Pemphigus

8

Clinical Types

1. *Pemphigus vulgaris*. Mucous membranes typically are affected first in pemphigus vulgaris. Patients have ill-defined, irregularly shaped, gingival, buccal, or palatine erosionslesions that may precede cutaneous lesions by weeks or months. Cutaneous lesions include flaccid blisters filled with clear fluid that arises on healthy skin or on an erythematous base.
2. *Pemphigus foliaceus*. The primary lesions are small, superficial blisters that are difficult to find because they are transient and transform into erosions. Typical pemphigus foliaceus has scaly, crusted erosions on an erythematosus base resembling those of sebhorrehic dermatitis.
3. *Pemphigus Herpetiformis*. Patients usually present with erythematous, vesicular, bullous, or papular lesions. Mucous membrane involvement is uncommon.
4. *Pemphigus IgA*. IgA pemphigus is characterized by tissue-bound and circulating IgA autoantibodies that target the desmosomal proteins of the epidermis. Lesions form within erythematous plaques or in skin without plaques. The initial, clear, fluid-filled blisters associated with IgA pemphigus fill with neutrophils and transform into pustules.
5. *Pemphigus Erythematosus*. Pemphigus erythematosus, also known as Senear-Usher syndrome, is an overlap syndrome with features of lupus erythematosus (LE) and pemphigus foliaceus. Lesions typically involve the scalp, the face, the upper part of the chest, and the back. Patients with classic pemphigus erythematosus present with small, flaccid bullae with scaling and crusting.
6. *Pemphigus vegetans*. Lesions in skin folds readily form vegetating granulations. In some patients, erosions tend to develop excessive granulation tissue and crusting, and these patients display more vegetating lesions.

Etiology and Pathophysiology

Pemphigus refers to a group of autoimmune or drug-induced blistering diseases of the skin and mucous membranes. These antibodies bind to keratinocyte desmosomes and to desmosome-free areas of the keratinocyte cell membrane which results in a loss of cell-to-cell adhesion, acantholysis. The antibody alone is capable of causing blistering without complement or inflammatory cells. Pemphigus is also reported to be linked to genetic factors. The elderly are more commonly affected. Occurrence is more common in patients with other autoimmune diseases [1–5].

Diagnosis

Direct Immunoflourescence (DIF) of preilesional skin reveals a "chicken wire" pattern of IgG deposition on intercellular cement substance. In the patient's serum, IDIF demonstrates the presence of circulating IgG autoantibodies that bind to epidermis. Circulating intercellular antibodies are detected using IDIF in 80–90 % of patients with pemphigus vulgaris.

Histopathology

Pemphigus is characterized histologically by intraepidermal blister and immunopathologically by the finding of in vivo bound and circulating immunoglobulin G (IgG) antibody directed against the cell surface of keratinocytes. Epidermal basal layer acantholysis is present in pemphigus vulgaris and vegetans. Subcorneal acantholysis is present in pemphigus foliaceus and erythematosus.

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Differential Diagnosis

Pemphigus can resemble several different imflammatory bullous diseases including bullous pemphigoid, dermatitis herpetiformis, erythema multiforme. Pemphigus vulgaris oral lesions may represent herpetic stomatitis or desquamative gingivitis. Pemphigus vegetans can resemble Hailey-Hailey disease, but differentiated by IF and histologic tests.

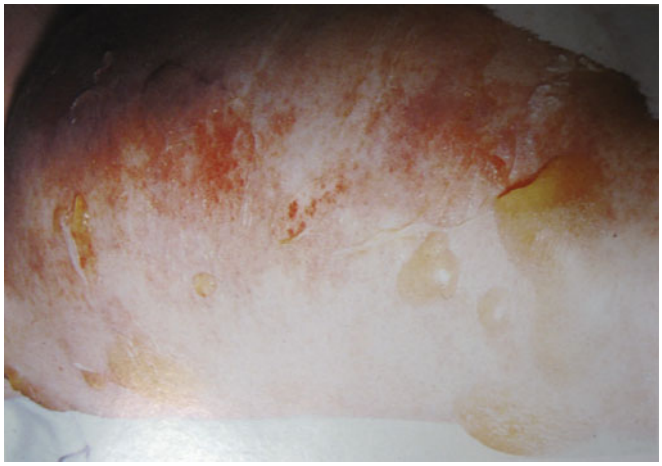
Therapy

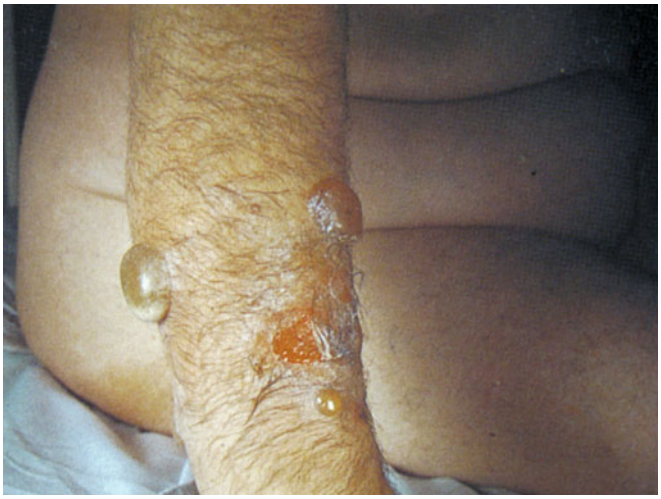
The aim of treatment is to decrease blister formation, promote healing of blisters and erosions, and determine the minimal dose of medication necessary to control the disease process.

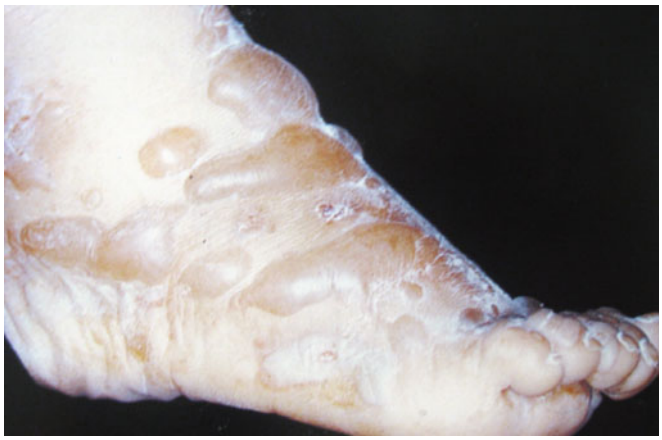
1. Corticosteroids have improved overall mortality. Prednisone, an anti-inflammatory agent, stabilizes lysosomal membranes and suppresses lymphocytes and antibody production.
2. Dapsone, Cyclophosphamide, Sulfasalazine, and Pentoxifylline have been reported as effective adjunctive treatments.
3. Mycophenolate, mofetil and azathioprine have been used as steroid-sparing agents
4. High-dose intravenous immunoglobulin has been reported to have a corticoid-sparing effect, but is quite expensive.
5. Many authorities now use rituximab as first- or second-line therapy. Rituximab (monoclonal antibody presumably targets B cells, the precursor of (auto) antibody-producing plasma cells. Given as intravenous therapy, it shows dramatic effect in some and at least partial remission in other patients.
6. Plasmapharesis reduces the level of circulating pemphigus antibodies.
7. Wet dressings, topical and intralesional glucocorticoid, antimicrobial therapy if documented bacterial infections, and correction of fluid and electrolyte imbalance. Topical care includes burn unit admission, whirlpool baths, topical antibiotics, and nonadherent dressings [6–8].

Prognosis

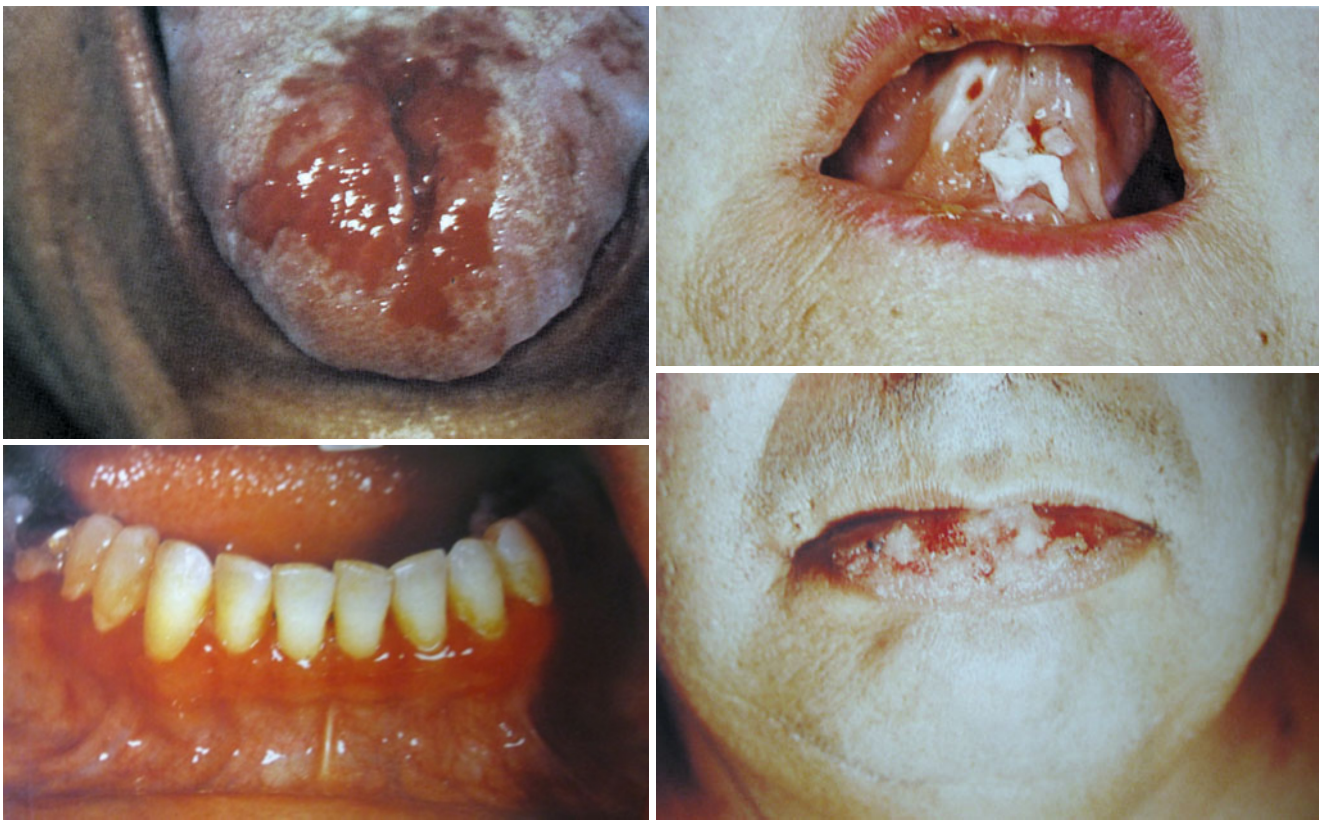
Therapy must be tailored for each patient, taking into account preexisting and coexisting conditions. The use of steroids has improved pemphigus related fatalities greatly, however untreated pemphigus is often fatal due to infections, fluid, and electrolyte disturbances. The outlook is worse in older patients and in patients with extensive disease.



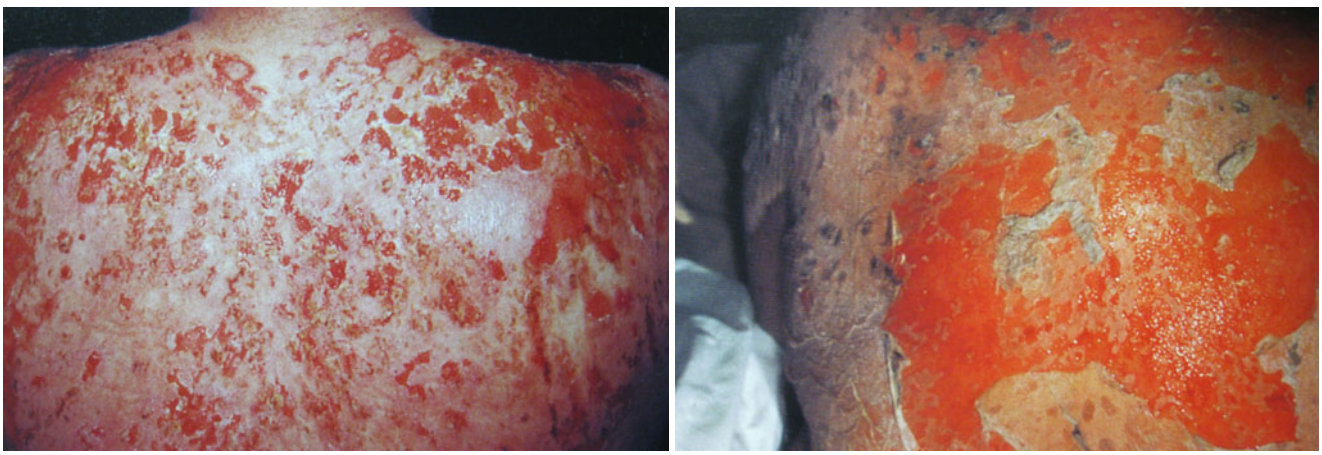




Figs. 8.1, 8.2, and 8.3 Flaccid bullae and erosions with a positive Nikolsky sign (production of blister by applying shearing force to clinically normal skin are the clinical diagnostic hallmarks of pemphigus vutqans



Figs. 8.4, 8.5, 8.6, and 8.7 Oral lesions, particularly ulcerations and erosions of the buccal mucosa, tongue, gingiva, and lips, are often the first sign of pemphigus, and occur in about 70 % of patients



Figs. 8.8 and 8.9 Extensive erosions must be treated as a severe burn with topical care and control of infection and of fluid and electrolyte balance

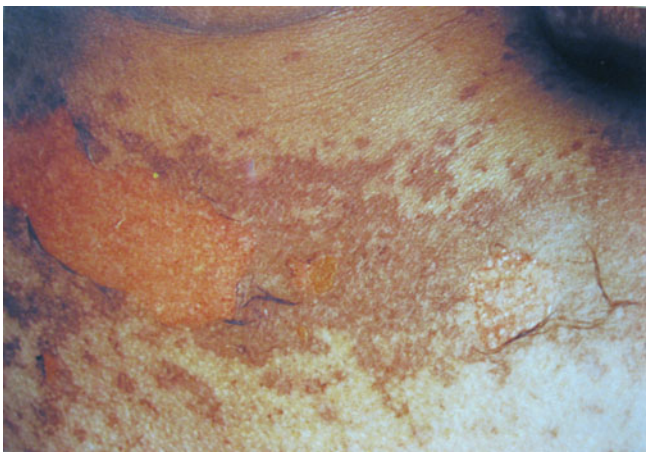
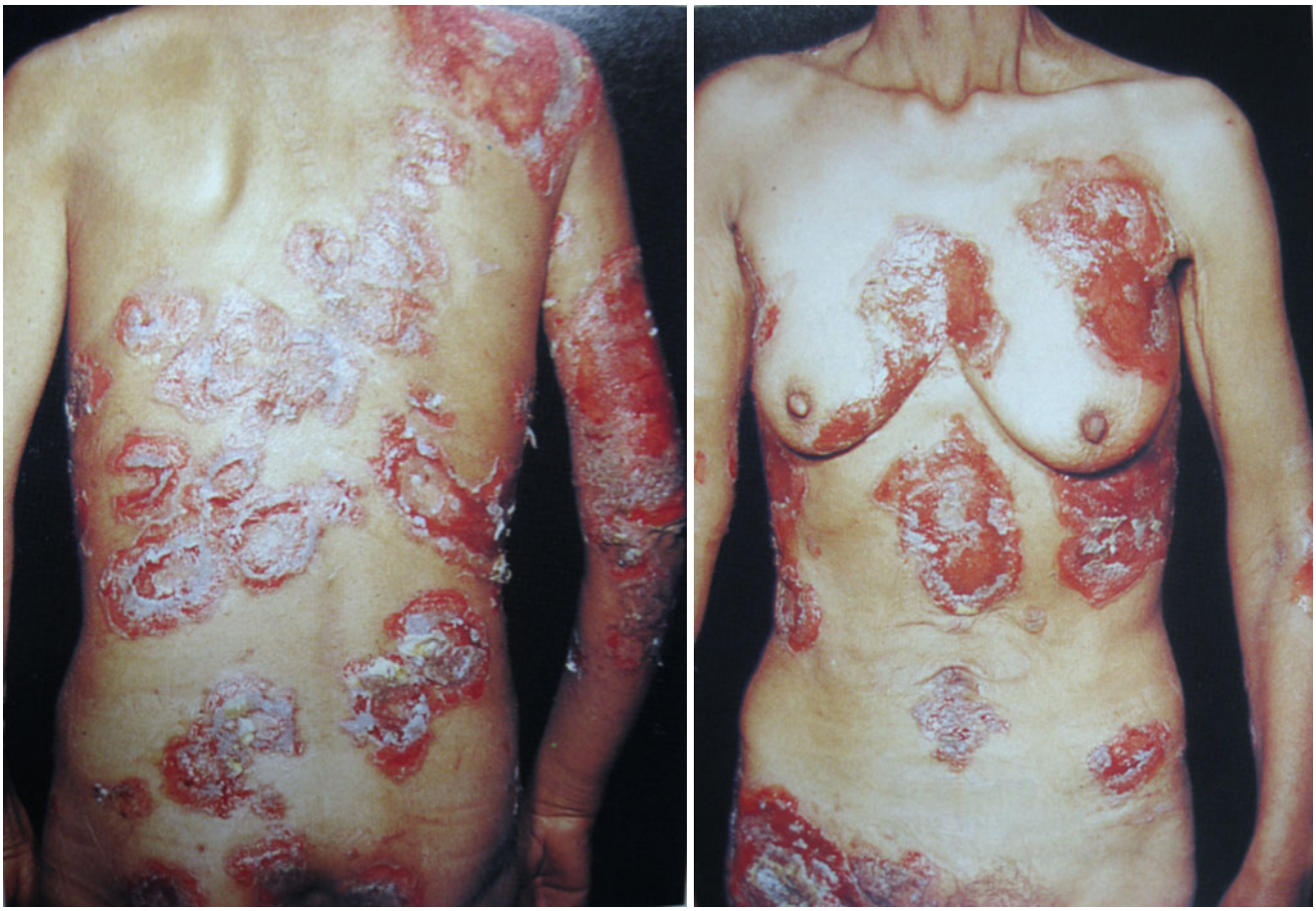


Fig. 8.10 Drug-induced pemphigus vulgaris and pemphigus foliaceus can occur with captopril, penicillamine, rifampin, penicillin, ampicillin, cephalexin, gold, propranolol, meprobamate, piroxicam, and phenobarbital



Figs. 8.11 and 8.12 Beefy, red erosions in a patient with severe pemphigus vulgaris

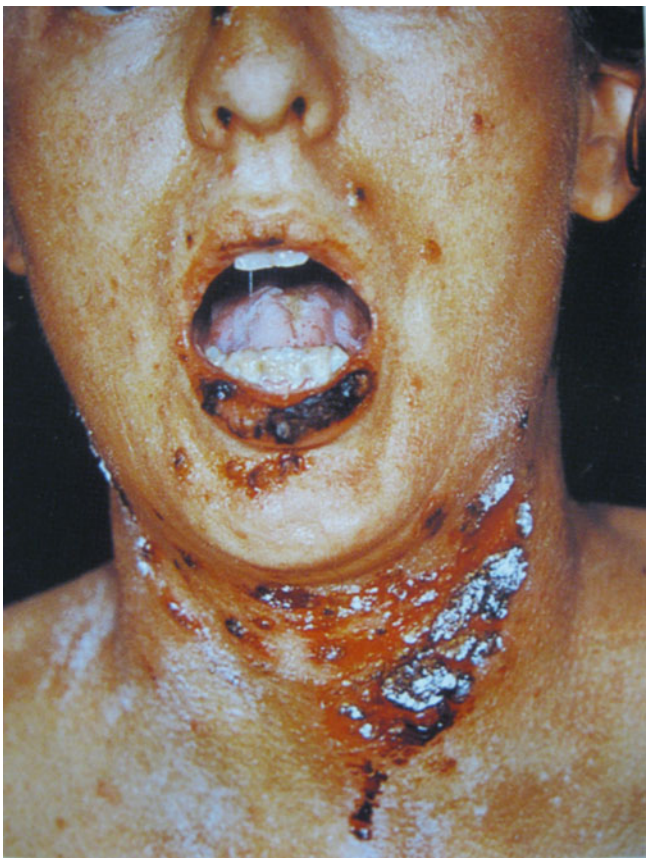
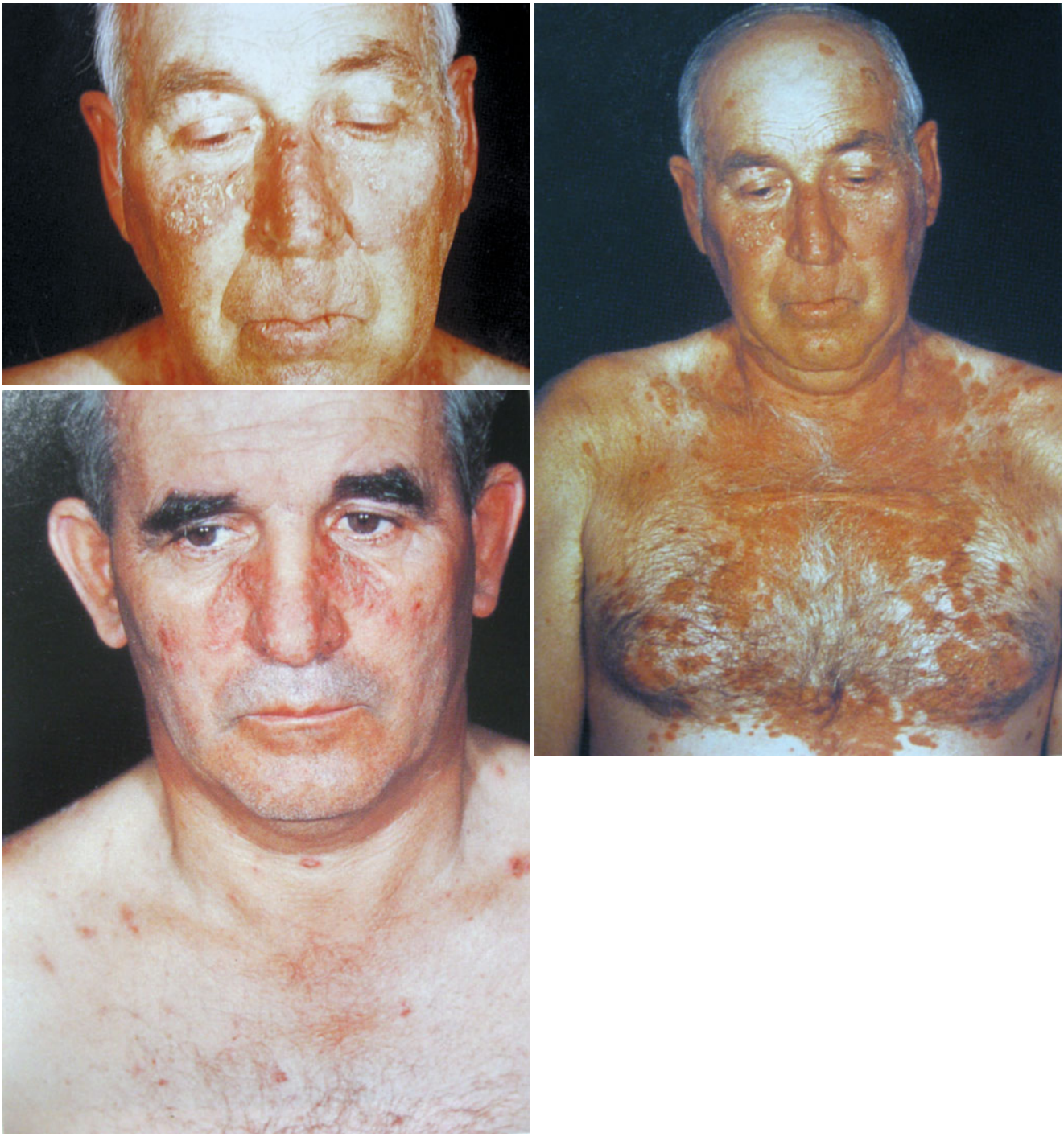
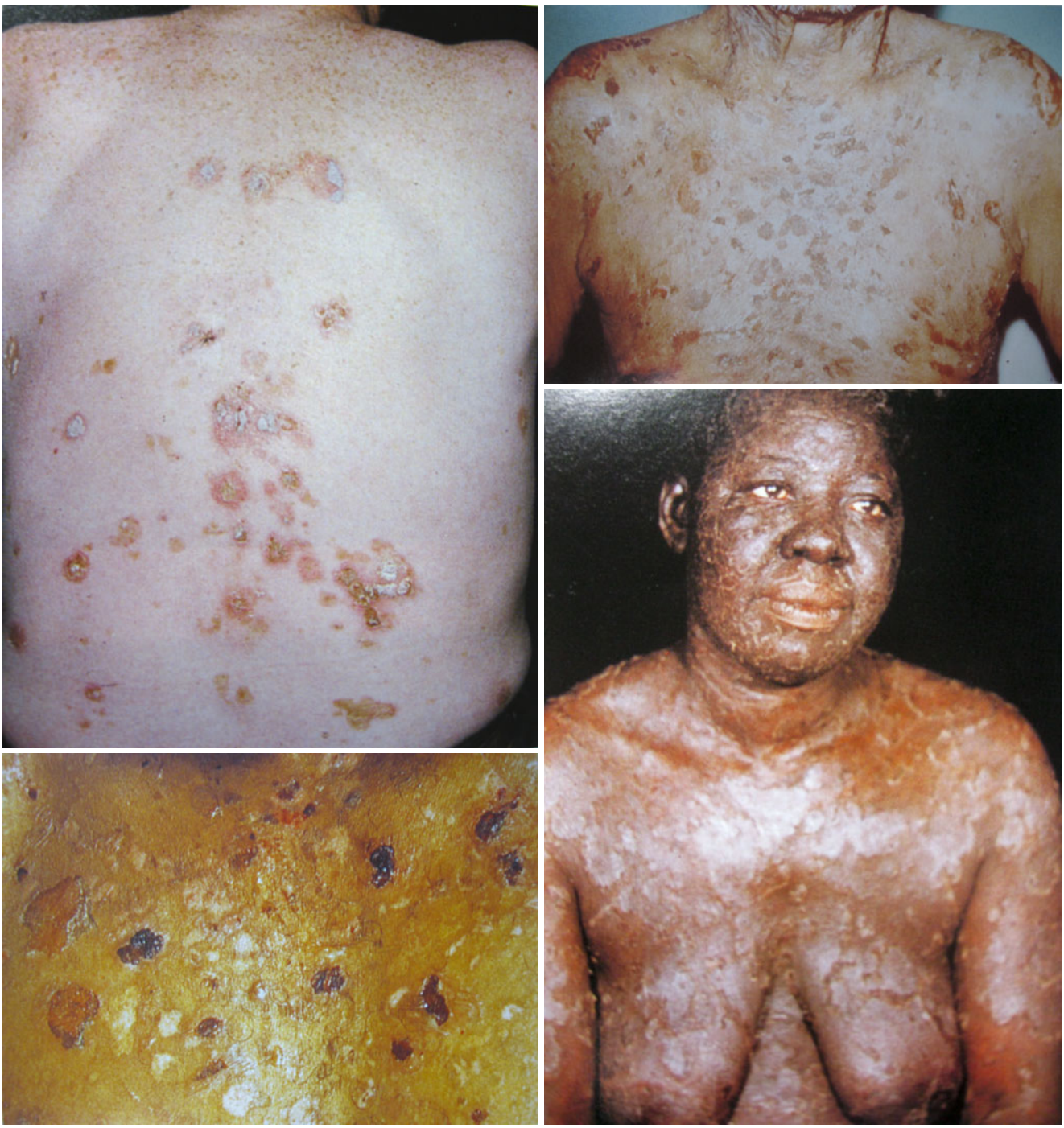


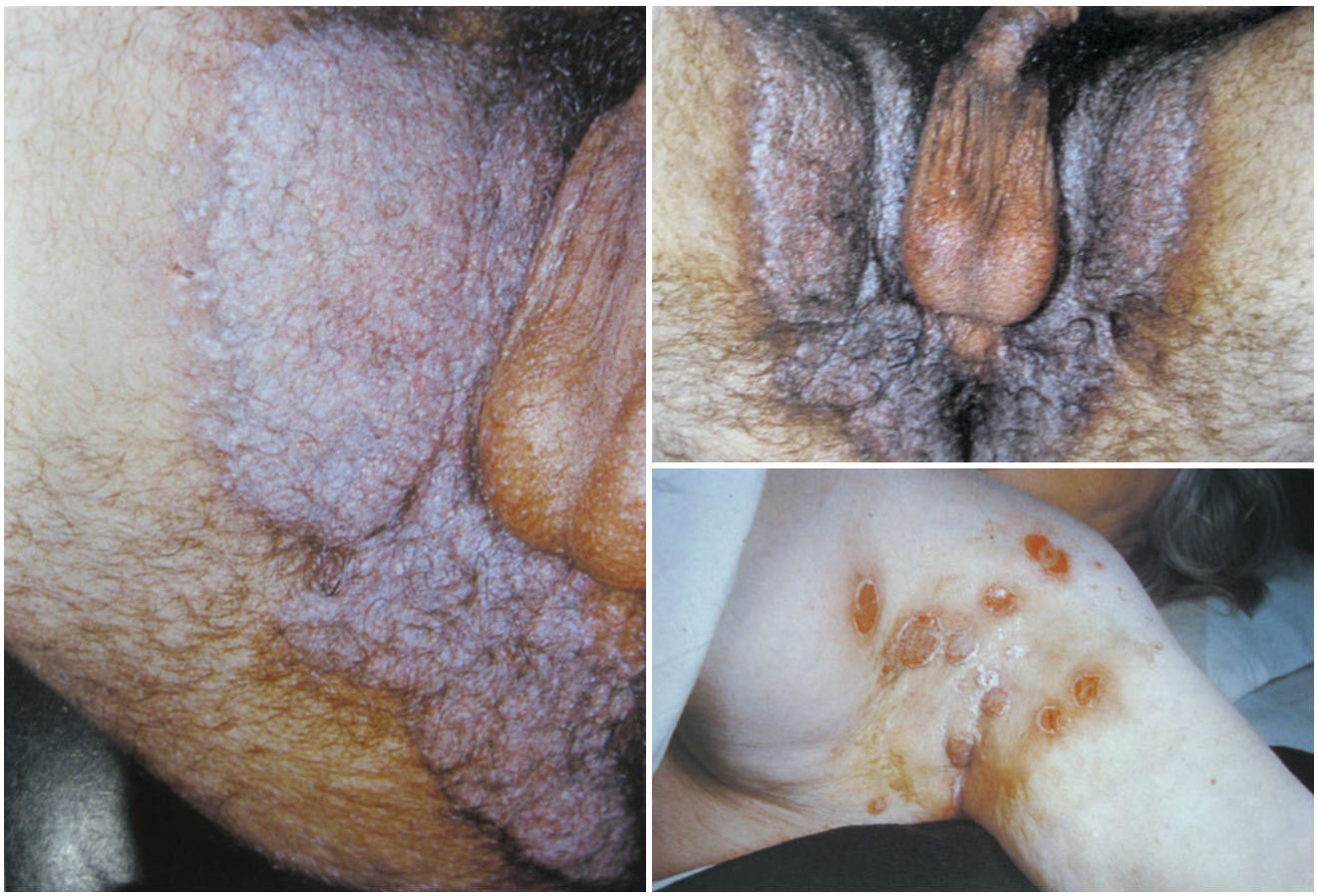
Fig. 8.13 Facial, oral, and neck lesions *in* a patient with pemphigus VUlgaris



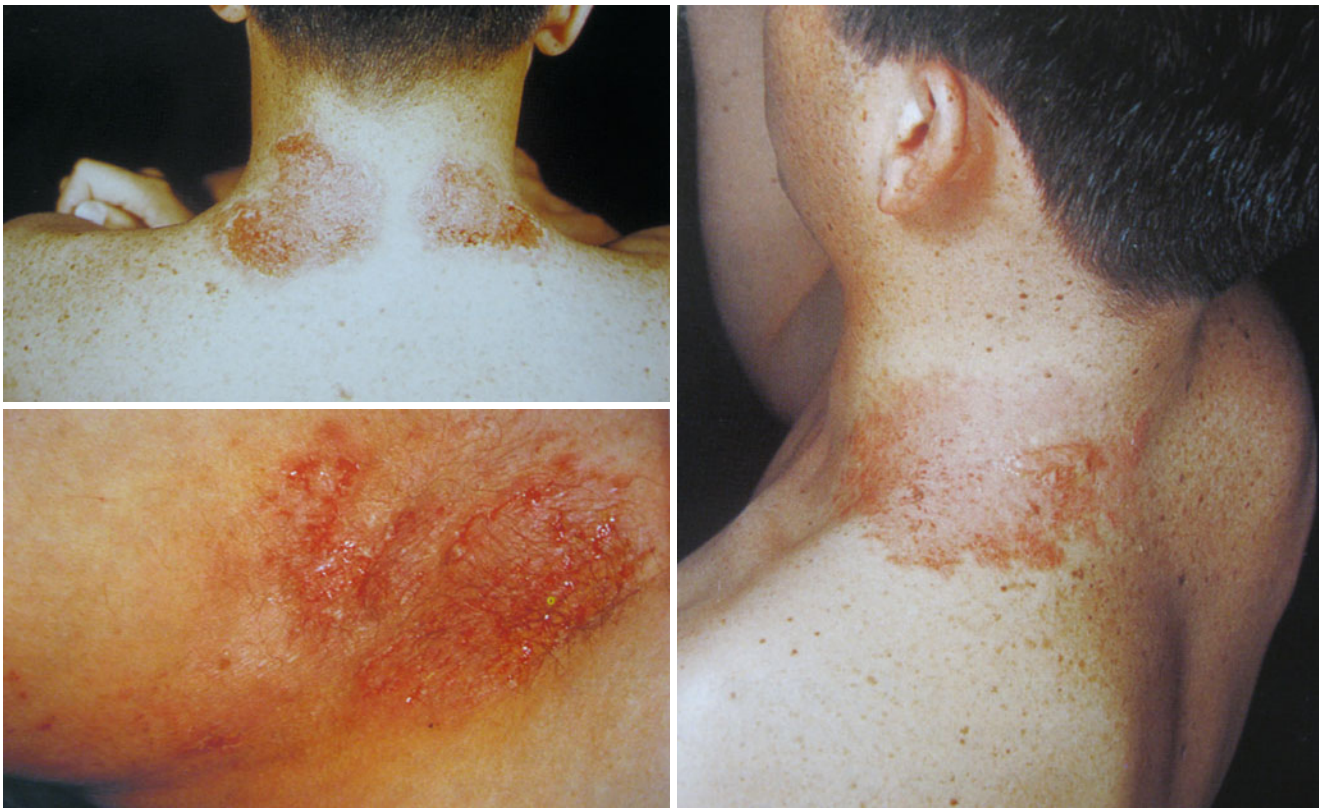
Figs. 8.14, 8.15, and 8.16 Pemphigus erythematosus (Senear-Usher syndrome) combines features of pemphigus vulgaris and lupus erythematosus: positive antinuclear antibody, facial butterfly rash, and positive direct immunofluorescence of IgG, M, and/or C3-a so-called lupus erythematosus band-along the dermal-epidermal junction, in addition to the intercellular staining



Figs. 8.17, 8.18, 8.19, and 8.20 Pemphigus foliaceus demonstrates superficial desquamation and erosions instead of fluid-filled blisters. It clinically resembles seborrheic dermatitis or, in generalized cases, exfoliative dermatitis



Figs. 8.21, 8.22, and 8.23 Pemphigus *vegetans* is manifested by verrucous, *vegetating*, moist eroded plaques in intertriginous areas, clinically resembling those of Hailey-Hailey disease (see Figs. 8.26, 8.27, and 8.28)



Figs. 8.24, 8.25, and 8.26 Hailey-Hailey disease (familial benign pemphigus) is an autosomal dominant condition with intertriginous vesicular plaques and erosions that rapidly become superinfected. Histologically, it shares features with both pemphigus vulgaris and Darier's disease (*see* Fig. 7.8). Direct and indirect immunofluorescence studies are *negative*, in contrast to pemphigus

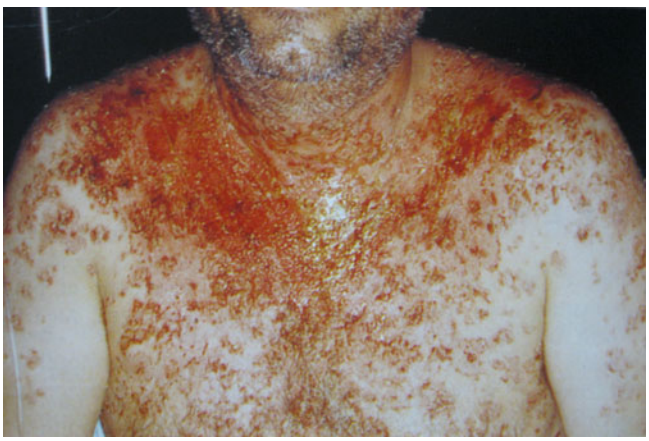
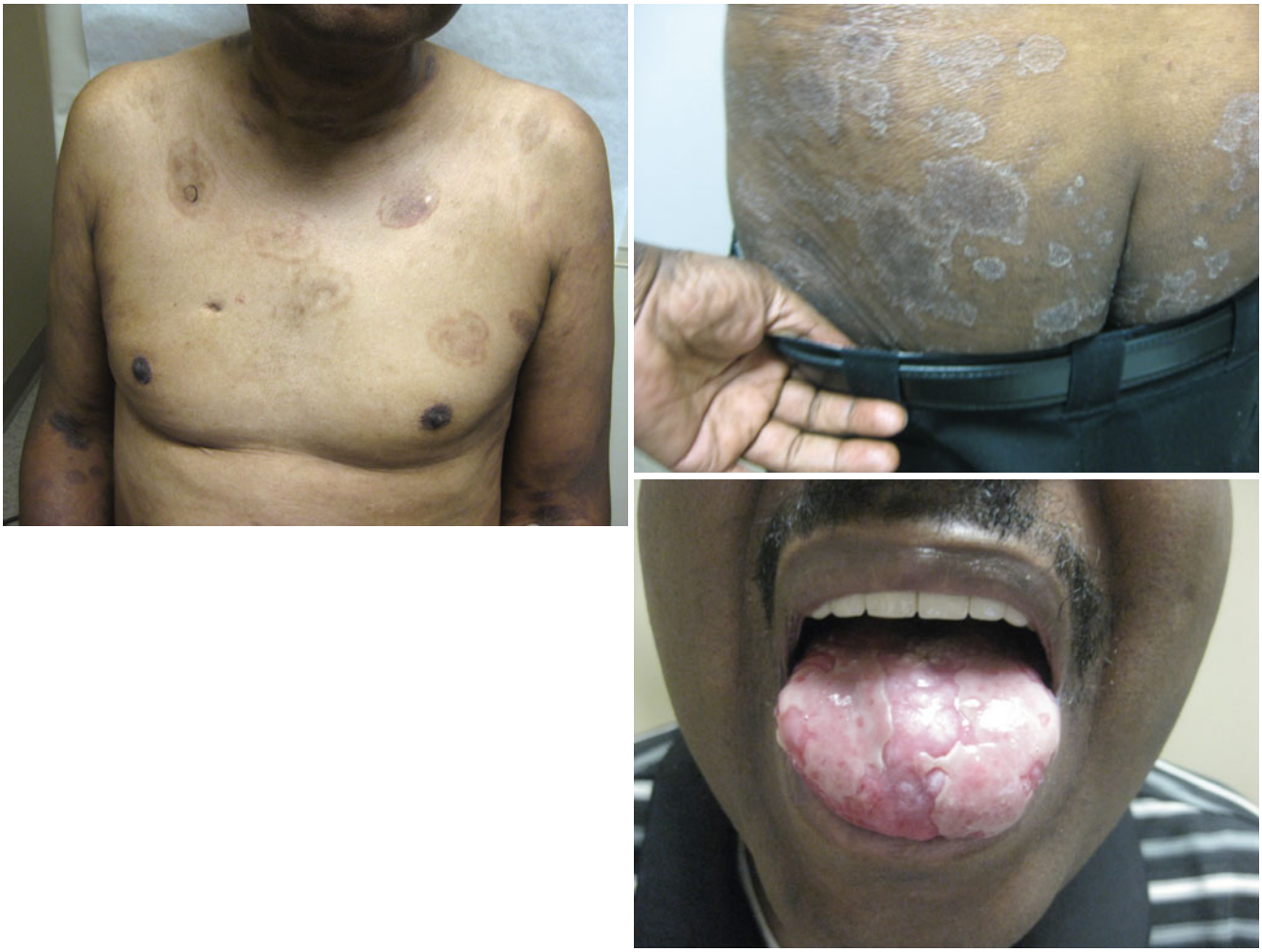


Fig. 8.27 Severe pemphigus vulgaris resembles a burn



Figs. 8.28, 8.29, 8.30 Pemphigus vulgaris affecting chest, buttocks and tongue

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