Solved Papers
Dermatology
for PG Students

A must for MD and DNB

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CHAPTER 21

Vesiculobullous Disorders

Q1. Describe the role of immunofluorescence in dermatology, and particularly its role in bullous disorders.

Ans.

Definition

Immunofluorescence is a specialized technique used for detection of a wide variety of antigens in tissues or cells in suspension.

Albert Coons developed IF in 1940s.

Principle

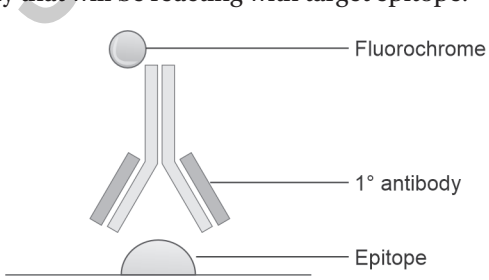
Viewing of antigen-antibody complexes under UV microscope using corresponding antibodies tagged to a fluorochrome.

Types

1. Direct immunofluorescence
2. Indirect immunofluorescence
3. Complement fixation
4. Immunofluorescence microscopy

Direct immunofluorescence (DIF)

- Single step procedure
- Substrate: Frozen section of skin
- Fluorophore label conjugated directly to primary antibody that will be reacting with target epitope.

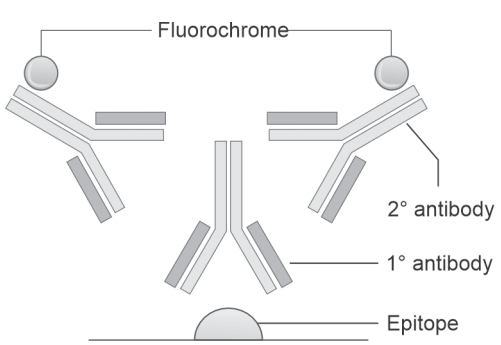


Diagnostic role in autoimmune mediated blistering disorders:

- Dermatitis herpetiformis
- HSP
- Cutaneous lupus erythematosus
- Pemphigus group

Indirect immunofluorescence

- Semi quantitative procedure
- Substrate: normal whole tissue, usually monkey esophagus
- Patient's serum layered on substrate followed by application of fluorinated antibodies.
- 2 step incubation process:
  1. Primary antibody bins to target epitope
  2. Tagged secondary antibody recognizes and binds to primary antibody

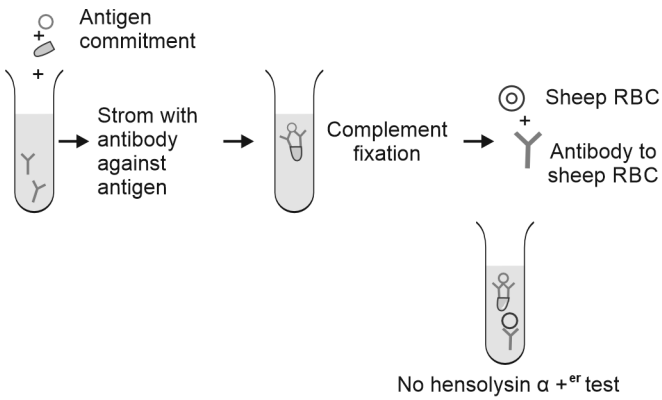


- Preferred over DIF due to:
  1. Increased sensitivity
  2. Single amplification
  3. Ability to detect several targets in same sample (excess reactivity)

Immunomapping—patient's own skin as substrate

Complement fixation—detects small quantities of complement fixing antibodies.

- Patient's serum layered on substrate-source of complement added.
- Glucocorticoid anti-complement antibodies added



Immunoelectron microscopy

- Analogues to DIF and IIF
- Instead of fluorinated antibodies, antibodies labelled with an enzyme such a horseradish peroxidase or a heavy metal (colloid god).
- Provides subcellular or ultrastructural localization of immunoreactants.
- Helpful in: Subtypes of hereditary Epidermolysis Bullosa.

Indications of Immunofluorescence:

1. Diagnostic
   - Bullous disorders
   - Pemphigus and pemphigoid
   - Herpes gestationis
   - Dermatitis herpetiformis
   - Linear IgA disease
   - EBA
   - Connective tissue diseases
2. Highly characteristic with some diagnostic value
   - Vascular diseases
   - HSP
   - Allergic vasculitis
   - PAN
   - Others
   - LP
   - Pemphigus
3. Suggestive of immunologic pathogenesis only
   - CTD
   - MCTD
   - SS
   - Dermatomyositis
   - Psoriasis

Sites of biopsy

1. Bullous diseases
   - Unblistered perilesional normal area of fresh lesion with part of fresh blister proportional to the level of split
   - Mucosa: Periphery of fresh lesion
   - DH: Normal appearing perilesional skin
2. Lupus erythematosus
   - Lesional and apparently normal sun exposed skin
   - Discoid lupus erythematosus: Only lesional
3. Vasculitis
   - Fresh lesions
4. Porphyrias
   - Dorsum of hand lesions and normal skin
5. Lichen planus
   - Non-sun exposed, normal skin
   - Inflamed skin and mucosa

Transport in:

- Phosphate buffered saline/normal saline
- Michel's media

Findings

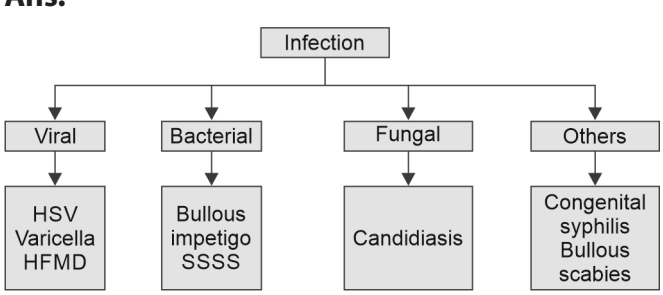
- PEMPHIGUS: Linear/granular deposition of immunoglobulins and C3 in epidermal intercellular spaces - 'chicken wire' or 'fish net pattern'
- PEMPHIGOID AND EBA: Subepidermal blistering with C3 ans/or IgG deposition
  1. BP: Localized in epidermal side
  2. EBA: Dermal side
- DH: Granular IgA at tips of dermal papillae

Advantages of IF

- Diagnosis
- Classification of disease
- Measure of disease activity

Q2. Classify vesiculobullous disorders in infants.

Ans.



Classification

1. Infection
   Viral Infections:
   - Herpes simplex virus (HSV)
   - Varicella
   - Hand, Foot, and Mouth Disease (HFMD)
   - Bacterial Infections
   - Bullous impetigo
   - Staphylococcal Scalded Skin Syndrome (SSSS)

   Fungal Infections:
   - Candidiasis

   Other Infections:
   - Congenital syphilis
   - Bullous scabies
2. Inflammatory
   - Intradermal split
   - Miliaria crystallina
   - Erythema toxicum neonatorum
   - Transient pustular melanosis
   - Suction blisters
   - Bullous IBR
   - Miliaria rubra spinous
3. Genodermatoses
   - Subepidermal
     - epidermolysis bullosa
     - Bullous congenital ichthyosiform erythroderma
   - Intraepidermal
     - Incontinentia pigmenti
4. Neoplastic/infiltrative
   - Bullous mastocytosis
   - Langerhans cell histiocytosis

Investigations

1. Tzanck smear
   HSV/Varicella/HZ: Ballooning multinucleated giant cells
   SSSS: Dyskeratotic acantholytic cells
   ICH: Atypical Langerhans cells
2. Gram stain
   - Bullous impetigo—gram positive
   - ETN—eosinophils
3. Bacterial culture (swab)
4. Viral culture/PCR for HSV DNA
5. Skin biopsy—level of split and deposition of immune complexes
6. Immunofluorescence—level of split and deposition of immune complexes
7. CBC to rule out infection/inflammation
8. Inflammation markers elevated
   - CRP—raised
   - ESR—raised
9. KOH—Candidiasis/Bullous scabies
10. Genetic testing for Epidermolysis Bullosa (COL7A1/COL7A2)
11. VDRL for syphilis

Treatment

1. Supportive care
   - Lateral drainage of bullae
   - Saline compresses for crusted erosions
   - Cleaning and dressing of wounds
   - Pain management
2. Viral
   - Acyclovir
   - Valacyclovir
3. Impetigo
   - Topical Mupirocin 2% ointment
   - Others like: Fusidic acid, Retapamulin
   - Systemic antibiotics: Amoxicillin, Cephalosporins
4. Candidiasis
   - Clotrimazole topically
5. Syphilis
   - Aqueous crystalline Penicillin G 100000–150000 MU/kg IV every 12 hours during first 7 days of life and every 8 hours thereafter for 10 days.
6. Scabies
   - Permethrin 5% cream once a week for 2 weeks
   - Ivermectin
   - Crotamiton
7. Bullous congenital ichthyosiform erythroderma
   - Oral retinoids
   - Physical therapy
   - Avoid friction
8. Reassurance
   - Erythema toxicum neonatorum
   - Suction blisters
   - Miliaria
9. Genetic counseling
   - Epidermolysis bullosa
10. LCH
    - Chemotherapy
    - Radiotherapy
    - Stem cell transplant

Q3. Write a short note on Nikolsky sign.

Ans.

Definition: It is a well described clinical sign which manifests as dislodgement of intact superficial epidermis by a shearing force, indicating a plane of cleavage in epidermis.

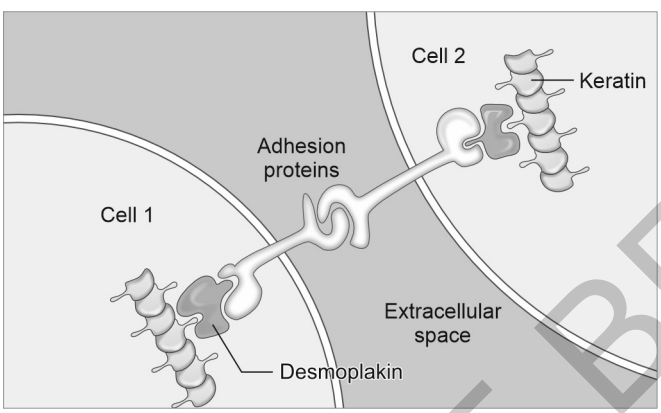
The sign basically differentiates between intra epidermal blisters from subepidermal blisters.

First described by Pyotr Vasilyevich Nikolsky.

Elicitation

Applying tangential/lateral pressure by a thumb or finger in the perilesional, affected or normal skin which results in a face that dislodges upper layers of epidermis from lower layers.

Pathophysiology



Core pathophysiology is acantholysis i.e., there is loss of coherence between epidermal cells because of breakdown of intercellular bridges.

Variants of Nikolsky sign

- Clinical Nikolsky sign: when tangential pressure is applied on apparently normal skin/mucosa or on perilesional skin/mucosa there is dislodging of upper layers of epidermis.
- Microscopic Nikolsky's sign: same as above but minimal damage at cellular level demonstrated only microscopically.
- Marginal Nikolsky's sign: Same as above but minimal damage at cellular level demonstrated inly microscopically.
- Marginal Nikolsky's sign: Extension of erosion on surrounding normal appearing skin by rubbing skin surrounding existing lesion.
- Direct Nikolsky sign: Induction of an erosion on normal appearing skin, distant from lesions (bony prominences).
- Wet and Dry Nikolsky sign: When eroded surface is "wet" or "dry".
- Modified Nikolsky sign: Peripheral extension of blisters on applying pressure to their surface.
- False Nikolsky sign/Sheklakov sign: Pulling of peripheral remnant roof of a ruptured blister thereby extending erosion on surrounding normal skin.
- "False" as subepidermal cleavage occurring in perilesional skin.
- Pseudo Nikolsky's sign: Epidermal peeling due to necrosis of epidermal cells seen in—SJS, TEN, burns, bullous ichthyosiform erythroderma.

Mauserung phenomenon: Nikolsky's sign elicited in rare Ichthyosis bullosa of Siemens.

Nikolsky's phenomenon: Superficial layer of epidermis felt to move over deeper layer and blister develops after sometime.

Implications of Nikolsky's sign

Diagnostic

- Pathognomonic of Pemphigus
- Differentiating various blistering disorders
  - Positive in intraepidermal blistering disorders
  - Negative in subepidermal blistering disorders (BP)

Prognostic

- Positive in active or progressive stage of disease/flares.
- Wet—active PV
- Dry—Re-epithelialization

Q4. Classify blistering disorders. Add a note on Butcher's Pemphigus.

Ans.

Classification according to the level of split

Intraepidermal

Subcorneal/Granular:

- Miliaria crystallina
- Bullous impetigo
- Staphylococcal scalded skin syndrome (SSSS)
- Pemphigus foliaceus and variants
- IgA pemphigus
- Subcorneal pustular dermatosis (SCPD)
- Erythema toxicum neonatorum (ETN)

- Transient neonatal pustular melanosis
- Acropustulosis of infancy

Spinous:
- Spongiotic dermatitis
- Friction blister
- Miliaria rubra
- Incontinentia pigmenti
- IgA pemphigus
- Epidermolytic hyperkeratosis
- Hailey-Hailey disease

Suprabasal:
- Pemphigus vulgaris (PV) and variants
- Paraneoplastic pemphigus (PNP)
- Dariers disease

Subepidermal:

1. Basal keratinocyte necrosis, cytolysis or damage
   - EBS
   - Thermal injury
   - EM
2. Epidermal BMZ destruction/disruption
   - Lamina lucida
     - BP
     - MMP
     - Herpes gestationis
     - DH
     - linear IgA bullous dermatosis
     - PCT
     - JEB
     - Suction blister
     - Thermal injury
   - Sublamina densa
     - Bullous SLE
     - EBA
     - EBD

Etiological classification
Immunobullous disorders
1. Intraepidermal blistering disorders
   - Pemphigus and variants
2. Subepidermal immune mediated disorders
   - Bullous pemphigoid
   - Mucoid membrane pemphigoid
   - Linear IgA bullous dermatosis
   - Epidermolysis bullosa acquisita
   - Herpes gestationis
   - Dermatitis herpetiformis

Infections:
- Bullous impetigo
- SSSS
- Varicella
- Herpes zoster
- Herpes simplex
- HFMD

Inherited:
- Epidermolysis bullosa
- Epidermolytic ichthyosis
- Incontinentia pigmenti
- Lipoid proteinosis

Drug induced:
- EM
- SJS/TEN
- Bullous FDE

Inflammatory:
- Pompholyx
- Id reactions
- Dermatitis (acute)
- ETN
- Transient neonatal pustular melanosis
- Miliaria

Metabolic:
- PCT
- Diabetic bullae
- Coma blisters
- Edema blisters

Butcher's Pemphigus
- Discovered by George Penet in 1890s
- Group of acute vesiculobullous eruptions frequently encountered among butchers
- Believed to be an infection following an injury due to unknown micro-organisms
- Also known as "acute bullous eruption" or "acute pemphigus"
- Also observed in other occupations handling animals
- Fatal in most cases

Clinical features:
- Long incubation period
- History of trauma present
- Large bullae and erosions
- Hemorrhagic bullae
- Lesions appear in crops
- Malodourous

- Epistaxis
- Fatty hepatomegaly
- Pericardial effusion
- Congestion in stomach/intestine

Treatment

Managed with Quinine

Q5. Classify and discuss clinical features of pemphigus group of disorders.

Ans.

Definition: "Pemphix" means bubble In Greek.

Pemphigus is a group of autoimmune blistering disorders characterized by intraepidermal split.

Pemphigus vulgaris is a common form.

Type	*Level of split*	*Target antigen*
Pemphigus vulgaris (PV), Pemphigus vegetans	Suprabasal	Desmoglein 3 (Dsg-3), Desmoglein 1 (Dsg-1), Desmocollin
Pemphigus foliaceus (PF), Pemphigus erythematosus (PE), Fogo selvagem	Subcorneal	Desmoglein 1 (Dsg-1), Desmocollin
Pemphigus herpetiformis	Subcorneal	Dsg-1 > Dsg-3
Drug-induced pemphigus	Subcorneal	Dsg-1 > Dsg-3
IgA pemphigus	Intraepidermal neutrophilic type Subcorneal pustular type	Dsg-1, Dsg-3, Desmocollin-1
Paraneoplastic pemphigus	Variable	Desmogleins, Plakins (Plectin, Desmoplakin, Envoplakin, Periplakin), BPAG-1
Neonatal pemphigus	Variable	Desmogleins

Newer variants of pemphigus

- Paraneoplastic pemphigus
- IgA pemphigus
- Pemphigus herpetiformis

Pathophysiology

- The main target antigen in pemphigus are Dsg1 and 3 expressed in skin and mucosal tissue.
- Desmoglein-1 is highly expressed in skin, particularly in epidermis.
- Dsmoglein-3 mainly found in basal and suprabasal layers.

Mucosa: Dsg 3 expressed throughout where Dsg 1 present at low levels.

Therefore, early and definite mucosal involvement in PV, whereas in PF only skin blistering

Antibodies against Dsg-1 cannot destabilize oral mucosa but have marked effect on skin.

IgG++(IgM, IgA, IgE)

- Antigen specific Th1 and Th2 cells present which helps in antibody production
- Associations: HLA-DRB1 or DQ-B1
- Acantholysis-key pathogenesis in PV and PF occurs due to:
  - Stearic hindrance—Anti-Dsg antibodies may sterically hinder Dsg mediated adhesion
  - Protease activation—by antibodies disrupt desmosomes
  - Disruption of intracellular signaling pathways that regulate desmoglein assembly and adhesion
  - Redistribution of desmoglein expression—due to Antibodies
  - Apoptolysis—acantholysis and keratinocyte damage due to EGFR activation, cell death cascades, basal cell shrinkage, degradation of structural proteins and apoptosis of acantholytic cells
  - Ultimate separation of keratinocytes and characterized by blistering

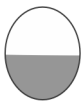
Clinical Features

Pemphigus vulgaris:

- Usually asymptomatic vesicles, bullae, erosions or crusted plaques on skin
- Oral erosions and ulcers
- Itching precedes development of new blisters
- Blisters rupture easily Painful erosions with ongoing
- Crusted Offensive odor (characteristic)
- Hard, neck, groins, trunk, axillae and pressure points

Progression and outcome:

- Lesions start as a vesicle or normal skin with or without surrounding erythema
- Gradually enlarges to form flaccid or tense bullae with clear or turbid fluid
- Hypopyon sign present heal with postinflammatory hyperpigmentation

• Hypopyon sign + 

- May leave behind SK-like changes—Post-pemphigus acanthomata

Other areas:

- Oral mucosa—painful, persistent, irregularly shaped erosions, ulcers or collapsed bullae
- Ocular mucosa—redness, photophobia
- Vaginal mucosa—erosions, dyspareunia
- Rectal mucosa—pain during defecation
- Nasal mucosa—epistaxis
- Laryngeal mucosa—hoarseness, throat pain
- Nail—acute paronychia, subungual hematoma, onycholysis

Variants:

- Pure cutaneous type
- Rarely switch to PF

Pemphigus vegetans:

- Rare and benign variant
- 2 forms:
  - Neumann—early type with vesiculopustulosis
  - Hallopeau—later vegetating type
- Vegetating lesions appear initially or over preexisting lesions
- May resolve or turn into PV
- Cerebriform tongue (Premalatha sign) and vegetating granulations in oral cavity
- Tumid, vegetating, papillomatous, hypertrophic plaques in intertriginous areas and flexures
- Local moisture, heat and friction contribute to development
- Subject symptoms minimal

Pemphigus foliaceus:

- Small, flaccid bullae with crusting
- Initial: scaly, moist papules or superficial flaccid bullae on normal skin or erythematous skin
- Bullae readily rupture resulting in moist erosions and cornflake like crusts
- Initially seborrheic areas—face, scalp, upper trunk—generalized
- Musty odor (Characteristic)
- Sharply demarcated unlike PV
- Oral erosions rare
- May evolve to become PV
- GC: fair
- Chronic benign course with intermittent crops

Endemic Pemphigus Foliaceus/Fogo Selvagem "wildfire".

- Striking distribution of lesions on sun exposed skin giving "burnt" appearance and painful burning sensation in lesions
- Occurs in dense forest areas of South America (Brazil)
- May be infectious disease caused by a virus transmitted by black flies (Simulium pruinosum)
- Frequently occurs in families and affects children and adolescents
- HLA-DRB1

Pemphigus erythematosus:

- Localized variant of PF
- Characterized by erythematous, scaly plaques, thin-walled bullae and denuded areas on face, upper back, chest and intertriginous areas
- Exacerbations on exposure to sunlight
- Oral involvement is absent
- Predilection for children and adolescents

Pemphigus herpetiformis:

- Rare subtype accounting for 7% of all pemphigus patients
- Clinical variant of PF/PV
- Dsh1>3, rarely Desmoglein 1 and 3
- Herpetiform arrangement of tense vesicles and pruritus
- Erythematous or urticarial plaques with central healing and peripheral papulovesicles.
- Mucosal involvement rare

IgA pemphigus/IEN IgA dermatosis/intercellular vesiculopustular dermatoses/IgA herpetiform pemphigus/ monoclonal IgA/IgA intercellular dermatosis.

Definition: Rare autoimmune eruption with neutrophilic infiltration, occasional acantholysis, and bound and circulating IgA autoantibodies targeting cell surface components of epidermis.

Epidemiology

- Affects middle-ages but can occur at any age including infancy
- Subtypes:
  - IEN type: DSG1 and 3
  - SCPD type: DSC-1

Clinical features

- Flaccid bullae or pustules in normal or erythematous skin
- Pustules tend to coalesce in an annular or circinate pattern with central crusting
- Mucosal lesions are rare
- Pruritus common

Course

- Chronic and benign coarse
- Responds well to treatment
- Lower IgA autoantibody titer and inability of IgA to inactivate complement by classical pathway may help differentiate from classical pemphigus
  Treatment:
- DOC: Dapsone
- Acitretin, Etretinate
- Psoralen: UVA, Systemic corticosteroids, Topical CS
- Colchicine
- MMF
- Adalimumab

Paraneoplastic pemphigus
Autoimmune disorders characterized recalcitrant blistering, erosive mucocutaneous lesions, associated neoplasm and high titers of "pemphigus-like" cell surface antibodies.

- Polymorphous cutaneous lesions resembling PV, BO, EM, GVHD, or LP
- HKA-DRB 03
- 45–70 years
- Existing neoplasm
  - Non-Hodgkins lymphoma
  - CLL
  - Castleman tumor
  - Thymoma
  - Waldenstrom's macroglobulinemia

Pathogenesis of PNP

Cellular autoimmune response
Autoreactive cellular cytotoxin mediated by:

- CD8+ cytotoxic T lymphocytes
- CD56+ natural killer cells
- CD68+ monocytes and macrophages

Humoral autoimmune response

- Antibodies predominant IgG1 directed against
  - Plakins (Desmoplakin 1 and Periplakin, BPAG1)
  - Dsg1 and 3
- Antibodies also deposited at GIT, respiratory epithelia, kidney, urinary bladder, smooth and striated muscle.

Mechanisms of pathogenesis:

1. Molecular mimicry: Immune response against tumor antigens cross reacts with normal epithelial proteins.
2. Cytokine dysregulation: Tumor causes cytokine dysregulation, leading to synthesis of antibodies to Dsg3/plakins
3. Epitope spreading: Tumor induced lichenoid ID which exposes hidden antigens

Clinical features:

- Recalcitrant oral stomatitis
- Painful oral erosions and ulcerations of oropharynx/lips
- Polymorphs, itchy skin lesions seen in Bullous pemphigoid, toxic epidermal necrolysis, erythema multiforme, lichen planus)
- Paronychial involvement present
- Conjunctiva (pseudomembranous conjunctivitis, symblepharon, visual impairment)
- Pulmonary (bronchiolitis obliterans)

Histopathological examination:

- Intraepidermal acantholysis
- Keratinocyte necrosis
- Vacuolar interface dermatitis
- DIF: IgG and C3 in epidermal intercellular spaces. Linear granular complement deposition along epidermal BMZ
- IIF: Serum autoantibodies binding to cell surface of skin and mucosa, simple, columnar and transitional epithelium

Diagnostic criteria: Anhalt's

1. Painful mucosal erosions and polymorphous skin eruption
2. Histopathological changes of intraepidermal acantholysis, keratinocyte necrosis and vacuolar interface dermatitis
3. DIF observation of immunoreactants
4. IIF serum autoantibodies binding to cell surface of skin and mucosa
5. Immunoprecipitation of a complex of 4 proteins:
   - Desmoplakin 1 and 11
   - BPAG 1
   - Periplakin

Differential diagnosis:

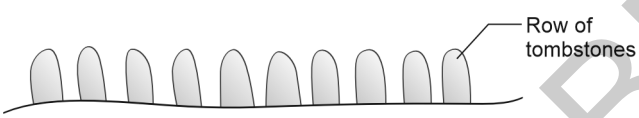
- Erythema Multiforme
- Pemphigus vulgaris
- cicatricial pemphigoid
- TEN/SJS
- LP
- Lichen planus pemphigoides
- Persistent Heroes Simplex
- GVHD

Prognosis:

- Remission after tumor resection
- Fatality rate: 90%
- Cause: Sepsis and respiratory failure

Treatment:
- Tumor excision
- Chemotherapy
- Oral corticosteroids
- Cyclophosphamide, Cyclosporine, MMF, Rituximab
- IV immunoglobulins
- Plasmapheresis
- Dapsone

Bedside tests and Investigations:
1. Nikolsky's sign
   - Positive
   - Direct/microscopic
   - Bulla spread sign/Lutz sign—angulated
   - Sheklakov sign positive
   - Tzanck smear—acantholytic cells
   - Skin biopsy
- Pemphigus vulgaris:
  - Suprabasal split with acantholytic cells in cavity
  - Basal layer keratinocytes lose adhesion with adjacent keratinocytes but remain attached at basement membrane



  - Erosion causes loss of upper epidermis
- Pemphigus vegetans
  - Suprabasal cleft
  - Papillomatosis and acanthosis
  - Occasional intraepidermal eosinophilic abscesses
- Pemphigus foliaceus/erythematosus
  - Superficial cleft usually beneath the granular layer
  - May develop into a bulla with acantholysis
  - Old: acantholysis, HK (hyperkeratosis), and papillomatosis
- Pemphigus herpetiformis
  - Eosinophilic spongiosis with slight or no acantholysis
  - Subcorneal pustules with neutrophils and eosinophils
- IgA pemphigus:
  - Intraepidermal pustules or blisters; subcorneal in SCPD, suprabasal in IEN type
  - Neutrophilic infiltration significant

6. DIF
   - High sensitivity early in disease
   - IgG antibodies seen in intercellular spaces—"fish net" or "chicken wire" appearance
   - PV: Intercellular space
   - PF: Superficial epidermis
   - PE: DEJ (dermo-epidermal junction)
   - IgA pemphigus: Upper/lower epidermis
   - PNP: Within epidermis & BM (basement membrane)
7. IIF
- Detects circulating IgG
- PV & PF react with upper and lower layers of substrate
8. ELISA
- High sensitivity and specificity for PV diagnosis
- Anti-Dsg 1 and 3 titers = disease activity
9. Immuno-electron microscopy
   - Detects location of antibody and complement deposits in the epidermis.

Treatment of pemphigus

1. Initial Therapy
   - Systemic corticosteroids
   - Prednisone: 1.5 mg/kg/day (alternative: dexamethasone)
   - Immunosuppressants
   - Azathioprine: 1–3 mg/kg/day
   - Mycophenolate mofetil: 2–3 g/day
   - Cyclophosphamide: 1–2 mg/kg/day
   - Methotrexate
   - Cyclosporine
2. Adjuvants
   - Rituximab (monoclonal antibody targeting CD20 cells)
   - IV Immunoglobulins: 2 g/kg over 3–5 days
   - Plasmapheresis
3. Maintenance
   - Corticosteroids → tapered
   - Immunosuppressants
   - Rituximab infusions
4. Topical
   - Topical corticosteroids and antibiotics
   - Antiseptic mouthwashes (for oral lesions)
   - Topical anesthetics
5. Newer and Advanced Therapies
   - DCP (Dexamethasone-Cyclophosphamide Pulse Therapy) and other pulses
   - Belimumab
   - Ibrutinib (Tyrosine kinase inhibitor)
   - Tocilizumab (IL-6 inhibitor)
   - Tofacitinib (JAK inhibitor)
   - Secukinumab (IL-17 inhibitor)
   - AHSCT (autologous hematopoietic stem cell transplantation)

Q6. Comment on the role of diet in pemphigus.

Ans.

Introduction: pemphigus vulgaris is a severe autoimmune blistering disorder characterized by the presence of painful blisters and erosions on skin and mucosa.

Several substances have been identified that can induce pemphigus. These substances are found in various foods and can trigger the disease through different mechanisms.

- Vegetables:
  Garlic, onion, mustard, turnip, broccoli, radish, cabbage, cauliflower, potato, leek, shallots, chives, tomato, ginger
- Fruits and nuts:
  Mango, raspberry, pistachio, avocado, cherry, cashew, banana, cranberry, pear, walnuts
- Masticatories and stimulants:
  Coffee, tea, betel leaf, cassava
- Beverages:
  Beer, wine, soft drinks
- Others:
  Ice cream, candy, baked foods, red chilies, sodium benzoate (preservative), coloring agents, tartrazine, nutritional supplements
- Water: High tannin content in river water (Brazil)—Fogo selvagem

Mechanism of induction of pemphigus:

- Thiols—compounds in garlic (allylmercaptan, allyl-methylsulfide, allylsulfide) induce acantholysis in vitro
- Isothiocyanates—present in mustard oil may be immunologically reactive
- Phenols:
  - Found in plants from toxicodendron family
  - Urushiol may trigger acantholysis
  - Found in mangoes, pistachios, cashew, aspartame and food additives
- Tannins:
  - These polyphenolic compounds can induce acantholysis, which can be blocked by anti-IL-1 alpha and anti-TNF alpha antibodies
  - Seen in various beverages, fruits and spices.

Management:

- Counseling patient to avoid these foods
- Monitoring
- Diet chart

Q7. Discuss pulse therapy in pemphigus.

Ans.

Introduction: Pulse therapy is a treatment approach where high doses of medications are administered intermittently to control severe, autoimmune diseases such as pemphigus.

GOAL: Achieve rapid disease control while minimizing long term side effects associated with continuous high dose therapy.

Types

- DCP therapy
- Methyl prednisolone therapy
- Dexamethasone therapy
- Rituximab therapy
- Methotrexate pulse
- Cyclophosphamide pulse

DCP pulse therapy

Dexamethasone cyclophosphamide pulse therapy was first introduced in management of pemphigus vulgaris by Dr Pasricha in 1984.

Advantages

- Faster healing
- Faster control of disease activity
- Reduction in total cumulative steroid dose
- Long term cure with minimal steroid side effects

Mechanism of action

Dexamethasone—causes shift of Th towards Th2—which decreases CD3, CD4 T-cell phenotypes that recover in 7 days

Cyclophosphamide—maximum suppression of B cells and moderate suppression of CD3 cells and NK cells that recover in 2–4 months

Phases

Phase 1: Monthly dose of 100 mg dexamethasone dissolved in 500 ml of 5% dextrose and given as slow IV infusion for 3 consecutive days, day 2: add 500 mg of cyclophosphamide in infusion.

In between 50 mg of daily oral cyclophosphamide, till no new lesions appear.

Phase 2: Patients on monthly DCP for 9 months

Phase 3: Only oral cyclophosphamide for 9 months

Phase 4: Drug free, disease free period. Follow up once a year for 10 years

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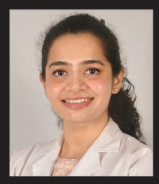

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