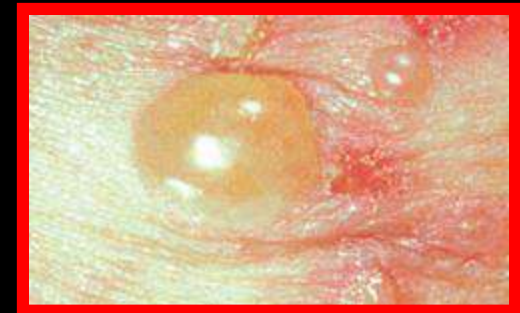


Diseases of Skin

- **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

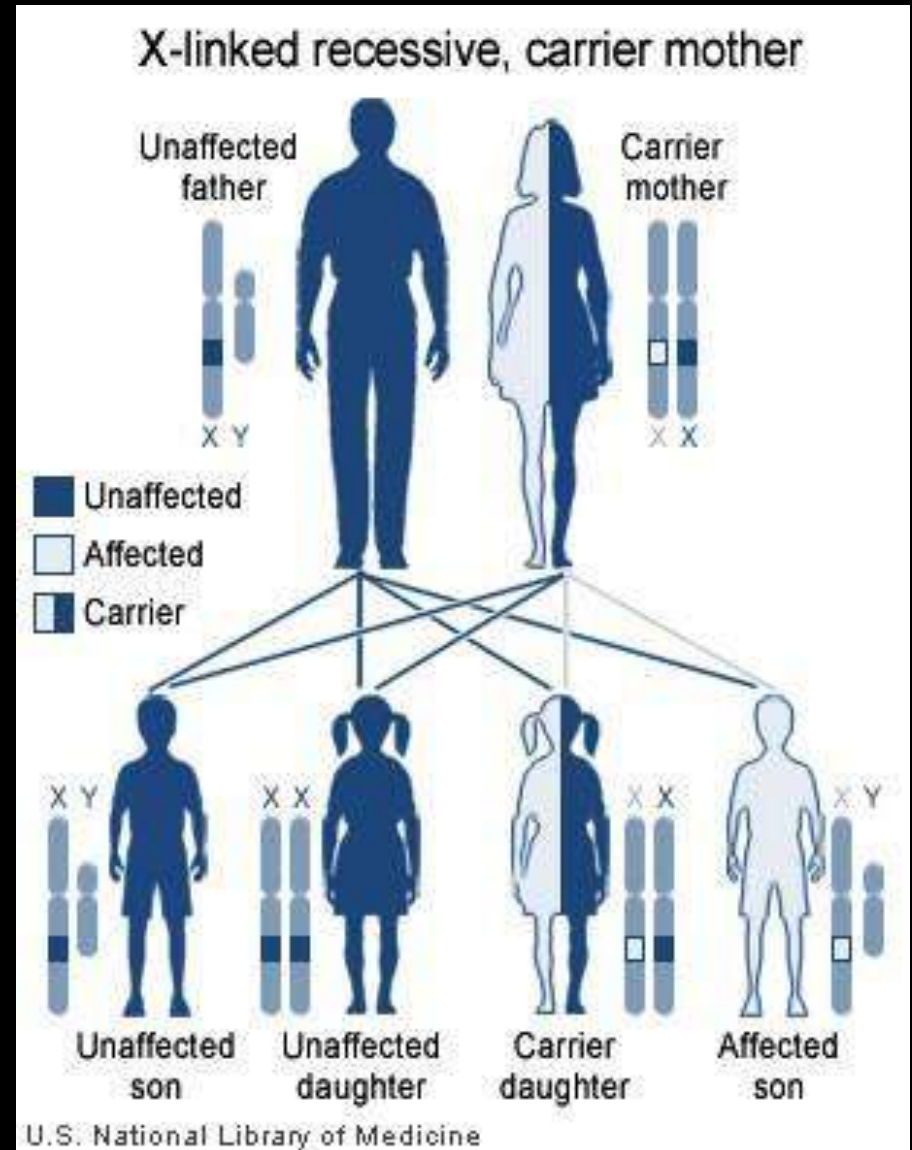
Papule: small, circumscribed, solid, elevated area varying in size from a pinhead to 5mm. The base is round/ ovoid & the surface configuration may be pointed/ rounded/ flattened

Ectodermal Dysplasia

Hereditary ectodermal dysplasia

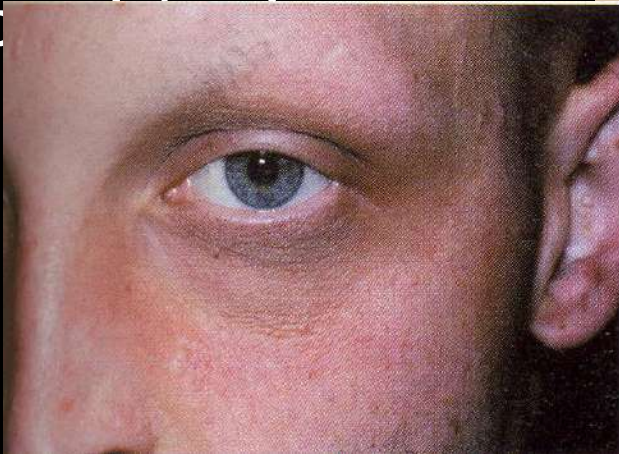
- Group of inherited conditions in which two or more ectodermally derived anatomic structures fail to develop
- Manifested as hypoplasia or aplasia of tissues such as
 - Skin
 - Hair
 - Nails
 - Teeth
 - sweat glands
 - Eyes
- Most common type → **“Hypohydrotic Ectodermal Dysplasia”**

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



Clinical features

- Hypohidrosis
- Onychodysplasia
- Hypotrichosis



- 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 teeth



- 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



- Nai



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



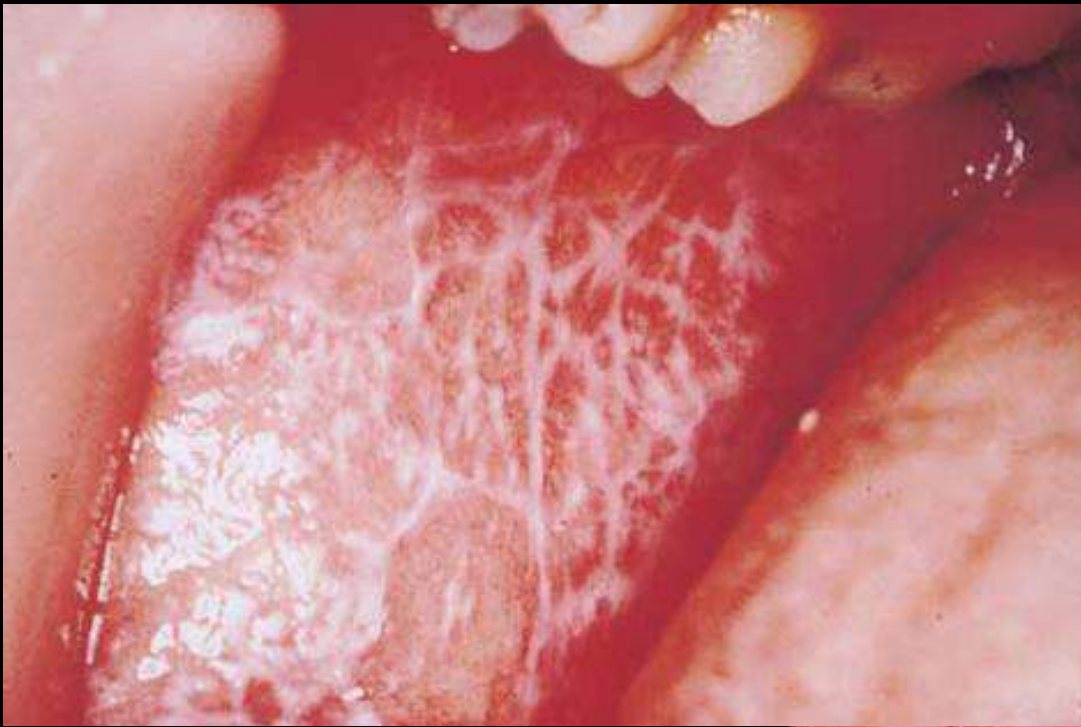
- “Severe pruritus” - most common symptom

- GRINSPAN’S SYNDROME

- Lichen planus
- Diabetes mellitus
- Vascular hypertension

Oral manifestations

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



- Reticular



- Plaque

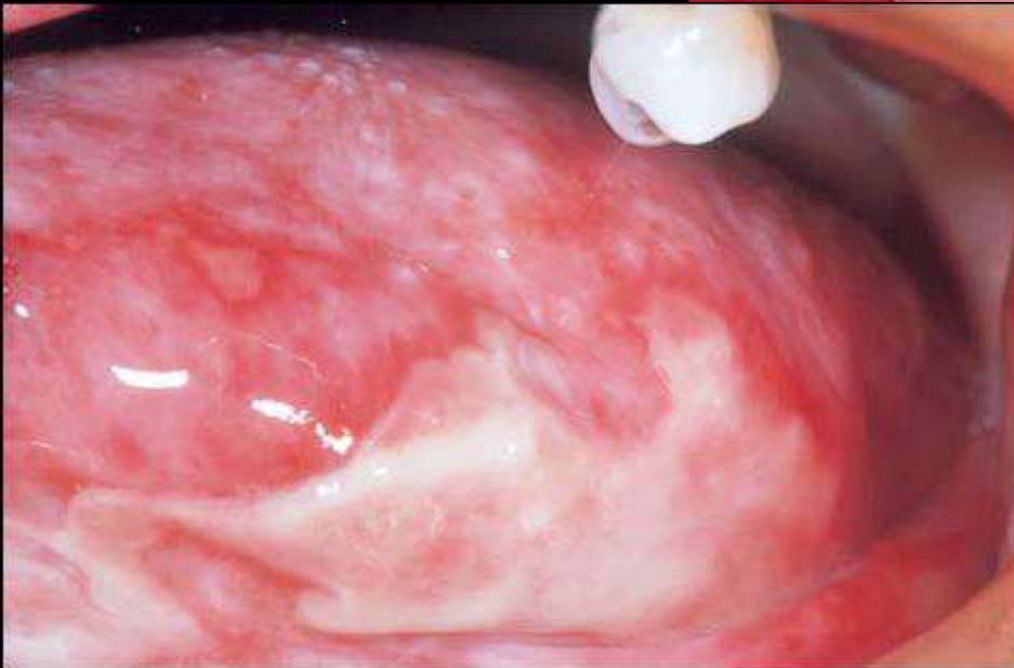
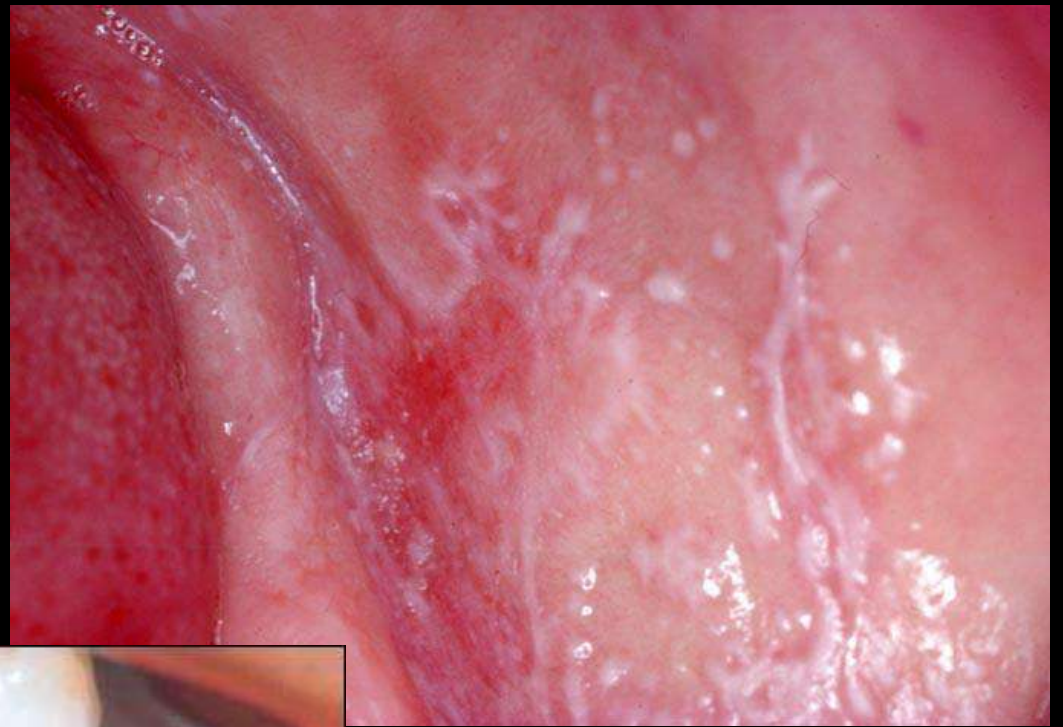




- Atrophic

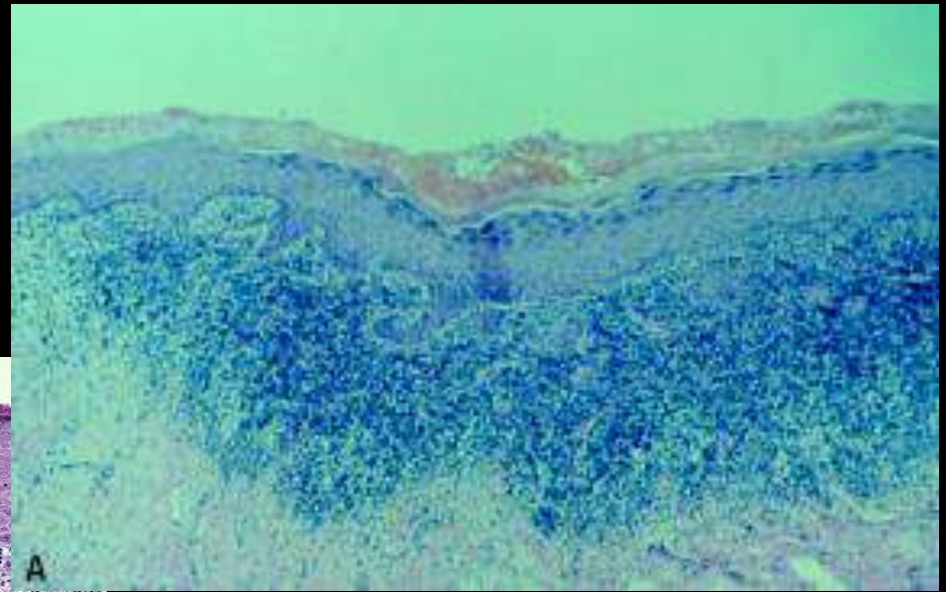
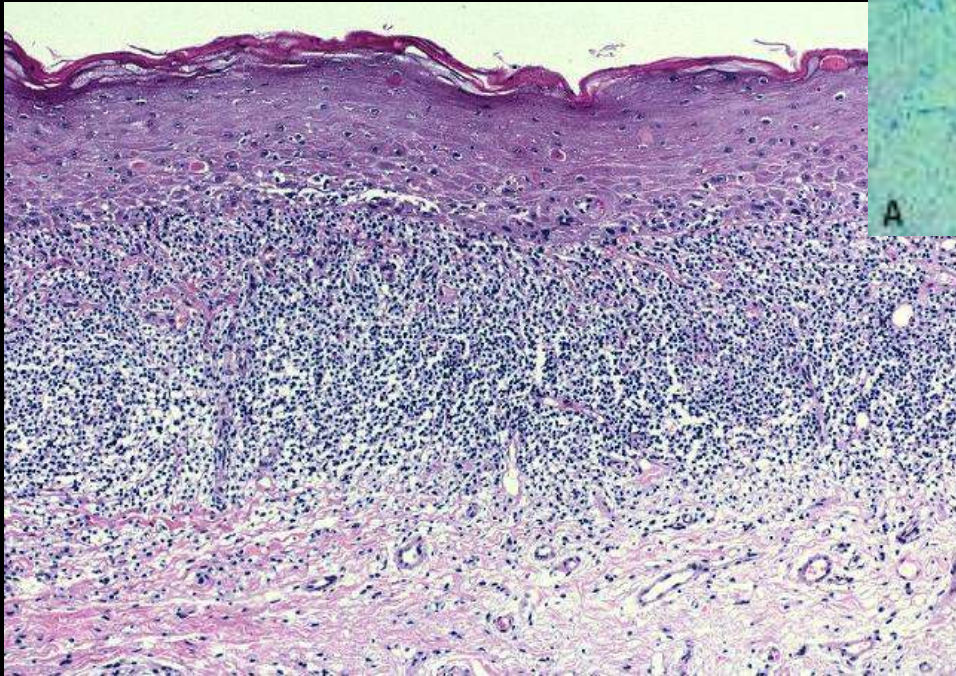


- Erosive

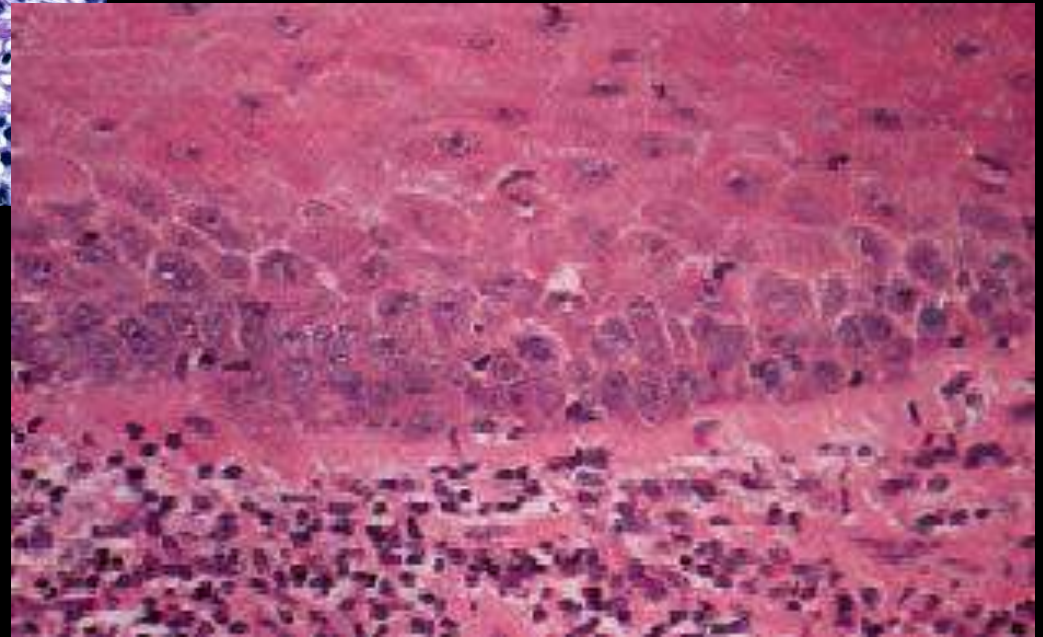
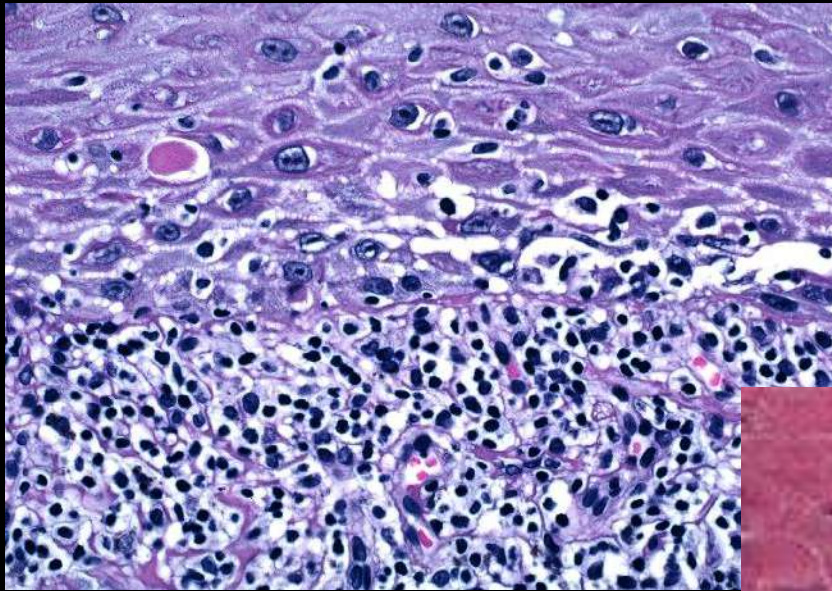


Histopathological features

- **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**

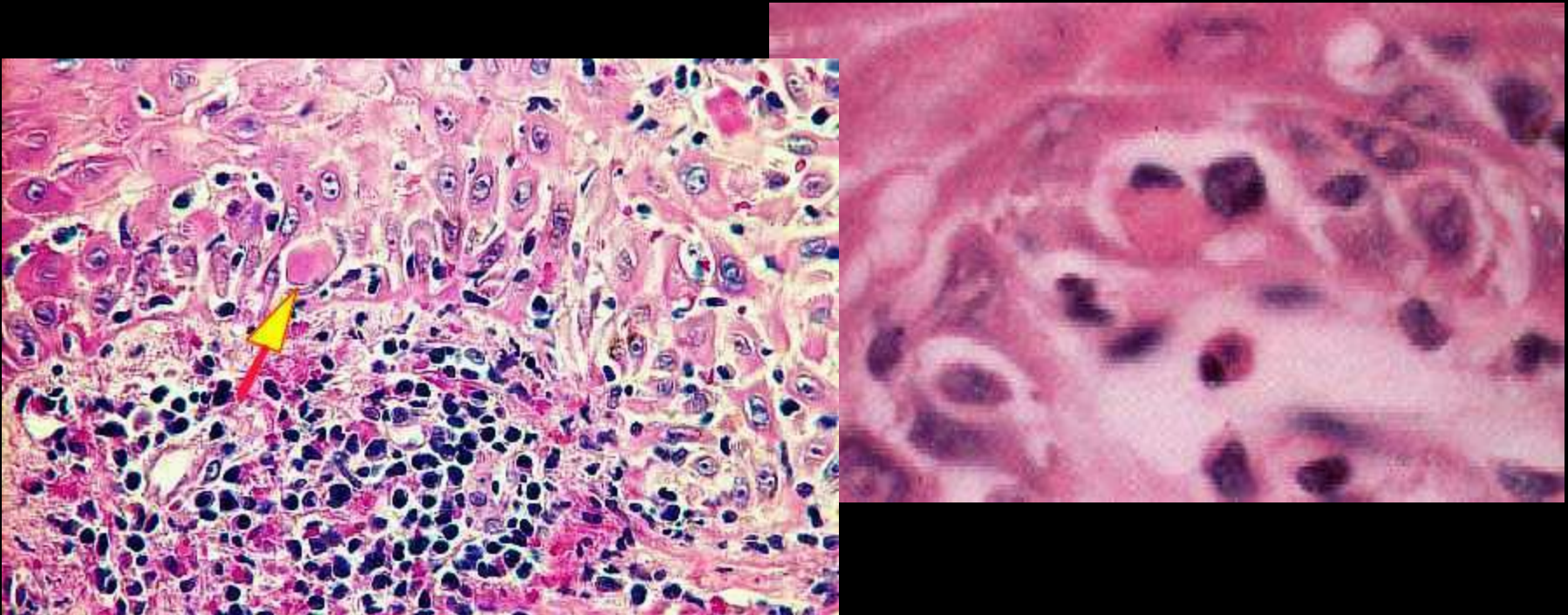


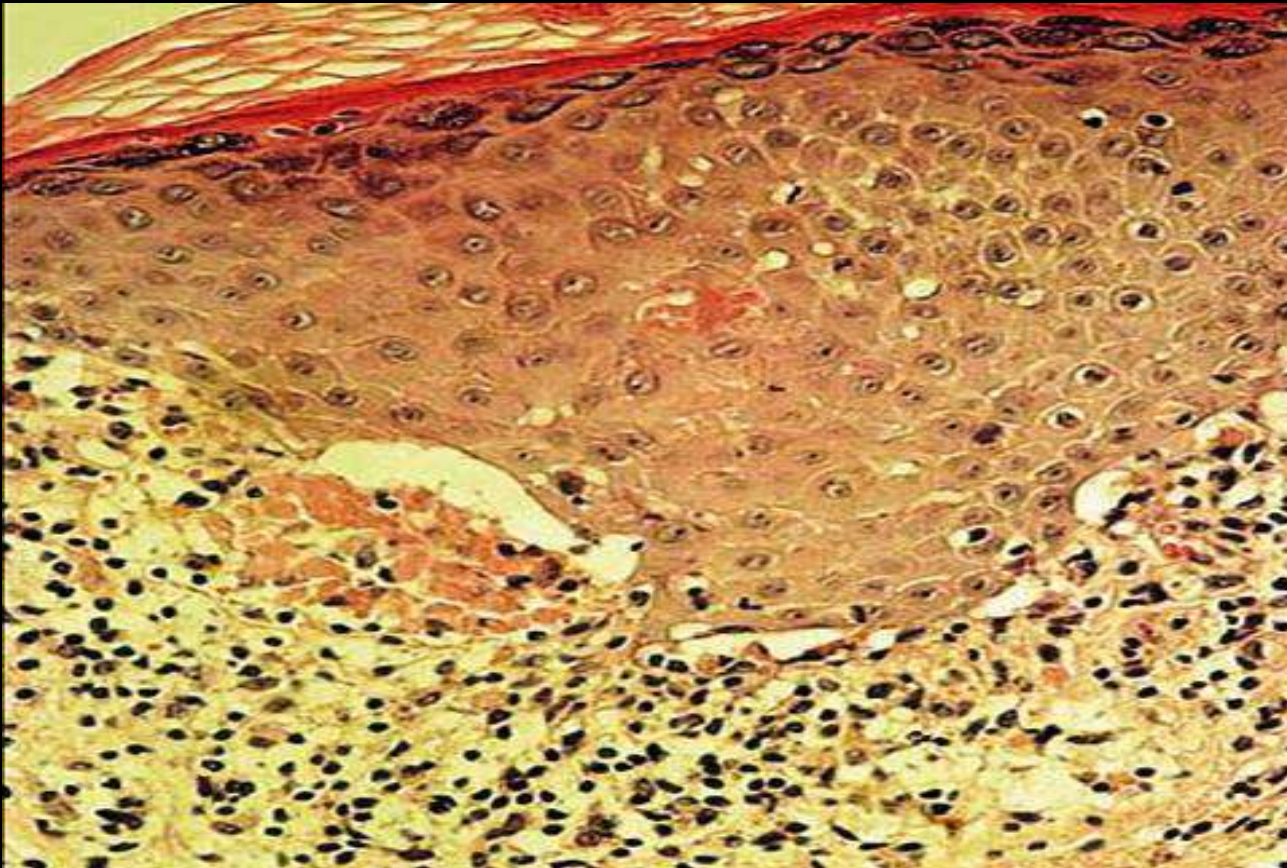
- OLP showing hyperkeratosis and a band like subepithelial lymphocytic infiltrate



- OLP showing vacuolar 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

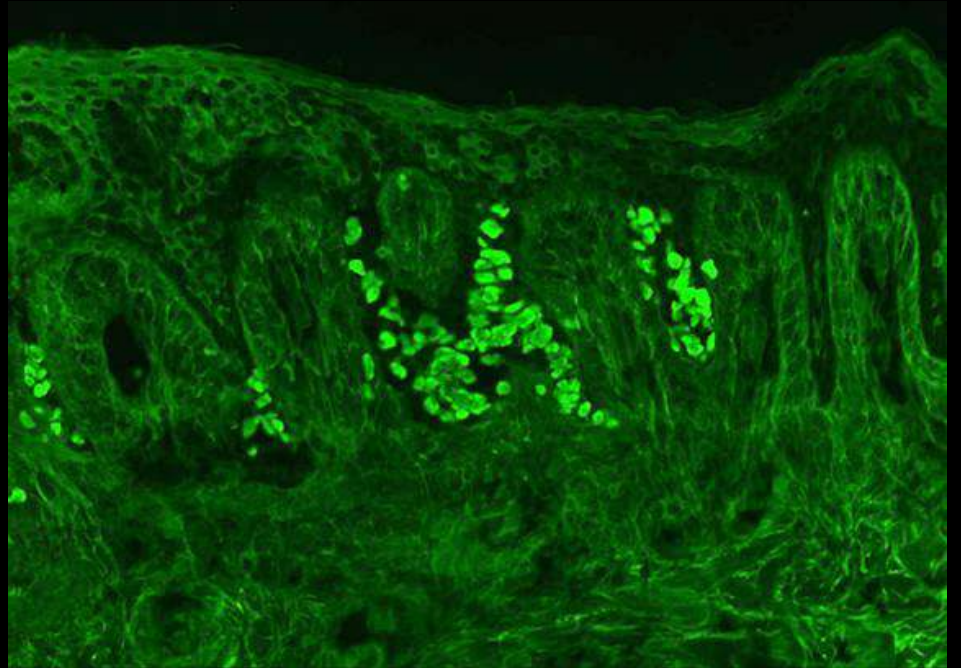
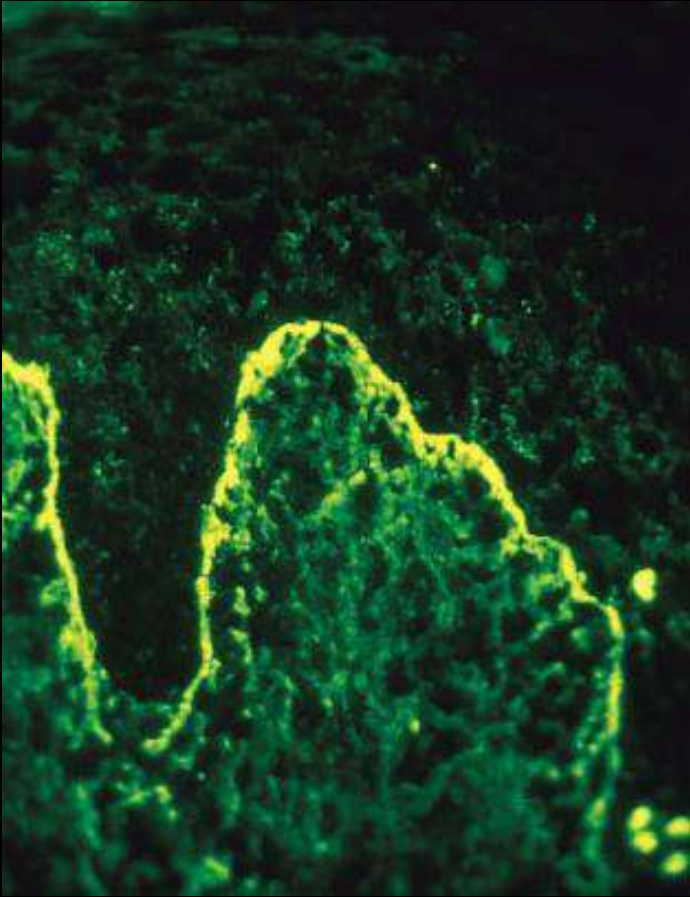




Max Joseph spaces

Immunofluorescence

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



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 manifestations of graft vs host disease
 - Lupus erythematosus

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**



• 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



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*.

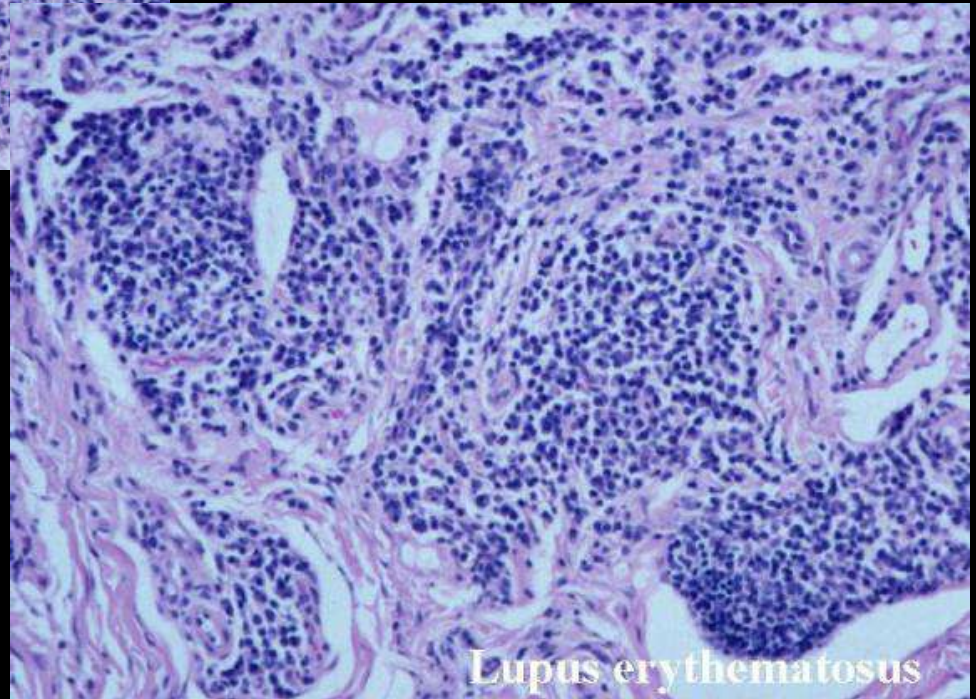
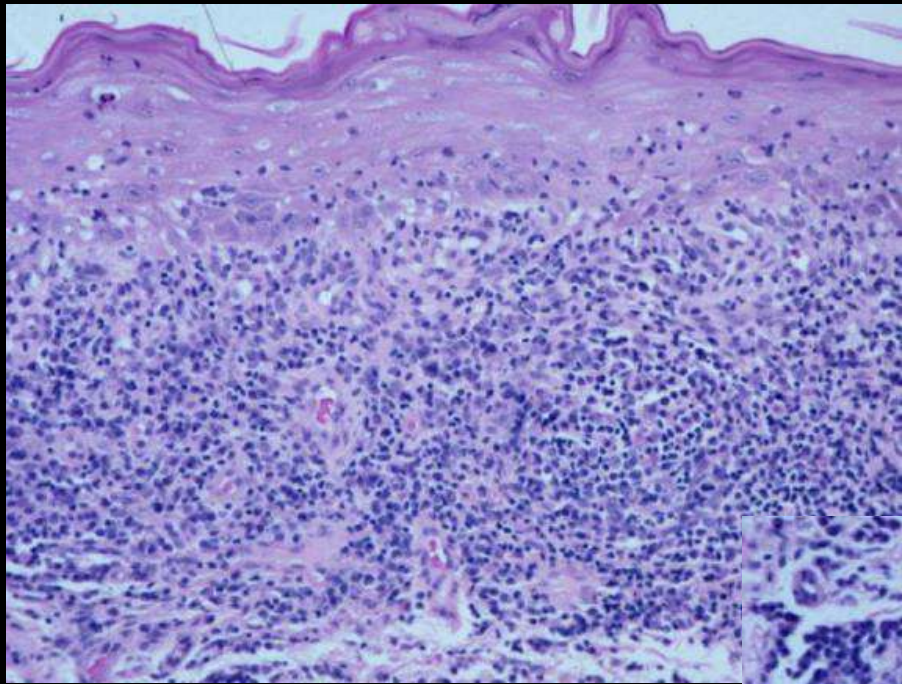


- As the lesions expand peripherally, there is central atrophy, scar formation, and occasional loss of surface pigmentation

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**

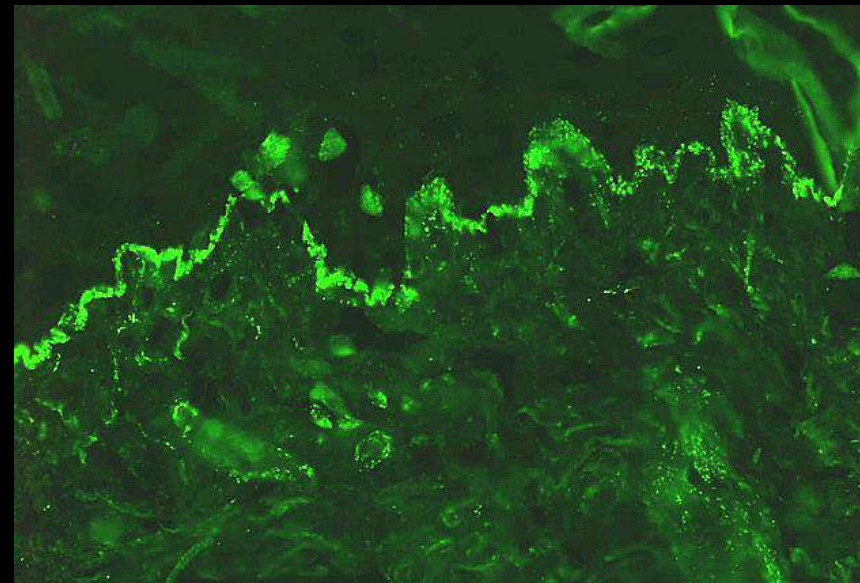


Lupus erythematosus

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**

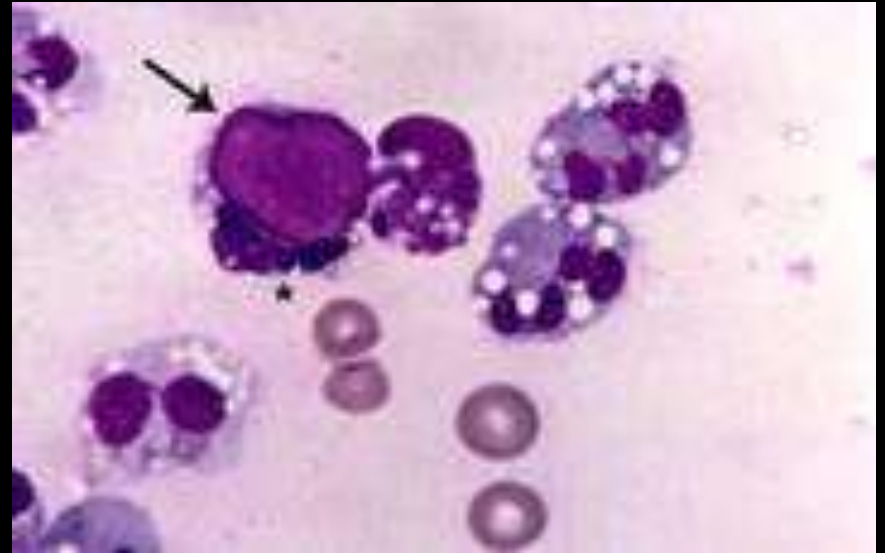
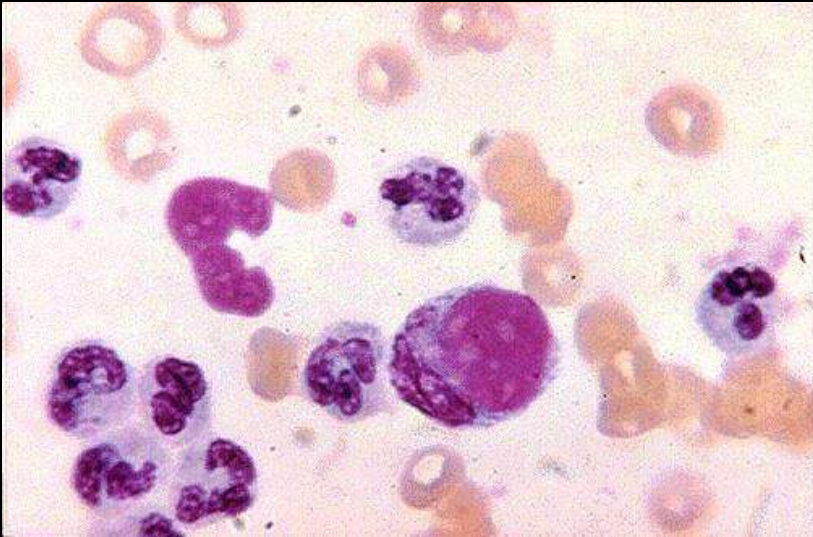


Laboratory diagnosis

- 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 foliaceus
- pemphigus erythematosus

Etiology

- *Autoimmune disorder*
- Malignant diseases
- Viral association (Pemphigus foliaceus) – 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 vesicle



Rupture to form erosions and ulcerations
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Clinical features

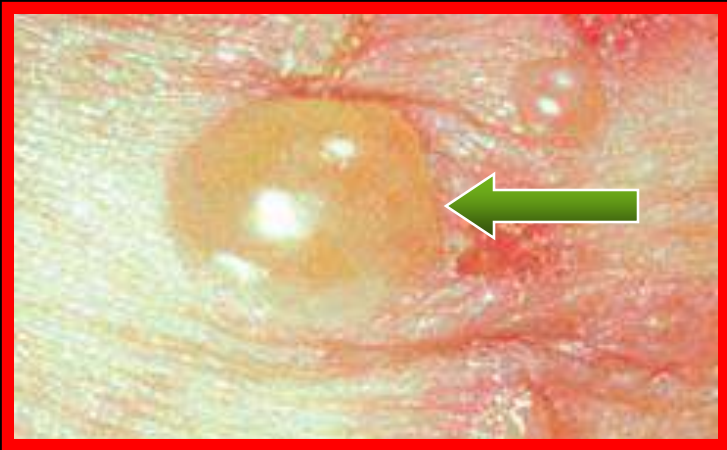
- Initial lesion → vesicle/ bulla
- Initial lesions → trunk, oral cavity
- 4th- 6th decade
 - Rare in children
- No sex predilection
- Common in Jewish persons
- Fever & malaise

Pemphigus vulgaris

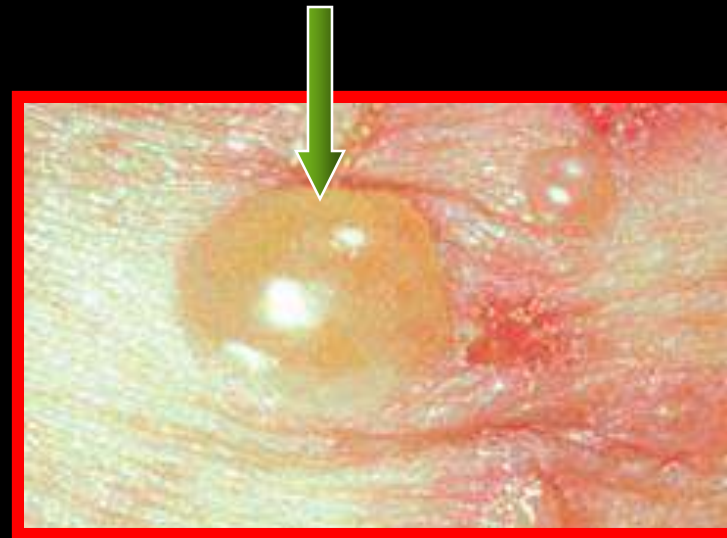
- Vesicle or bullae of varying sizes
 - Contain thin watry fluid
 - Vesicles rupture to form raw eroded surface
- Positive **Nikolsky's sign** and **Asboe Hansen's phenomenon**



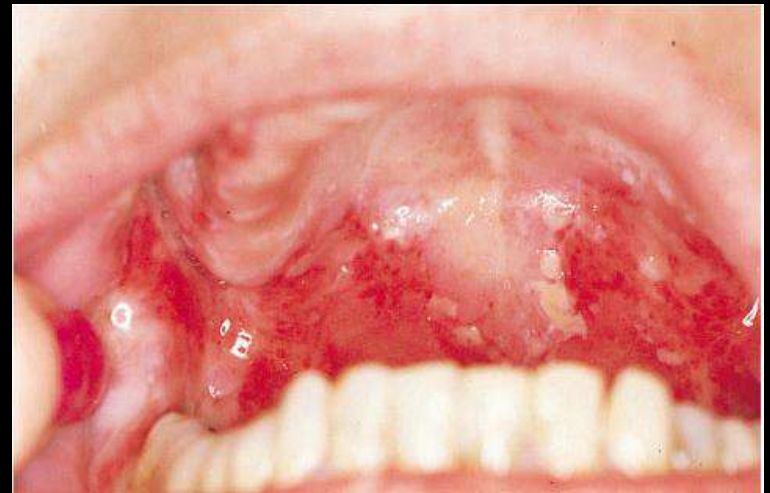
- **Nikolsky's sign**- formation of a lesion after gentle mechanical pressure applied laterally on clinically normal skin adjacent to the vesicle



- **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 manifestations
 - 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



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



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Pemphigus foliaceus

- 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. foliaceus, found in tropical regions; often occur in children & frequently in family groups*



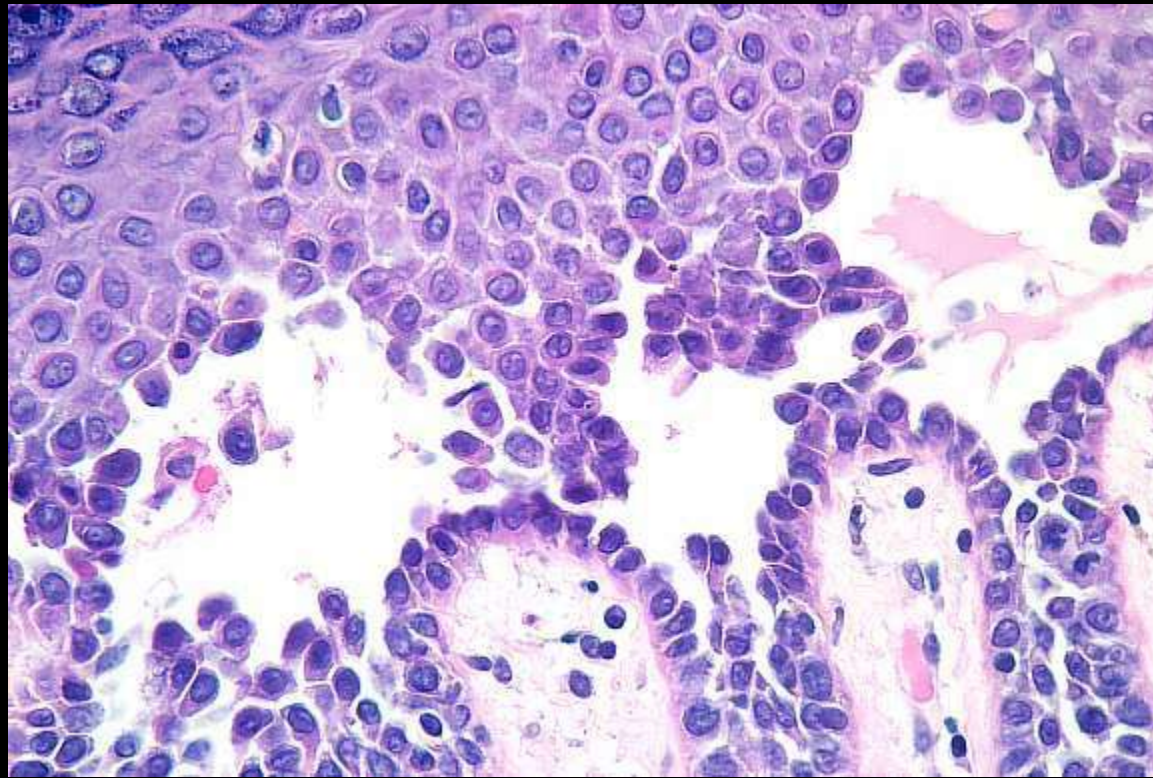
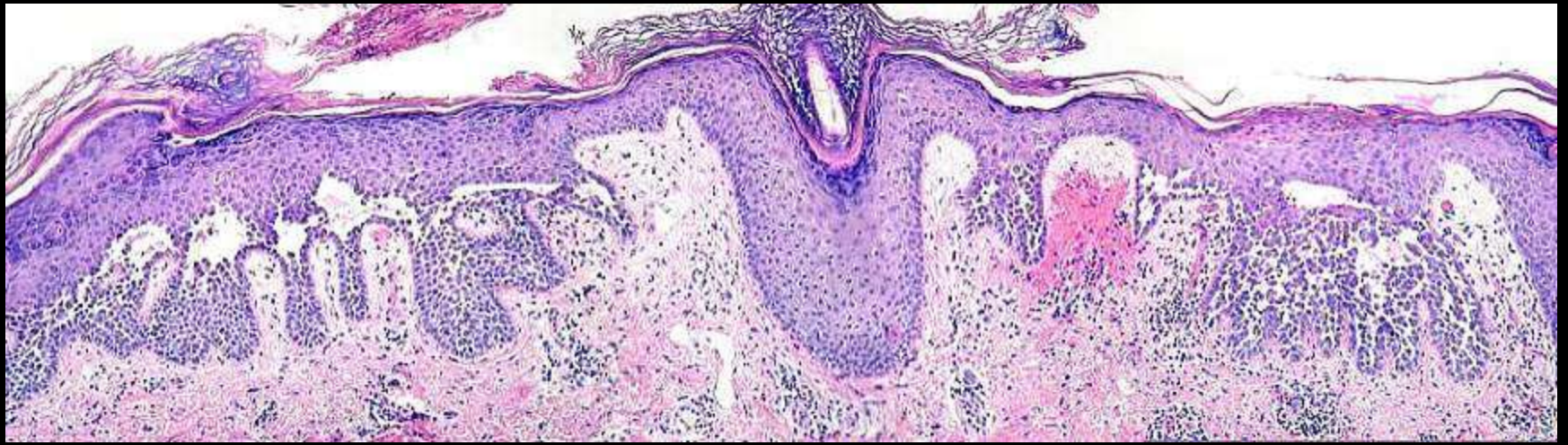
Prof. Shaleen Chandra

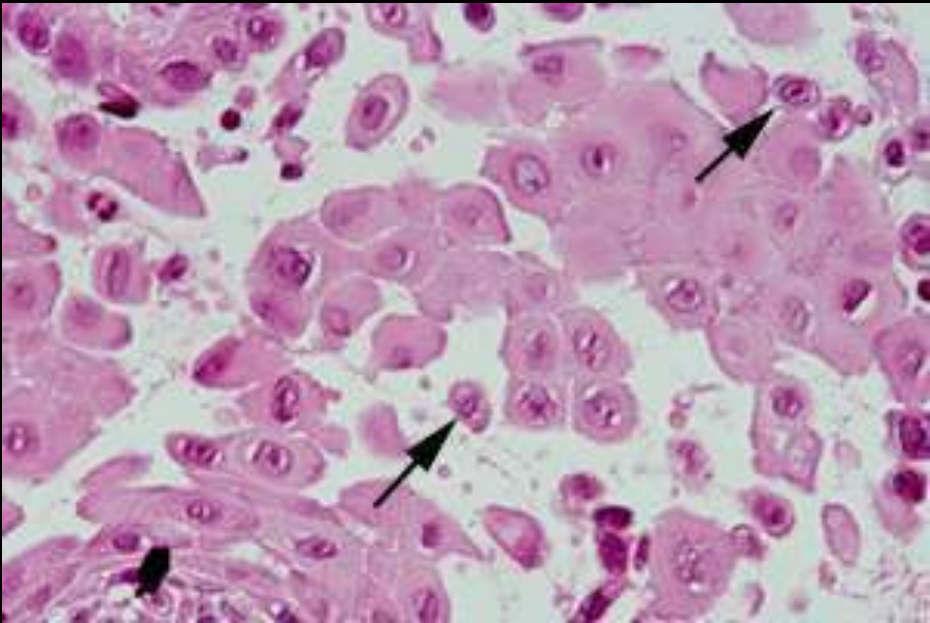
Pemphigus erythematosus

- Senear-Usher syndrome
- Along with bullae & vesicles, concomitant with the appearance of crusted patches resembling seborrheic dermatitis/ LE
- Most cases terminate in *P. vulgaris*

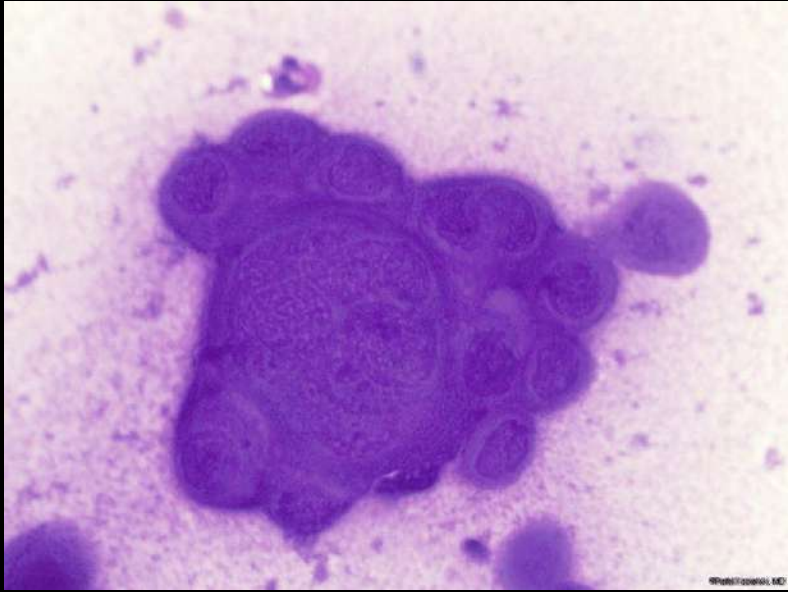
Histopathologic features

- Suprabasilar split in the epithelium with intraepithelial vesicle formation
- Intercellular junctions 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)





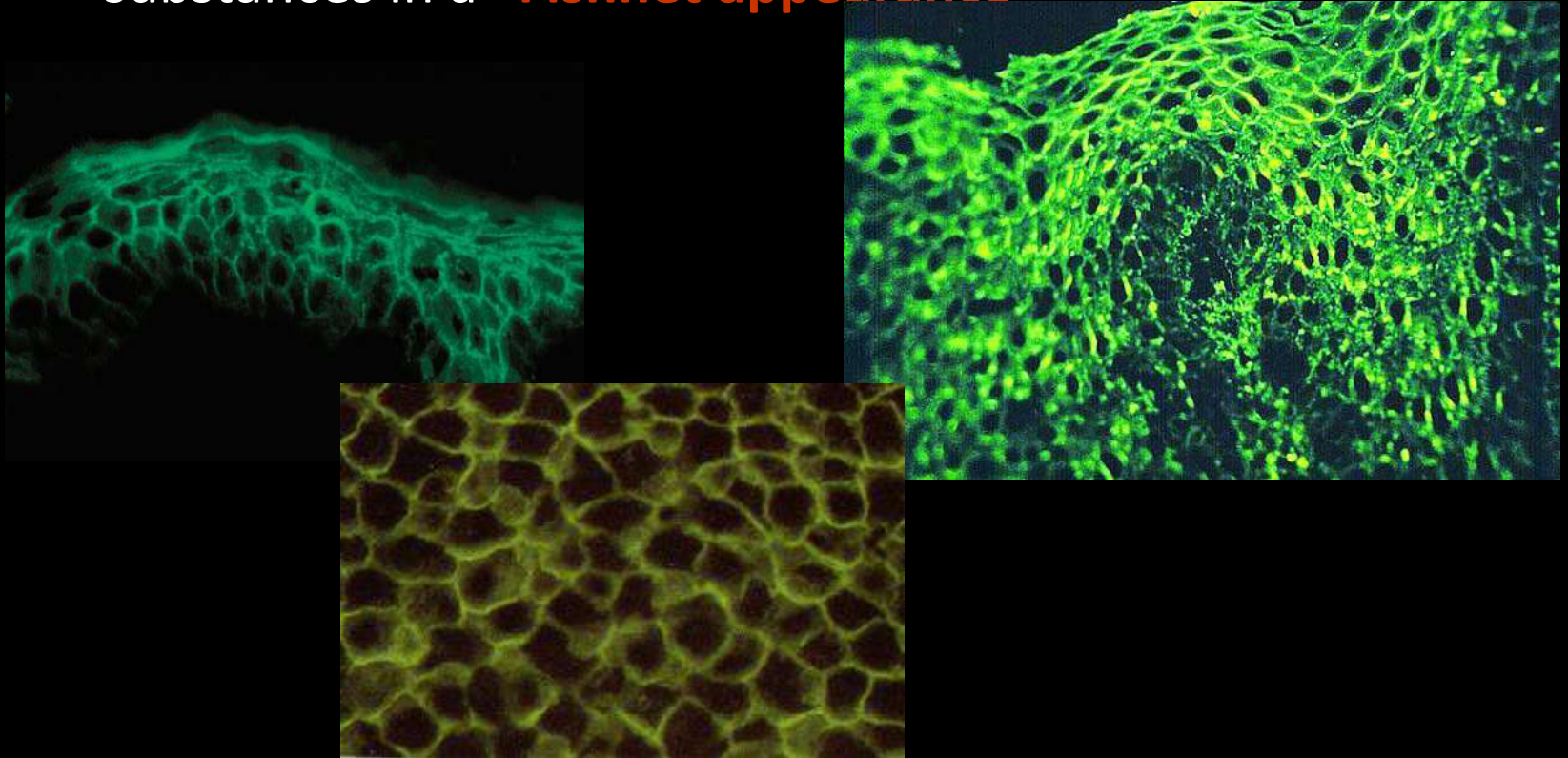
- Tzanck cells



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

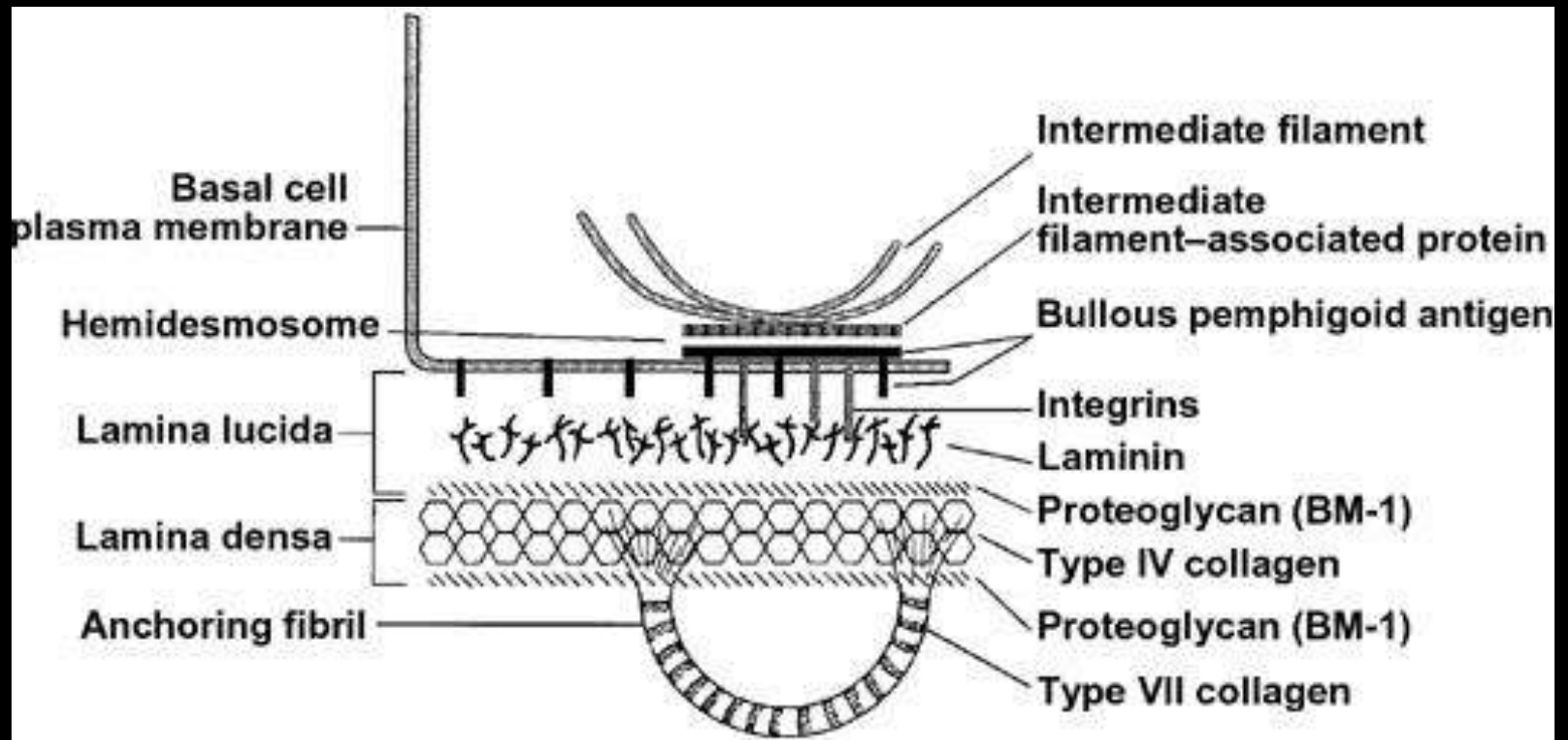
Benign mucous membrane Pemphigoid

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)



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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

- **Ocular 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

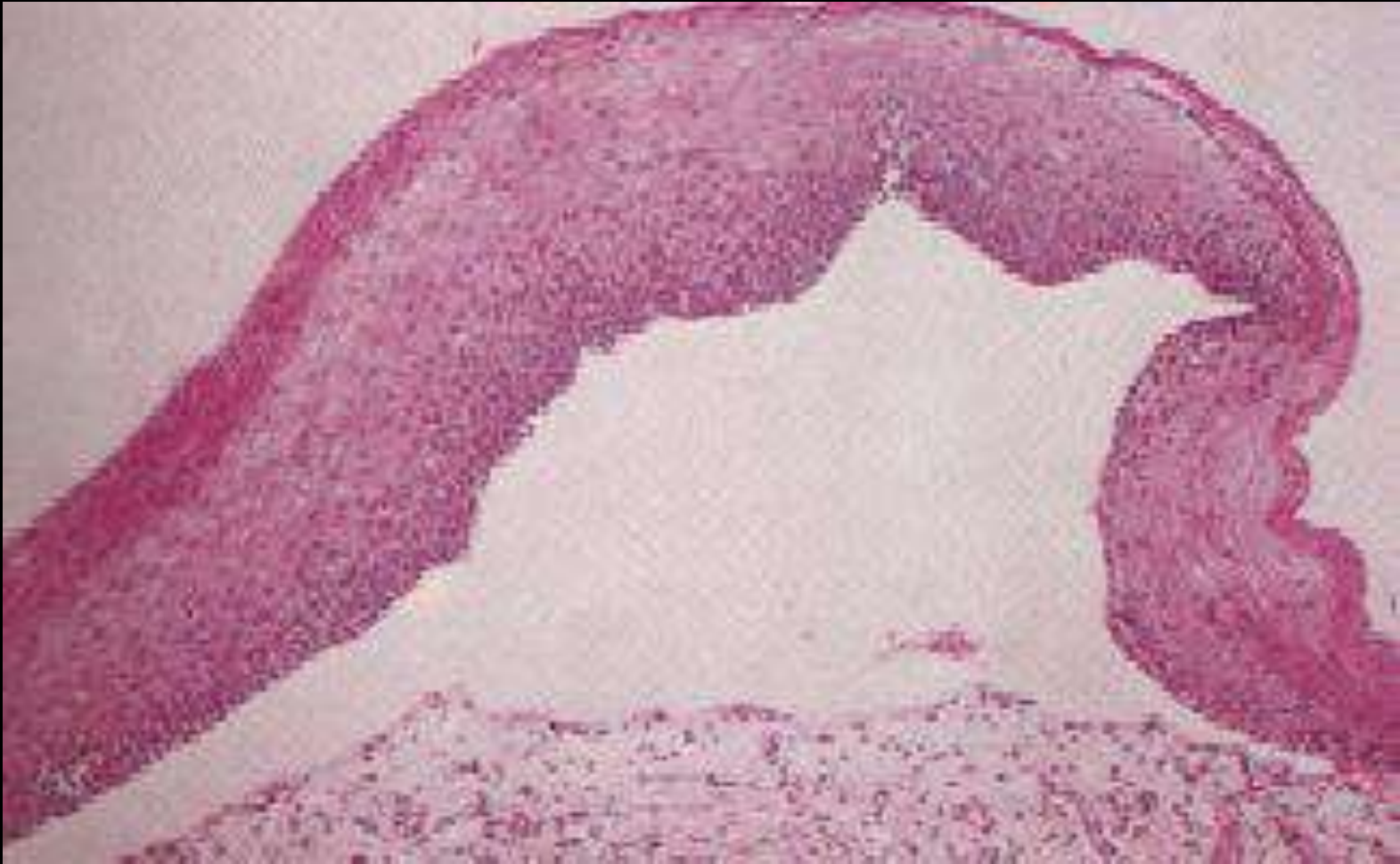
Oral manifestation

- 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”



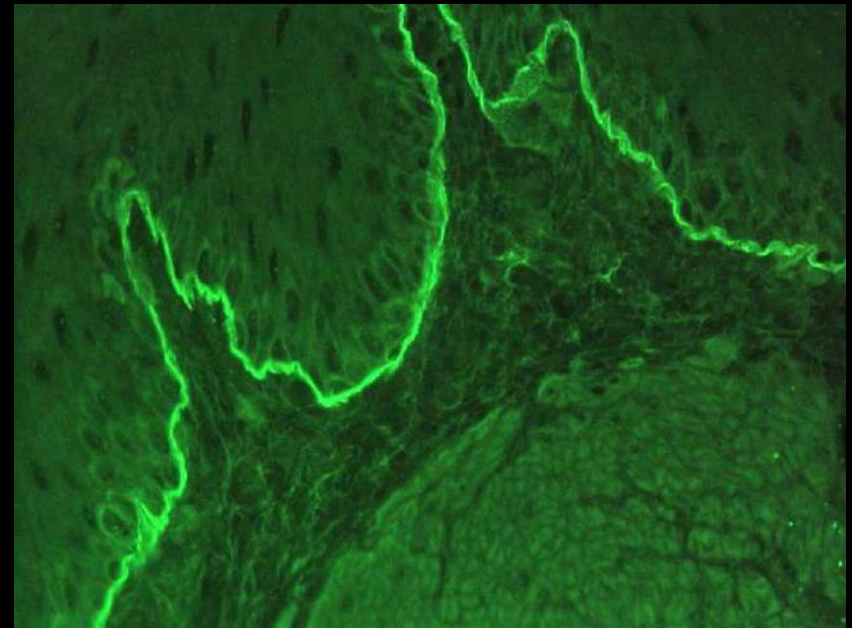
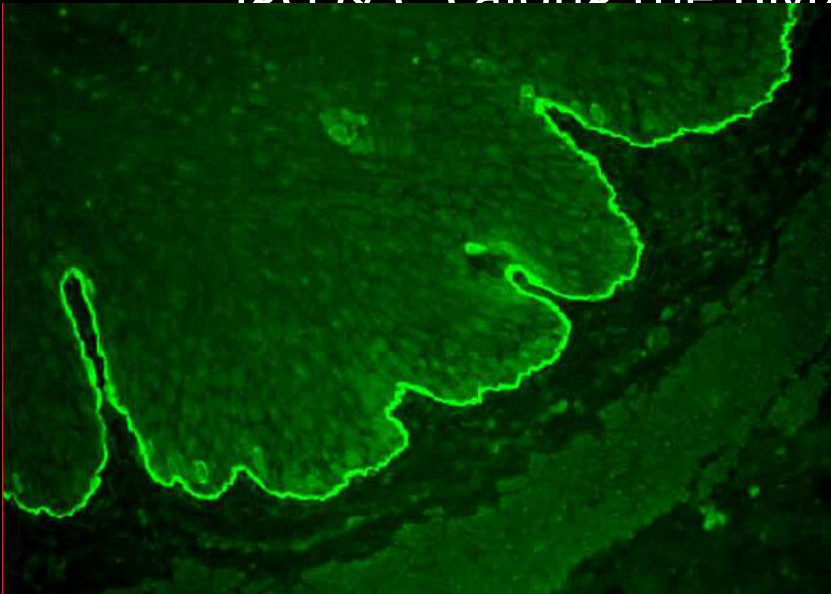
Histopathologic features

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



Immunofluorescence findings

- **Direct Immunofluorescence**
 - IgG & C3 along the RMZ



- **Indirect Immunofluorescence**

- ANTI EPILIGRIN ANTIBODIES 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

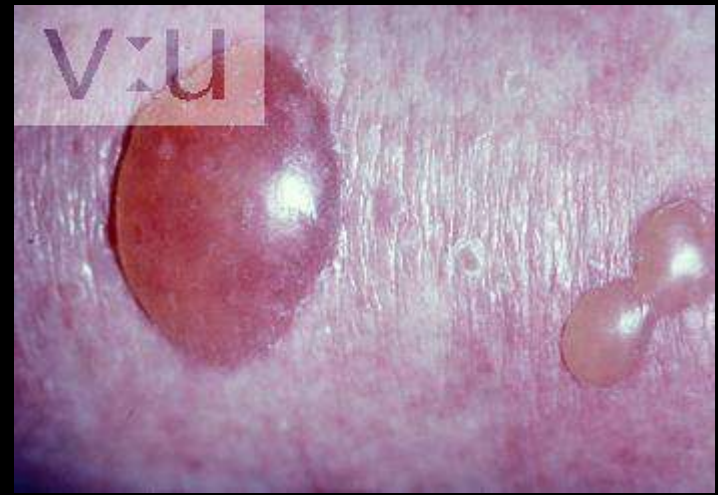
Bullous pemphogoid

Parapemphigus

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

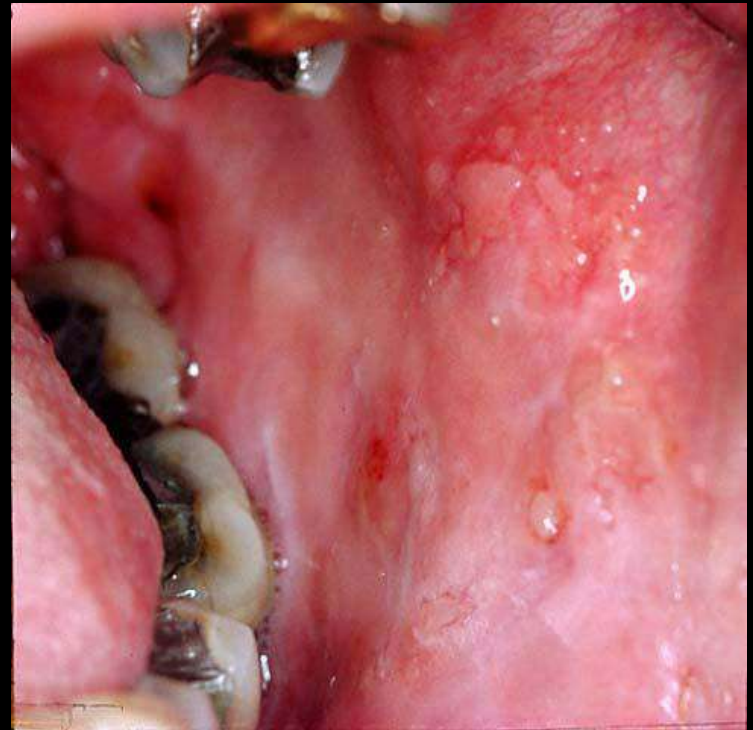
Clinical features

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



Oral manifestation

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

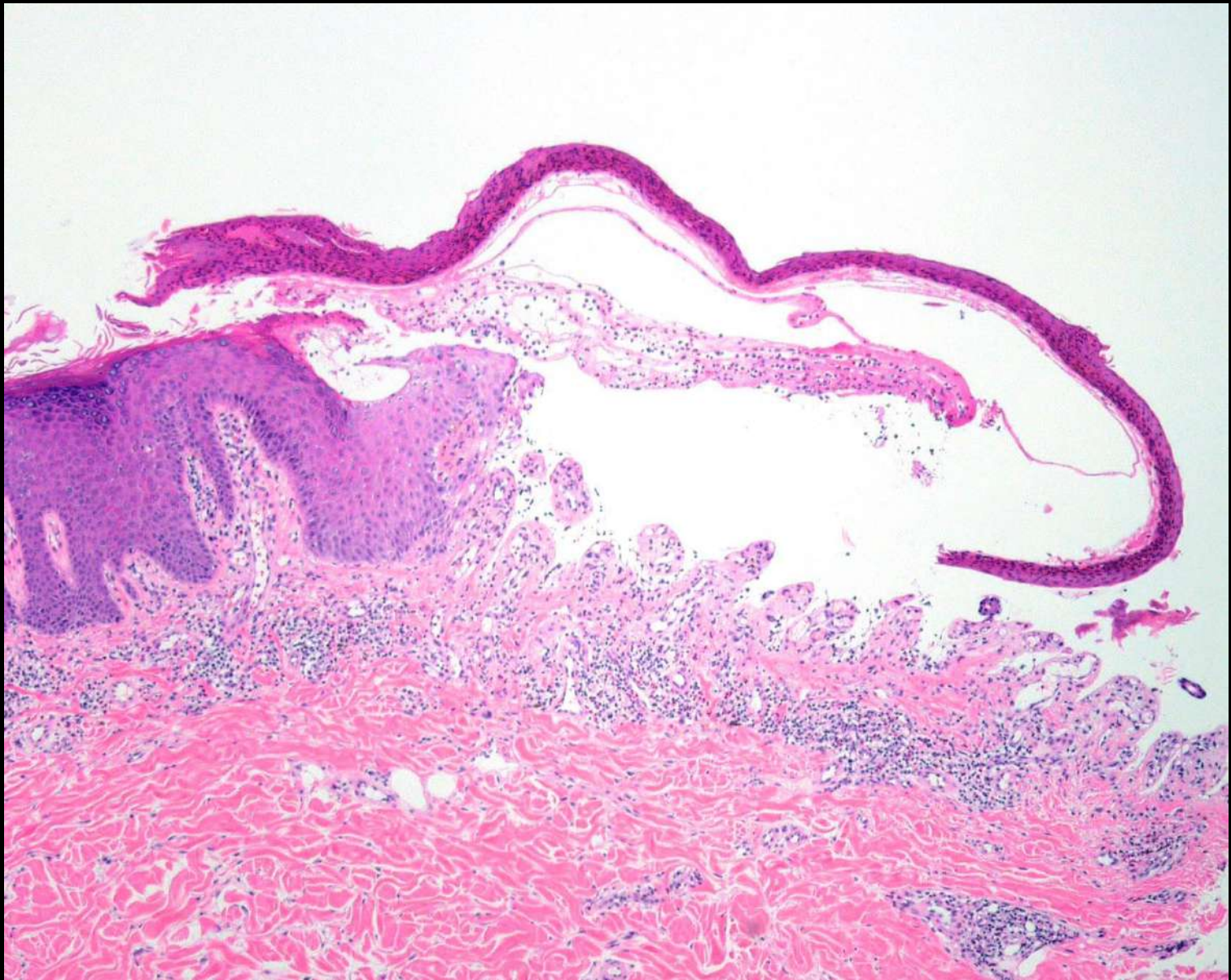


Histopathologic features

- 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)



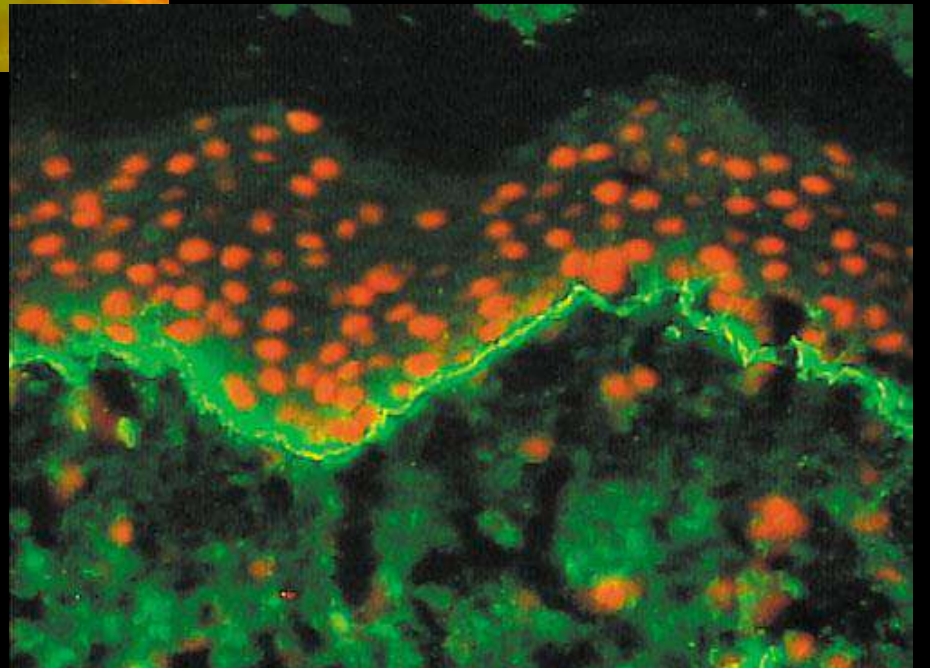
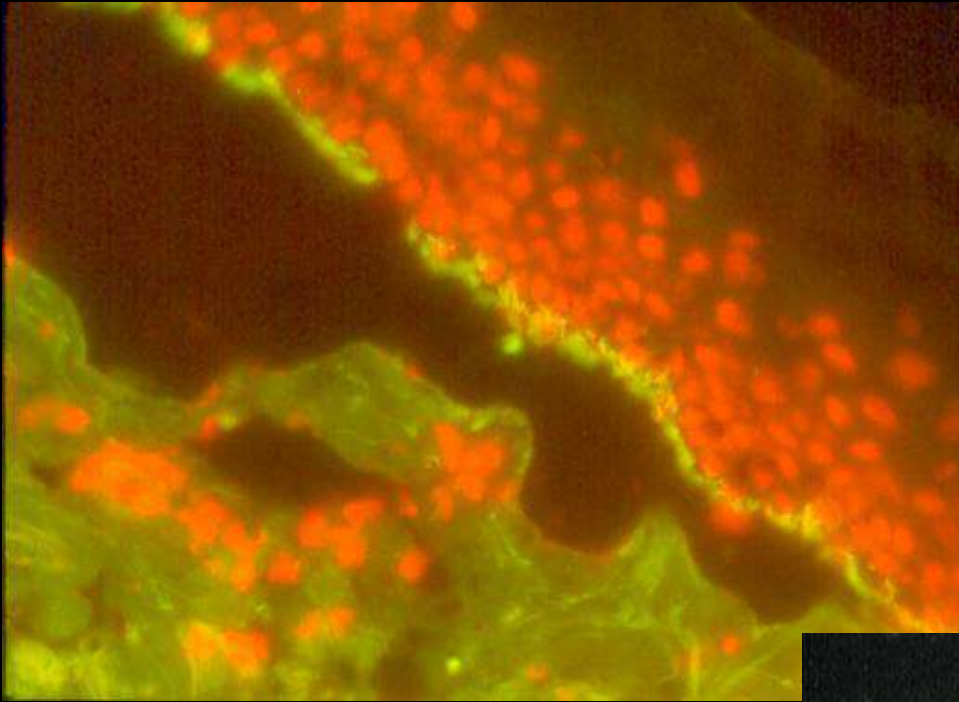
Immunofluorescence findings

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



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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 severe mucosal and skin disease which may be potentially life threatening

Etiology

- Drugs
- Infectious agents
 - HSV
 - Mycoplasma

Clinical features

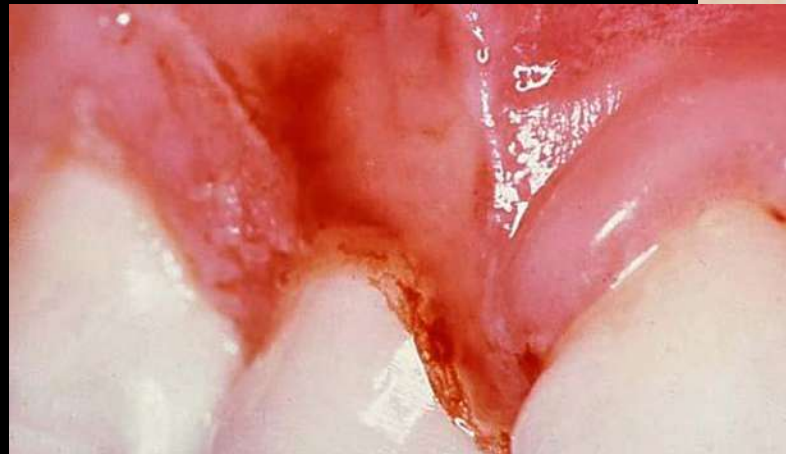
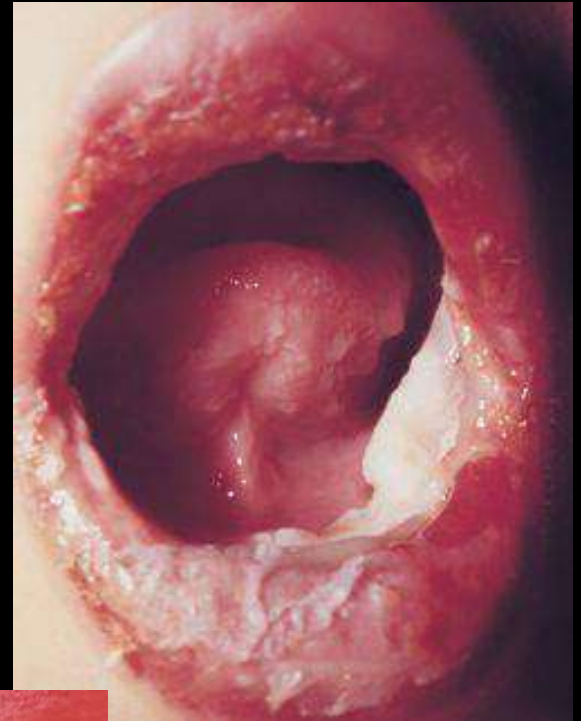
- Young adults
 - 2nd to 4th decade
- Males are affected more
- Asymptomatic, erythematous, discrete macules or papule (rarely vesicles or bullae)
- Distributed in symmetrical pattern
 - Hand, legs, face, neck

- 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



Stevens-Johnson Syndrome

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

- **Clinical presentation**

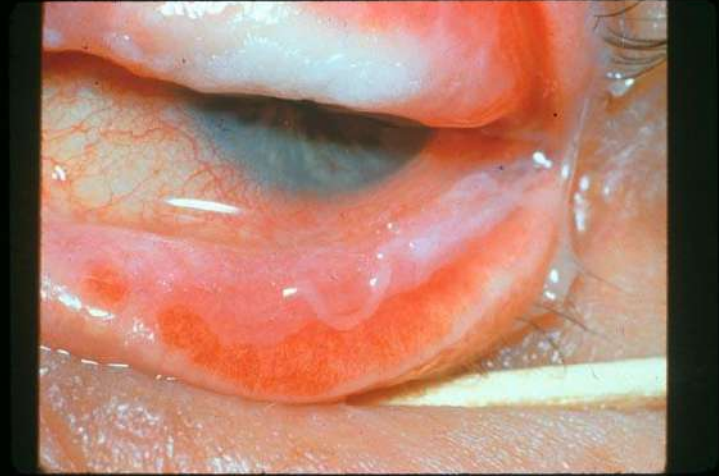
- Fever, malaise, photophobia
- Eruptions of oral mucosa, genitalia, and skin
- Lesions are similar to EM but are commonly hemorrhagic

- Oral lesions

- Extremely severe 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