

Blistering Diseases

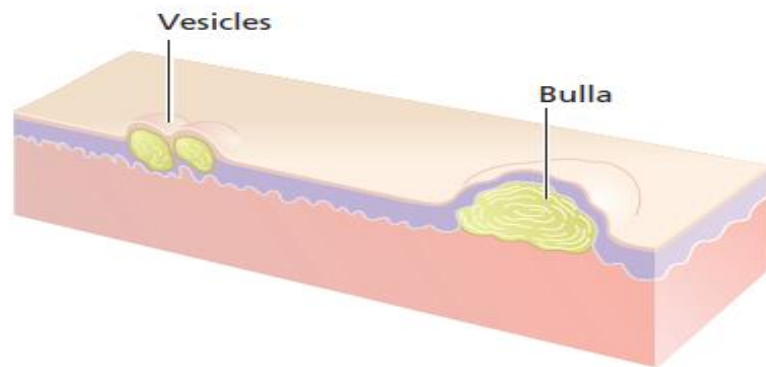
Salim Alkeraye
Assistant Professor and
Consultant
Department of Dermatology- KSU

Blistering Diseases

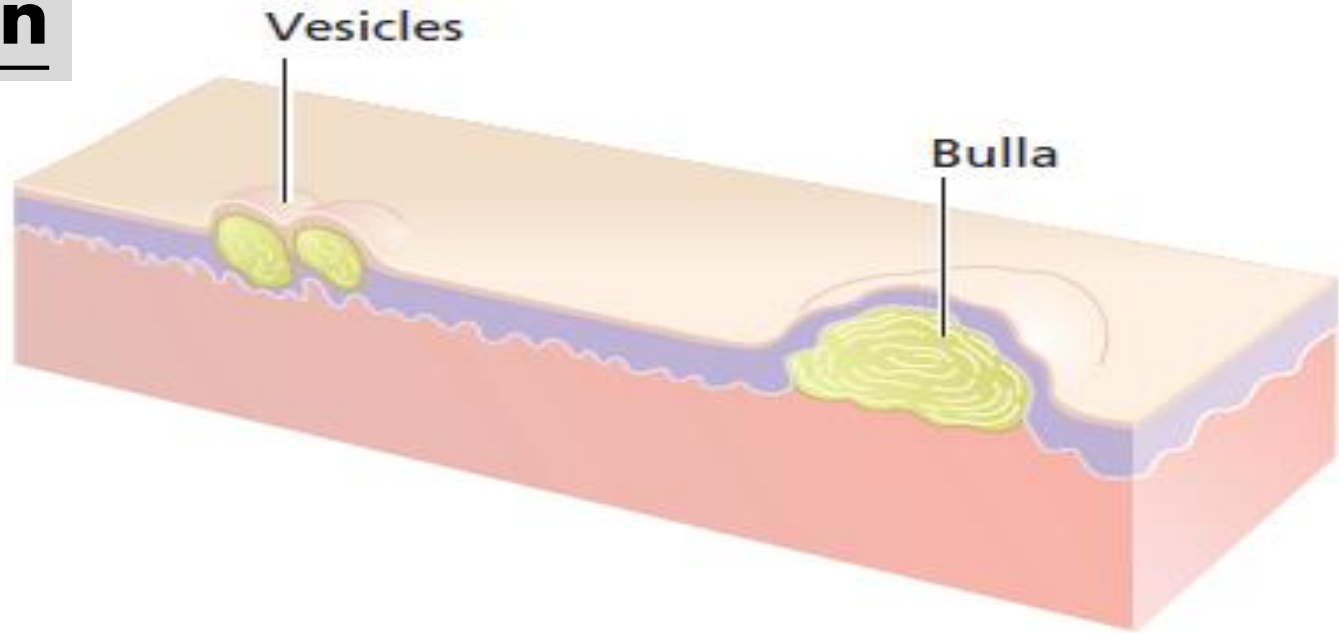
Objectives

- To know the definition & classification of Blistering diseases
- To recognize the primary presentation of different types of main blistering diseases
- To understand the possible pathogenesis of the main types of blistering diseases
- To have an overview about managements lines of these diseases





definition

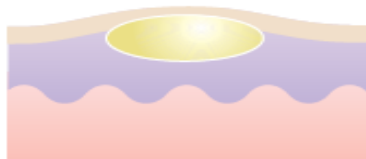


- **Vesicles and bullae are raised lesions that contain fluid.**
- **A vesicle is less than 0.5 cm in diameter.**
- **A bulla is larger than 0.5 cm in diameter.**

CLASSIFICATION OF VESICULOBULLOUS DISEASES

INTRA EPIDERMAL BLISTERS

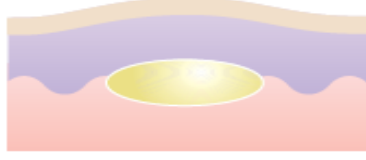
The lesion is formed within the epidermis

Location of bullae	Diseases
 <p style="text-align: center;">Subcorneal bulla</p>	<p>Bullous impetigo Miliaria crystallina Staphylococcal scalded skin syndrome</p>

 <p style="text-align: center;">Intra-epidermal bulla</p>	<p>Acute eczema Viral vesicles Pemphigus Miliaria rubra Incontinentia pigmenti</p>
--	--

SUB EPIDERMAL BLISTERS :

Lesions formed between the epidermis and the dermis

 <p style="text-align: center;">Subepidermal bulla</p>	<p>Bullous pemphigoid Cicatricial pemphigoid Pemphigoid gestationis Dermatitis herpetiformis Linear IgA disease Bullous erythema multiforme Bullous lichen planus Bullous lupus erythematosus Porphyria cutanea tarda Toxic epidermal necrolysis Cold or thermal injury Epidermolysis bullosa</p>
--	---

1. PEMPHIGUS VULGARIS

2. BULLOUS PEMPHIGOID

**3. CHRONIC BULLOUS DISEASE
OF CHILDHOOD**

**4. PARANEOPLASTIC
PEMPHIGUS**

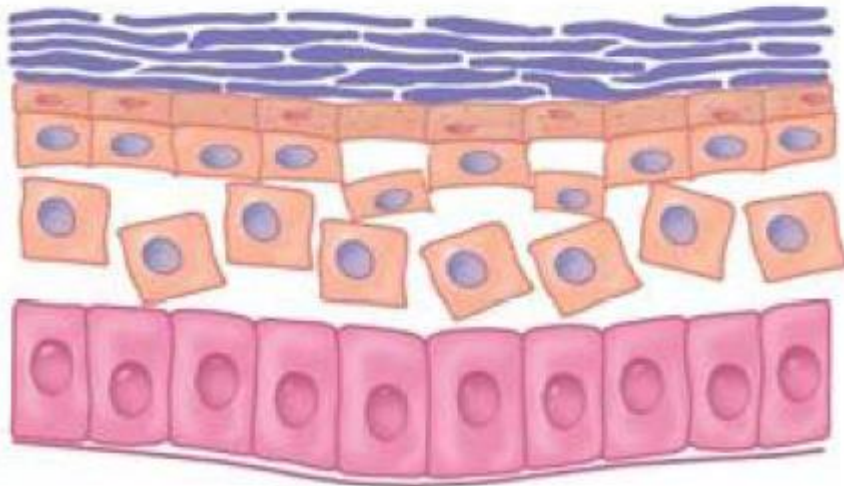
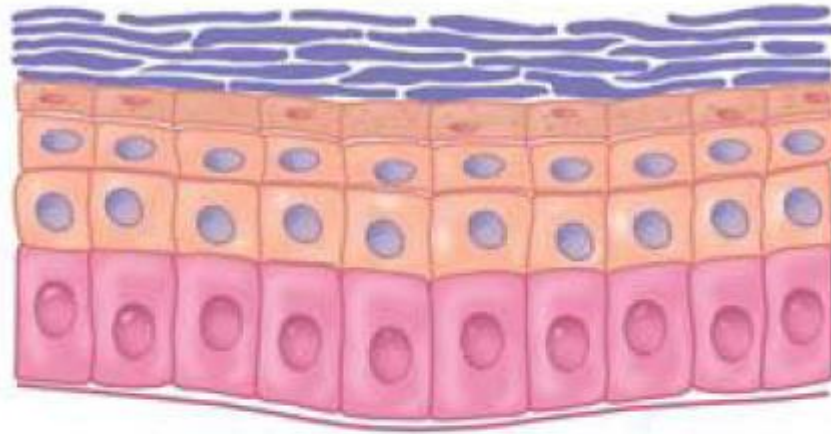
Blistering Diseases

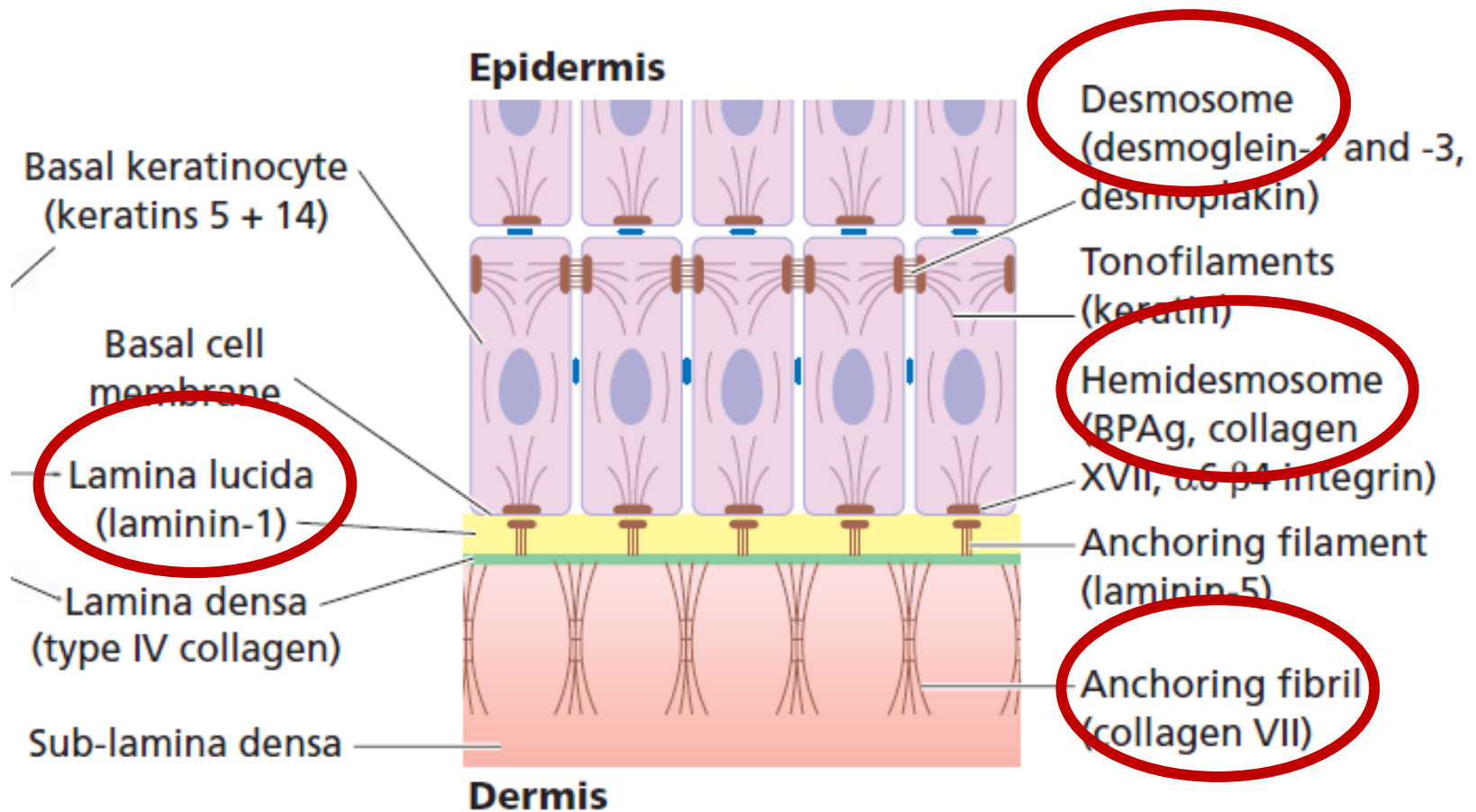
Objectives

- **To know the definition & classification of Blistering diseases**
- **To recognize the primary presentation of different types of main blistering diseases**
- **To understand the possible pathogenesis of the main types of blistering diseases**
- **To have an overview about managements lines of these diseases**

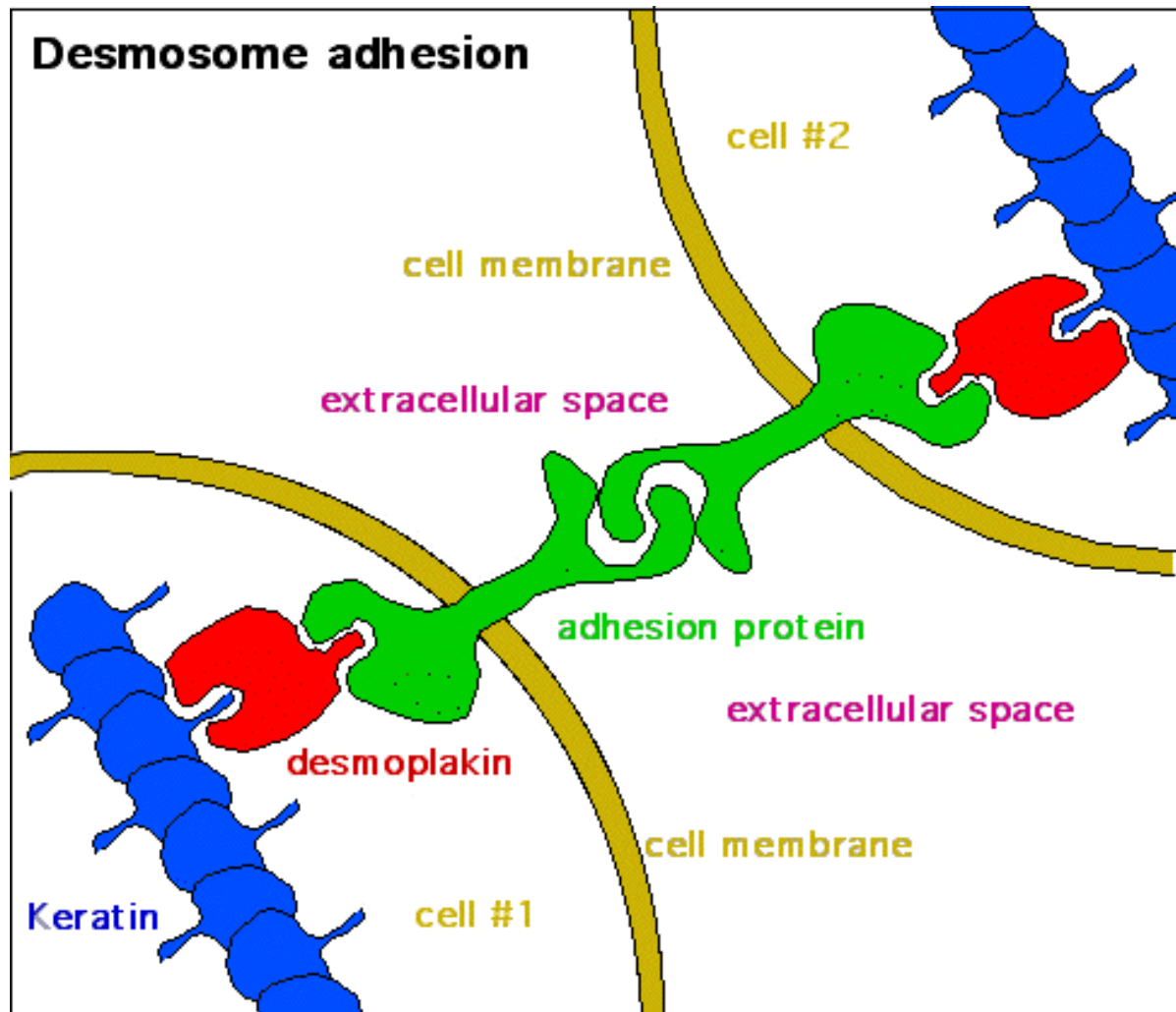


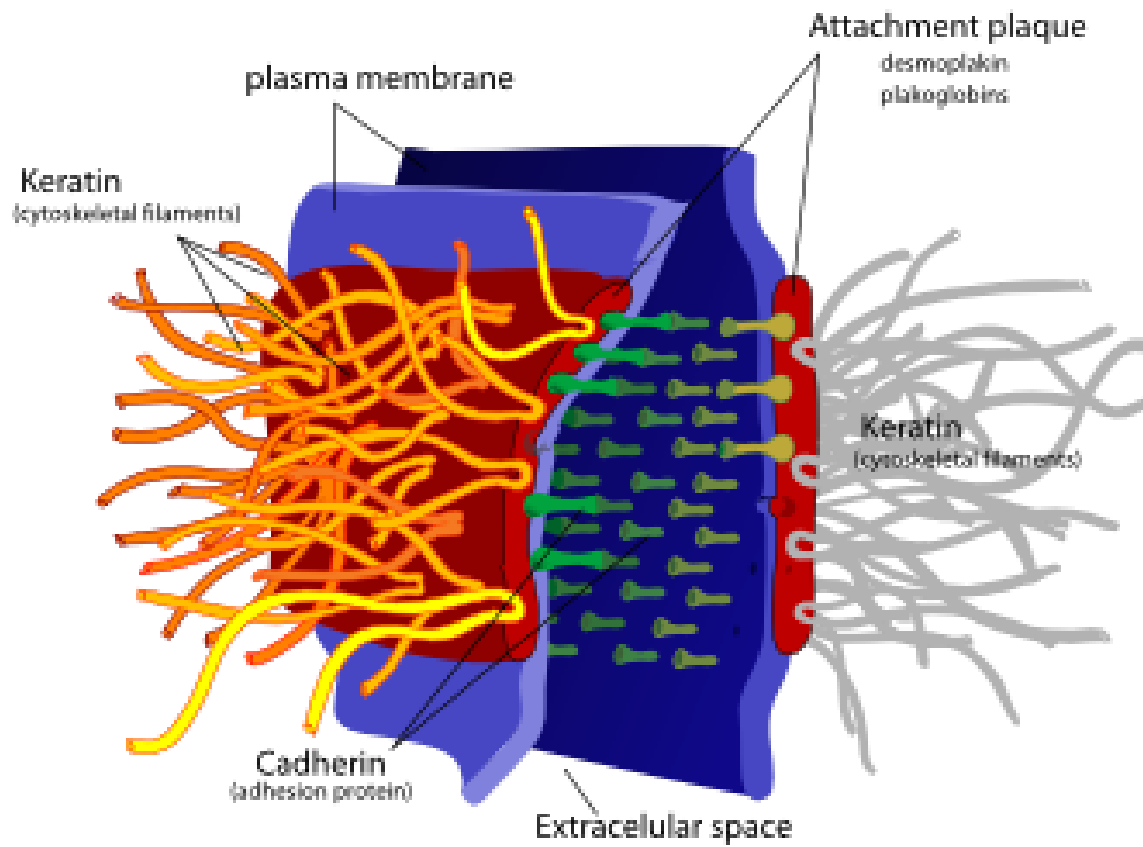
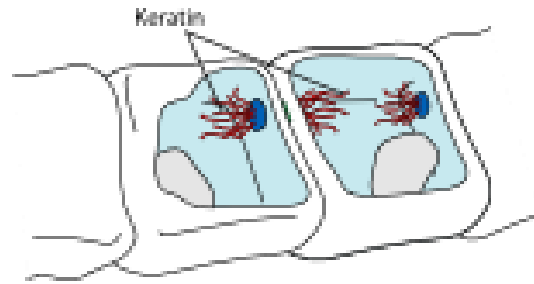
Skin

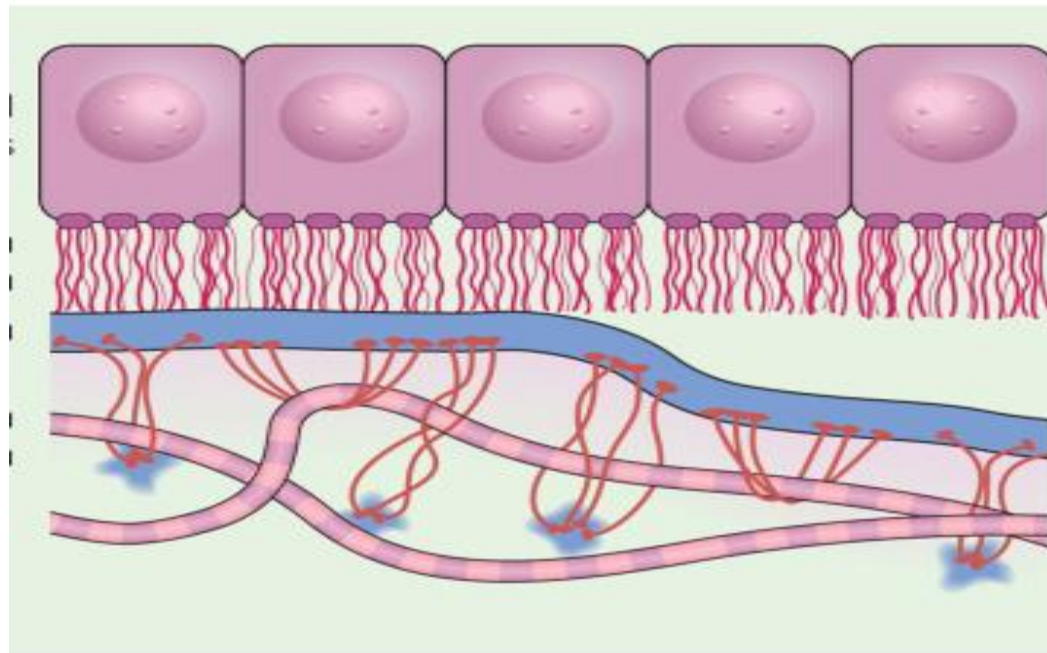
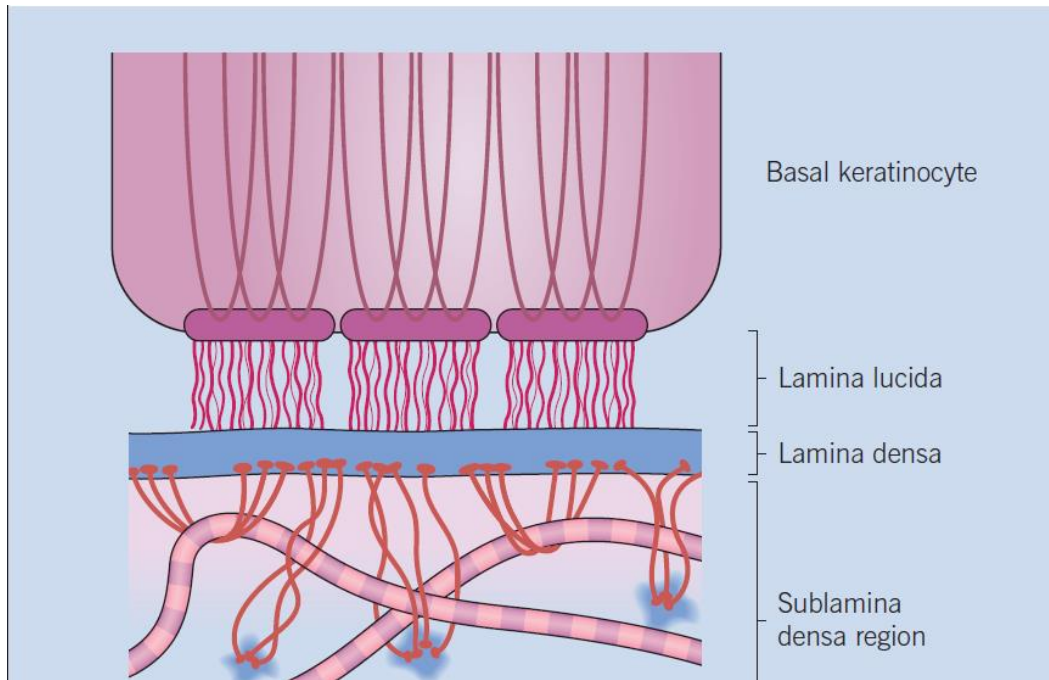




Dermo-edidermal junction





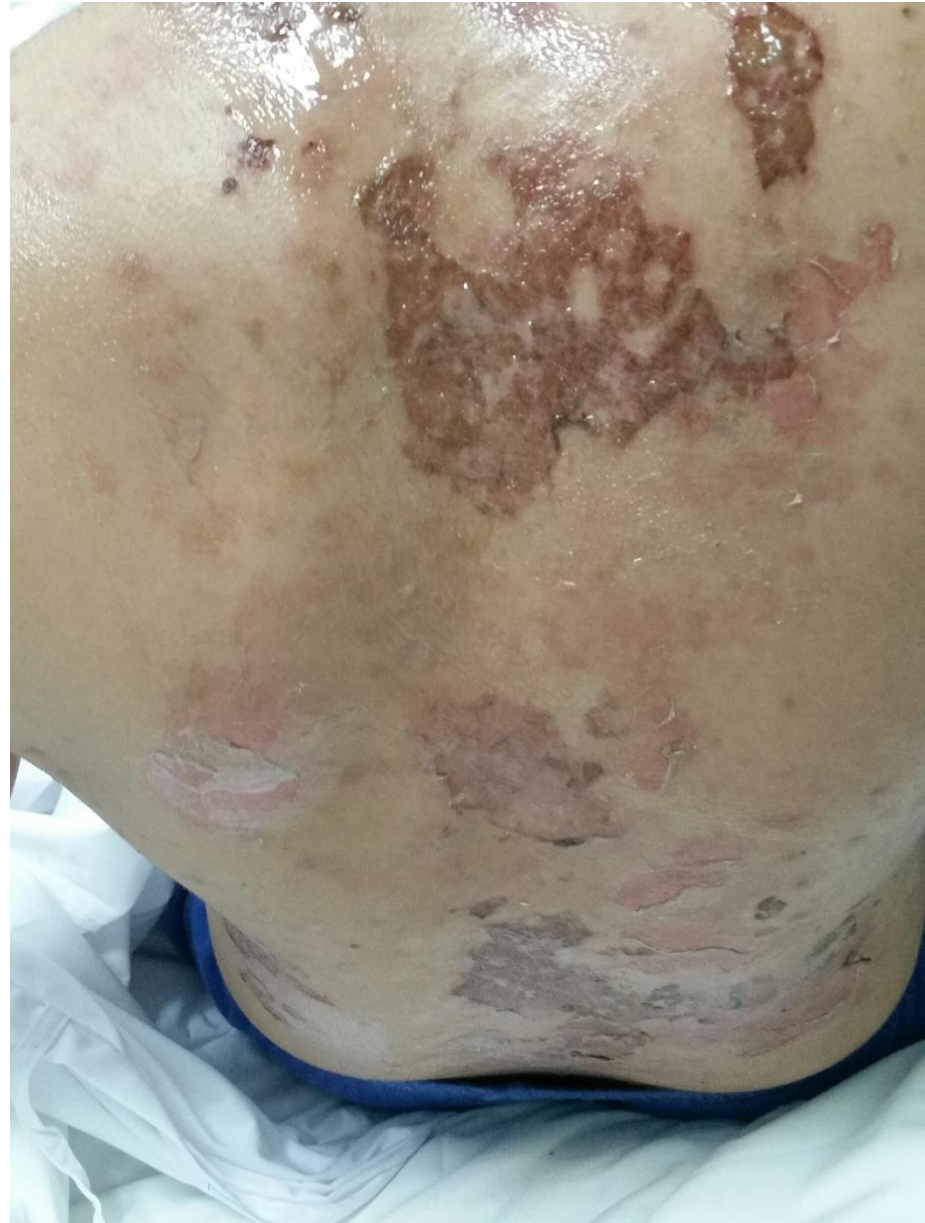


1. PEMPHIGUS VULGARIS

2. BULLOUS PEMPHIGOID

**3. CHRONIC BULLOUS DISEASE
OF CHILDHOOD**

**4. PARANEOPLASTIC
PEMPHIGUS**



- **Accurate pathological diagnosis requires 2 biopsies of a small newly formed lesion and perilesional skin for immunopathological studies.**

Diagnostic tests

1. Routine histology

- Lesional sample –small bulla or edge of large one.

2. Direct immunofluorescence

- Perilesional sample

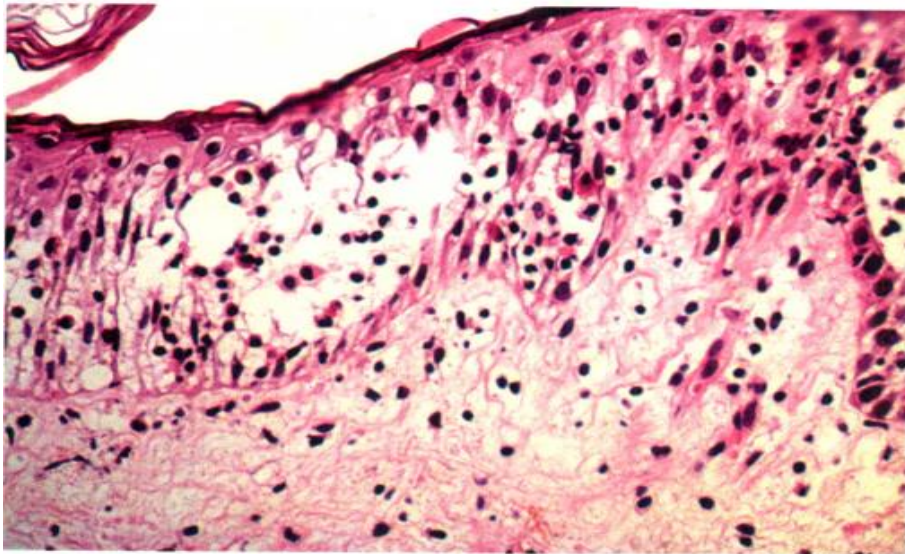
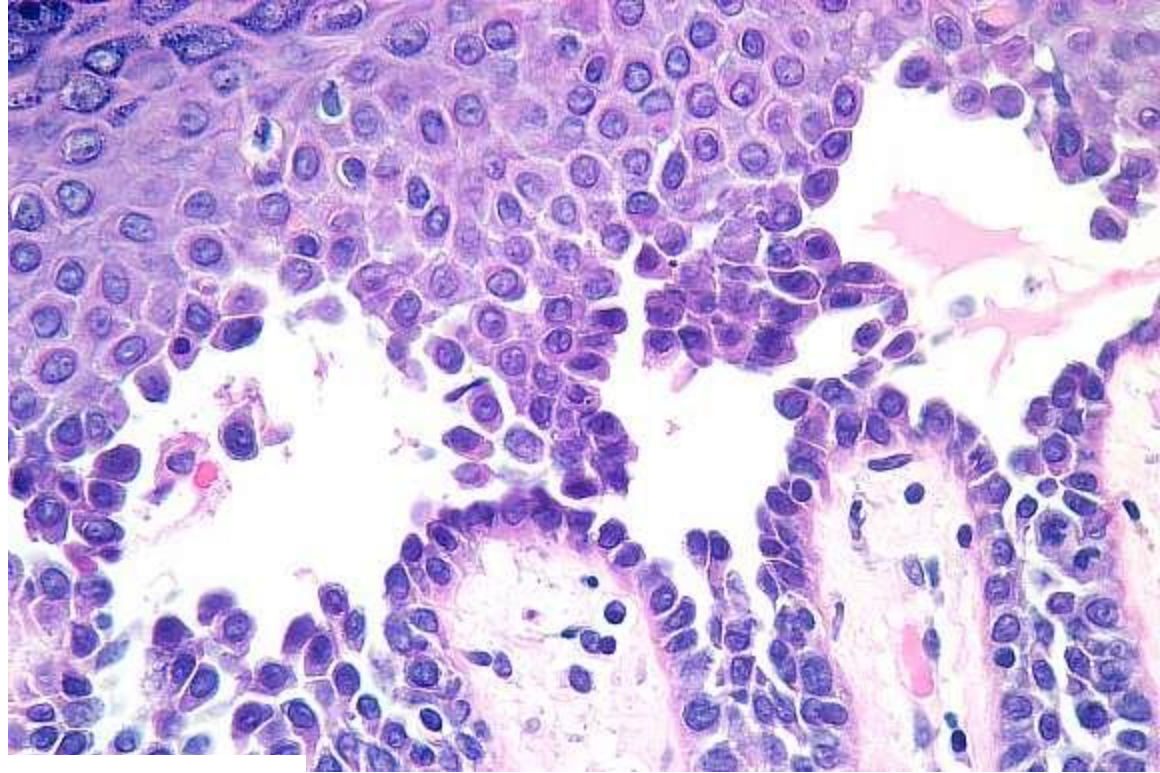
3. Indirect immunofluorescence

- Patient's serum is added to specific substrates that express antigen of interest.

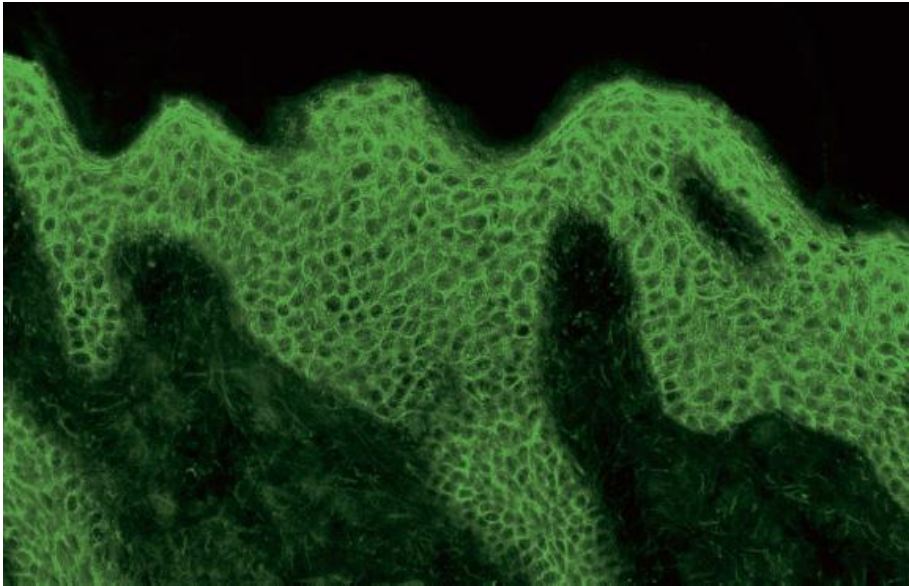
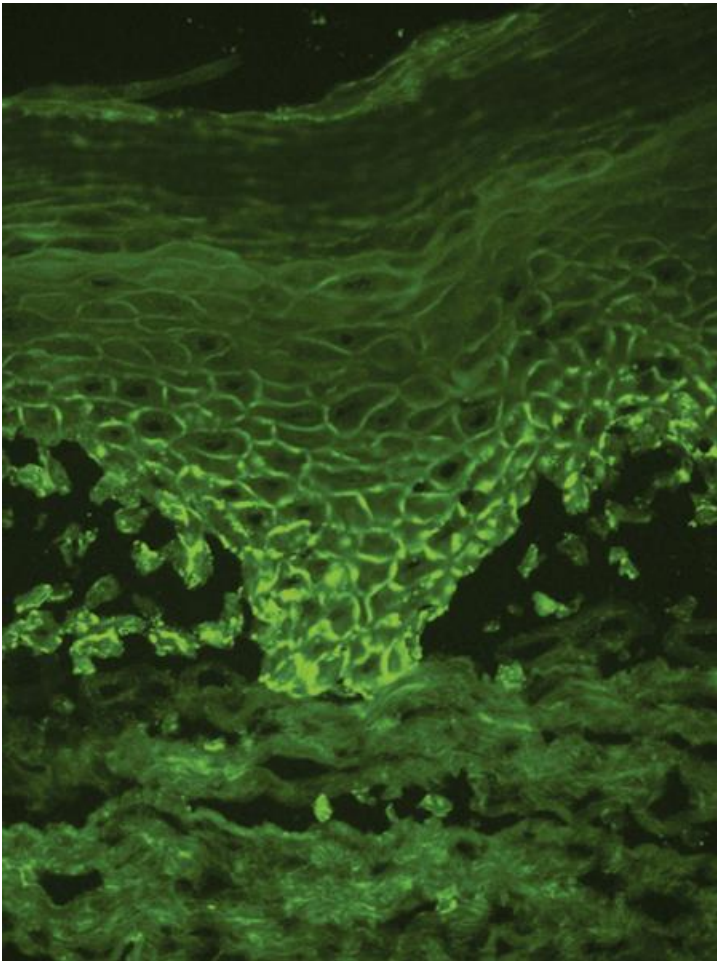
4. Electron microscopy.



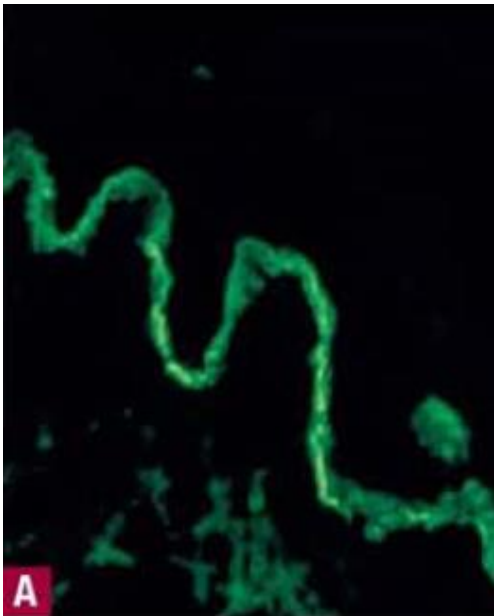
1. Routine histology

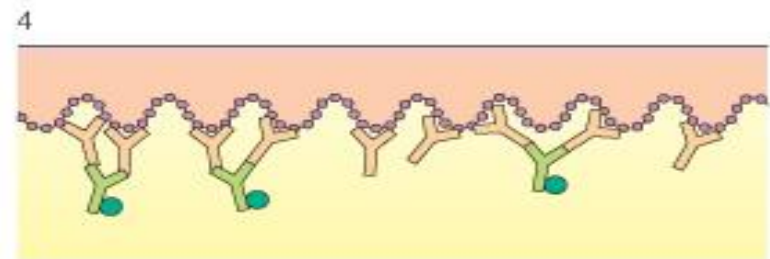
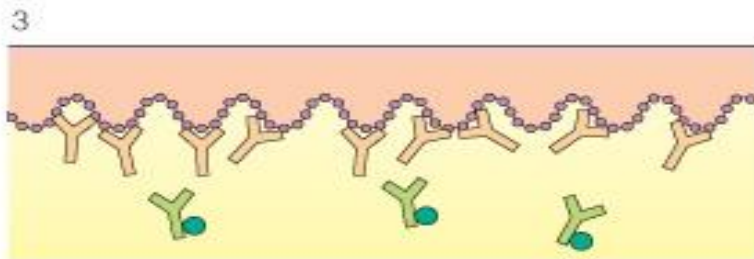
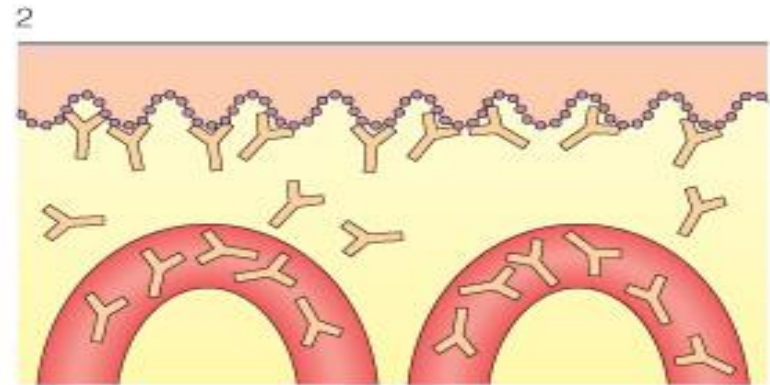
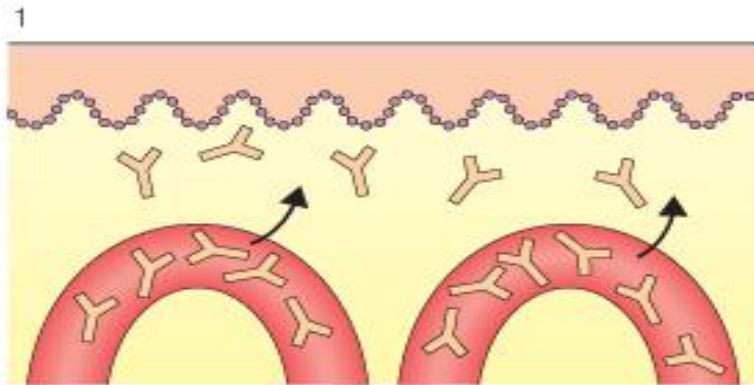



immunofluorescence



IgG
C3
IgA





 Patients skin in vivo (1,2) and as laboratory sections (3,4):
Note the basement membrane zone expressing bullous pemphigoid antigen (BPA)



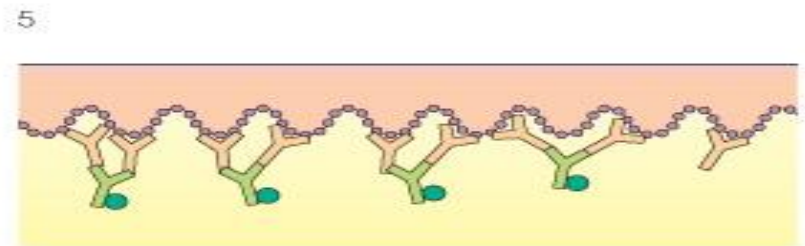
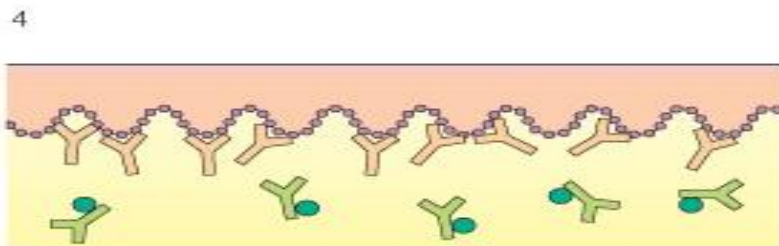
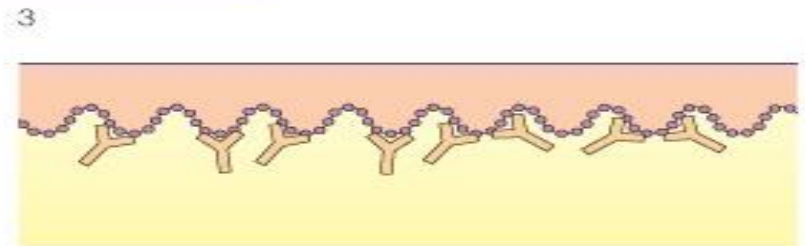
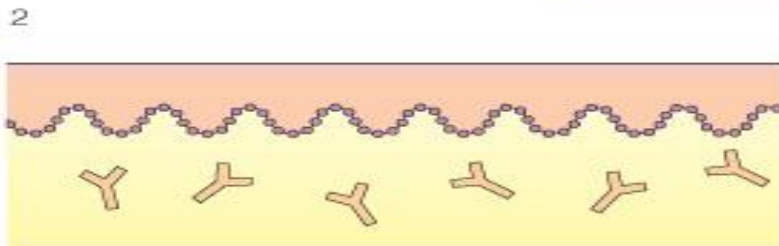
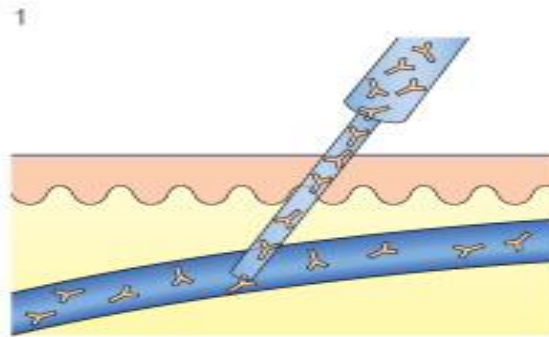
Capillary vessel







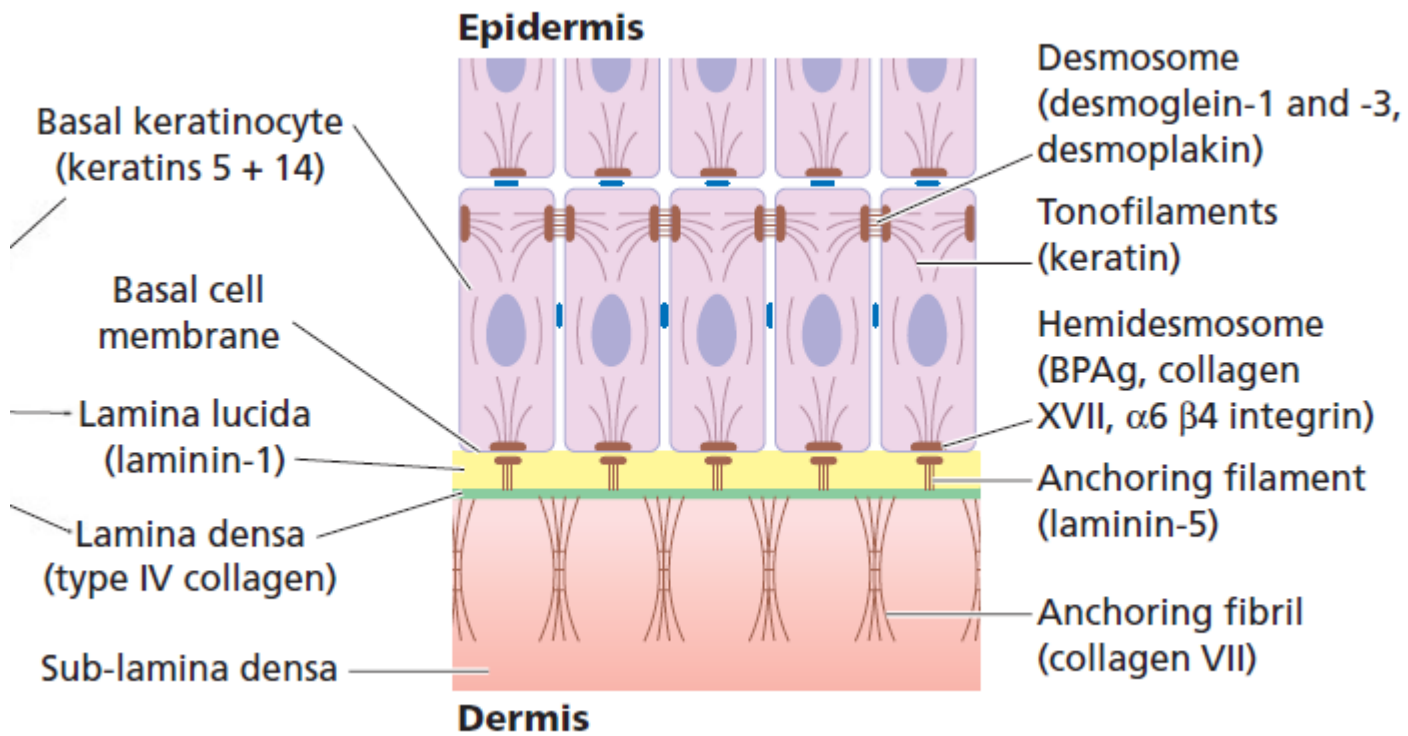
Patient's IgG autoantibody against BPA



Fluorescein-labeled antibody, e.g. goat anti-human IgG, added in laboratory



-  Sample skin or esophagus:
Note the basement membrane zone expressing bullous pemphigoid antigen (BPA)
-  Patient's vein with blood sample being extracted
-  Patient's IgG autoantibody against BPA, added (in patient's serum) to the sample skin or esophagus in the laboratory
-  Fluorescein-labeled antibody, e.g. goat anti-human IgG, added in the laboratory



1. PEMPHIGUS VULGARIS

2. BULLOUS PEMPFIGOID

3. CHRONIC BULLOUS DISEASE OF CHILDHOOD

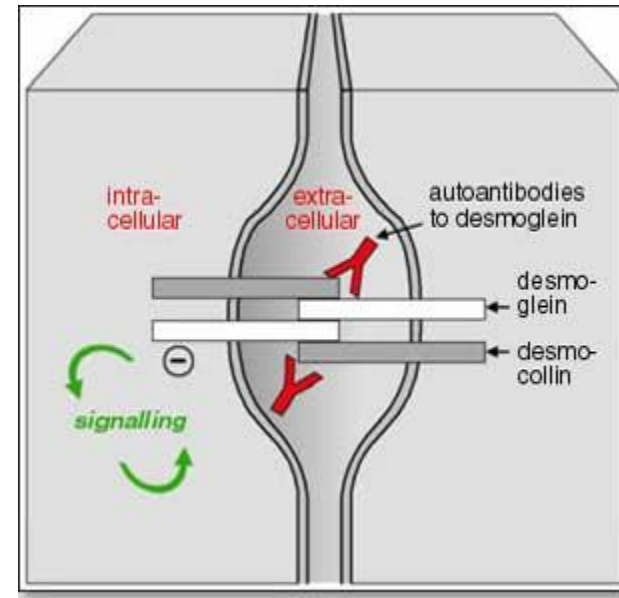
4. PARANEOPLASTIC PEMPFIGUS

Blistering Diseases

PEMPHIGUS VULGARIS

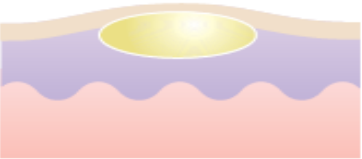
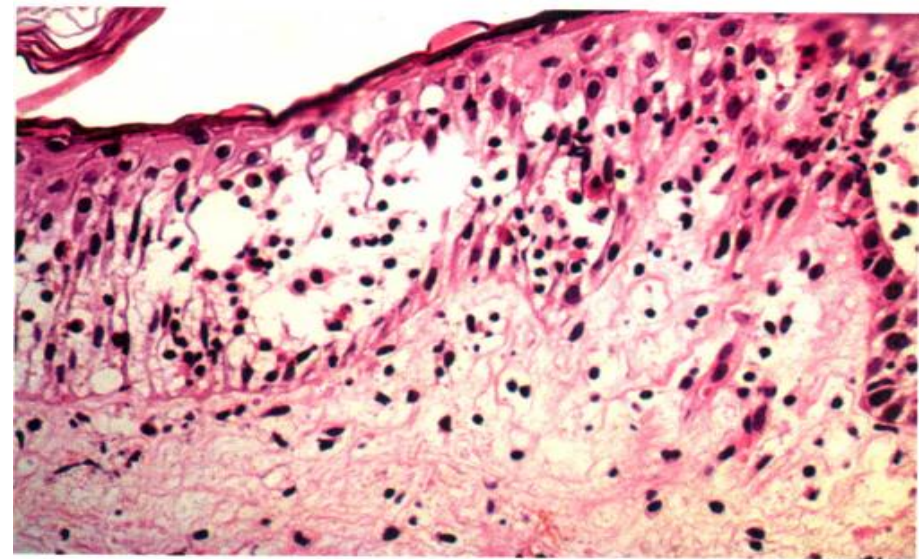
Pemphigus

- **Pemphigus is a group characterized by blistering of the skin and mucous membranes.**
- **Auto-antibodies against DESMOSOMES in epidermis and mucosal surface.**



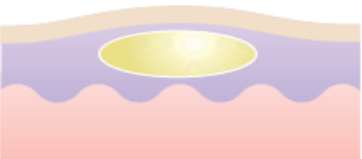
Location of bullae

Diseases



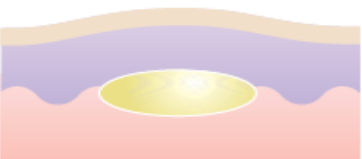
- Bullous impetigo
- Miliaria crystallina
- Staphylococcal scalded skin syndrome

Subcorneal bulla



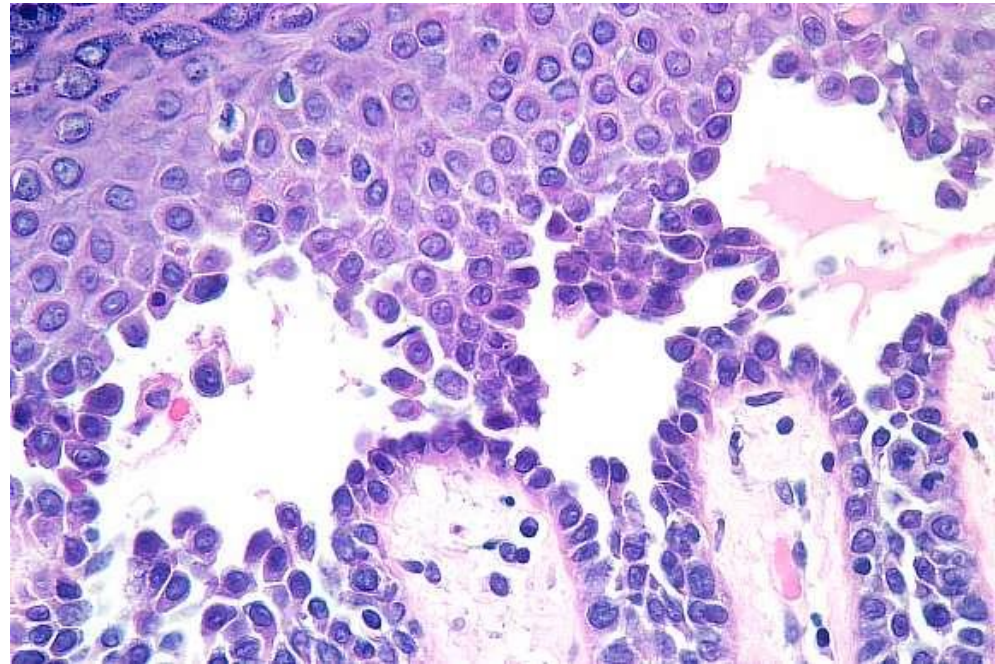
- Acute eczema
- Viral vesicles
- Pemphigus
- Miliaria rubra
- Incontinentia pigmenti

Intra-epidermal bulla



- Bullous pemphigoid
- Cicatricial pemphigoid
- Pemphigoid gestationis
- Dermatitis herpetiformis
- Linear IgA disease
- Bullous erythema multiforme
- Bullous lichen planus
- Bullous lupus erythematosus
- Porphyria cutanea tarda
- Toxic epidermal necrolysis
- Cold or thermal injury
- Epidermolysis bullosa

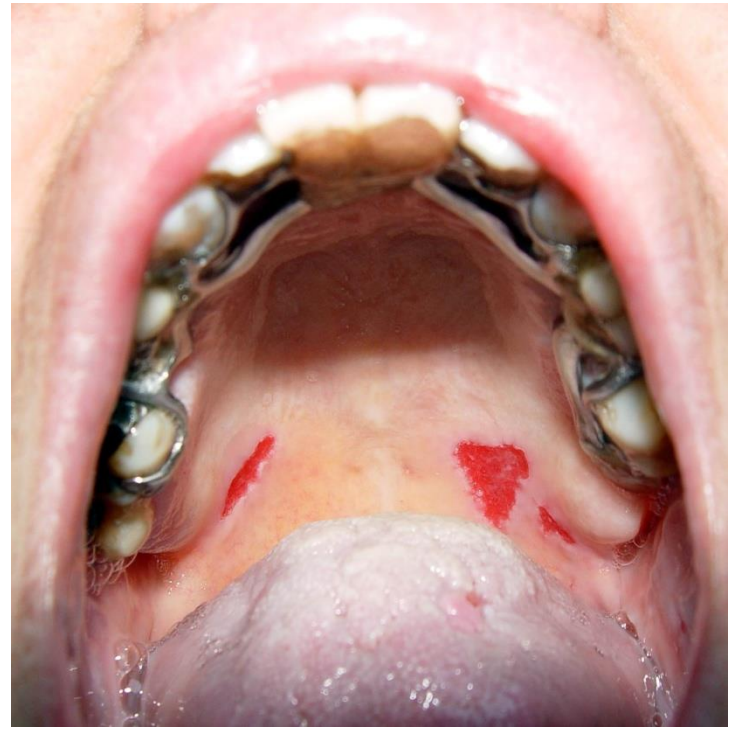
Subepidermal bulla



Four sub-clinical variants :

Pemphigus Vulgaris: is the most common Pemphigus variant, and the form usually responsible for oral lesions

Foliacious, vegetens, erythematosus



Pemphigus Vulgaris

- **Begins with erosions on mucous membrane then other skin areas.**
- **Very painful.**
- **+ve Nikolsky's sign**

+ve *Nicholsky* sign

- Twisting pressure on normal skin shears skin.**

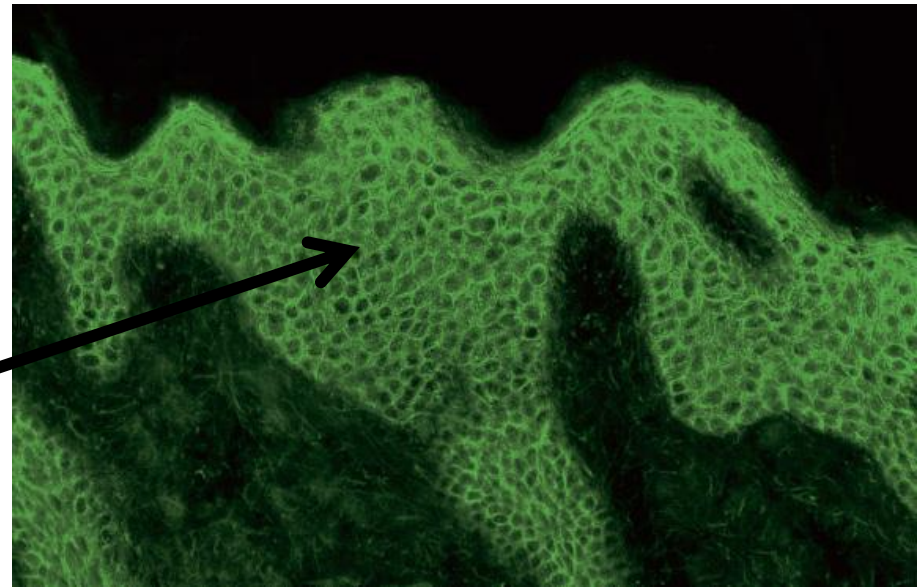
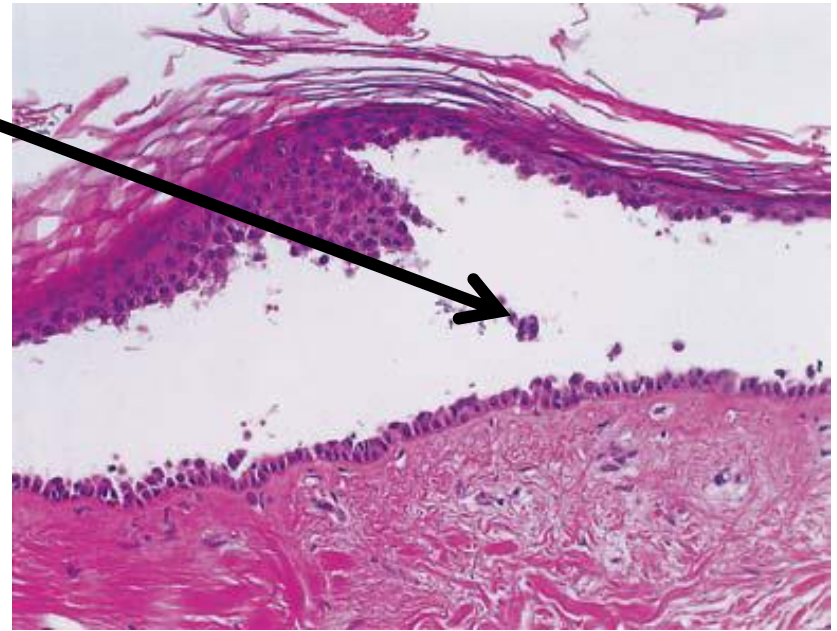
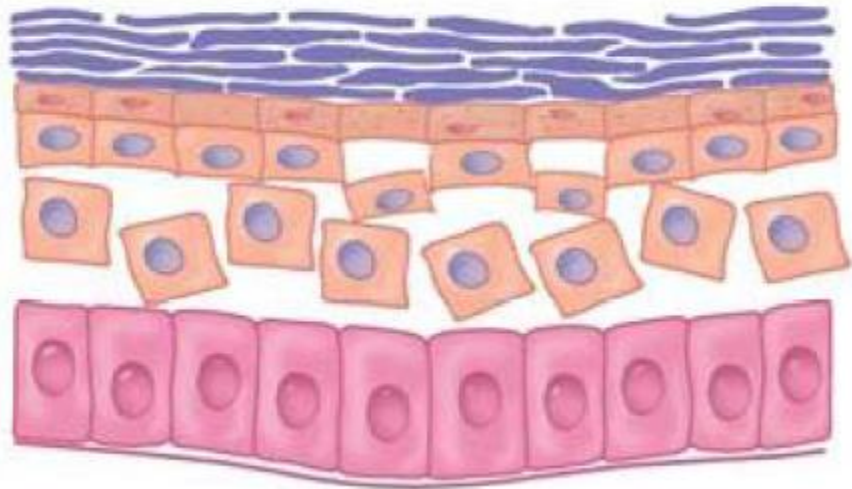


Pemphigus Vulgaris

- **Begins with erosions on mucous membrane then other skin areas.**
- **Very painful.**
- **+ve Nikolsky's sign.**
- **Age: middle-age 40-60 years.**
- **Secondary infection and disturbance of fluid and electrolyte balance are common complications .**

Pathology and immunopathology

Acantholysis



Immunofluorescence
IgG and C3

Treatment

- **High dose systemic steroids 60-100 mg of prednisolone.**
- **Immunosuppressive agent such as azathioprine cyclophosphamide , Methotrexate or mycophenolate**
- **Patient will probably have to remain on systemic steroids for long time.**
- **Antibiotics; to treat superinfection**

Biological Rx:

1- Rituximab

- IV

86% free of
disease after 3 y

2-IVIG (intravenous immunoglobulin)

Drug induced blistering diseases

Drug-induced PV

Drugs can induce PV

Drugs reported most significantly in association with PV are;

Penicillamine

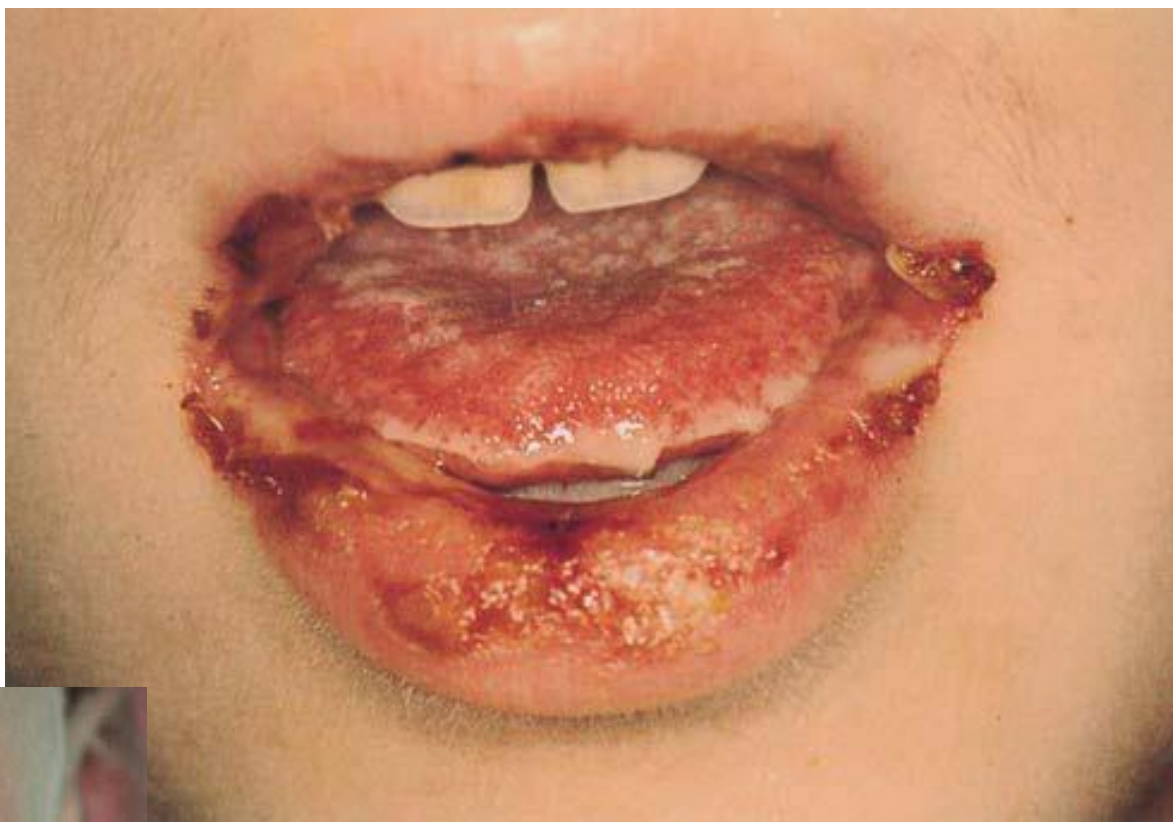
Captopril

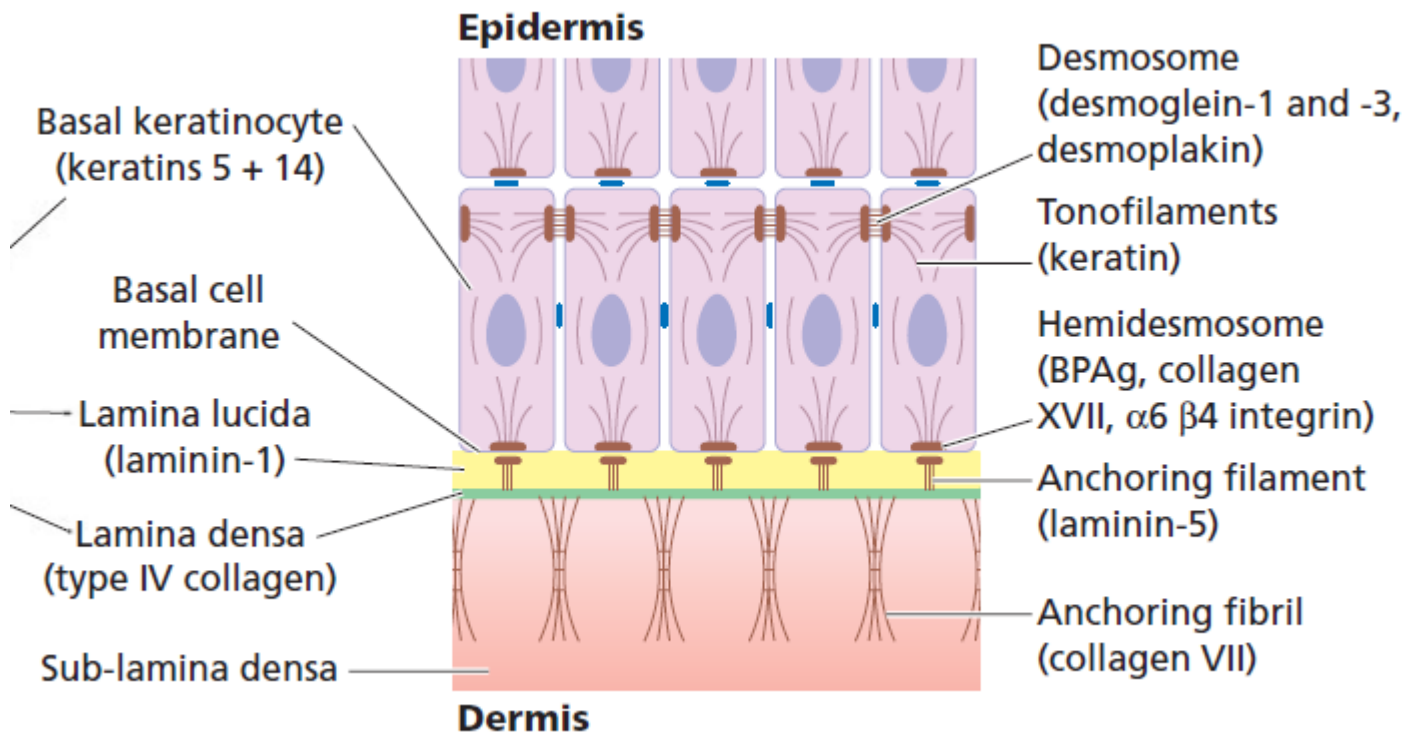
Anti epileptic phenytoin and carbamazepine

1. **PEMPHIGUS VULGARIS**
2. **BULLOUS PEMPFIGOID**
3. **CHRONIC BULLOUS DISEASE OF CHILDHOOD**
4. **PARANEOPLASTIC PEMPFIGUS**

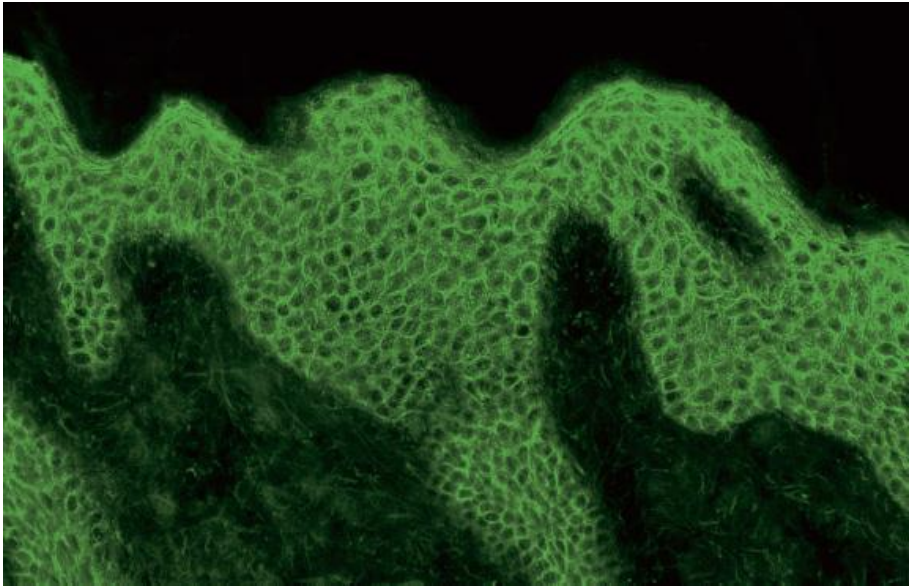
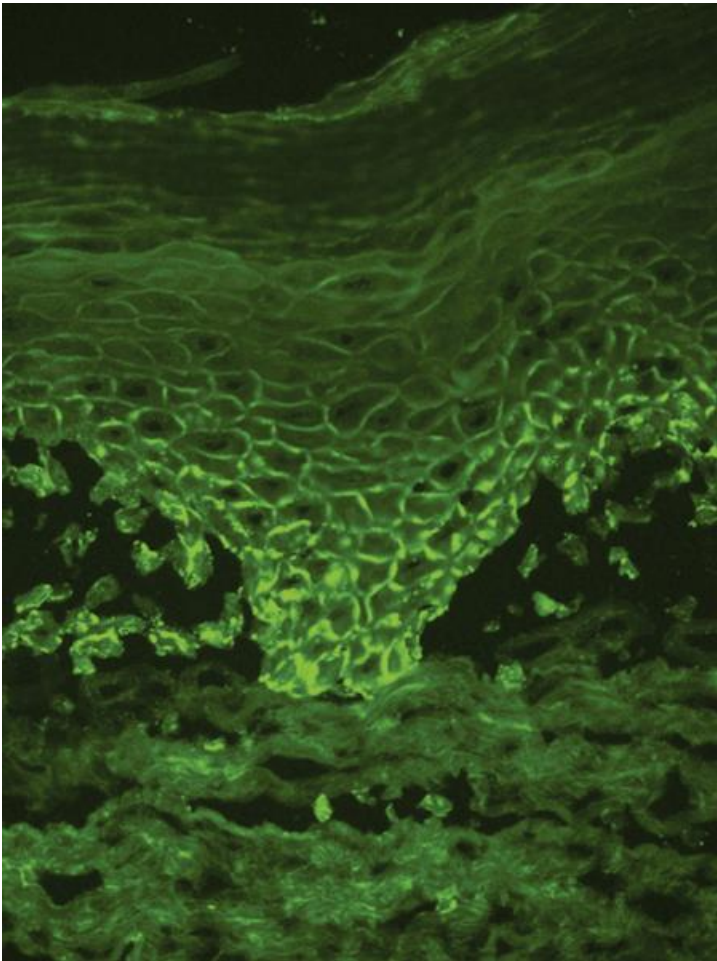
Paraneoplastic pemphigus

- The least common and most severe type of pemphigus is **paraneoplastic pemphigus (PNP)**. This disorder is a complication of **cancer**,
- usually **lymphoma** and **Castleman's disease**. It may precede the diagnosis of the tumor. Painful sores appear on the **mouth, lips, and the esophagus**.
- **Complete removal and/or cure of the tumor may improve the skin disease,**

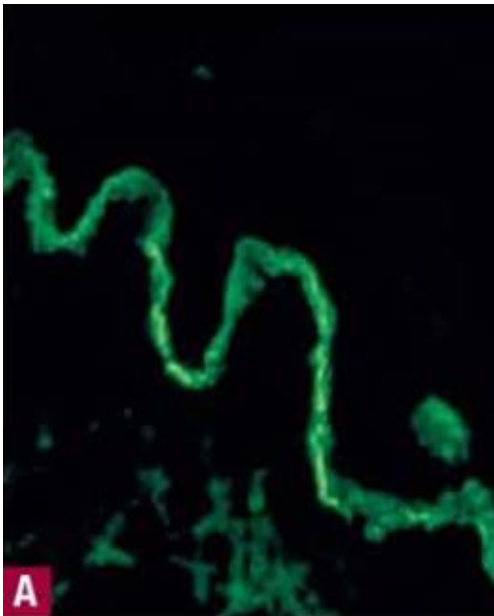




immunofluorescence



IgG
C3
IgA



1. **PEMPHIGUS VULGARIS**

2. **BULLOUS PEMPFIGOID**

3. **CHRONIC BULLOUS DISEASE OF
CHILDHOOD**

4. **PARANEOPLASTIC PEMPFIGUS**

Bullous pemphigoid

- **Characterized by large blisters on an erythematous base.**
- **Mainly in older age group more than 60 y.**
- **The prognosis is usually good.**

Clinical features

- **Elderly patents.**
- **Large tense blisters on upper arms and thighs.**
- **Eczematous base .**
- **Itch rather than pain.**
- **Oral lesions are less frequent than pemphigus.**

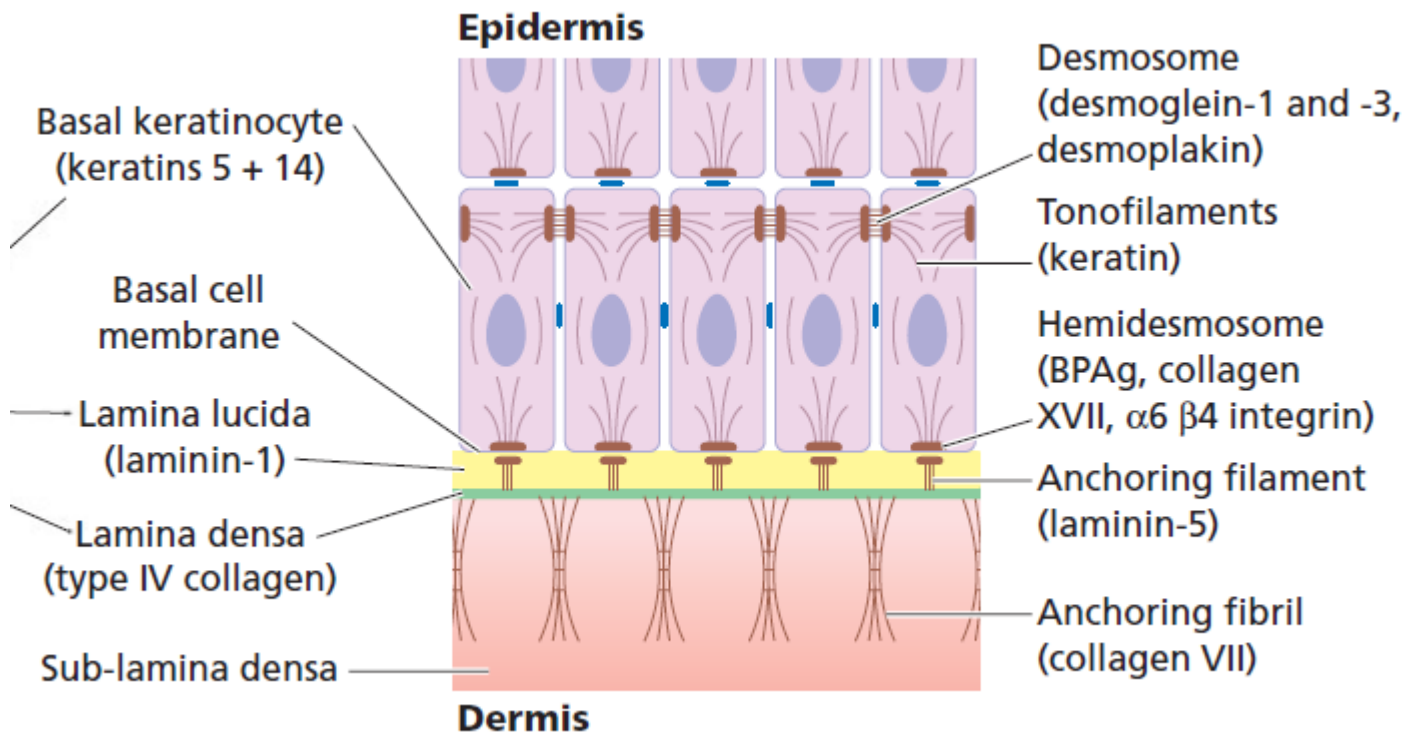


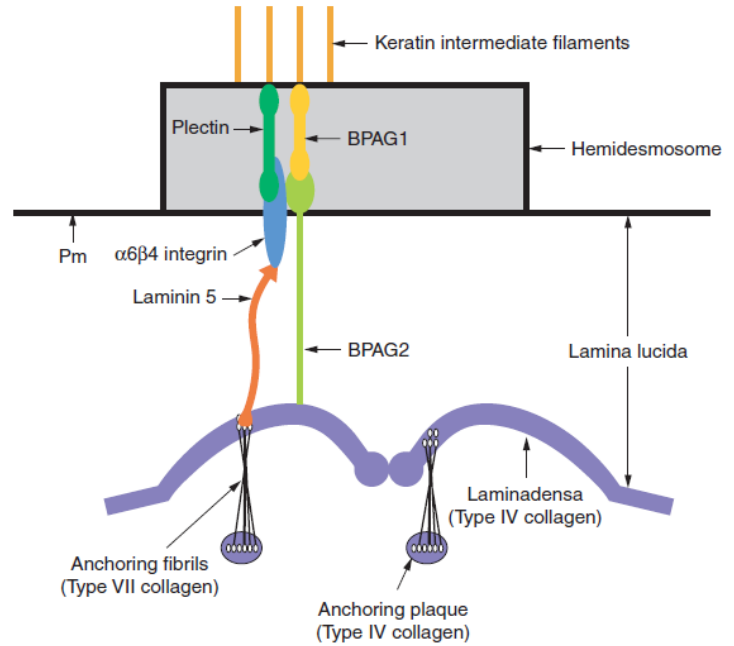
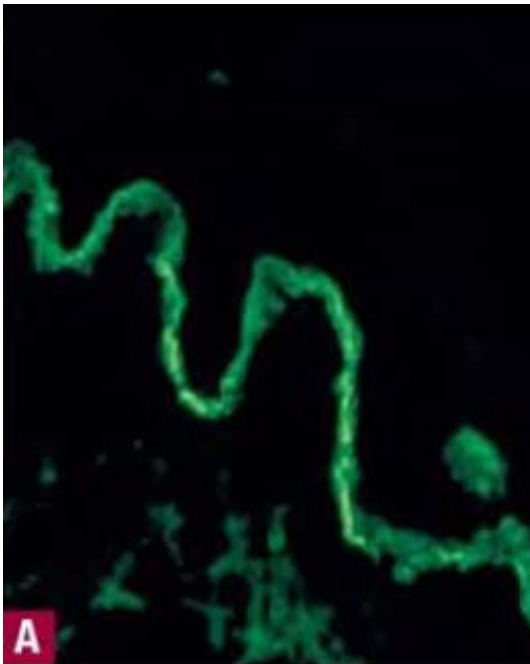


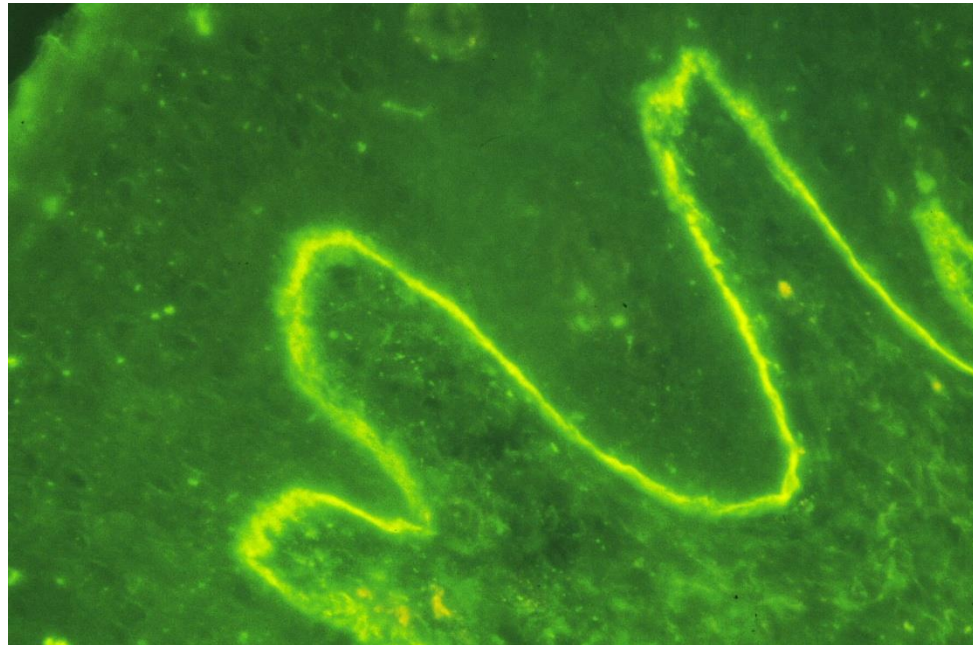
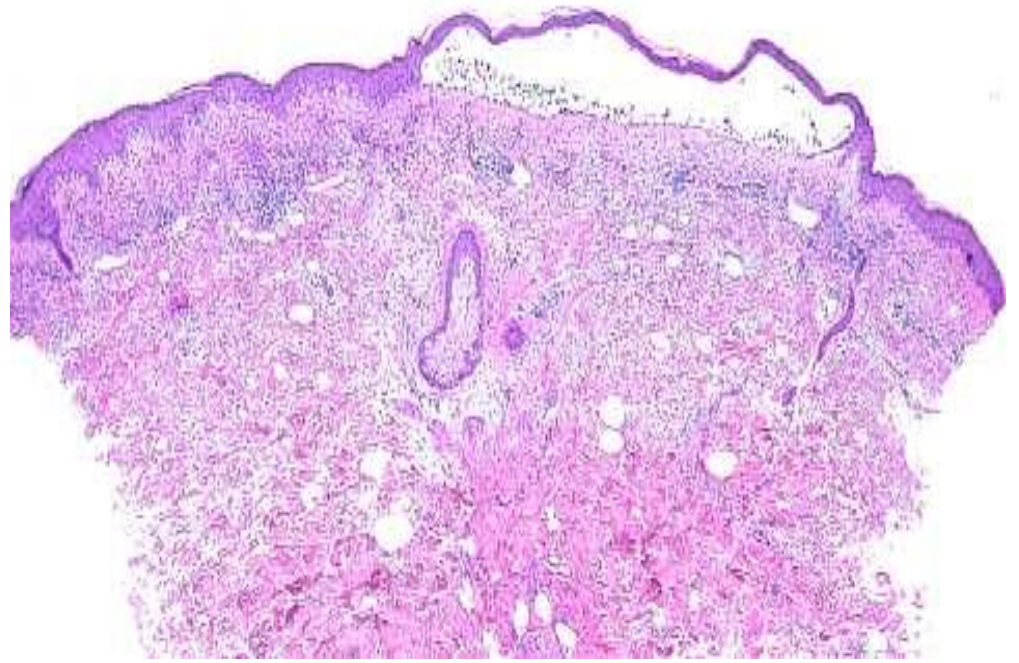
Pathology



- **Sub epidermal between epidermis and dermis the epidermis forms the roof of the blister.**
- **Antigens identified are BP 1 and BP 2.**
- **Immunoglobulin and complement are deposited in the lamina lucida of the basement membrane in a linear band.**







Treatment

- **Mild may also respond very well to potent or moderately potent topical steroids alone.**
- **Severe pemphigoid :Systemic steroids , but unlike pemphigus, it may be possible to discontinue.**
- **The addition of either azathioprine enable the oral steroid dose to be reduced more rapidly.**

1. **PEMPHIGUS VULGARIS**
2. **BULLOUS PEMPFIGOID**
3. **CHRONIC BULLOUS DISEASE
OF CHILDHOOD**
4. **PARANEOPLASTIC PEMPFIGUS**



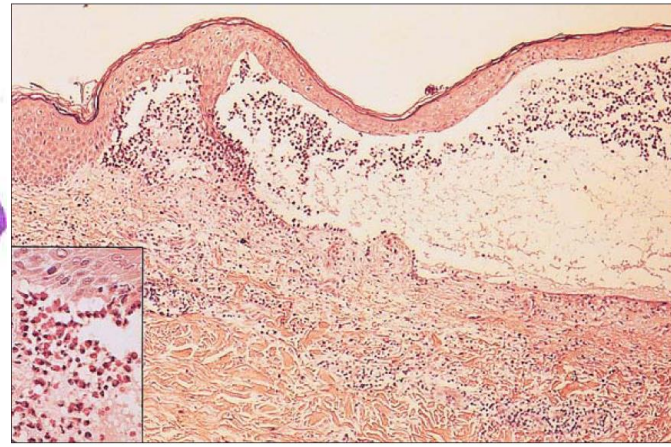
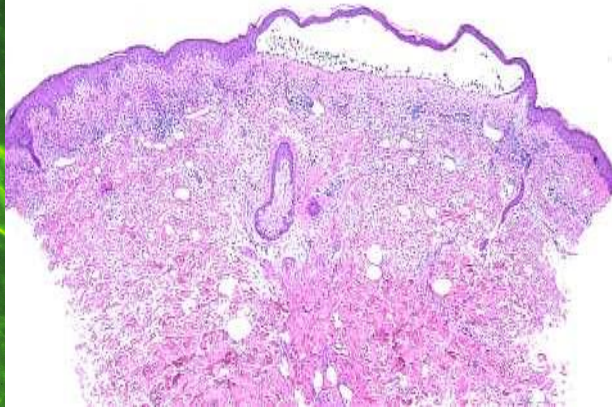
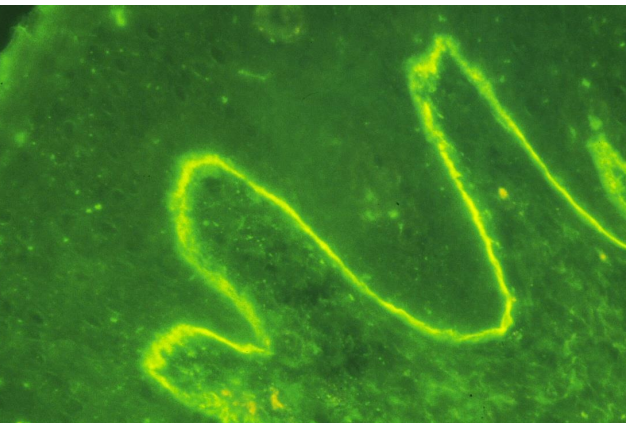
CLINICAL FEATURES

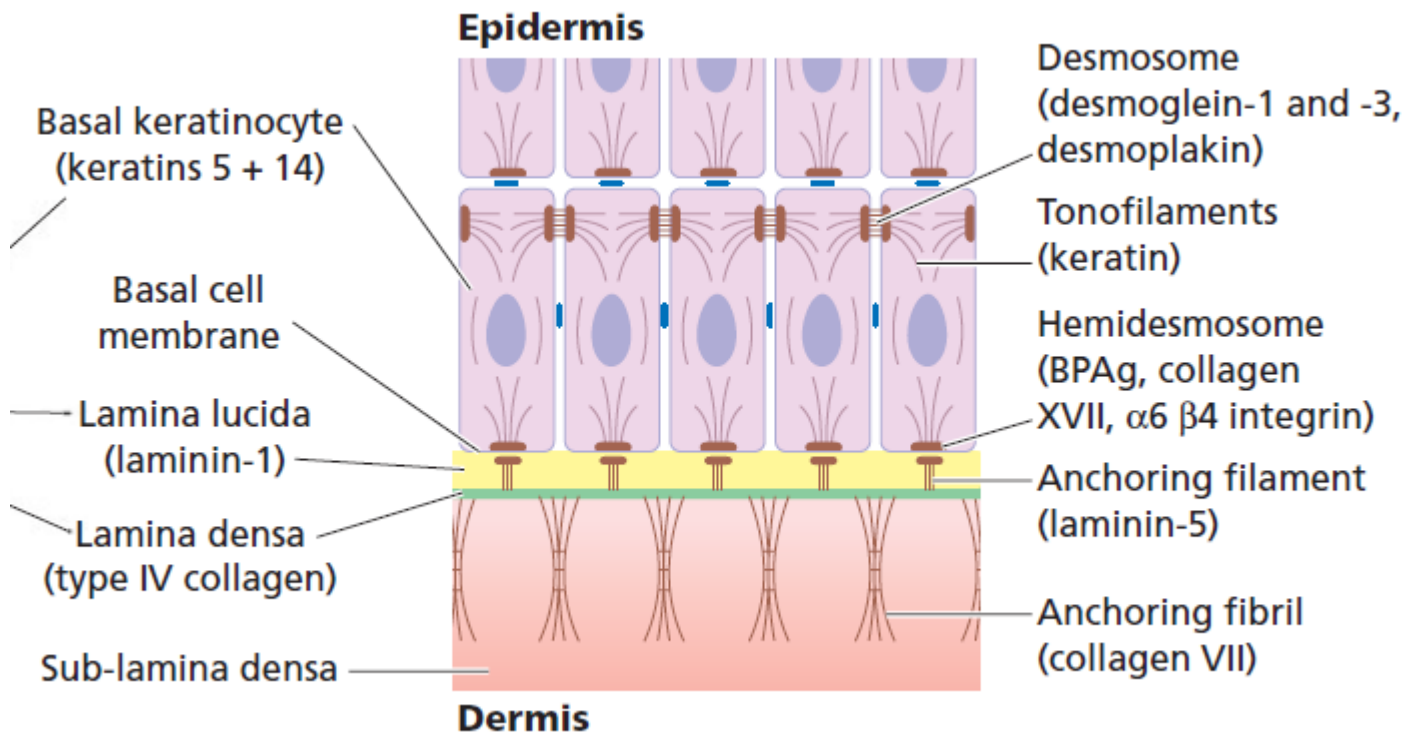
- **Circular clusters of large blisters like the type seen in pemphigoid (cluster of jewels)**
- **It involves the perioral area, lower trunk, inner thighs and genitalia**
- **Blistering may spread all over the body**

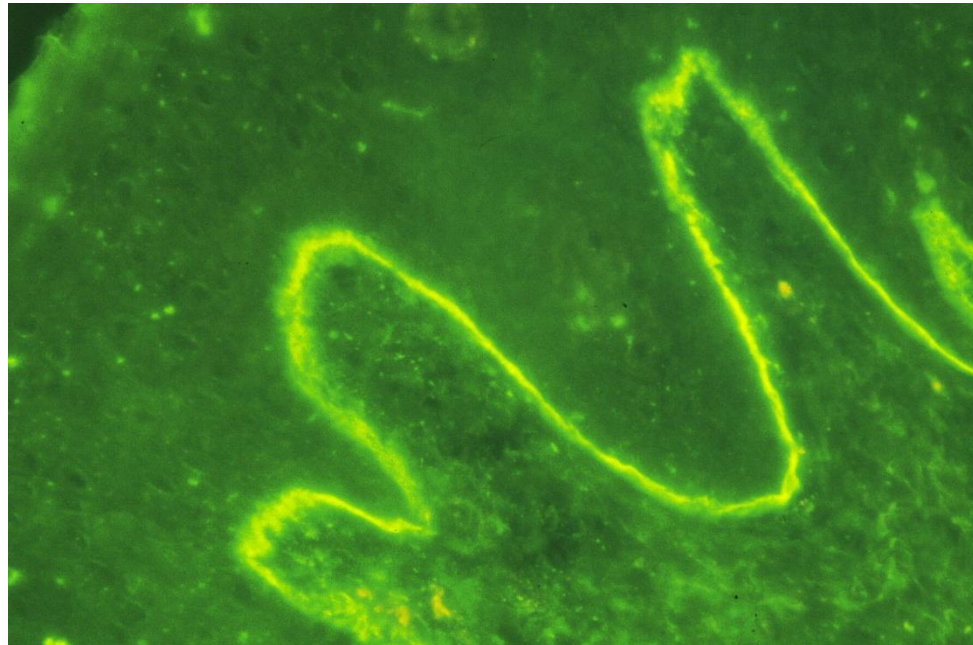
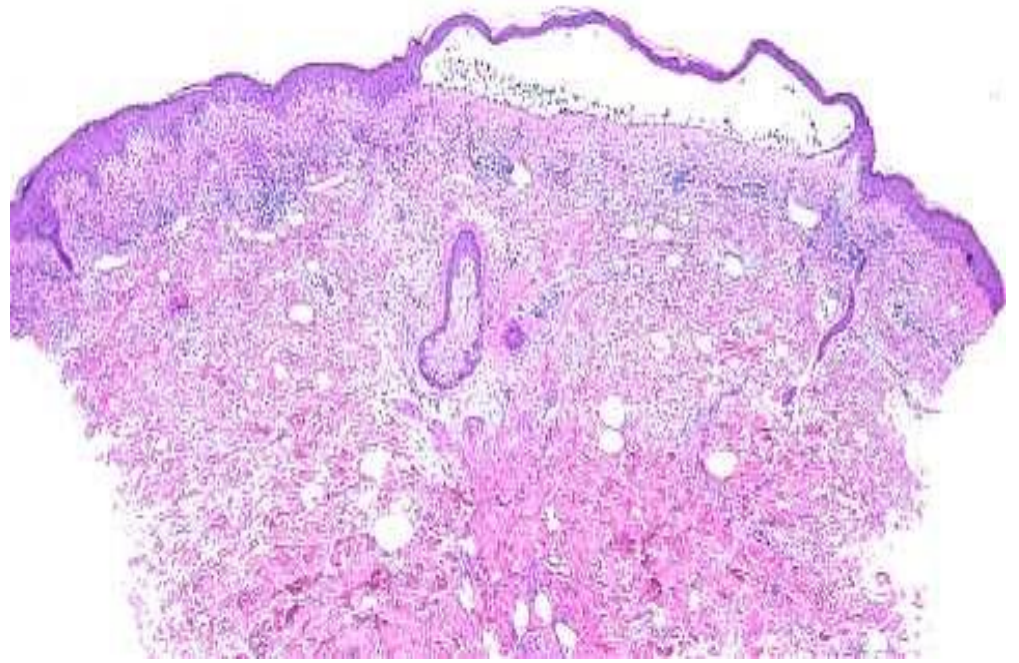


INVESTIGATION

- **Skin Biopsy** will show subepidermal splits
- **Direct IF** reveals **IgA** along the BM of the epidermis in a **linear** pattern







TREATMENTS

- **Oral dapsone 50-200mg daily (Ad/E)**
- **Sulphonamides and immunosuppressants**
- **Erythromycine**
- **Flucloxacillin : 7 cases reported from
KKUH**