Patterns and mechanisms of inflammatory skin conditions: the pathologist's survival kit

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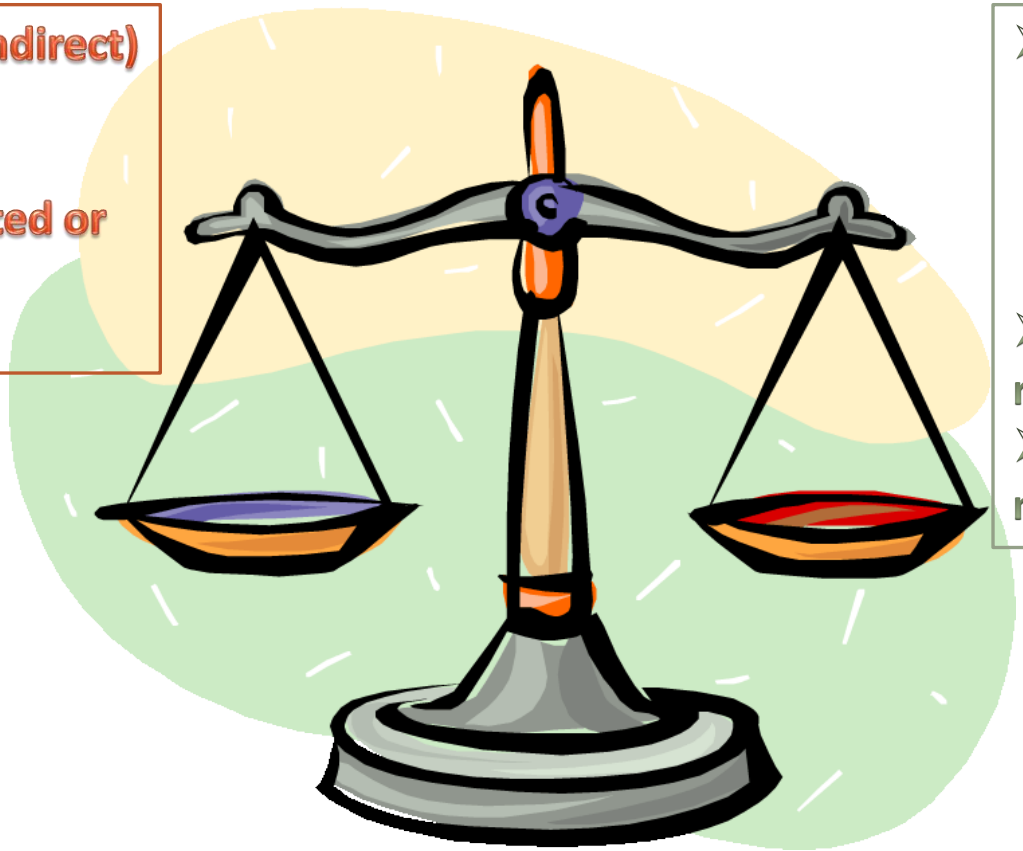
BAHRAIN, APRIL 2017

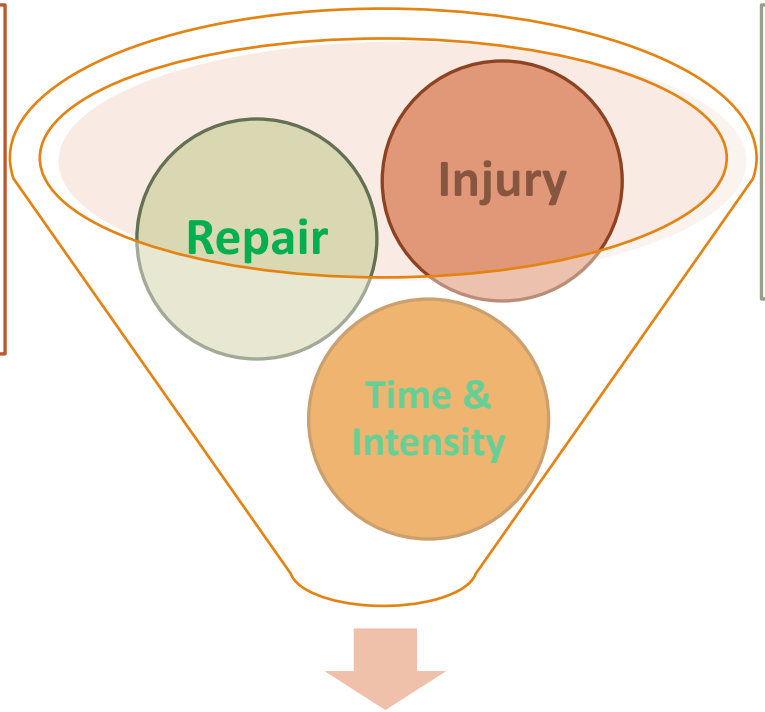
Basic Elements of Lesions

- Toxic (Direct/Indirect)
- Vascular
- Inflammatory (immune-mediated or not)
- Trophic



- Inflammation
  - Vascular component
  - Cellular component
- Regeneration/ reparation
- Intracellular mechanisms

- Toxic (Direct/Indirect)
- Vascular
- Inflammatory (immune-mediated or not)
- Trophic



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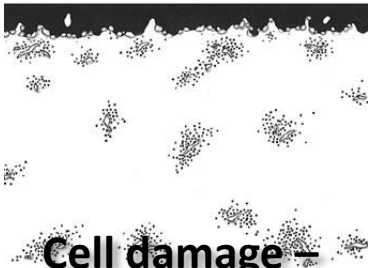
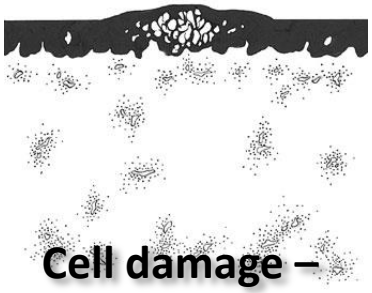
Patterns

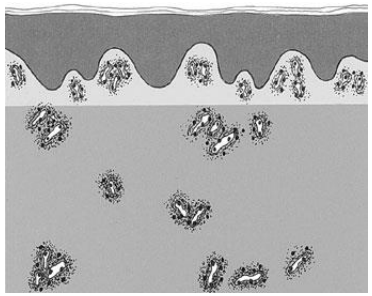


Cell damage – oncosis

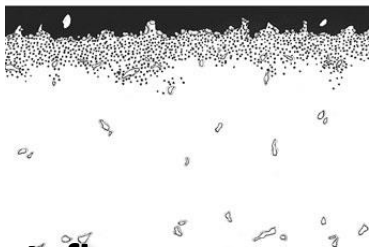
Hyperplastic reaction



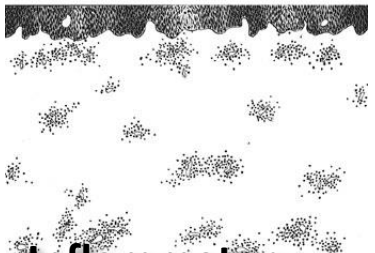
Cell damage – cytopathic



Combined



Inflammatory – cellular



Inflammatory – Extracellular/vascular

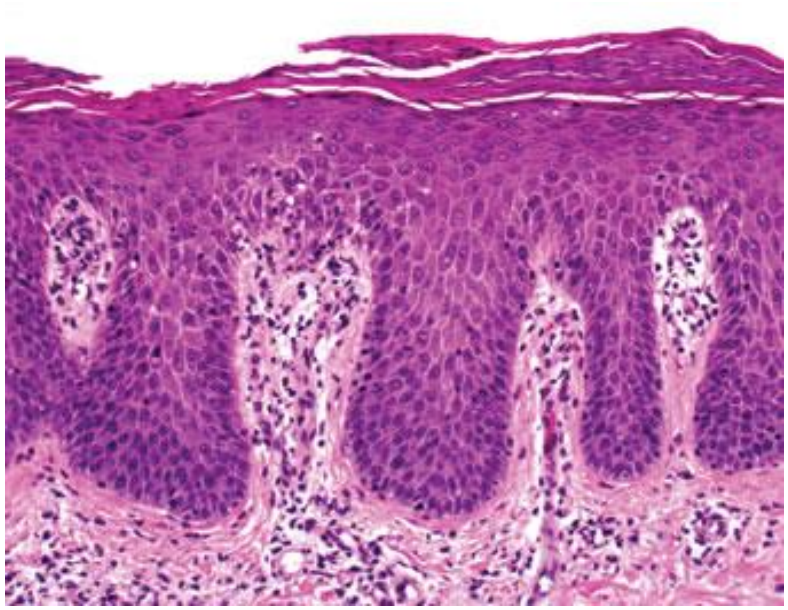
Biological Basis of Elementary Lesions

- **Cellular response**
  - **Cell perpetuation pathway**
  - **Cell differentiation pathway**
  - **Activation of “default” pathway – cell death**
- **Tissue effects**
  - **Parenchyma and stroma interactions**
- **Combination of findings depending on the primary damage target**

Biological Processes and Pathology

Primary Biological Process	General Pathology
Increased keratinocyte turnover	Hyperplastic changes Lack of full cell differentiation Relative increase of cell loss
Decreased keratinocyte turnover	Relative atrophy Full cell differentiation Decreased cell loss
Inflammation	Vascular changes and permeability Cellular infiltrate Cell damage (stroma, vessels, epithelia)
Cell damage	Reversible Irreversible Regeneration and reparation

Psoriasiform Acanthosis



Dermatophytosis

Psoriasis

Seborrheic dermatitis

Allergic contact / nummular dermatitis

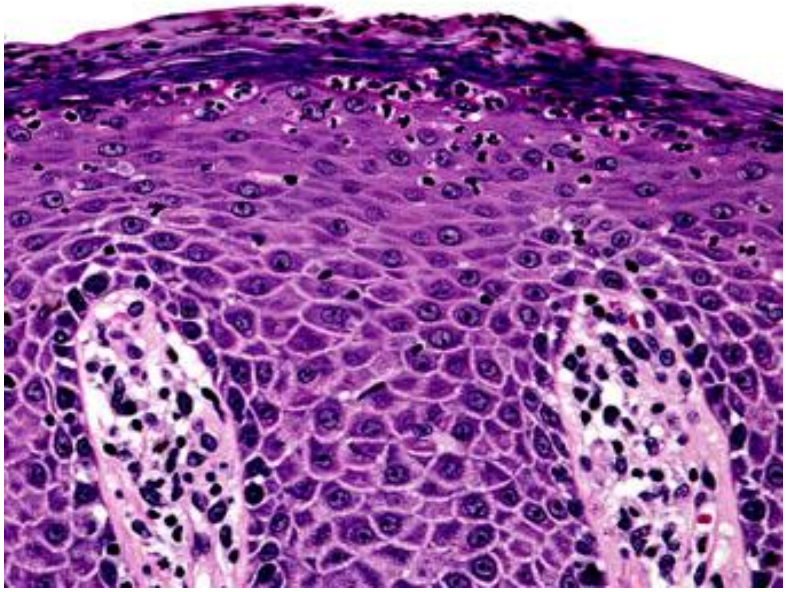
PRP

Secondary syphilis

Scabies, Norwegian type

MF

Psoriasiform Dermatitis

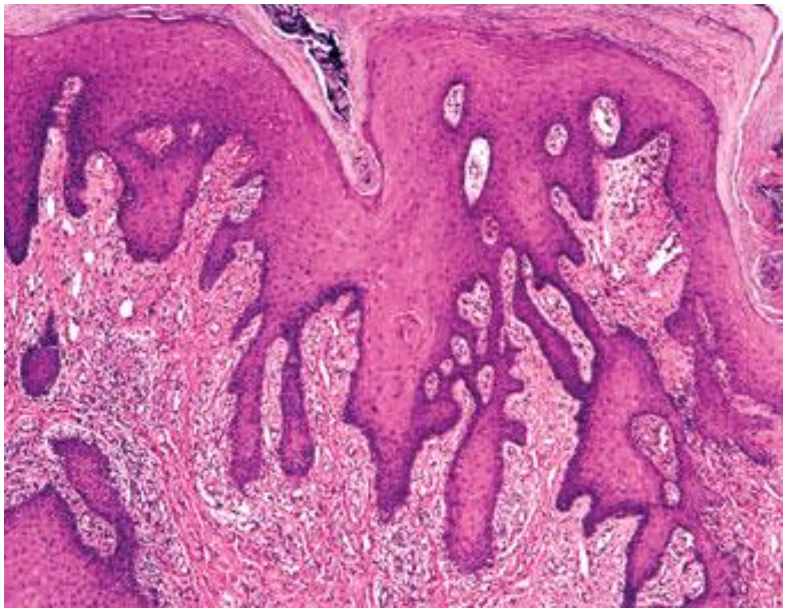


Neutrophils within parakeratosis

Superficial perivascular dermatitis

Psoriasis

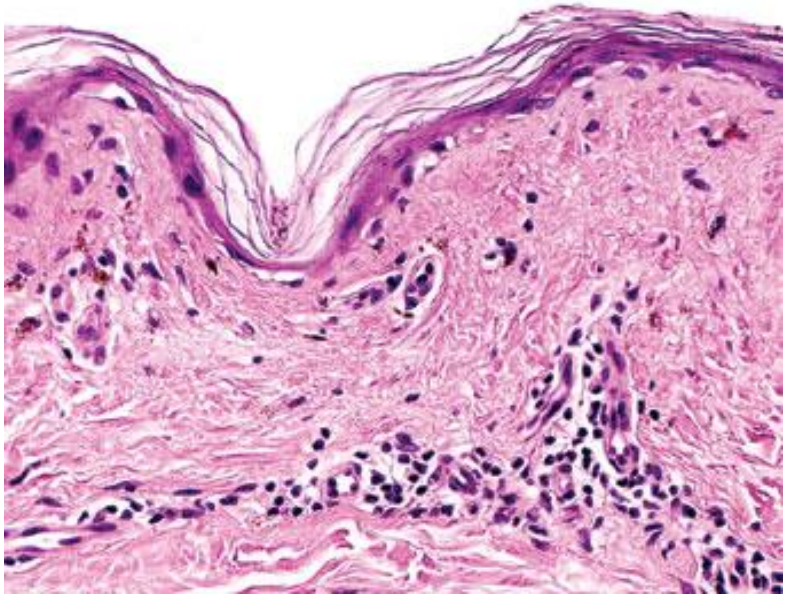
Irregular Epidermal Hyperplasia



Pseudoepitheliomatous hyperplasia
Suppurative granulomatous dermatitis

Deep mycosis, atypical mycobacterias

Markedly Thinned Epidermis



Dermatomyositis/DLE

DLE

GVHD

LP, atrophic

LP-like keratosis

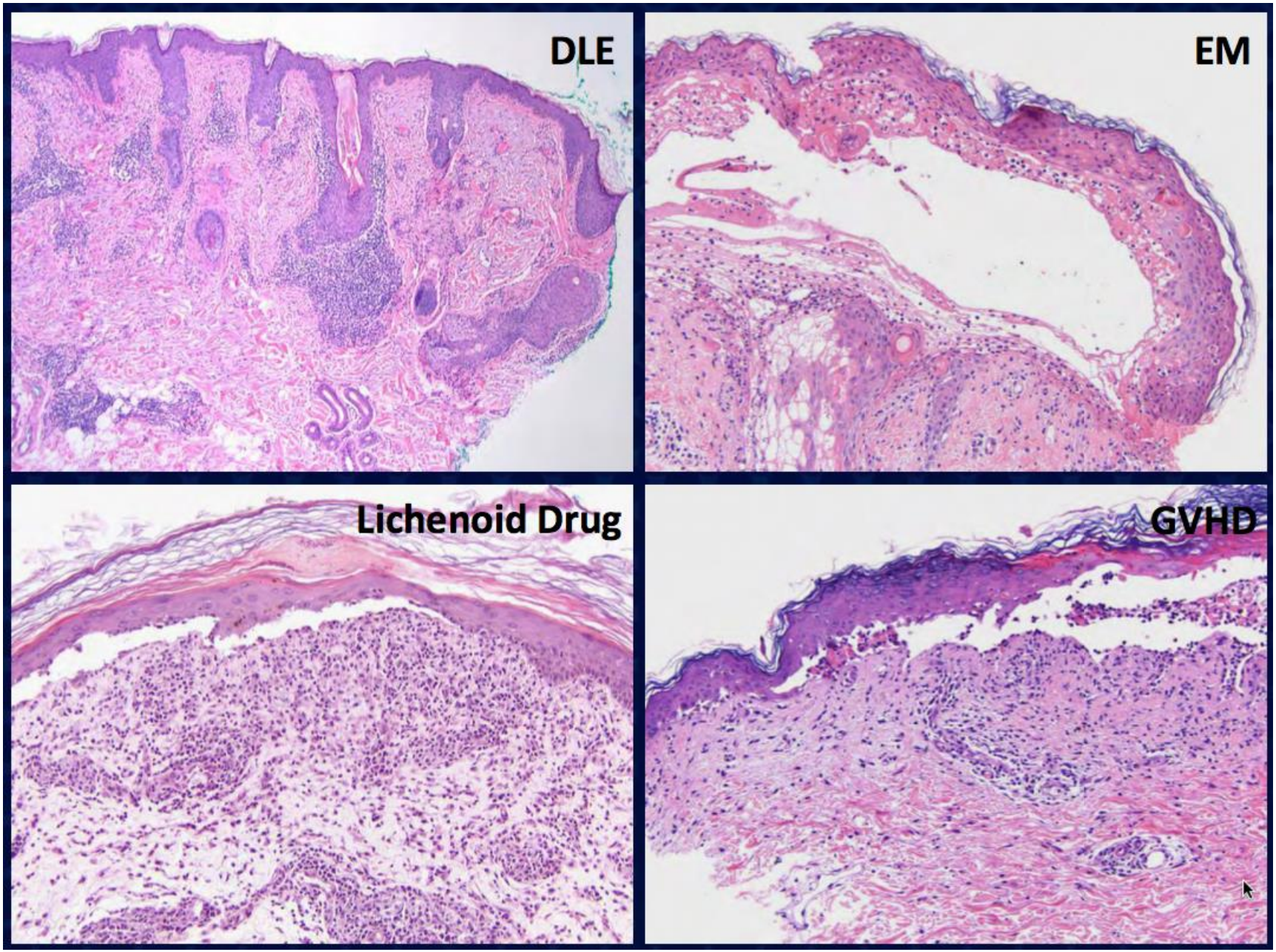
Porokeratosis

Lichen sclerosus

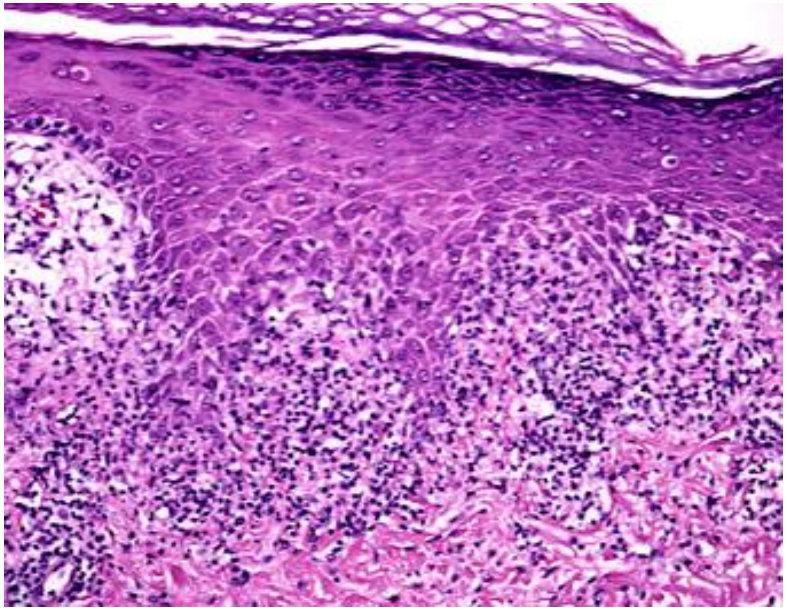
Degos' disease

Interface Dermatitis

- **Leukocyte infiltration of the dermis**
- **Vacuolar change of basilar epidermis**
- **Papillary dermal melanophages**
- **Necrosis of keratinocytes**
- **AKA: lichenoid tissue reaction pattern, vacuolar interface dermatitis**


DLE
EM
Lichenoid Drug
GVHD

Lichenoid Interface Dermatitis

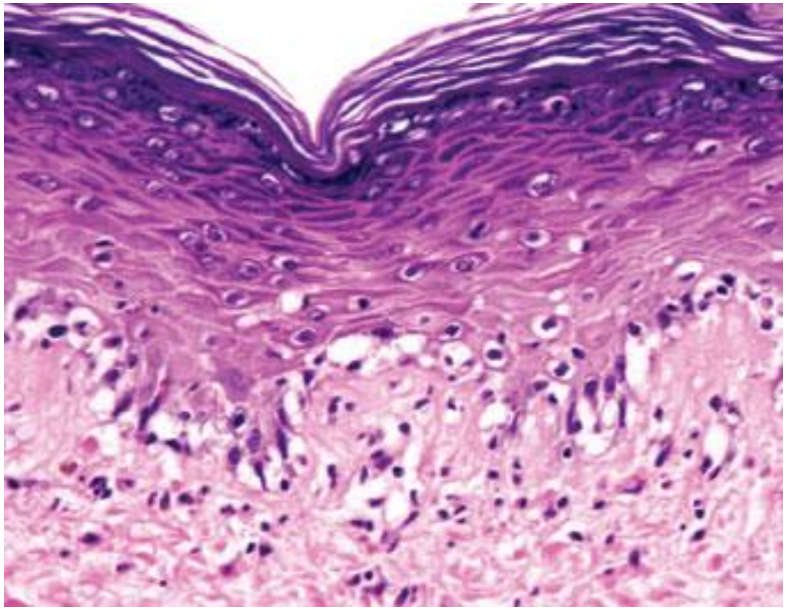


Wedge-shaped hypergranulosis

Lichenoid infiltrate

Lichen planus

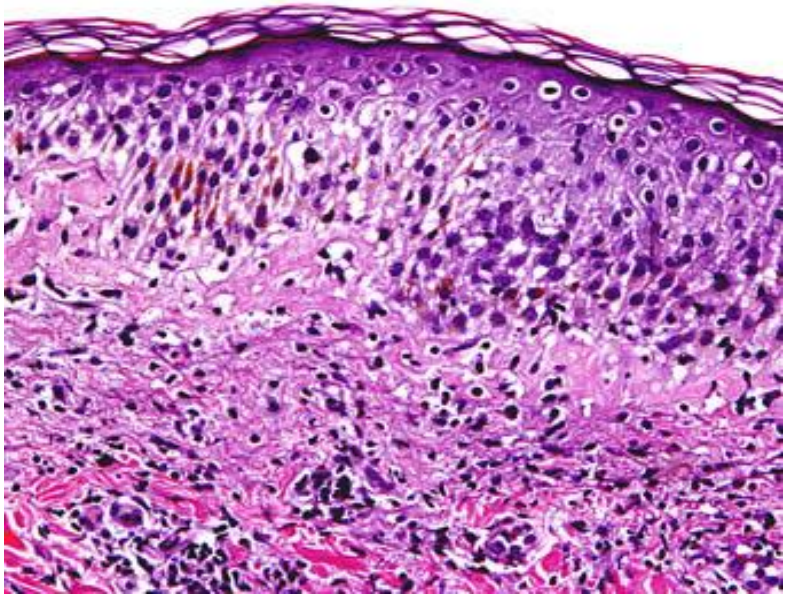
Vacuolar Interface Dermatitis



Necrotic keratinocytes
Vacuolar alteration
Lichenoid inflammation
Superficial perivascular lymphohistiocytic

Erythema Multiforme

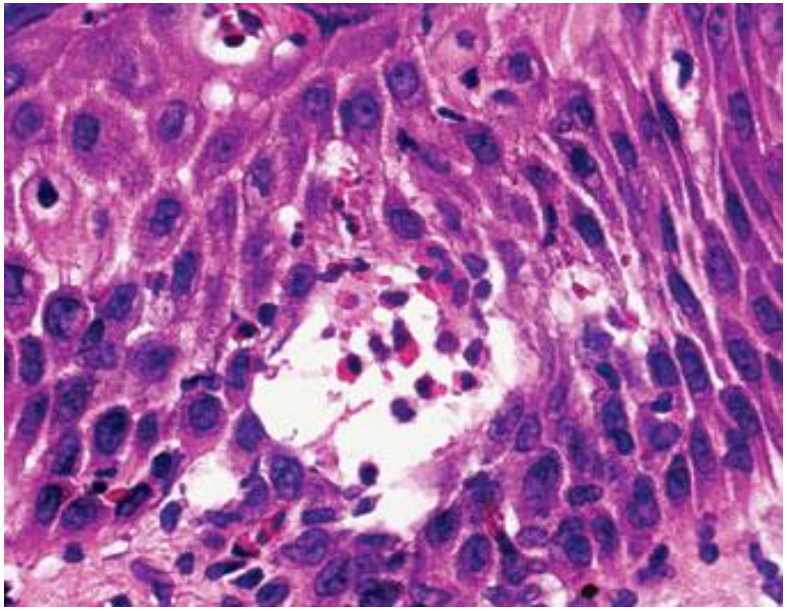
Spongiotic Dermatitis



Spongiosis around acrosyringia

Miliaria rubra

Eosinophilic Spongiosis



BP/HG, urticarial

Allergic dermatitis

Pemphigus vulgaris, urticarial

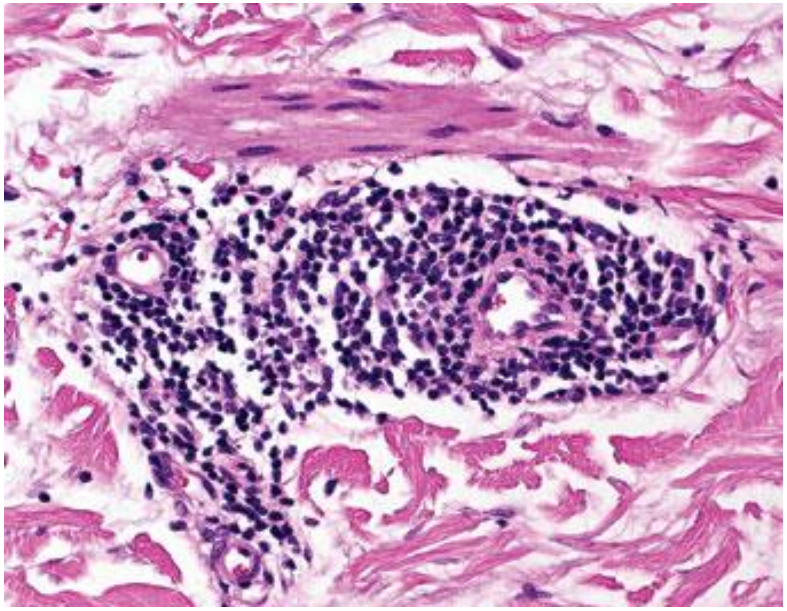
Arthropod assault

Dermatophytosis

Incontinentia pigmenti, vesicular

Toxic erythema of newborn

Lymphocytic Infiltrate



DLE, tumid

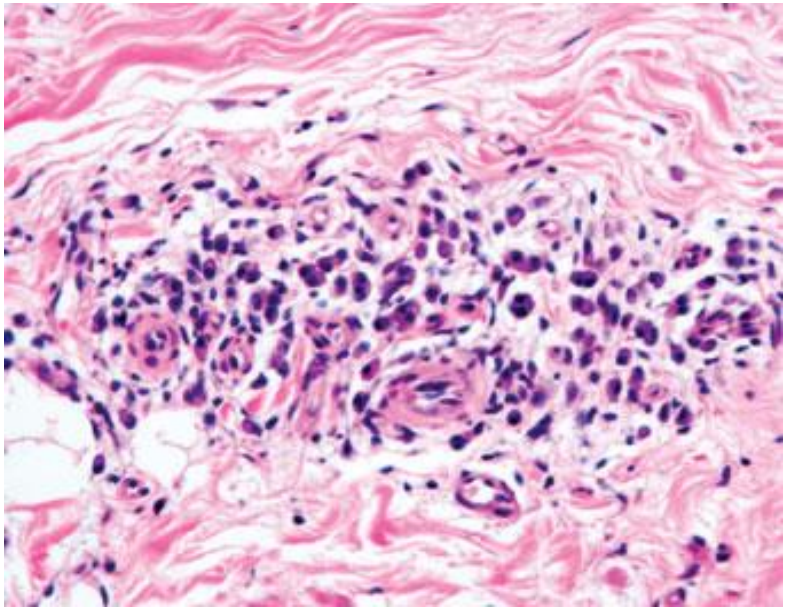
Pernio

PLE

Insect bite

Erythema figuratum

Perivascular Lympho-plasmacytic Infiltrate



Acrodermatitis chronica atrophicans

Erythema chronicum migrans

Secondary syphilis

Necrobiosis lipoidica

Morphea

Exocytosis vs. Epidermotropism

EXOCYTOSIS	EPIDERMOTROPISM
Random through epidermis to surface	Lower third/half epidermis
Spongiotic tissue reaction	Tendency to aggregate
Inflammatory processes	No/little spongiosis
	Feature of MF

Superficial and Deep Inflammation

Light reaction

Lymphoma

Leprosy

Lues

Lichen striatus

Lupus erythematosus

Lipoidica (necrobiosis)

Lepidoptera (+ other arthropods)

Dermatophyte

Reticular erythematous mucinosis

Urticarial stages (BP)

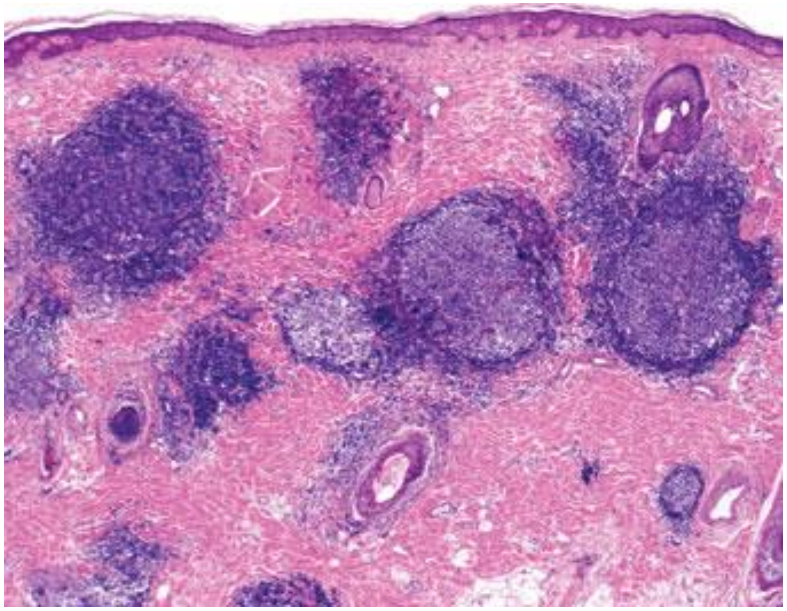
Gyrate erythemas

Scleroderma (localized)

Drug reactions

8Ls + DRUGS

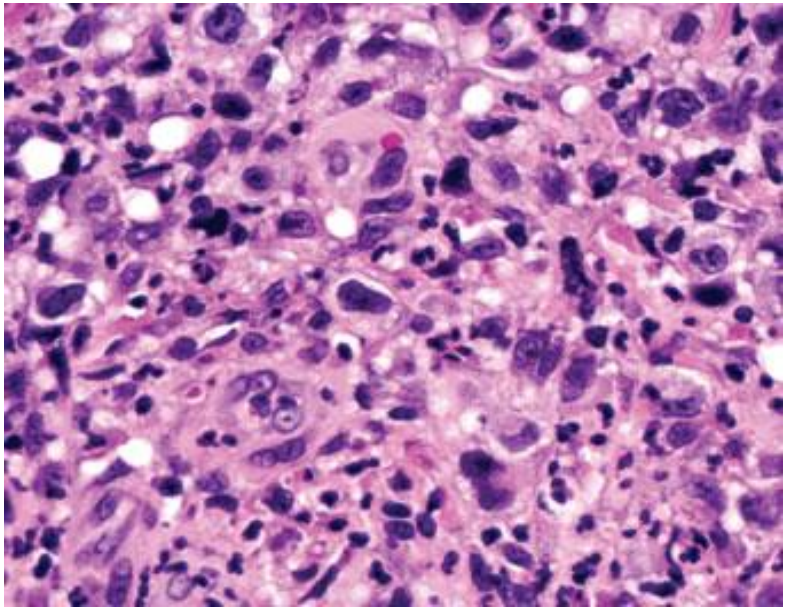
Nodular Dermatitis



Germinal centers in a dense nodular or diffuse infiltrate

Delayed hypsersensitivity reaction

Abnormal Lymphocytes in Mixed Cell Infiltrate



Tick bite reaction

Herpesvirus

Dermatophytosis

Ruptured molluscum

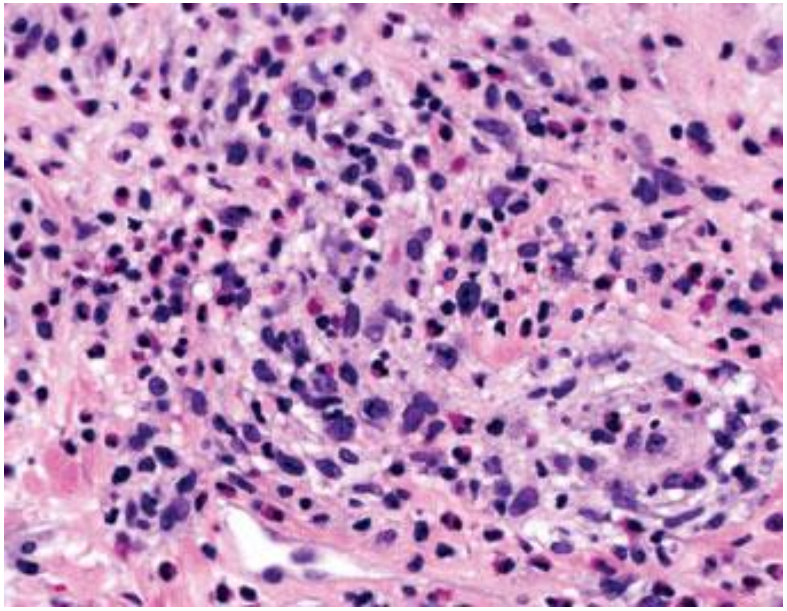
Kikuchi's disease

Gianotti-Crosti

Lymphomatoid papulosis

MF

Dense Mixed Inflammation

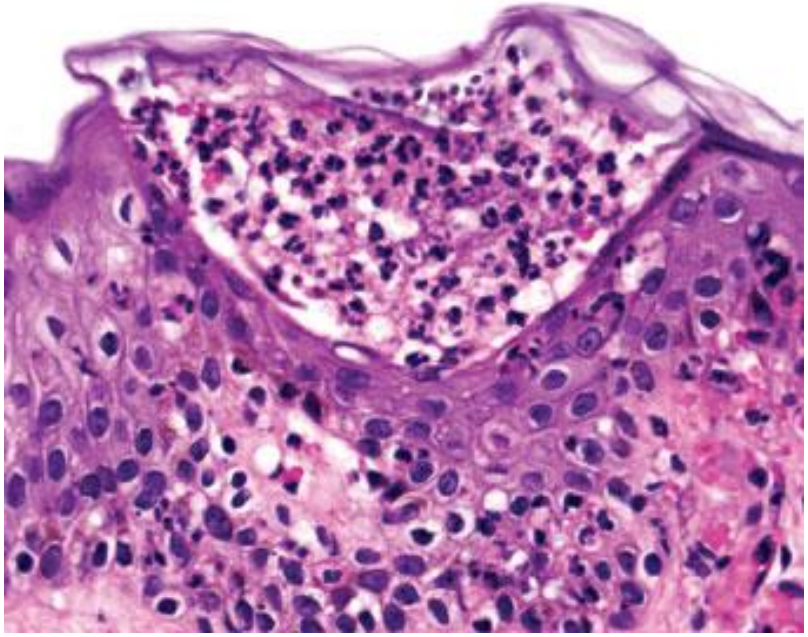


Granuloma faciale / Erythema elevatum diutinum

Nodular scabies

Tick bite reaction

Subcorneal Pustule



Dermatophytosis

Candidiasis

Impetigo

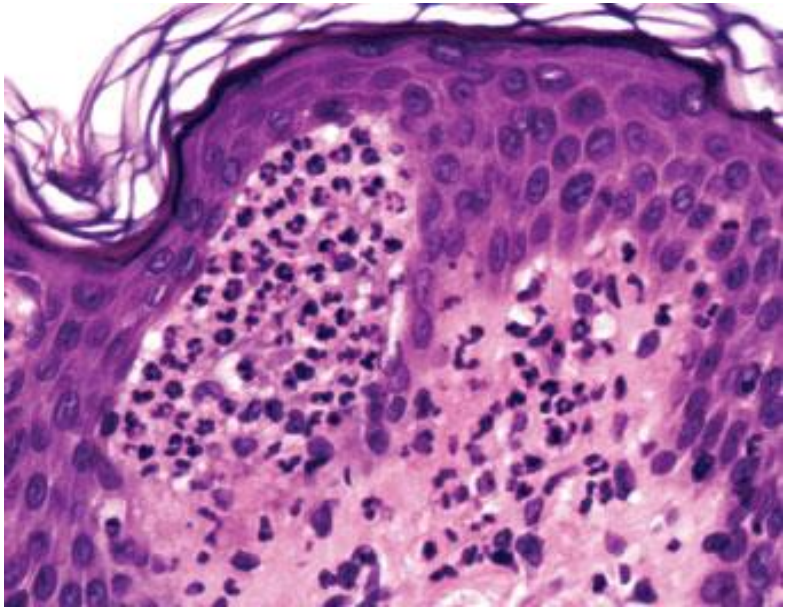
Suppurative infundibulitis

Pemphigus foliaceus

Pustular psoriasis

Prurigo pigmentosa

Papillary Micro-abscesses



DH / linear IgA dermatitis, drug eruptions

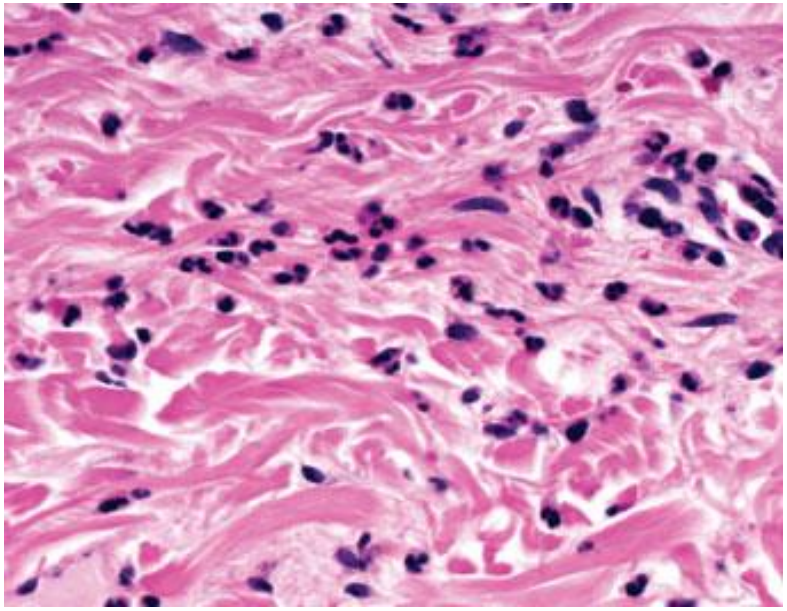
Acquired EB

DLE

Bullous LE

LCC vasculitis

Interstitial Neutrophils in Reticular Dermis



Urticaria

Cutis laxa

DH / linear IgA dermatitis

Bullous LE

Fixed drug eruption

Cellulitis

Flea bite

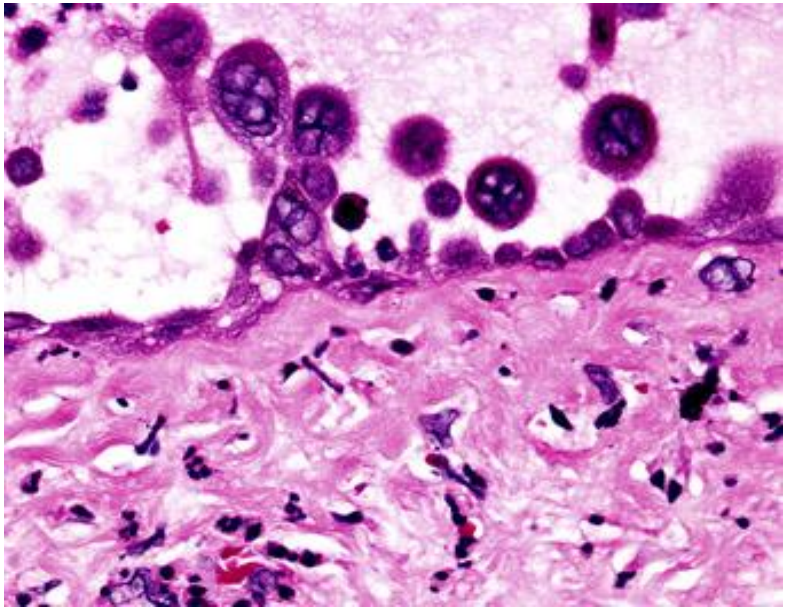
Pustular infundibular dermatitis

LCC vasculitis

Sweet's / PG

Lymphomatoid papulosis

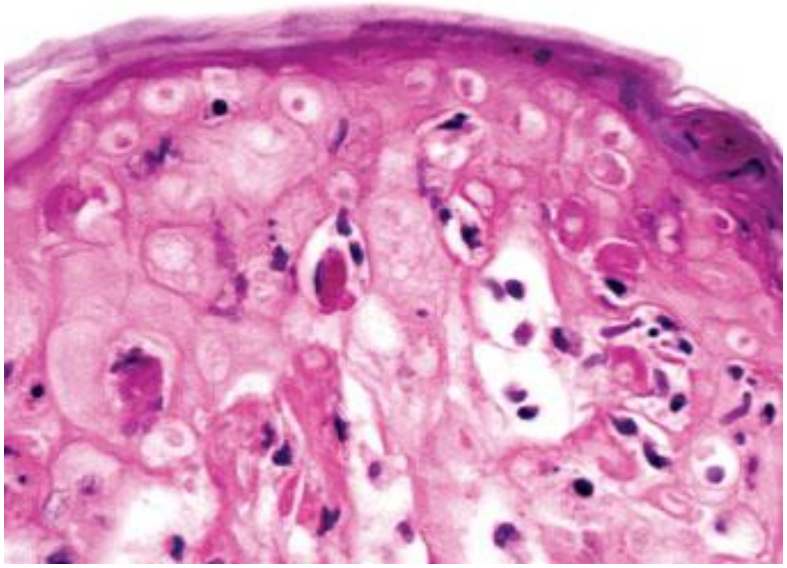
Cytopathic Dermatitis



Acantholytic separation
Multinucleated epithelial giant cells

Herpesvirus infections

Ballooning



EM

Fixed drug eruption

Mucha-Haberman

Prurigo pigmentosa

Hand-foot-mouth disease

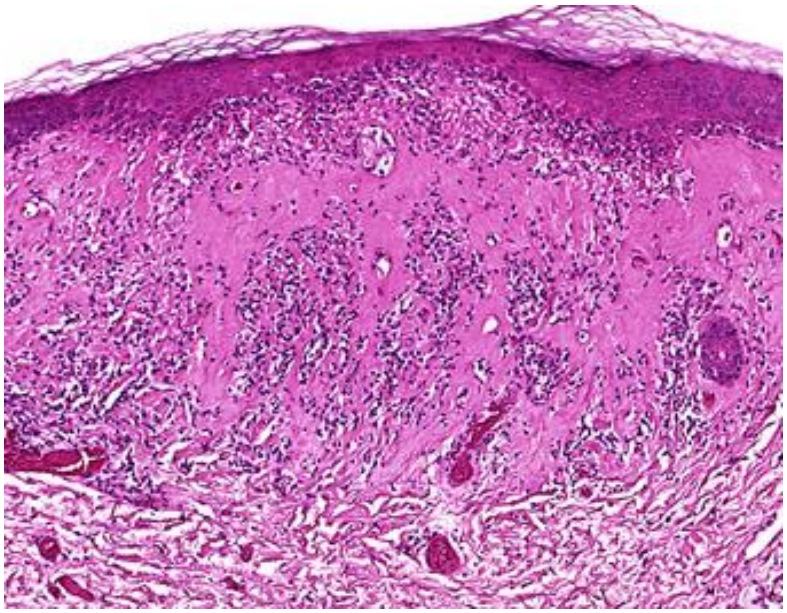
Herpesvirus

Milker's nodule/orf

Irritant contact dermatitis

Burn

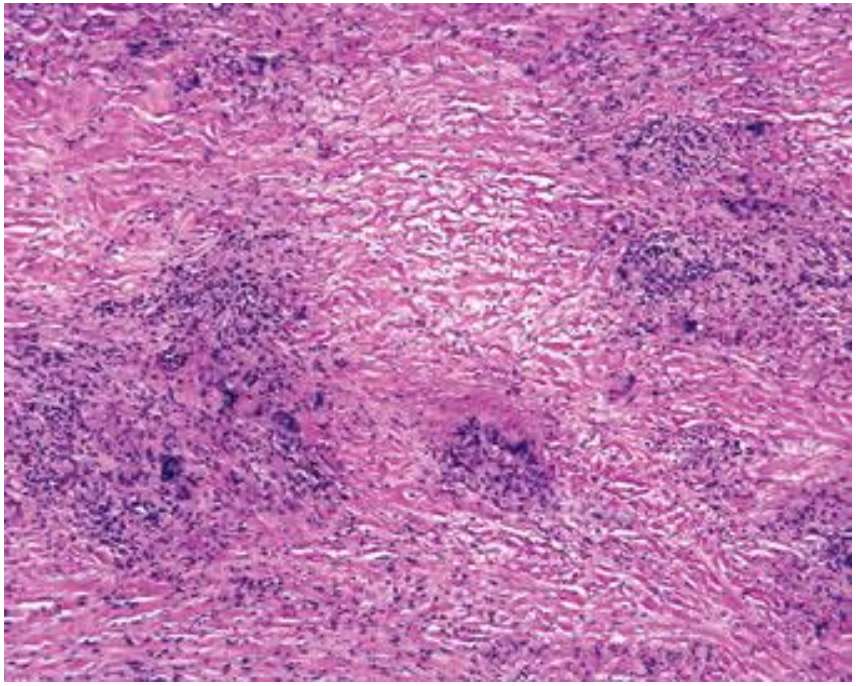
Fibrosing Dermatitis



Thinned epidermis
Thickened edematous / sclerotic papillary dermis
Underlying mononuclear infiltrate

Lichen sclerosus

Fibrosing Dermatitis



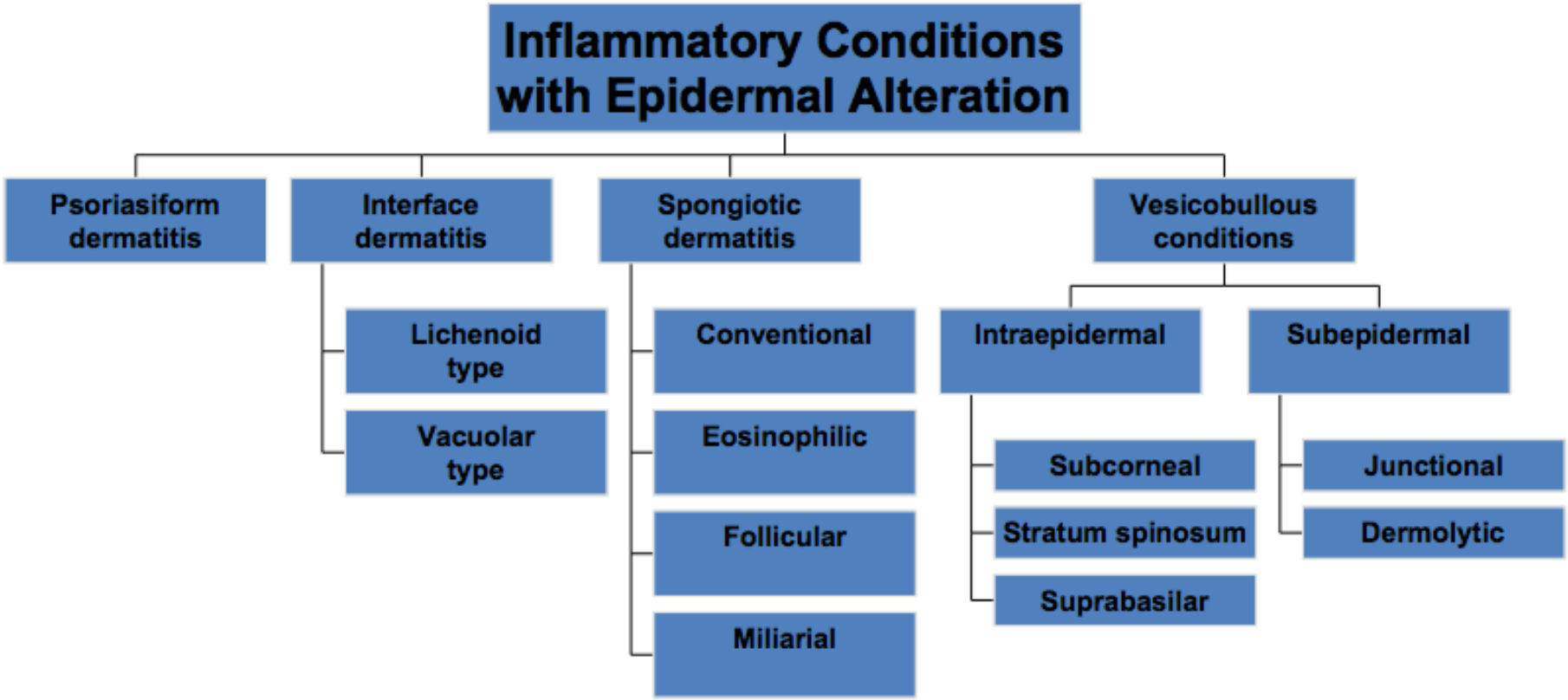
Decreased number of adnexal structures

Fibrosing inflammatory of neoplastic conditions

Elements of Pattern Recognition

- **With/without epidermal changes**
  - **Spongiotic, interface, hyperplastic, atrophic**
- **Distribution of inflammatory infiltrate**
  - **Topography – Superficial vs. superficial & deep**
  - **Microanatomy – Perivascular, interstitial, nodular, diffuse**
- **Type of inflammatory infiltrate**
  - **Mononuclear – Lymphocytes ± histiocytes**
  - **Mixed – Mono- and polymorphonuclear**
  - **Polymorphonuclear ± eosinophils**

Approach to Microscopic Diagnosis

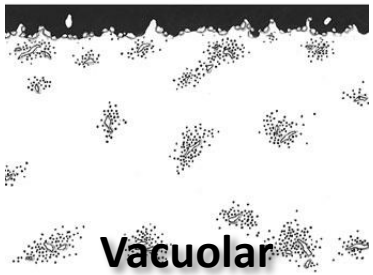


Inflammatory Conditions with Epidermal Alteration

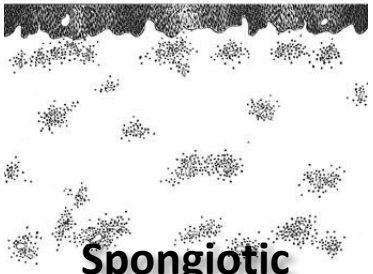
- Psoriasiform dermatitis
- Interface dermatitis
  - Lichenoid type
  - Vacuolar type
- Spongiotic dermatitis
- Vesicobullous conditions
  - Intraepidermal
  - Subepidermal
- Cytopathic Dermatitis

Psoriasiform dermatitis

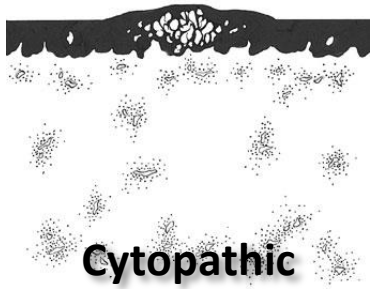
Lichenoid dermatitis



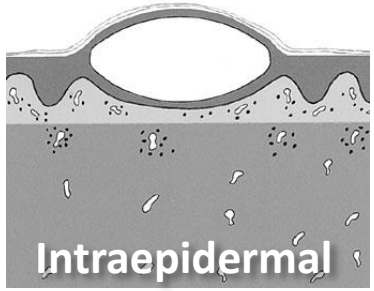
Vacuolar dermatitis



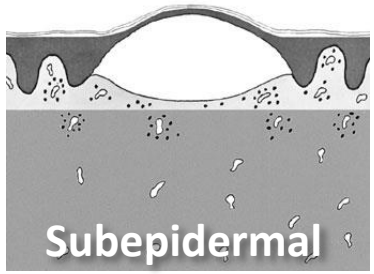
Spongiotic dermatitis



Cytopathic dermatitis

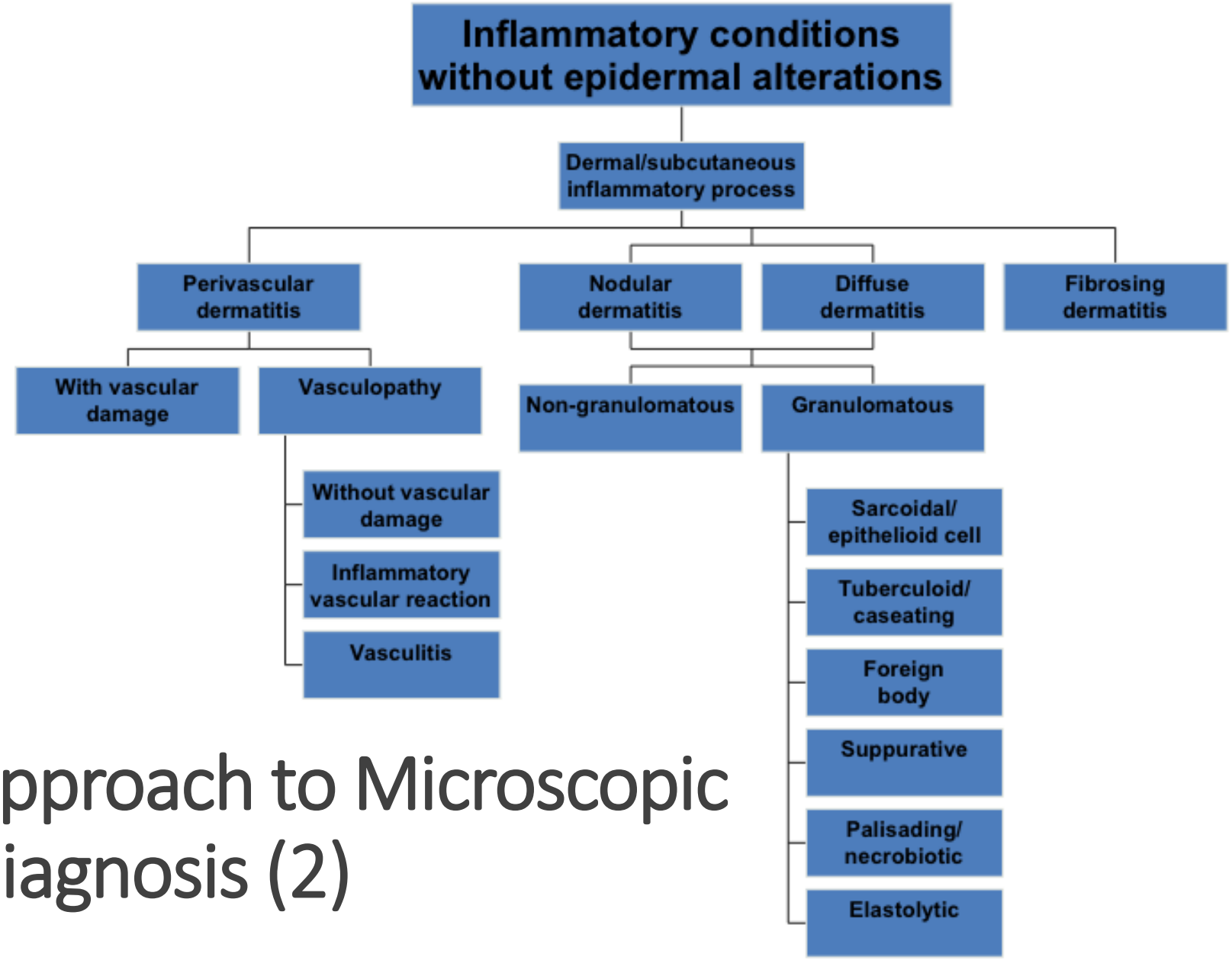


bullous dermatitis



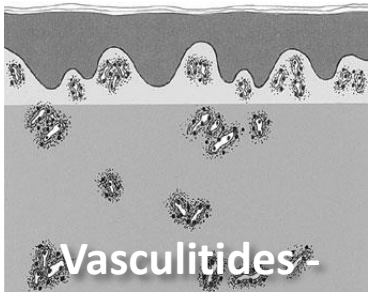
bullous dermatitis

Approach to Microscopic Diagnosis (2)

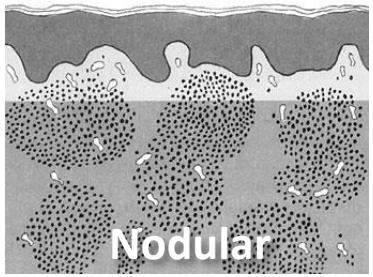


Inflammatory conditions without epidermal alterations

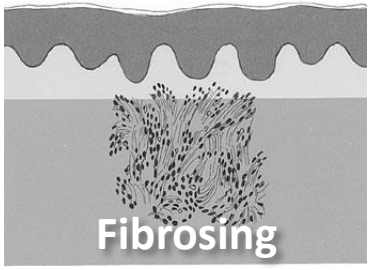
- Dermal/subcutaneous inflammatory process
  - Perivascular dermatitis
    - With vascular damage
    - Vasculopathy
  - Nodular dermatitis
    - Non-granulomatous
    - Granulomatous
  - Diffuse dermatitis
  - Fibrosing dermatitis



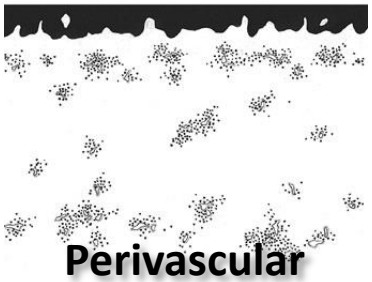
Vasculitides - dermatitis



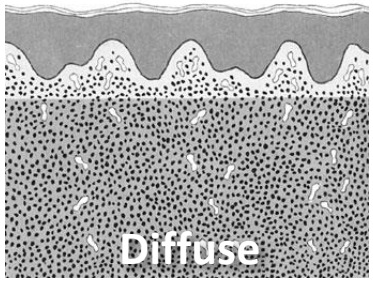
Nodular dermatitis



Fibrosing dermatitis



Perivascular dermatitis



Diffuse dermatitis

Lesions by Topography

Adnexal structures

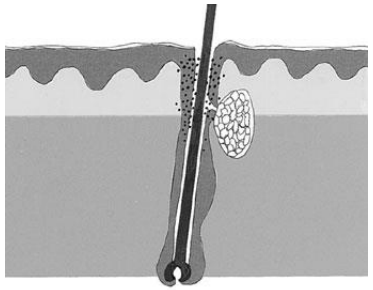
- **Folliculitis and perifolliculitis**
- **Follicular lesions with alopecia**

Subcutaneous soft tissue

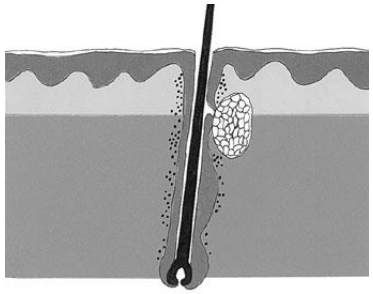
- **Panniculitis**

Inflammatory conditions without epidermal alterations

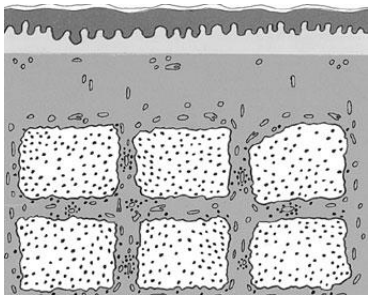
- Dermal/subcutaneous inflammatory process
  - Skin appendages disorders
    - Folliculitis/ perifolliculitis
    - Alopecia
  - Panniculitis/ fasciitis
    - Septal
    - Lobular



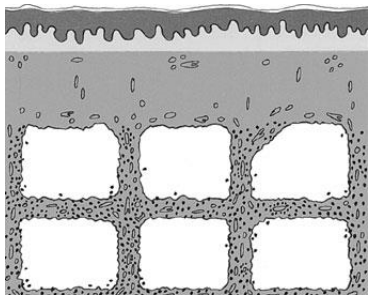
Folliculitis



Perifolliculitis

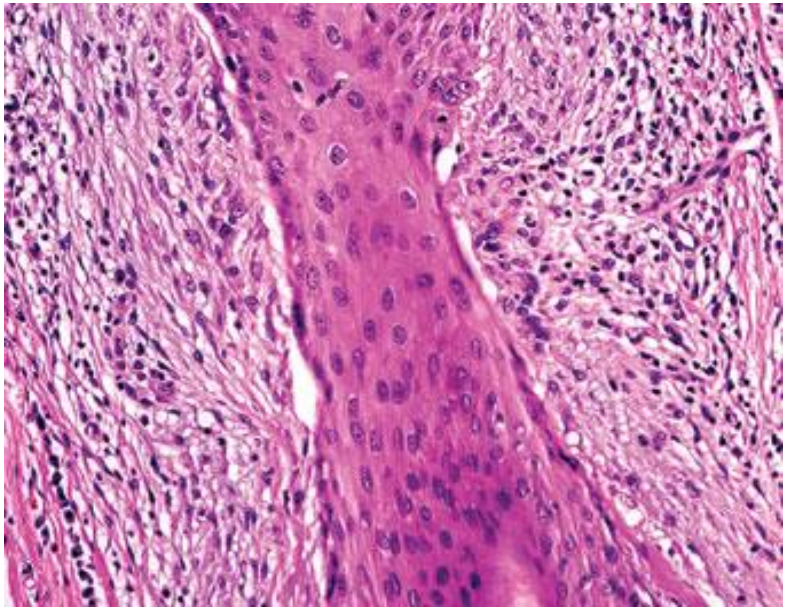


Lobular panniculitis



Septal panniculitis

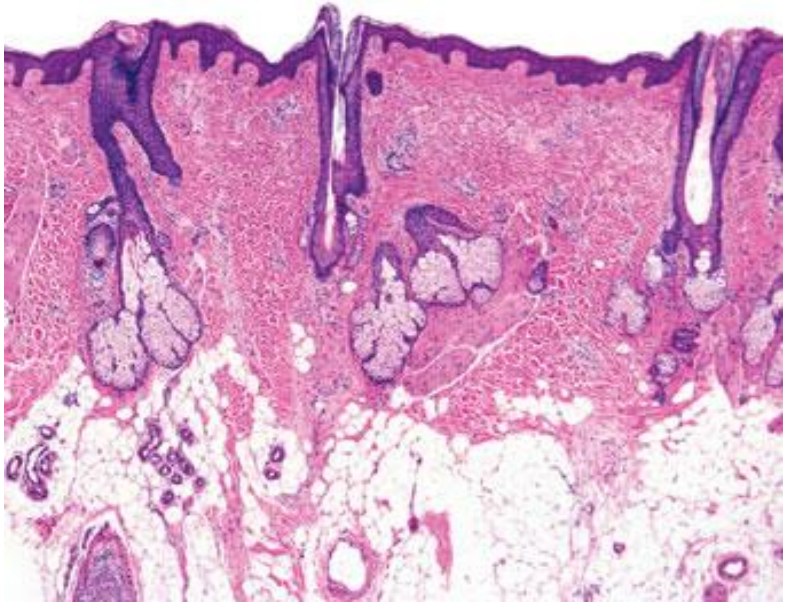
Perifolliculitis



Peri-infundibular and perifollicular fibroplasia

Long-standing perifolliculitis (traction alopecia, LPP)

Non-scarring Alopecia



Catagen or telogen follicles

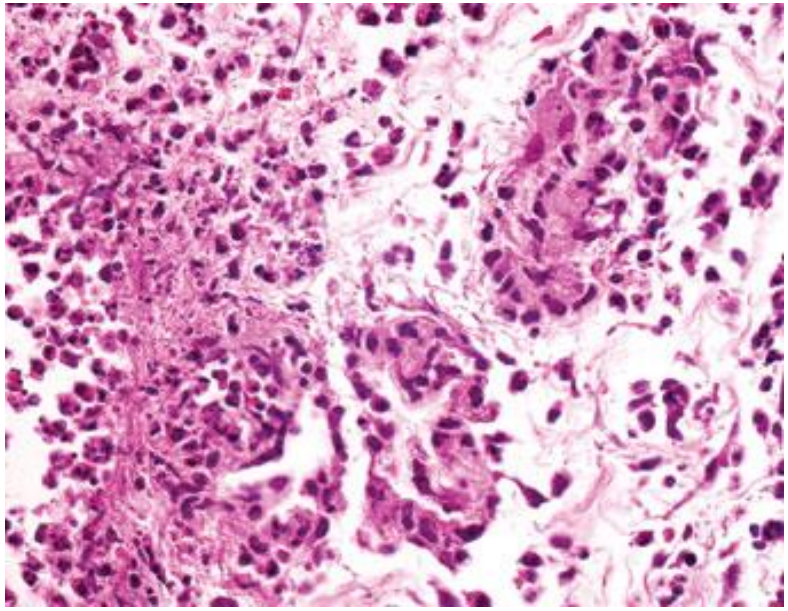
NO inflammatory infiltrate

Other findings:

- **Plucked hair**
- **All telogen hairs**

Common baldness, telogen effluvium, trichotillomania

Mostly Septal Panniculitis

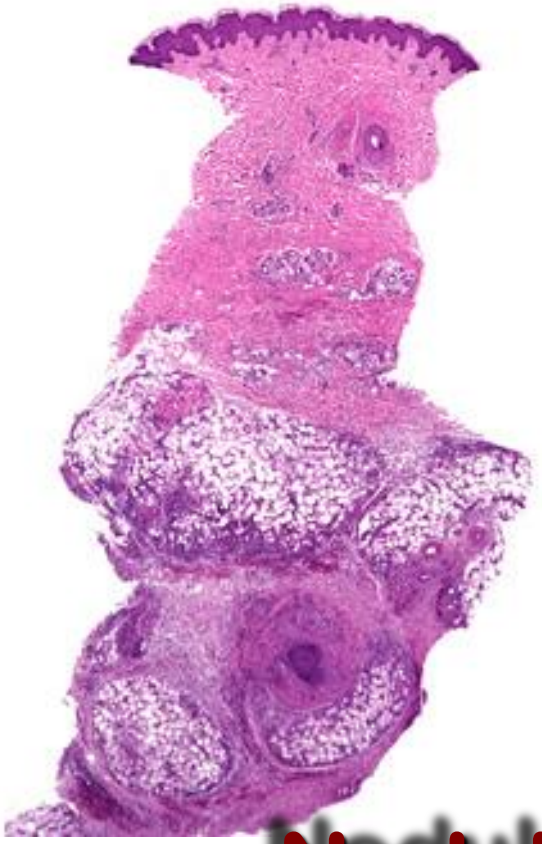


Miescher's radial granuloma

- **Linear spaces containing lipids**
- **Tiny collections of neutrophils**
- **Palisading histiocytes**

Erythema nodosum

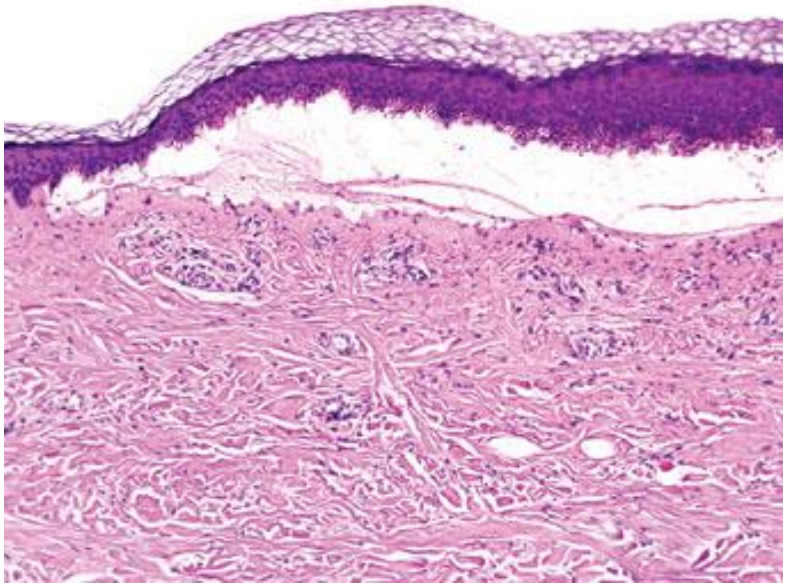
Mostly Lobular Panniculitis



Arteritis
Fat necrosis
Suppuration
Granulomas
Fibrosis

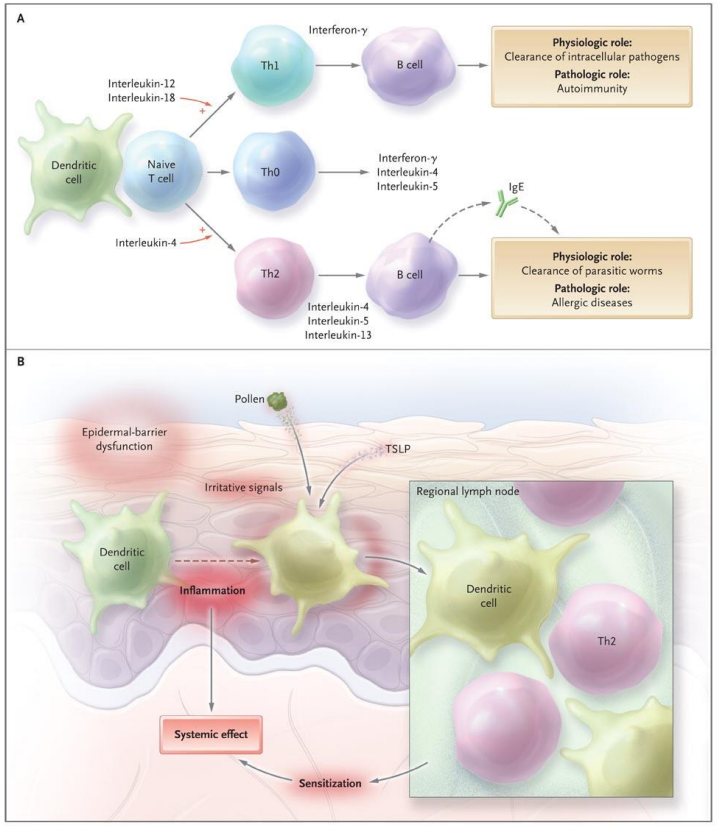
Nodular vasculitis

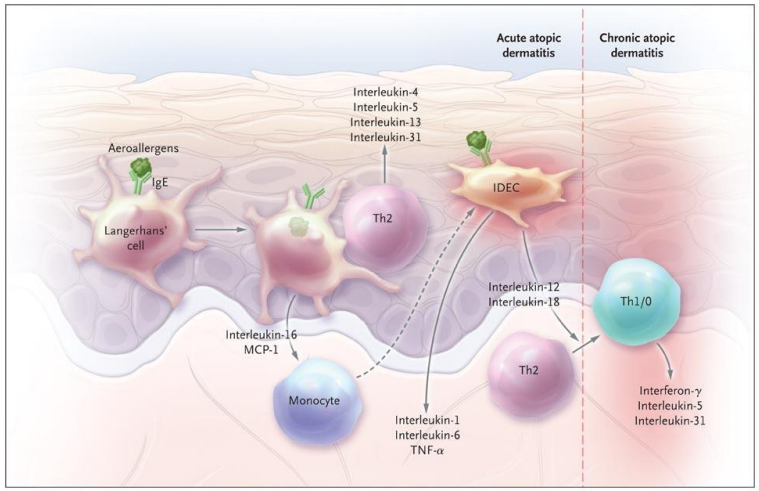
“Cell-Poor” Subepidermal Blister



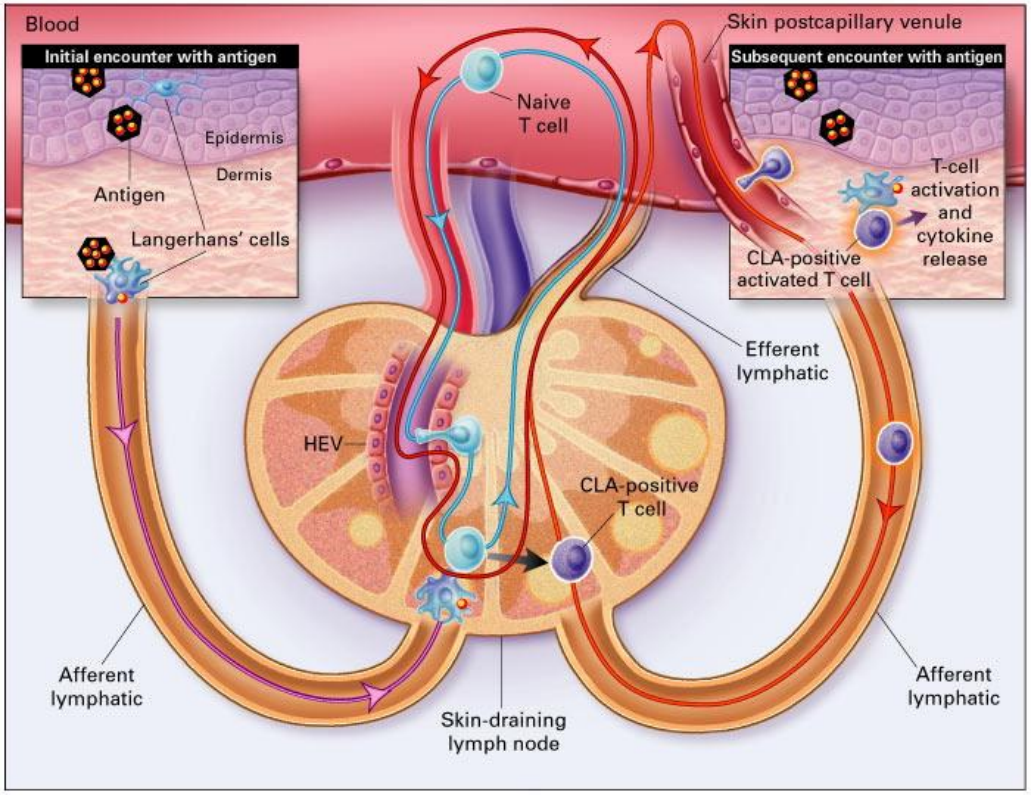
Suction blister
Gas gangrene
Porphyria cutanea tarda
Bullous dermatosis of hemodialysis
Bullous amyloid
Blister above scar
Hypoxemia blister
Electric current
Second-degree burn
Bullous pemphigoid
EB
Darier’s disease, systematized epidermal nevus
Grover’s disease
Porokeratosis
Solar keratosis

Antigen Presentation, Inflammation & Hypersensitivity

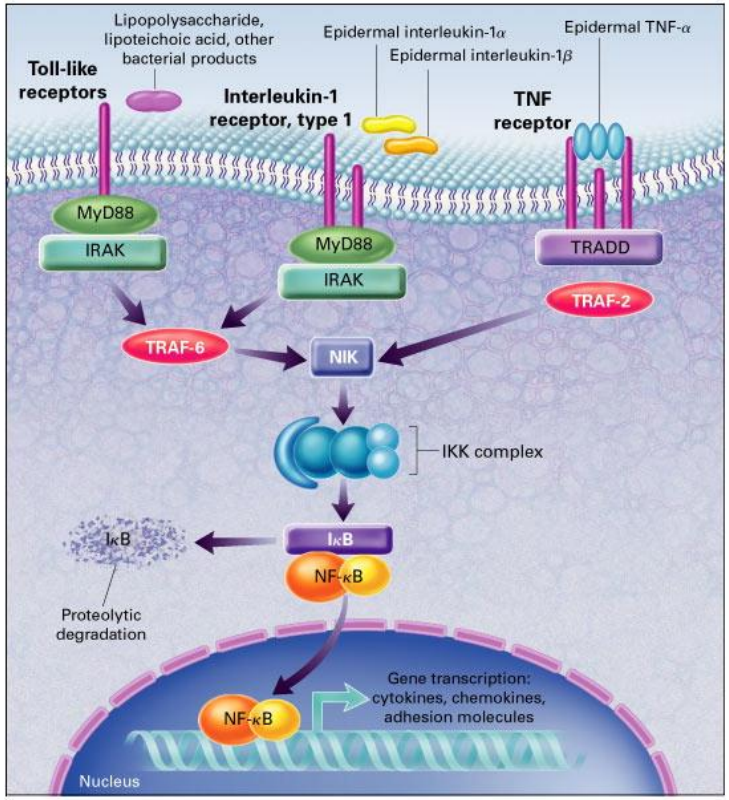


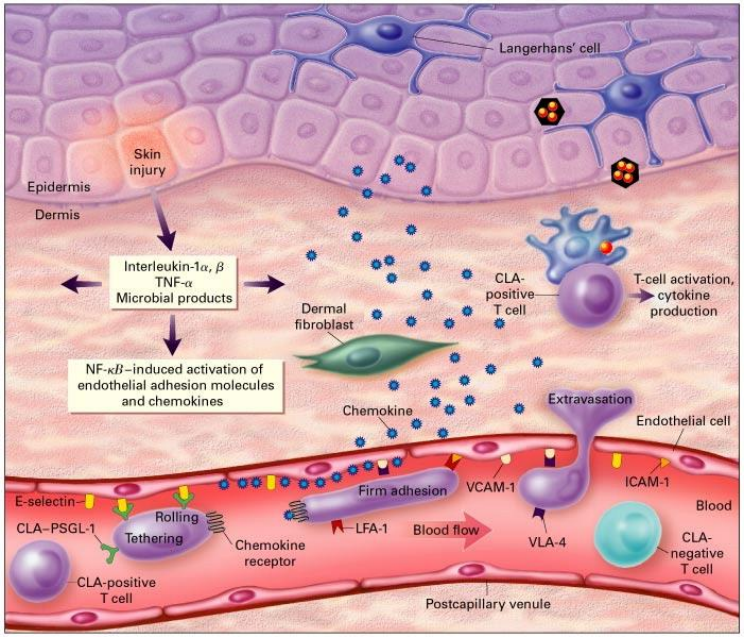


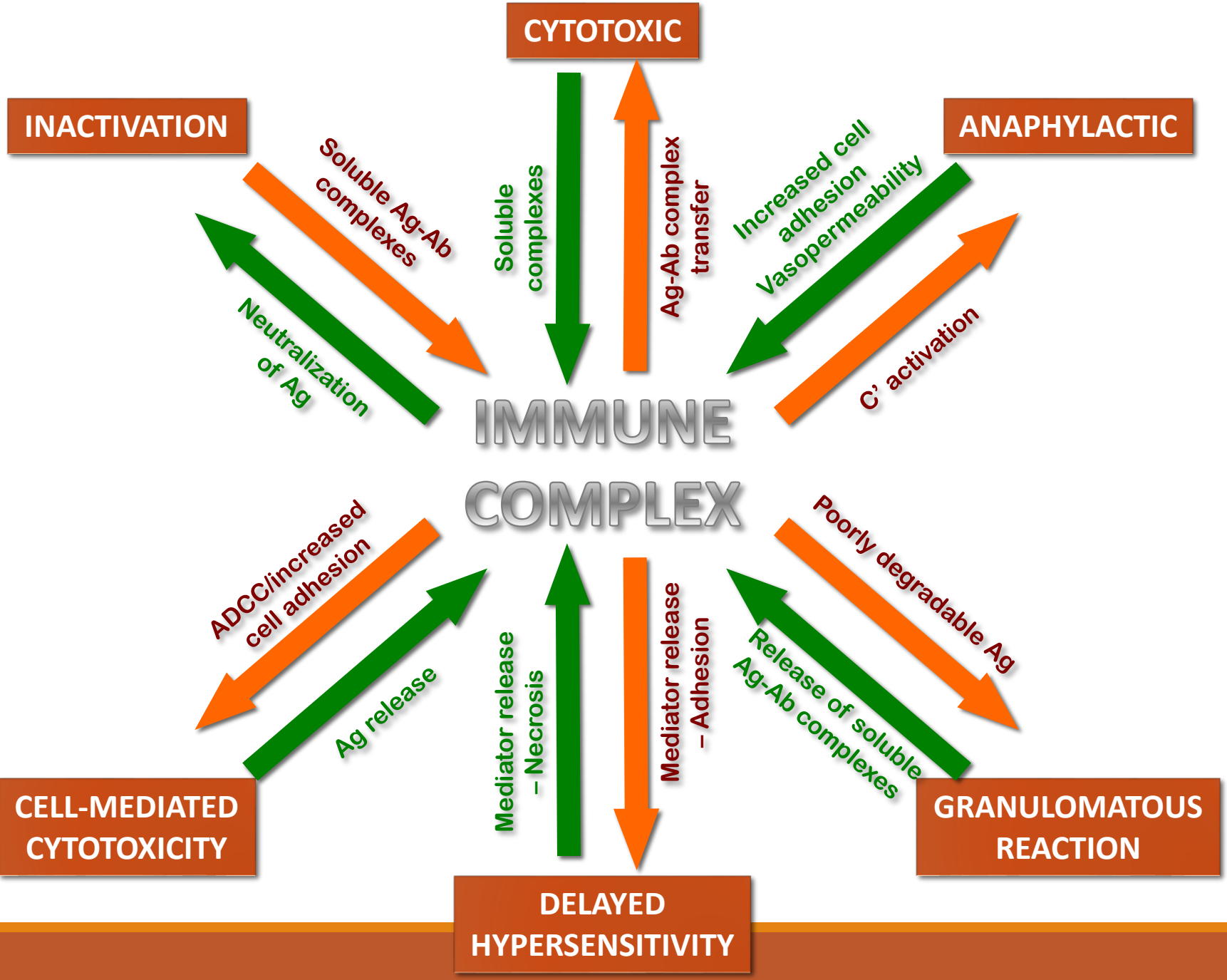
Antigen Processing



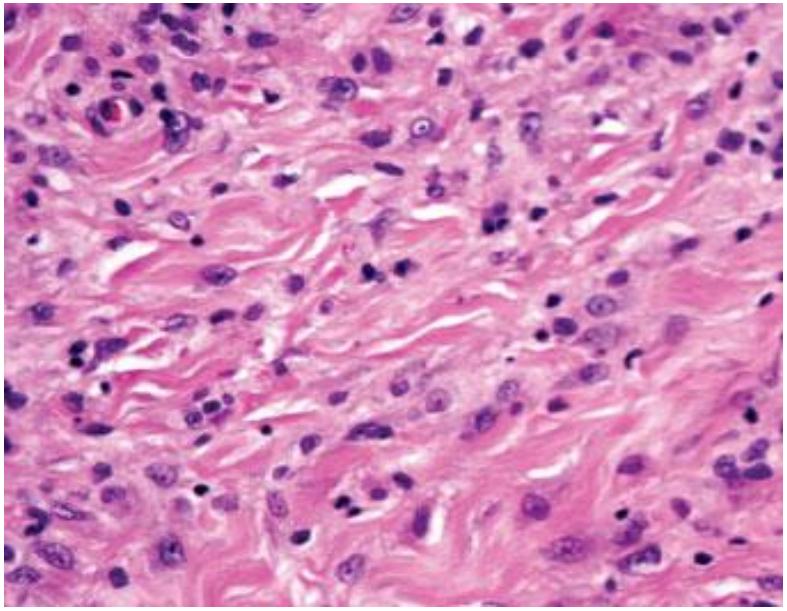
Inflammatory and Cellular Response after Injury






CYTOTOXIC
INACTIVATION
ANAPHYLACTIC
Soluble Ag-Ab complexes
Neutralization of Ag
Soluble complexes
Ag-Ab complex transfer
Increased cell adhesion
Vasopermeability
C' activation
IMMUNE COMPLEX
ADCC/increased cell adhesion
Ag release
Mediator release – Necrosis
Mediator release – Adhesion
Poorly degradable Ag
Release of soluble Ag-Ab complexes
CELL-MEDIATED CYTOTOXICITY
DELAYED HYPERSENSITIVITY
GRANULOMATOUS REACTION

Interstitial Granulomatous Infiltrate



Granuloma annulare

Dermatofibroma

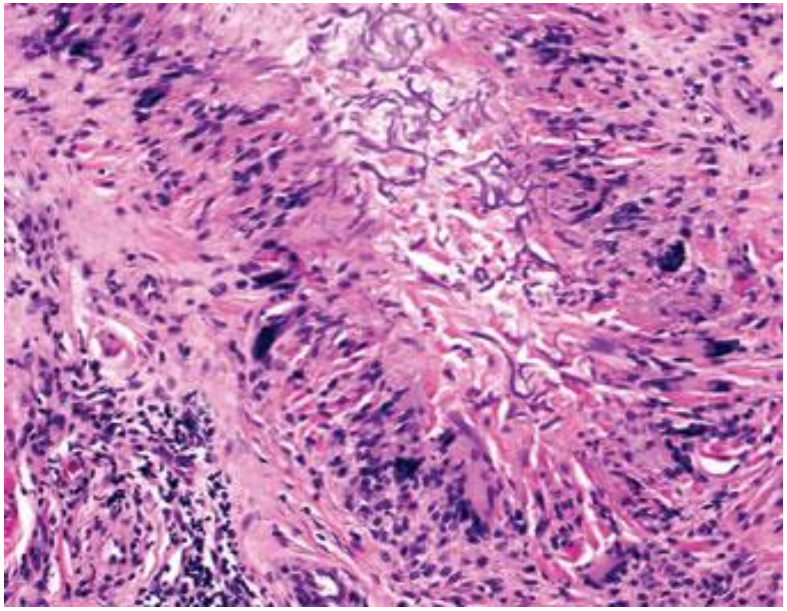
Interstitial granulomatous dermatitis

Necrobiosis lipoidica

MF, interstitial type

MF (granulomatous slack skin)

Palisaded Granuloma



Granuloma annulare

Gout

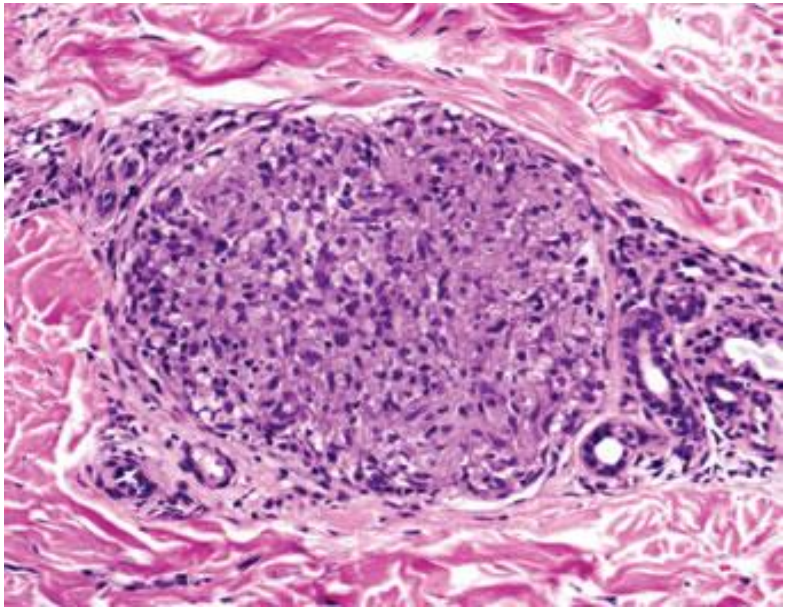
Rheumatoid nodule

Interstitial granulomatous dermatitis

Necrobiosis lipoidica

Necrobiotic xanthogranuloma

Sarcoidal granulomas

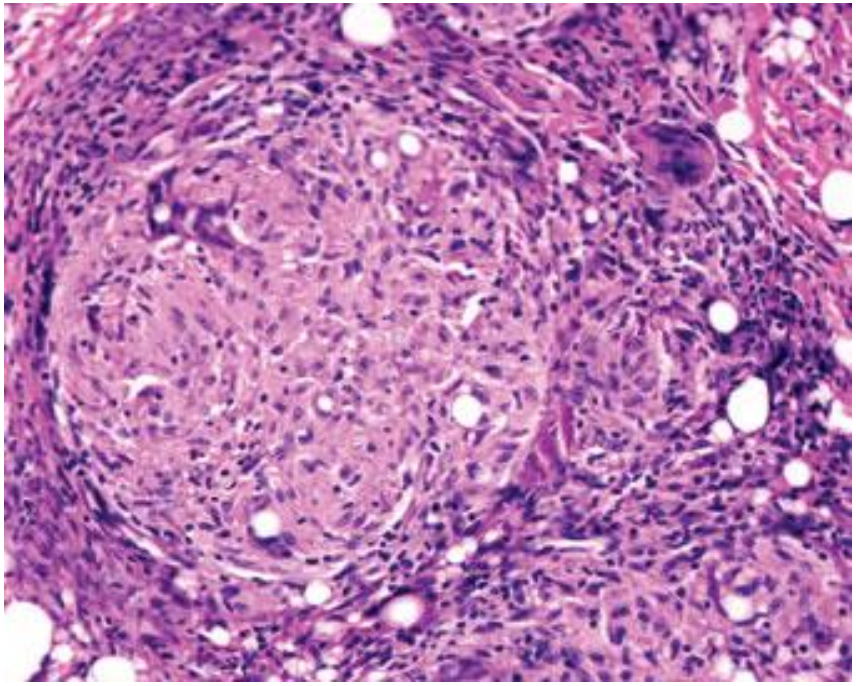


Sarcoidal granulomatous pattern

- **Cohesive epithelioid histiocytes**
- **Few or no lymphocytes**

Sarcoidosis, hallogenoderm

Tuberculoid granulomas

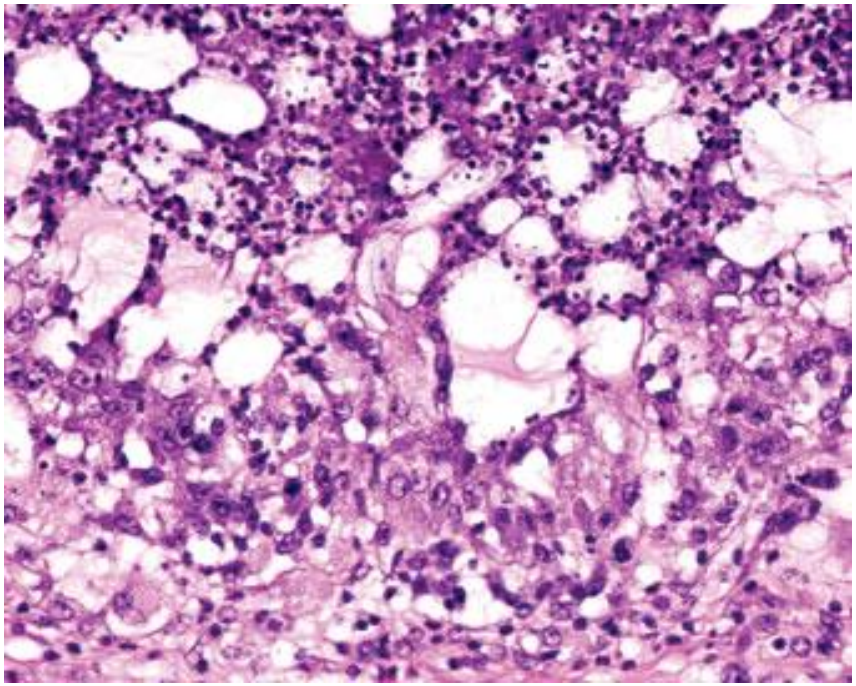


Tuberculoid granulomatous pattern

- **Collections of epithelioid histiocytes**
- **Lymphocytes and plasma cells**

Mycobacterial infections, leishmania, subcutaneous sarcoid

Suppurative granulomas

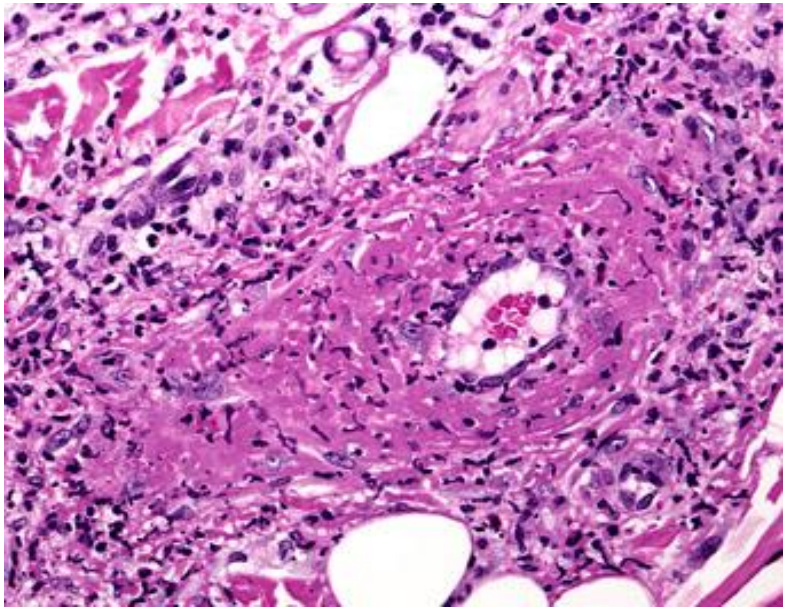


Suppurative granulomatous inflammation

- **Neutrophils and necrotic debris**
- **Histiocytes**
- **Few or no lymphocytes**

Rupture infundibular cyst, sporotrichosis, dermatophytes

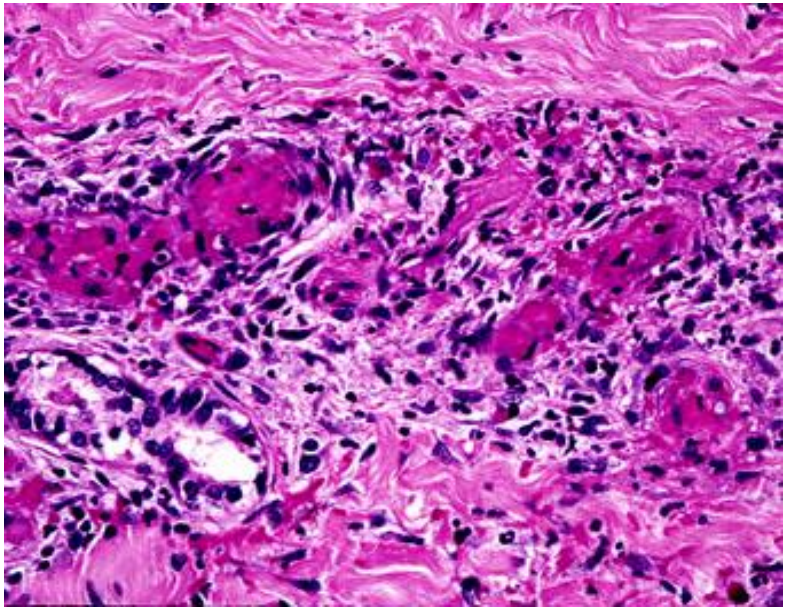
Vasculitis



Neutrophils, nuclear dust and fibrin in small blood vessel walls

Leukocytoclastic vasculitis

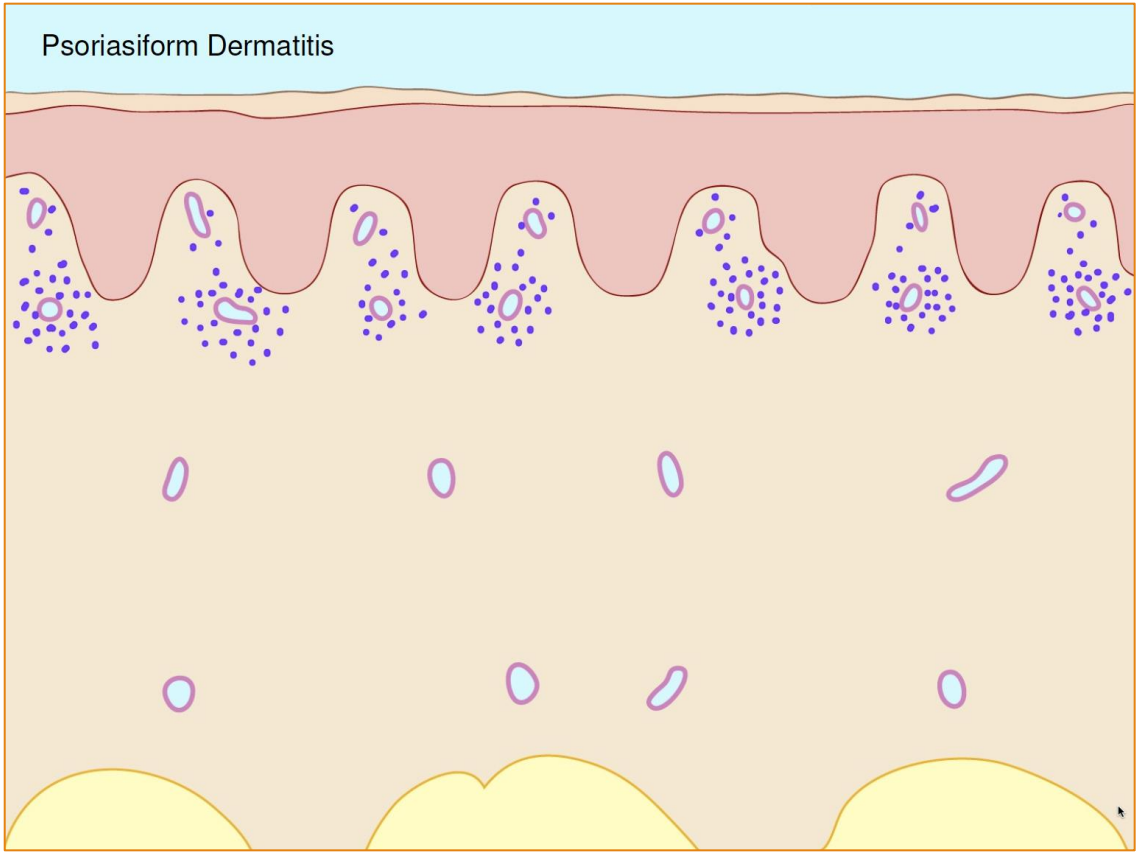
Vasculitis



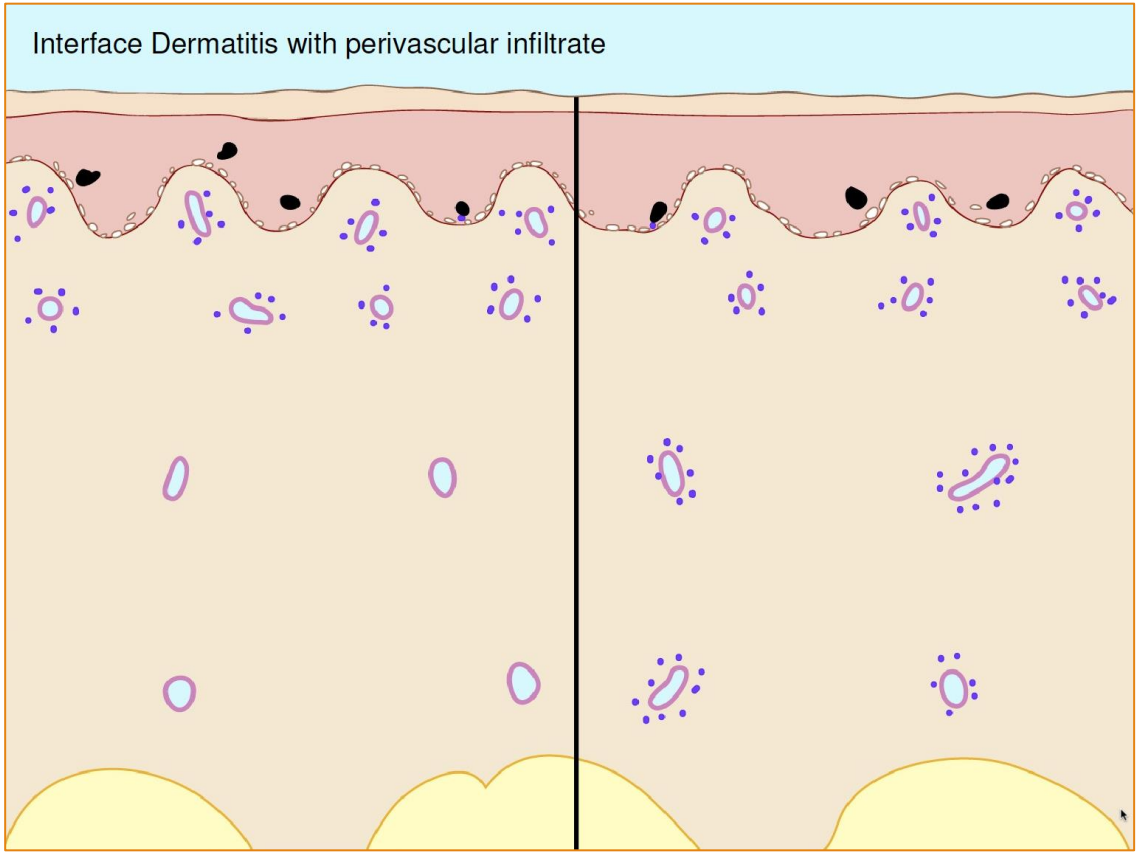
Neutrophils, nuclear dust and fibrin in small blood vessel walls
Thrombi within their lumina

Septic vasculitis

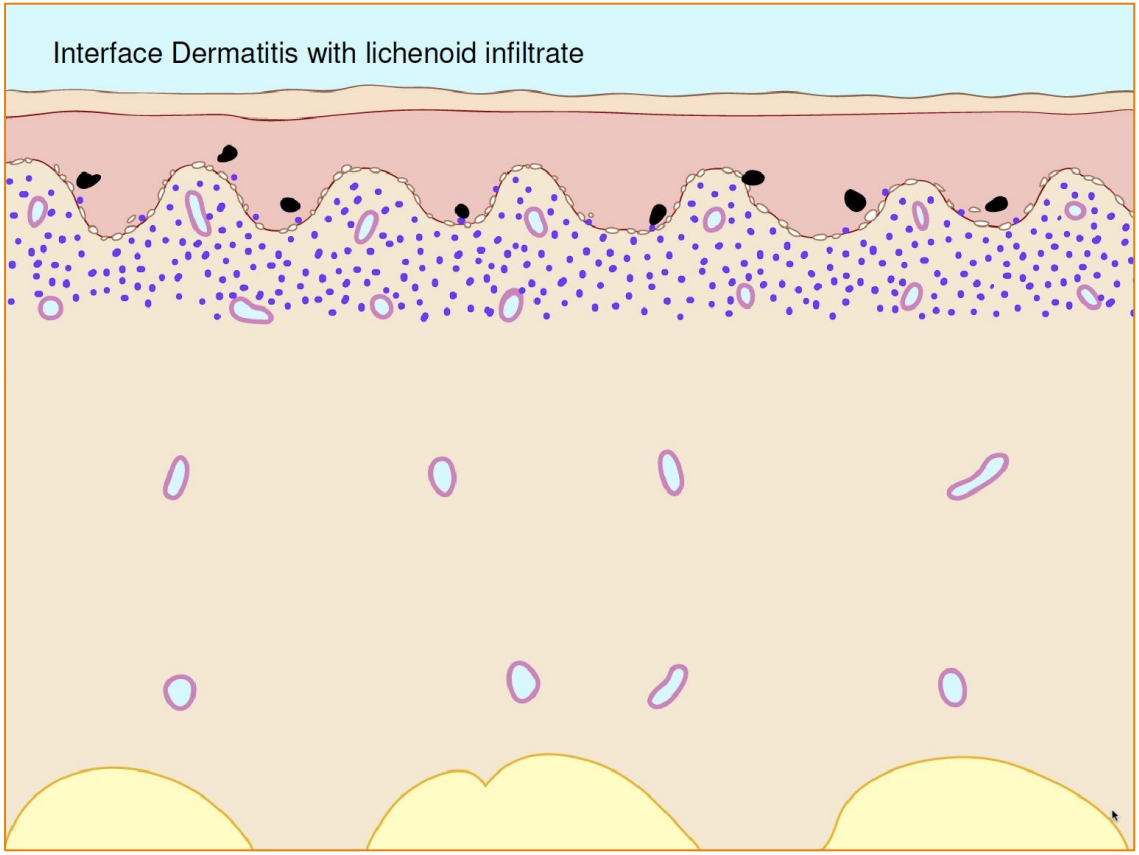
Psoriasiform Dermatitis



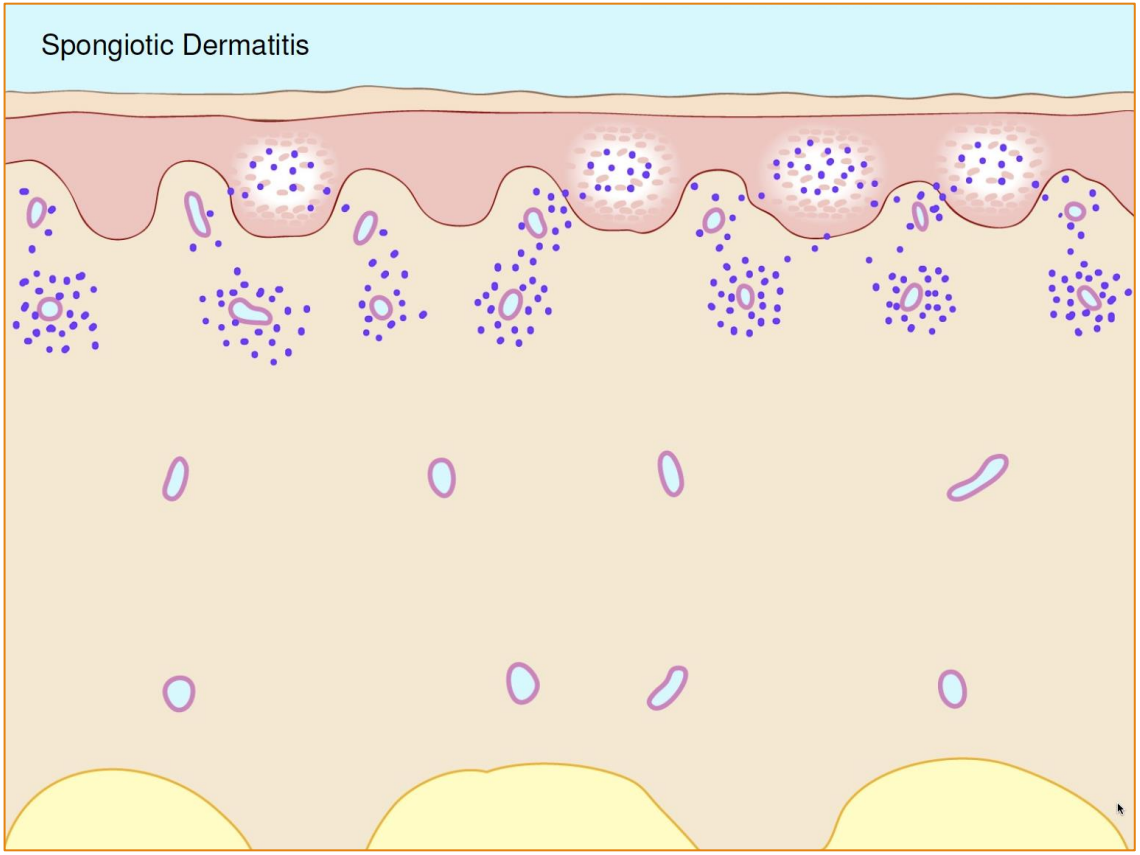
Vacuolar Interface Dermatitis



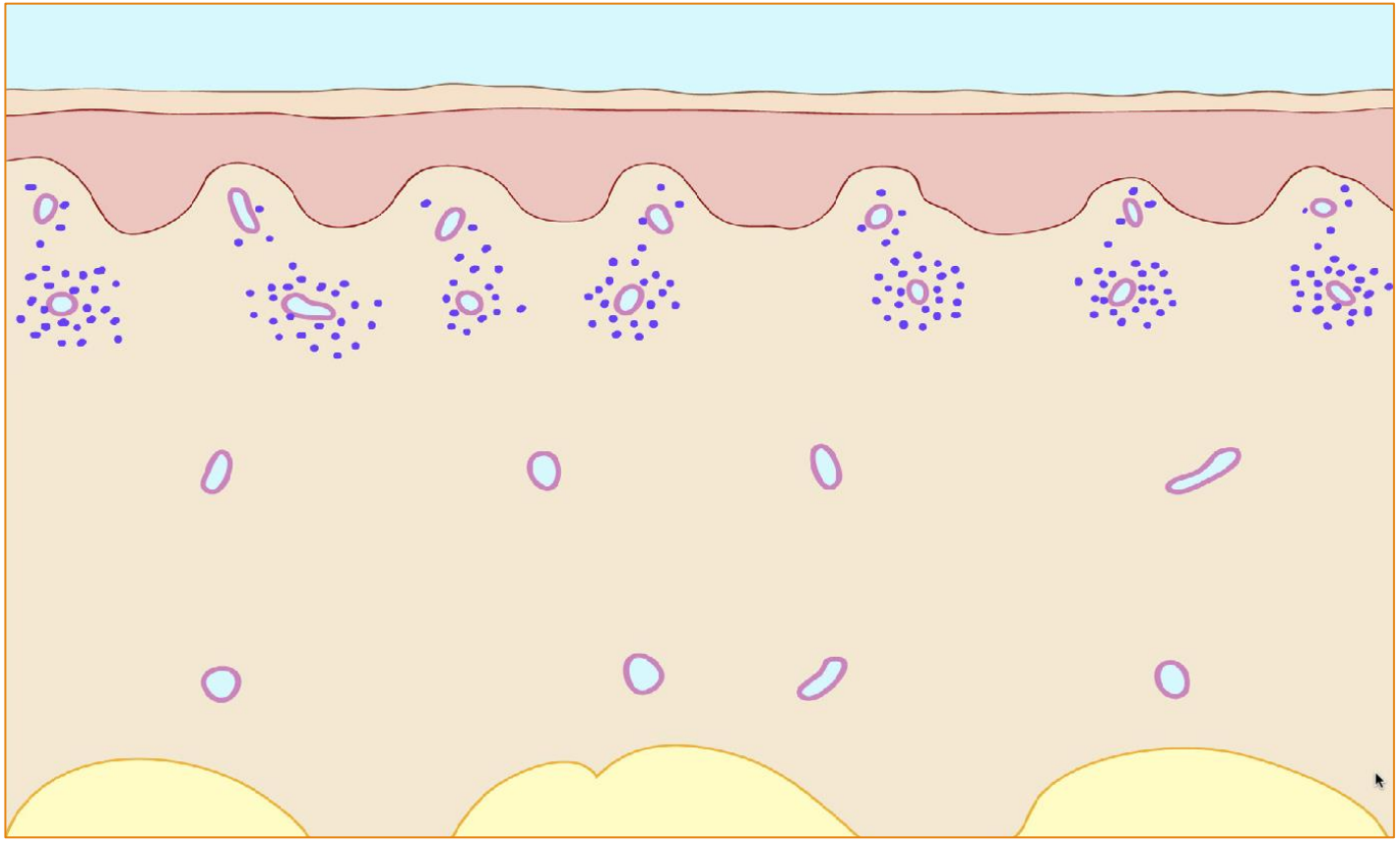
Lichenoid Interface Dermatitis



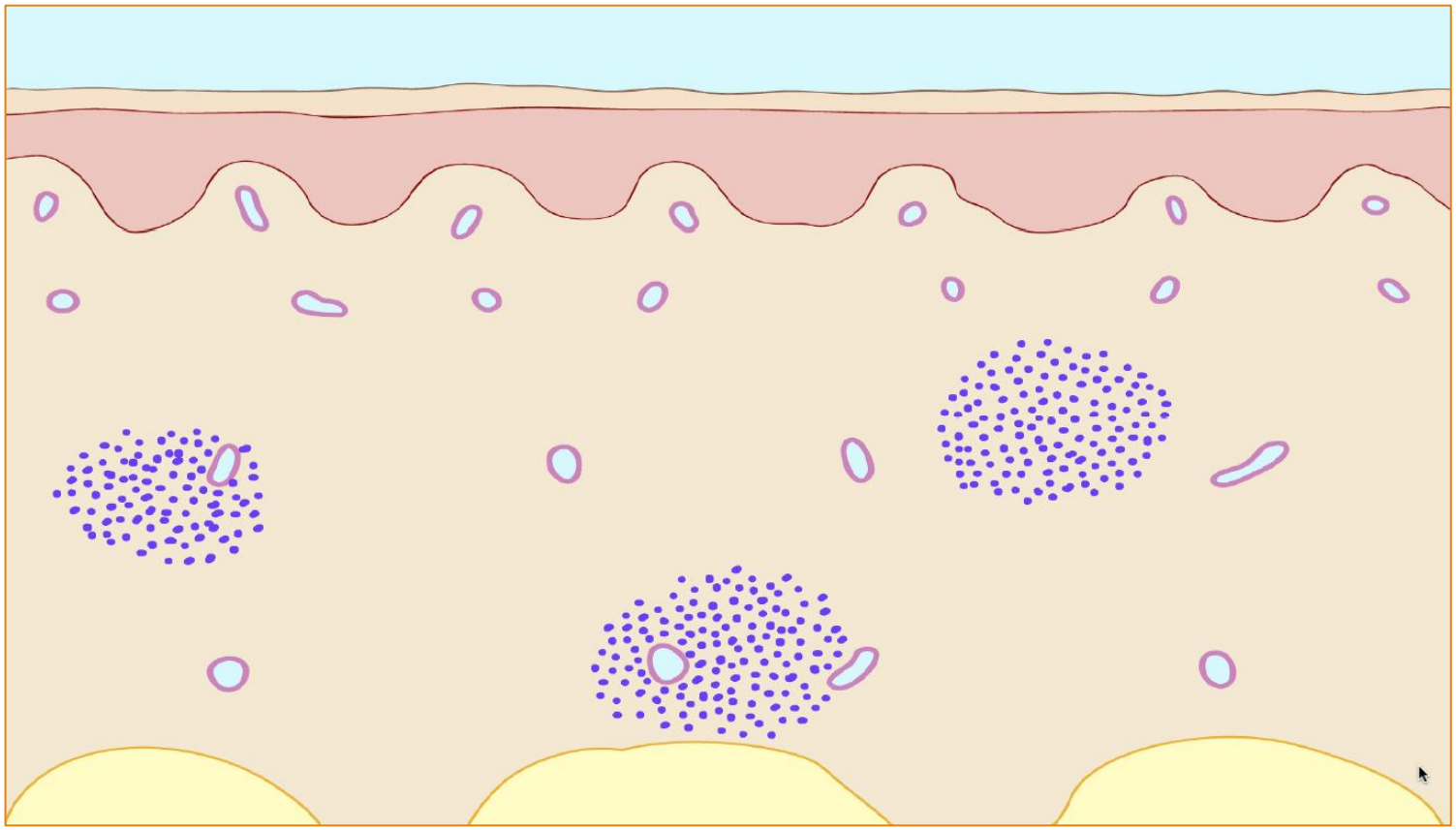
Spongiotic Dermatitis



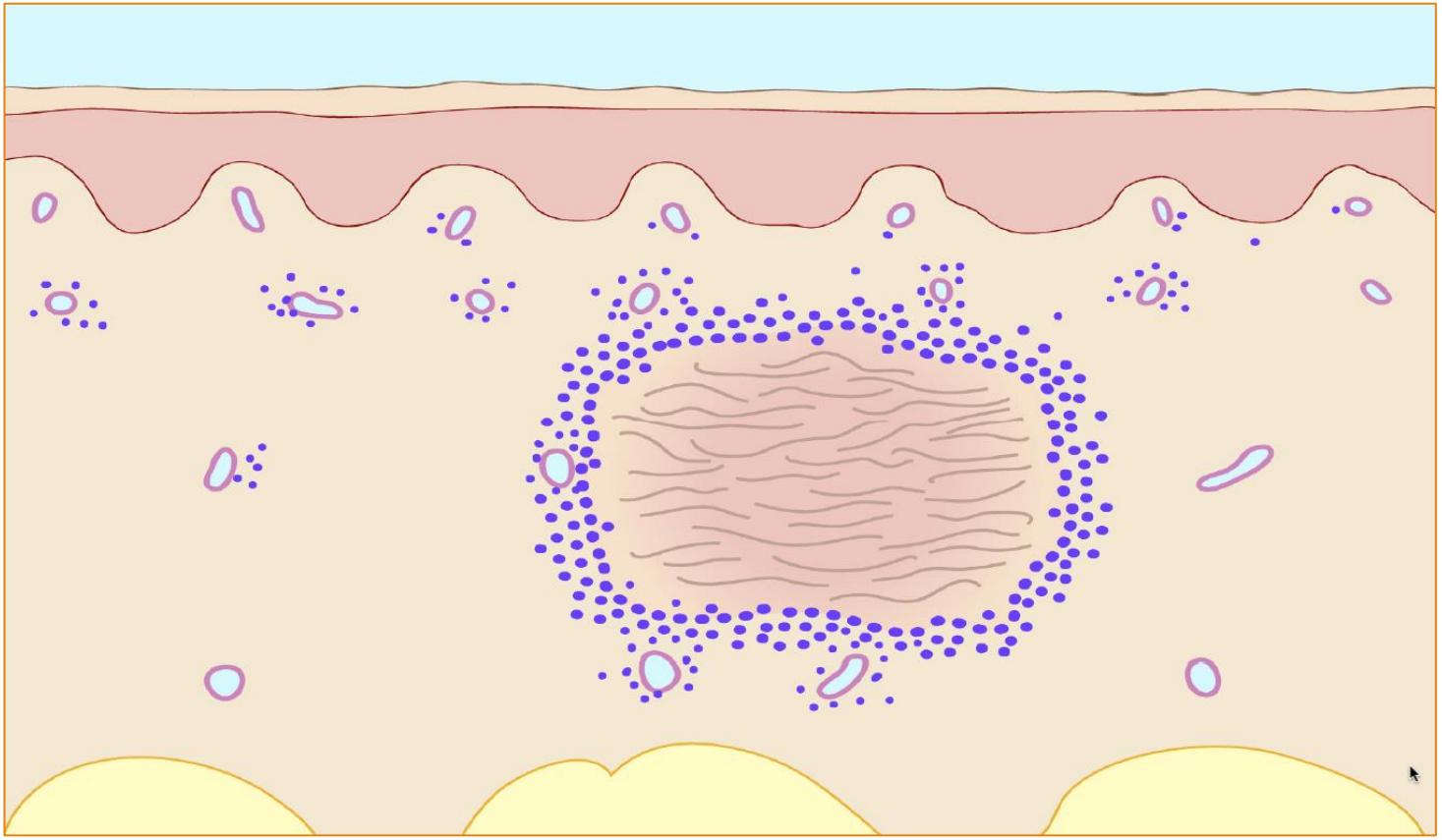
Superficial PV Dermatitis



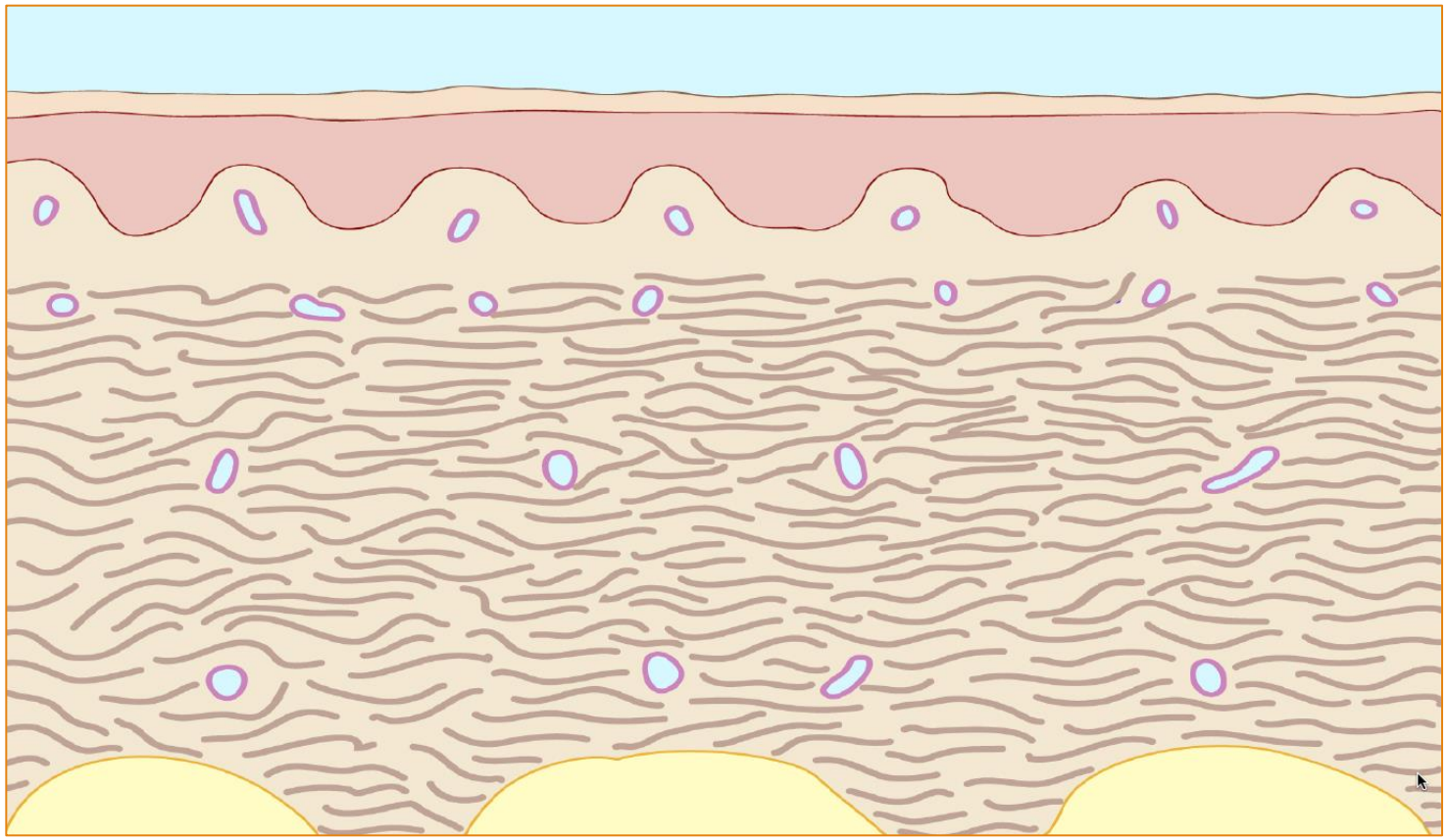
Nodular Dermatitis



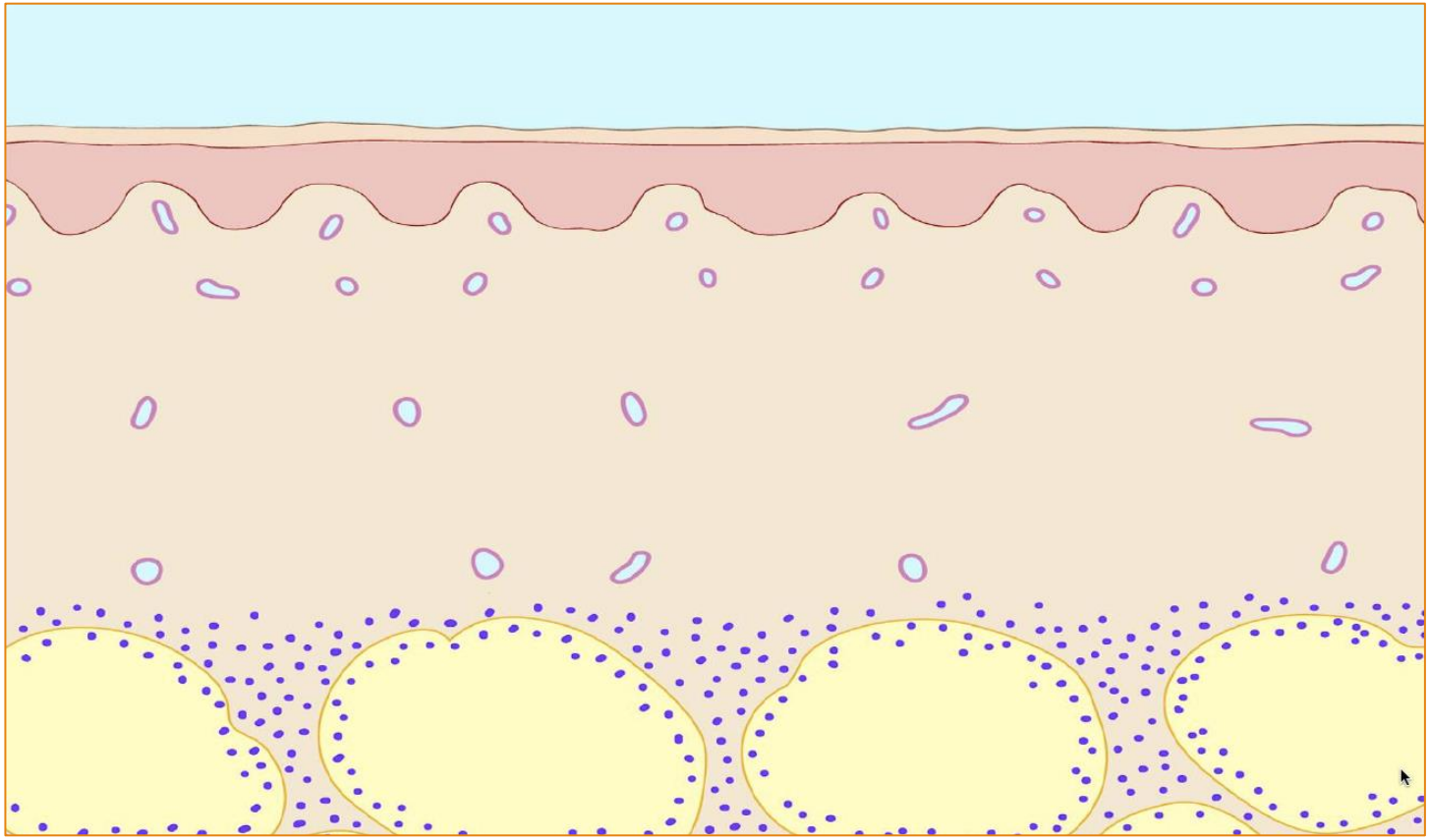
Granulomatous Dermatitis



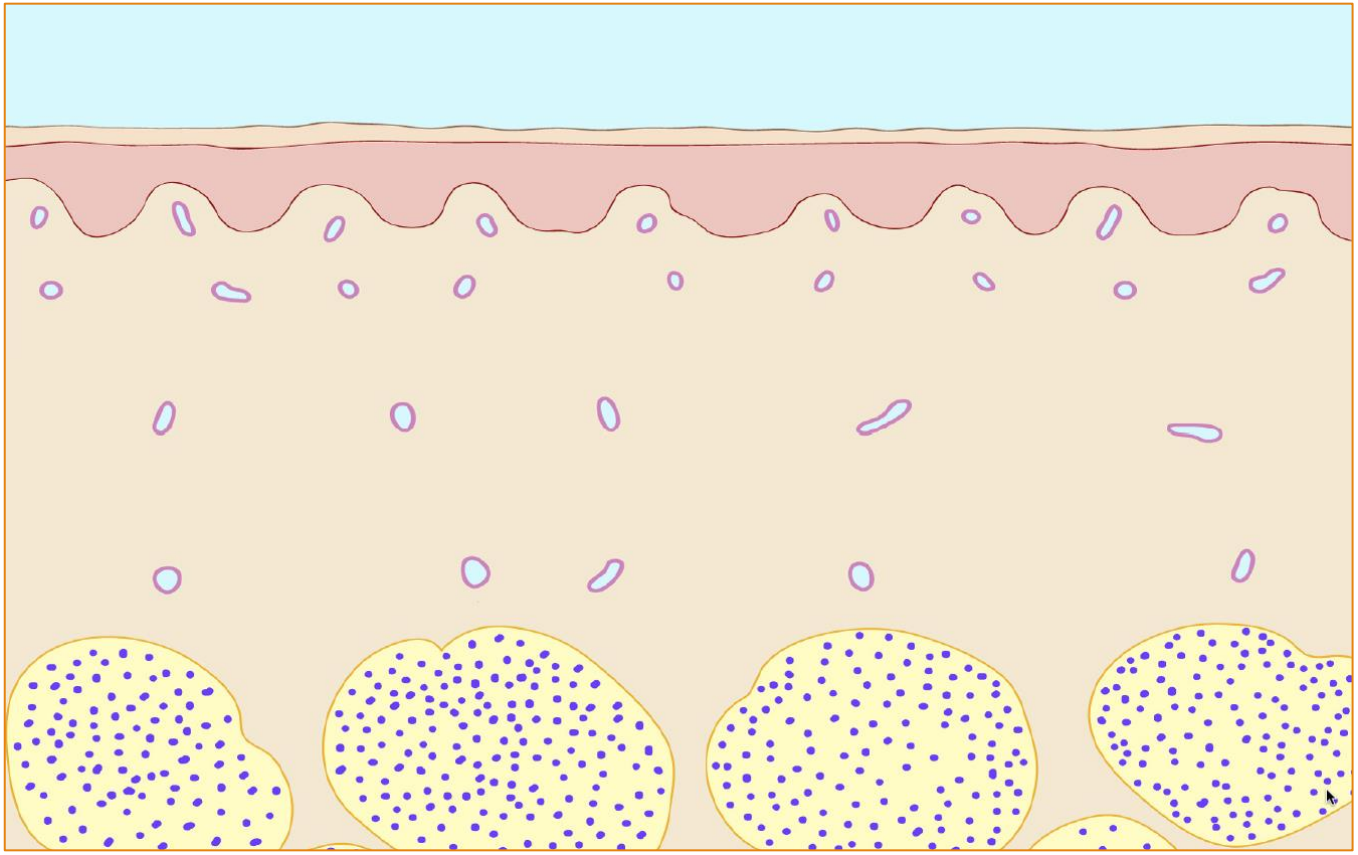
Fibrosing Dermatitis



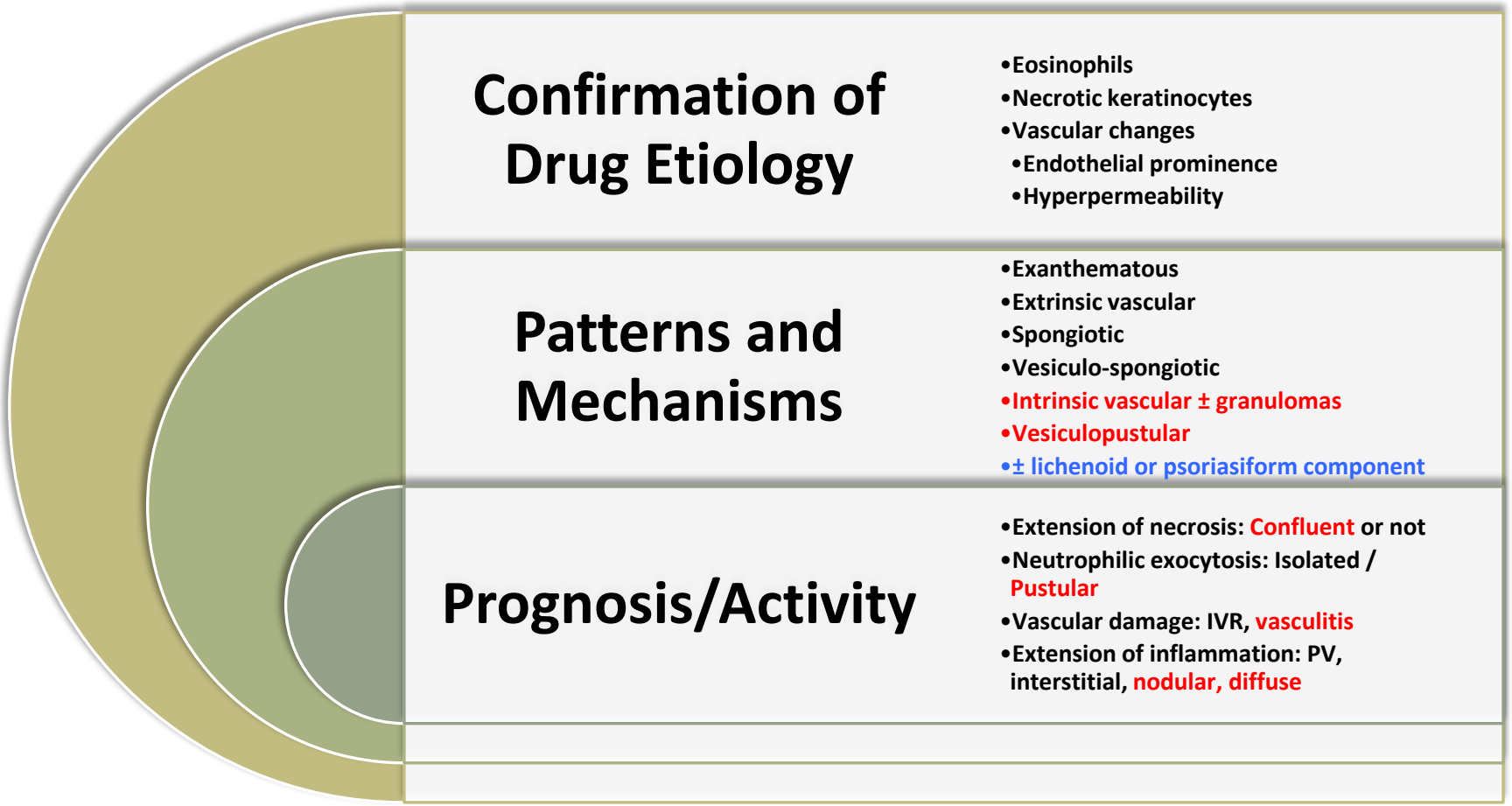
Mostly Septal Panniculitis

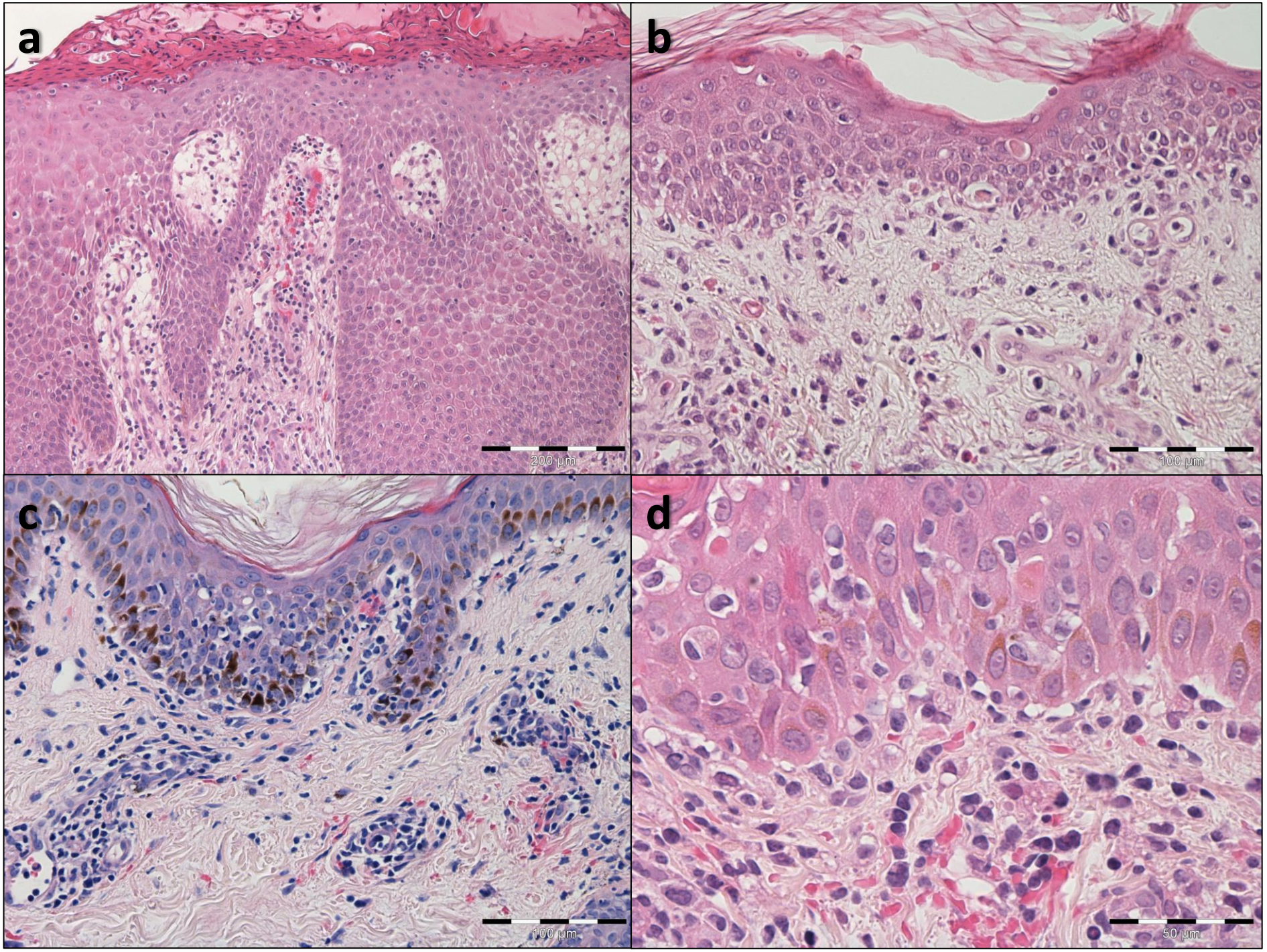


Mostly Lobular Panniculitis



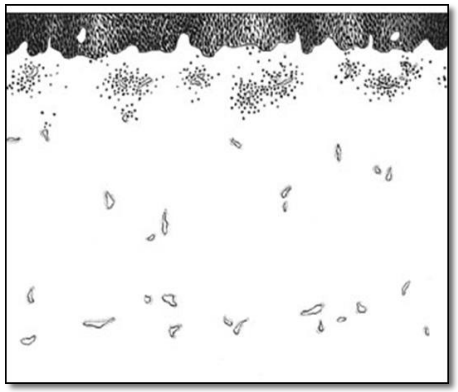
Pathology for ADR Evaluation




a
200 µm
b
100 µm
c
100 µm
d
50 µm

Patterns: Common Basic and Secondary

Exanthematous



Commonest pattern

Basic profile

Psoriasiform

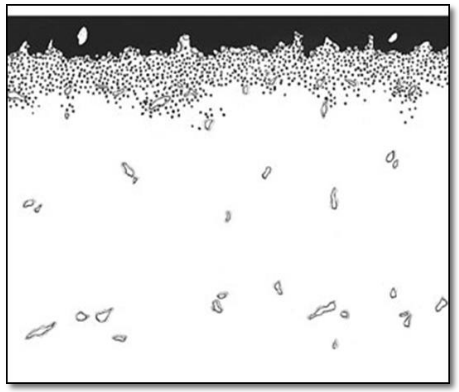
Chronicity

Relative low risk

Common as secondary pattern

Certain drugs if pseudoepitheliomatous

Lichenoid



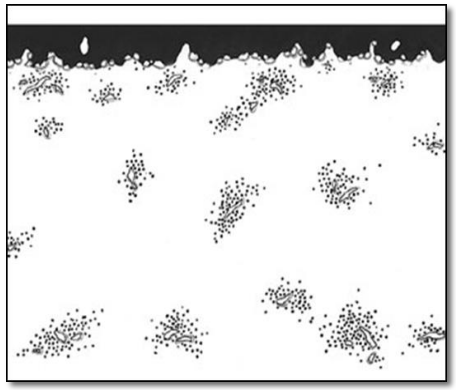
Chronicity

Relative low risk

Common as secondary pattern

Epithelial Damage and Necrosis

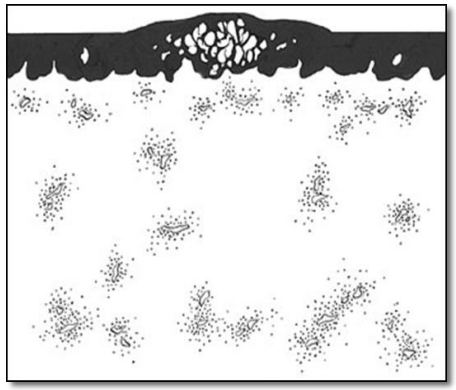
Basal cells



Isolated, cytotoxic

Barrier effect maintained

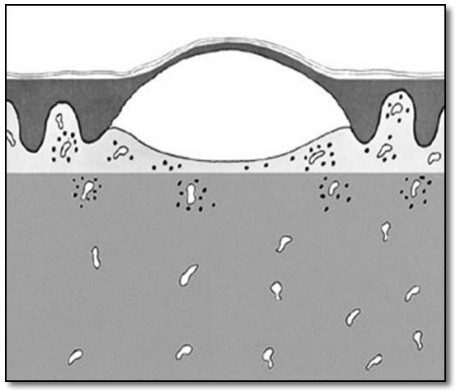
Multifocal



Clustering, cytotoxic

Barrier effect maintained

Confluent

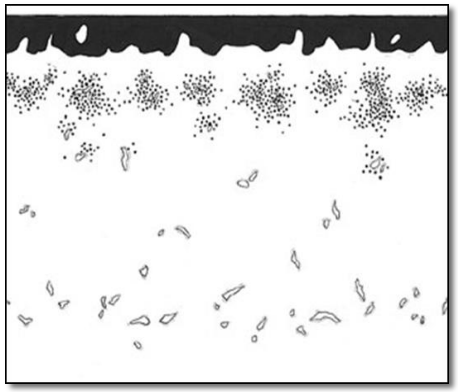


Multifactorial

Barrier effect lost

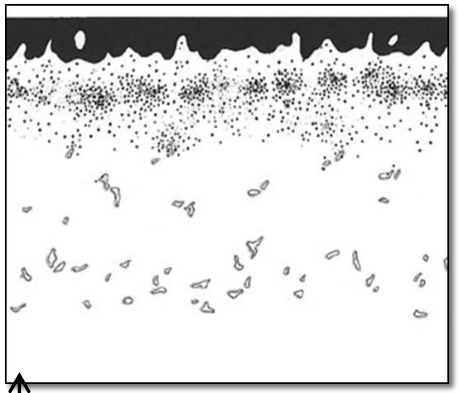
Vascular Changes and Damage

Perivascular



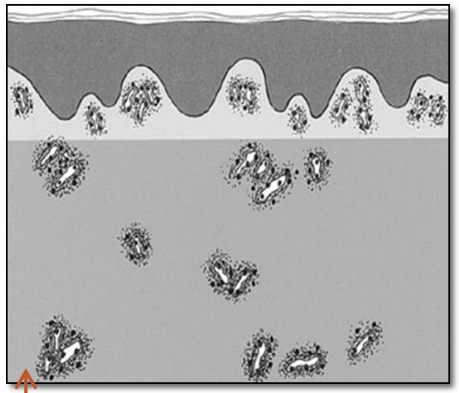
Basic profile

IVR

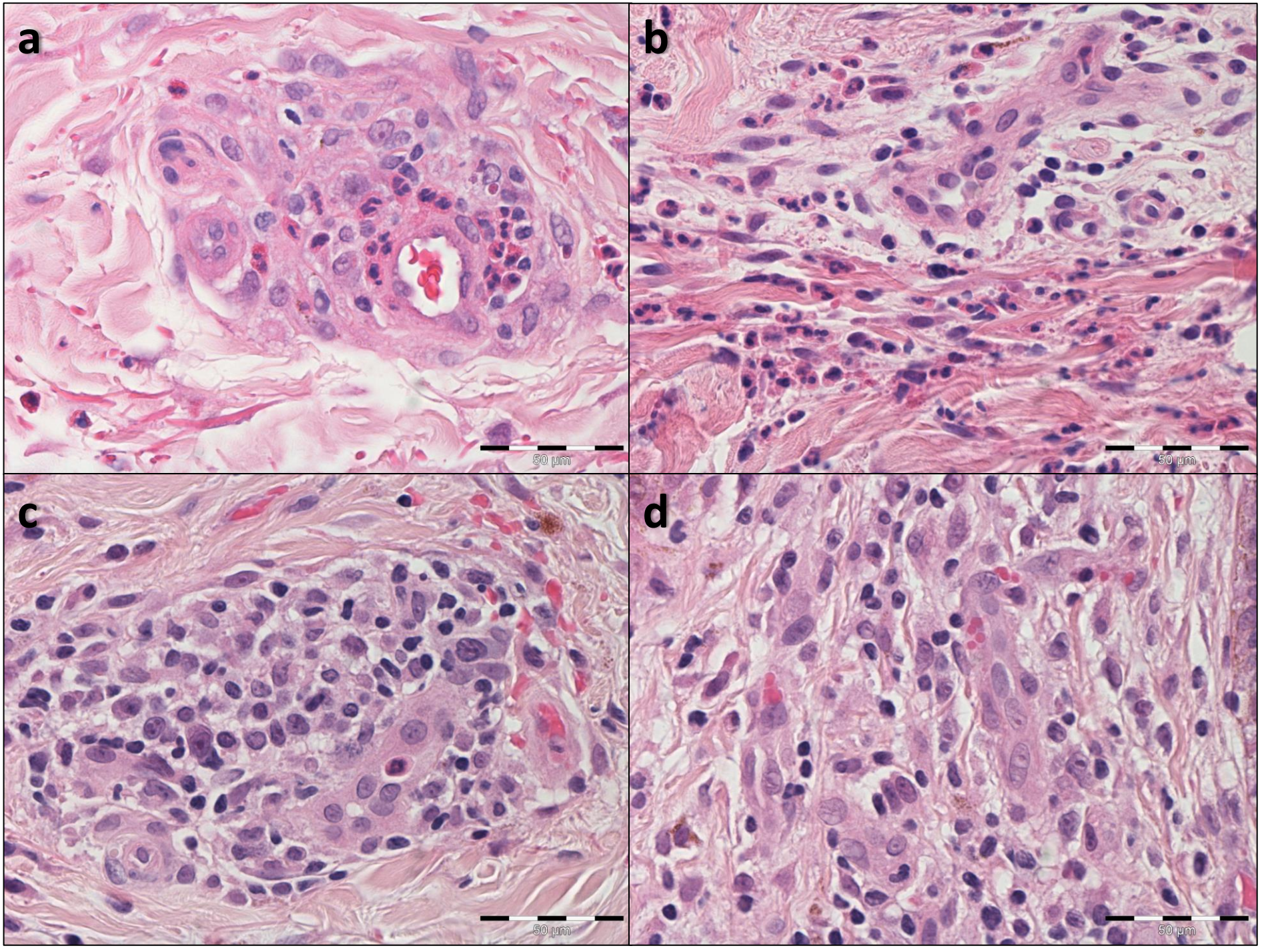


Permeability
Minor vessel wall damage

Vasculitis

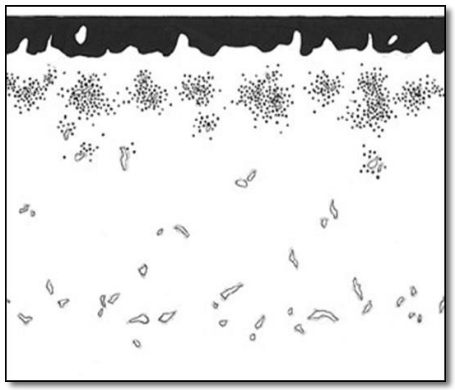


Permeability
Major vessel wall damage


a
50 µm
b
50 µm
c
50 µm
d
50 µm

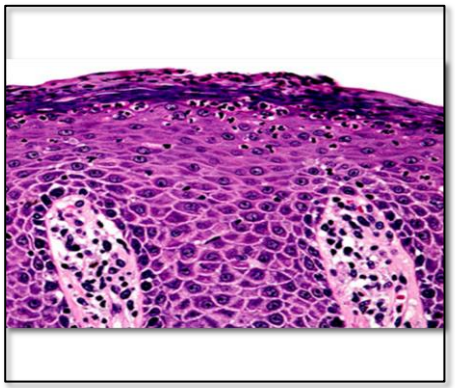
Neutrophilic Activity

Perivascular



Basic profile

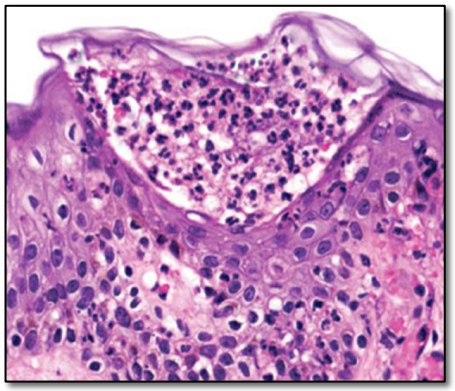
Single cell exocytosis



Spongiosis

No keratinocyte damage/necrosis

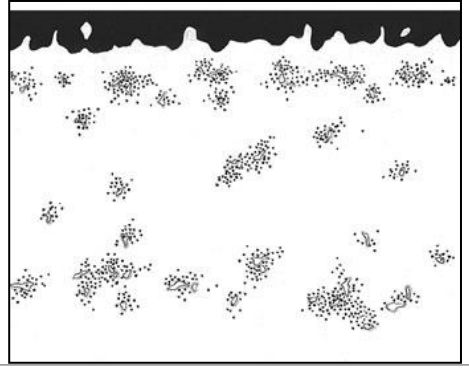
Pustular



Spongiosis

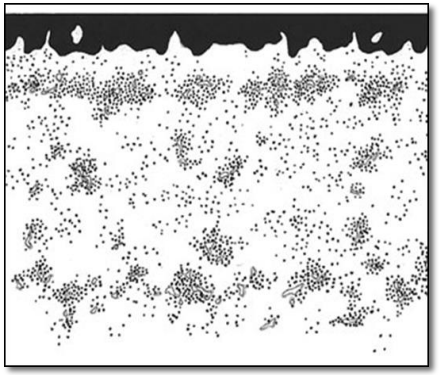
With keratinocyte damage/necrosis

Infiltrate Extension



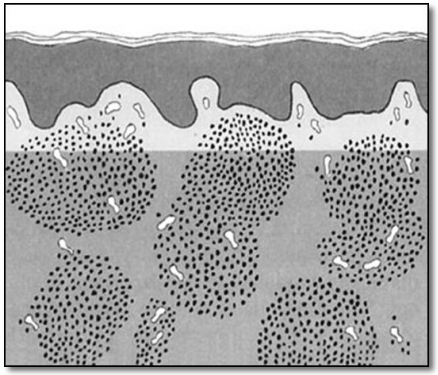
Basic - Perivascular

PV + Interstitial



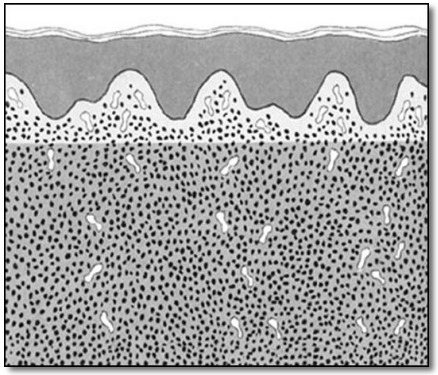
Low grade progressive

Nodular



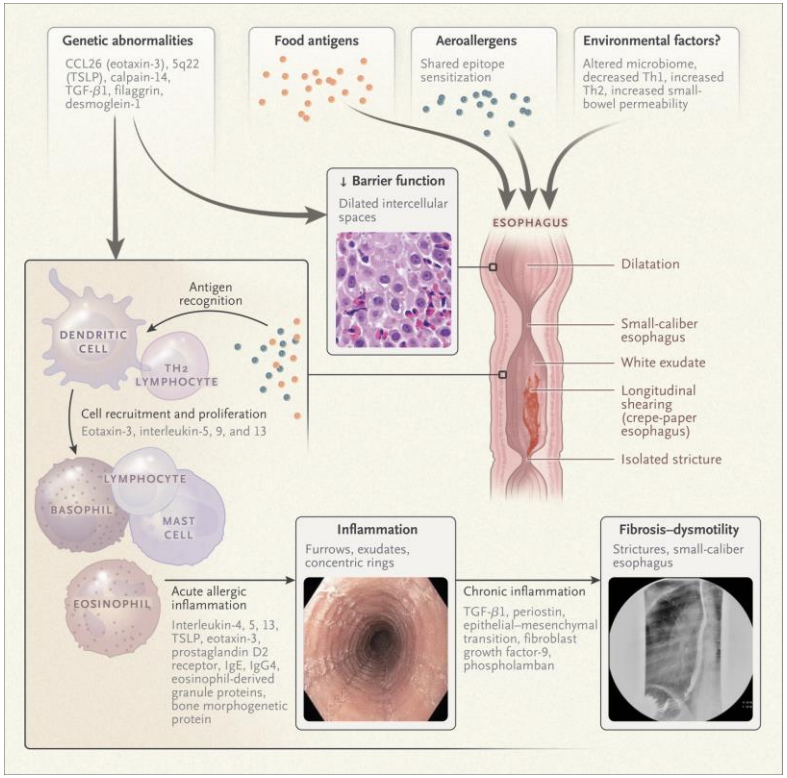
Severe

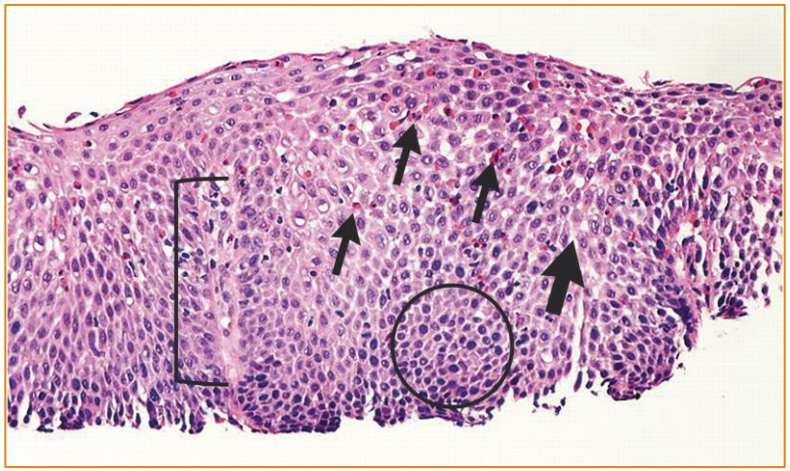
Diffuse



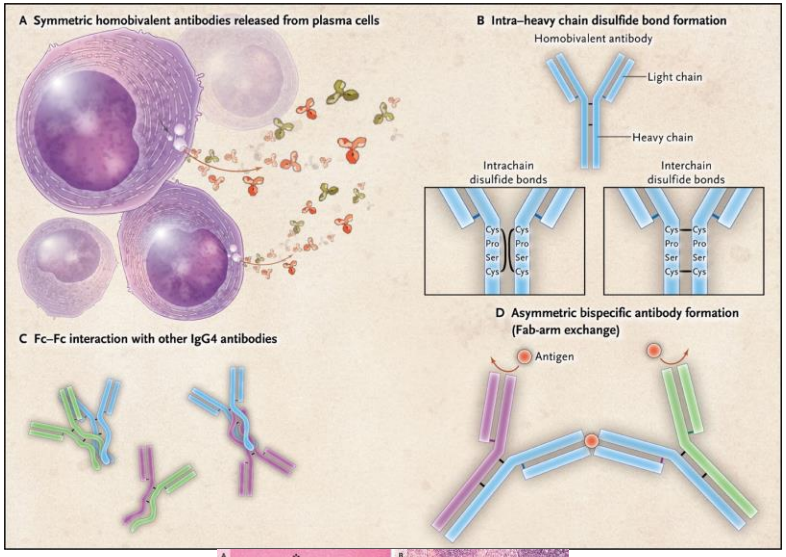
Severe & Tissue Damaging

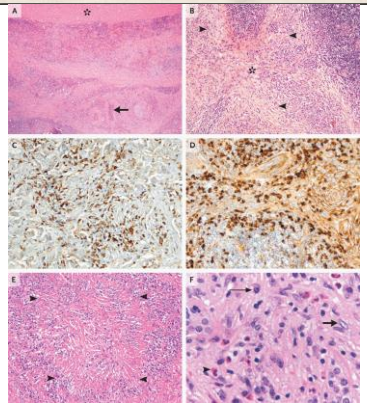
Type I Hypersensitivity

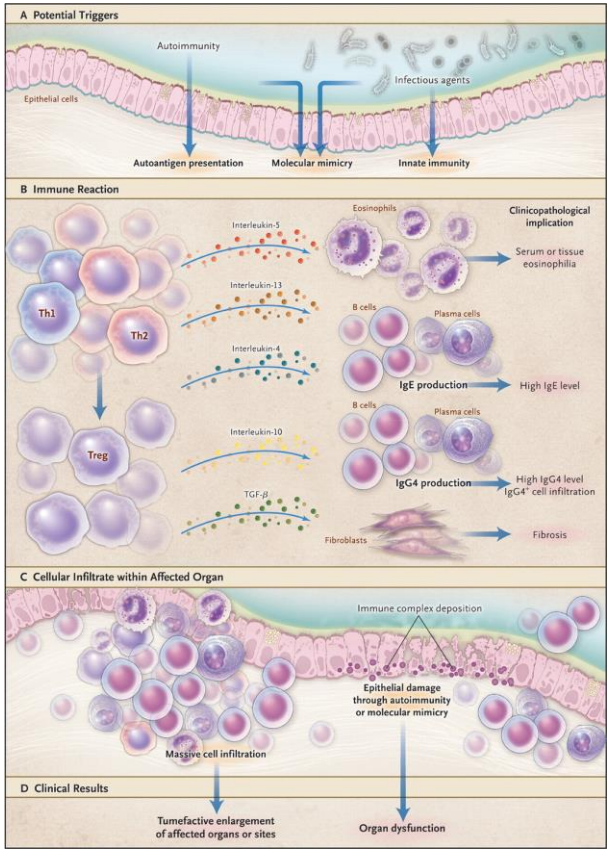




IgG4-mediated Reactions







Inflammatory Skin Lesions

- **Patterns are the result of the interaction of injury agents and tissue response, modulated in intensity and time**
- **Elementary lesions will depend on:**
  - **basic epidermal reaction (based on cellular turnover and maturation),**
  - **vascular and cellular inflammatory components,**
  - **types of cells, and**
  - **distribution of cells (topography and microanatomy)**
- **Activity should be evaluated a from target damage (epithelial necrosis, vasculitis), exocytosis (neutrophilic), and density of infiltrate**
- **Morphological and clinico-pathologic correlation should be included in the conclusion**