# Stomatological profile of some dermatoses:
# Pemphigus,
# Lichen planus,
# Erythema multiforme,
# Stevens-Johnson syndrome,
# Toxic epidermal necrolysis
# (Lyell syndrome)

# Pemphigus

# Definition

- Pemphigus family is a group of autoimmune blistering diseases.

- Pemphigus vulgaris, the prototype of the pemphigus family, is a serious, acute or chronic, bullous, autoimmune disease of skin and mucous membranes that is often fatal unless treated with immunosuppressive agents.

# Epidemiology and Etiology

- Age of onset: 40 to 60 years
- Sex: equal incidence in males and females
- Etiology: autoimmune disorder

# Pathogenesis

- A loss of normal cell-to-cell adhesion in the epidermis occurs as a result of circulating antibodies of the IgG class;
- These antibodies bind to cell surface glycoproteins of the epidermis and induce acantholysis, probably by the activation of serine proteases;
- The superficial subtypes of pemphigus are associated with autoantibodies to desmoglein 1, a 160 kD transmembrane desmosomal component;
- The deep subtypes of pemphigus are associated with autoantibodies to desmoglein 3, a 130 kd transmembrane desmosomal component, and to desmoglein 1.

# Pemphigus Classification

- Deep forms of pemphigus:
- Pemphigus vulgaris
- Pemphigus vegetant
- Superficial forms of pemphigus:
- Pemphigus foliaceus
- Pemphigus erythematosus
- Endemic pemphigus (fogo selvageum)
- Paraneoplastic pemphigus
- Drug-Induced pemphigus

# Pemphigus Vulgaris (PV)
# History

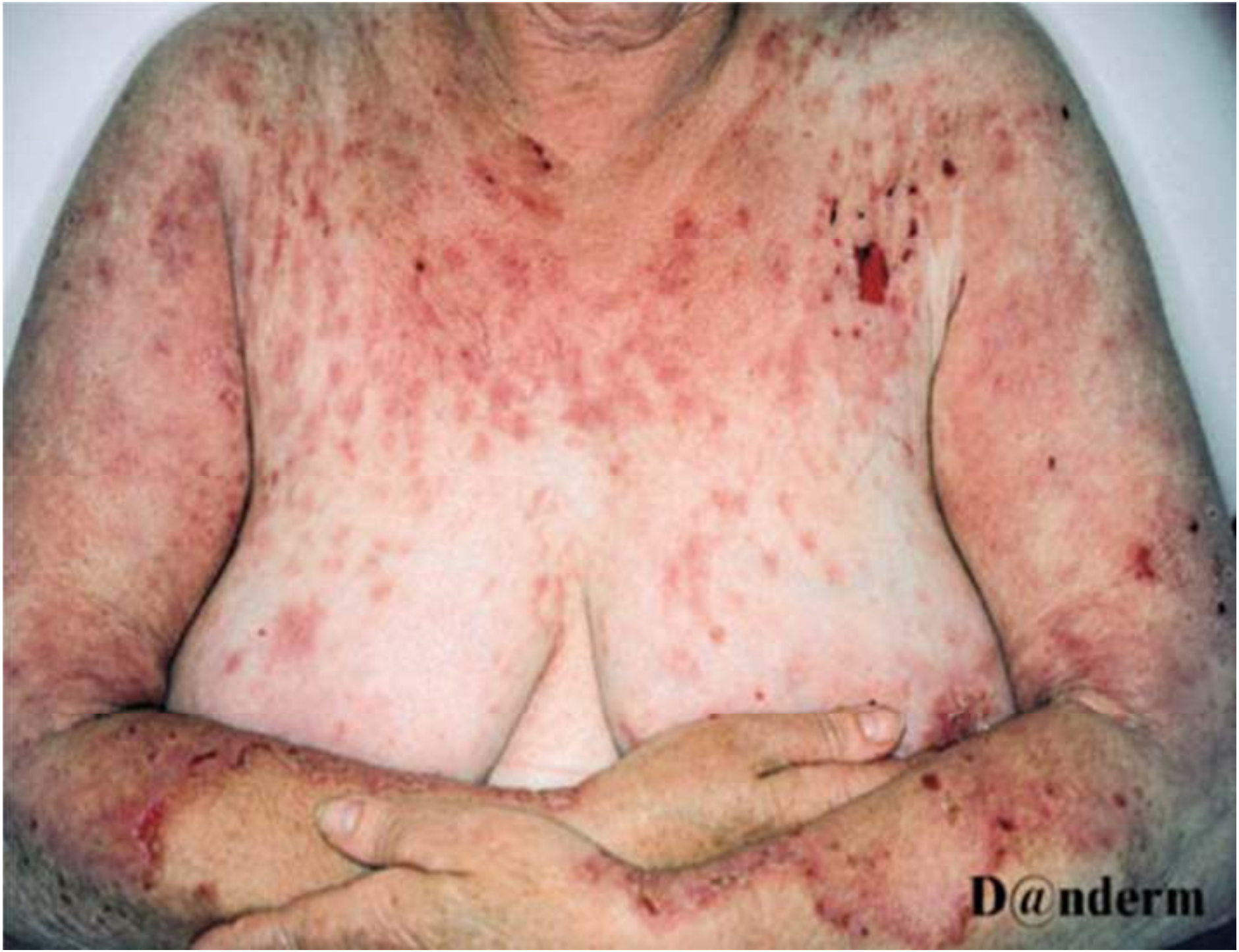
- PV usually starts in the oral mucosa, and months may elapse before skin lesions occur
- Lesions may be localized for 6 to 12 months, after which generalized bullae occur
- No pruritus, but burning and pain
- Painful and tender mouth lesions may prevent adequate food intake
- Epistaxis, hoarseness, dysphagia
- Weakness, malaise, weight loss (with prolonged mouth involvement).

# Physical examination

- Skin lesions: round or oval vesicles and bullae with serous content, flaccid, easily ruptured, and weeping, arising on normal skin, randomly scattered, discrete
- Localized to mouth or generalized with a random pattern
- Extensive erosions that bleed easily, crusts particularly on scalp
- Since blisters rupture so easily, only erosions are seen in many patients.

# Physical examination

- Nikolsky's sign: dislodging of epidermis by lateral finger pressure in the vicinity of lesions, which leads to an erosion
- Asboe-Hansen sign: pressure on bulla leads to lateral extension of blister
- Pear sign: pear-like bulla in patient's vertical position
- Sites of predilection: scalp, face, chest, axillae, groin, umbilicus; extensive involvement of back in bed-ridden patients
- Mucous membranes: bullae rarely seen, erosions of mouth and nose, pharynx and larynx, vagina.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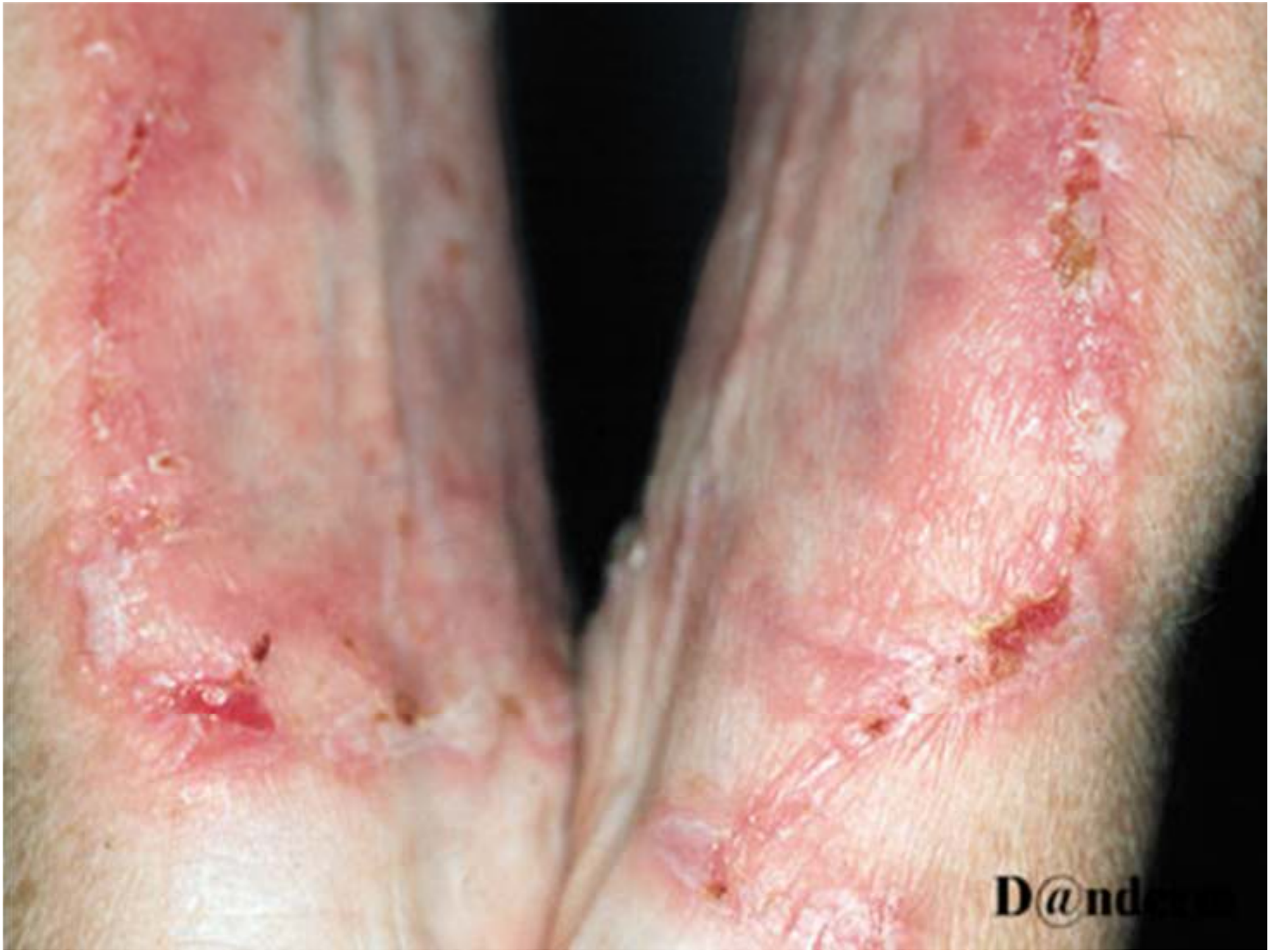
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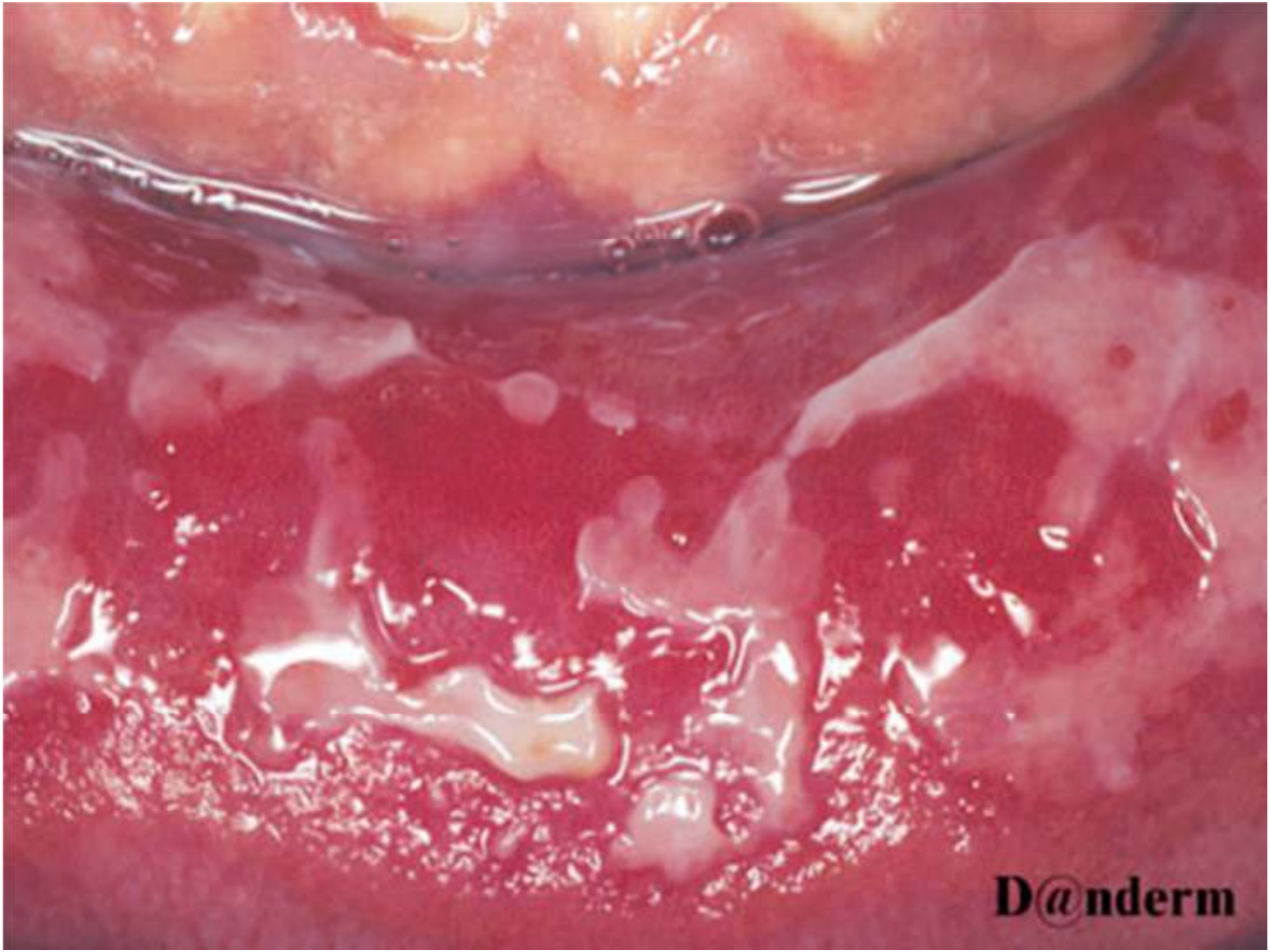
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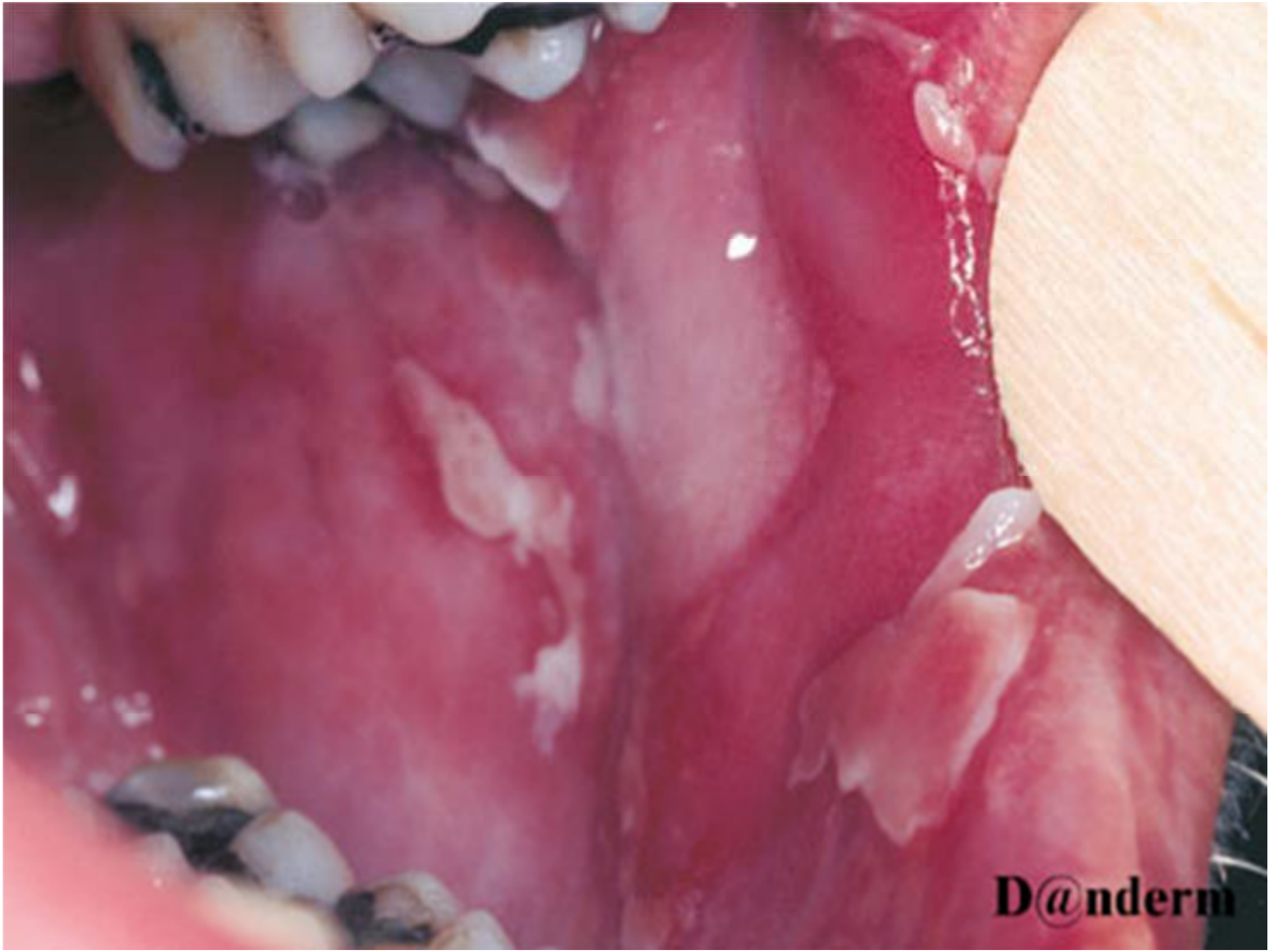
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# Laboratory Examinations

PV dermatopathology (histopathology) in light microscopy:

- (1) loss of intercellular cohesion in lower part of epidermis, leading to
- (2) acantholysis (separation of keratinocytes) and to
- (3) bulla that is split just above the basal cell layer and contains separated, smaller, rounded-up keratinocytes, so-called acantholythic cells.

# Laboratory Examinations

PV immunofluorescence (IF)

- direct IF staining reveals IgG and often C3 deposited in lesional and paralesional skin in the intercellular substance of the epidermis
- indirect IF detects serum circulating autoantibodies (IgG) of anti-desmoglein 3. Titer usually correlates with activity of disease process.

# Course

- The disease inexorably progresses to death unless treated aggressively with immunosuppressive drugs

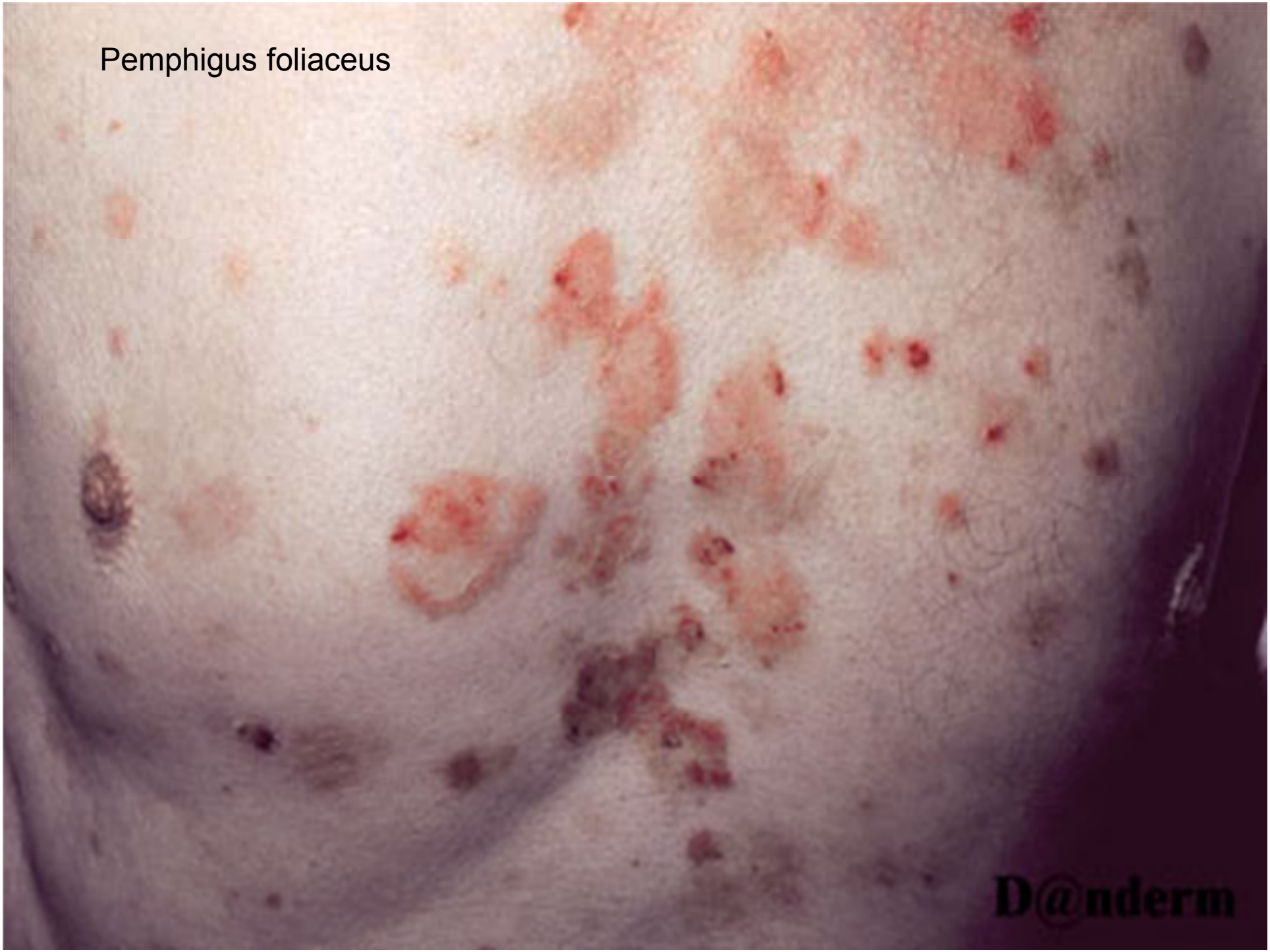
- The mortality rate has been markedly reduced since treatment has become available

# Other Variants: Pemphigus Vegetant (PVeg)

- Usually confined to intertriginous regions, perioral area, neck and scalp;
- Granulomatous vegetating purulent plaques that extend centrifugally;
- Suprabasal acantholysis with intraepidermal abscesses containing mostly eosinophils, epidermis hyperplasia and granulation tissue
- IgG autoantibodies as in PV
- PV may evolve into PVeg and vice versa

# Other Variants: Pemphigus Foliaceus (PF)

- Most commonly on face, scalp, upper chest, and abdomen, but may involve the entire skin, presenting as exfoliative erythroderma
- Superficial form of pemphigus with acantholysis in the granular layer of the epidermis
- Bullae hardly ever present, lesions consist of erythematous patches and erosions covered with crusts
- PF is mediated by circulating autoantibodies to desmoglein 1, which is a superficial intercellular antigen in the desmosomes of keratinocytes.
- That explains the different sites of acantholysis (in the granular layer) and thus the different clinical appearances from PV without mucous membranes involvement.


Pemphigus foliaceus
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# Other Variants: Pemphigus Erythematosus (PE)

- Also called Senear-Usher syndrome
- A localized variety of pemphigus foliaceus largely confined to seborrheic sites
- Erythematous, crusted, and erosive lesions in the “butterfly” area of the face, forehead, presternal, and interscapular regions
- There are immunoglobulin and complement deposits at the dermal-epidermal junction and positive antinuclear antibodies (as in case of lupus erythematosus), in addition to typical intercellular pemphigus antibodies (as in case of pemphigus foliaceus).

# Other Variants: Paraneoplastic Pemphigus

- Mucous membranes primarily and most severely involved
- Lesions combine features of pemphigus vulgaris and erythema multiforme, clinically and histologically.
- Usually associated with lymphoma, thymoma, less commonly with sarcoma/other tumors
- Usually recalcitrant to therapy

# Other Variants: Drug-Induced Pemphigus

- A pemphigus vulgaris or foliaceus – like syndrome can be induced by D-penicilamine and less frequently by captopril and other similar drugs.

- In most, but not all, instances the eruption resolves after termination of therapy with the offending drug

# Pemphigus treatment
# Systemic corticosteroids

- This is the mainstay of therapy for most subtypes of pemphigus.
- Most flares can be controlled with between 1-3 mg/kg/day of prednisone divided into two doses.
- As blistering activity subsides, this daily dose can initially be tapered at a rate of 10 mg/week assessing closely for any recurrence of blisters.
- Once the patient reaches 60 mg/day, a single daily dose can be given.
- After patients have reached the 40 mg/day of prednisone point in their taper, further tapering of the average daily dose should be performed more cautiously, not more than an average of 5 mg/day decrease in dose per week as reflares occur frequently at this point.
- The dose of 20-30 mg/day (sustaining dose) has to be maintained for at least 5 years or for life.

# Pemphigus treatment
# Steroid sparing agents

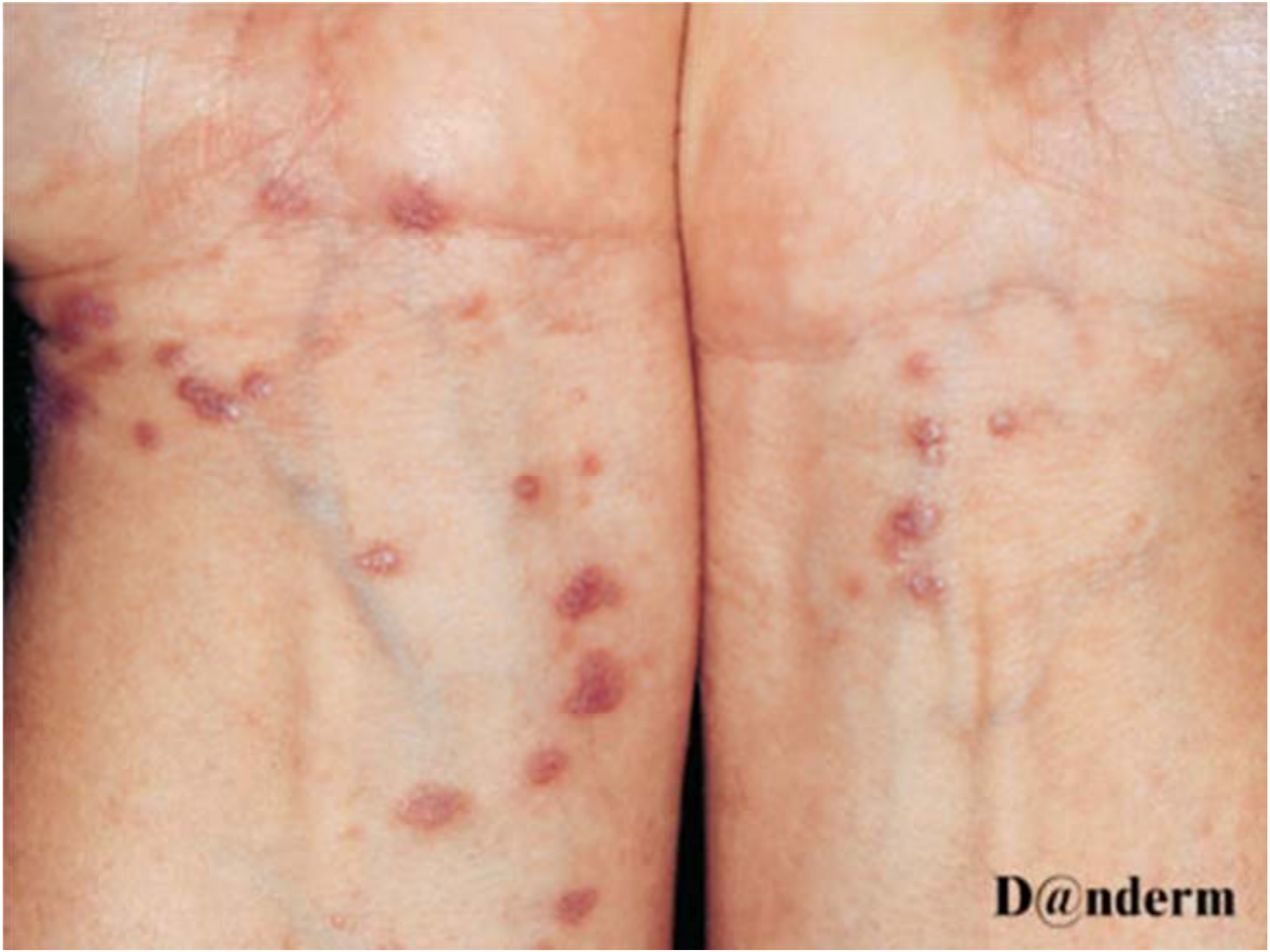
- The use of a steroid sparing agent reduces the side effects encountered with systemic corticosteroids but care needs to be taken to monitor for systemic toxicity of the steroid sparing agents themselves including the increased risks of infection and malignancy.
- Probably the lease toxic steroid sparing regimen is the use of tetracycline 2g/day and nicotinamide 2g/day.
- Cyclophosphamide and azathioprine are the drugs most commonly used as a steroid sparing agents in pemphigus subtypes. Cyclophosphamide has significant potential systemic toxicity and patients must be carefully monitored during treatment which usually is a single daily dose of 1-2 mg/kg. Azathioprine in general has less systemic toxicity than cyclophosphamide but it works more slowly. It is given at a dose of 1-3 mg/kg/day.
- Other steroid sparing modalities for pemphigus which are sometimes effective include cyclosporin, chlorambucil and plasmapheresis. Intramuscular gold has also been reported to be of benefit to patients with pemphigus subtypes.

# Pemphigus treatment

- Plasmapharesis: in conjunction with glucocorticoids and immunosuppressive agents in poorly controlled patients, in the initial phases of treatment to reduce antibody titers;
- Gold therapy: for milder cases. After an initial test dose of 10 mg IM, 25-50 mg of gold sodium thiomalate is given IM at weekly intervals to a maximum cumulative dose of 1 g.

# Lichen planus

- Lichen planus (LP) is a pruritic, papular eruption characterized by its violaceous color; polygonal shape; and, sometimes, fine scale. It is most commonly found on the flexor surfaces of the upper extremities, on the genitalia, and on the mucous membranes. LP is most likely an immunologically mediated reaction.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# Oral lichen planus

- Oral lichen planus (OLP) is a chronic inflammatory disease that causes bilateral white striations, papules, or plaques on the buccal mucosa, tongue, and gingivae. Erythema, erosions, and blisters may or may not be present.

# Pathophysiology

- LP is a cell-mediated immune response of unknown origin.
- LP may be found with other diseases of altered immunity; these conditions include ulcerative colitis, alopecia areata, vitiligo, dermatomyositis, morphea, lichen sclerosis, and myasthenia gravis.
- An association is noted between LP and hepatitis C virus infection, chronic active hepatitis, and primary biliary cirrhosis.

# OLP Pathophysiology

- Current data suggest that OLP is a T-cell–mediated autoimmune disease in which autocytotoxic CD8+ T cells trigger apoptosis of oral epithelial cells.

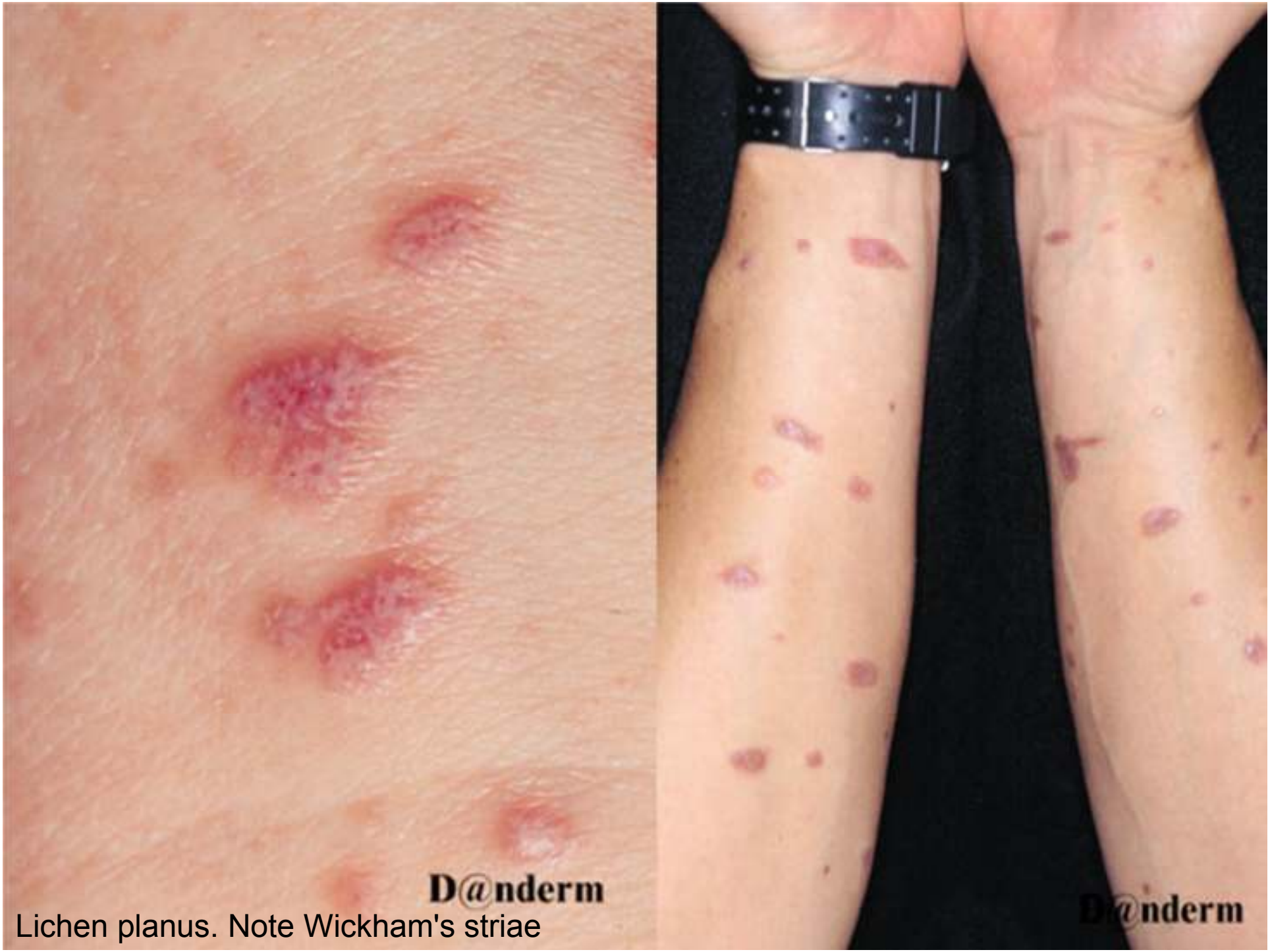
# History

- The initial lesion is usually located on the flexor surface of the limbs, such as the wrists. After a week or more, a generalized eruption develops with maximal spreading within 2-16 weeks.
- Pruritus is common but varies in severity depending on the type of lesion and the extent of involvement. Hypertrophic lesions are extremely pruritic.
- Oral lesions may be asymptomatic or have a burning sensation, or they may even be painful if erosions are present.
- In more than 50% of patients with cutaneous disease, the lesions resolve within 6 months, and 85% of cases subside within 18 months. On the other hand, oral LP had been reported to have a mean duration of 5 years. Large, annular, hypertrophic lesions and mucous membrane involvement are more likely to become chronic.

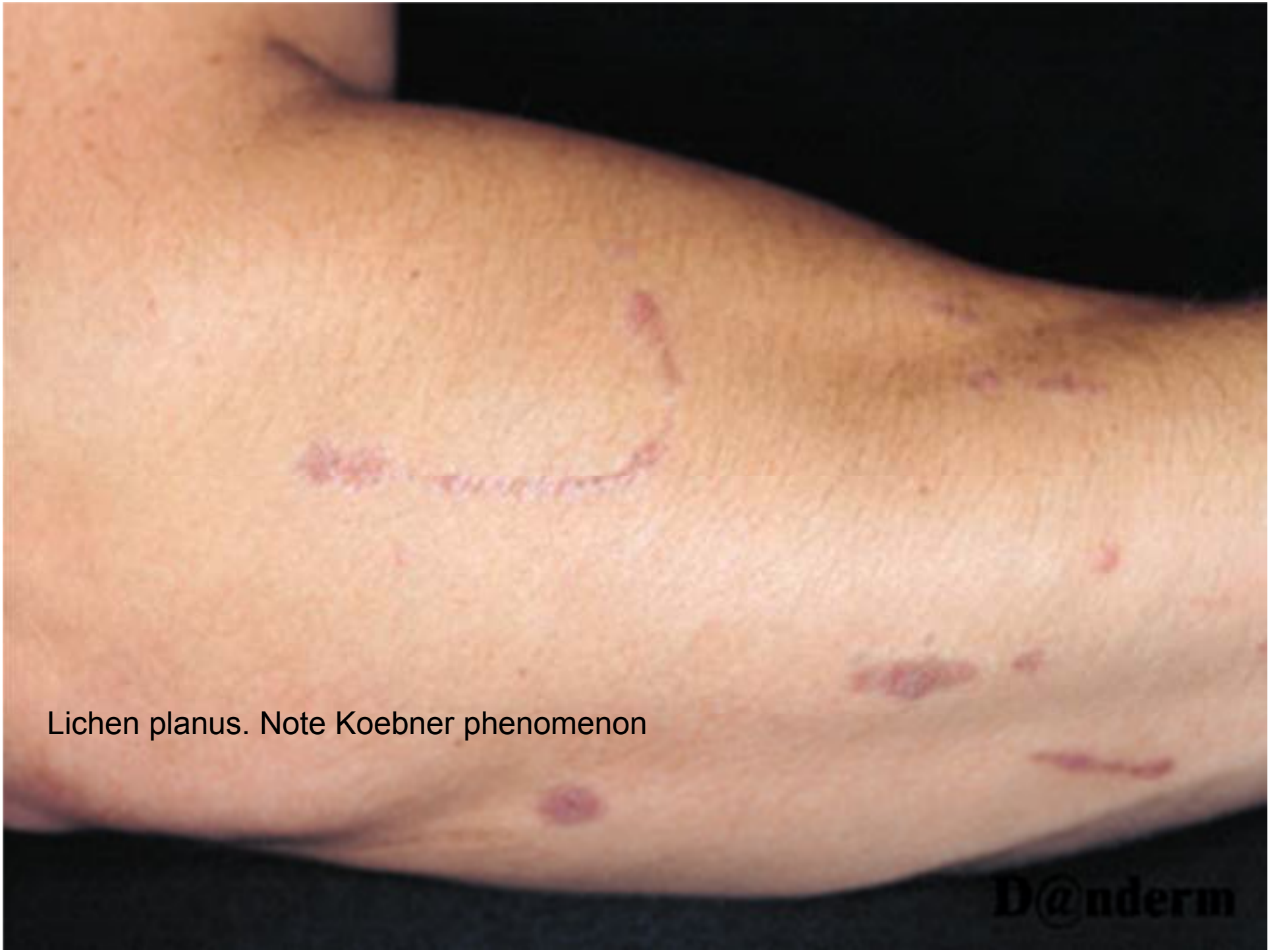
- Approximately two thirds of patients with OLP report oral discomfort, especially in association with atrophic and erosive lesions.
  - Erythematous and erosive lesions are often sensitive or painful.
  - Symptoms vary from mucosal sensitivity to continuous debilitating pain.
- Oral mucosal lichenoid lesions may occur after the administration of systemic drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs), sulfonylureas, antimalarials, beta-blockers, and some angiotensin-converting enzyme (ACE) inhibitors. The period between the commencement of the drug therapy and the clinical appearance of OLP-like disease varies.
- In rare cases, oral mucosal lichenoid lesions occur after a dental restoration is performed or after the patient starts using a denture; the lag period varies. Patients with an associated allergy to metals or components of the appliance should be evaluated by means of patch testing.
- Up to 44% of patients with OLP develop coincident skin lesions. Conversely, more that 70% of patients with cutaneous lichen planus develop coincident OLP.
- The genitals are involved in as many as 25% of women with OLP, compared with only 2-4% of men with OLP.
- In patients with OLP, scalp involvement (lichen planopilaris) is rare.
- Nail involvement in patients with OLP is uncommon.
- In a small group of patients, lichen planus may involve the esophagus.

# Physical

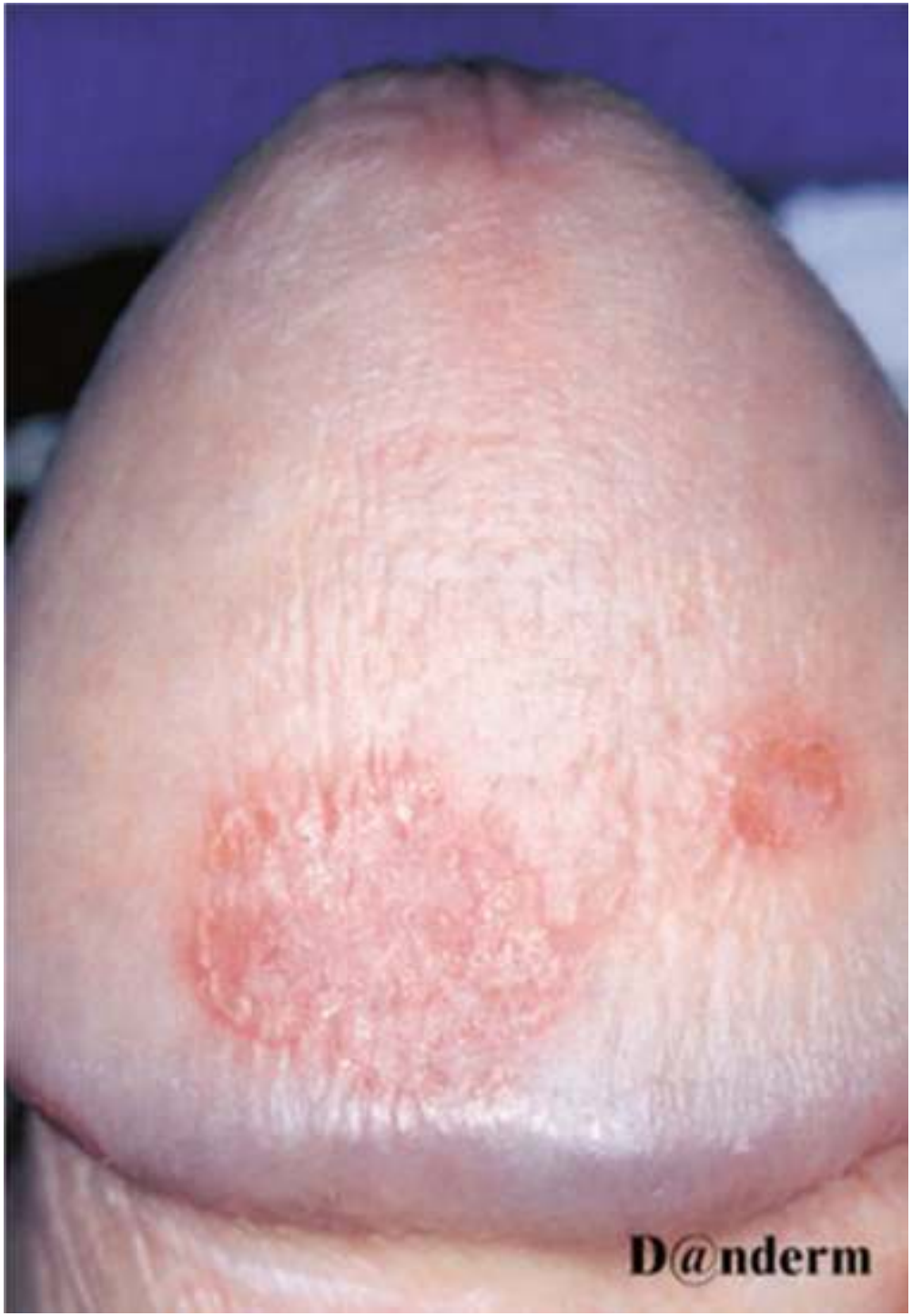
- In addition to the cutaneous eruption, LP can involve the mucous membranes, the genitalia, the nails, and the scalp.
- The clinical presentation of LP has several forms: actinic, annular, atrophic, erosive, follicular, hypertrophic, linear, pigmented, and vesicular/bullous.
- The papules are violaceous, shiny, and polygonal; varying in size from 1 mm to greater than 1 cm in diameter. They can be discrete or arranged in groups of lines or circles.
- Characteristic fine, white lines, called Wickham stria, are often found on the papules




Lichen planus. Note Wickham's striae




Lichen planus. Note Koebner phenomenon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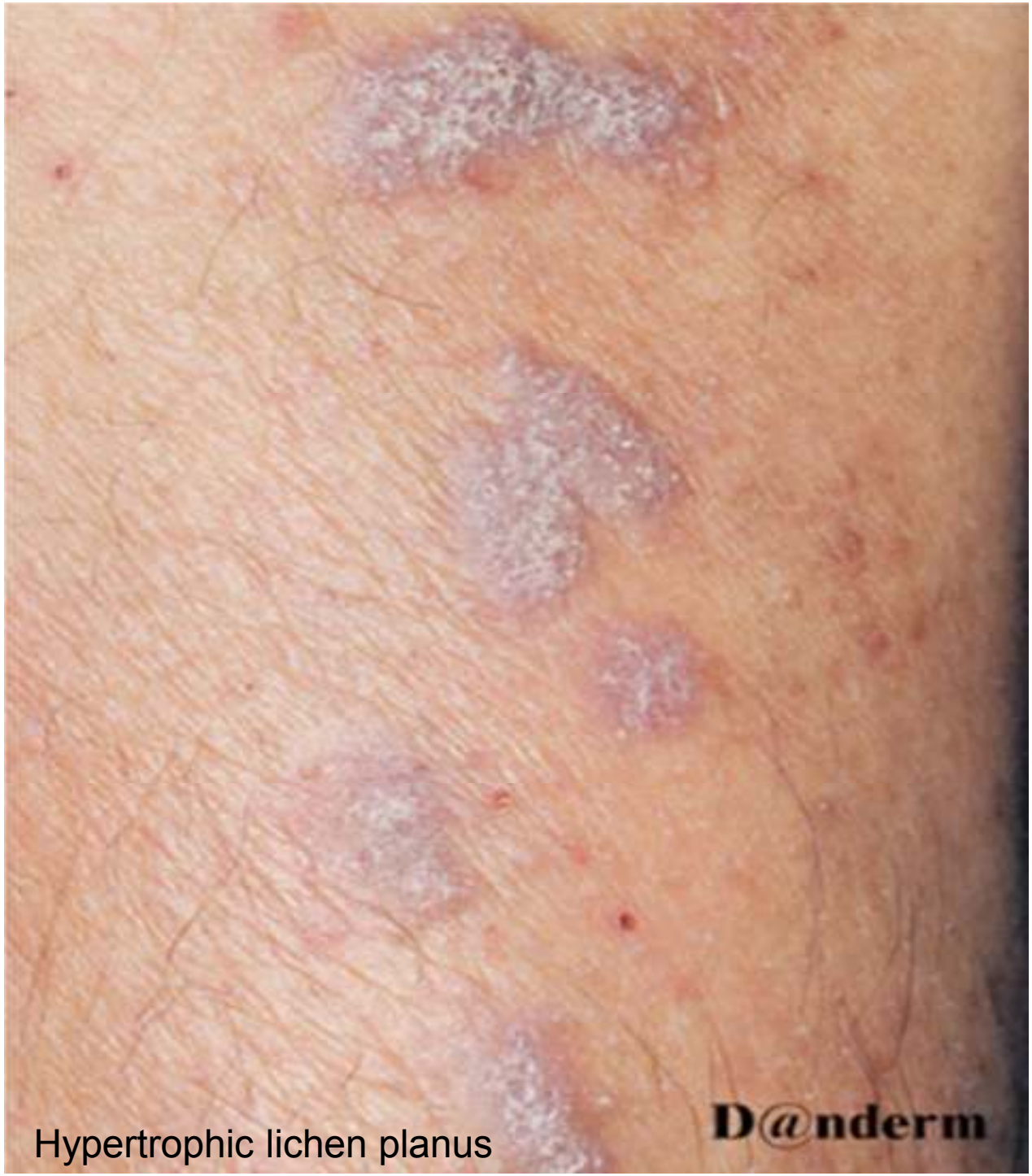
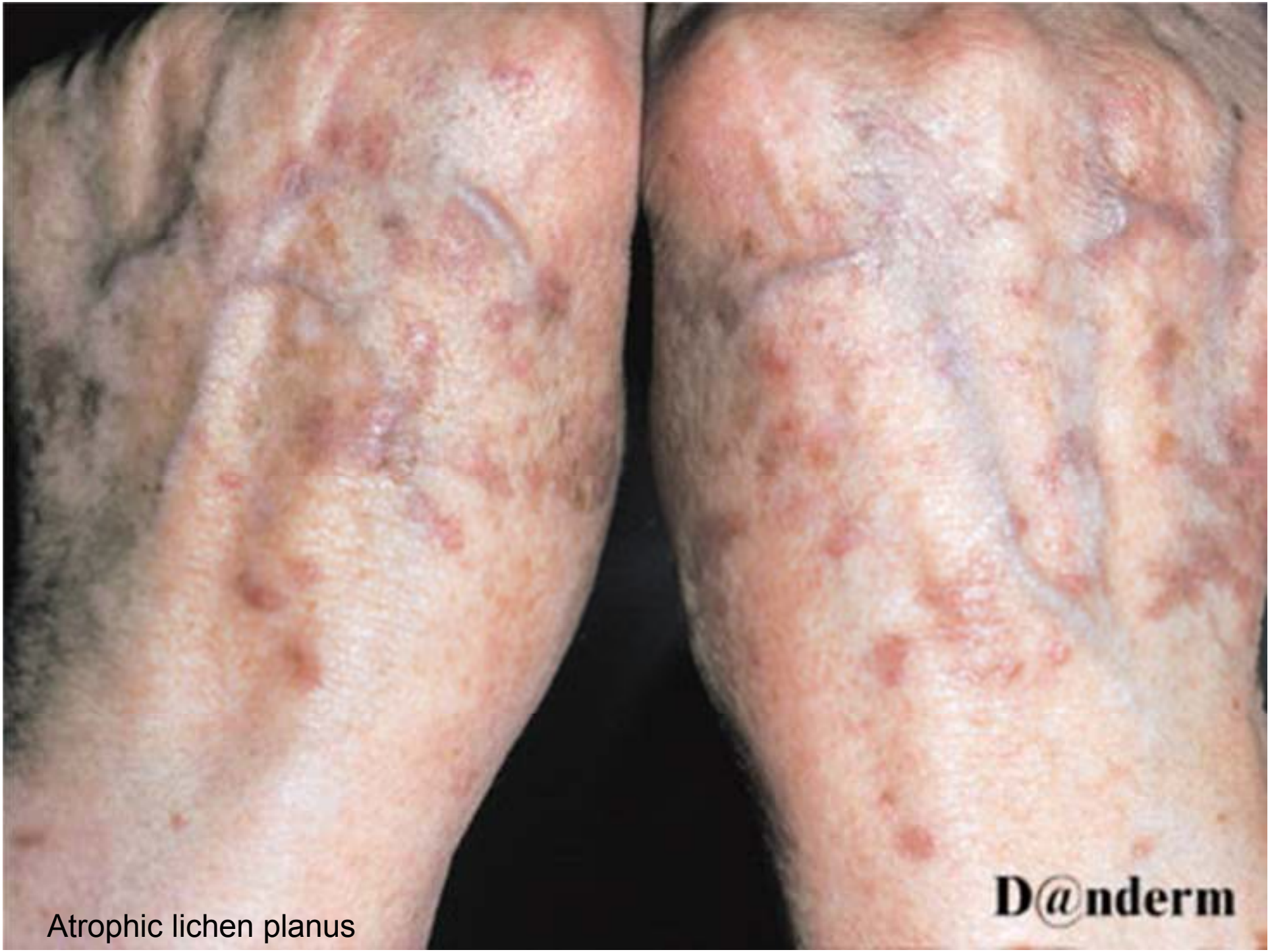



Hypertrophic lichen planus



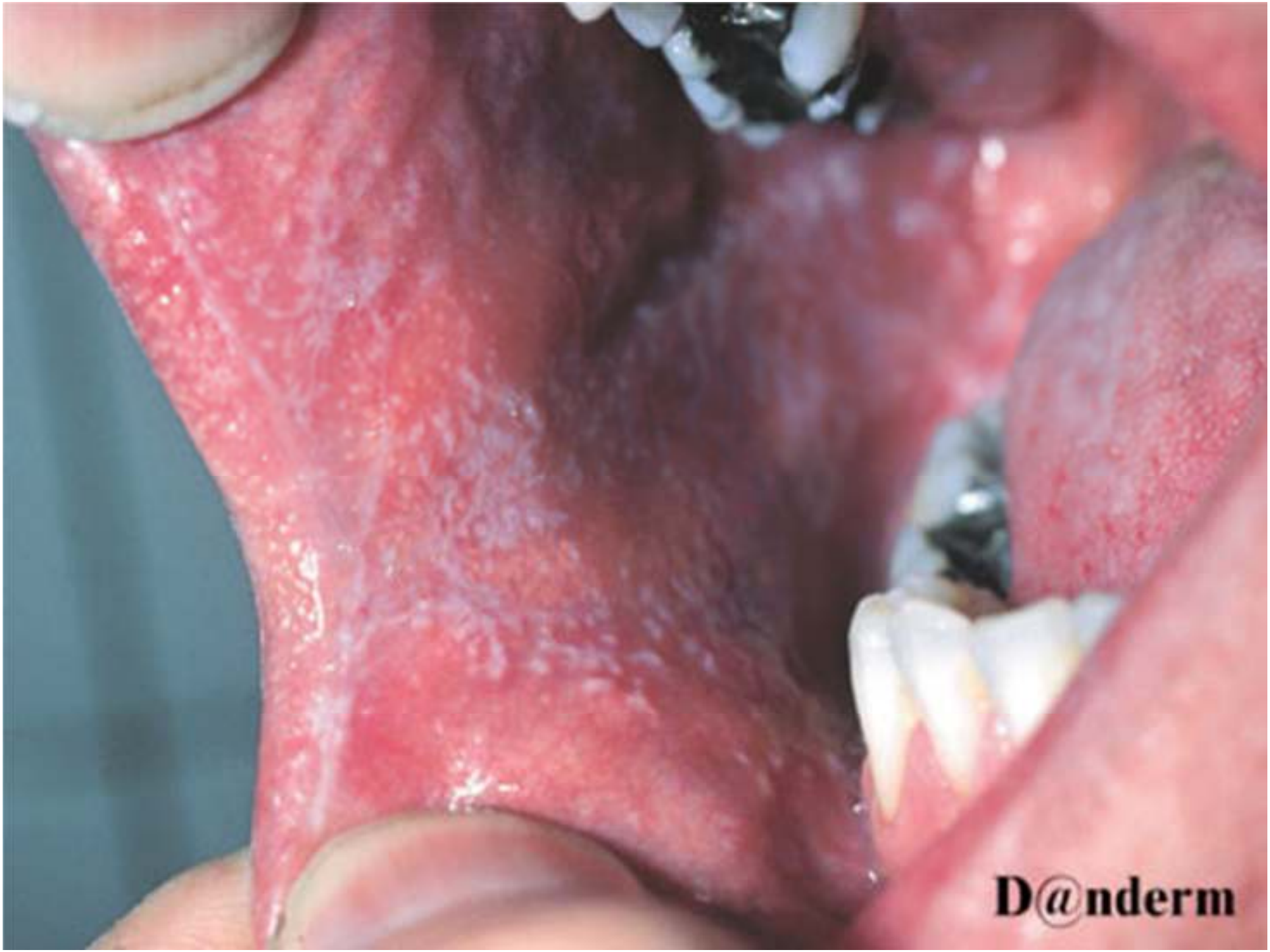

Atrophic lichen planus

# Physical

- Mucous membrane involvement is common and may be found without skin involvement.
- Lesions are most commonly found on the tongue and the buccal mucosa; they are characterized by white or gray streaks forming a linear or reticular pattern on a violaceous background.
- Oral lesions are classified as reticular, plaquelike, atrophic, papular, erosive, and bullous.
- Ulcerated oral lesions may have a higher incidence of malignant transformation in men, but this observation may be confounded by other factors, such as smoking and chewing tobacco.
- Lesions may also be found on the conjunctivae, the larynx, the tonsils, the bladder, the vulva, and the vaginal vault; throughout the gastrointestinal tract; and around the anus.

# OLP Physical

- The lesions predominantly affect the buccal mucosa, tongue, and gingivae, although other oral sites are occasionally involved.
- The lesions are usually bilateral.
- The lesions may appear as a mixture of clinical subtypes. For example, white streaks and gray streaks may form a linear or reticular pattern on an erythematous background. Alternatively, a central area of shallow ulceration (erosion) may have a yellowish surface (fibrinous exudate) surrounded by an area of erythema.
- In most patients, telltale white striations or papules are evident on the buccal mucosa or on the lateral margin of the tongue, either alone or in combination with other lesions.
- Gingival lesions commonly appear with a fiery red erythema that affects the entire width of the attached gingiva, a condition previously called desquamative gingivitis.
- In patients predisposed to pigmentation, OLP lesions may be associated with patchy brown melanin deposits in the oral mucosa (inflammatory melanosis).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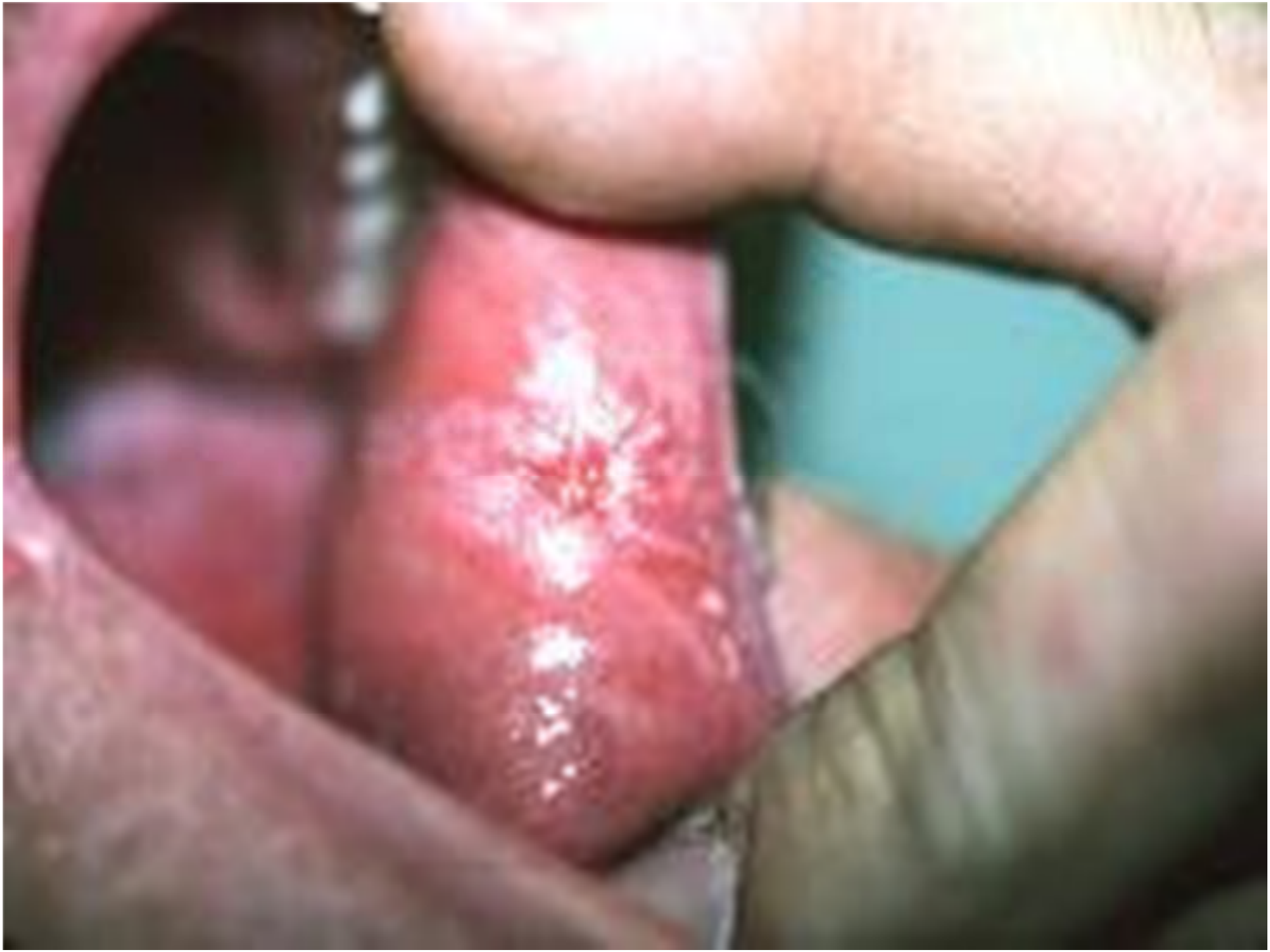
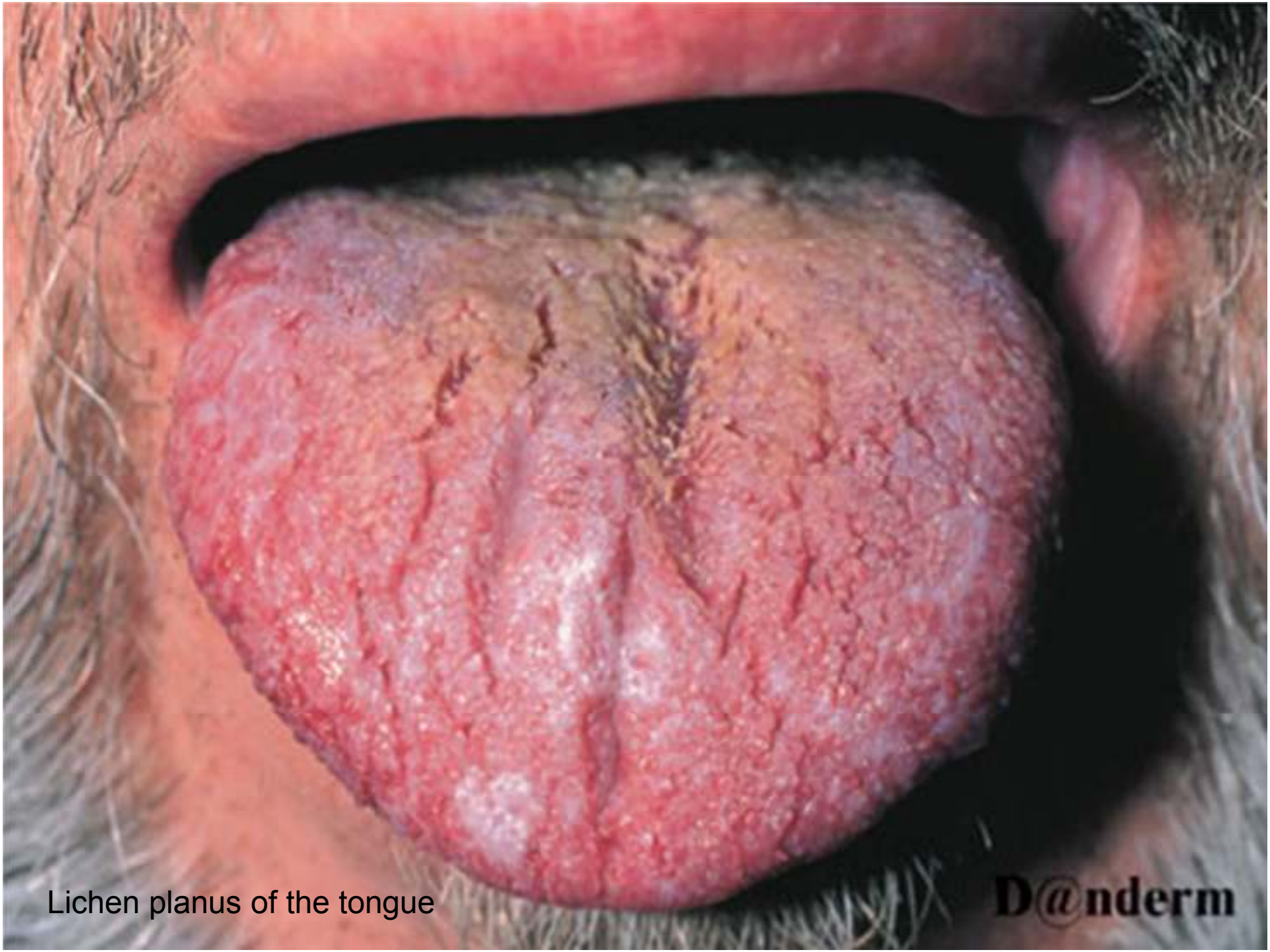
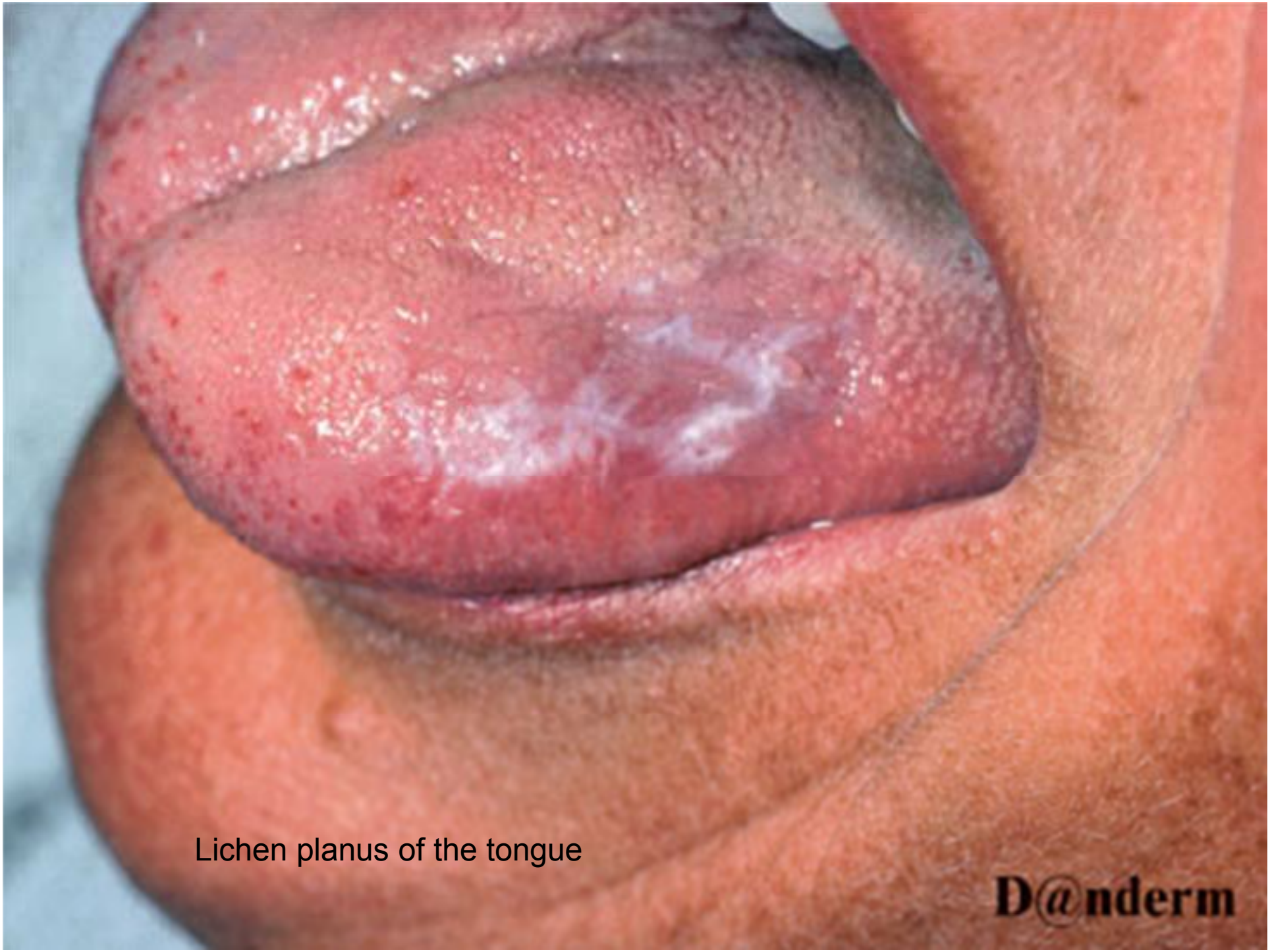
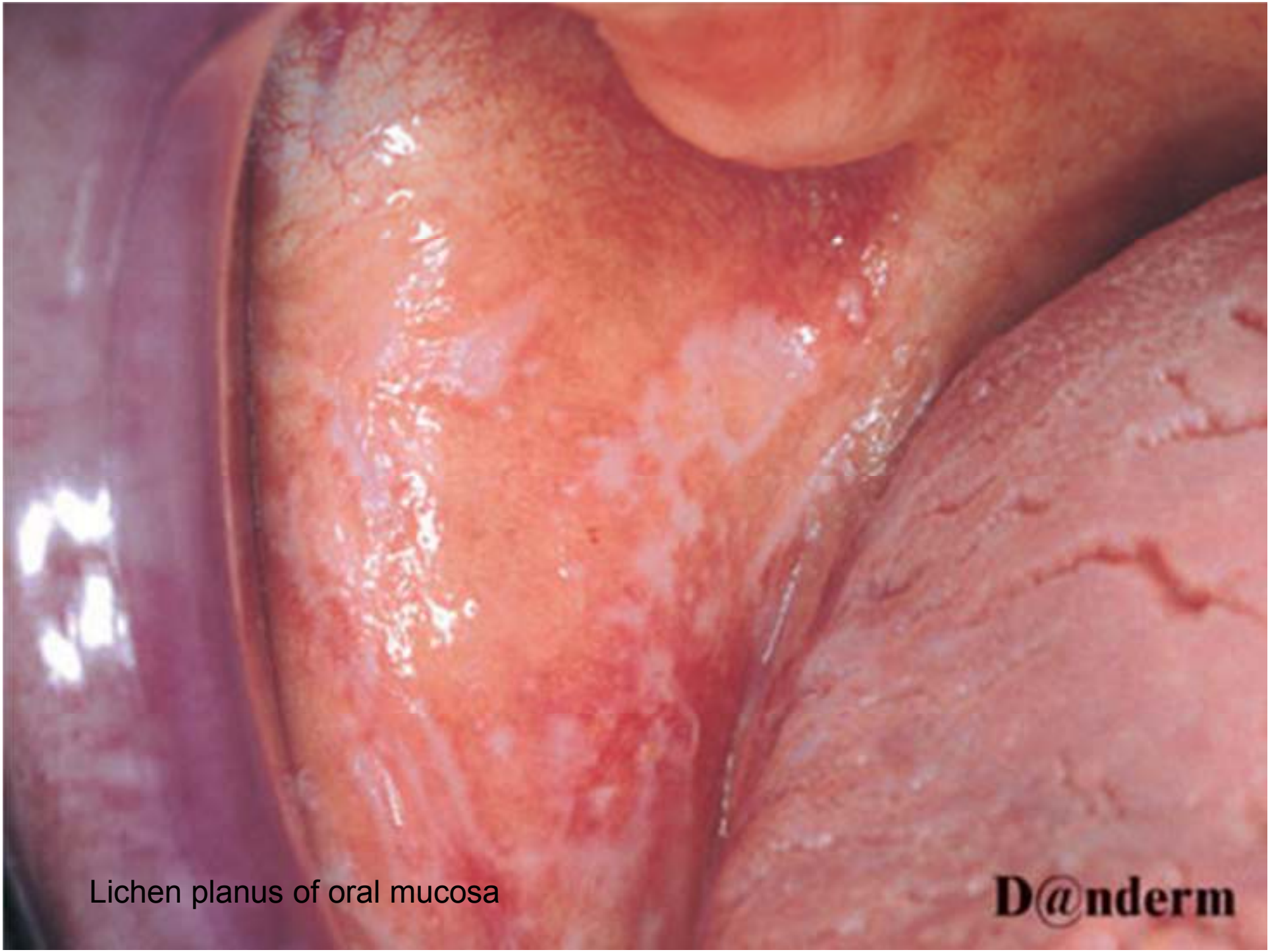




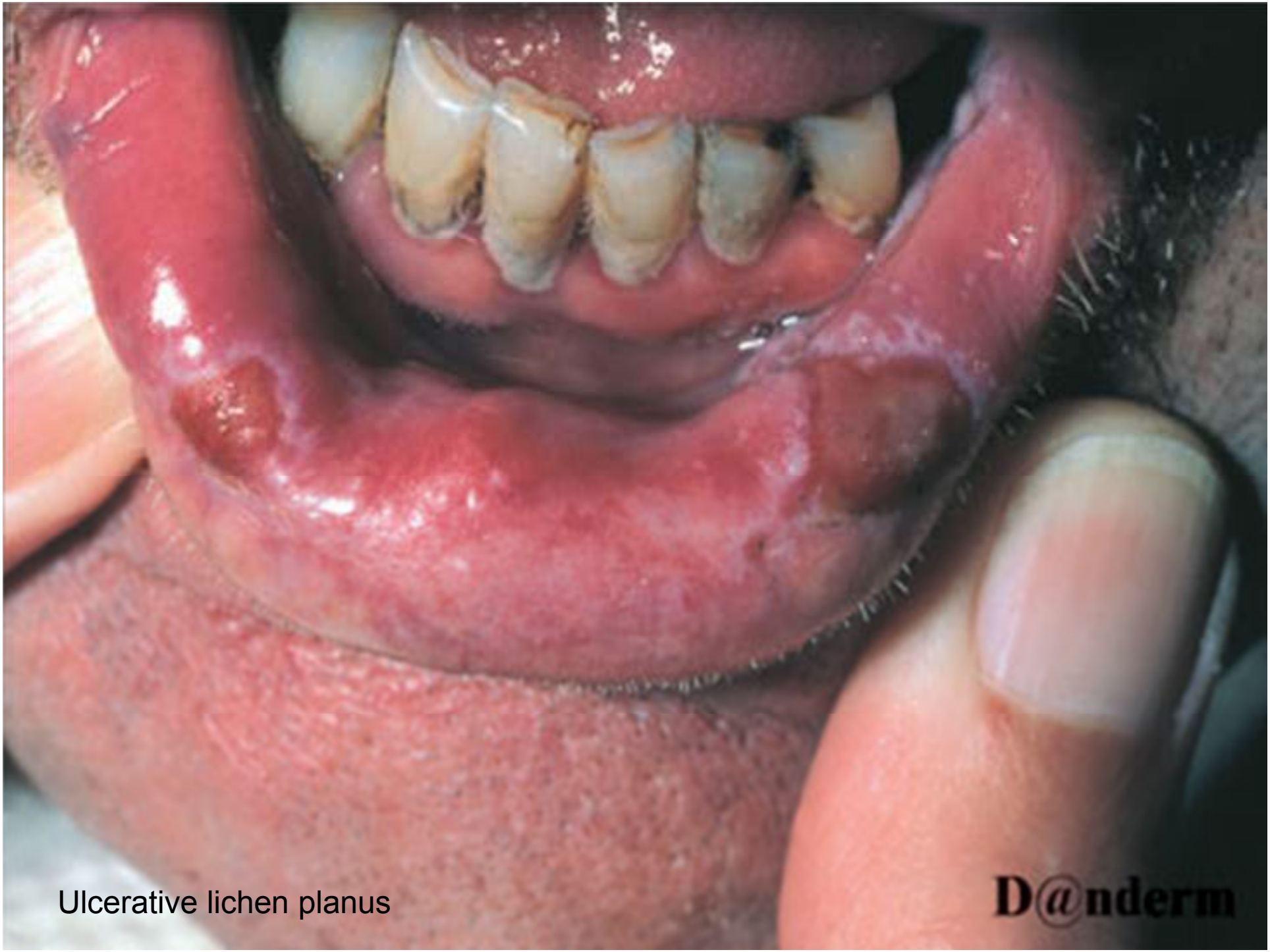

Lichen planus of the tongue




Lichen planus of the tongue




Lichen planus of oral mucosa




Ulcerative lichen planus

# Physical

- In 10% of patients, ungual findings are present. Most commonly, nail plate thinning causes longitudinal grooving and ridging. Hyperpigmentation, subungual hyperkeratosis, onycholysis, and longitudinal melanonychia can result from LP. Rarely, the matrix can be permanently destroyed with prominent pterygium formation. LP has been linked to childhood idiopathic nail atrophy and may overlap with twenty-nail dystrophy of childhood.

# Histologic Findings

- The histopathologic features distinguish LP based on the presence of irregular acanthosis and colloid bodies in the epidermis with liquefactive degeneration and linear fibrin deposition in the basal layer. The upper dermis has a bandlike infiltrate of lymphocytes and histiocytes.
- The inflammatory reaction pattern is characteristic. The epidermis is hyperkeratotic with irregular acanthosis and focal thickening in the granular layer. Degenerative keratinocytes, known as colloid or Civatte bodies, are found in the lower epidermis. In addition to apoptotic keratinocytes, colloid bodies are composed of globular deposits of IgM (occasionally immunoglobulin G [IgG] or immunoglobulin A [IgA]) and complement. Linear or shaggy deposits of fibrin and fibrinogen and liquefaction are in the basement membrane zone.
- The upper dermis has a bandlike infiltrate of lymphocytic (primarily helper T) and histiocytic cells with many Langerhans cells. The infiltrate is very close to the epidermis and often disrupts the dermal-epidermal junction.

# OLP Lab Studies

- The history, typical oral lesions, and skin involvement are usually sufficient to diagnose OLP, though laboratory studies and biopsy may be required.
- Direct immunofluorescence testing can help in distinguishing erosive or the rare bullous OLP from pemphigus vulgaris, benign mucous membrane pemphigoid, dermatitis herpetiformis, and linear immunoglobulin A (IgA) disease. However, OLP has no specific features at direct or indirect immunofluorescence testing.
- Some studies show an increased incidence of *C albicans* infection in patients with OLP.
  - Periodic acid-Schiff (PAS) staining of biopsy specimens and candidal cultures or smears may be performed. However, these tests may be of limited clinical value because oral *C albicans* is present in more than 70% of the population.
  - The presence of *C albicans* and the oral load of this organism do not aid either the diagnosis or the treatment of OLP.

# Treatment

- The first-line treatments of cutaneous LP are topical steroids, particularly class I or II ointments.
- A second choice would be systemic steroids for symptom control and possibly more rapid resolution. Many practitioners prefer intramuscular triamcinolone 40-80 mg every 6-8 weeks.
- Oral acitretin has been shown to be effective in published studies.
- Many other treatments are of uncertain efficacy because of the lack of randomized controlled trials. For LP of the oral mucosa, topical steroids are usually tried first. Topical and systemic cyclosporin has been tried with some success; however, a recent randomized double-blind study indicated that topical cyclosporin was a less effective but much more costly regimen than clobetasol. Other options include oral or topical retinoids. Even with these effective treatments, relapses are common.

# Treatment

- Psoralen with ultraviolet light A (PUVA) therapy for 8 weeks has been reported to be effective. Risks and benefits of this treatment should be considered. PUVA is carcinogenic. Long-term risks include dose-related actinic degeneration, squamous cell carcinoma, and cataracts. A phototoxic reaction with erythema, pruritus, phytophotodermatitis, and friction blisters could occur.
- UV-A therapy combined with oral psoralen consists of oral psoralen (0.6 mg/kg), 1.5-2 hours before ultraviolet light, which usually starts at 0.5-1 J/cm2 and is increased by 0.5 J/cm2 per visit. Use of topical ointment at the time of receiving UV-A treatment may decrease the effectiveness of PUVA. Precaution should be taken for persons with a history of skin cancers or hepatic insufficiency.

# Complications

- Oral ulcerations have the potential to become malignant. Malignant transformation has been reported in ulcerative oral lesions in men.
- Infection, osteoporosis, adrenal insufficiency, bone marrow suppression, renal damage, hyperlipidemia, and growth retardation in children may occur due to medication.
- Alopecia is often permanent.
- Hypertrophic lesions may leave residual hyperpigmentation.
- Vulvar lesions can be pruritic and painful.

# Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis (Lyell syndrome)

- First described in 1922, Stevens-Johnson syndrome (SJS) is an immune-complex–mediated hypersensitivity complex that is a severe expression of erythema multiforme.
- It is known by some as erythema multiforme major.
- Most authors and experts consider SJS and toxic epidermal necrolysis (TEN), alias Lyell syndrome, as different manifestations of the same disease.

# Definitions

- Toxic epidermal necrolysis (TEN) is an acute dermatologic disease, the presentation of which may constitute a true emergency. The disorder is characterized by widespread erythematous macules and targetoid lesions; full-thickness epidermal necrosis, at least focally; and involvement of more than 30% of the cutaneous surface. Commonly, the mucous membranes are also involved. Nearly all cases of TEN are induced by medications, and the mortality rate can approach 40%.
- Stevens-Johnson syndrome (SJS) may also present as a dermatologic emergency characterized by purpuric macules and targetoid lesions; full-thickness epidermal necrosis, although with lesser detachment of the cutaneous surface; and mucous membrane involvement. As with TEN, medications are important inciting agents, although *Mycoplasma* infections may induce some cases. The mortality rate is much lower and approaches 5% of cases.
- Erythema multiforme (EM) is generally a far more benign process characterized by target or targetoid lesions, with or without blisters, in a symmetric acral distribution. Oral lesions are common. Severe presentations may have widespread involvement of the mucous membranes and epidermal detachment with a loss of less than 10% of the cutaneous surface. Most cases are secondary to prior infection with a herpes virus. The condition generally has low morbidity and no mortality and is often recurrent. SJS may have features of both EM and TEN, which has led to confusion in nosology.

# Classification

Although several classification schemes have been reported, the simplest (French, *Allergol Int,* 2006) breaks the disease down as follows:

- SJS - a "minor form of TEN," with less than 10% body surface area (BSA) detachment
- Overlapping SJS/TEN - detachment of 10-30% BSA
- TEN - detachment of more than 30% BSA

# Pathophysiology

- SJS is an immune-complex–mediated hypersensitivity disorder that may be caused by many drugs, viral infections, and malignancies. Cocaine recently has been added to the list of drugs capable of producing the syndrome. In up to half of cases, no specific etiology has been identified.
- Pathologically, cell death results causing separation of the epidermis from the dermis. The death receptor, Fas, and its ligand, FasL, have been linked to the process. Some have also linked inflammatory cytokines to the pathogenesis.

# Mortality/Morbidity

- Mortality is determined primarily by the extent of skin sloughing. When BSA sloughing is less than 10%, the mortality rate is approximately 1-5%. However, when more than 30% BSA sloughing is present, the mortality rate is between 25% and 35%.
- Lesions may continue to erupt in crops for as long as 2-3 weeks. Mucosal pseudomembrane formation may lead to mucosal scarring and loss of function of the involved organ system. Esophageal strictures may occur when extensive involvement of the esophagus exists. Mucosal shedding in the tracheobronchial tree may lead to respiratory failure.
- Ocular sequelae may include corneal ulceration and anterior uveitis. Blindness may develop secondary to severe keratitis or panophthalmitis in 3-10% of patients. Vaginal stenosis and penile scarring have been reported. Renal complications are rare.

# Causes

The 4 etiologic categories are:

(1) Infectious - herpes simplex virus (HSV), AIDS, coxsackie viral infections, influenza, hepatitis, mumps, mycoplasmal infection, lymphogranuloma venereum, rickettsial infections, and variola, group A beta streptococci,diphtheria, *Brucellosis,* mycobacteria

(2) Drug-induced - penicillins and sulfa antibiotics; anticonvulsants including phenytoin, carbamazepine, valproic acid, lamotrigine, and barbiturates

(3) Malignancy-related - various carcinomas and lymphomas,

(4) Idiopathic (25-50% cases).

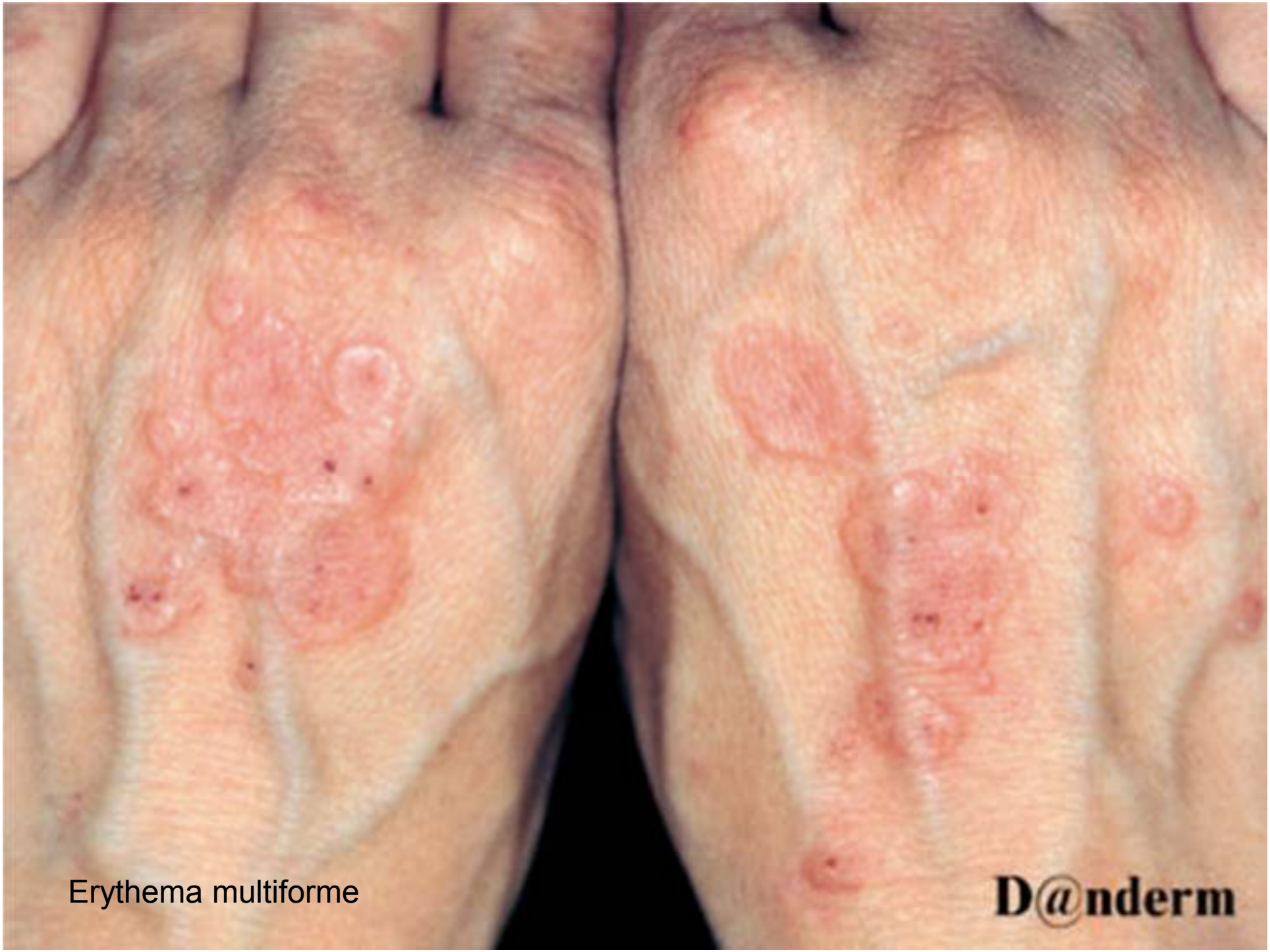
# History

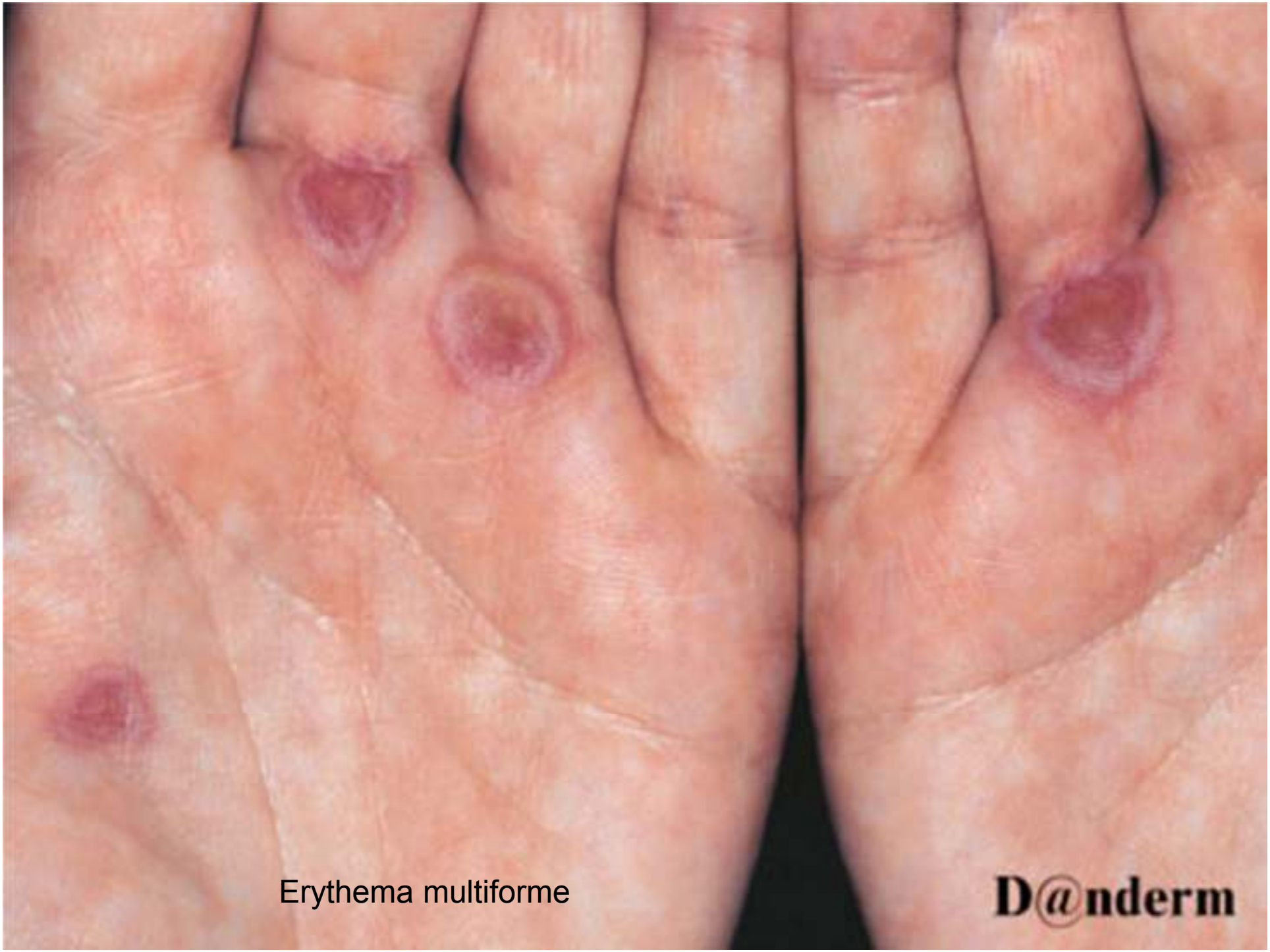
- Typically, the disease process begins with a nonspecific upper respiratory tract infection.
  - This usually is part of a 1- to 14-day prodrome during which fever, sore throat, chills, headache, and malaise may be present.
  - Vomiting and diarrhea are occasionally noted as part of the prodrome.
- Mucocutaneous lesions develop abruptly. Clusters of outbreaks last from 2-4 weeks. The lesions are typically nonpruritic.
- A history of fever or localized worsening should suggest a superimposed infection; however, fever has been reported to occur in up to 85% of cases.
- Involvement of oral and/or mucous membranes may be severe enough that patients may not be able to eat or drink.
- Patients with genitourinary involvement may complain of dysuria or an inability to void.
- A history of a previous outbreak of Stevens-Johnson syndrome (SJS) or of erythema multiforme may be elicited. Recurrences may occur if the responsible agent is not eliminated or if the patient is reexposed.

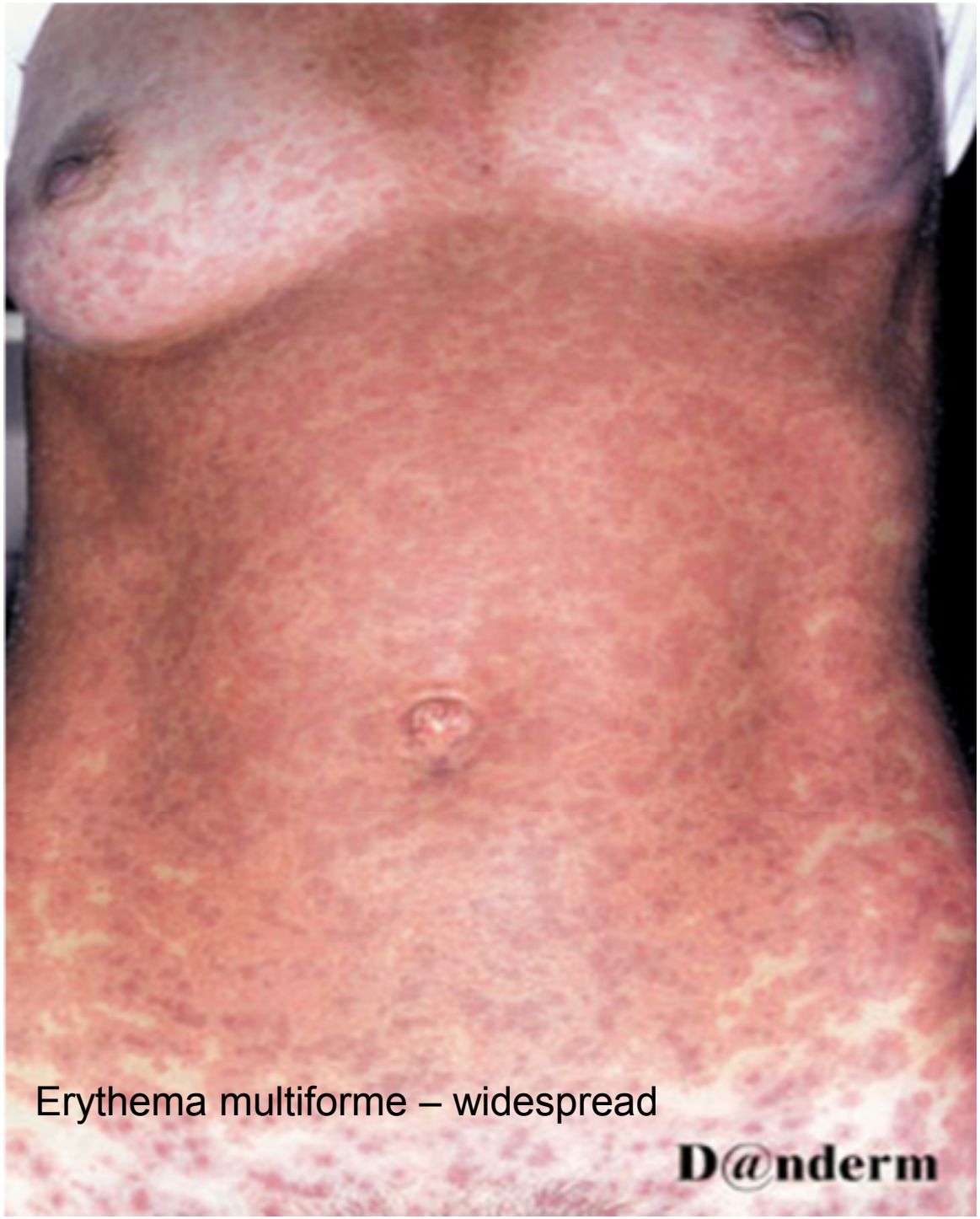
# Physical

The rash can begin as macules that develop into papules, vesicles, bullae, urticarial plaques, or confluent erythema.

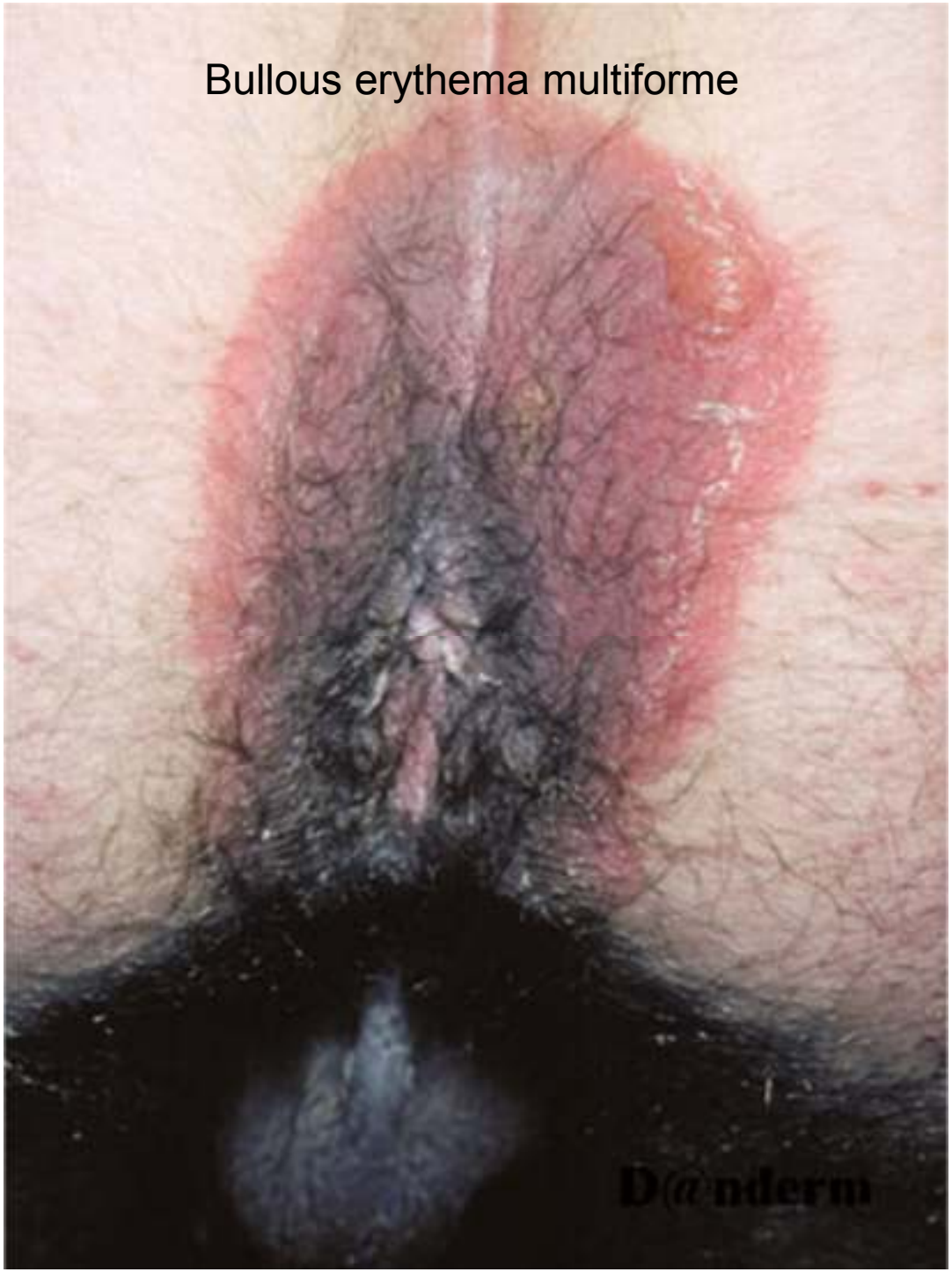
- The center of these lesions may be vesicular, purpuric, or necrotic.
- The typical lesion has the appearance of a target. The target is considered pathognomonic. However, in contrast to the typical erythema multiforme lesions, these lesions have only two zones of color. The core may be vesicular, purpuric, or necrotic; that zone is surrounded by macular erythema. Some have called these targetoid lesions.
- Lesions may become bullous and later rupture, leaving denuded skin. The skin becomes susceptible to secondary infection.
- Urticarial lesions typically are not pruritic.
- Infection may be responsible for the scarring associated with morbidity.
- Although lesions may occur anywhere, the palms, soles, dorsum of the hands, and extensor surfaces are most commonly affected.
- The rash may be confined to any one area of the body, most often the trunk.
- Mucosal involvement may include erythema, edema, sloughing, blistering, ulceration, and necrosis.
- Although some have suggested the possibility of SJS without skin lesions, most believe that mucosal lesions alone are not enough to establish the diagnosis.


Erythema multiforme
D@nderm

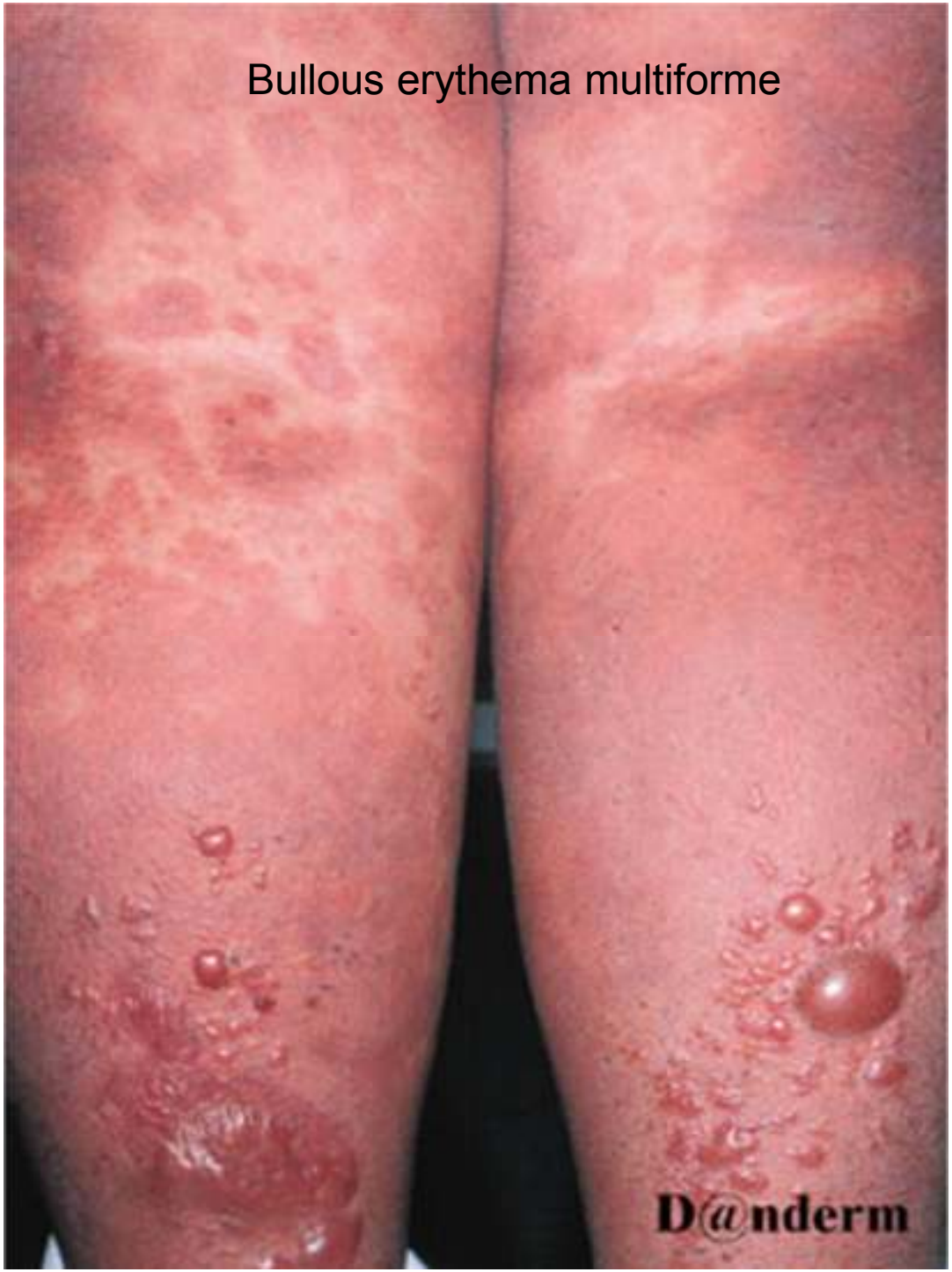

Erythema multiforme
D@nderm

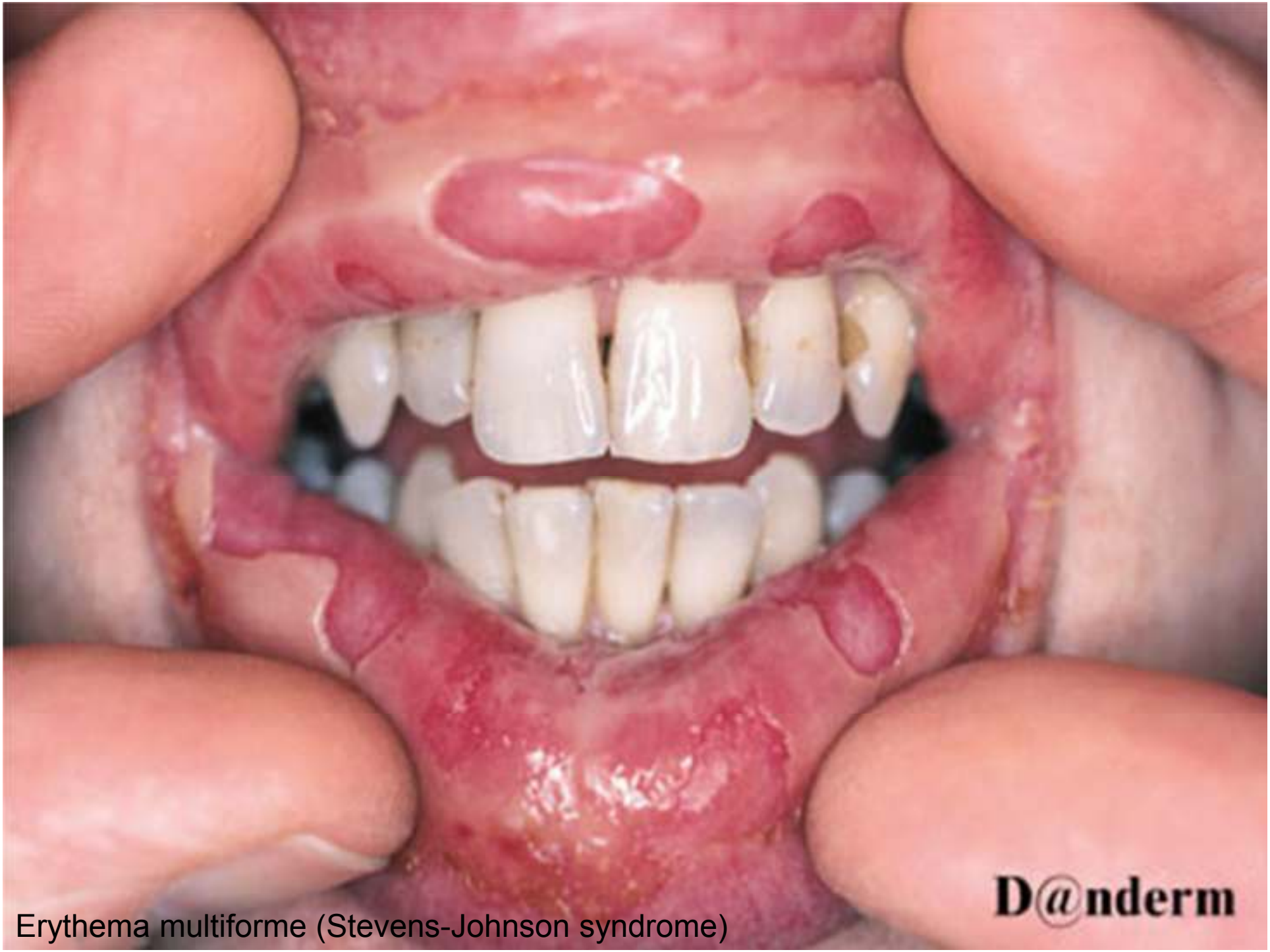

Erythema multiforme – widespread
D@nderm

Bullous erythema multiforme



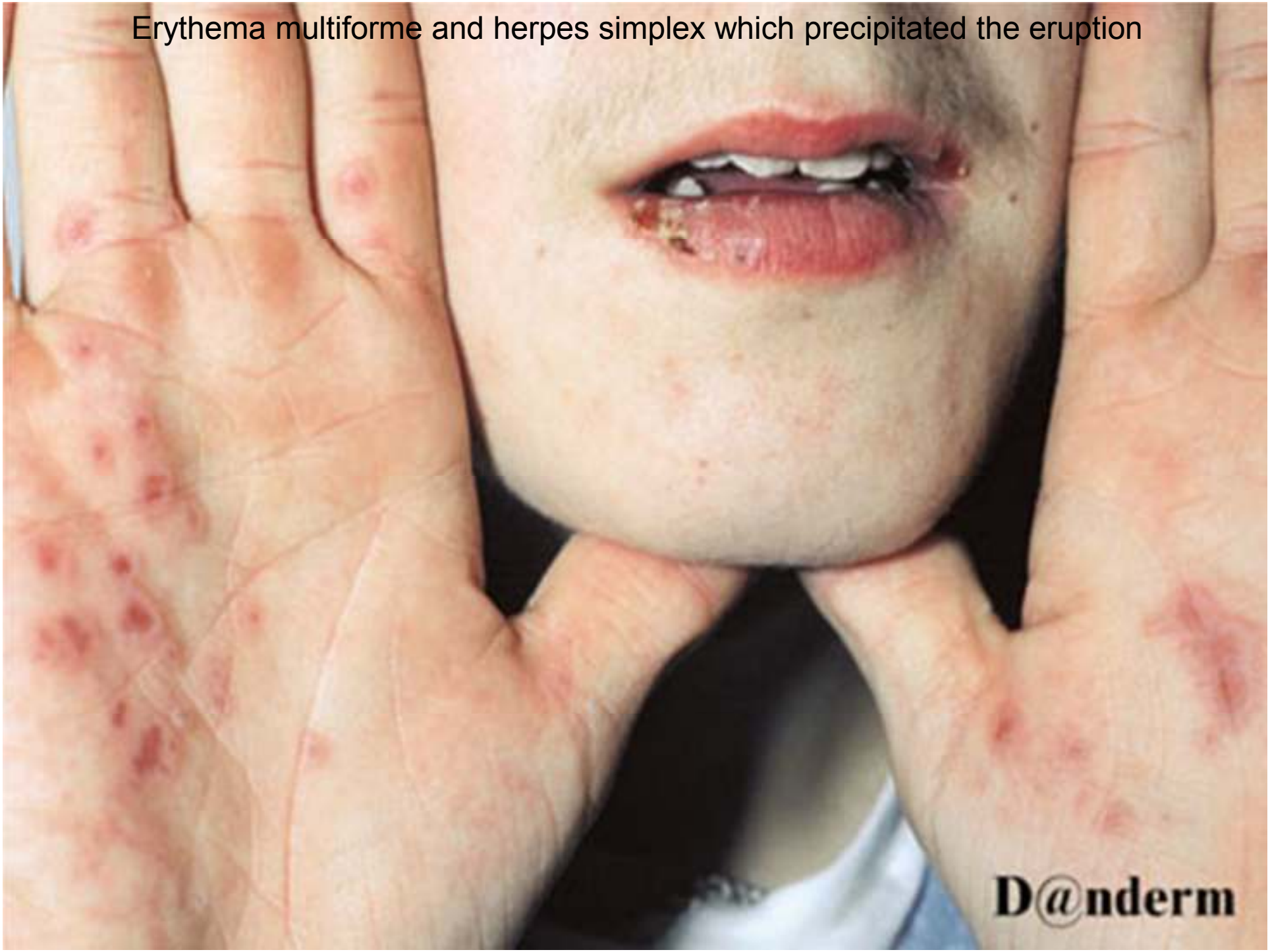
Bullous erythema multiforme






Erythema multiforme (Stevens-Johnson syndrome)

Erythema multiforme and herpes simplex which precipitated the eruption



# Complications

- Ophthalmologic - Corneal ulceration, anterior uveitis, panophthalmitis, blindness
- Gastroenterologic - Esophageal strictures
- Genitourinary - Renal tubular necrosis, renal failure, penile scarring, vaginal stenosis
- Pulmonary - Tracheobronchial shedding with resultant respiratory failure
- Cutaneous - Scarring and cosmetic deformity, recurrences of infection through slow-healing ulcerations

# Lab Studies

- No laboratory studies (other than biopsy) exist that can aid the physician in establishing the diagnosis.
- A complete blood count (CBC) may reveal a normal white blood cell (WBC) count or a nonspecific leukocytosis. A severely elevated WBC count indicates the possibility of a superimposed bacterial infection.
- Determine renal function and evaluate urine for blood.
- Electrolytes and other chemistries may be needed to help manage related problems.
- Cultures of blood, urine, and wounds are indicated when an infection is clinically suspected.
- Bronchoscopy, esophagogastroduodenoscopy (EGD), and colonoscopy may be indicated.

# Histopathology

- Skin biopsy is the definitive diagnostic study but is not an emergency department (ED) procedure.
  - Skin biopsy specimens demonstrate that the bullae are subepidermal.
  - Epidermal cell necrosis may be noted.
  - Perivascular areas are infiltrated with lymphocytes.

# Treatment

- No specific drug treatment exists for Stevens-Johnson syndrome. The choice of antibiotic depends on the associated infection. The use of systemic corticosteroids is controversial. They are useful in high doses early in the reaction, but morbidity and mortality actually may increase in association with corticosteroid use.
- Human intravenous immunoglobulin has been described as both treatment and prophylaxis.