Recurrent aphthous ulcers and herpes simplex account for the majority. Persistent and deep aphthous ulcers can be idiopathic or can accompany HIV/AIDS. Aphthous lesions are often the presenting symptom in *Behçet's syndrome* **(Chap. 364)**. Similar-appearing, though less painful, lesions may occur in reactive arthritis, and aphthous ulcers are occasionally present during phases of *discoid* or *systemic lupus erythematosus* **(Chap. 360)**. Aphthous-like ulcers are seen in *Crohn's disease* **(Chap. 326)**, but, unlike the common aphthous variety, they may exhibit granulomatous inflammation on histologic examination. Recurrent aphthae are more prevalent in patients with *celiac disease* and have been reported to remit with elimination of gluten.

Of major concern are chronic, relatively painless ulcers and mixed red/white patches (erythroplakia and leukoplakia) of >2 weeks' duration. Squamous cell carcinoma and premalignant dysplasia should be considered early and a diagnostic biopsy performed. This awareness and this procedure are critically important because early-stage malignancy is vastly more treatable than late-stage disease. High-risk sites include the lower lip, floor of the mouth, ventral and lateral tongue, and soft palate–tonsillar pillar complex. Significant risk factors for oral cancer in Western countries include sun exposure (lower lip), tobacco and alcohol use, and human papillomavirus infection. In India and some other Asian countries, smokeless tobacco mixed with betel nut, slaked lime, and spices is a common cause of oral cancer. Rarer causes of chronic oral ulcer, such as tuberculosis, fungal infection, granulomatosis with polyangiitis, and midline granuloma, may look identical to carcinoma. Making the correct diagnosis depends on recognizing other clinical features and performing a biopsy of the lesion. The syphilitic chancre is typically painless and therefore easily missed. Regional lymphadenopathy is invariably present. The syphilitic etiology is confirmed with appropriate bacterial and serologic tests.

Disorders of mucosal fragility often produce painful oral ulcers that fail to heal within 2 weeks. *Mucous membrane pemphigoid* and *pemphigus vulgaris* are the major acquired disorders. While their clinical features are often distinctive, a biopsy or immunohistochemical examination should be performed to diagnose