

chapter 13

DERMATOLOGIC DISEASES

HEREDITARY HYPOHIDROTIC ECTODERMAL DYSPLASIA

Figs. 13.1 and 13.2

Hereditary hypohidrotic ectodermal dysplasia is a genetic disorder characterized by defective formation of various ectodermally derived structures. It is most commonly inherited as an X-linked recessive trait, although autosomal-dominant and autosomal-recessive transmission also rarely may occur. Affected individuals have a marked reduction or absence of sweat glands resulting in the inability to tolerate heat. Severe fever may occur during infancy and early childhood and can be fatal. The skin is soft and dry, with wrinkling and hyperpigmentation often occurring around the eyes. The scalp hair is sparse, fine, and blond, with eyebrows, eyelashes, and other body hair being sparse or absent. There is often frontal bossing and a depressed nasal bridge. Many patients have atopic disease.

The lips are often protuberant and may exhibit pseudorhagades, or fissures. Hypoplasia of the mucoserous glands may lead to xerostomia and chronic rhinitis. The most characteristic oral finding is hypodontia or, in some cases, total anodontia. The teeth that do develop are typically malformed and conical in shape. Taurodontism is a common radiographic finding. Female carriers of the trait may show these tooth anomalies to a milder degree because of partial expression of the condition (Lyon hypothesis).

Treatment of the dental defects depends on the severity of the disease; removable prosthetic replacement is the most common treatment modality, including the use of complete dentures, partial dentures, or overdentures. In the child, the prostheses must be remade periodically to accommodate the growth of the dental arches. Osseointegrated dental implants also have been used with success.

HEREDITARY HEMORRHAGIC TELANGIECTASIA (RENDU-OSLER-WEBER DISEASE)

Fig. 13.3

Hereditary hemorrhagic telangiectasia is an autosomal-dominant disorder characterized by multiple vascular defects throughout the body in the form of telangiectasias and arteriovenous malformations. Weakness of the vascular wall and surrounding connective tissue predisposes patients to hemorrhagic episodes. Epistaxis is usually the earliest and most common symptom, often beginning in childhood. Cutaneous telangiectasias may become evident in the second and third decades, with oral lesions characteristically involving the lips and tongue. Oral and gastrointestinal tract bleeding may occur, as well as hemoptysis and intracranial hemorrhage. Treatment for hereditary hemorrhagic telangiectasia may require blood transfusions, laser ablation of skin and mucosal lesions, and surgical resection or embolotherapy of pulmonary and intracranial arteriovenous malformations. Epistaxis can be treated with septal dermoplasty and laser ablation.

► **Figure 13.1**
HEREDITARY HYPOHIDROTIC ECTODERMAL DYSPLASIA

Patient exhibiting frontal bossing and sparse, fine, blond hair. (Courtesy of Drs. Charles Hook and Bob Gellin.)



► **Figure 13.2**
HEREDITARY HYPOHIDROTIC ECTODERMAL DYSPLASIA

Patient from Figure 13.1 exhibiting hypodontia and conical-shaped teeth. (Courtesy of Drs. Charles Hook and Bob Gellin.)



► **Figure 13.3**
HEREDITARY HEMORRHAGIC TELANGIECTASIA

Telangiectasias of lips.



Figs. 13.4, 13.5, and 13.6

Pachyonychia congenita is a rare genetic syndrome inherited as an autosomal-dominant trait, although occasional cases have appeared to exhibit autosomal-recessive inheritance. At birth, or shortly thereafter, the fingernails and toenails become thickened, elevated, and tubular in shape with accumulation of a yellowish brown, horny material on the undersurface. This material causes the nails to project upward along the free edge. Recently, a late-onset form of the condition has been described (pachyonychia congenita tarda). The nails may have to be surgically removed or later may become hypoplastic. Hyperkeratosis of the palms and soles may occur during the first few years of life, with development of painful bullae that can burst and become infected. Palmar and solar hyperhidrosis also may be seen, as can follicular keratosis of the knees and elbows.

The principal oral manifestation is the development of white, hyperkeratotic lesions, especially in areas of increased trauma. The dorsum of the tongue and the buccal mucosa along the occlusal plane are the most common sites involved. These lesions are not predisposed to malignant degeneration. Neonatal teeth and angular cheilitis also have been reported.

► **Figure 13.4**
PACHYONYCHIA CONGENITA
Hypoplastic nails. (Courtesy of Dr. John Lenox.)



► **Figure 13.5**
PACHYONYCHIA CONGENITA
Hyperkeratosis of the soles. (Courtesy of Dr. Lou Young.)



► **Figure 13.6**
PACHYONYCHIA CONGENITA
Hyperkeratotic lesions on the lateral tongue. (Courtesy of Dr. John Lenox.)



WHITE SPONGE NEVUS

Fig. 13.7

White sponge nevus is a rare, autosomal-dominant abnormality of squamous epithelial differentiation that affects mucosal surfaces but not skin. Typically, spongy white plaques with a folded or corrugated surface occur bilaterally on the buccal mucosa and may also be seen at other oral mucosal sites. Lesions may be present at birth or first be noted in childhood or adolescence. Extraoral lesions may involve the vagina, labia, anorectal mucosa, and nasal cavity. Diagnosis often can be made on the basis of clinical appearance and family history. Cytologic smears, or sometimes biopsy, may help confirm the diagnosis. White sponge nevus is a benign condition, and no treatment is necessary. Interestingly, the lesions may improve with the use of systemic antibiotics, such as penicillin or tetracycline, or after application of topical tetracycline.

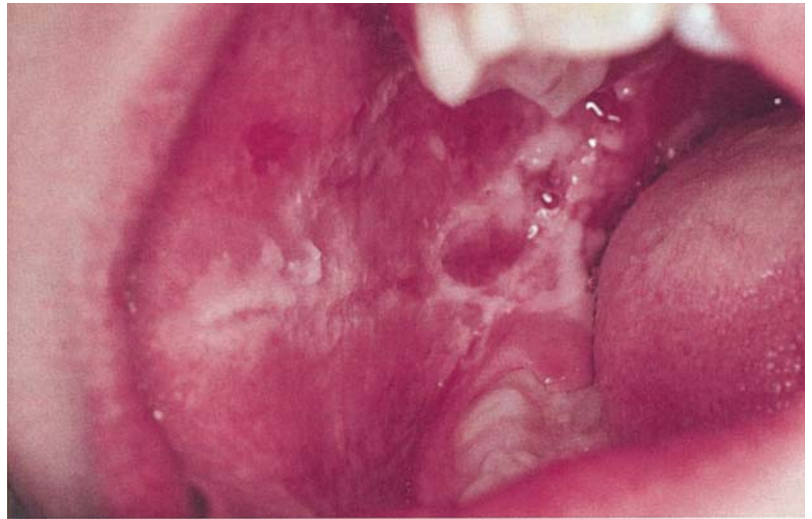
DARIER'S DISEASE (KERATOSIS FOLLICULARIS)

Figs. 13.8 and 13.9

Darier's disease is a rare genodermatosis inherited as an autosomal-dominant trait. The disease usually first manifests itself during childhood or adolescence with the development of red to yellowish brown papules behind the ears, around the nose, and on the neck, chest, back, and extremities. These papules become hyperkeratotic and crusty, eventually producing greasy plaques that may become secondarily infected and exude an offensive odor. Hyperkeratotic, papular lesions often involve the palms and soles and may become so severe that the patient has difficulty walking. The nails often are splintered and fissured and may exhibit longitudinal discoloration or subungual hyperkeratosis. The disease typically worsens during the summer months. Management includes frequent cleansing with antibacterial soaps and systemic antibiotics when necessary. Systemic retinoids often are helpful but may not be tolerated because of undesirable side effects.

Oral involvement has been reported in 15 to 50% of patients with Darier's disease. Rough, gray-white papules occur on the hard palate and gingiva and, less commonly, on the tongue and buccal mucosa. The palatal lesions may resemble papillary hyperplasia or nicotine stomatitis. No treatment is indicated for the mucosal lesions. Intermittent obstructive sialadenitis of the major salivary glands has been reported in some patients, probably secondary to squamous metaplasia of the ductal lining. In rare instances, this sialadenitis may become severe enough to necessitate excision of the affected gland.

- **Figure 13.7**
WHITE SPONGE NEVUS
Thickened white plaque of the buccal mucosa.



- **Figure 13.8**
DARIER'S DISEASE
Crusted, hyperkeratotic lesions of the leg and foot. (Courtesy of Weathers DR, Olansky S, Sharpe LO. Darier's disease with mucous membrane involvement. Arch Dermatol 1969;100:50–53.)



- **Figure 13.9**
DARIER'S DISEASE
Papular lesions of the palate. (Courtesy of Weathers DR, Olansky S, Sharpe LO. Darier's disease with mucous membrane involvement. Arch Dermatol 1969;100:50–53.)



Figs. 13.10 to 13.12

Tuberous sclerosis is a rare syndrome characterized by epilepsy, mental retardation, and hamartomatous growths in multiple organ systems. Although this syndrome is inherited as an autosomal-dominant trait, about 50 to 75% of cases have no family history and apparently represent new mutations. The earliest skin sign is the presence of congenital white, hypopigmented, ash-leaf-shaped macules on the trunk and limbs. Later, during the first decade, angiofibromas slowly develop, appearing as pink to red nodules most prominent in the nasolabial folds, cheeks, forehead, and scalp. These angiofibromas were once termed “adenoma sebaceum” in the mistaken belief that they represented tumors of the sebaceous glands. Subungual fibromas may elevate the nail bed. Orange-peel-like shagreen patches may occur in the lumbar area.

Numerous smooth, hard masses of glial tissue and ganglion cells occur in the brain and are responsible for the related mental retardation and epilepsy. The name “tuberous sclerosis” is derived from these potato-like tumors of the central nervous system. Intracranial calcifications, renal angiomyolipomas, cardiac rhabdomyomas, and other hamartomatous lesions may be seen.

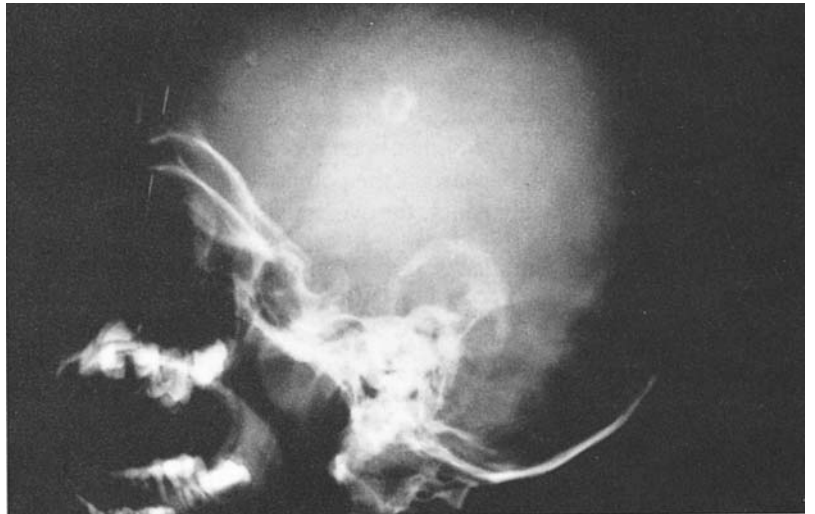
Fibromatous lesions of the anterior gingiva and other oral mucosal sites have been reported in 11 to 56% of patients. Intrabony fibrous or myxomatous tumors of the jaws also may occur. Generalized gingival hyperplasia secondary to anticonvulsant therapy may be seen. Pitting defects of the enamel have been described in 90% of patients; identification of these pits can be aided with the use of dental plaque disclosing solution.

Management of tuberous sclerosis often is directed primarily at controlling the associated seizures. Facial angiofibromas can be removed for cosmetic reasons. In general, patients have a slightly reduced life span, with death sometimes related to complications of central nervous system and kidney disease.

▶ **Figure 13.10**
TUBEROUS SCLEROSIS
Angiofibromas of the face. (Courtesy of
Dr. E. R. Costich.)



▶ **Figure 13.11**
TUBEROUS SCLEROSIS
Intracranial calcifications.



▶ **Figure 13.12**
TUBEROUS SCLEROSIS
Fibrous lesion of the gingiva.



DYSKERATOSIS CONGENITA

Figs. 13.13 and 13.14

Dyskeratosis congenita is a rare syndrome that is characterized by multiple defects of ectodermal structures plus bone marrow hypofunction. More than 80% of reported cases have occurred in males, and the condition is believed to be transmitted most frequently as an X-linked recessive trait. However, autosomal-dominant and autosomal-recessive transmission also are believed to occur, which accounts for sporadic cases seen in female patients.

Despite the disease's name, clinical manifestations typically are not congenital but begin to be noticed between 5 and 10 years of age. Reticulated hyperpigmentation is seen on the skin, especially the face, neck, upper arms, and chest. The nails become dystrophic, with longitudinal ridging and splitting. The palms and soles exhibit hyperhidrosis (excessive sweating), frequently in association with hyperkeratosis. Progressive bone marrow failure occurs in half of all cases, causing thrombocytopenia, anemia, and leukopenia. Other frequent findings include alopecia, dysphagia, and obstruction of the nasolacrimal duct.

Oral involvement may begin with the development of vesiculoerosive lesions on the tongue and buccal mucosa. The dorsum of the tongue may exhibit atrophy of the papillae and become smooth and shiny. The most significant oral feature is the frequent development of leukoplakia, which may involve the tongue, buccal mucosa, and labial mucosa. These leukoplakic lesions can undergo malignant transformation at an early age. Patients also have a predisposition to other malignancies, especially carcinomas of the gastrointestinal system. Rapidly progressive periodontal disease has been reported.

Because of the potential complications related to bone marrow failure and development of malignancy, the average life span for more severely affected patients is 32 years. The pancytopenia may be treated with bone marrow transplantation or administration of granulocyte colony-stimulating factor and erythropoietin.

PEUTZ-JEGHERS SYNDROME

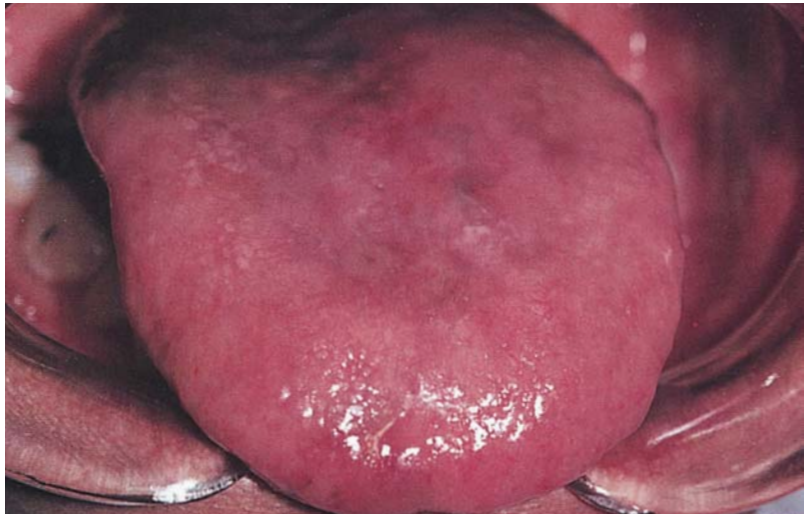
Fig. 13.15

Peutz-Jeghers syndrome is a rare autosomal-dominant condition characterized by multiple hamartomatous gastrointestinal polyps and mucocutaneous melanin pigmentation. The pigmented lesions are often congenital and are most common on the labial mucosa and perioral skin. They present as round to oval macules 1 to 5 mm in diameter, and are light brown to blue-black. Similar lesions may occur around the eyes, the nose, on the hands and feet, and intraorally. The intestinal polyps are most common in the small intestine, often leading to abdominal pain from small-bowel intussusception. Patients are at increased risk for carcinomas of the gastrointestinal tract, uterus, ovary, pancreas, and possibly breast. These tumors may develop at a young age, and close medical evaluation and monitoring are recommended. If desired, cosmetic removal of the pigmented lip lesions can be accomplished with laser ablation.

▶ **Figure 13.13**
DYSKERATOSIS CONGENITA
Dystrophic nail changes.



▶ **Figure 13.14**
DYSKERATOSIS CONGENITA
Atrophy of the dorsal tongue mucosa.



▶ **Figure 13.15**
PEUTZ-JEGHERS SYNDROME
Macular pigmentation of the lips.
(Courtesy of Dr. Ahmed Uthman.)



MELANOTIC MACULE (FOCAL MELANOSIS)

Figs. 13.16 and 13.17

The term melanotic macule has been used to describe a benign pigmented lesion of the oral cavity characterized by an increase in melanin pigmentation along the basal cell layer of the epithelium. The melanotic macule is typically a well-circumscribed flat area of pigmentation that most frequently exhibits a brown color but also may appear black, blue, or gray. Most lesions are less than 1 cm in diameter, although occasional cases may be larger. Most occur as single lesions, but multiple lesions can be seen. The most common location is the vermillion border of the lip, with a predilection for the midportion of the lower lip. The gingiva, buccal mucosa, and palate are the most common intraoral locations. The melanotic macule is most common in young and middle-aged adults, and females are affected more frequently than males.

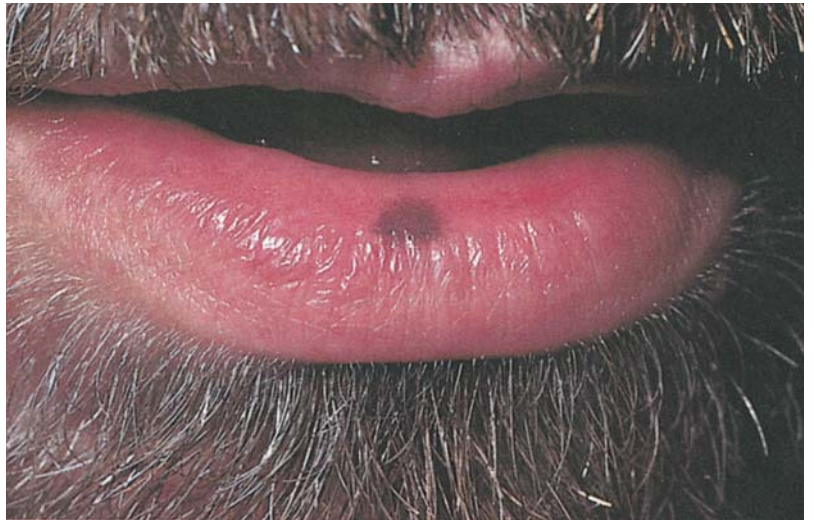
Treatment usually consists of surgical excision to rule out the possibility of early melanoma, although long-standing lesions exhibiting no evidence of change may be followed clinically, especially those on the lips. Biopsy is recommended especially for pigmented lesions of the hard palate–maxillary gingiva complex because this is the most common site for oral melanoma. Labial melanotic macules have been treated successfully with the use of a Q-switched ruby laser, which causes selective damage to pigmented cells in the tissue.

ORAL MELANOACANTHOSIS (ORAL MELANOACANTHOMA)

Fig. 13.18

Oral melanoacanthosis is a rare pigmented lesion that probably represents a reactive hyperplasia of melanocytes in response to local trauma. It is most common in young adults and occurs almost exclusively in blacks. Oral melanoacanthosis often has a sudden onset, sometimes exhibiting rapid growth over a period of several weeks to months. The buccal mucosa is the most common location, and bilateral involvement may occur. Lesions have been described as dark blue, brown, or black and range from less than 5 mm in diameter to extensive lesions several centimeters in size. The pigmentation often resolves spontaneously after removal of irritating factors or incomplete excision.

▶ **Figure 13.16**
MELANOTIC MACULE
Pigmented lesion on the lower lip.



▶ **Figure 13.17**
MELANOTIC MACULE
Flat, pigmented lesion of the maxillary gingiva.



▶ **Figure 13.18**
ORAL MELANOACANTHOSIS
Pigmented lesion of the buccal mucosa.



ERYTHEMA MIGRANS (GEOGRAPHIC TONGUE, BENIGN MIGRATORY GLOSSITIS, ECTOPIC GEOGRAPHIC TONGUE, MIGRATORY STOMATITIS)

Figs. 13.19, 13.20, and 13.21

Erythema migrans is a common inflammatory condition that usually affects the tongue, where it is known as “geographic tongue” or “benign migratory glossitis.” Most studies indicate that the prevalence of geographic tongue is in the range of 1 to 3% of the population. The condition occurs at all ages, and women are affected almost twice as often as men. Concomitant fissured tongue also may be present. The cause of erythema migrans is unknown, although a family history or association with stress or atopy may be seen. An increased prevalence of certain histocompatibility antigens has been reported in affected patients, supporting the theory that genetic influences play a role in the pathogenesis of this condition. Because of their histopathologic similarities and cases showing coexistence of both conditions, it has been suggested that erythema migrans may represent an oral manifestation of psoriasis. Although the relationship between these two conditions is still debated, one study did show a significantly increased prevalence of erythema migrans in patients with psoriasis.

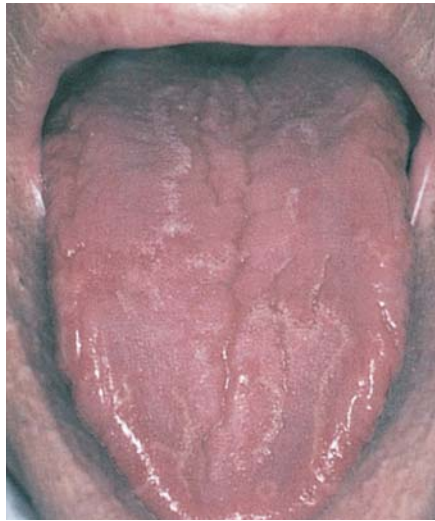
Geographic tongue typically affects the dorsal and lateral surface of the tongue, presenting as red patches caused by loss of the filiform papillae but with preservation of the fungiform papillae. These red patches are usually, but not always, surrounded by an elevated, circinate white or yellow border. The red patches rapidly enlarge and may coalesce, producing large areas devoid of filiform papillae. The filiform papillae rapidly regrow, however, returning the area to its normal appearance. The loss of papillae often begins in another area, resulting in an ever-changing pattern of papillae loss and regrowth, hence the name “benign migratory glossitis.” This changing pattern is a rapid process; daily differences can be noted in the maplike pattern. Most patients are without symptoms, although some may experience soreness or sensitivity to spicy foods.

Although involvement of the dorsal and lateral tongue is common, involvement of the ventral tongue and other oral mucosal sites is seen much less frequently. These lesions, however, have the same migrating pattern as the tongue lesions, presenting as atrophic, erythematous patches, usually with a raised, circinate, white border. Extralingual lesions usually occur on the buccal and labial mucosa. Almost all patients with “ectopic geographic tongue” also have typical dorsal tongue involvement.

Erythema migrans is a persistent condition that may exhibit periods of remission and exacerbation. No treatment is indicated, except possibly palliative therapy in some instances when significant tenderness is present. Topical application of corticosteroids, diphenhydramine, or anesthetic agents have been used with variable success.

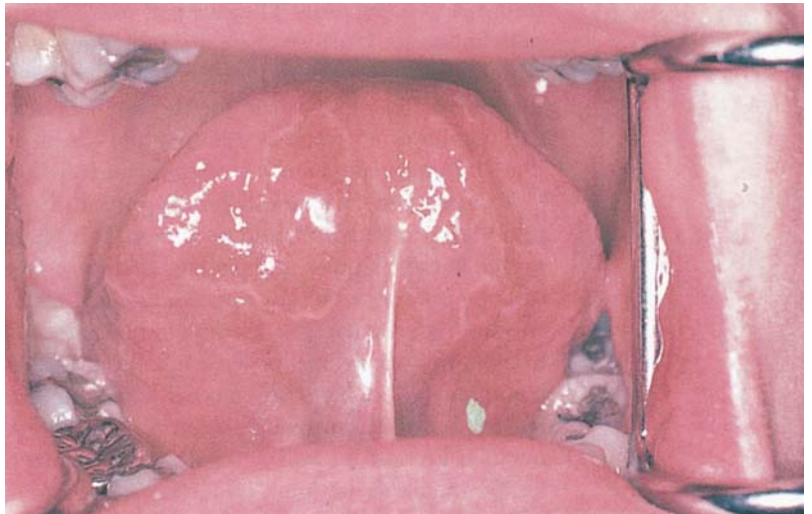
► **Figure 13.19**
ERYTHEMA MIGRANS

Loss of filiform papillae with a raised white border. Associated fissured tongue is also present.



► **Figure 13.20**
ERYTHEMA MIGRANS

Ventral tongue involvement.



► **Figure 13.21**
ERYTHEMA MIGRANS

Lesions on the soft palate.

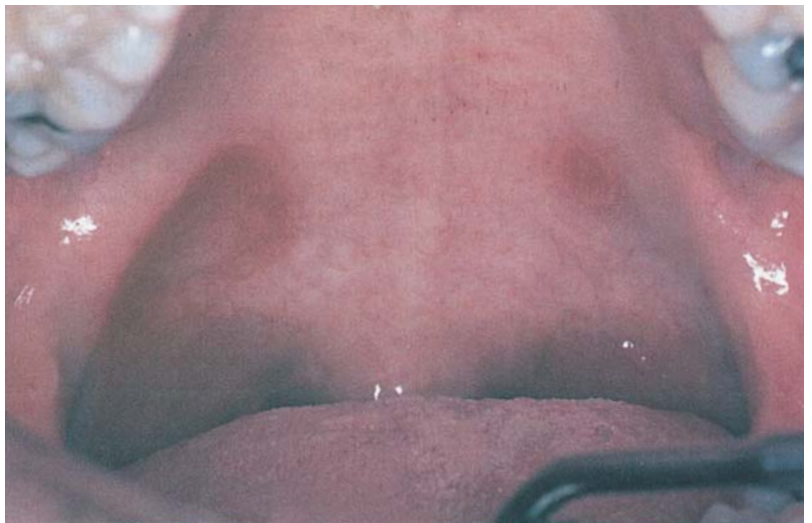


Fig. 13.22

Transient lingual papillitis is a common condition that is characterized by the development of enlarged and painful fungiform papillae on the tongue. One or more fungiform papillae become swollen and exhibit a red, white, or yellow color. The lesions typically resolve spontaneously within several hours to days, but periodic recurrences are not unusual. Despite its common occurrence, little was known about this entity until a recent article by Whitaker and colleagues. In their survey, they found that these lesions were reported by 56% of their study population and were most common in young women. A subsequent study, which apparently reported the same entity, showed a familial clustering of cases. The cause is unknown, although it has been speculated that the lesions may result from local trauma or a viral infection. The term "lie bumps" is derived from the popular superstition that these lesions are caused by telling lies. There is no effective treatment in most cases, although some individuals have found relief with over-the-counter mouthrinses or salt water rinses.

PSORIASIS

Figs. 13.23 and 13.24

Psoriasis is a common chronic inflammatory skin disorder that is estimated to affect 1 to 3% of the world's population. The cause of psoriasis seems to be multifactorial, but there is a strong genetic influence because one-third of patients with psoriasis have affected relatives. In addition, patients with psoriasis demonstrate an increased frequency of certain histocompatibility antigens. Factors that can exacerbate the disease include psychological stress, infections, alcohol abuse, and certain drugs, such as lithium and beta blockers. A strong association between psoriasis and human immunodeficiency virus infection has been shown.

Psoriasis most frequently has its onset during the second and third decades of life and shows periods of exacerbation and remission. It is characterized clinically by the development of erythematous papules and plaques that are covered by a silvery scale. If the scales are scraped off, one may observe tiny pinpoint areas of bleeding (Auspitz sign). However, eliciting the Auspitz sign is currently discouraged because of the aforementioned possible association with human immunodeficiency virus infection. Lesions are often bilaterally symmetrical and most commonly affect the scalp, elbows, knees, and sites of local trauma (Koebner phenomenon). Itching is not an unusual complaint. More severe forms of the disease may exhibit generalized pustular lesions. A small percentage of patients develop psoriatic arthritis, which may involve the temporomandibular joint. Oral lesions are rare and have been variably described as appearing as white plaques, erythematous patches, or ulcerations. An increased prevalence of erythema migrans has been reported, and some authors believe that this represents an oral manifestation of psoriasis. This association is strongest for pustular forms of the disease. An increased frequency of fissured tongue also is reported.

No treatment may be necessary for mild forms of psoriasis. For moderate cases, topical corticosteroids or coal tar derivatives may be used. Severe cases may require ultraviolet light treatment or systemic drug therapy with methotrexate, retinoids, or cyclosporine. Symptomatic oral lesions may be treated with warm salt water rinses or application of topical anesthetics, antihistamines, or corticosteroids.

► **Figure 13.22**
TRANSIENT LINGUAL PAPILLITIS
Painful white papules along the anterior margin of the tongue.



► **Figure 13.23**
PSORIASIS
Scaly lesions on the elbow.



► **Figure 13.24**
PSORIASIS
Erythematous lesions of the hard palate.



Figs. 13.25, 13.26, and 13.27

Systemic sclerosis is an unusual disorder of unknown cause that best fits into the category of autoimmune collagen-vascular diseases. Although the term “scleroderma” describes well the principal and most obvious site of involvement in most patients, the term “systemic sclerosis” better denotes the multisystem nature of the disorder.

Systemic sclerosis usually has its onset in middle age and is more common in females than in males. There is thickening and induration of the skin caused by dermal fibrosis, which may lead to clawlike flexion contractures of the hands and a masklike facial appearance. In long-standing scleroderma, ulcerations develop over pressure points due to trauma. Hyperpigmentation and hypopigmentation of the skin may occur. The fibrosis is not confined to the skin but may involve internal organs such as the lungs, heart, gastrointestinal tract, and kidneys, resulting in loss of normal visceral function. Other common features include Raynaud phenomenon, telangiectasias, soft-tissue calcifications, arthritis, an elevated erythrocyte sedimentation rate, and the presence of antinuclear antibodies in the serum.

Oral manifestations include difficulty opening the mouth and loss of tongue mobility because of perioral and lingual fibrosis. The anterior maxillary teeth often are exposed because of retraction of the lips. Crenations of the buccal mucosa and tongue have been reported. A classic radiographic finding is generalized symmetric widening of the periodontal ligament space, which occurs to at least some degree in almost all patients. Bony erosions may occur at the angle of the mandible, or they may destroy the coronoid and condylar processes. Xerostomia and dysphagia are also common findings. The salivary changes are similar to those seen in Sjögren syndrome.

Systemic sclerosis pursues an unpredictable course, but is typically a progressive disorder with no cure. Patients with diffuse involvement may exhibit rapid progression of their disorder, with death occurring within several years after onset. In other patients, the disease is less severe, with slow progression over a period of many years or periods of rapid spread and quiescence. The 5-year survival has been reported to be between 50 and 70%; 40 to 60% of patients survive for 10 years. Internal organ complications include pulmonary fibrosis, heart failure, renal insufficiency, and hypertension. Death usually results from complications of internal organ involvement. Renal disease formerly was the leading cause of morbidity and mortality, but since the advent of angiotension-converting enzyme inhibitor therapy for kidney disease, pulmonary complications are now the primary cause of death in patients with systemic sclerosis.

► **Figure 13.25**
SYSTEMIC SCLEROSIS

(A) Fibrosis of the skin resulting in a masklike facial expression. (B) The fibrosis has caused marked atrophy of the mandibular ramus. Note the widened periodontal ligament space around the mandibular molar.



► **Figure 13.26**
SYSTEMIC SCLEROSIS

Fibrosis of the hands with flexion contractures and blunting of digits.



► **Figure 13.27**
SYSTEMIC SCLEROSIS

Symmetric widening of the periodontal ligament space.



Fig. 13.28

The CREST syndrome is a clinical variant of systemic sclerosis. The term “CREST” is an acronym for the five major components of the disorder: calcinosis cutis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasias. The telangiectasias often are most prominent on the face and lips and also can be seen intraorally. Although considered a variant of systemic sclerosis, the CREST syndrome is often less severe than the more common systemic variety.

LUPUS ERYTHEMATOSUS

Figs. 13.29 and 13.30

Lupus erythematosus (LE) is an autoimmune disorder that usually has its onset in young adults and is considerably more common in women than in men. Chronic cutaneous LE (CCLE) primarily affects only the skin and mucous membranes, whereas systemic LE (SLE) affects the skin and multiple other tissues and organs. A third form of the disease, subacute cutaneous LE, has clinical features intermediate between SLE and CCLE.

Skin involvement is most common in areas of sun exposure. In SLE, patients often present with an erythematous rash in a butterfly distribution across the bridge of the nose and malar areas. Other features that may be seen in SLE include Raynaud phenomenon, arthritis, proteinuria, pericarditis, pleuritis, psychosis, convulsions, anemia, leukopenia, thrombocytopenia, and circulating antinuclear antibodies. The characteristic skin manifestation of CCLE is the development of discoid lesions, which present as elevated, erythematous, indurated plaques with an adherent scale and central atrophy and scarring. Although the term “discoid LE” sometimes has been used synonymously with CCLE, it should be emphasized that discoid skin lesions may be seen in all forms of the disease.

Oral lesions occur in 10 to 40% of patients with LE and seem to be more common in those with SLE. The most characteristic lesion consists of a central atrophic, speckled, erythematous area surrounded by a slightly elevated border exhibiting radiating white striae and telangiectasias. These lesions are most common on the buccal mucosa and may mimic lichen planus. Later stages can be indistinguishable from oral leukoplakia. Other oral manifestations include scaling lip lesions, erythema, nonspecific ulcers, and secondary Sjögren syndrome (see Figs. 8.5 and 8.6).

Management of LE depends on the extent and severity of the disease. Treatment usually consists of antimalarial drugs, topical and systemic corticosteroids, or both. The prognosis for CCLE is excellent, with only about 5% of cases progressing to systemic involvement. In SLE, the most common cause of death is renal failure, although most cases can be controlled with appropriate medications. The 5-year survival rate for SLE is approximately 95%, but survival drops to around 75% after 15 years.

► **Figure 13.28**
CREST SYNDROME
Facial telangiectasias.



► **Figure 13.29**
SYSTEMIC LUPUS ERYTHEMATOSUS
Lesions of the malar area.



► **Figure 13.30**
CHRONIC CUTANEOUS LUPUS ERYTHEMATOSUS
Speckled erythematous lesion with peripheral radiating white striae on the buccal mucosa.



Figs. 13.31, 13.32, and 13.33

The term “pemphigus” refers to a group of autoimmune disorders characterized by development of vesiculobullous lesions on the skin and mucous membranes. It is most common in middle-aged adults and affects both sexes equally. An increased prevalence has been noted in Ashkenazi Jews. Patients with pemphigus develop autoantibodies directed toward an antigen on the surface of squamous epithelial cells, destroying the intercellular attachments and resulting in intraepithelial blister formation. Although several clinical variants are recognized, pemphigus vulgaris is the most common form and the type most likely to exhibit oral manifestations.

On the skin, the primary lesions of pemphigus vulgaris are vesicles and bullae that can arise on normal skin or on an erythematous base. These blisters are fragile and rupture easily, producing painful, raw, denuded areas. In later stages of the disease, extensive areas of epidermis may be sloughed. Scaling and crusting of the ulcerated areas are common. A characteristic feature is the Nikolsky sign, which is the ability to elicit the formation of a bulla by the application of firm lateral pressure on normal-appearing skin.

Oral involvement in pemphigus vulgaris is extremely common: more than 90% of patients develop oral lesions at some time during the course of their disease. In fact, the mouth is the most common presenting site for lesions of pemphigus vulgaris, with some studies showing more than half of all cases originating there. The oral lesions often have a slow, insidious onset with symptoms present for many months before a diagnosis is made or skin lesions develop. Lesions may be found anywhere but are most common on the palate, buccal mucosa, and gingiva. Although the oral lesions are vesiculobullous in nature, intact blisters rarely are seen; patients usually exhibit collapsed bullae, ulcers, or widespread areas of erosion. Gingival involvement may produce “desquamative gingivitis.” Pain and resultant weight loss are common complaints.

Diagnosis is established by biopsy and immunofluorescent studies. Titers on indirect immunofluorescence often correlate to the severity of the disease. Before the advent of systemic corticosteroid therapy, pemphigus vulgaris was fatal in 60 to 90% of the patients because of general debilitation, malnutrition, and protein loss. Even today, pemphigus vulgaris is a serious disease, with a mortality of approximately 10%. Many of these deaths arise from complications of corticosteroid therapy. Other immunosuppressive drugs, such as azathioprine, also are frequently used to reduce the amount of systemic corticosteroids needed.

▶ **Figure 13.31**
PEMPHIGUS VULGARIS
Crusted vesiculobullous lesion of the elbow.



▶ **Figure 13.32**
PEMPHIGUS VULGARIS
Ulcer at the commissure.



▶ **Figure 13.33**
PEMPHIGUS VULGARIS
Extensive ulcerative lesions of the buccal mucosa and soft palate.



PARANEOPLASTIC PEMPHIGUS (NEOPLASIA-INDUCED PEMPHIGUS)

Figs. 13.34 and 13.35

Paraneoplastic pemphigus is a recently recognized vesiculobullous disorder that arises secondary to an underlying malignancy, most frequently non-Hodgkin's lymphoma or chronic lymphocytic leukemia. It is believed that antibodies that are produced against the tumor cross-react against antigens of the adhesion complex of the epithelium.

Paraneoplastic pemphigus presents a variable clinical and histopathologic picture that can be confused with other vesiculobullous disorders. The condition often has a rather sudden onset, with the development of multiple blisters and ulcers affecting the skin and oral mucosa. In some instances, the skin lesions are papular and pruritic, resembling lichen planus. The oral lesions can affect any location but frequently involve the lips to produce hemorrhagic crusting that may mimic erythema multiforme. Ocular involvement can produce scarring lesions similar to mucous membrane pemphigoid.

The diagnosis of paraneoplastic pemphigus is made on the basis of light microscopy, direct immunofluorescence, indirect immunofluorescence, and, sometimes, immunoprecipitation studies. The indirect immunofluorescence should be performed on transitional-type epithelium, which shows a highly specific pattern of antibody deposition in the intercellular areas of the epithelium. Treatment usually consists of systemic immunosuppressive medications such as prednisone and azathioprine. Unfortunately, patients usually have a poor prognosis, with death resulting from complications of the vesiculobullous lesions or the underlying malignancy. However, occasional long-term survivors have been described.

CHRONIC ULCERATIVE STOMATITIS

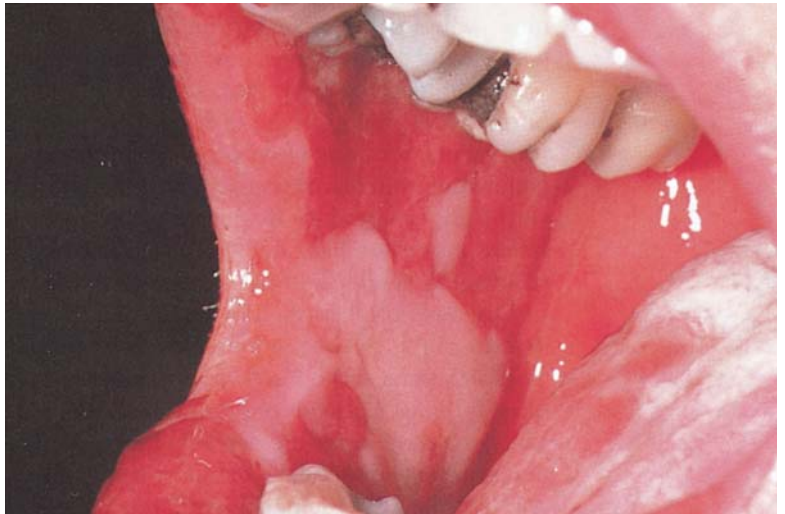
Fig. 13.36

Chronic ulcerative stomatitis is a recently described condition with clinical and light microscopic features that mimic erosive lichen planus. However, both direct and indirect immunofluorescent studies demonstrate specific autoantibodies directed against the nuclei of stratified squamous epithelial cells. The condition is most common in middle-aged and older women who present with chronic symptoms of desquamative gingivitis or ulcerations of the buccal mucosa or tongue. Associated Wickham's striae may be present, as well as lichenoid skin lesions. Unfortunately, unlike lichen planus, chronic ulcerative stomatitis is less responsive to topical and systemic corticosteroid therapy. Hydroxychloroquine has been reported to be successful in controlling the lesions in some patients.

► **Figure 13.34**
PARANEOPLASTIC PEMPHIGUS
Crusting, hemorrhagic lip lesions.
(Courtesy of Dr. Carl Allen.)



► **Figure 13.35**
PARANEOPLASTIC PEMPHIGUS
Extensive erosive lesions of the buccal mucosa. (Courtesy of Dr. Carl Allen.)



► **Figure 13.36**
CHRONIC ULCERATIVE STOMATITIS
White and red erosive changes on the dorsal tongue.



Figs. 13.37, 13.38, and 13.39

Pemphigoid is an autoimmune disorder characterized by the development of vesiculobullous lesions on the skin or mucous membranes. Patients develop autoantibodies directed toward the epithelial basement membrane zone that result in the formation of subepithelial blisters. Two major forms are recognized: bullous pemphigoid and mucous membrane pemphigoid.

Bullous pemphigoid primarily affects the skin of middle-aged and older adults. It is characterized by the development of tense blisters on the trunk, arms, and legs. Oral lesions have been reported in 8 to 39% of patients.

Mucous membrane pemphigoid primarily affects mucosal surfaces; skin involvement is uncommon. In some sites, the ulcerative lesions may result in scar formation—hence the name “cicatricial” pemphigoid. This condition is most common in middle-aged and older adults and shows a female predilection. The oral cavity is affected in most cases; the eyes are the second most common location. Although lesions may occur anywhere in the mouth, the gingiva is the most commonly affected site, with patients often presenting with a clinical “desquamative gingivitis.” As with pemphigus vulgaris, mucous membrane pemphigoid usually has a slow, insidious onset, with lesions present for many months before a diagnosis is made. Patients usually present with painful erythematous or erosive lesions; intact blisters rarely are seen.

Ocular involvement is characterized by conjunctivitis, with patients often complaining of burning and photophobia. As the disease progresses, a mucoid discharge may develop and scarring occurs, resulting in symblepharon formation (adhesions between the lid and eyeball). Inflammation, vascularization, and scarring of the cornea may lead to blindness. Esophageal involvement can produce dysphagia and stricture formation that may require dilatation. Laryngeal lesions may cause pain and hoarseness and can be life-threatening, though this is rare. Nasal, pharyngeal, genital, and anorectal lesions also can occur.

Diagnosis is established by biopsy and immunofluorescent studies. Treatment depends on the severity of the disease but often involves topical or systemic corticosteroids. For desquamative gingival lesions, custom soft acrylic trays can be fabricated to hold the topical corticosteroid in place for longer periods of time. When systemic corticosteroids are needed, azathioprine also may be used to lower the needed corticosteroid dosage. Dapsone may be effective in some patients, as may tetracycline and nicotinamide. In patients who present with only oral disease, an ophthalmologic examination is still recommended to evaluate for the possibility of early ocular disease.

► **Figure 13.37**
MUCOUS MEMBRANE PEMPHIGOID
Erythematous and erosive gingival lesions
("desquamative gingivitis"). (Courtesy of
Dr. Lynn Wallace.)



► **Figure 13.38**
MUCOUS MEMBRANE PEMPHIGOID
Lesions of the palate.



► **Figure 13.39**
MUCOUS MEMBRANE PEMPHIGOID
Symblepharon formation of the eye.



Figs. 13.40 to 13.54

Lichen planus is an inflammatory disorder of unknown cause that can affect both the skin and the oral cavity. The disease is relatively common and has been estimated to affect approximately 1% of the general population. Although stress has been suggested as a possible etiologic factor, a definite cause-and-effect relationship has not been established. A variety of drugs can cause lichenoid lesions (lichenoid drug reactions) that may be clinically and microscopically indistinguishable from idiopathic lichen planus. The disease most often has its onset in middle-aged adults. Females seem to be affected more often than males, especially with oral lichen planus. Studies show a wide variation in the relative prevalence of oral and skin lesions, which depends on whether the patient was seen primarily in a dermatology clinic or a dental clinic. In patients seen primarily for skin lesions, about 70% also show oral involvement. In patients seen initially for oral lesions, 20 to 40% show skin lesions.

The characteristic skin lesion of lichen planus is a flat-topped, polygonal papule with a red to violet color. The surface of the papule may exhibit a fine scale or lacy white streaks known as "Wickham's striae." Papules may coalesce to form hypertrophic plaques, especially on the lower legs and ankles. In rare instances, bullous lesions can arise. Pruritis, which can be severe, occurs in most cases. The most common sites of involvement are the flexor surfaces of the wrists, the legs, the abdomen, and the back. Lesions may develop in a linear distribution in areas of trauma (Koebner phenomenon). Nail involvement is seen in 6 to 10% of cases, usually producing longitudinal ridging and roughening of the surface. The clinical course of lichen planus of the skin is variable; some patients develop localized lesions, others develop a more generalized eruption.

Oral lesions begin as small white papules that usually coalesce to form an interlacing network of white lines (reticular lichen planus). These interlacing lines also are known as Wickham's striae. Hypertrophic white plaques sometimes occur, especially on the dorsum of the tongue. Erythematous atrophic areas and erosive lesions (erosive lichen planus) are common. In rare instances, intact bullae (bullous lichen planus) are seen. Although lesions may occur anywhere in the oral cavity, the buccal mucosa is involved in 78 to 87% of cases. The gingiva and tongue are also common sites of involvement. Oral lesions tend to be bilateral and symmetric in their distribution. Reticular lichen planus is often asymptomatic, except for a feeling of roughness of the mucosa. Atrophic or erosive lichen planus, however, is usually tender or painful and may interfere with eating. When erosive lesions involve the gingiva, they may present clinically as a "desquamative gingivitis."

Because of its characteristic features, classic reticular lichen planus may not require biopsy, although biopsy is often advisable for atrophic or erosive lichen planus to rule out a dysplastic process or other vesiculoerosive disorder. Oral lichen planus and lupus erythematosus (see Figs. 13.29 and 13.30) can have similar clinical features; therefore, biopsy and immunofluorescent studies may be indicated for oral lichenoid lesions if skin lesions suggestive of lupus erythematosus are present. Biopsy and immunofluorescent studies also may be indicated for lichenoid lesions that are not responsive to therapy.

Oral lichen planus is typically a chronic condition that may exhibit exacerbations and remissions over many years. If the lesions are asymptomatic, no treatment is necessary. For symptomatic atrophic or erosive lesions, treatment usually consists of topical corticosteroids, such as fluocinonide gel. Topical corticosteroid therapy affords only temporary control of the disease, and patients should be advised that the lesions will probably recur and require reapplication of the medication. In rare instances, systemic corticosteroids may be needed to bring the disease under control. A potential complication of corticosteroid therapy is the development of iatrogenic candidiasis, but this usually responds to appropriate antifungal therapy.

Considerable controversy exists concerning the malignant potential of oral lichen planus. A number of series and individual cases have been reported that show carcinoma developing in a small percentage (0.4–2.5%) of patients with oral lichen planus, especially the erosive form. Other authors have questioned this association, however, suggesting that in many cases the original diagnosis actually may have been a hyperkeratotic or dysplastic process with clinical or histopathologic features that mimicked lichen planus. In any case, periodic follow-up of patients with oral lichen planus seems to be prudent.

► **Figure 13.40**
LICHEN PLANUS
Violaceous papules on the wrist.



► **Figure 13.41**
LICHEN PLANUS
Hypertrophic, excoriated lesions on the shin.



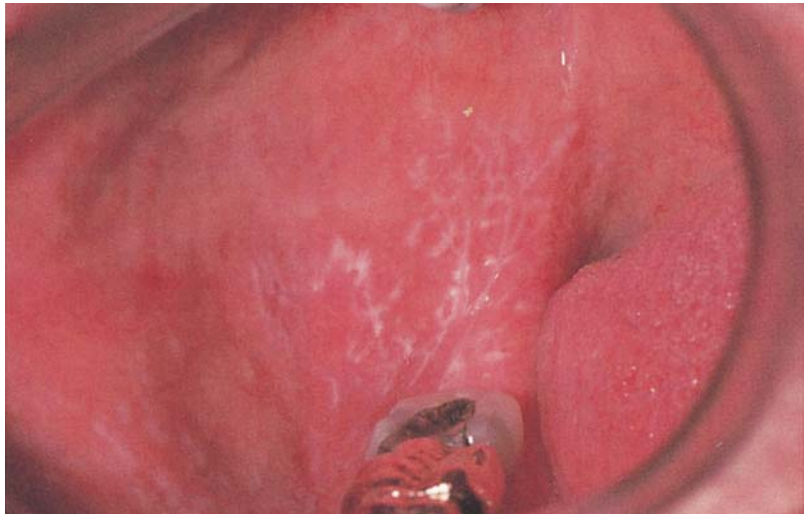
► **Figure 13.42**
LICHEN PLANUS
Nail involvement.



► **Figure 13.43**
LICHEN PLANUS
White papules and striae on the buccal mucosa.



► **Figure 13.44**
LICHEN PLANUS
White striae on the posterior buccal mucosa.



► **Figure 13.45**
LICHEN PLANUS
Confluent reticular lesions on the buccal mucosa.



► **Figure 13.46**
LICHEN PLANUS

White papules and plaquelike lesion of the dorsum of the tongue.



► **Figure 13.47**
LICHEN PLANUS

White papules and striae on the lower lip mucosa.



► **Figure 13.48**
LICHEN PLANUS

White plaque with peripheral striae on the hard palate.



► **Figure 13.49**
LICHEN PLANUS
Red, erosive gingival lesions
("desquamative gingivitis").



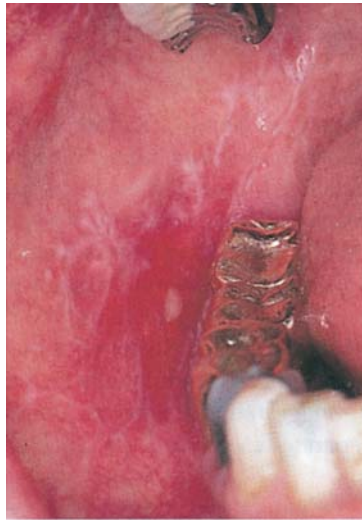
► **Figure 13.50**
LICHEN PLANUS
Erosive lesions of the mandibular facial gingiva.



► **Figure 13.51**
LICHEN PLANUS
Erosive lesion of the palatal gingiva. Note
the peripheral white striae.



► **Figure 13.52**
LICHEN PLANUS
Erosive lesion of the buccal mucosa.



► **Figure 13.53**
LICHEN PLANUS
Severe erosive lesions of the buccal mucosa before treatment.



► **Figure 13.54**
LICHEN PLANUS
Same patient as depicted in Figure 13.53 after 10 days of topical fluocinonide therapy.



Figs. 13.55, 13.56, and 13.57

Erythema multiforme is an acute vesiculoerosive disorder of the skin and mucous membranes. It is seen most commonly in young adults but may occur at almost any age. Males are affected more often than females. Although the clinical features of erythema multiforme suggest an immune or allergic reaction, in many instances a specific precipitating agent is never identified. The best-documented precipitating factors include various infections, especially herpes simplex and *Mycoplasma pneumoniae*. Several drugs also have been implicated as causing erythema multiforme, including sulfonamides, penicillins, and cephalosporins. Erythema multiforme has a wide range of severity; the terms “Stevens-Johnson syndrome” and “toxic epidermal necrolysis” (Lyell disease) have been used traditionally for more severe forms of the disease. However, some recent studies have suggested that Stevens-Johnson syndrome and toxic epidermal necrolysis may represent a separate disease process. Such cases are more likely to be triggered by a drug than by an infection.

Skin lesions of erythema multiforme usually begin as round, erythematous papules that enlarge to produce the characteristic iris or target lesions. The target lesion is created by a central area of epithelial necrosis or blister formation surrounded by an erythematous inflammatory zone and a lighter ring of edema at the periphery. These skin lesions may develop anywhere but are most common on the extremities, with a predilection for the extensor surfaces. A nonspecific rash also may be seen. In rare instances, blistering or necrotic lesions may coalesce to produce extensive areas of sloughing (toxic epidermal necrolysis).

Mucosal involvement is commonly seen and may affect the oral cavity, eyes, and genitalia. More severe cases affecting multiple mucosal sites and the skin are referred to as Stevens-Johnson syndrome. Oral lesions are typically sudden in onset and are characterized by multiple painful ulcers and erosions that often cause difficulty in eating and may lead to dehydration. Lesions may occur anywhere in the mouth but are most typical on the lips, where they often result in hemorrhagic crusting. Ocular involvement can be manifested by conjunctivitis, periorbital edema, and photophobia, rarely leading to scarring and permanent visual impairment.

Erythema multiforme is usually a self-limiting process that runs its course in 2 to 4 weeks, although severe cases of Stevens-Johnson syndrome and especially toxic epidermal necrolysis can be life-threatening. Recurrent episodes are not uncommon. Treatment consists of supportive care, including oral topical anesthetic agents and possibly intravenous rehydration if the patient cannot eat. Topical corticosteroids also may be helpful in the management of oral lesions. Systemic corticosteroid therapy has been used traditionally for erythema multiforme, but some authors have questioned the advisability of such treatment, especially for severe forms of Stevens-Johnson syndrome and toxic epidermal necrolysis. Such cases may be managed best in a hospital burn unit. In recurring cases of erythema multiforme that are precipitated by herpes simplex infections, prophylactic acyclovir therapy often is helpful in preventing further outbreaks. Some authors also have reported success using azathioprine or levamisole.

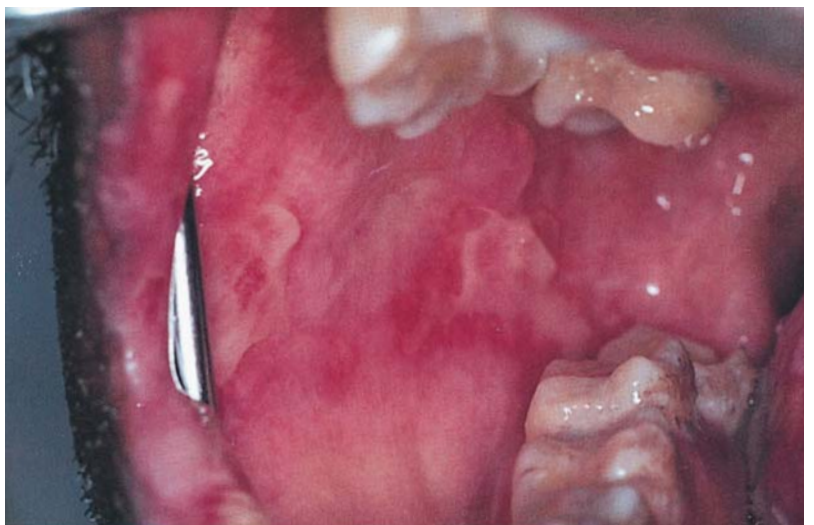
► **Figure 13.55**
ERYTHEMA MULTIFORME
Target lesions of the palm.



► **Figure 13.56**
ERYTHEMA MULTIFORME
Hemorrhagic, crusting lesions of the lips and nostrils.



► **Figure 13.57**
ERYTHEMA MULTIFORME
Ulcers of the buccal mucosa.



Figs. 13.58 and 13.59

The term “epidermolysis bullosa” (EB) is used for a group of mechanobullous diseases characterized by the development of blisters in areas of minor trauma. At least 23 distinct forms of the disease have been recognized. Most of these have a hereditary basis, with onset of blistering lesions at birth or within the first few years of life. Epidermolysis bullosa acquisita is not hereditary, however, and appears to be an autoimmune disorder, with lesions typically arising during adolescence or adulthood. The various types are characterized by spontaneous or trauma-induced blister formation caused by degeneration of basal or parabasal epithelial cells (EB simplex), lack of hemidesmosomes (junctional EB), or defects in anchoring fibrils in the connective tissue (dystrophic EB).

A wide range of severity is seen, from EB of Weber-Cockayne, with minor blisters of the hands and feet, to EB letalis, with extensive bullous lesions and shedding of sheets of skin. Scarring occurs in some forms of EB and is especially prominent in recessive dystrophic EB, in which scarring may result in encasement and fusion of fingers and toes, plus flexion contractures. Oral lesions are common in several types of EB and may result in painful erosions and severe scarring. Enamel hypoplasia is a common finding in junctional forms of EB. Rampant dental caries frequently is seen in patients with junctional EB and severe recessive dystrophic EB. Development of squamous cell carcinoma of the tongue has been reported in several cases of recessive dystrophic EB.

The prognosis for EB depends on the specific subtype: EB letalis is usually fatal during the first few months of life because of fluid loss and sepsis; dystrophic recessive EB is often fatal before patients reach adulthood; milder forms of EB are usually compatible with a normal life span.

► **Figure 13.58**
EPIDERMOLYSIS BULLOSA
Scarring vesiculobullous oral lesions.



► **Figure 13.59**
EPIDERMOLYSIS BULLOSA
Scarring and fusion of toes.



Hereditary Hypohidrotic Ectodermal Dysplasia

- Clarke A, Phillips DIM, Brown R, et al. Clinical aspects of X-linked hypohidrotic ectodermal dysplasia. *Arch Dis Child* 1987;62:989.
- Crawford PJM, Aldred MJ, Clarke A. Clinical and radiographic dental findings in X linked hypohidrotic ectodermal dysplasia. *J Med Genet* 1991;28:181.
- Davarpanah M, Moon JW, Yang LR, et al. Dental implants in the oral rehabilitation of a teenager with hypohidrotic ectodermal dysplasia: report of a case. *Int J Oral Maxillofac Implants* 1997;12:252.
- Kupietzky A, Hout M. Hypohidrotic ectodermal dysplasia: characteristics and treatment. *Quintessence Int* 1995;26:285.
- Pigno MA, Blackman RB, Cronin RJ Jr. Prosthodontic management of ectodermal dysplasia: a review of the literature. *J Prosthet Dent* 1996;76:541.

Hereditary Hemorrhagic Telangiectasia

- Flint SR, Keith O, Scully C. Hereditary hemorrhagic telangiectasia: family study and review. *Oral Surg Oral Med Oral Pathol* 1988;66:440.
- Guttmacher AE, Marchuk DA, White RI Jr. Hereditary hemorrhagic telangiectasia. *N Engl J Med* 1995;333:918.
- Haitjema T, Westermann CJJ, Overtom TTC, et al. Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease): new insights in pathogenesis, complications, and treatment. *Arch Intern Med* 1996;156:714.
- Siegel MB, Keane WM, Atkins JP Jr, et al. Control of epistaxis in patients with hereditary hemorrhagic telangiectasia. *Head Neck Surg* 1991;105:675.

Pachyonychia Congenita

- Feinstein A, Friedman J, Schewach-Millet M. Pachyonychia congenita. *J Am Acad Dermatol* 1988;19:705.
- Haber RM, Rose TH. Autosomal recessive pachyonychia congenita. *Arch Dermatol* 1986;122:919.
- Maser ED. Oral manifestations of pachyonychia congenita. *Oral Surg Oral Med Oral Pathol* 1977;43:373.
- Paller AS, Moore JA, Scher R. Pachyonychia congenita tarda: a late onset form of pachyonychia congenita. *Arch Dermatol* 1991;127:701.
- Su WPD, Chun SI, Hammond DE, et al. Pachyonychia congenita: a clinical study of 12 cases and review of the literature. *Pediatr Dermatol* 1990;7:33.

White Sponge Nevus

- Jorgenson RJ, Levin LS. White sponge nevus. *Arch Dermatol* 1981;117:73.
- McDonagh AJG, Gawkrödger DJ, Walker AE. White sponge nevus successfully treated with topical tetracycline. *Clin Exp Dermatol* 1990;15:152.
- Morris R, Gansler TS, Rudisill MT, et al. White sponge nevus: diagnosis by light microscopic and ultrastructural cytology. *Acta Cytol* 1988;32:357.
- Nichols GE, Cooper PH, Underwood PB Jr, et al. White sponge nevus. *Obstet Gynecol* 1990;76:545.

Darier's Disease

- Adams AM, Macleod RI, Munro CS. Symptomatic and asymptomatic salivary duct abnormalities in Darier's disease: a sialographic study. *Dentomaxillofac Radiol* 1994;23:25.
- Burge SM, Wilkinson JD. Darier-White disease: a review of the clinical features in 163 patients. *J Am Acad Dermatol* 1992;27:40.
- Macleod RI, Munro CS. The incidence and distribution of oral lesions in patients with Darier's disease. *Br Dent J* 1991;171:133.
- Weathers DR, Driscoll RM. Darier's disease of the oral mucosa. *Oral Surg Oral Med Oral Pathol* 1974;37:711.

Tuberous Sclerosis

- Harrison MG, O'Neill ID, Chadwick BL. Odontogenic myxoma in an adolescent with tuberous sclerosis. *J Oral Pathol Med* 1997;26:339.
- Kwiatkowski DJ, Short MP. Tuberous sclerosis. *Arch Dermatol* 1994;130:348.

- Miyamoto Y, Satomura K, Rikimaru K, et al. Desmoplastic fibroma of the mandible associated with tuberous sclerosis. *J Oral Pathol Med* 1995;24:93.
- Mlynarczyk G. Enamel pitting: a common symptom of tuberous sclerosis. *Oral Surg Oral Med Oral Pathol* 1991;71:63.
- Scully C. Orofacial manifestations in tuberous sclerosis. *Oral Surg Oral Med Oral Pathol* 1977;44:706.

Dyskeratosis Congenita

- Alter BP, Gardner FH, Hall RE. Treatment of dyskeratosis congenita with granulocyte colony-stimulating factor and erythropoietin. *Br J Haematol* 1997;97:309.
- Anil S, Beena VT, Raji MA, et al. Oral squamous cell carcinoma in a case of dyskeratosis congenita. *Ann Dent* 1994;53:15.
- Drachtman RA, Alter BP. Dyskeratosis congenita: clinical and genetic heterogeneity: report of a new case and review of the literature. *Am J Pediatr Hematol Oncol* 1992;14:297.
- Yavuzylmaz E, Yamalik N, Yetgin S, et al. Oral-dental findings in dyskeratosis congenita. *J Oral Pathol Med* 1992;21:280.

Peutz-Jeghers Syndrome

- DePadova-Elder SM, Milgraum SS. Q-switched ruby laser treatment of labial lentigines in Peutz-Jeghers syndrome. *J Dermatol Surg Oncol* 1994;20:830.
- Giardiello FM, Welsh SB, Hamilton SR, et al. Increased risk of cancer in the Peutz-Jeghers syndrome. *N Engl J Med* 1987;316:1511.
- Hizawa K, Iida M, Matsumoto T, et al. Cancer in Peutz-Jeghers syndrome. *Cancer* 1993;72:2777.
- Rodu B, Martinez MG Jr. Peutz-Jeghers syndrome and cancer. *Oral Surg Oral Med Oral Pathol* 1984;58:584.

Melanotic Macule

- Ashinoff R, Geronemus RG. Q-switched ruby laser treatment of labial lentigos. *J Am Acad Dermatol* 1992;27:809.
- Buchner A, Hansen LS. Melanotic macule of the oral mucosa. *Oral Surg Oral Med Oral Pathol* 1979;48:244.
- Ho KK-L, Dervan P, O'Loughlin S, et al. Labial melanotic macule: a clinical, histopathologic, and ultrastructural study. *J Am Acad Dermatol* 1993;28:33.
- Kaugars GE, Heise AP, Riley WT, et al. Oral melanotic macules: a review of 353 cases. *Oral Surg Oral Med Oral Pathol* 1993;76:59.
- Weathers DR, Corio RL, Crawford BE, et al. The labial melanotic macule. *Oral Surg Oral Med Oral Pathol* 1976;42:196.

Oral Melanoacanthosis

- Goode RK, Crawford BE, Callihan MD, et al. Oral melanoacanthoma. *Oral Surg Oral Med Oral Pathol* 1983;56:622.
- Heine BT, Drummond JF, Damm DD, et al. Bilateral oral melanoacanthoma. *Gen Dent* 1996;44:451.
- Tomich CE, Zunt SL. Melanoacanthosis (melanoacanthoma) of the oral mucosa. *J Dermatol Surg Oncol* 1990;16:231.

Erythema Migrans

- Bánóczy J, Szabó L, Csiba Á. Migratory glossitis: a clinical-histologic review of seventy cases. *Oral Surg Oral Med Oral Pathol* 1975;39:113.
- Brooks JK, Balciunas BA. Geographic stomatitis: review of the literature and report of five cases. *J Am Dent Assoc* 1987;115:421.
- Espelid M, Bang G, Johannessen AC, et al. Geographic stomatitis: report of 6 cases. *J Oral Pathol Med* 1991;20:425.
- Fenerli A, Papanicolaou S, Papanicolaou M, et al. Histocompatibility antigens and geographic tongue. *Oral Surg Oral Med Oral Pathol* 1993;76:476.
- Morris LF, Phillips CM, Binnie WH, et al. Oral lesions in patients with psoriasis: a controlled study. *Cutis* 1992;49:339.
- Sigal MJ, Mock D. Symptomatic benign migratory glossitis: report of two cases and literature review. *Pediatr Dent* 1992;14:392.

Transient Lingual Papillitis

- Lacour J-P, Perrin C. Eruptive familial lingual papillitis: a new entity? *Pediatr Dermatol* 1997;14:13.
- Whitaker SB, Krupa JJ III, Singh BB. Transient lingual papillitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82:441.

Psoriasis

- Hietanen J, Salo OP, Kanerva L, et al. Study of the oral mucosa in 200 consecutive patients with psoriasis. *Scand J Dent Res* 1984;92:50.
- Morris LF, Phillips CM, Binnie WH, et al. Oral lesions in patients with psoriasis: a controlled study. *Cutis* 1992;49:339.
- Ulmansky M, Michelle R, Azaz B. Oral psoriasis: report of six new cases. *J Oral Pathol Med* 1995;24:42.
- Zhu J-F, Kaminski MJ, Pulitzer DR, et al. Psoriasis: pathophysiology and oral manifestations. *Oral Dis* 1996;2:135.

Systemic Sclerosis and CREST Syndrome

- Marmary Y, Glaiss R, Pisanty S. Scleroderma: oral manifestations. *Oral Surg Oral Med Oral Pathol* 1981;52:32.
- Mitchell H, Bolster MB, LeRoy EC. Scleroderma and related conditions. *Med Clin North Am* 1997;81(1):129.
- Nagy G, Kovács J, Zeher M, et al. Analysis of the oral manifestations of systemic sclerosis. *Oral Surg Oral Med Oral Pathol* 1994;77:141.
- Rout PGJ, Hamburger J, Potts AJC. Orofacial radiological manifestations of systemic sclerosis. *Dentomaxillofac Radiol* 1996;25:193.
- Velayos EE, Masi AT, Stevens MB, et al. The "CREST" syndrome: comparison with systemic sclerosis (scleroderma). *Arch Intern Med* 1979;139:1240.
- Wood RE, Lee P. Analysis of the oral manifestations of systemic sclerosis (scleroderma). *Oral Surg Oral Med Oral Pathol* 1988;65:172.

Lupus Erythematosus

- Callen JP. Lupus erythematosus. In: Demis DJ, ed. *Clinical dermatology*. Philadelphia: Lippincott-Raven, 1992.
- Laman SD, Provost TT. Cutaneous manifestations of lupus erythematosus. *Rheum Dis Clin North Am* 1994;20:195.
- Pisetsky DS, Gilkeson G, St Clair EW. Systemic lupus erythematosus: diagnosis and treatment. *Med Clin North Am* 1997;81(1):113.
- Rhodus NL, Johnson DK. The prevalence of oral manifestations of systemic lupus erythematosus. *Quintessence Int* 1990;21:461.
- Schiødt M. Oral manifestations of lupus erythematosus. *Int J Oral Surg* 1984;13:101.

Pemphigus Vulgaris

- Chrysomallis F, Loannides D, Teknetzis A, et al. Treatment of oral pemphigus vulgaris. *Int J Dermatol* 1994;33:803.
- Korman N. Pemphigus. *J Am Acad Dermatol* 1988;18:1219.
- Lamey PJ, Rees TD, Binnie WH, et al. Oral presentation of pemphigus vulgaris and its response to systemic steroid therapy. *Oral Surg Oral Med Oral Pathol* 1992;74:54.
- Robinson JC, Lozada-Nur F, Frieden I. Oral pemphigus vulgaris: a review of the literature and a report on the management of 12 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997;84:349.
- Williams DM. Vesiculobullous mucocutaneous disease: pemphigus vulgaris. *J Oral Pathol Med* 1989;18:544.

Paraneoplastic Pemphigus

- Anhalt GJ, Kim S, Stanley JR, et al. Paraneoplastic pemphigus: an autoimmune mucocutaneous disease associated with neoplasia. *N Engl J Med* 1990;323:1729.
- Camisa C, Helm TN, Liu Y-C, et al. Paraneoplastic pemphigus: a report of three cases including one long-term survivor. *J Am Acad Dermatol* 1992;27:547.
- Helm TN, Camisa C, Valenzuela R, et al. Paraneoplastic pemphigus: a distinct autoimmune vesiculobullous disorder associated with neoplasia. *Oral Surg Oral Med Oral Pathol* 1993;75:209.

Perniciaro C, Kuechle MK, Colón-Otero G. Paraneoplastic pemphigus: a case of prolonged survival. *Mayo Clin Proc* 1994;69:851.

Chronic Ulcerative Stomatitis

- Beutner EH, Chorzelski TP, Parodi A, et al. Ten cases of chronic ulcerative stomatitis with stratified epithelium-specific antinuclear antibody. *J Am Acad Dermatol* 1991;24:781.
- Church LF Jr, Schosser RH. Chronic ulcerative stomatitis associated with stratified epithelial specific antinuclear antibodies: a case report of a newly described disease entity. *Oral Surg Oral Med Oral Pathol* 1992;73:579.
- Jaremko WM, Beutner EH, Kumar V, et al. Chronic ulcerative stomatitis associated with a specific immunologic marker. *J Am Acad Dermatol* 1990;22:215.
- Lewis JE, Beutner EH, Rostami R, et al. Chronic ulcerative stomatitis with stratified epithelium-specific antinuclear antibodies. *Int J Dermatol* 1996;35:272.

Mucous Membrane Pemphigoid

- Lamey P-J, Rees TD, Binnie WH, et al. Mucous membrane pemphigoid: treatment experience at two institutions. *Oral Surg Oral Med Oral Pathol* 1992;74:50.
- Lilly JP, Spivey JD, Fotos PG. Benign mucous membrane pemphigoid with advanced periodontal involvement: diagnosis and therapy. *J Periodontol* 1995;66:737.
- Poskitt L, Wojnarowska F. Minimizing cicatricial pemphigoid orodysphagia with minocycline. *Br J Dermatol* 1995;132:784.
- Poskitt L, Wojnarowska F. Treatment of cicatricial pemphigoid with tetracycline and nicotinamide. *Clin Exp Dermatol* 1995;20:258.
- Silverman S Jr, Gorsky M, Lozada-Nur F, et al. Oral mucous membrane pemphigoid: a study of sixty-five patients. *Oral Surg Oral Med Oral Pathol* 1986;61:233.
- Vincent SD, Lilly GE, Baker KA. Clinical, historic, and therapeutic features of cicatricial pemphigoid: a literature review and open therapeutic trial with corticosteroids. *Oral Surg Oral Med Oral Pathol* 1993;76:453.
- Williams DM. Vesiculo-bullous mucocutaneous disease: benign mucous membrane and bullous pemphigoid. *J Oral Pathol Med* 1990;19:16.

Lichen Planus

- Duffey DC, Eversole LR, Abemayor E. Oral lichen planus and its association with squamous cell carcinoma: an update on pathogenesis and treatment implications. *Laryngoscope* 1996;106:357.
- Eisenberg E, Krutchkoff DJ. Lichenoid lesions of oral mucosa: diagnostic criteria and their importance in the alleged relationship to oral cancer. *Oral Surg Oral Med Oral Pathol* 1992;73:699.
- Gorsky M, Raviv M, Moskona D, et al. Clinical characteristics and treatment of patients with oral lichen planus in Israel. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82:644.
- Porter SR, Kirby A, Olsen I, et al. Immunologic aspects of dermal and oral lichen planus: a review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997;83:358.
- Silverman S Jr, Gorsky M, Lozada-Nur F. A prospective follow-up study of 570 patients with oral lichen planus: persistence, remission, and malignant association. *Oral Surg Oral Med Oral Pathol* 1985;60:30.
- Thompson DF, Skaehill PA. Drug-induced lichen planus. *Pharmacotherapy* 1994;14:561.
- Vincent SD, Fotos PG, Baker KA, et al. Oral lichen planus: the clinical, historical, and therapeutic features of 100 cases. *Oral Surg Oral Med Oral Pathol* 1990;70:165.

Erythema Multiforme

- Barone CM, Bianchi MA, Lee B, et al. Treatment of toxic epidermal necrolysis and Stevens-Johnson syndrome in children. *J Oral Maxillofac Surg* 1993;51:264.
- Côte B, Wechsler J, Bastuji-Garin S, et al. Clinicopathologic correlation in erythema multiforme and Stevens-Johnson syndrome. *Arch Dermatol* 1995;131:1268.
- Farthing PM, Maragou P, Coates M, et al. Characteristics of the oral lesions in patients with cutaneous recurrent erythema multiforme. *J Oral Pathol Med* 1995;24:9.
- Lozada-Nur F, Cram D, Gorsky M. Clinical response to levamisole in thirty-nine patients with erythema multiforme: an open prospective study. *Oral Surg Oral Med Oral Pathol* 1992;74:294.
- Nazif MM, Ranalli DN. Stevens-Johnson syndrome: a report of fourteen pediatric cases. *Oral Surg Oral Med Oral Pathol* 1982;53:263.
- Schofield JK, Tatnall FM, Leigh IM. Recurrent erythema multiforme: clinical features and treatment in a large series of patients. *Br J Dermatol* 1993;128:542.

Stewart MG, Duncan NO III, Franklin DJ, et al. Head and neck manifestations of erythema multiforme in children. *Otolaryngol Head Neck Surg* 1994;111:236.

Epidermolysis Bullosa

Harel-Raviv M, Bernier S, Raviv E, et al. Oral epidermolysis bullosa in adults. *Spec Care Dent* 1995;15:144.

Pearson RW. Clinicopathologic types of epidermolysis bullosa and their nondermatological complications. *Arch Dermatol* 1988;124:718.

Wright JT, Fine J-D, Johnson LB. Oral soft tissues in hereditary epidermolysis bullosa. *Oral Surg Oral Med Oral Pathol* 1991;71:440.

Wright JT, Fine J-D, Johnson L. Hereditary epidermolysis bullosa: oral manifestations and dental management. *Pediatr Dent* 1993;15:242.

Wright JT, Fine J-D, Johnson L. Dental caries risk in hereditary epidermolysis bullosa. *Pediatr Dent* 1994;16:427.