Vesiculobullous Diseases

This group of lesions are immune mediated, characterized by the eruption of vesicles and bullae affecting the oral mucosa and skin. These lesions are caused by the production of autoantibodies by the body directed against various constituents that hold epithelial cells together, or that bind the epithelial surface to the underlying connective tissue. The resultant damage produced by the interaction of these autoantibodies with the host tissue is seen clinically as a disease process termed as immune-vesiculobullous diseases. The major vesiculobullous disease affecting oral mucosa are:

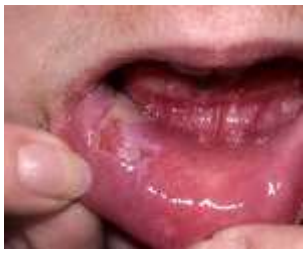
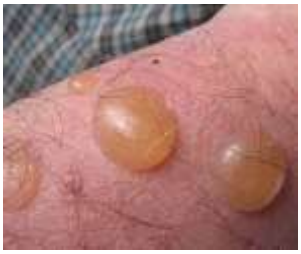
Pemphigus Vulgaris (PV):

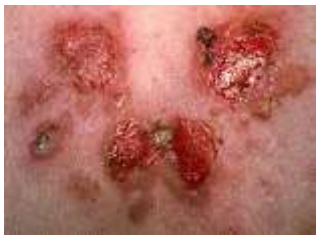
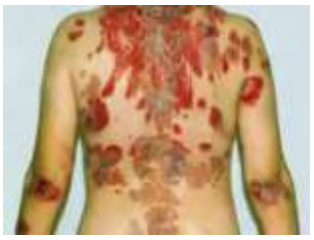
Is the most common among this group. It is a chronic vesiculobullous disease of the skin and oral mucosa. It is a serious condition because if untreated, it often results in patient's death. Furthermore, the oral lesions are often the first sign of the disease.

In this disease, there is epithelial desquamation due to autoantibodies that attack the desmosomes of the intercellular cohesive system, as a result loss of adhesion occurs between the cells located in the zone above die basal cell layer and leads to suprabasilar bullous formation. Destruction of the adhesive factors of suprabasilar spinous cells referred to as acantholysis.

Clinically:

PV affects patients in 40-60 years old. The initial manifestations involve the oral mucosa. Patients usually complain from oral soreness, and examination showed superficial, ragged erosions and ulcerations haphazardly distributed on the oral mucosa. The lesions affect any oral mucosa location, although the palate, labial mucosa, ventral tongue and gingivae are often involved. Vesicles and bullae rarely seen by the clinician because of early rupture of the thin, friable roof of the blisters.

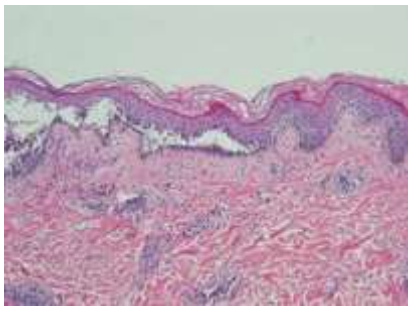
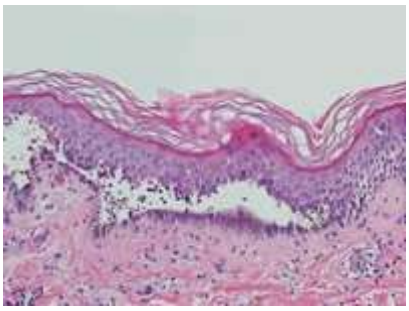



The skin lesions appear as flaccid bullae, that rupture quickly, usually within hours to a few days, leaving an erythematous denuded surface.

Without proper treatment, the oral and cutaneous lesions tend to persist and progressively involve more surface area. A characteristic feature of PV is that the bulla can be induced on normal-appearing skin if firm lateral pressure is exerted. This is called a positive Nikolsky sign.

Histopathologic features:

Microscopic appearance of PV exhibits epithelium of normal thickness. Mild inflammation is found in the underlying CT. The basal cell layer is intact, but the cells of the suprabasilar layer separated (acantholysis) and float freely in a fluid-like intraepithelial space. The cells lose their polygonal shape and become rounded with less cytoplasm visible around the nucleus. These cells named as Tzanck cells and are characteristic finding in the intraepithelial split in PV. Immunofluorescence is a valuable aid in the diagnosis of PV, the test reveals the presence of IgG AB in a fishnet pattern due to its attachment to the periphery of the cells in the spinous layers of the epithelium.

Treatment:

Treatment is aggressive and requires a prolonged high dose of corticosteroid (prednisolone) in a range of 150-360mg daily for 6-10 weeks. Then the dose is reduced and it is usually used in combination with other non-steroid immunosuppressant drug such azathioprine. Gradual reduction of corticosteroid is required after cure to reduce the risk complication of this therapy.

Before the development of corticosteroids, 60-80% of patients die as a result of infection, protein loss and electrolytic imbalance from the extensive skin vesiculobullous rupture and ulcerations.

Classification of Pemphigus

1. Superficial pemphigus

a. Foliaceous pemphigus

- Endemic

b. Erythematous or seborreic pemphigus

- Isolated

- Associated to systemic lupus erythematosus

2. Deep Pemphigus

a. Pemphigus vulgaris

b. Pemphigus vegetans

c. Paraneoplastic pemphigus

Mucous Membrane pemphigoid(MMP): Cicatritial Pemphigoid

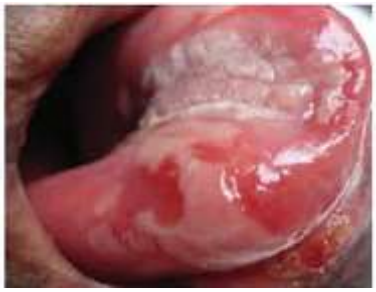
A desquamating condition of the mucous membrane in which the autoimmune reaction occurs at a level of the basement membrane and commonly affects the gingival before extending to other mucosal locations. The patient suffers from involvement of the mucous membrane of the eyes that result in scar formation (cicatrix) leading to a (symblepharon formation) of the eyes, and accordingly, the condition is termed by the dermatologists as cicatritial pemphigoid associated with nasal mucosal lesions in addition to oral lesions. Occasionally, patient develops skin lesions mostly on head and neck areas.

In any involved area, there is atrophy of epithelium followed by separation from CT at the level of B.M. If the disease involves the oral mucosa only it is termed as mucous membrane pemphigoid, When the disease restricted to the gingiva it is called desqumative gingivitis.

Clinical features:

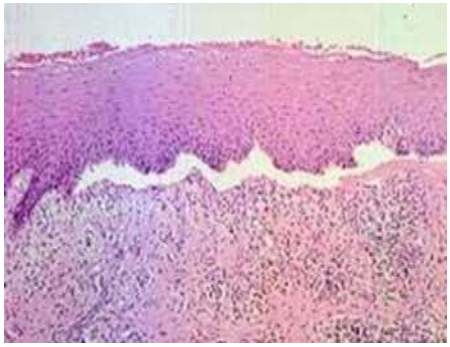
Cicatritial pemphigoid usually affects adults of an average age 50-60 years, females are affected most commonly than males. Oral lesions are seen in most patients, but other sites, such as conjunctival, nasal, esophageal, laryngeal as well as skin may be involved.

The oral lesions begin as vesicles or bullae that may be identified clinically in contrast to pemphigus. The explanation to this difference is that pemphigoid blisters forms in a subepithelial location, producing a thicker, stronger roof than intraepithelial, acantholytic pemphigus blisters. Eventually, vesicles rupture, leaving large superficial. The ulcerations are usually painful and persist for some weeks to months if untreated.



Histologic features:

The antibodies directed towards the B.M. and cause separation or splitting of epithelium from underlying C.T. to form subepithelial vesicle or bulla, there is no evidence of acantholysis, also there is chronic inflammatory cells infiltration in the CT.



Diagnosis:

The major goal in diagnosis of MMP is to differentiate it from PV and this depend on:

1- History and clinical features

2- Histopathology

3- Direct immunofluorescence study shows a continuous linear band of IgG and C3 localized at the basement membrane zone.

Treatment:

Systemic immunosuppressive therapy. Prednisolone dialy dose combined with azathioprine.

Erythema Multiforme (EM):

It is a blistering and ulcerative mucocutaneous condition of uncertain etiology. It is probably an immunmediated process. It presented with wide spectrum of manifestations and varying degree of severity.

Common precipitating factors are:

1- Infections such as herpes simplex.

2- Drugs: most commonly sulfas, penicillin, dilantin, barbiturate and salicylates.

3- Gastro-intestinal conditions: as Crohn's disease and ulcerative colitis

4- Other conditions: as malignancies, radiation therapy and vaccination

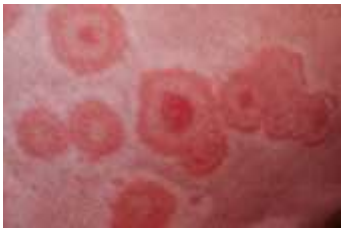
Clinical features:

EM usually has an acute onset with wide spectrum of clinical disease. On the mild end of the spectrum, ulcerations affecting the oral mucosa. In the severe form, diffuse sloughing and ulceration of the entire skin and mucosal surfaces may be seen and the condition called (toxic epidermal necrolysis).

EM is noted most frequently in young adults and children unlike PV and MMP. There is male sex predilection.

Oral lesions, variable in appearance, almost all are painful. Any area may be involved, lesions tend to show diffuse distribution, including the lips, tongue, floor of the mouth, labial and buccal mucosa. The lips are frequently grossly swollen, split, crusted and bleeding. There is also wide spread of fibrin-covered erosions, erythema and ulcerations in the mouth. Lesions tend to be symmetrical and there are periods of remission.

Skin lesions: Typically, early lesions develop on the extremities and are flat, round, they presented in a unique picture, consisting of a central area of vesiculation, surrounded by concentric circular erythematous rings resembling a target or bull's eye (target lesion).

Erythema Multiforme Major: A more severe form of the disease, known as Stevens-Johnson syndrome, is usually triggered by a drug rather than infection. The diagnosis of this condition depends on the involvement of ocular or genital mucosae in addition to oral and skin lesions. With severe ocular involvement, scarring (symblepharon formation) may occur similar to cicatritial pemphigoid.

Histopathologic features:

Reveals a characteristic but not pathognomonic. Subepithelial or intraepithelial vesicle may be seen. A mixed inflammatory cells infiltration in the C.T arranged in perivascular orientation,

Diagnosis: Because the immunopathologic features are nonspecific, the diagnosis is based on the

-clinical presentation and the exclusion of other vesiculobullous diseases.

Treatment:

1- Systemic corticosteroids administration.

2- If the patient is dehydrated as a result of inability to eat because of pain, intravenous rehydration, with topical anesthetic agent to reduce discomfort.

Epidermolysis Bullosa (EB):

Is a general term that describes a heterogenous group one **acquired** and several **genetic (inherited)** mucocutaneous varieties, each has a specific defect in the attachment mechanisms in the epithelial cells, either to each other, or to the underlying connective tissue, that are basically characterized by the formation of vesicles and bulla at the site of minor trauma.

The acquired is termed **Epidermolysis aquisita**. It is unrelated to other types and precipitated by exposure to specific drugs. In this type, IgG antibodies directed against type VII collagen of the anchoring fibrils.

The genetic types are (Simplex, Junctional & Dystrophic). These types range from autosomal dominant to autosomal recessive in origin. In these types circulating antibodies are not evident. But there are genetic defects in basal cells, hemidesmosomes or anchoring C.T filaments depending on the disease subtype.

Clinical Features:

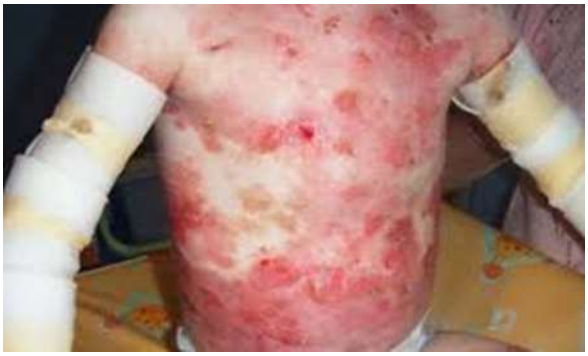
- Common features to all subtypes of EB is bulla formation from minor trauma usually over areas of stress such as the elbows or knees.

- In hereditary forms the onset of disease is during infancy or early childhood

- In acquired type, the onset during adulthood,

- Blisters may be widely spread and severe and may result in scarring and atrophy. Nails may be dystrophic in some forms of this disease.

- Oral lesions are common and severe in inherited types and uncommon in the acquired type. The oral lesions include bulla that heal with scar formation, a constricted oral orifice resulting from scar contracture and hypoplastic teeth.



Treatment & Prognosis:

Prognosis depend on the subtype of ED, ranging from life threatening (in junctional subtype) to debilitating in the other forms.

Therapy includes avoidance of trauma, supportive measures and chemotherapeutic agents.