



## Derma Team 436

# Blistering Diseases

### Course 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

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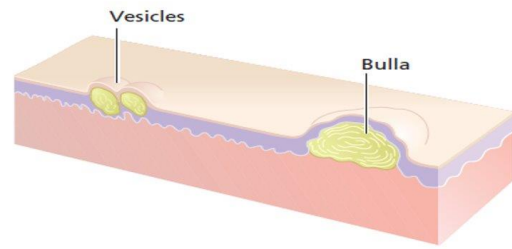
Before you start. [CHECK THE EDITING FILE](#)

**Sources:** doctor's slides and notes

[ Color index: **Important** | 435 notes | gold | doctor notes | Extra ]

## ❖ Definition:

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



## ❖ CLASSIFICATION OF VESICULOBULLOUS DISEASES:

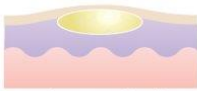
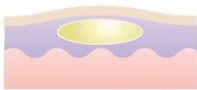
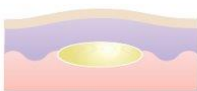
### DISEASES:

1. **INTRA EPIDERMAL BLISTERS:** The lesion is formed within the epidermis:
  - **PEMPHIGUS VULGARIS,**
  - **PARANEOPLASTIC PEMPHIGUS.**
2. **SUB EPIDERMAL BLISTERS:** Lesions formed between the epidermis and the dermis:
  - **BULLOUS PEMPHIGOID,**
  - **CHRONIC BULLOUS DISEASE OF CHILDHOOD.**

-Location of bullae is identified by skin biopsy

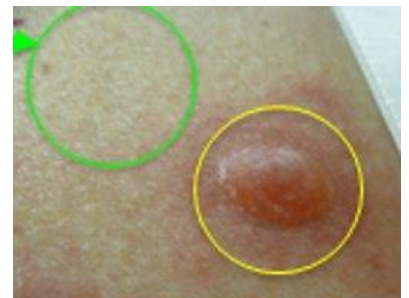
ممکن يعطيك بالاختبار وحدة من الامراض الي يمينا ويسألك بأي ليفل مثال:

bullous pemphigoid ? **Subepidermal**

Location of bullae	Diseases
 <p>Subcorneal bulla</p>	Bullous impetigo Miliaria crystallina Staphylococcal scalded skin syndrome
 <p>Intra-epidermal bulla</p>	Acute eczema Viral vesicles Pemphigus Miliaria rubra Incontinentia pigmenti
 <p>Subepidermal bulla</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

## ❖ 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.



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

-First biopsy on the lesion to know the level of separation

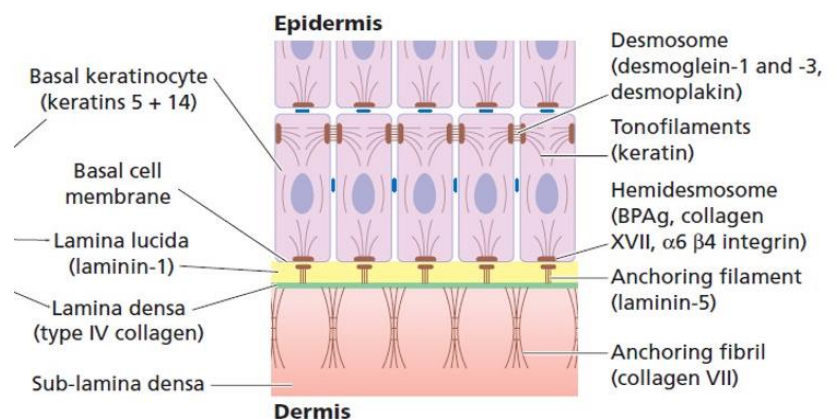
-Second biopsy on the intact skin to do direct immunofluorescence

## ❖ Pemphigus sub-clinical variants:

there are four sub-clinical variants to Pemphigus: **Vulgaris** is the most common Pemphigus variant, and the form usually responsible for oral lesions. other variants include: **Follicularis**, **vegetans**, **erythematosus**.

## ❖ Pemphigus Vulgaris:

- Pemphigus is a group characterized by blistering of the skin and mucous membranes.
- Auto-antibodies against DESMOSOMES in epidermis and mucosal surface.  
Antibodies against desmoglein 3 (Dsg3) and later desmoglein 1 (Dsg1).

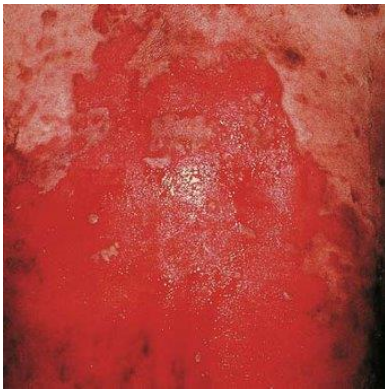


different disease depends on which Protein (list on the right) is attacked by autoantibodies

## ❖ Clinical Features:

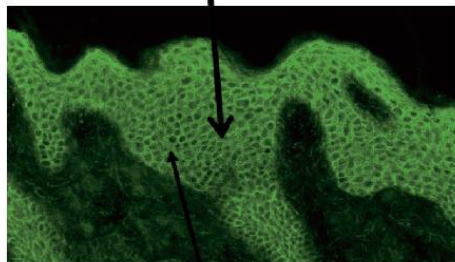
- Begins with erosions on mucous membrane then other skin areas.
- Pemphigus usually starts in the oral mucosa, so pts would go to dentist and they start them on antifungal treatment thinking that this is an infection, but they won't benefit.
- Any mucosal membrane not only the mouth such as anal, vaginal
- **Very painful.**
- **+ve Nikolsky's sign.**
- Age: middle-age 40-60 years.
- Secondary infection and disturbance of fluid and electrolyte balance are common complications.

Peeling and erosion of the skin



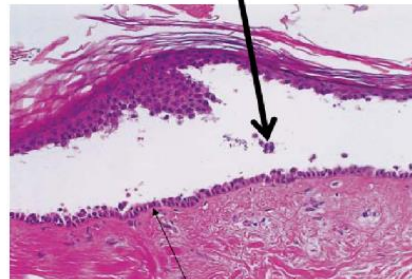
### Pathology and immunopathology:

#### Immunofluorescence IgG and C3



Fish net appearance

#### Acantholysis



Tombstone appearance

#### ❖ Treatment:

- High dose systemic steroids 60-100 mg of prednisolone.
- Immunosuppressive agents 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:
  - IV86% free of disease after 3 y
2. IVIG (intravenous immunoglobulin)

### ❖ Drug-induced Pemphigus Vulgaris:

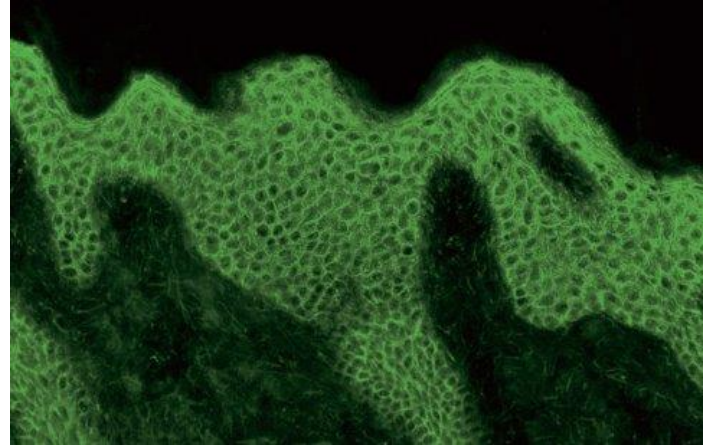
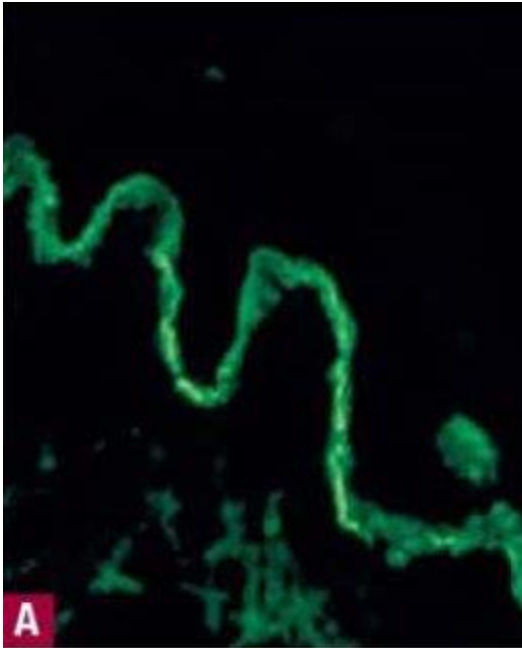
- Drugs can induce PV.
- Drugs reported most significantly in association with PV are;
  1. Penicillamine.
  2. Captopril.
  3. Antiepileptic: phenytoin and carbamazepine.

### ❖ 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.
- Important: It's associated with many malignancies (lymphoma is the main one)
- Important: desmoplakin is the targeted protein by autoantibody in paraneoplastic pemphigus



Paraneoplastic pemphigus shows both pattern of pemphigoid (IgG in the basement membrane) and pemphigus (IgG in the epidermis) in immunofluorescent.



### ❖ 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 patients.
- Large tense blisters on upper arms and thighs.
- Eczematous base.
- Itch rather than pain.
- Oral lesions are less frequent than pemphigus.

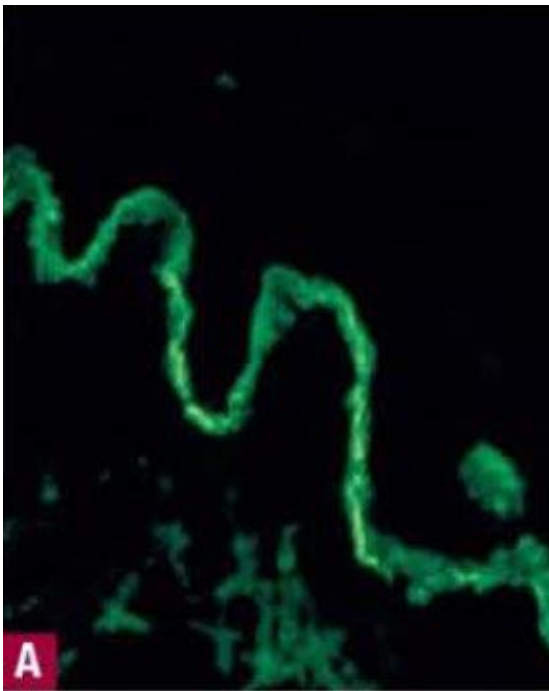
Pts usually present with tense bullous (not ruptured yet)



### ❖ Pathology and immunopathology:

- 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.

IgG in the basement membrane



❖ **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 enables the oral steroid dose to be reduced more rapidly.

<b>Pemphigus Vulgaris</b>	<b>Bullous Pemphigoid</b>
Very painful	Very itchy
More mucosal involvement	More skin involvement
+ve Nikolsky's sign	-ve Nikolsky's sign

## ❖ CHRONIC BULLOUS DISEASE OF CHILDHOOD:

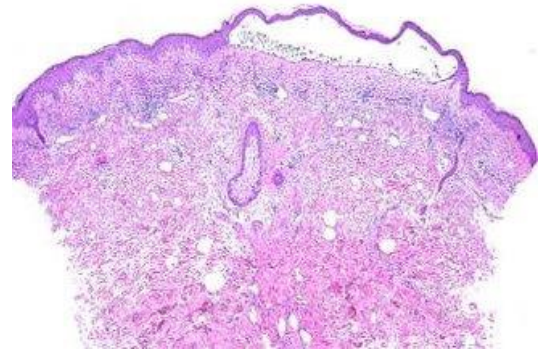
### ❖ Clinical Features:

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



### ❖ Investigations:

- Skin Biopsy will show **subepidermal splits**.
- Direct immunofluorescence reveals **IgA** along the basement membrane of the epidermis in a **linear** pattern.



### ❖ Treatment:

- Oral dapsone 50-200mg daily (Ad/E) .  
Dapsone is the drug of choice, act as anti-neutrophilic (anti-inflammatory)
- Sulphonamides and immunosuppressants.
- Erythromycin
- Flucloxacillin: 7 cases reported from KKHU.

