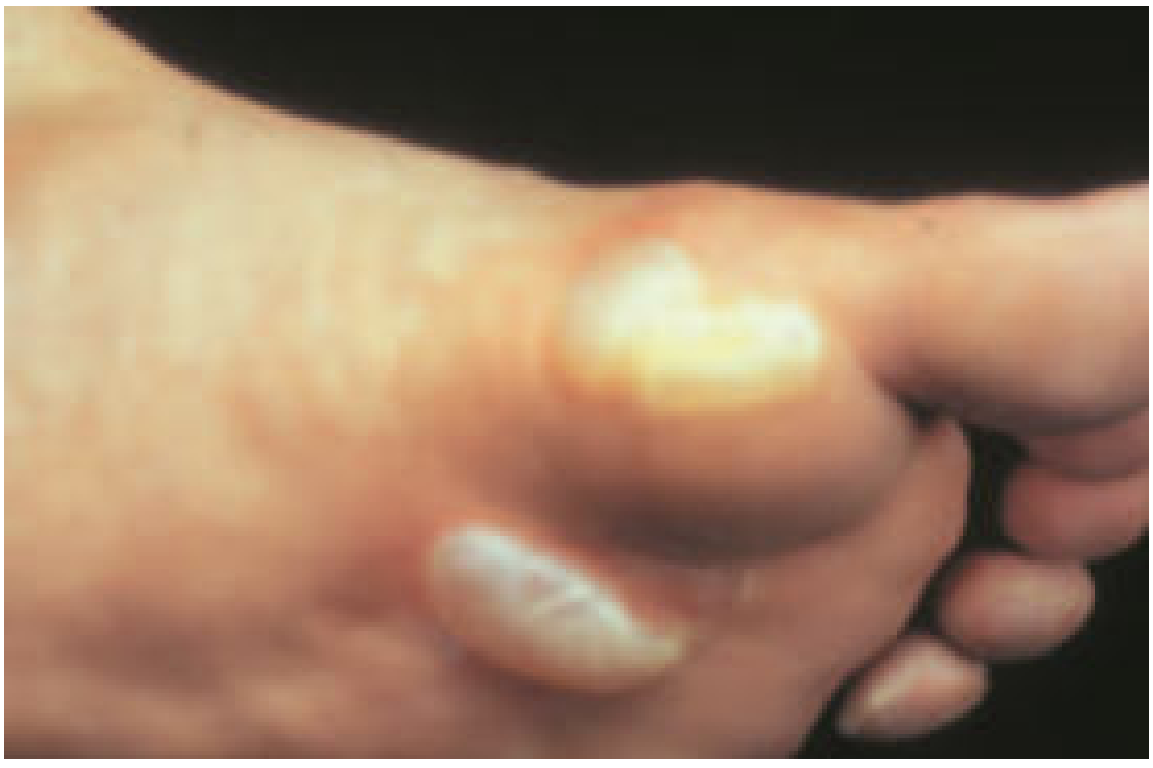
Immunobullous disorders

- Blister: fluid filled cavity formed within or beneath the epidermis

- Vesicle: blister < 0.5cm
- Bullae: >0.5cm



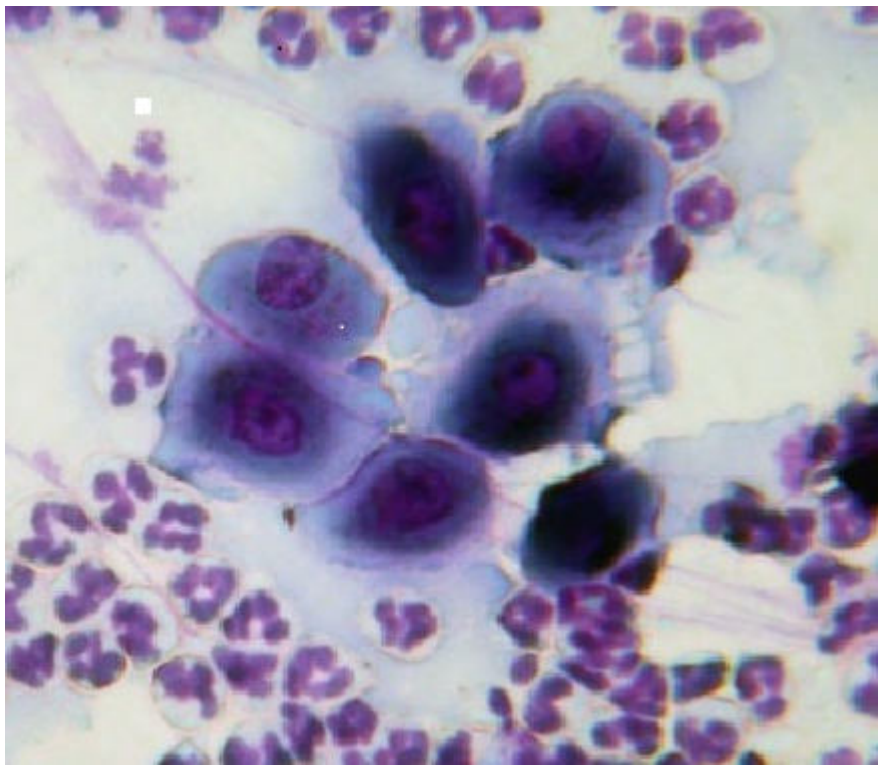
Mechanism of blister formation:

- 1. spongiosis: extracellular fluid in epidermis

  Eg eczema, miliaria crystallina
- 2. Acantholysis: loss of keratinocyte cell to cell contact…….. Rounded keratinocytes…… condensed cytoplasm…large nuclei…. Peripheral condensation of chromatin and prominent nucleoli

  Eg: pemphigus, hailey hailey ds, darriers dis

Tzanck smear



- Reticular degeneration – ballooning degeneration (intracellular oedema)
  - eg: viral infections
- Cytolysis- friction and heat

- Basement membrane zone destruction –
- primary structural deficiency
- immunologically mediated damage- BP, linear Ig A disease, DH

TABLE 9-1. DISEASES AND MECHANISMS OF BLISTER FORMATION

Disease	Blister Formation Mechanisms
Spongiosis	Eczematous dermatitis
	Miliaria
	Pemphigus (early)
	Transient acantholytic dermatosis (one pattern)
Acantholysis	Pemphigus
	Transient acantholytic dermatosis (some patterns)
	Hailey–Hailey disease
	Darier's disease
	Irritant dermatitis (some)
Reticular degeneration	Viral infections
	Eczematous dermatitis (late stage)
Cytolysis	Epidermolysis bullosa simplex
	Epidermolytic hyperkeratosis
	Friction blister
	Erythema multiforme (in part)
	Irritant dermatitis (some)
Basement membrane zone destruction	Bullous pemphigoid
	Cicatricial pemphigoid
	Linear IgA dermatosis
	Dermatitis herpetiformis
	Epidermolysis bullosa acquisita
	Epidermolysis bullosa letalis
	Epidermolysis bullosa dystrophica

Based upon plane of separation

- Intraepidermal-

  A. subcorneal- miliaria crystallina, SSSS, P. foliaceous, Bullous impetigo, SCPD

  B. Spinous- Eczema, Hailey Hailey, Miliaria Rubra

  C. Suprabasal- Pemphigus vulgaris, Paraneoplastic pemphigus, Darriers Disease

- Subepidermal:
  - Bullous Pemphigoid
  - DH
  - Linear Ig A disease
  - Porphyria cutanea tarda

Classification

Immune-mediated bullous disorders

Intraepithelial blistering group of disorders

Pemphigus and its variants

Subepidermal immune mediated disorders

Bullous pemphigoid
Mucous membrane pemphigoid
Linear IgA bullous dermatosis
Epidermolysis bullosa acquisita
Pemphigoid gestationis
Dermatitis herpetiformis

Bullous disorders without associated autoantibodies

Inherited

Epidermolysis bullosa

Metabolic

Porphyrias

Inflammatory

Erythema multiforme
~~Staphylococcal scalded skin syndrome~~
Grover's disease

Immunobullous disorders Introduction

- The immunobullous diseases are characterized by pathogenic autoantibodies directed at target antigens whose function is either cell-to-cell adhesion within the epidermis or adhesion of stratified squamous epithelium to dermis or mesenchyme.
- These diseases are often associated with significant morbidity and some can even cause mortality, if left untreated.

- Adhesion between keratinocytes: Desmosomes (transmembrane glycoproteins)

- 1. desmogleins- 1,2,3

  desmoglein 3 – in basal and suprabasal layers and mucosae
- 2. desmocollins

- Others: non glycosylated proteins
  - Plakoglobin; desmoplakin 1 and 2; plakophilin

Intraepidermal immunobullous disorders

Table 41.1 Types of pemphigus.

Pemphigus vulgaris
variant: pemphigus vegetans
Pemphigus foliaceus
variant: pemphigus herpetiformis
variant: pemphigus erythematosus
Induced pemphigus
Intercellular IgA dermatosis
Paraneoplastic pemphigus

Table 41.3 The intraepidermal immunobullous diseases: immunopathology and immunogenetics.

Disease	Direct IMF	Isotype	Target antigens	Antigens (kDa)	Epitopes	Location	Immunogenetics MHC class I and II
Pemphigus vulgaris/ pemphigus vegetans	Intercellular	IgG, (few IgM, IgA)	Desmoglein 3 Sometimes desmoglein 1 desmocollins	130	Amino-terminal of extracellular domain	Desmosome	DRB1*0402 DRB1*14
Pemphigus foliaceus	Intercellular	IgG	Desmoglein 1 Sometimes desmocollins	160	Amino-terminal of extracellular domain	Desmosome	HLA-DRB1*14
Endemic pemphigus foliaceus	Intercellular	IgG	Desmoglein 1 Sometimes desmocollins	160	Amino-terminal of extracellular domain	Desmosome	Several susceptibility alleles, all with same amino acid sequence in *DRB-1* gene DRB1*0102 DRB1*0404, *1402 or *1406
Paraneoplastic pemphigus	Intercellular and subepidermal	IgG	Plakins (desmoplakin, envoplakin BP230, periplakin)		Various	Desmosomes, BMZ; stratified, simple and transitional epithelia	Unknown

BMZ, basement-membrane zone; HLA, human leukocyte antigen; IMF, immunofluorescence; MHC, major histocompatibility complex.

Table 41.2 The intraepidermal immunobullous diseases: clinical features.

Disease	Patients	Cutaneous distribution	Mucosal involvement	Lesions	Disease associations	Treatment	Prognosis
Pemphigus vulgaris	Middle age	Scalp, face, flexures, may be generalized	Always oropharynx, conjunctiva, genital	Flaccid blisters, erosions, flexural vegetations	Autoimmune disease, thymoma	Steroids, immunosuppressives, dapsone	Variable, may remit
Pemphigus vegetans	Middle age	Flexural	Oral	Vesicles, pustules, erosions, vegetating plaques		Steroids, immunosuppressives, dapsone	Variable, may remit
Pemphigus foliaceus	Middle age	Scalp, face, chest, upper back, rarely generalized 'seborrhoeic'	None	Scaly papules, crusted erosions, erythroderma		Steroids (topical, intralesional, systemic), immunosuppressives	Benign but chronic
Endemic pemphigus foliaceus	Children, young adults	Head, neck, generalized	Uncommon	Flaccid blisters, erosions, verrucous lesions, erythroderma		Steroids, immunosuppressives, antimalarials	Chronic mortality < 10%
Intercelluar IgA dermatosis	Adults children	Axillae, groins, face, scalp, proximal limbs	Uncommon	Flaccid pustules annular or circinate configuration	IgA monoclonal gammopathy	Dapsone	Chronic indolent
Paraneoplastic pemphigus	Adults, children	Upper body, palmo-plantar	Severe mucositis	Polymorphous, bullae, erosions, 'target lesions'	Lymphoprolife-rative disease, Castleman's, other malignancies	Tumour resection, steroids, immunosuppression	Very poor

Pemphigus vulgaris

- The term pemphigus stems from the Greek '*pemphix*' meaning blister or bubble.
- Pemphigus is a group of autoimmune blistering disease of skin & mucous membranes characterized by:
  - Histologically, intraepidermal blisters due to loss of cell-cell adhesion of keratinocytes.
  - Immunopathologically, the finding of *in vivo* bound & circulating IgG autoantibodies directed against the cell surface of the keratinocytes.

Pemphigus vulgaris

- All patients develop painful oral erosions. More than half of patients also have flaccid blisters and widespread cutaneous erosions.
  - Mucosa: painful erosions over buccal & palatine mucosa. Intact blisters are rare. Esophagus, conjunctiva, & nasal mucosa may develop these lesions.
  - Skin lesions: primary lesions are flaccid, thin walled easily ruptured blisters. Blisters are fragile and soon rupture to form painful erosions.
    - Erosions often become large and partially covered with crusts. Some lesions on healing leave hyperpigmentation but no scarring.

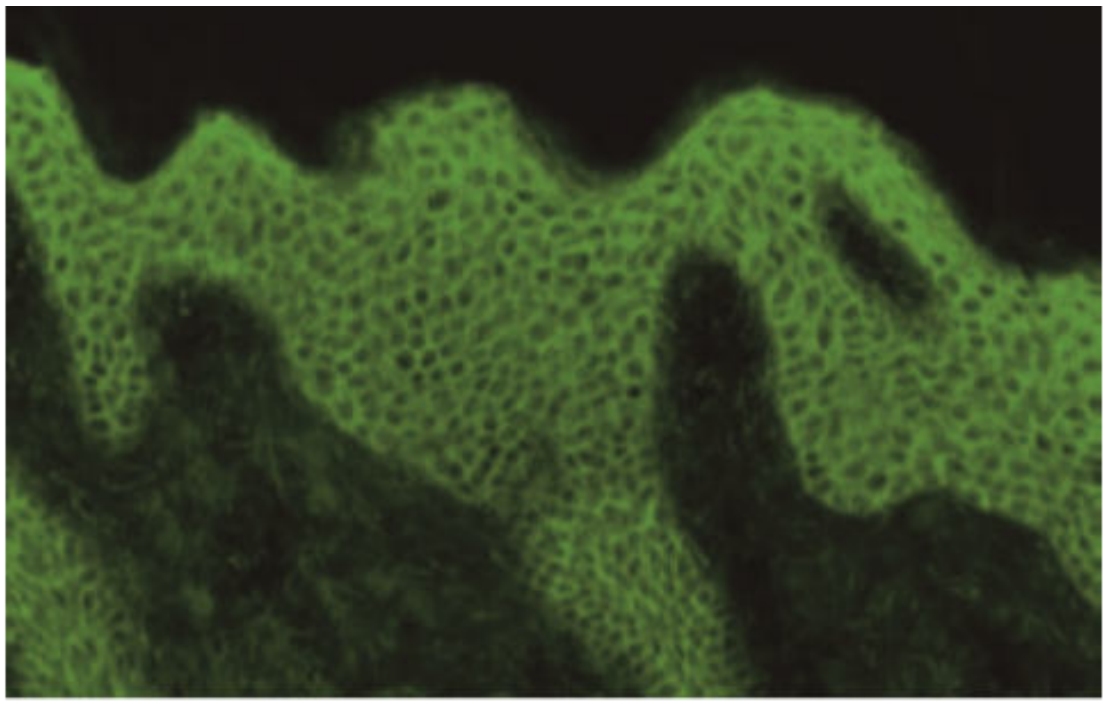


Fig. 41.2 Immunofluorescence showing intercellular IgG throughout the epidermis of a patient with pemphigus vulgaris.

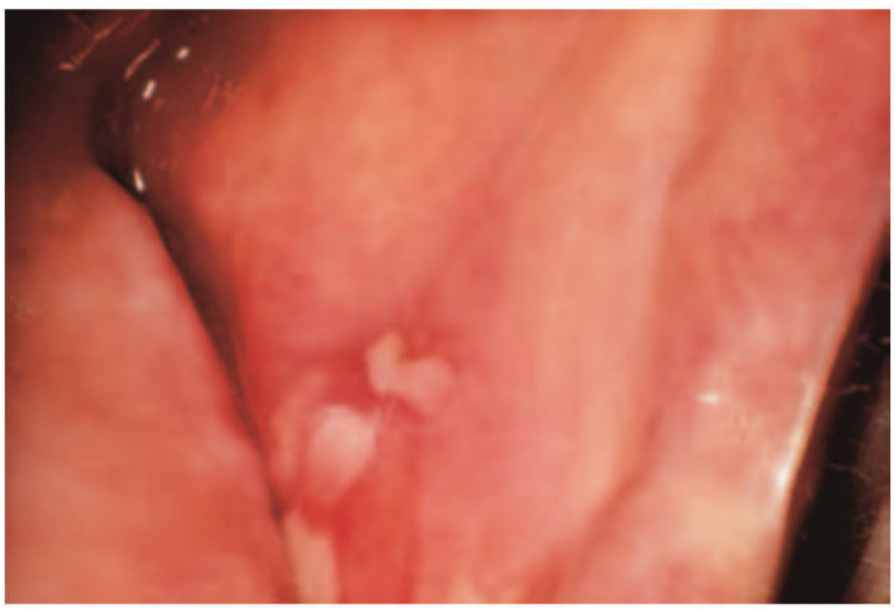


Fig. 41.3 Pemphigus vulgaris. Erosions in mouth. (Courtesy of Dr R.J. Pye, Addenbrooke's Hospital, Cambridge, UK.)

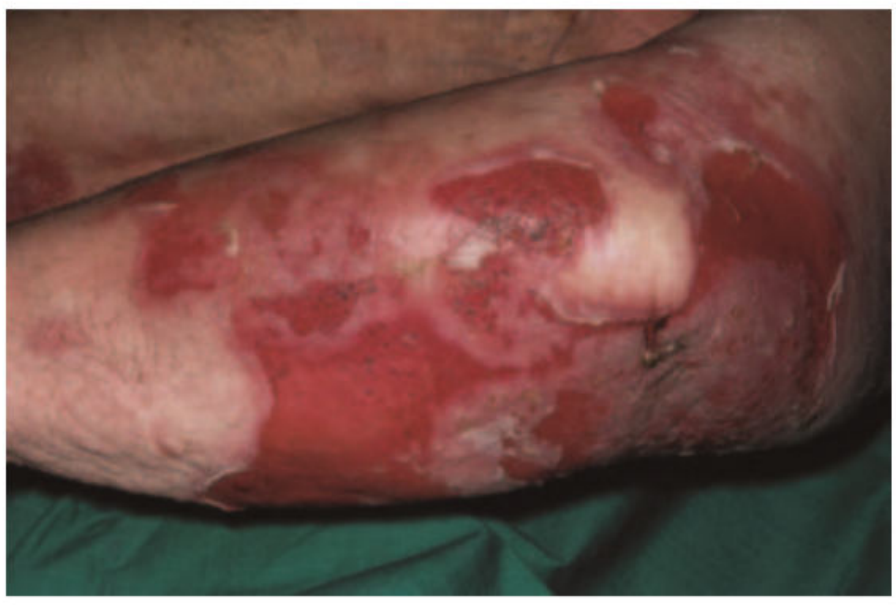
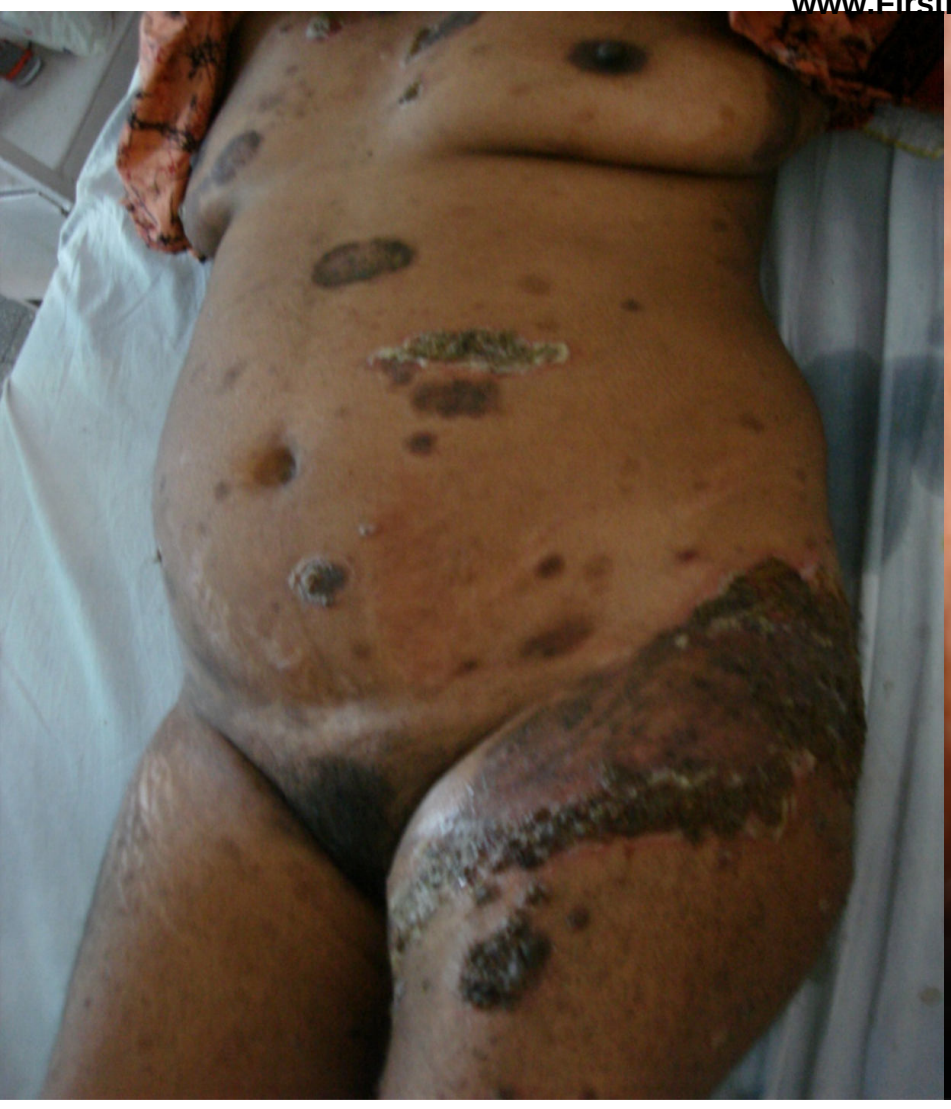
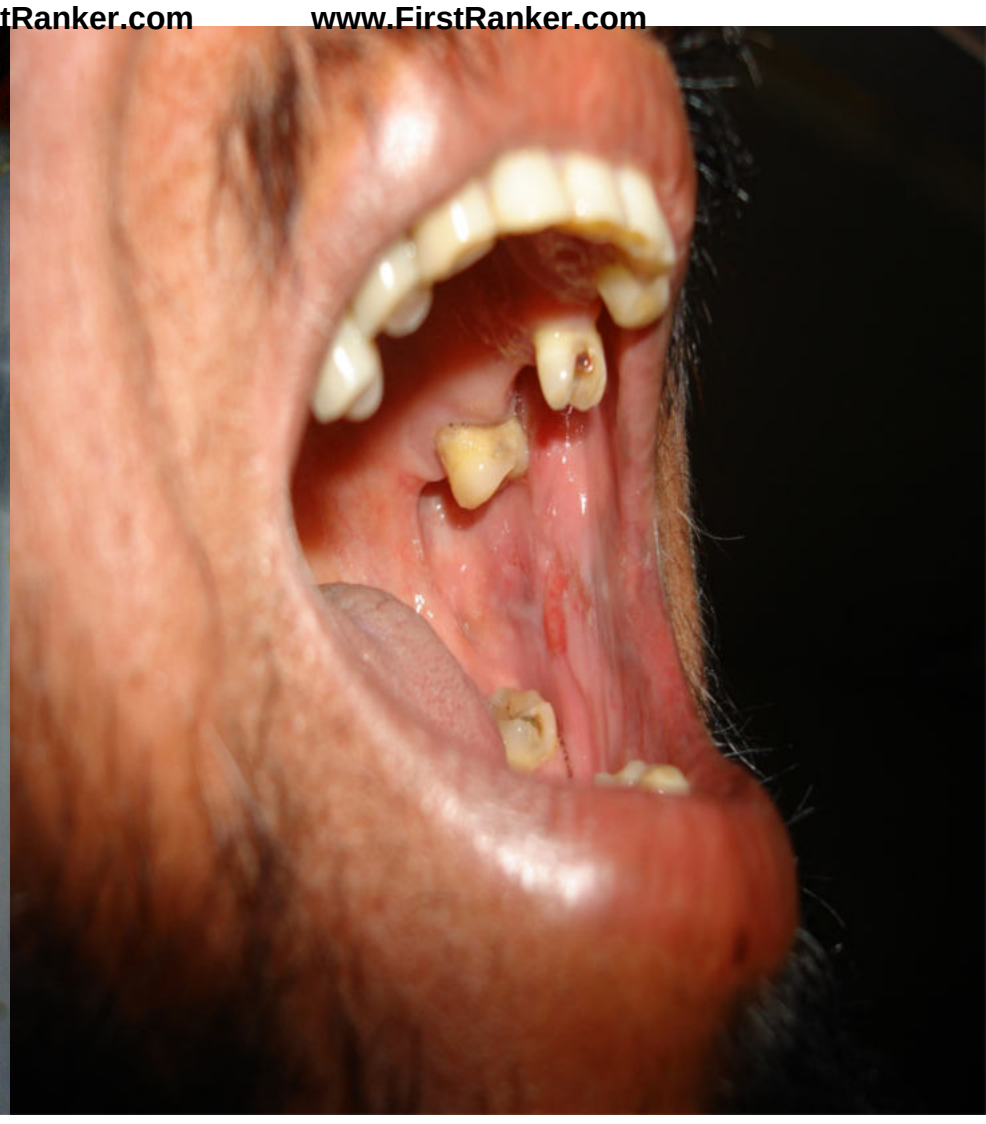


Fig. 41.5 Pemphigus vulgaris. Flaccid bullae and erosions on the forearm. (Courtesy of Dr R.J. Pye, Addenbrooke's Hospital, Cambridge, UK.)

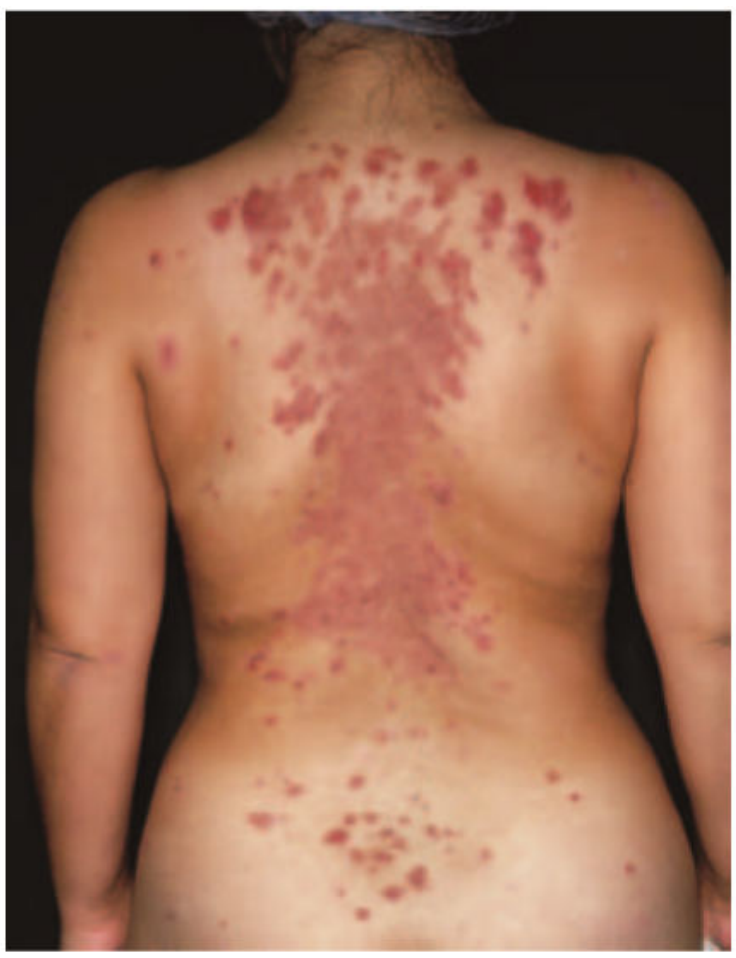


Skin lesions



Oral mucosal lesions

PEMPHIGUS VULGARIS



- Nikolsky sign : positive

- Tzanck smear: Acantholytic cells

Pemphigus vegetans

- Rare vegetative variant of pemphigus vulgaris.
- Flaccid blisters that become erosions and then form papillomatous projections especially in intertriginous areas and on scalp or face.
- Two subtypes:
  - Neumann type: severe
  - Hallopeau type: mild

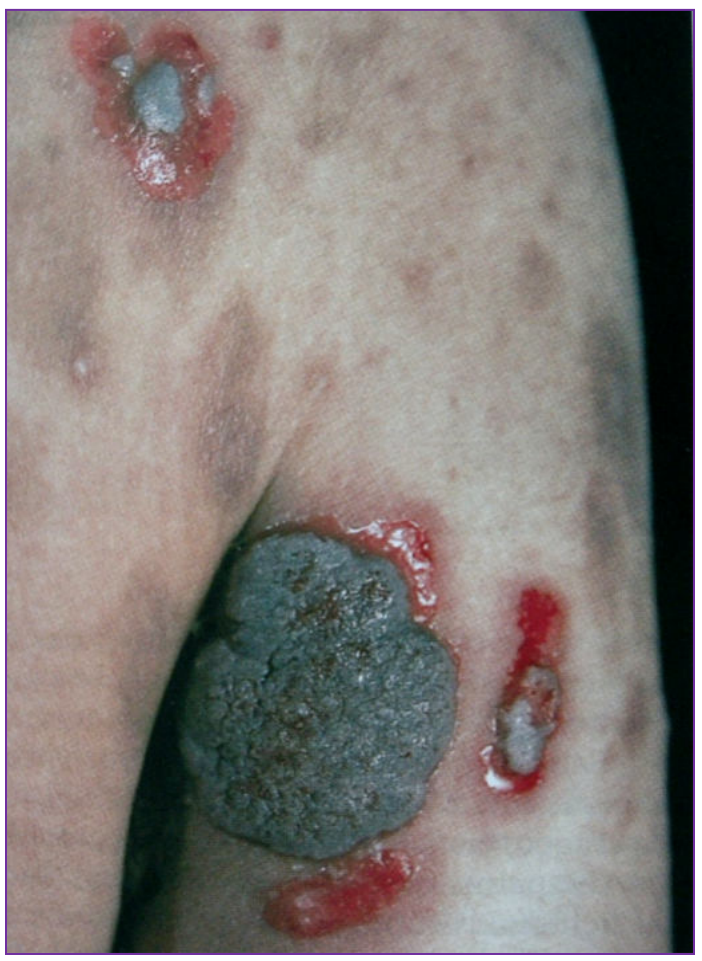
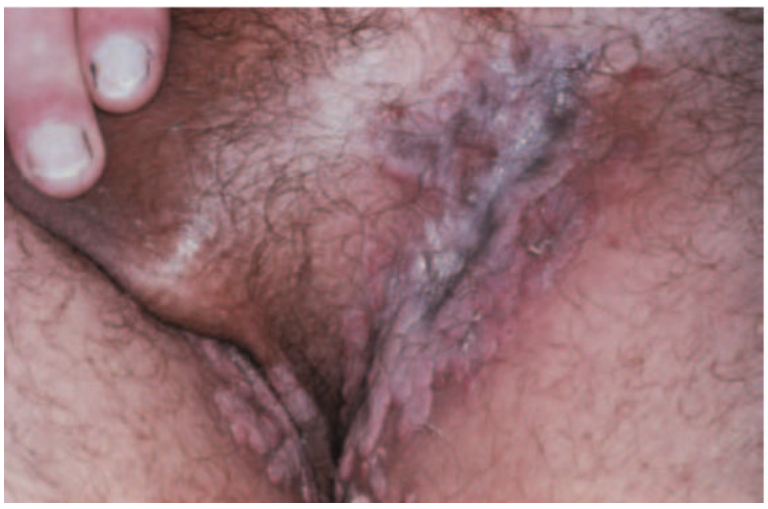


Figure: pemphigus vegetans. Extensive vegetating papillomatous lesions



Pemphigus foliaceus

- Patients develop scaly, crusted cutaneous erosions, often on an erythematous base.
  - Lesions are well demarcated and have a seborrhoeic distribution, i.e. they favor the face, scalp and upper trunk
- No clinically apparent mucosal involvement.
- Patients are not severely ill.
- Disease may remain localized for years or it may rapidly progress, in some cases to erythrodermic exfoliative dermatitis.

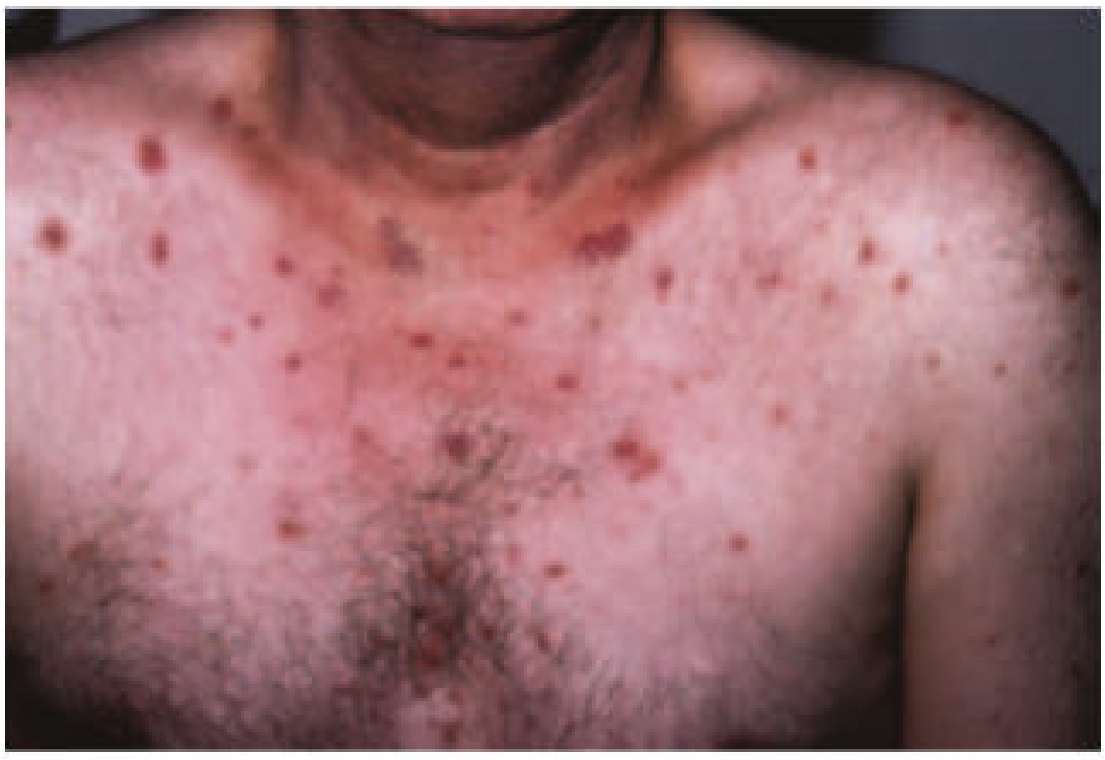


Fig. 41.7 Pemphigus foliaceus. Well-demarcated crusted lesions scattered over the chest.

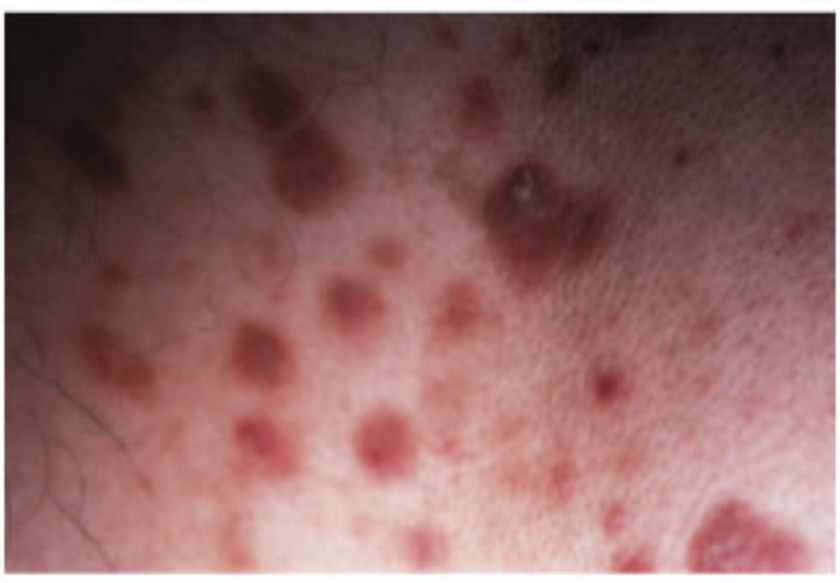
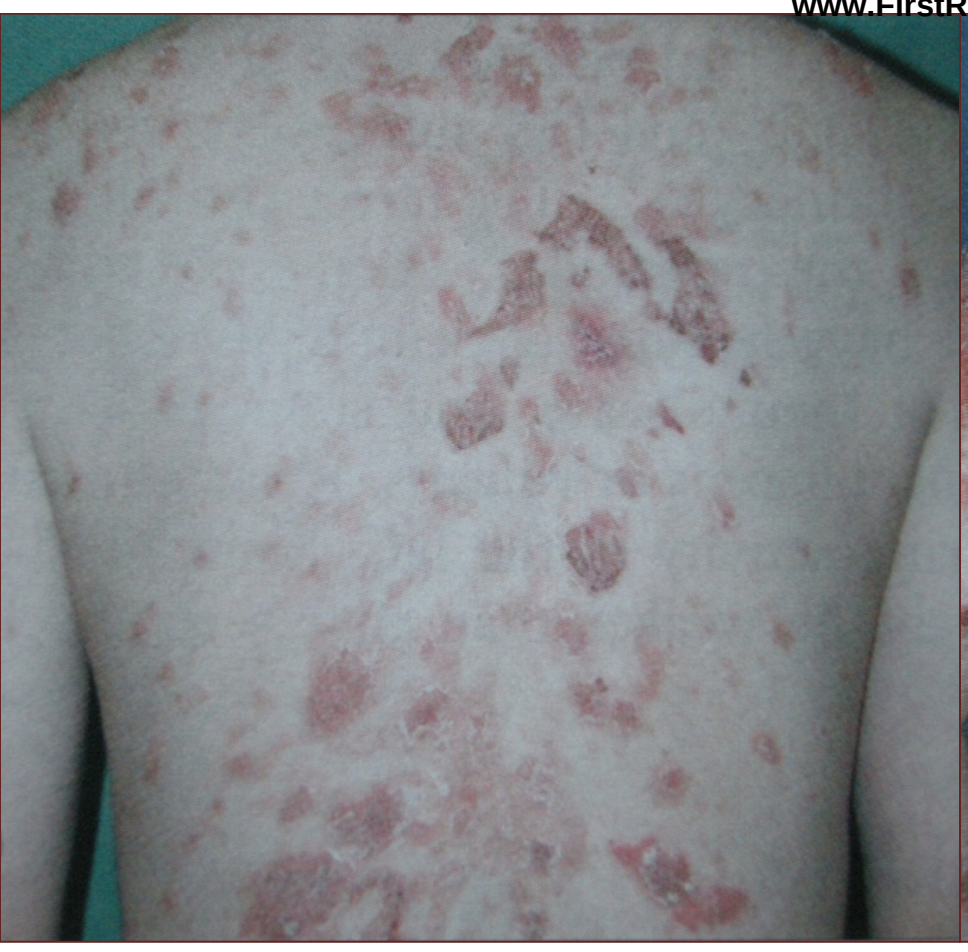
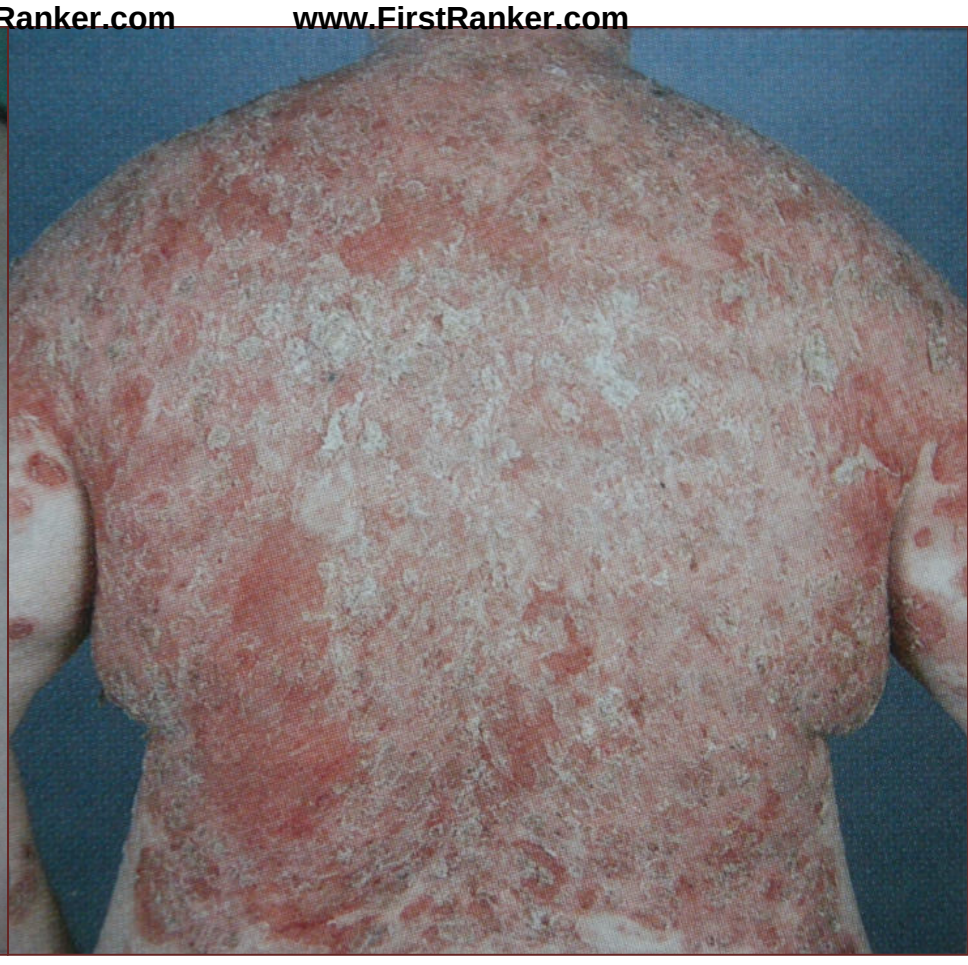


Fig. 41.8 Pemphigus foliaceus. Sharply demarcated areas of erythema, crusting and scaling with no obvious bullae.



Early disease: Scaly crusted erosions on the back



Progressive disease: Lesions have become confluent

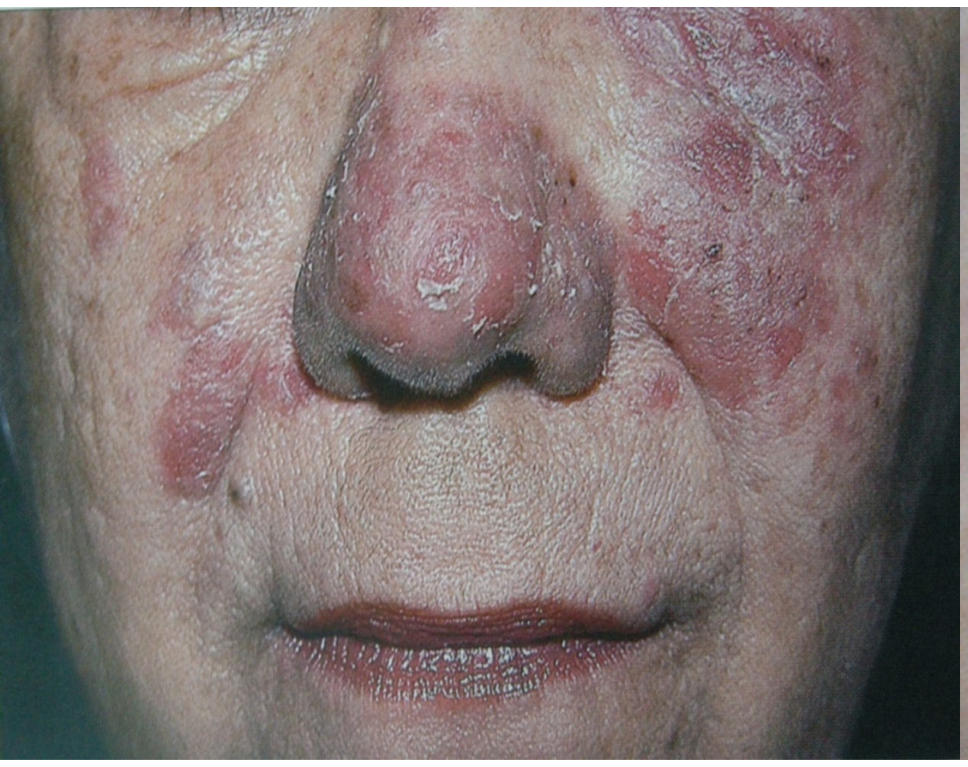
PEMPHIGUS FOLIACEUS

Pemphigus erythematosus (Senear -Usher Syndrome)

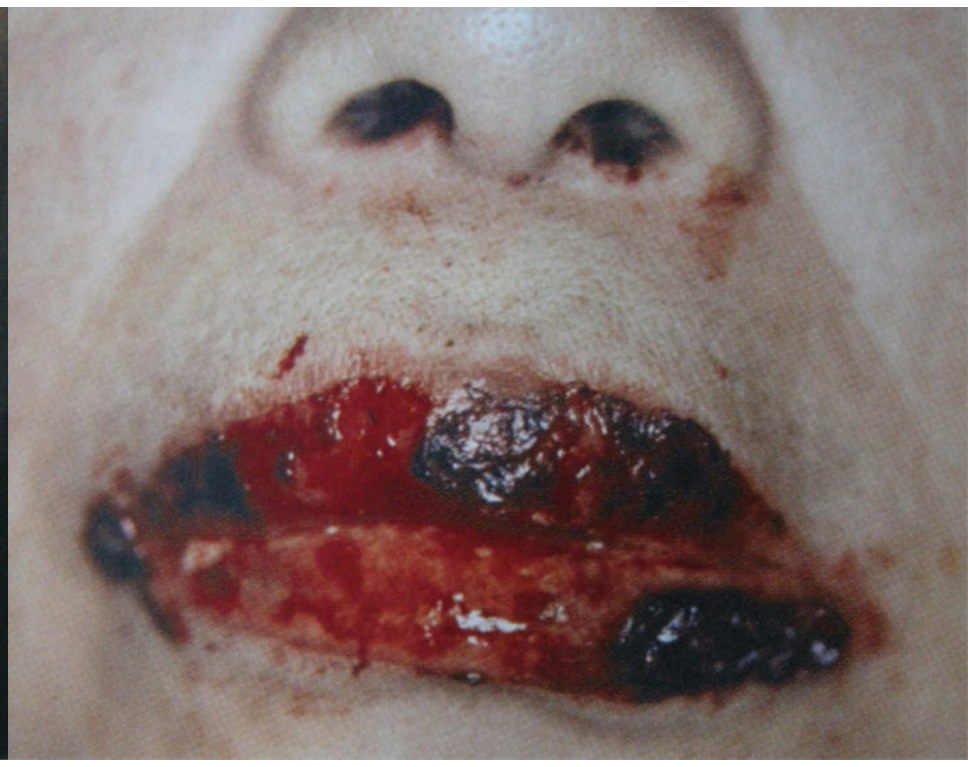
- Localized variant of pemphigus foliaceus.
- Scaly and crusted lesions of pemphigus foliaceus appear in the malar region of face and in other 'seborrheic' areas.
- Immunologic features of both lupus erythematosus and pemphigus.
  - In vivo IgG and C3 deposition on cell surface of keratinocytes as well as basement membrane zone, in addition to circulating antinuclear antibodies(ANA).

Paraneoplastic pemphigus

- Associated with underlying neoplasms, both malignant and benign.
- Most commonly associated neoplasms are non-Hodgkin lymphoma(40%), chronic lymphocytic leukemia(30%), Castleman's disease , thymomas, sarcomas
  - In children and adolescents, Castleman's disease is the most commonly associated tumor.
- Most constant clinical feature is intractable stomatitis. Cutaneous findings are pleomorphic and may present as macules, flaccid/tense blisters, Erythema Multiforme like lesions, lichenoid eruption.



: scaly crusted erosions are seen on the nose and malar area.



: severe stomatitis extending onto vermilion lip

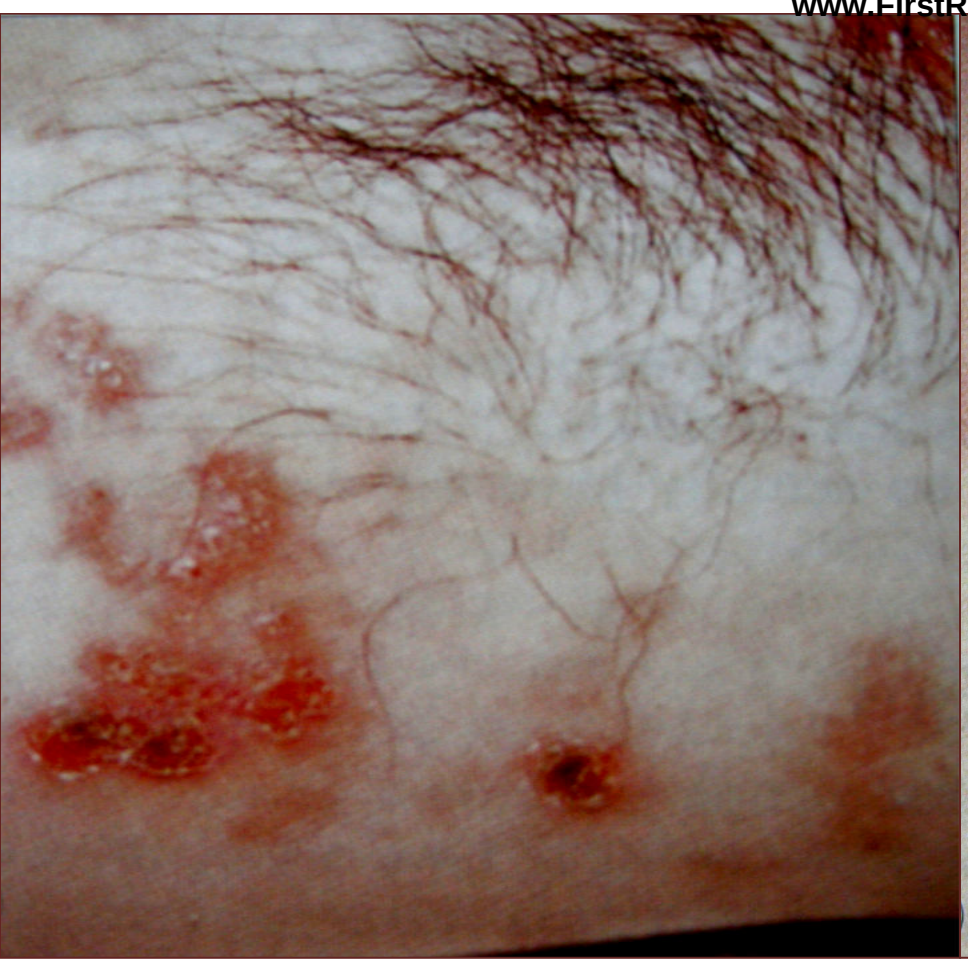
IgA Pemphigus = intercellular Ig A dermatosis

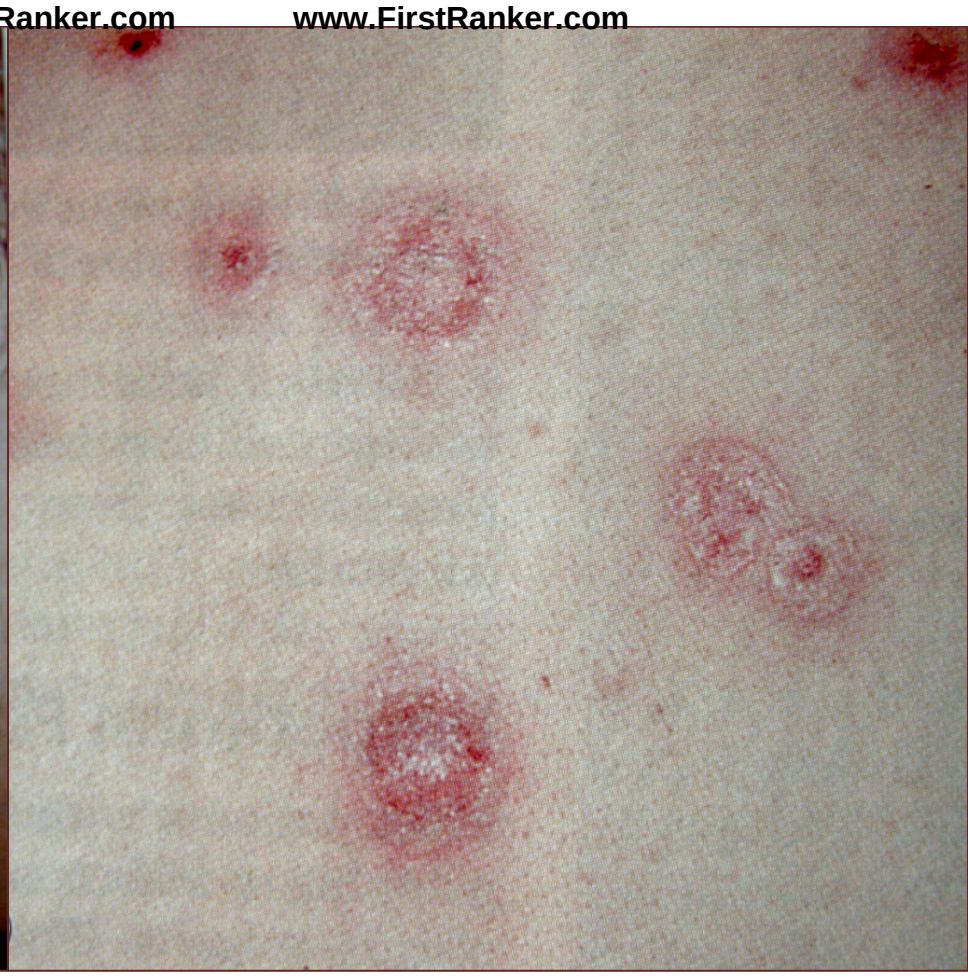
- Intraepidermal antikeratinocyte IgA
- vesicopustular

1. Subcorneal pustular dermatosis (SCPD) type:
   - Presents as flaccid vesicles or pustules on either erythematous or normal skin.
   - Pustules tend to coalesce to form an annular or circinate pattern with crusts in the center of the lesion.
   - Most commonly involved sites are axilla and groin.
   - Mucus membrane involvement is rare.
   - Pruritus is a significant symptom.

IgA Pemphigus

2. Intraepidermal neutrophilic (IEN) type:
   - Presents as flaccid vesicles or pustules on either erythematous or normal skin.
   - Pustules tend to coalesce to form an annular or circinate pattern with crusts in the center of the lesion
   - Sunflower -like configuration of pustules is a characteristic sign of the IEN type.
   - Most commonly involved sites are axilla and groin





Subcorneal pustular dermatosis(SCPD) type: pustules coalescing in annular or circinate pattern with central crusting.

Intraepithelial neutrophilic (IEN) type: characteristic sunflower-like configuration of pustules is seen.

IgA PEMPHIGUS

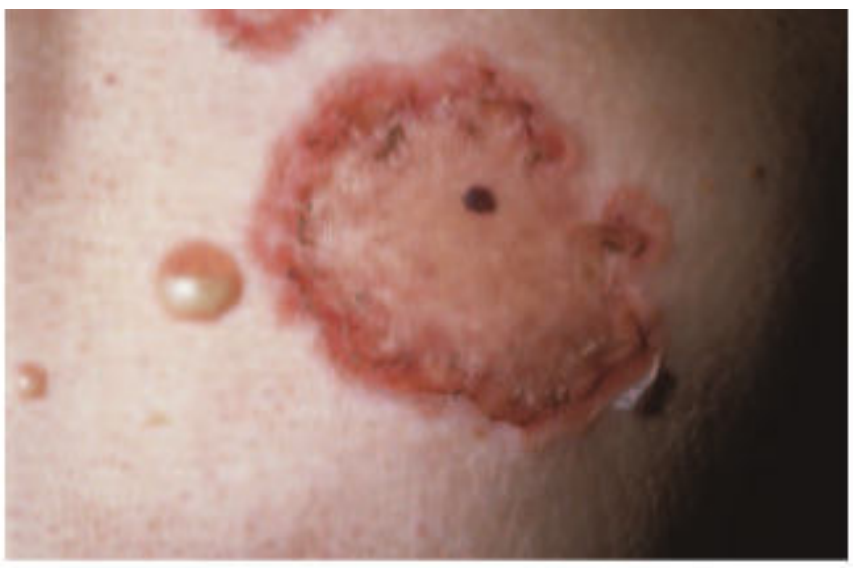


Fig. 41.10 Subcorneal pustular dermatosis. Annular lesions with a scaly margin and surrounding pustules. Pus has accumulated in the lower half of the flaccid pustule leaving clear fluid in the upper half.

Induced Pemphigus

- Drugs: penicillamine
  captopril
- Radiotherapy
- Thermal burns

SUBEPIDERMAL IMMUNOBULLOUS DISEASES

Table 41.4 The subepidermal immunobullous diseases.

Bullous pemphigoid
variant: pemphigoid nodularis
variant: localized pemphigoid
variant: localized vulvar pemphigoid
variant: pemphigoid vegetans
variant: lichen planus pemphigoides
Mucous membrane pemphigoid
variant: oral pemphigoid
variant: Brunsting–Perry pemphigoid
Pemphigoid gestationis
Linear IgA disease
variant: chronic bullous disease of childhood
variant: linear IgA disease of adults
variant: dermal associated linear IgA disease
variant: linear IgA mucous membrane pemphigoid
variant: mixed immunobullous disease
Epidermolysis bullosa acquisita
Bullous systemic lupus erythematosus
Dermatitis herpetiformis

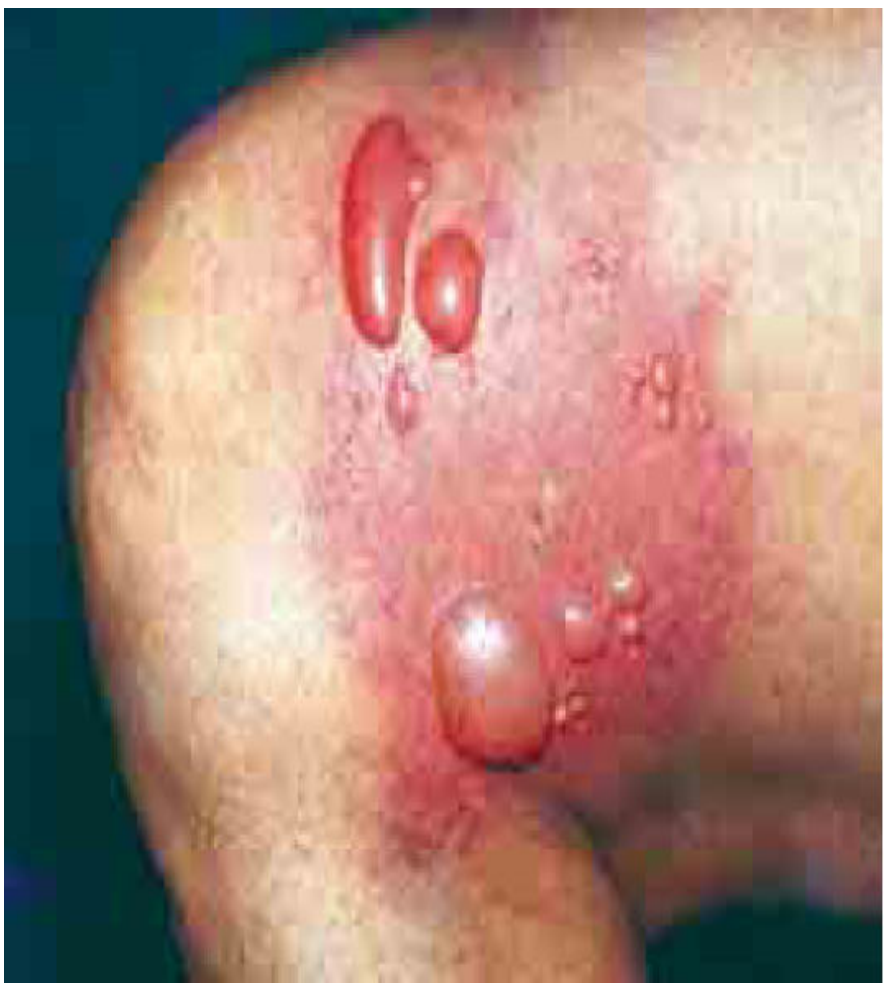
BULLOUS PEMPHIGOID

- Bullous pemphigoid is an acquired non-scarring autoimmune blistering disease of the elderly age group characterized histologically by subepidermal bullae and immunopathologically by deposition of antibodies and complement along the epidermal basement membrane zone (BMZ).

- The median age of onset ranges from 60 to 75 years.

- tense blisters, hemorrhagic or filled with thick fibrinous fluid, on normal appearing skin or on an erythematous base.
- The blisters range from vesicles to large bullae and may be seen all over the body, the commonest sites of involvement being the lower abdomen, inner thighs, groin and the flexor aspects of the limbs.
- The flexural and intertriginous areas are often affected.
- Vesicles may also develop on the palms and soles.
- Nikolsky's sign is negative.

- For blisters that rupture, the resulting erosions and may become covered with a crust.
- The erosions heals without scarring, but transient pigmentary changes and milia formation can occur.
- Pruritus is generally present, but the degree is variable, ranging from none to intense.
- Mucosal lesions have been reported in 10%– 40% of patients
- They are often mild and transient.



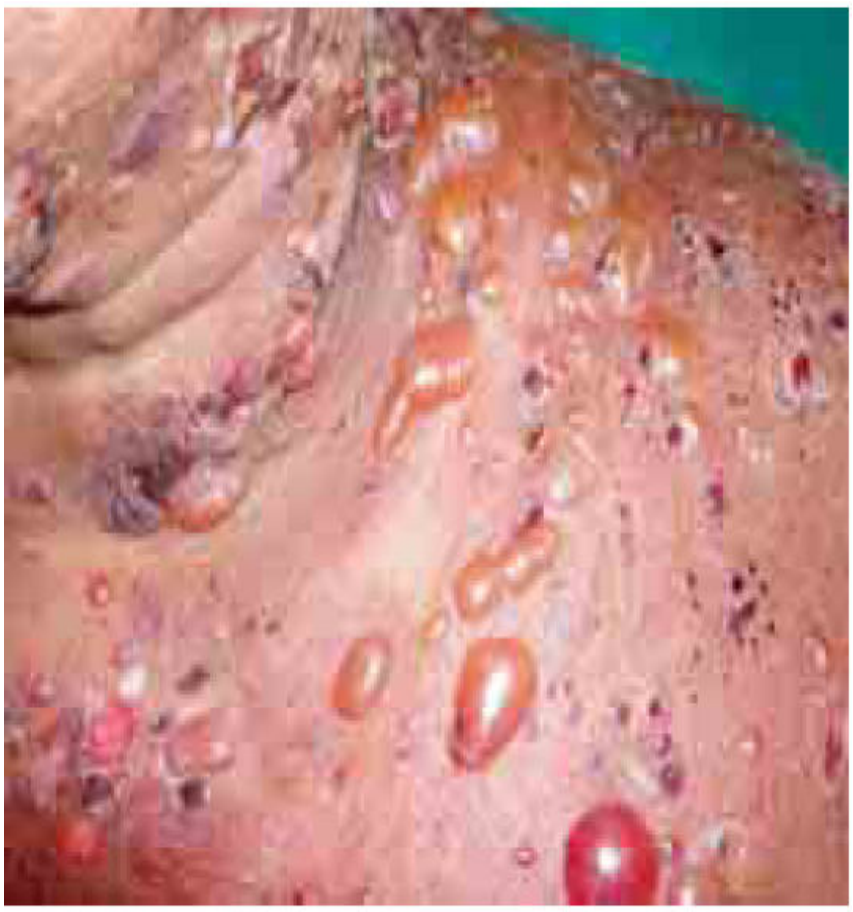


Fig. 32.25: Bullous pemphigoid: Multiple tense bullae

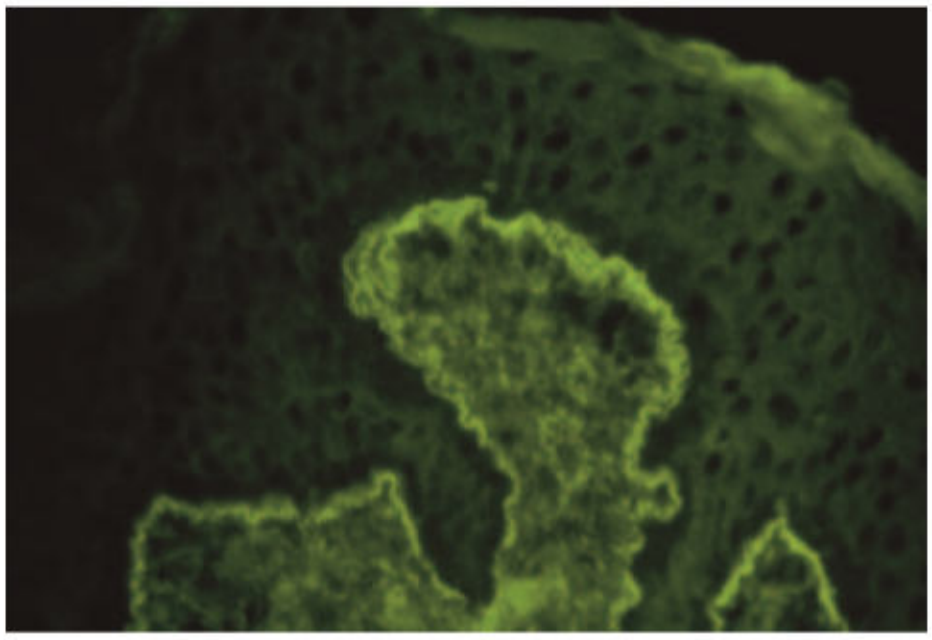


Fig. 41.13 Immunofluorescence showing IgG at the basement-membrane zone in a patient with pemphigoid. (Courtesy of Dr R.J. Pye, Addenbrooke's Hospital, Cambridge, UK.)

MUCOUS MEMBRANE PEMPHIGOID (SYN. CICATRICIAL PEMPHIGOID)

- Mucous membrane pemphigoid (MMP) is a group of chronic inflammatory, autoimmune, subepithelial blistering diseases predominantly affecting mucous membranes and is characterized by linear deposition of IgG, IgA, or C3 along the epithelial basement membrane zone (BMZ).
- Scarring is the clinical hallmark, but is not always obvious, particularly in the oral mucosa.

- Mucous membrane pemphigoid is a rare disease that primarily affects the elderly (the peak incidence is between the age of 60 and 80 years).
- It affects twice as many women as men.
- The onset is usually insidious.
- The oral mucosa is most commonly involved (approximately 85% of patients), followed by the ocular, nasal, nasopharyngeal, anogenital, skin, laryngeal, and esophageal mucosa in descending order of involvement.

- In the oral cavity, the gingival and palatal mucosae and less commonly the labial, glossal, and buccal mucosae are affected.
- There may be swollen, bright, erythematous, focal or generalized, mildly painful erosions on the gingiva (termed 'desquamative gingivitis')
- The presentation may also be as fluid- or sometimes blood-filled blisters.
- The lips are rarely involved.

- The eyes are affected in about two-thirds of patients, most often by a unilateral chronic cicatricial conjunctivitis with symptoms of burning, irritation and excessive lacrimation.
- Genital involvement has been observed in about 20% of cases, as blisters and erosions on the glans and prepuce or the labia.
- Skin lesions occur in 10%–30% of patients, and are of two types: scarring and nonscarring.
- Flaccid blisters develop on erythematous plaques on the head, neck and upper trunk, and heal with atrophic scars.
- This eruption tends to be localized and recurrent.

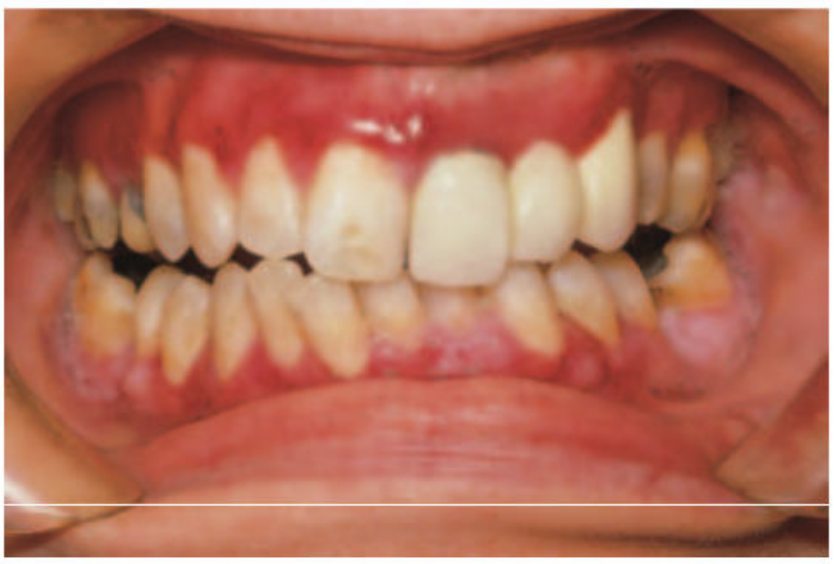


Fig. 41.18 Mucous membrane pemphigoid. Erosions around the gingival margins. (Courtesy of Dr R.J. Pye, Addenbrooke's Hospital, Cambridge, UK.)

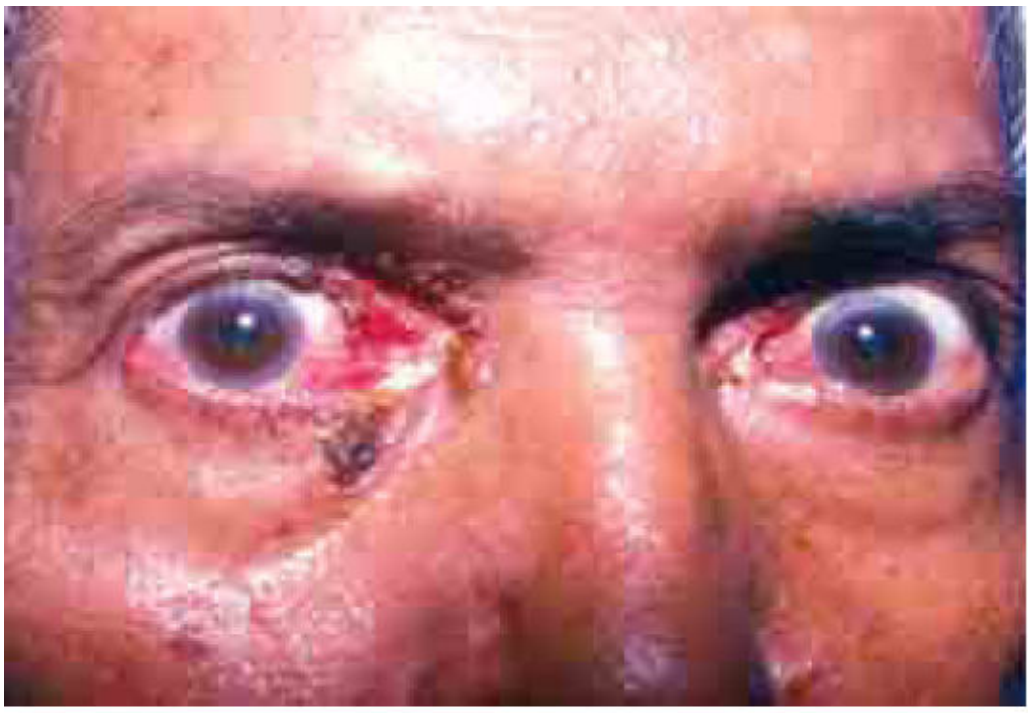


Fig. 32.29: Cicatricial pemphigoid: Ocular involvement

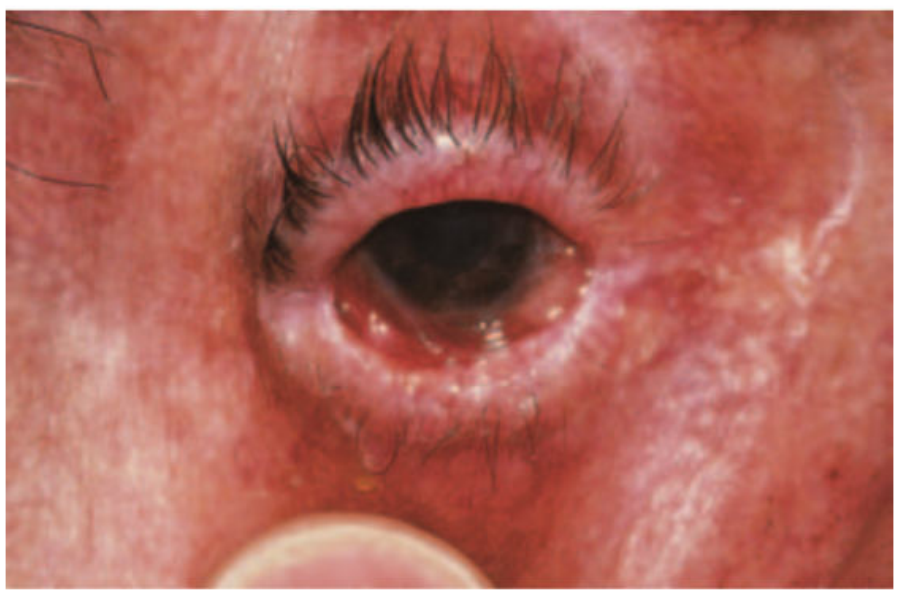


Fig. 41.20 Mucous membrane pemphigoid. Severe scarring and blindness. (Courtesy of Dr R.J. Pye, Addenbrooke's Hospital, Cambridge, UK.)

PEMPHIGOID GESTATIONIS

- Pemphigoid gestationis (PG), also known as herpes gestationis, is a rare autoimmune pruritic polymorphic dermatosis of pregnancy and puerperium.
- pemphigoid gestationis is undoubtedly under hormonal influence since it occurs only with pregnancy, menstruation, oral contraceptive ingestion, hydatidiform mole or choriocarcinoma.
- The PG antigen is the 180 kDa BP antigen (BP180 or BPAG2),that is present in the hemidesmosomes of the basement membrane.

- PG may occur in the first or any subsequent pregnancy.
- It usually begins in the second or third trimester, though it can begin at any time between the first trimester and the immediate postpartum period.
- Intense pruritus usually accompanies but occasionally precedes a polymorphic eruption of erythematous urticarial papules and plaques, vesicles or bullae arising on inflamed or normal skin.
- Classically, there are erythematous urticarial plaques rimmed by blisters, and crusts that enlarge peripherally to form annular or polycyclic patterns.

- The eruption usually begins on the abdomen, especially around the umbilicus, or on the extremities and then spreads to the rest of the trunk, palms and soles.

- Facial and mucosal lesions are rare.

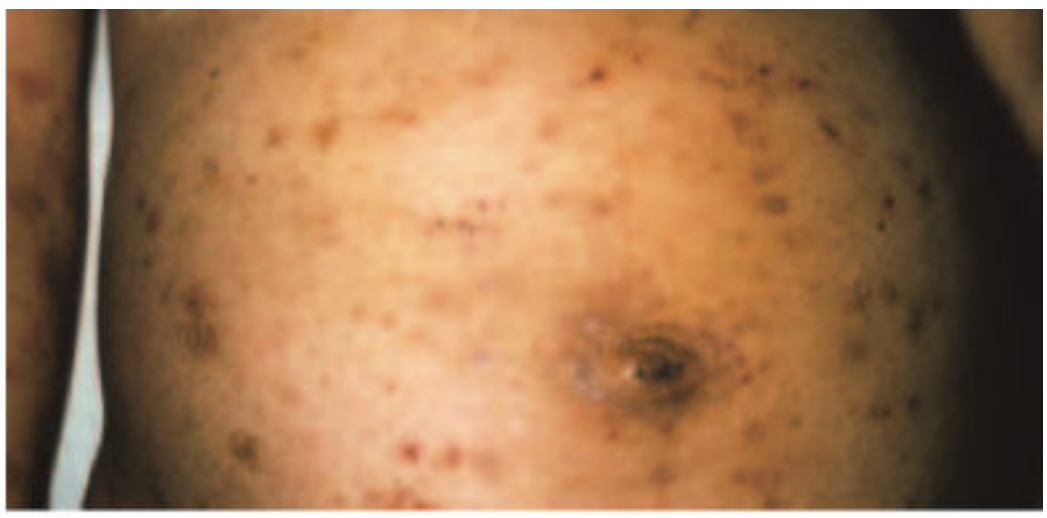


Fig. 41.21 Pemphigoid gestationis. Early pruritic erythematous stage. (Courtesy of Dr P. Hudson, Peterborough Hospital, Peterborough, UK.)

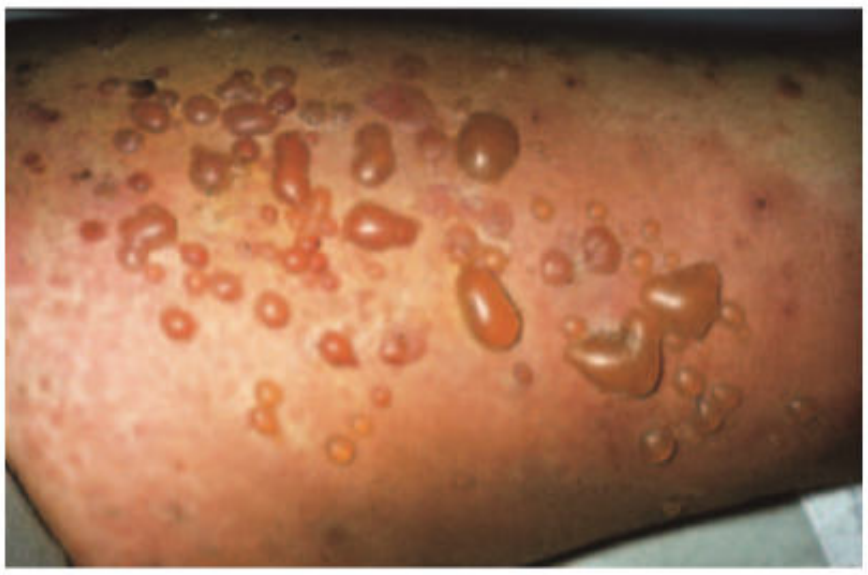


Fig. 41.22 Pemphigoid gestationis. Bullae arising on urticated erythematous skin on the thigh. (Courtesy of Dr P. Hudson, Peterborough Hospital, Peterborough, UK.)

DERMATITIS HERPETIFORMIS

- Dermatitis herpetiformis is a rare chronic blistering skin disease characterized clinically by intensely pruritic grouped vesicles arising on an erythematous base, by granular IgA deposits in the dermal papillae on direct immunofluorescence, and associated with gluten-sensitivity and a mostly asymptomatic enteropathy.
- It presents most often in the second or third decades, but the disease can occasionally occur in children also.
- A slight male predominance has been reported.

- Onset may be acute or gradual.
- The eruption is characteristically polymorphous, although at a given time any one type of lesion (e.g. papular, urticarial, vesicular or bullous) may predominate.
- The primary lesion is classically, a small vesicle on an
- erythematous, edematous base, or an erythematous papule, or an urticarial plaque.
- The vesicles may be grouped in a herpetiform manner on an erythematous plaque.
- Intense itching or a burning or stinging sensation is a common

- If the rash is chronic, there are often lichenified plaques at the sites of involvement.
- The areas of predilection are the elbows, knees, buttocks, sacrum, shoulders, posterior hairline and scalp.
- **The lesions** are symmetrically distributed over the extensor surfaces of the limbs.
- The face is occasionally affected, but the mucous membranes, only rarely.

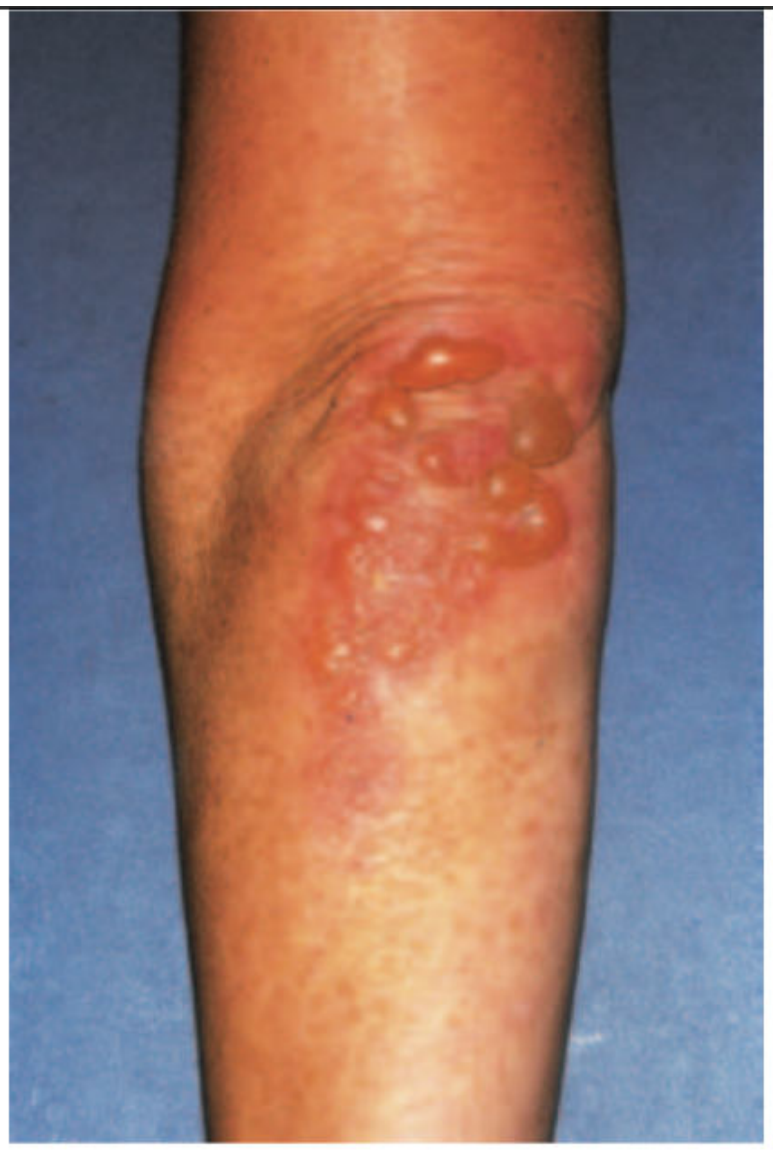


Fig. 41.27 Dermatitis herpetiformis. Intact tense bullae on the elbow.

LINEAR IgA DISEASE

- Linear IgA disease can be clinically categorized into two disorders with two distinct presentations: CBDC, which begins in childhood, and adult LAD, which begins in adult life.
- In children, the disease usually starts below the age of 5.
- The onset is usually abrupt, with large tense bullae filled with clear or hemorrhagic fluid on or near the genitalia.
- They gradually involve other areas such as the buttocks, scalp and
- face, especially the perioral **and periocular areas.**

- Blisters may also appear in a generalized but asymmetric distribution.
- Typical features include herpetiform clustering of blisters, formation of bizarre, irregularly shaped bullae as they enlarge and coalesce, and ‘rosettes’ or ‘clusters of jewels’ which represent the annular arrangements of new, small, tense blisters around a crusted healing erythematous plaque (the ‘string of pearls’ sign) .
- **Pruritus is variable in intensity.**
- In adults, the onset may be insidious or abrupt, with symptoms varying from mild pruritus to severe pruritus and burning.

- There may be flexural and truncal involvement with scattered vesicles and tense blisters similar to BP.
- The bullae may be somewhat linear, sausage- shaped and hemorrhagic.
- A few patients of LAD may present with a DH like itchy eruption with grouped papulovesicles involving the extensor surfaces.
- Perineal and perioral involvement is less common than in children.
- Approximately 80% of adults and children with LAD have mucosal lesions

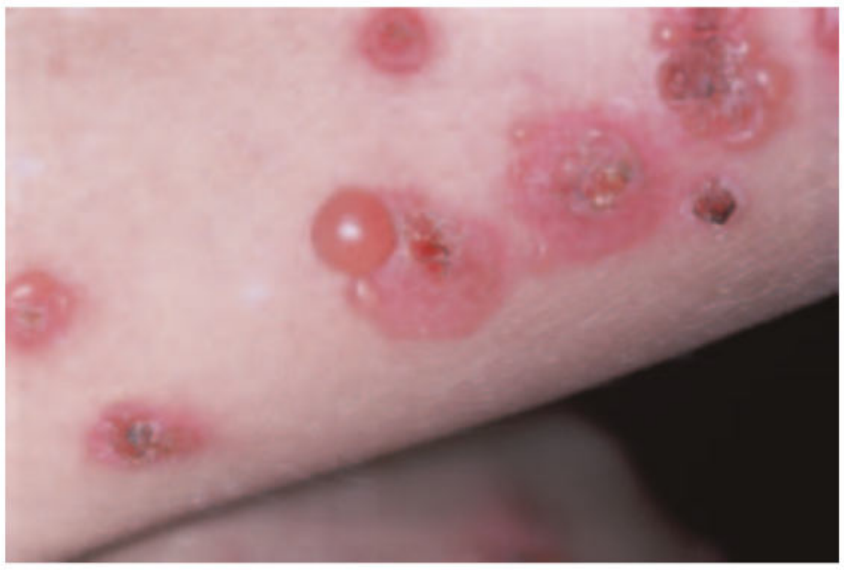


Fig. 41.24 Linear IgA disease. Intact tense bullae on the thigh and annular lesions. (Courtesy of Dr P. Hudson, Peterborough Hospital, Peterborough, UK.)

Treatment of Immunobullous disorders

- Management includes-

1. Investigations
2. Treatment

INVESTIGATIONS

1-Routine

- Full blood count and differential
- Fasting blood sugar
- Liver function tests
- Renal function tests
- Chest x-ray
- Urinalysis

2-Specific –for diagnosis

- Tzanck smear
- Histopathological examination
- DIF
- IIF
- Immunoblotting
- Immunoelectron microscopy
- ELISA

TREATMENT

- The treatment of immunobullous diseases consists of three phases: control, consolidation, and maintenance.
- ***control phase-*** intense therapy is given to suppress disease activity until no new lesions appear.
- ***consolidation phase*** during which drugs and doses are maintained until complete clearance of lesions.
- Finally, medications can be gradually tapered in the **maintenance phase**, aiming for the lowest dose that prevents new lesions from appearing .

- Aim of therapy is to prevent the appearance of new lesions & produce healing of existing lesions.

- The choice of therapy

➢ Severity of the disease at presentation.

➢ Patient-related
- age
- general health
- associated medical illnesses

➢ Drug-related
- onset of action
- efficacy
- adverse effects
- cost

TREATMENT PHASES

- **GENERAL THERAPY**
- **PHARMACOLOGICAL THERAPY-**

A. **TOPICAL**

B. **SYSTEMIC**

General measures

- It includes-

1. General nursing care-

- Proper and regular dressing of the raw area is done until re-epithelization takes place.
- This is performed with sterile petroleum gauze or gauge impregnated with topical antibiotics.

2.Adequate Nutrition –

- Oral supplementation with protein and high calorie fluids.
- Soft easily chewable diet in case of oral lesions

3. control of secondary infection-antibiotics should be given preferably following culture and sensitivity report.
4. restoring fluid and electrolyte equilibrium

Topical therapy

- Is indicated in more local oral lesion with less aggressive behaviour.
- Skin lesions-

1. clobetasol propionate .05% may reduces the requirement of oral steroid.
2. Potassium permanganate and antiseptics to reduce the risk of secondary infection.

❑ **Oral lesions-**

- soft diets, soft toothbrushes help to minimize local trauma.
- Topical analgesics or anaesthetics - benzydamine hydrochloride 0.15% (Oral Rinse) are useful in alleviating oral pain, particularly prior to eating or tooth brushing.

- Tooth brushing should be encouraged and antiseptic mouthwashes may be used such as
  - chlorhexidine gluconate 0.2%
  - hexetidine 0.1%
  -01:4 hydrogen peroxide solutions.

- Patients are susceptible to oral candidiasis which should be treated.
- Topical Corticostreoid therapy may help to reduce the requirement for systemic agents.
- It include application of clobetasol gel .05%
- Clobetasol gel may be used with occlusive vehicle mainly in desquamative gingivitis

- Soluble betamethasone sodium phosphate 0.5 mg tablet dissolved in 10 mL water may be used up to four times daily, holding the solution in the mouth for about 5 minutes.

- Isolated oral erosions could be treated with application of triamcinolone acetonide 0.1% in adhesive paste

- 2.5 mg hydrocortisone lozenges or sprayed directly with an asthma aerosol inhaler, for example beclomethasone dipropionate 50-200 micrograms or budesonide 50-200 micrograms.

- Topical ciclosporin (100 mg/mL) in oral pemphigus has been described and may be of some benefit but is expensive

- Tetracyclines are successful in pemphigus vulgaris and cicatricial pemphigoid

- Tacrolimus is indicated in oral resistant cicatricial pemphigoid

SYSTEMIC THERAPY

- **Corticosteroids:**
  - Oral
  - Pulse IV

- **Adjuvant drugs**

  - Azathioprine
  - Oral cyclophosphamide
  - Pulsed cyclophosphamide and dexamethasone
  - MMF
  - Gold
  - Methotrexate
  - Ciclosporin
  - Tetracyclin and nicotinamide
  - Dapsone
  - Chlorambucil

Newer treatment modalities

- IVIG
- Cholinomimetic drugs
- Plasma exchange
- Extracorporeal photophoresis
- Biologicals
- Immunoadsorption

THANKS