologic accumulation of glycoproteins in most bodily tissues. Hoarseness or a weak cry from infancy develops because of vocal cord infiltration. The skin develops vesicles that, after healing, appear as acneform scars with altered pigmentation; later, pale yellow nodules evolve. Multiple papules or nodules develop in the oral cavity, particularly on the tongue, buccal mucosa, and soft palate. Intracranial calcifications, particularly of the dorsum sellae, and seizures occur, as does decreased sensitivity to pain. Reported dental defects include hypodontia, primarily involving the maxillary lateral incisors and premolars.

TREATMENT

There is no known treatment for the systemic manifestations. Missing teeth may be replaced prosthetically.

Additional Reading

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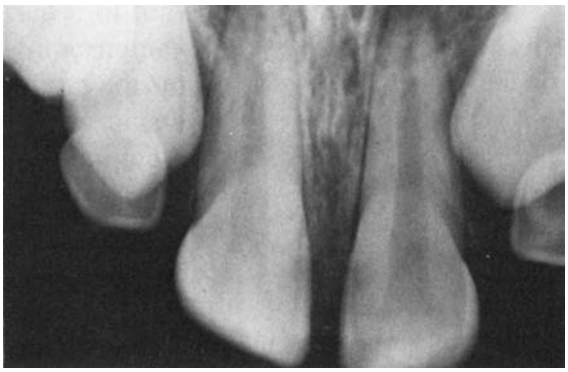

FIGURE 11-3
Missing lateral incisors in a child with hyalinosis cutis et mucosae.

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MANDIBULO-OCULO-FACIAL DYSCEPHALY

Figure 11-4

Sex: No predilection

CLINICAL FEATURES

The mandibulo-oculo-facial dyscephaly syndrome, also known by the eponym Hallermann-Streiff syndrome, is characterized by brachycephaly with frontal bossing, small face, beak-like nose, mandibular retrognathia, temporomandibular joint anomalies, open sutures, and microphthalmia with blue sclera. Hypotrichosis with absent brows, cutaneous atrophy, spinal deformities, and mild retardation are also featured. Hypodontia is seen with retention of deciduous teeth, although supernumerary teeth can also be present. Dental malformations are also commonly encountered. The syndrome is usually sporadic.

TREATMENT

As long as the deciduous dentition remains sound, it can be retained. Severe caries and malocclusion, which are common in this syndrome, should be treated accordingly. The craniofacial anomalies can be treated by orthognathic and plastic surgery.

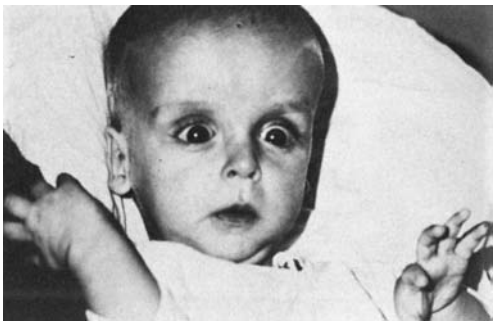

FIGURE 11-4
Mandibulo-oculo-facial dyscephaly. (Courtesy of Dr. Ray Stewart.)

Additional Reading

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HEREDITARY ECTODERMAL DYSPLASIA

Figure 11-5

Sex: Male predilection

CLINICAL FEATURES

Ectodermal dysplasia is a group of disorders with similar features and differing modes of inheritance. Usually inherited as an X-linked recessive trait, ectodermal dysplasia is seen in males. One of the few inherited structural defects to show genetic heterogenicity, ectodermal dysplasia may also show an autosomal dominant form of transmission, whereby females manifest the trait. A variety of forms are now

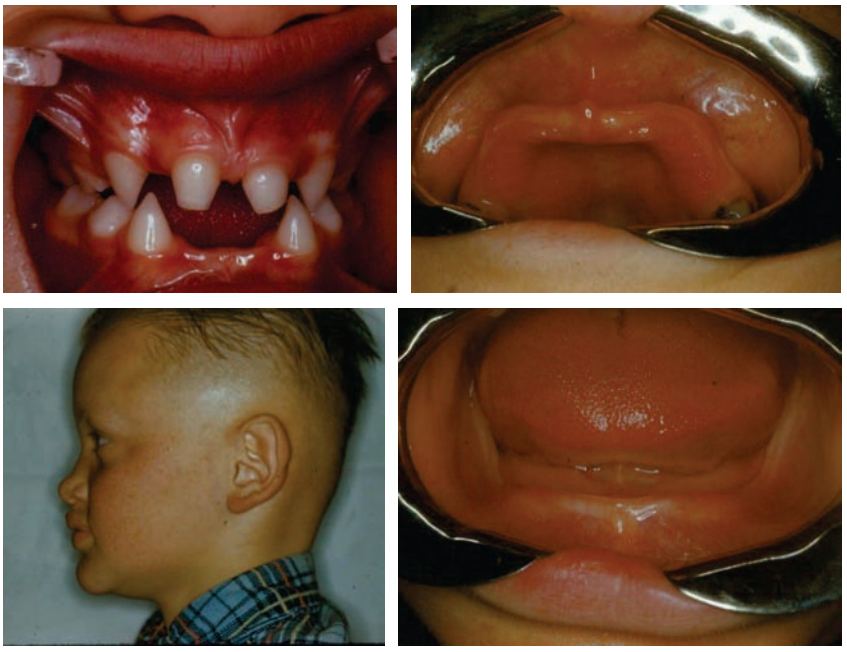

FIGURE 11-5
Ectodermal dysplasia. Multiple missing teeth conical cusps, lanugo hair. Complete anodontia on right.

recognized. Ectodermal appendages including hair, teeth, and sweat glands either fail to develop or are rudimentary. Children may be completely bald or possess lanugo hair. Heat intolerance is a common finding because of the sweat gland agenesis. Complete anodontia is sometimes seen; however, in most cases, the cuspids are present, albeit malformed, with conical crown structure. Salivary hypoplasia with xerostomia is sometimes seen. Other anomalies including pili torti (kinky hair), cleft palate, popliteal pterygium, cleft lip, and ectrodactyly may occur in variant forms of ectodermal dysplasia (Rapp-Hodgkin syndrome, Rosselli-Gulienetti syndrome).

TREATMENT

In most affected children, prosthetic appliances are well tolerated; if xerostomia is severe, dentures with a soft liner may be used. In some cases, however, prostheses cannot be tolerated. Because affected children cannot stand hot humid climates, relocation to cool climates and/or air-conditioned living quarters are recommended.

Additional Reading

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CHONDROECTODERMAL DYSPLASIA

Figure 11-6

Sex: No predilection

CLINICAL FEATURES

Inherited as an autosomal recessive trait, the Ellis-van Creveld syndrome or

chondroectodermal dysplasia represents a developmental disorder involving both epidermal and mesodermal tissues. The skin anomalies include dysplasia of the nails and hair. Sweat glands may be normal. Congenital absence of some or numerous teeth and fusion of the upper lip to the anterior maxillary alveolar ridge are noted. Eruption is often retarded. As with ectodermal dysplasia, the teeth that do form often evince conical crown forms. The mesodermal defects are most prominent in endochondral bones. The limbs are short, and polydactyly is observed on both hands and feet. The same features are typical of chondroplastic dwarfism. Congenital heart defects are present in one half of the individuals affected with the syndrome. The dental anomalies are similar to those encountered in ectodermal dysplasia. Chondroplastic dwarfism in conjunction with ectodermal defects and hypodontia are the diagnostic features of chondroectodermal dysplasia.

TREATMENT

If their root length is adequate, the existing teeth may be used as abutments for either removable or fixed dental prostheses. When congenital heart disease is present and oral surgical procedures are required, prophylactic antibiotic coverage should be instituted to prevent subacute bacterial endocarditis.

Additional Reading

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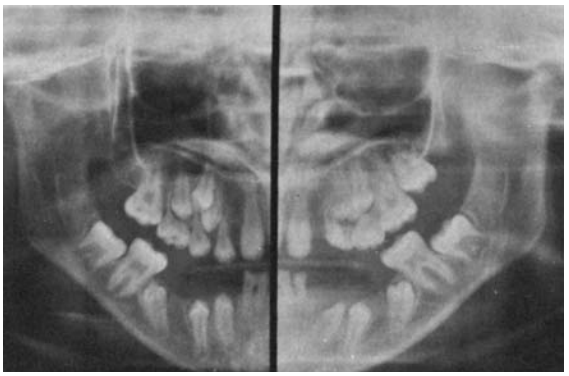

FIGURE 11-6
Hypodontia in chondroectodermal dysplasia. (Courtesy of Dr. Stefan Levin.)

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Alterations in Number: Supernumerary Teeth

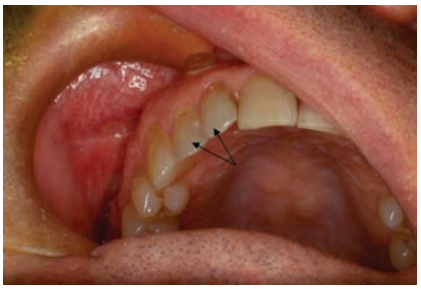
HYPERDONTIA

Figure 11-7

Sex: No predilection

CLINICAL FEATURES

Simple hyperdontia is not uncommon. The supernumerary teeth may be eumorphic but are usually heteromorphic. The most common supernumerary tooth is the mesiodens, which is formed in the midline of the maxilla, either erupted or impacted, and may occur singly or in pairs. It is heteromorphic with conical crown form. Maxillary fourth molars, also generally heteromorphic, may be located behind the third molars (distomolars), or they may erupt laterally on the buccal aspect of the normal maxillary molar dentition (paramolars). Maxillary lateral incisors, mandibular incisors, and bicuspids occasionally are supernumerary; extra cuspids are rarely encountered. Extra deciduous teeth are rare.



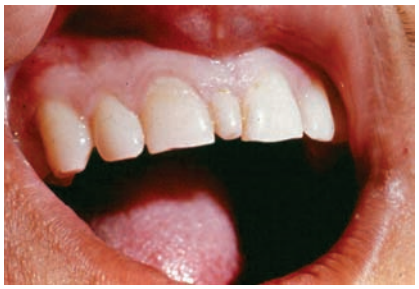


FIGURE 11-7
Supernumerary teeth, mesiodens upper right.

TREATMENT

Supernumerary teeth that have erupted usually are afunctional and should be extracted. Impacted supernumerary teeth may interfere with normal tooth position and can develop dentigerous cysts. For this reason, they too should be surgically extracted as soon as they are identified.

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CLEIDOCRANIAL DYSPLASIA

Figure 11-8

Sex: No predilection

CLINICAL FEATURES

Cleidocranial dysplasia may occur sporadically or as an autosomal dominant trait. The disease affects the bones of the shoulder and craniofacial complex. The cranial fontanels remain open into adult life, the frontal eminence is prominent with bossing, and the maxillary sinuses are rudimentary. The clavicles may be absent or hypoplastic so that the patient may be able to adduct the shoulders almost to the point of touching. Other bones may show anomalous development as well. The oral manifestations are striking, particularly on dental radiographs. The deciduous teeth may show delayed exfoliation, and both dental arches are virtually filled with unerupted permanent and supernumerary teeth. It has been suggested that the defect in eruption is linked to the absence or paucity of cementum on the permanent tooth roots. The locus for this disease was mapped to chromosome 6p21. RUNX2 is a member of the runt family of transcription factors and its expression is restricted to developing osteoblasts and a subset of chondrocytes.

TREATMENT

Deciduous tooth retention and numerous impactions provide for a monumental orthodontic problem. Removal of the deciduous teeth does not usually allow for eruption of the secondary dentition. Attempts to surgically uncover, wire, and orthodontically erupt the impacted teeth may be successful.

Additional Reading

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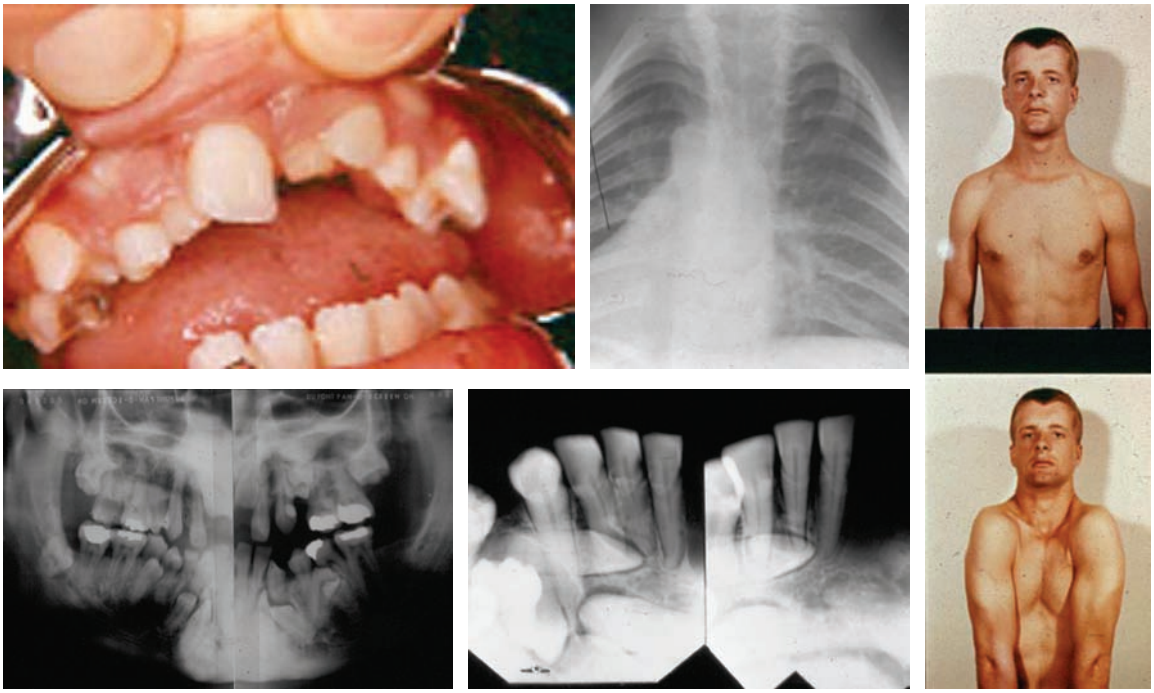

FIGURE 11-8
Multiple impactions and supernumerary teeth in cleidocranial dysplasia. Absence of clavicles.

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GARDNER'S SYNDROME

Figure 11-9

Sex: No predilection

CLINICAL FEATURES

Familial adenomatous polyposis (FAP) is characterized by multiple colonic polyps that make their appearance in the second decade; ultimately many of these polyps transform into adenocarcinoma. Extraintestinal manifestations include osteomas and dental abnormalities (unerupted teeth, congenital absence of one or more teeth, supernumerary teeth, and odontomas). In addition, congenital hypertrophy of the retinal pigment epithelium, desmoid tumors, and extracolonic cancers including thyroid, liver, bile ducts, and central nervous system are encountered. There is a less aggressive form in which fewer polyps are present and cancerous transformation is less frequent. Craniomandibular osteomas, dental abnormalities, and fibromas on the scalp, shoulders, arms, and back typify the Gardner variant. Classic FAP is inherited in an autosomal dominant manner and results from a germline mutation in the adenomatous polyposis (*APC*) gene. A *MUTYH* mutation causes a recessively

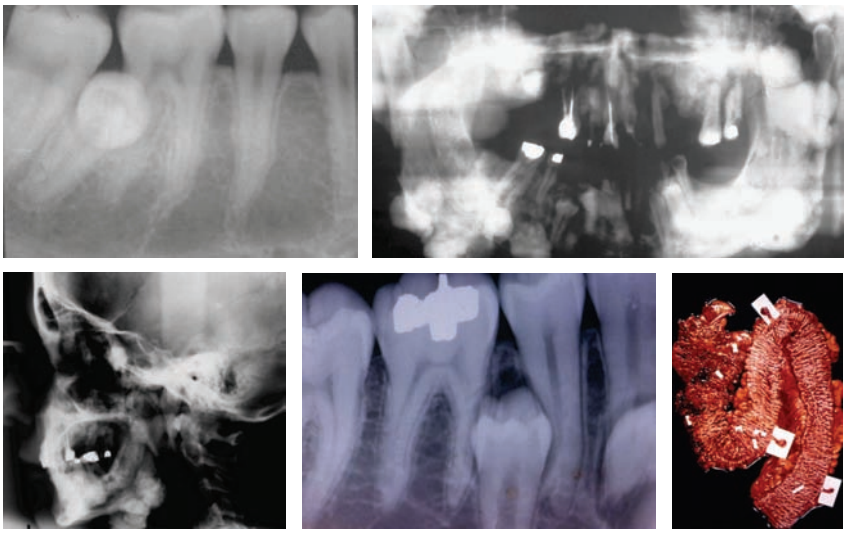

FIGURE 11-9
Supernumerary teeth in Gardner's syndrome, osteomas, premalignant adenomatous intestinal polyps.

inherited polyposis condition, also at lower risk than classic FAP for development of carcinoma.

TREATMENT

The primary concern in Gardner's syndrome is detection of the entity so that the patient can be referred to a gastroenterologist for management of the potentially malignant intestinal polyps. The maxillofacial osteomas may require surgical removal, and orthodontic therapy may be instituted to restore the occlusion.

Additional Reading

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Ida M, Nakamura T, Utsanomiya J. Osteomatous changes and tooth abnormalities in the jaw of patients with adenomatosis coli. *Oral Surg Oral Med Oral Pathol*. 1981;52:2.

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Alterations in Morphology

MICRODONTIA AND MACRODONTIA

Figure 11-10

Sex: No predilection

CLINICAL FEATURES

Variations in the size of teeth may be generalized, involving the entire dentition, or localized to one or a few teeth; the latter is more common. Generalized microdontia, extremely rare, is encountered among pituitary dwarfs, whereas macrodontia may be a feature of pituitary gigantism. Macrodontia restricted to one half the teeth in unilateral distribution is a feature of facial hemihypertrophy. Localized microdontia most often affects the maxillary lateral incisors, with formation of conical crown forms. The disorder is usually familial. Third molars are commonly small and malformed as well. Localized macrodontia is less often observed than microdontia. The incisors are most commonly affected, but geminated or fused teeth may show features that could be confused with true mac-

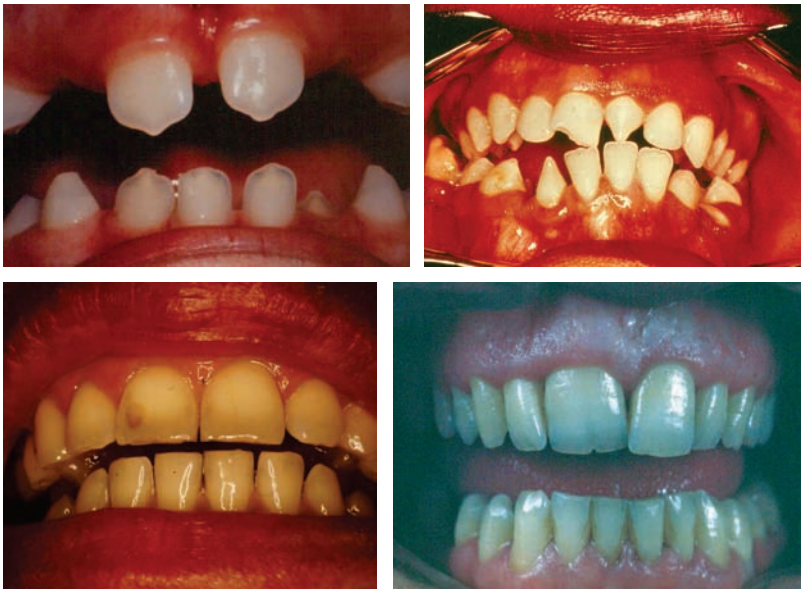

FIGURE 11-10
Microdontia above, macrodontia below.

rodontia. Syndromic associations are seen such as the microdontia, microtia, and sensorineural hearing loss syndrome in which there is a mutation in the fibroblast growth factor number 3 gene.

TREATMENT

Microdontia and macrodontia of a localized nature are usually of no consequence. Orthodontics may be required if an arch length problem develops. Crown and bridge prosthodontic reconstruction may help to achieve an esthetic appearance.

Additional Reading

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ACCESSORY CUSPS AND ROOTS

Figure 11-11

Sex: No predilection

CLINICAL FEATURES

Accessory cusps are commonly encountered on the lingual surface of maxillary first molars as the so-called cusps of Carabelli. Indeed, rudimentary forms may affect as many as 90% of all such teeth in whites, although they are extremely rare among Eskimos and Asians. Buccal accessory cusps are occasionally encountered on both molars and premolars. Dens evaginatus represents an accessory cusp emanating occlusally from the central groove of premolars and molars. This anomaly is rare and is most often encountered among Eskimos. A pulp horn may extend into this central occlusal cusp. Excluding the cusp of Carabelli, the most common accessory cusp represents an anomalously enlarged lingual tubercle on an incisor. Accessory roots are most frequently seen on maxillary molar teeth and secondly on mandibular

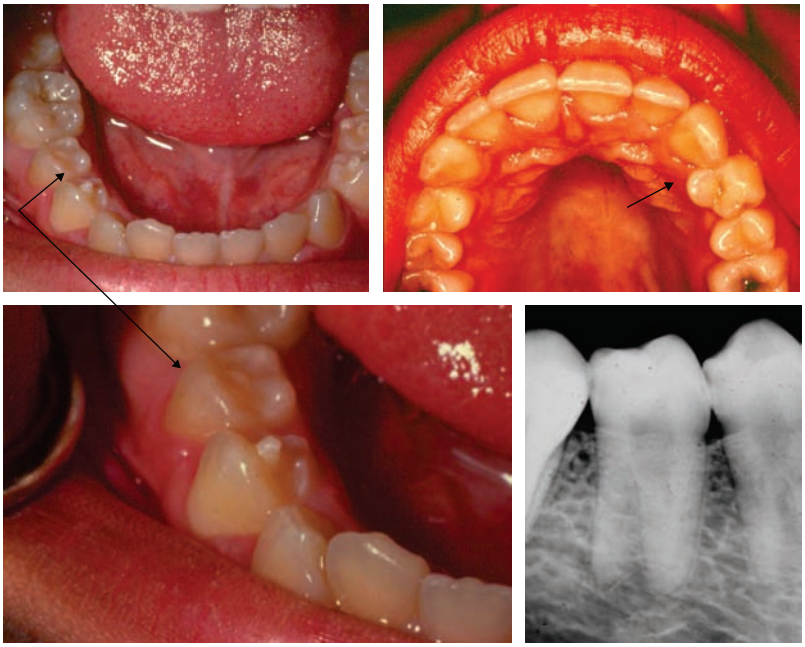

FIGURE 11-11
Accessory cusps, roots, and Dens evaginatus.

molars. Premolars and maxillary cuspids and incisors may have accessory or appendicial roots; however, mandibular cuspid or incisor accessory roots are extremely rare.

TREATMENT

Accessory cusps are rarely in occlusion so that no treatment is required unless, in the case of buccal accessory cusps, periodontal pocket formation is encountered. In this case, tooth reduction and placement of a restoration to avoid exposure of dentin are recommended. Dens evaginatus may pose a problem, because the cusps are in occlusion. It must be remembered that pulp horns extend into these areas. A knowledge of the existence of accessory roots is significant when endodontic therapy is required.

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DENTAL TRANSPOSITION

Figure 11-12

Sex: No predilection

CLINICAL FEATURES

Teeth may erupt into inappropriate positions. A second premolar may be interposed between a first and second molar, or a cuspid may erupt into position between the premolars. Although rare, a tooth may erupt into the opposite quadrant. Many examples of so-called "transposition" are instances of supernumerary teeth, particu-

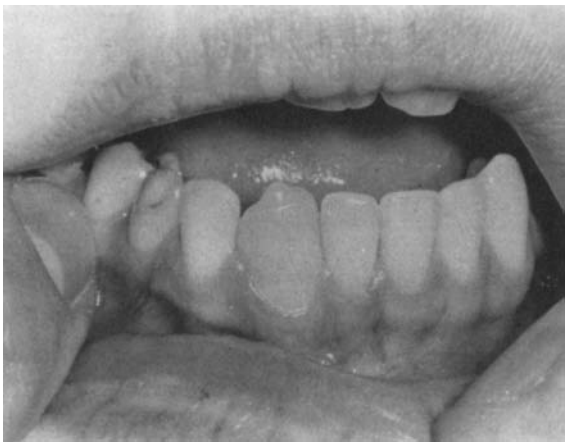

FIGURE 11-12
Transposition of lateral incisor and canine.

larly in the molar region. These supernumerary molars are small and malformed and often show occlusal anatomy analogous to premolars. Seventy-five percent of transpositions involve the maxillary dentition. Unilateral transposition accounts for 88% of cases; the most common transposition involves the maxillary canine and first premolar. Data regarding any genetic tendency for true transposition are insufficient.

TREATMENT

If crowding and malocclusion are not significant, no treatment is required. Otherwise, extraction and/or orthodontic therapy may be indicated.

Additional Reading

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ENAMEL PEARL

Figure 11-13

Sex: No predilection

CLINICAL FEATURES

Enamel pearls or droplets are white, dome-shaped calcific concretions of enamel, usually located at the furcation areas of molar teeth. Maxillary molars are most often affected. Encountered fairly frequently, enamel pearls probably represent a histologic abnormality occurring in Hertwig's sheath. The sheath epithelium retains ameloblastic potential in a focal area so that a nodule of enamel forms in place of cementum. Occasionally, a dentin core extends into the enamel-surfaced excrescence.

TREATMENT

Treatment is necessary only when periodontal disease involves a furcation area with an enamel pearl. Because the region is difficult to maintain in a hygienic state, the pearl should be removed with dental burrs or stones.

Additional Reading

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DILACERATION

Figure 11-14

Sex: No predilection

CLINICAL FEATURES

Dilaceration refers to a defect in root development, whereby a bend or curve develops.

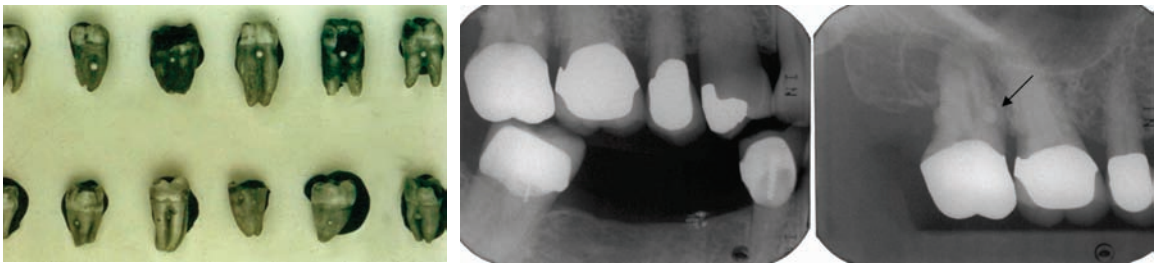

FIGURE 11-13
Molar teeth with enamel pearls.

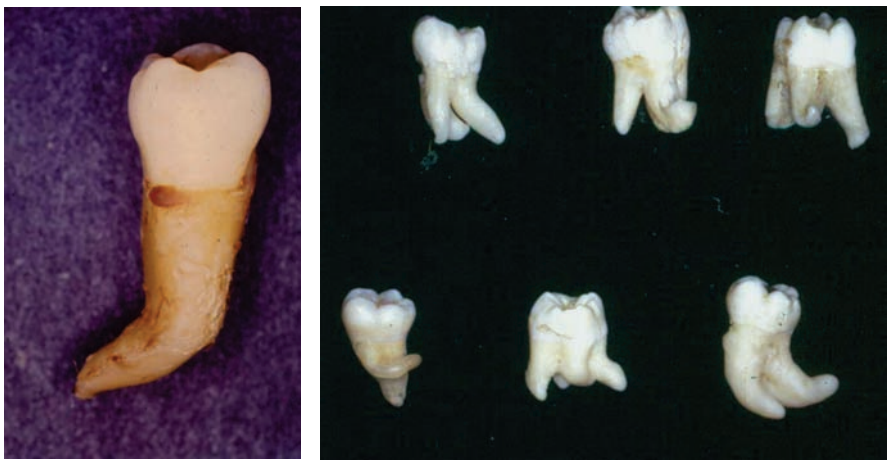

FIGURE 11-14
Dilaceration of roots.

This flaw, which is not the result of a true laceration of Hertwig's sheath, probably evolves subsequent to trauma or some defect in development that alters the angulation of the tooth germ during root formation. The angulation may occur at any location along the root. Any tooth, deciduous or permanent, may show this anomaly. Dilaceration of the coronal portion of the tooth has also been reported.

TREATMENT

No treatment is required. When extraction or endodontic therapy is necessary, knowledge of this defect and its identification on dental radiographs aids in circumventing complications that could occur when these procedures are performed on such anomalous teeth.

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DENS INVAGINATUS (DENS IN DENTE)

Figure 11-15

Sex: No predilection

CLINICAL FEATURES

Dens invaginatus represents a defect in morphologic development, whereby the coronal enamel and dentin become inverted into the pulp chamber. The defect, which is generally localized to a single tooth, occasionally involves multiple teeth and frequently involves the same tooth bilaterally. The coronal invagination may be limited to the crown region, or it may extend deeply into the radicular pulp. The defect is most often encountered in the maxillary lateral incisor and in mesiodens. Clinically, the incisor may manifest only an enlarged lingual pit. The defect is easily demonstrated radiographically as an invaginated radiopaque, ribbon-like enamel structure, giving the impression of a small tooth within the coronal pulp cavity. The invaginated core is patent; food debris with accompanying microorganisms enter this canal, predisposing the affected tooth to caries, pulp infection, and periapical disease.

TREATMENT

When dens invaginatus is encountered shortly after eruption, prophylactic restoration of the invaginated channel is recommended to prevent pulpal necrosis.

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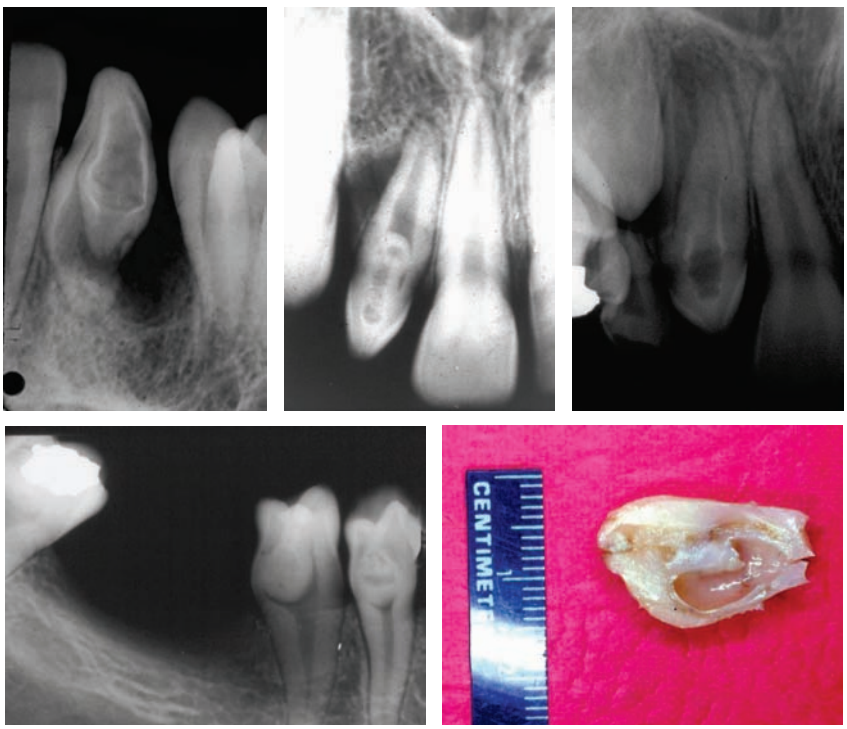

FIGURE 11-15
Dens invaginatus.

TAURODONTISM

Figure 11-16

Sex: No predilection

CLINICAL FEATURES

Taurodontism means bull teeth; the term is appropriate because this human dental defect involves an elongated pulp chamber with rudimentary root formation mimicking, to some extent, the normal morphology of the ungulate dentition. The defect is observable only in dental radiographs; there is no clinically obvious malformation. Molars are affected and give the appearance of having been "stretched," with the root furcation occurring at the apical third. One or more molars may show this change. Taurodonts may be encountered in patients suffering from various developmental craniofacial deformities. Specifically, in the trichodentoosseous syndrome, hypoplastic-hypocalcified amelogenesis imperfecta (AI), kinky hair, and cortical osteosclerosis are seen along with taurodontism. Among patients with hypodontia, one third also have a taurodont. Interestingly, similar dental morphology has been encountered among fossil hominoids, particularly the Neanderthals.

TREATMENT

No treatment is required. The enlarged pulp chamber is of significance when endodontic therapy is required.

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GEMINATION

Figure 11-17

Sex: No predilection

CLINICAL FEATURES

Gemination is the result of either schizodontism, the splitting of a tooth germ during development, or synodontism, the fusion of a normal tooth bud with one from a developing supernumerary tooth. Both forms represent abortive attempts at forming supernumerary buds. The deciduous mandibular incisors and permanent maxillary incisors are most often affected. Gemination may be distinguished from fusion by the fact that the full complement of teeth is present in the former, whereas

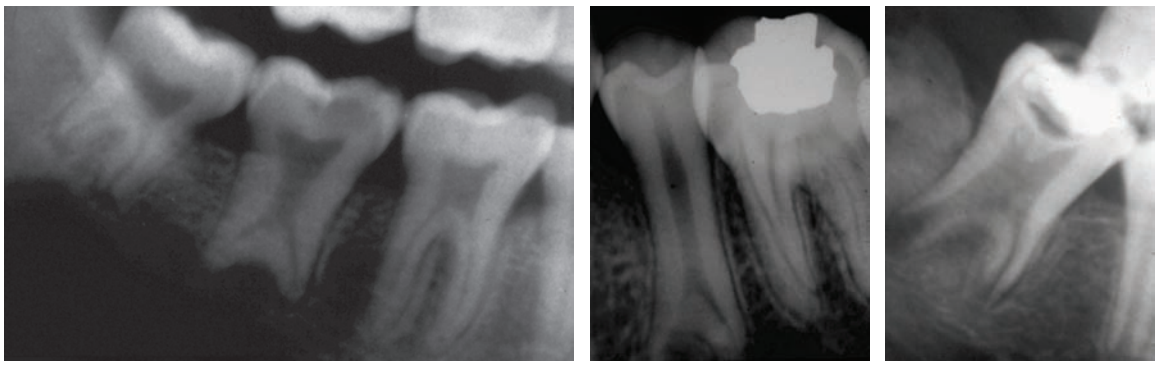

FIGURE 11-16
Taurodontism.

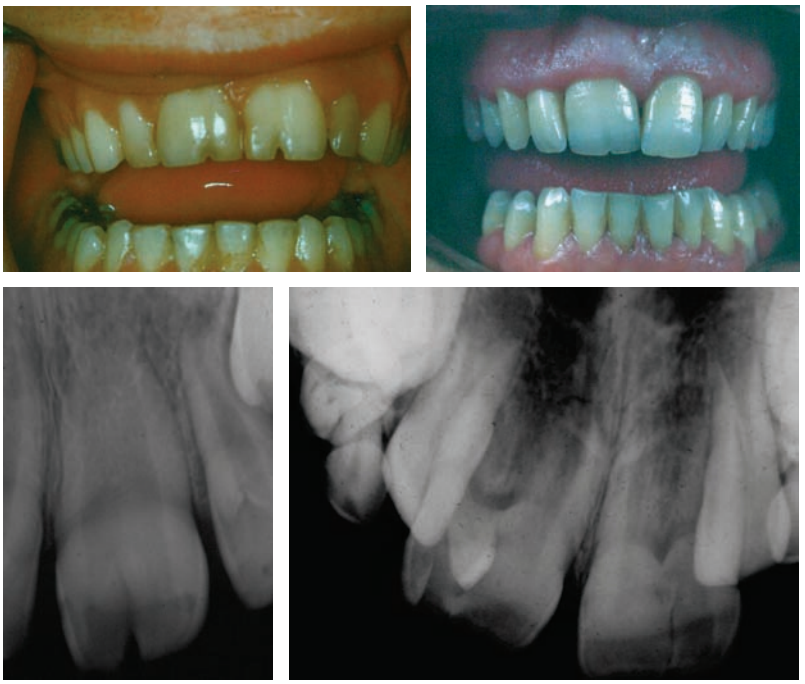

FIGURE 11-17
Gemination.

a tooth is missing in the latter. Geminate teeth usually show doubling of both the crown and root. The crown may be excessively widened or may actually show an indentation or groove delineating the two crown forms. A hereditary pattern is sometimes evident.

TREATMENT

Gemination of anterior teeth represents a prosthetic challenge. Depending on the morphologic character of the defect, a fixed anterior bridge may be constructed, using the anomalous tooth as an abutment. Alternatively, to ensure an adequate esthetic result, the affected teeth are extracted and the cuspids are used as abutments.

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FUSION

Figure 11-18

Sex: No predilection

CLINICAL FEATURES

Fusion represents a junction at the level of dentin between juxtaposed normal tooth germs, so that one enlarged anomalous crown form exists in place of two normal teeth. A single, enlarged root or two roots are observed. A hereditary pattern is often encountered. Either deciduous or permanent teeth can be affected; however, the anomaly has been reported to be more common in deciduous teeth. In both dentitions, the incisors are most often affected.

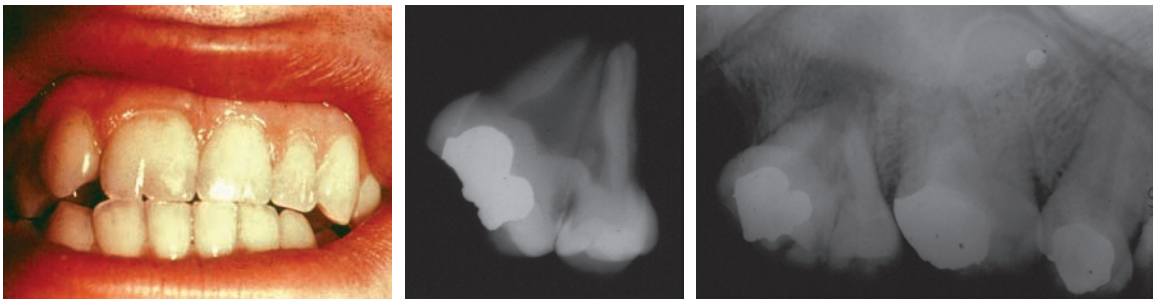

FIGURE 11-18
Fusion.

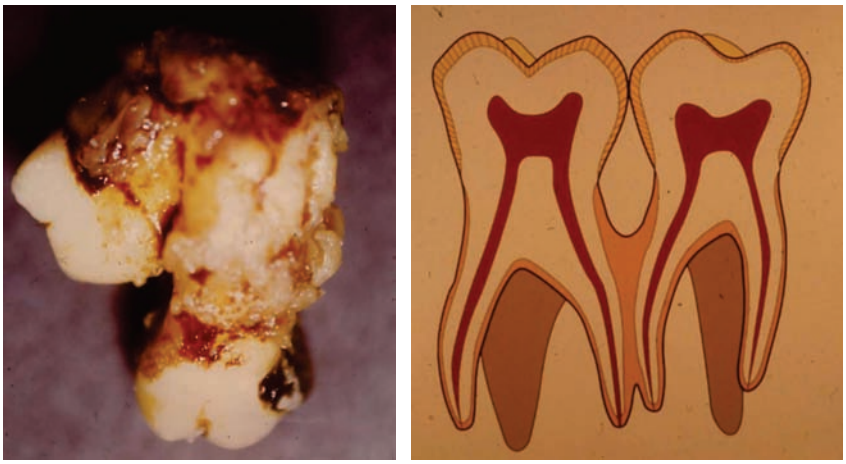

FIGURE 11-19
Concrescence in molar teeth.

TREATMENT

Depending on the morphologic features of the fused teeth, a fixed prosthetic appliance may include the anomalous tooth as an abutment, or the tooth may be extracted with subsequent bridge fabrication to achieve optimal esthetics.

Additional Reading

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CONCRESCENCE

Figure 11-19

Sex: No predilection

CLINICAL FEATURES

Concrescence represents union between juxtaposed teeth at the level of the cementum; there is no interdentinal combination. The maxillary molars are usually affected by this developmental abnormality. Confluency of cementum between adjacent teeth may occur with two normal molars, yet is perhaps more often encountered between a normal molar

and a supernumerary molar (i.e., paramolar or distomolar). Concrescence may occur in both impacted and erupted teeth.

TREATMENT

Concrescent teeth are either in malocclusion or impacted, usually necessitating extraction. If such a condition is suspected from radiographic features, care during extraction is necessary, particularly to avoid fracturing excessive amounts of alveolar bone.

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ATTRITION

Figure 11-20

Age: Adults, particularly elderly people
Sex: No predilection

CLINICAL FEATURES

Attrition represents the physiologic loss of tooth structure. The pattern of loss is characteristic in that the enamel and dentin become abraded on their occlusal and incisal surfaces in a generalized fashion. Normal occlusal attrition has been calculated at 30 µm/year for molar teeth. The process is related to diet, and is more severe in individuals who partake of a food such as maize or use their teeth in the preparation of hides. It is, therefore, common among older American Indians and Eskimos. Tooth wear has been correlated with erosive degenerative changes in the temporomandibular joint among aboriginals. It may be difficult to differentiate between attrition and bruxism with abrasion by noting only the pattern of tooth wear.

TREATMENT

No treatment is required as secondary dentin proceeds at a rate commensurate with the attritional wear. When the crowns are worn down to the gingival margin, an overdenture may be constructed to improve function.

Additional Reading

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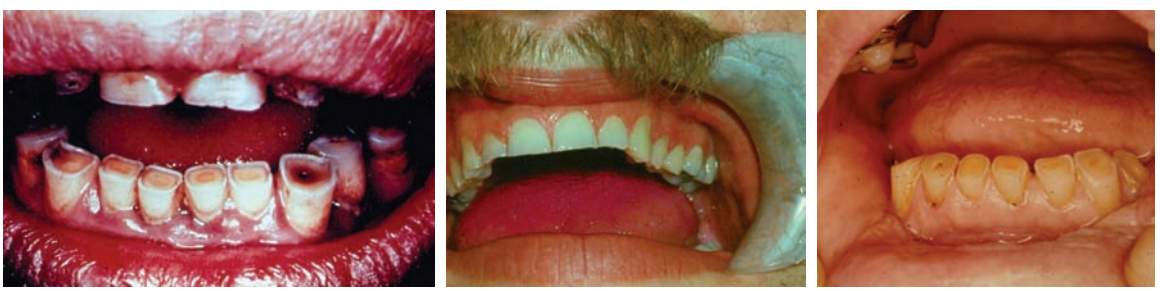

FIGURE 11-20
Physiologic tooth wear or attrition.

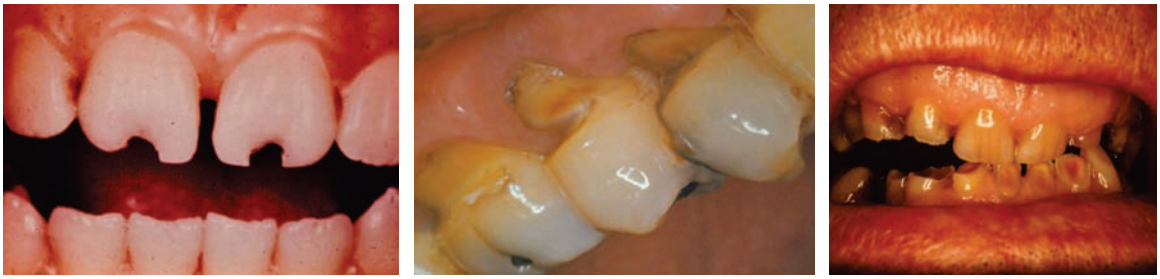

FIGURE 11-21
Pathologic tooth wear or abrasion.

ABRASION

Figure 11-21

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Abrasion represents the pathologic wear of tooth structure. The location of tooth structure loss is in keeping with the nature of the etiology or habit responsible for excessive abrasion. Notching of incisors is seen in hairdressers who hold bobby pins between their teeth; grooving of both maxillary and mandibular incisors is observed in pipe smokers; cervical abrasion occurs in individuals who brush excessively in a horizontal plane. In the last instance, pulp exposure may ensue. Isolated foci of abrasion are observed in patients with occlusal prematurities appearing as cuspal wear facets. A common occlusal anomaly leading to widespread abrasion occurs in patients who show incisal guided protrusive movement. The incisal portion of the mandibular incisors shows abrasion, as do the incisal and lingual surfaces of the maxillary incisors and cuspids. It is important to recognize that abrasion related to occlusal disharmony may be associated with advancing periodontal disease about the affected teeth. Patients with bruxism display generalized abrasion that mimics physiologic attrition in its distribution. Pathologic tooth wear has been found to be prevalent among mentally retarded patients.

TREATMENT

Limited forms of abrasion require elimination of the incriminating habit and restoration of normal tooth contour if function or esthetics is a problem. Abrasion related to malocclusion may require occlusal rehabilitation and a complete periodontal evaluation. Night-guard appliances may limit abrasion in patients with bruxism.

Additional Reading

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Oilo G, Hatle G, Gad AL, Dahl BL. Wear of teeth in a mentally retarded population. *J Oral Rehabil*. 1990;17:173.

EROSION

Figure 11-22

Age: Adult predilection
Sex: No predilection

CLINICAL FEATURES

Erosion represents the demineralization of tooth structure as a result of chemical action, usually that of acidic compounds. Although a definite history of oral contact with acids

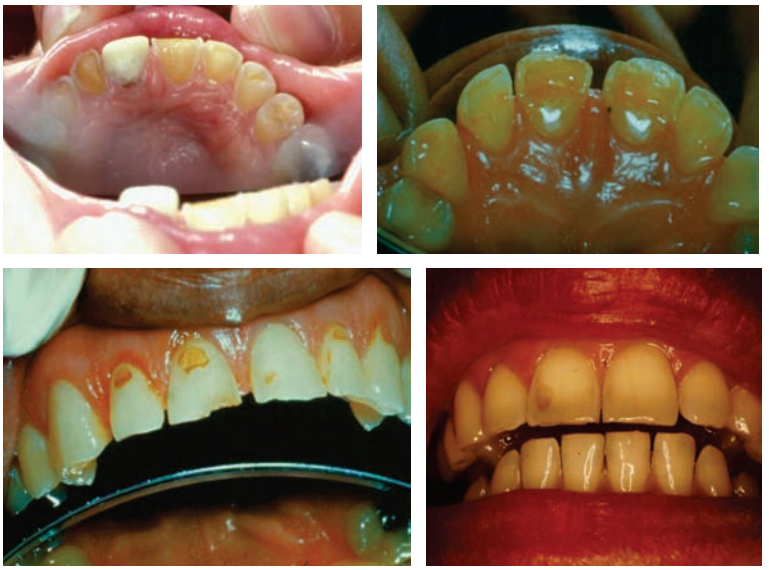

FIGURE 11-22
Idiopathic erosion of facial enamel. Lingual erosion in anorexia nervosa/bulimia with chronic vomiting.

can be elicited in most instances, occasionally a cause is not readily apparent. The more common agents associated with erosion are chronic vomiting, habitual carbonic acid intake from cola or soft drinks, or habitual contact with citric acid as in lemon sucking. When vomiting is the cause, a smooth homogeneous loss of enamel with exposure of dentin is observed on the lingual surfaces. Both facial and lingual loss of surface tooth structure can be seen in persons who imbibe acidic fruits or beverages. Idiopathic erosion occurs on the cervical and middle thirds of the incisors, cuspids, and bicuspids as a smooth cupped-out depression.

TREATMENT

Areas of erosion may be sensitive and should be restored with conventional operative procedures.

Additional Reading

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HYPERCEMENTOSIS

Figure 11-23

Age: Middle-aged and elderly adults
Sex: No predilection

CLINICAL FEATURES

Excessive deposition of secondary cementum may develop on one tooth or may be generalized. Generally no cause can be found; occasionally, contributing factors can be detected (periapical inflammation and hypofunction as seen when an opposing tooth is missing). Pain is not a feature. The roots show laminated layers of secondary cementum, usually of the lamellar type, which is most extensive in the apical third of the root. The radiographic features are characteristic, showing bulbous enlarged

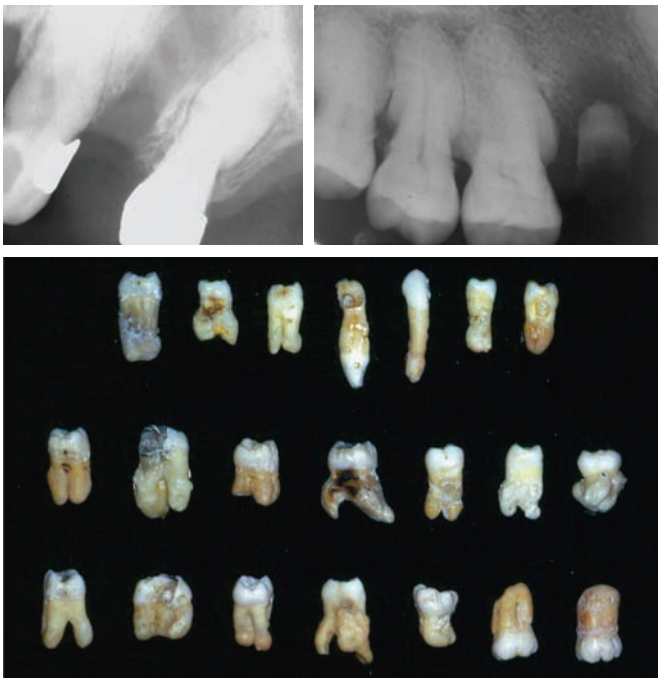

FIGURE 11-23
Hypercementosis.

roots. Generalized hypercementosis may occur alone or may be seen in conjunction with a ground-glass or cotton-wool-appearing alveolar bone in osteitis deformans. A serum alkaline phosphatase assay is helpful.

TREATMENT

No treatment is required. Extraction of teeth with hypercementosis may require sectioning to facilitate removal.

Additional Reading

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Alterations in Structure

DENTAL CARIES

Figure 11-24

Sex: No predilection

CLINICAL FEATURES

Dental caries represents the most common disease to affect the teeth. Most evidence supports a bacterial etiology, whereby teeth accumulate material known as plaque that provides a carbohydrate substrate for acid-producing bacteria, primarily *Streptococcus mutans*. Acid generation induces a chemical demineralization of hydroxyapatite crystals in the enamel. When the enamel has been penetrated, other microorganisms gain access to the protoplasm of the dentinal tubules, and the carious process proceeds pulpally. Once the pulp has been invaded by bacteria, inflammation ensues; ultimately, necrosis with spread of infection occurs through the apical foramen or accessory root canals. In children, pits and fissures are the most common sites along

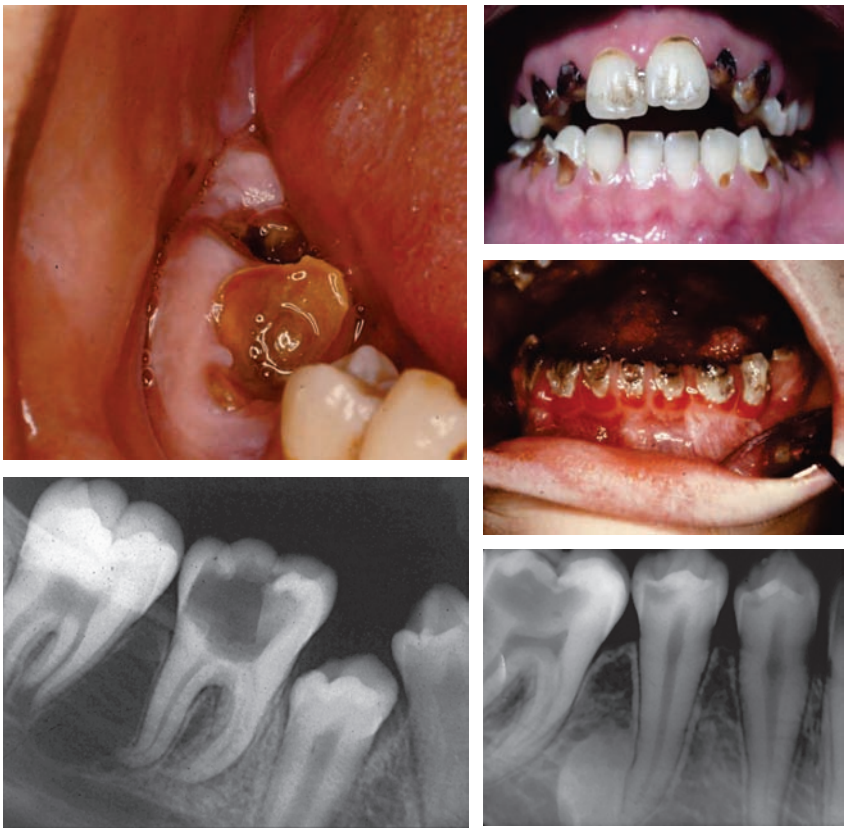

FIGURE 11-24
Dental caries. Upper right: crystal meth caries in an addict who consumes sugar drinks and candy while stoned. Middle right: post radiation therapy caries associated with xerostomia.

with interproximal areas. Clinically, pit and fissure caries is characterized by either a chalky appearance or a brown discoloration. A sharp dental explorer can be forced into a carious fissure or pit and will be retained, requiring somewhat forceful removal. Interproximal caries can often be detected as pits or irregularities on instrument exploration; however, bite-wing radiographs are the major diagnostic aid. Immediately below the point of tooth-to-tooth contact, a funnel-shaped radiolucency can be detected with its apex directed toward the dentin. Dentinal caries also appears triangular and undermines the overlying intact enamel. Cervical and root caries on the facial or buccal gingival one third of the crown are more frequently encountered among adults. It may involve cementum and extend below the marginal gingiva. Cervical caries begins as white opaque areas that become discolored brown or yellow-brown. Severe or rampant caries occurs in children who eat excessive amounts of candy and other sweets. In adults, severe caries occurs in xerostomia secondary to the Sjögren's syndrome or after radiation therapy for head and neck cancer.

TREATMENT

All carious enamel and dentin must be removed before restoration with amalgam, cast gold, or resin materials. Pit and fissure sealants effectively prevent dental decay among children. Patients with xerostomia from immunopathic sialadenitis or radiation should be treated with daily fluoride gel.

Additional Reading

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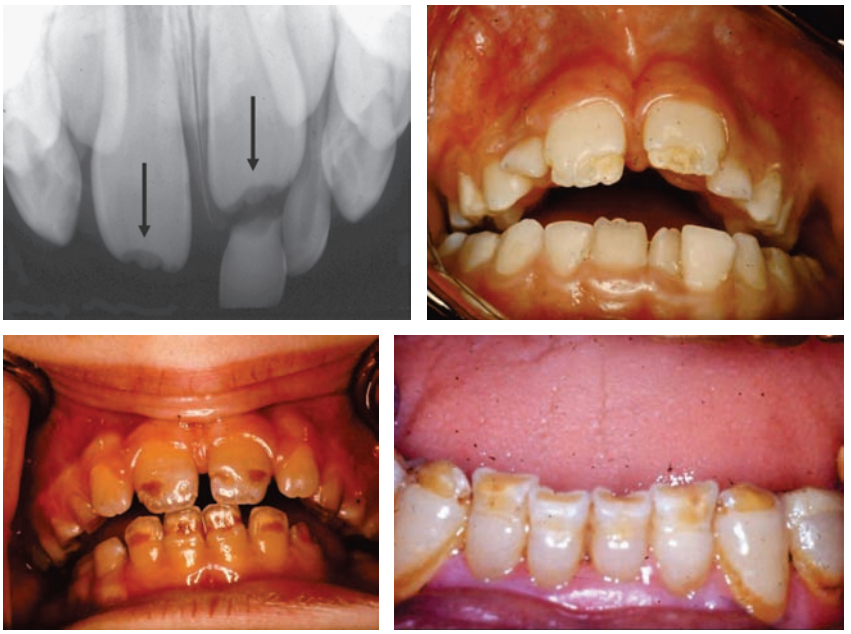

FIGURE 11-25
Turner's hypoplasia of centrals. Enamel pitting occurs in teeth at the same stage of odontogenesis when a stressor on the enamel organ occurs during development.

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ENAMEL HYPOPLASIA

Figure 11-25

Sex: No predilection

CLINICAL FEATURES

Damage to ameloblasts during odontogenesis, if severe, results in defective enamel formation. A variety of infectious, nutritional, chemical, and traumatic factors play a role. (Because of their unique characters, congenital syphilis and dental fluorosis are considered separately). Perhaps, the most common form of enamel hypoplasia is seen in isolated permanent teeth, whereby caries with periapical spread of infection or trauma to a deciduous tooth results in damage to ameloblasts forming the crown of the subjacent developing permanent tooth. The affected tooth, so-called Turner's tooth, is yellow or brown, and the enamel surface is pitted or chalky. Occasionally, many teeth show pitting or rough, poorly calcified enamel matrices. In these instances, one of the childhood infectious diseases associated with prolonged elevated temperature may have resulted in ameloblastic injury, in which case only that portion of the teeth under development at the time of infection manifests hypoplastic changes. Children of low birth weight have a high incidence of enamel hypoplasia, which may be a consequence of oxygen deprivation and mineral depletion during perinatal development. Enamel hypoplasia with a similar distribution as that seen with febrile childhood infections may occur in rickets, congenital hypoparathyroidism, and birth injuries. Enamel defects have been reported to be a common accompaniment to celiac disease.

TREATMENT

When the pulp chambers have receded to an appropriate level, permanent restorations may be fabricated. In the interim, resin restorative materials may be periodically placed to achieve a desirable esthetic appearance.

Additional Reading

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CONGENITAL SYPHILIS

Figure 11-26

Sex: No predilection

CLINICAL FEATURES

Congenital syphilis is contracted in utero from a mother who has active treponemal infection. The clinical manifestations are protean, as the infection may involve virtually any tissue or organ, particularly bone, tooth, and nerve. Saber shins, rhagades, frontal bossing, and saddle nose are common structural anomalies. Hutchinson's triad consists of blindness, deafness, and dental anomalies. The classic dental changes involve the maxillary incisors and first permanent molars. The central incisors are notched, the laterals are peg shaped, and the molars manifest a crumpled, discolored occlusal surface (so-called mulberry molars). Not all patients manifest all components of Hutchinson's triad, nor do they all show the three dental anomalies together. The fact that children with congenital syphilis may continue to carry spirochetes, may be infectious, and may show any of the signs of acquired syphilis is extremely important.

TREATMENT

Children should be referred to a pediatrician to determine whether or not active disease persists. The anomalous teeth may be restored by the usual operative procedures.

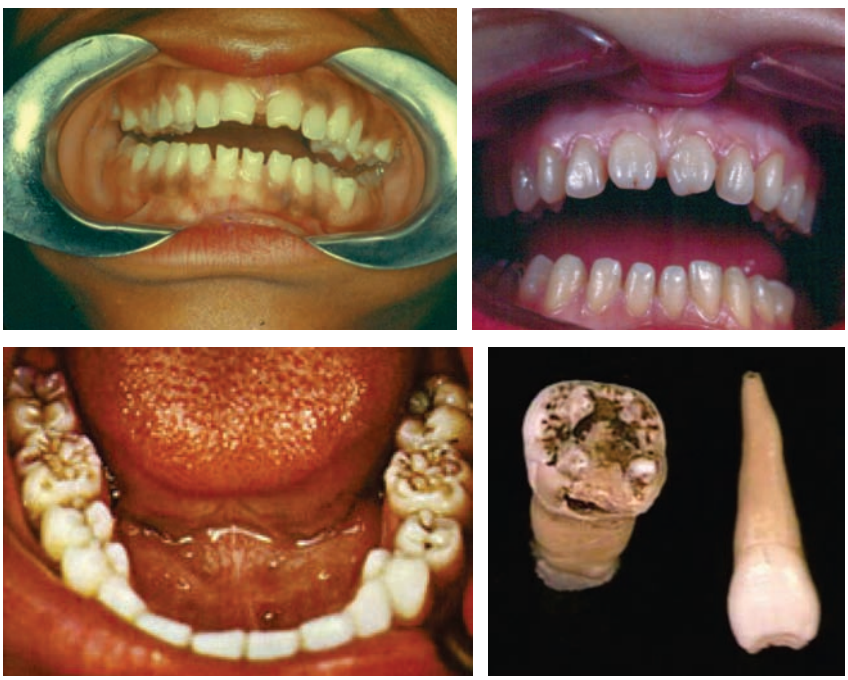

FIGURE 11-26
"Screwdriver" centrals and "mulberry" molars in congenital syphilis.

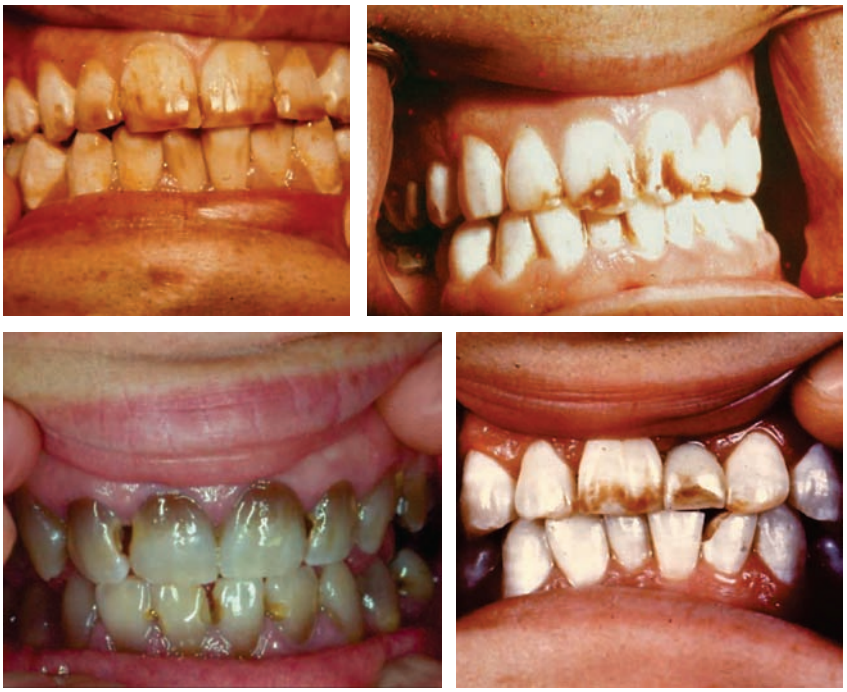

FIGURE 11-27
Fluorosis prior to age 1 resulting in discoloration and chalky enamel.

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DENTAL FLUOROSIS

Figure 11-27

Sex: No predilection

CLINICAL FEATURES

When fluoride levels in the drinking water exceed 1 ppm, mottling of enamel may occur. Certain regions of the world have natural drinking water supplies in which the fluoride content is extremely high. Fluoride in concentrated levels is toxic to ameloblasts; during amelogenesis, cell damage leads to defective enamel formation. The affected teeth, deciduous or permanent, vary considerably regarding the extent of hypoplasia. The surface may be chalky, opaque, and flecked, or the enamel may show extensive flaking, fracturing, and brown or black pigmentation. The condition is generalized, affecting all teeth exposed to excess fluoride during development.

TREATMENT

No treatment can remineralize the defective surface. Temporary resin restorations should be employed during childhood, and full-coverage fixed prostheses can be fabricated after the pulp chamber has sufficiently receded. Treatment is elective because the teeth are not any more susceptible to decay than the normal dentition.

Additional Reading

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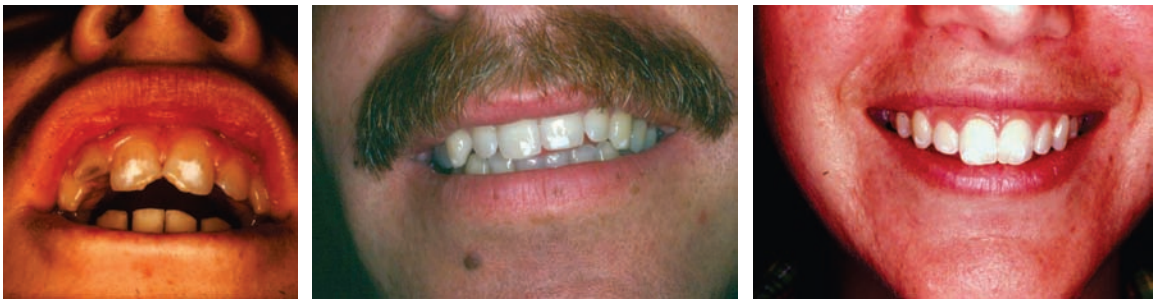

FIGURE 11-28
Opaque regions on incisal one third of maxillary central incisors and cuspids representing snow-capped teeth.

Dean HT, Arnold FA. Endemic dental fluorosis or mottled teeth. *J Am Dent Assoc*. 1943;30:1278.
Dean HT. Chronic endemic fluorosis. *J Am Med Assoc*. 1936;107:1269.
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SNOW-CAPPED TEETH

Figure 11-28

Sex: No predilection

CLINICAL FEATURES

This autosomal dominantly inherited disorder is relatively common. The incisors, cuspids, and occasionally even posterior teeth manifest a white, chalky opaque discoloration of the incisal and occlusal third of the crown. This opacified region of the enamel reflects an anomaly of mineralization; however, the involved hard tissue is neither structurally weakened nor more susceptible than normal tooth structure to caries. Recently, a rare X-linked form of snow-capped teeth has been described and has been classified as a form of AI, hypomaturation type. This form resembles the common variety in that the incisal one third of the teeth exhibit an opaque appearance; it differs in that a brownish discoloration also is observed. Scanning electron microscopic studies indicate a structural defect in the outer prismless enamel layer.

TREATMENT

No treatment is required.

Additional Reading

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AMELOGENESIS IMPERFECTA, HYPOPLASTIC TYPES

Figure 11-29

Sex: Predilection varies according to mode of inheritance.

CLINICAL FEATURES

The amelogenin gene encodes for enamel matrix protein and is probably heritably

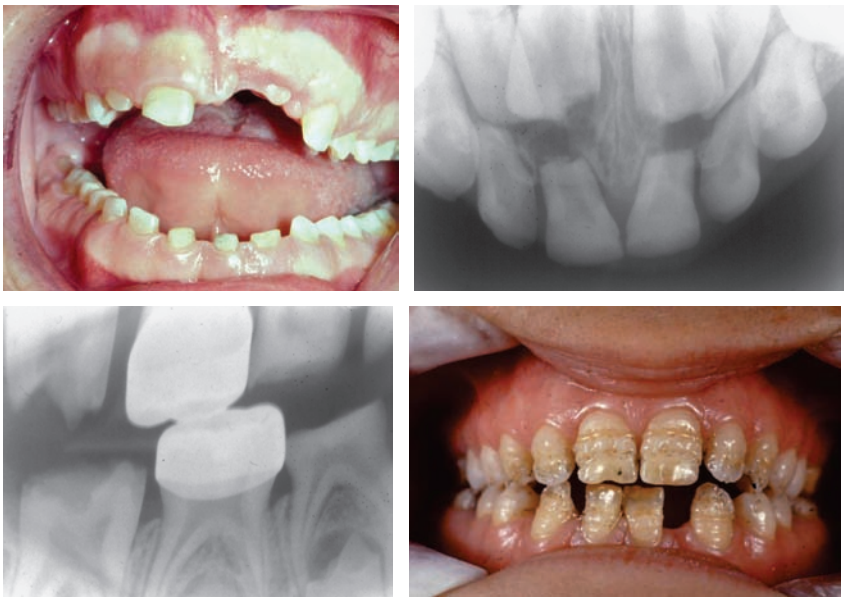

FIGURE 11-29
Amelogenesis imperfecta, smooth hypoplastic type, no incisal flare, no enamel seen radiographically. Lower right: amelogenesis imperfecta, local hypoplastic type showing midcoronal pitting.

defective in the various forms of AI. Two major forms of AI exist; the hypoplastic types exhibit a deficient amount of surface enamel, whereas the hypomaturation forms show adequate enamel thickness with defective mineralization. This subdivision is often confusing because both hypoplastic and hypomineralized enamel may coexist. The hypoplastic forms have been subcategorized according to clinical, microscopic, and genetic features. This group has the following general features. The enamel is thin, teeth fail to evince mesiodistal contacts, and pitting or fissuring, either horizontal or vertical, occurs. The *autosomal dominant pitted hypoplastic variety* affects both primary and secondary dentitions that manifest multiple pinpoint pits randomly distributed over the crowns. *Autosomal dominant local hypoplastic AI* is characterized by horizontal rows of pits located on the middle one third of the crown; the immediately adjacent enamel is hypocalcified, and the occlusal third is usually unaffected. The *autosomal dominant smooth hypoplastic form* is devoid of pits, being smooth and approximately one fourth normal thickness; clinically, newly erupted teeth are yellow and later appear opaque white or slightly brown. Radiographically, the teeth may appear to be devoid of enamel. The *autosomal dominant rough hypoplastic form* is represented by hard granular white or yellow-white enamel, one fourth normal thickness, that chips away from the underlying dentin. There is some degree of incisal flare. Radiographically, the enamel layer is readily identified, yet extremely thin. In contrast, the *autosomal recessive rough hypoplastic type* is nearly devoid of enamel and is also termed enamel agenesis. The surface exhibits a granular, ground-glass appearance and a yellow discoloration. Impaction with resorption is frequently witnessed. Last, *X-linked dominant smooth hypoplastic AI* varies according to sex. Hemizygous males show smooth yellowish-brown thin enamel with significant abrasion; a thin opaque enamel capping is observed radiographically. Female heterozygotes show vertically banded fissures, alternating with enamel

striations of normal thickness (Lyonization effect). These vertical striae are radiographically evident. In all forms of AI, there is a tendency for development of anterior open bite. In families with an X-linked form, it has been shown that the disorder may result from mutations in the amelogenin gene, *AMELX*. The enamelin gene, *ENAM*, is implicated in the pathogenesis of the dominant forms of AI.

TREATMENT

Full crown prostheses are recommended for esthetic reasons and to eliminate sensitivity. Dentitions affected by AI are not inherently caries prone.

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AMELOGENESIS IMPERFECTA, HYPOMATURATION/ HYPOCALCIFICATION TYPES

Figure 11-30

Age: Infants
Sex: Predilection varies according to mode of inheritance.

CLINICAL FEATURES

Hypomaturation and hypocalcification forms of AI exhibit normal enamel thickness with mesiodistal contacts, yet are poorly mineralized, mottled, discolored, and tend to show chipping of enamel away from the dentin. The hypocalcified enamel

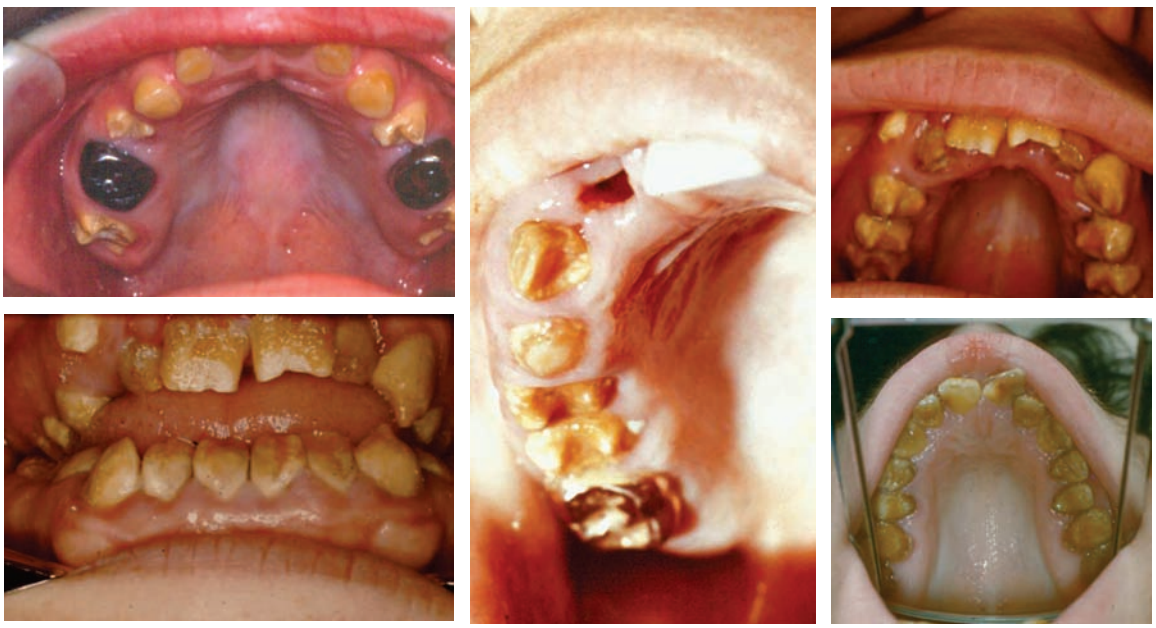

FIGURE 11-30
Amelogenesis imperfecta, pigmented hypomaturation type.

is no more radiodense than dentin, having a higher protein content than normal enamel. *Autosomal dominant hypocalcified AI* is the most common form, occurring once in every 20,000 births. The enamel is normal in thickness yet is soft, cheesy, and crumbly, and is penetrable with a dental explorer. Newly erupted teeth are without luster and are opaque white or orange. The enamel wears away rapidly, and calculus deposition is often a striking feature. Radiographically, multiple moth-eaten foci are observed over the crowns. An *autosomal dominant hypomaturation-hypoplastic form* of AI occurs in conjunction with taurodontism, which may represent a variation of expressivity of the trichodento-osseous syndrome (see Syndrome-Associated Enamel Defects). *X-linked recessive hypomaturation AI* affects both primary and adult dentitions. Males show more severe changes. The permanent teeth are nearly normal in thickness and are in contact, yet are yellowish-brown and mottled. The cervical collar is minimally involved. In females, wavy vertical banding is seen and has the appearance of dripping wax. These striae are not seen radiographically. *Autosomal recessive pigmented hypomaturation AI* affects both primary and adult dentitions. Although thickness approaches normalcy, the enamel chips, particularly around restorations, and is brown. The incisal and occlusal surfaces are usually eroded. These teeth tend to accumulate calculus that fluoresces red-violet. Radiographically, the enamel layer is poorly defined. In families with an X-linked form, it has been shown that the disorder may result from mutations in the amelogenin gene, *AMELX*. The enamelin gene, *ENAM*, is implicated in the pathogenesis of the dominant forms of AI.

TREATMENT

Full coverage prostheses are indicated for esthetic reasons. In addition, full crowns minimize calculus deposition, which would otherwise predispose to periodontal inflammation.

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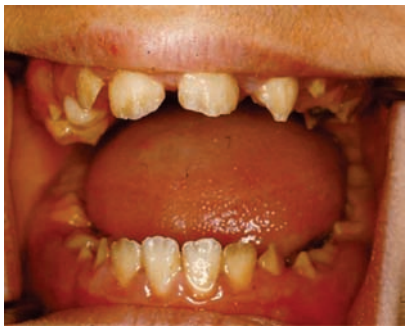
SYNDROME-ASSOCIATED ENAMEL DEFECTS

Figure 11-31

Sex: Predilection varies according to mode of inheritance.

CLINICAL FEATURES

A vast number of rare syndromes have been described in which dental anomalies have been observed. Some of these syndromes show enamel defects as the sole dental anomaly; others affect enamel as well as other dental tissues. *Epidermolysis bullosa* occurs in at least four genetic forms and is a bullous disease of skin and mucous membranes. Dental defects are observed in some of these forms and consist of thin hypoplastic enamel with random pitting, yielding a honeycomb pattern. The *mucopolysaccharidoses* (MPS) are heritable diseases of defective mucopolysaccharide metabolism. In type IV, Morquio's syndrome, the enamel is hypoplastic with pointed peak-like cusp tips. The teeth are grey and pitted, and the pits tend to be vertically oriented. The teeth in type III, Sanfilippo's syndrome, exhibit loss



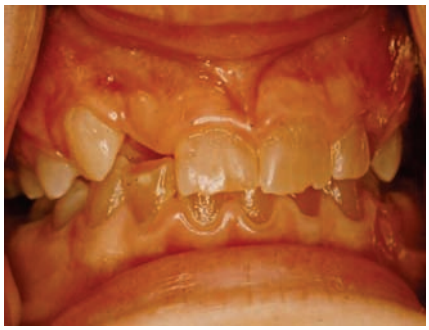


FIGURE 11-31
A variety of syndromes are associated with hypodontia and defective enamel.

of enamel with excessive and defective dentinogenesis, yielding radiographic evidence of pulp obliteration. In *tuberous sclerosis,* linear enamel pits may pock the facial enamel surfaces; these pits are usually apparent as punctate radiolucencies. *Oculodento-osseous dysplasia* is characterized by microphthalmus, iridal anomalies, bony anomalies of the digits and syndactyly, thickened mandibular bone, and enamel hypoplasia. The teeth show large multifocal hypoplastic defects and pitting, yielding a moth-eaten pattern radiographically. *Oculodentodigital dysplasia* is a subvariant of the former disorder and involves mutations in the Connexin 43 gene (*GJA1*). The syndrome is characterized by abnormal facial features, central nervous system involvement, syndactyly and clinodactyly of fourth and fifth fingers, dry and lusterless hair, generalized enamel hypoplasia, and odontodysplasia. In the *amelo-onychohypohidrotic syndrome,* defective nails with subungual hyperkeratosis are seen in conjunction with sweat gland hypofunction, seborrheic dermatitis, and severe hypoplastic-hypocalcified enamel. Many resorbing unerupted teeth are observed in this syndrome.

The *trichodento-osseous syndrome* also shows enamel defects in conjunction with morphologic dental anomalies. These patients have tightly curled, kinky hair, with osteosclerosis of bone cortices. The enamel is hypoplastic and hypocalcified, lacking mesiodistal contact with pitting. Taurodontism is a feature, and many of the teeth remain unerupted. In *vitamin D refractory rickets,* the incisal or occlusal one third is hypoplastic with granular enamel. The pulp chambers are large and pulp horns extend to the dentinoenamel junction. *Pseudohypoparathyroidism* exists in two forms. In both forms, parathyroid hormone levels are intact; however, there is an inability to eliminate phosphate through the kidneys. Males are more severely affected in this X-linked disease. Features include round facies, short neck, short fourth metacarpals, falx cerebri and basal ganglia calcifications, and hypocalcemia with tetany. In addition, isolated secondary teeth, usually molars and premolars, show pitted enamel defects, are wedge shaped, and have short roots with wide root canals and open apices. In the odontogenic fibroma-like hamartoma/enamel hypoplasia syndrome, enlarged pericoronal follicles are seen around unerupted molars and enamel resembles that of AI.

TREATMENT

The dental defects included here are all characterized by enamel hypoplasia with pitting, and can be restored with full crowns.

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DENTINOGENESIS IMPERFECTA

Figure 11-32

Sex: No predilection

CLINICAL FEATURES

Dentinogenesis imperfecta is inherited as an autosomal dominant trait and is occasionally associated with osteogenesis imperfecta (OI) with blue sclera. Not all OI syndromes are associated with dentinal defects. Furthermore, there is no correlation between dentinogenesis imperfecta and severity of the osseous diseases in OI; rather, it appears that OI pedigrees either consistently exhibit dentinogenesis imperfecta or show no evidence of heritable dental disease. Dentinogenesis imperfecta without associated osseous disease is encountered more frequently than OI-associated disease. Both deciduous and permanent dentitions are affected. The teeth show a yellowish to blue-gray opalescent,

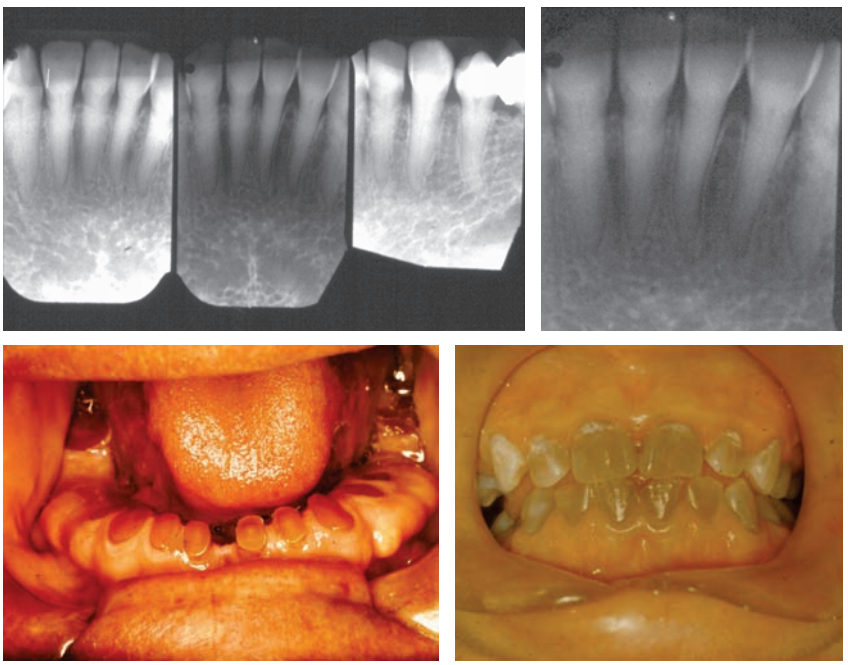

FIGURE 11-32
Dentinogenesis imperfecta with opalescent teeth, which are subject to enamel fragmentation and advanced abrasion. Radiographs show obliteration of root canals.

polished appearance. The defective dentin pervades both the coronal and radicular regions. A severe form of dentinogenesis imperfecta was first described in a triracial isolate group in Maryland. Opalescent bell-shaped crowns are seen; radiographically, dentin is rudimentary with large pulp chambers (shell teeth, Brandywine type, Shields type III). Originally it was thought that a defective dentinoenamel junction was extant; scanning electron microscopic studies have disclosed a normal junction. There is a propensity for enamel loss, and the cleavage of enamel likely occurs within defective dentin underlying the dentinoenamel junction. The exposed dentin rapidly abrades in many instances so that the coronal surface may fail to extend beyond the gingival crest. Radiographically, the cervix region is constricted, the roots are spiked, and the pulp chambers and root canals manifest calcific obliteration. Because dentinal tubules are haphazardly arranged and often devoid of odontoblastic processes, the teeth are not particularly sensitive, even when most of the enamel surface has been lost. Microscopically, the pulp chamber is nearly obliterated. The dentinal tubules are poorly formed and fail to radiate in parallel fashion; rather, they are serpentine and haphazardly arranged.

TREATMENT

Affected teeth are not more prone than normal teeth to dental caries. Full crowns can be fabricated, even at an early age, because of the small, obliterated pulp chambers. Root fractures are relatively common. When severe abrasion exists, an overdenture may be considered.

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OSTEOGENESIS IMPERFECTA

Figure 11-33

Sex: No Predilection

OI is a genetic disease involving mutations in collagen that have great impact on osteogenesis. There are numerous variants of the disorder, one of which is associated dentinogenisis imperfecta type I. Fractures are the most problematic aspect of the disease and may occur without traumatic provocation. Hearing loss may occur in adult life. A hallmark of the disease is the presence of blue sclera. The clinical spectrum ranges from severe skeletal deformities and short stature with mobility impairments to mild forms with limited history of fractures. In all forms, most fractures occur in the lower extremities. Seven variant types of OI are now identified. Radiographically, fractures are seen along with Wormian bones, "codfish" vertebrae, and osteopenia. Assays of bone collagen type I demonstrate perturbations in 98% of the cases of OI type II and somewhat less in the other variants.

About 90% of individuals with OI types I, II, III, and IV (but none with OI types V, VI, and VII) have an identifiable mutation in either *COL1A1* or *COL1A2*. Types I to V are autosomal dominant, whereas type VII is inherited in an autosomal recessive manner, and the mode of inheritance of type VI has yet to be illuminated. The features of dentinogenesis imperfecta (DI) mirror those cases without OI association (DI type II). There is also an OI phenotype in which

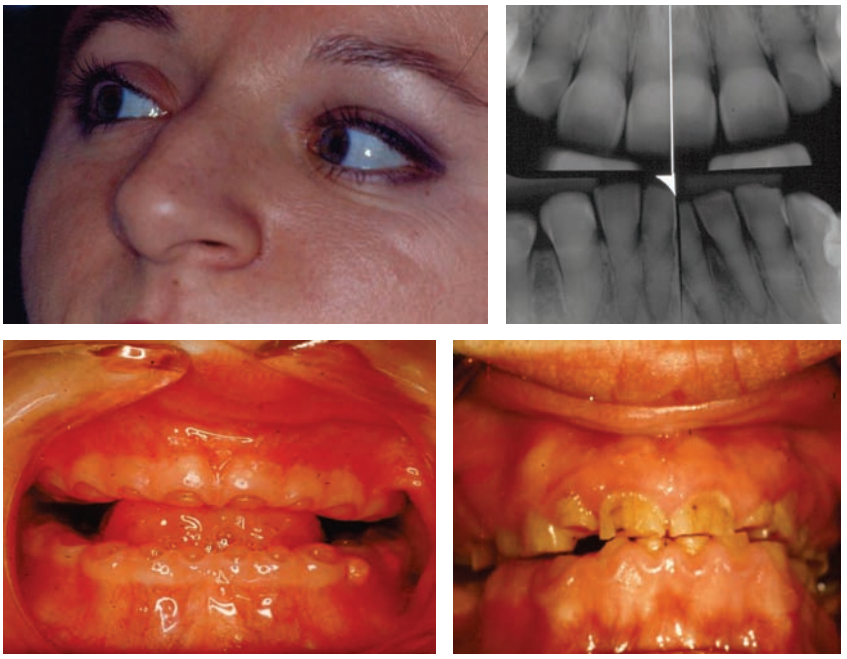

FIGURE 11-33
Osteogenesis imperfecta with type I dentinogenesis imperfecta. Blue sclera.

benign fibro-osseous lesions similar to florid osseous dysplasia are present in multiple jaw quadrants.

DIFFERENTIAL DIAGNOSIS

Various forms of dwarfism must be considered in severe forms and other conditions that predispose to fracture should be considered (e.g., osteoporosis and osteomalacia). Pathologic fractures also occur with intraosseous tumors including cancers metastatic to bone.

TREATMENT

There is no preventive treatment for this genetic group of disease. Orthopedic management of fractures is required throughout life. When dentinogenesis is present, full coverage prosthodontics can be performed for both functional and esthetic reasons.

Additional Reading

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DENTIN DYSPLASIA TYPE I

Figure 11-34

Sex: No predilection

CLINICAL FEATURES

Dentin dysplasia type I is a rare disease of dentin and is inherited as an autosomal dominant trait that affects both the deciduous and permanent dentitions. It represents a peculiar disturbance in the development of radicular dentinogenesis in that the coronal morphologic and histologic features are normal. Unlike dentinogenesis imperfecta, enamel fragmentation is not encountered. Clinically, the crowns usually appear normal, yet in some individuals subtle opalescent gray discoloration is noted. Radiographically, the roots are rudimentary with tapering and blunting. The root canals are obliterated and the pulp chambers are malformed, appearing

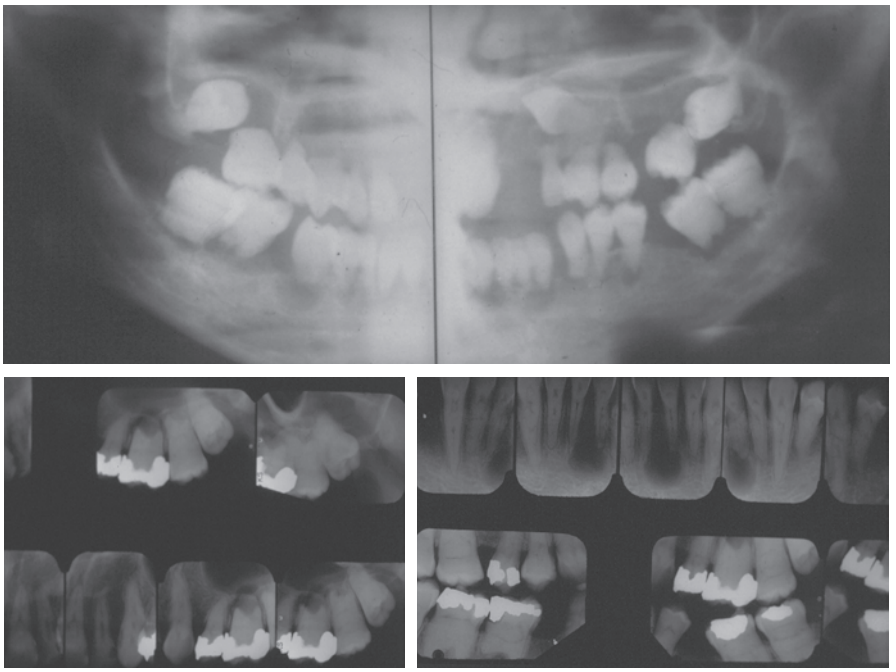

FIGURE 11-34
Dentin dysplasia type I. Rootless teeth with obliterated root canals and pulp chambers.

as horizontal crescents. Periapical radiolucencies of unknown origin underlie many of the teeth. The microscopic appearance of extracted teeth is pathognomonic. The coronal dentin shows normal tubular orientation, whereas the radicular dentin is whorled, giving the appearance of cascading waterfalls. The pulp chamber and root canal cannot be identified. The short roots are functionally unstable, so that loosening of teeth is a feature. Dentin dysplasia type I has been reported to occur in conjunction with diffuse generalized osteosclerosis in some patients and radiographically anomalous teeth similar to that of dentin dysplasia may be seen in conjunction with periarticular tumoral calcinosis. The genetic basis of this disorder has not been elucidated.

TREATMENT

No specific treatment is recommended. When teeth are lost as a result of shortened roots, adjacent teeth should not be used as prosthetic abutments.

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DENTIN DYSPLASIA TYPE II

Figure 11-35

Sex: No predilection

CLINICAL FEATURES

Dentin dysplasia type II, coronal type, is inherited as an autosomal dominant disorder. The deciduous teeth are amber/gray

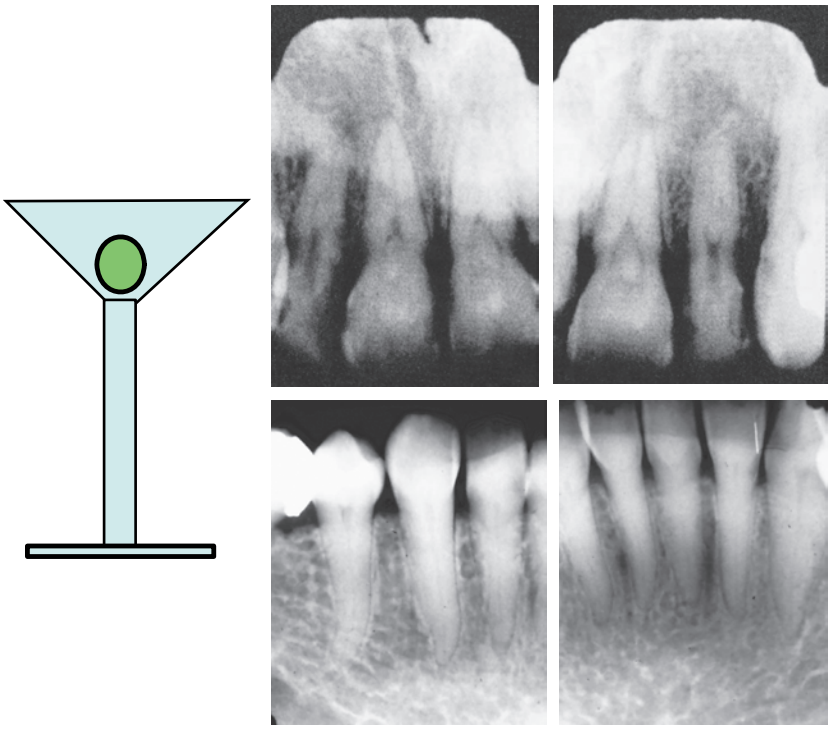

FIGURE 11-35
Dentin dysplasia type II showing denticles. Martini glass or thistle shaped pulps.

and translucent with radiographic evidence of pulp chamber and root canal obliteration, thereby resembling dentinogenesis imperfecta. The permanent dentition is clinically normal; radiographically, pronounced cervical constriction is not featured. Large, flame-shaped pulp chambers contain many denticles; root canals may be partially obliterated. The dentin sialophosphoprotein (*DSPP*) gene on chromosome 4q21.3 encodes the major noncollagenous protein in tooth dentin and is mutated in dentin dysplasia type 2 as well as dentinogenesis imperfecta types II and III.

TREATMENT

No special treatment is required, because enamel fracturing is not a problem and root length is essentially normal.

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REGIONAL ODONTODYSPLASIA

Figure 11-36

Sex: No predilection

CLINICAL FEATURES

Occurring as a sporadic anomaly, regional odontodysplasia is a localized developmental dental defect restricted to a single tooth or group of contiguous teeth in one quadrant. Although most instances fail to

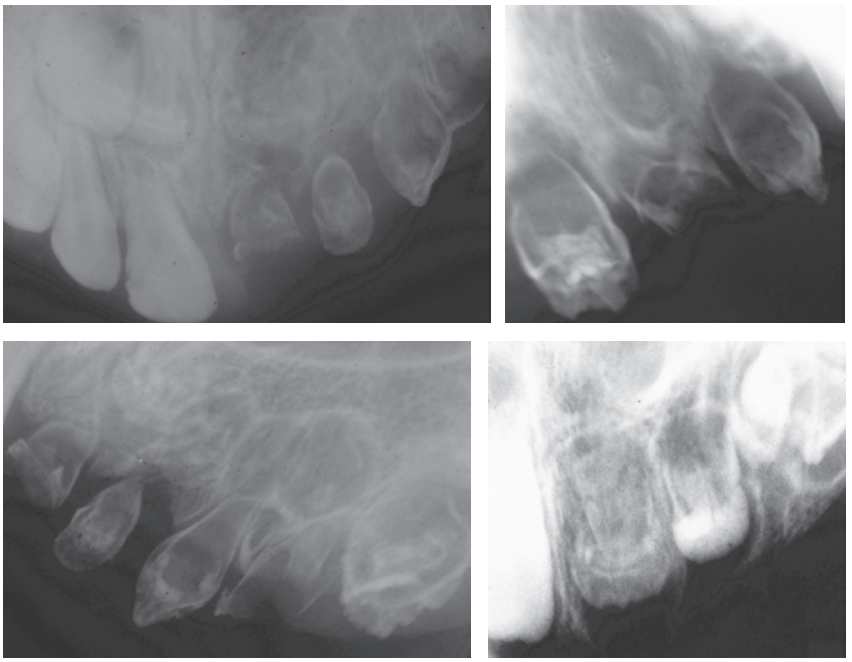

FIGURE 11-36
Ghost teeth in regional odontodysplasia.

show gingival enlargement in the affected area, patients with hyperplastic appearing tissue have been reported. The involved teeth are usually the central and lateral incisors and cuspid in the maxilla. They fail to erupt completely. On radiographs, both enamel and dentin formation are deficient, yielding a subdued appearance with patent dilated pulp chambers. The appearance accounts for the term *ghost teeth*. The cause is unknown; however, the distribution in the maxilla often corresponds to the neurovascular supply, suggesting that an ischemic phenomenon may be responsible. In fact, many cases have been reported in which vascular nevi involve the area of the face that harbors the hypoplastic teeth. Both permanent and deciduous predecessors may be affected. Microscopically, large pulp chambers are noted and the dentin is thin and globular. The enamel layer is attenuated and disrupted. The reduced enamel epithelium persists, and the follicular connective tissue contains many enameloid droplet calcifications.

TREATMENT

The teeth are nonfunctional; because eruption is not evident or is only partial, extraction with fabrication of a prosthetic appliance is recommended.

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HYPOPHOSPHATASIA

Figure 11-37

Sex: No predilection

CLINICAL FEATURES

Inherited as an autosomal recessive trait, hypophosphatasia represents an enzyme-deficiency metabolic bone disease characterized by absence or diminution of alkaline phosphatase in osteoblasts, intestines, and kidneys, among other tissues. It occurs in infantile, juvenile, and adult forms; the infantile form has the worst prognosis. Those individuals capable of survival show osteomalacia with hypomineralization similar to that seen in acquired rickets. The chief dental manifestation is premature tooth loss from cemental agenesis with lack of secure periodontal fiber attachment to the teeth. In addition, the teeth are often hypocalcified with large pulp chambers resembling shell teeth or odontodysplasia. Both primary and secondary teeth are affected. Histologically, a thin layer of dentin is observed with cemental agenesis. The serum alkaline phosphatase level is lowered; in many cases, hypercalcemia and urinary phosphoethanolamine are demonstrable. Mutations in *ALPL*, the gene encoding alkaline phosphatase, and tissue-nonspecific isozyme (*TNSALP*) *ALPL* occur in hypophosphatasia.

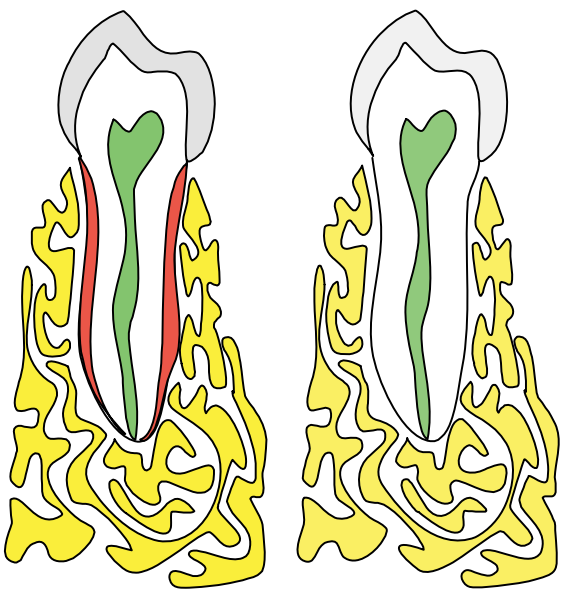

FIGURE 11-37
Drawing depicting normal cementogenesis (left), cemental agenesis in hypophosphatasia (right).

TREATMENT

No successful treatment is available. High-dose vitamin D therapy has been used with limited success.

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VITAMIN D REFRACTORY RICKETS

Figure 11-38

Sex: Males are affected more severely

CLINICAL FEATURES

Vitamin D refractory or hypophosphatemic rickets is a heritable disorder with X-linked dominant transmission. The clinical features, osteomalacia causing osseous deformities similar to those seen in ordinary rickets, do not show resolution with administration of vitamin D. Serum phosphorus

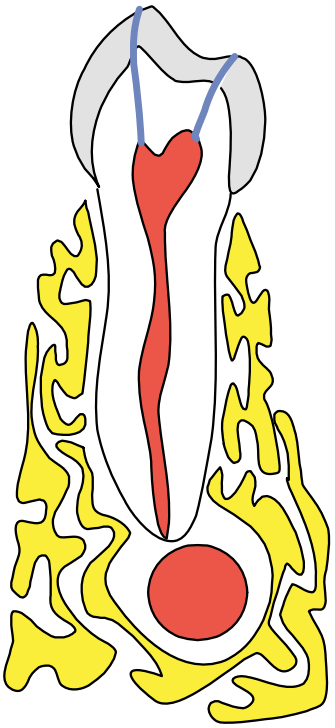

FIGURE 11-38
Elongated pulp horns in region of coronal fissures in vitamin D refractory rickets.

levels are depressed. Patients lack an enzyme necessary for conversion of intestinally absorbed vitamin D_3 into the active 1α-25 dihydroxyvitamin D_3. The resultant deficit in active vitamin leads to poor phosphate absorption and deficient mineralization of osteoid. There is also some evidence to support a defect in renal tubular handling of phosphate. Affected children have difficulty walking. Globular dentin is prominent; fissures develop and extend from the pulp horns, which are elongated, to the cusp tips. These fissures are patent, allowing oral microorganism to gain access to the pulp chamber in the absence of caries. This exposure, in turn, leads to periapical disease, demonstrated radiographically, with clinical evidence of widespread fistulae. The supportive alveolar bone often shows an osteoporotic pattern of trabeculation. The long-bone epiphyseal plates show pericartilaginous deposition with failure to mineralize.

Ordinary rickets fails to show the dental defects encountered in hypophosphatemic rickets, and the former disease responds rapidly to vitamin D therapy. A mutation in the vitamin D receptor gene has been identified.

DIFFERENTIAL DIAGNOSIS

Widespread dental abscess formation may be seen in diabetes of juvenile onset, yet diabetes rarely becomes severe enough to produce these changes in young children. Assessment of serum phosphorus levels and a skeletal radiographic survey should be done with children showing widespread periapical disease in the absence of dental caries. The presence of a familial pattern also helps to limit the differential diagnosis.

TREATMENT

Administration of 1α-25 dihydroxyvitamin D_3 results in significant improvement. The patient should be referred to an internist or endocrinologist. Occlusal sealants will not prevent pulpal and periapical infection. Complete pulpectomy of affected teeth is recommended with placement of zinc oxide and engenol.

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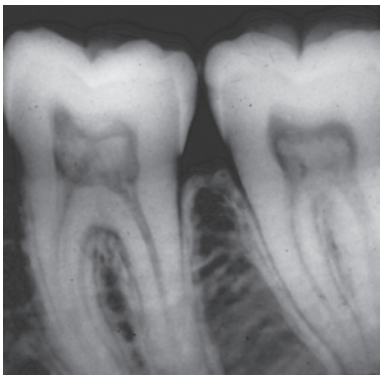
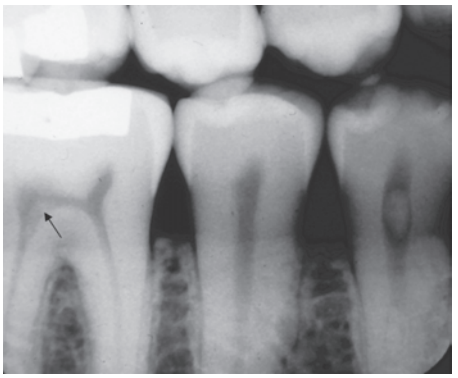

FIGURE 11-39
Pulp stones.

DENTICLES AND PULP CALCIFICATION

Figure 11-39

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Pulpal calcifications are identified on dental radiographs and may be located either within the pulp chamber, appearing as focal intrapulpal radiopacities, or within the root canals, as diffuse radiopacities giving the appearance of calcific obliteration. The calcifications in the coronal pulp chamber are referred to as *denticles or pulp stones*; root canal calcification has been referred to as *calcific metamorphosis of pulp*. In either case, no cause can be identified either locally or systemically. The teeth are vital, even when canals appear to be obliterated, and there is no relationship between pulp calcification and facial pain. Denticles are classified as "true" if composed of dentin or "false" if composed of laminated dystrophic calcific concretions. Furthermore, either type may be attached or free, depending on whether the calcified mass is confluent with the normal tooth dentin. Type II dentin dysplasia is characterized by large pulp chambers with denticle formation. Pulp stones are also frequently encountered in certain forms of OI. Microscopically, calcific metamorphosis of the root canal is characterized by multifocal dystrophic calcifications that tend to align themselves in a vertical plane throughout the radicular pulp.

TREATMENT

No treatment is required.

Additional Reading

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SEGMENTAL ODONTOMAXILLARY DYSPLASIA

Figure 11-40

Age: Teens
Sex: No predilection

CLINICAL FEATURES

This anomaly is sporadic and is first noted during teenage years when routine dental or orthodontic radiographs are procured or when facial asymmetry becomes appar-

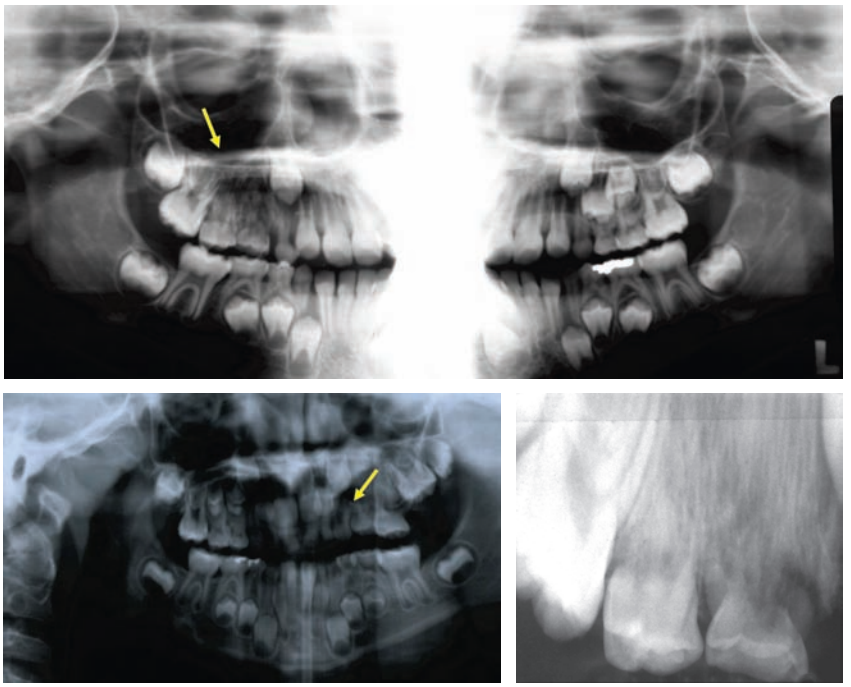

FIGURE 11-40
Segmental odontomaxillary dysplasia.

ent. Unilateral asymmetry with maxillary enlargement is usually mild and may not be particularly noticeable. Radiographically, the area of alveolar enlargement shows a somewhat ground glass appearance that is vertically streaked yielding a "falling rain or sleet" pattern. One or both premolar teeth are missing and retained deciduous teeth are morphologically anomalous.

MICROSCOPIC FEATURES

Pathologic changes in the affected maxillary bone are characterized by osteocytic hyperplasia (increased number of intralacunar osteocytes per unit area of bone), lacunar enlargement, and sheet-like arrangements of woven bone. Osteoblastic and osteoclastic activity appears decreased. The fibrous marrow element is hypocellular, mature, or myxoid. Affected teeth show variability in dentinal tubule diameter.

DIFFERENTIAL DIAGNOSIS

Fibrous dysplasia may be a consideration, yet does not show anomalous or missing teeth.

TREATMENT

No treatment is necessary. Any unerupted teeth in the area of lesional bone should be extracted. If maxillary enlargement is a cosmetic concern, surgical contouring may be undertaken.

Additional Reading

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INTERNAL RESORPTION

Figure 11-41

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

As opposed to most of the diseases showing structural deformities, internal resorption is acquired later in life and fails to follow any hereditary pattern. The cause is unknown, although trauma has been suggested. Caries with pulpitis may be present, but this is not a prerequisite. Pain is not a feature when caries is absent. When internal resorption develops in the coronal pulp, the tooth may resorb to the point where the vascularity of the pulp tissue is observed through a thin dental hard tissue layer with a pink appearance (pink tooth of Mummery). Radiographs show a circular or ovoid radiolucency within the region of the pulp chamber either in the coronal or, more commonly, in the radicular region. The maxillary central incisors are most often afflicted. Internal resorption may accompany external resorption, particularly with impacted teeth. Microscopically, the pulp chamber contains viable fibrous connective tissue, which in unexposed pulps is devoid of inflammation. The dentin shows scalloping with osteoclastic resorption. Attempts at repair may exist, with deposition of osteodentin over zones of resorption.

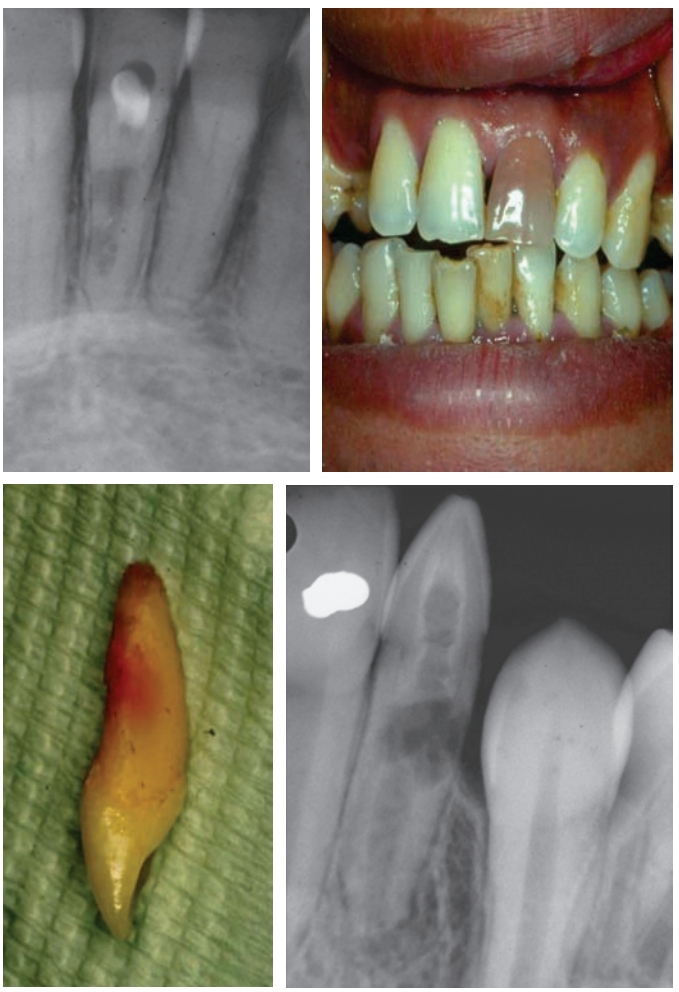

FIGURE 11-41
Internal resorption manifesting an intradental radiolucency.

TREATMENT

No treatment is required. Endodontic therapy is not feasible because of the inaccessibility of the resorbed recesses to instrumentation. As the disease progresses, root fracture may occur, necessitating extraction. Often, the resorption becomes static.

Additional Reading

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EXTERNAL RESORPTION

Figure 11-42

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The cementum and underlying dentin may show resorption as a consequence of pressure or trauma generated by tumors and cysts, orthodontic forces, reimplantation, or periapical inflammation. Impacted teeth of long standing may also show internal and external resorption of both coronal and radicular hard tissues. Resorption of roots on erupted teeth where no cause can be determined is termed *idiopathic resorption*. Some degree of root resorption probably occurs in most adults; however, it is minimal. Occasionally, for no apparent reason, many teeth show advanced resorption

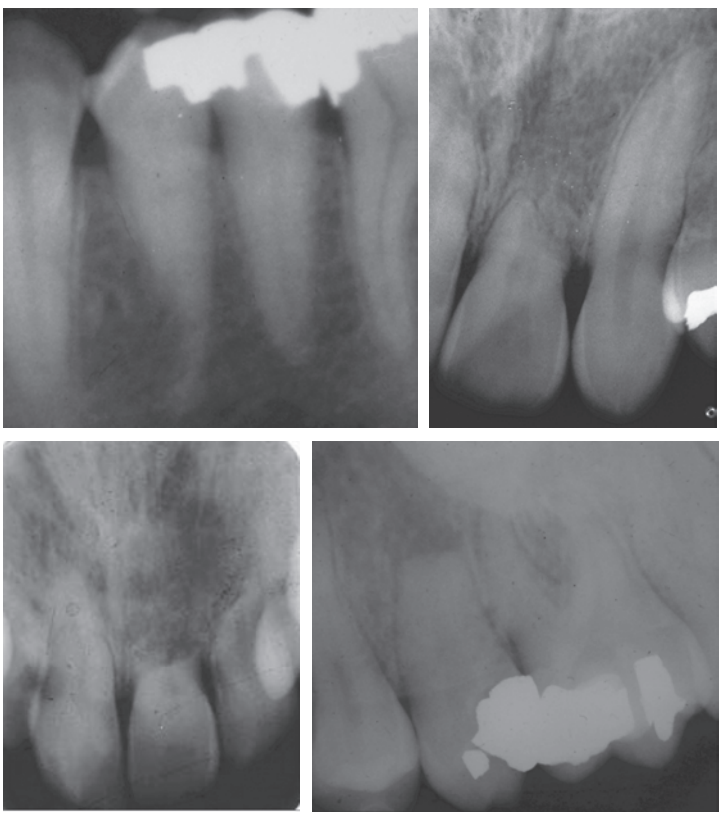

FIGURE 11-42
External root resorption.

with blunting of the roots. The maxillary premolars, incisors, and molars are most often affected. Neither periodontal disease nor periapical inflammation bears any relationship to idiopathic generalized resorption. The apices show osteoclast-mediated resorption of cementum and dentin, with no alteration in the periodontal ligament or underlying periodontal bone that replaces the zone previously occupied by dental root structure.

TREATMENT

No form of treatment has been shown to arrest the process. Resorption may proceed progressively until the involved teeth become loose. Extraction may then become necessary.

Additional Reading

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SUBCERVICAL RESORPTION

Figure 11-43

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Subcervical resorptive foci may be isolated, yet usually multiple lesions are seen, even as many as 20 in any given patient. The resorptive lesions may be focal, on only one side of a tooth or they may become circumferential. Their number increases with time. There is no association with any specific systemic or other dental disease and the resorptive foci are not carious. Radiographically, radiolucencies at the cervical region are seen and are usually smooth and well demarcated.

MICROSCOPIC FEATURES

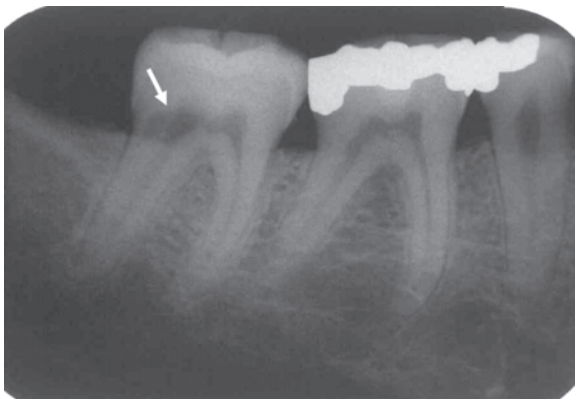
Granulation tissue, chronically inflamed, occupies the resorptive foci and osteoclastic activity is identifiable.

DIFFERENTIAL DIAGNOSIS

Cervical/root caries is differentiated from subcervical resorption on the findings of hard tissue softness using a sharp probe.

TREATMENT

Circumferential lesions may condemn the tooth to extraction. Focal lesions can be restored with composite or full crowns can



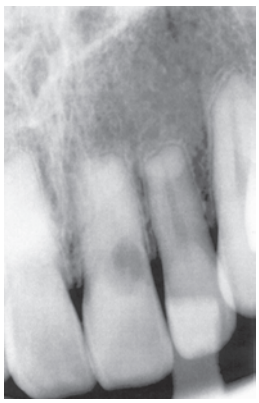


FIGURE 11-43
Subcervical erosion.

be fabricated especially in teeth that may be in danger of fracture.

Additional Reading

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CORONAL FRACTURE

Figure 11-44

Age: Children and teens
Sex: Male predilection

CLINICAL FEATURES

Rambunctious kids engaging in daredevil feats, tend to fall off of bikes and skateboards, many invariably landing on their face. Incisal fractures are the most common injuries. There are classification systems for dental fractures that are designed for determining the most appropriate restorative treatment. Fractures that do not intersect the pulp chamber may not predispose to pulpitis because of pulp exposure; however, if tooth luxation occurs, the pulp may be devitalized in the absence of pulp exposure. Fractures that intersect and expose the pulp will result in pulpitis leading to necrosis and periapical spread of infection.

MICROSCOPIC FEATURES

Not applicable.

DIFFERENTIAL DIAGNOSIS

A history of trauma eliminates developmental defects.

TREATMENT

Avulsed teeth may be reinserted into the socket and immobilized. Pulpotomy in

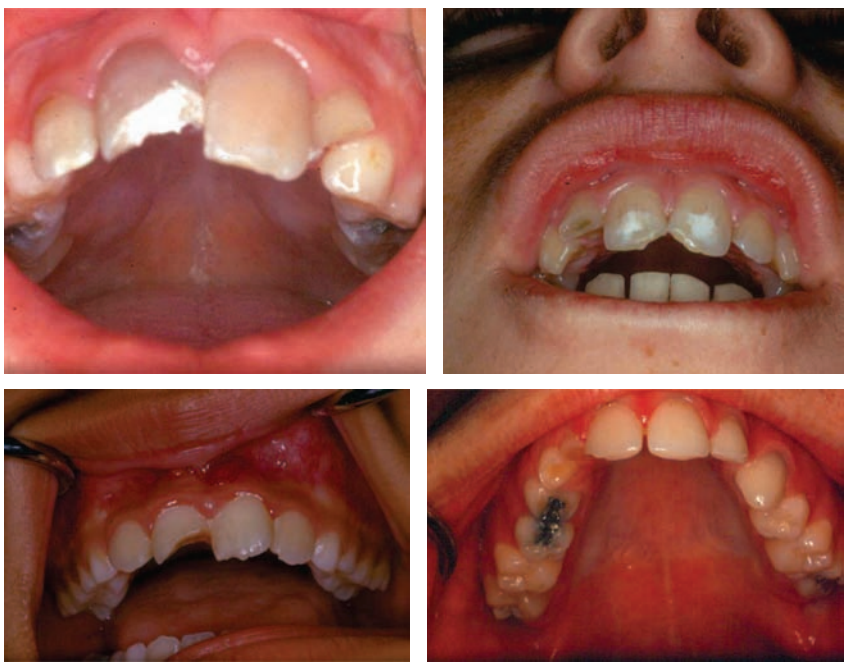

FIGURE 11-44
Incisal trauma with fractures.

pulpally exposed deciduous teeth is recommended; in permanent incisors and cuspids, root canal therapy is required.

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Alterations in Eruption/ Exfoliation Times

PREMATURE ERUPTION

Sex: No predilection

CLINICAL FEATURES

Early eruption of teeth may occur with both deciduous and permanent dentitions in the absence of any underlying systemic disorder. Indeed, 10% of the population may manifest precocious eruption as early as 3 months for deciduous and 4 years for permanent dentitions. Natal or neonatal teeth are deciduous teeth, usually mandibular incisors, that are present at birth or erupt soon thereafter. This condition seems to be genetically determined and is most frequently encountered among isolated tribes and ethnic groups. Often, prematurely erupted deciduous teeth fail to complete root development and are prematurely exfoliated. A variety of craniofacial syndromes are associated with premature eruption of teeth: clefts, oculomandibulodyscephaly, chondroectodermal dysplasia, and hemifacial hypertrophy. Hyperthyroidism of congenital or childhood onset may also be associated with early eruption.

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DELAYED ERUPTION

Sex: No predilection

CLINICAL FEATURES

Great variation exists with regard to eruption dates; thus, delayed eruption may not herald the presence of any underlying disorder but may merely represent a variation in normal physiology. Certain systemic illnesses and syndromes may be associated with generalized delayed eruption, and these conditions must be considered when a patient exhibits alteration in eruption dates. In particular, patients with cleidocranial dysostosis show hypoplastic or aplastic clavicles, cranial anomalies, and multiple unerupted and supernumerary teeth. In cryptodontic brachymetacarpia, the metacarpals and metatarsals are shortened and teeth fail to erupt. Many of the syndromes described in conjunction with enamel defects show retarded eruption or unerupted teeth. Hypothyroidism and hypopituitarism (pituitary dwarfism) are often associated with delayed eruption. Multiple impacted teeth are encountered in cleidocranial dysplasia and Gardner's syndrome. Generalized delayed eruption may also be encountered in Down's syndrome, rickets, vitamin D refractory rickets, lead poisoning, and osteopetrosis. Isolated or individual teeth showing retarded eruption often indicate the presence of an intrabony odontogenic neoplasm or cyst, requiring radiographs to determine whether or not a radiolucent or radiopaque lesion

is associated with the impacted tooth. In addition to impaction, congenitally missing teeth, of course, give the impression that eruption is retarded. This may be generalized in hereditary ectodermal dysplasia and chondroectodermal dysplasia.

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IMPACTION

Figure 11-45

Sex: No predilection

CLINICAL FEATURES

Impaction or retention of teeth is one of the most common developmental dental defects encountered in man. Failure of teeth to erupt may be the result of a physical barrier, unexplained loss of eruption force, or a tumor or cyst of the jaws arising from odontogenic or nonodontogenic tissues. The mandibular third molars and maxillary canines are most frequently involved, followed by the maxillary third molars. Maxillary central incisors, mandibular canines, and premolars in both arches are also retained with some degree of frequency. Supernumerary teeth such as mesiodens and premolars often fail to erupt. Multiple impactions and supernumerary teeth are encountered in cleidocranial dysostosis, which is characterized by the aforementioned dental defect in conjunction with agenesis or hypoplasia of the clavicles and craniofacial anomalies including Wormian bones, open fontanels, hypoplastic sinuses, and other defects of both membranous and endochondral bones. Gardner's syndrome is also associated with multiple dental impactions. Impacted teeth are also seen in various forms of AI and in syndromes associated with enamel defects. The significance of impacted teeth rests with the latent potential of the follicular tissues to undergo cystic or neoplastic transformation. A complication of impacted mandibular third molar removal is paresthesia.

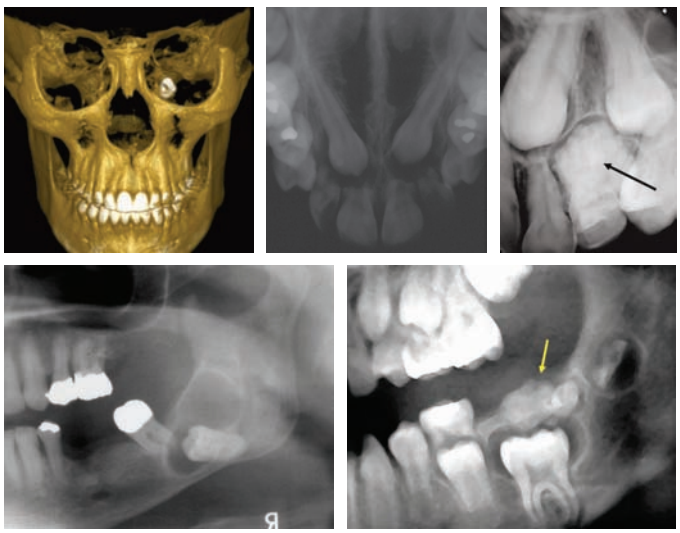

FIGURE 11-45
Impacted teeth. Arrows: odontomas.

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PREMATURE EXFOLIATION

Sex: No predilection

CLINICAL FEATURES

Premature loss of deciduous teeth in conjunction with precocious eruption is usually no clinical significance because the succedaneous dentition also commonly erupts early. Premature exfoliation limited to a localized region may be an ominous sign. Loosening of either deciduous or permanent teeth in children, teenagers, or young adults may be indicative of an underlying destructive process of the alveolar bone: leukemia, sarcoma, histiocytosis X, or a benign neoplasm. Generalized premature loss of the incisors and molars is a feature of periodontosis; when seen in conjunction with palmar-plantar hyperkeratosis, the Papillon-Lefevre syndrome should be considered. Generalized early tooth loss is also encountered in hypophosphatasia, juvenile onset diabetes, cyclic neutropenia, agranulocytosis, acrodynia, scurvy, and dentin dysplasia. Full-mouth dental radiographs or a panorex radiograph should be obtained when teeth become loose prior to their normal exfoliation times.

Additional Reading

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Pigmentations

ERYTHROBLASTOSIS FETALIS

Figure 11-46

Sex: No predilection

CLINICAL FEATURES

Hemolytic anemia develops in infants when an Rh-positive fetus is nurtured in the womb of an Rh-negative mother who has developed anti-Rh antibodies from a previous pregnancy. When antibodies pass the placental membrane and enter the fetal circulation, they agglutinate fetal erythrocytes, bind complement, and cause hemolysis. This same immunologic lesion may evolve as a consequence of ABO isoantigen incompatibility, in which the fetus is A, B, or AB and the mother lacks A or B isoantigens. If the anemia is prolonged, hemolyzed erythrocytes liberate hemosiderin pigment, which may become deposited in developing dentin matrices. Teeth at a comparable stage of development (usually only deciduous) then show pigmentation; they are brown, black, green, or blue. The pigment is transmitted from the deeper layers of dentin. When

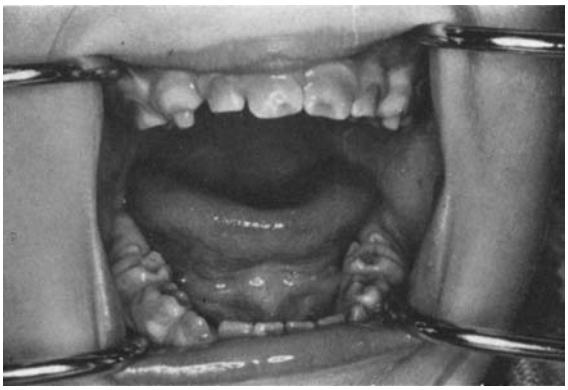

FIGURE 11-46
Teeth in erythroblastosis fetalis darkened as a result of hemosiderin pigment deposition in dentin. (Courtesy of Drs. R. Abrams, R. Adams, and R. Sobel.)

icterus develops, hypoplasia of enamel may be seen.

DIFFERENTIAL DIAGNOSIS

The pigment of erythroblastosis is not associated with a chalky enamel surface as is often encountered in fluorosis. Staining from tetracycline occurs more often in permanent teeth, is yellow, and fluoresces with ultraviolet light. Red fluorescence is seen in porphyria. Bilirubin-stained teeth are also green, so that various other forms of neonatal jaundice must be considered. Extrinsic stains can be removed with scalers.

TREATMENT

No treatment is required. On exfoliation, the permanent teeth are usually of normal color.

Additional Reading

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BILIARY ATRESIA

Figure 11-47

Sex: No predilection

CLINICAL FEATURES

Atresia of the biliary ducts, or other liver disorders such as neonatal hepatitis, may cause retention of either conjugated or unconjugated bilirubin. The bile pigments become elevated in serum and may then become incorporated into the organic matrices of developing teeth. In the icteric state, the deposited bilirubin imparts a green hue to the deciduous teeth. If the child is able to thrive and if the jaundice can be corrected, he or she will have a normal secondary dentition. The prognosis with biliary atresia is poor. Other forms of neonatal jaundice such as erythroblastosis and hepatitis are reversible in most cases.

DIFFERENTIAL DIAGNOSIS

The diagnosis of biliary atresia is made on the basis of biochemical and radiologic studies for liver function. A conjugated hyperbilirubinemia prevails, and cholangiograms disclose a rudimentary biliary tree. Liver biopsy may also be required to make the diagnosis. Fever with jaundice in newborns may indicate neonatal hepatitis. Needle biopsies may aid in obtaining a definitive diagnosis. By the time the patient is seen by the dentist, a diagnosis has usually been rendered.

TREATMENT

Provided that jaundice has been corrected, the secondary dentition will be normal.

Additional Reading

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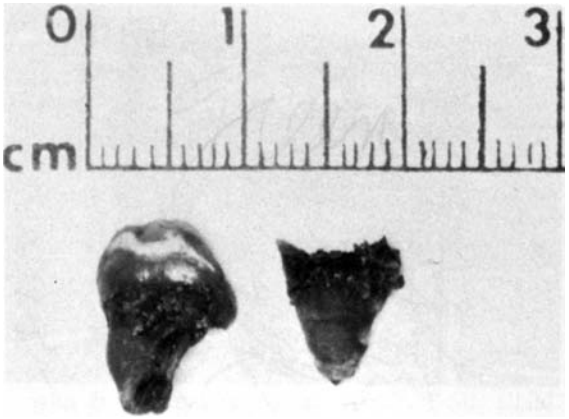

FIGURE 11-47
Exfoliated teeth stained green by bilirubin pigment in biliary atresia.

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POSTMORTEM PINK TEETH

Age: After death
Sex: No predilection

CLINICAL FEATURES

The pink teeth phenomenon in corpses, although uncommon, is a well-recognized postmortem change. Predisposing factors include unnatural death, exposure to humid conditions or submersion of the corpse in water, and probable gravitational stasis of blood at the time of death. Thus, postmortem pink teeth are most often, yet not exclusively, observed in drownings. Clinically, all, most, or just a few teeth may be discolored, ranging from pale pink to a robust red. The pigmentation is most obvious in the root, with the apical one third being of normal color. The cervical areas of the crowns are involved; the occlusal surfaces are not. In all cases, the radicular coloration is of a darker hue than that seen in the crown. Furthermore, anterior teeth are darker than molars. Histologic and chemical assays have disclosed that the pigment is undegraded hemoglobin rather than hemosiderin or bilirubin, and this pigment collects in the pulp as well as in dentinal tubules. Gross evidence of pigmentation is more striking in the roots of extracted teeth, yet histologic sections disclose that more pigment actually accumulates in the coronal dentin and fades distally from the pulp chamber on out to the dentinoenamel junction.

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PORPHYRIA

Figure 11-48

Sex: No predilection

CLINICAL FEATURES

Accumulations of porphyrin compounds in tissues may result from certain infections or from an inborn error in metabolism. The most important form associated with dental pigmentation is congenital erythropoietic porphyria, which is inherited as an autosomal recessive trait. The first sign is red coloration of the urine by uroporphyrin. Photosensitivity becomes progressively worse as the child ages and a vesiculobullous dermatitis develops. Both deciduous and permanent dentitions show pigmentation, usually brown. Under ultraviolet light, the teeth show a striking red

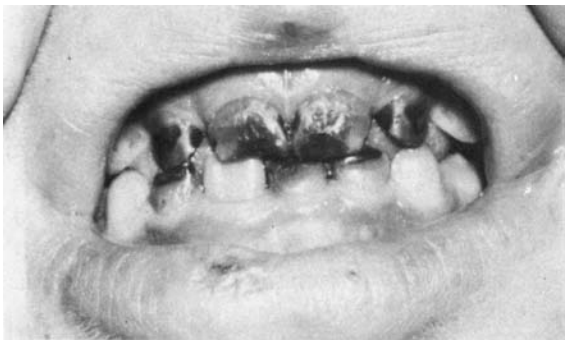

FIGURE 11-48
Porphyrin deposits in porphyria. (Courtesy of Dr. R. Gorlin.)

fluorescence. Ground sections disclose porphyrin pigments deposited in enamel, dentin, and cementum.

DIFFERENTIAL DIAGNOSIS

The stain in porphyria often has a reddish tinge. Under fluorescent light, the red fluorescence is pathognomonic. The cutaneous manifestations of porphyria, in conjunction with other clinical features of the disease, allow for differentiation from other disorders that show dental pigmentation.

TREATMENT

No treatment is available. The discolored teeth may be cosmetically restored with porcelain-veneered crowns.

Additional Reading

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DENTAL FLUOROSIS

Figure 11-49

Sex: No predilection

CLINICAL FEATURES

Fluorosis, a common cause of dental pigmentation, is discussed with structural dental defects. In addition to the hypoplastic changes, a mottled or blotchy brown pigmentation is present in the enamel layers. Both deciduous and permanent teeth are affected if excess fluoride is consumed in drinking water during the period of tooth development. Concentrations in excess of 1 ppm are required to produce dental mottling. Severe pigmentation is usually not seen unless the fluoride concentration exceeds 5 ppm.

DIFFERENTIAL DIAGNOSIS

Dental fluorosis is usually associated with chalky enamel surfaces, and the pigmentation is generally irregular and blotchy, as opposed to that of other dental pigmentations. The pigment shows no fluorescent properties. A history of residence in a geographic region known to contain high levels of fluoride in the water is significant in limiting the differential diagnosis.

TREATMENT

Teeth with fluorosis pigmentation can be restored with esthetic porcelain crowns.

Additional Reading

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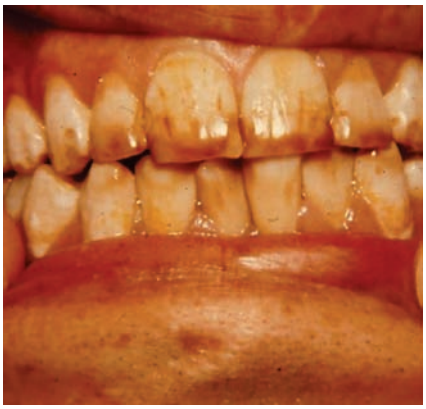

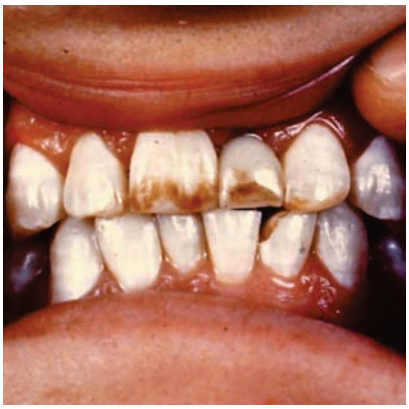

FIGURE 11-49
Teeth with fluorosis showing brown pigmentation.

McClure FS, Lipkins RC. Fluorine in human teeth studied in relation to fluorine in the drinking water. *J Dent Res*. 1951;30:172.

Pendrys DG, Stamm JW. Relationship of total fluoride intake to beneficial effects and enamel fluorosis. *J Dent Res*. 1990;69:529-556.

TETRACYCLINE STAINING

Figure 11-50

Sex: No predilection

CLINICAL FEATURES

Tetracycline antibiotics act as a vital dye, being incorporated into bone and dentin during osteogenesis and dentinogenesis, respectively. The antibiotic becomes highly concentrated in dentin and renders the teeth yellow or yellowish brown. Under ultraviolet light, a bright yellow or yellowish-green fluorescence is observed. Discoloration as seen clinically depends on dose and duration of drug administration. The drug is deposited only during dentinogenesis. Most examples of severe discolorations are seen in children requiring long-term antibiotic therapy; relatively short courses of drug use usually fail to produce any significant clinical manifestations. Ground sections of teeth examined under fluorescence microscopy show linear deposits in dentin corresponding temporally to drug intake.

DIFFERENTIAL DIAGNOSIS

When staining is seen as a result of tetracycline administration, it is generally diffuse and uniform as opposed to that of fluorosis, which is brown and mottled. Tetracycline fluoresces yellow, whereas porphyria is associated with red fluorescence. A history of drug use is, of course, the key in making the diagnosis.

TREATMENT

Severely discolored anterior teeth may be cosmetically corrected by porcelain-veneered crowns when bleaching methods are unsuccessful.

Additional Reading

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Sánchez AR, Rogers RS 3rd, Sheridan PJ. Tetracycline and other tetracycline-derivative staining of the teeth and oral cavity. *Int J Dermatol*. 2004;43(10):709-715.

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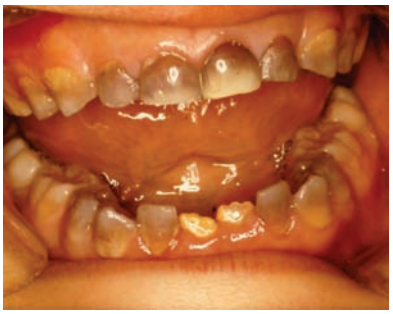


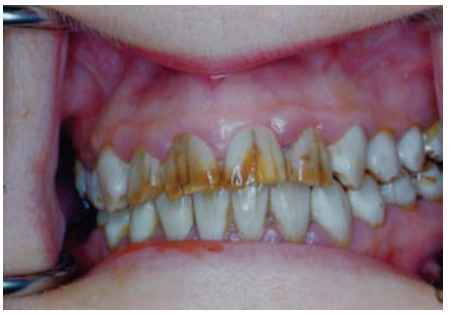
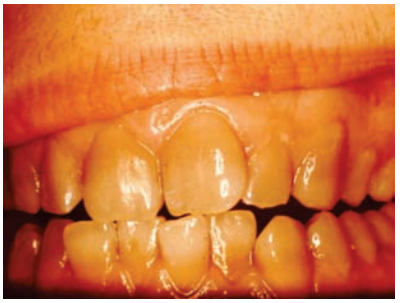


FIGURE 11-50
Brownish-yellow pigmentation in teeth of patients receiving tetracycline over a long period of time. Patient on left has porcelain-fused-to-metal (PFM) crowns on lower anterior teeth.



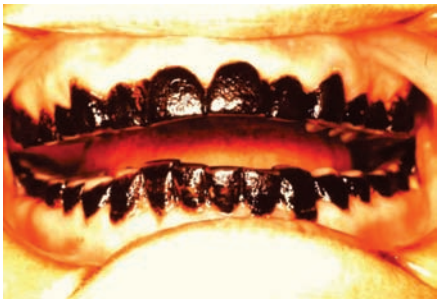


FIGURE 11-51
Right: extrinsic stain from betel nut chewing. On the left: chromogenic bacteria impart a yellow stain to the dental biofilm.

EXTRINSIC STAINING

Figure 11-51

Sex: No predilection

CLINICAL FEATURES

Extrinsic staining is generally confined to the cervical enamel, whereby extrinsic pigments become incorporated into dental plaque or calculus deposits. The color of the deposit varies according to the agent responsible. In children, green stain is most frequent. It is common and most prominent on maxillary anterior teeth. The cause has not clearly been identified but may represent chlorophyll or deposits of chromogenic bacteria. Orange stain, also seen in children, is believed to evolve as a result of colonization by chromogenic bacteria. Neither green nor orange stains have any pathogenic consequences. Rarely, black or brown stains are encountered on deciduous teeth and, as with green or orange stains, chromogenic bacteria are probably responsible. In adults, brown or black stains are usually attributable to tobacco or caffeine.

DIFFERENTIAL DIAGNOSIS

Extrinsic stains can be differentiated from the other forms of dental pigmentation included here on the basis of location, being confined to the cervical one third of the tooth crown, and the fact that they can be scaled from the tooth surface.

Additional Reading

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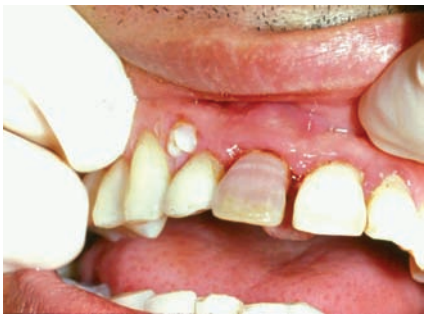

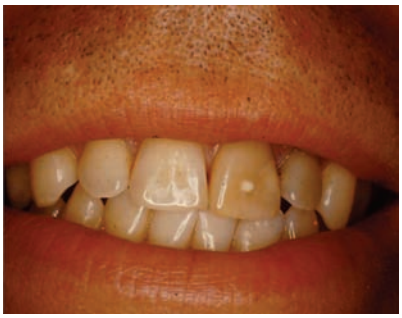

FIGURE 11-52
Focal dental pigmentation in pulp necrosis of central incisor, left, pink tooth Mummery due to internal resorption.

FOCAL PIGMENTATION

Figure 11-52

Sex: No predilection

CLINICAL FEATURES

Pigmentation of a single tooth is seen in pulp necrosis and internal coronal resorption. In pulp necrosis, the affected tooth shows a brown or gray discoloration, which results from deposition of hemosiderin pigment and necrotic tissue products. Radiographs usually disclose the presence of a periapical radiolucency; coronal internal resorption has no known etiology, yet may be the result of trauma. The affected tooth appears pink (pink tooth of Mummery) because of pulpal enlargement subsequent to internal resorption of dentin. Radiography discloses focal pulp chamber enlargement.

DIFFERENTIAL DIAGNOSIS

The other pigmentations listed here are generalized or involve more than one tooth. Internal coronal resorption can be easily differentiated from the pigmentation associated with pulp necrosis on the basis of color differences, radiographs, and response to pulp testing.

TREATMENT

Because pink teeth with coronal internal resorption fracture easily, pulp extirpation with endodontic therapy and a prosthetic crown are indicated. Pigmented nonvital teeth should be treated similarly, and the discoloration can be managed by peroxide bleaching.

Additional Reading

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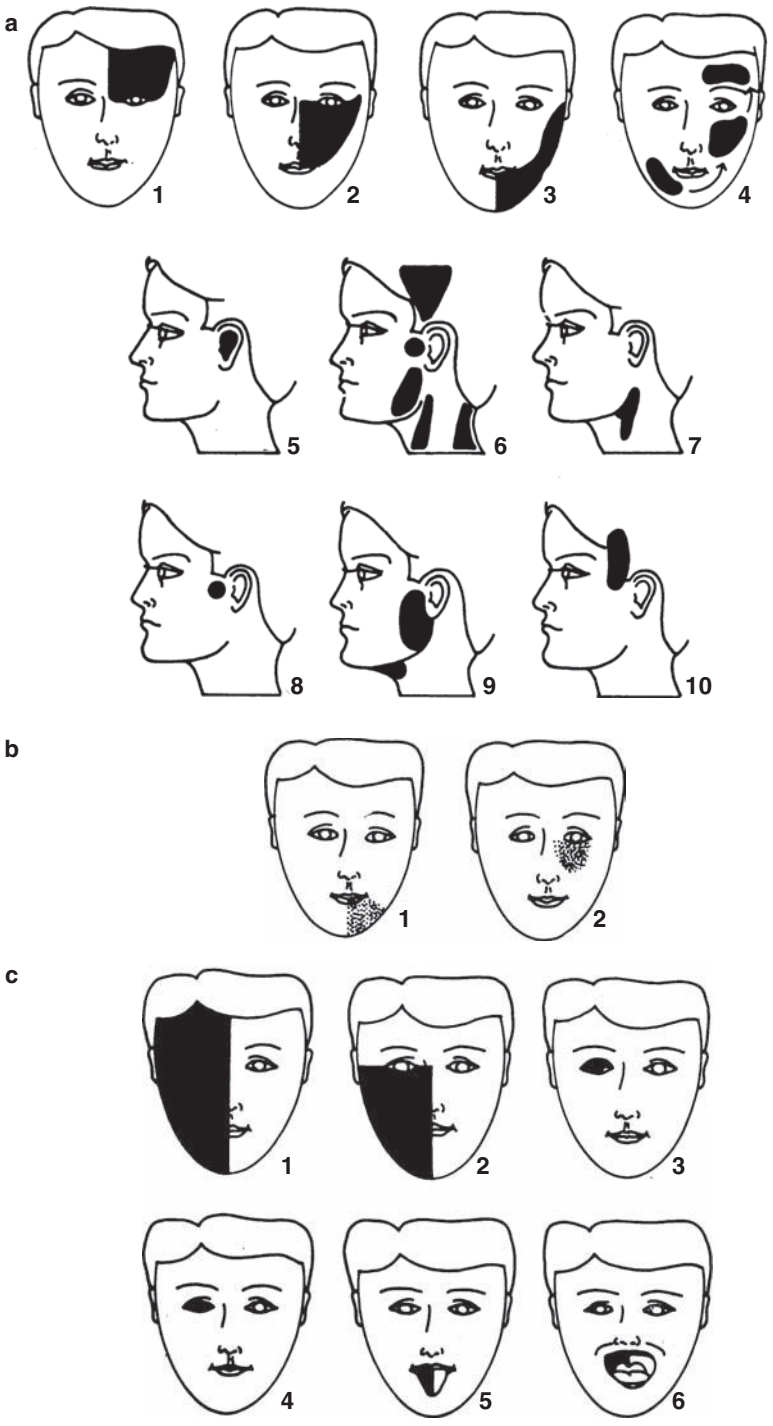
Padayachee A. Pigmentation of teeth: a review. *J Forensic Odonto-Stomatol*. 1988;6:67.

Sweet APS. Internal resorption, a chronology. *Dent Radiogr Photogr*. 1965;38:75.



Pain and Neuromuscular Disorders

a-1, Ophthalmic division pain; a-2, Maxillary division pain; a-3, Mandibular division pain; a-4, Wandering pain; a-5, Otologic pain; a-6, Myofascial pain; a-7, Upper cervical pain; a-8, TMJ internal derangement; a-9, Sialogenic pain; a-10, Temporal pain; b-1, Mental nerve paresthesia/hypoesthesia; b-2, Infraorbital paresthesia/hypoesthesia; c-1, Peripheral nerve VII paralysis; c-2, CNS nerve VII paralysis; c-3, Horner's syndrome; c-4, Ophthalmoplegia; c-5, Nerve XII paralysis; c-6, V Motor paralysis, X paralysis

Facial Pain and Neuromuscular Disorders

12

*Refer to TMJ Region Pain.
†Refer to Maxillary Division Pain.
‡Refer to Mandibular Division Pain.
§Refer to Otogenic Pain.
**Refer to Limited and Deviant Mandibular Opening

Pain in the maxillofacial region is usually, and significantly, a symptom heralding the presence of an infectious or inflammatory disease process. The more prevalent sources of facial pain include odontogenic infections, trauma, periodontal infections (abscess), sinusitis, otitis, salivary obstruction, internal derangements of the temporomandibular joint (TMJ), and myofascial psychofunctional disorders. Most organic diseases manifest acute pain, whereas rare pain syndromes and psychogenic pain disorders are chronic. Patients who have organic disorders usually present obvious clinical signs uncovered by a thorough dental, oral, and facial physical examination. After appropriate tests have been performed (including sensitivity testing of teeth to hot and cold stimuli, percussion of teeth, occlusal stressing and fiberoptic evaluation for cracked teeth, vitalometric testing, and periodontal probing), a diagnosis can usually be rendered.

Many of the diseases included in this chapter show no identifiable organic lesions. They represent defects in sensory perception, vasodilatory phenomena, or symptoms associated with psychologic disorders such as endogenous depression, conversion reactions, stress-associated myospasm, or delusionary phenomena. As mentioned previously, most of these disorders have not been found to be associated with any histopathologic alteration in the tissues and are usually characterized by chronic pain. Furthermore, paroxysmal chronic pain is more often seen as a symptom of trigeminal neuralgia or vasoactive pain (cluster or migrainous facial pain).

To aid the clinician in developing a differential diagnosis, the pain symptoms are classified according to location. The more common entities such as organic pain of odontogenic, periodontal, sinus, and salivary origin are described first, followed by the more esoteric entities representing vasoactive, neuralgic, and psychogenic disorders.

When no organic source for facial pain can be detected, the clinician is always concerned that a brain tumor or abscess is potentially causative. Lethal nervous system malignancies rarely cause facial pain; yet, when they do, there is usually a persistent paresthesia with a concomitant deficit in motor function of ocular, facial, or masticatory muscles.

Many pain disorders share common symptoms. The specific disorders can often be differentiated on the basis of the character, location, and duration of sensory alterations considered in conjunction with the physical and radiographic findings. A definitive diagnosis of some diseases requires an extensive work-up, cranial nerve function tests, therapeutic trials, laboratory data, and expert psychiatric analysis. The characteristics allowing for a definitive diagnosis along with recommendations for the work-up protocol are outlined for each entity.

The diagnosis of chronic facial pain can be problematic and evasive. In addition, those patients with psychiatric disorders are frequently demanding, abrasive, and otherwise difficult to manage; a team approach is recommended in such cases. Furthermore, the clinician should be advised that more than one process may be involved, and therefore more than one diagnosis may be made. For example, a given patient may suffer from concurrent myogenic pain, an internal derangement of the TMJ, and migraine headaches.

This chapter also includes motor function disorders that involve the muscles of facial expression and mastication. The gnathologic apparatus may be affected by diseases causing pain in the TMJ area. Some of these TMJ pain problems exhibit an attending motor defect such as limitation in opening or deviant function. Alternatively, jaw functional movements may exist in the absence of pain. TMJ diseases are included here under both categories. In addition, rare neurologic and muscular disease processes

of a systemic nature can affect the facial musculature. Differentiation among the specific disorders requires evaluation of the muscle groups involved in paralysis or deviant function.

Ophthalmic Division Pain

ODONTOGENIC INFECTION

Figure 12-1

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Frontal pain of odontogenic origin is rare. It represents referred pain from an acute pulpitis or acute apical periodontitis associated with the maxillary incisors or canines. Pain is usually experienced in the infected tooth as well, yet occasionally may be referred solely to the medial supraorbital area. The frontal pain is a constant moderate ache with or without throbbing. Patients complaining of medial frontal pain should be examined for an incriminating anterior maxillary tooth; thus, evaluation for dental caries, tooth percussion sensitivity, pulp test response, and periapical radiographic changes are required. Rarely, an odontogenic infection may spread to the orbit, resulting in orbital cellulitis.

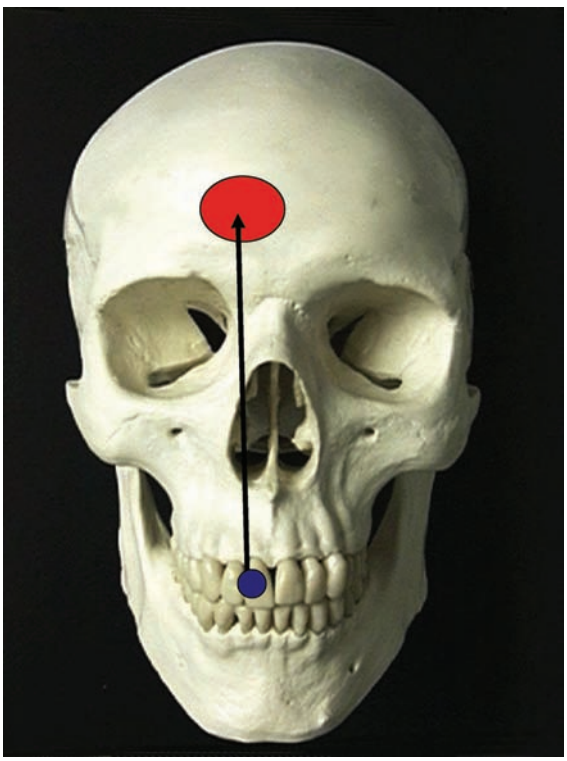


FIGURE 12-1
Frontal pain referral from anterior maxillary odontogenic infection.

DIFFERENTIAL DIAGNOSIS

Odontogenic infection is easily differentiated from the other entities included here if the clinician is aware that dental infections can refer pain to this region.

TREATMENT

The infected tooth should be treated endodontically and subsequently restored with a crown of porcelain fused to metal. When evidence of suppuration is observed, it is advisable to obtain a culture with sensitivity. When facial swelling and fever are present, antibiotic therapy is indicated: a 1-week course of penicillin, or erythromycin for patients with penicillin allergy. In the absence of response, the possibility of staphylococcal or anaerobic infection must be considered with selection of appropriate antibiotics (e.g., cloxacillin or clindamycin, respectively).

Additional Reading

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Sicher H. Problems of pain in dentistry. *Oral Surg Oral Med Oral Pathol.* 1954;7:149.

FRONTAL/ETHMOIDAL SINUSITIS

Figure 12-2

Age: Primarily adults
Sex: No predilection

CLINICAL FEATURES

The frontal sinuses may be chronically inflamed because of allergy; patients are generally asymptomatic, although some complain of pressure or a mild dull ache. Allergic frontal sinusitis is rarely localized; the other sinus cavities are also inflamed, and chronic rhinitis is usually observed. Acute frontal sinusitis is usually infectious; it frequently occurs after water is forced into the nose, thus affecting swimmers. A deviated septum or presence of nasal polyps also may predispose to frontal sinusitis. The patient complains of severe throbbing pain in the medial supraorbital region. Water's sinus radiographs generally exhibit opacification as a result of accumulation of a purulent exudate within the sinus cavity. Lowering the head often exacerbates or intensifies the pain. *Hemophilus influenzae* and anaerobic organisms are the more prevalent microbial agents. If left untreated, swelling and redness of the upper eyelid may be seen and brain abscess can occur. Also, the infection may progress to an acute osteomyelitis with frontal swelling and pain *(Pott's puffy tumor)* and may progress to death.

DIFFERENTIAL DIAGNOSIS

Acute frontal sinusitis may be confused with referred pain of odontogenic origin. Dental examination and evaluation of sinus radiographs aid in arriving at a diagnosis. Myogenic pain involving the frontalis muscle is usually bilateral, dull, and diffuse; electromyographic readings from the frontalis muscle are elevated. The other disorders listed here manifest specific symptoms, allowing for exclusion from the differential diagnosis of acute ophthalmic division pain.

TREATMENT

As the nasofrontal communication is usually blocked because of edema, a nasal decongestant spray should be used in conjunction with antibiotics. Penicillin or one of the cephalosporins is the antibiotic of choice. When the patient's response is poor, the sinus may require irrigation or surgical intervention.

Additional Reading

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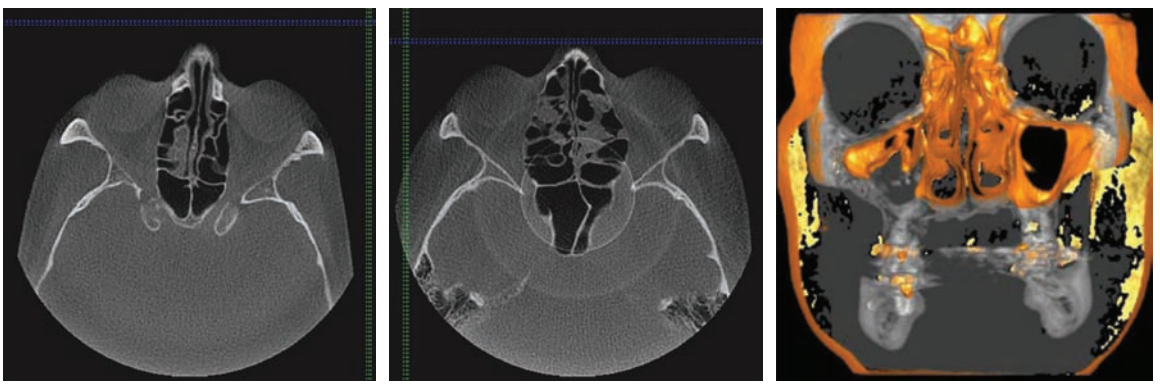

FIGURE 12-2
Clouded ethmoid sinuses in acute sinusitis.

McDermott C, O'Sullivan R, McMahon G. An unusual cause of headache: Pott's puffy tumour. *Eur J Emerg Med*. 2007;14(3):170-173.
Singletary EM, Reilly JF, Jr. Acute frontal sinus barotrauma. *Am J Emerg Med.* 1990;8:329.
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VASCULAR OCCLUSIVE DISEASE AND ANEURYSMS

Figure 12-3

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Thrombosis of the internal or common carotid may cause unilateral cranial edema with headache occurring on the affected side. Transient ischemia may also be associated with pain. Aneurysms and arteriovenous malformations have been associated with headache often mimicking migraine with contralateral visual disturbances; intracranial bruit is usually detectable. Ruptured aneurysms lead to subarachnoid hemorrhage and often follow sexual intercourse or physical exertion. Other neurologic deficits are often encountered, including hemiparesis, third nerve palsy, or palsy involving other cranial motor nerves. Some of these central nervous system (CNS) vascular lesions cause parietal or occipital headache, yet many patients complain of unilateral frontal and retro-orbital pain, which is frequently throbbing.

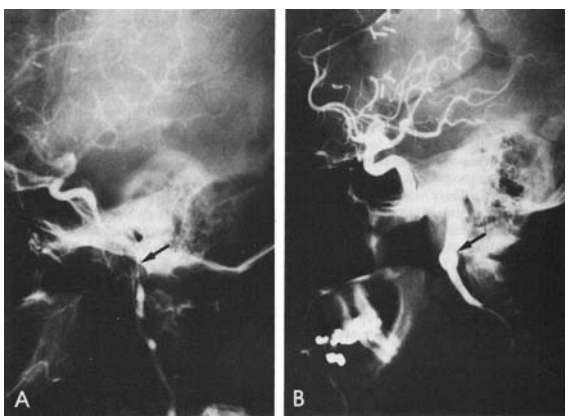

FIGURE 12-3
Frontal area pain is occasionally associated with *A:* vascular occlusive disease or *B:* aneurysms (carotid angiography).

DIFFERENTIAL DIAGNOSIS

When the classic signs and symptoms of both cluster and tension headache are lacking and frontal sinus and odontogenic pain sources have been excluded, a CNS lesion, either vascular or neoplastic, should be suspected, particularly when other neurologic deficits can be detected.

TREATMENT

When other pain syndromes have been eliminated and a vascular occlusive or aneurysmal source is suspected, referral to a neurologist is recommended. A spinal tap, computed tomographic (CT) scans, and carotid angiograms are of great importance diagnostically for localizing the lesion.

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Grindal AB, Toole JF. Headache and transient ischaemic attacks. *Stroke.* 1974;5:603.
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Maxillary Division Pain

ODONTOGENIC INFECTION

Figure 12-4

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Maxillary teeth with pulpitis or pulp necrosis with acute apical periodontitis will exhibit pain in the maxilla. The pain

is localized to the infected tooth or may be diffusely distributed over the malar region. It is a dull aching pain or may progress to severe throbbing. The tooth is sensitive to heat, cold, and/or percussion. Periapical radiographs should be obtained to evaluate for apical widening of the periodontal ligament space or a gross periapical radiolucency. When radiographs yield negative findings and no carious lesions are encountered, fiberoptic examination for cracks should be performed. Local infiltration anesthesia may be used diagnostically.

DIFFERENTIAL DIAGNOSIS

A variety of pain syndromes affect the second division region of the trigeminal nerve. These disorders generally manifest characteristic symptoms, yet many mimic toothache. Identification of an acutely infected or necrotic tooth, relief of pain by infiltration anesthesia, and favorable response to analgesic drugs allow for a definitive diagnosis.

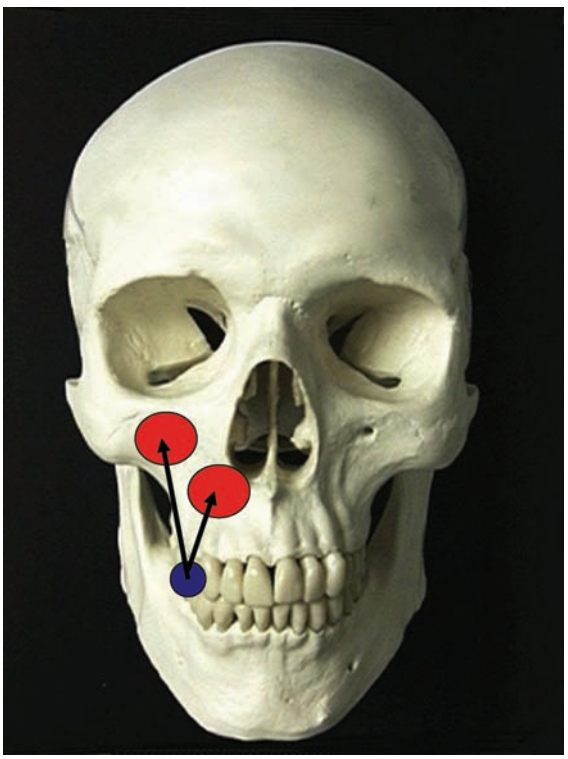

FIGURE 12-4
Paranasal pain referred from maxillary odontogenic infection.

TREATMENT

Root canal therapy or extraction, when the affected tooth is nonrestorable, is the treatment of choice. When patients are febrile or show facial swelling, 10-day treatment with penicillin or erythromycin, in the presence of penicillin allergy, is advisable. Patients who do not respond should be reevaluated for staphylococcal penicillinase-positive organisms or anaerobes, especially bacteroides. In these instances, penicillinase-resistant antibiotics or clindamycin should be prescribed, respectively.

Additional Reading

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MAXILLARY SINUSITIS

Figure 12-5

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Chronic maxillary sinusitis is usually allergic in origin and develops secondary to chronic rhinitis. As the nasal mucous membranes become congested and edematous secondary to allergen:IgE-mediated inflammation, the ostium of the maxillary sinus becomes occluded. The sinus membranes

may become inflamed and thickened, or the antral cavity may partially or entirely fill with secretions. The pain is dull, aching, and constant. All posterior maxillary teeth on the affected side ache and are sensitive to percussion; malar tenderness to percussion also may be witnessed. Pain increases when the head is lowered between the knees. Nasal examination discloses edematous and erythematous mucous membranes over the lateral wall and turbinates. Water's sinus radiographs or maxillary sinus tomograms fail to show osseous destruction or expansion. The sinus membrane is thickened, a fluid level may be detected, or the entire antral cavity may be diffusely opacified. Acute sinusitis, which is usually infectious in origin, manifests similar radiographic changes; the patient experiences intense acute throbbing pain. In addition, a periodic purulent nasal discharge may be experienced and should be cultured. *Hemophilus influenzae, Streptococcus pneumoniae,* and *Staphylococcus aureus* are the bacteria most frequently cultured. Occasionally, acute sinusitis is caused by odontogenic infection, thus necessitating a thorough dental examination.

DIFFERENTIAL DIAGNOSIS

Chronic maxillary sinusitis may have features suggesting odontogenic infection. Cluster headaches and trigeminal neuralgia are severe and paroxysmal. Neoplasms of sinus or cranial base origin generally manifest a sensory and/or motor deficit. Dull aching pain with rhinitis, congestion, and pandental percussion sensitivity in the affected maxilla along with radiographic evidence of nondestructive antral disease are usually adequate signs and symptoms

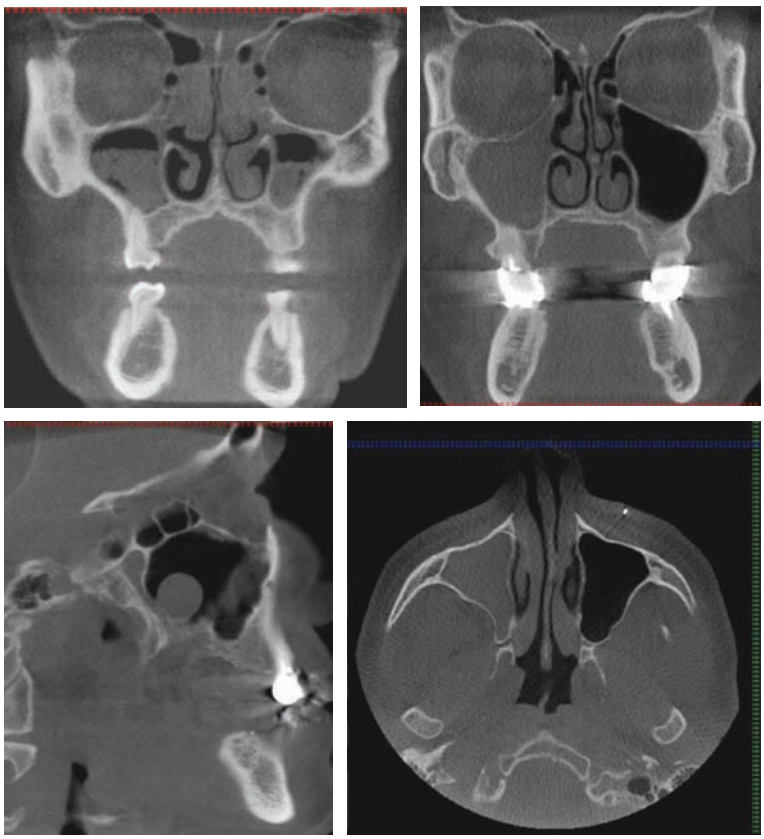

FIGURE 12-5
Clouded sinuses in chronic maxillary sinusitis: air/fluid level (upper left), diffuse opacification (upper right), antral polyp (lower left), diffuse opacification (lower right).

for diagnosis. If osseous destruction or expansion is noted radiographically, an antral biopsy should be performed.

TREATMENT

Chronic sinusitis should be treated with nasal decongestant sprays, such as phenylephrine hydrochloride, and antihistamines. Occasionally, sinus irrigation and lavage are necessary. Acute sinusitis should be treated promptly with penicillin or erythromycin, in the presence of penicillin allergy; if a purulent exudate is present, culture and sensitivity tests are required.

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PATHOLOGIC JAWBONE CAVITIES

Figure 12-6

Age: Middle-aged and elderly adults
Sex: No predilection

CLINICAL FEATURES

The existence of radiologically nondemonstrable bone cavities in extraction site foci within the jaws has been reported to be etiologically related to both atypical facial pain and trigeminal neuralgia. This condition is also termed *neuralgia-inducing cavitational osteonecrosis.* Both jaws are affected and many patients experience both maxillary and mandibular pain; furthermore, while most cases fail to show pathology, lucent foci may sometimes be seen. The focus is usually located within one jaw with upper-to-lower or lower-to-upper pain referral patterns. Patients may complain of classic trigeminal neuralgia symptoms with an identifiable trigger zone, or they may present with constant, dull, aching, or burning pain with unilateral distribution. The pain develops after tooth extraction either immediately or many years later. In the absence of odontogenic or antrogenic infection, radiographs are used to identify edentulous zones on the ipsilateral side for diagnostic infiltration anesthesia. Three percent mepivicaine, 0.25 ml, is injected subperiosteally over the suspected site. Abolition of pain then warrants surgical exploration of the edentulous region. Failure to achieve pain relief by local infiltration anesthesia requires readministration to a closely adjacent site until pain ablation is achieved, thereby precisely pinpointing the location of the suspected bone cavity. Surgery will reveal cavitation of the medullary region with soft tissue contents. Histologically, these bone cavities are represented by vascular connective tissue and occasionally exhibit a mononuclear inflammatory cell infiltrate. Microbiologic studies have disclosed the presence of a mixed aerobic-anaerobic flora. Some of these patients have an associated coagulopathic hematologic disorder.

DIFFERENTIAL DIAGNOSIS

Odontogenic and antrogenic sources of pain should be ruled out initially. Reported pain referral patterns associated with pathologic bone cavities are often diffuse and may extend beyond the alveolus to involve the maxillary, temporal, or TMJ regions; therefore, myogenic facial pain, internal derangements of the TMJ, and temporal arteritis should be considered in the differential diagnosis. Elimination of pain with local infiltration anesthesia over an extraction site supports a diagnosis

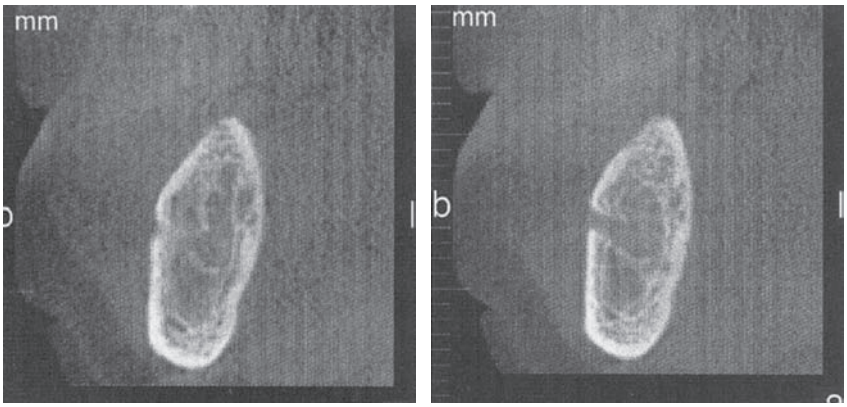

FIGURE 12-6
Idiopathic bone cavitation: vague radiolucent foci in the mandible associated with jaw pain.

of bone cavity–related neuralgia. It should be noted that this entity is controversial and is not accepted by many surgeons.

TREATMENT

The edentulous site is approached surgically after a flap reflection. The contents are curetted and the space is packed with gauze impregnated with 500 mg tetracycline/ml sterile water. This packing is replaced until healthy granulation tissue appears, after which the packing is removed. Chloromycetin also has been used in the packing. It should be noted that most clinicians reporting this form of treatment for facial pain have not included follow-up evaluation over 18 months for most patients; however, a small number of patients have been pain free for 2 to 5 years.

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ANTRAL AND MAXILLARY NEOPLASMS

Figure 12-7

Age: Predilection depends on nature of disease
Sex: Male predilection

CLINICAL FEATURES

Maxillary and antral neoplasms are often asymptomatic in the early stages of proliferation. Pain may develop later in the course of the disease and is usually accompanied by paresthesia. Infraorbital paresthesia and pain occur when the neoplasm, usually a malignant tumor, grows superiorly to involve the sinus roof. Antral carcinomas often undergo foci of necrosis with secondary infection, which can result in release of endogenous pain mediators. The pain is usually deep seated and may be maxillary, retro-orbital, or dental in distribution. Water's radiographs, maxillary sinus tomograms, and CT scans disclose diffuse antral opacification with sinus wall erosion.

DIFFERENTIAL DIAGNOSIS

Pain associated with sinus cancer is usually coexistent with paresthesia. Occasionally, no sensory deficit is encountered. In these instances, the pain symptoms mimic

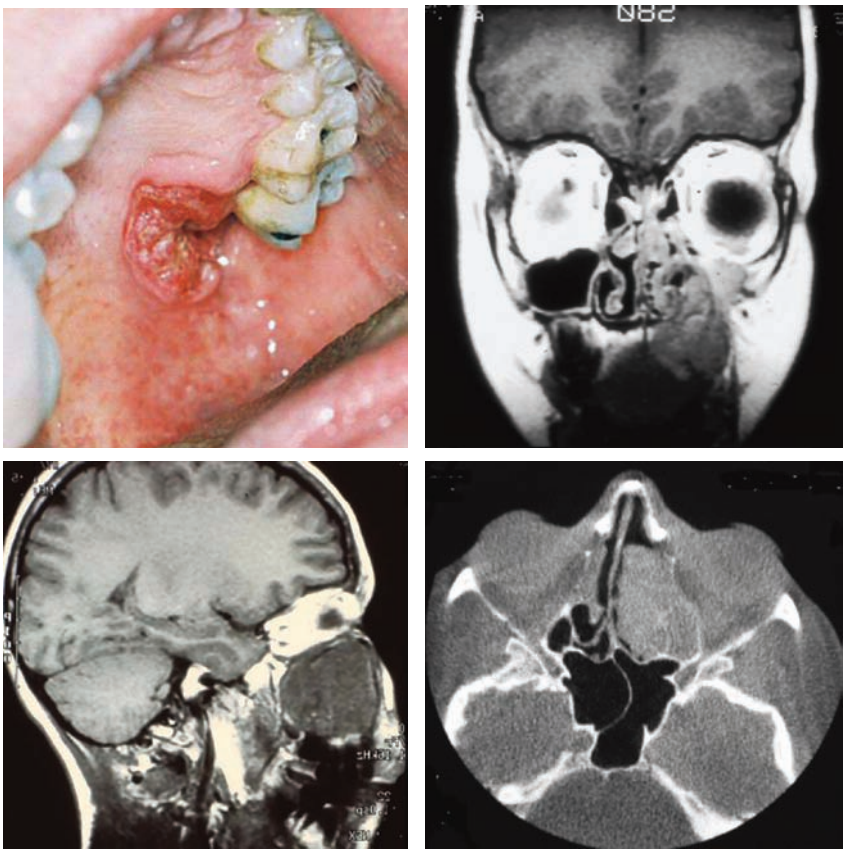

FIGURE 12-7
Antral carcinoma with palatal bone perforation; magnetic resonance imaging and computed tomographic scans showing opacification and bony expansion.

odontogenic pain or acute sinusitis. Radiographic opacification along with sinus wall erosion or expansion warrants a Caldwell-Luc access or endoscopy with biopsy.

TREATMENT

Most sinus tumors with pain and paresthesia are malignant. Squamous cell carcinoma and adenocarcinoma are managed by hemimaxillectomy. Because the tumor may perforate into the nasal cavity, other paranasal sinuses, or the cranium, a thorough clinical and radiographic evaluation is needed to determine the extent of disease and the form of treatment.

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CLUSTER HEADACHE

Figure 12-8

Age: Middle-aged adults
Sex: Male predilection

CLINICAL FEATURES

A variety of eponymic designations, which relate to the precise location of pain, have been applied to a group of midface vasoac-

tive headaches (Vail's syndrome, Horton's headache, Sluder's neuralgia, Charlin's syndrome). Sphenopalatine neuralgia, vidian neuralgia, petrosal neuralgia, and ciliary neuralgia are all forms of midface cluster or vasoactive headaches. Two clinical presentations are observed. The chronic form persists throughout the year, whereas the episodic form is seasonal with pain attacks being more frequent in the spring. In both forms, the nature of the pain attacks is similar. The pain is severe and sharp, lasting 15 to 20 minutes, being unilaterally located in the maxilla, retro-orbital, or supraorbital region. There is no trigger zone. The attacks occur once or twice daily, and nocturnal episodes following random eye movement sleep are common. Patients report no visual scotomata or other "aura" prodromal changes as seen in classic migraines. The concurrent observation of ipsilateral conjunctival erythema, palpebral edema, lacrimation, and nasal stuffiness is significant diagnostically. Patients with cluster headache often exhibit a ruddy facial complexion. Alcoholism, peptic ulcer, and hypertension are also common concomitants. Although the cause is unknown, vasodilation of the cranial or internal maxillary artery branches is thought to be pathogenetically related to the condition. Platelet-rich plasma serotonin and histamine levels are elevated, and the platelet count is decreased during attacks. Electroencephalograms, CT scans, and radionuclide brain scans are usually normal.

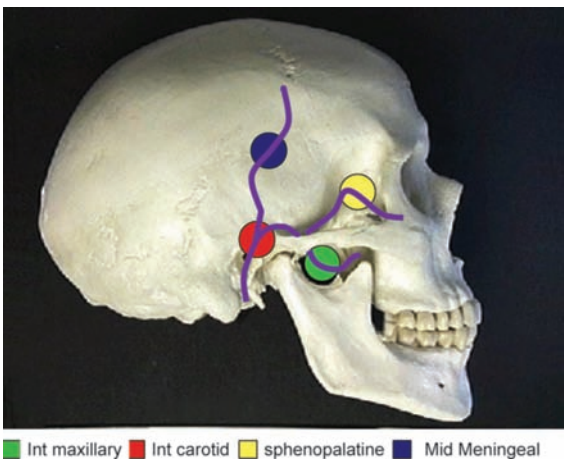

FIGURE 12-8
Vessels involved in vasodilation cluster headache: sphenopalatine (Sluder's neuralgia); middle meningeal (Charlin's neuralgia), internal carotid (Horton's headache), internal maxillary (Vail's neuralgia).

DIFFERENTIAL DIAGNOSIS

Cluster headaches, being paroxysmal, may be confused with trigeminal neuralgia involving the maxillary division. Absence of a trigger zone, presence of autonomic signs and symptoms (lacrimation, nasal stuffiness, conjunctival erythema), and other aforementioned features are characteristic for cluster headache. The other lesions causing maxillary pain fail to manifest the episodic paroxysmal symptoms of cluster headache.

TREATMENT

In the past, the treatment of choice was sublingual ergotamine tartrate or ergotamine tartrate and caffeine rectal suppositories, which are used during a pain attack. Methysergide and prednisone are effective in the prevention of cluster headache, and lithium carbonate has been shown to be efficacious. Administration of 100% oxygen at 7 L/minute flow is more effective for aborting pain if given at the onset of the attack. Ergot alkaloids are contraindicated in patients with hypertension, cardiac, or cerebral vascular occlusive disease. Recently, calcium channel blockers such as nifedipine (10 mg t.i.d.) have been successful in relief of pain from classic, seasonal-type of cluster headache. Verapamil has proved efficacious in patients with chronic cluster headaches.

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TRIGEMINAL NEURALGIA

Figure 12-9

Age: Middle-aged and elderly adults
Sex: Slight female predilection

CLINICAL FEATURES

Trigeminal neuralgia or tic douloureux is a pain syndrome involving the trigeminal nerve divisions and is of unknown etiology. It has been speculated that this neuralgia is the result of ganglionic compression over the petrous ridge or by an artery or vein. Electron microscopic evidence of myelin degeneration of nerves is observed; these findings support a peripheral etiology and suggest a herpetic ganglioneuritis. The clinical symptoms are unique and diagnostic. The pain is sudden, paroxysmal, severe, and stabbing; it follows one or more divisions of the trigeminal nerve. The right side of the face is most frequently affected, and the pain is precipitated by touching a specific area of the skin or mucous membrane referred to as a "trigger zone." A patient's trigger zone is consistently in the same region, usually at the lip commissure or the nasal ala. Local anesthetic infiltration of the trigger zone causes the pain to abate temporarily. During the early onset of pain paroxysms, a discrete trigger zone may not be apparent. In addition to pain, many patients experience paresthesia along the involved nerve division. Most cases are unilateral; 5% of patients develop bilateral involvement. The symptoms of trigeminal neuralgia are occasionally encountered in association with a CNS neoplasm. Also, trigeminal neuralgia is known to occur in some patients with multiple sclerosis and progressive systemic sclerosis (scleroderma).

DIFFERENTIAL DIAGNOSIS

Sharp stabbing paroxysmal pain with identification of a discrete trigger zone allows for a straightforward clinical diagnosis. Atypical trigeminal neuralgias, which have no discrete trigger zone, may be confused with other facial pain syndromes such as midface cluster headache and psychogenic atypical facial pain. Eventually, a trigger zone becomes evident in most instances. Because neoplasia may, albeit rarely, underlie the condition, both brain and CT scans are recommended.

TREATMENT

The treatment of choice is carbamazepine or carbamazepine with phenytoin. High doses of carbamazepine induce bone marrow sup-

FIGURE 12-9
Trigeminal neuralgia (tic doloreau). Trigger points (yellow) and distribution of pain paroxysms along trigeminal pathways (red).

pression, thus necessitating regular blood count monitoring. Some patients cannot tolerate the drugs and are candidates for thermal nucleolysis, peripheral neurectomy, or vascular decompression neurosurgical intervention. Surgical treatment is temporary when peripheral neurectomies are performed, offering, on the average, 1.5 to 2 years of pain relief. Radiofrequency thermal nucleolysis to specific tracts within the trigeminal ganglion is effective, yet pain often recurs within 1 or 2 years. Because the procedure is not particularly invasive, it can be readministered. Vascular decompression of the ganglion is also effective, yet not universally. Gamma knife surgery is effective among patients who have not had previous surgical interventions.

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POSTHERPETIC NEURALGIA

Figure 12-10

Age: Middle-aged and elderly adults
Sex: No predilection

CLINICAL FEATURES

Varicella-zoster infection, causing herpes zoster or shingles, results in a painful vesicular eruption along sensory nerve pathways. The virus initially infects sensory ganglia and subsequently disseminates along the sensory nerve terminals in skin or mucosa. The lesions persist for 2 to 3 weeks and are accompanied by a stinging pain. When the trigeminal ganglion is infected, the lesions generally localize in the region of the ophthalmic division; however, both maxillary and mandibular divisions may be involved. In older patients, the pain may persist after the lesions have resolved; if this symptom prevails after 6 to 8 weeks, the condition represents postherpetic neuralgia. The character of the pain changes somewhat in that stinging is replaced by burning, aching, and paresthesia. This pain is usually chronic and persistent. Scarified zones in areas of old vesicular lesions are hypesthetic when pinched with a needle. The pain may persist for months or even years after infection and, needless to say, results in tremendous emotional upset. Occasionally, paroxysmal stabbing pains mimic trigeminal neuralgia, although trigger zones are lacking.

DIFFERENTIAL DIAGNOSIS

The pain of postherpetic neuralgia is limited to a single division of the trigeminal nerve in most instances, and is restricted to the superficial skin or mucosal surfaces. Nevertheless, it may be confused with trigeminal neuralgia or even cluster headache. A history of vesicular eruption (shingles) is diagnostic.

TREATMENT

Postherpetic neuralgia is difficult to control. Cutaneous stimulation with an electric physiologic stimulator offers some degree of palliation. Other therapies that may cause relief include the lidocaine patch, opioid analgesics, nortriptyline, amitriptyline, and gabapentin.

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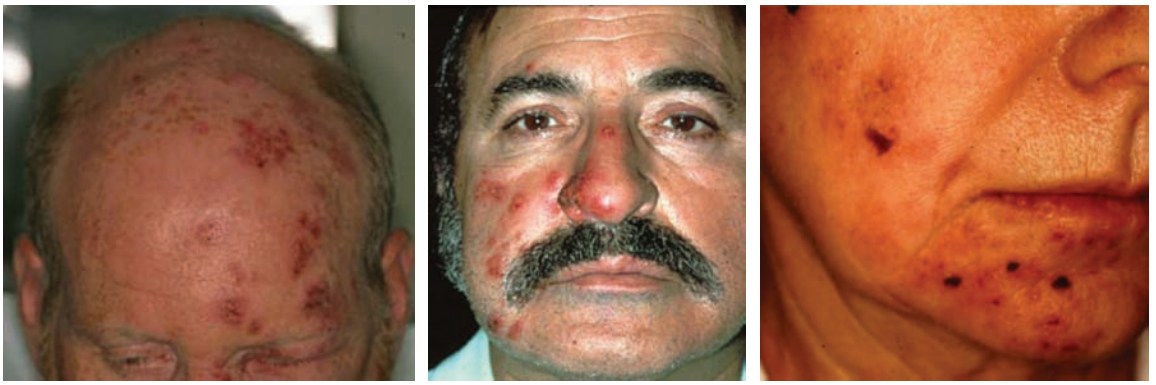

FIGURE 12-10
Herpes zoster vesicular lesions may be distributed along the trigeminal I, II, or III divisions preceding the onset of postherpetic neuralgia.

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COMPLEX REGIONAL PAIN SYNDROME (CAUSALGIA)

Figure 12-11

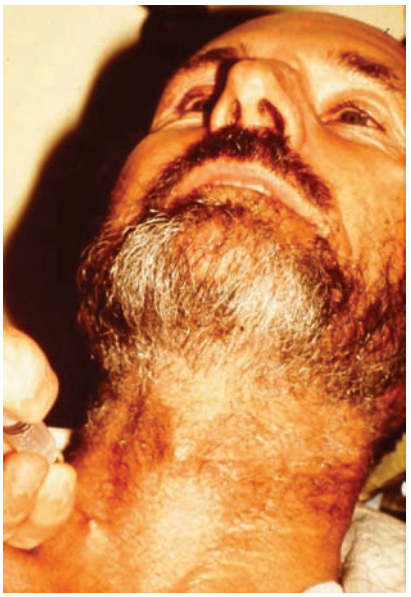
Age: Adults
Sex: No predilection

CLINICAL FEATURES

Complex regional pain syndrome is now divided into two clinical entities: type I is formerly identified as *reflex sympathetic dystrophy*; type II is the new term for *causalgia* that always coexists with documented nerve injury. This rare facial pain syndrome is usually localized to the extremities after an episode of severe trauma. Facial causalgia is characterized by hyperesthesia of the affected skin; often, a trophic response is observed with erythema and dermatitis. The pain is burning and may be deep, yet there is invariably a superficial component. A light touch or even a blast of air will provoke a hyperesthetic response. The pain may be constant or episodic, and in some patients, cutaneous erythema is observed during intensity peaks; this vasodilation phenomenon subsequently wanes. Facial trauma or surgery usually precedes onset of the syndrome. The mechanism is not clearly understood; however, mediation by the sympathetic nervous system appears to be an important factor. Afferent nociceptor pathways are apparently stimulated by locally released catecholamines. A stellate ganglion block with bupivacaine causes relief of symptoms and is therefore the most important diagnostic tool when causalgia is suspected.

DIFFERENTIAL DIAGNOSIS

A variety of facial pain syndromes should be included in the differential diagnosis. Many cases of causalgia have probably gone undiagnosed, being labeled as atypical facial pain. Hyperesthesia, burning pain, vasodilatory cutaneous signs, and a history of facial surgery or trauma should alert the clinician to the probability of causalgia. Abolition of pain subsequent



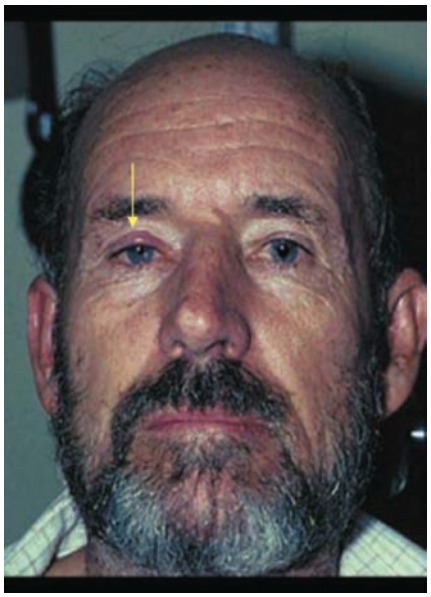


FIGURE 12-11
Complex regional pain syndrome (Causalgia). Stellate ganglion block (left), resultant Horner's syndrome and pain relief (right).

to a stellate ganglion block confirms the diagnosis.

TREATMENT

Biweekly stellate ganglion blocks, confirmed by initiation of Horner's syndrome, often are curative after 6 to 10 injections. If relief is not achieved, surgical stellate ganglion sympathectomy may be required. This will, of course, result in a permanent hemifacial sympathetic blockade with ptosis, miosis, and anhidrosis.

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CRANIAL BASE AND CNS NEOPLASMS

Figure 12-12

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Neurologic deficits are encountered in neoplastic processes that encroach on cranial nerves above or below the exit through the cranial base foramina. Metastatic tumors to the cranial base or middle fossa, cerebellopontine angle tumors, and nasopharyngeal tumors often compress or invade one or two, or all three, divisions of the trigeminal nerve, thus resulting in paresthesia, hypesthesia, and/or pain. The fact that a sensory deficit or pain symptom is rarely encountered in the absence of a motor deficit is significant. Although a variety of eponymic syndromes have been described depending on the localization of signs and symptoms, the commonality is tumor compression of nerves. Many of these eponymic syndromes exhibit overlapping features that are confusing to the clinician; therefore, a topographic nosol-

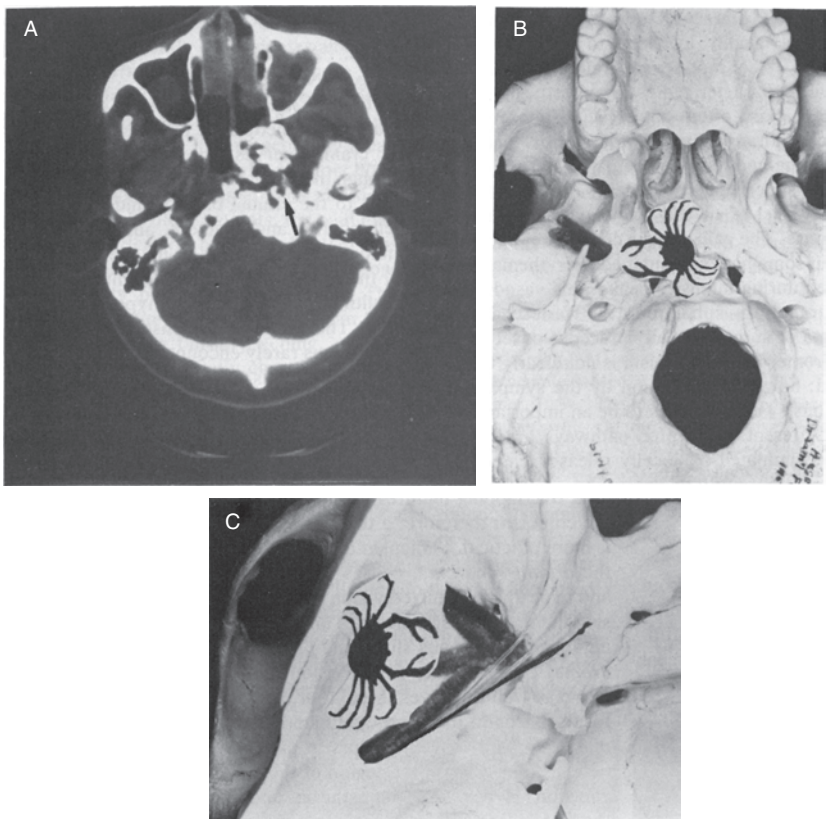

FIGURE 12-12
A: CT scan illustrating a cranial base chondrosarcoma with sphenoid sinus extension. *B:* Site of tumor in parasellar syndrome in relation to trigeminal and ocular motor nerves. *C:* Site of nasopharyngeal/cranial base tumor in relation to V-3 and motor root of the trigeminal nerve.

ogy is more practical. Malignant disease of the orbit, the *orbital syndrome,* causes supraorbital pain and hypesthesia, blurred vision or diplopia, ptosis, and/or ophthalmoplegia. Tumors encroaching on the cavernous sinus, the *parasellar syndrome,* compress the first division of the fifth nerve as well as nerves 3, 4, and 6; the result is frontal pain and ophthalmoplegia. The *middle fossa syndrome* occurs in patients with neoplastic disease in the region of the gasserian ganglion. Hypesthesia, paresthesia, and pain of the second and third divisions are common; numbness without pain also is encountered. Ocular muscle paralysis is common, and paresis of the masticatory muscles may be detected (i.e., deviated mandibular opening, masseteric weakness, unilateral soft palate paralysis, etc.). Foramina or intracranial extension by a nasopharyngeal carcinoma may cause similar signs and symptoms, including a unilateral hearing deficit resulting from eustachian tube extension. The *jugular foramen syndrome* is characterized by dysphagia, hoarseness, glossopharyngeal neuralgia-like pain, palate weakness, and vocal cord paralysis. Hypoglossal weakness is also common, but it occurs more frequently in the *occipital condyle syndrome,* which is heralded by occipital pain that is exacerbated by neck flexion.

DIFFERENTIAL DIAGNOSIS

Malignant neoplasia that is primary within the CNS, secondary to nasopharyngeal extension, or metastatic may cause facial pain and be confused with a variety of local pain syndromes. The triad of sensory deficit (numbness or paresthesia), pain, and motor deficit (ocular, masticatory, facial, or glossal) constitutes an ominous finding. Although routine radiographs often fail to uncover a

lesion, magnetic resonance imaging (MRI) or CT scans will reveal a pathologic process. A history of cancer may indicate the probability of cranial base metastasis.

TREATMENT

Any patient with pain, numbness, and cranial nerve motor weakness should be evaluated by a neurologist; a CT scan of the cranium should be performed. Treatment is determined when the process has been definitively diagnosed.

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ATYPICAL FACIAL PAIN

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Atypical facial pain occurs in the maxilla or the mandible, but current evaluative and diagnostic methods do not reveal an organic cause. The diagnosis requires exclusion of other known pain syndromes including the true neuralgias, vasoactive headaches, and myogenic pain disorders. Then one is left with a pain patient whose signs, symptoms, or chemical and laboratory findings do not allow for a definitive diagnosis. By exclusion, one attaches the appellation "atypical facial pain," which probably includes a heterogeneous constellation of disorders. Pathologic jawbone cavities have been identified in some of these patients and are discussed separately. The symptoms of atypical pain are inconsistent from one patient to the next. Some patients complain of localized dull aches; others say the pain is dull and wanders from one site to another; yet others complain of paroxysms of acute pain without a trigger zone. Many instances of atypical facial pain probably represent symptoms of a psychiatric disorder, usually depression or histrionic personality. Postherpetic ganglioneuritis associated with herpes simplex may be responsible for some instances of atypical pain, particularly when mild paresthesia is present or motor weakness of facial muscles is observed. No hard data are available to support a viral etiology; however, demyelinating peripheral lesions can follow herpes hominis infections and could eventuate in pain, paresthesia, and seventh- or fifth-nerve motor weakness. Atypical odontalgia can be included as a form of atypical facial pain. Patients complain of aching pain in a tooth or group of teeth in which objective pulp testing and radiographs fail to show evidence of pulpal disease. These patients are insistent and demand endodontic therapy or extraction. Typically, endodontic therapy is given, but pain persists; then, apicoectomy is performed, but pain continues. Ultimately, the tooth is removed; subsequently, the patient complains of pain in an adjacent tooth. In these instances, psychogenic causes should be suspected. The clinician should consider depression and conversion symptoms with secondary gain or guilt complex.

DIFFERENTIAL DIAGNOSIS

The symptoms encountered in atypical facial pain can mimic organic, neuralgic, vasoactive, or myogenic pain syndromes. The clinician is obliged to rule out odontogenic, antrogenic, and sialogenic sources first. Secondly, muscle palpation and muscle trigger point tenderness should be assessed

with subcutaneous or intramuscular local anesthesia to evaluate elimination of myogenic referred pain to teeth or the jaws. When edentulous regions are observed, a pathologic bone cavity should be considered; selective infiltration anesthesia is useful diagnostically. Although central neural or cranial base neoplasms may cause facial pain, they rarely do so in the absence of paresthesia or motor deficit.

TREATMENT

Unfortunately, and by definition, the causal process is unknown. When a psychogenic origin is suspected, patients rarely accept this diagnosis and refuse psychiatric care. A 6-week trial of tricyclic antidepressant therapy is recommended. This treatment has been beneficial for some patients with atypical facial pain.

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Mandibular Division Pain

ODONTOGENIC INFECTION

Figure 12-13

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

The most common cause of mandibular pain is odontogenic infection. The pain is usually sharp and severe in acute pulpitis. Sensitivity to heat, cold, and percussion is characteristic. The pain often awakens the patient or prevents sleep. In most instances, clinical and radiographic examination disclose a large carious lesion encroaching on the pulp or pulp horns. Acute pain during mastication or when firm lateral pressure is applied to cusps and the presence of cold sensitivity are indicative of tooth fracture. Fiberoptic light examination often uncovers a fracture line; however, some fractures underlie restorations, thus necessitating removal of the material before fiberoptic examination. Dull chronic aching pain is more often associated with periapical disease related to a necrotic tooth. Alternatively, many patients with pulp necrosis and periapical granulomas or cysts are pain free or have a history of pain that eventually resolves. Radiographs uncover a periapical radiolucency, and the tooth fails to respond to electric pulp test stimulation. Most teeth with pulp necrosis are grossly carious. A maxillary tooth seldom refers pain to the mandible. Furthermore, the pain, particularly in molar teeth, may be referred to the TMJ and ear.

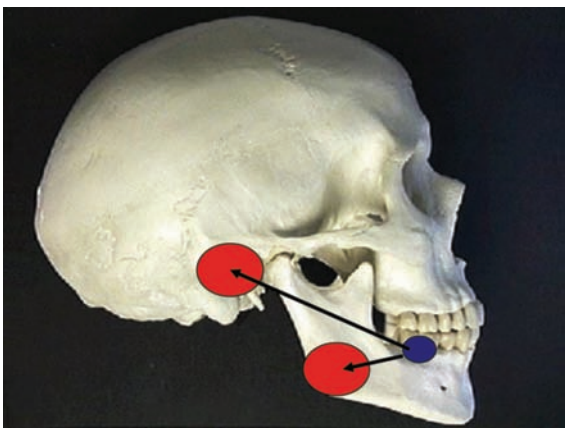

FIGURE 12-13
Pain referral routes to TMJ, ear, and mandibular angle from mandibular odontogenic infection.

DIFFERENTIAL DIAGNOSIS

Most mandibular pains are of odontogenic origin; therefore, a dental source should be sought before other pain syndromes involving the third division of the trigeminal nerve are considered. The suspected tooth (teeth) should be tested with heat, cold, percussion, electric stimulation, and fiberoptics; radiographs should be obtained. When no dental source can be uncovered in the mandible, the maxillary dentition should be evaluated. Periodontal probing should be undertaken, after all dental sources are ruled out, if a periodontal abscess cannot be found easily. Failure to uncover either a dental or periodontal source of the pain will direct attention to other pain syndromes included in this section.

TREATMENT

Restorable teeth should be treated endodontically. In some cases, cracked teeth can be managed by full crown coverage; however, large cracks may require extraction. When fever or a facial swelling is present, penicillin or erythromycin (when patients are allergic to penicillin) should be prescribed for 10 days. Response failure may indicate penicillinase-producing organisms or anaerobes. In these instances, penicillinase-resistant antibiotics or clindamycin should be used, respectively.

Additional Reading

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OSTEOMYELITIS

Figure 12-14

Age: Any age
Sex: No predilection

CLINICAL FEATURES

Osteomyelitis is an acute, subacute, or chronic bacterial infection of the bone marrow. In the jaws it usually arises from the spread of infection from a necrotic tooth or from a periapical infectious focus. In some instances an anachoretic infection may be responsible. Osteomyelitis of the jaws usually affects the mandible, and the incriminating tooth tends to be a posterior one. Pain may be dull and aching or severe and pounding depending on the virulence of the infectious organisms, some of which may be anaerobes. Radiation therapy for oral carcinoma results in vascular damage and predisposes to osteomyelitis if an endodontic infectious source is extant. Another predisposing factor is bisphosphonate therapy for osteoporosis and metastatic bone cancer. Sequestration of bone and fistulous tracts may occur in all forms of osteomyelitis. Radiographs show radiolucencies with a moth-eaten pattern, being poorly marginated.

MICROSCOPIC FEATURES

Bony sequestra show lacunae devoid of osteocyte nuclei and may be engulfed by bacteria, and actinomycete colonies may predominate. Marrow spaces are typically infiltrated with inflammatory cells, neutrophils if acute, round cells if chronic.

DIFFERENTIAL DIAGNOSIS

The presence of sequestra, fistulae, and radiolucent lesions along with elevated temperature usually clinch the diagnosis. Both aerobic and anaerobic cultures with antibiotic sensitivity should be employed.

TREATMENT

Antibiotic therapy should be initiated with a penicillin-related antibiotic or cepha-

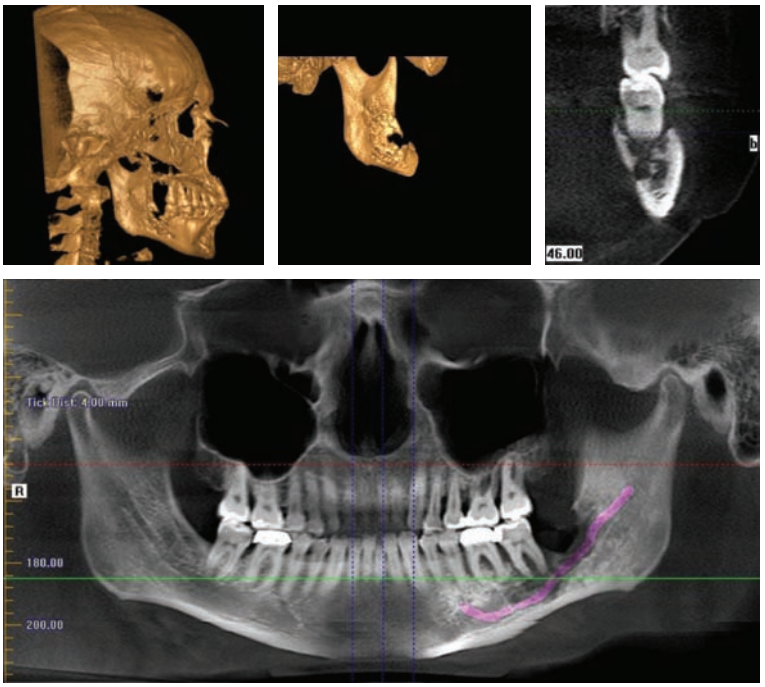

FIGURE 12-14
Moth-eaten radiolucencies seen in the mandible on cone beam computed tomography (CT) 3D reconstructions, CT cuts and panoramic radiographs occur in osteomyelitis, bisphosphonate osteonecrosis, and osteoradionecrosis.

losporins until results are obtained from sensitivity testing. In severe cases, hyperbaric oxygen can be administered along with analgesics. Surgical debridement should be undertaken diligently and selectively.

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TRAUMATIC NEUROMA

Figure 12-15

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Severance of a nerve trunk results in axonal degeneration of the distal segment with regeneration by the proximal axonal segment, which canalizes the distal nerve sheath tract. When the severed nerve ends are not readily approximated, the regenerating axon may, in the process of searching for the distal sheath, become hyperplastic and tortuous, creating a painful nodule. Traumatic neuromas of soft tissue are usually detected visually as swelling, or they are palpable. Compression initiates pain. Occasionally, traumatic neuromas arise central in bone subsequent to tooth extraction or alveolar bone trauma. The pain is deep and intraosseous, and can be moderate or severe. The canine and mental foramen areas are the most common sites; the pain can be triggered by denture pressure or digital compression over the involved area, simulating a trigger zone in trigeminal neuralgia. Local anesthesia eliminates the symptoms. Occasionally, a radiolucency can be seen on periapical films.

DIFFERENTIAL DIAGNOSIS

When compression of a palpable nodule overlying the mental foramen or alveolus causes a pain paroxysm, traumatic neuroma

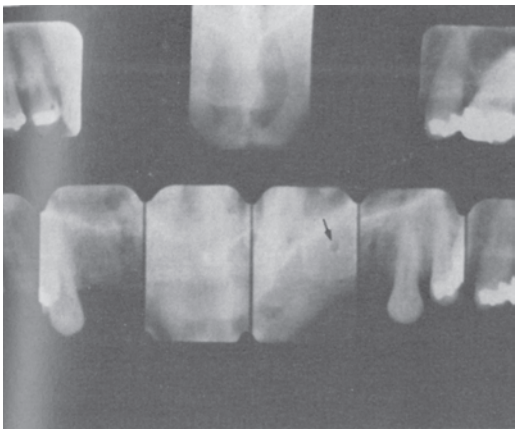

FIGURE 12-15
Small radiolucency in anterior maxilla representing a traumatic neuroma causing severe pain. These lesions are actually more common in the mandible.

should be suspected. Alternatively, centrally located neuromas are not palpable, and the pain episodes may mimic trigeminal neuralgia or be classified as atypical facial pain. Any radiolucency in the vicinity of the pain should be tested for abolition of pain by local infiltration anesthesia; pending a positive result, the area should be explored surgically.

TREATMENT

Painful nodules or radiolucent foci suspected of representing traumatic neuroma should be excised. A definitive diagnosis requires microscopic confirmation. Step serial sections may be needed to identify the neuromatous tissue in marrow curettings.

Additional Reading

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SUBACUTE THYROIDITIS

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Subacute thyroiditis usually evolves subsequent to an upper respiratory infection; the prevailing evidence supports a viral etiology, probably coxsackievirus. The pain, which is located in the thyroid region, is aggravated by swallowing or turning the head. Pain radiation to the mandible, ear, and/or occipital region is a common finding; indeed, the patient's chief complaint may be jaw pain. Other symptoms include nervousness, palpitations, and lassitude. Fever may be severe. Palpation of the thyroid discloses diffuse swelling and acute tenderness. The overlying skin is often erythematous. Occasionally, the disease is asymptomatic. Most patients are euthyroid with normal thyroid function tests. The condition usually resolves of its own accord within 4 to 6 weeks.

DIFFERENTIAL DIAGNOSIS

Acute thyroiditis with mandibular pain being the primary complaint may be mistaken for a variety of organic and functional diseases involving the mandibular nerve distribution. In addition, the styloid and hyoid syndromes, carotidynia, and cardiogenic pain may be suspected. Elevated temperature and exquisite pain on palpation of the thyroid gland usually suffices for the clinical diagnosis. Tenderness and pain on palpation are rarely featured in goiter, Graves' disease, Hashimoto's thyroiditis, or thyroid neoplasia.

TREATMENT

Palliative care includes the use of analgesics and antipyretics. The disease is self-limited and although thyrotoxicosis has

been reported to occur, most patients fail to suffer from any residual thyrometabolic complications.

Additional Reading

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STOMATODYNIA/ GLOSSOPYROSIS

Age: Middle-aged and elderly adults
Sex: Female predilection

CLINICAL FEATURES

Burning mouth or tongue (glossopyrosis) is a common symptom and in younger patients is usually associated with one of the vesiculo-bullous-ulcerative diseases. Older patients may also present with this symptom in the absence of oral lesions. Rarely, burning tongue is a symptom in patients with organic diseases including pernicious anemia and diabetes mellitus. In the former, the tongue is often beefy red and denuded of papillae. In the majority of patients, no physical evidence of disease is encountered. There are special sensory deficits in taste threshold, implicating involvement of the chorda tympani pathway. Most elderly patients with stomatodynia suffer from psychiatric illness, with chronic depression being the most prevalent diagnosis. Loss of enthusiasm, sleep disturbances, loss of libido, and concurrent anxiety are often present. Patients with long-standing endogenous depression usually manifest elevated blood cortisol levels after challenge with oral steroids (dexamethasone suppression test). Anxiety is also prevalent in patients with burning mouth. Guilt, conversion reactions, and overt schizophrenia may be encountered; many of these patients are cancerophobic as well.

DIFFERENTIAL DIAGNOSIS

A fasting blood sugar or, preferably, a 2-hour postprandial glucose test should be performed along with a hemogram in order to rule out diabetes and megaloblastic anemia, respectively. Negative laboratory findings and normal-appearing oral soft tissues lead to a diagnosis of psychogenic stomatodynia. A psychiatric work-up augmented with psychometric testing (e.g., Minnesota Multiphasic Personality Inventory [MMPI]) and a dexamethasone suppression test will aid in establishing a diagnosis of depressive illness.

TREATMENT

Once a diagnosis of depression is confirmed, treatment with one of the tricyclic antidepressants should be instituted. Doxepin, 100 mg 2 hours before retiring, can be prescribed for 1 week; a final dosage of 200 to 250 mg per day will affect an elevation in mood with resolution of pain symptoms for most patients. Beneficial results usually require 3 or 4 weeks of therapy. Most patients with this symptom are postmenopausal women, and estrogen therapy has been found to alleviate the burning symptoms. α-lipoic acid and gabapentin also provide relief in some subjects. After medical treatment has proven efficacious, psychotherapy should be considered.

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CARDIOGENIC FACIAL PAIN

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Although myocardial ischemia classically produces angina pectoris with referred pain over the left shoulder and down the arm, the pain is occasionally referred to the left mandible. Indeed, some patients may complain of jaw pain without a substernal component. Pain referred to the mandible has been explained on the basis of converging nociceptor pathways from cardiac pain fibers that ascend the cord subsequent to synapsing in the thoracic dorsal horn and communicate with neurons located in the subnucleus caudalis of the trigeminal nerve. Typically, the pain is precipitated by exertion or stress and is usually described as an ache. Administration of a nitroglycerin tablet sublingually usually, yet not invariably, relieves the symptoms. An electrocardiogram (ECG) often displays S-T or T wave anomalies indicative of myocardial ischemia. Normal resting ECG results do not rule out coronary vascular disease.

DIFFERENTIAL DIAGNOSIS

Because many common local processes can cause mandibular pain, a cardiogenic etiology is often overlooked. Pain on exertion or left mandibular pain with concurrent chest pain should arouse suspicion of coronary ischemia.

TREATMENT

Referral to a physician is recommended when cardiac origin is suspected. Resting and stress ECG readings then aid in establishing the diagnosis, and appropriate medical management controls the jaw symptoms.

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Otogenic Pain

ACUTE OTITIS MEDIA

Figure 12-16

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Acute inflammation of the middle ear is usually bacterial in origin with β-hemolytic streptococci, *Streptococcus pneumoniae*, and *Hemophilus influenzae* being the predominant infectious organisms. Viral agents are rarely responsible, yet may predispose to bacterial infection by inducing eustachian tube edema and obstruction. Pain is severe and persistent; otoscopic examination reveals a bulging hyperemic tympanic membrane. Conductive hearing loss is a

FIGURE 12-16
Tympanic membrane in: normal ear (top); acute otitis media with bulging drum and loss of landmarks (bottom). *Source:* Reprinted by permission from Dr. R. A. Buckingham, *Some Pathological Conditions of the Eye, Ear and Throat*, Abbott Laboratories, 1955.

feature; the eustachian tube mucosa in the nasopharynx is usually hyperemic. Eventually, the patient becomes febrile and may manifest an exudate with perforation of the drum. Coalescent mastoiditis develops, and opacification of the middle ear chamber and mastoid air cells can be detected radiographically. Subsequent to perforation and drainage, the lesion may resolve, or complications such as subperiosteal abscess, dural abscess, or brain abscess may evolve.

DIFFERENTIAL DIAGNOSIS

Acute otitis media is usually not confused with other otalgic disorders because of the classic clinical changes that involve the tympanic membrane along with acute severe persistent pain.

TREATMENT

Penicillin or erythromycin therapy is indicated; myringotomy may help to relieve pain when exudation has not yet occurred. Referral to an otolaryngologist is recommended.

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CHRONIC OTITIS MEDIA

Figure 12-17

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Chronic otitis media is far more complex than acute infectious otitis. The onset may be insidious, and pain is not common. *Staphylococcus aureus* and *Bacillus proteus* are most frequently cultured. Many factors are believed to predispose to chronic otitis, including progression of acute otitis, eustachian tube obstruction, and allergy. Ear pain, if present, is dull and usually mild to moderate. Occasionally, acute exacerbations with sharp pain surface. Persistent otitis media of long standing is accompanied by destructive changes within the middle ear and mastoid air cells. Otoscopic examination may disclose a perforation of the pars tensa, and a discharge may or may not be seen. Small perforations may not interfere with normal hearing; however, hearing loss occurs with larger perforations. In chronic tubotympanic otitis, the perforation may be filled with edematous polypoid mucosa. Otitis represented by excessive middle ear keratinization (keratoma, cholesteatoma) is probably the result of drum perforation

FIGURE 12-17
Tympanic membrane in: normal ear (top); bulging drum (bottom left); and perforated drum (bottom right). *Source:* Reprinted by permission from Dr. R. A. Buckingham, *Some Pathological Conditions of the Eye, Ear and Throat*, Abbott Laboratories, 1955.

with epidermal migration from the meatus. Retraction and pitting with loss of ossicle definition are indicative of disease. Chronic otitis can become severely destructive.

DIFFERENTIAL DIAGNOSIS

Chronic otalgia can be seen in referred pain of odontogenic origin or in diseases of the TMJ. Changes in the tympanic membrane warrant a thorough otologic evaluation. In the absence of drum changes, pain with hearing loss suggests middle ear disease. Significantly, otitis media can result from tubal obstruction secondary to nasopharyngeal carcinoma. In histiocytosis, histiocytic infiltrates involve the middle ear; however, pain is usually not a complaint.

TREATMENT

When clinical signs and symptoms indicate chronic otitis media, referral to an otolaryngologist is indicated. Surgery is often necessary, particularly when keratoma is present.

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HERPES ZOSTER OTICUS

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Also known as geniculate ganglion neuralgia or the Ramsay-Hunt syndrome, herpes zoster oticus causes aural and postauricular pain. Pain is acute and burning, and often represents a prodromal symptom preceding the onset of a vesicular eruption involving the postauricular cleft. The external ear canal receives sensory innervation from geniculate ganglion fibers of the seventh nerve that innervate the aural skin and travel with branches of the tenth nerve. Branches from the auriculotemporal also innervate the auditory canal anteriorly. Regardless of which nerves are affected by the varicella-zoster virus, the signs and symptoms are the same. A coexistent ipsilateral facial paralysis frequently follows the vesicular eruption. Vesicles are occasionally seen in the ipsilateral pharynx.

DIFFERENTIAL DIAGNOSIS

Prior to onset of the aural vesicular eruption, the diagnosis may be enigmatic, simulating other diseases causing otalgia. Within a few days, the vesicles appear; a cytologic smear discloses viral epithelial cell changes. Elevated serum varicella-zoster antibody titers can be detected after the appearance of vesicles.

TREATMENT

The disease is self-limited and resolves of its own accord. Facial paralysis may require 4 to 6 weeks to resolve. Intravenous acyclovir (10 mg/kg) every 8 hours has been recommended for resolution of vesicles as well as paralysis.

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MIDDLE EAR NEOPLASMS

Figure 12-18

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

Neoplastic and neoplasm-like proliferations of the middle ear, temporal bone, and mastoid air cells are usually painless; however, otalgia can be a major complaint, particularly when secondary infection occurs. Histiocytosis and granulomatous inflammatory diseases are the more frequently encountered reactive lesions. Pain with erosion of the mastoid region and acute mastoiditis are more often encountered in histiocytosis. Glomus jugulare tumors, meningiomas, facial nerve neuromas, squamous cell carcinomas, and adenocarcinomas are the common primary tumors in this region; acute ear pain, particularly nocturnal, is often reported by patients with squamous cancer. Metastatic lesions and invasion by tumors arising from contiguous tissues of the brain, meninges, external ear, nasopharynx, and parotid gland can also cause bone destruction, otitis media, and otalgia. Visual inspection of the tympanic membrane often discloses drum perforation, a retrotympanic mass, or suppurative otitis. Invasion of the temporal bone, inner ear, and facial canal cause a variety of signs and symptoms, including unilateral pulsatile tinnitus, neurosensory hearing loss, and paresis of cranial nerves VII, IX, X, XI, and XII.

DIFFERENTIAL DIAGNOSIS

Differentiation of tumor from other lesions causing otalgia is not always straightforward on clinical grounds alone. Cranial nerve deficits, hearing loss, and tinnitus should arouse suspicion of tumor. Angiography and tomography are then employed, and if significant bony destruction is observed, biopsy is indicated.

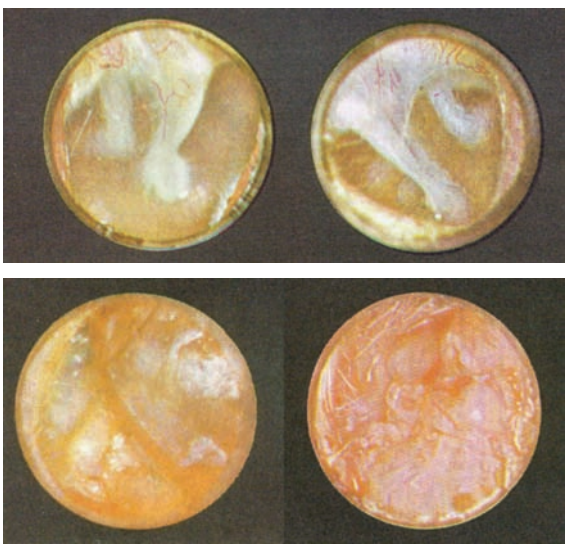

FIGURE 12-18
Normal ear drum (top); cholesteatoma middle ear with anterior polyp (bottom left); squamous cell carcinoma filling external canal (bottom right). Source: Reprinted by permission from Dr. R. A. Buckingham, *Some Pathological Conditions of the Eye, Ear and Throat*, Abbott Laboratories, 1955.

TREATMENT

Most middle ear complex tumors are treated by surgical resection. Referral to an otolaryngologist or head and neck surgeon is recommended; the extent of disease along with the specific microscopic diagnosis help to determine the treatment.

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Neck and Throat Pain

STYLOHYOID SYNDROME (EAGLE'S SYNDROME)

Figure 12-19

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Eagle's syndrome is characterized by pain during mandibular movement or twisting of the head and neck; it is stabbing, originates in the tonsillar region, and radiates to the region of the TMJ and base of the tongue. When the jaws are closed, the pain subsides. The pain is caused by dystrophic calcification of the stylohyoid ligament and a past history of trauma to the area is significant. In some instances, the ligament calcifies in childhood and symptoms appear later in life. Lateral jaw or panographic radiographs demonstrate a slender radiopaque spicule emanating from the region of the styloid process. Other elongated protuberances, such as the hamular process and cervical transverse process, may impinge upon nerves in their vicinity, thus causing pain and discomfort. Calcified stylohyoid ligaments are frequent and are usually asymptomatic.

DIFFERENTIAL DIAGNOSIS

Pain associated with a calcified stylohyoid ligament may simulate the pain associated with other causes of TMJ and upper cervical pain. When the pain originates in the throat or tonsillar region, glossopharyngeal neuralgia must be considered in the differential diagnosis; however, a trigger zone is not present in Eagle's syndrome and pain is elicited on mandibular opening. Radiographs disclose the presence of a calcified stylohyoid ligament.

TREATMENT

Symptomatic elongated styloid processes can be surgically removed, using an intraoral approach.

Additional Reading

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HYOID SYNDROME

Age: Middle-aged and elderly adults
Sex: Female predilection

CLINICAL FEATURES

The hyoid syndrome results from elongation of the greater cornu with impingement

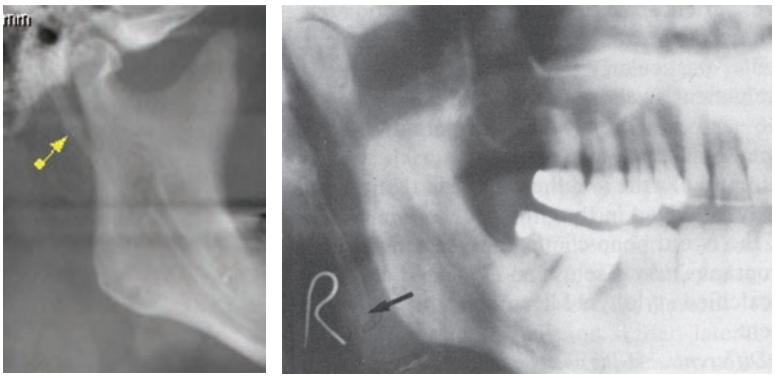

FIGURE 12-19
Calcified stylohyoid ligament associated with upper lateral neck pain.

on adjacent laryngeal tissues. Pain is experienced in the lateral neck/carotid area at the tip of the greater hyoid cornu. Pain may be acute, particularly when the neck is turned or the patient swallows. Ipsilateral referred pain to the ear is common, and syncope may be a feature. Many patients experience a chronic persistent dull ache and the sensation that a foreign body is lodged in the throat. Lateral movement of the hyoid bone elicits pain. Significantly, radiographs may disclose an elongated cornu, and a calcified stylohyoid ligament is usually not evident.

DIFFERENTIAL DIAGNOSIS

Carotidynia, styloid syndrome, and superior laryngeal neuralgia mimic hyoid syndrome because they manifest pain in virtually the same location. The clinical features and tenderness on palpation or lateral displacement of the hyoid bone allow for a definitive diagnosis.

TREATMENT

Surgical excision of the affected greater cornu is the treatment of choice. This procedure is usually performed through a cutaneous incision, which follows local anesthetization.

Additional Reading

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GLOSSOPHARYNGEAL NEURALGIA

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Affecting the left side of the face more often than the right, glossopharyngeal neuralgia appears to represent a disorder similar to tic douloureux but involving cranial nerve IX. Excruciating, stabbing, and paroxysmal pain develops after stimulation of a trigger zone located in the tonsil region or throat. Swallowing may stimulate an attack. Pain evolves at the base of the tongue or in the pharynx, radiating to the ear. Other signs, such as coughing and even syncope, may appear during an attack. A few affected patients also suffer from trigeminal neuralgia.

DIFFERENTIAL DIAGNOSIS

Paroxysmal pain in the throat and base of the tongue differentiates glossopharyngeal neuralgia from trigeminal neuralgia. Few

organic lesions cause paroxysms of pain; however, a thorough physical examination of the pharynx and hypopharynx should be undertaken to rule out infection or neoplasm. The cocaine test is useful in making the diagnosis. Application of 10% cocaine to the site of pain almost invariably eliminates the symptoms in glossopharyngeal neuralgia.

TREATMENT

Phenytoin and carbamazepine are the drugs of choice; however, they are usually less effective in glossopharyngeal neuralgia than in trigeminal neuralgia. When medical treatment fails, surgical sectioning of the rootlets of nerve IX may be required. Some neurosurgeons also recommend sectioning of laryngeal fibers from nerve X, which may also contribute to the pain paroxysms. The primary surgical choice is vascular decompression.

Additional Reading

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CAROTIDYNIA

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Carotidynia is believed to represent a vasodilation-mediated pain response located in the vicinity of the common carotid artery directly below the bifurcation area. In this respect, it is probably closely related to the other atypical facial pain syndromes described as midface cluster headaches. The pain may be unilateral or bilateral, lasting for a few days or a week, with localization in the lateral neck, ear, and angle of the mandible. It is intense and can be accentuated when the carotids are manually pressed posterolaterally against the cervical transverse processes. Inhalation of 100% oxygen may cause pain relief, such as that encountered with midface cluster headaches. In most instances, the disorder is self-limiting with spontaneous remission of symptoms.

DIFFERENTIAL DIAGNOSIS

The localization of pain in the region of the carotid artery is considered to represent carotidynia only when all organic disease has been eliminated from consideration. Neoplasms, aneurysms, and inflammatory conditions of the lateral pharynx must be ruled out, as must odontogenic inflammation arising from infected mandibular teeth. Parotitis, sialadenitis, arteritis, and otitis may all exhibit pain centered around the carotid bifurcation and angle of the mandible.

TREATMENT

Ergotamine tartrate administered as an anal suppository induces transient vasoconstriction and relief of pain. This drug should not be given to patients who are pregnant or hypertensive. Most cases eventually resolve of their own accord. In recalcitrant cases, denervation of the carotid bulb may offer relief.

Additional Reading

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SUPERIOR LARYNGEAL NEURALGIA

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Superior laryngeal neuralgia, like trigeminal and glossopharyngeal neuralgias, is a pain syndrome of unknown etiology characterized by acute lancinating paroxysmal pain localized above the thyroid cartilage in the region of the hyoid bone. The disorder is usually unilateral; however, bilateral cases have been reported. A trigger mechanism prevails; an acute pain attack, which lasts a few seconds, can be precipitated by yawning, swallowing, sneezing, or touching the skin over the hyoid bone. During a pain attack, the patient may exhibit uncontrolled swallowing and belching. Local anesthesia in the region of the hypothyroid membrane or in the pyriform sinus ablates the pain when trigger zones are stimulated; this represents an important diagnostic finding.

DIFFERENTIAL DIAGNOSIS

Superior laryngeal neuralgia may be confused with glossopharyngeal neuralgia. The former is localized to the thyrohyoid region, whereas the latter affects the base of the tongue and supraglottic region of the pharynx. Local disease of the larynx should be ruled out by palpation of the neck and thyroid area, and laryngoscopy should be performed. The absence of organic pathosis along with a history of acute lancinating pain with a trigger mechanism is usually sufficient for a definitive diagnosis. Nevertheless, the hyoid syndrome may evince similar, if not identical, features. The hyoid should be palpated and shifted laterally; if this maneuver does not elicit pain, a true neuralgia of the superior laryngeal nerve is the likely diagnosis.

TREATMENT

Carbamazepine (Tegretol), 200 to 1200 mg daily, is usually adequate for control; the drug can be withdrawn slowly. Periodic blood counts should be obtained. Surgical intervention with nerve resection should be reserved for when this disorder cannot be managed medically.

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LARYNGEAL NEOPLASMS

Figure 12-20

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Most neoplastic processes that arise in the larynx originate on the true or false cords and pyriform recess. Benign neoplasms rarely are painful. Malignant laryngeal tumors usually result in hoarseness without pain. Nevertheless, pain can be a sign of larynx cancer, particularly in large necrotic squamous carcinomas and in smaller tumors of the aryepiglottic fold, vallecula, and epiglottis. The pain is often referred to the ear. Invasion of cartilage or contiguous laryngeal soft tissues may produce induration with loss of the normal laryngeal cartilage crepitus on palpation. Direct or indirect laryngoscopy should be performed in patients with hoarseness, with or without upper cervical or larynx pain. White keratotic, red, ulcerated, and tumefactive lesions

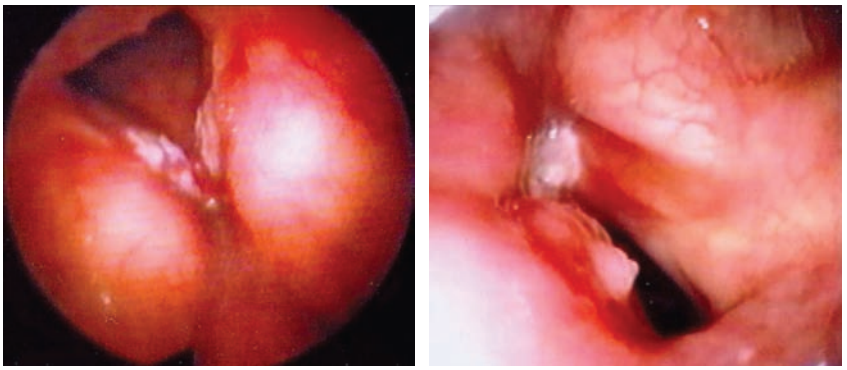

FIGURE 12-20
Keratotic squamous cell carninomas of the true cord associated with hoarseness and throat pain.

should arouse suspicion of carcinoma and warrant biopsy.

DIFFERENTIAL DIAGNOSIS

Pain associated with larynx cancer is usually a mild-to-moderate dull ache, yet may manifest occasional sharp twinges. When throat pain is present, laryngitis or one of the other pain syndromes listed here is more likely than cancer. Regardless, cancer should be considered as a potential cause of laryngeal pain, particularly among smokers.

TREATMENT

Laryngeal carcinoma is treated according to clinical staging and should be managed by a head and neck surgeon in conjunction with a radiotherapist.

Additional Reading

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TMJ Region Pain

Figure 12-21

MYOGENIC PAIN

Figure 12-22

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Myogenic pain represents one of the most common disorders causing facial pain. It is included with TMJ pain because myospasm can refer pain to the joint region with or without diffuse distribution over the facial musculature. Nevertheless, localized pain from myospasm without a more diffuse distribution over the masseteric and temporal regions is not common in the absence of joint sounds. When it does occur, the patient complains of a dull ache in the TMJ area; it is chronic and usually persistent. Often the pain is worse in the morning, in nocturnal bruxism, or in the late afternoon if parafunctional clenching or bruxing habits are correlated with work stress. The mandible may or may not deviate to the affected side; a full range of opening is observed, although maximal opening may be painful. The patient should be evaluated for myogenic TMJ pain by palpating the muscles for trigger point tenderness. The lateral pterygoid is most often involved, followed by the masseter and temporalis. Persistent

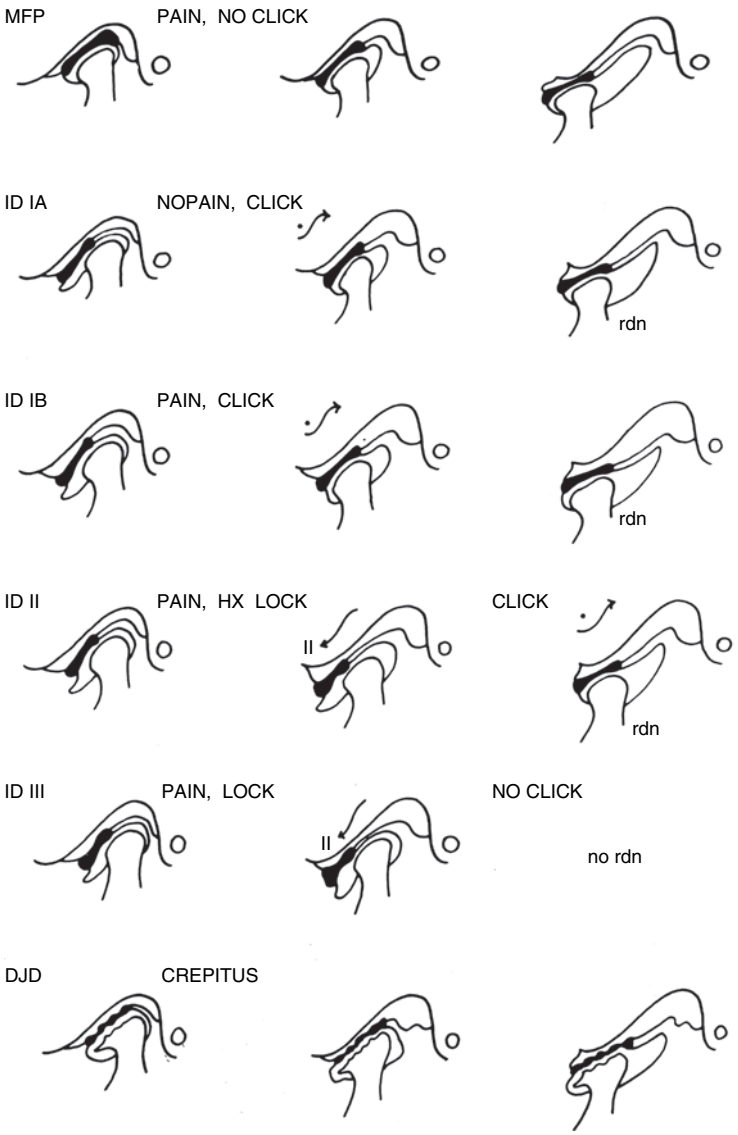

FIGURE 12-21
Classification of functional and internal derangements of TMJ. (DJD, degenerative joint disease; ID, internal derangement; MFP, myogenic facial pain; RDN, reduction of meniscus). See text for explanation.

digital pressure on the muscle trigger point usually intensifies the joint pain, and local anesthetic infiltration of the muscle eliminates the pain. In uncomplicated myogenic facial pain, clicking or popping cannot be palpated or auscultated. Rarely, facial myalgia may be associated with generalized myalgia and fibrositis syndromes.

DIFFERENTIAL DIAGNOSIS

Internal derangements can be excluded from the differential when no joint sounds are detectable and a full range of opening is observed. Organic lesions such as arthritis can be ruled out when joint swelling is absent or when tomograms fail to show pathologic changes indicative of arthritis. Muscle splinting secondary to a high restoration or odontogenic infection should be ruled out by conducting a thorough dental examination. Pain of myogenic origin may also mimic toothache in which the pain symptoms are referred to the maxilla or mandible.

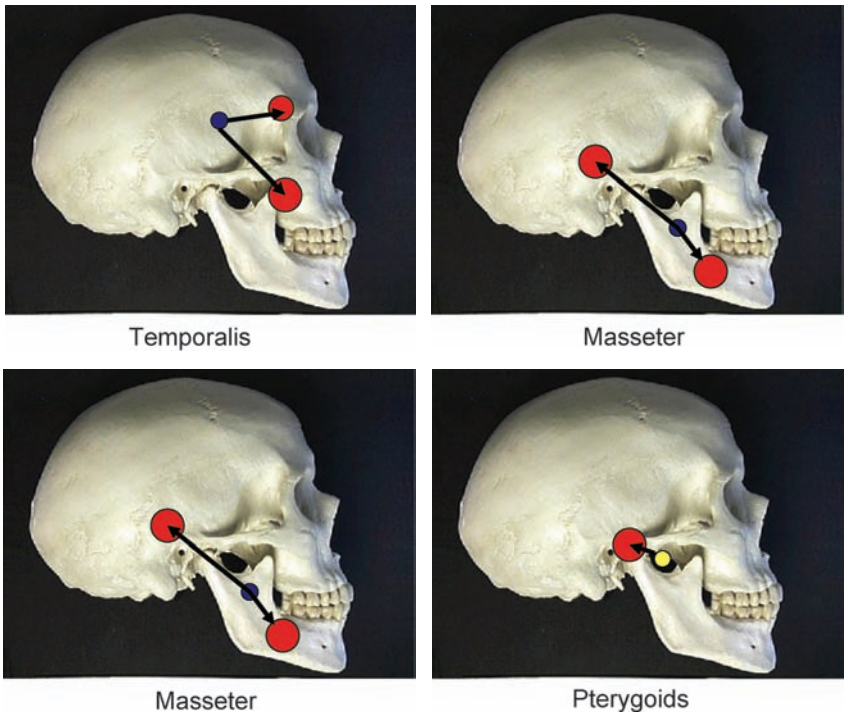

FIGURE 12-22
Trigger points (small blue and yellow dots) and pain referral patterns (red circles) in myogenic pain of masticatory and strap muscles.

TREATMENT

Myogenic TMJ pain can be managed in a variety of ways. All methods are directed toward minimizing myospasm and parafunctional activities. Electromyographic biofeedback with stress management behavioral medicine is highly effective. Occlusal splints may be employed, especially for nocturnal bruxism and clenching. Ultrasound applied over affected muscles may also relieve myogenic pain. Last, trigger point injections of a local anesthetic without a vasoconstrictor into affected muscle may be useful as an adjunctive management technique.

Additional Reading

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TYPE I INTERNAL DERANGEMENT (REDUCING)

Figure 12-23

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Type I derangements may be subdivided into two variants. Type IA is characterized by clicking or popping of the affected joint without pain, whereas type 1B is characterized by clicking or popping with pain. Both opening and closing clicks occur, and the fact that they are detected at different condylar positions is important. The pain may be a constant dull ache in the joint area, or it may be periodic and sharp, particularly when the patient eats hard or tough foods. Notably, the patient has no history of

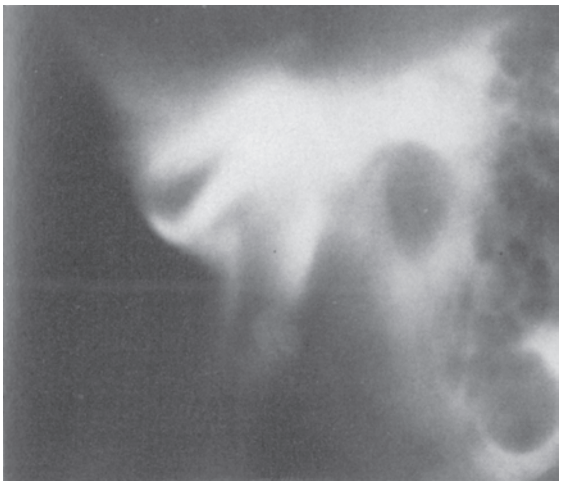

FIGURE 12-23
Arthrogram illustrating anterior displacement of the meniscus in a type IB internal derangement.

locking. The problem is usually unilateral, yet can be bilateral. On opening, the mandible often deviates to the affected side, the click occurs, and the mandible then shifts to the midline, reaching a full open position. The pathogenesis of this disorder is related to anterior displacement of the TMJ meniscus. The etiology has not been clarified and is probably multifactorial. Bruxing, clenching, occlusal disharmony, yawning, mandibular trauma, and overextension of the joint from intubation or prolonged opening have been implicated. Many patients with a type IB internal derangement may manifest concurrent myospasm with trigger point tenderness of masticatory and/or strap muscles of the neck. Tomograms fail to show pathologic osseous changes; however, the condyle(s) on the affected side(s) may appear to be retroposed, a finding that is not always consistent. CT and MRI may be used to confirm anterior displacement of the disc, and arthroscopic examination is useful in the diagnosis and detection of fibrous adhesions that may limit disc function.

DIFFERENTIAL DIAGNOSIS

Uncomplicated myogenic pain can be ruled out when no joint sounds are apparent. A history of locking or a persistent closed-lock places the derangement into type II and III, respectively. Tomograms should be obtained to rule out degenerative joint disease.

TREATMENT

Evidence indicates that this type of derangement may be reversible. Alternatively, some patients become progressively worse, and progress to type II or III derangements, and ultimately develop degenerative joint disease. Because muscle spasm may occur in conjunction with clicking or pain and clicking, the muscles should be palpated for trigger point tenderness, and electromyographic scanning is advisable. Splint therapy, along with muscle relaxation and stress management strategies, is the treatment of choice. Occlusal equilibration may be performed, particularly if the occlusion tends to retropose the mandible. Alternatively, recent studies tend to minimize the role of occlusion in the etiology of this disorder. Arthroscopic intervention in recalcitrant cases is advisable because fibrous adhesions may need to be freed.

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TYPE II INTERNAL DERANGEMENT (TRANSIENT LOCK)

Figure 12-24

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Anterior displacement of the meniscus with clicking or popping and pain in the affected joint(s) along with a history of locking characterize the type II internal derangement. The displaced disc in patients with a history of locking may not be a reversible phenomenon. The retrodiscal tissues (bilaminar zone) have been overdistended, and the meniscus cannot be firmly positioned over the condylar head. Fibrous adhesions may be present, augmenting the displacement. At surgery, the entire meniscus may be found to be loose ("floppy disc"). Patients may complain of transient closed lock whereby they are unable to open more than 15 to 25 mm, yet with automanipulation of the mandible they are able to open full range. In these instances, the displaced disc precludes translation of the condyle, yet reduction of the disc is ultimately achieved. Alternatively, transient open locks may occur, presumably related to entrapment of a reduced disc. An open lock should not be confused with true subluxation of the condyles, which lock anterior to a steep eminence. The mandible may deviate laterally on opening, and in some patients, the deviation corrects at the fully open position. Pain is usually dull and aching, but sharp episodes can occur during transient locking or when hard foods are eaten. In addition, muscle trigger points and elevated electromyographic readings may be noted, as patients with type II derangements sometimes manifest coexistent myogenic pain.

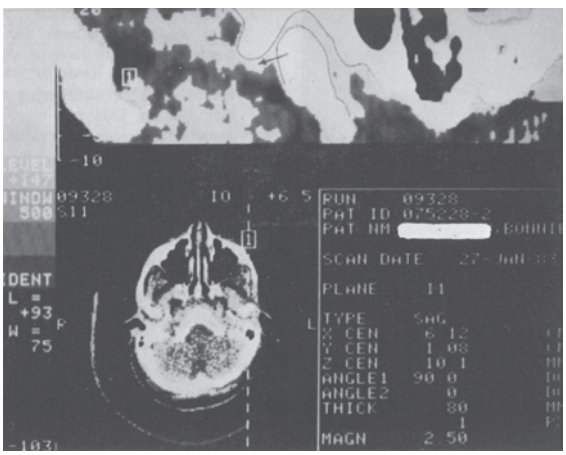

FIGURE 12-24
Computed tomographic scan (blink mode) showing anterior meniscus displacement in a patient with transient locking, a type II internal derangement.

DIFFERENTIAL DIAGNOSIS

The other TMJ pain syndromes listed here usually can be eliminated with the confirmation that locking occurs, yet is transitory.

TREATMENT

Splint therapy with muscle relaxation and stress therapy should be attempted initially. If no progress is achieved after 6 months or if the patient proceeds to a type III derangement with persistent, nonreducing closed lock, arthroscopic surgery with release of adhesions is recommended or surgical intervention with meniscus repositioning may be necessary.

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TYPE III INTERNAL DERANGEMENT (CLOSED LOCK)

Figure 12-25

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Whereas types I and II manifest pain and clicking of the affected joint(s), type III derangement is characterized by locking with pain. Average jaw opening is 20 mm. The disc is forward and precludes translation of the condyle; therefore, no click can be palpated or auscultated, and the jaw deviates to the affected side. In bilateral involvement, the jaw fails to deviate. Pain is chronic with a dull ache, and may be exacerbated during masticatory function. Occasionally, the examiner can reduce the disc with manual manipulation of the condyle; however, the patient is unable to do so unassisted. Arthrotomograms demonstrate anterior dislocation of the disc without reduction. As with the other types of internal derangements, a myogenic pain component may be extant. Studies have shown that about 20% of type I or II internal derangement patients progress to closed lock within 6 months, and this progression can be correlated with degree of pain and a deep anterior recess.

DIFFERENTIAL DIAGNOSIS

The other types of internal derangements can be excluded from consideration when closed lock is encountered. Other disorders unrelated to TMJ dysfunction must be considered in the differential diagnosis when unilateral locking is encountered. Not all of these conditions are associated with pain symptoms. Postinjection trismus, infections, and tumors of the pterygoid space and lateral pharynx must be considered. These disorders are discussed in detail under the heading *Limited and Deviant Mandibular Opening.*

TREATMENT

If left untreated, type III derangement will most likely progress to degenerative joint disease (localized osteoarthritis). Patients with closed lock can be treated by meniscus reattachment surgery; however, supe-

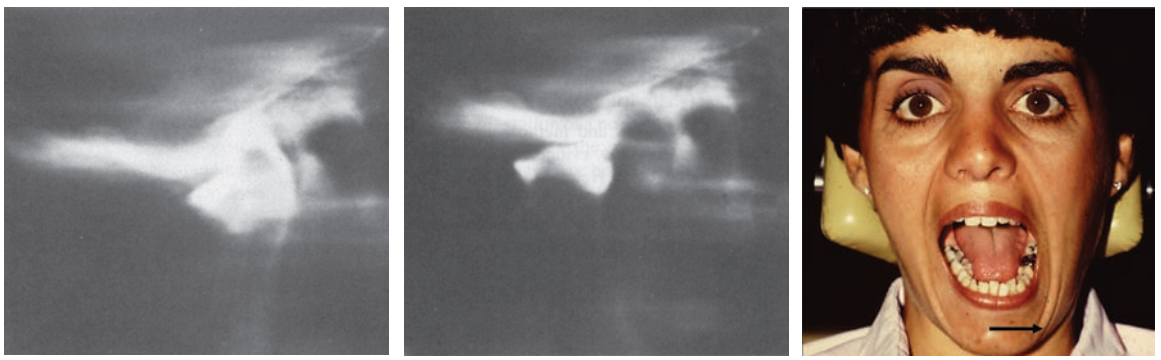

FIGURE 12-25
Arthrograms in type III internal derangement. Left: Closed with anterior disc displacement. Right: Open without reduction, the disc remains forward. Jaw deviates on opening to affected side.

rior joint space arthroscopic surgery with lysis of adhesions usually relieves pain and increases range of motion. If myogenic pain is a concomitant, electromyographic (EMG) biofeedback with stress management therapeutic methods are recommended following postoperative recovery. Interestingly, patients receiving no therapy with a follow-up of 2 years have significant diminution of symptoms despite a chronically displaced disc.

Additional Reading

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MENISCUS PERFORATION

Figure 12-26

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Perforation of the meniscus may occur subsequent to chronic anterior displacement, whereby the condylar head articulates with the loose connective tissues of the retrodiscal or bilaminar zone. Alternatively, perforations may occur in the fibrotic intermediate zone or even anterior to the anterior band of the meniscus. In these instances, the condyle has no cushion and may rub directly against the glenoid fossa incline. Characteristically, the patient has a history of clicking and locking and exhibits limited opening. Auscultation reveals crepitus. During arthrographic evaluation with fluoroscopy, contrast media introduced to the lower compartment can be seen to flow into the upper compartment simultaneously. Arthrotomograms also reveal dye opacity in both joint spaces. Superior joint space arthroscopic examination may also be diagnostic; however, some false-negative results have been reported.

DIFFERENTIAL DIAGNOSIS

Similar findings are encountered in degenerative joint disease, which, of course, may coexist with a perforation. Crepitus may also be detected in synovial chondromatosis as well as in other types of chronic arthritis.

TREATMENT

Surgical correction is the treatment of choice. A simple retrodiscal perforation can be closed primarily. Large perforations with adhesions may require placement of a disc prosthesis. Any condylar osteophytes should be eliminated by arthroplasty

Additional Reading

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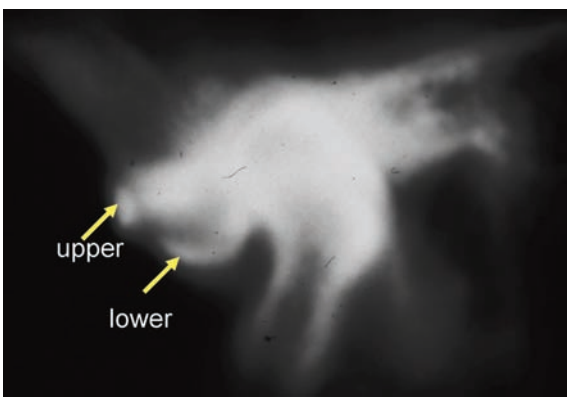

FIGURE 12-26
Arthrogram showing contrast media in both upper and lower joint spaces in cases of meniscus perforation. *A:* Closed. *B:* Open.

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OSTEOARTHRITIS (DEGENERATIVE JOINT DISEASE)

Figure 12-27

Age: Middle-aged and elderly adults
Sex: Female predilection

CLINICAL FEATURES

Generalized osteoarthritis is a degenerative process involving, primarily, weight-bearing joints and metacarpophalangeal joints. The latter may evince nodular excrescences referred to as Heberden's nodes. Limitation of motion and pain are also featured. The TMJ is not often involved in generalized degenerative joint disease, localized TMJ osteoarthritis being more common. Localized arthritis of the TMJ may evolve secondary to trauma; evidence increasingly implicates untreated internal derangements with an anterior meniscus as a precursor to degenerative disease. When the condyle is no longer protected by the meniscus or when the meniscus is loosely attached, perforation may occur, resulting in bone-to-bone contact between the mandibular condylar head and the articular fossa. Erosions, eburnation, and osteophyte formation evolve with resultant chronic pain. Most patients with degenerative joint disease have crepitant joint sounds while opening and closing. Tomograms reveal flattening of the condylar head, eburnation with deformation, erosions, and anterior or superior osteophytic lipping. Similar changes occur on the articular fossa; however, these changes rarely are radiographically demon-

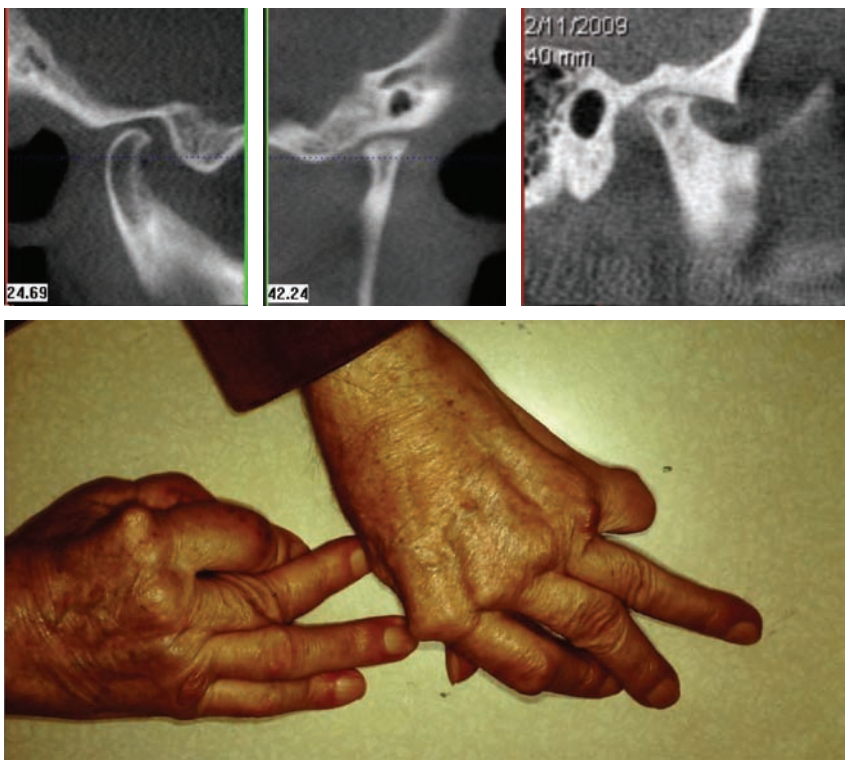

FIGURE 12-27
Degenerative joint disease (osteoarthritis). TMJ showing "bird break" anterior osteophytes, condylar head flattening, and Ely cyst in condylar neck (right).

strable. In chronic osteoarthritis of long standing, the patient, despite crepitus, may be pain free. Alternatively, ankylosis may develop, but this is unusual.

DIFFERENTIAL DIAGNOSIS

A diagnosis of localized TMJ degenerative joint disease is based on the presence of crepitus on auscultation with radiographic confirmation of osseous changes. A history of trauma or of symptoms that indicate a preexistent internal derangement, in conjunction with the aforementioned criteria, provides insight into the possible pathogenesis of the disease. The radiographic changes in TMJ osteoarthritis are similar if not identical to those encountered in rheumatoid arthritis. The latter is a TMJ manifestation of a polyarthritic condition.

TREATMENT

When the pain is mild, management with analgesics or nonsteroidal prostaglandin inhibitors may be adequate. When pain is moderate and problematic, condylar contouring or condylectomy with placement of a prosthesis may be indicated along with meniscoplasty. Surgical procedures of this nature may alter the occlusion, thus requiring orthodontic or restorative correction.

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RHEUMATOID ARTHRITIS

Figure 12-28

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Rheumatoid arthritis is a collagen disease associated with poststreptococcal immunopathic tissue changes localized in the joints. This progressive disorder is variable in its regional distribution; however, there is a tendency for symmetric involvement. The second and third metacarpophalangeal and proximal interphalangeal joints are most frequently involved, followed by the knee, wrist, shoulder, ankle, elbow, and vertebrae. The chief extra-articular manifestation of the disease is anemia. The affected joints are warm to the touch, swollen, and painful. The TMJ is frequently involved; when it is, bilateral pain is accompanied by generalized joint disease. Crepitation with stiffness is more commonly noted than pain. In rheumatic joint disease of childhood onset, involvement of the TMJ may result in retarded development of the mandible and a class II malocclusion with open bite. Condylar destruction and TMJ ankylosis occur in rare instances. Transcranial radiographs or, preferably, TMJ tomograms often disclose pathologic alterations, including irregular condylar articulating surfaces, flattening of the condyle, and osteophyte formation with increased joint space dimension. Rheumatoid nodules of the preauricular soft tissues have not been encountered. Rheumatoid factor as assayed by latex agglutination from a serum sample is the primary laboratory finding of diagnostic importance.

DIFFERENTIAL DIAGNOSIS

The pain of TMJ rheumatoid arthritis may be confused with that of other arthritides and the myofascial pain dysfunction syndrome. The bilateral nature and association with generalized joint pain and swelling are

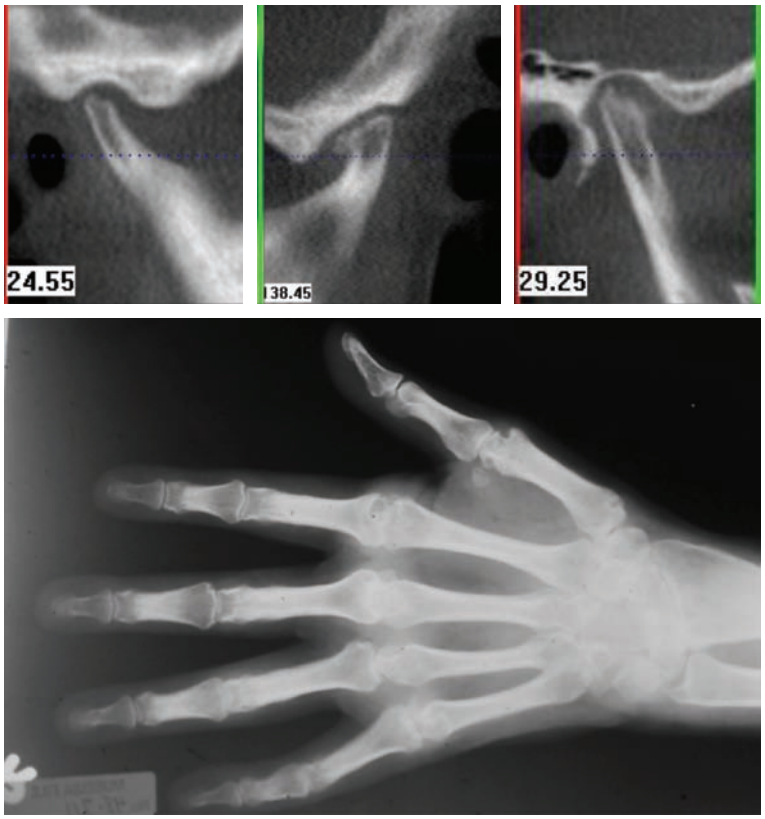

FIGURE 12-28
Rheumatoid arthritis. Condylar flattening, atrophy and erosion. Hand film showing erosions of proximal interphalangeal joints.

highly suggestive of rheumatoid arthritis, particularly when rheumatoid nodules are found over extremity joints. The rheumatoid factor is generally a positive finding in the serum along with elevated glutamate.

TREATMENT

Treatment for TMJ arthritis is not specific. The generalized disease should be managed by a physician and includes the use of steroids or other immunosuppressive drugs along with analgesics. When fibrous ankylosis or severe joint destruction is present, surgical intervention may be indicated.

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ACUTE INFECTIOUS ARTHRITIDES

Age: Young adults
Sex: No predilection

CLINICAL FEATURES

Acute or suppurative TMJ arthritis is usually the result of a bacteremia with pyogenic organisms. Gonococcal, streptococcal, and staphylococcal organisms are seen most

frequently in test cultures. The preauricular tissues are swollen and erythematous; they are acutely tender when palpated, both directly and intrameatally. The patient restricts opening; deviation of the mandible toward the affected side is apparent. Aspiration yields an exudate, and a culture should be obtained for specific identification of the infectious agent. Acute arthritis is rare, but chronic granulomatous arthritis, which is usually related to tuberculosis, is even less frequent. In tuberculosis arthritis, pain and tenderness are uncommon; however, a preauricular swelling may be present. Acute arthritis causes exudate accumulation in the joint spaces, and tuberculous arthritis causes granulomas; consequently, the joint space dimensions may be enlarged on TMJ tomograms, and a posterior open bite can be seen on the affected side.

DIFFERENTIAL DIAGNOSIS

Acute arthritis is unique in that swelling and acute pain coexist with limited opening and deviation. In addition, joint sounds are absent. Aspiration of the periarticular area with evidence of a purulent exudate confirms the initial clinical impression of acute arthritis.

TREATMENT

Aspiration and drainage should be performed initially, followed by culture and sensitivity testing of the aspirated exudate. An appropriate antibiotic may then be prescribed. Jaw movement exercises during the recovery period prevent the development of adhesions.

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MISCELLANEOUS ARTHRITIDES

Figure 12-29

Age: Adults
Sex: Predilection depends on specific disease

CLINICAL FEATURES

On rare occasions, polyarthritic disease associated with hyperuricemic gout, pyrophosphate arthritis, psoriasis, ankylosing spondylitis, lupus erythematosus, and scleroderma affect the TMJ. Most patients with these arthritides do not manifest significant TMJ signs or symptoms. In gout, the synovial tissues are the site of urate crystal formation, which initiates an inflammatory reaction with hyperplasia of the periarticular tissues. With progressive deposition of

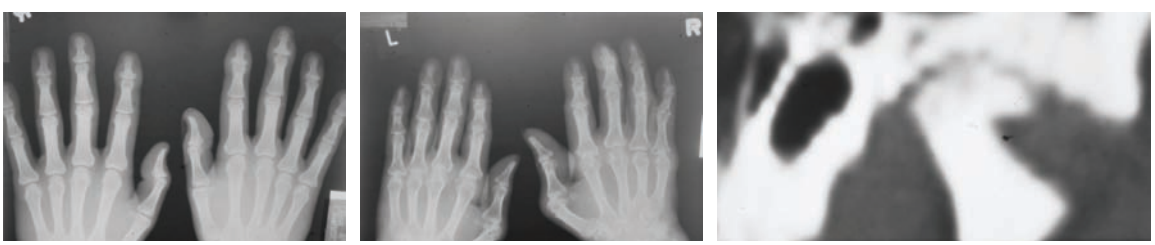

FIGURE 12-29
Miscilaneous arthritides. Gout (left), psoriatic (center), erosions and osteophyte (right) in TMJ psoriatic arthritis.

urates, pain and limitation of motion may be observed along with osseous resorption late in the course of the disease. A small fraction of psoriasis patients develop arthritis in the form of monoarticular or oligoarticular symptoms. Ankylosing spondylitis is an asymmetric oligoarthropathy that primarily affects the spine, particularly the sacroiliac joint, while, in general, sparing small peripheral joints. In systemic lupus erythematosus, fibrinoid necrotic foci may occur in the articular tissue. Dystrophic calcifications and articular erosions may occur in the later stages of systemic sclerosis (scleroderma). In some instances, these arthritides affect the TMJ, and the patient may suffer pain, joint swelling, and limited opening. Radiographic evidence of condylar erosions may be identified on tomograms.

DIFFERENTIAL DIAGNOSIS

The jaw signs and symptoms appearing in these miscellaneous arthropathies do not differ from those encountered in rheumatoid or degenerative TMJ arthritis. The specific diagnosis is based on distribution of joint symptoms throughout the skeleton in conjunction with other clinical and laboratory findings.

TREATMENT

In general, conservative therapy is indicated; many other joints are involved, and pain symptoms beyond the craniomandibular articulation tend to be more troublesome. Physical therapy, ultrasound, occlusal splints, and nonnarcotic analgesics often alleviate the symptoms. Most of these patients are under the care of a physician, and treatment should be pursued after medical consultation. When unrelenting pain is a feature and is refractory to conservative management, surgical intervention may be indicated.

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CONDYLAR FRACTURE

Figure 12-30

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Although trauma to the mandible may occur at any age, condylar neck and symphysis fractures are commonly seen in

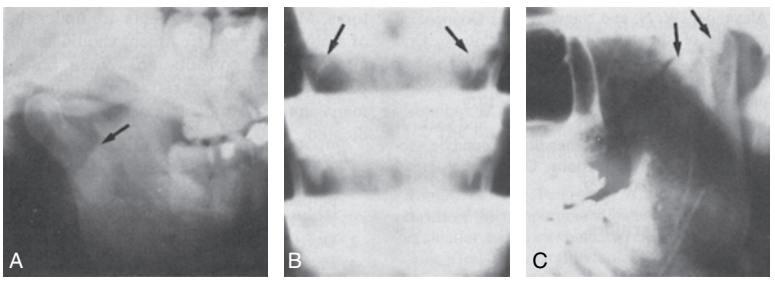

FIGURE 12-30
Condylar Fractures. *A:* Lateral jaw showing low subcondylar fracture. *B:* AP tomograms showing bilateral subcondylar fractures with medial displacement. (Courtesy of Dr. William Donlon.) *C:* Double condyle occurring subsequent to nonreducing condylar fracture.

children. The fracture may be unilateral or bilateral, greenstick, complete, or comminuted. In unilateral subcondylar fractures, the occlusion is altered with a shift of the mandible toward the affected side. Palpation of the preauricular area causes pain, which may be severe; in most cases, swelling is detectable. The jaw deviates on opening, and movement is painful. In bilateral complete fractures, the patient presents with a gagged occlusion that is characterized by retropositioning and an anterior open bite. Towne's, panoramic, ramus lateral jaw, and anteroposterior or submental vertex radiographs disclose the site of fractures. In complete fractures, the condyle is usually anteromedially displaced. Greenstick fractures in children may not show any condylar displacement.

DIFFERENTIAL DIAGNOSIS

Restricted or deviant opening associated with subcondylar fracture is, of course, preceded by a traumatic blow to the mandible; therefore, the diagnosis is readily suspected and easily confirmed by obtaining radiographs.

TREATMENT

Most surgeons agree that open reduction is rarely necessary for the treatment of condylar neck fractures. Closed reduction with intermaxillary fixation is the treatment of choice. At long-term follow-up, function is adequate; however, radiographs may disclose bilobed condyles.

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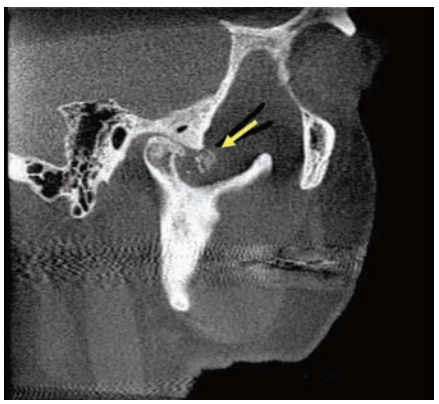
SYNOVIAL CHONDROMATOSIS

Figure 12-31

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Synovial chondromatosis is a reactive phenomenon that is seldom encountered in the periarticular tissues of the TMJ. Single or multiple ovoid bodies composed of hyaline cartilage form in the subsynovial connec-



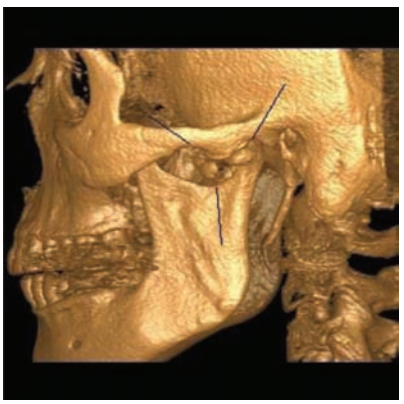


FIGURE 12-31
Synovial chondromatosis. Computed tomography and 3D reconstruction showing "joint mice" anterior to condyle.

tive tissue; they enlarge and then become detached, thus forming loose bodies within the joint spaces. Alternatively, it has been suggested that some are generated when osteophytic projections in arthritic joints become detached to form loose bodies. In fact, in some cases, these cartilaginous nodules remain in continuity with the articular tissues, meniscus, or condylar head. They calcify or undergo endochondral ossification and can be visualized as focal radiopacities radiographically. The mandible usually deviates toward the affected side, and the chondroid bodies may cause cross-bite or open-bite occlusion. Pain, particularly during mastication, is often a complaint. Larger lesions may be palpable over the condyle, and clicking or crepitus can be auscultated. Multiple chondroid bodies may be present with resultant double or triple clicks on opening and closing. Synovial chondromatosis may occur in conjunction with reactive synovial proliferation (villonodular synovitis).

DIFFERENTIAL DIAGNOSIS

Internal derangements with meniscus displacement or perforation and arthritic joints manifest similar clinical features. Transcranial and TMJ tomograms disclose the presence of joint space opacities when calcification is present. It is probable that if contrast media arthrography were used, noncalcified joint bodies would be demonstrable in relief.

TREATMENT

Surgical removal is the treatment of choice. Meniscus displacement, fibrous adhesions, villonodular synovitis, and arthritic changes may be present; they also require surgical correction.

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PIGMENTED VILLONODULAR SYNOVITIS

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Pigmented villonodular synovitis is a reactive proliferation of the synovial lining cells and underlying periarticular connective tissue with a predilection for the knee joint. The lesion is rare in the TMJ. It can be experimentally induced by intra-articular injections of blood and saline, thus suggesting the possibility of traumatic hemarthrosis in its genesis. Microscopically, villous proliferations extend into the joint space, and the supportive fibrovascular tissue contains multinucleated giant cells and hemosiderin pigment deposition. Many of the cases reported in the TMJ have been associated with chondroid metaplasia, thus suggesting the coexistence of synovial condromatosis. In other joints, osseous erosion is uncommon, yet may occur. In the TMJ, radiographic and surgical evidence of condylar erosion may be observed. Clinical findings include pain, swelling, limited opening, and deviation toward the affected side.

DIFFERENTIAL DIAGNOSIS

Pigmented villonodular synovitis is diagnosed on the basis of microscopic features. Clinically, the disease may mimic internal

derangements, neoplasms, synovial chondromatosis, and arthritis. When condylar erosion is radiographically evident and when a palpable preauricular mass can be detected, surgical intervention with biopsy of the periarticular mass is recommended.

TREATMENT

Surgical excision and repair of the articular soft tissues is the treatment of choice. Condylar destruction may necessitate placement of a joint prosthesis.

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Sialogenic Pain

SIALOLITHIASIS

Figure 12-32

Age: Adults
Sex: Male predilection

CLINICAL FEATURES

Salivary calculi are more common in the submandibular duct than in the parotid duct. The pain associated with salivary calculi is experienced during salivation and therefore is notable during meals. Blockage of the main excretory duct causes saliva distention throughout the duct tree, producing a drawing or stinging pain. The submandibular area is often swollen during pain episodes, and the swelling may be tender

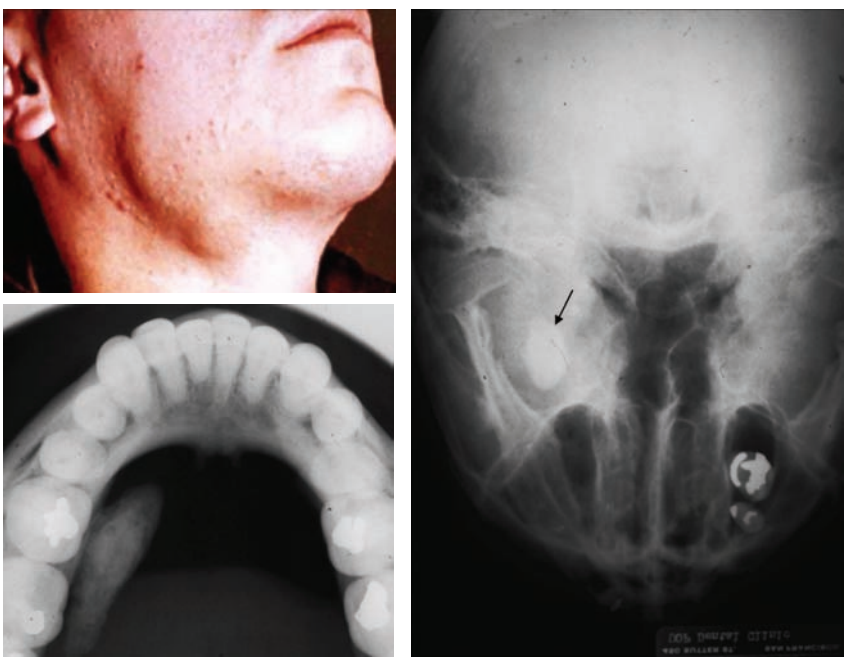

FIGURE 12-32
Sialolith in submandibular duct, causing pain and swelling at mealtimes. Parotid duct stone (right).

to palpation. Prolonged blockage may predispose to acute bacterial sialadenitis with constant pain. Occlusal radiographs should be obtained in both anterior and posterior regions. Most stones are located anteriorly; however, some may be found posteriorly underlying the retromylohydoid ductal flexure. A panoramic radiograph or lateral skull radiograph should be obtained when a parotid stone is suspected. When symptoms indicate sialolithiasis yet radiographs fail to uncover a stone, the gland should be milked to evaluate salivary flow. When no flow can be elicited, a sialogram should be ordered to evaluate for the possibility of a noncalcified blockage or focal duct stenosis.

DIFFERENTIAL DIAGNOSIS

Pain in the region of the submandibular gland could represent submandibular lymphadenopathy that is secondary to odontogenic infection or is a nonspecific sign of viral infection. The dentition should be evaluated when radiographs are negative for a sialolith.

TREATMENT

Small stones can occasionally be manipulated digitally and extruded from the duct orifice. Surgery is required in most cases. When duct blockage has persisted for a long time, thus causing sclerosing sialadenitis, sialectomy may be required to prevent multiple recurrent episodes of acute suppurative sialadenitis.

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ENDEMIC PAROTITIS (MUMPS)

Figure 12-33

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

Endemic parotitis is a paramyxovirus infection of the parotid glands causing bilateral parotid swelling and moderate to severe pain. Occasionally, the submandibular glands are enlarged and painful. Pain increases when sour or bitter foods are ingested. Milking the gland often causes exudation at the ori-

FIGURE 12-33
Endemic parotitis.

fice of Stensen's duct. Constitutional signs and symptoms of infectious disease include malaise, fever, and cervical lymphadenopathy. Orchitis or oophoritis are complications. The serum amylase level is elevated. Since development of the mumps vaccine, the disease has become less prevalent.

DIFFERENTIAL DIAGNOSIS

The swelling seen in mumps should not be confused with benign lymphoepithelial lesion of Sjögren's syndrome, which is painless. Acute suppurative sialadenitis is encountered in elderly adults. If a bacterial infection is suspected, the duct secretions or exudate can be cultured.

TREATMENT

Endemic parotitis resolves within 2 weeks. A bland diet, bed rest, and aspirin are recommended in conjunction with medical consultation because of possible orchitis, oophoritis, or meningitis.

Additional Reading

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ACUTE SUPPURATIVE SIALADENITIS

Age: Middle-aged and elderly adults
Sex: Male predilection

CLINICAL FEATURES

Acute bacterial sialadenitis is usually caused by streptococcal or staphylococcal microorganisms. Two predisposing factors are associated with nonviral sialadenitis. Surgical mumps is uncommon, representing a suppurative bacterial parotitis in elderly patients recovering from surgery (usually abdominal). It has also been reported to occur in xerostomic patients receiving phenothiazine therapy. The parotids are enlarged and painful, and Stensen's ducts usually have a purulent exudate. Postobstruction sialadenitis is a suppurative bacterial infection that develops in an occluded gland. The occlusion may be the consequence of calculus or a focal excretory duct stricture. The involved gland is swollen and painful. If the obstruction is still present and exudate cannot escape, draining cutaneous or oral fistulas may develop. Regardless of the predisposing conditions, fever and malaise are common but not invariable findings.

DIFFERENTIAL DIAGNOSIS

Acute suppurative sialadenitis must be differentiated from endemic parotitis and simple, uncomplicated sialithiasis. Pain and swelling are common to all three diseases. Both an exudate and cultivatable pathogenic organisms are required for the diagnosis.

TREATMENT

The exudate should be cultured, and penicillin should be prescibed. Pending results of culture and sensitivity, an alternative antibiotic may be necessary, particularly when penicillinase-producing staphylococci are the predominant pathogens.

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Temporal Pain

MIGRAINE

Age: Young adults
Sex: Female predilection

CLINICAL FEATURES

Migraine headache has been reported to affect 20% of the female population. It is not nearly as prevalent among males. The pain is usually unilateral (hemicrania), yet can be bilateral. The classic form of migraine is characterized by prodromal or concurrent symptoms including nausea, vomiting, flashing lights, scotomas, hemianopia, and/or photophobia. Speech disorders, paresthesias, and confusion are frequently encountered. The pain is moderate to severe, throbbing, and often incapacitating. The episodes may occur 2 or 3 times monthly, and pain may persist for many hours. It is localized around the temporal area and often involves the frontal and retro-orbital regions. The disorder is familial, and emotional problems may precipitate an attack. Evidence supports a vascular source subsequent to vasodilation of the external carotid branches. The superficial temporal vessels are often dilated during an attack; thermograms show a decrease in facial skin temperature, presumably resulting from shunting of blood away from the skin. Blood serotonin levels are decreased during attacks.

DIFFERENTIAL DIAGNOSIS

The signs and symptoms of migraine are characteristic and usually pathognomonic. Regardless, CNS neoplasms and organic rather than functional vascular disease must be considered in the differential diagnosis, as these conditions may mimic the symptomatology of migraine. Furthermore, migraine may be accompanied by tension headache, with episodic classic attacks being superimposed over constant dull aching pain of the frontalis and temporalis areas.

TREATMENT

Ergotamine tartrate (with or without caffeine) suppositories or sublingual tablets usually relieve pain. Skin temperature and EMG biofeedback along with stress management have been highly successful. Medical prophylactic management with propranolol has been effective, as has verapamil (320 mg/day). For menstrual cycle–associated migraine, tiptan drugs have proven effective.

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MYOGENIC PAIN (TENSION HEADACHE)

Age: Young and middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Muscle tension headaches are the most common form of headache. The pain may be referred to the TMJ; however, diffuse pain over the temporal, frontal, and masseteric regions is more often the chief symptom. Suboccipital, shoulder, and neck pain

may occur. Myogenic pain is the result of prolonged and sustained muscle contraction that is related to anxiety or stress. The pain itself is thought to arise subsequent to muscular accumulation of lactic acid. Myogenic facial pain is characterized by a constant dull to moderate ache, which is usually poorly localized. Palpation of the frontalis, temporalis, masseter, pterygoids, sternomastoid, trapezius, and strap muscles of the neck locate acutely tender foci, referred to as muscle trigger points. Prolonged pressure on a trigger point often causes diffuse referred pain in the areas constituting the chief complaint. Indeed, specific muscles show predictable routes of pain referral. Patients with uncomplicated myogenic facial pain do not manifest clicking or popping joints. Nevertheless, because of muscle spasm and soreness, deviant jaw opening may be a feature.

DIFFERENTIAL DIAGNOSIS

A diagnosis of uncomplicated myogenic facial pain is made when no joint sounds are heard and when no palpable clicks are detected in the TMJ. Myospasm can develop secondarily if other pain disorders are extant. A newly placed high dental restoration or a painful tooth may initiate muscle guarding or splinting to protect against occluding of the tooth in question.

TREATMENT

Myogenic facial pain is a stress disorder. Treatment is directed toward breaking the myospasm pain cycle. Stress management and electromyographic biofeedback are extremely beneficial in this regard; when bruxism or clenching coexists, an occlusal splint may be employed. Short-term use of muscle relaxants, anxiolytics, and analgesics are initially beneficial, yet should be phased out as the other forms of treatment begin to achieve results. Injection of muscle trigger points with an anesthetic devoid of vasoconstrictor is also beneficial as an adjunctive procedure.

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GIANT CELL ARTERITIS

Figure 12-34

Age: Elderly adults
Sex: Female predilection

CLINICAL FEATURES

Giant cell arteritis (GCA), also termed temporal arteritis, is related to polymyalgia rheumatica (PMR), a disorder characterized by shoulder and pelvic girdle pain with muscular weakness, absence of joint disease, and presence of an elevated erythrocyte sedimentation rate. GCA and PMR often coexist. Giant cell arteritis is a granulomatous disease of unknown etiology affecting the muscular-intimal layers of arteries, primarily cranial and facial vessels. The disease is characterized by episodic pain over the temple or temple and maxilla along with palpation tenderness of vessels, fever, anorexia, and eventual blindness. The pain is sharp or shooting with intervening periods of persistent dull ache. The temporal artery may be prominent and visibly

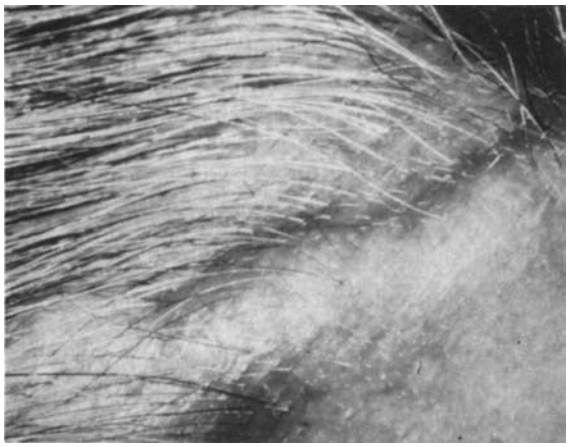

FIGURE 12-34
Prominent artery in giant cell (temporal) arteritis.

tortuous. The overlying skin is often erythematous and hyperalgesic. Involvement is not confined to the temporal artery. Indeed, many vessels supplying the head and neck area may be involved. Cerebral infarction is a complication. Notably, the erythrocyte sedimentation rate and C-reactive protein are elevated. Ultrasonography is a first-line diagnostic test and when negative, arterial wall biopsy is procured.

DIFFERENTIAL DIAGNOSIS

The episodic or paroxysmal nature may simulate a true neuralgia. When the patient's age is considered in conjunction with arterial tenderness and elevated sedimentation rate, a preliminary diagnosis of temporal arteritis can be made. Arterial biopsy is then indicated.

TREATMENT

Prednisone, 20 to 30 mg daily, usually controls the pain associated with temporal arteritis.

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Paresthesia

MENTAL PARESTHESIA

Figure 12-35

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Paresthesia, hypesthesia, or anesthesia of the mental nerve distribution over the lower lip usually represents a complication of a mandibular fracture or third molar extraction with trauma of the inferior alveolar nerve. Rarely, paresthesia may occur in response to overfilling during root canal therapy. Sensitivity to a light touch or a pinprick may be diminished or absent; the ipsilateral mandibular teeth may fail to respond to vitalometer testing. When there is no history of trauma or tooth extraction, metastatic carcinoma to the jaw should be suspected. Periapical and panoramic radiographs disclose a poorly marginated or moth-eaten radiolucency of the mandibular body. Occasionally, a central or cranial base lesion compresses the third division; when this occurs, the motor trunk of the fifth nerve is often compressed, resulting in soft palate paresis and/or masticatory muscle weakness.

DIFFERENTIAL DIAGNOSIS

With a documented history of trauma or third molar removal, the symptom usually resolves in 6 weeks; however, some patients do not report resolution for 6 months. In

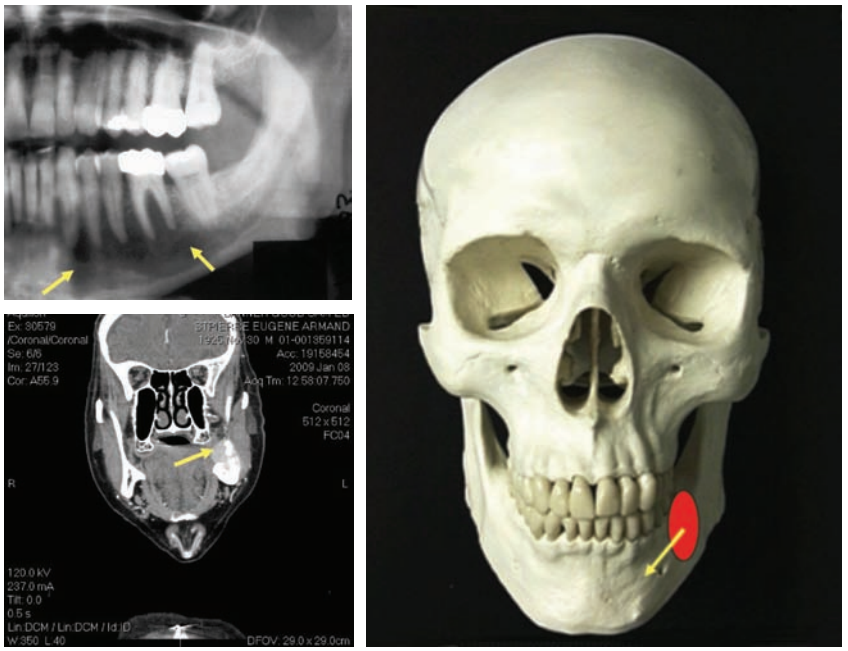

FIGURE 12-35
Mental paresthesia occurs following physical trauma to the inferior alveolar nerve or to malignant neoplasms, particularly metastatic tumors that encroach upon the nerve.

some instances of trauma, the paresthesia never resolves, but this is rare. When there is no history of nerve injury, a panoramic radiograph should be ordered; biopsy of any suspicious radiolucent or mixed radiolucent and radiopaque regions should be performed. In the absence of jaw disease, CT scans should be used to evaluate for CNS or cranial base lesions.

TREATMENT

There is no treatment for posttraumatic mental paresthesia; spontaneous resolution evolves as axis cylinders regenerate. When the sensory deficit persists beyond 6 months, a microsurgical nerve graft procedure may be successful. Metastatic tumor should be managed by an oncologist.

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INFRAORBITAL PARESTHESIA

Figure 12-36

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Included under this title of infraorbital paresthesia are other forms of sensory neurologic deficit, including hypesthesia and anesthesia of the infraorbital nerve distribution. In instances of complete anesthesia, light-touch and pinprick test-

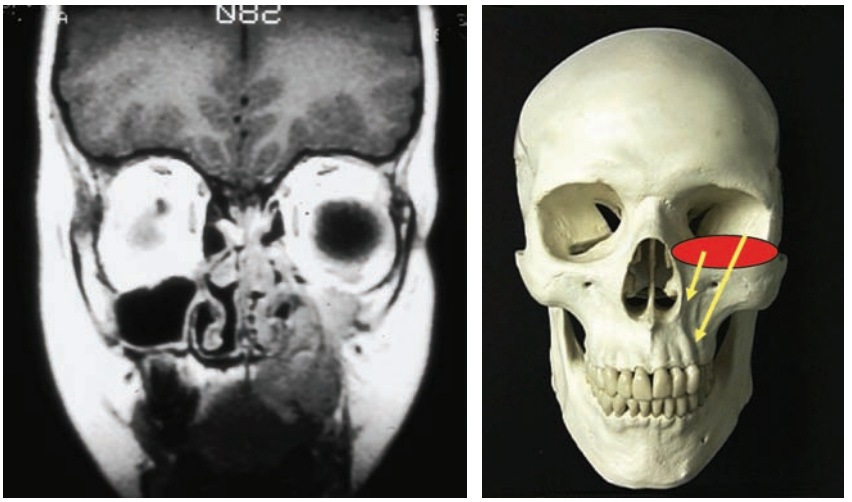

FIGURE 12-36
Infraorbital paresthesia may be secondary to V-2 injury or neoplasia along the course of the nerve.

ing over the infraorbital skin and usually the ipsilateral palate are not felt by the patient. In hypesthesia, either a pinprick, a light touch, or both may be affected to some degree. In other words, patients may detect these forms of stimulation to a lesser degree than they would on unaffected cutaneous regions. Patients with paresthesias may show a normal response to pinprick and light-touch tests, yet subjectively describe numbness and tingling of the affected skin. In general, loss of sensation to both a pinprick and a light touch indicates a peripheral nerve lesion, whereas differential loss suggests a central lesion. Antral carcinoma and cranial base tumors are the more common causes of infraorbital sensory deficits when the second division fibers are involved after exit from the skull. Cerebellopontine angle tumors with involvement of the gasserian ganglion are the most prevalent central lesions accounting for these symptoms. Other causes of sensory neuropathy in this area are multiple sclerosis, Bell's palsy, trauma, vertebrobasilar vascular disease, and connective tissue immunopathic disorders. Trigeminal (sensory) neuropathy is a less frequently encountered disorder in which no organic source can be detected. The sensory deficit is usually temporary with spontaneous resolution. Some of these instances may represent a viral neuritis or a psychologic conversion symptom. A few patients with idiopathic atypical facial pain may also experience an attending paresthesia. In all instances of infraorbital paresthesia, hyperthesia, or anesthesia, the remaining cranial nerves should be evaluated for accompanying motor deficits; antral tomograms as well as CT scans should be used to identify a tumor.

DIFFERENTIAL DIAGNOSIS

As mentioned previously, loss of both pinprick and light-touch sensation necessitates a search for a central lesion. The presence of ophthalmoplegia or other motor paresis is another sign that suggests a CNS or cranial base tumor. Maxillary or palatal expansion implicates an antral neoplasm.

TREATMENT

When the cause has been determined and a biopsy diagnosis has been procured, treatment must be planned according to this diagnosis. If an antral source has been ruled out, patients should be referred to a neurologist.

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Localized Motor Deficits

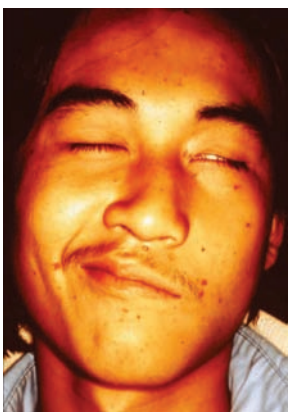
FACIAL PARALYSIS

Figure 12-37

Age: Varies according to etiology
Sex: Varies according to etiology

CLINICAL FEATURES

Seventh nerve paralysis is usually self-limited, and normal function returns within 2 months. Paralysis of this nature is referred to as Bell's palsy. Notably, the entire distribution of the seventh nerve is involved from the onset; therefore, the patient is unable to raise the eyebrow, close the eye, or smile on the affected side (i.e., complete hemifacial paralysis). Although it has been suggested that Bell's palsy is a herpesvirus neuritis, a variety of other diseases, lesions, and trauma of the temporal region, brain stem, facial canal, middle ear, and infratemporal fossa may produce partial, sequential, or complete seventh nerve palsy. The cortical tracts communicating with the motor nucleus ambiguus of the facial nerve cross over to innervate the lower face musculature, while the upper face fibers are ipsilateral proximal to the nucleus. A cortical lesion, therefore, causes contralateral lower face palsy; a lesion of the brain stem, main trunk, or peripheral fibers results in a total hemifacial paralysis. The nervus intermedius carries parasympathetic secretory fibers to the lacrimal and salivary glands. Lesions of the main trunk and facial canal are, therefore, frequently accompanied by ipsilateral xerophthalmia; xerostomia may not be evident because of normal contralateral function. Facial canal and middle ear neoplasms are usually associated with sensorineural hearing loss when seventh nerve palsy is a feature. Tumors of the cranial base, parapharyngeal space, and infratemporal fossa, particularly malignant parotid tumors, often cause seventh nerve palsy and neuropathy of other cranial nerves. CT scans disclose osseous destructive changes in the temporal bone or a soft tissue mass, depending on the location of the lesion. Lastly, neurologic involvement in Lyme disease (Bannwarth's syndrome) can result in either unilateral or bilateral facial paralysis.



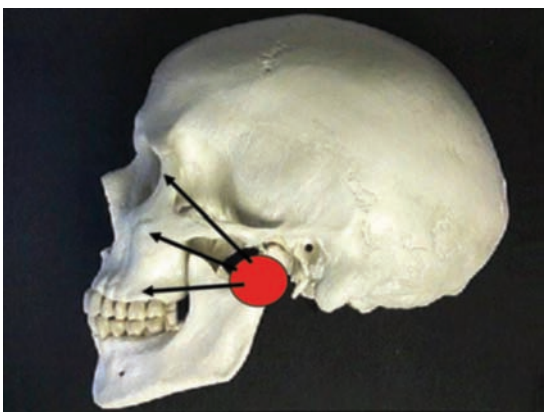


FIGURE 12-37
Complete facial nerve paralysis is seen in Bell's palsy and parotid adenocarcinomas that invade nerve VII.

DIFFERENTIAL DIAGNOSIS

Evaluation of a patient with seventh nerve paralysis must include the following chief factors: precise muscle groups involved, temporal progression of muscle group paresis, middle ear disease, vestibular function, hearing loss, tinnitus, and presence of other cranial nerve deficits. It should also be noted that seventh nerve palsy accompanies cheilitis granulomatosa in the Melkerson-Rosenthal syndrome and, recently, idiopathic paresis has been observed among human immunodeficiency virus (HIV)–positive patients. Special radiographic and neurologic procedures are required to secure a definitive diagnosis. Referral to an otolaryngologist or neurologist is recommended.

TREATMENT

Systemic steroids or corticotropin injections have been successful in treating Bell's palsy. Even in the absence of treatment, the paralysis generally disappears within 2 months. Lesions arising along the intracranial, temporal bone, and peripheral distributions of the seventh nerve are treated in accordance with the ultimate and definitive diagnosis.

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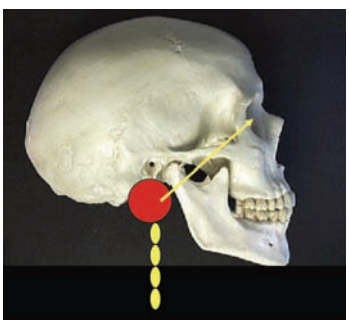
HORNER'S SYNDROME

Figure 12-38

Age: Elderly adults
Sex: Male predilection

CLINICAL FEATURES

Horner's syndrome is a neurological facial sign indicative of a lesion compressing the stellate ganglion, usually bronchogenic carcinoma arising adjacent to the apex of the lung. The sympathetic fibers emerging from the ganglion normally pass into the head and neck regions and innervate the pupil dilator, smooth muscle elevator of the upper eyelid, and periorbital sweat glands. Compression of the ganglion leads to miosis or contraction of the pupil, ptosis of the upper eyelid, and anhydrosis of the periorbital and facial skin. In addition to lung cancer, other neoplasms, infections, or aneurysms adjacent to the cervical spine may encroach upon the ganglion or sympathetic fibers arising therefrom. Lyme disease, and rarely CNS vascular occlusive disease or aneurysms, can result in sympathetic paresis.



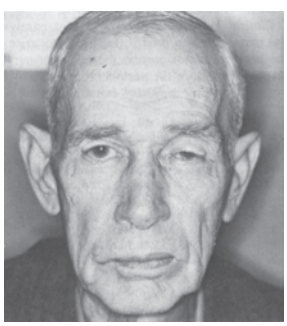


FIGURE 12-38
Ptosis and miosis in Horner's syndrome associated with carcinoma of lung apex.

DIFFERENTIAL DIAGNOSIS

The etiology of Horner's syndrome is variable and represents a medical problem. Referral to an internist or neurologist is recommended.

TREATMENT

The cause must be eliminated. Horner's syndrome may herald the presence of a serious illness such as cancer or an aneurysm.

Additional Reading

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OPHTHALMOPLEGIA

Figure 12-39

Age: Varies according to disease
Sex: Varies according to disease

CLINICAL FEATURES

Eye movement paralysis has many complex origins. Lesions may arise in the cerebral motor cortex, the nuclei of nerves III, IV, and VI, or the peripheral nerves may be compressed after they have exited from the brain stem. A lesion of the motor cortex causes a defect in contralateral conjugate gaze. The consequences of a left cerebral lesion are inability of both eyes to engage in right-sided gaze and a tendency for bilateral left deviation. In other words, the patient "looks toward the lesion." The mechanism involves impairment of neural pathway conduction prior to synapse with the nuclei of III (ipsilateral) and VI (contralateral). Internuclear ophthalmoplegia is characterized by inability to move one eye medially while the opposite eye is directed laterally, despite the fact that the patient is able to converge both eyes. This apparent paradox is reconciled when one realizes that the pathway for convergence is different from the pathway for lateral conjugate gaze. Multiple sclerosis is usually the underlying disease involving internuclear ophthalmoplegia. Lesions involving each specific nucleus of the three nerves controlling eye movement manifest specific signs. Bilateral involvement of the abducens nuclei causes convergent gaze owing to defective motor supply to the lateral rectus. Divergent gaze is the consequence of a bilateral lesion of the oculomotor nerve. Compression of the peripheral nerves is caused by hemorrhage or tumor. Alternatively, entrapment of ocular muscles may occur in orbital blow-out fractures or in localized orbital lesions. A lesion located in the middle fossa/cavernous sinus region may compress one, two, or all three motor nerves to the eye. Compression of the oculomotor (CN-III) causes unilateral gaze with pupillary dilation. The cold caloric test confirms the finding. Involvement of the trochlear nerve (CN-IV) causes inability to move the affected eye inferolaterally. Unilateral paralysis of the abducens (CN-VI) is characterized by medial gaze of the affected eye. *Progressive supranuclear palsy* is a primary neurologic disorder that causes paralysis of the extraocular muscles and may be due to a perturbation in mitochondria.

DIFFERENTIAL DIAGNOSIS

Because of the aforementioned clinical signs gleaned from cranial nerve examination of nerves III, IV, and VI, observation of eye position at rest, comparison of pupil size, and use of the cold caloric test, the examiner will have a concept of where the

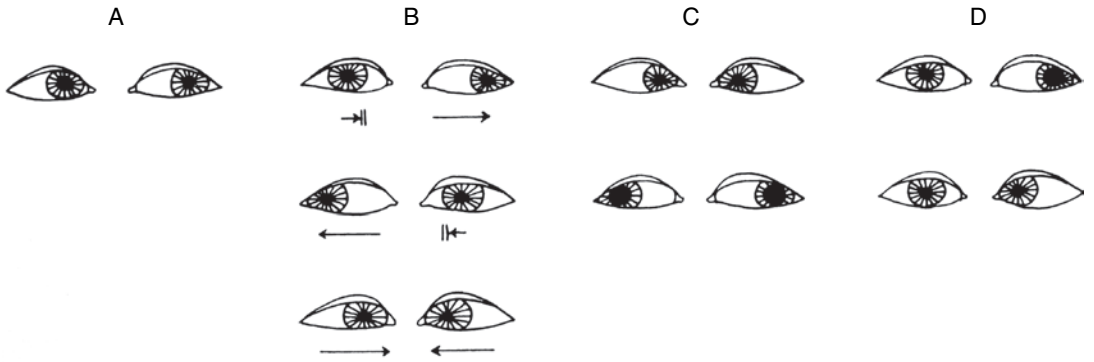

FIGURE 12-39
Ophthalmoplegia. *A:* Left cerebral lesion with conjugate gaze. *B:* Medial longitudinal fasciculus lesion with inability to look medially when directed to look left or right, convergence intact. *C:* Bilateral nuclear lesions of abducens (above) and oculomotor (below). *D:* Left unilateral nuclear or peripheral nerve paresis of oculomotor (above) and abducens (below).

lesion lies. Because the etiology of ophthalmoplegias is so protean, a definitive diagnosis requires a variety of other clinical, radiologic, and laboratory tests. A detailed differential diagnosis of ophthalmoplegia is beyond the scope of this book.

TREATMENT

Patients with eye muscle paresis should be examined by an ophthalmologist or a neurologist when it has been determined that the etiology is not a maxillary or orbital fracture.

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HYPOGLOSSAL PARALYSIS

Figure 12-40

Age: Adults
Sex: No predilection

CLINICAL FEATURES

The hypoglossal or twelfth nerve supplies motor fibers to the tongue and exits the medulla inferior to the olive. Unilateral injury or a lesion of the nucleus or nerve

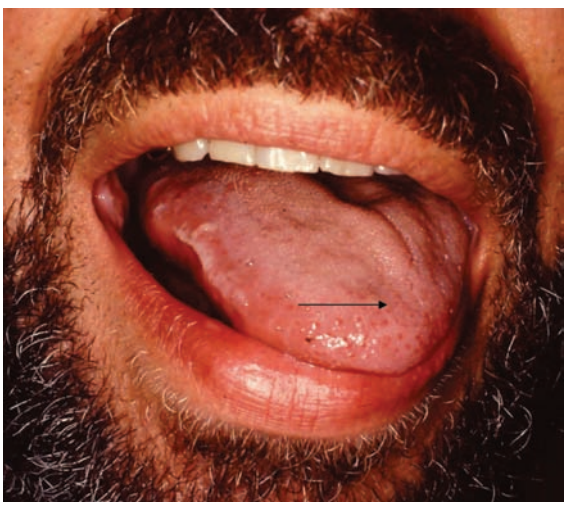

FIGURE 12-40
Twelfth nerve paralysis. Tongue deviate toward the affected side.

causes the affected side of the tongue to undergo atrophy, and on protrusion, the tongue deviates toward the affected side. Attempted movements of the protruded tongue to the normal side are absent or weak. At rest, lying in the floor of the mouth, the tongue deviates slightly toward the healthy side; retrusion of the tongue on the affected side is defective. A lesion may be located within the medulla or along the peripheral course of the nerve. Basilar artery occlusion causes a lesion of the medulla with ipsilateral tongue paralysis and contralateral arm and leg paralysis. Neoplasms in the vicinity of the occipital condyle frequently compress the hypoglossal nerve with paralysis, dysarthria, and severe pain that is worsened when the neck is flexed. Neoplasms in the lateral neck along the course of the nerve may also cause unilateral paresis or palsy. Bilateral twelfth nerve palsy is rare. Fibrillation of the tongue is seen in syringobulbia, amyotrophic lateral sclerosis, and chronic alcoholism.

DIFFERENTIAL DIAGNOSIS

Because unilateral hypoglossal paralysis may be either central or peripheral in origin, complete neurologic examination is required to explore other deficits indicative of a lesion within the medulla. CT scans should be obtained to evaluate the possibility of a cranial base primary or metastatic tumor. Palpation of the upper lateral neck for indurated swellings should also be performed.

TREATMENT

Referral to a neurologist is recommended. Treatment is determined when the source of the lesion is located and a definitive diagnosis is rendered.

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SOFT PALATE PARALYSIS

Figure 12-41

Age: Varies depending on disease
Sex: No predilection

CLINICAL FEATURES

The soft palate muscles include the tensor veli palatini, supplied by the motor root of the fifth nerve, and the levator veli palatini, palatoglossus, and palatopharyngeous, all supplied by branches of the tenth nerve from the nucleus ambiguus. Brain stem lesions involving the nucleus or cranial base and parapharyngeal space lesions may cause paralysis with resultant drooping of the palate and loss of the palatal

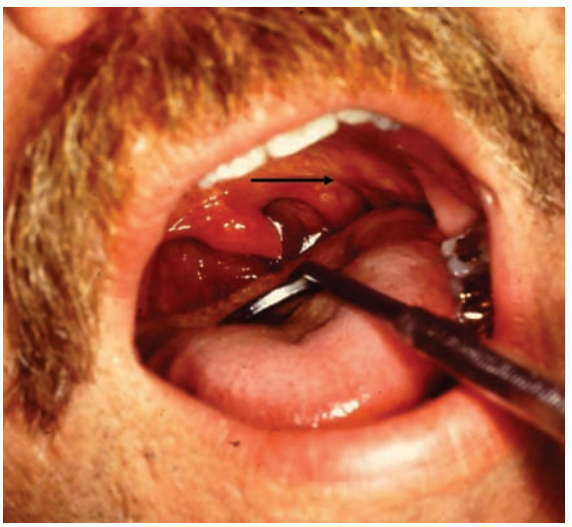

FIGURE 12-41
Soft palate paralysis. Uvula deviates toward normal side.

reflex. Bilateral paralysis results in velopharyngeal insufficiency, thus causing nasal speech and difficulty with velar sounds such as "N" and "NG." Bilateral paralysis is associated with poliomyelitis, diphtheritic polyneuropathy, myasthenia gravis, and brain stem infarction. Unilateral paralysis is characterized by inability of the affected side to elevate when the patient says "ah"; the uvula deviates toward the normal side. An ipsilateral nuclear lesion, cranial base neoplasia, nasopharyngeal carcinoma, foraminal narrowing, or varicella zoster may be causative. When pharyngeal constrictor paralysis and sternomastoid weakness is observed, the clinical findings are termed *Vernet syndrome,* and when nerves IV, X, and XI are involved, the term *Jugular syndrome* is used.

DIFFERENTIAL DIAGNOSIS

As previously mentioned, a variety of neurologic diseases can cause bilateral palatal paralysis. Unilateral paralysis warrants a thorough nasopharyngeal examination, which should include CT scans of the cranial base to detect the presence of a tumor.

TREATMENT

Because a variety of neurologic and neoplastic disorders can cause palatal paralysis, referral to a neurologist is recommended.

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Limited and Deviant Mandibular Opening

MUSCLE SPLINTING

Figure 12-42

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

When patients feel pain, they protect themselves by limiting motion of the associated joint. For instance, wide opening may be painful; thus, the patient may consciously maintain closure or limited opening. The splinting may be unilateral, causing deviation of the mandible on opening. A variety of organic lesions may initiate this protective phenomenon; they include trauma, fracture, pericoronitis, odontogenic infection, salivary gland inflammation, primary TMJ articular disease, and avoidance of a recently placed high dental restoration. Prolonged splinting may actually lead to myospasm, although

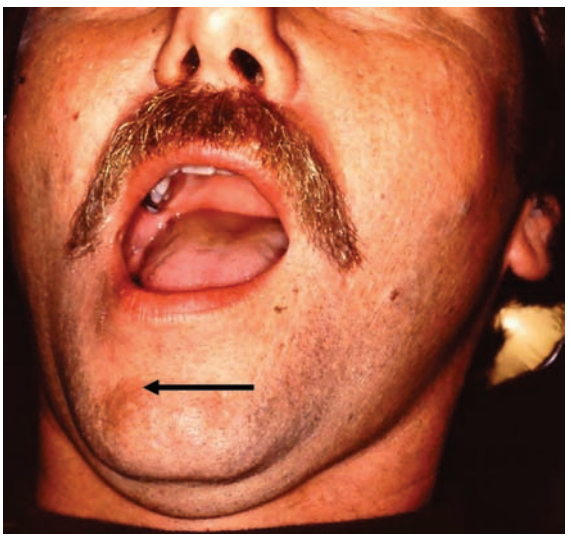

FIGURE 12-42
Deviant jaw opening secondary to muscle splinting.

this is rare. Amelioration of the problem or local anesthesia to the tissues suspected in its etiology permit the patient to fully depress the mandible. Dystrophic calcification or myositis ossificans of the pterygoid muscles also decreases ability to open.

DIFFERENTIAL DIAGNOSIS

Limited opening because of muscle splinting may leave the erroneous impression that the problem is a primary muscle disorder (i.e., myogenic facial pain). Physical evaluation of teeth, occlusion, and periodontium and perioral tissues along with radiographs disclose the presence of disease. The inflamed or traumatized tissue can be anesthetized so that amelioration of the inability to open can be evaluated.

TREATMENT

Resolution of the cause eliminates the effect.

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POSTINJECTION/ POSTINFECTION TRISMUS

Age: Middle-aged adults
Sex: No predilection

CLINICAL FEATURES

Limitation in jaw opening may evolve from inferior alveolar nerve block. Occasionally, the patient complains of pain; however, most patients do not experience pain unless they forcefully attempt full depression of the mandible. The closed-lock phenomenon appears 1 to 6 days after a dental procedure that necessitated inferior nerve block anesthesia. Most patients are unable to open beyond 20 mm. Although the pathogenesis is unknown, the condition probably occurs because a needle has pierced a vessel and caused hematoma followed by organization and scar formation. Occasionally, trismus is encountered in patients with acute pericoronitis or alveolitis sicca. Inflammatory extension into the pterygomandibular space may develop; but in most instances, pain may induce muscle splinting or guarding that prevents a full range of opening.

DIFFERENTIAL DIAGNOSIS

Although limited opening may be seen in a variety of disorders, a closed-lock situation related to injection can be readily diagnosed on the basis of history. Inflammation of a pericoronal operculum or extraction site accounting for trismus is also easily recognized on the basis of examination and history.

TREATMENT

Postinjection trismus usually resolves after a 3-week course of physiotherapy that includes ultrasound to masticatory muscles, hot packs, and jaw opening exercises 3 times a week. Forced opening under general anesthesia may be required for patients who do not respond to the aforementioned conservative regimen. Rarely, surgical intervention is required to sever a scar band that may form in the pterygoid space. Pericoronitis should be treated with hydrogen peroxide irrigation and antibiotics when fever and malaise are present. With resolution of symptoms, the hyperplastic tissue should be excised with extraction of the associated third molar. A full range of opening should return within a few days.

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CONVERSION TRISMUS

Age: Young and middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Conversion reactions are encountered among patients with hysterical or histrionic personality. The etiology is apparently related to an underlying emotional crisis with which the subject cannot cope, whereby the emotional conflict is converted to a physical sign or symptom. Motor deficits (paralysis), sensory deficits (paresthesia or numbness), and visual loss represent the more common hysterical conversion reactions; notably, the deficits usually do not follow neuroanatomic pathway distributions. Conversion or hysterical trismus is rare and is characterized by inability to open the mouth in the absence of organic disease in the TMJ. Prolonged closure may, however, lead to myospasm with masticatory muscle weakness. The personality profile is important in the diagnosis, and psychometric testing with the MMPI shows elevation of the hysteria scale. Patients with histrionic or hysterical personalities exaggerate their symptoms and make multiple unfounded organ-system somatic complaints, yet they maintain an indifferent attitude about their problems (belle indifference). In addition, patients tend to be theatrical with overuse of cosmetics and adornment. The trismus can be reversed with restoration of normal opening while the patient is under general anesthesia or heavy sedation.

DIFFERENTIAL DIAGNOSIS

Because many organic disorders result in limited opening or trismus, a thorough work-up for joint, muscle, and infectious disease must be pursued. Differentiation from a true closed-lock type III internal derangement is difficult on clinical grounds alone. Psychiatric consultation and MMPI testing should be included in the data base collection. Restoration to normal function after intravenous diazepam sedation with manipulation of the mandible aids in establishing the diagnosis.

TREATMENT

The immediate problem is easily ameliorated by manipulation of the jaw under general anesthesia or intravenous sedation. Long-term management rests with psychotherapy.

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ANKYLOSIS

Figure 12-43

Age: Children or adults
Sex: No predilection

CLINICAL FEATURES

Unilateral or bilateral ankylosis of the TMJ is the consequence of trauma, destructive infectious arthritis, or rheumatoid arthritis. The ankylosis may be fibrous or bony. When a joint lesion arises during childhood, mandibular retrognathism occurs because of the arrest of condylar growth on the affected side(s). The patient may be able to open the jaw only a few millimeters or it may be completely closed. Severe limitation of opening is seen even in unilateral ankylosis, and

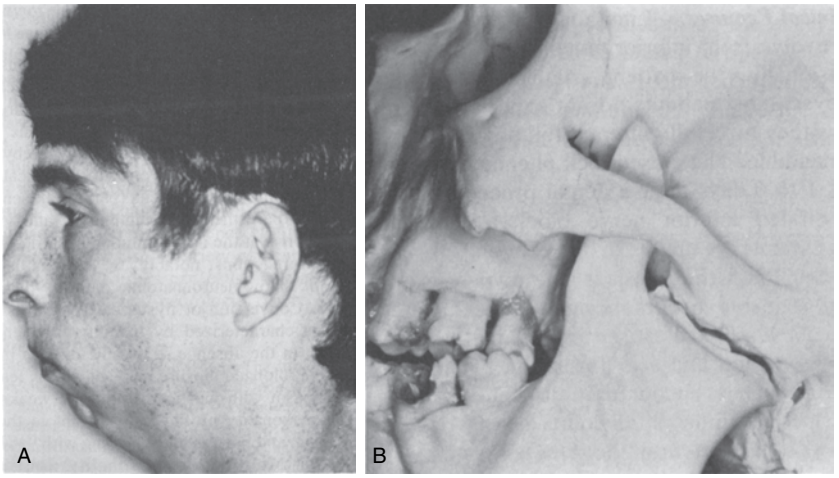

FIGURE 12-43
A: Retrognathia in bilateral TMJ ankylosis. *B:* Skull specimen in TMJ ankylosis.

deviation of the mandible to the affected side is generally not detected because the ankylosed joint often prevents translation of the unaffected condyle. TMJ tomograms disclose an absent or anomalous-appearing condyle without joint space radiolucency.

DIFFERENTIAL DIAGNOSIS

In most of the other disorders showing limitation of opening, the restriction is incomplete. A history of trauma, acute arthritis, or juvenile rheumatoid arthritis and mandibular retrognathia, when considered in conjunction with the radiographic findings, allows for establishment of the diagnosis.

TREATMENT

Ankylosis may be corrected by surgical resection, reconstruction, and/or placement of a joint prosthesis.

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HECHT-BEALS-WILSON SYNDROME

Age: Childhood onset
Sex: No predilection

CLINICAL FEATURES

Inherited as an autosomal dominant trait, the Hecht-Beals-Wilson syndrome is characterized by limited mandibular opening, campylodactyly resulting from foreshortened flexor tendons of the fingers and wrists, shortened leg and hamstring muscles with consequently short stature, and, occasionally, foot deformities (club foot). The limitation in opening is the result of bilateral abnormal ligaments located within the masseteric region. This fibrotic band can usually be easily palpated bidigitally in the buccal mucosa just anterior and confluent with the masseter.

DIFFERENTIAL DIAGNOSIS

This syndrome exhibits classic features allowing for a definitive diagnosis. Limited opening in conjunction with buccal

mucosal fibrous bands and flexion of the finger when the wrist is dorsiflexed confirms the diagnosis. Other family members may be affected.

TREATMENT

The masseteric fibrous bands may be surgically severed. Some surgeons advocate coronoidectomy to free any inhibition of opening as a consequence of temporalis fibrosis, which may be present.

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CORONOID HYPERPLASIA

Age: Children
Sex: Males

CLINICAL FEATURES

A rare developmental disorder, coronoid hyperplasia is bilateral and causes painless restriction of mandibular opening. Most patients are unable to open beyond 20 mm. The enlarged coronoids impinge upon the posterior aspect of the zygoma, thereby restricting translation of the condyles secondarily. There is no deviation on opening as both coronoids are involved. Although some cases are probably sporadic, others have been reported among siblings. The diagnosis must be confirmed radiographically. A lateral skull, high panoramic, or lateral tomograms disclose enlarged coronoid processes extending high above the zygomatic arch.

DIFFERENTIAL DIAGNOSIS

Restricted opening without pain or deviation in a young male should arouse suspicion of coronoid hyperplasia. Although the other entities included here must be considered in the differential diagnosis, they are more common in older patients or exhibit restriction of opening with deviation or pain. Radiographs confirm the diagnosis of condylar hyperplasia.

TREATMENT

When patients are not bothered by their inability to open and they are able to function adequately, no treatment is necessary. With severe limitation, bilateral coronoidectomy is the treatment of choice.

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CONDYLAR HYPERPLASIA

Figure 12-44

Age: Children and young adults
Sex: Female predilection

CLINICAL FEATURES

Unilateral hyperplasia of the mandibular condyle is of unknown etiology yet is considered to be a developmental defect. Clinically, facial asymmetry is seen and the patient exhibits either an open bite on the affected side or a cross bite with open bite.

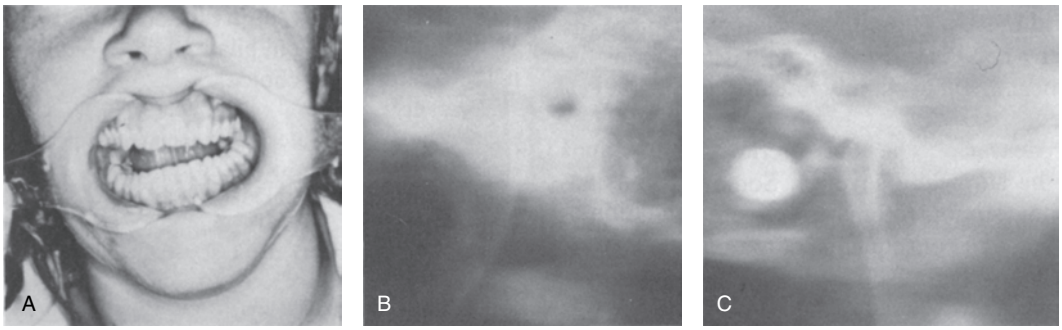

FIGURE 12-44
Condylar hyperplasia. *A:* Asymmetry with unilateral open bite on affected side. *B:* Hyperplastic condyle. *C:* Normal condyle for comparison. (Courtesy of Dr. John Ditmer.)

The face is elongated on the affected side, and restricted opening may or may not be observed. Similarly, deviation toward the affected side is a variable finding. TMJ tomograms disclose a significantly thickened condyle, which may represent a two- or threefold increase in dimension when compared radiographically with the normal condyle.

DIFFERENTIAL DIAGNOSIS

Condylar hyperplasia is easily differentiated from the other disorders included here with restricted or deviant mandibular movement. The facial asymmetry, open bite or cross bite, and radiographic evidence of an enlarged condyle confirm the diagnosis of condylar hyperplasia. Condylar hypoplasia is rare yet must be considered in the differential diagnosis because the normal side may be mistaken for hyperplasia.

TREATMENT

Surgical correction with subcondylar osteotomy is the treatment of choice. The case should be planned with models and radiographs because bilateral procedures may be required to obtain optimal results. Orthodontic consultation should be obtained; most patients require combined orthodontic and surgical therapy.

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TMJ REGION NEOPLASMS

Figure 12-45

Age: Variable
Sex: Variable

CLINICAL FEATURES

Most so-called neoplasms of the TMJ region are, in actuality, represented by hyperplastic or reactive processes including synovial chondromatosis and villonodular tenosynovitis. These reactive lesions involve the joint space or synovium and rarely distort or erode the condylar bone. Nevertheless, true benign and malignant neoplasms, although extremely rare, do arise in the region of the TMJ. The most

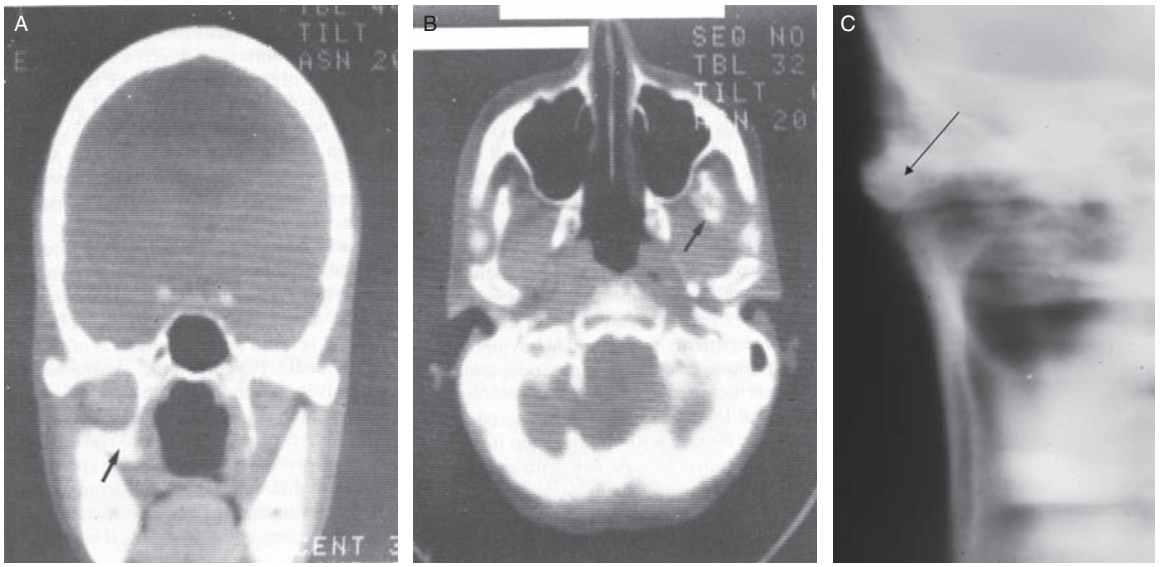

FIGURE 12-45
TMJ neoplasms. A and B: Osteochondroma of coronoid fused to pterygoid plate. C: Osteoma overlying condyle.

common benign tumor is osteochondroma. The lesion arises from the cortex as an exostotic projection with a narrow neck. Actually, most osteochondromas arise from the coronoid process. Limitation of opening with deviation toward the affected side is a common sign; pain usually is not a complaint, although it certainly can be. Radiographs disclose a radiopaque nodular projection emanating from either the condyle or coronoid; the projection is usually oriented medially or superiorly. Other benign neoplasms including osteomas, hemangiomas, and nerve sheath neoplasms may arise within articular tissues and cause restricted opening. Sarcomas are extremely rare, whereas parotid adenocarcinomas are not uncommon. These malignancies may proliferate within the infratemporal space and cause limited opening, cranial nerve deficits, and condylar or coronoid erosion as evidenced radiographically. In these instances, a parapharyngeal mass is usually palpable with deflection of the tonsillar region or soft palate.

DIFFERENTIAL DIAGNOSIS

Submental vertex, TMJ tomograms, CT scans, and/or MRI should be obtained when patients present with unilateral restricted opening and jaw deviation. Soft tissue opacification; irregular foci of resorption, particularly below the articular cortex; and soft tissue swelling over the joint or in the parapharyngeal region should arouse suspicion of neoplasia, and a biopsy should be obtained.

TREATMENT

Treatment is usually surgical, and the extent of surgical removal depends on the microscopic diagnosis.

Additional Reading

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SCLERODERMA

Age: Adults
Sex: Female predilection

CLINICAL FEATURES

Scleroderma or progressive systemic sclerosis is grouped with the collagen diseases: although the etiology is unknown, evidence suggests an immunopathic or autoimmune mechanism. Although the onset is early adult life, many years evolve before severe symptoms develop. Progressive fibrosis of the skin, lungs, and esophagus is the end result with expressionless facies, board-like skin, sclerodactyly, and dysphagia. The CREST syndrome is a variant and is characterized by soft tissue calcinosis, Raynaud's phenomenon, esophageal stricture, sclerodactyly, and telangiectasia of the skin. Microstomia with restricted opening occurs late in the course of the disease. The major cause is fibrosis of the perioral tissues including the buccal mucosa. The fibrous induration is palpable and may restrict opening severely. In addition, some patients manifest TMJ symptoms, usually crepitus, and radiographs occasionally exhibit arthritic erosive changes.

DIFFERENTIAL DIAGNOSIS

Because scleroderma is a systemic disease with multisystem involvement, the diagnosis in a patient with restricted mandibular opening is usually straightforward. Board-hard facial skin, microstomia, widened periodontal ligament spaces, loss of attached gingiva with foci of stripping, and xerostomia are all head and neck manifestations of the disease.

TREATMENT

There is no effective therapy for the restricted opening observed in scleroderma. Plasmapheresis has been beneficial for the other manifestations of the disease.

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ORAL SUBMUCOUS FIBROSIS

Figure 12-46

Age: Adults
Sex: No predilection

CLINICAL FEATURES

Betel nut chewing is a pervasive habit in Malaysia, Pakistan, India, Inodnesia, and the Philipines among adults. Betel, or areca is ground and chewed alone or in combination with tobacco leaves and slaked lime (Pan). Betal nut chewing leads to mucosal changes most prominently seen in the buccal mucosa where white scar bands form causing restricted mouth opening. Diffuse multifocal melanotic pigmentation, which is probably an expansion of physiologic pigmentation in this population, may also

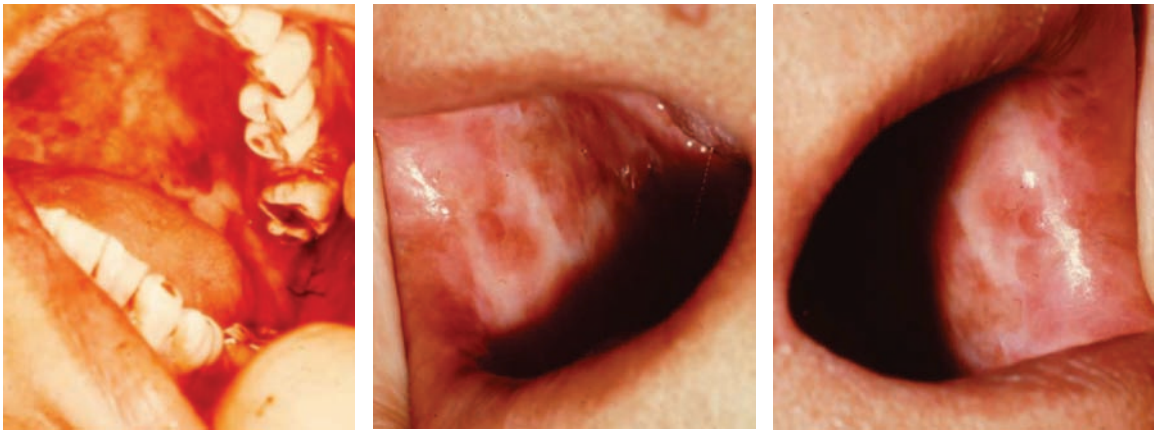

FIGURE 12-46
Restricted opening in betel nut chewer causing oral submucous fibrosis with multifocal pigmentation and white fibrous scar bands.

occur, as may leukoplakias. The latter are precancerous lesions that may become dysplastic and progress to squamous cell carcinoma. It is noteworthy that oral cancer is one of the most prevalent malignancies in India. Tumefactive indurated masses are indicative of carcinoma.

MICROSCOPIC FEATURES

Oral submucous fibrosis is characterized by epithelial atrophy and marked fibrosis of the submucosal connective tissue. When leukoplakia is an accompaniment, keratosis is observed and dysplastic changes may be seen including foci of invasion.

DIFFERENTIAL DIAGNOSIS

Scleroderma and Hecht-Beals-Wilson syndrome show similar clinical appearances.

TREATMENT

Curtailing the habit of betal chewing is the primary preventive strategy. Leukoplakias require close clinical monitoring.

Additional Reading

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TETANUS

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

Tetany represents sustained tonic muscular contraction and is seen in *Clostridium tetani* infection and in hypoparathyroidism secondary to hypocalcemia. Infectious tetanus occurs primarily as a result of accidental injury from fomites on which *C tetani* spores reside. The organism secretes the tetanus toxin that is transported to the CNS and acts on autonomic nerves, end plates, the spinal cord, and the brain, where it binds to gangliosides. Headache is a prodromal sign followed

by generalized muscle rigidity. During the early stages of the disease, masticatory muscle trismus occurs along with facial muscle spasms, producing a distorted demoniacal grin referred to as *risus sardonicus*. This head and neck, early manifestation is sometimes referred to as cephalic tetanus, and seventh nerve paralysis is often an accompaniment. The myotonic spasm becomes progressively generalized with dysphasia, laryngospasm, and autonomic effects including hypertension, cardiac arrythmias, elevated pulse rate, and profuse perspiration. Hyperflexia is also featured. Death may result from asphyxia. In hypoparathyroidism, low serum calcium levels initiate neuromuscular electrolyte disturbances with appearance of convulsions and tetanus. Jaw trismus is rarely seen alone or as the chief presenting sign. Carpopedal spasm is the predominant finding. Latent tetany is evaluated by trapping the preauricular skin over the facial nerve that is followed by facial muscle contraction (Chvostek's sign) and by producing carpal spasm by reducing blood flow to the arm by means of a blood pressure cuff (Trousseau's sign). In addition, lowered-threshold electric excitability of nerves is observed (Erb's sign). In addition to tetany and convulsions, other features of the disease include basal ganglia calcifications, dry skin with alopecia and atrophic nails, and cataracts. The serum calcium level may dip to 5 mg/100 mL with acalciuria; the serum phosphate value is elevated.

DIFFERENTIAL DIAGNOSIS

Unlike most of the other disorders with limited opening, tetanus is a systemic disorder involving numerous other muscle groups. The diagnosis is made on the basis of the aforementioned signs, symptoms, and laboratory findings.

TREATMENT

Infectious tetanus is treated by administration of tetanus antitoxin. Hypoparathyroid tetany is treated by management of the etiology of parathyroid dysfunction and restitution of electrolyte balance by administration of calcium and dihydrotachysterol. The care of these patients should be managed by a physician.

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Generalized Motor Function Disorders

AURICULOTEMPORAL SYNDROME

Age: No predilection
Sex: No predilection

CLINICAL FEATURES

A complication of conservative parotid surgery, the auriculotemporal syndrome may also develop as a consequence of trauma or infection of the parotid or preauricular tissues. The syndrome, also termed *gustatory sweating*, is characterized by preauricular sweating, flushing, and sometimes pain after ingestion of food or visual stimulation by foods that initiate salivation. These symptoms emerge after severance of the auriculotemporal nerve, which, in addition to its sensory function, supplies parasympathetic fibers to the parotid. The fibers regenerate, become misdirected, and follow the course of sympathetic fibers to the skin and sweat glands. Parasympathetic fibers that would

ordinarily induce salivation inadvertently stimulate the preauricular dermal sweat glands and arterioles, causing hydrosis and vasodilation. A similar disorder may accompany facial nerve palsy of surgical or traumatic origin in which parasympathetic fibers are misdirected into the lacrimal gland, causing gustatory lacrimation (crocodile tears).

DIFFERENTIAL DIAGNOSIS

Gustatory sweating, dysgeusia, and crocodile tears have been reported to occur with CNS tumor.

TREATMENT

Control of gustatory sweating may be maintained for up to 3 days by topical application to the affected skin of 1% glycopyrrolate lotion or cream. Intracutaneous injections of botulinum toxin A (Botox, Allergan Inc, USA) are effective.

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JAW-WINKING PHENOMENON

Age: Childhood or congenital
Sex: Slight male predilection

CLINICAL FEATURES

The jaw-winking phenomenon is a misnomer in that this bizarre neuromuscular disorder is characterized by exaggerated opening of the eye on moving of the mandible in a contralateral direction. The involved eye shows ptosis at rest. The pupils of both eyes show normal reflexes without miosis of the ptotic eye. One half of the affected patients manifest exaggerated opening by simply abducting the jaw; the other half show this change only when the jaw is depressed with lateral movement to the opposite direction of the ptotic eye. The etiology and pathogenesis are unknown. It has been theorized that neural fiber crossovers occur between the pterygoid innervation and innervation to the upper lid. Supranuclear involvement has also been suggested as responsible.

DIFFERENTIAL DIAGNOSIS

Unilateral ptosis as seen in the jaw-winking phenomenon may be confused with Horner's syndrome. In the former, miosis with anhydrosis is lacking; conversely, the upper lid fails to open on depression of the mandible in Horner's syndrome.

TREATMENT

Surgical treatment by unilateral levator resection and by the frontalis muscle flap or orbicularis oculi muscle flap results in diminution of the anomaly.

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MOTOR SYSTEM DISEASE

Age: Varies according to subtype
Sex: Male predilection

CLINICAL FEATURES

The motor system diseases include progressive muscular atrophy, which begins in childhood and involves the extremities; amyotrophic lateral sclerosis (ALS); and progressive bulbar palsy. The motor system diseases result from degeneration of the corticospinal and anterior horn cells. The latter two variants begin in adulthood and result in bulbar signs. These two disorders may show a familial pattern or may develop after a neurotropic infection. In ALS, patients show ambulatory difficulties and weakness of the oropharyngeal musculature evidenced by difficulty with swallowing and speech. In progressive bulbar palsy, deglutition and articulation defects are present in conjunction with atrophy of masticatory and facial muscles. Fasciculation of the tongue is often present in both forms with bulbar manifestations. There are 16 distinct forms of spinal motor atrophy, 14 of which manifest mutations in genes that encode proteins involved in transcriptional regulation, RNA processing, and cytoskeletal dynamics: TRPV4, ATP7A, VRK1, and HSPB3. Genetic testing is now available for many of these mutations.

DIFFERENTIAL DIAGNOSIS

Difficulty with swallowing and articulation, cardinal signs of bulbar degenerative motor system disorders, may also be seen in organic disease such as cancer of the larynx or base of the tongue. For this reason, a thorough physical examination is required when these symptoms emerge. Bulbar lesions subsequent to cerebrovascular accident may cause similar signs and symptoms.

TREATMENT

No known treatment exists. The motor system diseases are progressive, eventually resulting in death.

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MULTIPLE SCLEROSIS

Age: Young adults
Sex: Slight female predilection

CLINICAL FEATURES

Multiple sclerosis is a demyelinating disease, probably of either viral or autoimmune origin, that involves the CNS without demyelinization of peripheral nerves. The disease is chronic with periods of remission and exacerbation. A variety of neurologic signs and symptoms are observed, depending on anatomic location and severity of lesions. These signs and symptoms can be extremely diverse; the more common include spasticity, hyper-reflexia, Babinski's sign, absent abdominal reflexes, intention tremor, nystagmus, sensory deficits, paresthesias, muscle weakness, ocular disturbance, urinary disturbance, and ataxia. Facially, the more prevalent or noteworthy manifestations are ocular (diplopia, blurring of vision, visual field defects, and scotoma), sensory (trigeminal paresthesia or neuralgia), and motor (seventh nerve pare-

sis and dysarthria). Cognitive impairments include memory, speed processing, executive function, attention, and concentration domains. The more significant laboratory abnormalities include elevated cerebrospinal fluid levels of immunoglobulin G and white cells. Cortical-evoked responses from visual, auditory, and sensorimotor stimulation have been shown to be of value in early diagnosis. CT scans often disclose ventricular enlargement, cortical atrophy, and periventricular plaques.

DIFFERENTIAL DIAGNOSIS

Myelinoclastic infectious diseases are easily confused with multiple sclerosis because the signs and symptoms can be identical. Neurologic lesions in other diseases including lupus erythematosus, polyarteritis nodosa, vascular malformations and gliomas of the brain stem, syringomyelia, and lymphoma may exhibit features similar to those enumerated for multiple sclerosis. Patients with unexplained facial weakness, paresthesia, or trigeminal neuralgia should be evaluated for the disease.

TREATMENT

Referral to a neurologist is recommended. The disease may be quite mild or may remain in long-term remission. Alternatively, in some instances, it is a progressive disease that leaves the patient severely disabled.

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MUSCULAR DYSTROPHIES

Age: Childhood onset
Sex: Male predilection

CLINICAL FEATURES

Muscular dystrophy of Duchenne is a generalized progressive disease of muscle with an X-linked recessive mode of inheritance, occurring in males. A restricted form, fascioscapulohumeral dystrophy, shows no sex predilection, and the disorder is restricted to muscles of the face, neck, and shoulder. The defective gene has been localized to chromosome 4. In all forms of muscular dystrophy, the primary defect lies in the muscle fiber; neural function and reflexes are not affected. In the generalized form, which is more common, early childhood onset is characterized by inability to ambulate, with pseudohypertrophy of the limb muscles. The increase in muscle bulk is the result of fatty infiltration so that weakness and poor function are encountered. The muscles eventually become atrophic. Masticatory, facial, and strap muscles are involved late in the course of the disease, with difficulty chewing, swallowing, and articulating. Serum creatinine phosphokinase levels are elevated early in the course of the disease. Fascioscapulohumeral dystrophy spares the lower limbs and does not show pseudohypertrophic enlargement. Onset may be later in life and is characterized by profound weakness of the arms, inability to close the eyes, drooping of the facies, and inability to purse the lips (which are protuberant). Cardiac failure is a common complication. The various forms of muscular dystrophy involve the complex dystrophin-associated glycoproteins of the extracellular matrix: CMD with merosin deficiency (CMD1A), collagen VI-related CMDs (Ullrich CMD and Bethlem myopathy), CMDs with abnormal glycosylation of α-dystroglycan (Fukuyama CMD, muscle-eye-brain disease, Walker-Warburg syndrome, CMD1C, CMD1D), and the much

rarer CMD with integrin deficiency. Yet other forms of CMDs are not related to the dystrophin/glycoproteins/extracellular matrix complex (rigid spine syndrome, CMD1B, CMD with lamin A/C deficiency)

DIFFERENTIAL DIAGNOSIS

The two forms of muscular dystrophy may be differentiated on the basis of age and distribution of muscle involvement. Both may show myopathic facies, which occur in the myotonias, and myasthenia gravis. A muscle biopsy may be helpful in determining whether the patient suffers from muscular dystrophy. Muscle fibers show variation in size with infiltration of adipose tissue, and enzyme histochemical stains are useful.

TREATMENT

No treatment is presently effective. In Duchenne's muscular dystrophy, survival beyond the second decade is rare. Fascioscapulohumeral muscular dystrophy is compatible with life; however, many patients develop cardiac failure.

Additional Reading

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MYOTONIAS

Age: Children and young adults
Sex: No predilection

CLINICAL FEATURES

The myotonias are characterized by failure of muscle relaxation after contraction. Two major forms exist: dystrophic and congenital myotonias. Myotonic contractions may also be acquired after trismus, with spread of infection to muscle. This form is most common, and in the head and neck area, myositis of the masticatory muscles generally develops as a complication of odontogenic infection or pericoronitis. Myotonia congenita is the result of mutations in the *CLCN1* gene that controls muscle membrane hyperexcitability caused by reduced sarcolemmal chloride conductance. The disorder may be transmitted as either an autosomal dominant or recessive trait. Dystrophic myotonia develops in late childhood as an autosomal dominant trait. In addition to sustained contractions after voluntary neuromuscular activity, atrophy of the masticatory and strap muscles occurs to yield the so-called myopathic facies. Masticatory weakness, malocclusion, and altered craniofacial morphology have been reported among patients with myotonic dystrophy. Testicular atrophy is often present. Congenital myotonia, a familial disorder, commences early in life and affects virtually all skeletal muscles. The myotonic contractions are severe but painless. The affected individuals manifest significant generalized muscular hypertrophy so that they appear to be muscle bound.

DIFFERENTIAL DIAGNOSIS

Dystrophic myotonia may resemble late muscular dystrophy and myasthenia gravis, as muscular atrophy with a myopathic facies may be seen in all three of these muscular disorders. Characteristic myotonic contractions are seen only in myotonia. The muscle hypertrophy of congenital myotonia is also accompanied by myotonic contraction, aiding in differentiating this disorder from pseudohypertrophic muscular dystrophy.

TREATMENT

No treatment is available for the familial myotonias. The dystrophic form is ultimately

fatal, whereas the congenital form carries a favorable prognosis. Acquired myotonia may be treated by removing the source of infection and employing antibiotics.

Additional Reading

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CONGENITAL FACIAL DIPLEGIA

Age: Congenital
Sex: No predilection

CLINICAL FEATURES

The Möbius syndrome is a nonfamilial congenital primary myopathy of the facial muscles with secondary degeneration of the abducens and facial nerves. Alternatively, in utero, necrosis of brain stem nuclei has been reported and may result from an episode of anoxia. The paralysis is bilateral with expressionless facies and inability to close the eyes. The muscles of mastication may also be affected, with difficulty in chewing and swallowing. Drooling is often uncontrollable. Patients also show a variety of other congenital defects including deafness, epilepsy, and club foot. MRI reveals brainstem hypoplasia with straightening of the fourth ventricle floor, a finding indicative of an abscent facial colliculus.

DIFFERENTIAL DIAGNOSIS

Congenital facial diplegia shows myopathic facies seen in other myopathies; however, onset at birth and restriction to the facial musculature allow for differentiation from these other disorders.

TREATMENT

No treatment is effective. The disease is not fatal.

Additional Reading

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HEMIFACIAL ATROPHY

Age: Teenagers
Sex: Female predilection

CLINICAL FEATURES

Unilateral progressive atrophy of the face, known as Romberg's syndrome, is an uncommon disorder of unknown origin. It begins during the second decade with slowly progressive atrophy of the skin, muscle, and often even the maxilla and mandible on one side of the face. The disease progresses for 3 or 4 years and ultimately becomes static. The teeth on the affected side may be smaller than normal, and eruption may be somewhat retarded. Contralateral epilepsy and trigeminal neuralgia may accompany the atrophic changes. The condition may be the result of a trophic malformation of the cervical sympathetic nervous system secondary to trauma, viral infections, heredity, endocrine disturbances, and autoimmunity, among others

DIFFERENTIAL DIAGNOSIS

The facial asymmetry with atrophy on one side may be confused with hemifacial hyper-

trophy. Close observation shows that the larger side of the face is normal, the smaller side is atrophic. Unilateral TMJ ankylosis may show features similar to Romberg's syndrome; however, in the former, only the mandible is atrophic, whereas in the latter, the entire hemiface is involved.

TREATMENT

Plastic surgery may be performed once the atrophic process has stabilized.

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MYASTHENIA GRAVIS

Age: Middle-aged adults
Sex: Female predilection

CLINICAL FEATURES

Myasthenia gravis is characterized by generalized muscular weakness involving only voluntary muscle, the heart being spared. Often the facial and masticatory muscles are the first to show fatigue after limited movement. As the disease progresses, ptosis with an expressionless myopathic facies develops. In advanced cases, the jaw and head droop; eventually, the respiratory muscles become fatigued. The cause for this condition is unknown but has been linked to immunopathologic mechanisms operating at the level of the neuromuscular junction with interference in the release-binding of acetylcholine. Thymic hyperplasia or thymoma is found in most patients with myasthenia gravis. Antiacetylcholine receptor antibody testing and single fiber electromyography are the more reliable diagnostic tests.

DIFFERENTIAL DIAGNOSIS

The myopathic facies with generalized muscular weakness is seen in muscular dystrophy, myotonias, and Möbius syndrome. The onset during midlife, predilection for females, lack of myotonic contraction, and lack of muscle hypertrophy favor a diagnosis of myasthenia. A muscle biopsy may be helpful in that perivascular lymphoid aggregates appear between muscle bundles in this disorder, but are not featured in the aforementioned disorders. A classic diagnostic finding is the ability of intramuscular injection of physostigmine to restore normal functions.

TREATMENT

Myasthenia gravis is treated with anticholinesterases such as neostigmine or related drugs and should be managed by an internist or neurologist.

Additional Reading

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Appendices

Appendix I. Classification of Certain Oral Cysts, Reactive Proliferations, and Neoplasms

I. ODONTOGENIC CYSTS

Dental lamina cyst
Gingival cyst
Primordial cyst
Lateral periodontal cyst
Dentigerous (follicular) cyst
Eruption cyst
Apical periodontal cyst
Calcifying cystic odontogenic tumor
Orthokeratotic odontogenic cyst
Odontogenic keratocyst (keratocystic odontogenic tumor)
Sialoodontogenic cyst

II. DEVELOPMENTAL AND NONODONTOGENIC CYSTS

A. Intraosseous Cysts
Incisive canal (nasopalatine) cyst
Median mandibular cyst
Surgical ciliated cyst of the maxilla
B. Soft Tissue Cysts
Epidermoid cyst
Dermoid cyst
Lymphoepithelial (branchial cleft) cyst
Benign cystic lymph node
Lingual gastric cyst (enterocystoma)
Thyroglossal duct cyst
Nasoalveolar (Kledstadt) cyst
Cyst of incisive papilla
True mucous cyst (sialocyst)
Mucous retention cyst of the sinus
C. Pseudocysts
Mucous retention phenomenon (mucocele)
Ranula (mucocele)
Traumatic (hemorrhagic) cyst
Aneurysmal bone cyst

III. BENIGN ODONTOGENIC NEOPLASMS AND HAMARTOMAS

A. Epithelial Group
Ameloblastoma
Invasive type
Unicystic type
Desmoplastic type
Calcifying epithelial odontogenic tumor
Odontogenic adenomatoid tumor
Epithelial odontogenic hamartoma
Squamous odontogenic tumor
B. Mixed Group
Ameloblastic fibroma
Ameloblastic fibrodentinoma
Ameloblastic fibro-odontoma

Odontoma
Odontoameloblastoma

C. Mesenchymal Group
Odontogenic fibroma
Odontogenic myxoma
Periapical cemental dysplasia (cementoma)
Benign cementoblastoma
Cementifying fibroma
Granular cell odontogenic tumor

D. Malignant Odontogenic Neoplasms
Malignant ameloblastoma
Ameloblastic carcinoma
Clear cell odontogenic tumor (carcinoma)
Intraosseous squamous cell carcinoma
Ameloblastic fibrosarcoma

IV. SALIVARY NEOPLASMS

A. Benign
Pleomorphic adenoma (mixed tumor)
Myoepithelioma
Monomorphic adenoma
Canalicular (basal cell) adenoma
Papillary cystadenoma lymphomatosum
Sialadenoma papilliferum
Oxyphilic adenoma (oncocytoma)
Intraductal papilloma
Ductal inverted papilloma
Sebaceous lymphadenoma
Glycogen-rich adenoma
Papillary cystadenoma
Sclerosing polycystic adenosis

B. Malignant
Adenoid cystic carcinoma (cylindroma)
Adenosquamous carcinoma
Mucoepidermoid carcinoma
Polymorphous low-grade adenocarcinoma
Malignant mixed tumor
Carcinoma ex pleomorphic adenoma
Ductal epidermoid carcinoma
Undifferentiated carcinoma
Small cell type
Large cell type
Malignant lymphoepithelial lesion
Acinic cell carcinoma
Epithelial-myoepithelial carcinoma of intercalated duct
Salivary duct carcinoma
Sialoblastoma
Mucinous adenocarcinoma
Papillary cystadenocarcinoma
Adenocarcinoma (not otherwise specified)

V. ORAL EPITHELIAL NEOPLASMS

A. Benign
Papilloma
Verruca vulgaris
Condyloma acuminatum
Keratoacanthoma

B. Malignant
Squamous cell carcinoma
Papillary exophytic squamous cell carcinoma
Verrucous carcinoma
Adenoacanthoma (pseudoglandular squamous cell carcinoma)
Spindle cell (sarcomatoid) carcinoma

VI. NEUROECTODERMAL HAMARTOMAS AND NEOPLASMS

Ephilis
Nevocellular nevi
Melanocytic nevi (blue nevus)
Spindle cells (Spitz) nevus
Melanotic neuroectodermal tumor of infancy
Hutchinson's freckle (superficial spreading melanoma)
Malignant melanoma

VII. MESENCHYMAL NEOPLASMS OF SOFT TISSUE

A. Benign
- Fibroma
- Giant cell fibroma
- Collagenoma
- Lipoma
- Leiomyoma
- Rhabdomyoma
- Granular cell tumor
- Neurofibroma
- Neurilemmoma (schwannoma)
- Palisaded encapsulated neuroma
- Solitary fibrous tumor
- Osseous and cartilaginous choristoma
- Benign fibrous histiocytoma
- Hemangioma
- Lymphangioma and cystic hygroma

B. Aggressive
- Hemangioendothelioma
- Hemangiopericytoma
- Myofibroma/myofibromatosis

C. Malignant
- Fibrosarcoma
- Liposarcoma
- Leiomyosarcoma
- Rhabdomyosarcoma
- Alveolar soft part sarcoma
- Liposarcoma
- Neurogenic sarcoma
- Malignant fibrous histiocytoma
- Synovial sarcoma
- Angiosarcoma
- Kaposi's sarcoma
- Malignant lymphoma (Hodgkin's and non-Hodgkin's types)

VIII. REACTIVE PROLIFERATIONS

- Pyogenic granuloma
- Traumatic fibroma
- Inflammatory fibrous hyperplasia (epulis fissuratum)
- Papillomatosis
- Peripheral ossifying fibroma
- Peripheral giant cell granuloma
- Nodular fasciitis
- Pseudosarcomatous fasciitis
- Myositis ossificans
- Proliferative myositis

IX. CENTRAL NONODONTOGENIC BONE TUMORS OF THE JAWS

A. Benign
- Desmoplastic fibroma (fibromatosis)
- Hemangioma
- Arteriovenous malformation
- Neurofibroma
- Neurilemmoma
- Leiomyoma
- Central ossifying fibroma
- Osteoma

B. Malignant
- Osteogenic sarcoma
- Chondrosarcoma
- Fibrosarcoma
- Neurogenic sarcoma
- Ewing's sarcoma
- Angiosarcoma
- Non-Hodgkin's lymphoma
- Burkitt's lymphoma
- Multiple myeloma

Appendix II. Classification of Benign Fibro-Osseous Lesions

I. GIANT CELL GROUP

Central giant cell granuloma
Hyperparathyroid brown tumor
Aneurysmal bone cyst
Cherubism (familial fibrous dysplasia)

II. NONGIANT CELL GROUP (PURE FIBRO-OSSEOUS)

Fibrous dysplasia
Osteitis deformans
Ossifying and cementifying fibromas
Juvenile aggressive ossifying fibroma (trabecular and psammomatoid)
Gigantiform cementoma
Periapical cemental dysplasia (cementoma)
Focal sclerosing osteomyelitis
Diffuse sclerosing osteomyelitis
Florid osseous dysplasia
Garre's proliferative periostitis

Appendix III. Oral Lesions Associated With HIV Infection

I. LESIONS ASSOCIATED WITH AIDS

Kaposi's sarcoma—red/purple macules or tumefactions
Non-Hodgkin's lymphoma—ulcerated masses
Histoplasmosis—granulomatous ulcerations
Herpes simplex lesions over 1 month duration—oral or labial vesiculoulcerative lesions

II. OTHER LESIONS ASSOCIATED WITH AIDS OR PRE-AIDS HIV-SEROPOSITIVE SUBJECTS

Viral
- Varicella zoster—shingles of the trigeminal pathways
- Cytomegalovirus—aphthaeform ulcers
- Epstein-Barr virus—oral hairy leukoplakia
- Human papillomavirus—condylomatous papillary lesions, Heck disease-like papules

Fungal
- Candidiasis—pseudomembranous, erythematous, hyperplastic, papillary, angular cheilitis
- Cryptococcosis—granulomatous ulcers, palatal perforation

Bacterial
- Mycobacterium avium intracellular—granulomatous mass or ulcer
- HIV gingivitis—erythematous band of marginal gingiva
- HIV periodontitis—focal painful lesions with cementum exposure
- HIV necrotizing stomatitis—progression of HIV periodontitis to adjacent tissues

Unknown etiology
- HIV polycystic disease of salivary glands
- Aphthous-like ulcerations

Appendix IV. Clinical Laboratory Parameters

The following diseases, which are associated with elevated or depressed values, are by no means all inclusive. Rather, they represent the more common disease states showing alterations in laboratory values.

I. HEMOGRAM

A. Red Blood Cell Count, Hemoglobin, and Hematocrit

1. *Elevated*
   - Fluid loss
   - Polycythemia vera
   - Secondary polycythemia

2. *Depressed*
   - Iron deficiency anemia
   - Pernicious anemia
   - Malaria
   - Hemorrhage
   - Thalassemia
   - Sickle-cell anemia
   - Hemolytic anemias
   - Leukemia
   - Metastatic cancer
   - Osteopetrosis
   - Multiple myeloma
   - Pancytopenia
   - Erythroblastosis fetalis
   - Renal disease

B. White Blood Cell Count

1. *Elevated*
   - Infections
   - Leukemia

2. *Depressed*
   - Certain viral infections
   - Leukemia (leukopenic phase)
   - Agranulocytosis
   - Cyclic neutropenia
   - Hemorrhage
   - Pancytopenia
   - Typhoid fever

C. Differential White Count

1. *Neutrophilic Leukocytosis*
   a. Pyogenic infections
   b. Myelogenous leukemia
2. *Lymphocytic Leukocytosis*
   a. Viral infections
   b. Typhoid fever
   c. Lymphocytic leukemia
   d. Infectious mononucleosis
3. *Eosinophilic Leukocytosis*
   a. Allergy
   b. Parasitic infections, particularly helminths

4. *Neutrophilic Leukopenia*
   a. Agranulocytosis
   b. Cyclic neutropenia
   c. Leukemia

D. Thrombocytes
1. *Depressed Count*
   Thrombocytopenic purpura
   Secondary thrombocytopenia
   Pancytopenia
   Leukemia
   Metastatic cancer
   Multiple myeloma
   Consumptive coagulopathy (DIC)
   Postinfections
2. *Delayed Aggregation*
   Thrombocytopathic purpura
   von Willebrand's disease
   Salicylates and other drugs

II. COAGULATION PANEL

A. Prothrombin Time Prolonged
Alcoholic cirrhosis
Biliary cirrhosis
Hepatitis
Idiopathic steatorrhea
Hypovitaminosis K
Coumadin therapy
Afibrinogenemia
Hypoprothrombinemia

B. Partial Thromboplastin Time Prolonged
Hemophilia
Christmas disease
von Willebrand's disease
Hageman deficiency
All disorders manifesting prolonged prothrombin time

C. Fibrin Split Products
Disseminated intravascular coagulation

III. SEROLOGY (ELEVATED OR POSITIVE TESTS)

A. VDRL, TPI, FTA—Syphilis
B. Monospot, Heterophil Antibody—Infectious Mononucleosis
C. Antistreptolysin-O—Scarlet Fever, Rheumatic Fever, Erysipelas, Streptococcal Sore Throat

D. RA Factor—Rheumatoid Arthritis
E. Antineutrophil cytoplasmic Antibody (C-ANCA, PR-3 ANCA)—Wegener's granulomatosis
F. Antinuclear Antibodies and Anti-DNA Antibodies—Lupus Erythematosus, Miscellaneous Collagen Diseases
G. Antimitotic Spindle Antibody—Scleroderma
H. Coombs' Test—Erythroblastosis Fetalis and Other Immune Hemolytic Anemias
I. HBS-AB—Immunity to Hepatitis B
J. HBS-AG, Hepatitis Core AG—Active or Carrier Status for Hepatitis B

IV. IMMUNOFLUORESCENCE

A. Antibasal Lamina Antibodies (Smooth)—Bullous Pemphigoid, Benign Mucous Membrane Pemphigoid
B. Antibasal Lamina Antibodies (Granular)—Lupus Erythematosus
C. Anti-Intercellular Cement Antibodies—Pemphigus Vulgaris
D. Antibasal Lamina Fibrinogen—Lichen Planus
E. Submucosal Papillae IgA Antibodies—Dermatitis Herpetiformis
F. Antiductal Salivary Antibodies—Sjögren's Syndrome
G. Speckled Antinuclear Epithelial Antibodies- Chronic Ulcerative Stomatitis

V. COMMONLY EMPLOYED IMMUNOHISTOCHEMICAL MARKERS IN HISTOPATHOLOGY

A. Epithelium: AE1-AE3 cytokeratins, specific cytokeratins, EMA (epithelial membrane antigen)
B. Connective tissues: Vimentin
C. Leukocytes: CD3 T cells, CD20 B cells, CD45 common leukocyte antigen, CD56 natural killer cells
D. Myeloid cells: myeloperoxidase
E. Cell division markers: PCNA, Ki67/MIB1
F. Nerve sheath and granular cell tumors: S-100
G. Vascular walls: Factor VIII, CD34, smooth muscle actin
F. Melanocytic tumors: S-100, HMB45
G. Langerhans cells: S-100, CD1a
H. Muscle: desmin, SMA (smooth muscle actin)
I. Neuroendocrine tumors: synaptophysin, chromogranin
J. Histiocytes: CD68
K. Specific microorganisms: HPV, HSV 1 and 2, CMV, EBV

VI. CLINICAL LABORATORY

Test	Elevated Values	Depressed Values
A. Glucose 70–110 mg/100 ml	Diabetes mellitus Acute pancreatitis Cushing's syndrome Pheochromocytoma Acromegaly Anabolic hormones Hemochromatosis	Insulinoma Addison's disease Liver disease Early diabetes Glycogenosis Renal glycosuria
B. Total Bilirubin 0.1–1.0 mg/100 ml	Biliary obstruction Liver diseases Hemolytic anemias Hepatitis Postextravasation Dubin-Johnson syndrome Gilbert's disease Crigler-Najar syndrome Rotor's syndrome Malnutrition	
C. Cholesterol 150–300 mg/100 ml	Atherosclerosis Diabetes mellitus Nephrotic syndrome Hypothyroidism Hyperlipoproteinemia Gout Myeloma Biliary obstruction	Liver disease Malnutrition Anemia
D. Uric Acid 2.5–8.0 mg/100 ml	Gout Malignancy Infectious mononucleosis Renal disease Tissue necrosis Anemias	Cirrhosis Renal tubular disease Various drugs Wilson's disease
E. Creatinine 0.05–1.5 mg/100 ml Renal disease	Muscle necrosis	
F. Total Protein 6–8 g/100 ml	Liver disease Collagen disease Chronic infection Myeloma Cryoglobulinemia	Renal disease Debilitating disease Malnutrition Burns Hypogammaglobulinemia

G. Albumin 3.5–5 g/100 ml			Liver disease Nephrotic syndrome Malnutrition Burns
H. Calcium 8.5–10.5 mg/100 ml	Hyperparathyroidism Milk-alkali syndrome Malignancy Sarcoidosis Hypothyroidism Addison's disease Hypophosphatasia		Renal disease Malnutrition Acute pancreatitis Hypoparathyroidism Vitamin D refractory rickets
I. Phosphorus 2.5–4.5 mg/100 ml Renal disease Hypoparathyroidism Milk-alkali syndrome Sarcoidosis Addison's disease	Malignancy in bone Malnutrition Osteomalacia Renal tubular disease Vitamin D refractory rickets Hypophosphatasia		Hyperparathyroidism
J. Alkaline Phosphatase 1.5–5 Bodansky U/ml 5–10 King-Armstrong U/ml	Bone metastasis Hepatobiliary disease Renal disease Paget's disease Bone fractures Fibrous dysplasia Ulcerative colitis Hyperthyroidism Pancreatitis Sarcoidosis Rickets Amyloidosis		Hypophosphatasia Malnutrition
K. SGOT 10–40 U/ml	Acute myocardial infarction Liver disease Skeletal muscle disease Congestive heart failure Renal infarction Pulmonary infarction Malignancy Burns Certain anemias Eclampsia Trauma		

Test	Elevated Values	Depressed Values
L. LDH 100–225 U/ml	Myocardial infarction Liver disease Skeletal muscle disease Renal infarction Pulmonary infarction Cerebral vascular accident Collagen vascular diseases Acute pancreatitis Trauma	

Appendix V. Prescriptions Useful in the Management of Oral Diseases

I. Antibiotics endocarditis prophylaxis is recommended only for high risk of adverse outcomes from endocarditis to include: prosthetic cardiac valve, previous endocarditis, select cyanotic congenital heart defects that include: 1. unrepaired cyanotic heart disease including those with palliative shunts and conduits, 2. completely repaired congenital heart disease with prosthetic material or device, whether placed by surgery or catheter intervention, during the first six months after the procedure, 3. repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization). Cardiac transplant recipients with valvular disease. In the above conditions, prophylactic coverage is recommended for periodontal, endodontic and mucosal perforation (surgery).

Antibiotic Prophylactic Regimens (1 hour before procedure)

Situation	Agent	Adults	Children
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral	Ampicillin	2 g IV or IM	50 mg/kg IV or IM
	or		
	Cefazoline	1 g IV or IM	50 mg/kg IV or IM
	Or Ceftriazone		
Allergic to Penicillin	Cephalexin*	2 g	50 mg/kg
	or		
	Clindamycin	600 mg	20 mg/kg
	or		
	Axithromycin	500 mg	15 mg/kg
Allergic to Penicillin	Clindamycin	600 mg IM or IV	20 mg/kg IM or IV
Unable to take oral	or		
	Cefazolin	1 g IM or IV	50 mg/kg IM or IV

II. ANTIBIOTICS (INFECTIONS)

Penicillin VK 500 mg
Dsp #40
Sig: 1 cap every 6 hours
Use: Odontogenic infections (i.e., abscess cellulitis), acute necrotizing ulcerative gingivitis with fever, oral gonorrhea

Amoxycillin 500mg/Clavulanic acid 125 mg
Dsp #30
Sig: 1 or each three times per day with snack or meal.
Use: Odontogenic infections

Erythromycin stearate 500 mg
Dsp #40
Sig: 1 cap every 6 hours
Use: Odontogenic infections in the patient allergic to penicillin

Ciprofloxacin 500 mg
Dsp #20
Sig: one tablet twice a day
Use: Odontogenic infections, cellulitis
Caution: may cause tendonitis and rupture several months after use, do not use if taking steroids

Dicloxacillin 150 mg
Dsp #40
Sig: 2 caps every 6 hours
Use: Possible drug of choice when penicillin is ineffective in 48 hours. Effective for staphylococci or penicillinase-secreting organisms.

Clindamycin 150 mg
Dsp #40
Sig: 2 caps every 6 hours
Use: Most effective against bacteroides infections.
Caution: May cause clostridia pseudomembranous ulcerative colitis.

Cephalexin 250 mg
Dsp #40
Sig: 1 cap every 6 hours
Use: Possible drug of choice when penicillin is ineffective in 48 hours. Often ineffective for penicillinase-secreting organisms.

Tetracycline oral suspension 250 mg/tsp
Dsp 4 oz
Sig: 1 tsp 4 times daily, rinse orally for 5 minutes and swallow
Use: Minor and major aphthous stomatitis

III. ANTIFUNGALS

Nystatin ointment
Dsp 30 g
Sig: Apply to affected area 4 times daily
Use: Denture-related candidiasis, angular cheilitis

Nystatin pastilles 200,000 U
Dsp #80
Sig: 2 tabs every 6 hours orally as lozenge
Use: Oral candidiasis
Clotrimazole troches 10 mg
Dsp #40
Sig: 1 tablet every 6 hours orally as lozenge
Use: Oral candidiasis
Ketoconazole (Nizoral) 200 mg
Dsp #10
Sig: 1 tab per day
Use: Oral candidiasis
Fluconazole 100 mg
Dsp #11
Sig: 2 tabs initial dose, 1 tab per day thereafter
Use: Oral candidiasis in HIV seropositive patients

IV. ANTIHISTAMINES AND TOPICAL ANESTHETICS

Diphenhydramine HCl (Benadryl) 50 mg
Dsp #20
Sig: 1 cap 3 times daily
Use: Allergic stomatitis of the immediate type, erythema multiforme
Promethazine (Phenergan) 12.5 mg
Dsp #20
Sig: 1 cap 3 times daily
Use: Allergic stomatitis of the immediate type, erythema multiforme
Diphenhydramine HCl (Benadryl) elixir 12.5 mg/tsp 50:50 with Kaopectate
Dsp 6 oz
Sig: 2 tsp as oral rinse 3 times daily
Use: Palliation of painful vesiculoulcerative lesions
Promethazine (Phenergan) syrup 6.25 mg/tsp 50:50 with Kaopectate
Dsp 6 oz
Sig: 2 tsp as oral rinse 3 times daily
Use: Palliation of painful vesiculoulcerative lesions
2% Xylocaine viscous
Dsp 4 oz
Sig: 3 drops with fingertip to oral sores p.r.n. for pain
Use: Palliation of painful vesiculoulcerative lesions
Caution: Instruct patient not to swallow medication to avoid anesthetizing gag reflex

V. STEROID AND OTHER ANTI-INFLAMMATORY PREPARATIONS

0.1% Triamcinolone in Orabase
Dsp 5-g tube

Sig: Apply to oral sores 4 times daily
Use: Erosive lichen planus, bullous pemphigoid, oral lesions of pemphigus vulgaris, contact (delayed) allergic stomatitis

0.05% fluocinonide (Lidex) ointment
Dsp 30 g
Sig: Apply to oral lesions 6 times daily
Use: Erosive lichen planus, bullous pemphigoid, pemphigus vulgaris, contact (delayed) allergic stomatitis

0.05% Clobetasol proprionate ointment (Temovate)
Dsp 30 g
Sig: Apply to oral lesions 6 times daily
Use: Erosive lichen planus, bullous pemphigoid, pemphigus vulgaris, contact (delayed) allergic stomatitis

Dexamethasone elixir 0.5 mg per 5 ml (Decadron)
Dsp 8 oz
Sig: 1–2 tsp as an oral rinse, expectorate.
Use: Minor aphthous ulcers, other erosive stomatitides

Dapsone 25 mg
Dsp #30
Sig: 1 tab daily for 3 days, then 2 tabs daily for 3 days, then 3 tabs daily for 3 days, followed by 2 tabs twice daily for 3 days
Use: Benign mucous membrane pemphigoid. Maintenance dose after accelerated schedule is between 100 and 150 mg daily.
Caution: Dapsone may cause hemolysis; red cell counts, hemoglobin, and hematocrit should be obtained regularly.

Prednisone 5 mg or dexamethasone 0.75 mg
Dsp #40
Sig: 1 tab every 6 hours for 7 days, followed by 1 tab every 12 hours for 4 days, followed by 1/2 tab every 12 hours for 3 days
Use: Severe erosive lichen planus, major aphthous stomatitis, benign mucous membrane pemphigoid, erythema multiforme
Caution: Do not prescribe for patients with existing infectious disease or diabetes mellitus

Methylprednisolone Dosepak
Dsp 2 packs
Sig: Take as directed, doubling the dose (i.e.: using the two packs simultaneously
Use: Severe erosive lichen planus, major aphthous stomatitis, benign mucous membrane pemphigoid, erythema multiforme
Caution: Do not prescribe for patients with existing infectious disease or diabetes mellitus

Tacrolimus 0.1%
Dsp 30 g
Sig: Apply to mouth sores four times daily
Use: Erosive lichen planus, major aphthous stomatitis, benign mucous membrane pemphigoid, erythema multiforme

Cyclosporin oral solution. 100mg/1ml
Dsp: 50 ml

Sig: ½ tsp, coat lining of mouth four times daily
Use: Erosive lichen planus, major aphthous stomatitis, benign mucous membrane pemphigoid, erythema multiforme

VI. ANTIVIRAL AGENTS

5% Acyclovir ointment
Dsp 15 g
Sig: Apply to lip sores 6 times daily
Use: Herpes labialis. Recommend application during onset of prodromal paresthesia if possible; otherwise apply directly over vesicles.
Acyclovir 200 mg
Dsp #120
Sig: 1 cap 4 times daily
Use: Prevention of recurrent herpes simplex and herpes-related erythema multiforme
Famciclovir 1 g
Dsp #60
Sig: 1g twice a day
Use: Prevention of recurrent herpes simplex and herpes-related erythema multiforme

VII. MUSCLE RELAXANTS

Chlorzoxazone (Paraflex) 250 mg
Dsp #100
Sig: 2 tabs every 4 hours
Use: Myogenic facial pain, tension headache
Chlorzoxazone and acetominophen (Parafon Forte) 500 mg
Dsp #100
Sig: 2 tabs every 4 hours
Use: Myogenic facial pain, tension headache
Baclofen (Lioresal) 10 mg
Dsp #60
Sig: 1/2 tab 3 times daily for 3 days, then 1 tab 3 times daily for 3 days, then 1 1/2 tab 3 times daily
Use: Myogenic facial pain, tension headache

VIII. ANXIOLYTICS

Diazepam (Valium) 5 mg
Dsp #20
Sig: 1–2 tabs daily
Use: Tension reduction prior to appointments, myogenic facial pain
Lorazepam (Ativan) 1 mg

Dsp #20
Sig: 1 tab daily
Use: Tension reduction prior to appointments, myogenic facial pain

IX. ANTIDEPRESSANTS

Doxepin HCl (Sinequan) 25 mg
Dsp #45
Sig: 1 cap each evening for 5 days, then 2 caps each evening for 5 days, then 4 caps each evening for 7 days
Use: Atypical facial pain of psychogenic origin and burning mouth syndrome, most effective in depressed patients with anxiety. Dexamethasone suppression test advisable initially. Maintenance dose varies from 100–200 mg daily
Trazodone HCl (Desyrel) 50 mg
Dsp #70
Sig: 2 tabs each evening for 5 days, then 3 tabs each evening for 5 days, then 3 tabs 3 times daily for 7 days
Use: Atypical facial pain of psychogenic origin and burning mouth syndrome, most effective in depressed patients. Dexamethasone suppression test advisable initially. Maintenance dose is 250–350 mg/day in divided doses.
Fluoxetine HCl 20 mg (Prozac)
Dsp #30
Sig: 1/2 cap daily
Use: Atypical facial pain of psychogenic origin and burning mouth syndrome, most effective in depressed patients.

X. ANALGESICS

Aspirin 325 mg or Tylenol
Dsp: OTC
Sig: 2 tabs every 6 hours, p.r.n. pain
Use: Mild pain
Ibuprofen (Motrin) 600 mg
Dsp #20
Sig: 1 tab every 4 hours, p.r.n. pain
Use: Mild pain
ASA #2 (Codeine 15 mg)
_#3 (Codeine 30 mg)
_#4 (Codeine 60 mg)
Dsp #20
Sig: 1 tab every 4 hours, p.r.n. pain
Use: Mild to moderate pain
Oxycodone HCl (Percodan or Percocet)
Dsp #20
Sig: 1 tab every 4 hours, p.r.n. pain
Use: Moderate pain

Meperidine HCl (Demerol) 50 mg
Dsp #12
Sig: 1 tab every 4 hours, p.r.n. pain
Use: Severe pain
Hydromorphone HCl (Dilaudid) 2 mg
Dsp #12
Sig: 1 tab every 4 hours, p.r.n. pain
Use: Severe pain
Carbamazepine (Tegretol) 100 mg
Dsp #40
Sig: 1 tab 2 times daily for 2 days, then 1 tab 3 times daily
Use: Trigeminal and glossopharyngeal neuralgias. Most patients can be maintained on 400–800 mg per day.
Caution: While escalating, complete blood counts should be monitored regularly as Tegretol induces a dose-related marrow suppression.

XI. VASOACTIVE DRUGS

Nifedipine 10 mg
Dsp #42
Sig: 1 cap twice daily
Use: Short-term therapy for cluster headache (sphenopalatine neuralgia)
Ergotamine tartrate and caffeine (Cafergot) suppositories
Dsp #10
Sig: Place 1 tab rectally at onset of pain attack
Use: Migraine headache, midface cluster headache, not to exceed 5 per week.
Caution: Contraindicated in gravid women; use cautiously in hypertensive patients.

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