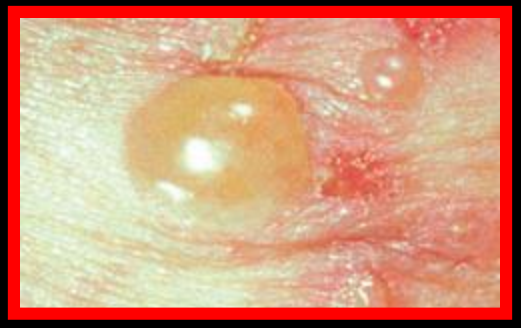
Diseases of Skin

- **Vesicle: Elevated blister containing clear fluid that are under 1cm in diameter.**

- **Bullae: Elevated blister-like lesions containing clear fluid that are over 1 cm in diameter.**



- **Macula:** circumscribed, non-raised area of altered coloration, varying in size from a pinhead to several cms in diameter; are usually deeper in color than the surrounding mucosa

Papule: small, circumscribed, solid, elevated area varying in size from a pinhead to 5mm. The base is round/ ovoid & the surface configuration may be pointed/ rounded/ flattened

Ectodermal Dysplasia

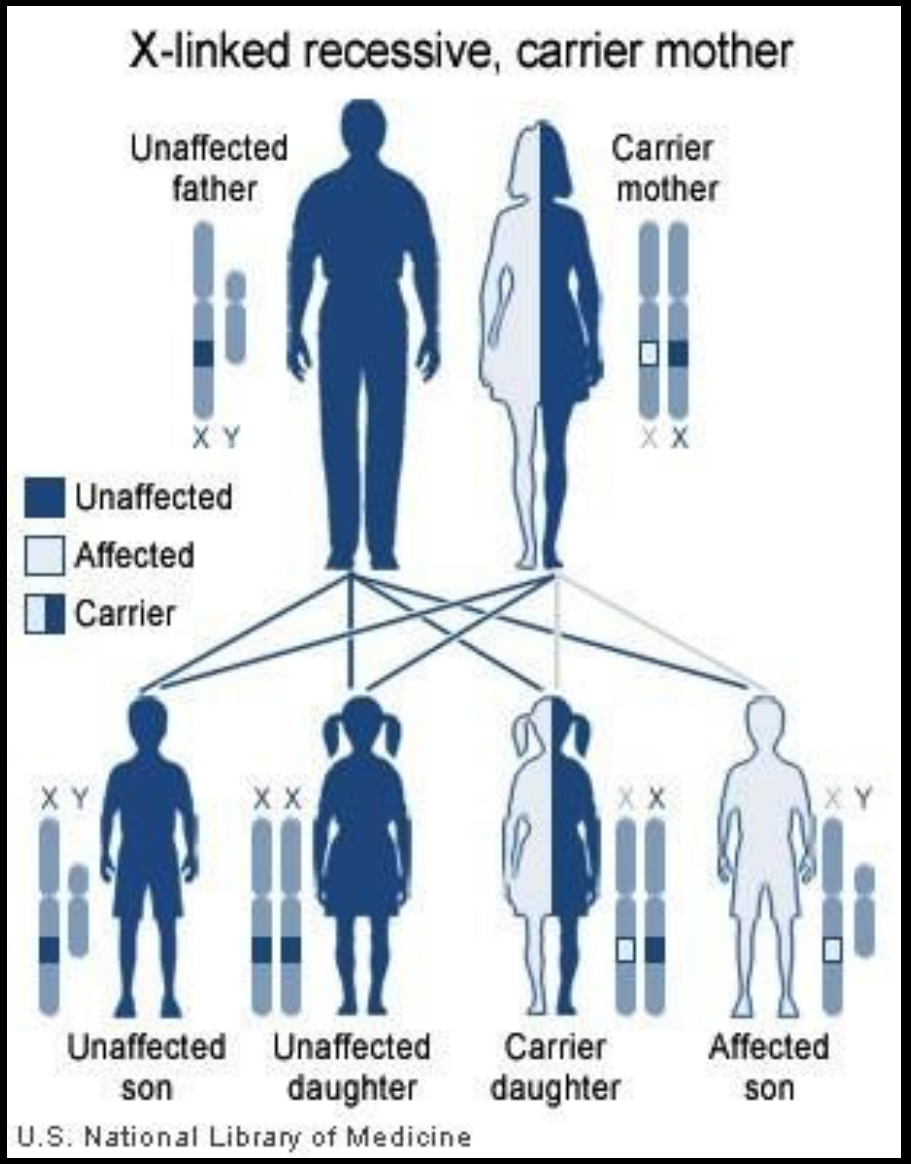
Hereditary ectodermal dysplasia

- Group of inherited conditions in which two or more ectodermally derived anatomic structures fail to develop

- Manifested as hypoplasia or aplasia of tissues such as
  - Skin
  - Hair
  - Nails
  - Teeth
  - sweat glands
  - Eyes

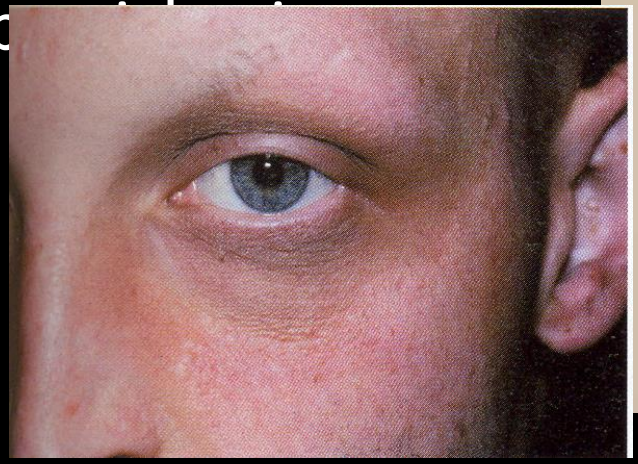
- Most common type → **“Hypohydrotic Ectodermal Dysplasia”**

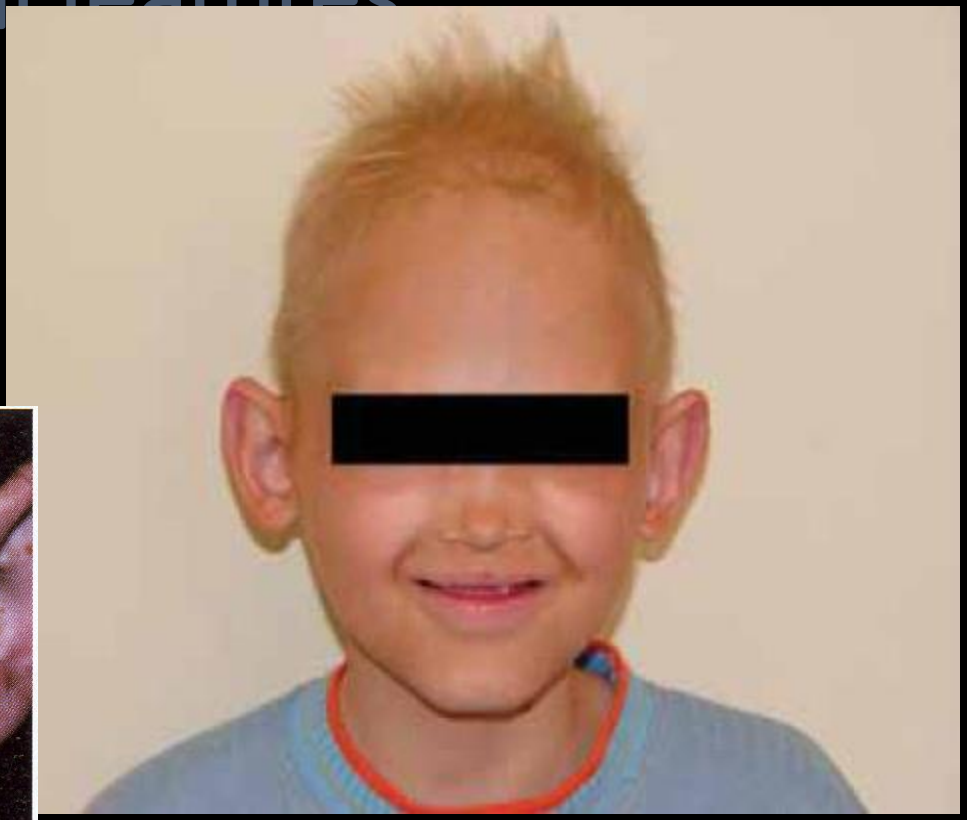
- X-linked recessive inheritance pattern
  - Male predominance
- Rarely autosomal dominant or autosomal recessive

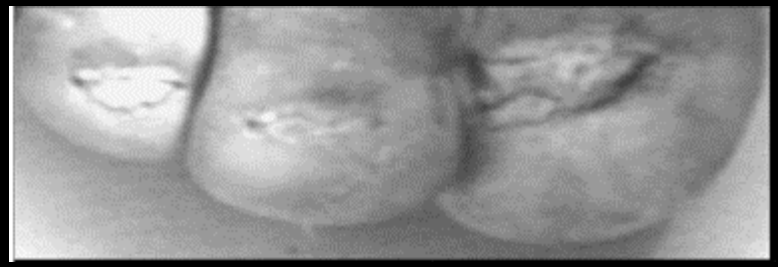


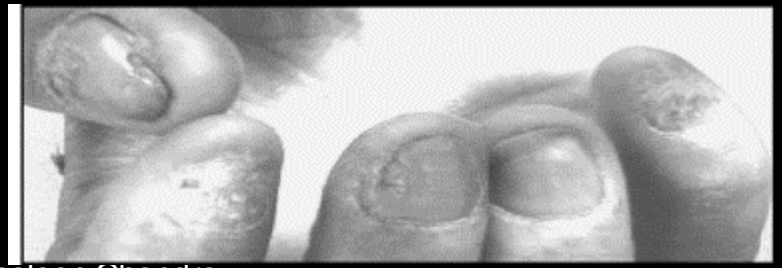
Clinical features

- Hypohidrosis
- Onychodysplasia
- Hyp



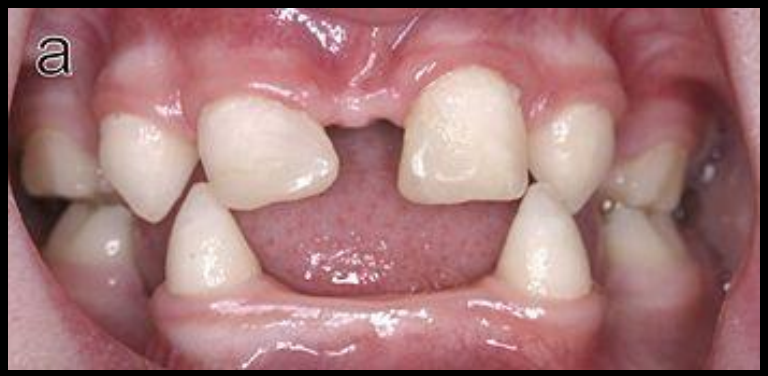


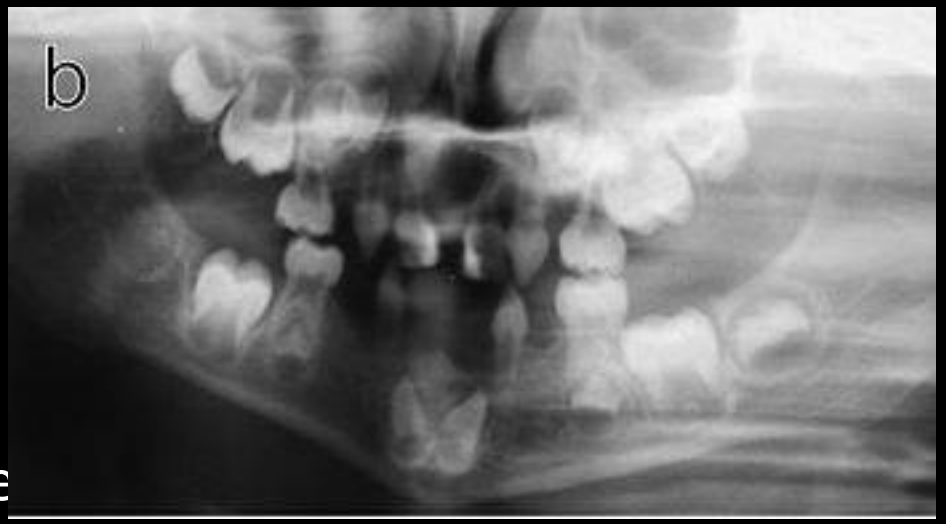




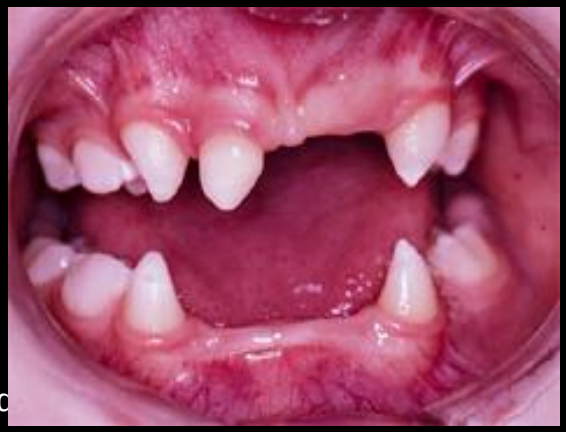
- Soft, smooth, thin, dry skin with partial/ complete absence of sweat glands
- No perspiration, hyperpyrexia, inability to endure warm temperature, fever
- Pronounced supraorbital ridges & frontal bossing
- Protuberant lips due to midface hypoplasia
- Dystrophic and brittle nails
- Extensive scaling of the skin

- Oral manifestations
  - Anodontia or hypodontia





  - Truncated or cone shaped te



- Delayed eruption
- Reduction in vertical dimension
- High arched palate or cleft palate
- Xerostomia

Histopathologic features

- Skin biopsy
  - Decreased number of sweat glands & hair follicles
  - Hypoplastic and malformed adnexal structures

Lichen Planus

- Common, chronic mucocutaneous disorder
- Most common dermatologic condition with oral manifestations
- 0.5% to 2.0% of the general population are affected
- Can effect either skin or mucosa or both

- About a third to half of the patients with skin lesions have oral lesions
- About 25% present with oral lesions alone
- More common in females

Etiology/ Predisposing features

- Unknown

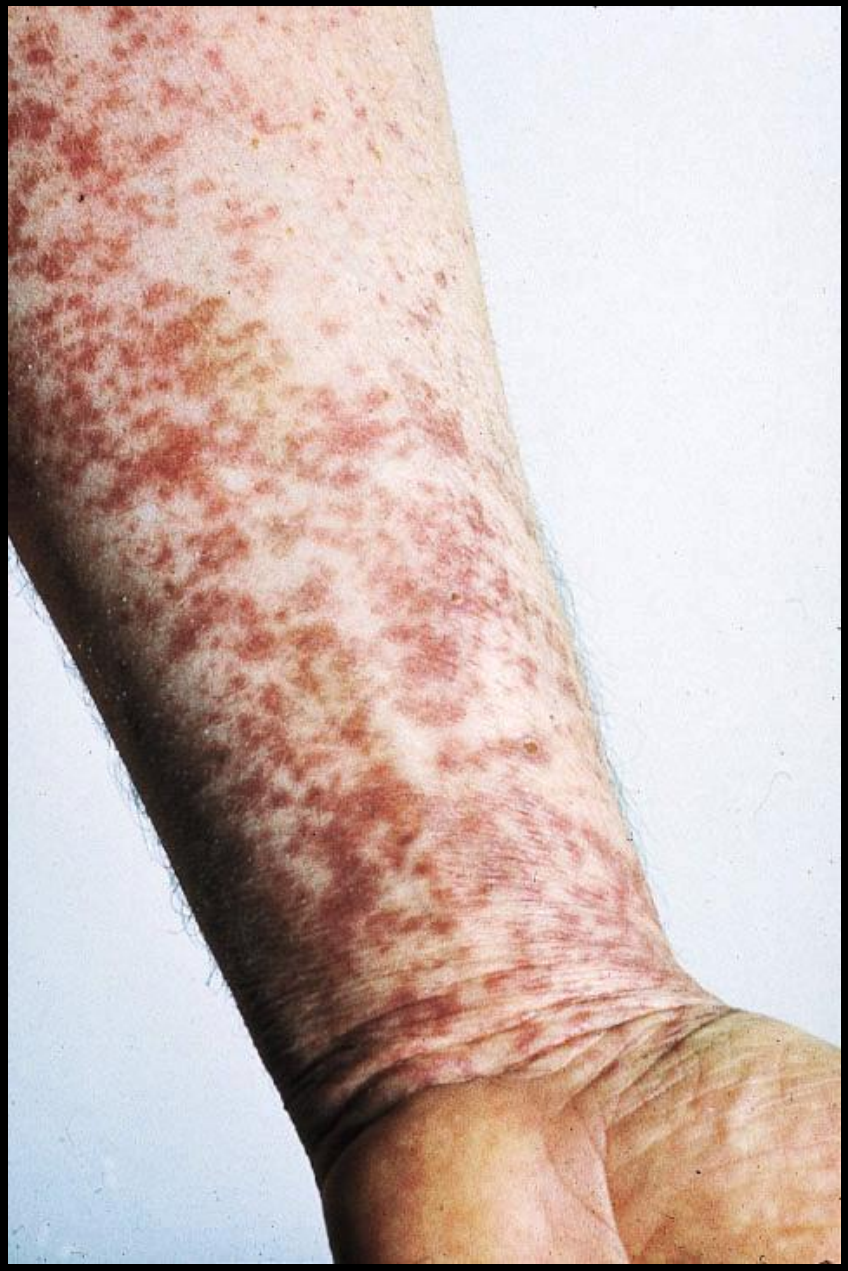
- Suggested etiologies
  - **Autoimmunity**
  - **Emotional stress**
  - Infection
  - Tobacco *(in plaque type of LP)*
  - Diabetes mellitus
  - Drugs & chemicals- antimalarials, NSAIDs, Diuretics, antihypertensive, antibiotics, heavy metal
  - Deranged tissue metabolism

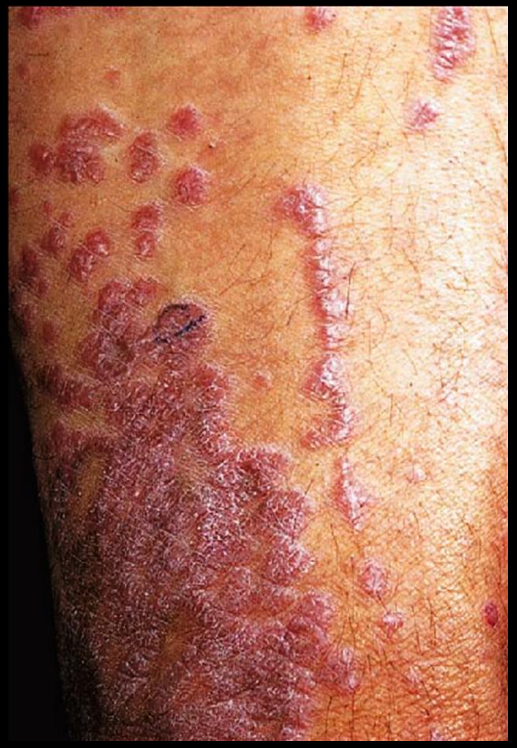
Clinical features

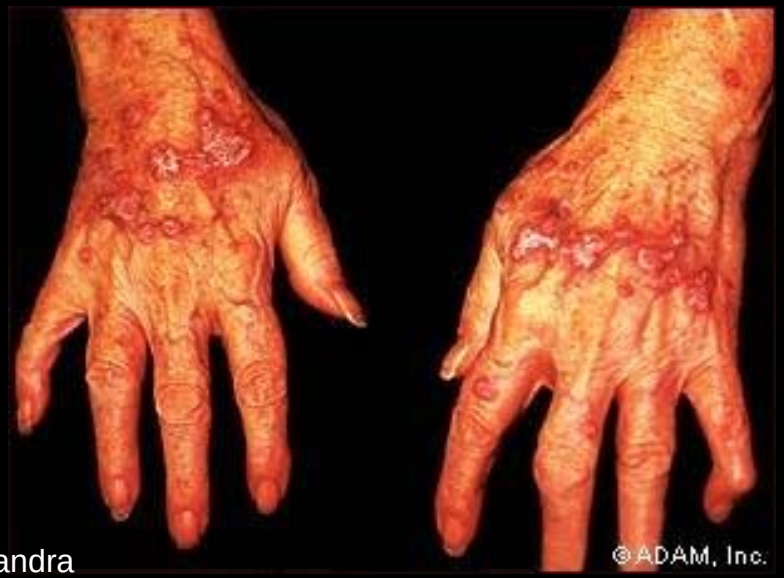
- Age
  - More common in adults
  - Middle age
- Sex
  - Females
  - 2/3rd to 3/4th of cases

Skin lesions:

- Small angular flat-topped papule (few mm) → coalesce to form plaques
- Covered by fine glistening scales
- Sharply demarcated from surrounding skin
- Initially red to reddish purple/ violaceous hue
- Centre of papule umbilicated
- Wickham's striae → whitish lines surrounding the lesions



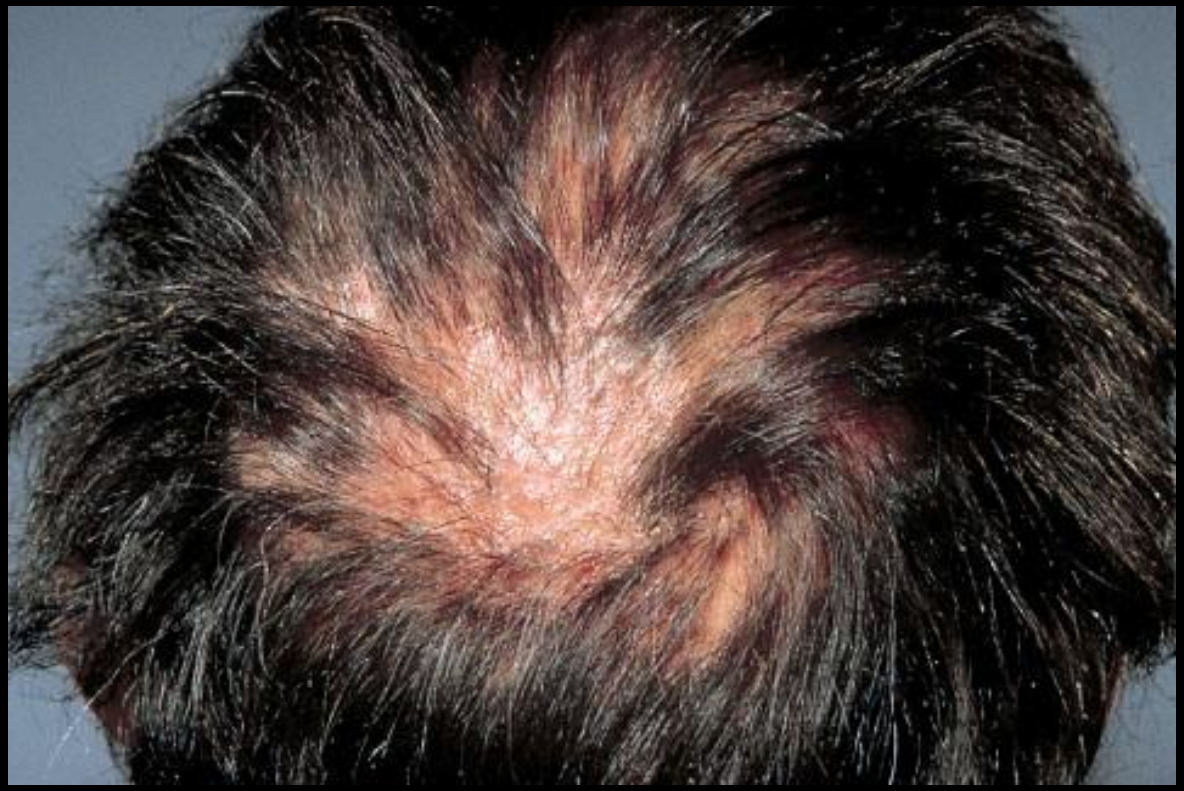




Prof. Shaleen Chandra

- Nai

- Graham Little syndrome
  - Lichen planus of scalp along with alopecia



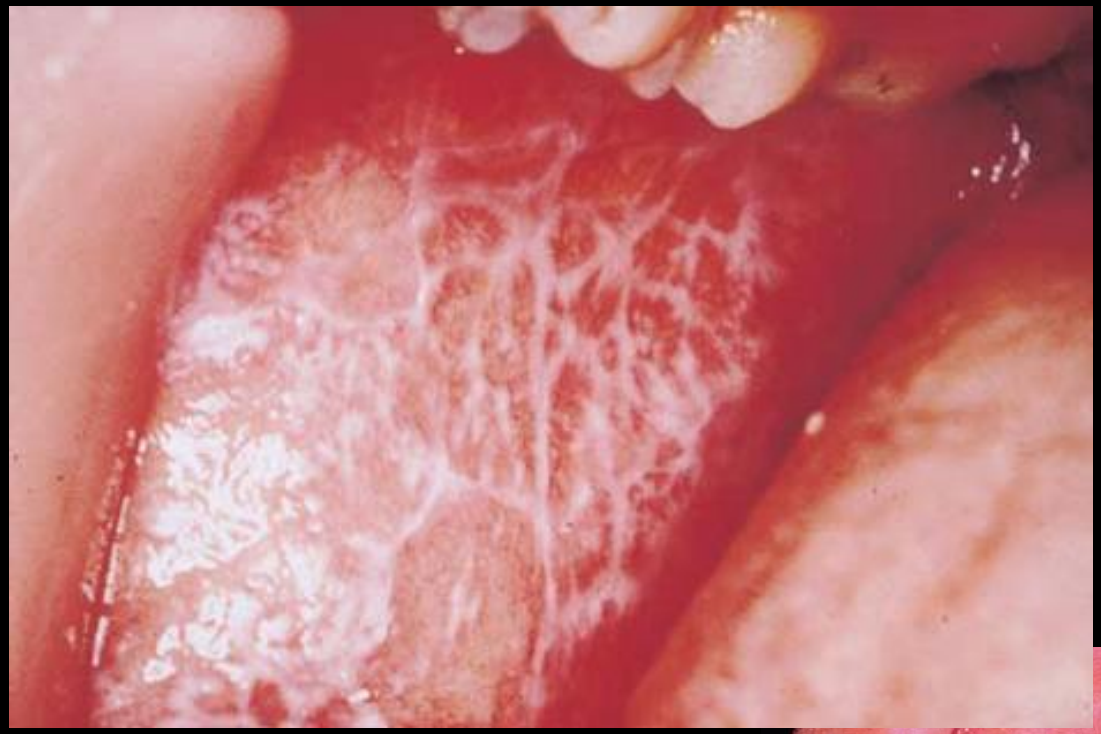
Prof. Shaleen Chandra

- “Severe pruritus”- most common symptom

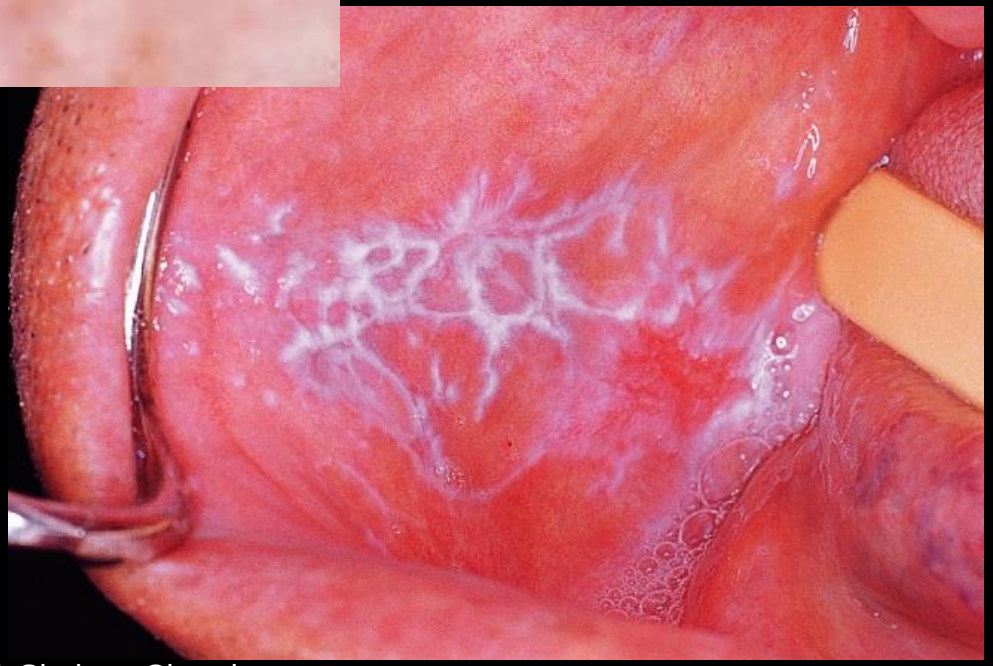
- GRINSPAN’S SYNDROME
  - Lichen planus
  - Diabetes mellitus
  - Vascular hypertension

Oral manifestations

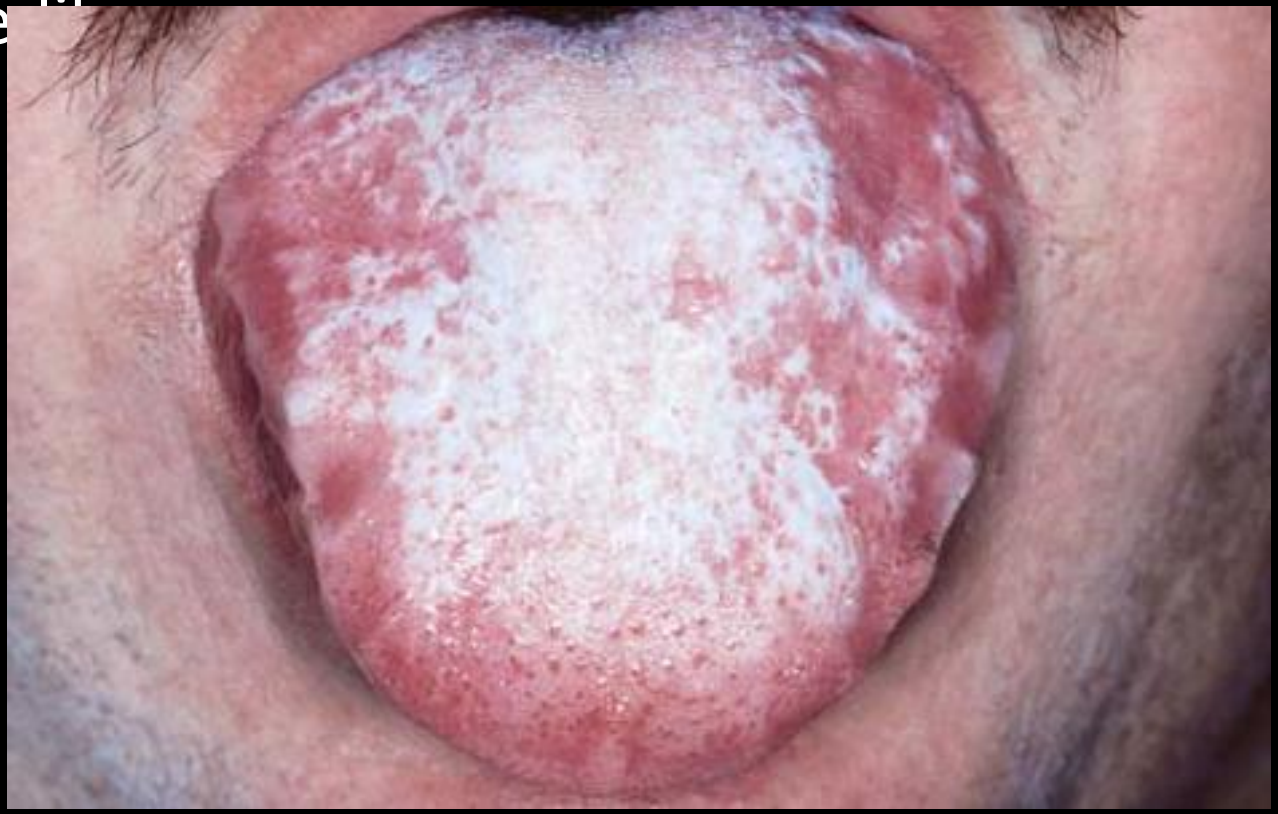
- **6 types**
  - **Reticular**
  - **Papular**
  - **Plaque-like**
  - **Atrophic**
  - **Erosive**
  - **Bullous**

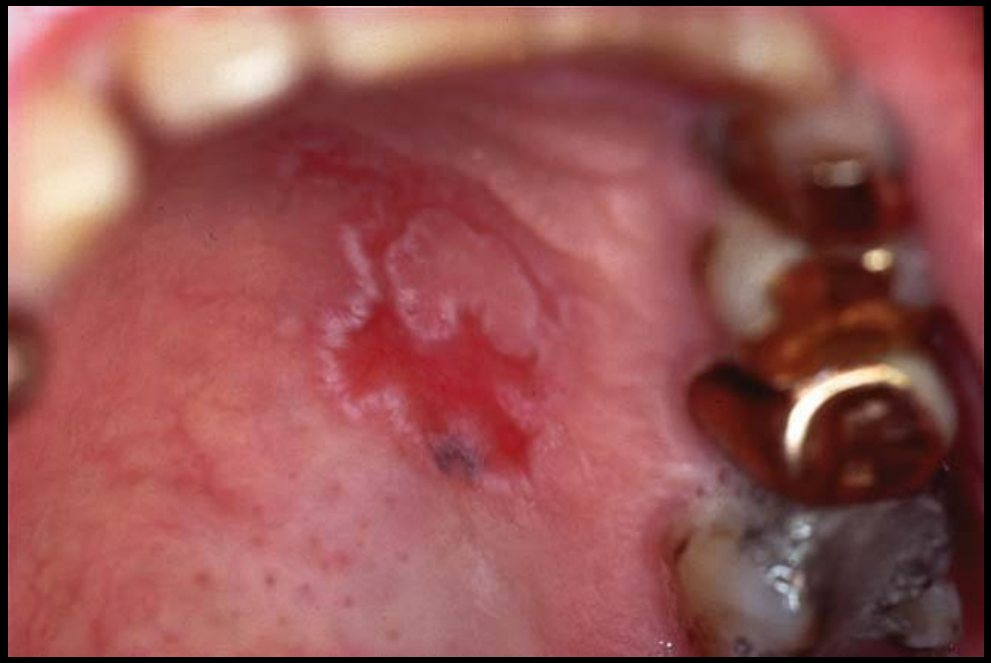


- Reticular

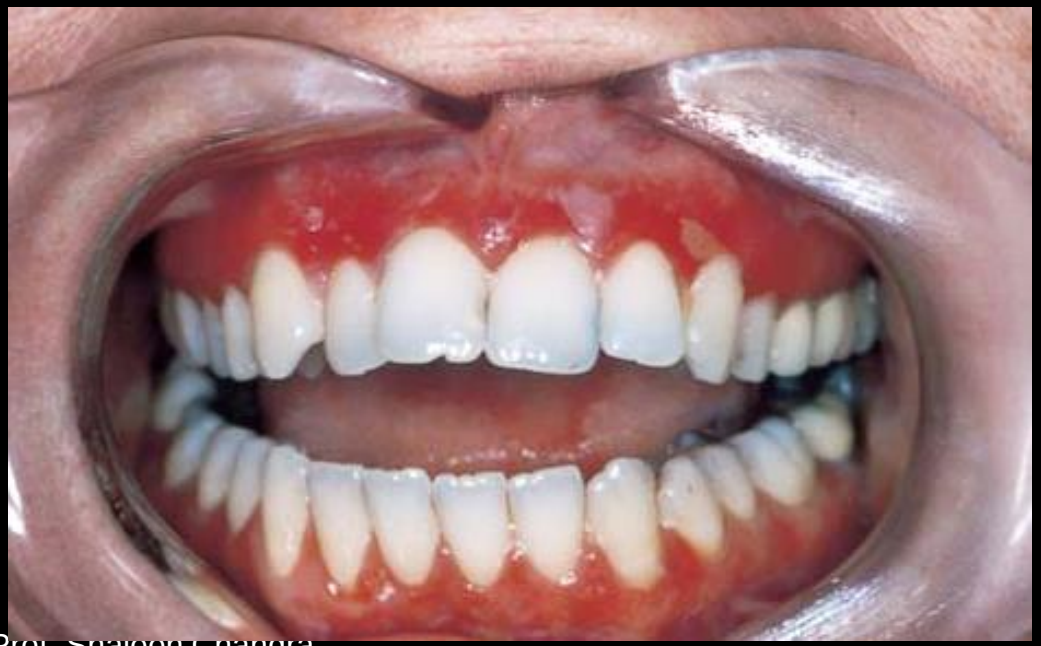


- Plaque-like

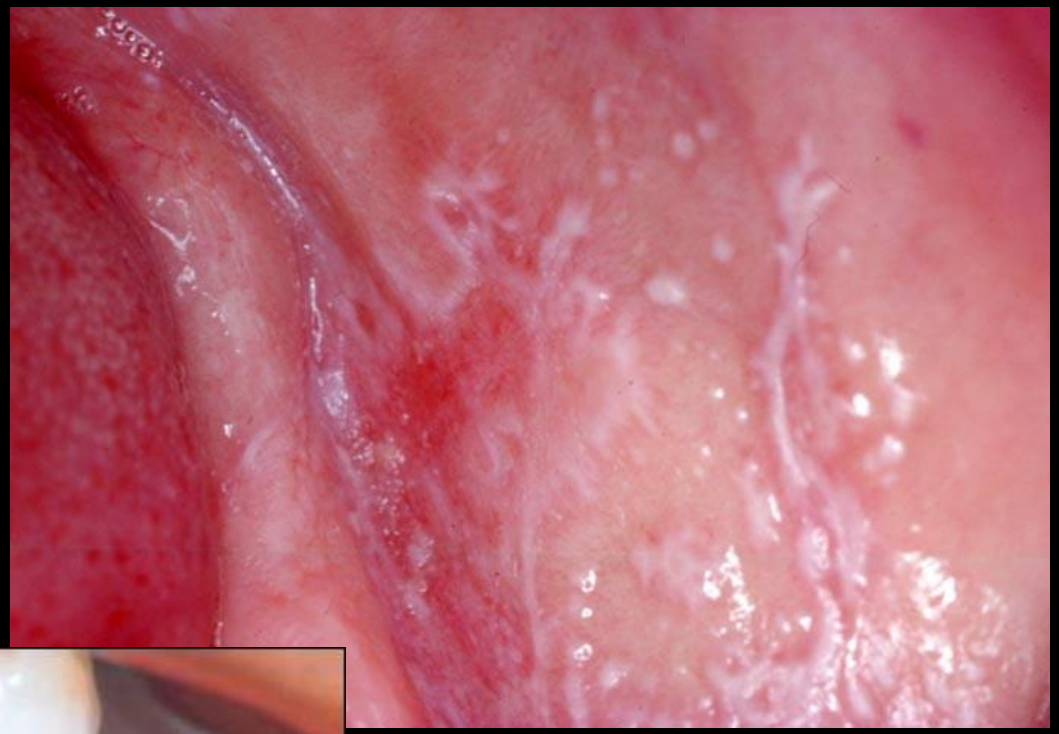


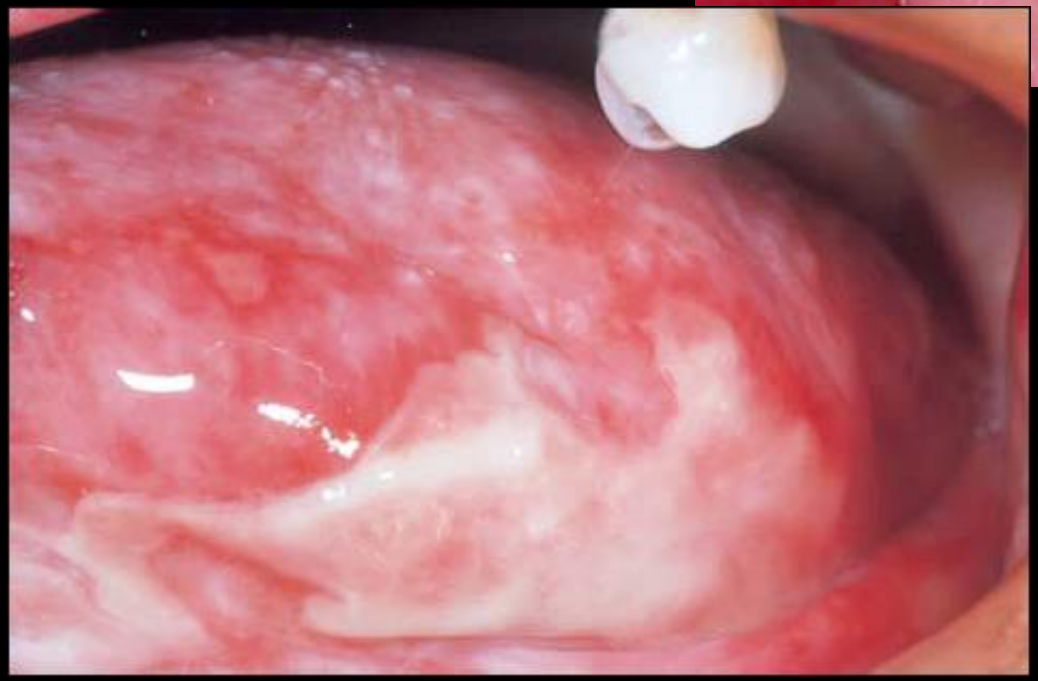


- Atrophic



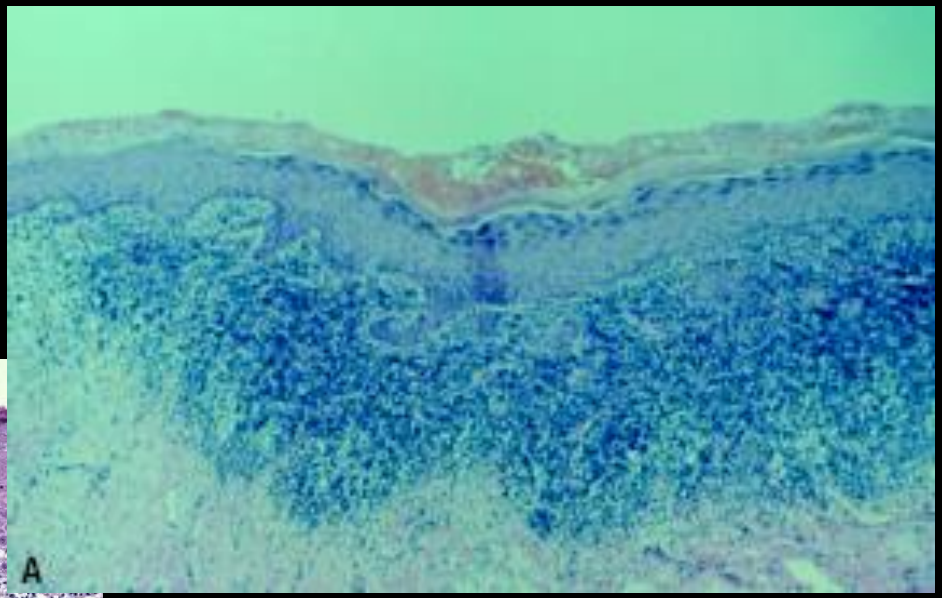
- Erosive

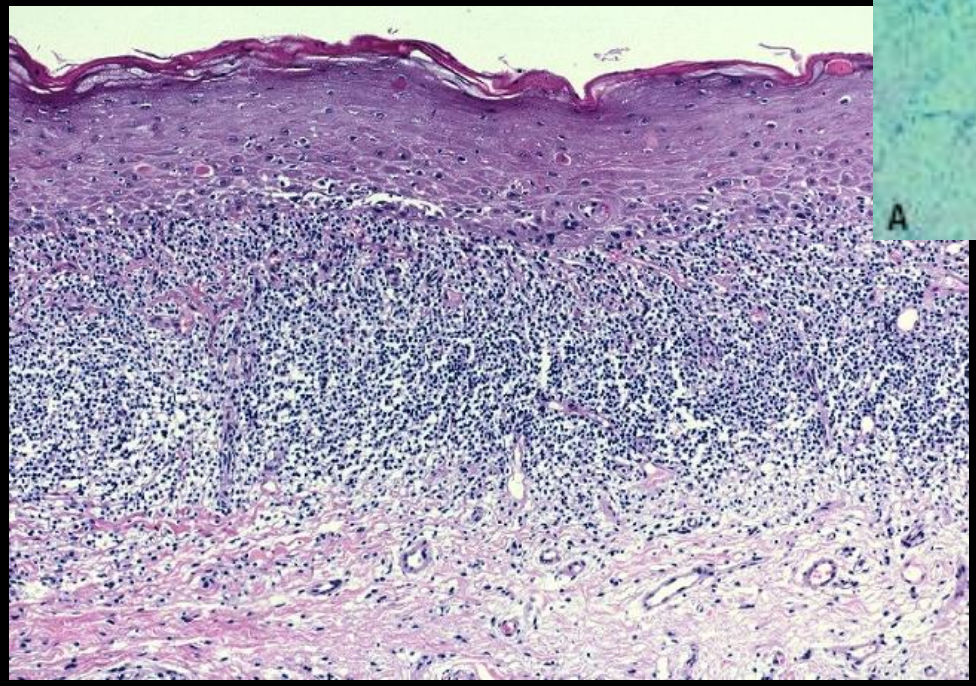




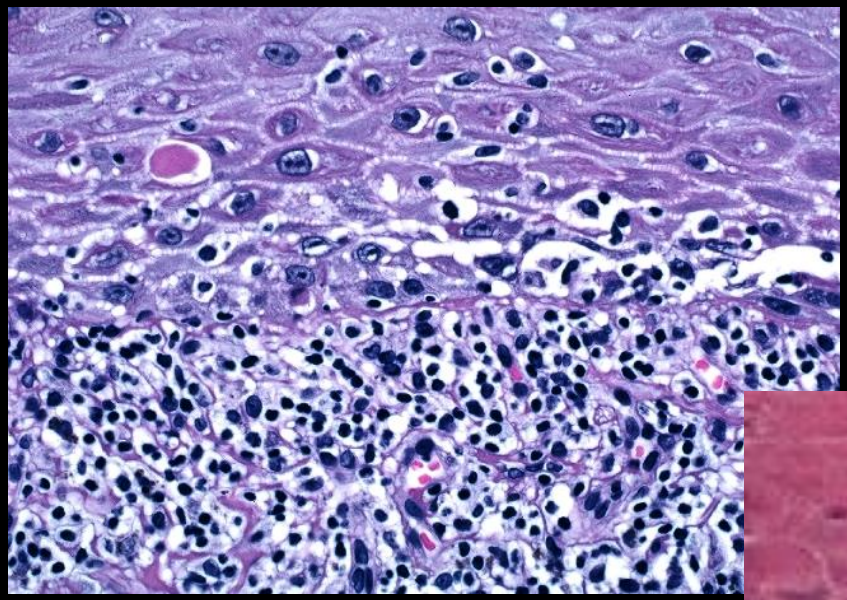
Histopathological features

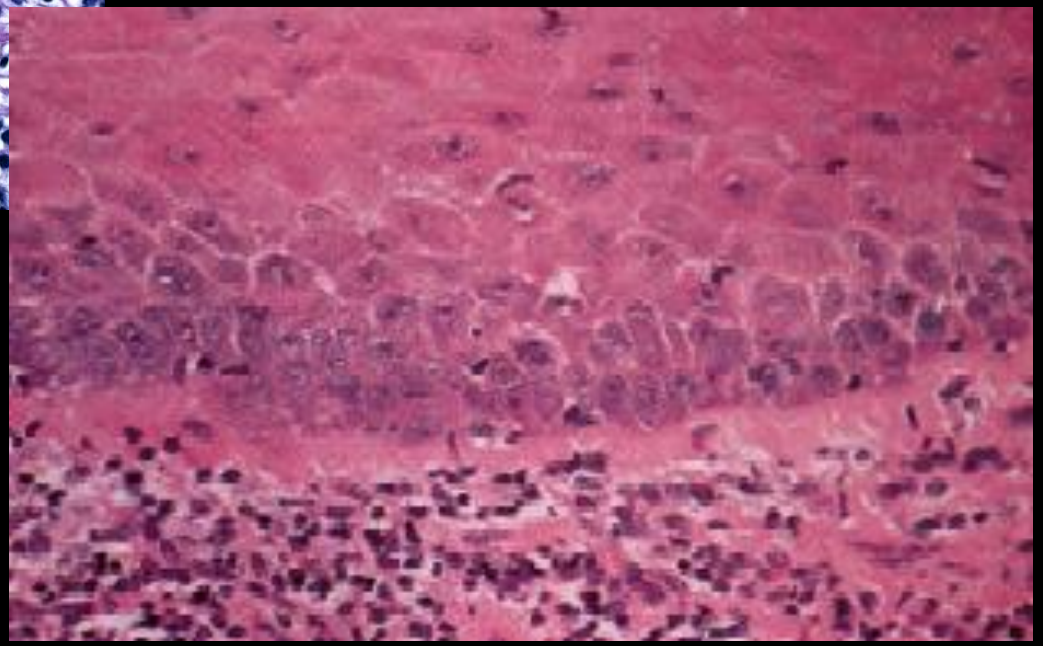
- **Hyperkeratosis/ orthokeratosis**
- **Thickening of the granular layer**
- **Acanthosis with intracellular edema of the spinous cells**
- **“Saw- tooth” appearance of the rete pegs**
- **Necrosis/ basal cell degeneration of basal cell layer with formation of a band of eosinophilic coagulum**
- **Lymphocytic infiltration & occasional plasma cells in subepithelial C.T**





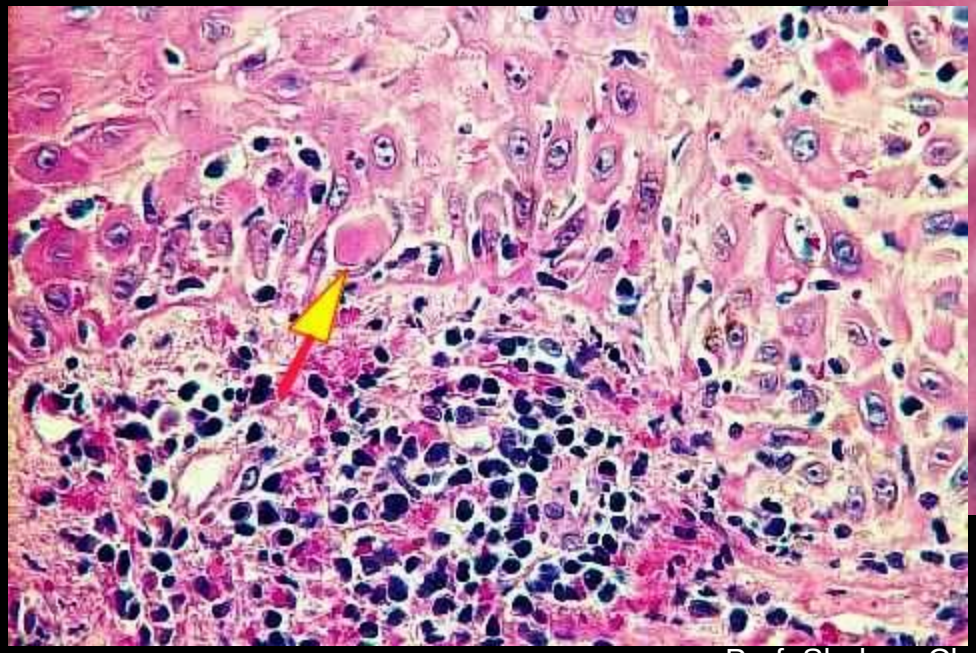
- OLP showing hyperkeratosis and a band like subepithelial lymphocytic infiltrate

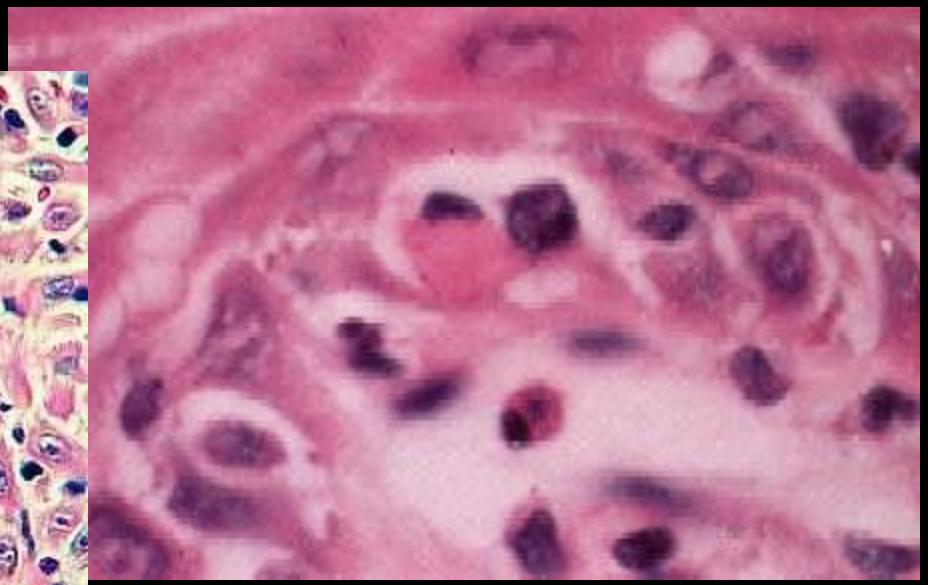


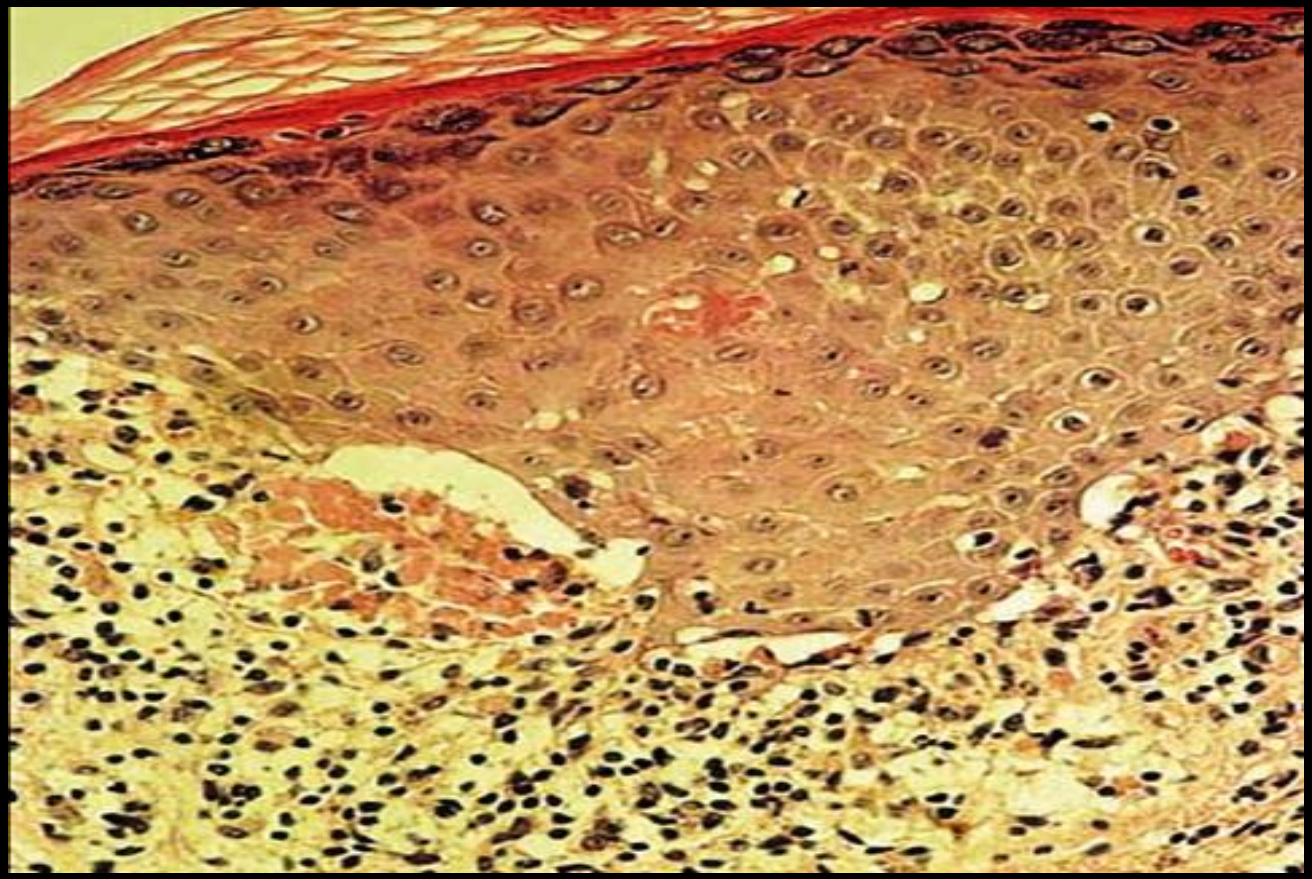


- OLP showing vacoular degeneration of basal cells and eosinophilic coagulum

- Colloid bodies/ Civette bodies/ Hyaline Bodies/ Fibrillar bodies in the basal/ spinous layers of epithelium
  - Degenerated epithelial cells/ phagocytosed epithelial cell remnant within microphages



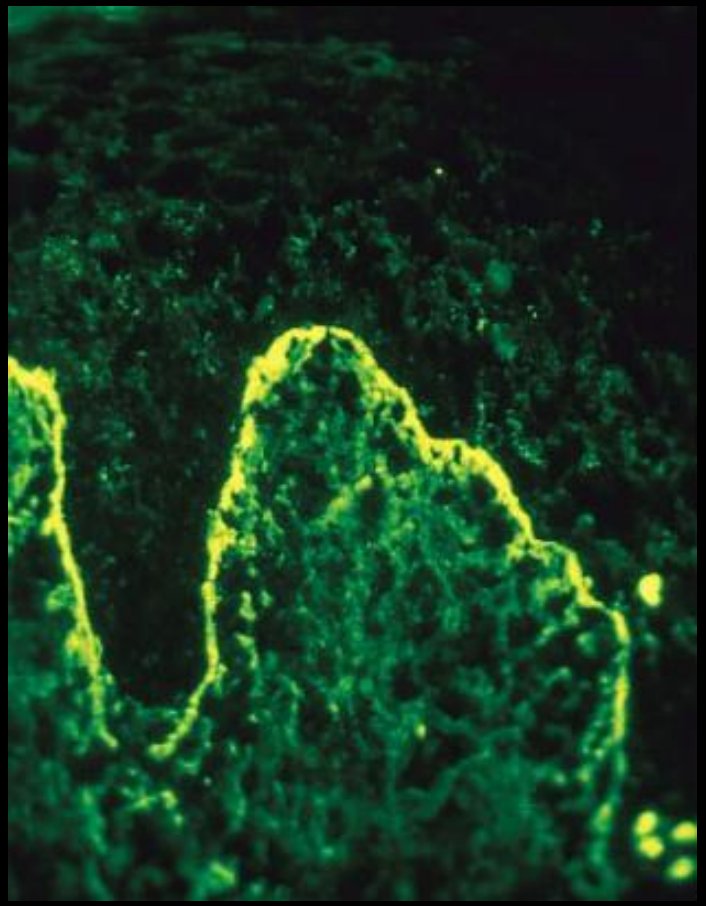


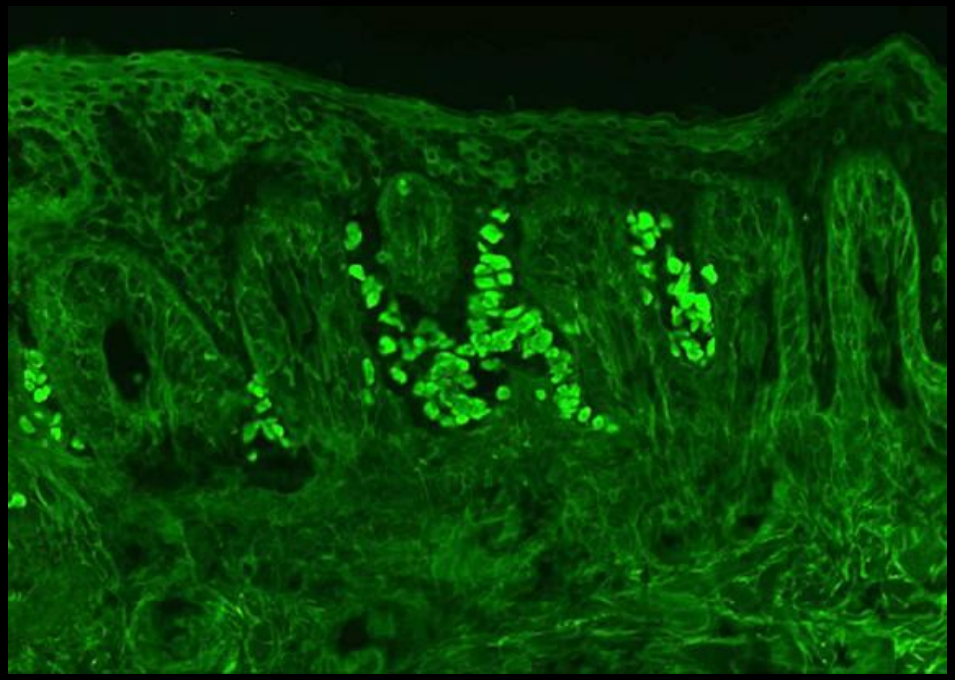


Max Joseph spaces

Immunoflorescence

- Direct immunofluorescence examination of involved skin or mucosa
  - Fibrinogen/fibrin deposited in a shaggy pattern at the dermal-epidermal junction
  - Numerous IgM-positive cytoid bodies at the dermal-epidermal junction





Prof. Shaleen Chandra

Differential Diagnosis

- Leukoplakia
- Candidiasis
- Pemphigus
- Cicatricial pemphigoid
- Erythema Multiforme
- Lupus Erythematosus

Malignant transformation

- Controversial
- Malignant transformation rate is low
  - 0.3%
- Most common type which undergoes malignant transformation
  - Erosive OLP
  - Plaque like OLP

- Lesions similar to lichen planus are called as “lichenoid lesions”
  - Lichenoid drug reaction
  - Lichenoid reaction
  - Oral manifestaions of graft vs host disease
  - Lupus erythematosis

Treatment

- **No specific treatment**
- **Arsenicals, mercurials & bismuth**
- **Vitamin and antioxidant therapy**
- **Corticosteroids (intralesional)**
- **Immunosuppressants**
  - **Cyclosporine**
  - **Tacrolimus**

Lupus Erythematosus

- Immunologically mediated condition

- Two basic forms- Systemic and discoid

Etiology

1.Genetic predisposition

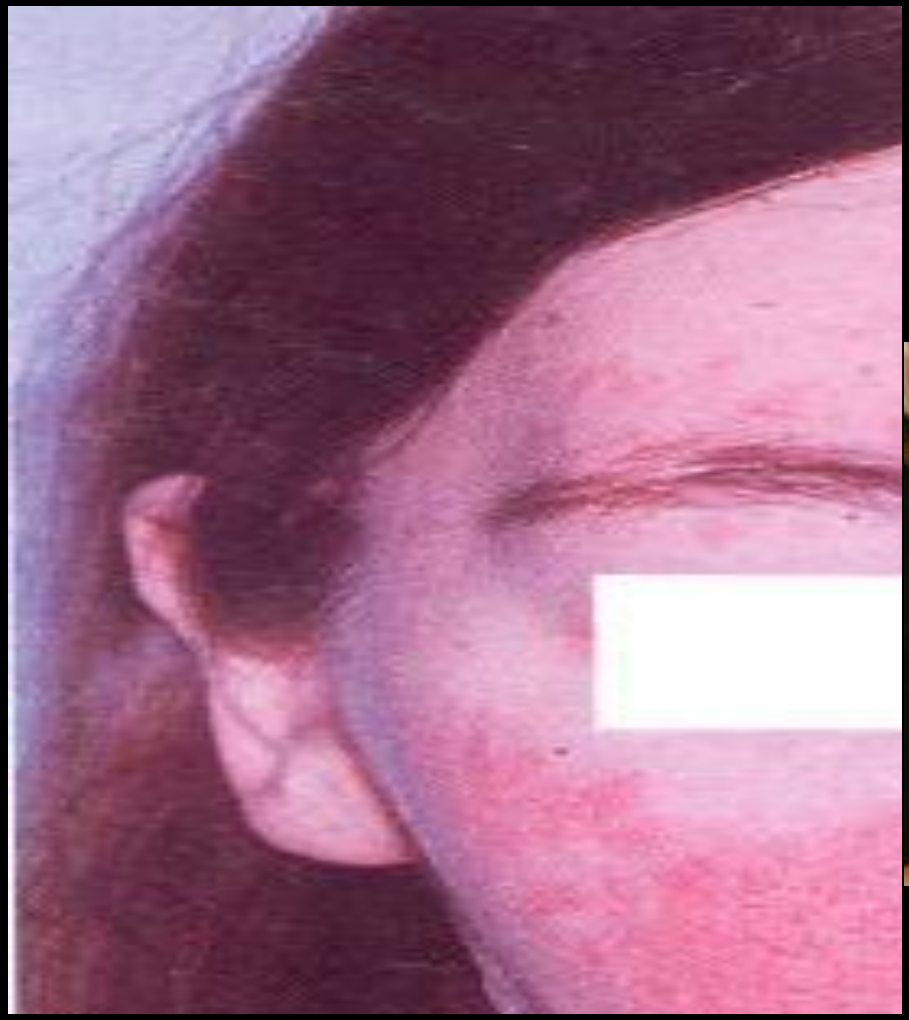
2.Deposition of Ag-Ab complexes

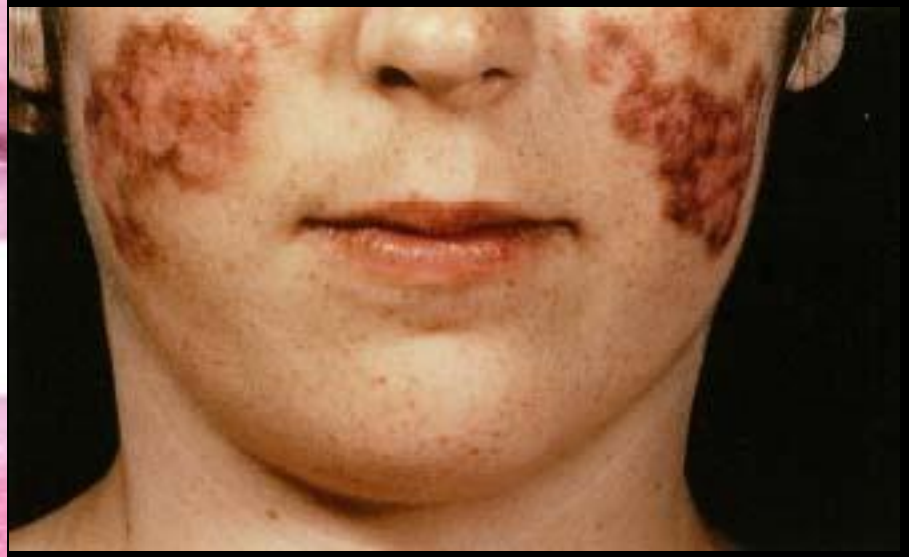
Systemic lupus erythematosus

- Serious multisystem disorder with a variety of cutaneous & oral manifestations
- Manifested by repeated remissions & exacerbations – difficult to diagnose in early stage
- Females > Males (8:1)
- 3rd decade of life

Clinical features

- Fever, weight loss, arthritis, fatigue & general malaise
- Rashes/ erythematous patches → Butterfly pattern (40- 50 % of affected pts) over malar area & nose
- Itching/ burning sensation, hyperpigmentation
- Lesions aggravate on sun exposure
- Involvement of various organs- kidney, heart





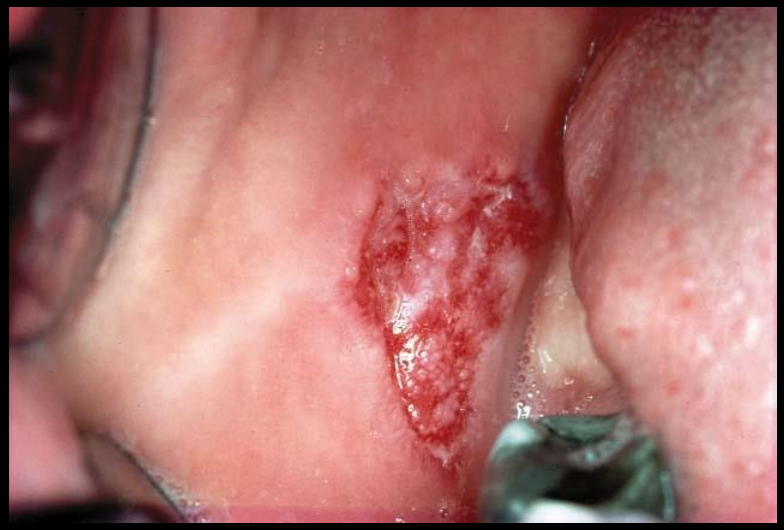
Prof. Shaleen Chandra

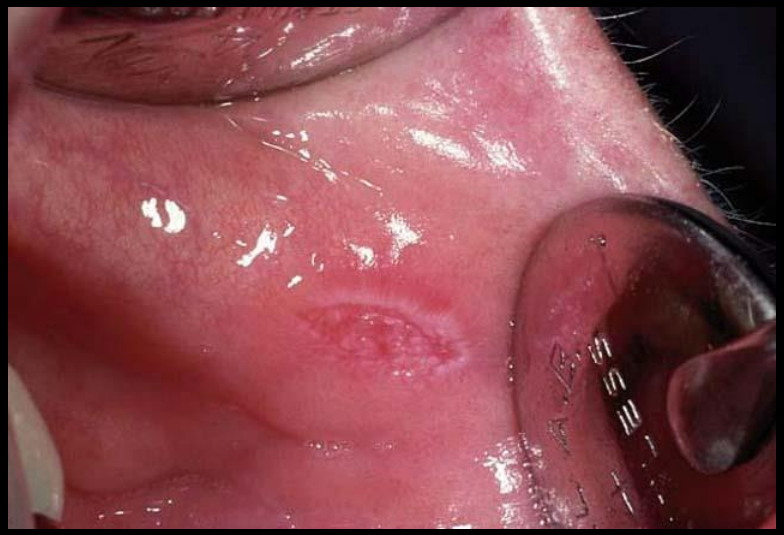
- **Oral manifestation**

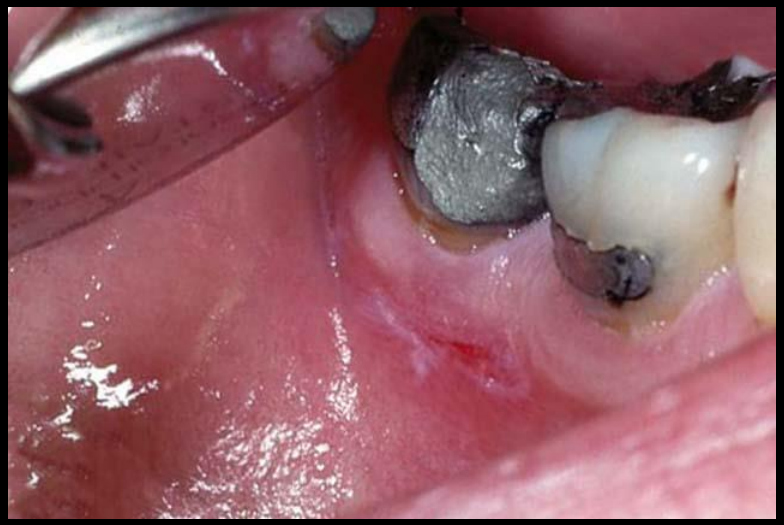
  - Erythema/ Surface ulceration/ Keratotic plaques/ White striae or papules

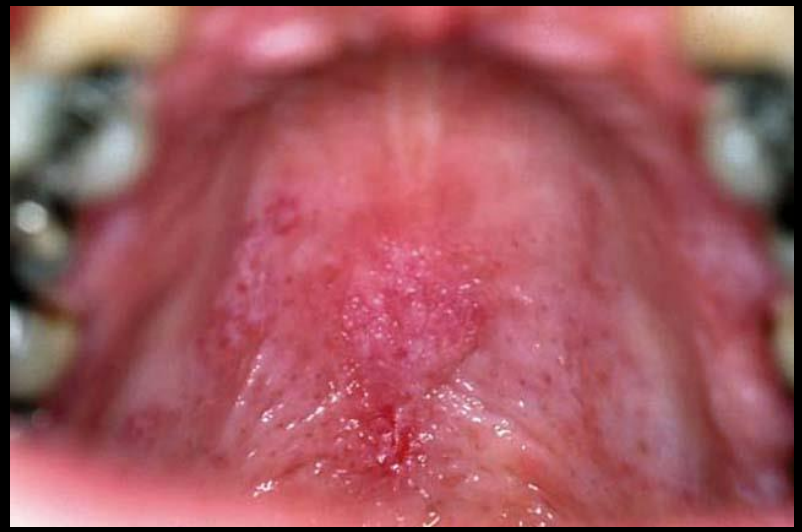
  - Lesions are frequently symptomatic, especially if the patient ingests hot or spicy foods

  - Xerostomia
  - Stomatodynia
  - Candidiasis
  - Periodontal diseases
  - Dysgeusia









Prof. Shaleen Chandra

Discoid Lupus Erythematosus

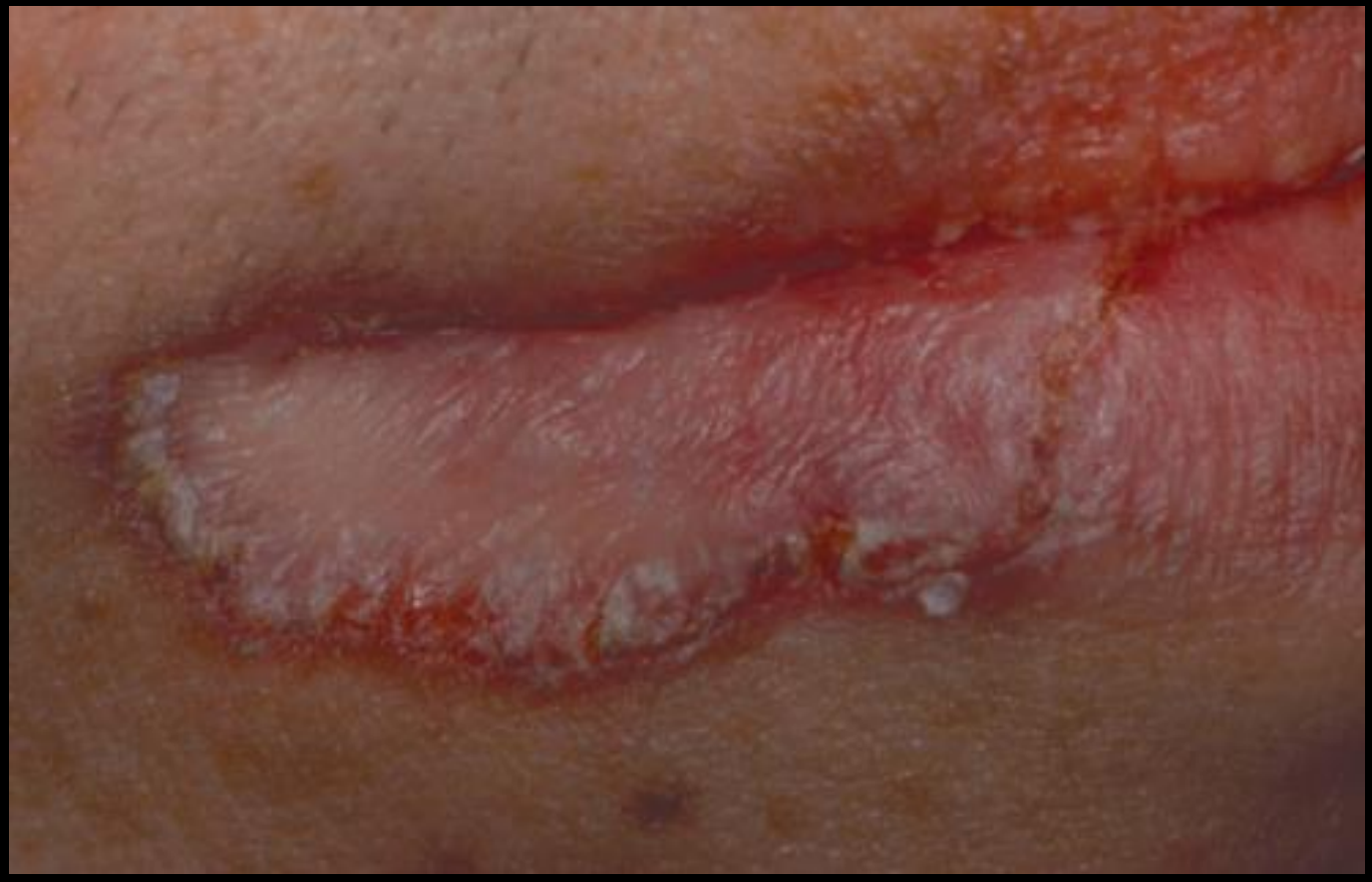
- Occurs predominantly in females in the third or fourth decade of life
- *Localized and disseminated forms*
- Also called *chronic cutaneous lupus*

Clinical features

- Red, scaly patches that favor sun-exposed areas such as the face, chest, back, and extremities

- Characteristically expand by peripheral extension and are usually disk-shaped

- Oral mucosal lesions of DLE frequently resemble *reticular or erosive lichen planus*.

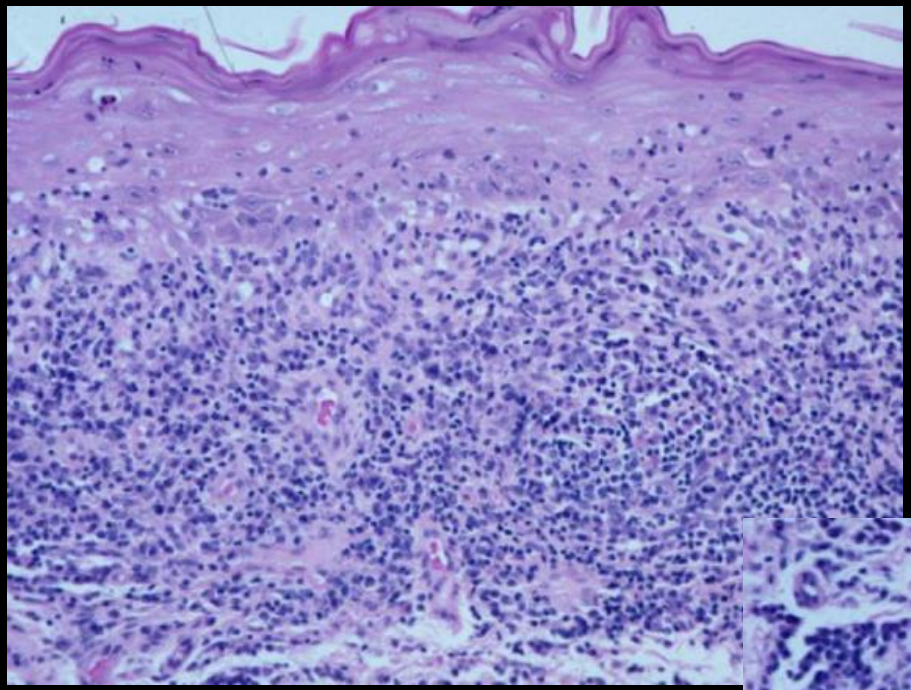


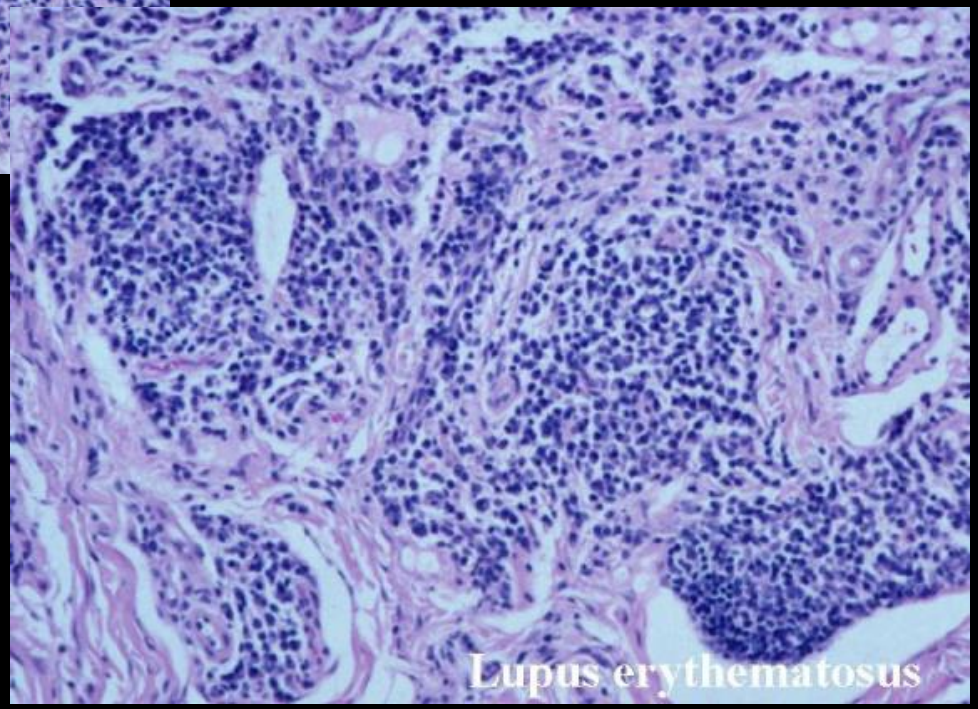
- As the lesions expand peripherally, there is central atrophy, scar formation, and occasional loss of surface pigmentation

Histopathologic features

- Skin lesions
  - Hyperkeratosis
  - Follicular plugging
  - Degeneration of basal cell layer
  - Patchy to dense aggregates of chronic inflammatory cells often arranged perivascularly
  - Thickening of basement membrane

- **Oral lesions**
  - **Hyperkeratosis**
  - **Alternating atrophy & thickening of the spinous cell layer**
  - **Degeneration of basal cell layer**
  - **Subepithelial lymphocytic infiltration**
  - **Resembles oral lichen planus but can be distinguished by**
    - **Patchy deposits of PAS positive material in the BMZ**
    - **Subepithelial edema**
    - **More diffuse, deep inflammatory infiltrate**

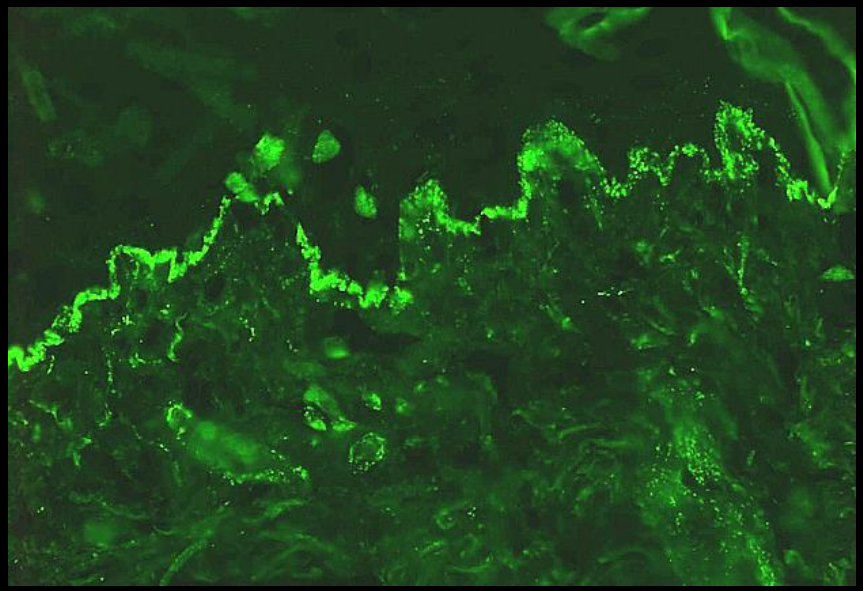




Prof. Shaleen Chandra

Immunofluorescence

- **Direct immunofluorescence**
  - Deposition of various immunoglobulins (IgG, M &A), fibrinogen and C3 in a granular band involving the basement membrane zone
  - This is called the positive Lupus band test

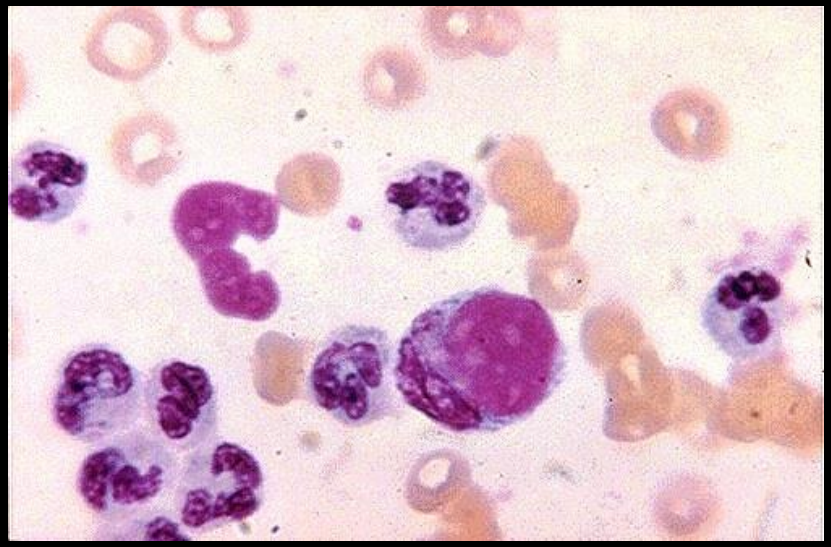


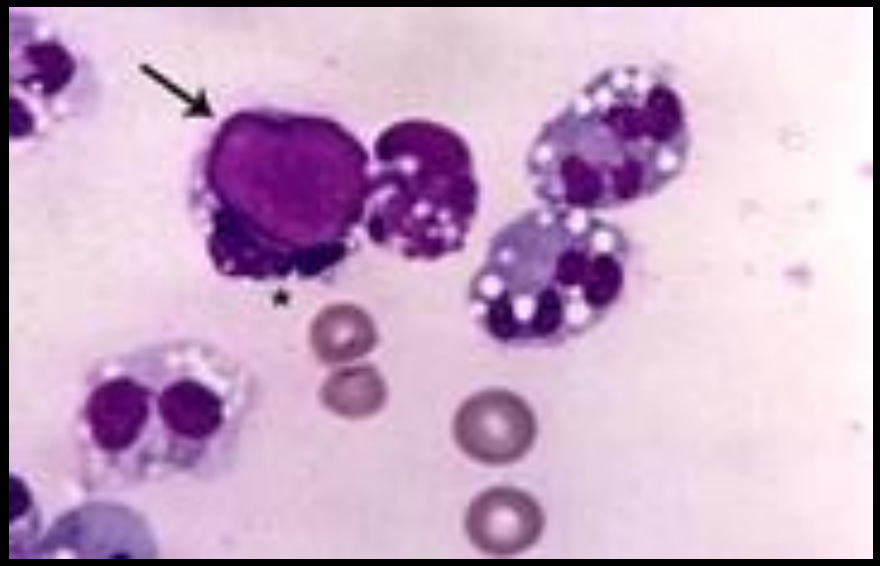
Laboratory diagnosis

- ANA
- Anti-DNA antibody,
- L.E. cell test
- Renal function test
- Increased ESR

L E cell test

- **L.E. cells**
  - **Rosettes of PMNLs surrounding nuclear mass of lymphocytes**





Pemphigus

- *Pemphix"* – Bubble or blister

- Autoimmune disorder in which intraepithelial vesicles & bullae are produced by the action of the autoantibodies

Types

- Pemphigus vulgaris (most common)
- Pemphigus vegetans
- Pemphigus foliaceous
- pemphigus erythematosus

Etiology

- ***Autoimmune disorder***

- Malignant diseases

- Viral association (Pemphigus foliaceous) – transmitted by an insect vector, endemic to brazil, in people living near river, rural areas.

- Drugs
  - Penicillamine

Pathogenesis

- Organ specific autoimmune disease

- Unique autoantibody specific for epidermal cell surface antigen **desmoglein (Dsg)**

Auto antibodies (IgG or IgA) directed against Desmosomal structural proteins

Dsg 1 & Dsg 3

↓

Destruction of desmosomes and hence decreased adhesion of epithelial cells to each other

↓

Formation of cleft between the cells

↓

Accumulation of fluid in the cleft

↓

Formation of intraepithelial vescicle

↓

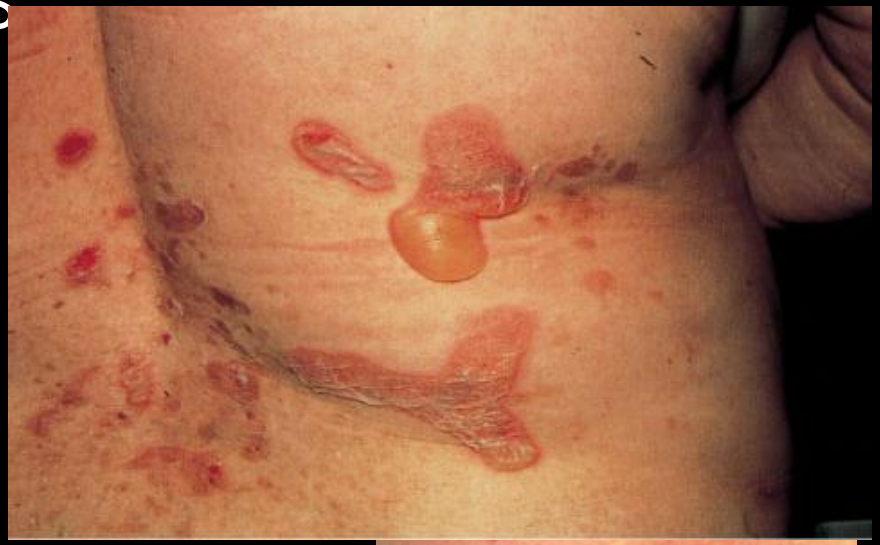
Rupture to form erosions and ulcerations

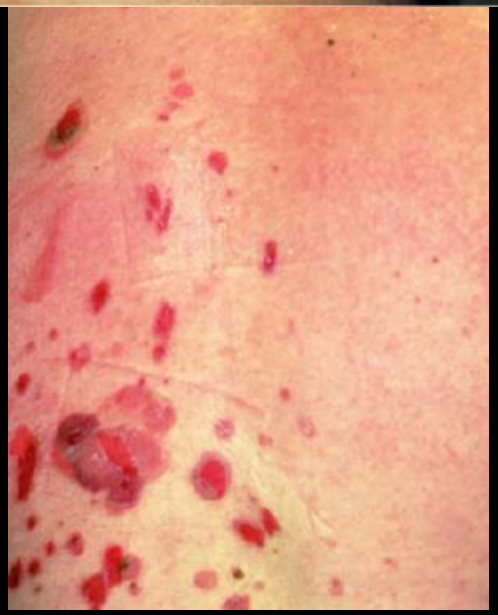
Clinical features

- Initial lesion → vesicle/ bulla
- Initial lesions → trunk, oral cavity
- 4^{th}- 6^{th} decade
  - Rare in children
- No sex predilection
- Common in Jewish persons
- Fever & malaise

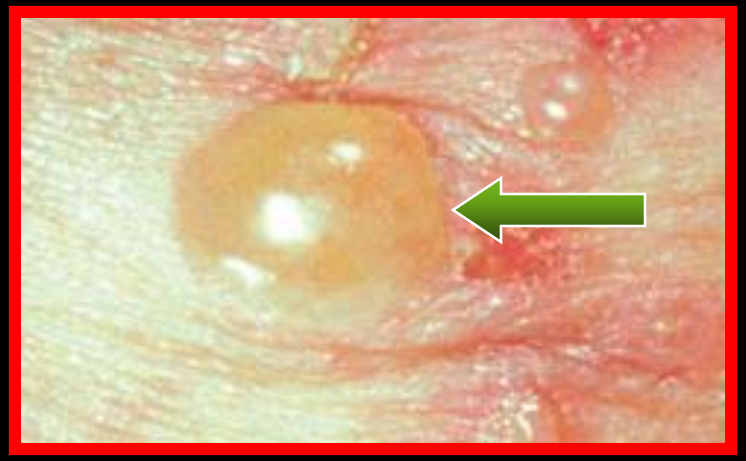
Pemphigus vulgaris

- Vesicle or bullae of varying sizes
  - Contain thin watry fluid
  - Vesicles rupture to form raw eroded surface
  - Positive **Nikolsky's sign** and **Asboe Hansen's phenomenon**

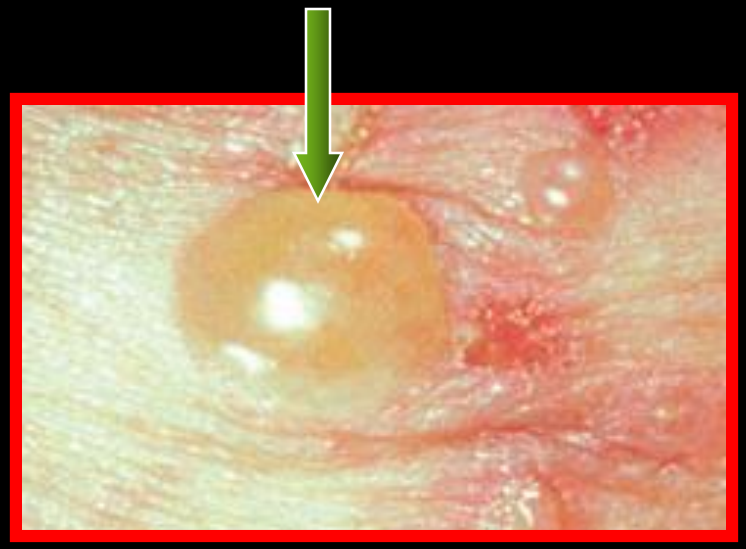




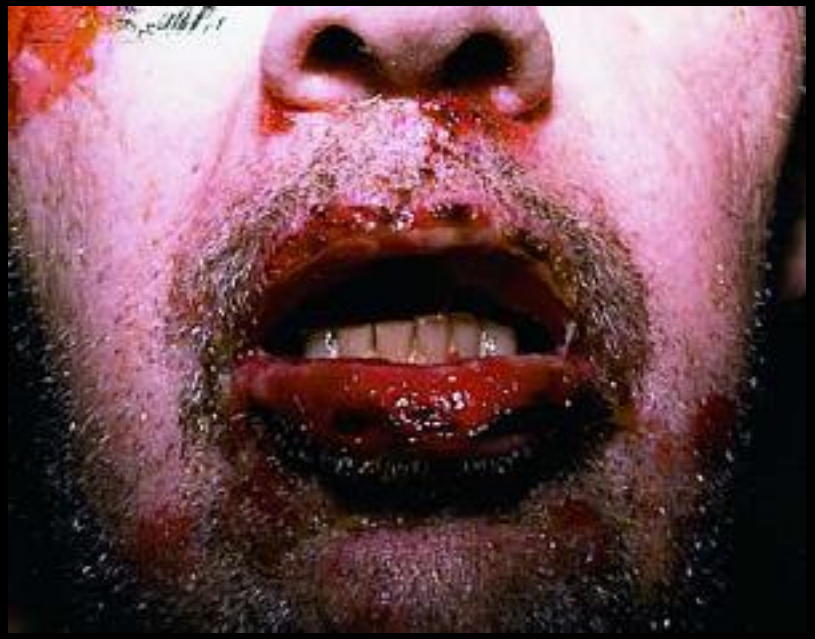
- **Nikolsky's sign-** formation of a lesion after gentle mechanical pressure applied laterally on clinically normal skin adjacent to the vesicle

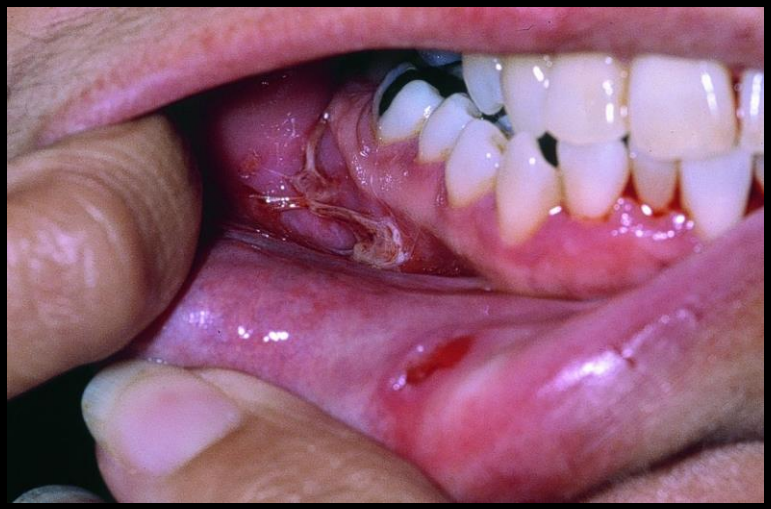


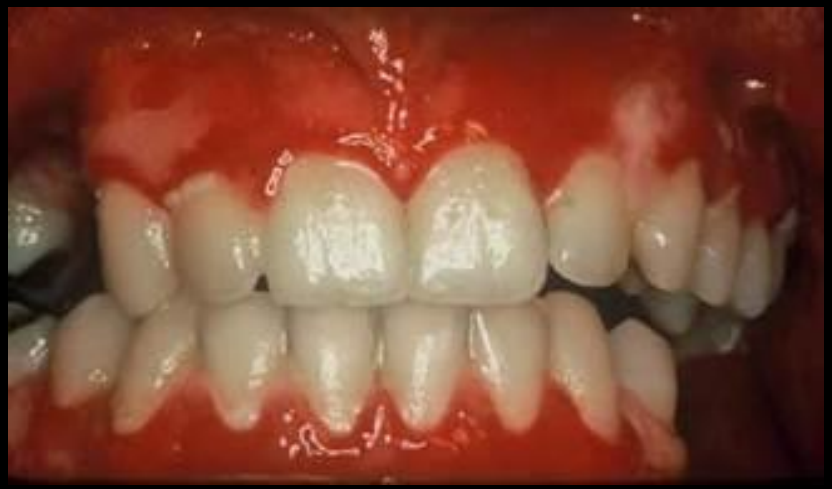
- **Asboe Hansen's phenomenon-** extension of a blister into apparently normal appearing skin as a consequent of applying direct pressure onto an intact blister

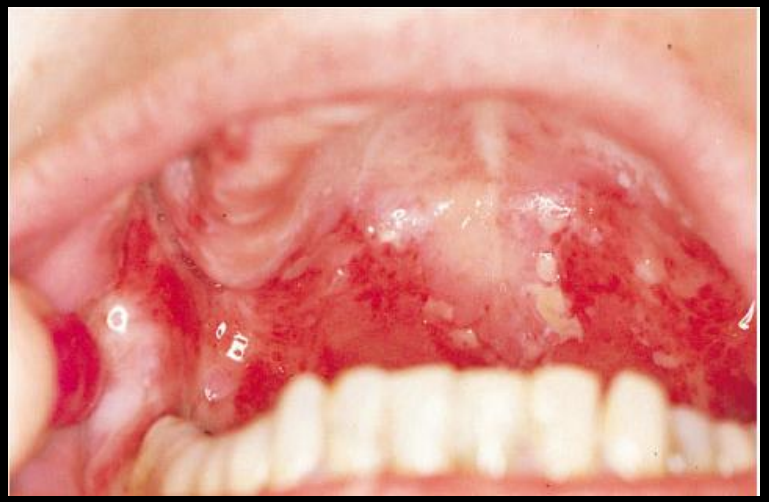


- Oral manifestaions
  - Seen in about 50-70% patients
  - Intact bullae are rare in oral cavity
  - Ill defined, irregularly shaped erosions
  - Painful and slow to heal
  - Inability to eat and speak





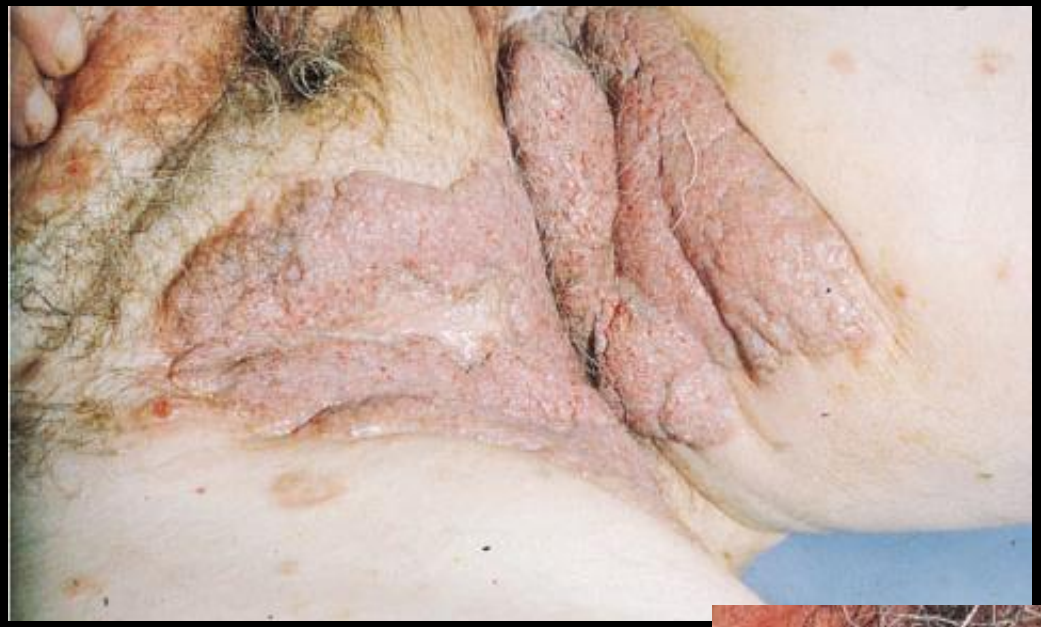


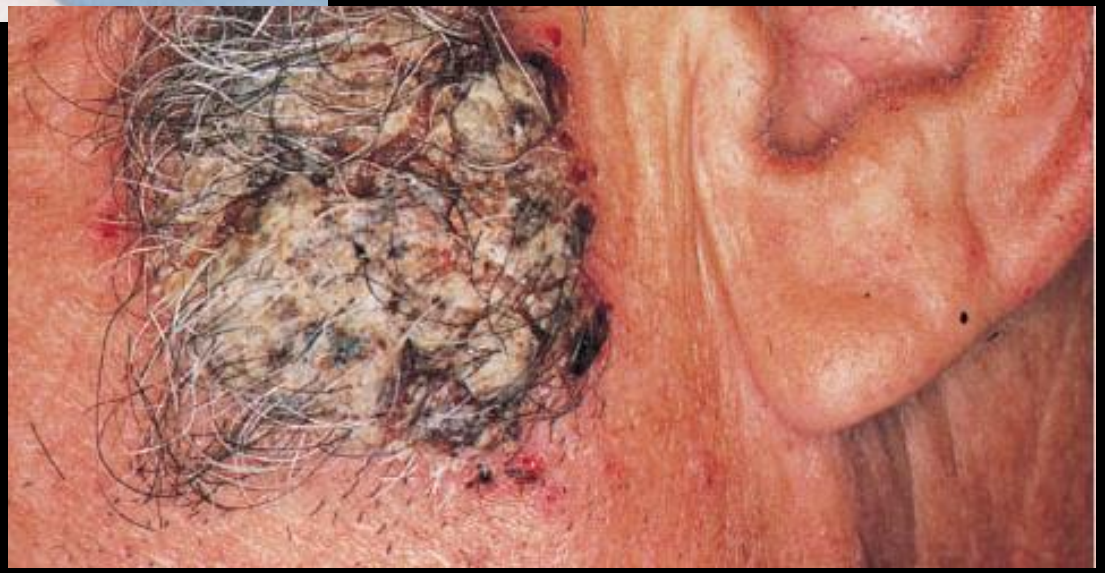


Prof. Shaleen Chandra

Pemphigus vegetans

- Flaccid bullae → eroded → form vegetations resembling fungus
- Covered by purulent exudate; inflamed border
- Frequently on the nose, mouth, axillae, anogenital regions
- Intraorally, affect buccal mucosa, hard &soft palate

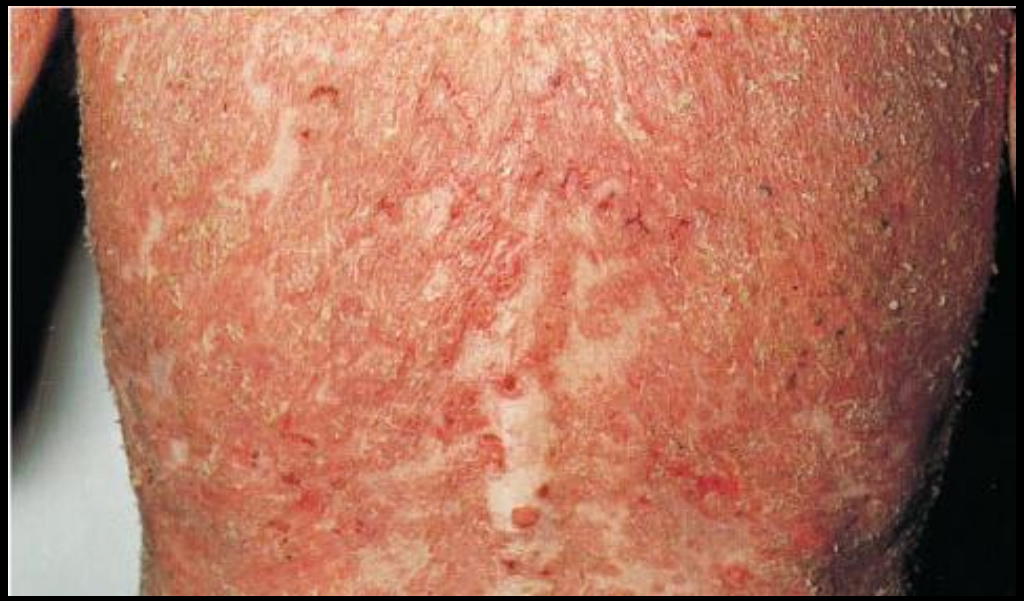


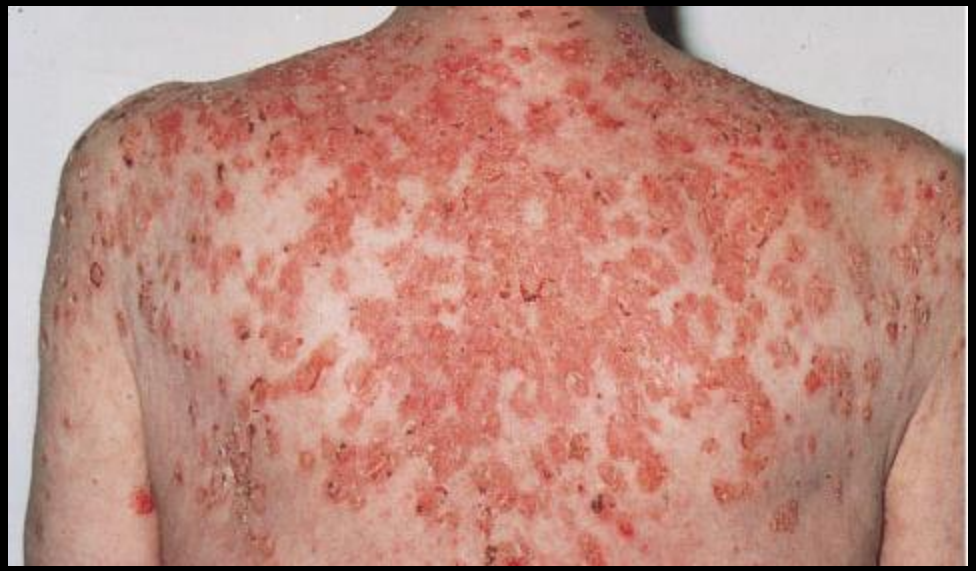


Prof. Shaleen Chandra

Pemphigus foliaceous

- Oral lesions rare
- Early bullous lesions → rupture → dry to leave masses of flakes/ scales
- Similar to exfoliative dermatitis/ eczema
- *Brazilian pemphigus/ Fogo selvagem/ Brazilian wildfire- mild form of P. foliaceous, found in tropical regions; often occur in children & frequently in family groups*





Prof. Shaleen Chandra

Pemphigus erythematosus

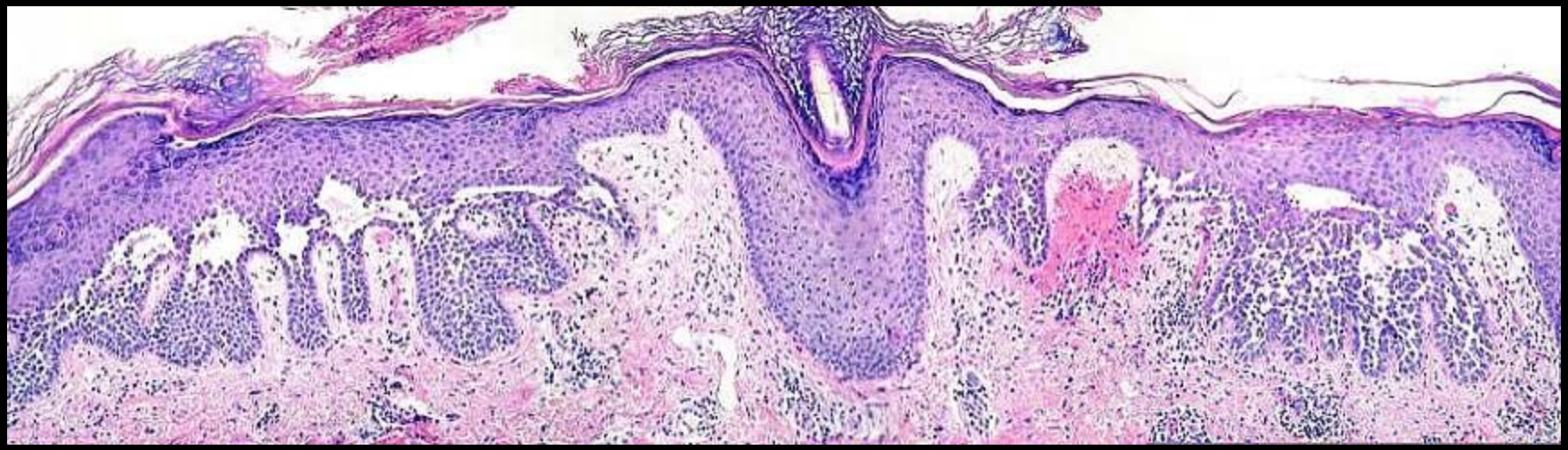
- Senear-Usher syndrome

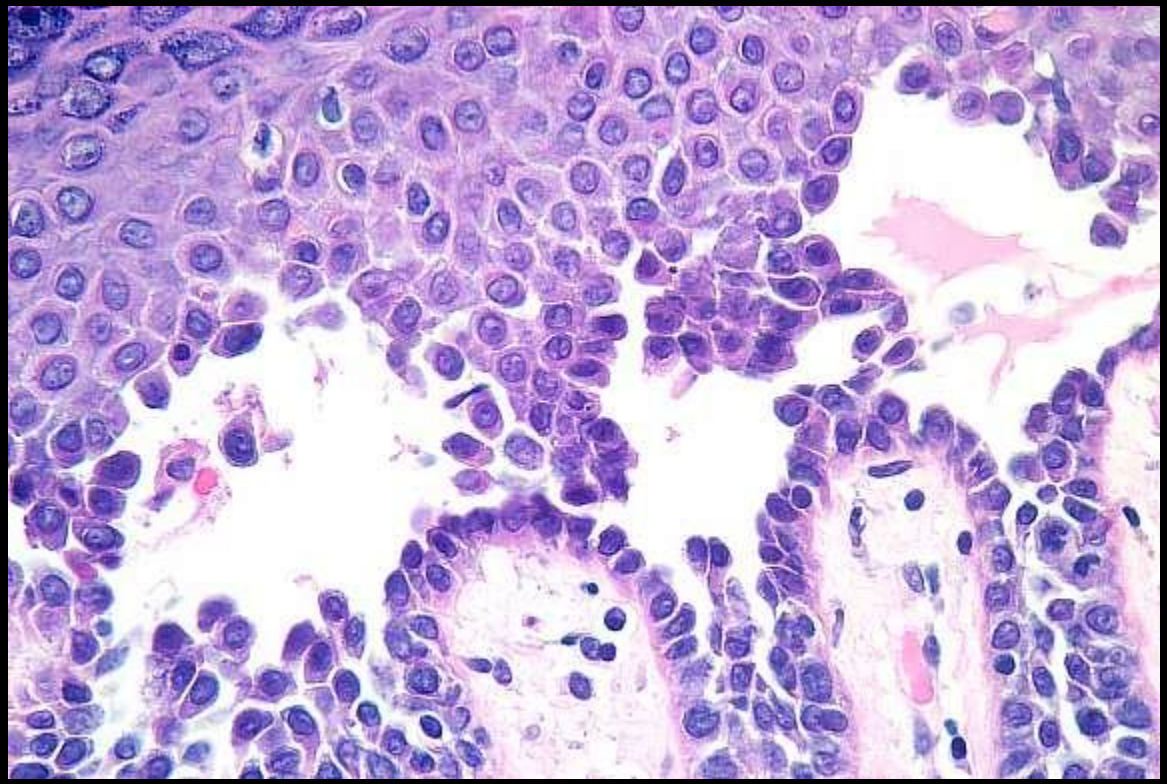
- Along with bullae & vesicles, concomitant with the appearance of crusted patches resembling seborrheic dermatitis/ LE

- Most cases terminate in P. vulgaris

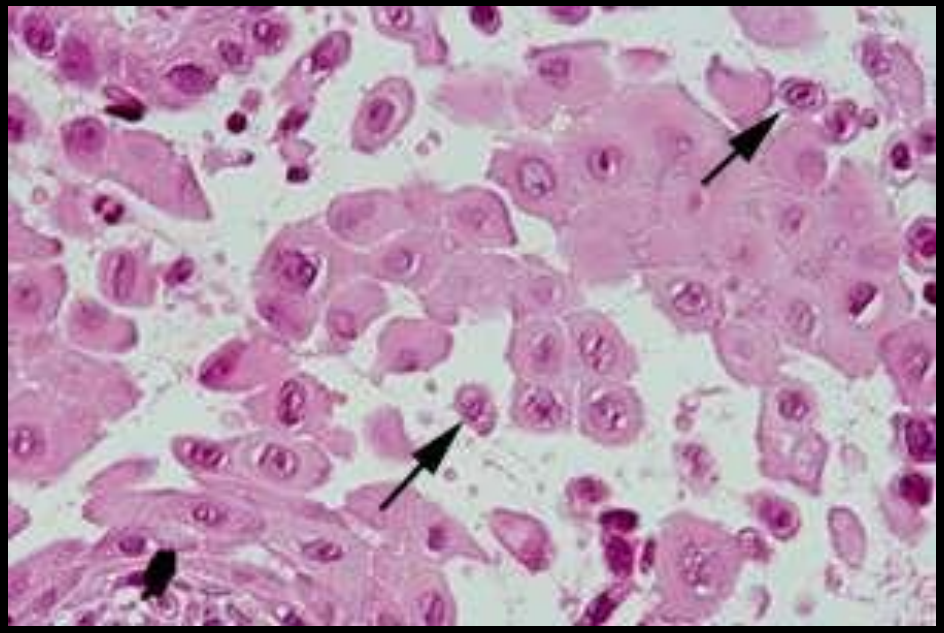
Histopathologic features

- Suprabasilar split in the epithelium with intraepithelial vesicle formation
- Intercellular juncions disappear
- Acantholysis
- **Tzanck cells** →clumps of epithelial cells lying freely in the vesicular space
  - Show degenerative changes, swelling of nuclei and hyperchromatic staining
- Variable number of neutrophils (relative lack of inflammatory cells)

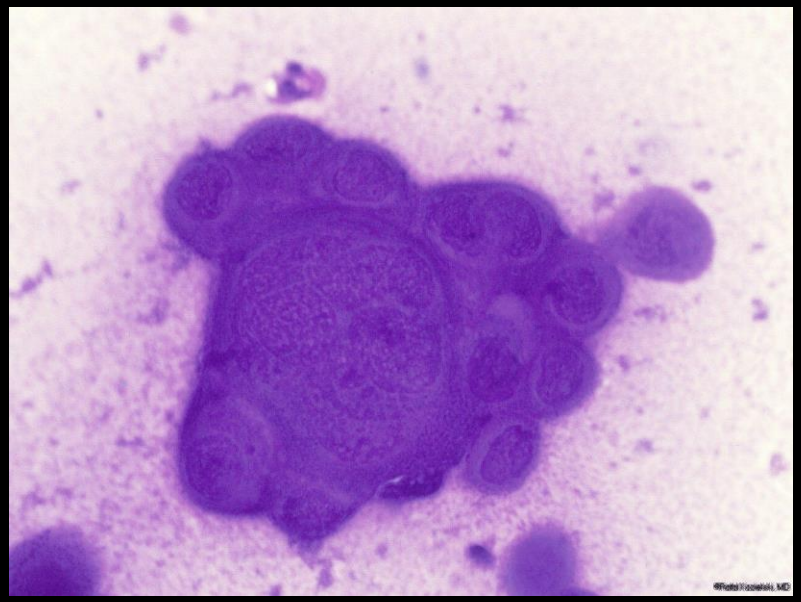




Prof. Shaleen Chandra

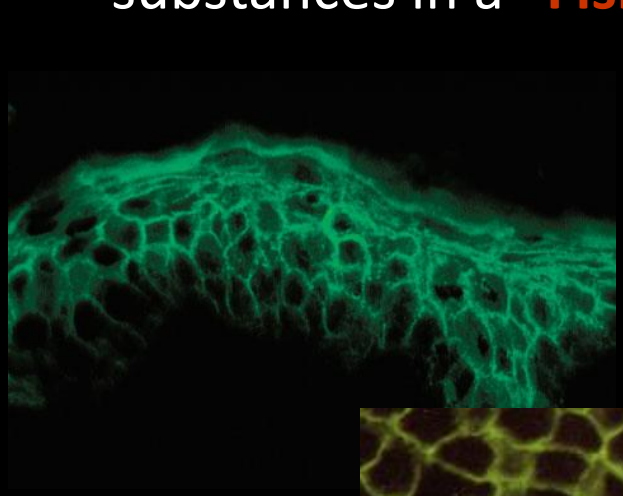


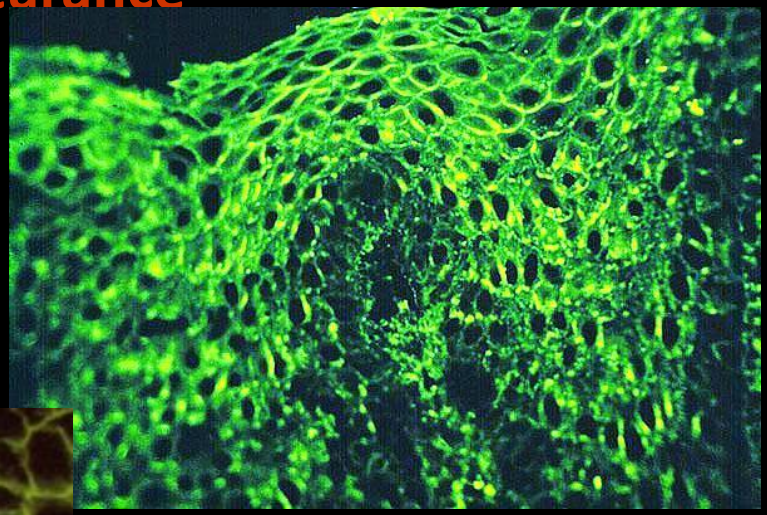
- Tzanck cells

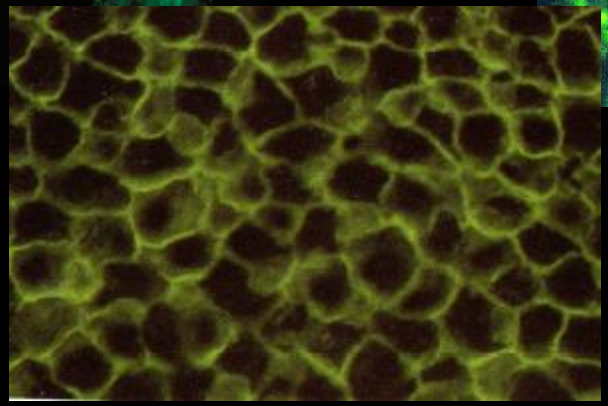


Immunofluorescence findings

- **Direct immunofluorescence**
  - Deposition of IgG, IgA, IgM, and C3 in the intercellular substances in a **"Fishnet appearance"**







Indirect immunofluorescence

- Substantiates the presence of circulating autoantibodies (chiefly IgG, sometimes also C3, IgA & IgM) which reacts with normal animal or human mucosa

- **Differential diagnosis**
  - Dermatitis herpetiformis
  - Erythema multiforme bullosae
  - Bullous lichen planus
  - Epidermolysis bullosa
  - Bullous pemphigoid
  - Cicatricial pemphigoid

- **Treatment**
  - Corticosteroids
  - Water electrolyte balance

Pemphigoid

- Group of vesiculobullous diseases clinically resembling Pemphigus
  - **Cicatricial Pemphigoid**
  - **Bullous Pemphigoid**

Cicatricial Pemphigoid

Benign mucous membrane Pemphigoid

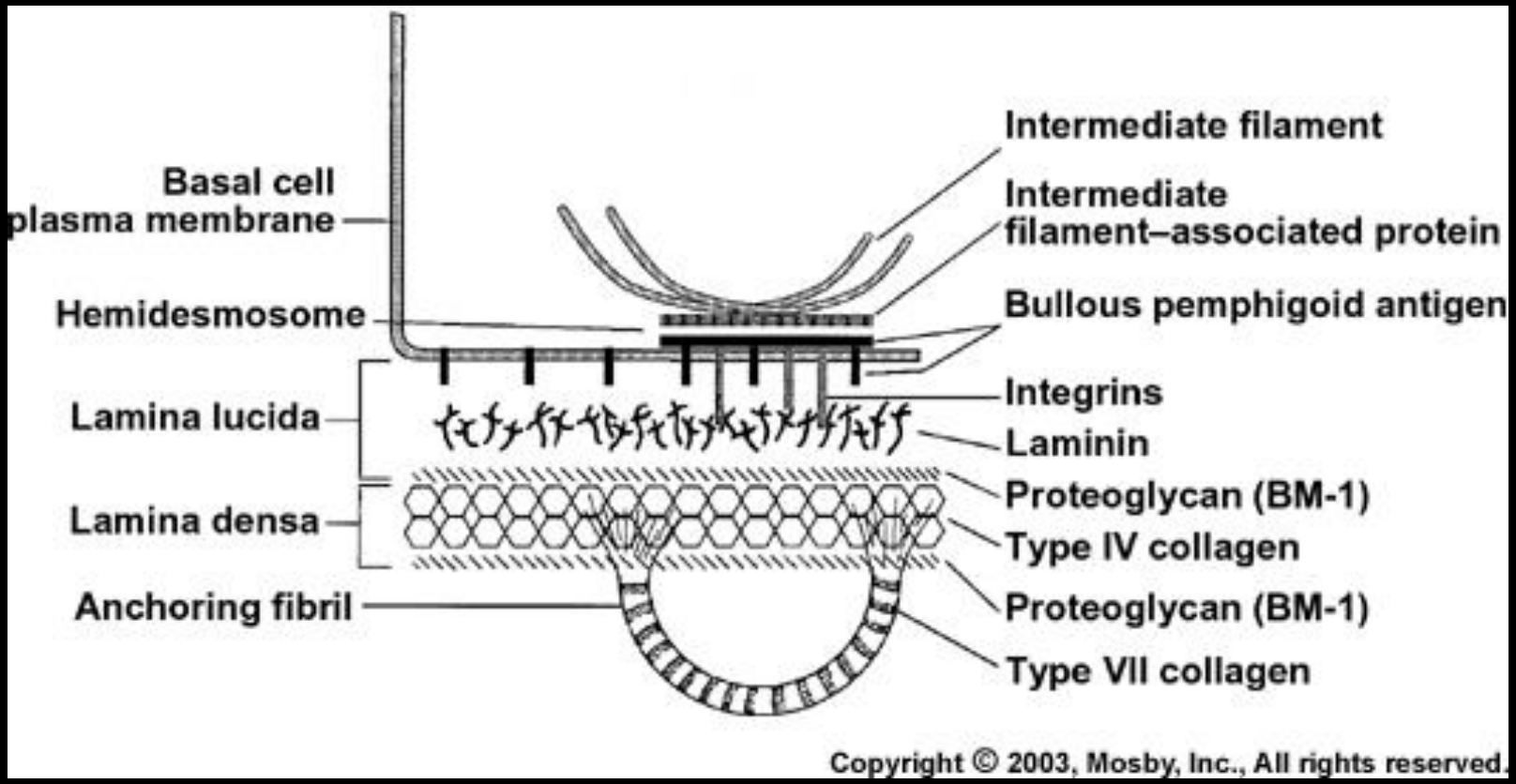
Mucous membrane Pemphigoid

- A chronic sub epithelial autoimmune disease, which predominantly involves mucosal surfaces & results in mucosal blistering, ulceration, & subsequent scarring

- 30% will have skin involvement

Etiopathogenesis

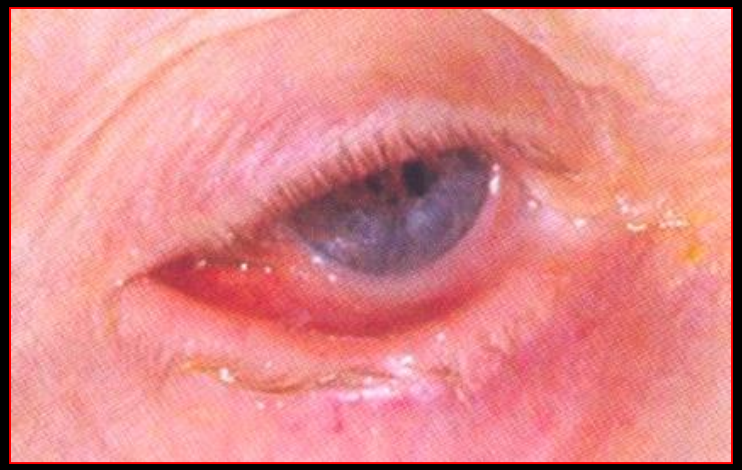
- Autoantibodies directed against basement membrane zone antigens
  - Bullous pemphigoid antigen 2 (BPAG2)
  - Epiligrin (laminin 5)

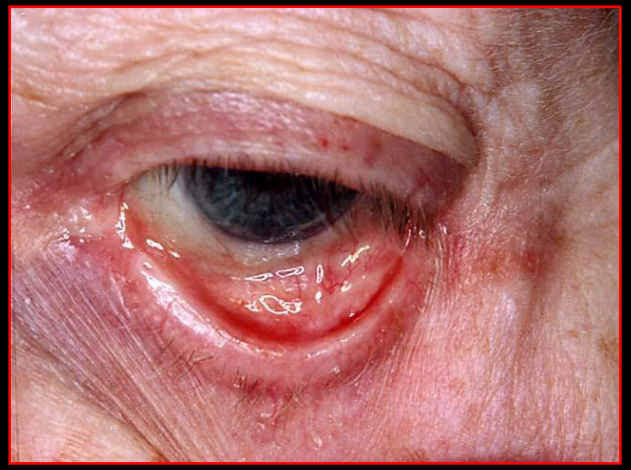

Basal cell plasma membrane
Hemidesmosome
Lamina lucida
Lamina densa
Anchoring fibril
Intermediate filament
Intermediate filament–associated protein
Bullous pemphigoid antigen
Integrins
Laminin
Proteoglycan (BM-1)
Type IV collagen
Proteoglycan (BM-1)
Type VII collagen
Copyright © 2003, Mosby, Inc., All rights reserved.

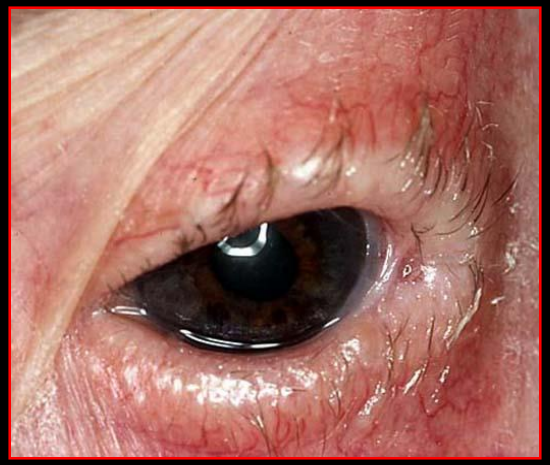
Clinical features

- Affects older individuals (40-60 yr age group)
- Females > males
- Oral/ conjunctival vesiculobullous lesions
- Skin lesions→ around genitalia & body orifices
- Lesions heal by scar formation particularly on conjunctiva
- Nose, larynx, pharynx, esophagus, vulva, vagina, penis & anus

- **Occular lesions→ most common complication**
  - Subconjunctival fibrosis
  - Scarring b/w bulbar & palpebral conjunctiva
  - Entropion→ eyelids turn inwards
  - Trichiasis → closure of opening of lacrimal glands → Eye becomes dry
  - Keratin production → BLINDNESS



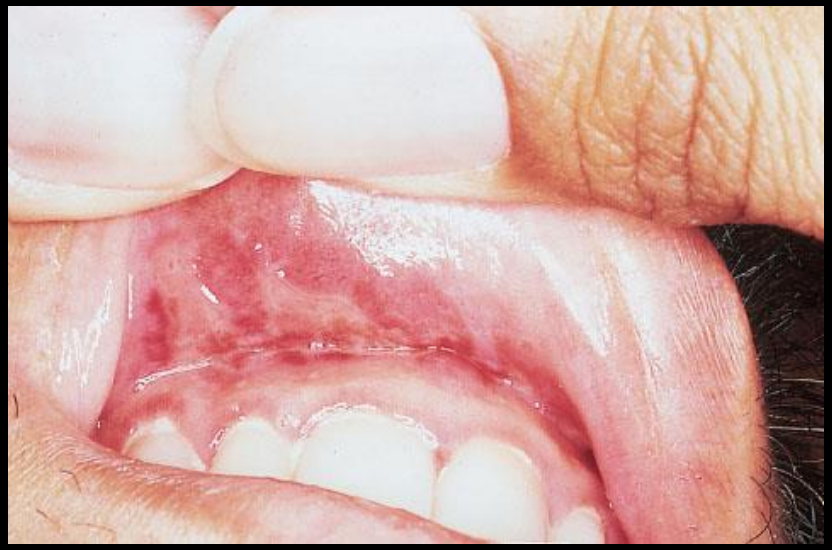


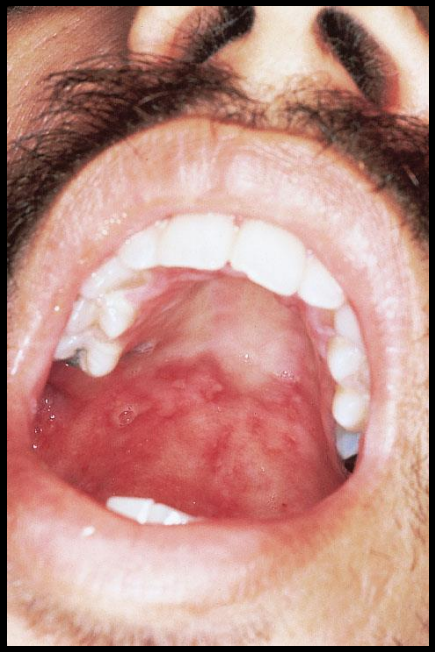


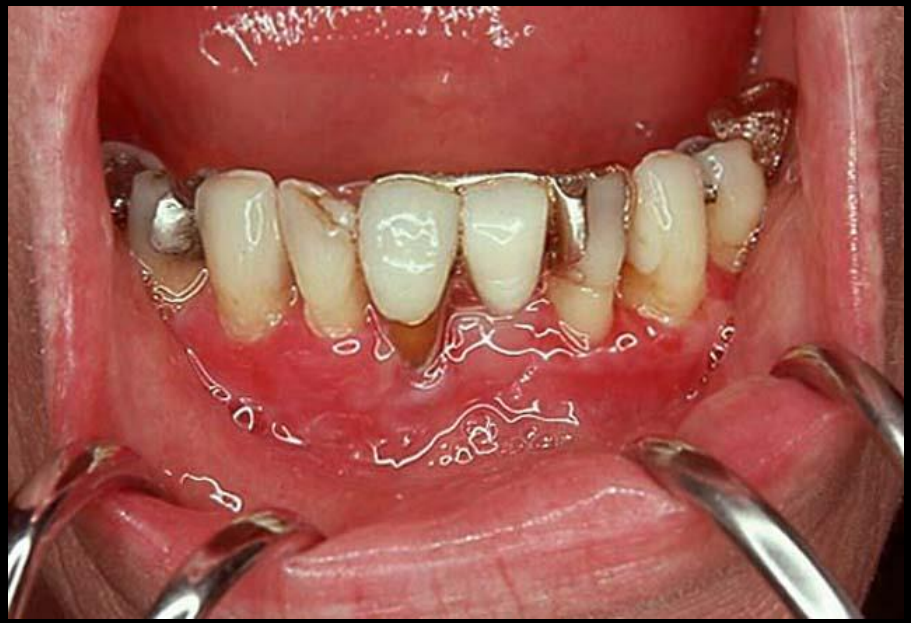
Prof. Shaleen Chandra

Oral manifestation

- Gingiva is most commonly affected
- Mucosal lesions as vesicles & bullae- relatively thick walled → rupture → leaves a raw, eroded bleeding surfaces
- Oral lesions rarely scar
- "Chronic desquamative gingivitis"



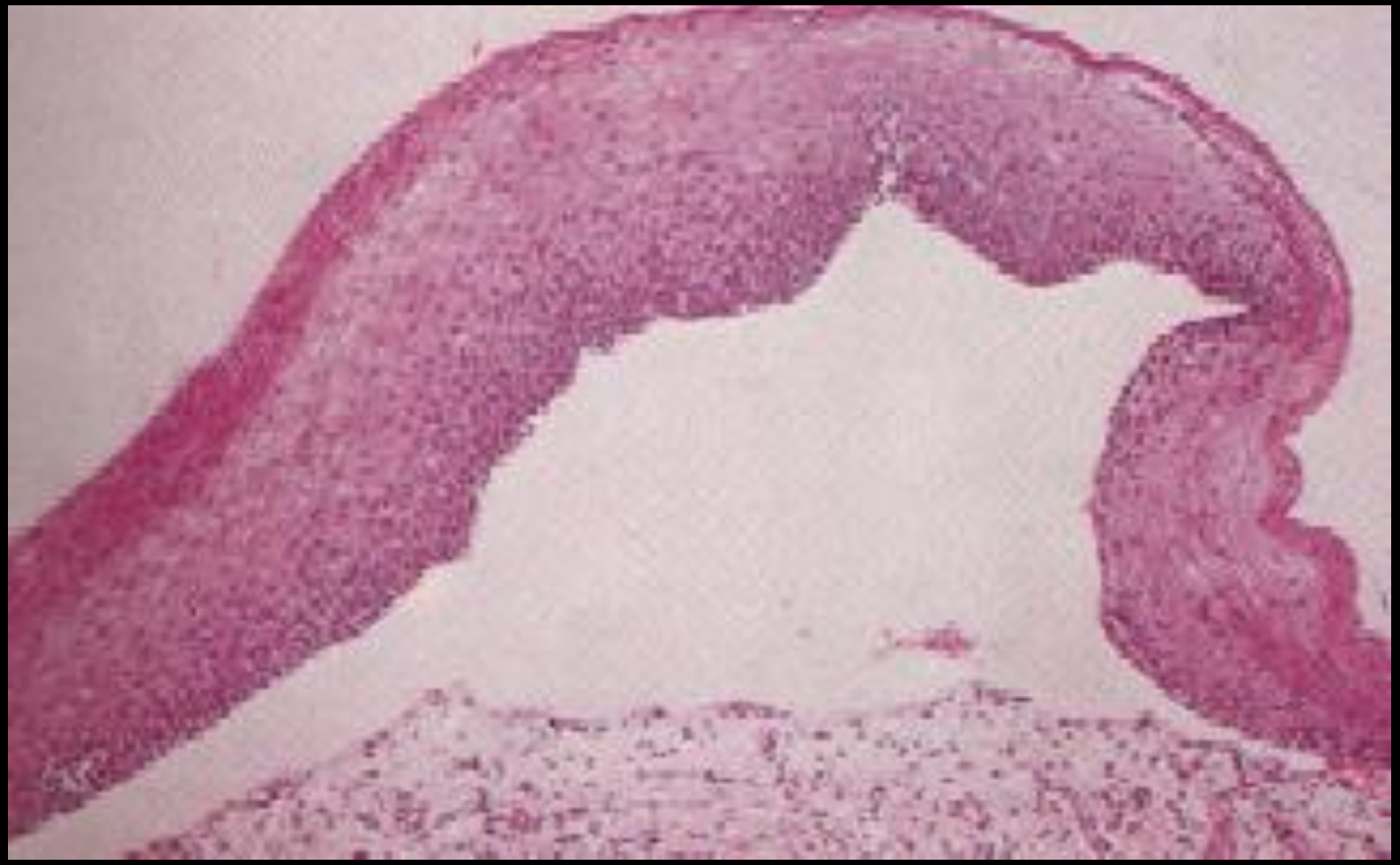




Prof. Shaleen Chandra

Histopathologic features

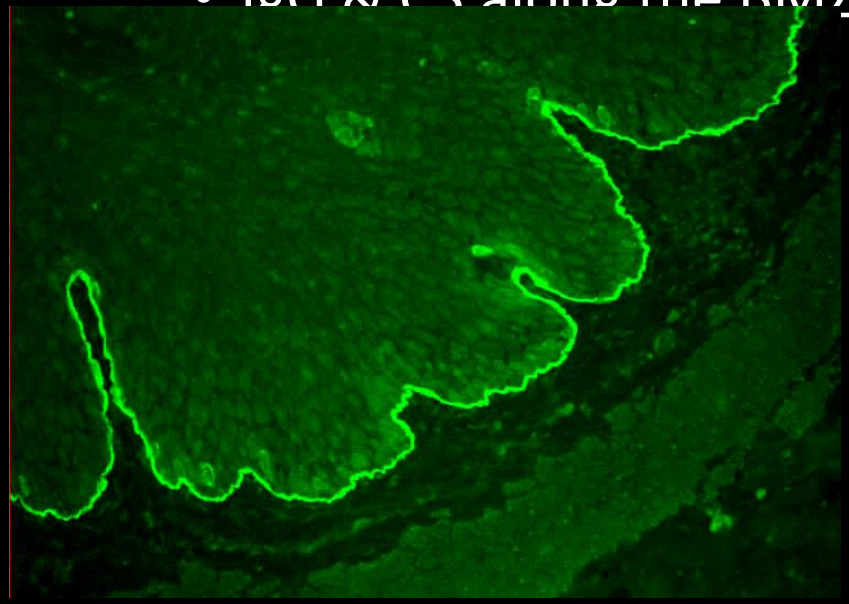
- Subepithelial vesicles/ bullae/ clefts
- Basement membrane apppears detached from the underlying CT
- No evidence of acantholysis
- Nonspecific chronic inflammatory cell infiltrate
  - Lymphocytes, plasma cells & eosinophils

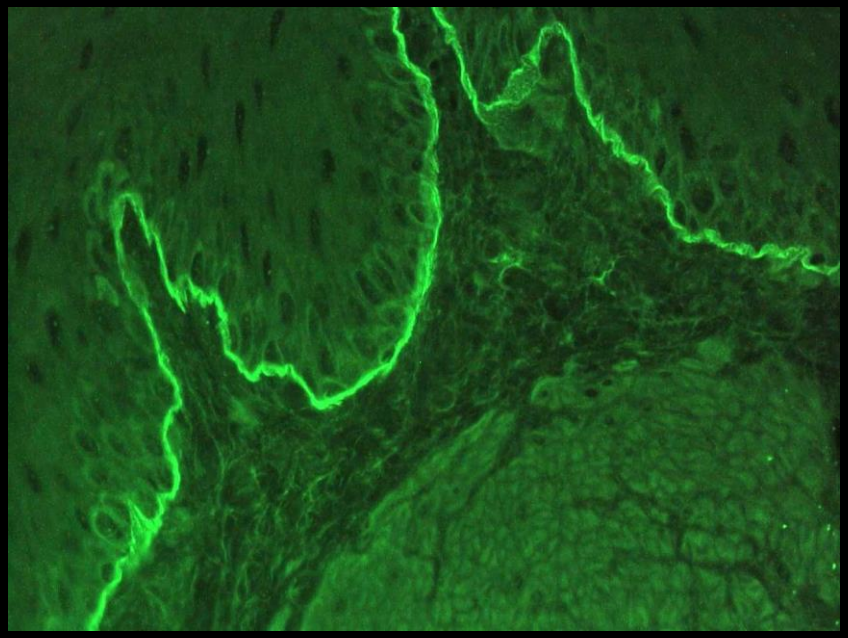


Prof. Shaleen Chandra

Immunofluorescene findings

- **Direct Immunofluorescene**
  - IgG & C3 along the BMZ





- **Indirect Immunofluorescene**
  - ANTI EPILIGRIN ANTOBODIES are demonstrated in patients serum

Differential diagnosis

- Pemphigus vulgaris
- Bullous pemphigoid
- Erosive lichen planus
- Bullous erythema multiforme

Treatment & prognosis

- In mild forms, no treatment required
- In severe cases, topical/ intralesional/ systemic corticosteroid therapy
- Immunosuppressive agents

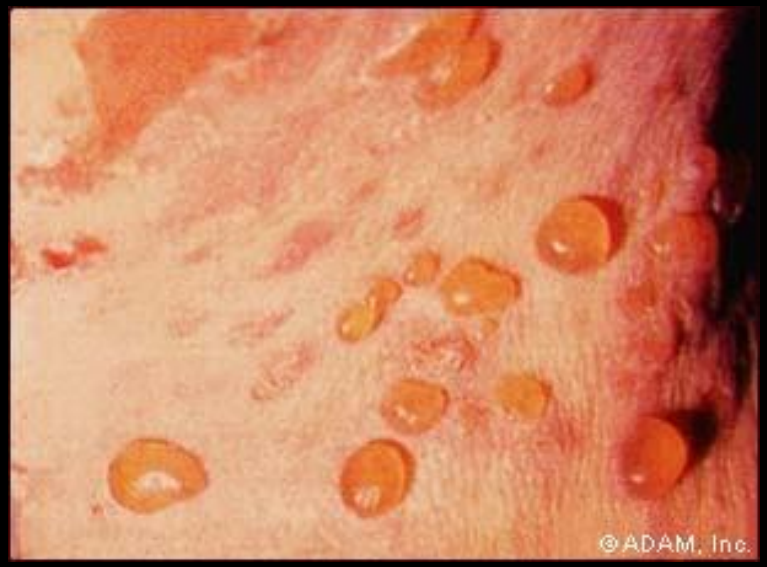
Bullous pemphogoid

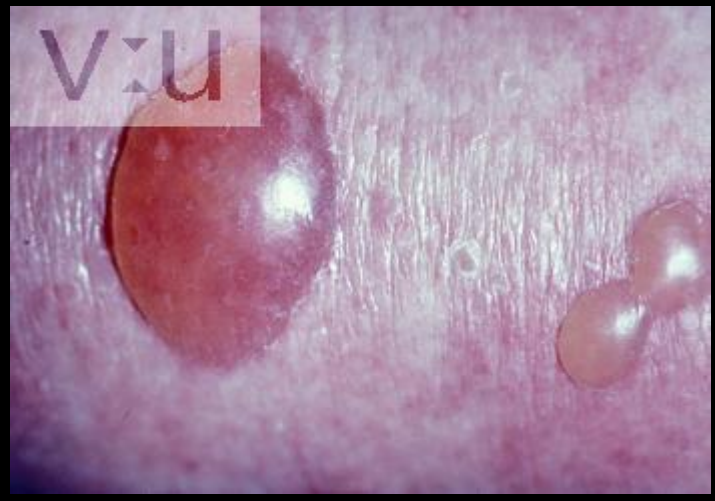
Parapemphigus

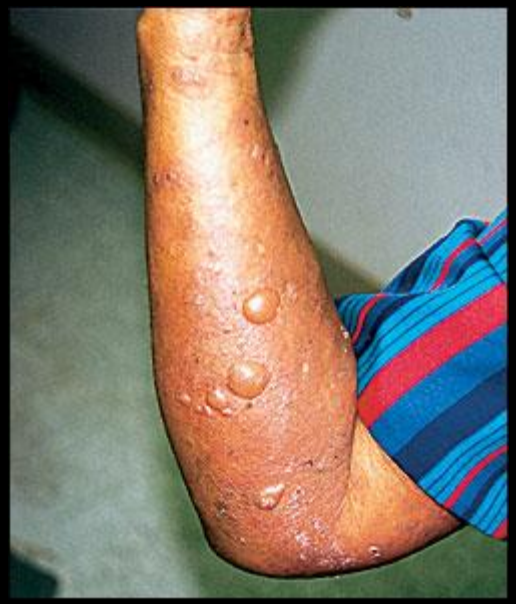
- Most common autoimmune blistering condition
- Subepidermal Bullous dermatoses
- Resembles Cicatricial pemphigoid in many respects
- Autoantibodies develop against BPAG1 and BPAG2

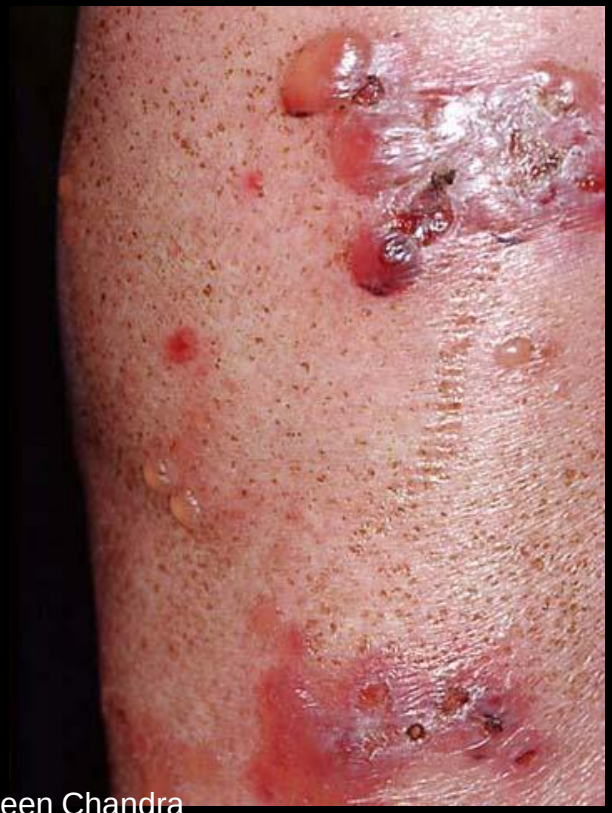
Clinical features

- 6^{th} – 8^{th} decade
- No sex predilection
- Generalized nonspecific rash → Multiple tense bullae → rupture → superficial erosion & crusting
- Healing occurs without scarring
- Pruritis is an early symptom





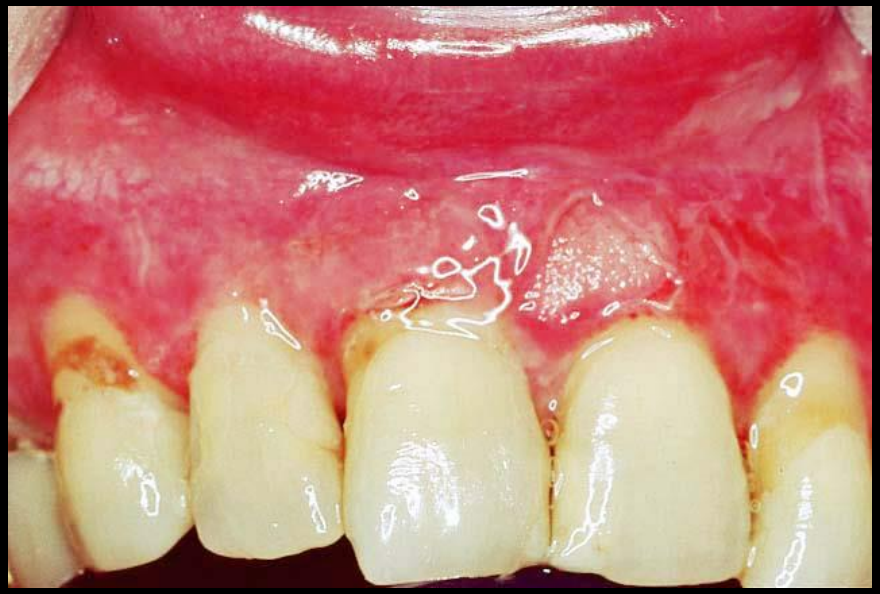


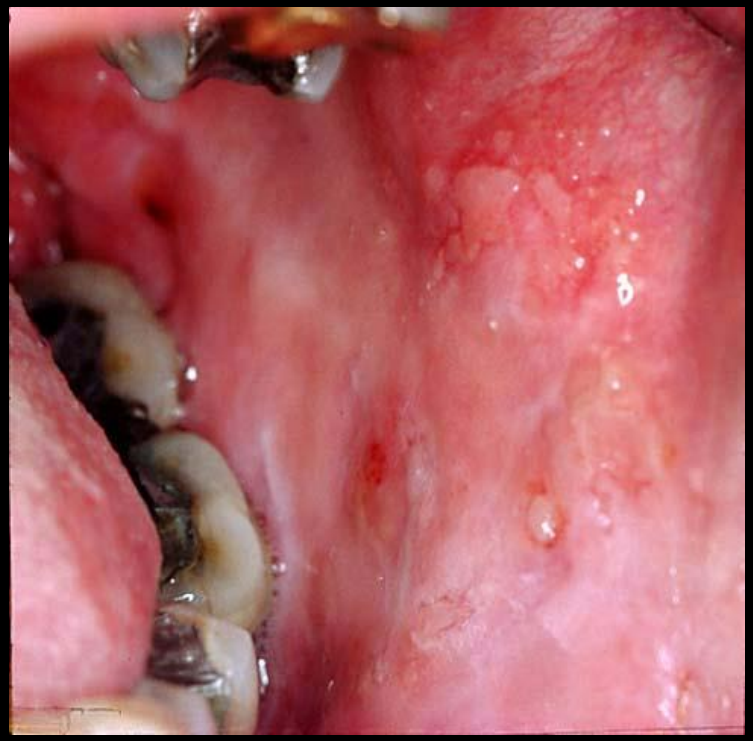


Prof. Shaleen Chandra

Oral manifestation

- Oral mucosal involvement uncommon
- Gingiva > buccal mucosa > Palate > floor of mouth > tongue
- Gingival lesion similar to Cicatricial pemphigoid





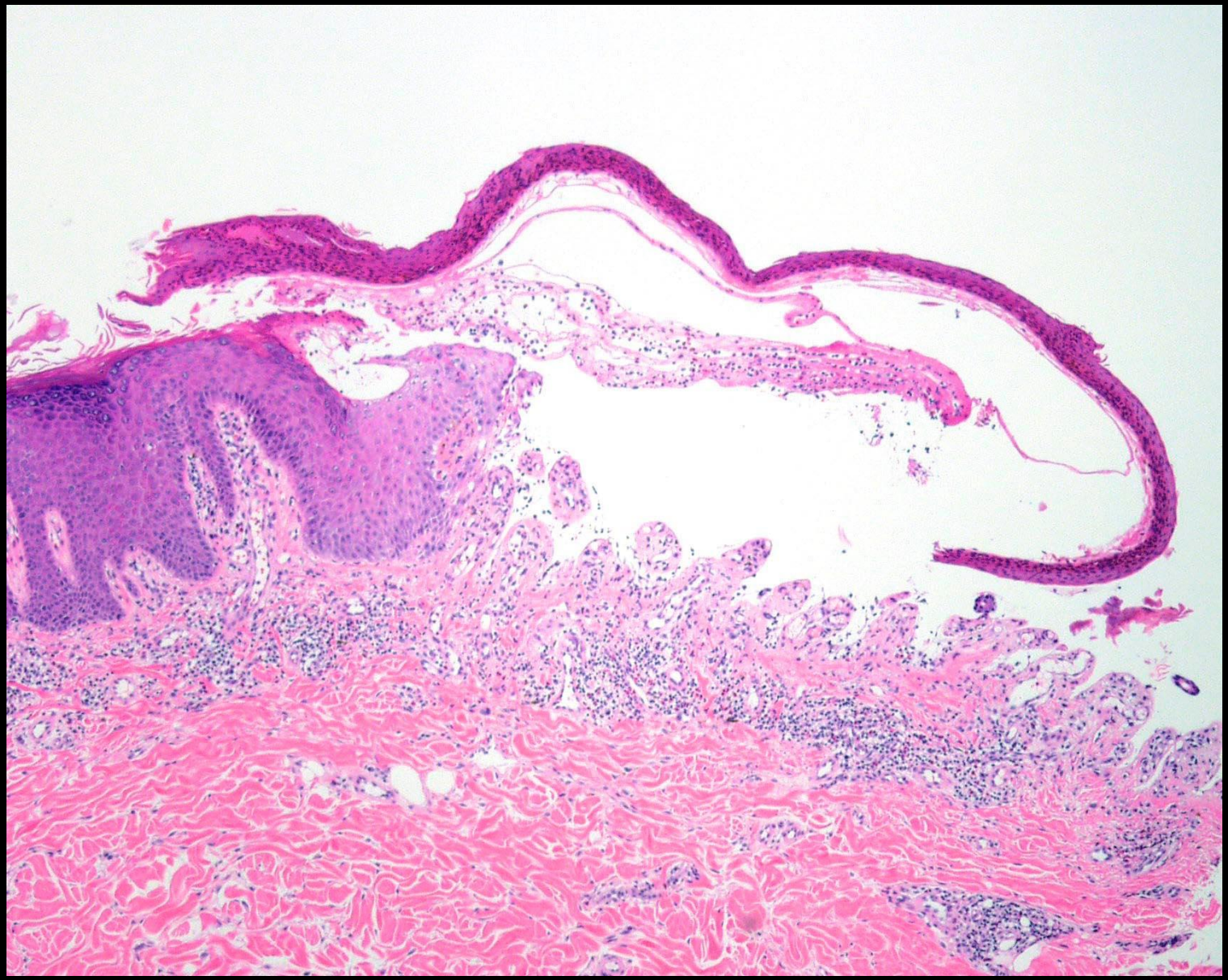
Prof. Shaleen Chandra

Histopathologic features

- Vesicles/ bullae are subepithelial & nonspecific
- No evidence of acantholysis
- Fibrinous exudate admixed with both acute & chronic inflammatory cells

Electron microscopy:

- Basement membrane remains attached to the CT rather than the overlying epithelium (in contrast to C. pemphigoid)



Prof. Shaleen Chandra

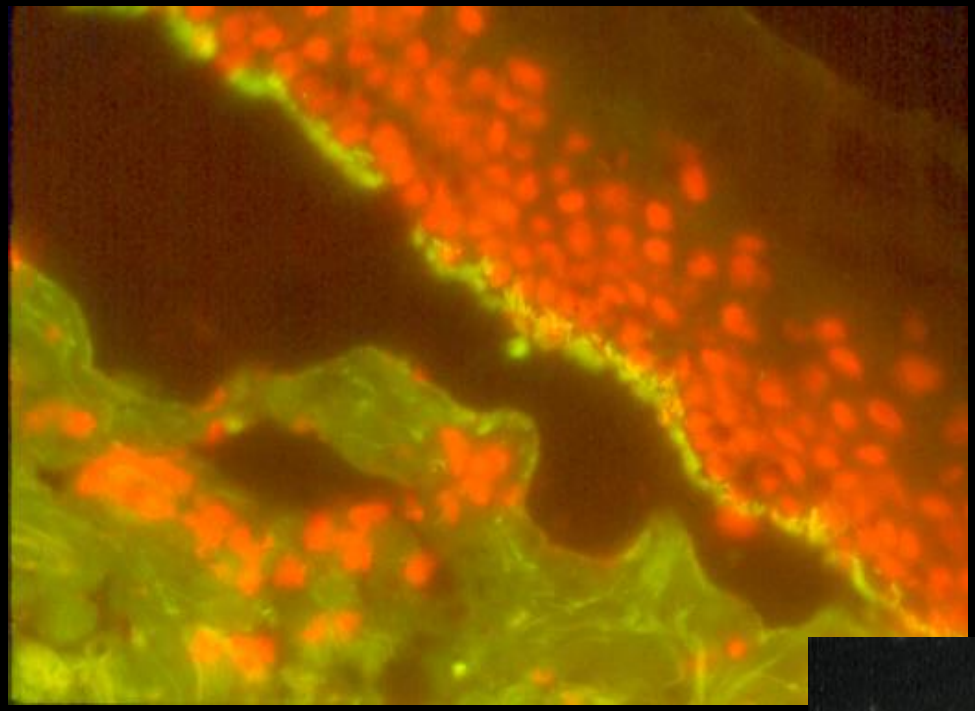
Immunofluorescence findings

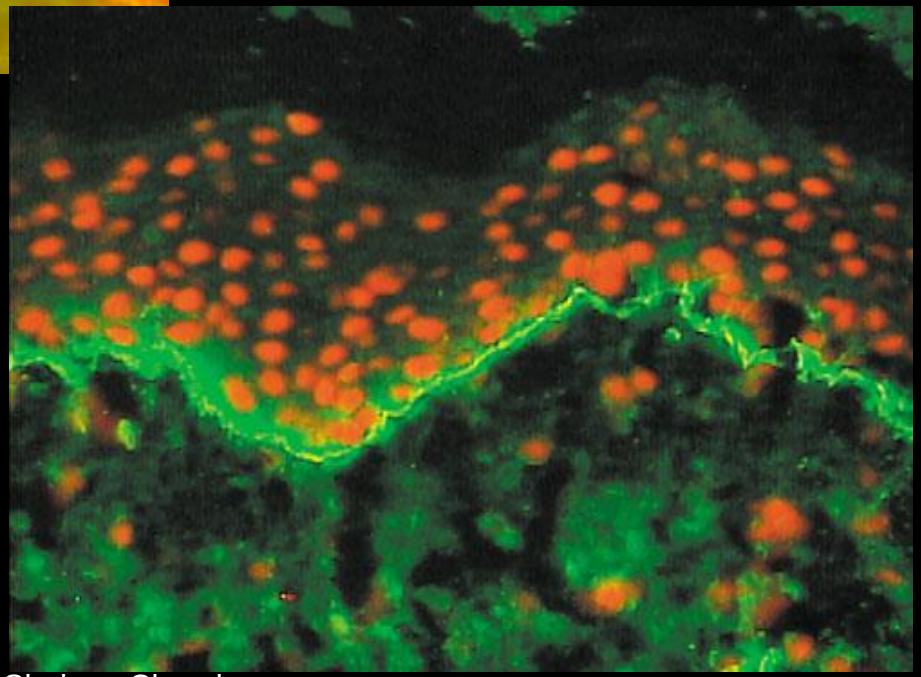
Direct immunofluorescence

- Continuous linear band of IgG, C3 in the BMZ of affected patients

Indirect immunofluorescence

- Patients have circulatory autoantibodies in the serum producing IIF pattern similar to DIF





Prof. Shaleen Chandra

Erythema Multiformae

- An acute self limiting dermatitis characterized by distinctive clinical eruptions manifested as iris or target lesions

- **EM minor** → localized eruption of the skin with mild or no mucosal involvement

- **EM major** → more sever mucosal and skin disease which may be potentially life threatening

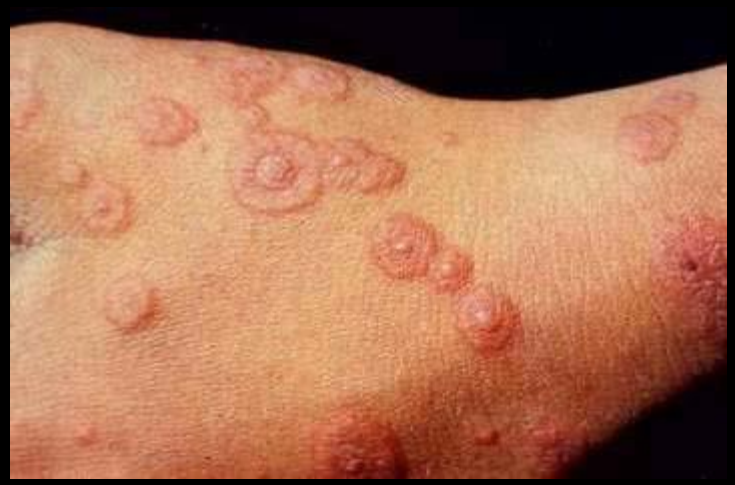
Etiology

- Drugs
- Infectious agents
  - HSV
  - Mycoplasma

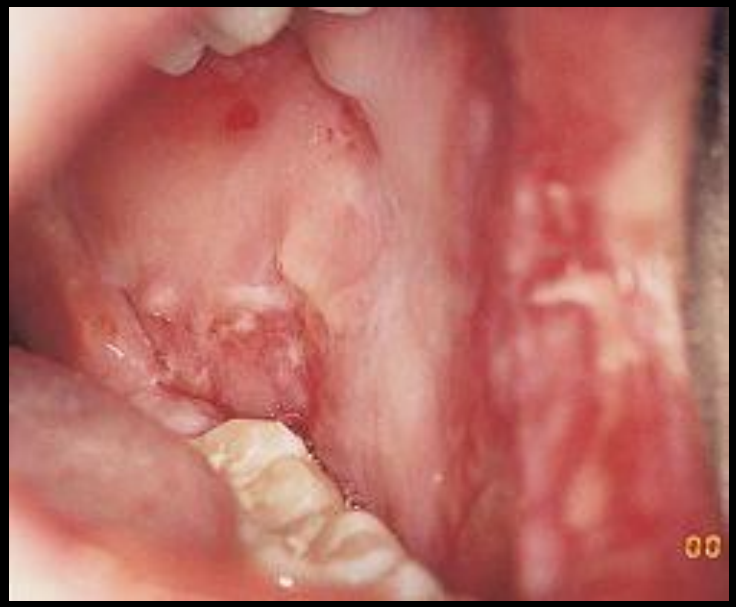
Clinical features

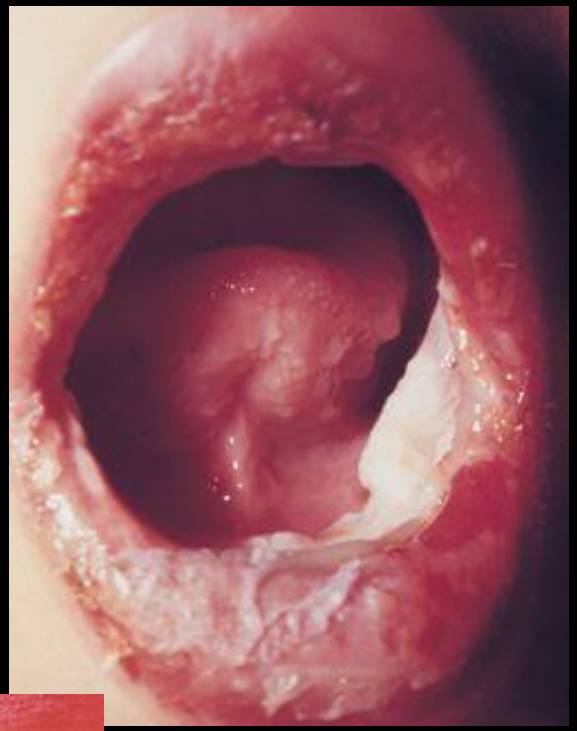
- Young adults
  - 2nd to 4th decade
- Males are affected more
- Asymptomatic, erythematous, discrete macules or papule (rarely vesicles or bullae)
- Distributed in symmetrical pattern
  - Hand, legs, face, neck

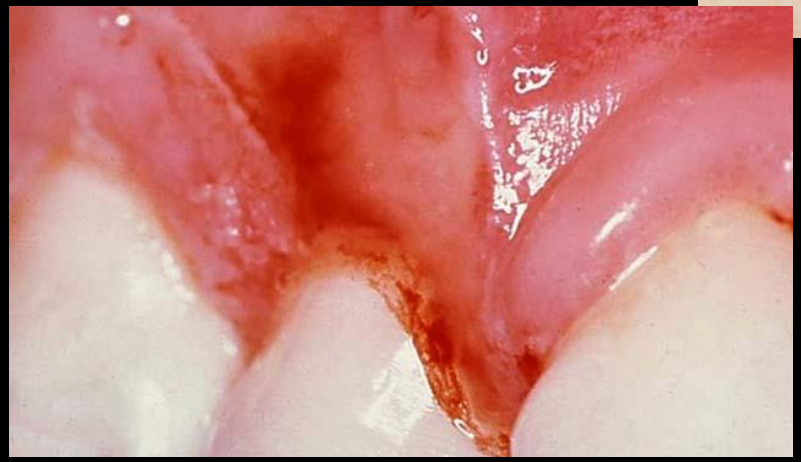
- Few centimeters in diameter
- Concentric ring like appearance
- Varying shades of erythema



- **Oral manifestations**
  - Pain and discomfort
  - Hyperemic macule, papules or vesicles
  - Become eroded or ulcerated and bleed freely
  - Tongue
  - Palate
  - Buccal mucosa
  - Gingiva
  - Oral lesions are present only along with dermal lesions







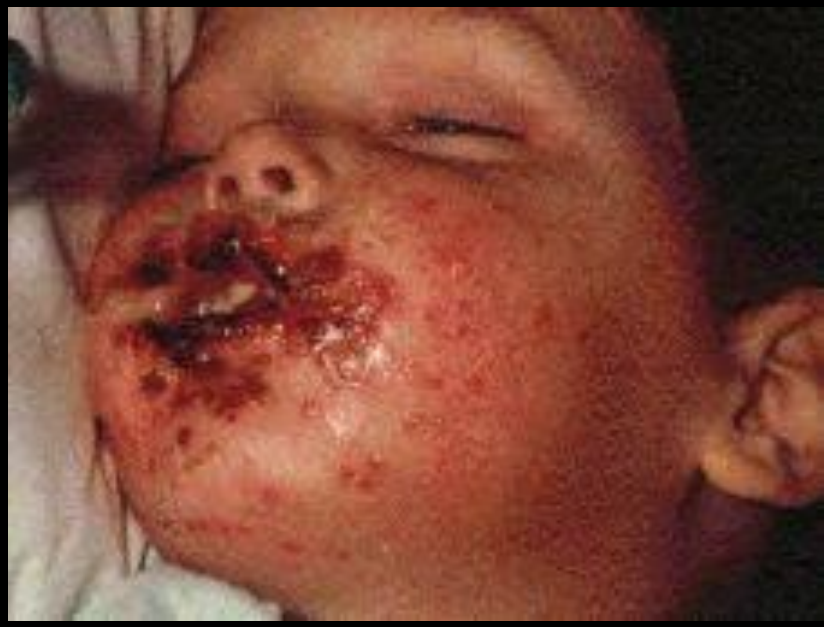
Prof. Shaleen Chandra

Stevens-Johnson Syndrome

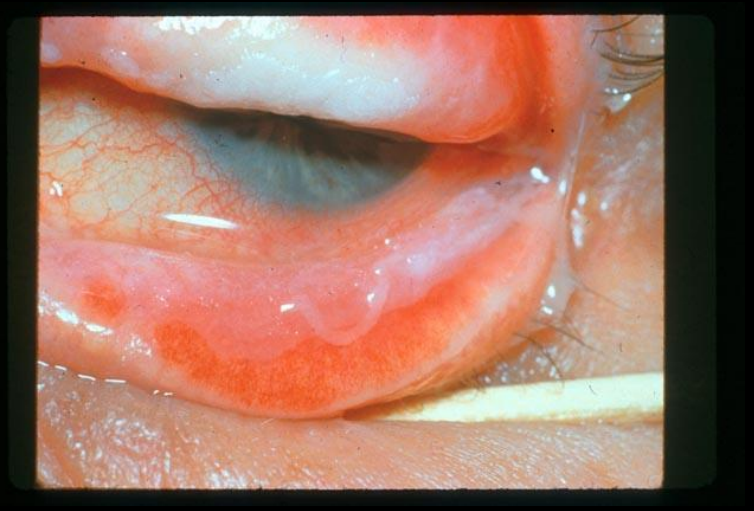
- Very sever bullous form of erythema multiformae
- Widespread involvement typically including skin, oral cavity, eyes, and genitalia

- **Clinical presentation**
  - Fever, malaise, photophobia
  - Eruptions of oral mucosa, genitalia, and skin
  - Lesions are similar to EM but are commomly hemorrhagic

- Oral lesions
  - Extremely sever and painful vesicles, bullae and ulcers
  - Thick white or yellow exudate
  - Erosion of pharynx
  - Ulceration and crusting of lips



- Eye lesions
  - Photophobia
  - Conjunctivitis
  - Panophthalmitis
  - Keratitis
  - Blindness



- Genital lesions
  - Urethritis
  - Balanitis
  - Vaginal ulcers

- Complications
  - Tracheobronchial ulcerations
  - Pneumonia
  - Secondary infection

Histopathologic features

- Not diagnostic
- Intracellular edema of the spinous layer of epithelium
- Intraepithelial/ Subepithelial vesiculation
- Necrosis of basal cells
- Dilatation of superficial capillaries / lymphatics
- Mixed inflammatory infiltrate

Diagnosis

- Clinical presentation and exclusion of other vesiculobullous diseases

- Direct and indirect immunofluorescence findings are not specific