Inflammatory dermatopathology in general medicine: Case review

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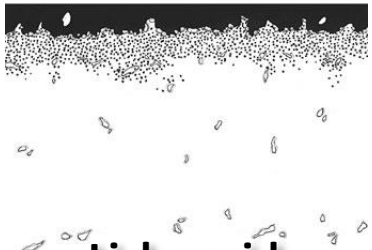
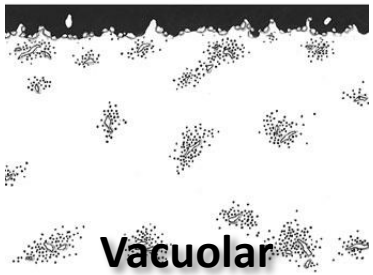
Inflammatory Conditions with Epidermal Alteration

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

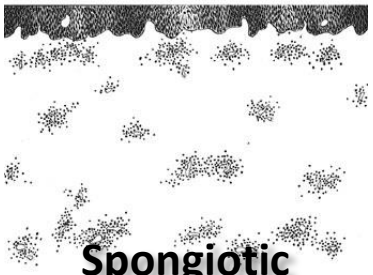
Psoriasiform dermatitis



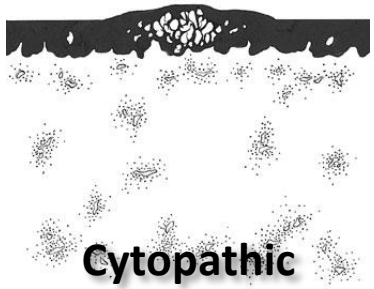
Lichenoid dermatitis



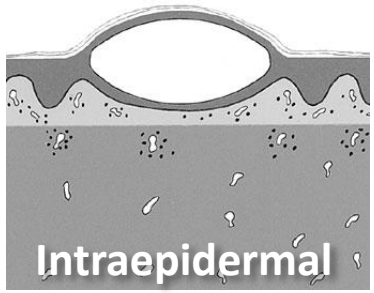
Vacuolar dermatitis



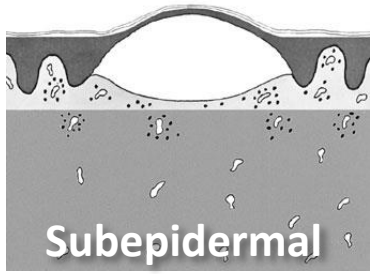
Spongiotic dermatitis



Cytopathic dermatitis



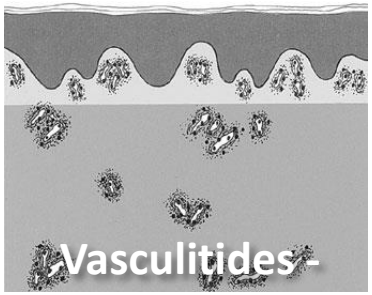
Intraepidermal bullous dermatitis



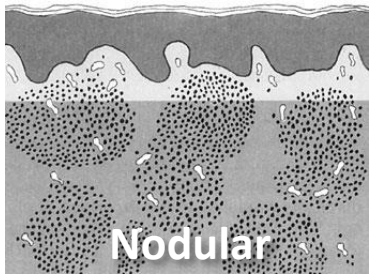
Subepidermal bullous dermatitis

Inflammatory conditions without epidermal alterations

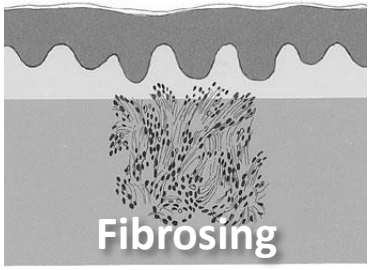
- Dermal/subcutaneous inflammatory process
  - Perivascular dermatitis
    - With vascular damage
    - Vasculopathy
  - Nodular dermatitis
    - Non-granulomatous
    - Granulomatous
  - Diffuse dermatitis
  - Fibrosing dermatitis



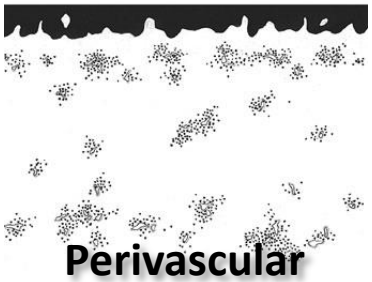
Vasculitides - dermatitis



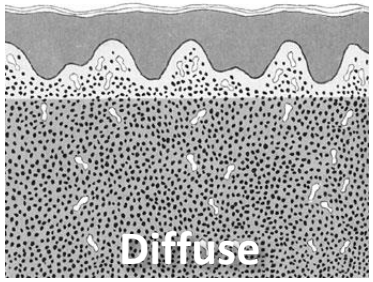
Nodular dermatitis



Fibrosing dermatitis



Perivascular dermatitis

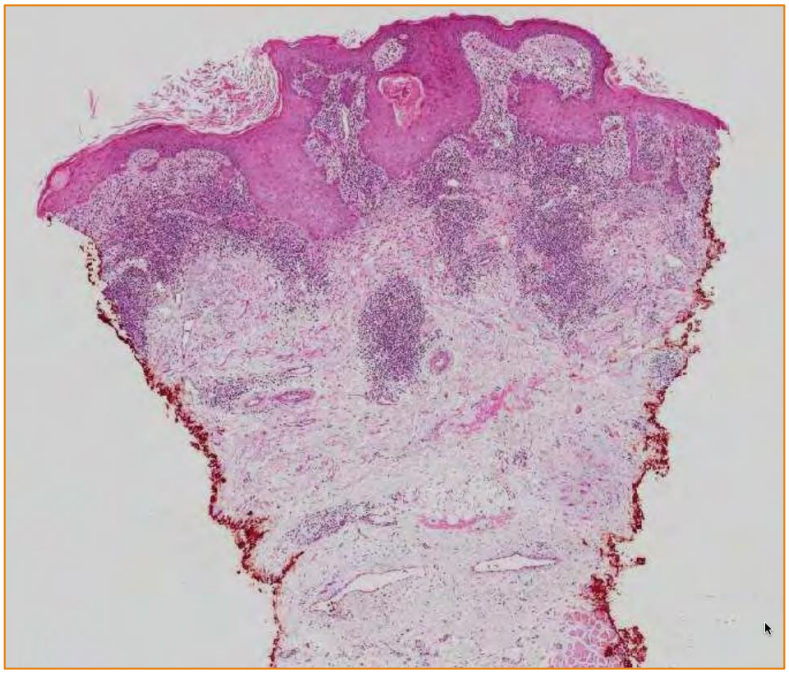


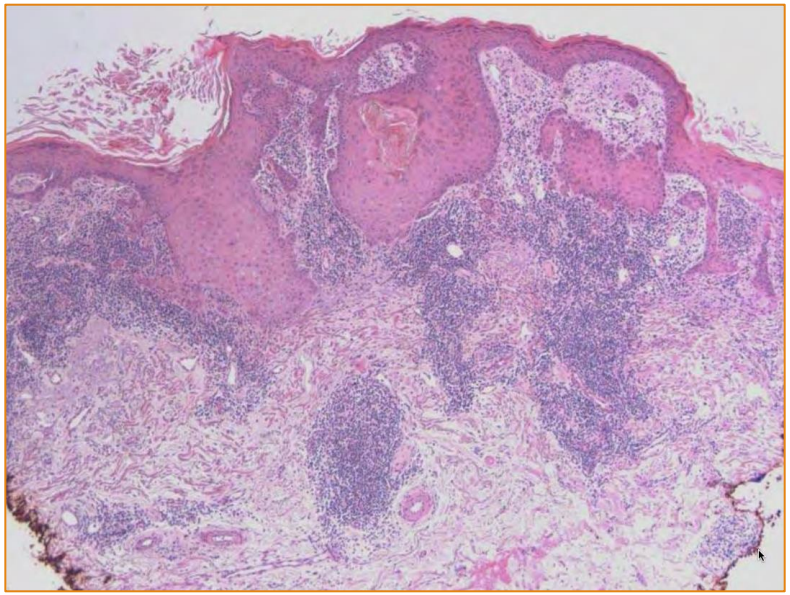
Diffuse dermatitis

Case 1

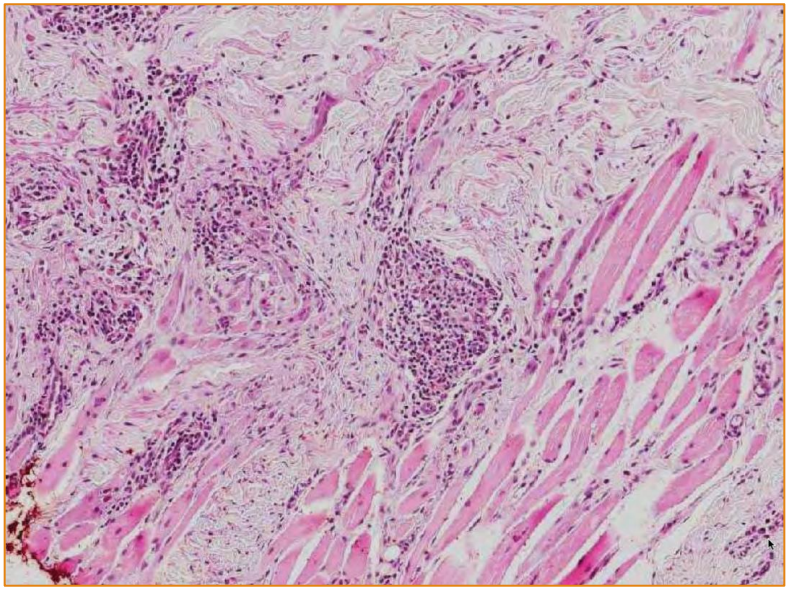
77 YEAR-OLD FEMALE WITH A LONG- STANDING WELL DEMARCATED SCALY VERRUCIFORM PLAQUE ON THE CHIN

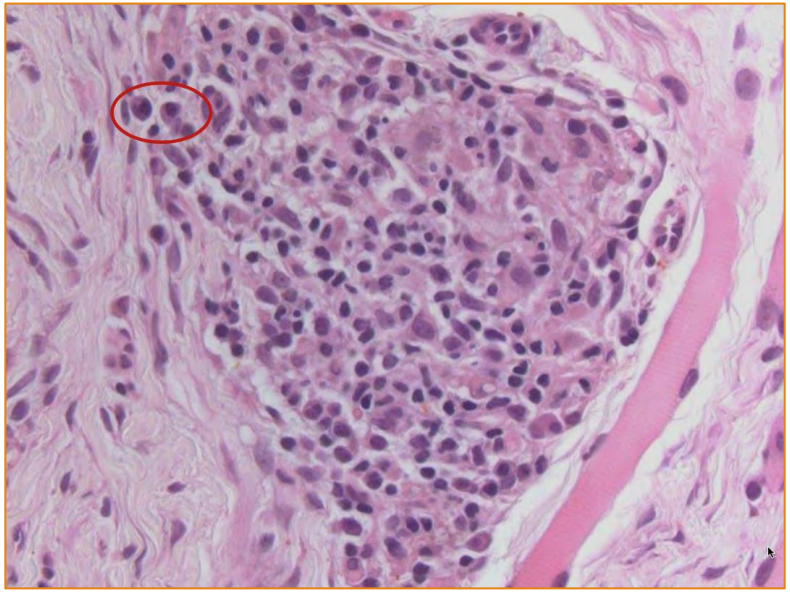
Scaly verruciform plaque



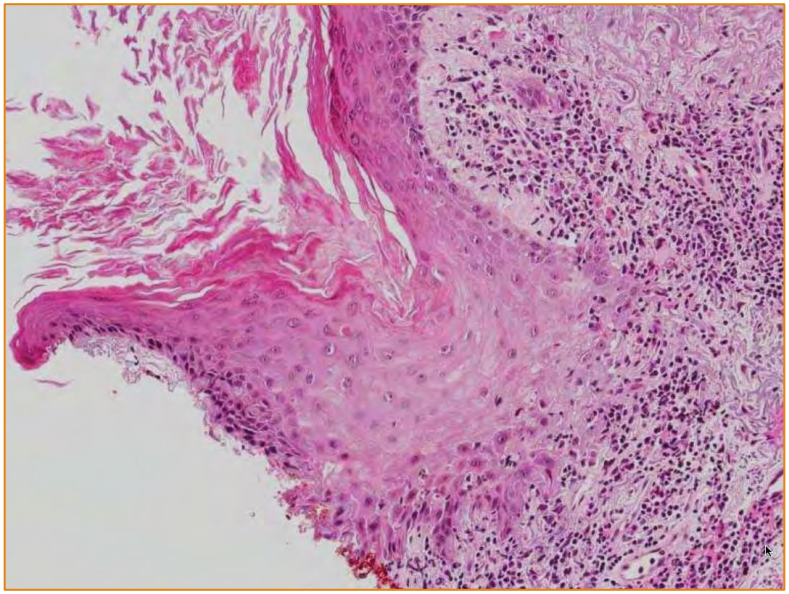


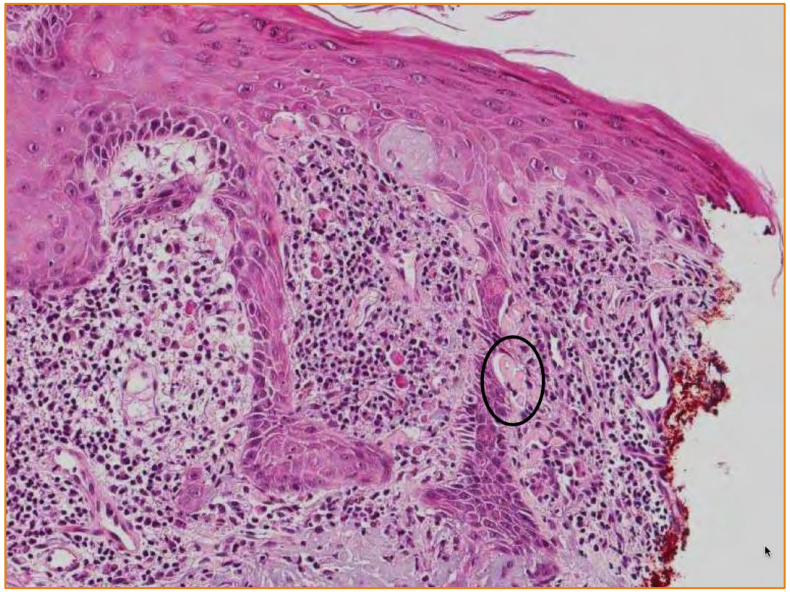
Scaly verruciform plaque





Scaly verruciform plaque





Hypertrophic LE

PATHOLOGY

- Basal vacuolar changes
- Superficial and deep perivascular lymphocytic infiltrate
- Variable apoptosis, follicular plugging, mucin and basement membrane thickening
- Hyperkeratosis with pseudoepitheliomatous epidermal hyperplasia

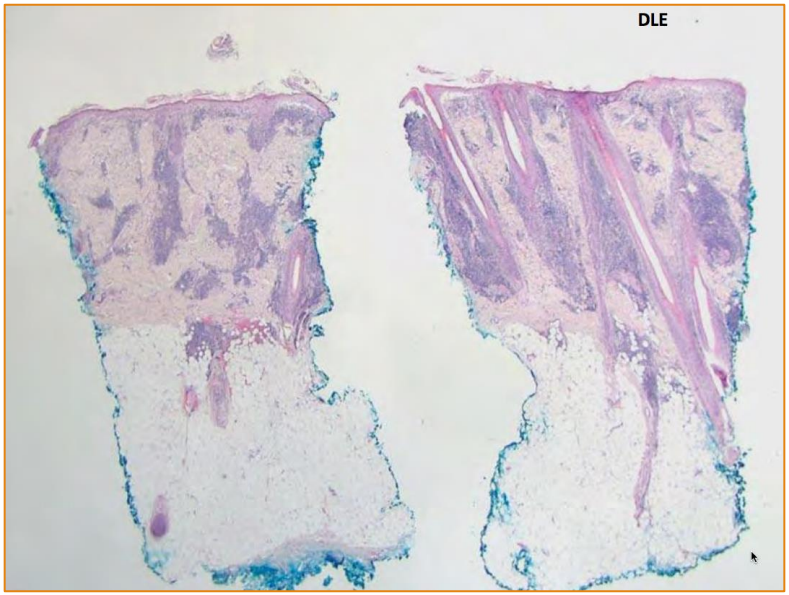
EVOLUTION

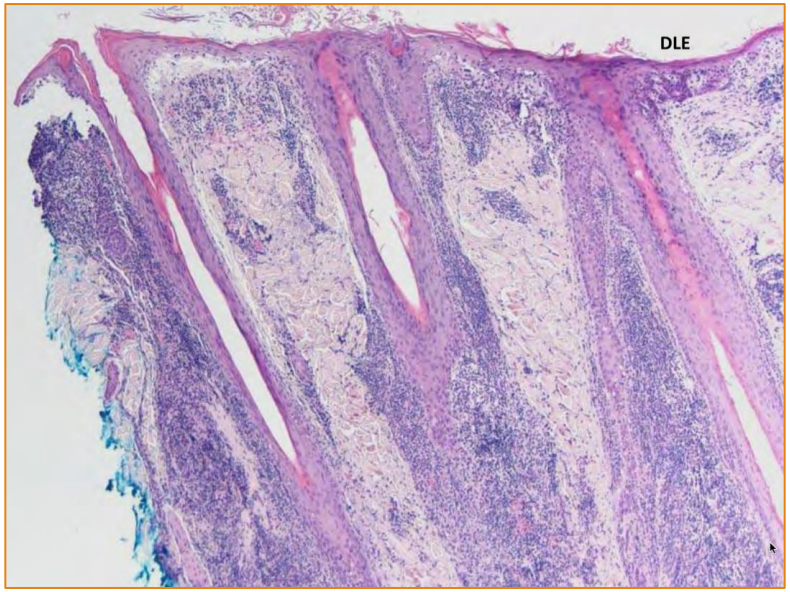
- Chronic relapsing condition
- Often refractory to conventional treatment
  - Some success with thalidomide & pulsed dye laser therapy
- Scarring is common
- SCC uncommon late complication

Hypertrophic LE

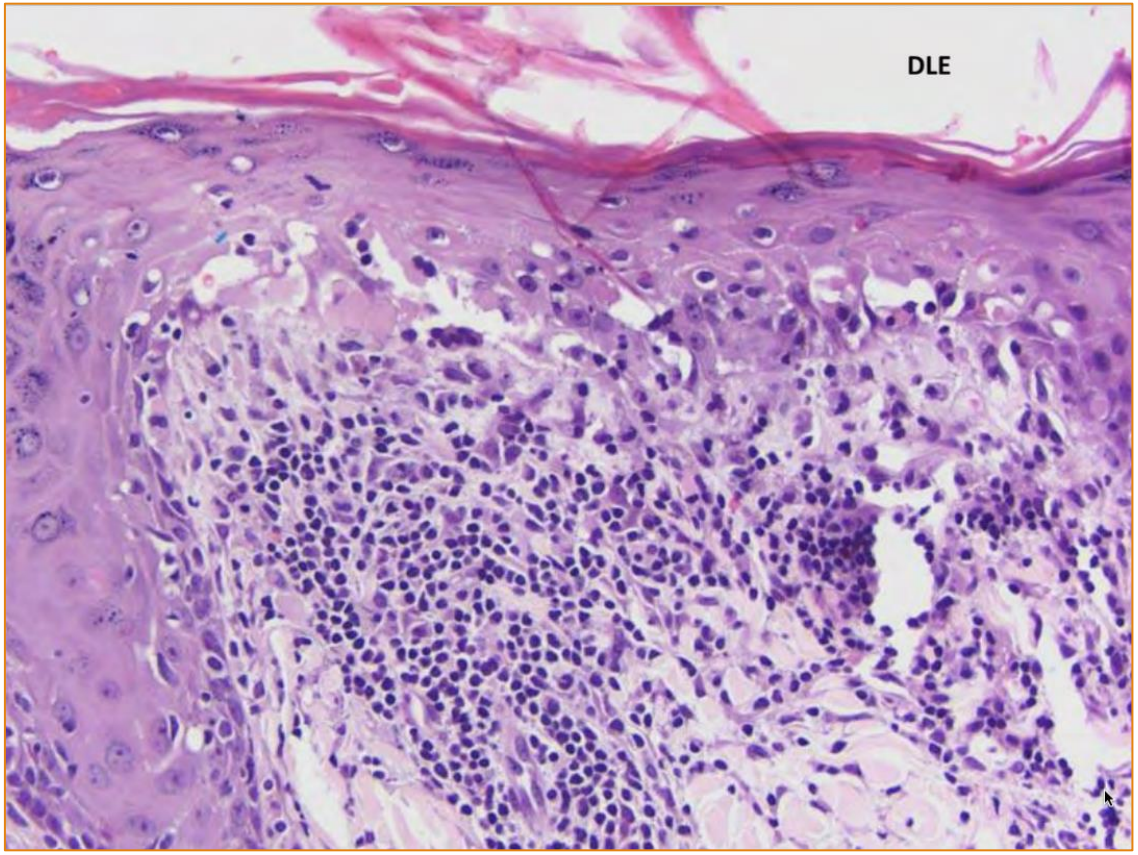
- **Lupus erythematosus hypertrophicus et profundus (Behçet 1940)**
- **Regarded as variant of DLE**
- **Erythematous verruciform plaques on sun damaged skin**
- **Face , arms, chest most common sites**
- **Typical lesions of DLE almost always present**

Discoid Lupus Erythematosus

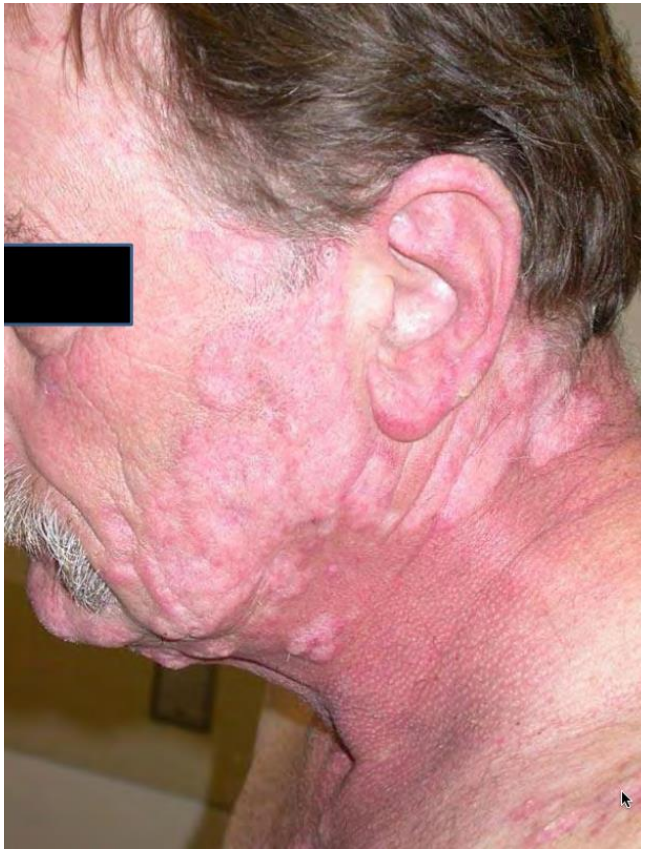


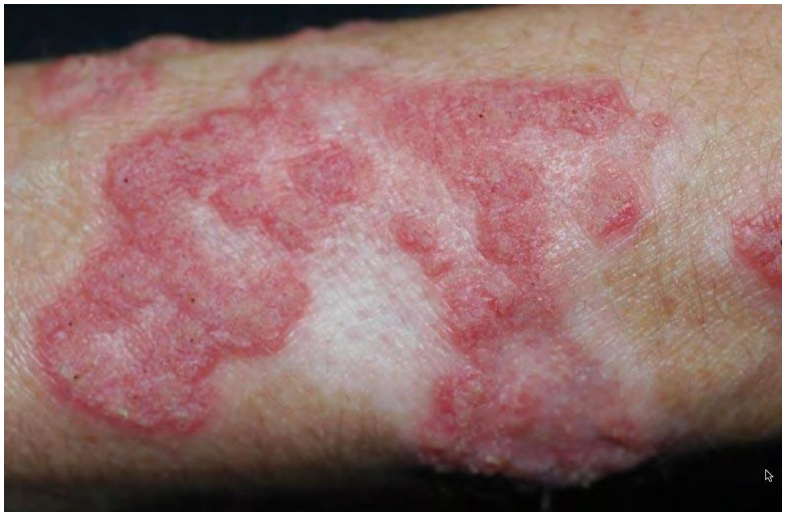


Discoid Lupus Erythematosus

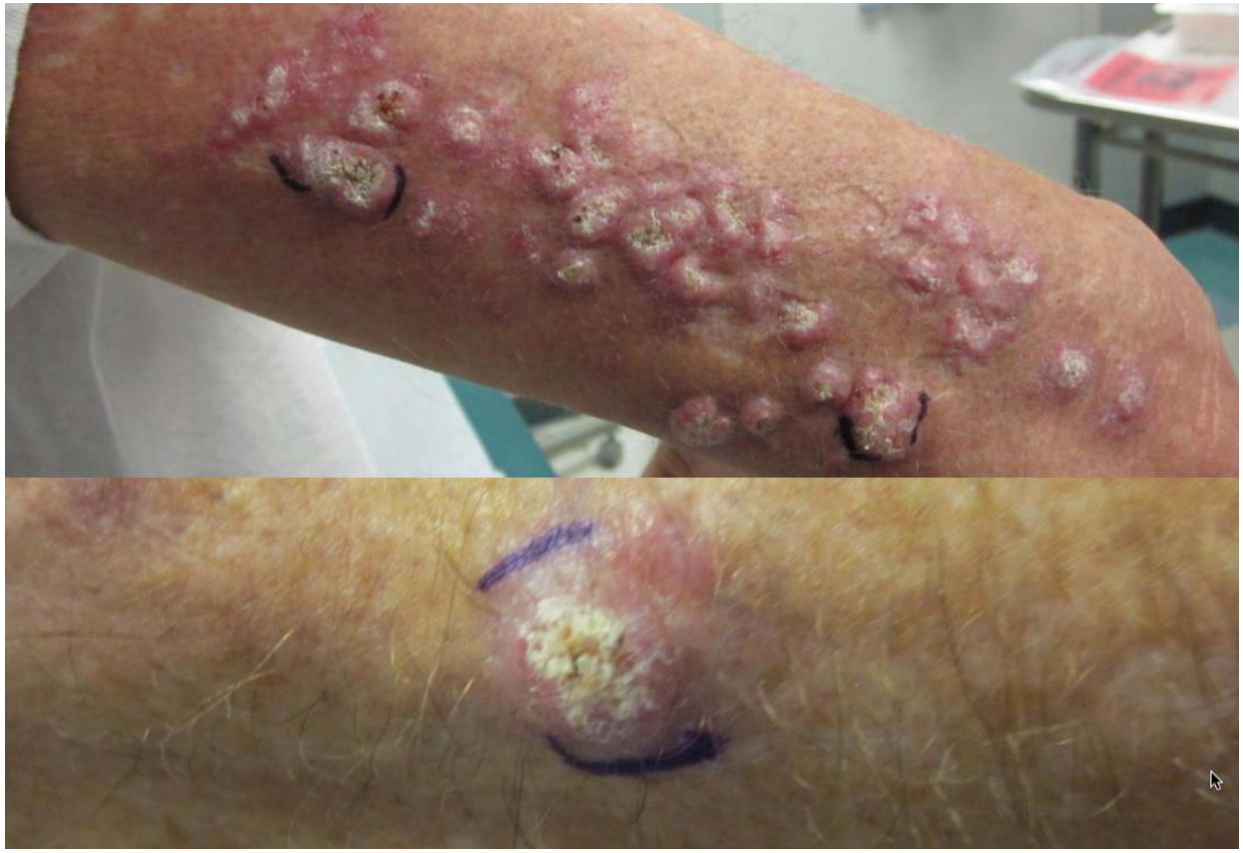


Discoid Lupus Erythematosus



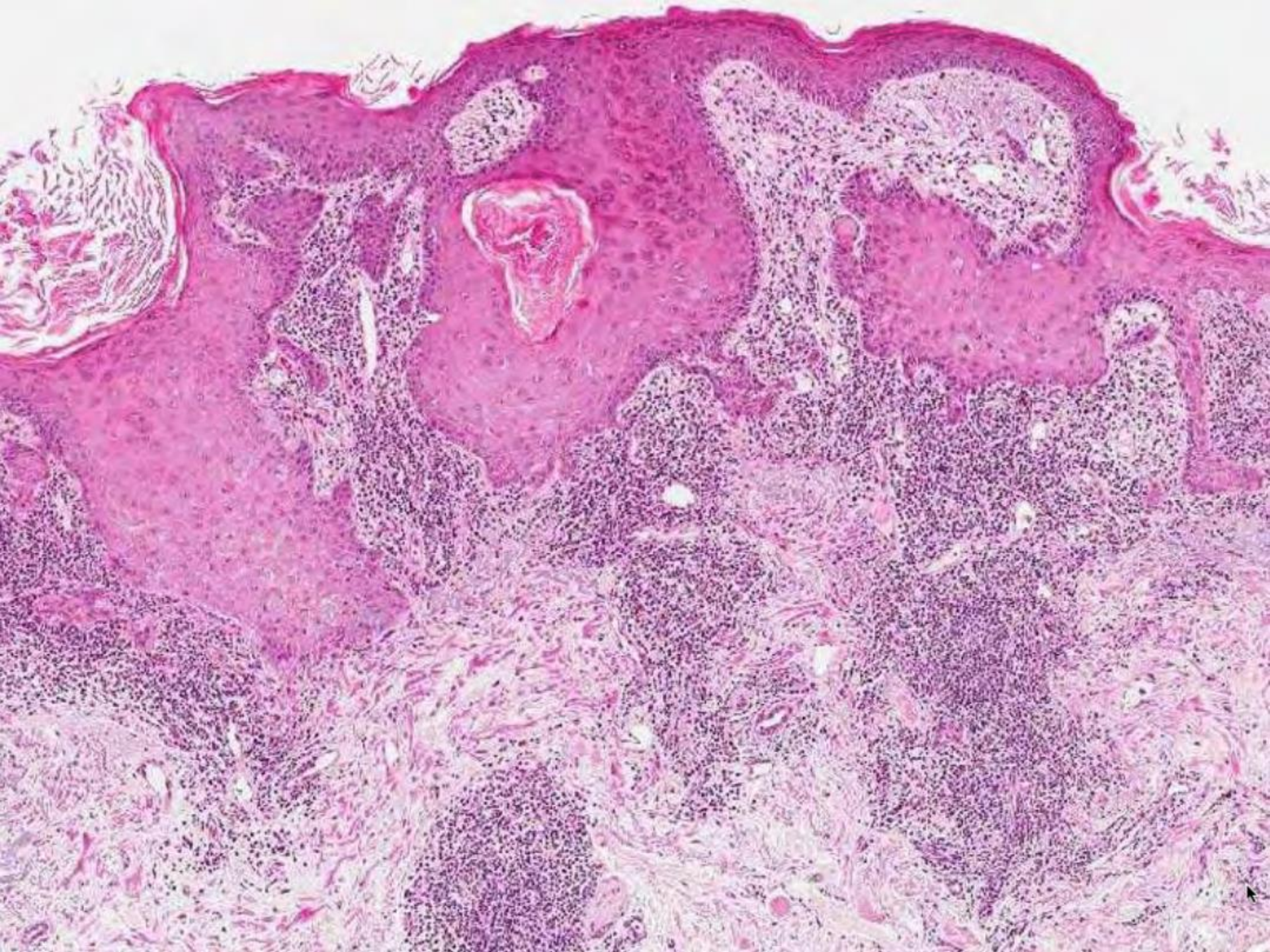


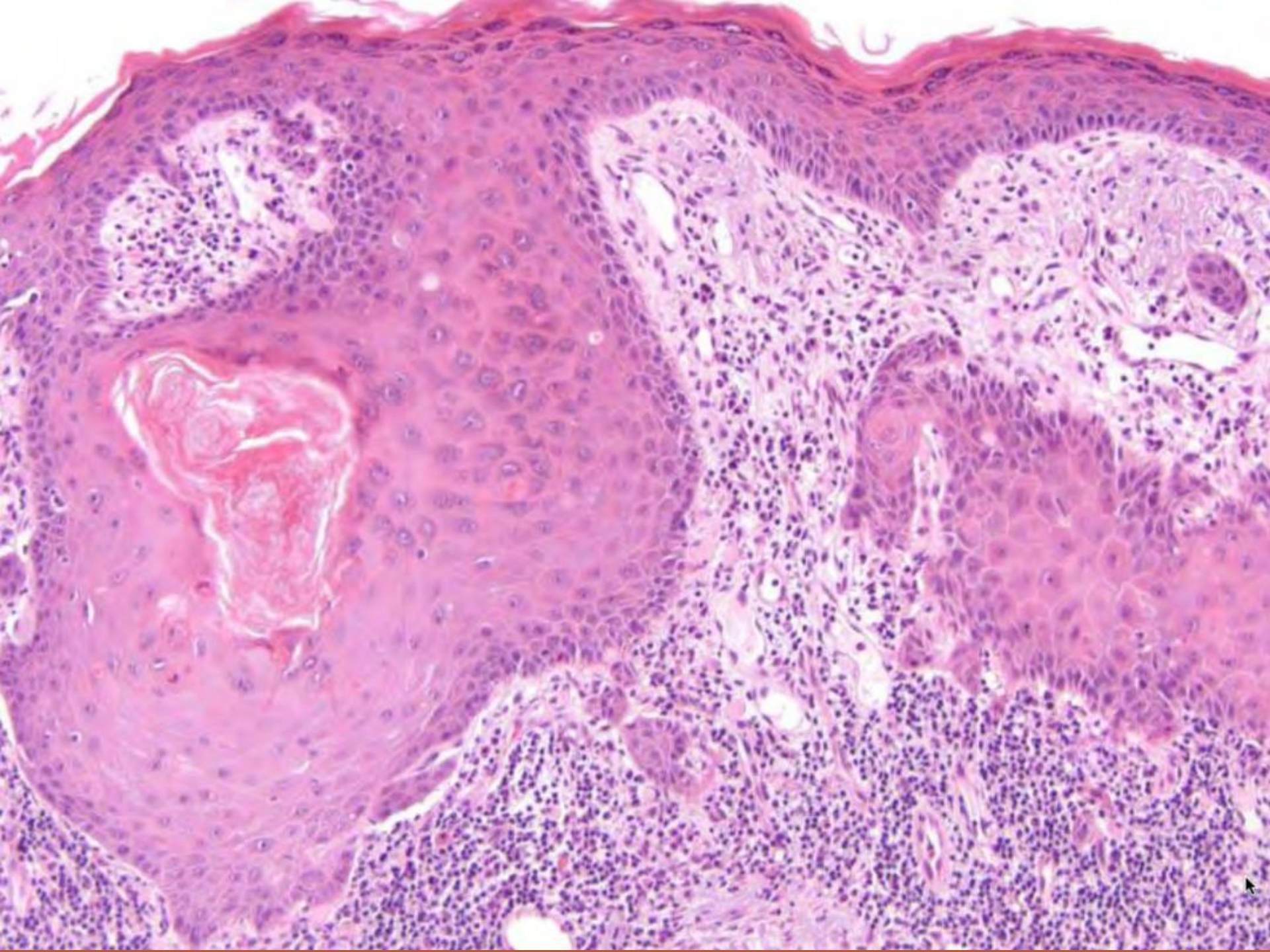
Discoid Lupus Erythematosus

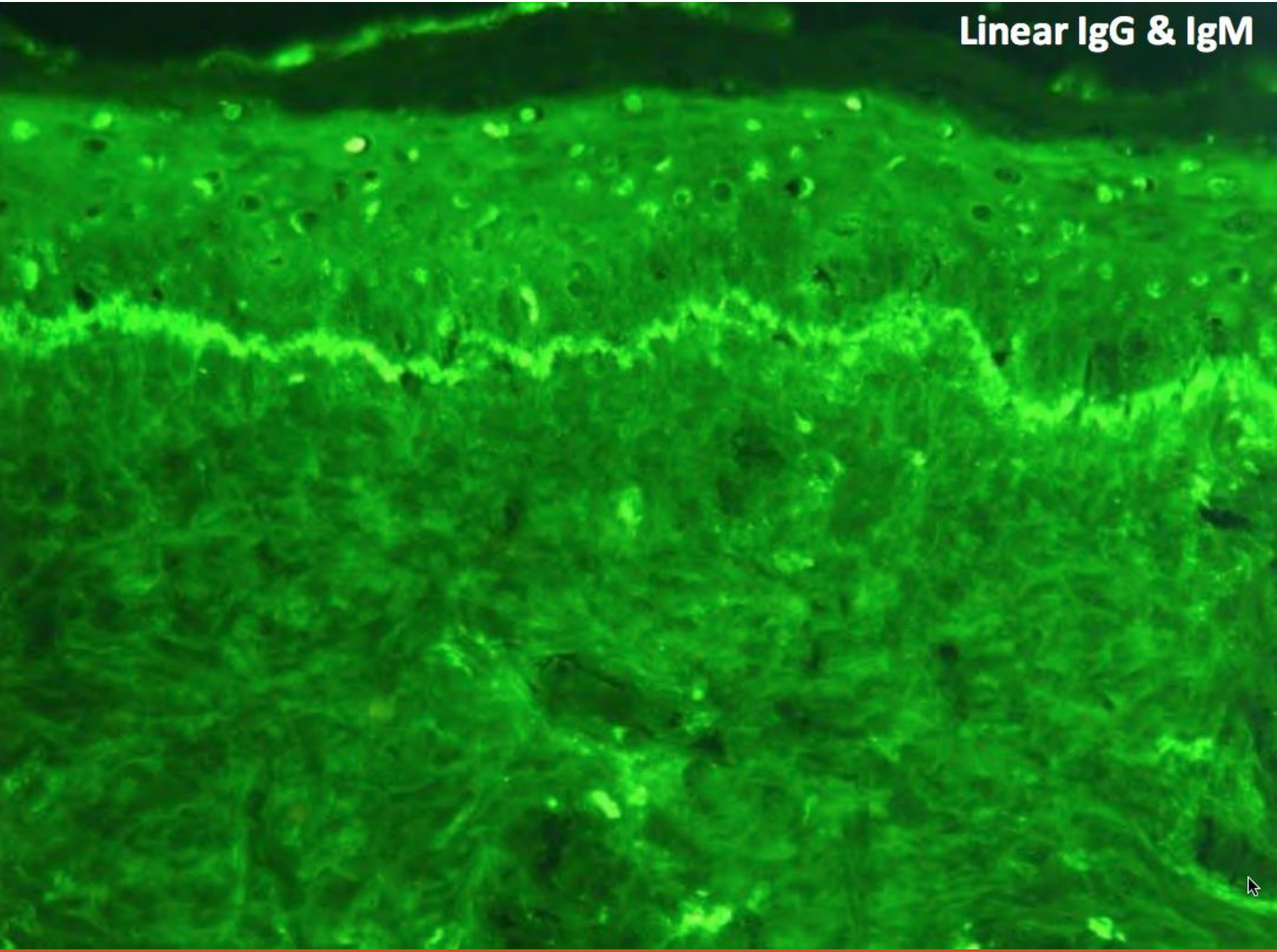


Hypertrophic LE

- **Elastic material between keratinocytes of retia**
- **KA-like lesions**
- **DIF may be useful- IgG & IgM along basement membrane 50-90% (similar to DLE)**
  - **May yield false positive when applied to sun-damaged skin**






Linear IgG & IgM

Hypertrophic LE - Ddx

- Hypertrophic lichen planus
- Lichenoid adverse drug eruptions
- Conditions with pseudoepitheliomatous hyperplasia
  - Halogenoderms
  - Deep fungal infections
  - Perforating disorders
  - Underlying slow growing neoplasms
    - Dermatofibroma
    - Granular cell tumor

Hypertrophic Inflammatory Lesions

HYPERTROPHIC LP

- Superficial
- Minor stromal reaction
- Rare adnexal involvement
- Distribution
  - Lower extremities (shin)

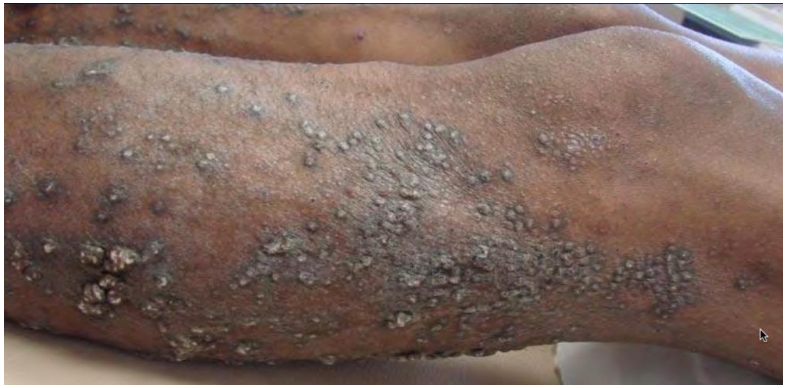
HYPERTROPHIC LE

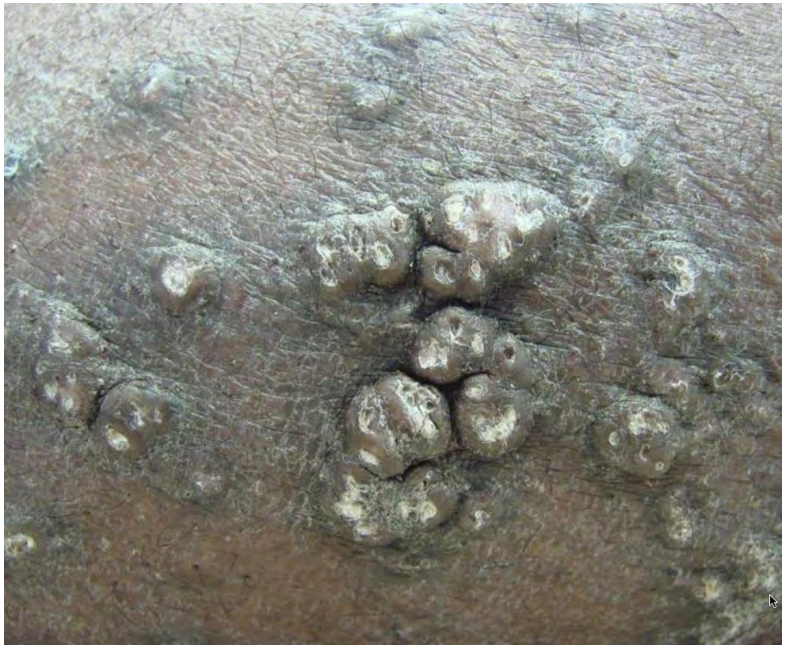
- Superficial and deep
- Prominent stromal reaction
- Common adnexal involvement
- Distribution
  - Face, arm, chest

Hypertrophic Lichen Planus

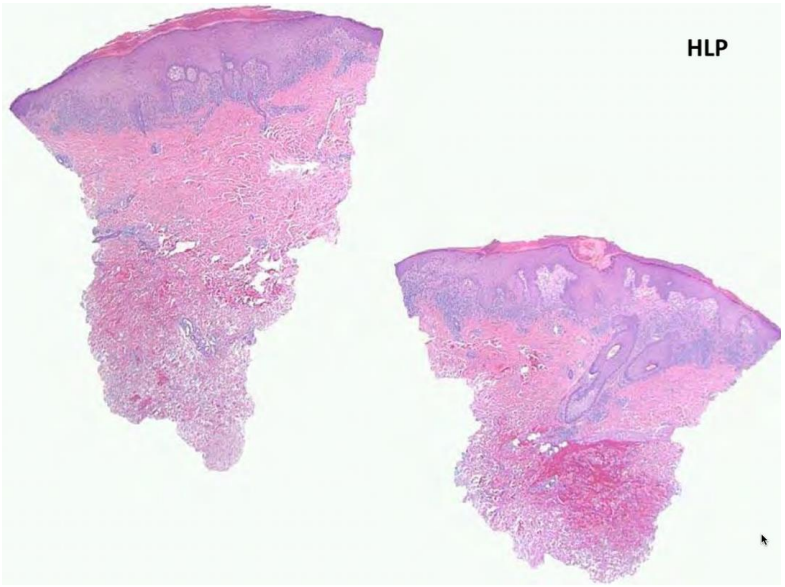
- **May look very similar to Hypertrophic LE**
- **Clinical completely different**
  - **HLE- face, arms, chest**
  - **HLP- lower extremities especially shins**

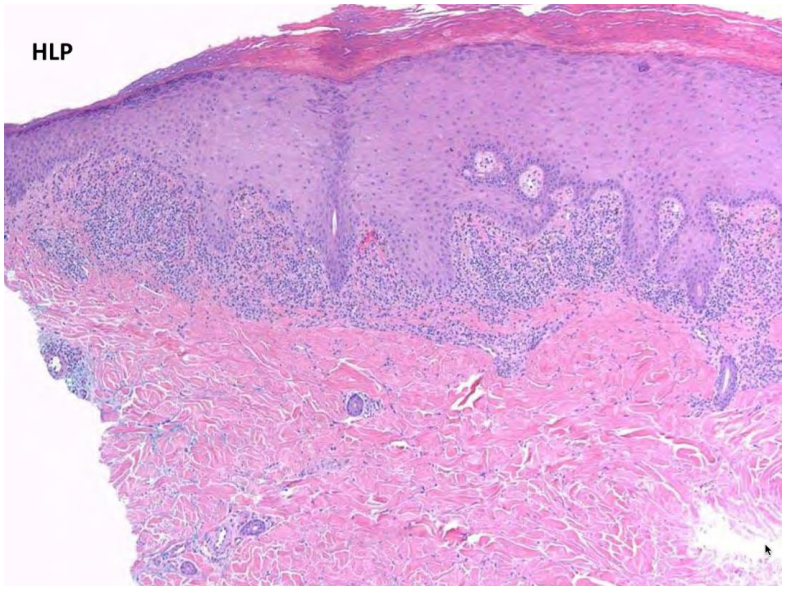
Hypertrophic Lichen Planus



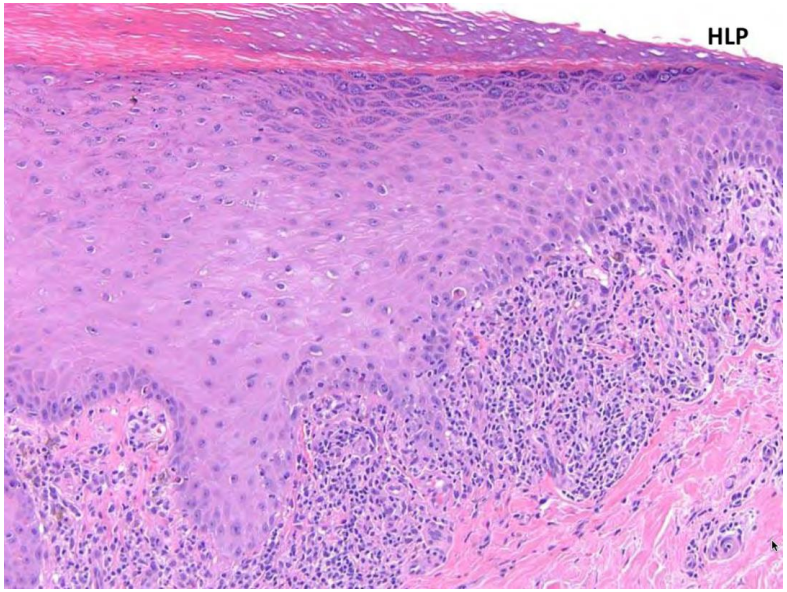


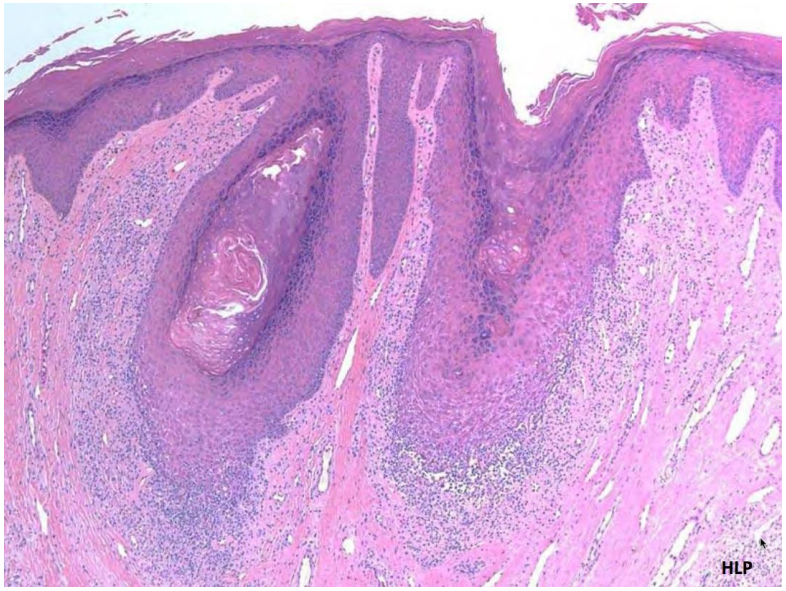
Hypertrophic Lichen Planus





Hypertrophic Lichen Planus

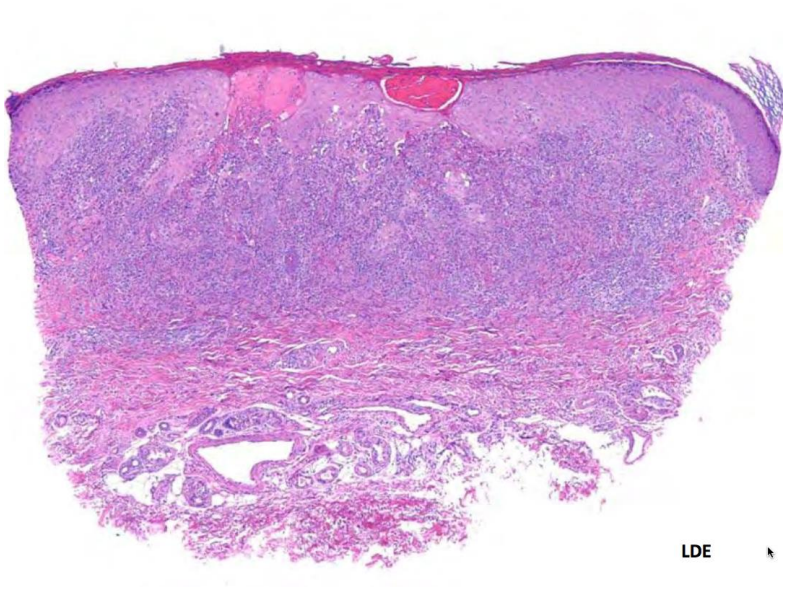


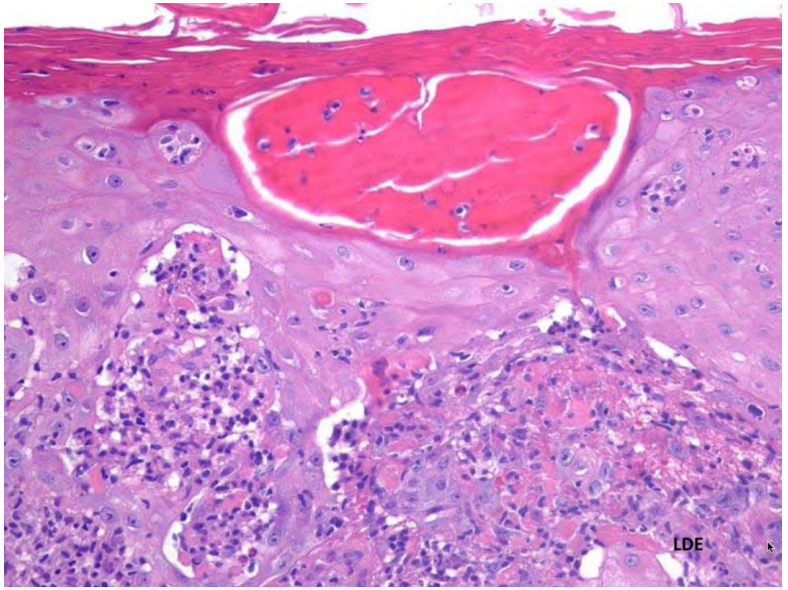


Lichenoid ADR

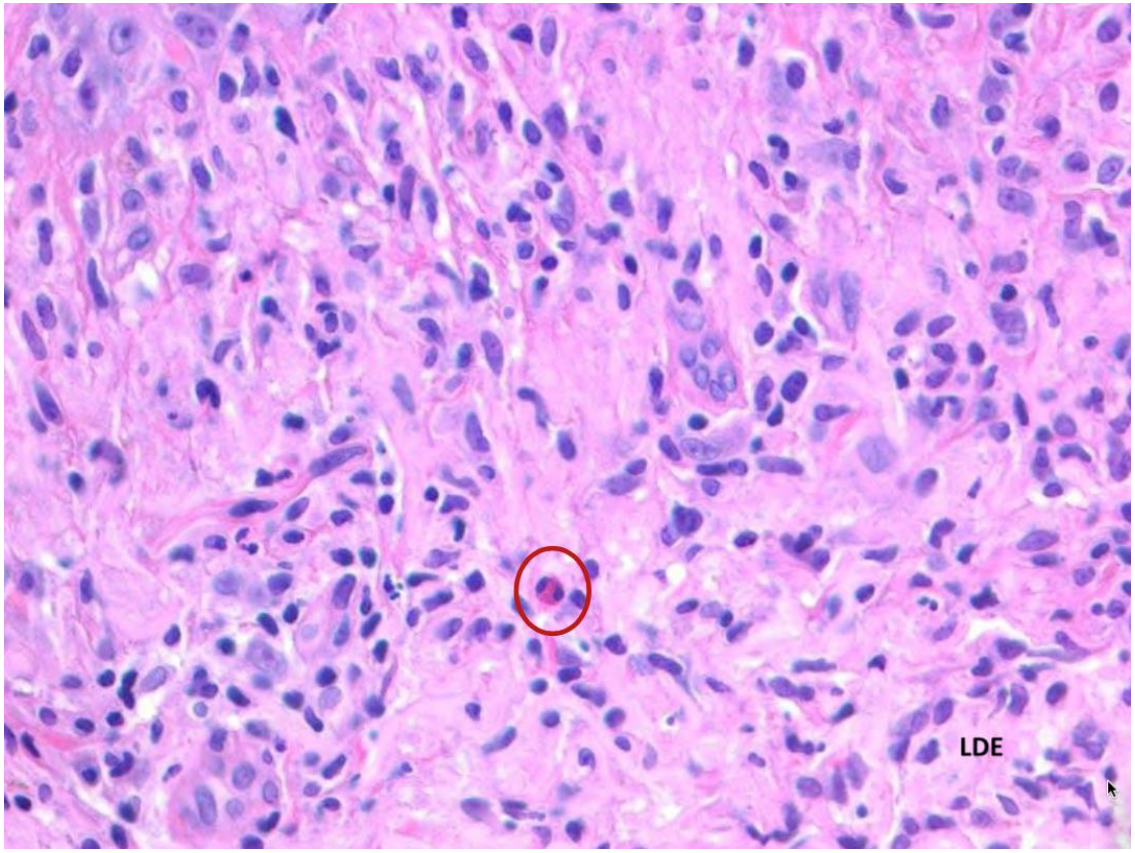
- **Drug history**
- **May have prominent epidermal hyperplasia, but no mucin, follicular plugging, intraepidermal elastic fibers, angiocentic lymphocytic inflammation**
- **Eosinophils and neutrophils**

Lichenoid ADR





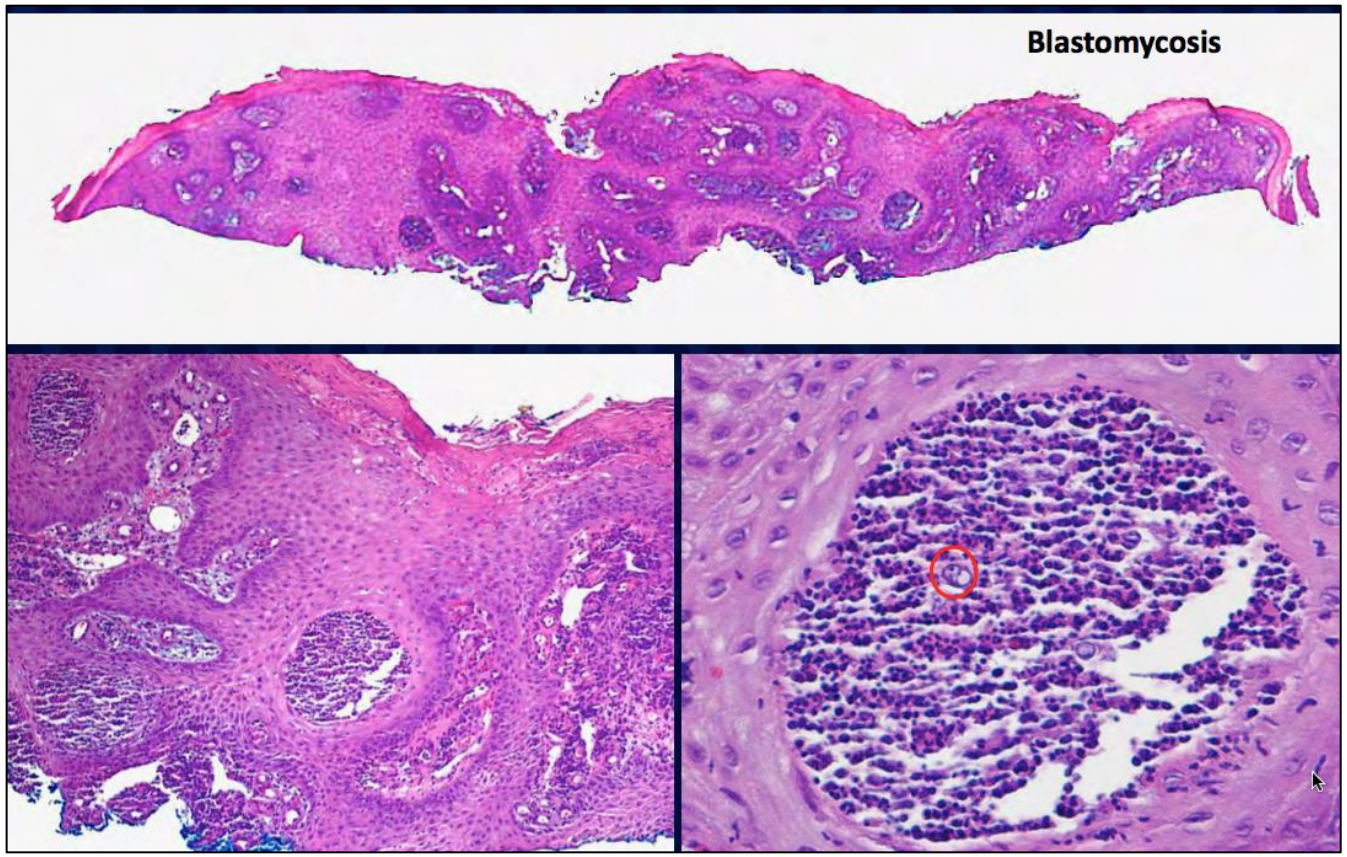
Lichenoid ADR



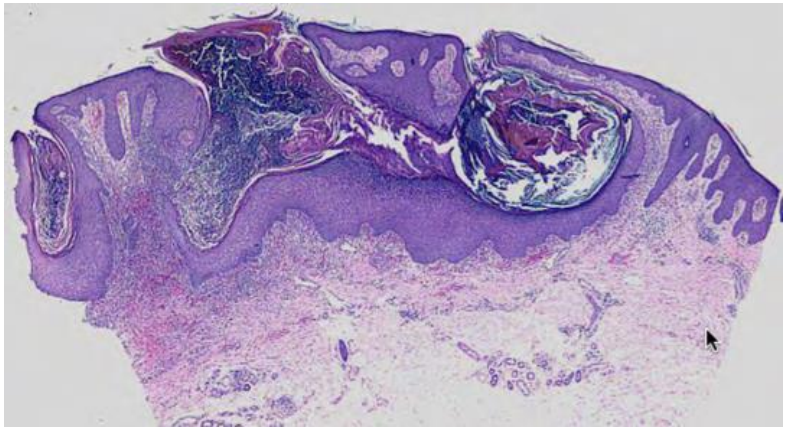
Secondary Irregular Epidermal Hyperplasia

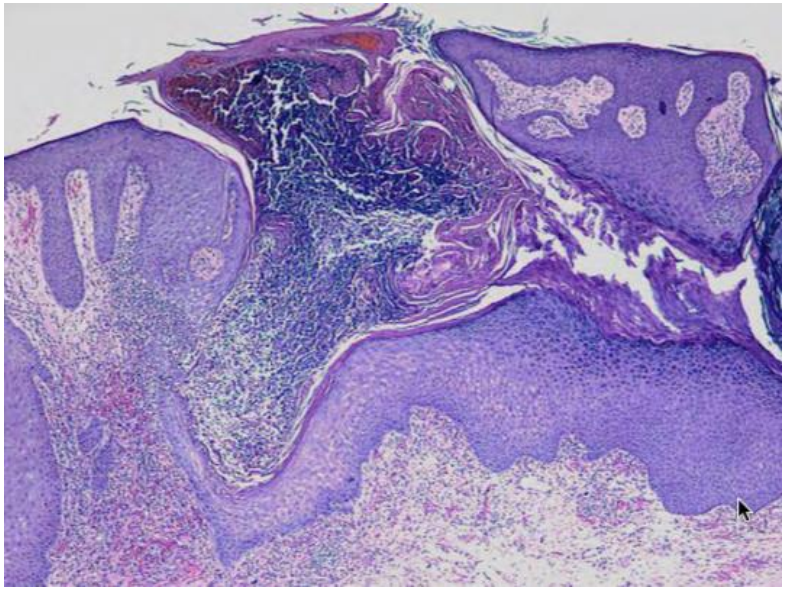
- **Halogenoderms**
  - **Intraepidermal microabscesses with neutrophils & eosinophils**
  - **Lacks interface changes**
  - **Chronic ingestion of halogens**
- **Deep fungal infections**
  - **Lacks interface changes**
  - **Bug stains positive**
- **Perforating disorders**
  - **Neutrophils & histiocytes**
  - **Fewer lymphocytes**
  - **Greater amounts of altered elastin & collagen**
  - **Extensive transepidermal elimination**

Epidermal Hyperplasia in Fungal Infections



Acquired Perforating Disorders

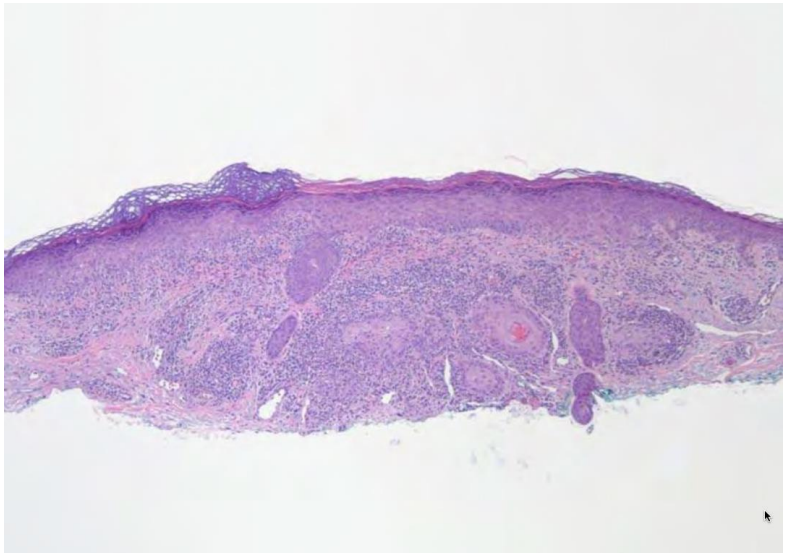


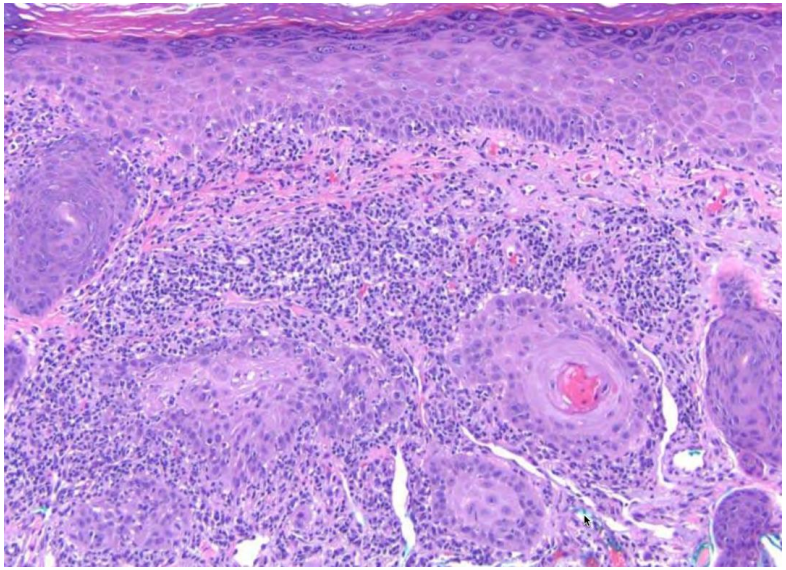


Atypical Squamo-Proliferative Lesions

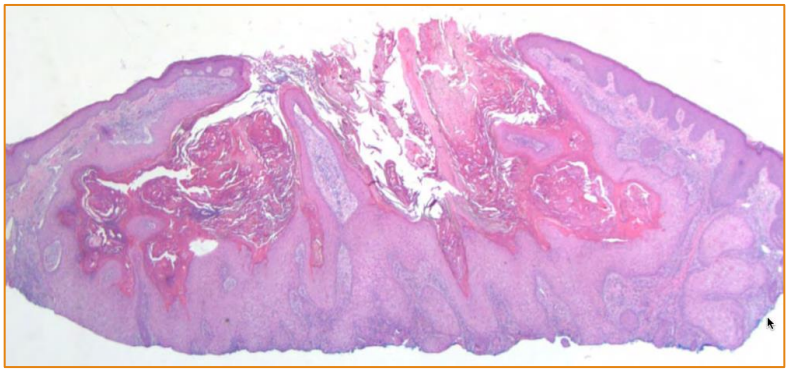
- **Lichenoid keratoses**
  - **Chest, forearm R/O BBC**
  - **Atypia does not extend beyond inflammation**
- **Lichenoid actinic keratoses**
  - **Atypia beyond inflammation**
  - **Alternating ortho- and parakeratosis**
- **Squamous cell carcinoma**
  - **In situ & invasive**
  - **KAs**

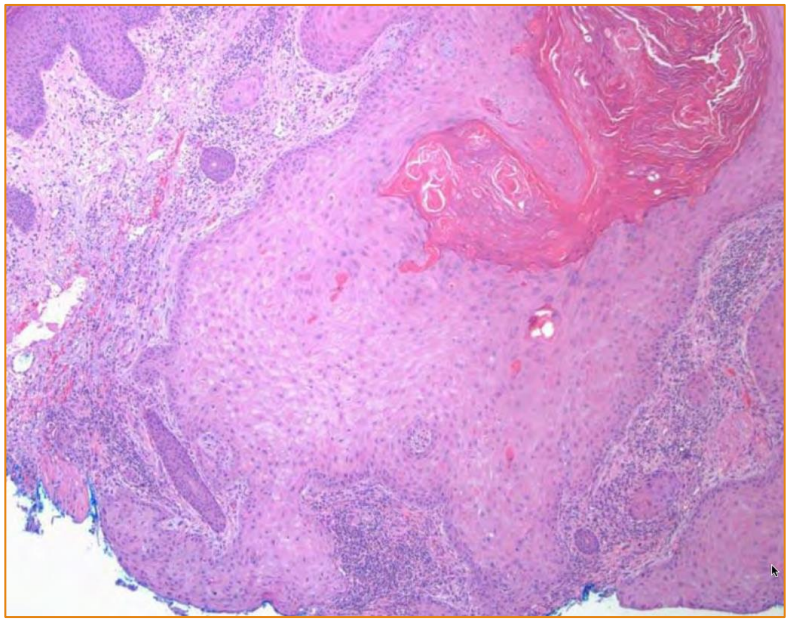
Atypical Squamo-Proliferative Lesions



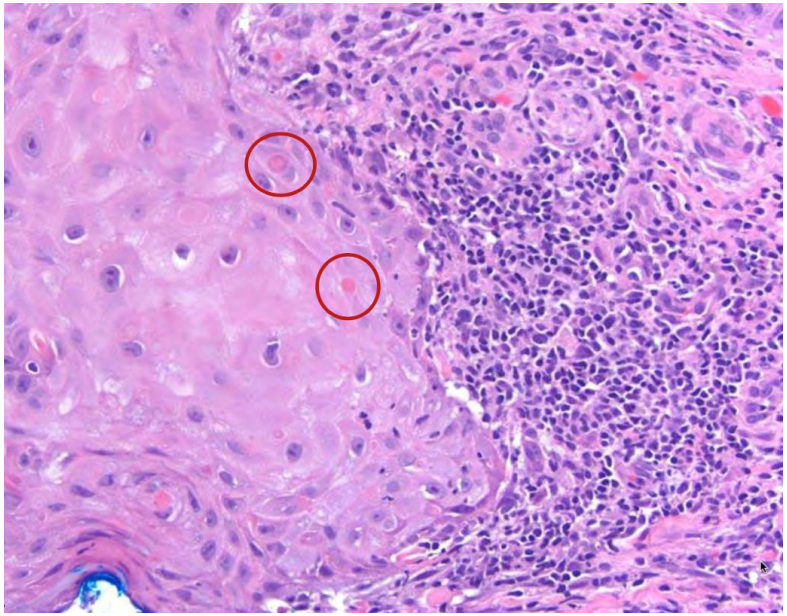


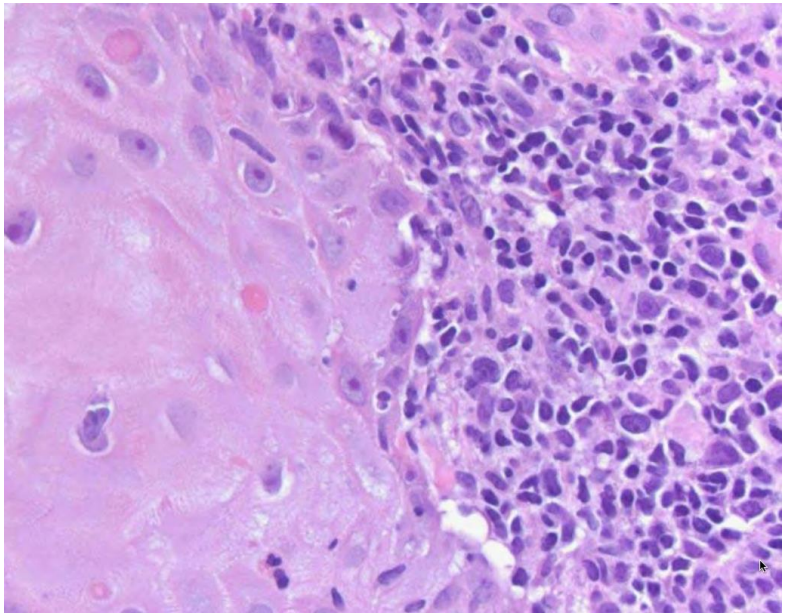
KA-like SCC





KA-like SCC

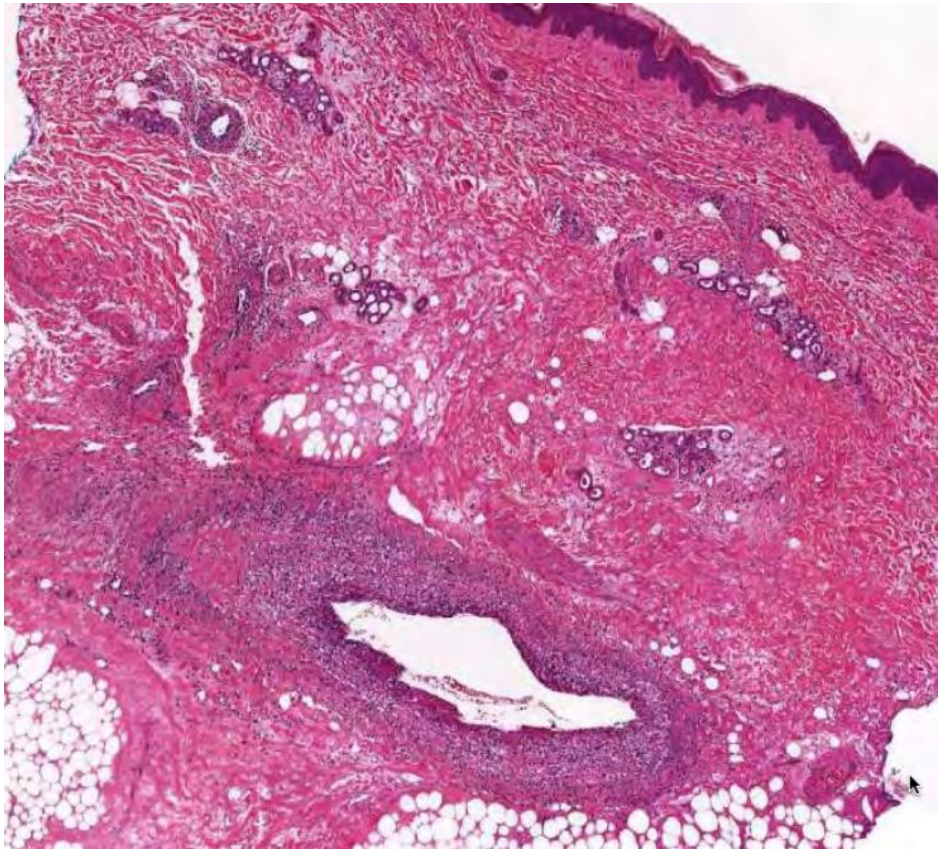




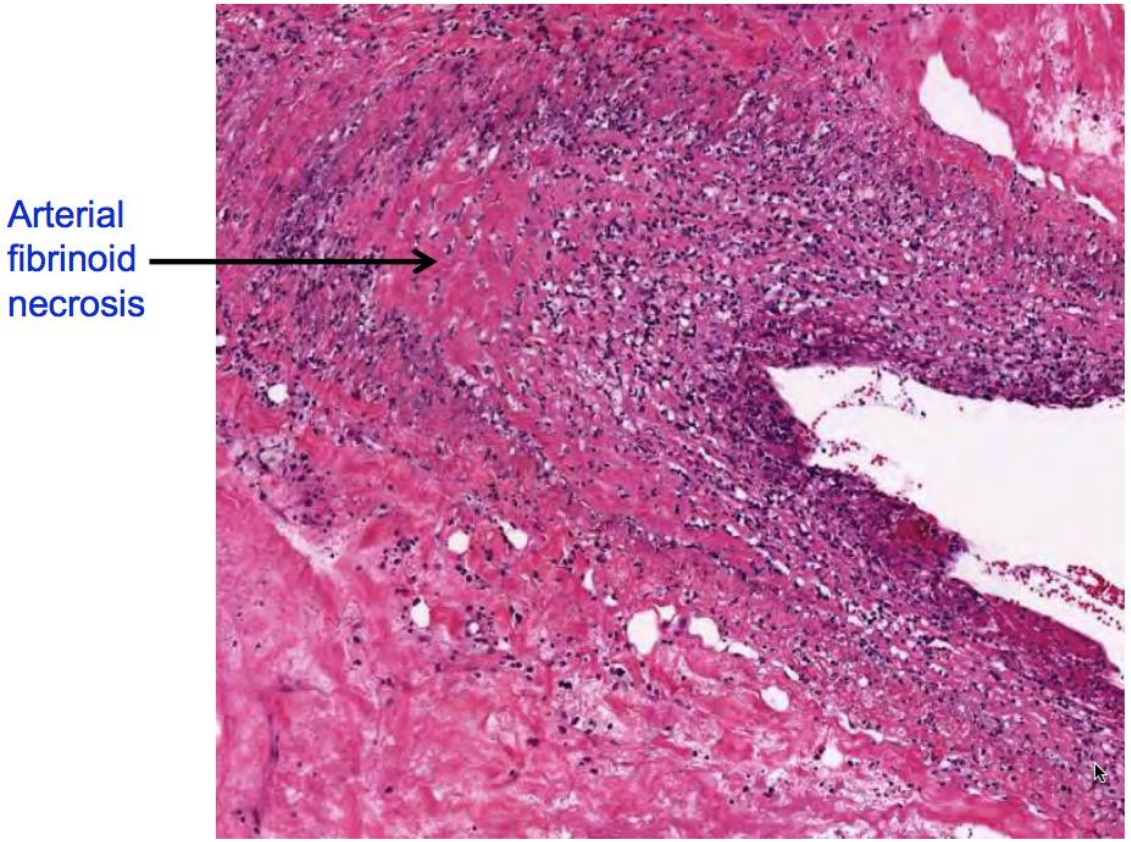
Case 2

A 43 year old man noted worsening arthralgias, myalgias, abdominal pain, and migrating “tingling” in both lower extremities. Physical examination revealed livido reticularis on his left lower extremity and an erythematous nodule in the calf. A biopsy of the skin nodule was performed.

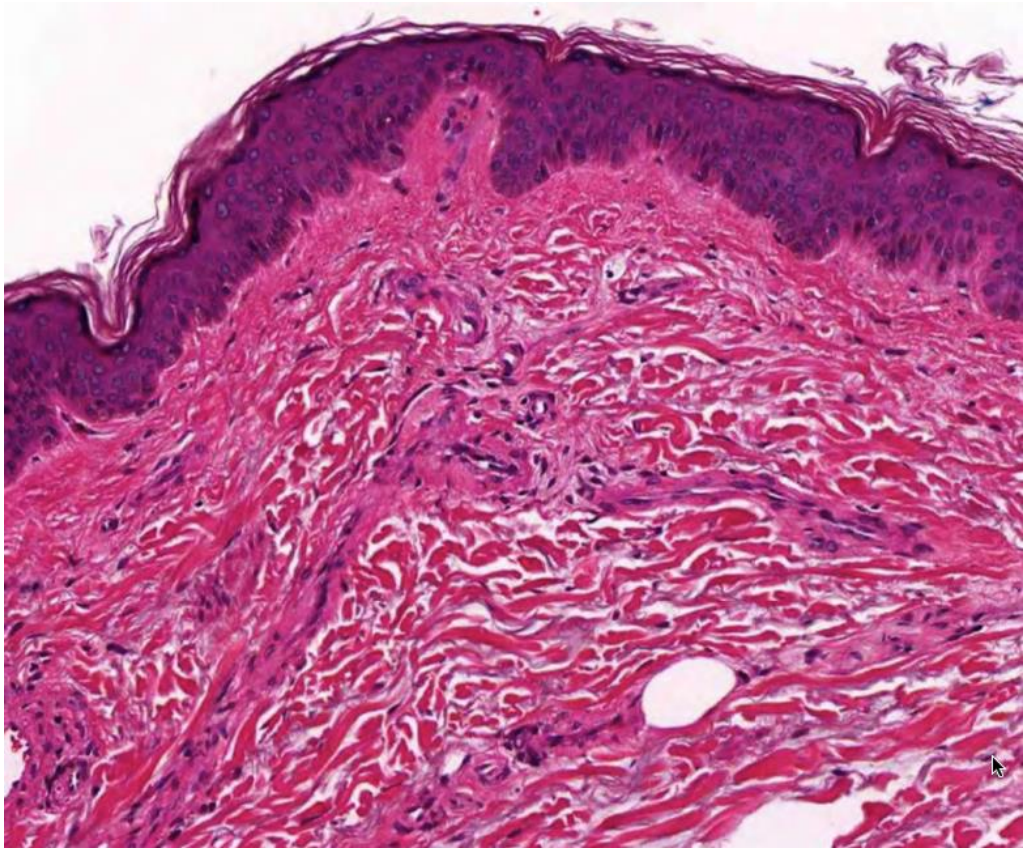
Erythematous nodule in the calf



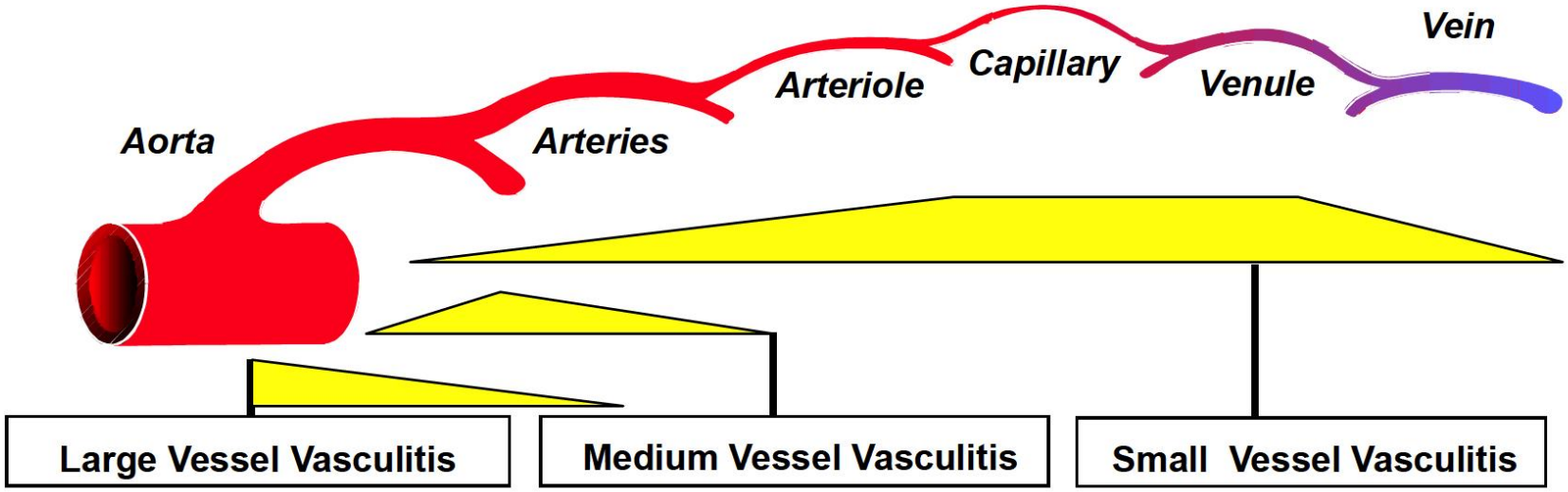
Erythematous nodule in the calf

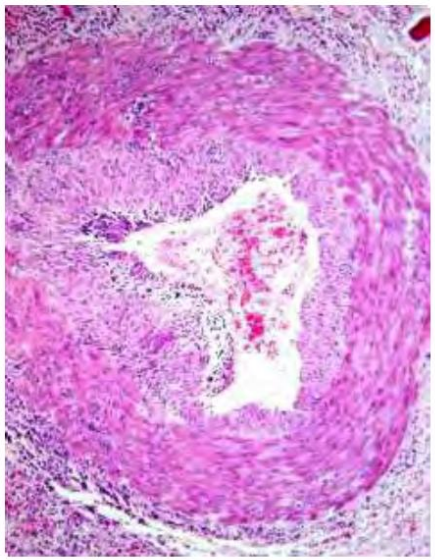


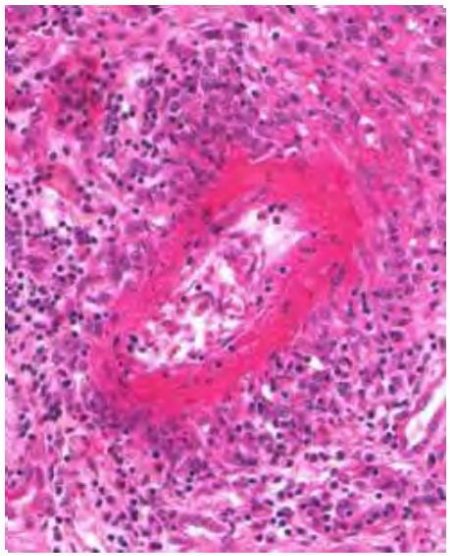
Erythematous nodule in the calf

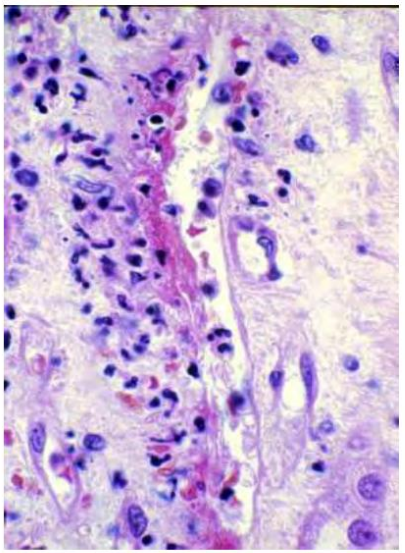


2012 CHCC Vasculitis Nomenclature



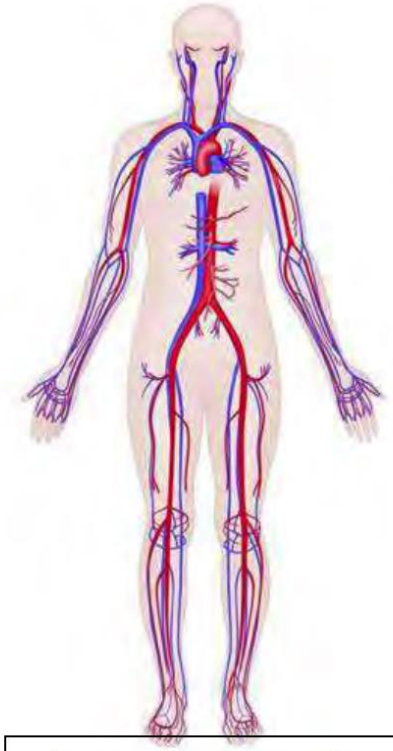






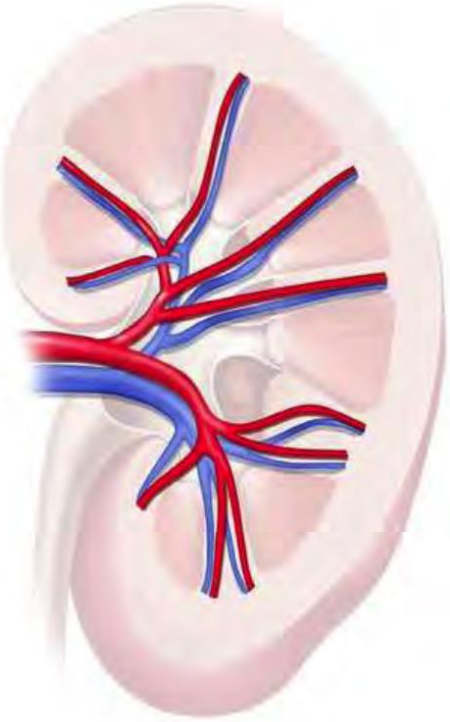
"Vessel size" refers to structural/functional type of vessel as well as size

Large Vessels



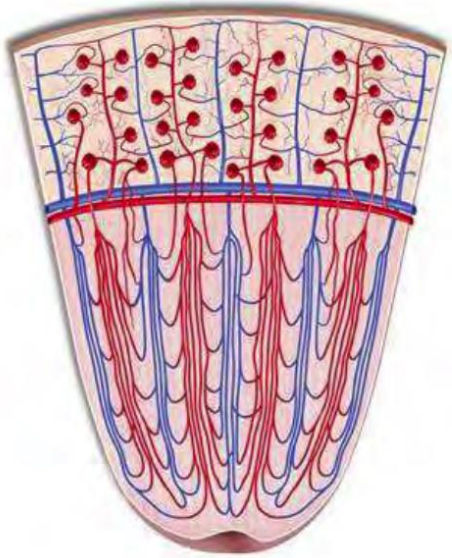
Large vessels are the aorta and its major branches and the analogous veins.

Medium Vessels



Medium vessels are the main visceral arteries and veins and their initial branches.

Small Vessels



Small vessels are intra-parenchymal arteries, arterioles, capillaries, venules and veins.

Jennette et al. Arthritis Rheum 2013;65:1-11

2012 CHCC Vasculitis Nomenclature

Immune Complex Small Vessel Vasculitis

Cryoglobulinemic Vasculitis

IgA Vasculitis (Henoch-Schönlein)

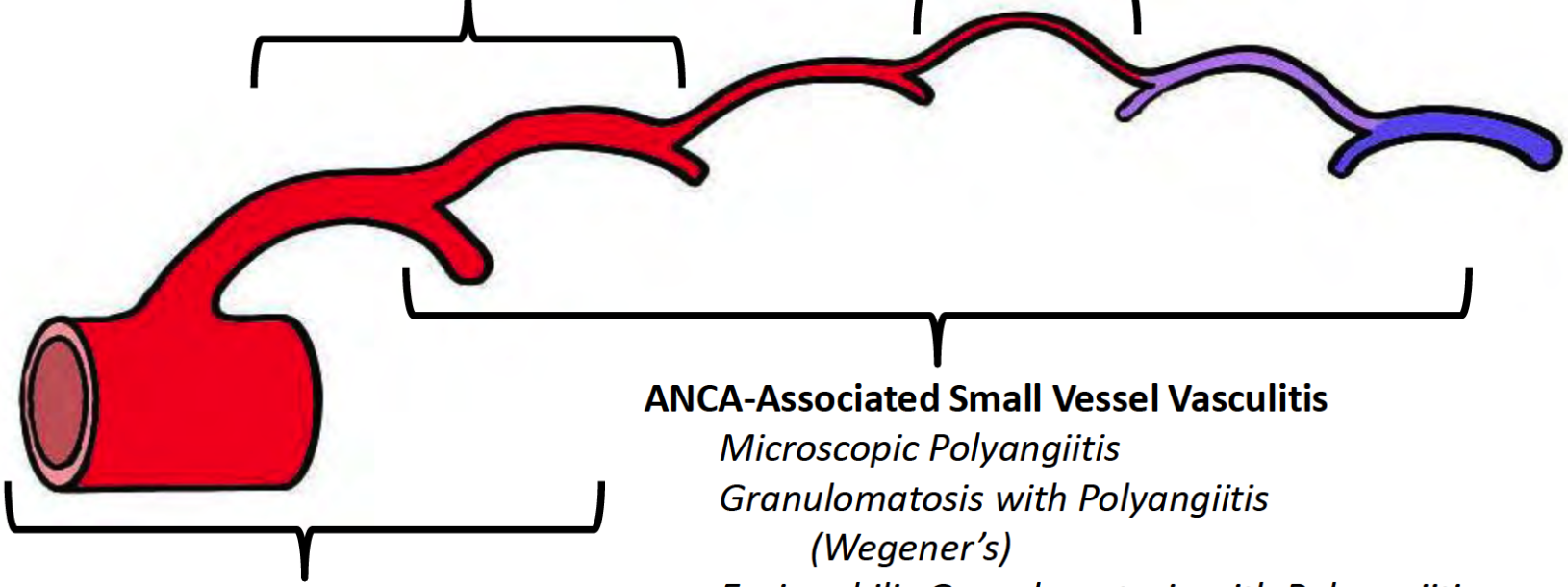
Hypocomplementemic Urticarial Vasculitis (Anti-C1q Vasculitis)

Medium Vessel Vasculitis

Polyarteritis Nodosa

Kawasaki Disease

Anti-GBM Disease



ANCA-Associated Small Vessel Vasculitis

Microscopic Polyangiitis

Granulomatosis with Polyangiitis (Wegener's)

Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss)

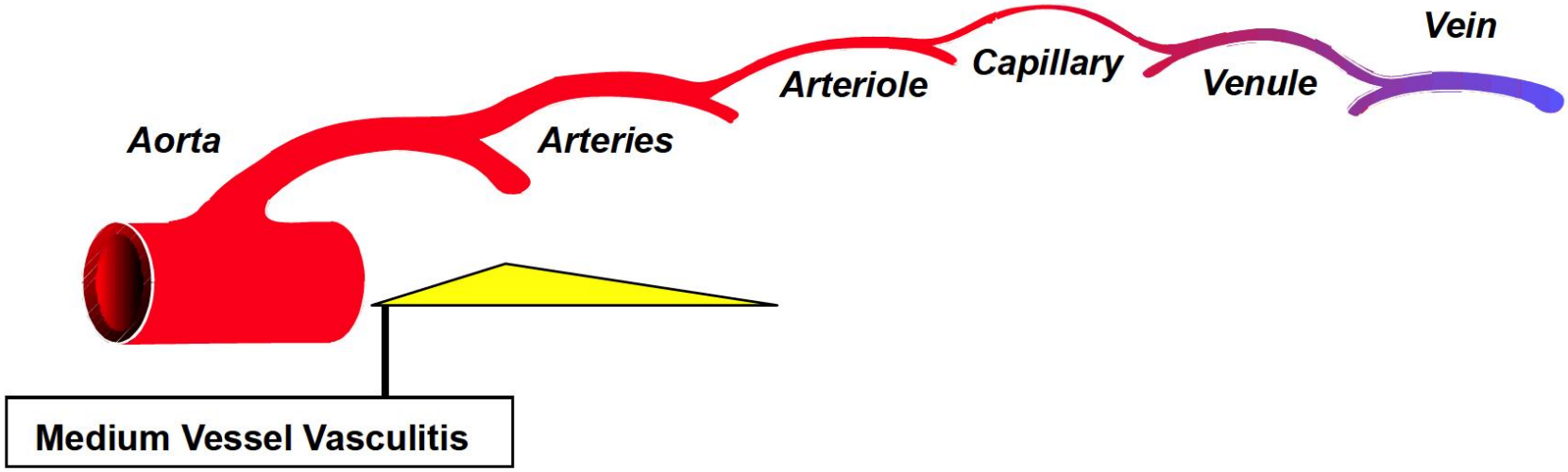
Large Vessel Vasculitis

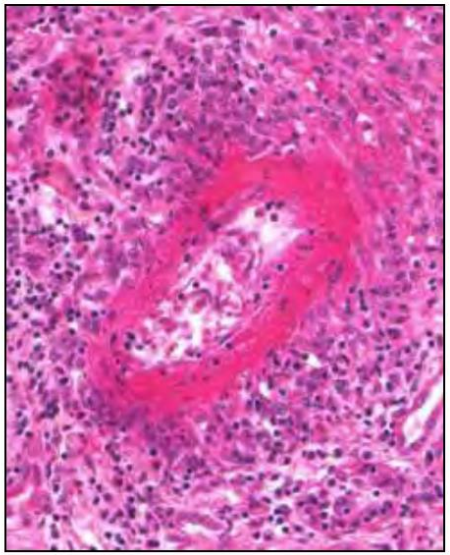
Takayasu Arteritis

Giant Cell Arteritis

Jennette et al. Arthritis Rheum 2013;65:1-11

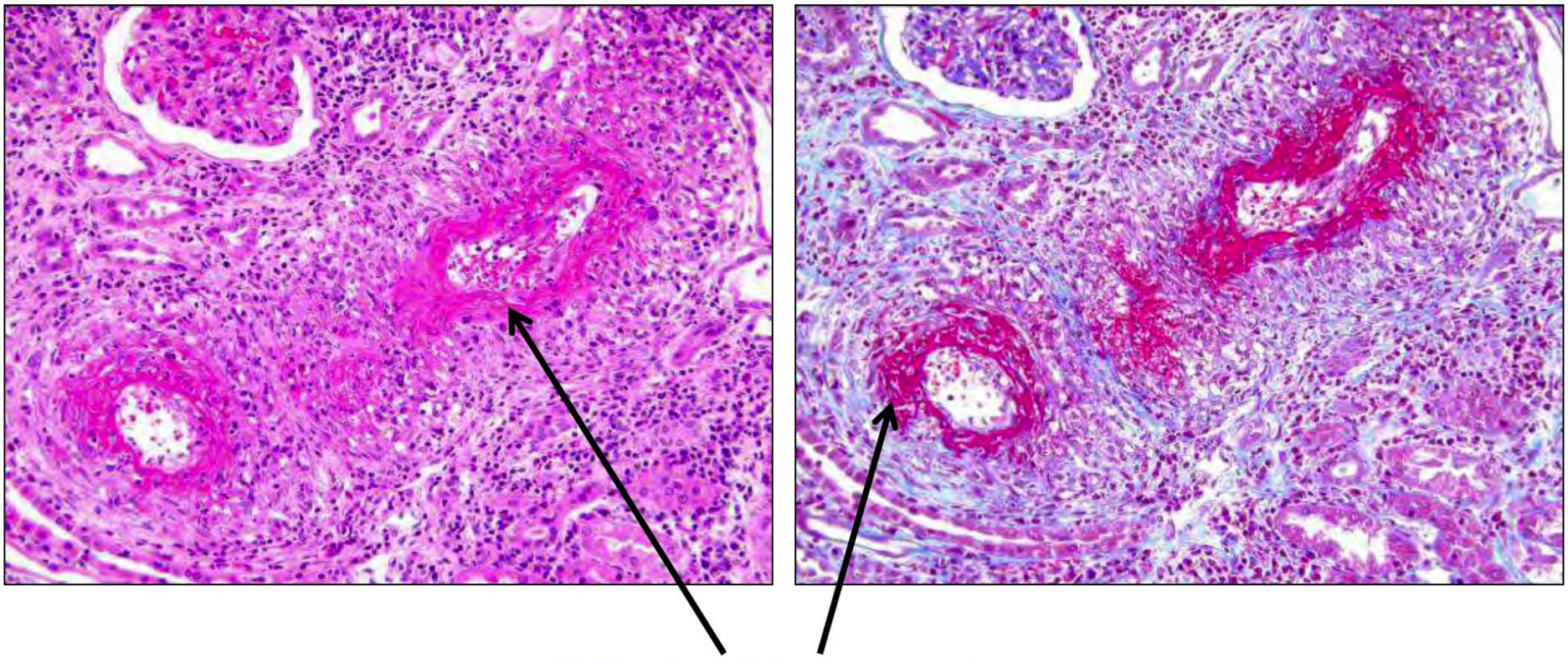
Medium Vessel Vasculitis 2012 CHCC Definition





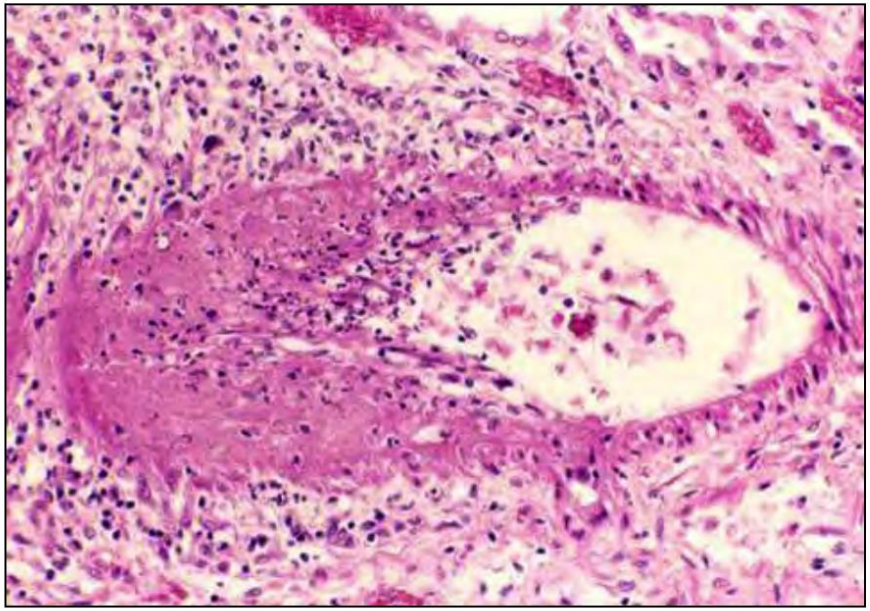
Vasculitis predominantly affecting medium arteries defined as the main visceral arteries and their branches. Any size artery may be affected. Inflammatory aneurysms and stenoses are common.

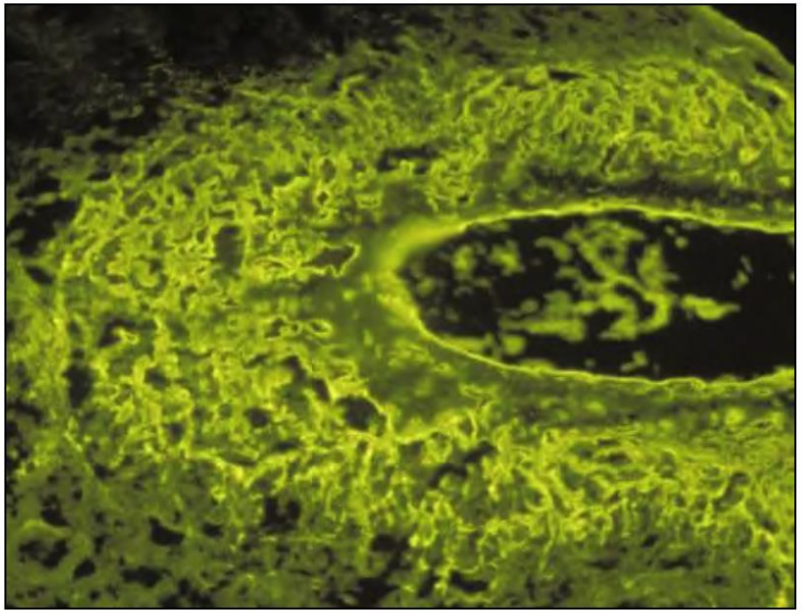
Necrotizing arteritis



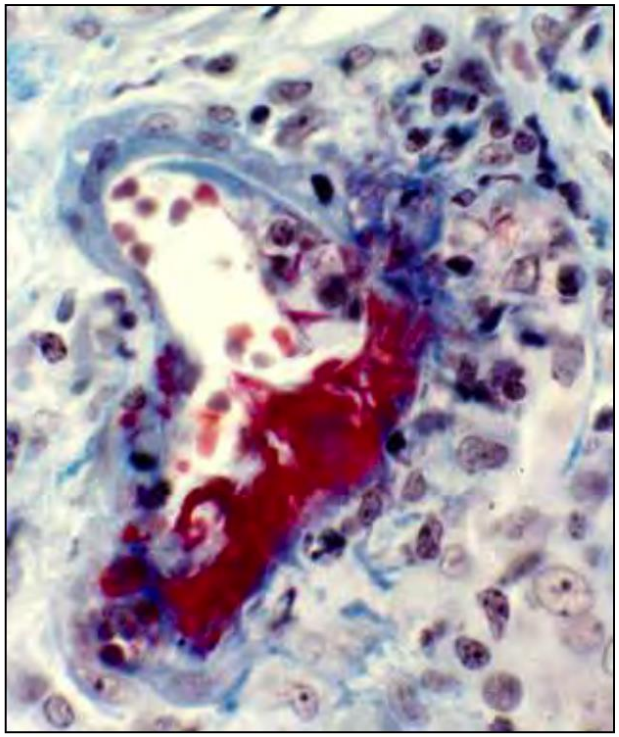
Necrotizing arteritis begins as a segmental necrotizing inflammation of arteries with conspicuous infiltration of neutrophils and monocytes.

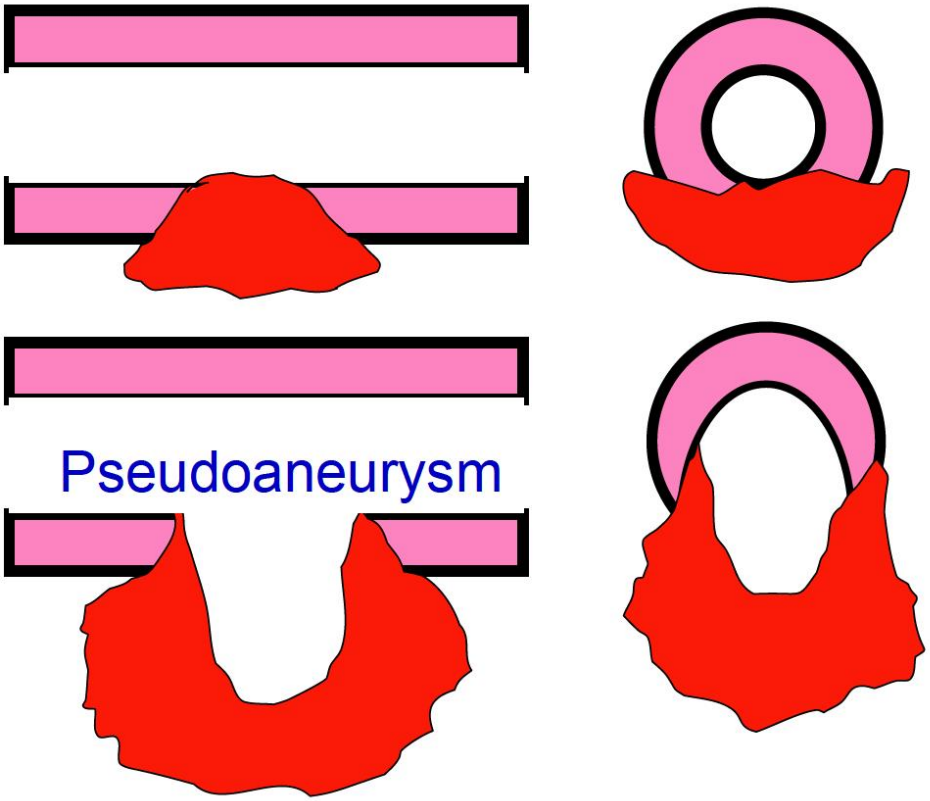
This typically induces fibrinoid necrosis characterized by accumulation of plasma proteins in injured tissue, including coagulation factors that are converted to fibrin.





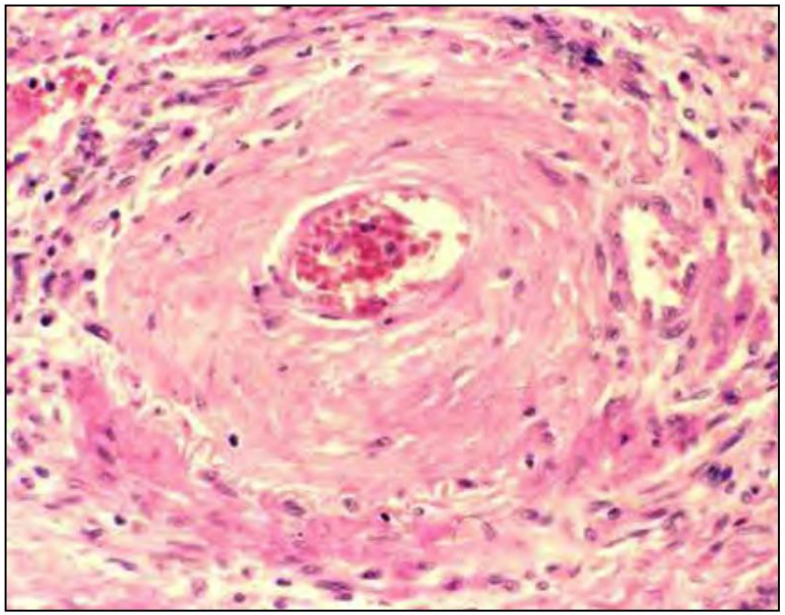
If the necrotizing inflammation extends through the vessel wall into the perivascular tissue, inflammatory aneurysms (pseudoaneurysms) will develop.

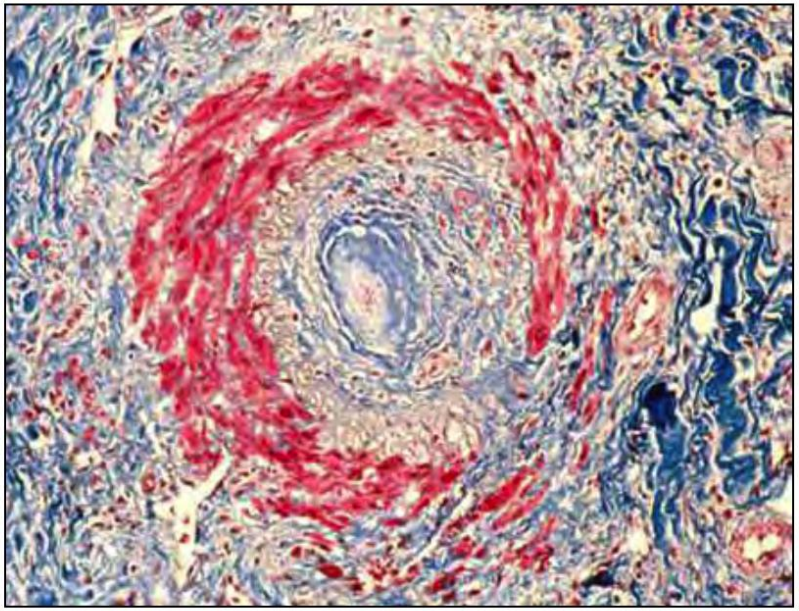




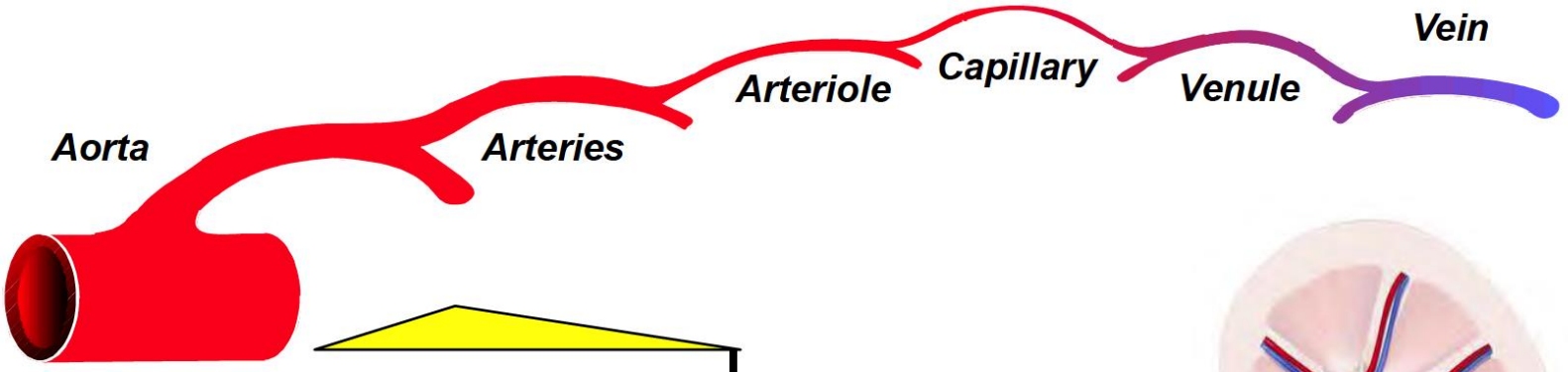
All necrotizing vasculitis enters a final common pathway of chronic inflammation and scarring.

The transformation to sclerotic lesions with a predominance of infiltrating T-lymphocytes and macrophages occurs as quickly as one or two weeks after the initiation of injury.



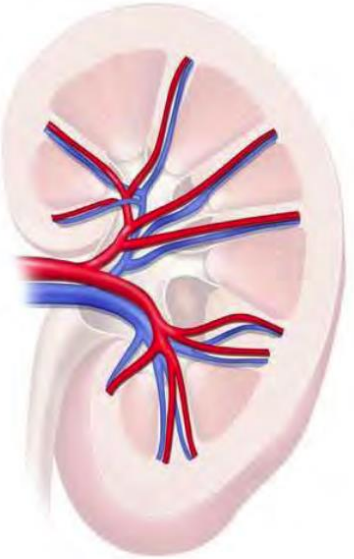


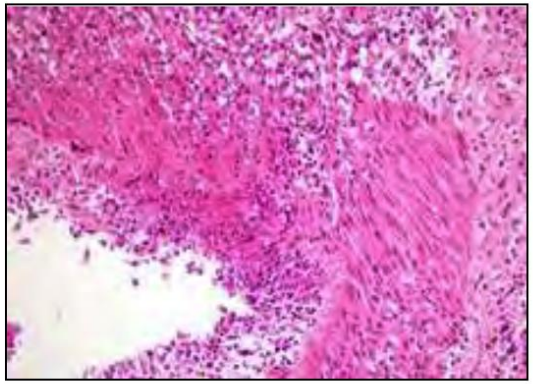
“Chronic” arteritis

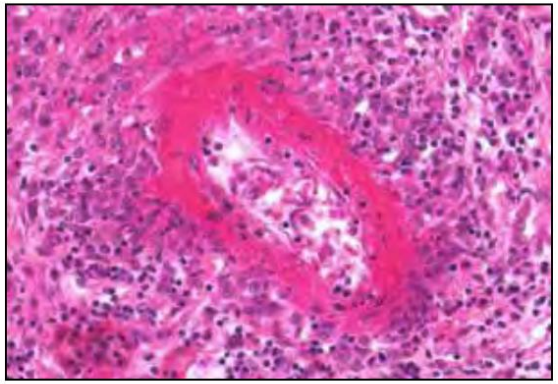


Medium Vessel Vasculitis

- necrotizing arteritis without MCLN syndrome → **Kawasaki Disease**
- necrotizing arteritis with MCLN syndrome → **Polyarteritis Nodosa**

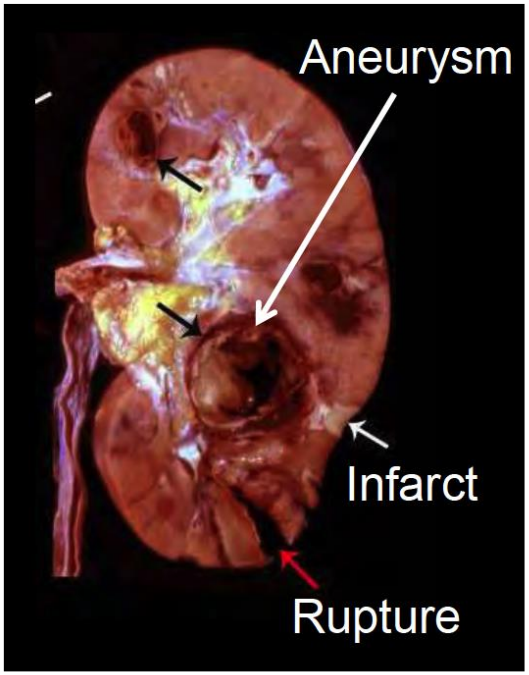


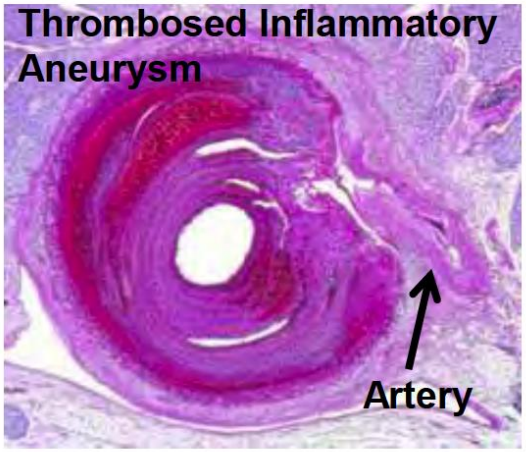




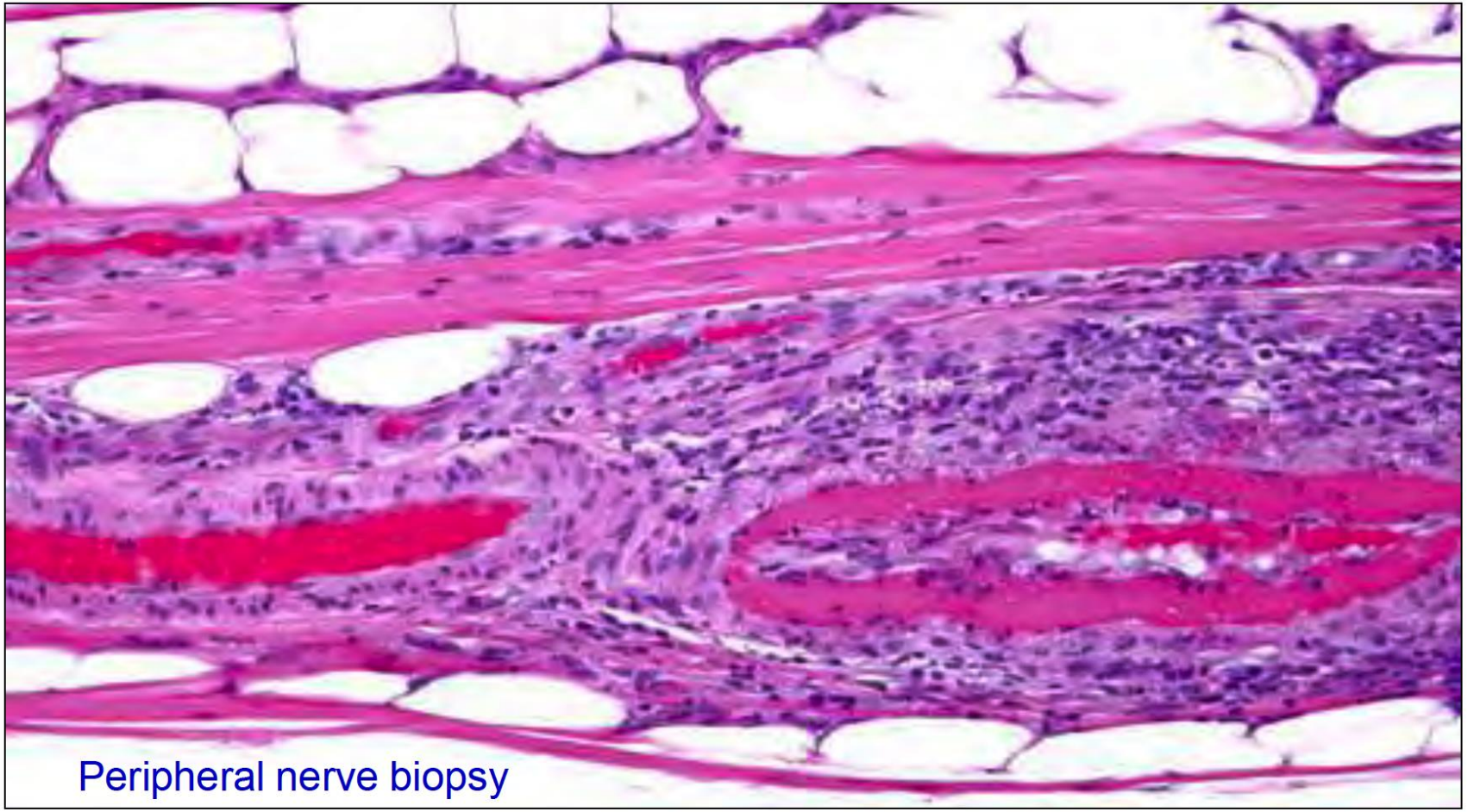
Polyarteritis Nodosa
2012 CHCC Definition

Necrotizing arteritis of medium or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules; and not associated with ANCA.



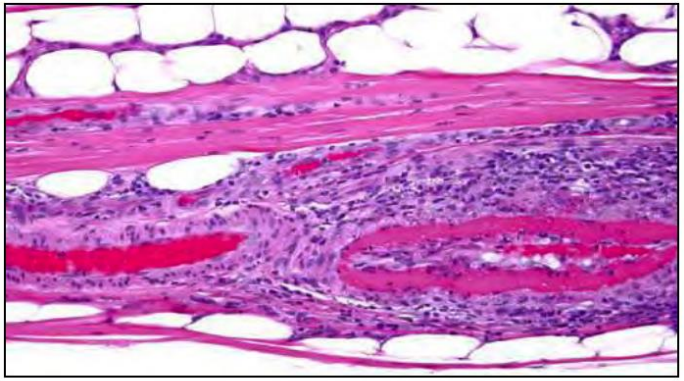


Necrotizing arteritis is not definitive for a specific category of vasculitis



Diagnosis: necrotizing arteritis, differential diagnosis includes polyarteritis nodosa and microscopic polyangiitis and other vasculitides that cause necrotizing arteritis (recommend ANCA serology)

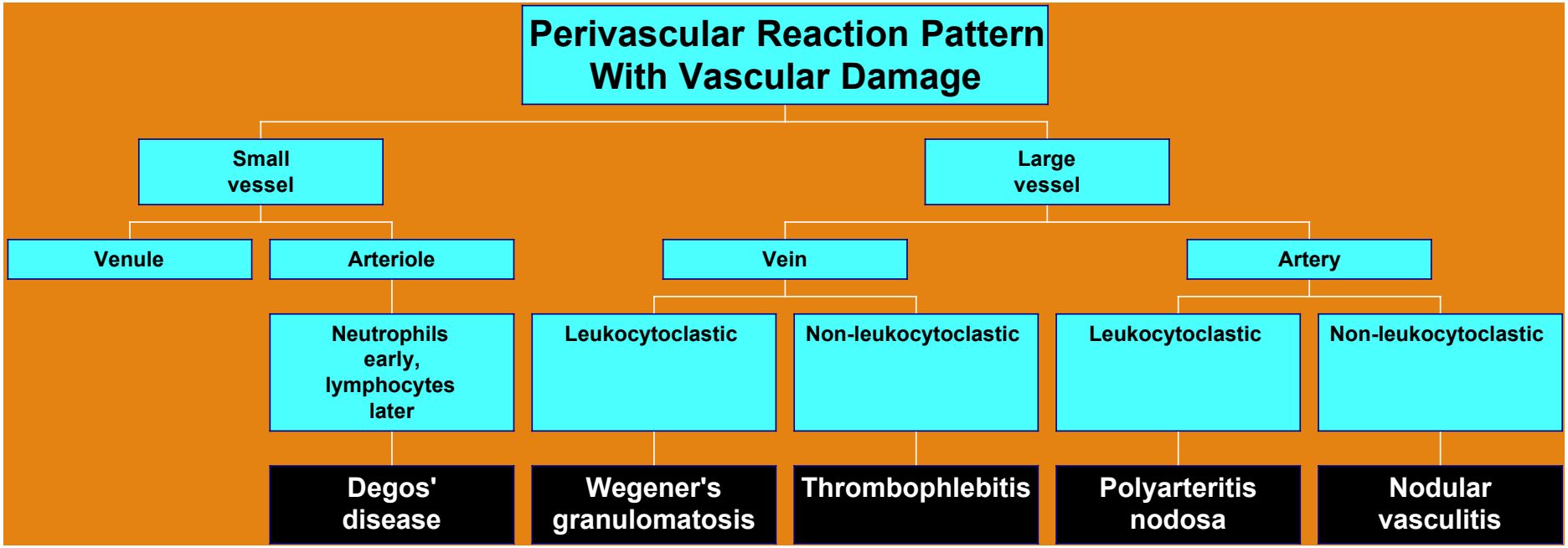
Names proposed by the 2011 Chapel Hill Consensus Conference on Vasculitis Nomenclature



- Large Vessel Vasculitis
  - Takayasu Arteritis
  - Giant Cell Arteritis
- Medium Vessel Vasculitis
  - Polyarteritis Nodosa
  - Kawasaki Disease
- Small Vessel Vasculitis
  - ANCA-Associated Vasculitis
    - Microscopic Polyangiitis
    - Granulomatosis with Polyangiitis (Wegener's)
    - Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss)
  - Immune Complex Vasculitis
    - Anti-GBM Disease
    - IgA Vasculitis (Henoch-Schönlein Purpura)
    - Cryoglobulinemic Vasculitis
    - Hypocomplementemic Urticarial Vasculitis (Anti-C1q Vasculitis)
- Variable Vessel Vasculitis (Behçet's Disease, Cogan's Syndrome)
- Single Organ Vasculitis (e.g. Primary CNS Vasculitis, Cutaneous PAN, etc.)
- Vasculitis Associated with Systemic Diseases (e.g. Rheumatoid, Lupus, etc.)
- Vasculitis Associated with Probable Etiologies (e.g. HBV, HCV, drug, etc.)

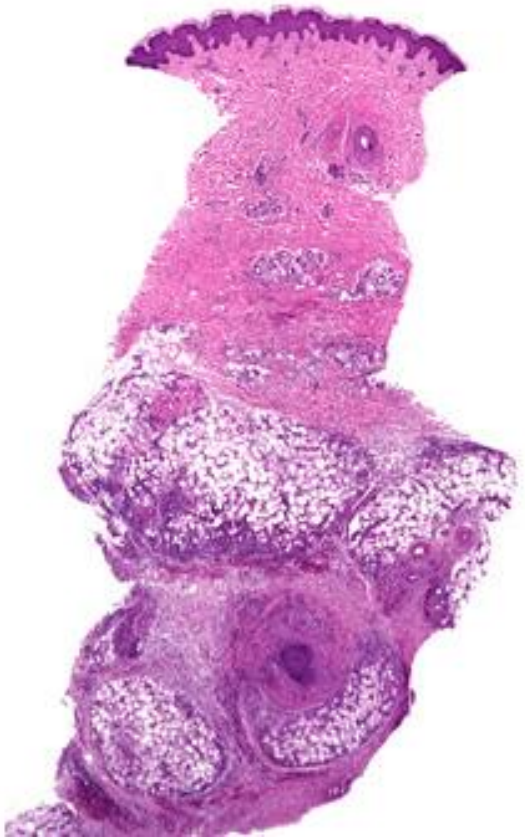
Necrotizing arteritis also can occur with

Vasculitis, Medium-Sized

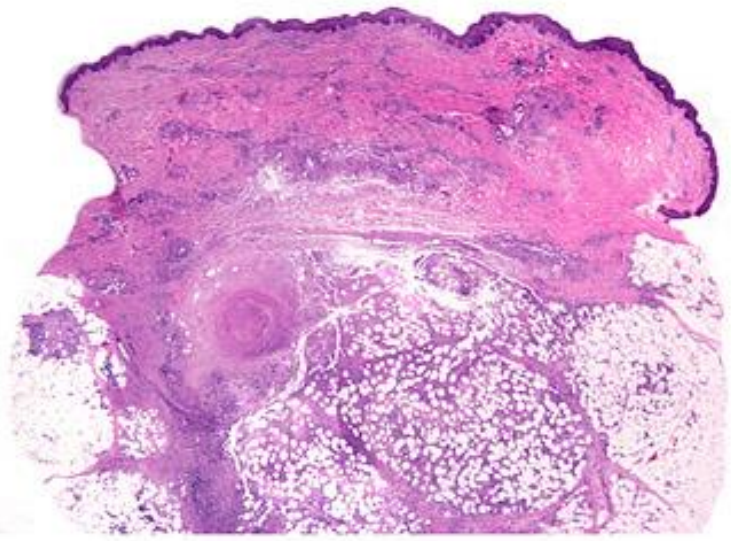


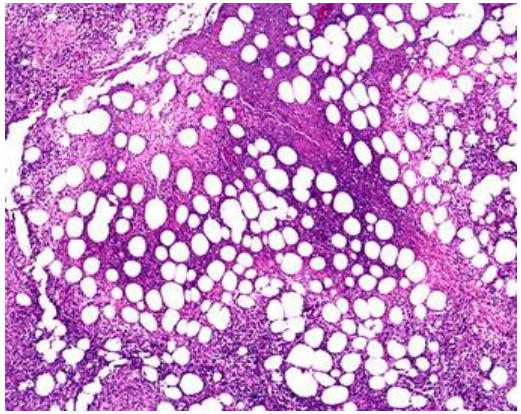
Nodular Vasculitis

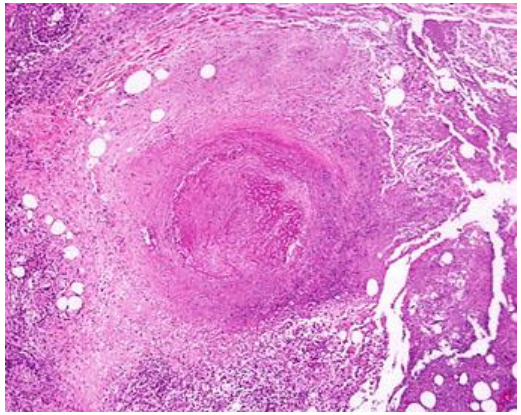
- **Epidermal ulceration**
- **Granular necrosis of collagen and fat**
- **±Granulomatous inflammation**
- **Necrotizing vasculitis**
- **Fibrosis in older lesions**



Nodular Vasculitis



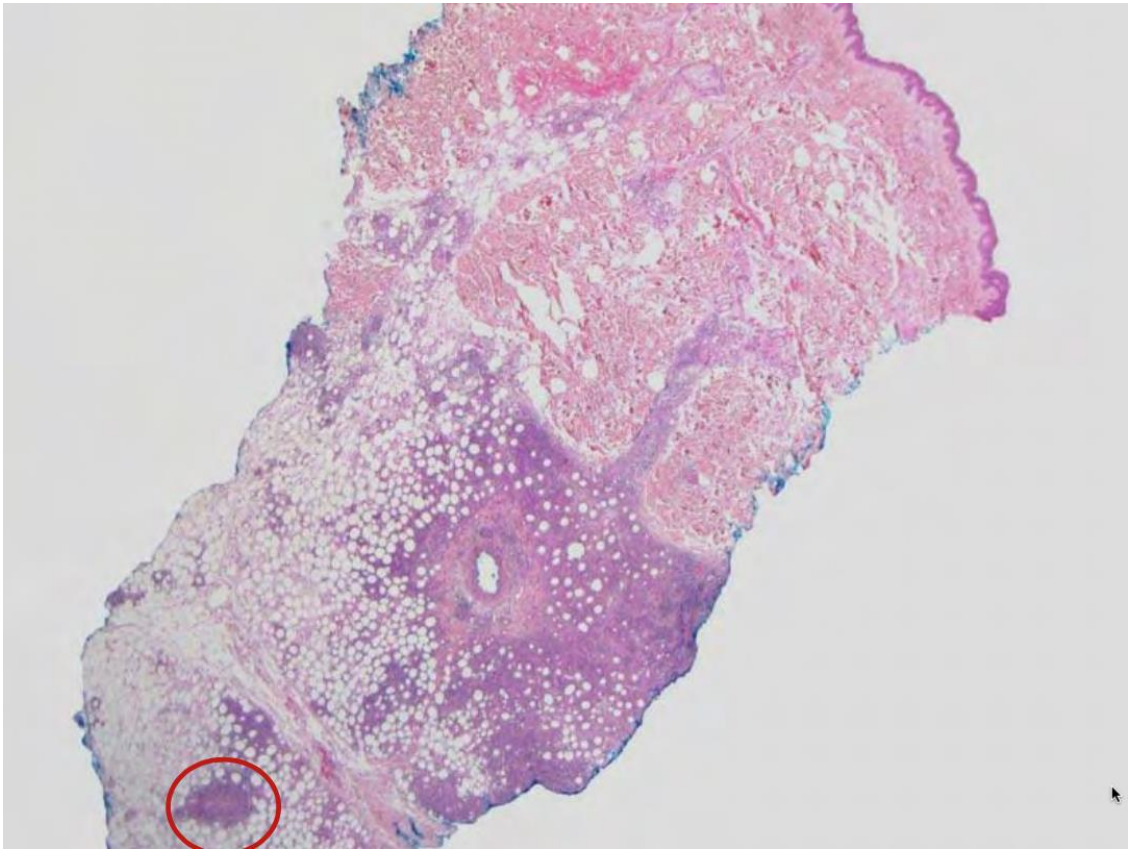




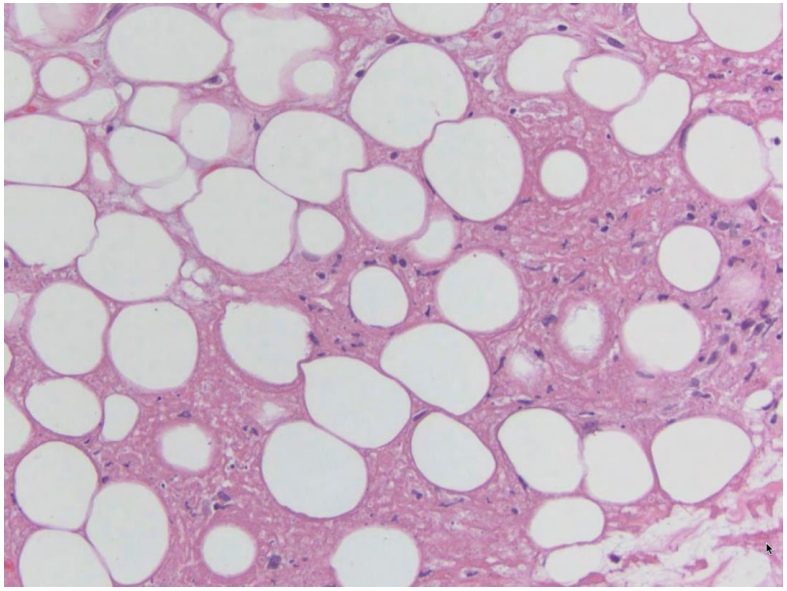
Case 3

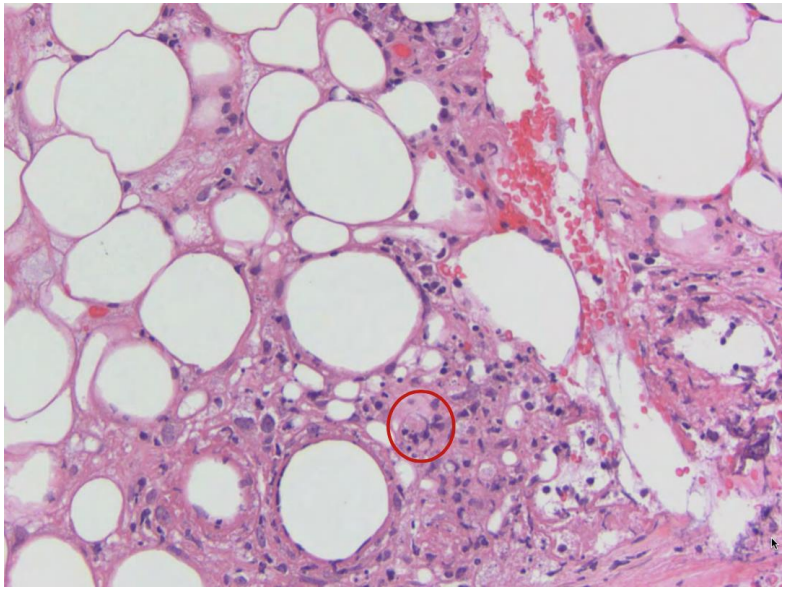
25 YEAR-OLD FEMALE WITH TENDER NODULES ON THE ARMS AND FLANKS

Tender nodules on the arms and flanks

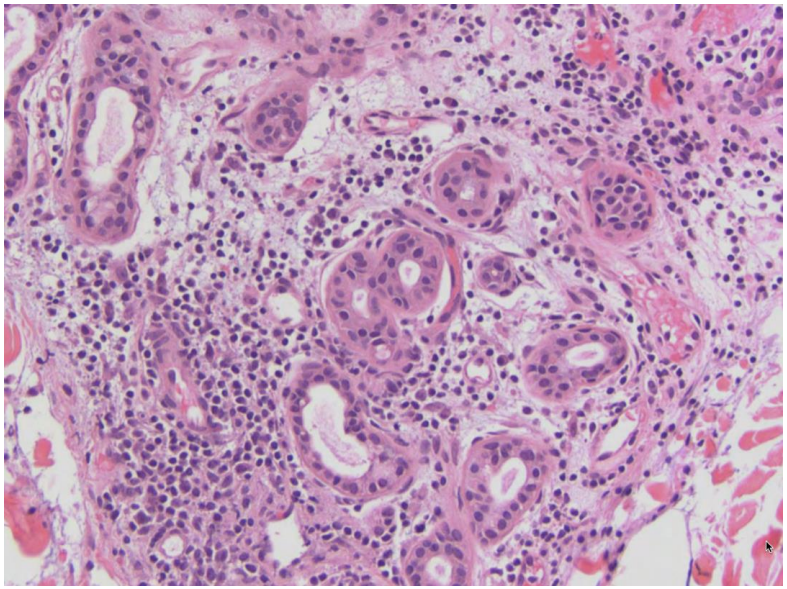


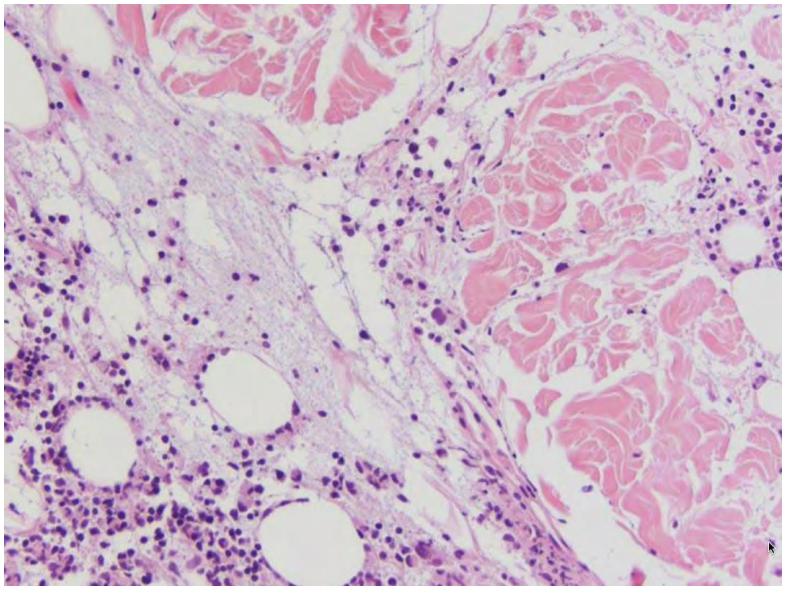
Tender nodules on the arms and flanks



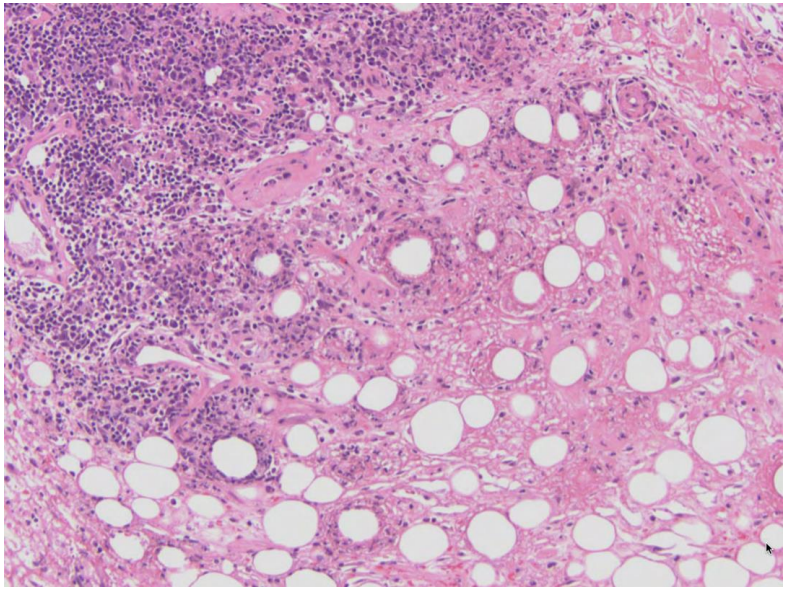


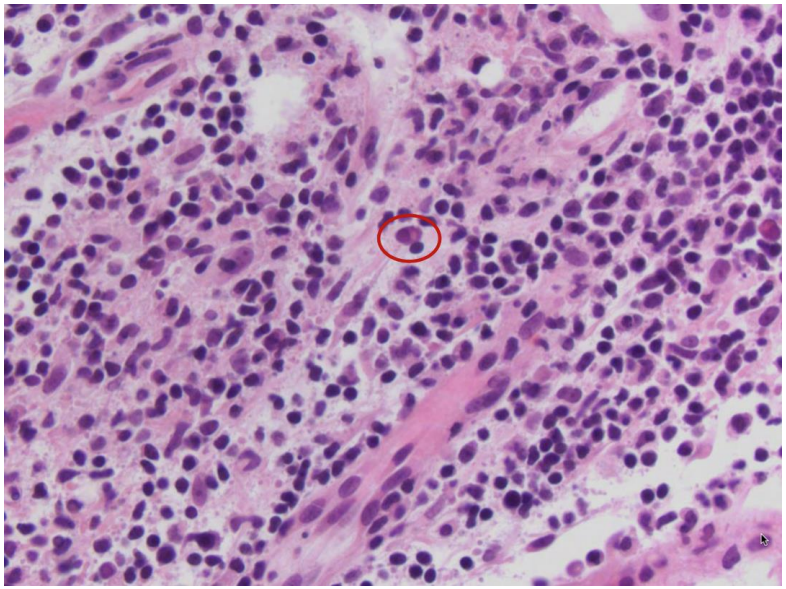
Tender nodules on the arms and flanks



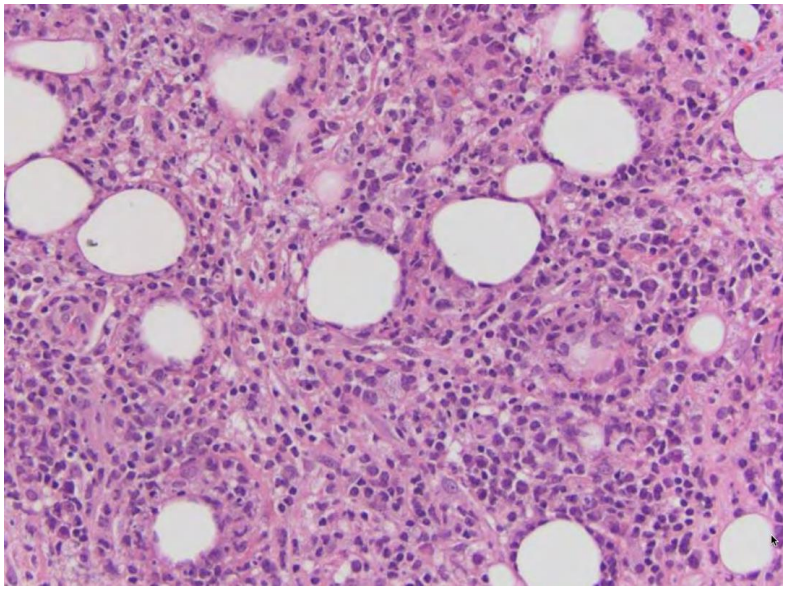


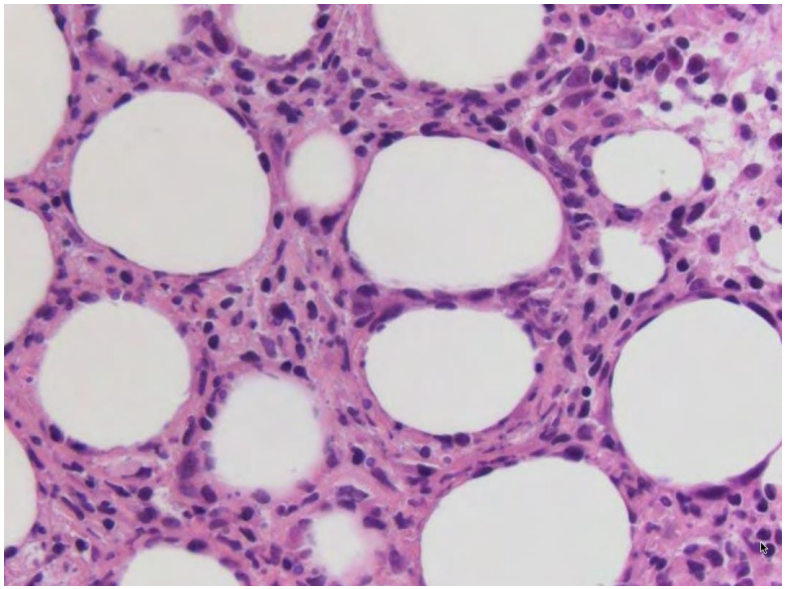
Tender nodules on the arms and flanks

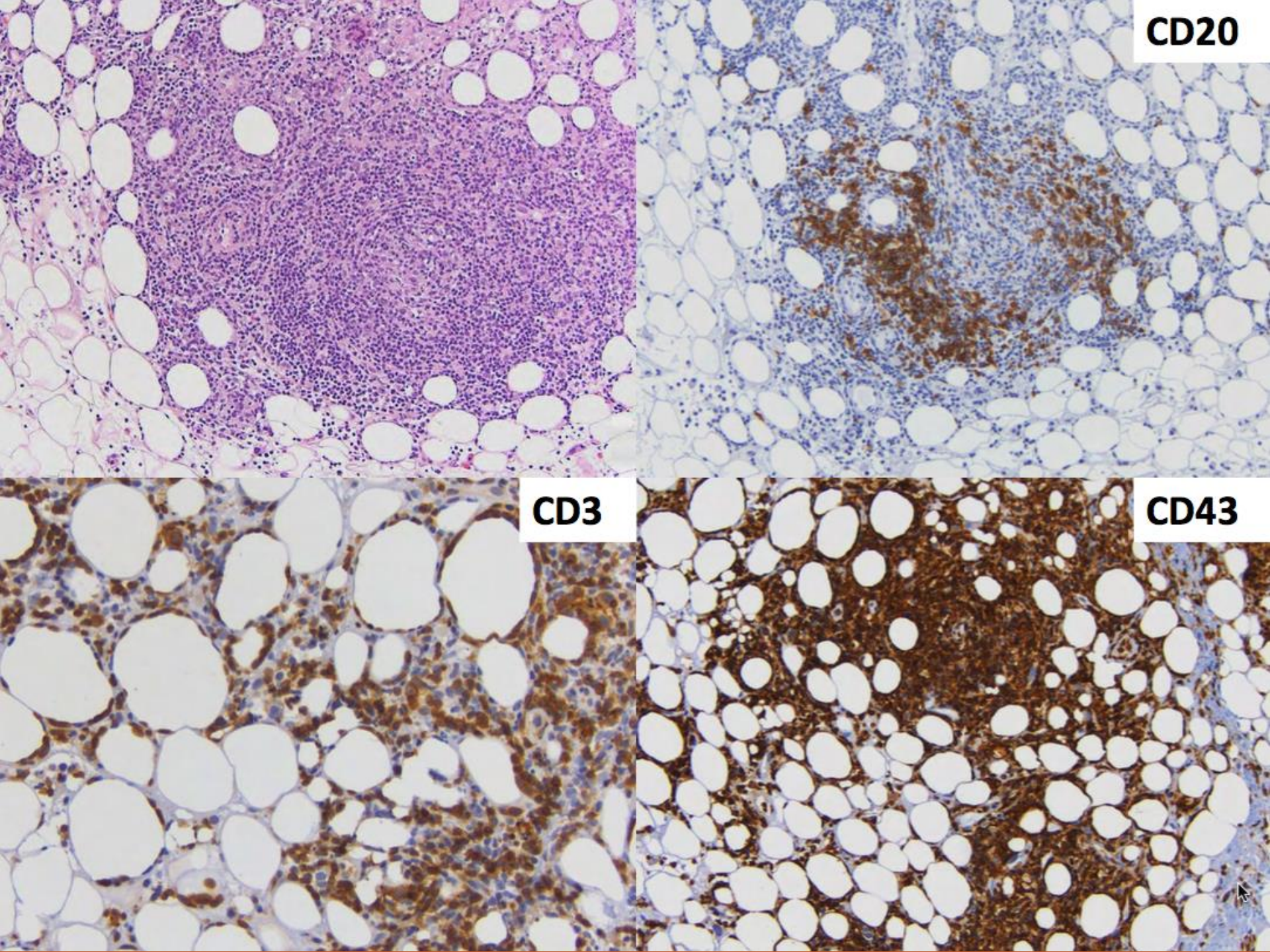




Tender nodules on the arms and flanks






CD20
CD3
CD43

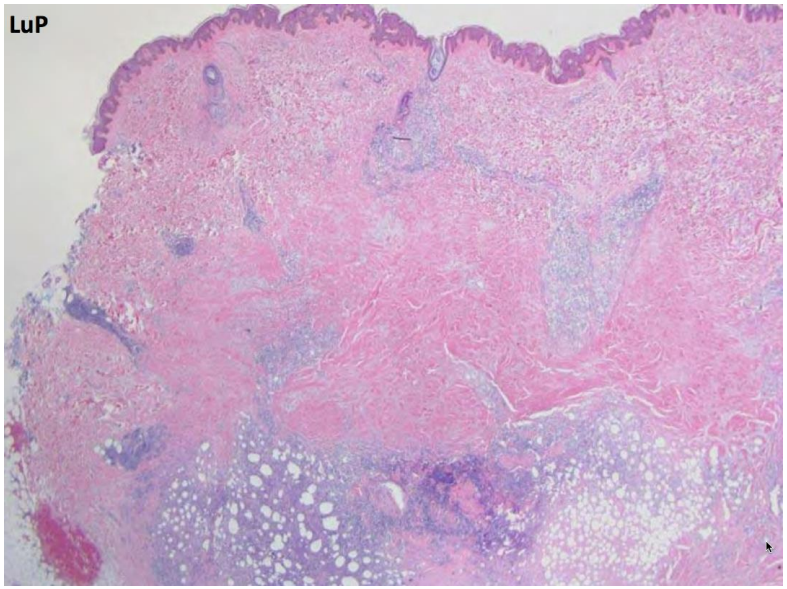
Lupus Profundus

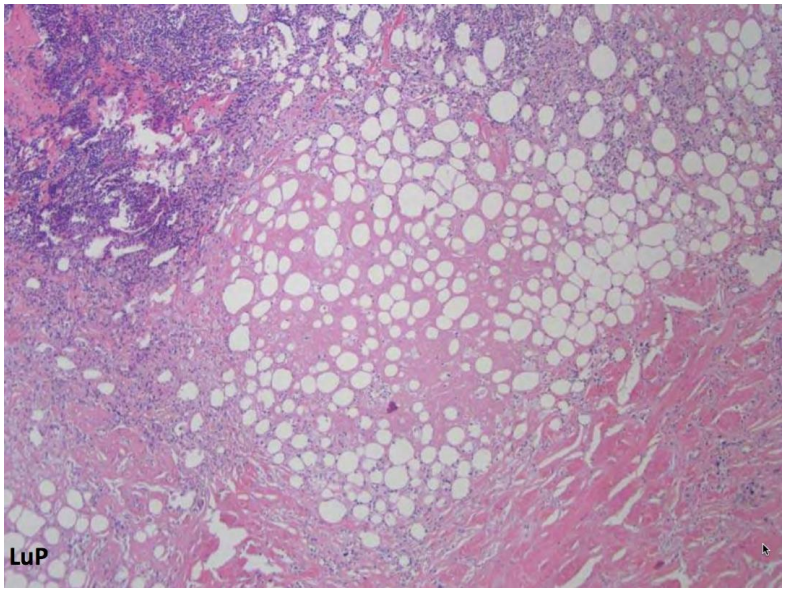
- 1883 Kaposi
- Erythematous or flesh-colored, tender, subcutaneous nodules or plaques
- Upper arms, shoulders, face, buttocks
- May arise in patients with DLE, SLE or as an isolated finding
- Develops in 1-3% of patients with cutaneous LE

Lupus Profundus

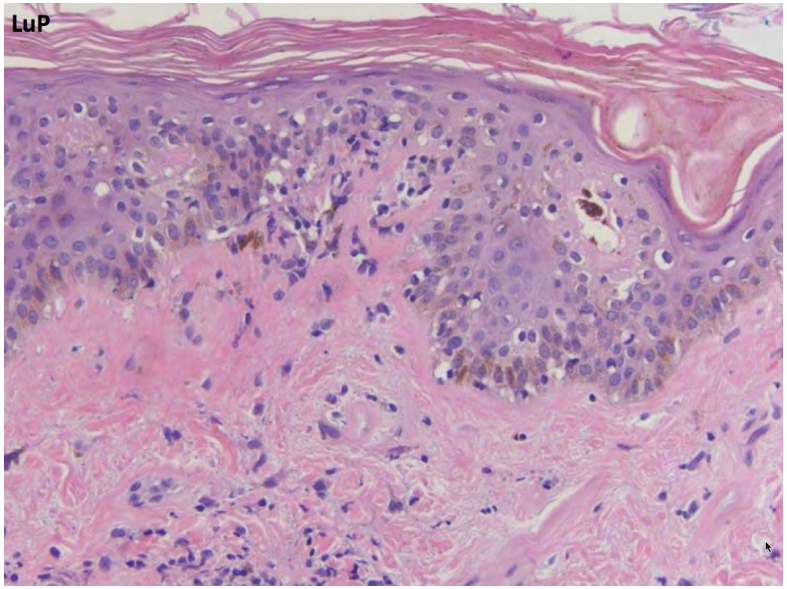
- Primarily lobular lymphocytic panniculitis
- Lymphoid aggregates with peripheral plasma cells
- Hyaline sclerosis
- Lymphocytic vascular reaction & mucin sometimes
- IgM & C3 along DEJ typical, subcutis less often
- >50% of cases changes of DLE
- ANAs in approximately 50% of cases

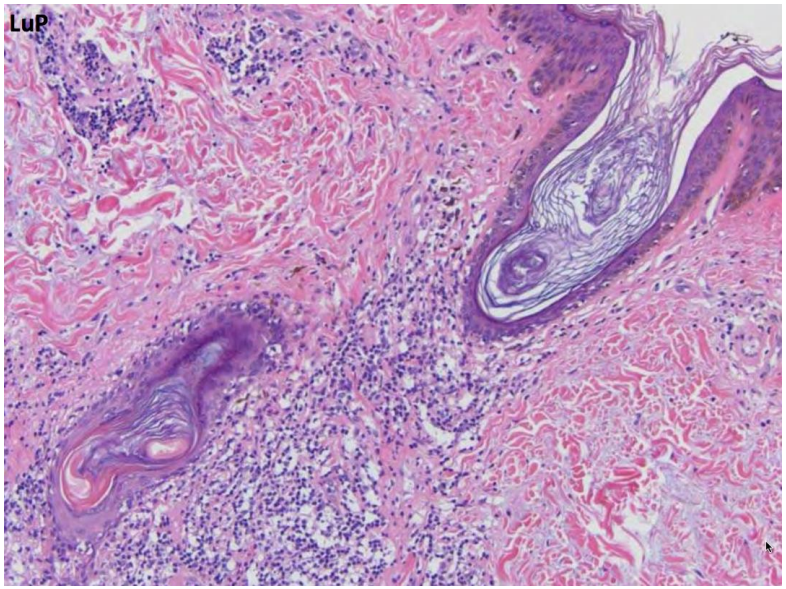
Lupus Profundus



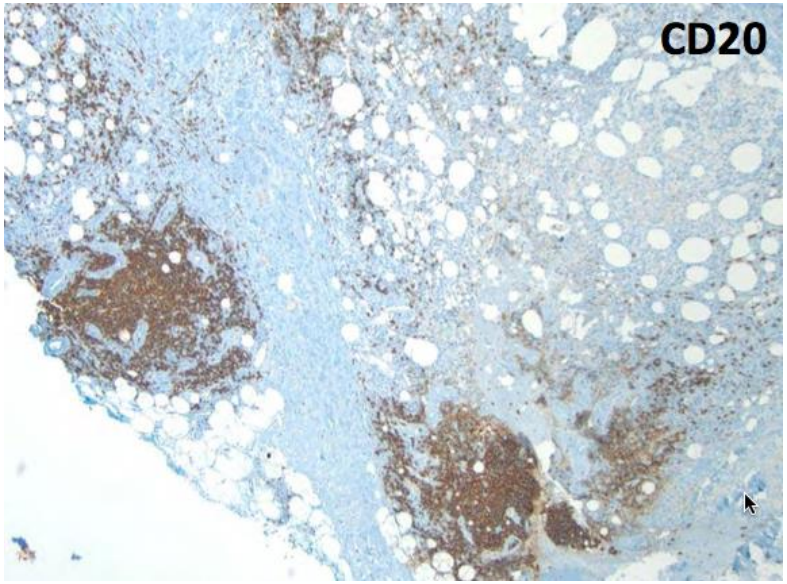


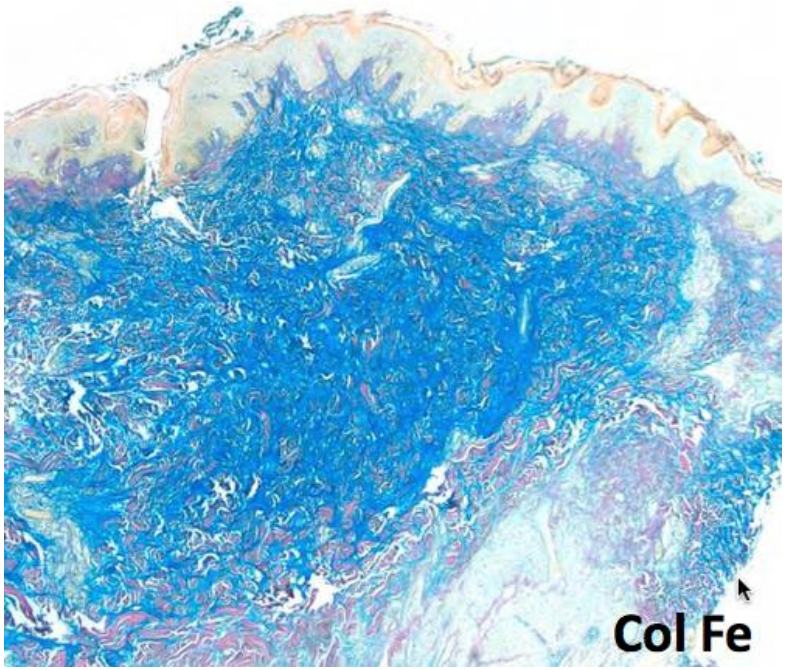
Lupus Profundus



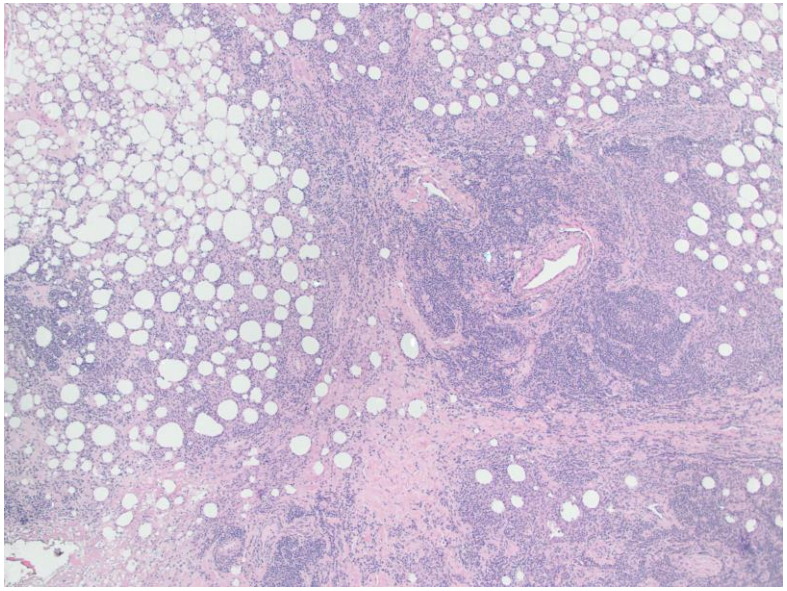


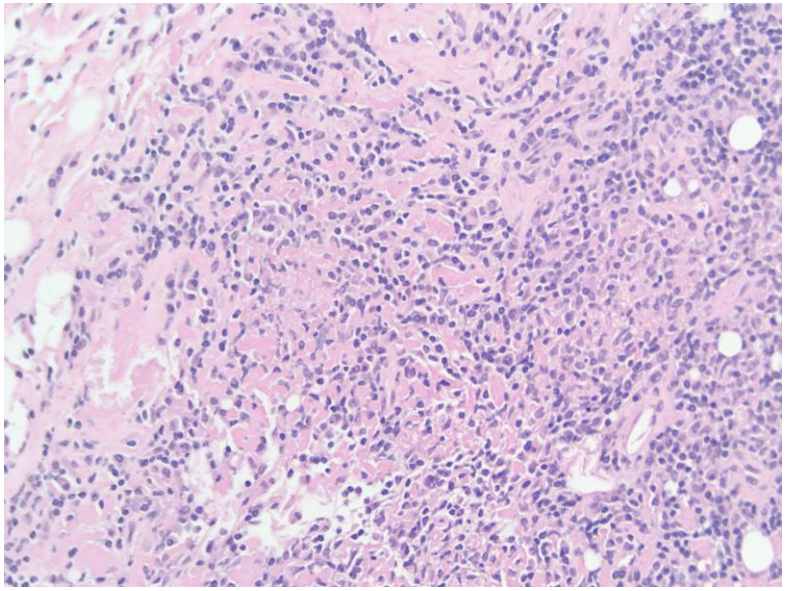
Lupus Profundus



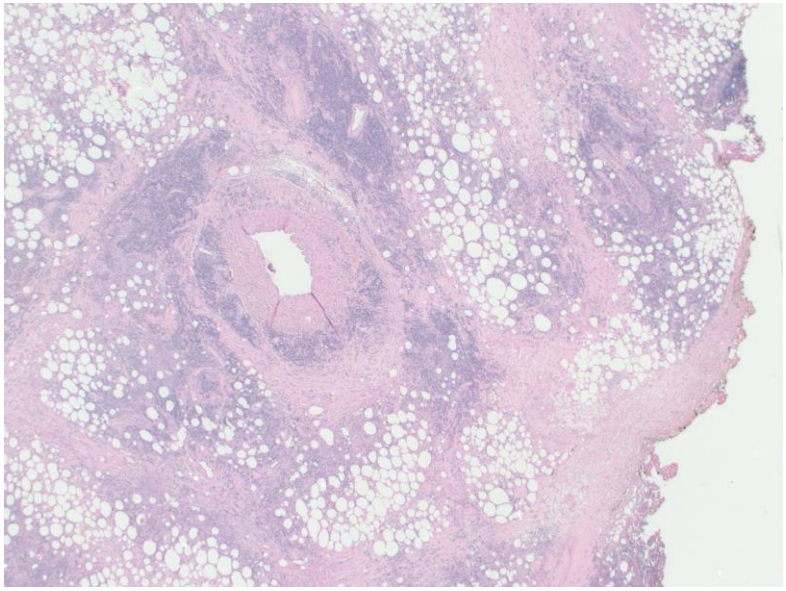


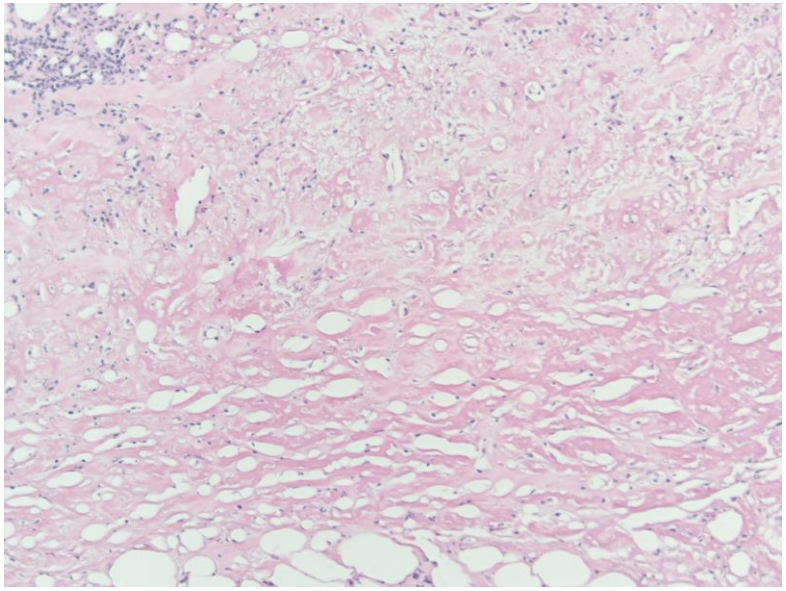
Lupus Panniculitis





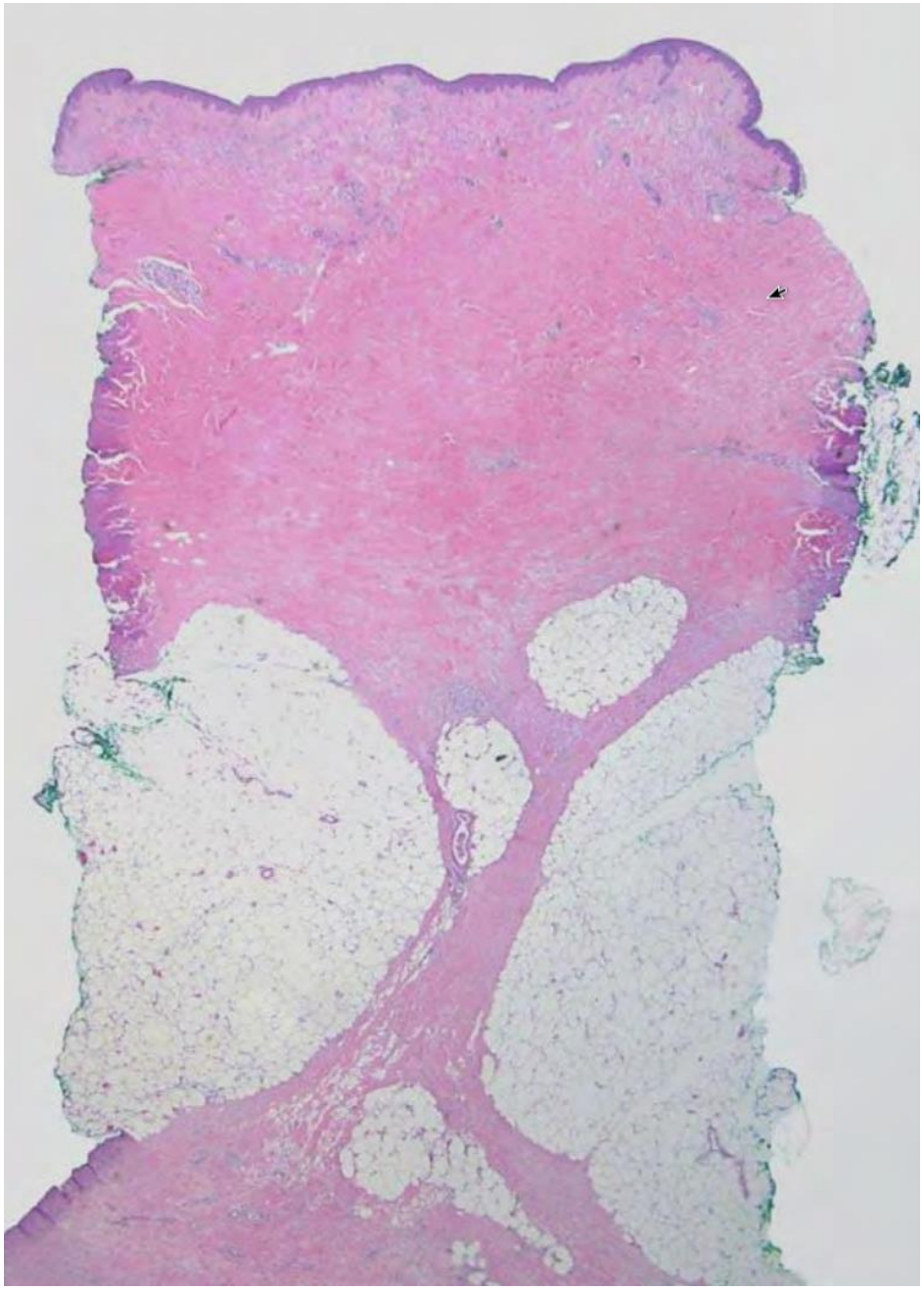
Lymphocytic Vascular Dermatitis – LE



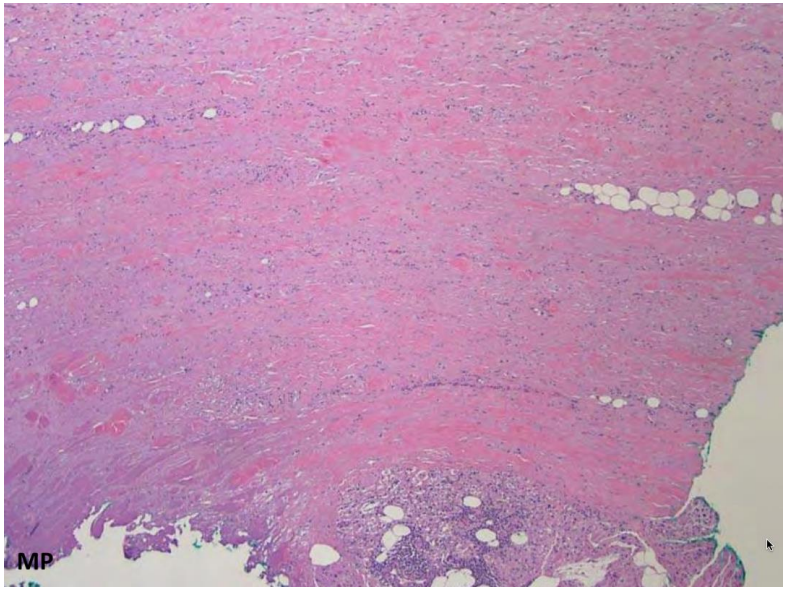


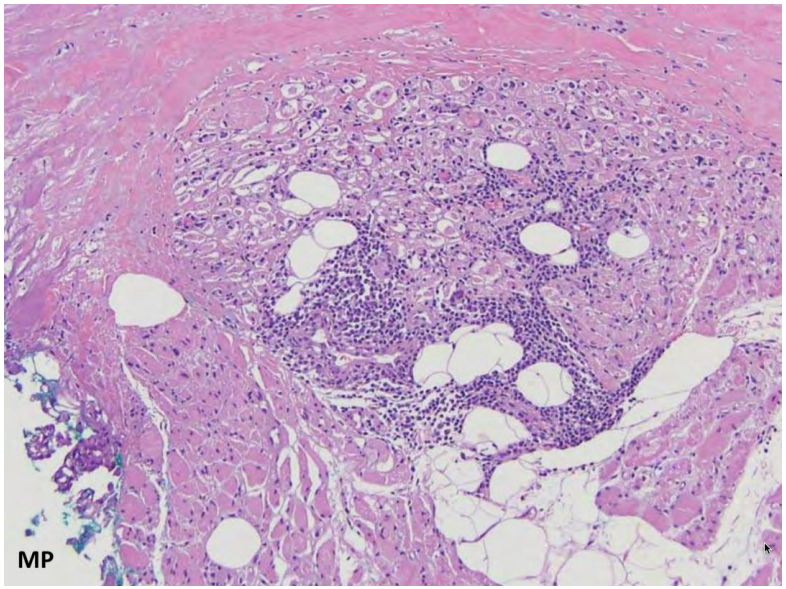
Morphea Profunda/ Eosinophilic Fasciitis

- **Connective tissue panniculitis**
- **Identical clinical to LuP**
- **Shared histopathologic features with LuP**
- **More prominent dermal sclerosis**
- **Prominent epidermal changes, mucin & hyaline septal & lobular sclerosis favor LuP**



Morphea Profunda/ Eosinophilic Fasciitis



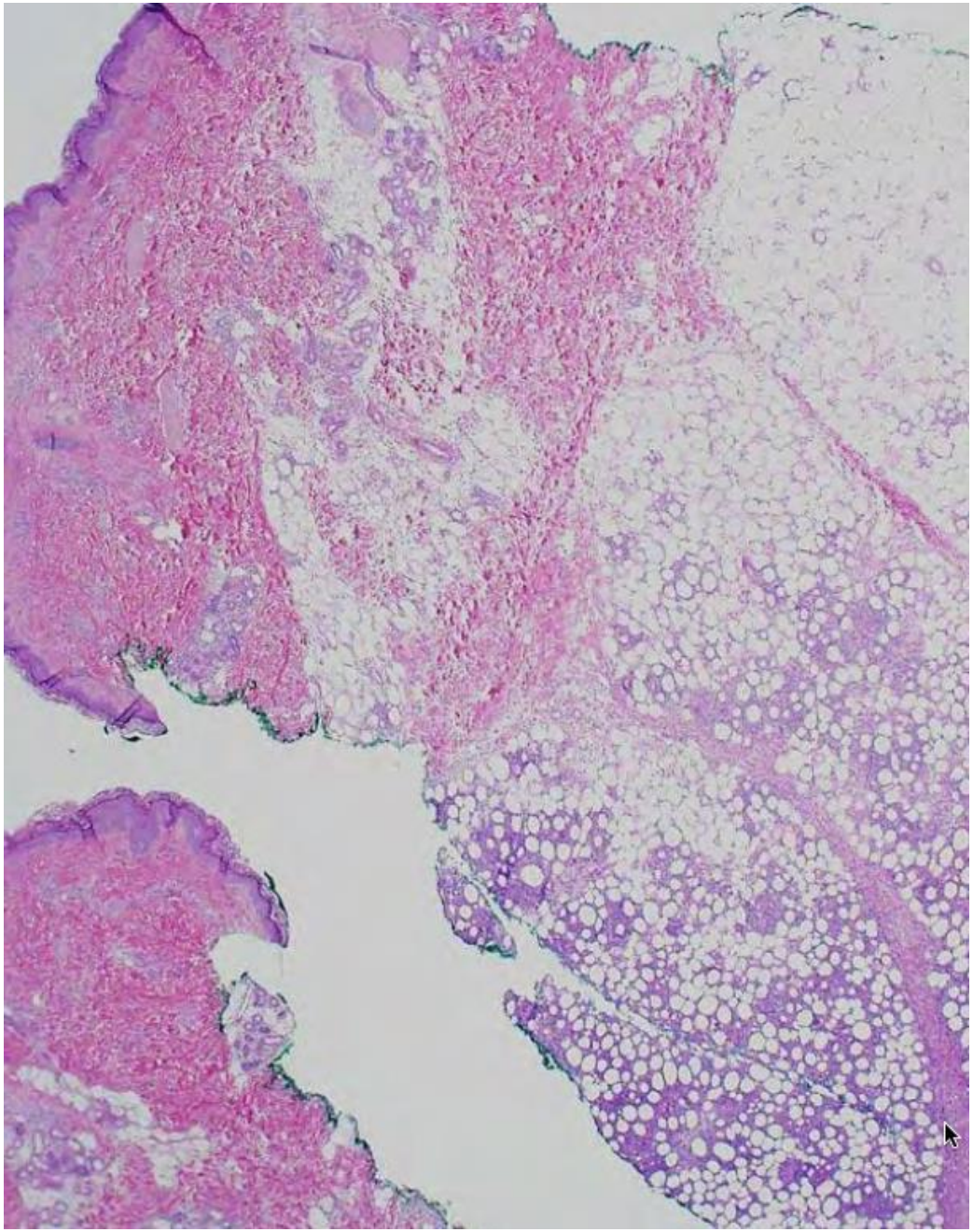


Subcutaneous Panniculitic-like T-cell Lymphoma

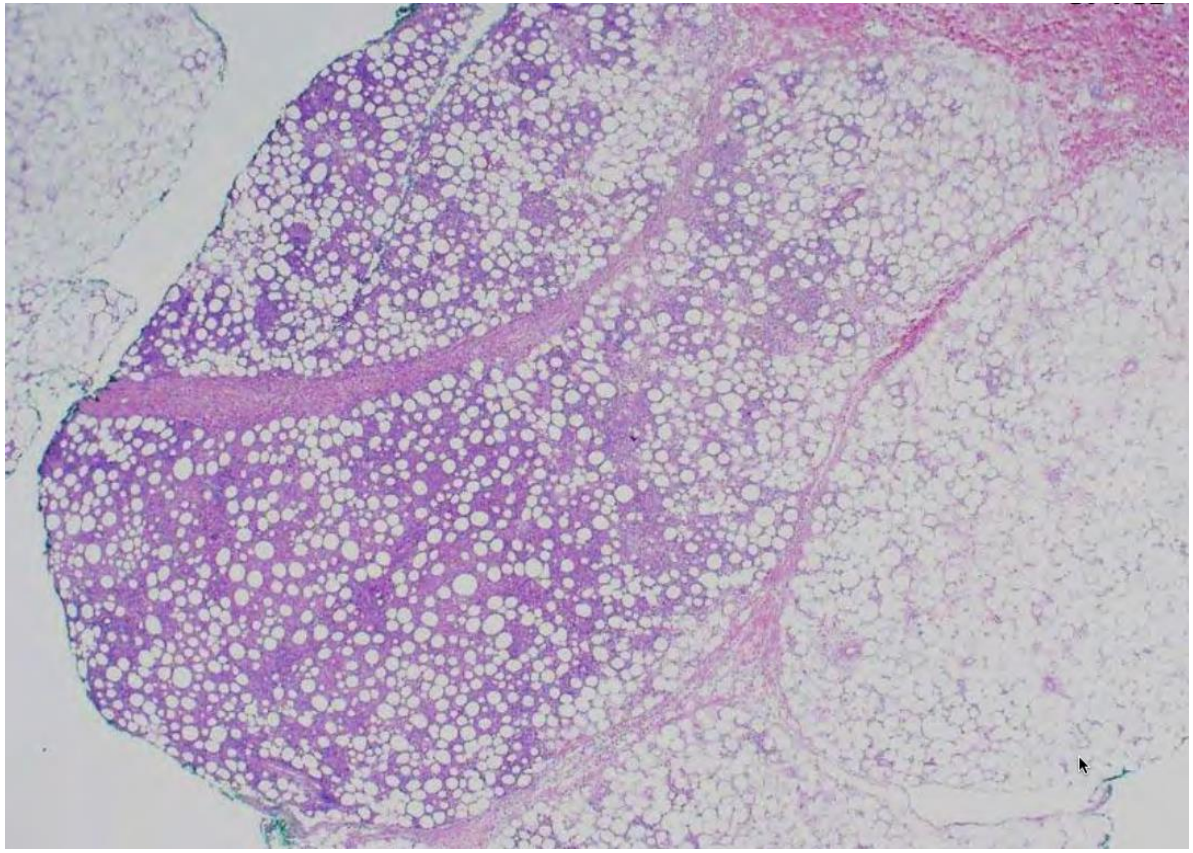
- **Cytotoxic TCL of subcutis**
- **Subset formerly “cytophagic histiocytic” panniculitis**
- **Subcutaneous nodules +/- ulceration**
- **Trunk & extremities (legs)**
- **Systemic signs may be present**
- **May be associated with hemophagocytic syndrome**

Panniculitic-like CTCL

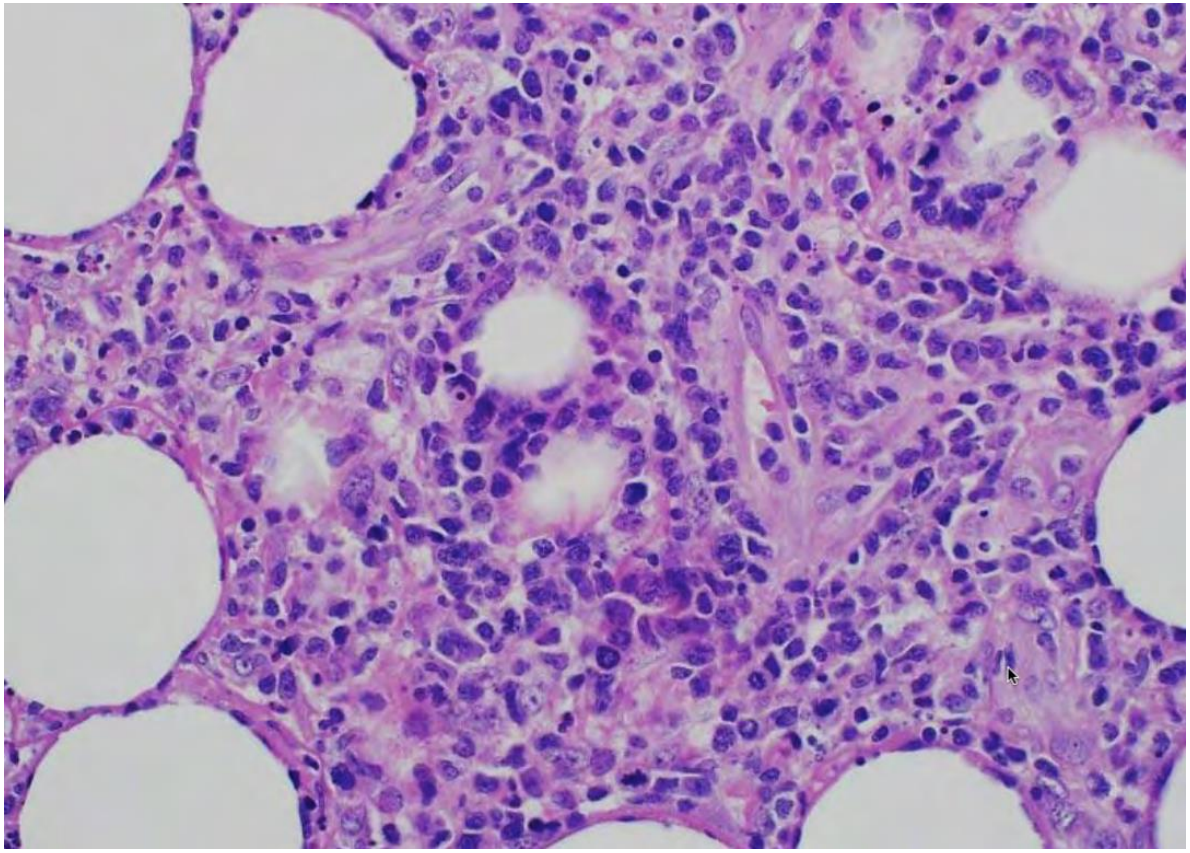
- **Subcutaneous infiltrate mimicking lobular panniculitis**
- **Small or medium-sized to large pleomorphic lymphoid cells**
- **Necrosis & granulomatous infiltrate**
- **Rimming of adipocytes by atypical neoplastic cells**
- **Plasma cells & eosinophils rare**



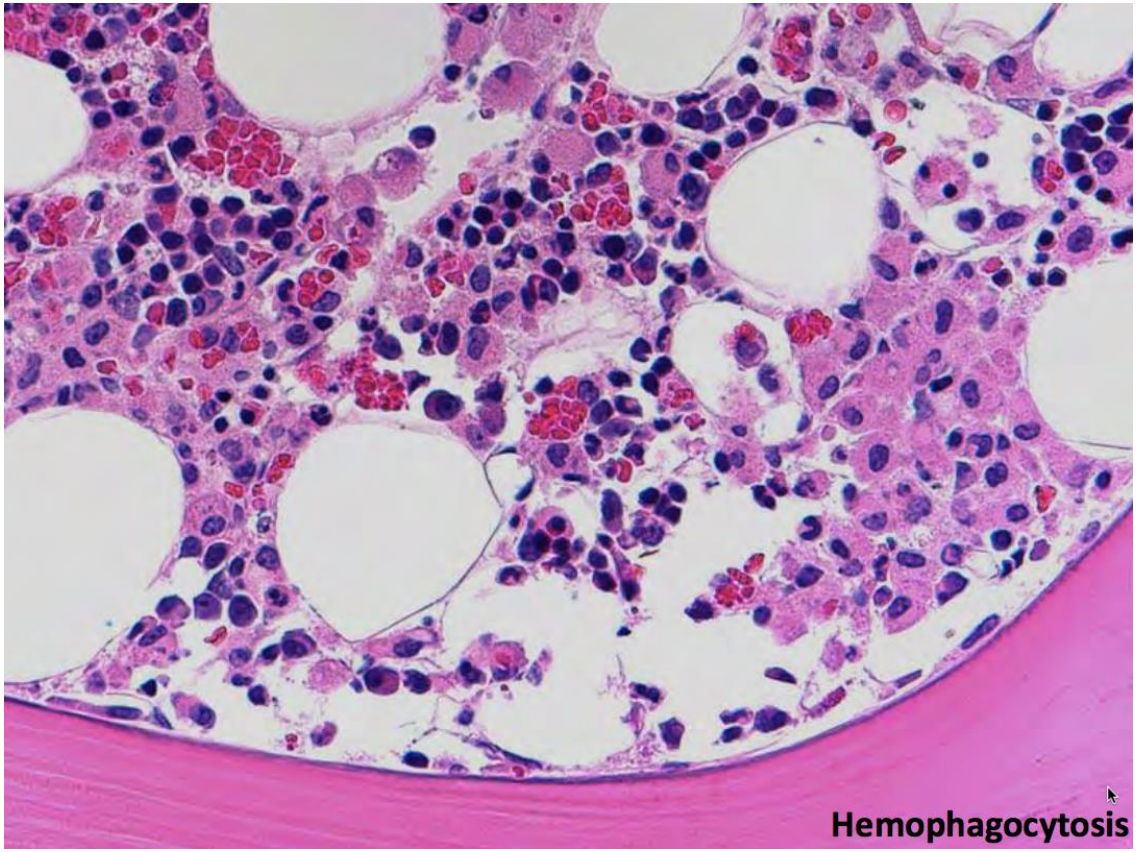
Panniculitic-like CTCL

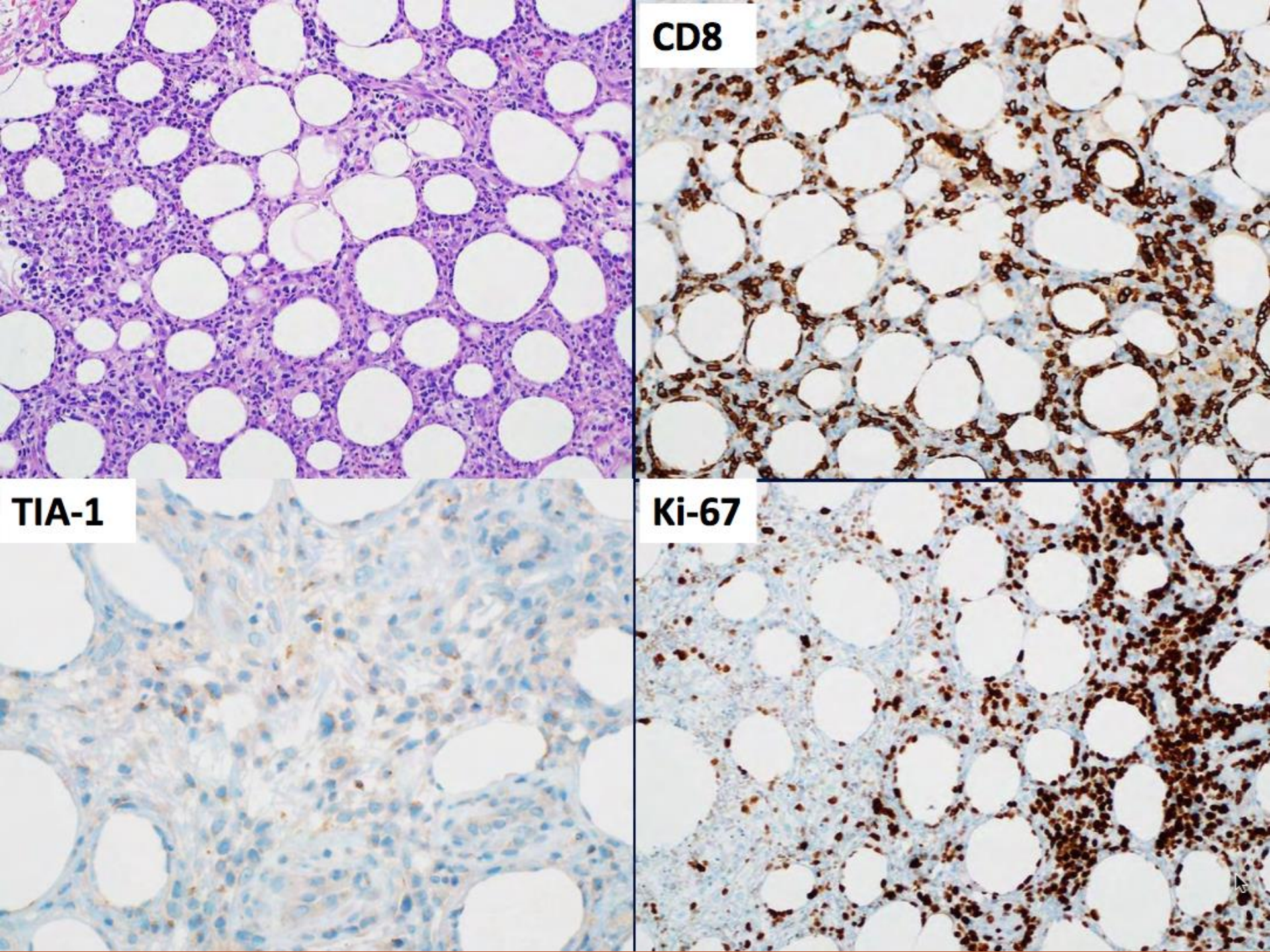


Panniculitic-like CTCL

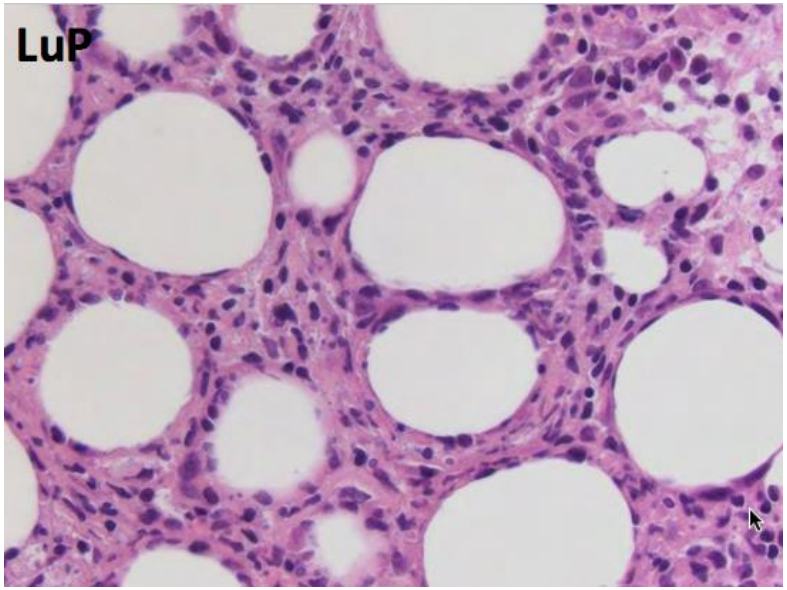


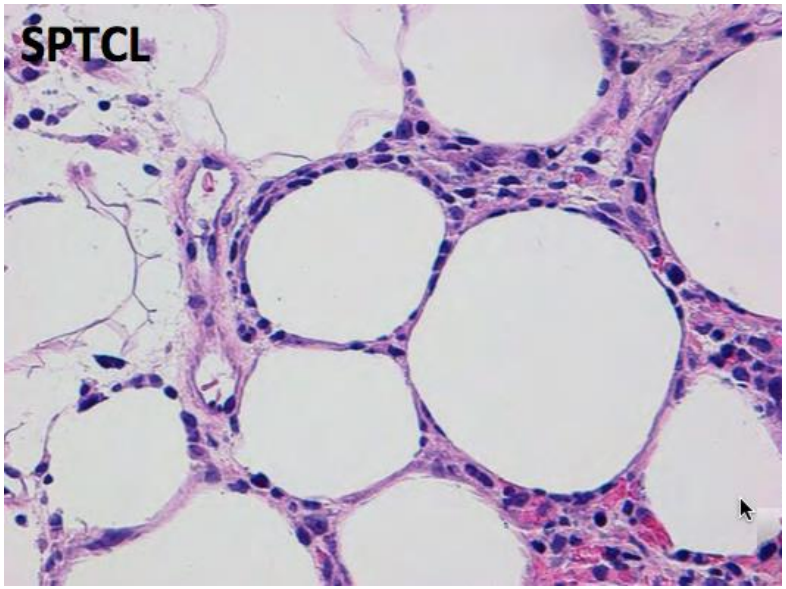
Panniculitic-like CTCL




CD8
TIA-1
Ki-67

Subcutaneous Lymphocytic Infiltrate





Subcutaneous Panniculitis-Like T-Cell Lymphoma With Overlapping Clinicopathologic Features of Lupus Erythematosus: Coexistence of 2 Entities?

Laura B. Pincus, MD, Philip E. LeBoit, MD,*† Timothy H. McCalmont, MD,*† Roberto Ricci, MD,‡ Carlo Buzio, MD,§ Lindy P. Fox, MD,* Fergus Oliver, MD,¶ and Lorenzo Cerroni, MD‖*

Abstract: We observed 5 patients with subcutaneous panniculitis-like T-cell lymphoma (SPTCL) who were unusual, in that they also exhibited features of lupus erythematosus (LE). This observation is in keeping with a recent study that reported an increased rate of autoimmune disease, including systemic lupus erythematosus (SLE), among patients with SPTCL. In all cases, attributes indicating SPTCL included an infiltrate of lymphocytes with pleomorphic nuclei involving subcutaneous lobules exhibiting a cytotoxic T-cell ($CD3^+/CD8^+/\beta F1^+$) immunophenotype. Additionally, a high proliferation rate and a monoclonal T-cell receptor-γ gene rearrangement were observed in most cases. The manifestations of LE in these patients included a spectrum of clinical and histopathological abnormalities. Clinical manifestations of LE included, in some patients, morphologic evidence of lupus erythematosus panniculitis (LEP) with subcutaneous nodules that healed with lipoatrophy on the face. In addition, all the patients exhibited serologic and/or extracutaneous end-organ abnormalities seen in patients with SLE, with 2 patients having sufficient findings to meet American College of Rheumatology criteria for SLE. Histopathological evidence of LE included vacuolar change at the dermal–epidermal interface in 3 patients, 2 of whom also showed interstitial deposition of mucin in the reticular dermis. One of these patients also had findings of LEP in the subcutaneous lobules with clusters of $CD20^+$ B cells partially arranged within germinal centers. In 2 patients in which neither the epidermis nor dermis was available for review, histopathological features of LE included, in one patient, a few small clusters of $CD123^+$ plasmacytoid dendritic cells within the adipose tissue and, in the other patient, a positive direct immunofluorescence test (lupus band) on clinically uninvolved and lesional skin. Our study shows that some patients show overlap between SPTCL and LE. We suspect that these patients may suffer from both diseases concomitantly. Furthermore, patients with LE, particularly LEP, should be monitored for evolution into SPTCL with biopsy of any subcutaneous lesion that is not typical of LEP. Additionally, screening for cutaneous LE and SLE could be considered in patients with SPTCL.

Key Words: cutaneous T-cell lymphoma, lupus erythematosus, lupus panniculitis, lupus profundus, subcutaneous panniculitis-like T-cell lymphoma

(*Am J Dermatopathol* 2009;31:520–526)

INTRODUCTION

A recent large European Organization for Research and Treatment of Cancer study of 63 patients with subcutaneous panniculitis-like T-cell lymphoma (SPTCL) indicated that 19% had an associated autoimmune disease, including 4 with systemic lupus erythematosus (SLE).[1] We encountered 5 patients in routine practice or in consultation who exhibited typical features of SPTCL but were unusual, in that they also had manifestations of lupus erythematosus (LE). The features of LE included a spectrum of findings from typical clinical cutaneous lesions, to serologic and extracutaneous end-organ abnormalities typical of SLE, to findings of LE seen on histopathological sections from skin biopsies.

Reports addressing a relationship between SPTCL and LE have focused primarily on delineating histopathological and clinical features that distinguish SPTCL from lupus erythematosus panniculitis (LEP).[2–5] Indeed, it can be very challenging to differentiate between SPTCL and LEP on histopathological grounds.[6,7] Microscopically, LEP is typically characterized by a lymphocytic infiltrate within subcutaneous lobules with little septal involvement, fat necrosis, and the presence of histiocytes containing karyorrhectic debris—although these features can also be seen in SPTCL. Microscopic findings that can help to distinguish LEP from SPTCL include features typical of cutaneous LE in the epidermis and dermis, including vacuolar change at the dermal–epidermal interface, periadnexal lymphocytic infiltrates, and interstitial deposition of mucin in the reticular dermis. The presence in the subcutis of lymphoid follicles with reactive germinal centers, clusters of B lymphocytes, and a mixed infiltrate with prominent plasma cells also favors LEP.[4] A recently elucidated clue to LEP is presence of clusters of $CD123^+$ plasmacytoid dendritic cells (pDCs) within the subcutaneous lobules and, if present, within the dermal infiltrates,

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Lupus profundus, indeterminate lymphocytic lobular panniculitis and subcutaneous T-cell lymphoma: a spectrum of subcuticular T-cell lymphoid dyscrasia

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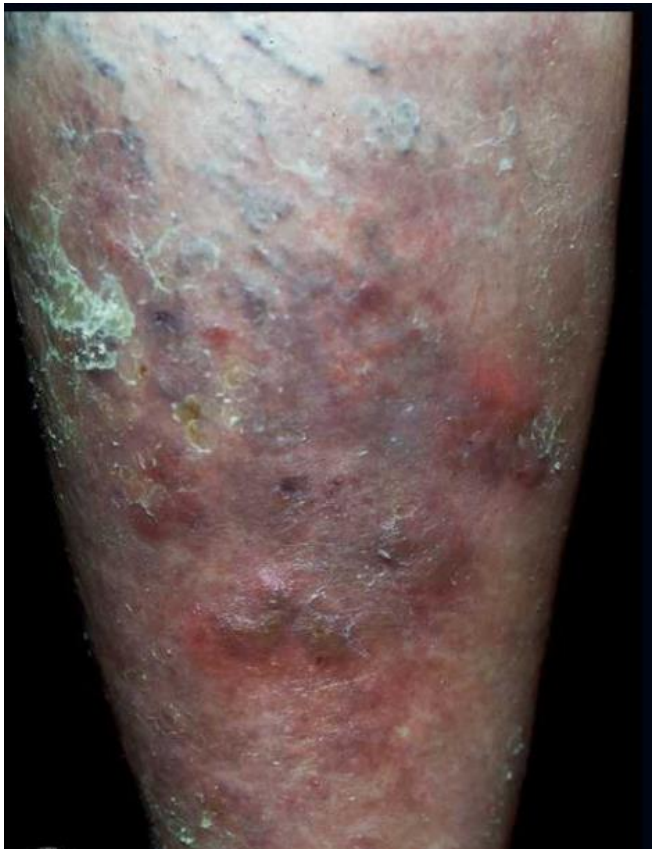
Introduction: The diagnosis and classification of lymphocytic lobular panniculitis (LLP) has historically proven to be a difficult challenge. We encountered 32 cases of primary LLP which could be categorized as: 1) lupus erythematosus profundus (LEP) (19 patients); 2) an indeterminate group termed *indeterminate lymphocytic lobular panniculitis* (ILLP) (6 patients); and 3) subcutaneous T-cell lymphoma (SCTCL) (7 patients).
Objective: We attempted to better define the subtypes of LLP by morphologic, phenotypic and genotypic features and to correlate those features to clinical presentation and outcome.
Method: Skin biopsy material was studied by conventional light microscopy, through immunophenotyping performed on sections from paraffin-embedded, formalin-fixed tissue and in some cases on sections of tissue frozen after receipt in physiological (Michel's) medium, and by polymerase chain reaction single-stranded conformational polymorphism analysis to assess for clonality of T-lymphocytes. Clinical features were correlated to histologic, phenotypic, and genotypic analyses.
Results: Patients with LEP had a prior diagnosis of LE or overlying skin changes which light microscopically were characteristic of LE. Patients with ILLP had no concurrent or prior history of LE, no systemic symptoms or cytopenias, and a clinical course not suggestive of lymphoma. Cases of SCTCL showed hemophagocytic syndrome and/or lesional progression with demise attributable to the disease. Lesions in all groups showed proximal extremity predilection. Females predominated in the LEP group. The average age of onset was 38, 40 and 55 years in the LEP, ILLP and SCTCL groups, respectively. Cytopenia was seen in 4 LEP patients; 1 also developed fever. In LEP and ILLP, lesions resolved with hydroxychloroquine and/or steroid therapy, with recurrences following cessation of therapy. In the SCTCL group 4 developed hemophagocytic syndrome, 4 died within 2 years of diagnosis, and 3 went into remission following chemotherapy. The LEP and SCTCL groups manifested histological similarities: dense perieccrine and lobular lymphocytic infiltration, lymphoid atypia, histiocytes with ingested debris, eosinophilic necrosis of the fat lobule and thrombosis. The atypical lymphocytes although pleomorphic did not have a cerebriform morphology. The infiltrate in ILLP had a

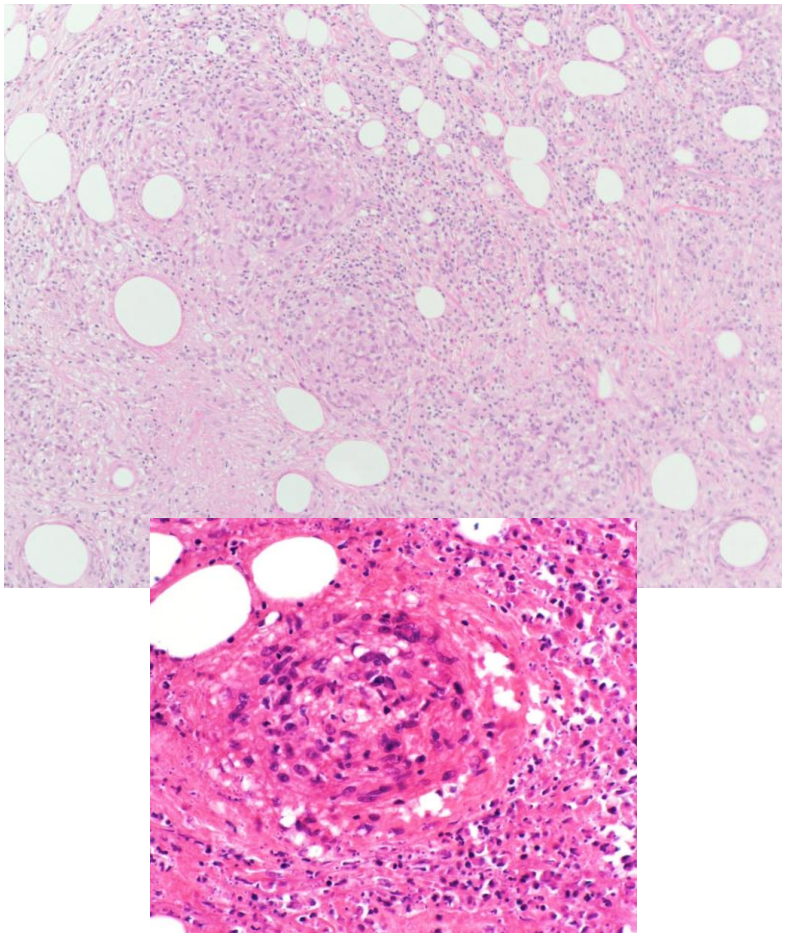
Erythema Induratum

- **Recurrent, painful nodules on calves**
- **Heal with scarring**
- **Associated with underlying tuberculosis infection in 30-80% of cases**



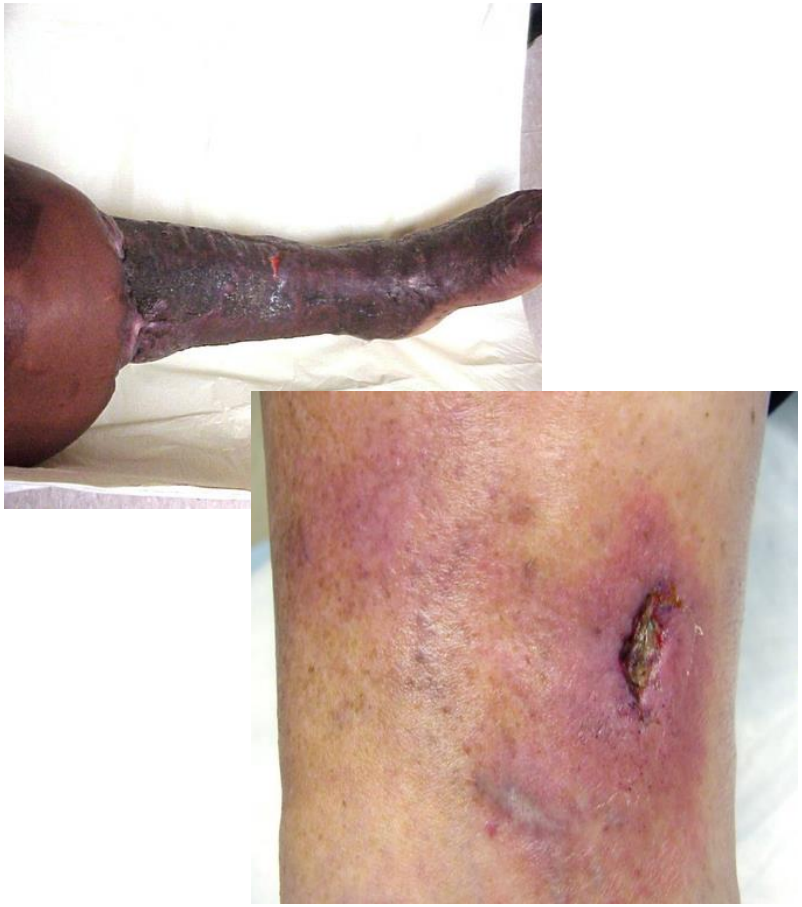
Erythema Induratum

- Acute vasculitis in septae affecting artery and/or veins
- Adjacent lobular panniculitis with granulomas and fat necrosis
- Septae may be widened in older lesions



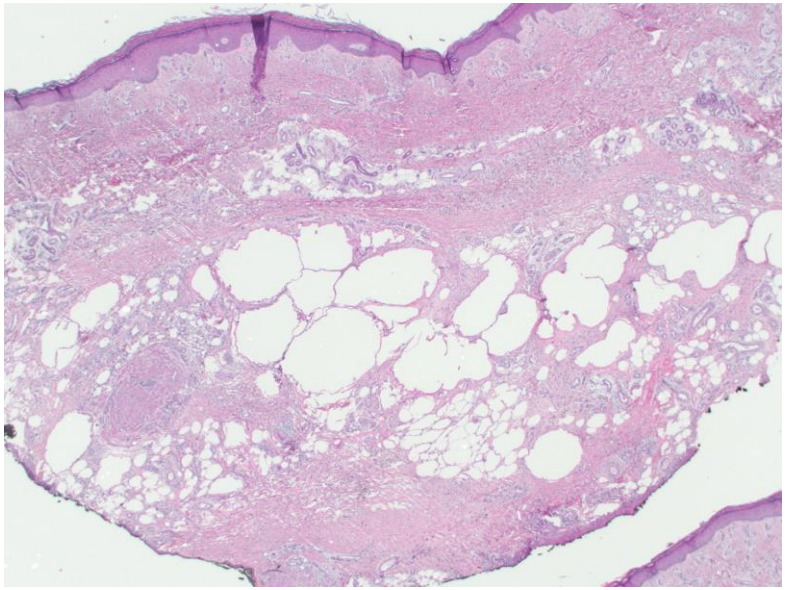
Lipodermatosclerosis

- Middle-aged or elderly women
- Usually bilateral indurated plaques on medial aspects of lower legs
- Associated with stasis changes secondary to venous insufficiency and obesity

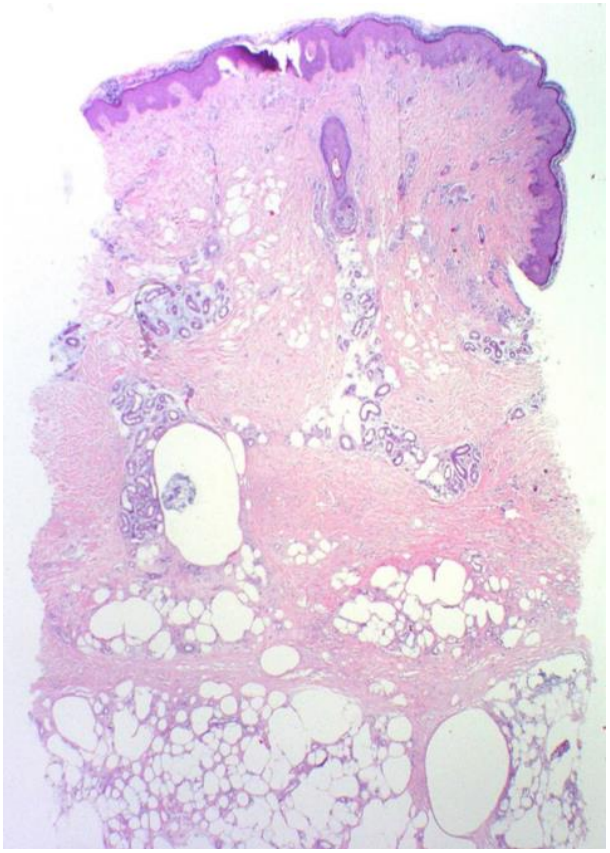


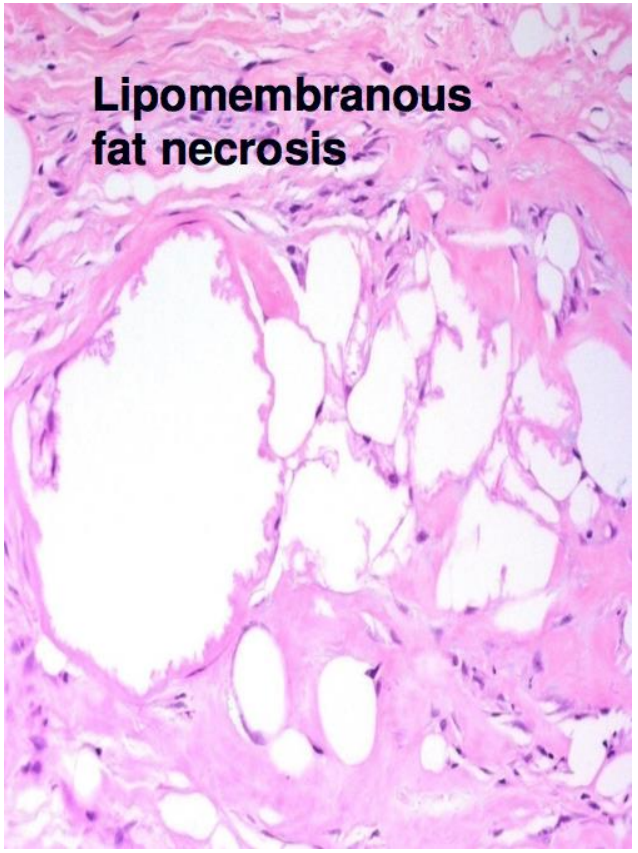
Lipodermatosclerosis

- Widened septae
- Lipomembranous fat necrosis (LMFN)
  - Cystic cavities lined by a crenulated, hyaline membrane that is PAS-positive
    - LMFN may be seen in other panniculitides
- Mild perivascular lymphocytic infiltrate
- Overlying features of stasis change in dermis and epidermis



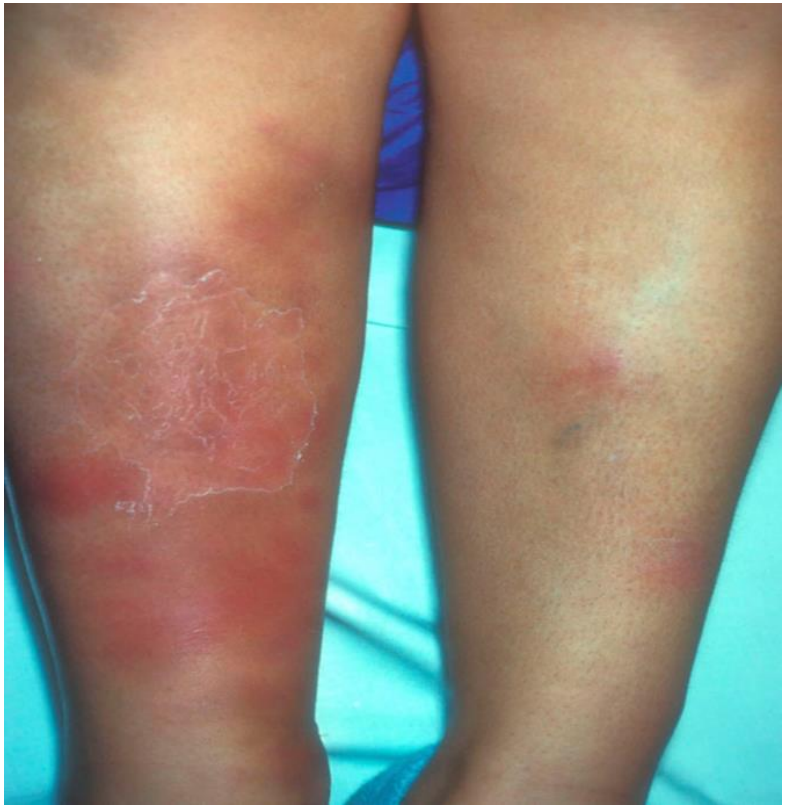
Lipodermatosclerosis





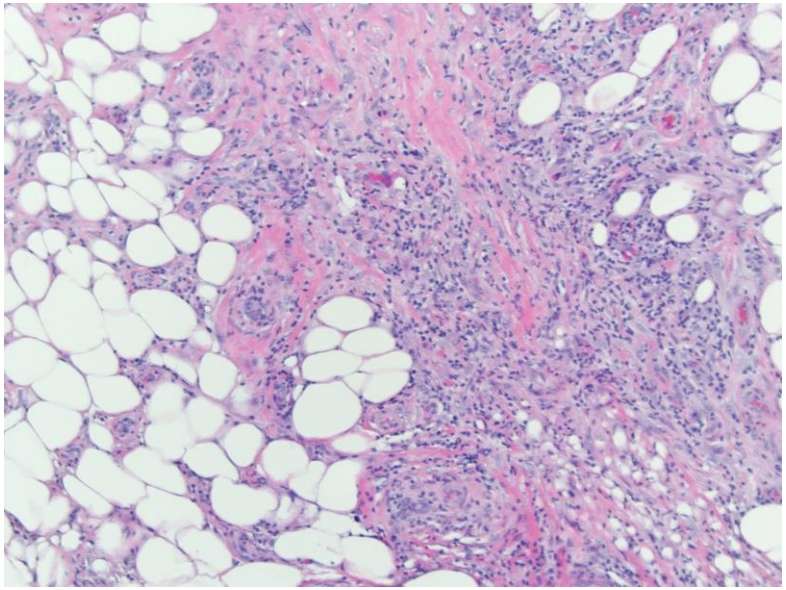
Erythema Nodosum

- Most common form of panniculitis
- Acute onset of tender, erythematous nodules
- Shins most common site, often bilateral
- Pathogenesis unclear: probably a hypersensitivity response to underlying antigen (infections, drugs, malignant and inflammatory disorders)
  - Adults: drugs, sarcoidosis, inflammatory bowel disease
  - Children: streptococcal infections

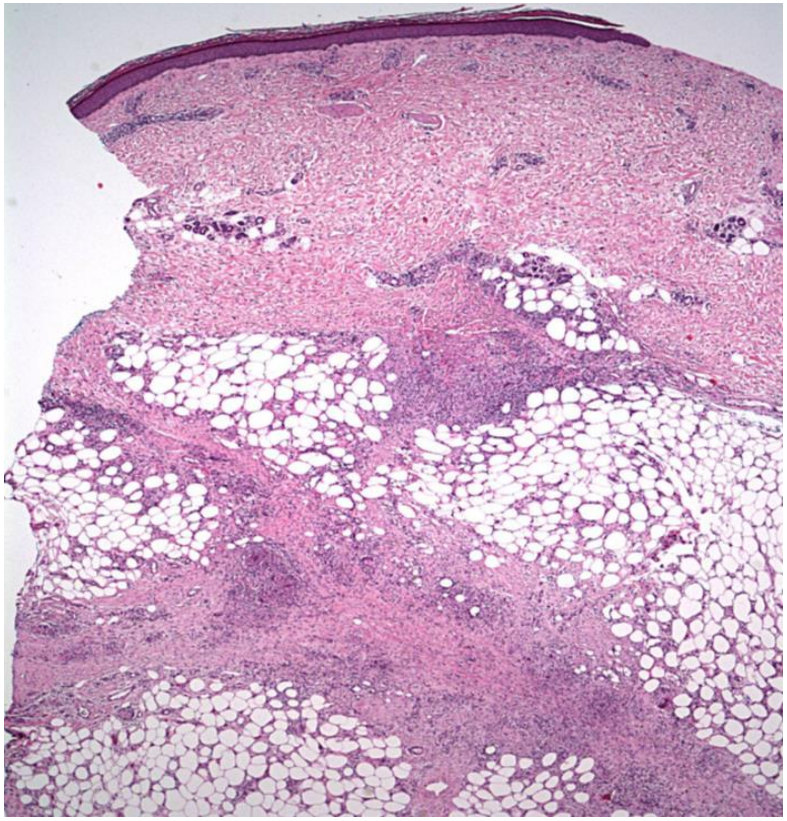


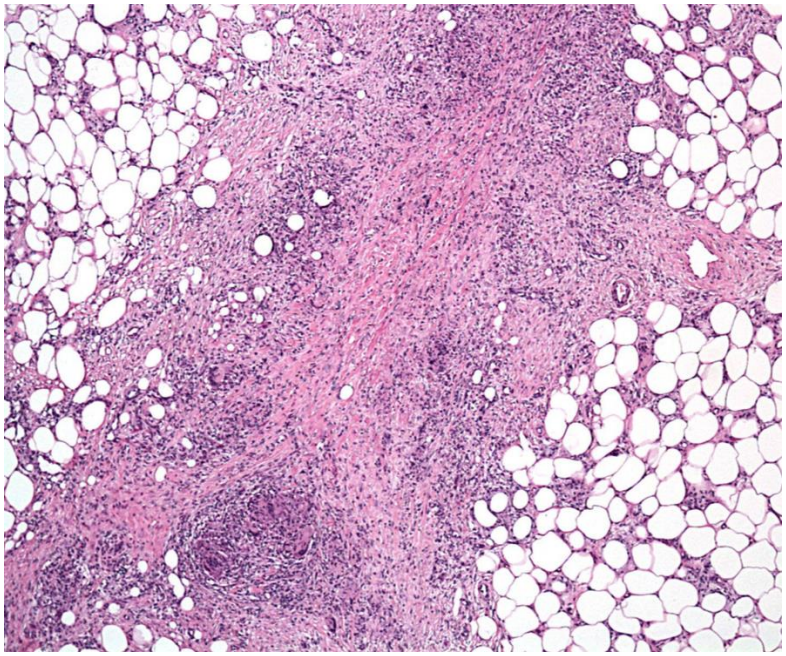
Erythema Nodosum

- Early lesions have more inflammation (neutrophils); and less fibrosis
- Later lesions demonstrate septal thickening, lymphocytes, histiocytes, multinucleated giant cells (current case)
- Miescher's radial granulomas: aggregates of small histiocytes around central cleft
- No vasculitis

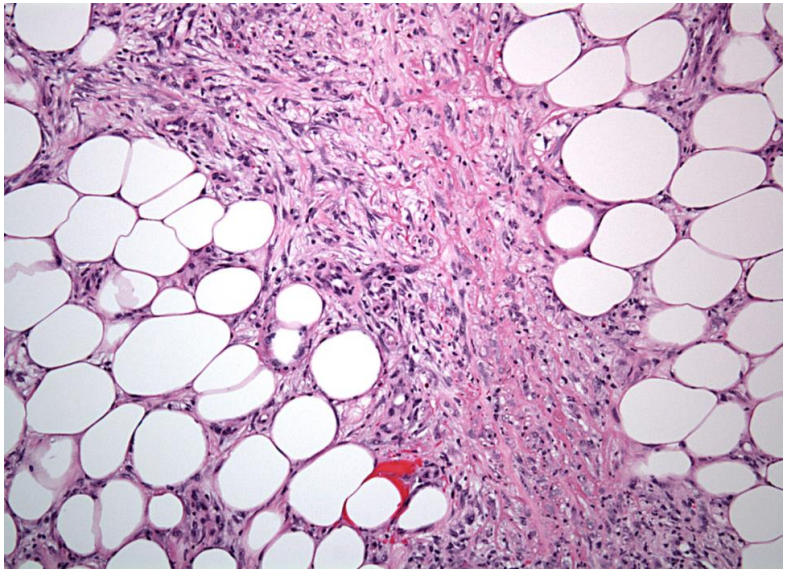


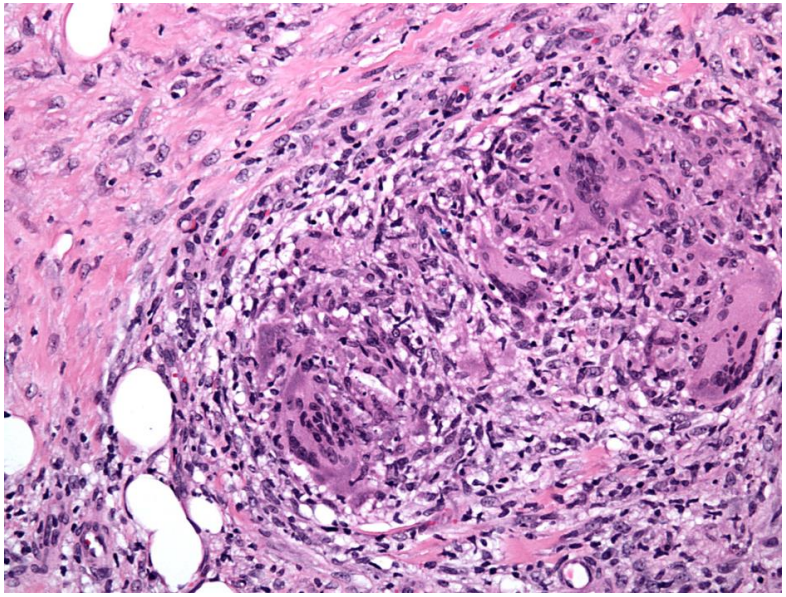
Erythema Nodosum

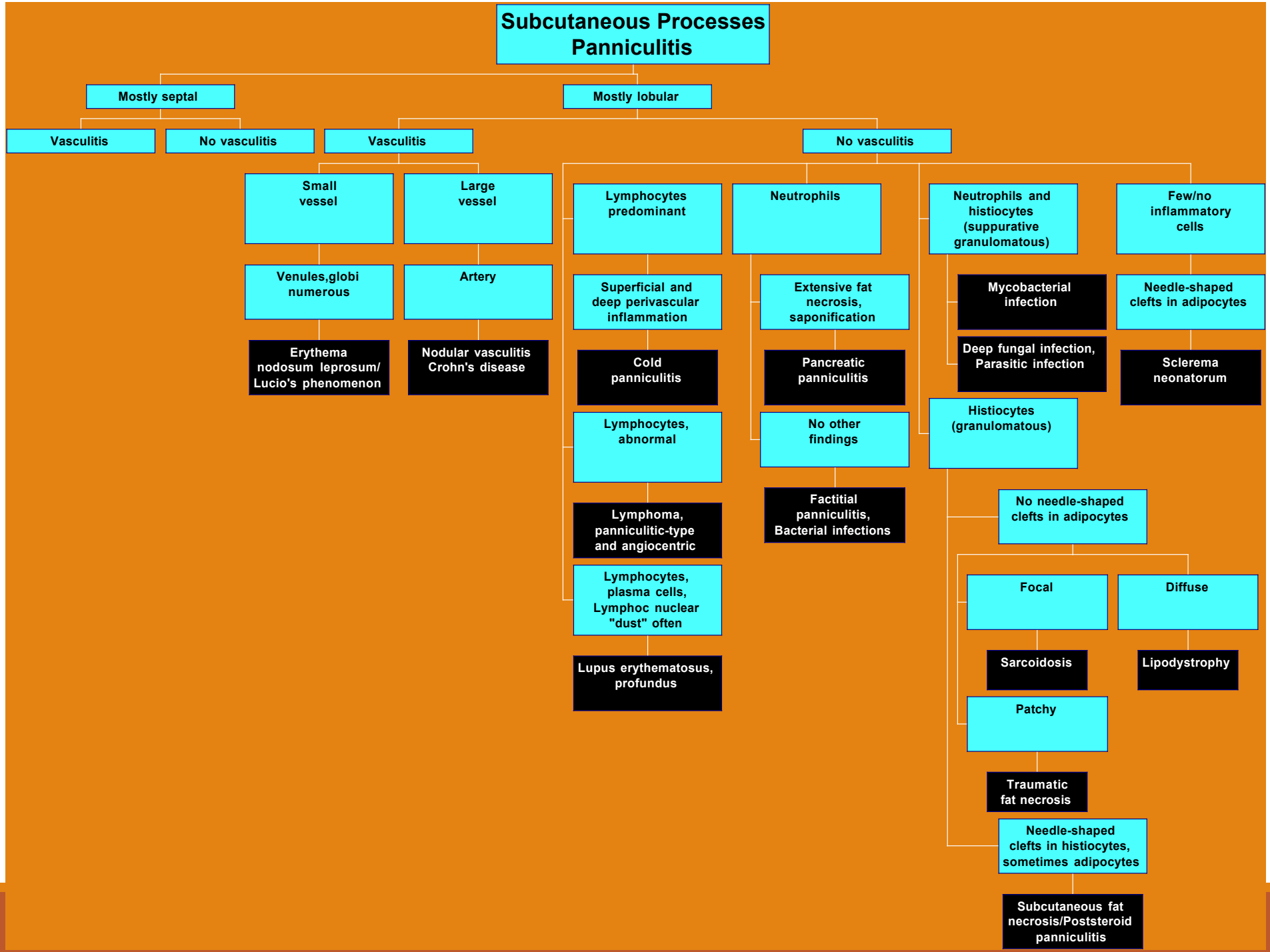




Erythema Nodosum



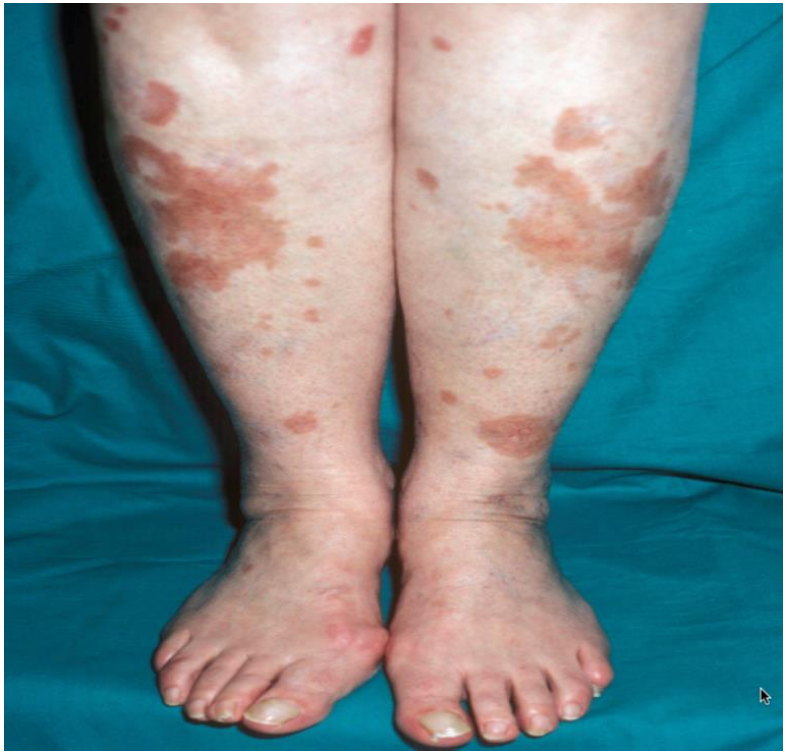


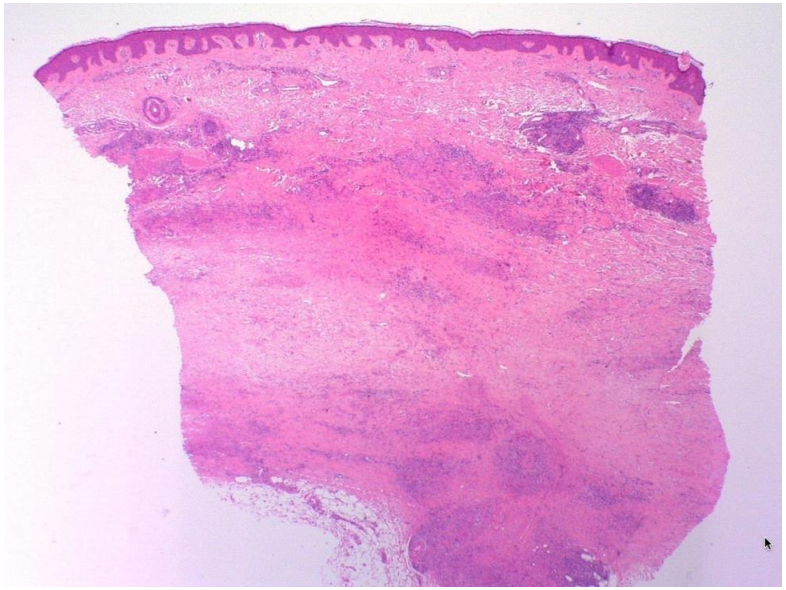

Subcutaneous Processes
Panniculitis
Mostly septal
Mostly lobular
Vasculitis
No vasculitis
Vasculitis
No vasculitis
Small vessel
Large vessel
Venules,globi numerous
Artery
Erythema nodosum leprosum/ Lucio's phenomenon
Nodular vasculitis Crohn's disease
Lymphocytes predominant
Neutrophils
Neutrophils and histiocytes (suppurative granulomatous)
Few/no inflammatory cells
Superficial and deep perivascular inflammation
Extensive fat necrosis, saponification
Mycobacterial infection
Needle-shaped clefts in adipocytes
Deep fungal infection, Parasitic infection
Sclerema neonatorum
Cold panniculitis
Pancreatic panniculitis
Lymphocytes, abnormal
No other findings
Histiocytes (granulomatous)
Factitial panniculitis, Bacterial infections
Lymphoma, panniculitic-type and angiocentric
No needle-shaped clefts in adipocytes
Lymphocytes, plasma cells, Lymphoc nuclear "dust" often
Focal
Diffuse
Sarcoidosis
Lipodystrophy
Lupus erythematosus, profundus
Patchy
Traumatic fat necrosis
Needle-shaped clefts in histiocytes, sometimes adipocytes
Subcutaneous fat necrosis/Poststeroid panniculitis

Case 4

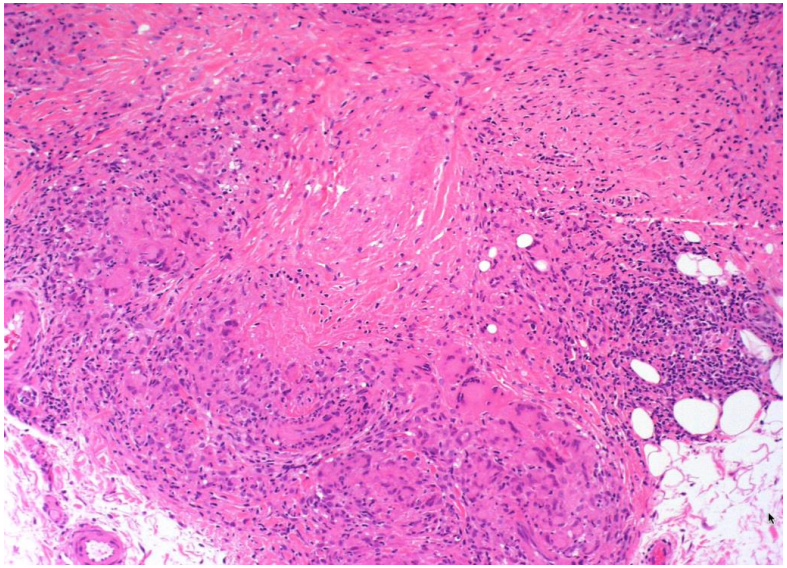
60-YEAR OLD FEMALE, YELLOWISH BRAWNY INDURATED PLAQUES ON LOWER EXTREMITIES (PRETIBIAL)

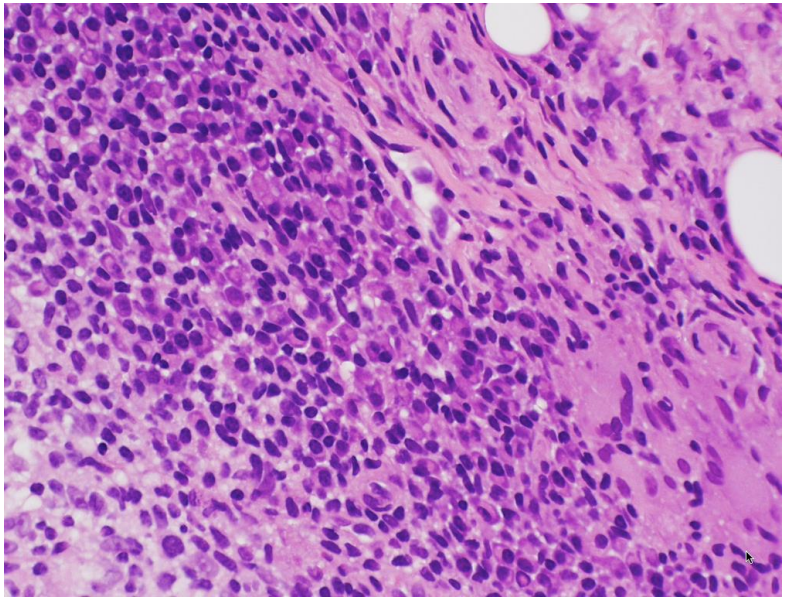
Pretibial indurated plaques

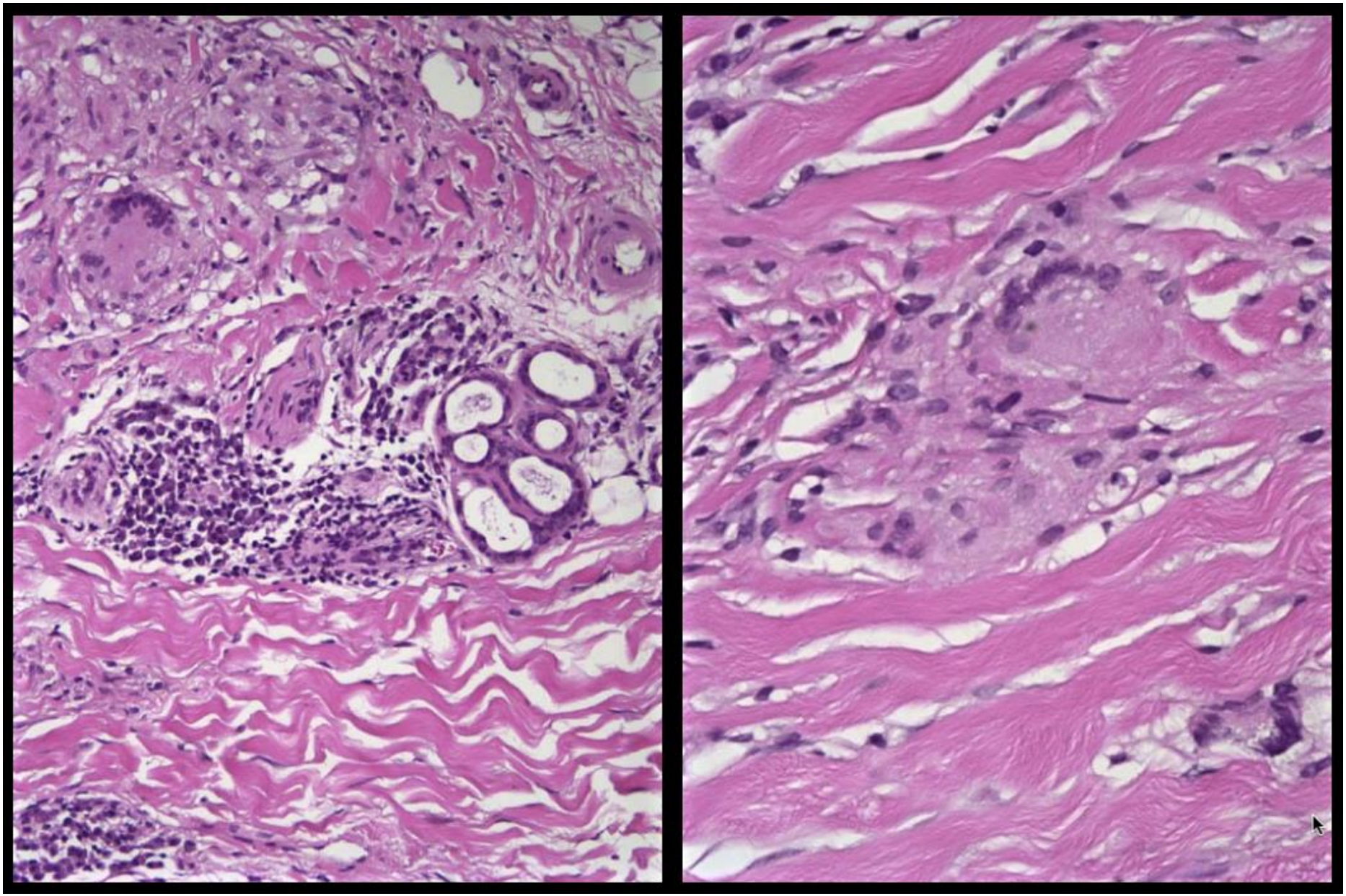


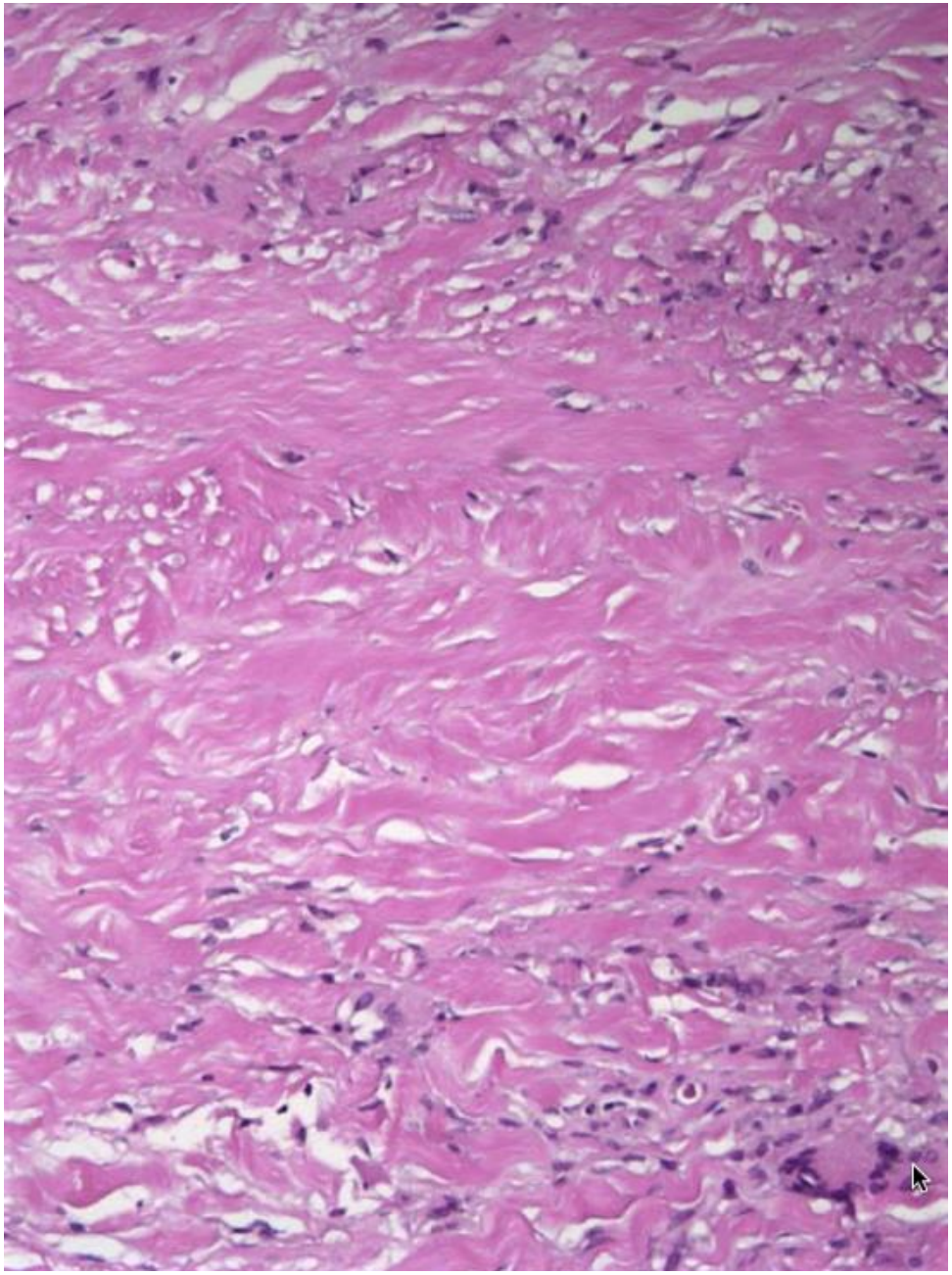


Pretibial indurated plaques









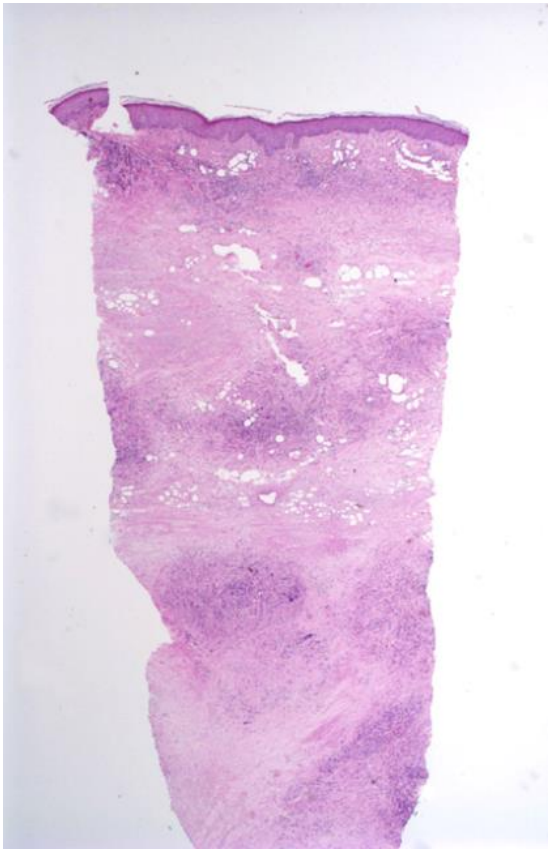
Necrobiosis Lipoidica

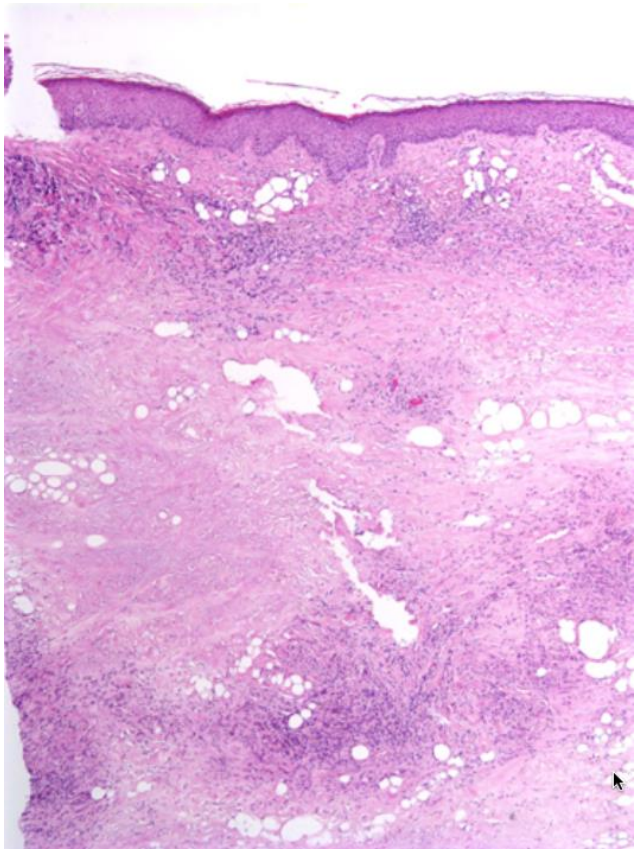
- **Atrophic epidermis**
- **Sclerotic and “layered” appearing dermis**
- **Areas of histiocytes palisading around pauci-cellular areas**
- **Scattered lymphocytes and plasma cells**
- **Vascular thickening**

Necrobiosis Lipoidica

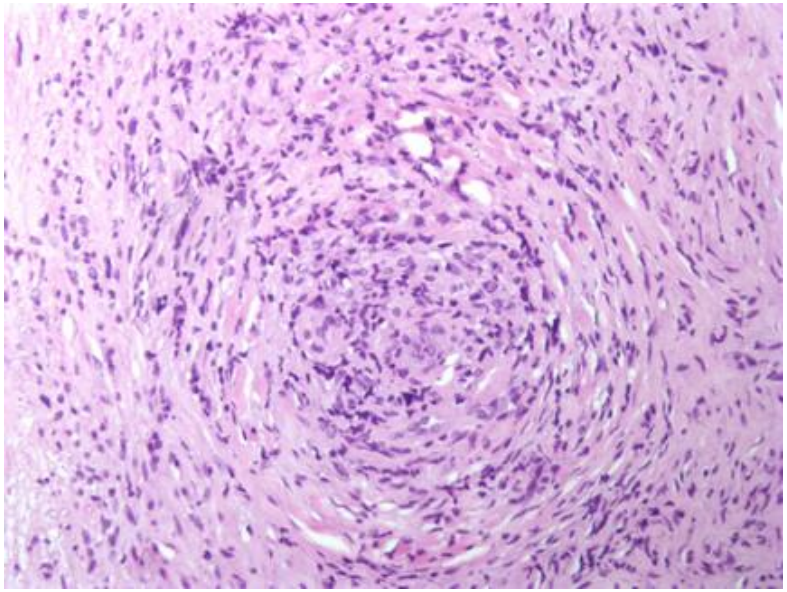
- Atrophic annular plaques, most common on shins
- Rarely occur on scalp, face
- More common in women
- 2/3 have frank diabetes
- Virtually 100% with glucose metabolism abnormality
- NL is a disease seen most commonly in patients with relatively advanced diabetes mellitus
- Not usually seen in early cases or in young patients
- Rare that it is presenting sign of disease

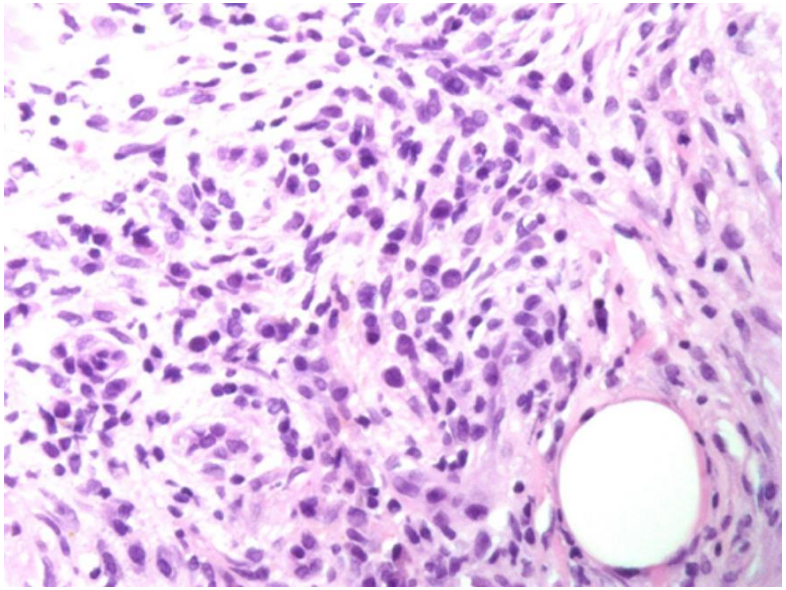
Necrobiosis Lipoidica





Necrobiosis Lipoidica

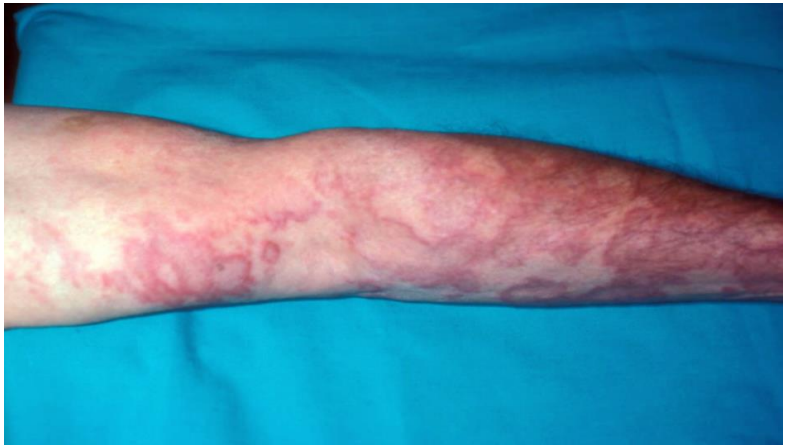


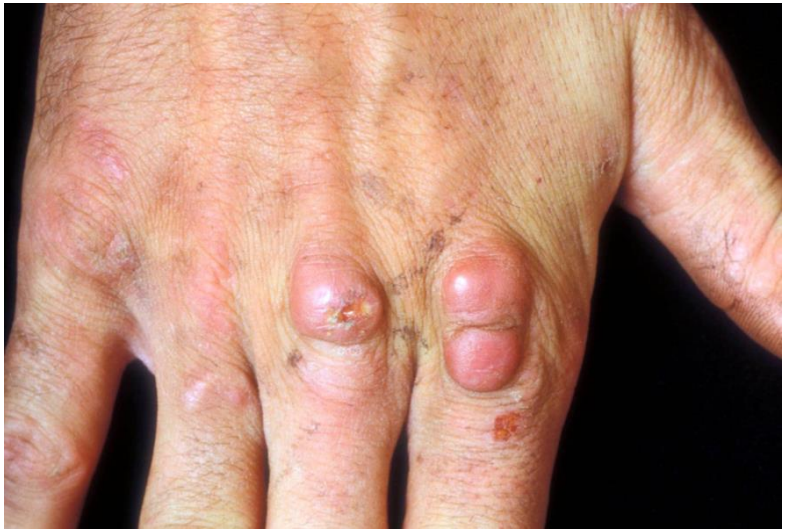


Necrobiosis Lipoidica - Ddx

- **Granuloma annulare**
- **Actinic granuloma (annular elastolytic granuloma)**
- **Rheumatoid nodule**
- **Necrobiotic xanthogranuloma**
- **Epithelioid sarcoma**

Granuloma Annulare

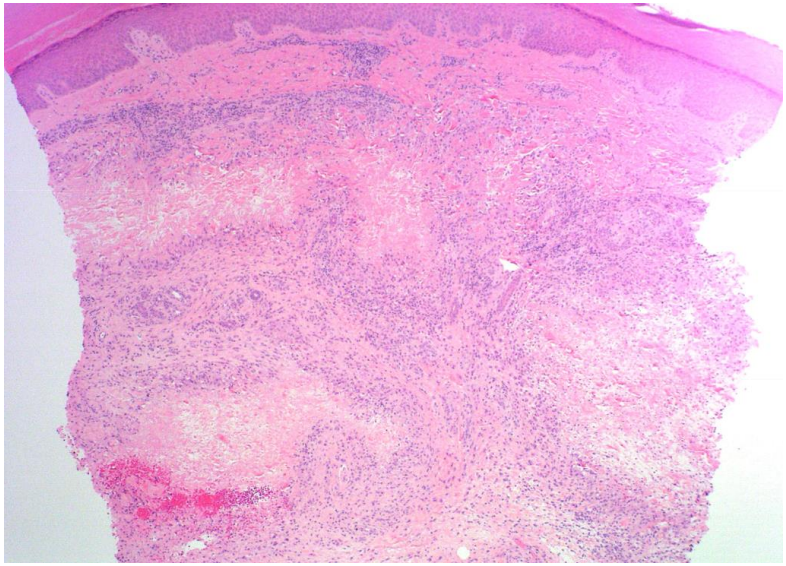


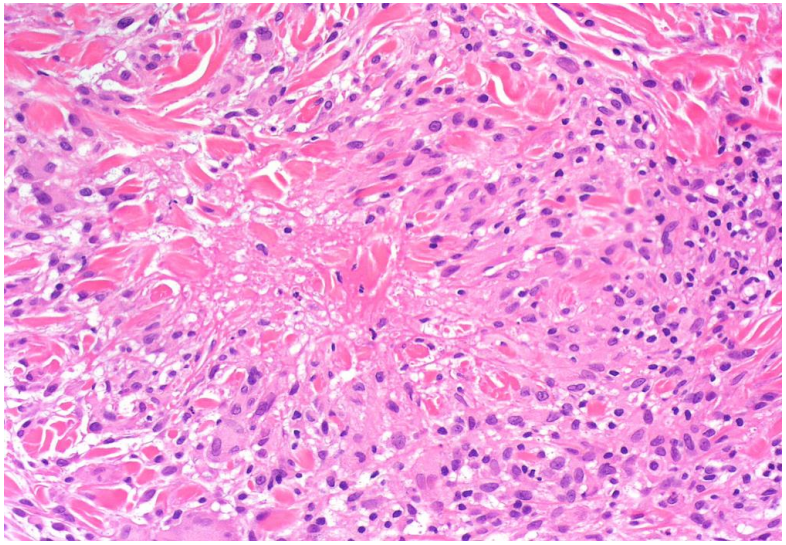


Granuloma Annulare

- Most commonly involves upper and mid reticular dermis
- Central zone of altered collagen fibers with associated dermal mucin surrounded by a palisade of histiocytes with some giant cells
- Interstitial pattern common
- Perivascular lymphocytic infiltrate with variable numbers of eosinophils
- Neutrophils may be prominent early
- Rarely may resemble sarcoidal granulomas
- Rarely may be confined to the subcutis (deep granuloma annulare)

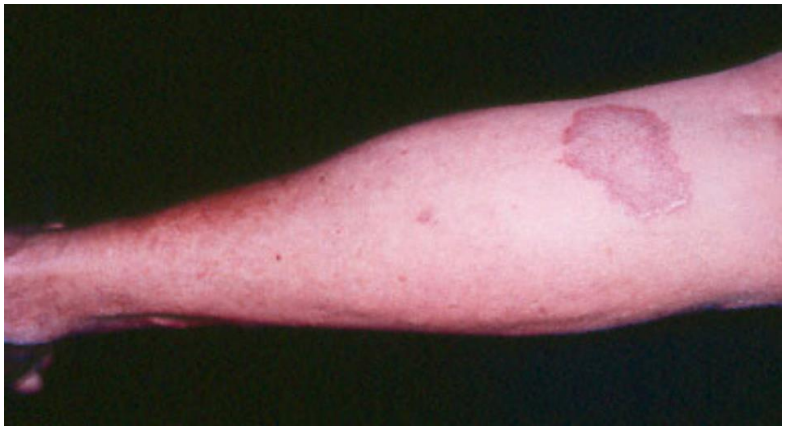
Granuloma Annulare

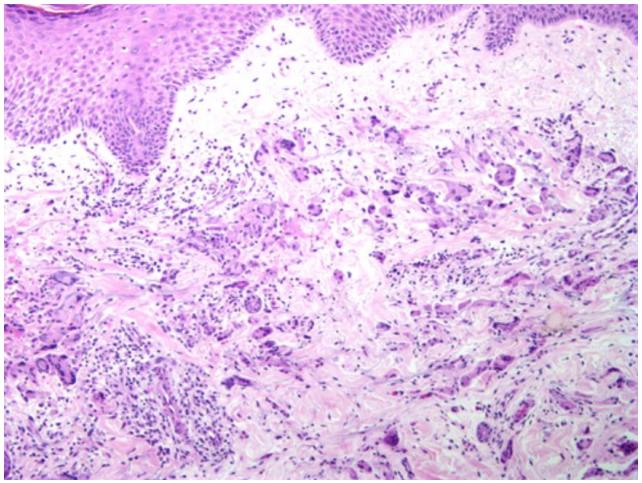




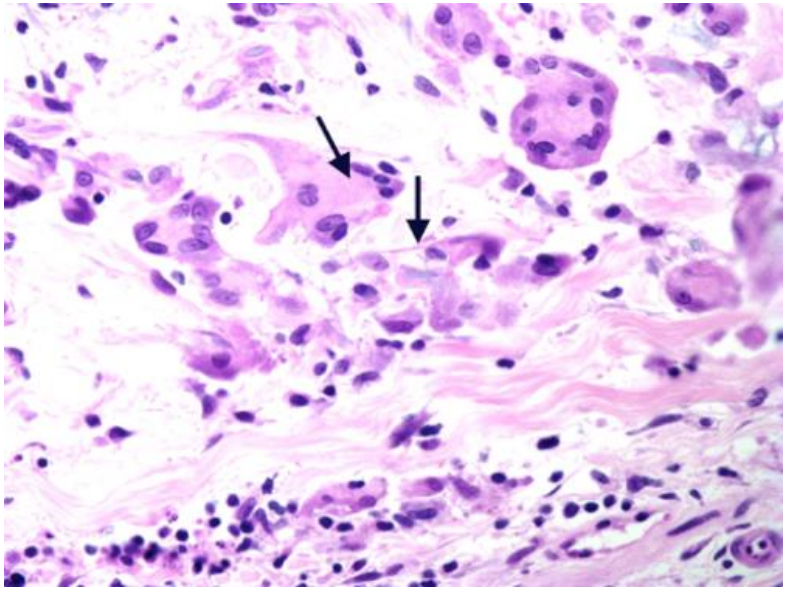
Actinic Granuloma

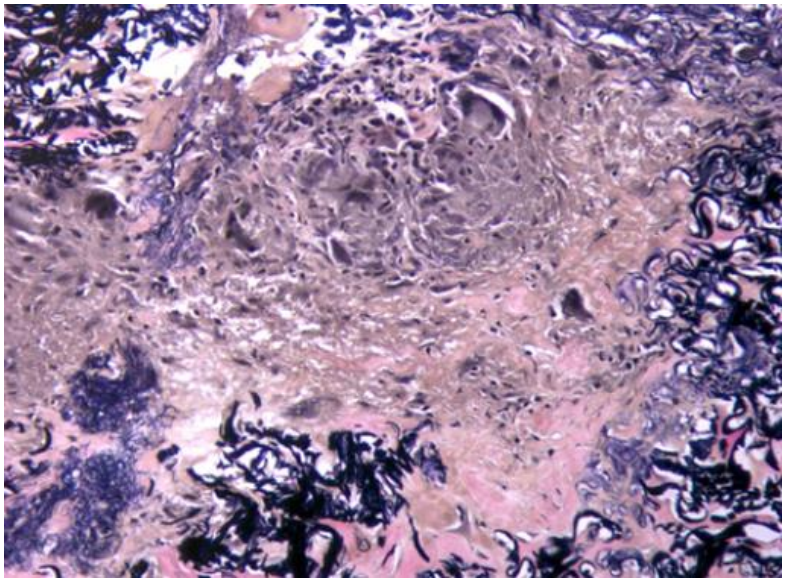
- May represent granuloma annulare occurring on sun-damaged skin
  - Usually multiple lesions on sun-exposed body sites
  - Small foci of granulomatous degenerationin superficial dermis
  - Multinucleated giant cells often containing degenerating elastotic material
  - Elastolysis in center of granulomatous foci



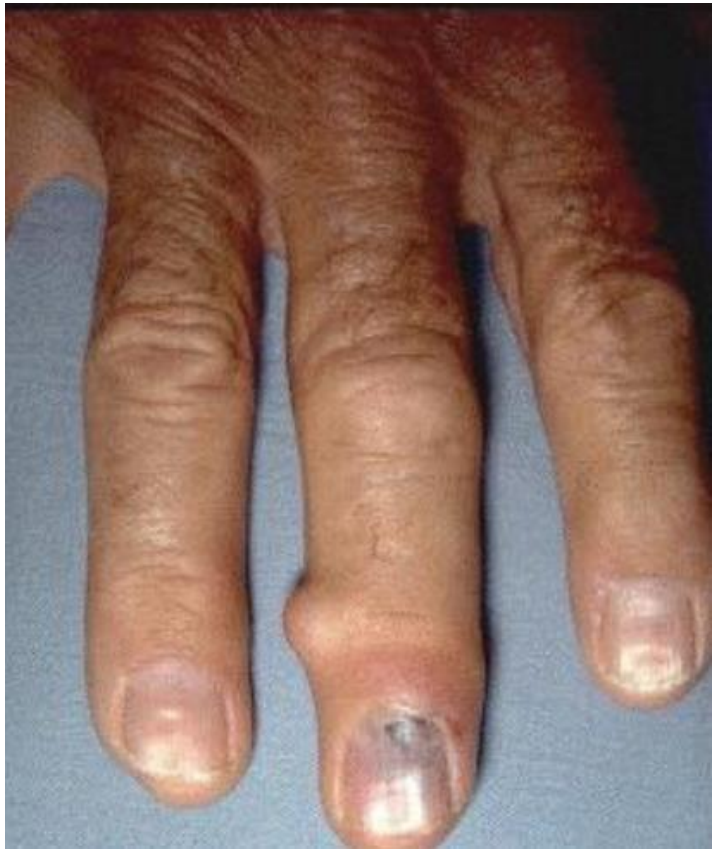


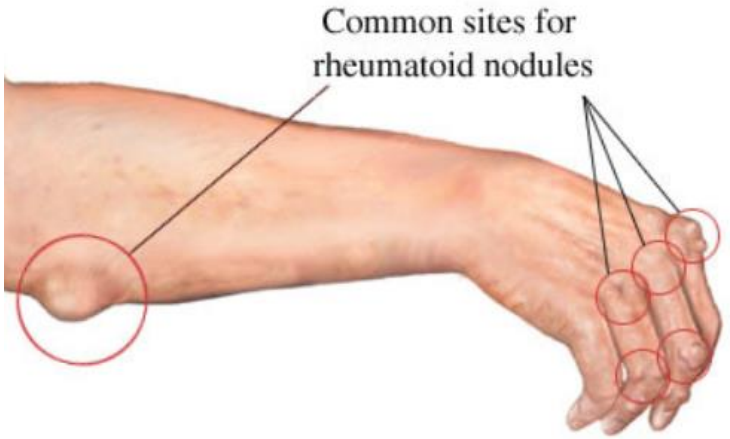
Actinic Granuloma





Rheumatoid Nodules





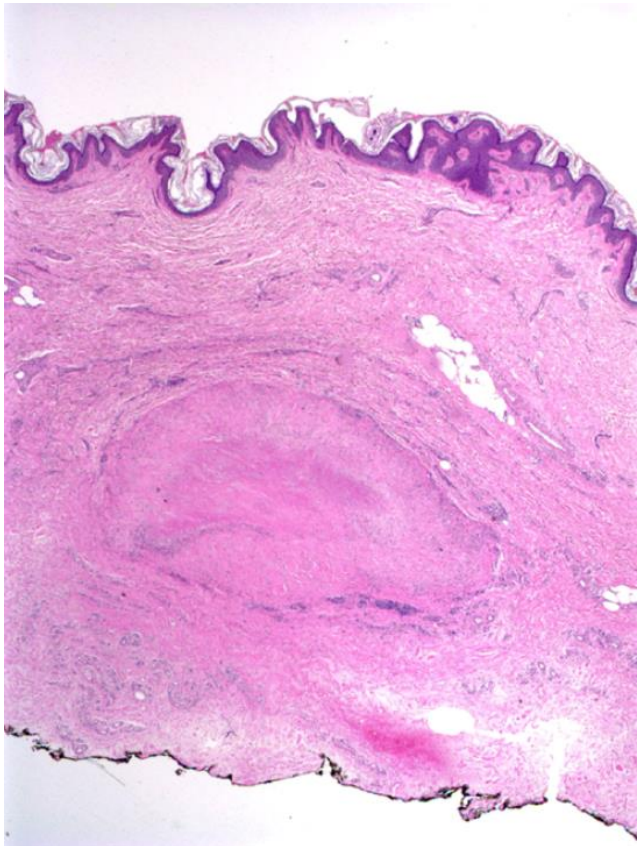
Rheumatoid Nodules

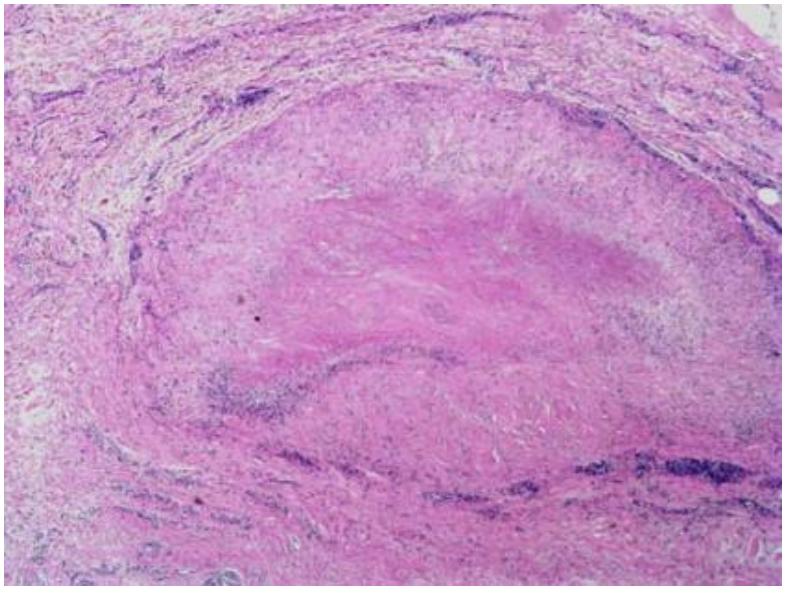
- **Lesions are located in the deep dermis, subcutaneous fat or soft tissue**
- **Central areas of acellular fibrin surrounded by histiocytes and giant cells in a palisaded pattern**
- **Lymphocytes, plasma cells and eosinophils may be present**

Rheumatoid Nodules

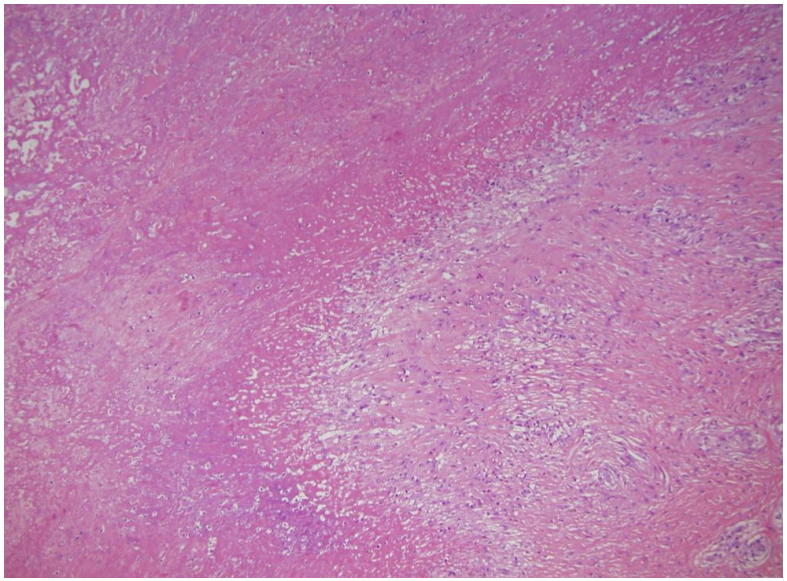
- Peri-articular nodules over smaller joints
- Little to no surface changes to skin
- Single large focus of granulomatous degeneration in dermal collagen
- Present in deep reticular dermis and into subcutaneous fat
- Fibrin covers collagen leading to brick-red color
- Well-circumscribed palisade of histiocytes including multinucleated cells

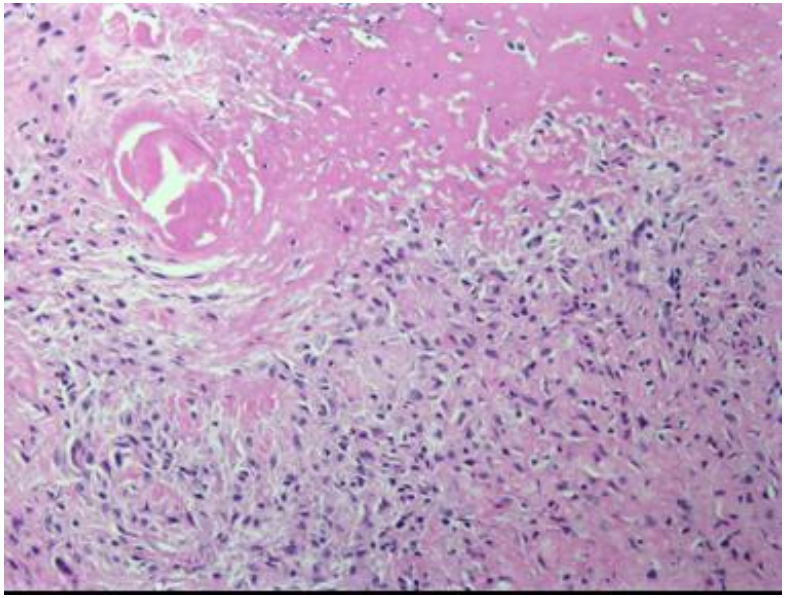
Rheumatoid Nodules





Rheumatoid Nodules

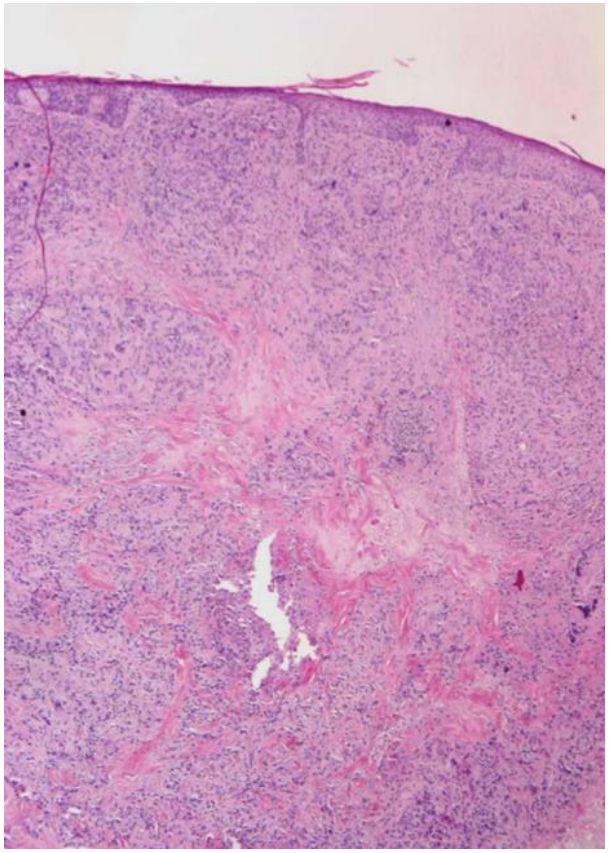


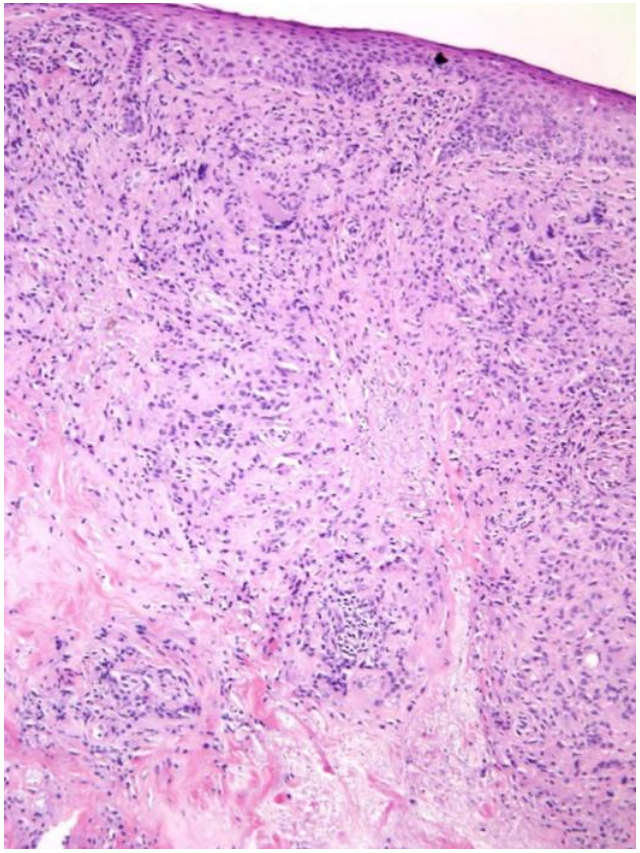


Necrobiotic Xanthogranuloma

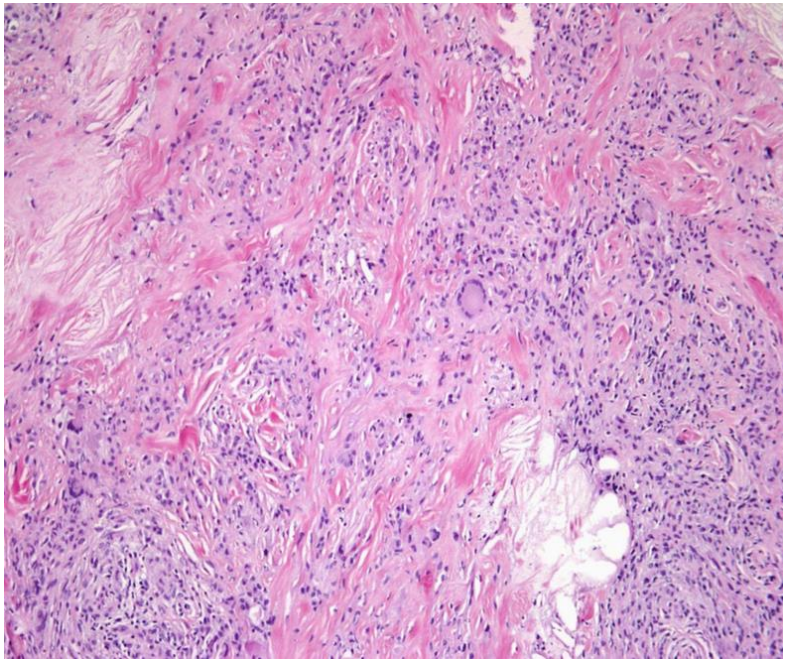
- **Low Power - Normal epithelium and rounded well-circumscribed dermal process**
- **Intermediate Power - Dermal palisade of histiocytes including foam cells and numerous giant cells with intervening zones of hyaline necrosis with cholesterol clefts and lymphoid follicles**
- **High Power - Giant cells of the Touton and foreign-body type often with irregular size, shape and distribution of the nuclei**

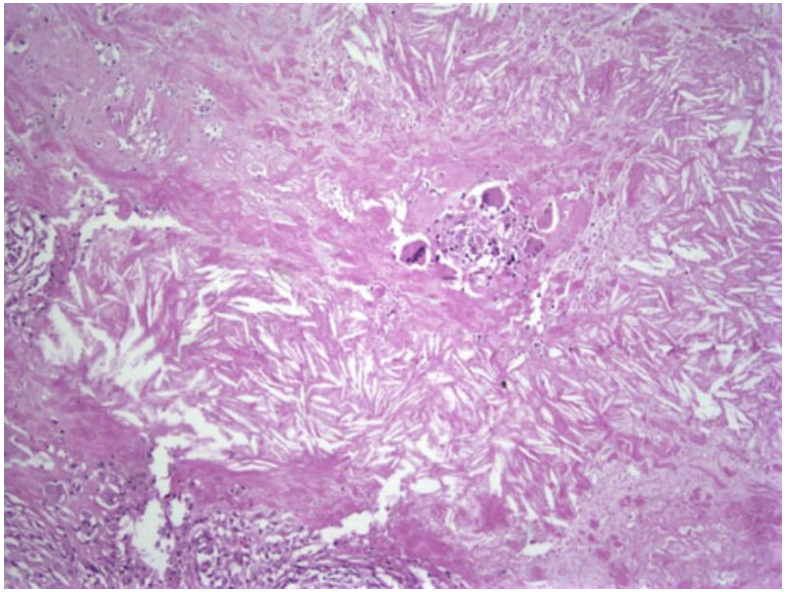
Necrobiotic Xanthogranuloma



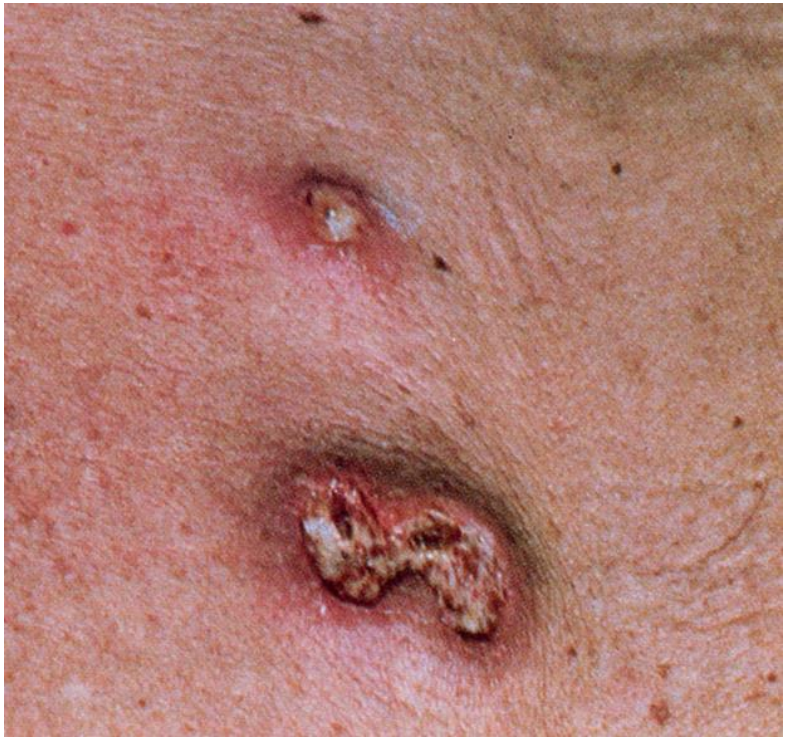


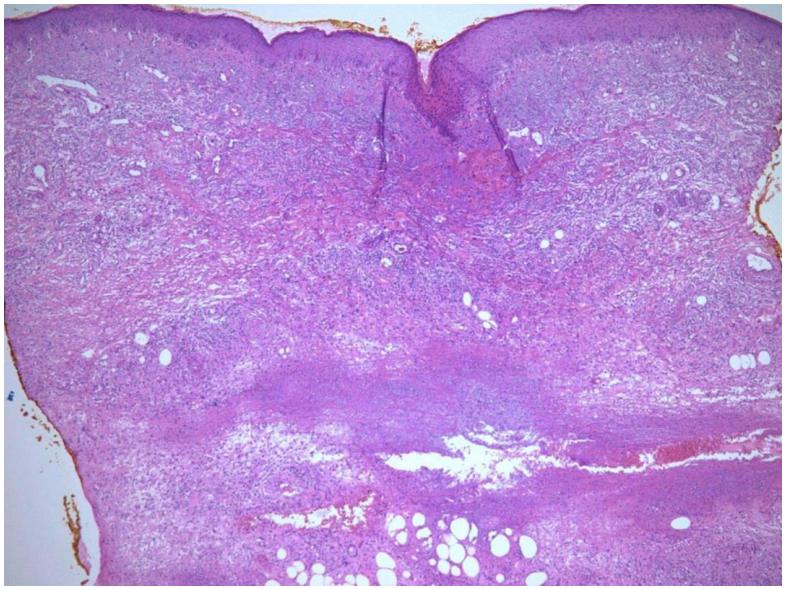
Necrobiotic Xanthogranuloma





Necrobiotic Xanthogranuloma

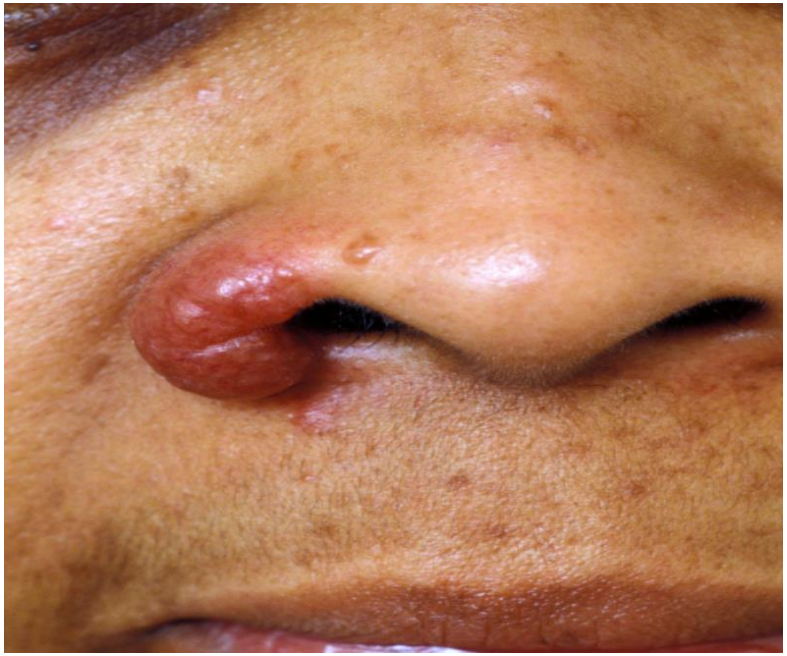


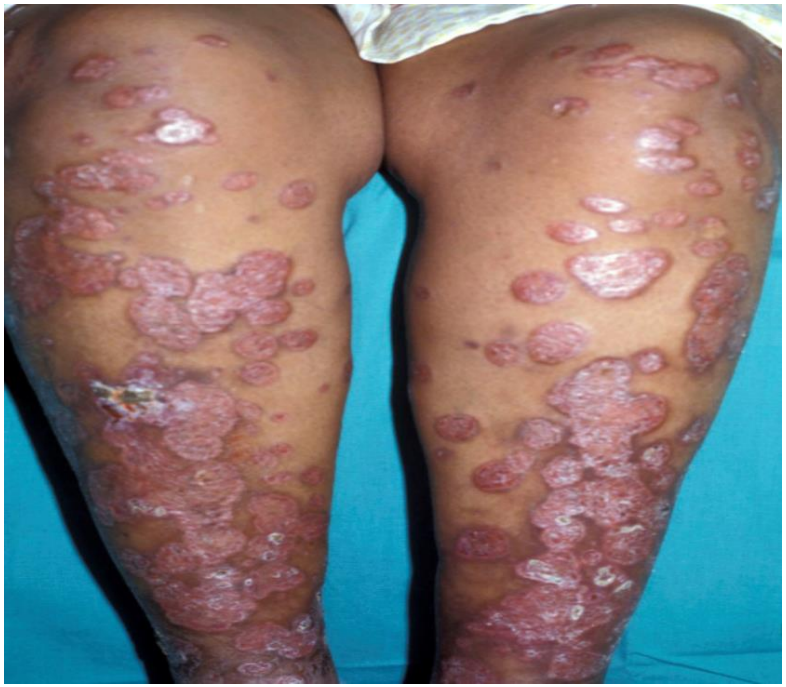


Necrobiotic Xanthogranuloma

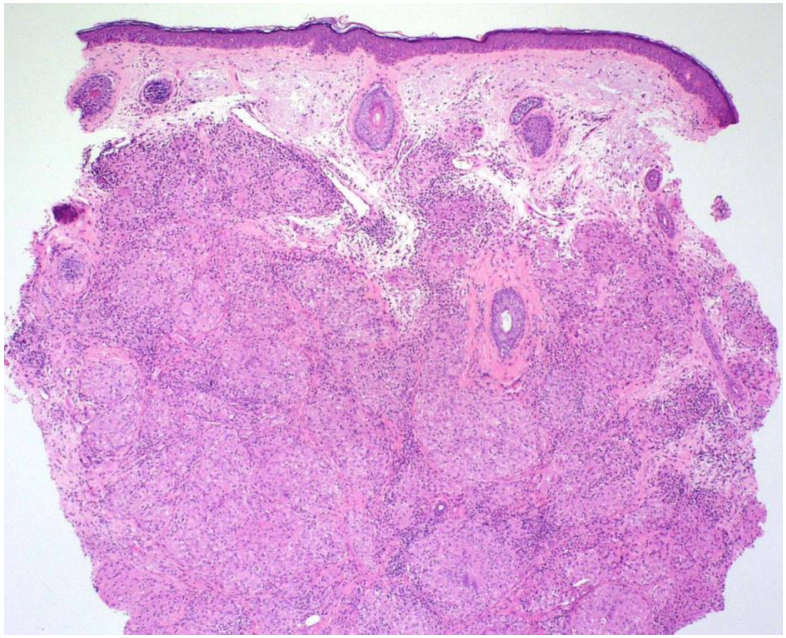
- **Yellow-red indurated nodules and plaques of the face, particularly the infraorbital area**
- **Rare condition, seen exclusively in adults, equal gender distribution**
- **Association with paraproteinemia, hyperlipidemia, scleritis and keratitis**

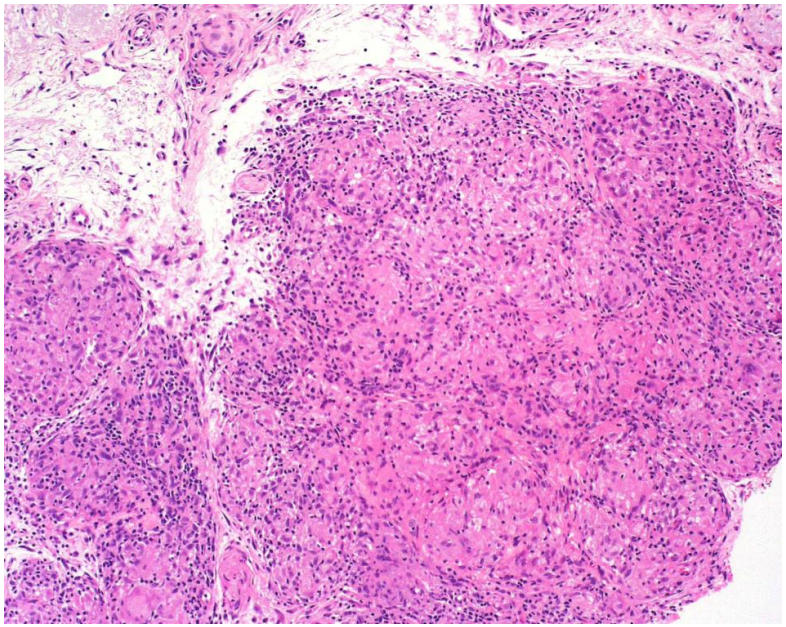
Sarcoidosis

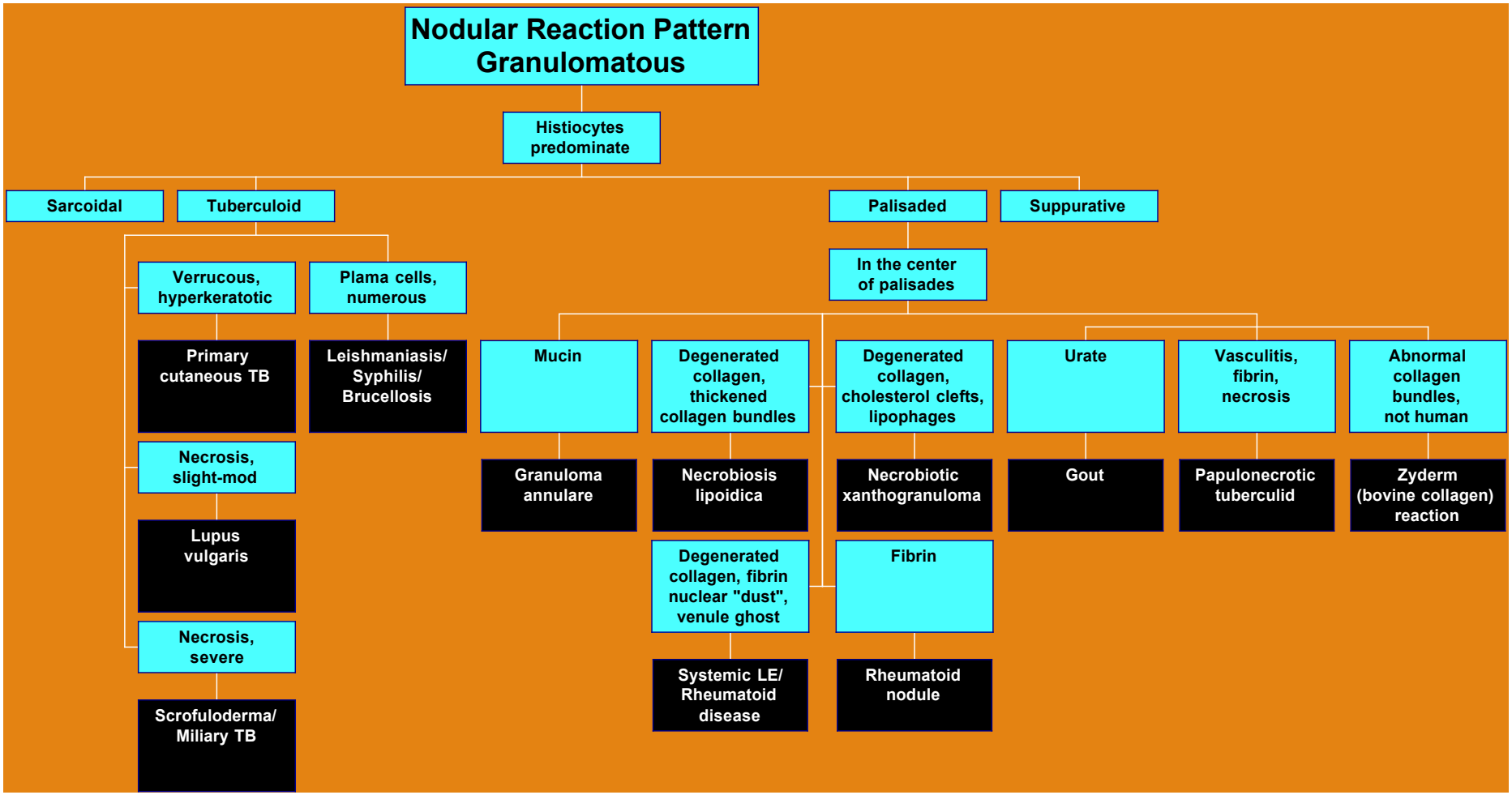


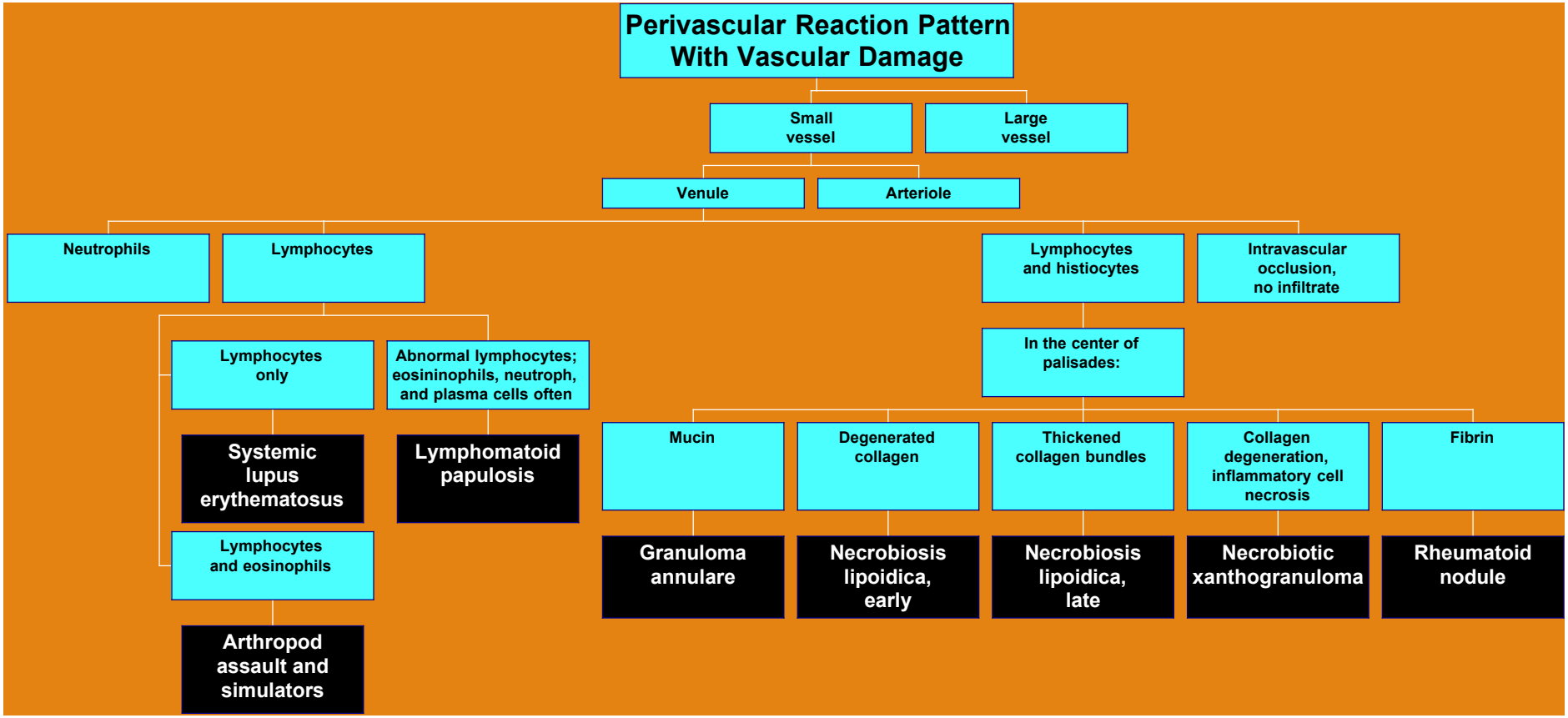


Sarcoidosis





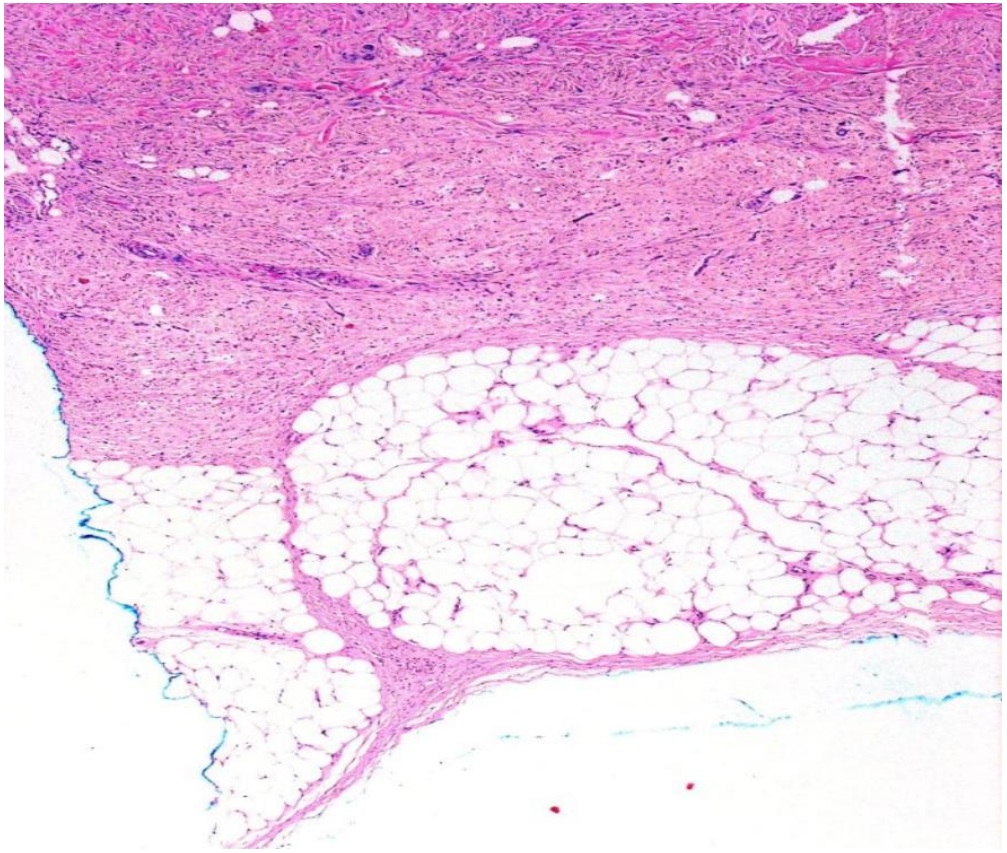

Nodular Reaction Pattern
Granulomatous
Histiocytes predominate
Sarcoidal
Tuberculoid
Palisaded
Suppurative
Verrucous, hyperkeratotic
Plama cells, numerous
In the center of palisades
Primary cutaneous TB
Leishmaniasis/ Syphilis/ Brucellosis
Mucin
Degenerated collagen, thickened collagen bundles
Degenerated collagen, cholesterol clefts, lipophages
Urate
Vasculitis, fibrin, necrosis
Abnormal collagen bundles, not human
Necrosis, slight-mod
Granuloma annulare
Necrobiosis lipoidica
Necrobiotic xanthogranuloma
Gout
Papulonecrotic tuberculid
Zyderm (bovine collagen) reaction
Lupus vulgaris
Degenerated collagen, fibrin nuclear "dust", venule ghost
Fibrin
Necrosis, severe
Systemic LE/ Rheumatoid disease
Rheumatoid nodule
Scrofuloderma/ Miliary TB


Perivascular Reaction Pattern With Vascular Damage
Small vessel
Large vessel
Venule
Arteriole
Neutrophils
Lymphocytes
Lymphocytes and histiocytes
Intravascular occlusion, no infiltrate
Lymphocytes only
Abnormal lymphocytes; eosininophils, neutroph, and plasma cells often
In the center of palisades:
Systemic lupus erythematosus
Lymphomatoid papulosis
Mucin
Degenerated collagen
Thickened collagen bundles
Collagen degeneration, inflammatory cell necrosis
Fibrin
Lymphocytes and eosinophils
Granuloma annulare
Necrobiosis lipoidica, early
Necrobiosis lipoidica, late
Necrobiotic xanthogranuloma
Rheumatoid nodule
Arthropod assault and simulators

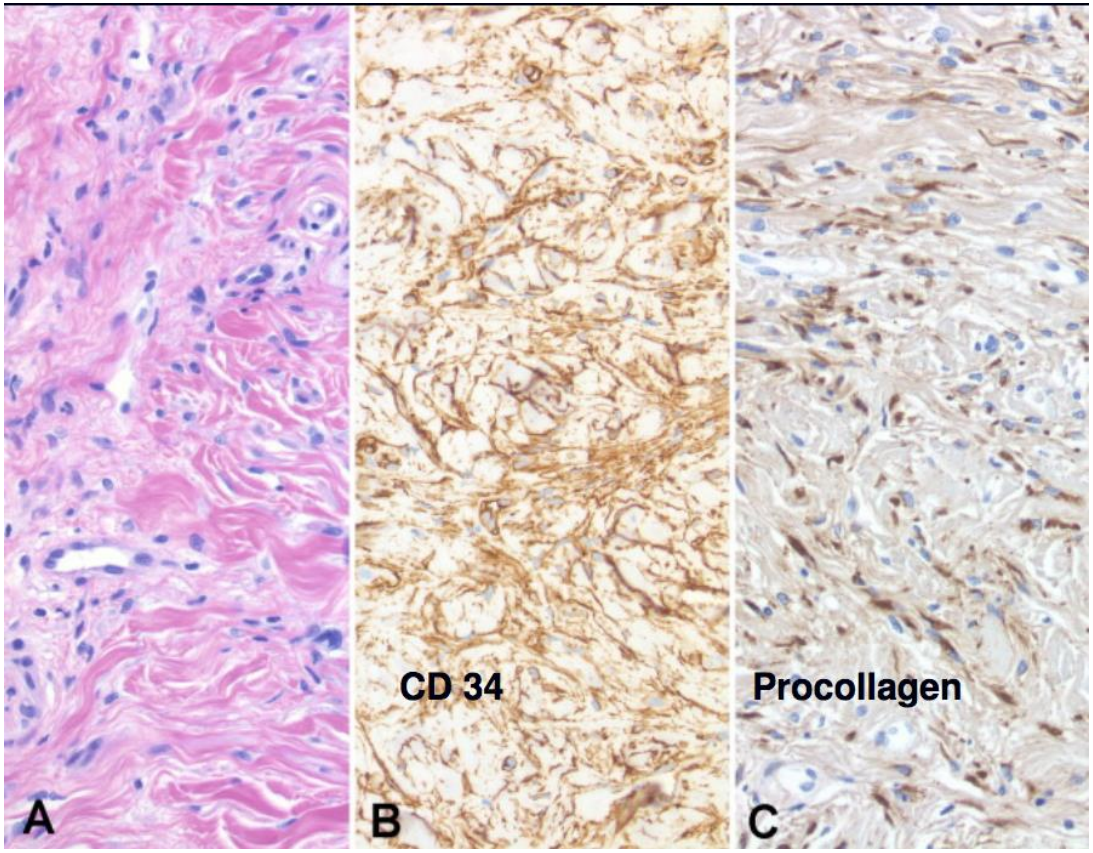
Case 5

45-YEAR OLD MALE WITH POLYCYSTIC KIDNEY DISEASE AND INDURATED PLAQUES IN LOWER EXTREMITIES

Indurated plaques in lower extremities



Indurated plaques in lower extremities



Nephrogenic Systemic Fibrosis

- **Nephrogenic systemic fibrosis (NSF),**
  - **Nephrogenic fibrosing dermopathy (NFD)**
  - **Systemic disorder with most prominent effects in the skin**
- **No cases identified prior to early 1997**
  - **Cowper SE et al described first patients in 2000**
  - **Scleromyxoedema-like cutaneous disease in renal-dialysis patients**
- **Occurs only in people with kidney disease.**
  - **Not related to disease duration or underlying cause**

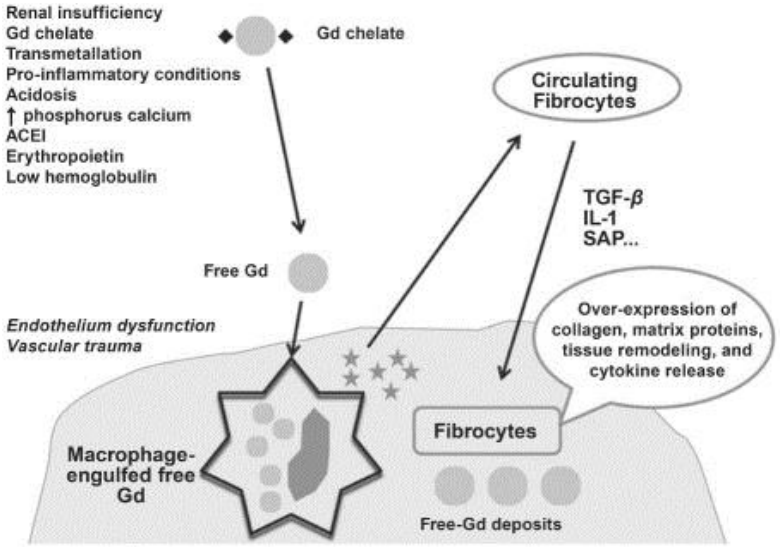
Nephrogenic Systemic Fibrosis

Indurated papules and plaques, brawny thickening of skin

- **Lower extremities 97%**
- **Upper extremities 77%**
- **Face is usually spared**

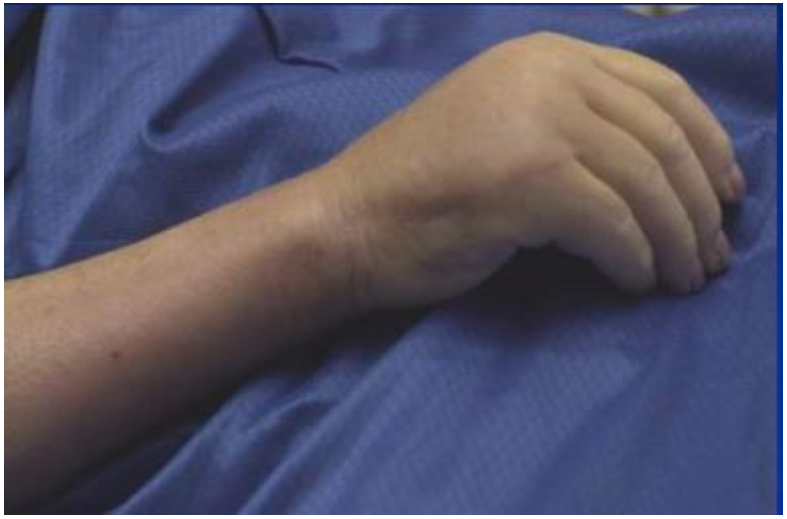
Systemic involvement

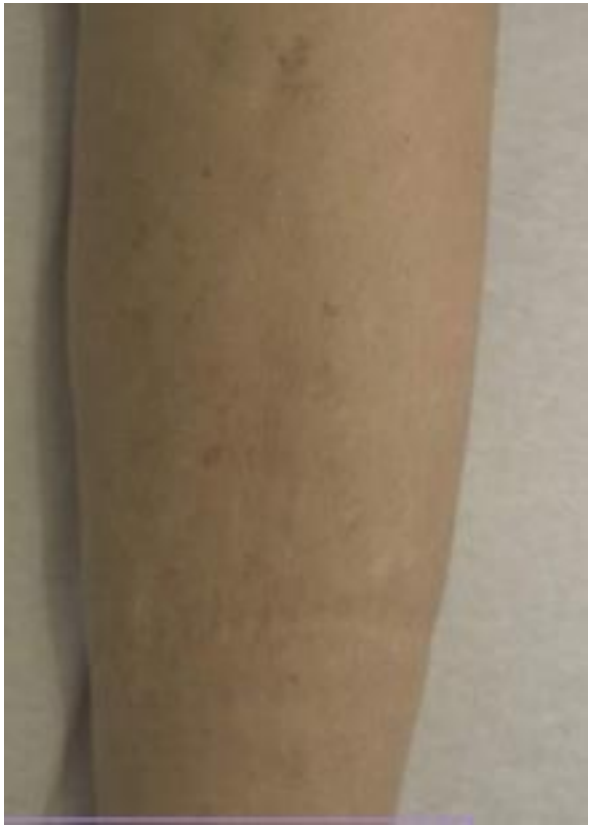
- **Joints and tendons**
- **Muscles and peripheral nerves**
- **Cardiovascular**
- **Pulmonary**



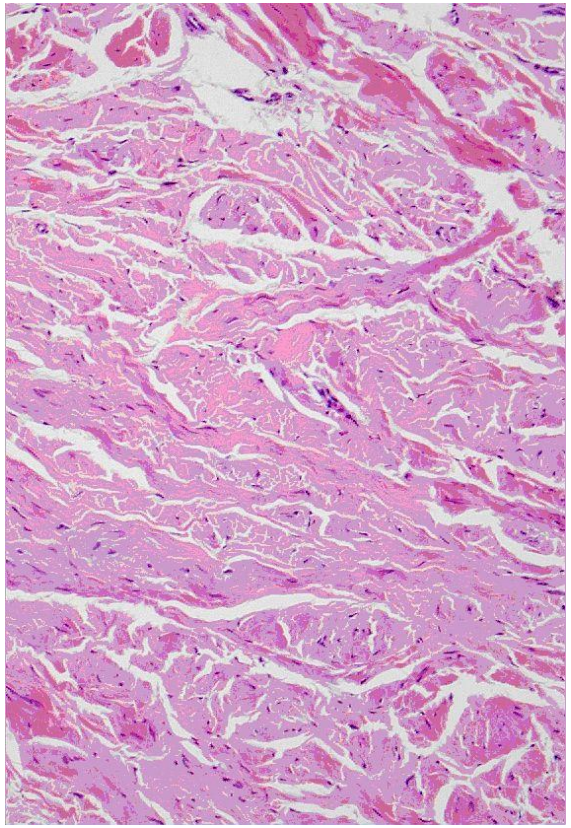
Jimenez SA, Arlett CM, Sandorfi N et al. Arthritis Rheum 2003; 50: 2660-66

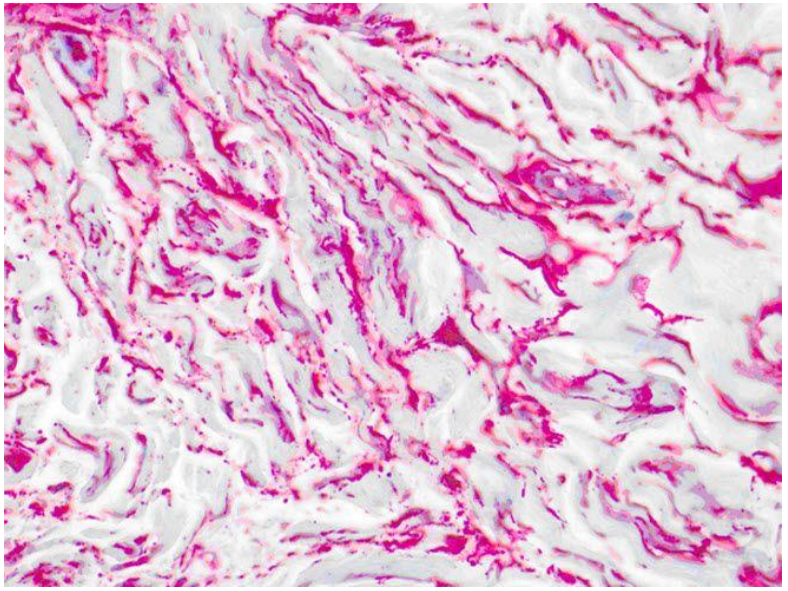
Nephrogenic Systemic Fibrosis



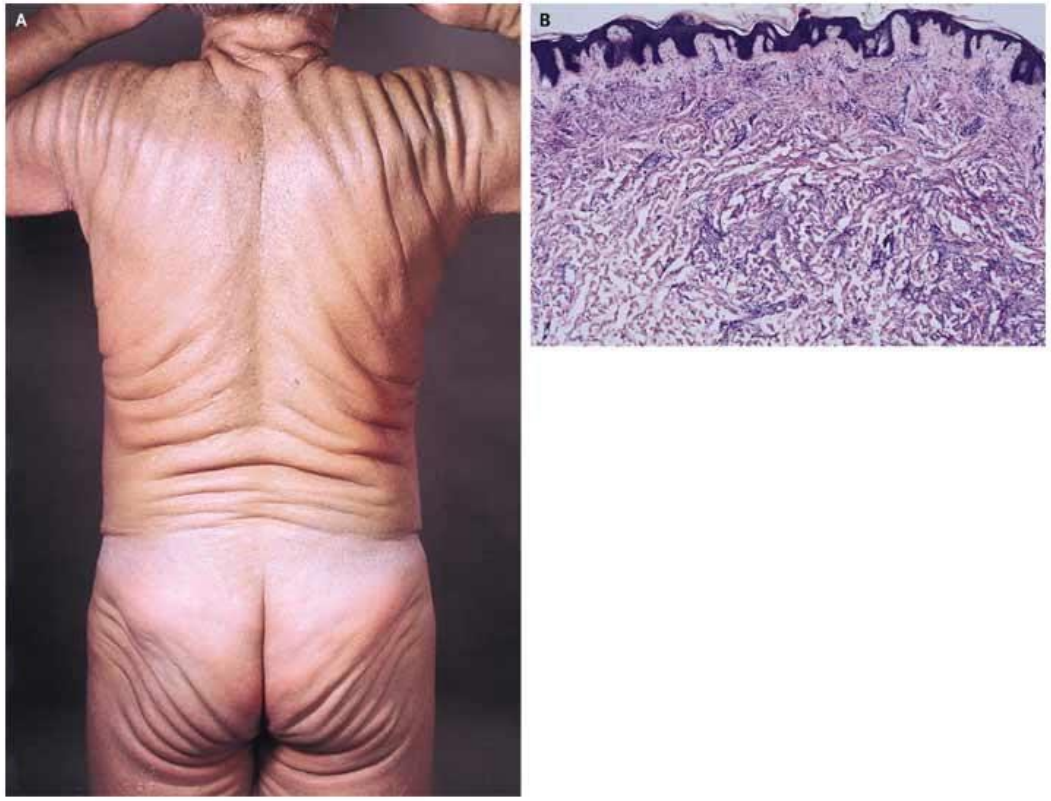


Nephrogenic Systemic Fibrosis





Scleromyxedema



Morphea

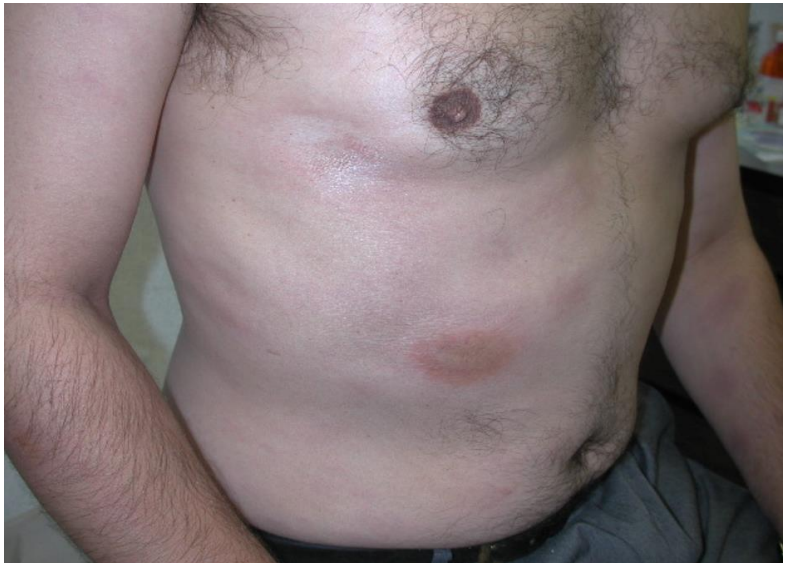
LOCALIZED

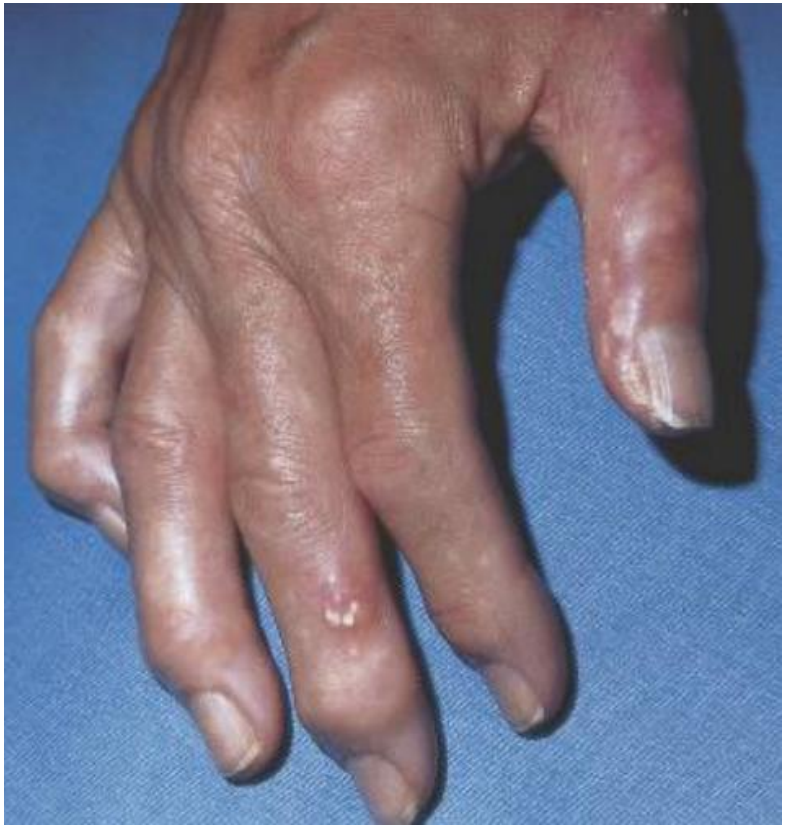
- **Localized scleroderma**
- **Indurated, dusky or hypopigmented plaques with surrounding violaceous zone of inflammation**
- **Plaque-like morphea most frequent variant**
- **No Raynaud's phenomenon or internal organ involvement**

SYSTEMIC

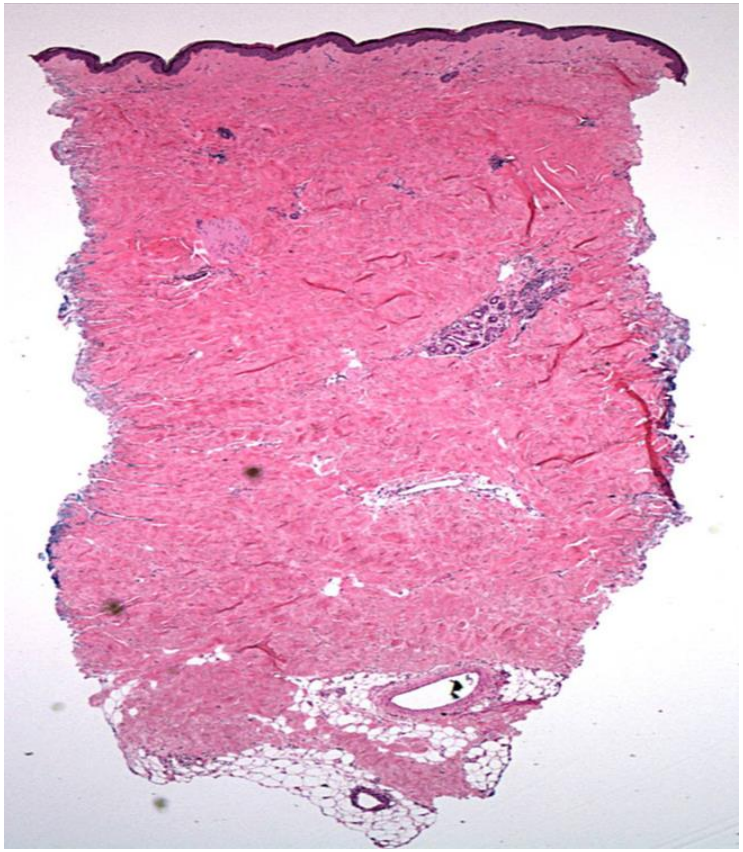
- **Multisystem connective tissue disease**
- **Two major clinical groups**
  - **Group 1: limited disease involving hands, forearms and face, often have CREST syndrome**
  - **Group 2: Diffuse cutaneous sclerosis and frequent visceral involvement**
- **Indurated skin, sclerodactyly, hypopigmentation with perifollicular pigment retention, telangiectasias**

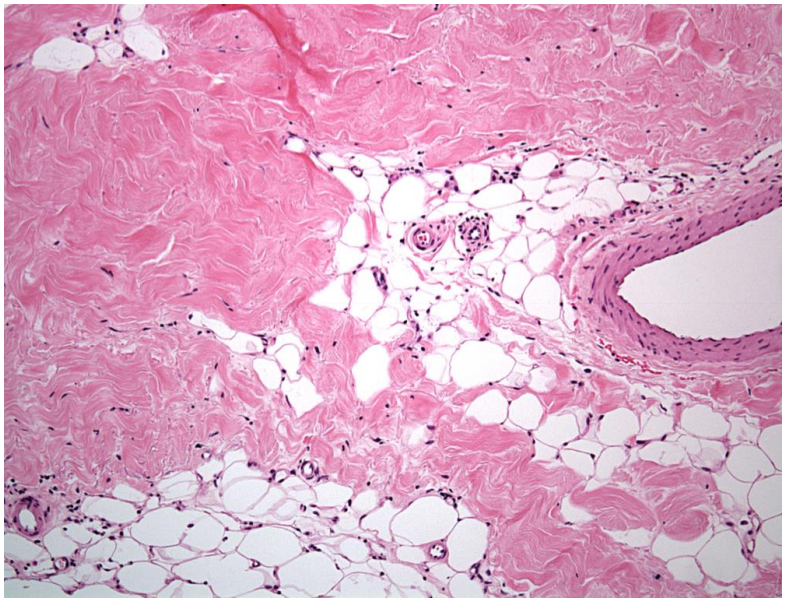
Morphea



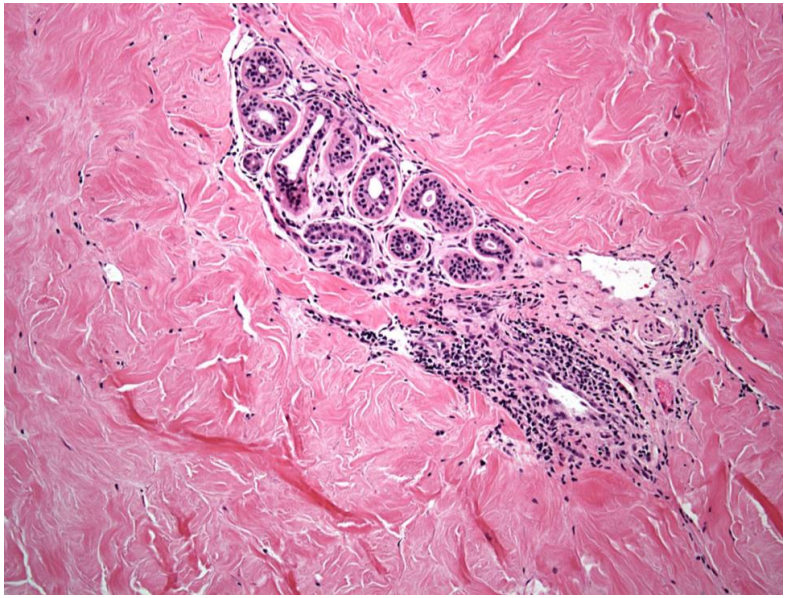


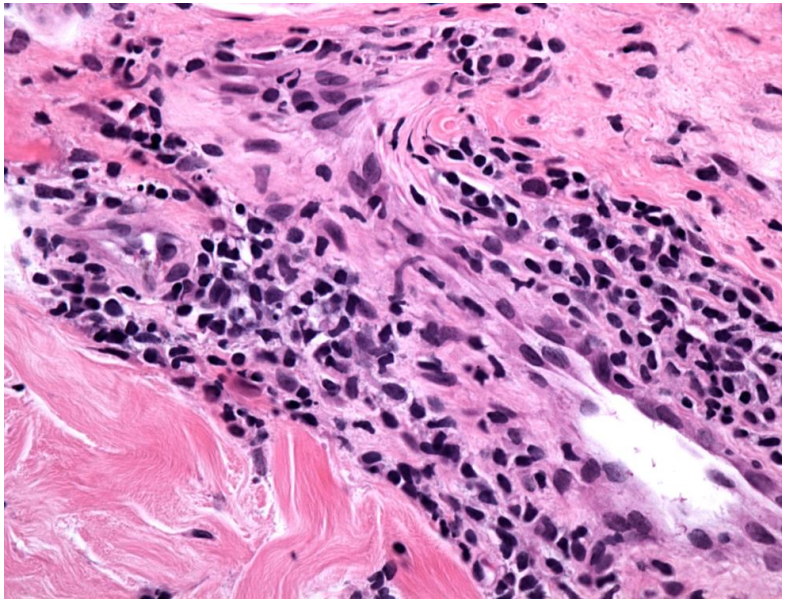
Morphea





Morphea





Morphea

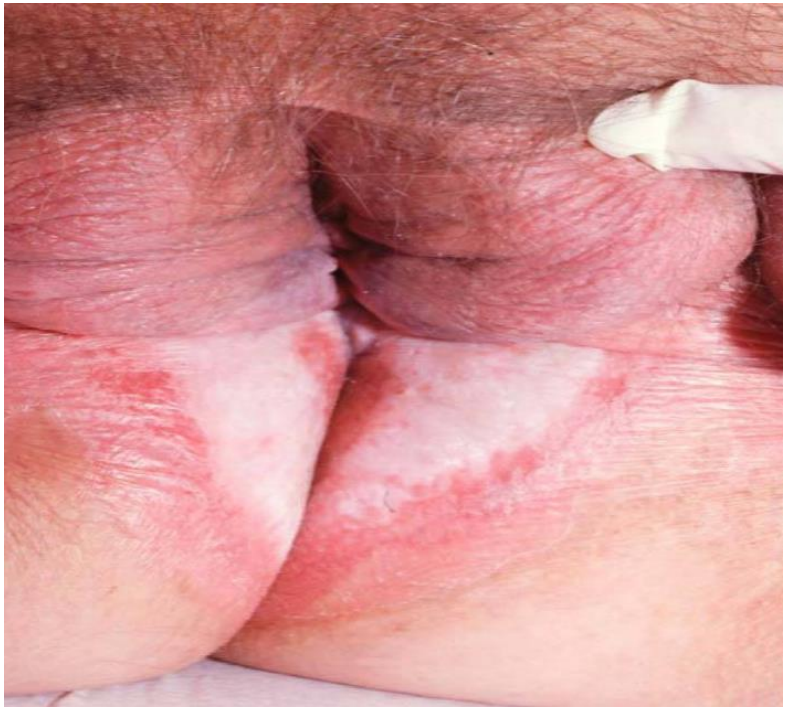
FINDINGS

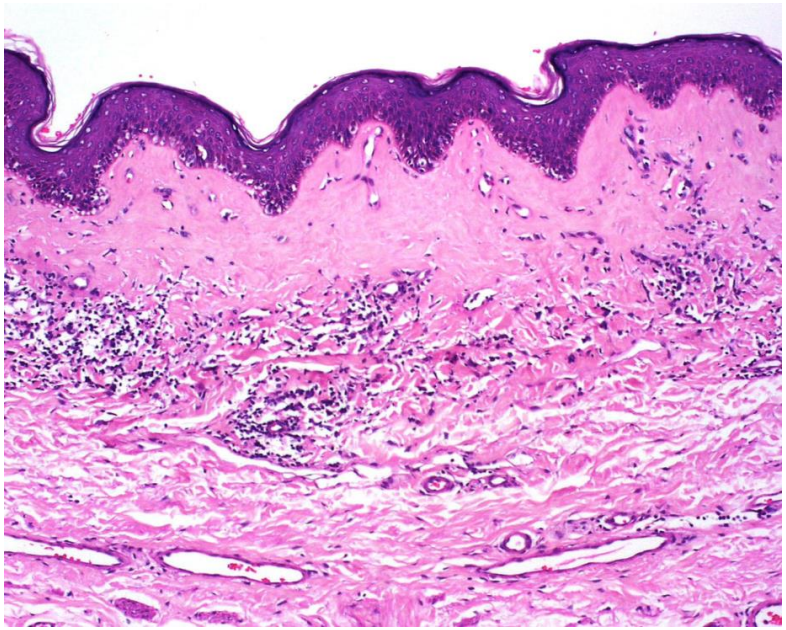
- **Early lesions**
  - **Superficial and deep interstitial mixed inflammatory infiltrate (lymphocytes, plasma cells)**
- **Fully developed**
  - **Thickened collagen bundles**
  - **Homogenization of papillary dermis**
- **Late**
  - **Sparse inflammation**
  - **Absent/degenerative adnexa**

TIPS

- **“Square” punch biopsy**
- **Differentiate from normal back**
- **Decreased spaces between collagen fibers**
- **Entrapped adnexal structures**
- **Elastic tissue stains useful in differentiated late stage NL vs. morphea**

Lichen Sclerosus



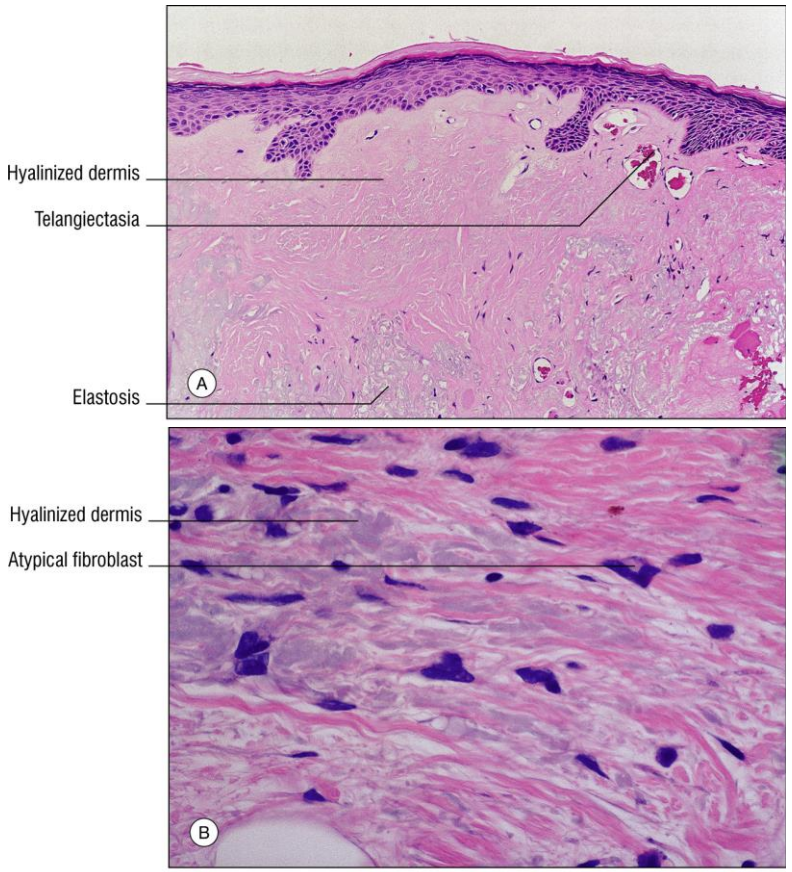


Lichen Sclerosus

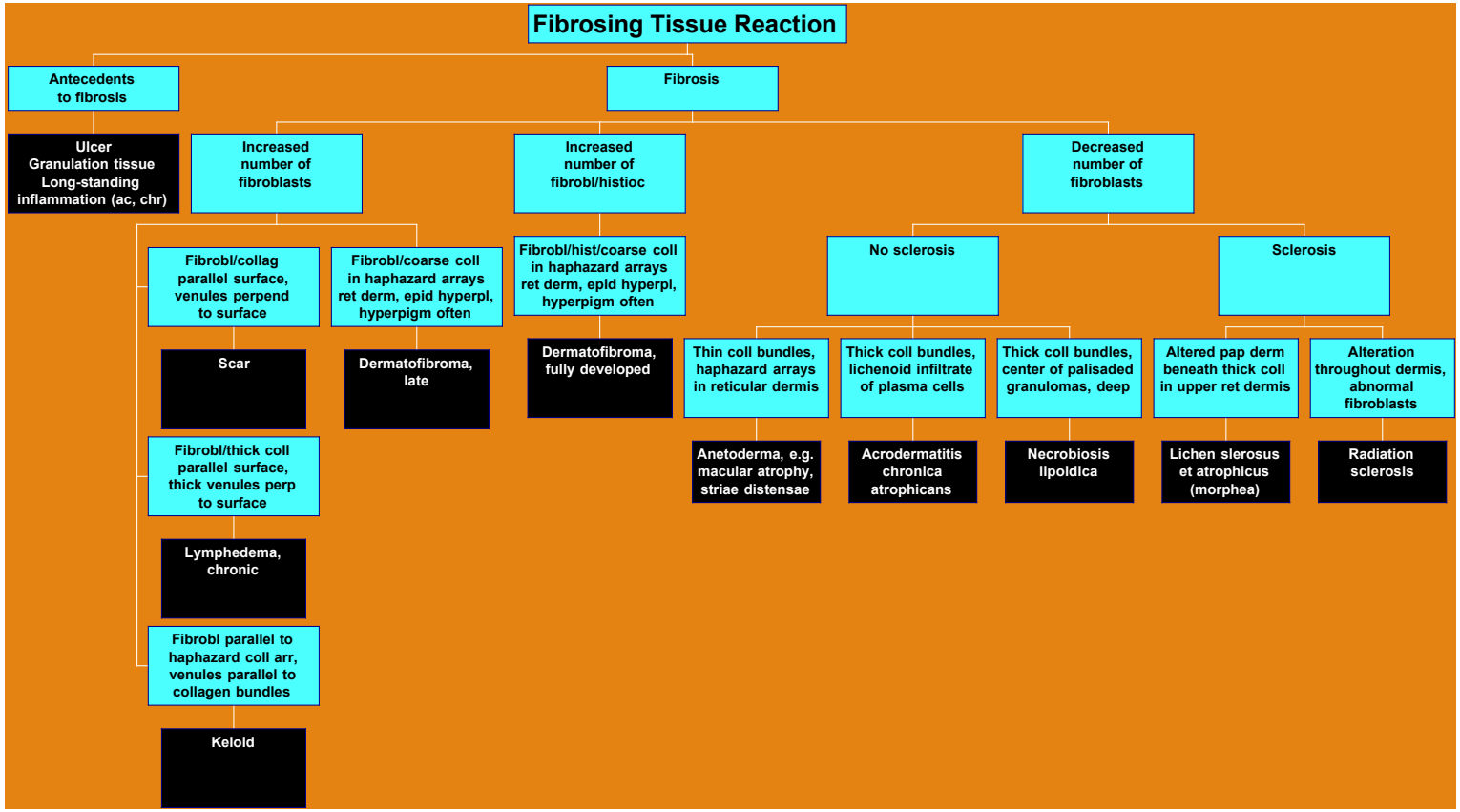
- **Consider possibility of early lichen sclerosus in any interface dermatitis of genital skin**
  - **Inflammatory lesions of LS may mimic MF!**
- **Remember that lichen sclerosus may occur outside the anogenital area**
- **Cases with histologic overlap with morphea: use descriptive diagnosis “fibrosing dermatitis”**

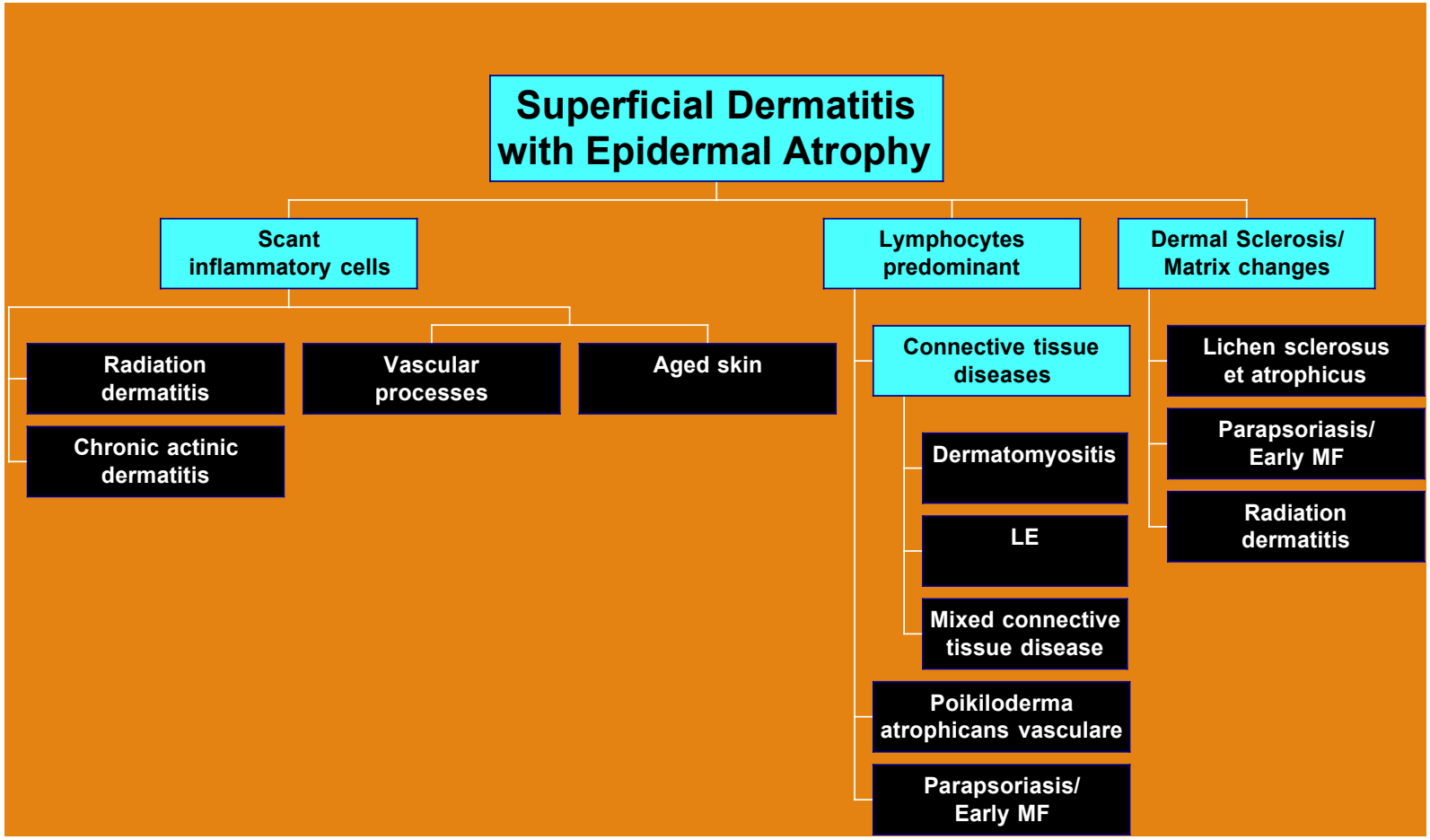
Radiation Dermatitis

- **Acute**
  - **Epidermal necrosis**
  - **Dermal edema and picnotic fibroblasts**
  - **Perivascular inflamation**
  - **Endothelial swelling**
- **Chronic**
  - **Hyper-, parakeratosis, atypia and dyskeratosis**
  - **± ulceration**
  - **Superficial ectatic vessels and melanophages**
  - **Dermal hyalinization with radiation fibroblasts**
  - **No pilosebaceous units, atrophic eccrine glands**



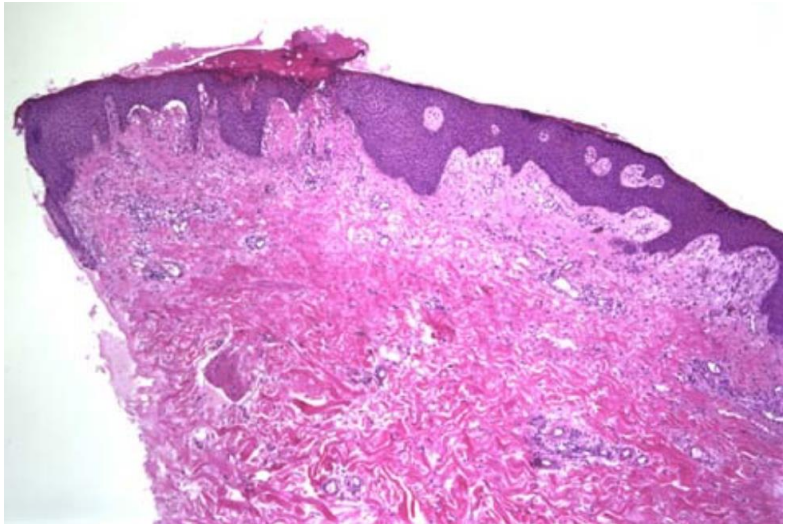
Fibrosing Dermatitis

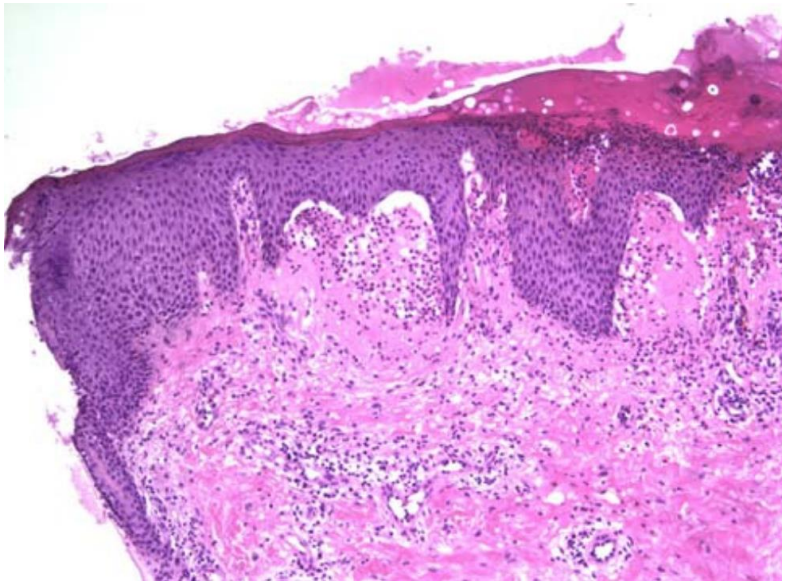


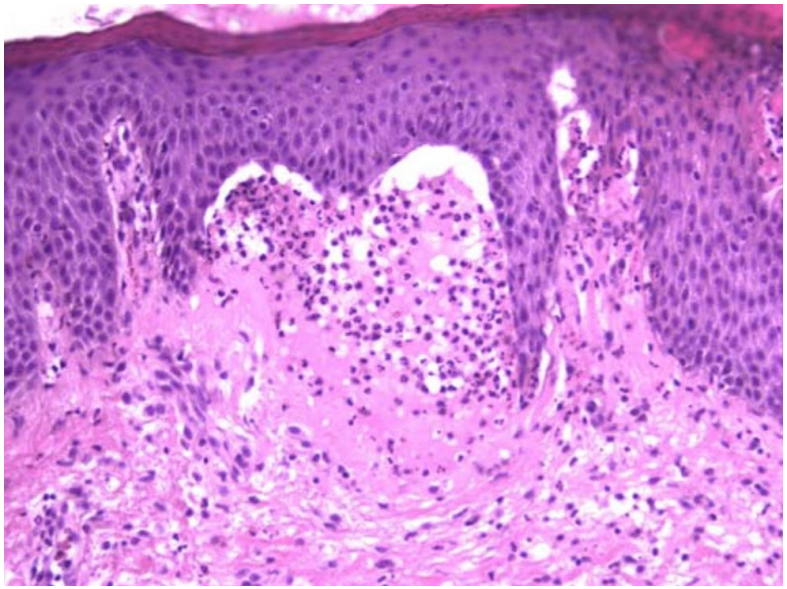

Superficial Dermatitis with Epidermal Atrophy
Scant inflammatory cells
Lymphocytes predominant
Dermal Sclerosis/ Matrix changes
Radiation dermatitis
Chronic actinic dermatitis
Vascular processes
Aged skin
Connective tissue diseases
Dermatomyositis
LE
Mixed connective tissue disease
Poikiloderma atrophicans vasculare
Parapsoriasis/ Early MF
Lichen sclerosus et atrophicus
Parapsoriasis/ Early MF
Radiation dermatitis

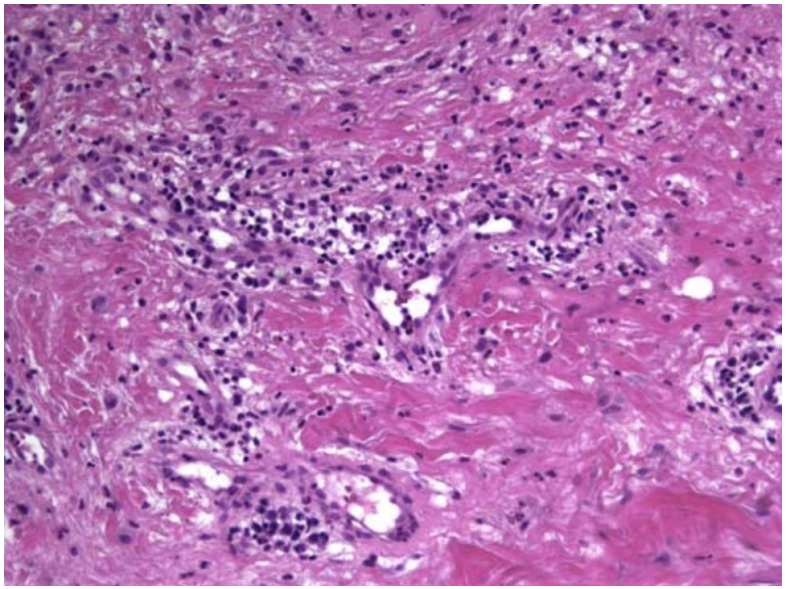
Case 6

35-YEAR OLD FEMALE WITH SYMMETRIC PRURITIC ERYTHEMATOUS PAPULES ON EXTENSOR SURFACE OF ELBOWS

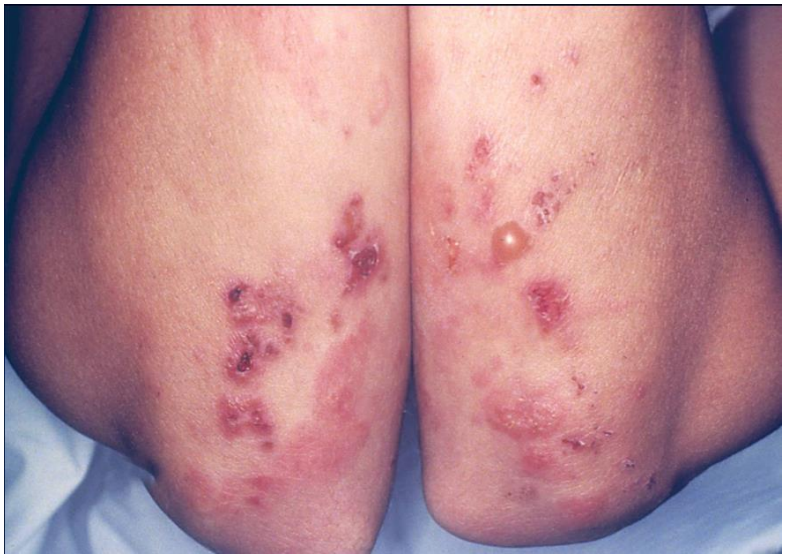






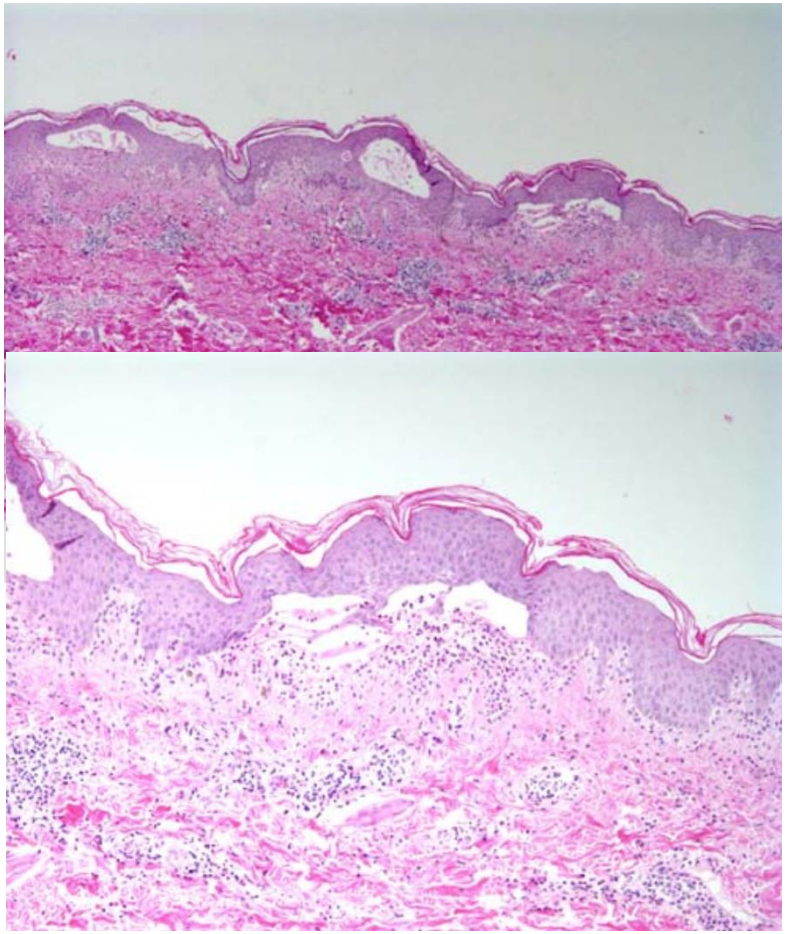


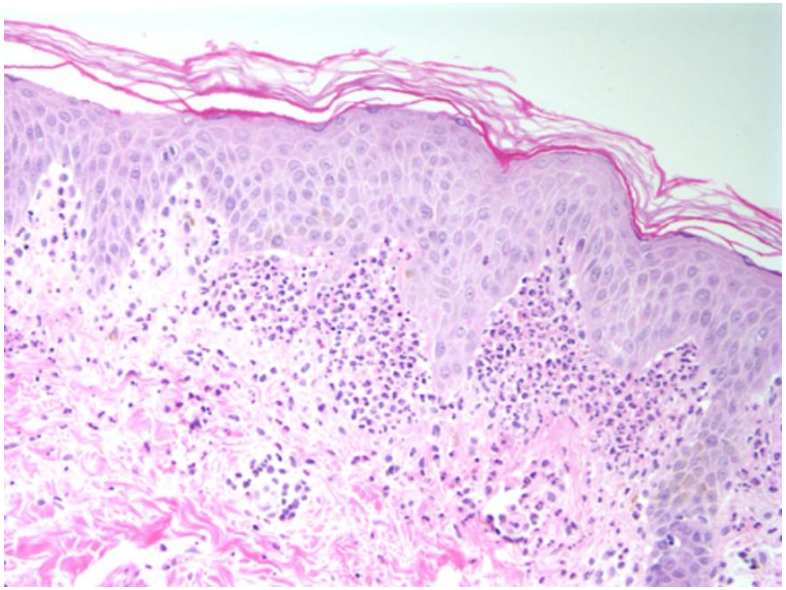
- Rare, chronic subepidermal blistering disorder
- Intensely pruritic papules and vesicles
- Elbows, knees, shoulders
- Associated gluten-sensitive enteropathy (subclinical but demonstrable on bowel biopsy)
- Skin disease improves when patients put on gluten- free diet

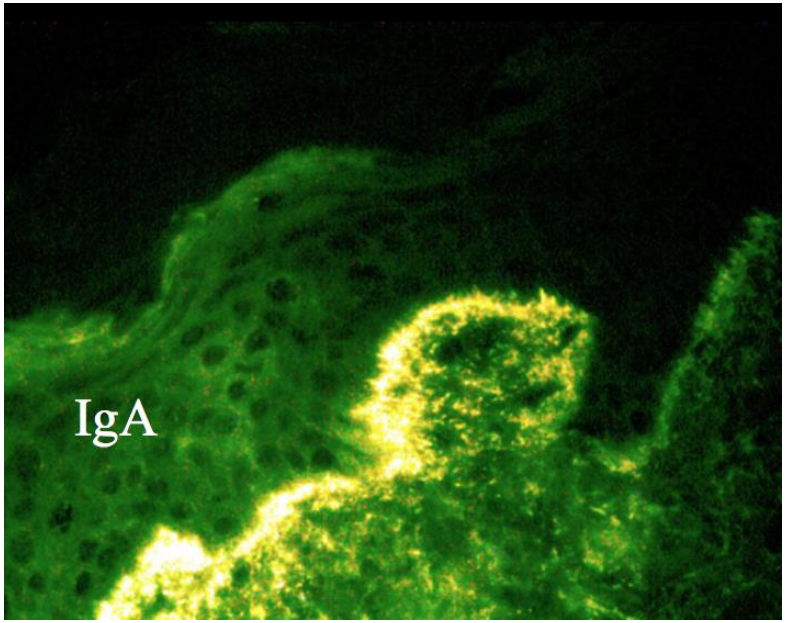


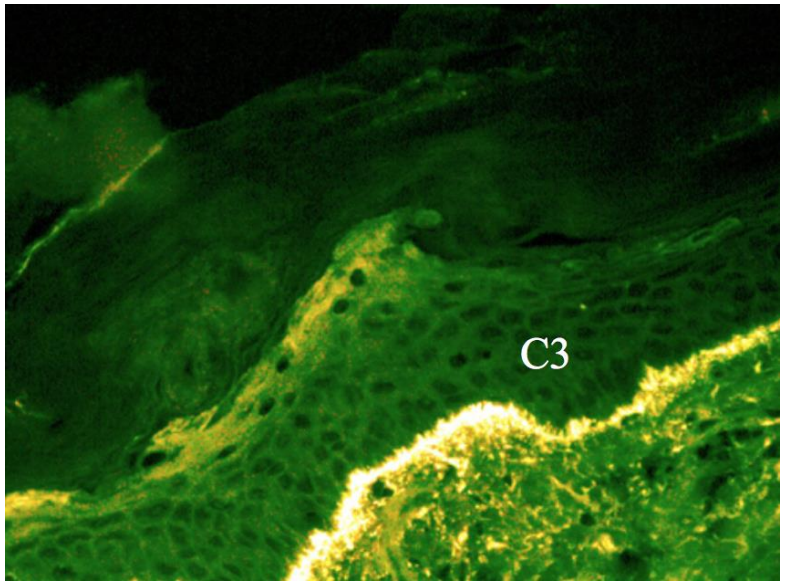
Dermatitis Herpetiformis

- Subepidermal blister
- Predominantly neutrophilic infiltrate
- No epidermal necrosis
- Inflammation largely confined to papillary dermis
- Eosinophils scant



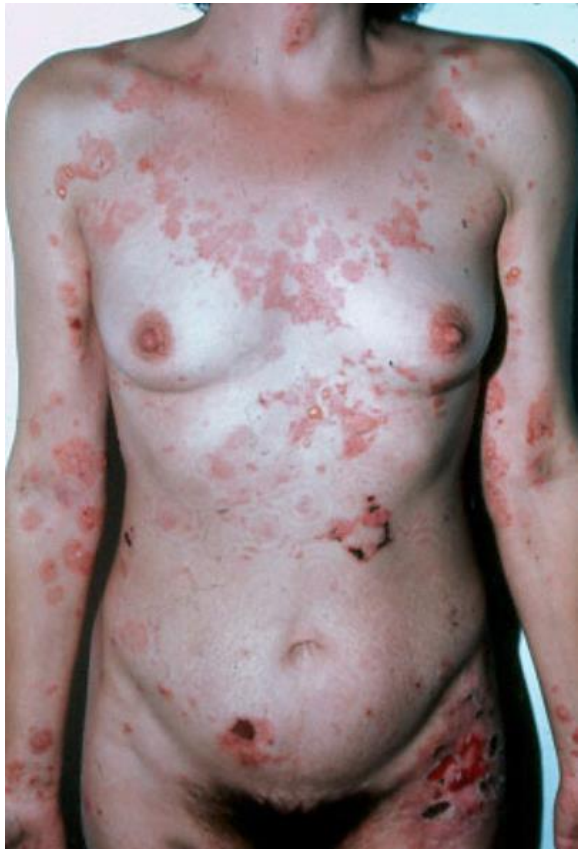


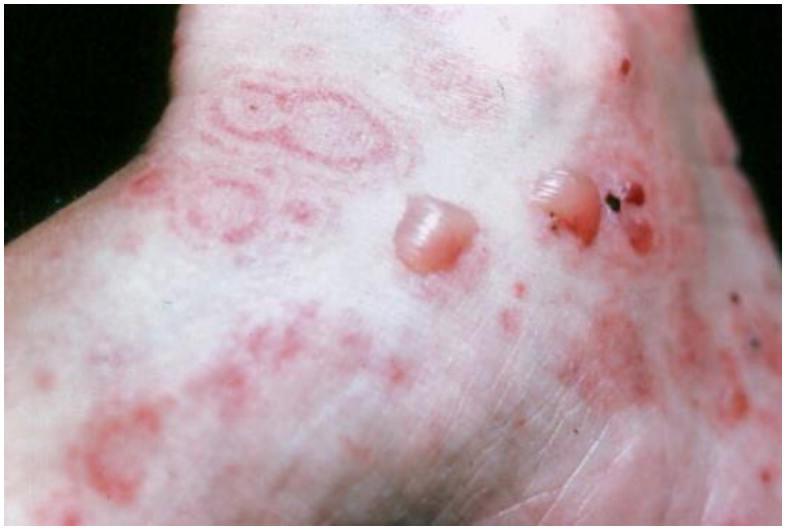

IgA

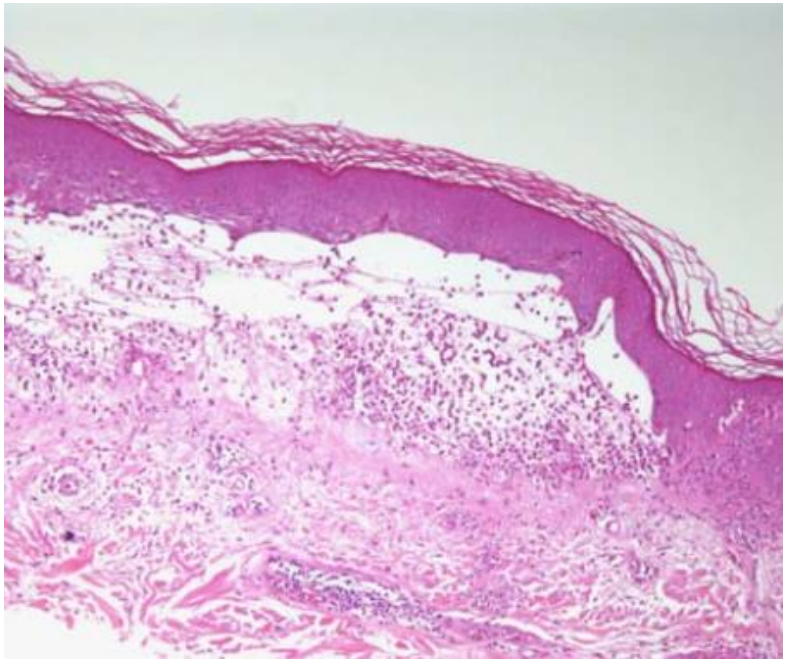

C3

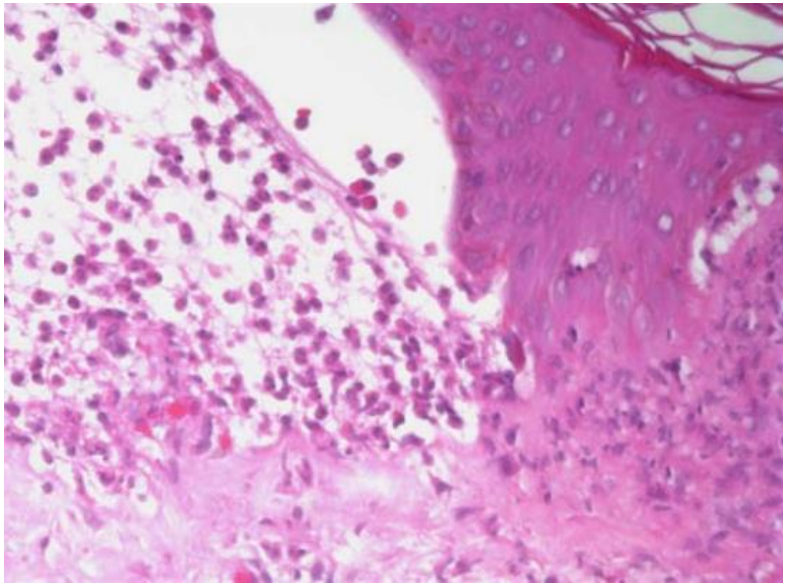
Linear IgA Bullous Dermatitis

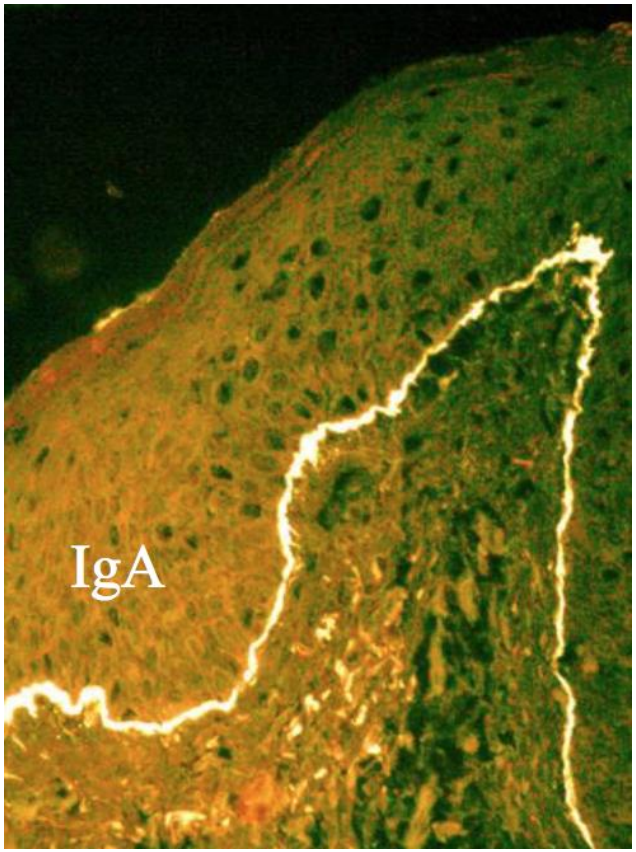
- **Larger blisters, may be intact – often associated with drug ingestion in adults (especially vancomycin)**
- **Larger subepidermal blisters with linear array of neutrophils in papillary dermis**
- **Linear IgA staining along dermal-epidermal junction**







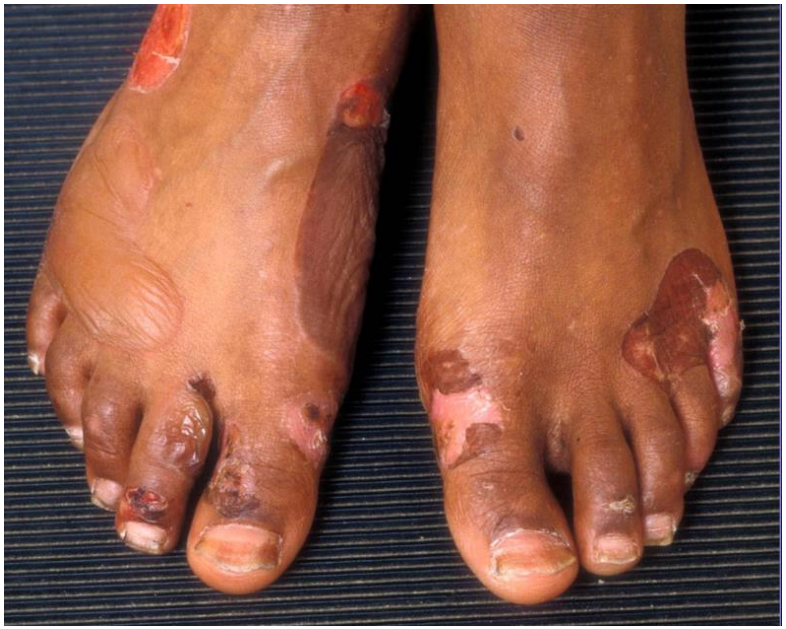



IgA

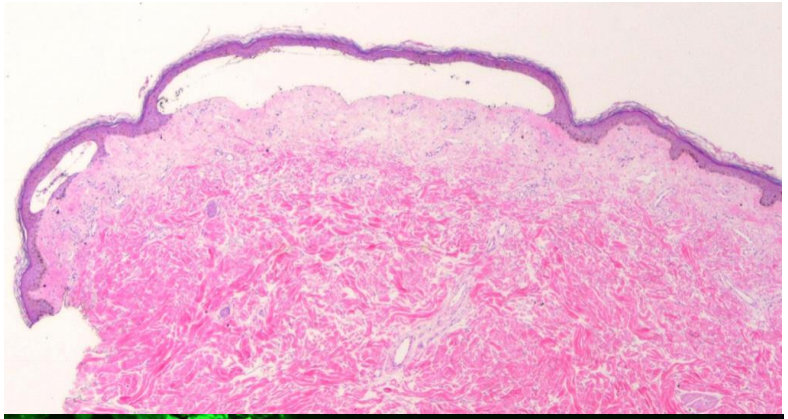
Epidermolysis Bullosa Acquisita

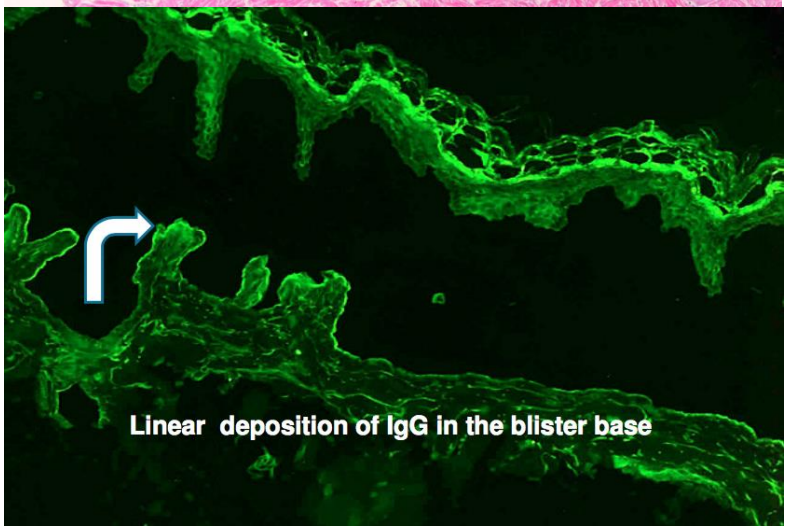
- **Blisters and milia formation often on extremities – at sites of repeated minor trauma**
- **Most cases non-inflammatory, but can be neutrophil-rich**
- **Scarring seen in older lesions**
- **DIF – linear IgG along the floor of the blister (Ab. directed against type VII collagen)**

- Rare, non-hereditary subepidermal bullous disorder
- Acrally distributed blisters that heal with scarring and milia formation (pauci-inflammatory)
- Occasional lesions may be vesiculo-bullous in nature (BP-like)



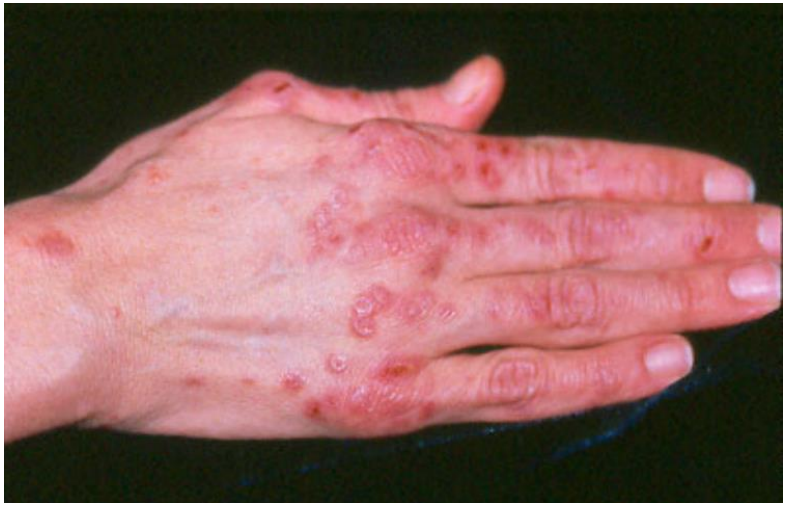
- Pauci-inflammatory subepidermal blister
- In older lesions dermal scarring and milia may be seen
- DIF: Linear IgG and C3 at the DEJ
- DIF on SSS: Antibodies bind to dermal side (vs. epidermal side for BP)

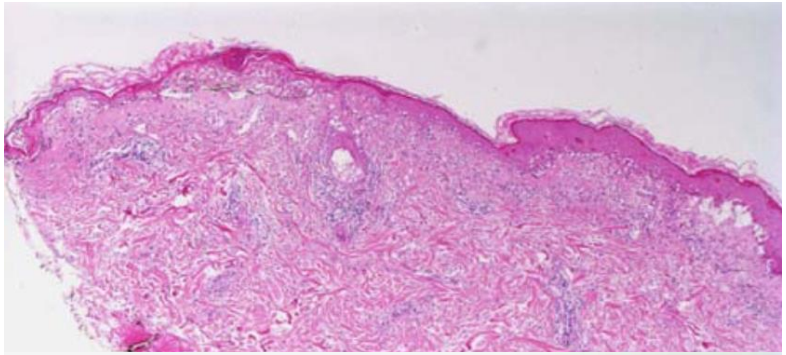


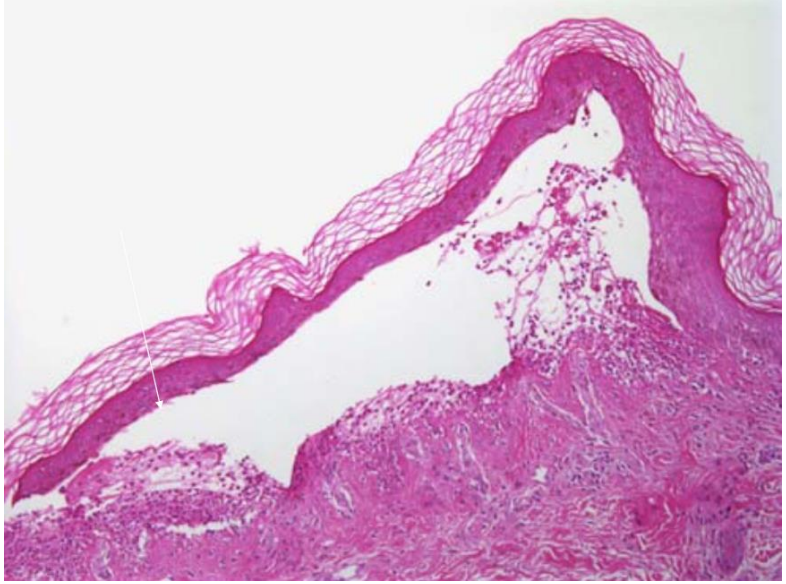


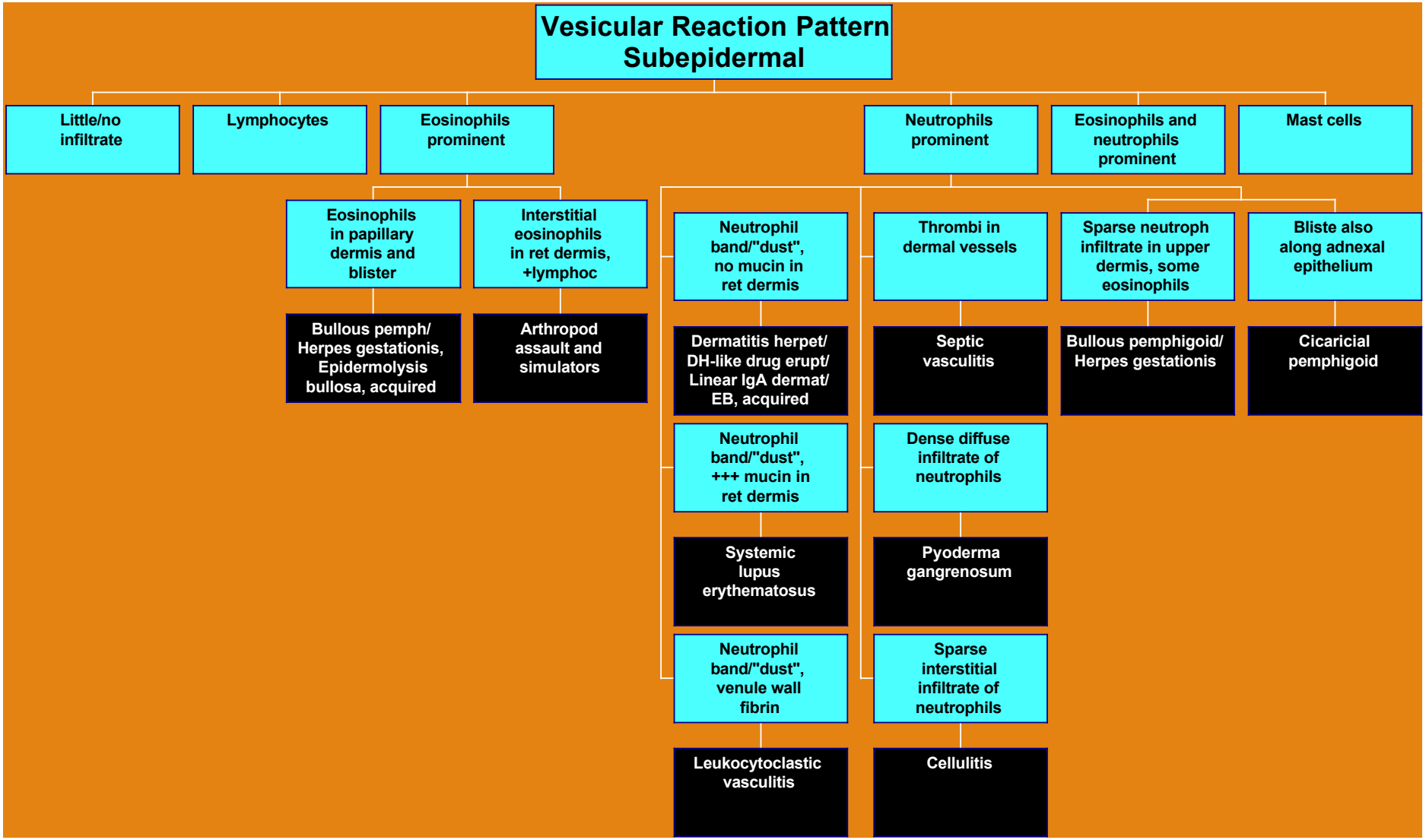
Bullos Lupus Erythematosus

- **Patients usually with other cutaneous manifestations of LE and focal blisters**
- **Often superficial and deep perivascular and peri-appendageal lymphocytic infiltrate along with the subepidermal blister and neutrophils**
- **DIF – granular IgG/IgM/C3 along DEJ (typical of LE)**

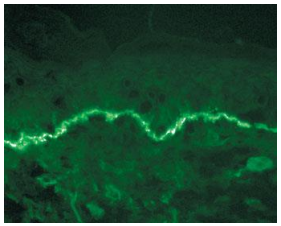







Vesicular Reaction Pattern
Subepidermal
Little/no infiltrate
Lymphocytes
Eosinophils prominent
Neutrophils prominent
Eosinophils and neutrophils prominent
Mast cells
Eosinophils in papillary dermis and blister
Interstitial eosinophils in ret dermis, +lymphoc
Neutrophil band/"dust", no mucin in ret dermis
Thrombi in dermal vessels
Sparse neutroph infiltrate in upper dermis, some eosinophils
Bliste also along adnexal epithelium
Bullous pemph/ Herpes gestationis, Epidermolysis bullosa, acquired
Arthropod assault and simulators
Dermatitis herpet/ DH-like drug erupt/ Linear IgA dermat/ EB, acquired
Septic vasculitis
Bullous pemphigoid/ Herpes gestationis
Cicaricial pemphigoid
Neutrophil band/"dust", +++ mucin in ret dermis
Dense diffuse infiltrate of neutrophils
Systemic lupus erythematosus
Pyoderma gangrenosum
Neutrophil band/"dust", venule wall fibrin
Sparse interstitial infiltrate of neutrophils
Leukocytoclastic vasculitis
Cellulitis

IMF in Subepidermal Bullous Conditions



Predominantly BMZ

Finely linear

Thick, glassy linear (IgG, often IgA)

Granular

C3 only

IgG (± C3)

IgA

Porphyria cutanea tarda / pseudoporphyria

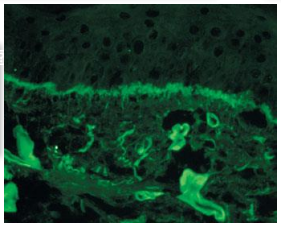
IgA

≥2 IgG (lupus band)

Pemphigoid (all forms), EHG

Salt split

Linear IgA dermatosis (including chronic bullous disease of childhood)

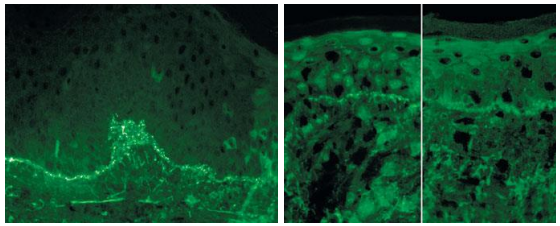


Dermatitis herpetiformis

?Lupus erythematosus

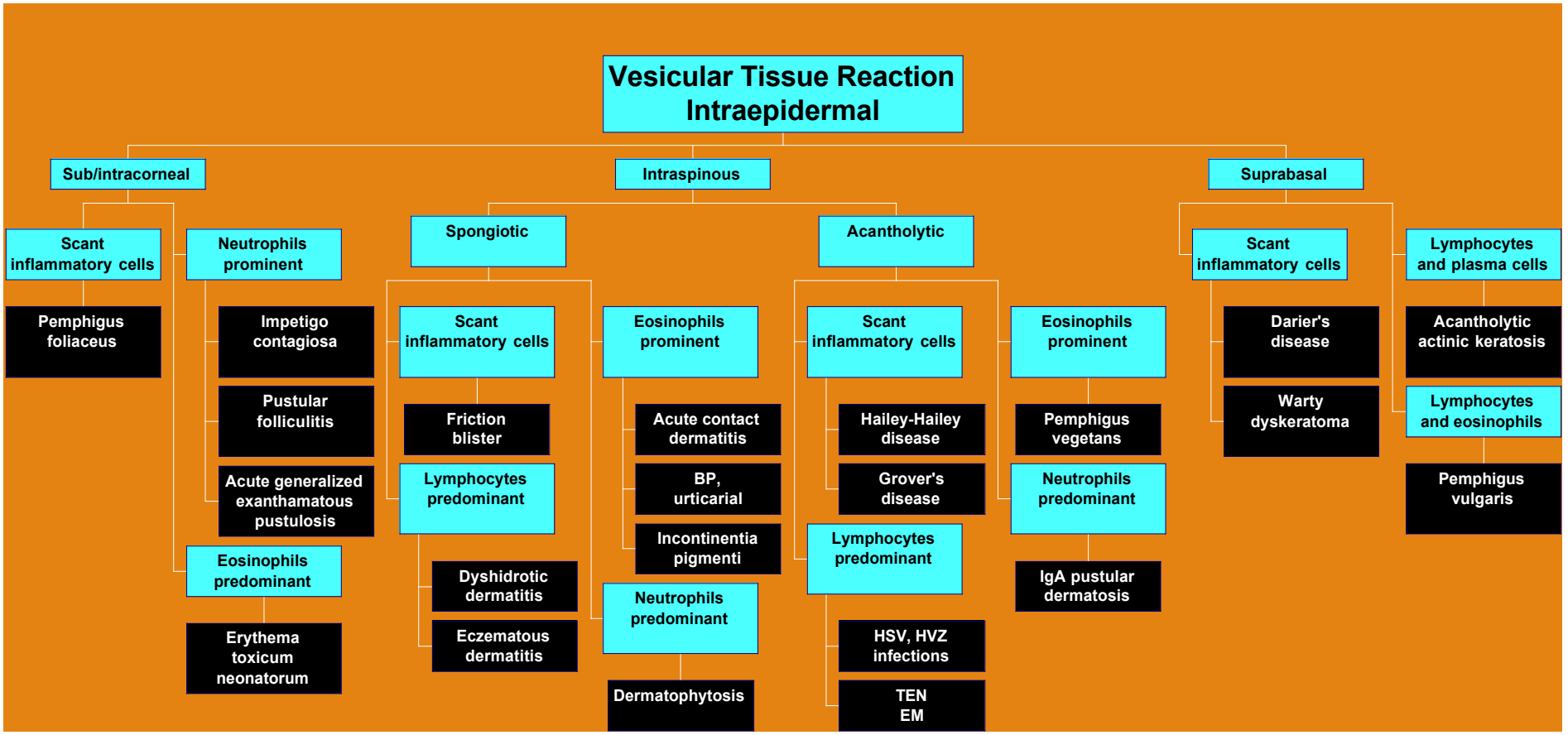
IgG on "roof"

IgG on "floor"

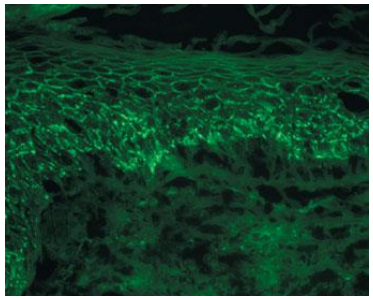


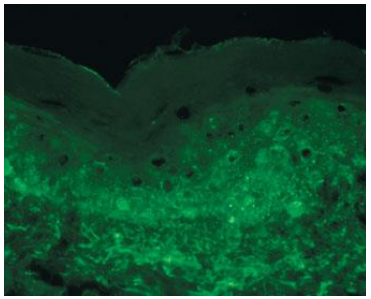
Pemphigoid (all forms), EHG

EBA, bullous LE, rare pemphigoid


Vesicular Tissue Reaction
Intraepidermal
Sub/intracorneal
Intraspinous
Suprabasal
Scant inflammatory cells
Neutrophils prominent
Spongiotic
Acantholytic
Scant inflammatory cells
Lymphocytes and plasma cells
Pemphigus foliaceus
Impetigo contagiosa
Pustular folliculitis
Acute generalized exanthamatous pustulosis
Eosinophils predominant
Erythema toxicum neonatorum
Scant inflammatory cells
Eosinophils prominent
Friction blister
Lymphocytes predominant
Dyshidrotic dermatitis
Eczematous dermatitis
Acute contact dermatitis
BP, urticarial
Incontinentia pigmenti
Neutrophils predominant
Dermatophytosis
Scant inflammatory cells
Eosinophils prominent
Hailey-Hailey disease
Grover's disease
Lymphocytes predominant
HSV, HVZ infections
TEN
EM
Pemphigus vegetans
Neutrophils predominant
IgA pustular dermatosis
Darier's disease
Warty dyskeratoma
Acantholytic actinic keratosis
Lymphocytes and eosinophils
Pemphigus vulgaris

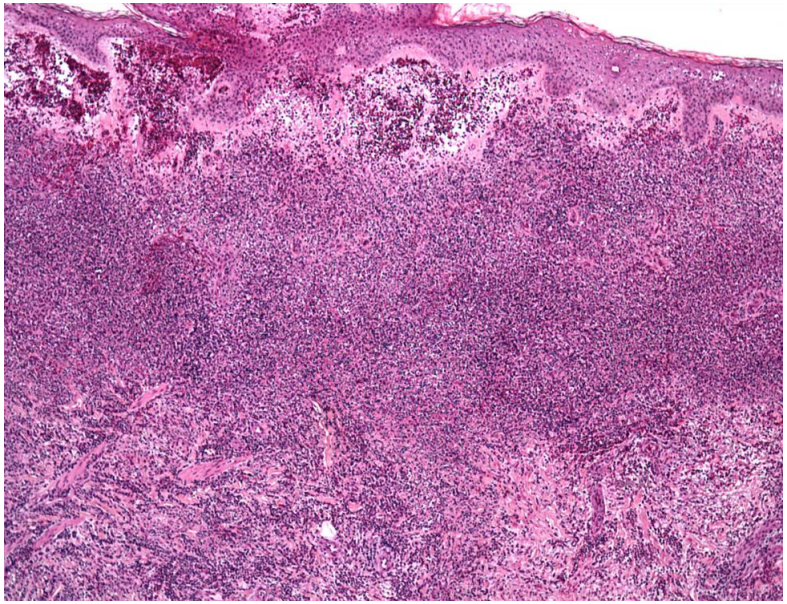
IMF in Intraepidermal Bullous Conditions

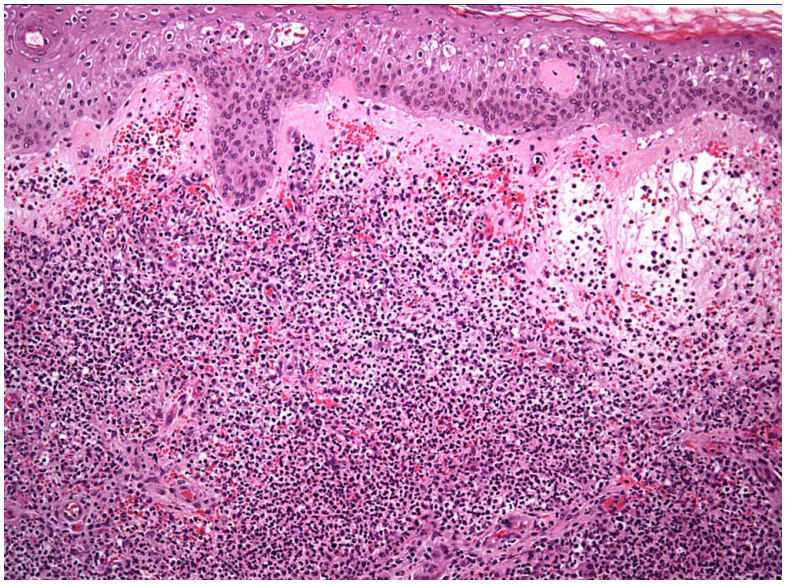


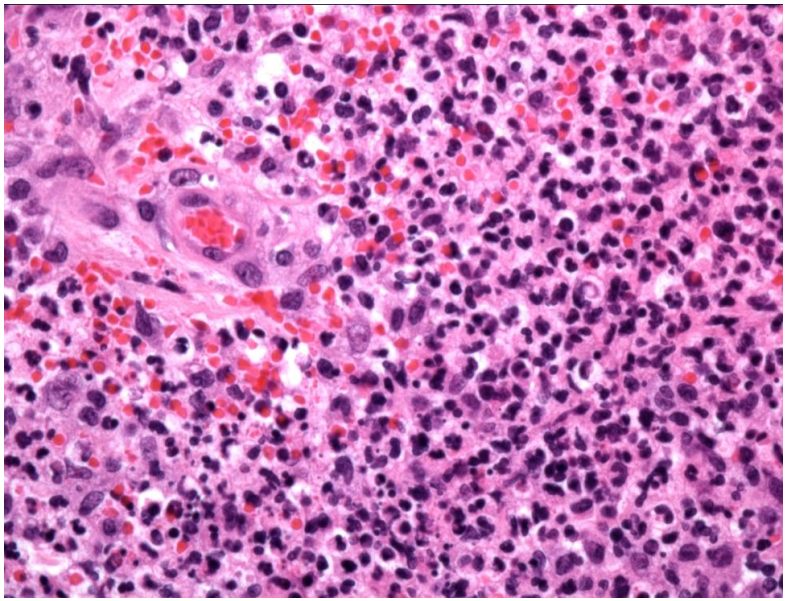


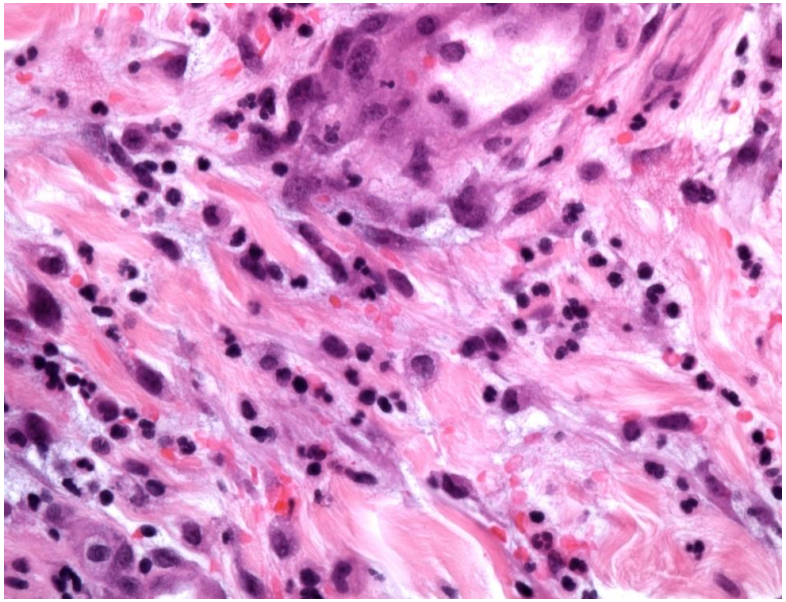
Case 7

A 32-YEAR-OLD MAN PRESENTED WITH TENDER ERYTHEMATOUS NODULES AND PLAQUES ON THE FACE









Neutrophilic Vascular Dermatitis

- **Neutrophilic infiltrate**
- **Lack of micro-organisms**
- **Clinical improvement on systemic steroid treatment**

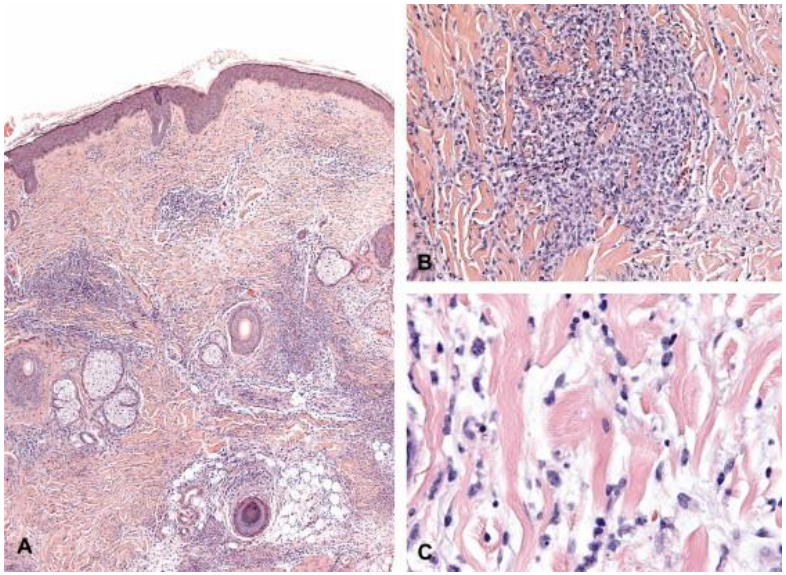
- **Granuloma faciale / EED**
- **Sweet syndrome**
- **Bowel-associated neutrophilic dermatitis**
- **Pyoderma gangrenosum**
- **Palisaded neutrophilic and granulomatous dermatitis**

Acute Febrile Neutrophilic Dermatitis

- **Fever, leukocytosis, arthralgias, violaceous tender nodules or plaques**
- **May be associated with underlying leukemia, systemic diseases, infection**
- **No or minimal epidermal change**
- **Dense infiltrate of neutrophils in superficial dermis**
- **Leukocytoclasis but no true vasculitis**

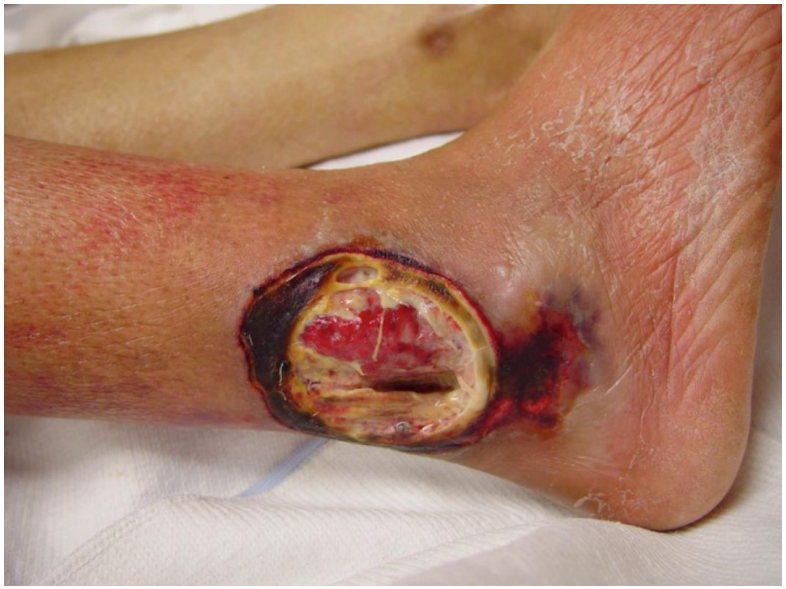
Palisaded Neutrophilic Granulomatous Dermatitis

- **Palisading and/or diffuse interstitial granulomatous inflammation**
- **Variable collagen necrobiosis**
- **Interstitial neutrophilia**
- **Vasculitis**



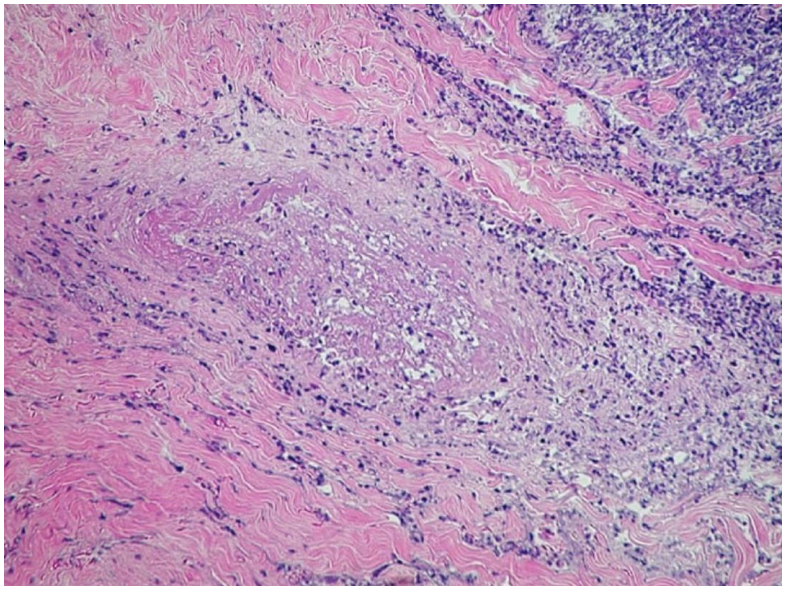
Pyoderma Gangrenosum

- Erythematous pustule or nodule which progresses to become a necrotic ulcer with an undermined and violaceous edge
- Variable size as (~20 cm)
- Satellite lesions
- Lower extremities, trunk, and occasionally head and neck
- Pathergy



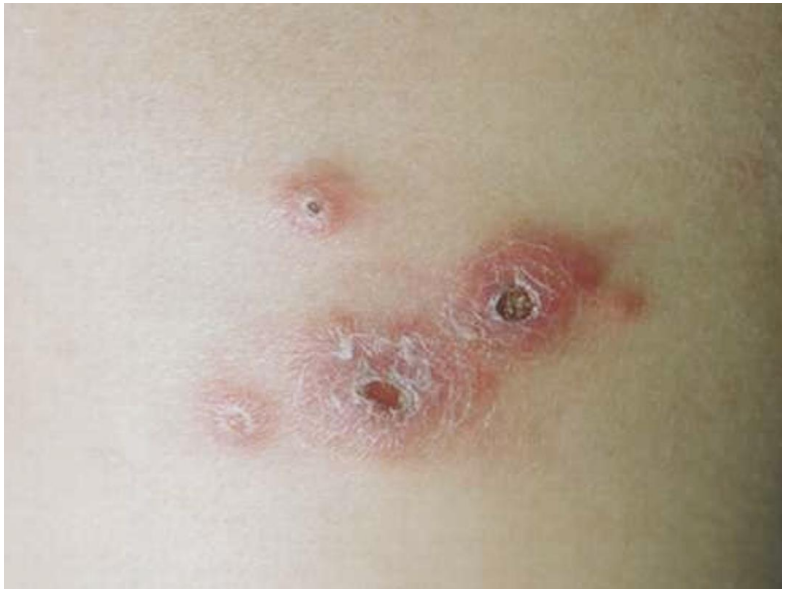
Pyoderma Gangrenosum

- **Variable changes depending upon site of biopsy and age of lesion**
- **Early lesions may show neutrophilic dermatosis**
- **Possible role of folliculitis**
- **Dx of exclusion: Rule out infection**



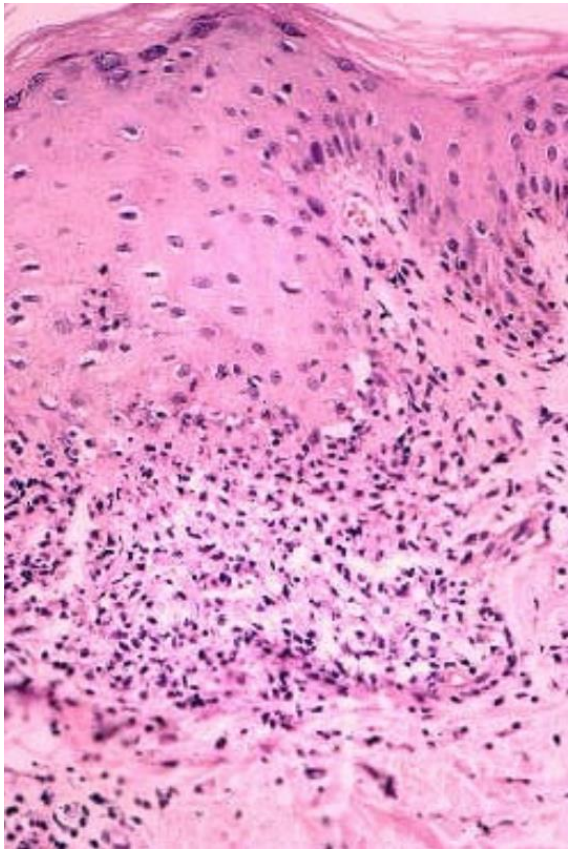
Behçet Syndrome

- Mucocutaneous lesions (oral ulcers-recurrent, at least three times per year)
- Patients must also meet two of the following four criteria:
  - Recurrent genital ulcerations
  - Eye lesions (uveitis or retinal vasculitis)
  - Positive pathergy test (trauma induced lesions)
  - Skin lesions as diagnostic of Behcet's disease

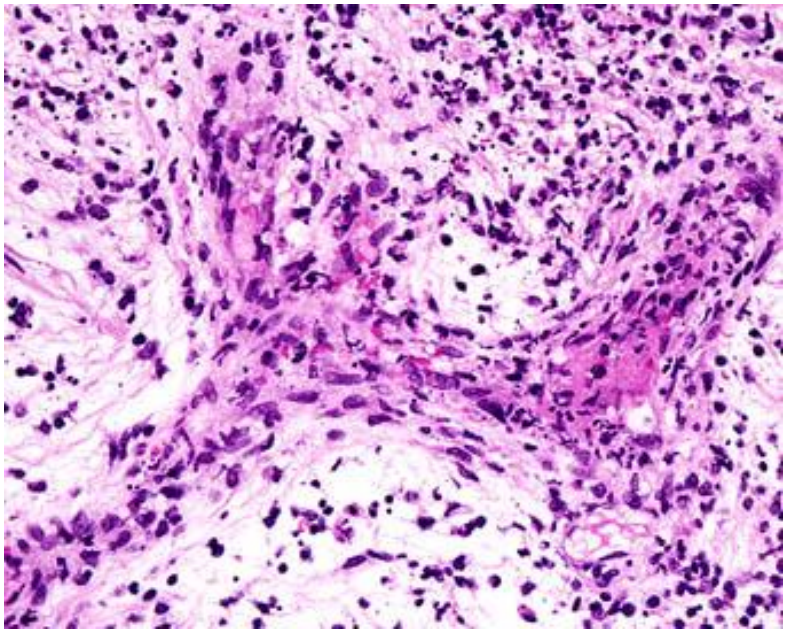


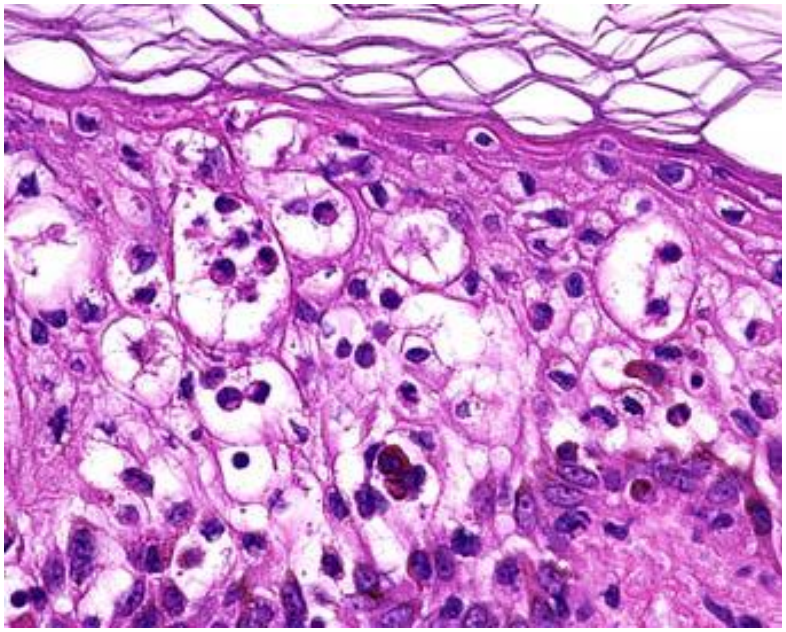
Behçet Syndrome

- **Neutrophilic dermatosis**
- **May have leukocytoclastic vasculitis**
- **Panniculitis change mimics erythema nodosum or erythema induratum**



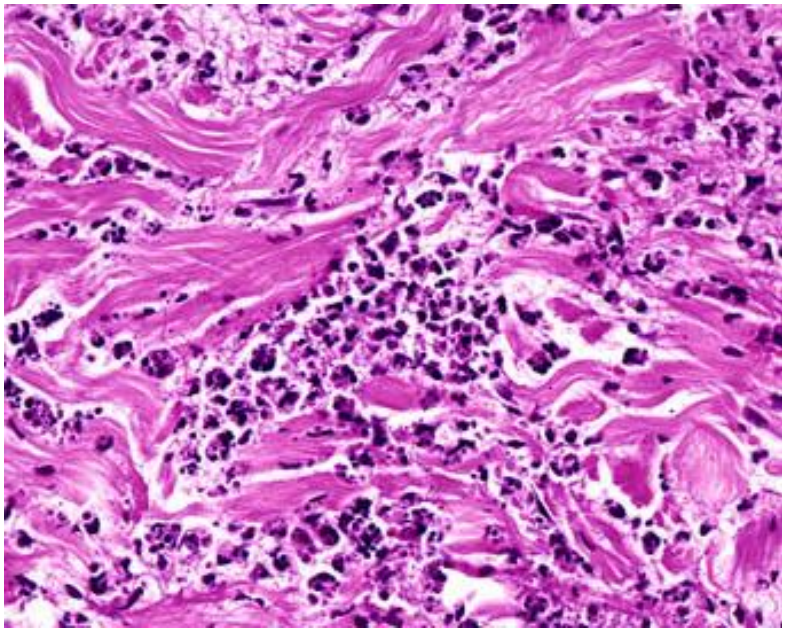
Behçet Syndrome





Behçet Syndrome

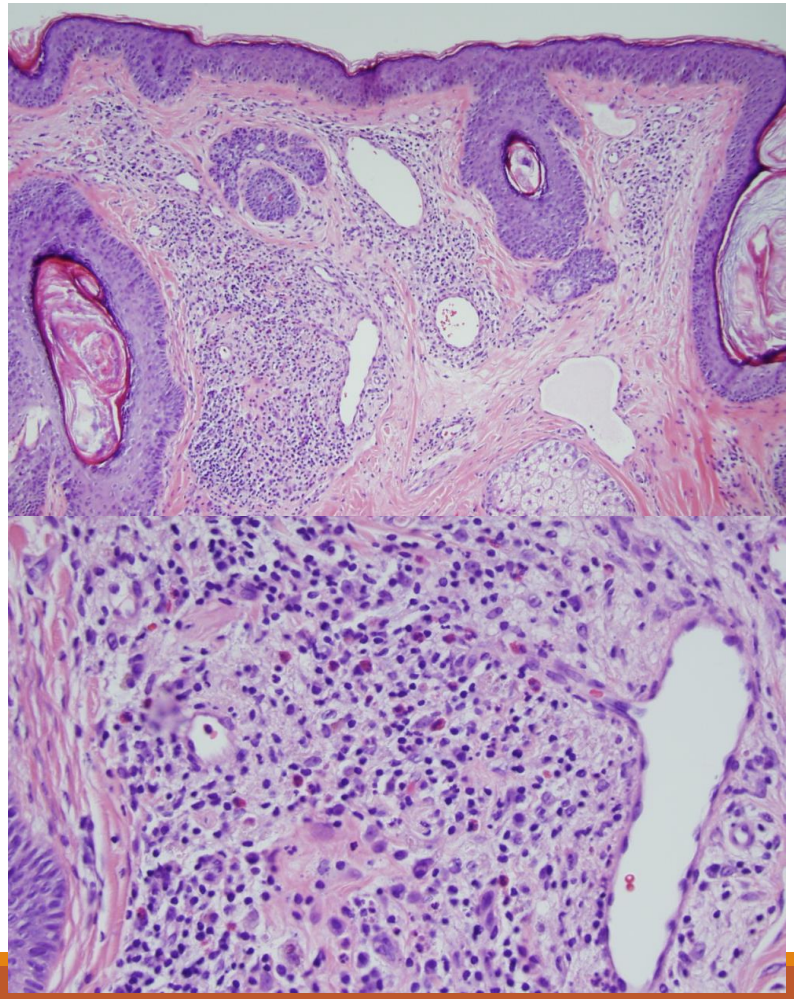
- **Early**
  - **Neutrophilic necrotizing vasculitis or**
  - **Pustular vasculitis**
- **Late**
  - **Lymphocytic and granulomatous vascular reactions**



Granuloma Faciale / EED

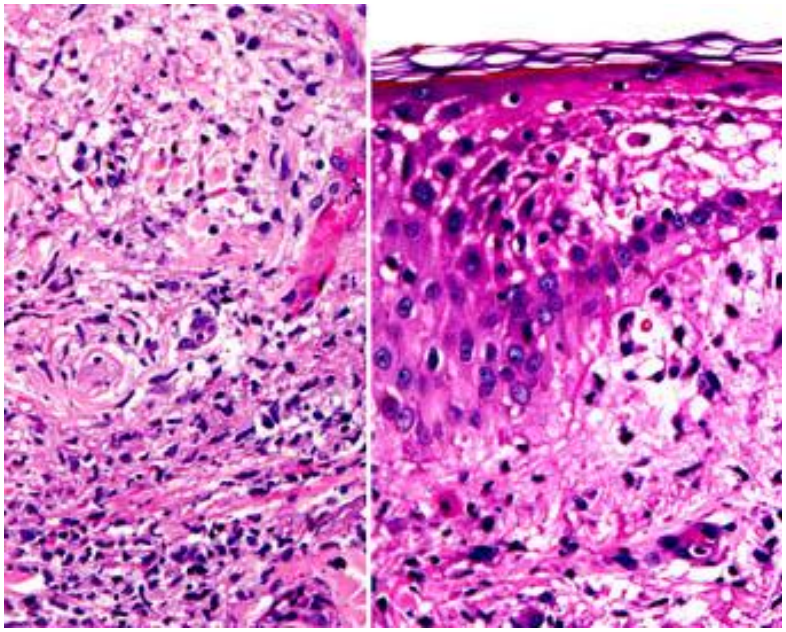
- Grenz zone
- Nodular/diffuse mixed infiltrate with eosinophils and PMN
- ± leukocytoclastic vasculitis

Lack of Grenz zone and predominance of neutrophils separate EED from granuloma faciale

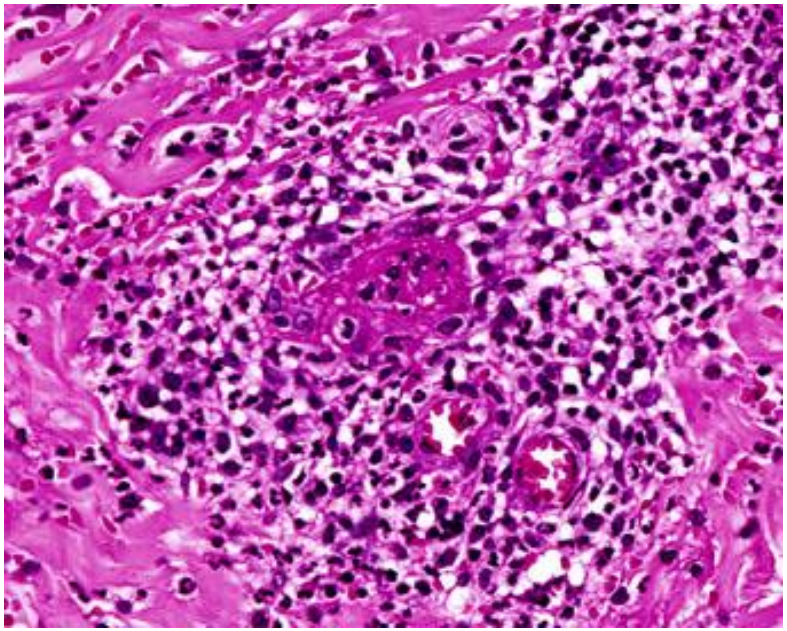


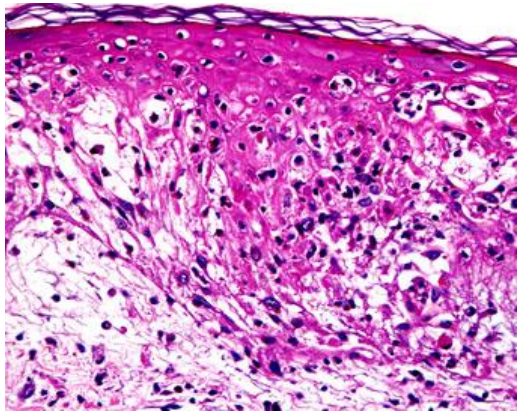
Septic Vasculitis

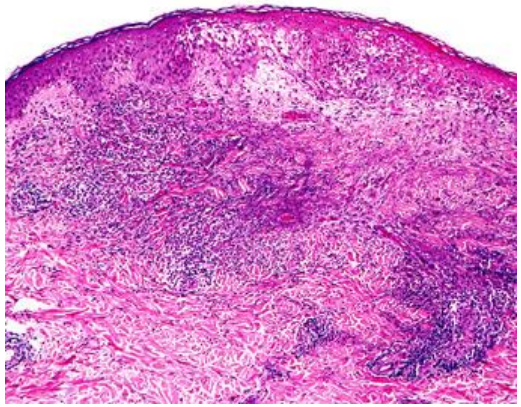
- **Neutrophilic pustules = pustular vasculitis**
- **Dense dermal neutrophilic infiltrate**
- **Intravascular fibrin thrombi ± micro-organisms**



Septic Vasculitis

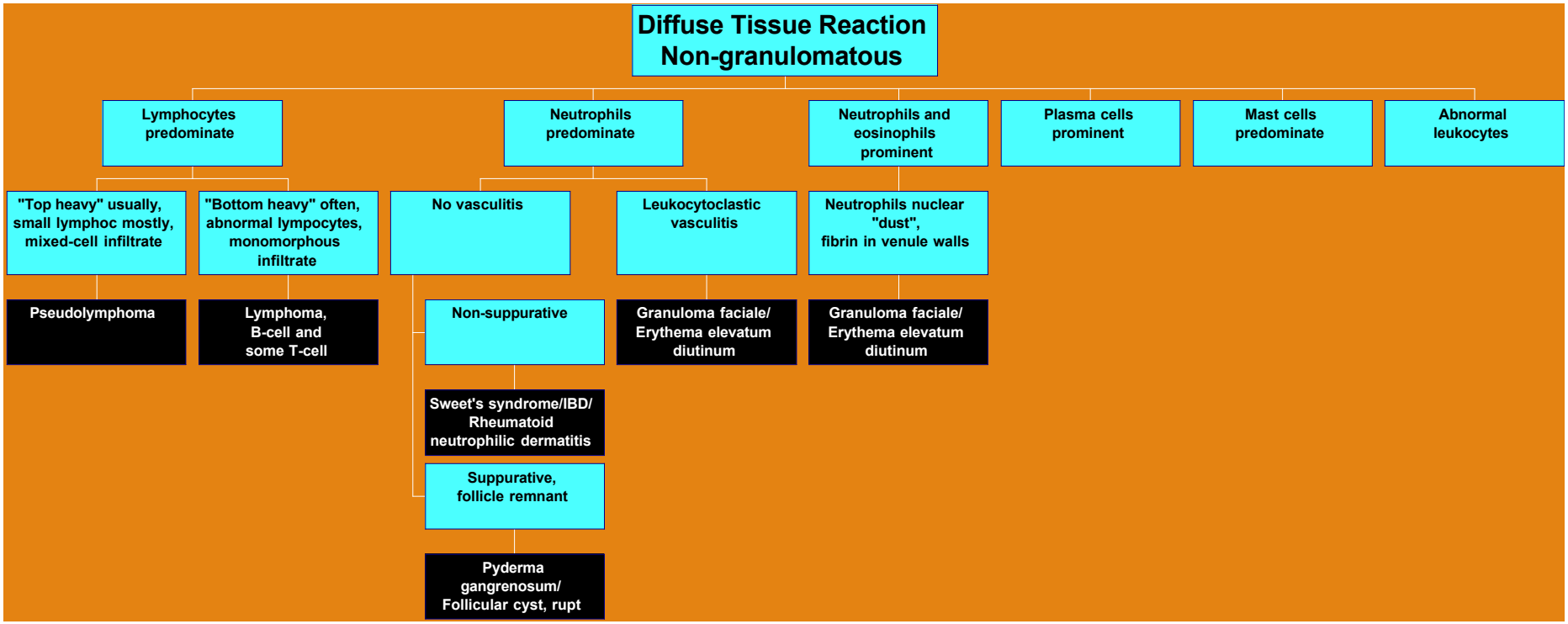






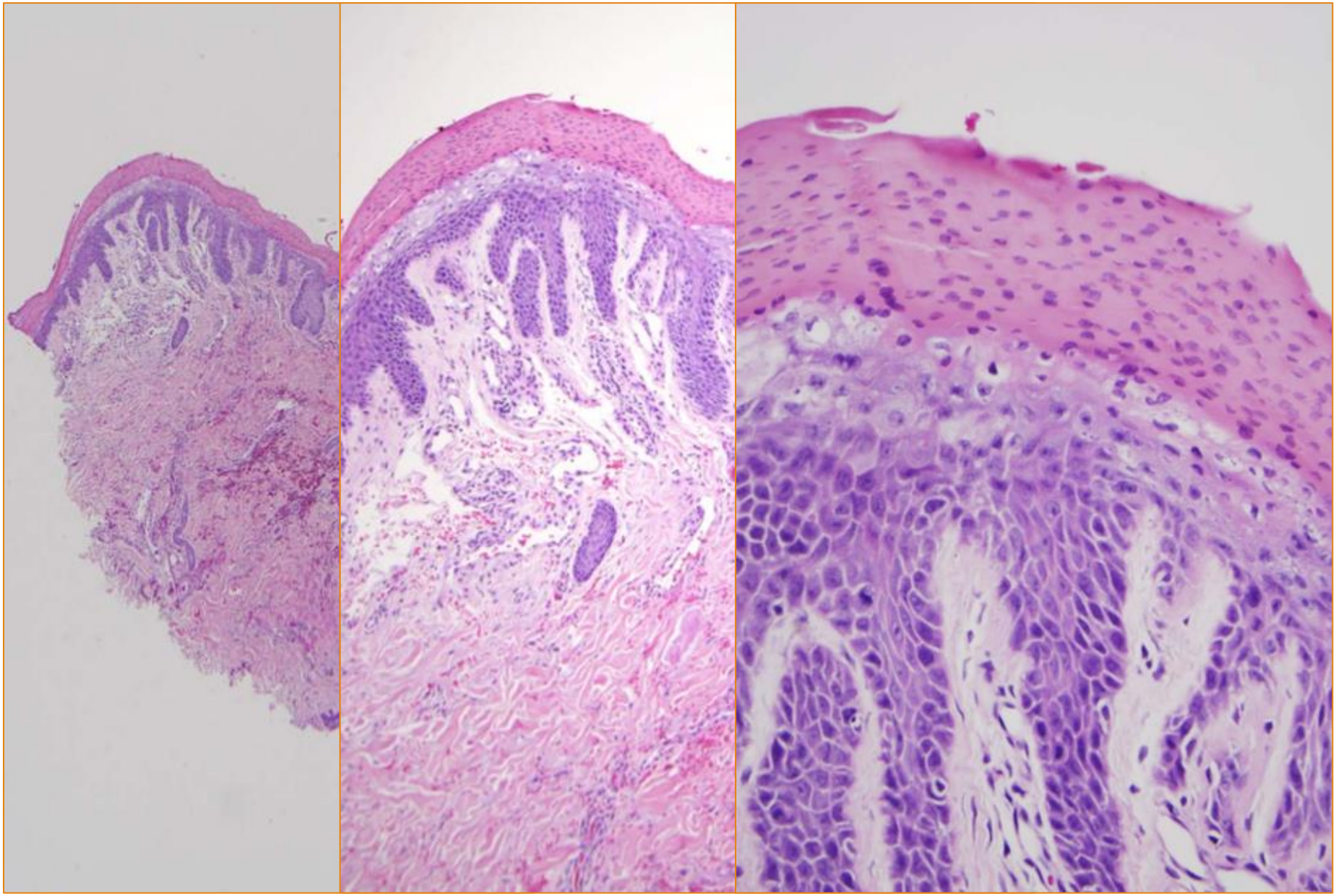
Blood infections by:

- Neisseria
- Staphylococcus


Diffuse Tissue Reaction
Non-granulomatous
Lymphocytes predominate
Neutrophils predominate
Neutrophils and eosinophils prominent
Plasma cells prominent
Mast cells predominate
Abnormal leukocytes
"Top heavy" usually, small lymphoc mostly, mixed-cell infiltrate
"Bottom heavy" often, abnormal lympocytes, monomorphous infiltrate
No vasculitis
Leukocytoclastic vasculitis
Neutrophils nuclear "dust", fibrin in venule walls
Pseudolymphoma
Lymphoma, B-cell and some T-cell
Non-suppurative
Granuloma faciale/ Erythema elevatum diutinum
Granuloma faciale/ Erythema elevatum diutinum
Sweet's syndrome/IBD/ Rheumatoid neutrophilic dermatitis
Suppurative, follicle remnant
Pyderma gangrenosum/ Follicular cyst, rupt

Case 8

A 52-YEAR OLD MAN WITH WEIGHT LOSS, CHRONIC DIARRHEA AND AN ERYTHEMATOUS RASH WITH BULLAE AND EROSIONS ON EXTREMITIES



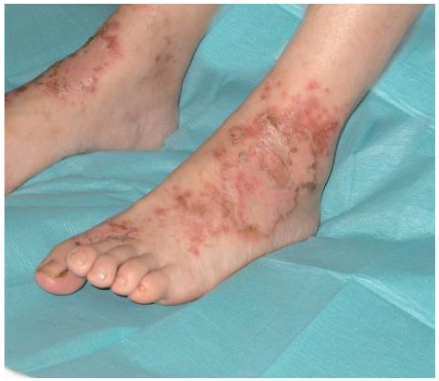
Glucagonoma

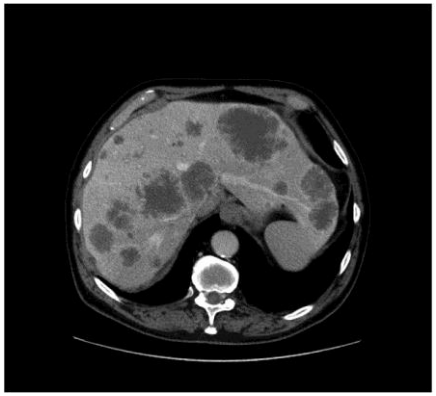
Crops of peripherally expanding annular erythematous patches with surmounted scale and bullae involving the trunk and proximal extremities

Associated with glucagon secreting pancreatic islet cell tumor (malignant 70% of cases)

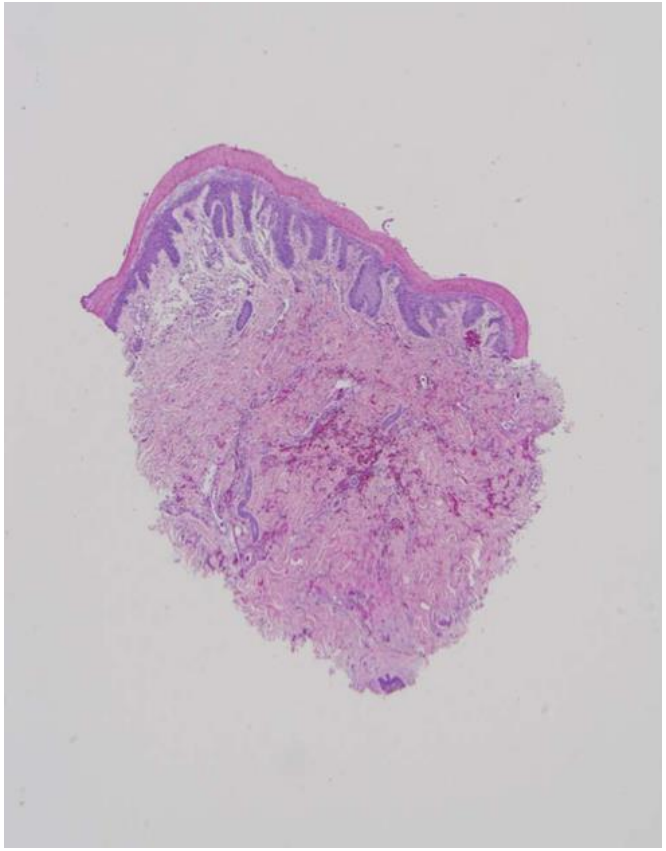
Other clinical manifestations include glossitis, stomatitis, weight loss and venous thrombosis

Laboratory findings include hyperglycemia, normochromic, normocytic anemia and decreased serum amino acids associated with spectacular elevations in the serum glucagon level





- Slightly thickened epidermis with normal dermis
- Broadly pale epithelium with confluent parakeratosis
- Abrupt transition to parakeratotic zone without an interposed granular layer
  - Pallor follows cytoplasmic vacuolar change with ballooning necrosis and intercellular cleft formation



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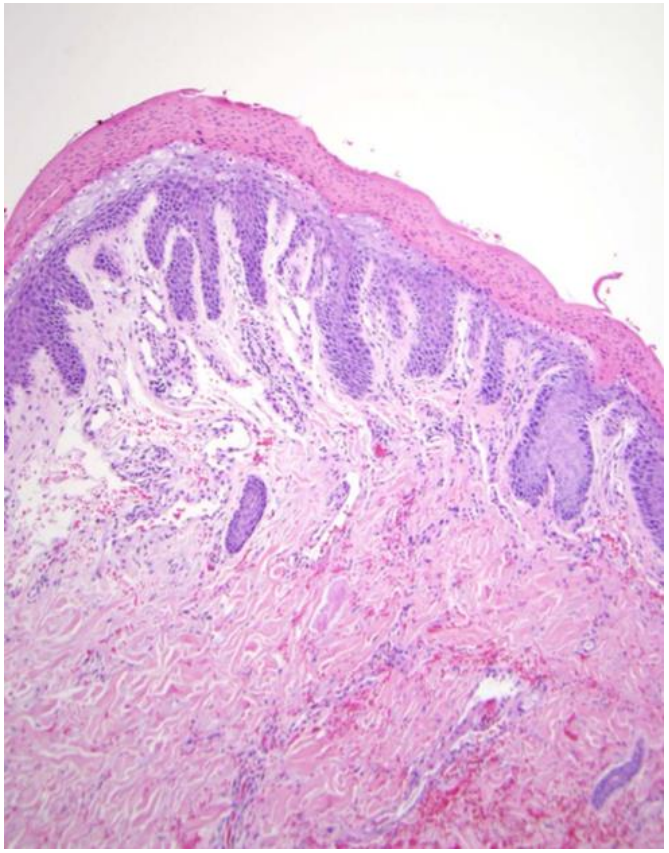

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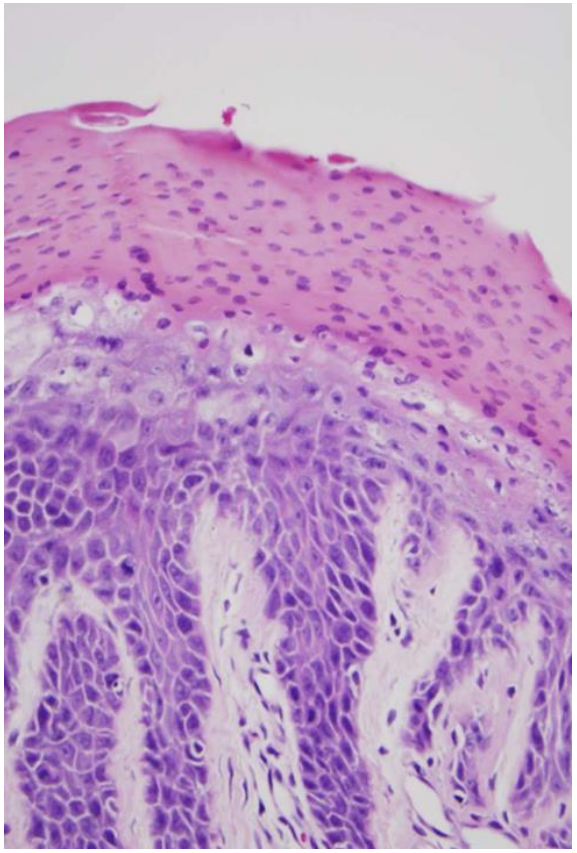
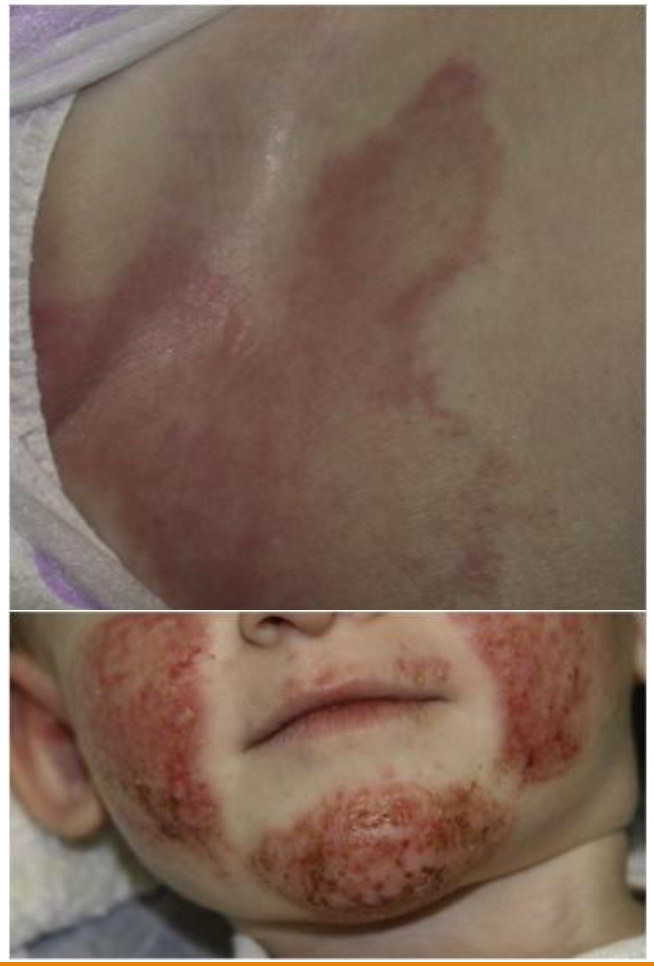


Acrodermatitis Enteropathica

- Autosomal recessive disorder of zinc metabolism
  - Triad of alopecia, diarrhea, scaly periorificial and acral rash seen in infants/children following weaning
  - Other features include photophobia, naildystrophy, short stature, and stomatitis
- Zinc deficiency also seen in adults with Crohn's disease, patients receiving total parenteral nutrition, following intestinal bypass surgery, AIDS, cystic fibrosis, and anorexia nervosa
- Pathogenesis thought to involve qualitative defect in zinc transporter or zinc deficiency

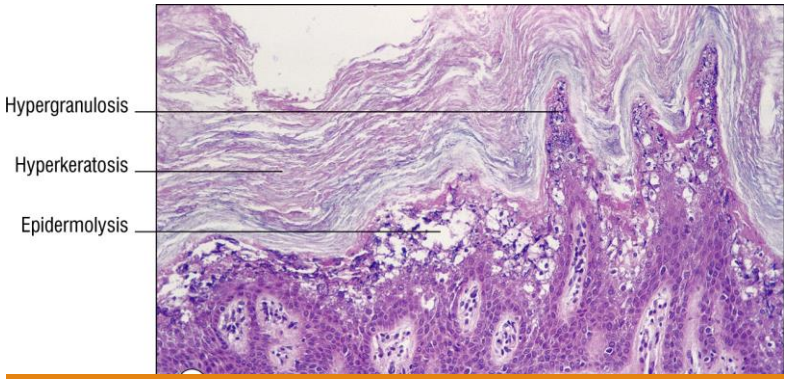


Pellagra/Hartnup Disease

- **Niacin deficiency with classic triad of dermatitis, diarrhea and dementia**
  - **Dermatitis involves a scaly annular hyperpigmented rash of the sun-exposed V-of-neck area, face and upper extremities**
  - **Hartnup disease is a rare autosomal recessive disorder of intestinal tryptophan absorption in gut and renal tubules**
  - **Also niacin deficiency with malabsorption syndromes, medications that interfere with tryptophan metabolism such as isoniazid, 5- fluorouracil and chloramphenicol, and carcinoid syndrome**

Epidermolytic Hyperkeratosis

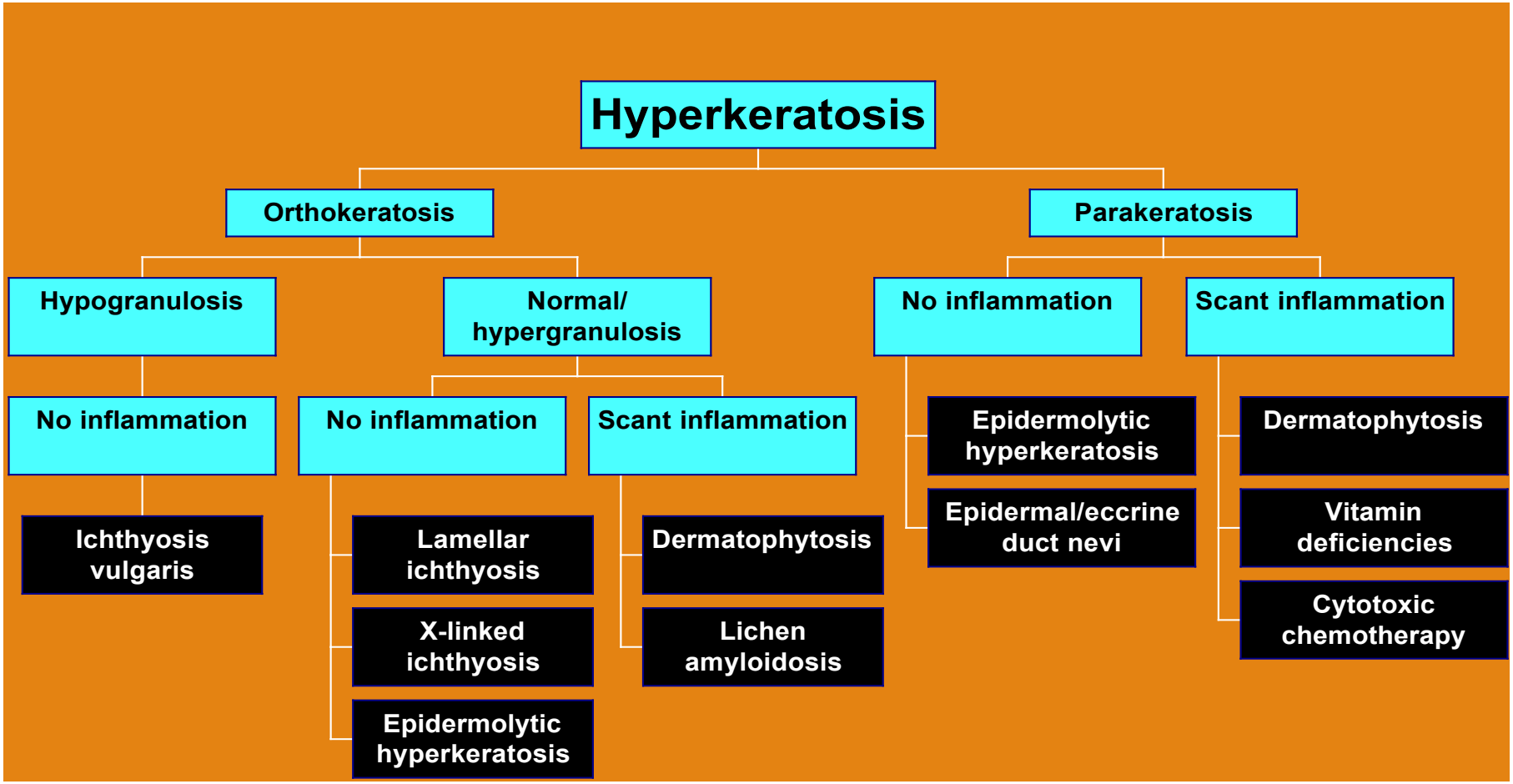
- **Compact hyperkeratosis**
- **Hypergranulosis with reticular degeneration with abnormal granules**
  - **Irregular basophilic keratohyaline and eosinoph trichohyaline-like granules**
- **Intercellular epidermal edema**



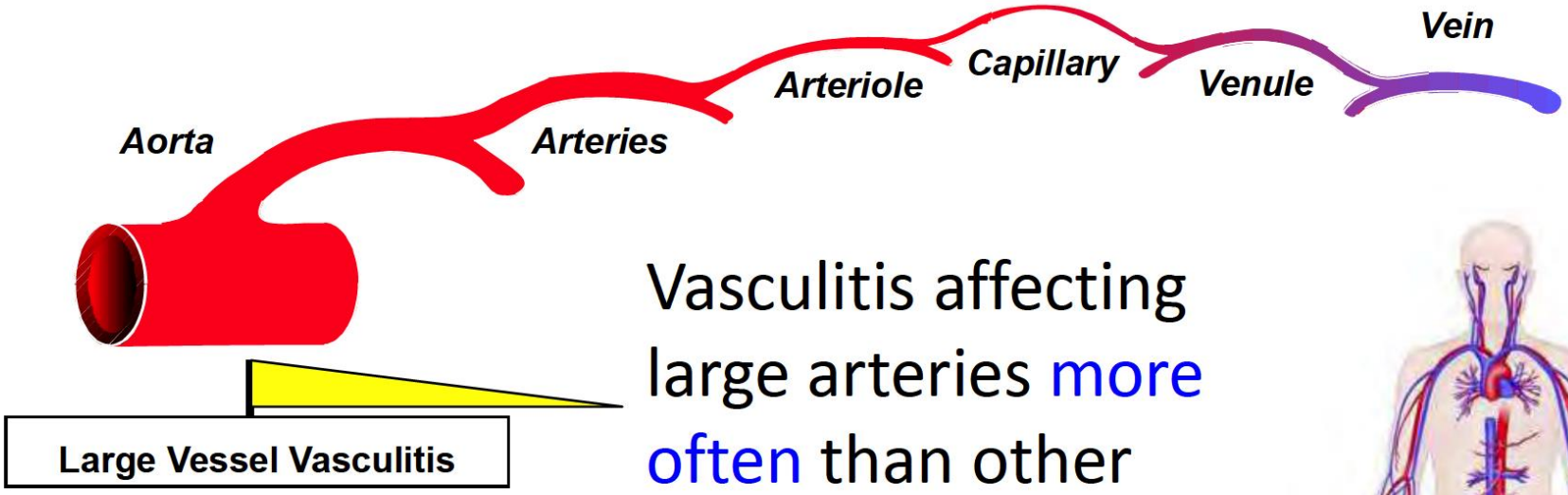
Foci may be seen in:

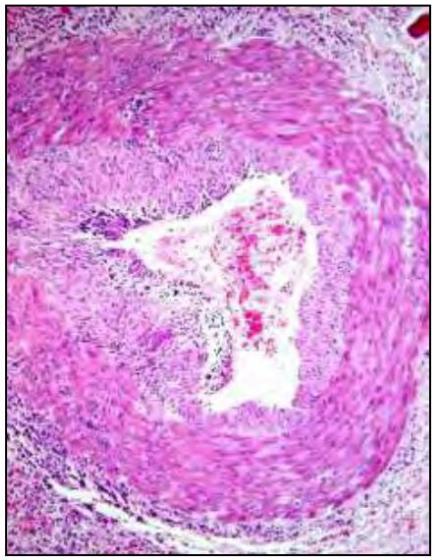
- Normal skin
- AK
- Epidermoid cyst
- Adjacent to SCC
- Seborrheic keratosis
- Granuloma annulare
- Verruca plana
- Dermatofibroma
- Systematized linear epidermal nevus

Epidermal Reaction with Hyperkeratosis

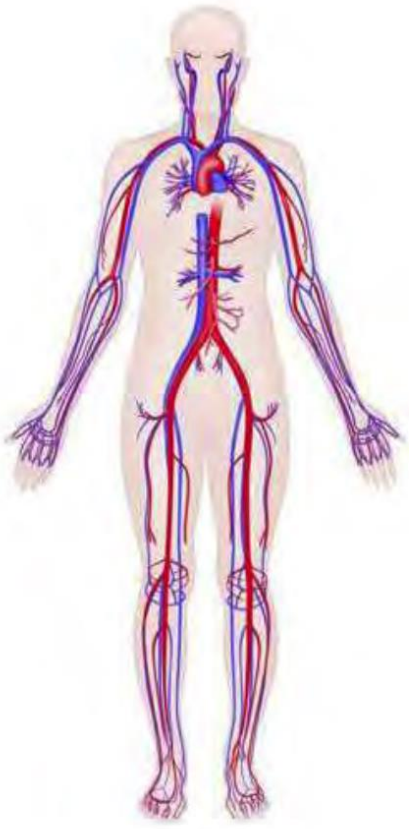


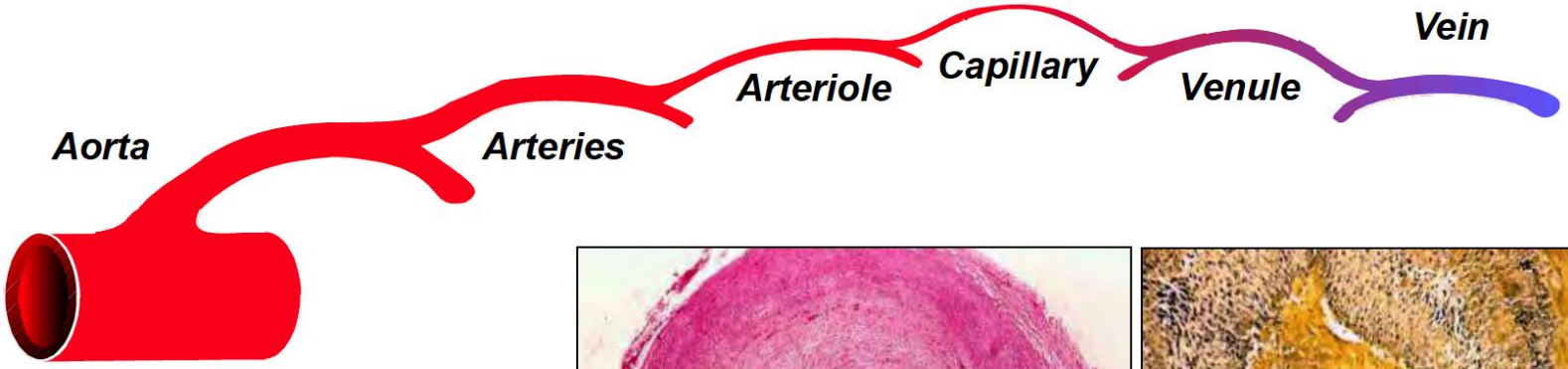
Large Vessel Vasculitis 2012 CHCC Definition





Vasculitis affecting large arteries more often than other vasculitides. Large arteries are the aorta and its major branches. Any size artery may be affected.

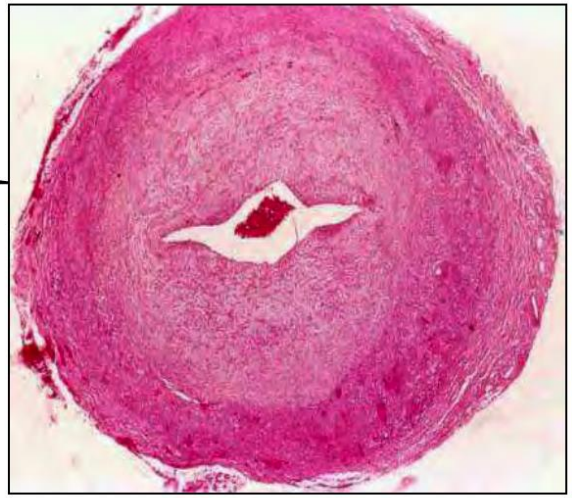


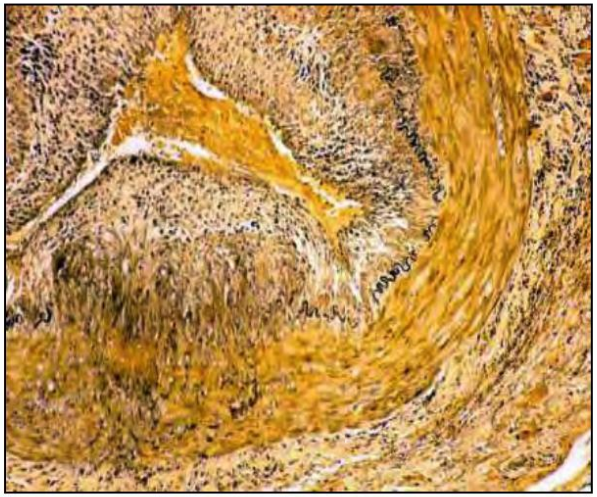


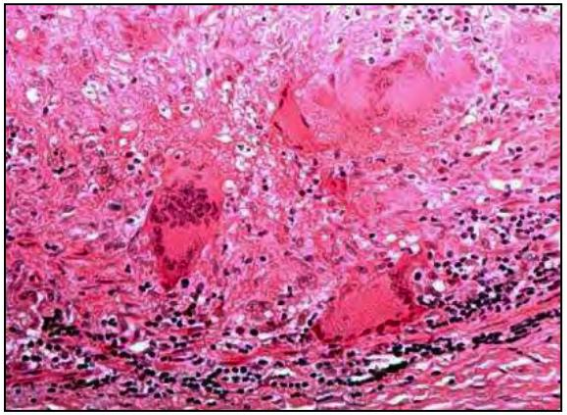
Large Vessel Vasculitis

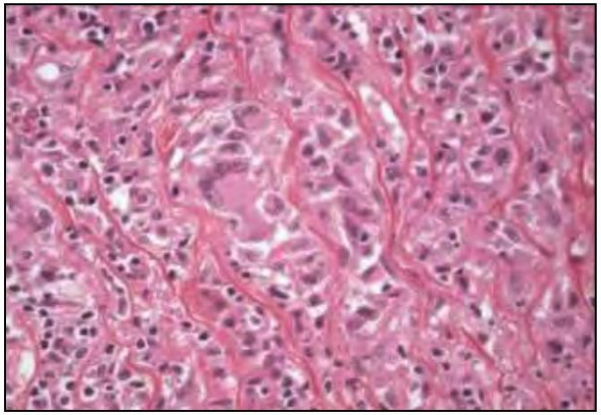
granulomatous arteritis in a patient >50 yo → **Giant Cell Arteritis**

granulomatous arteritis in a patient <50 yo → **Takayasu Arteritis**

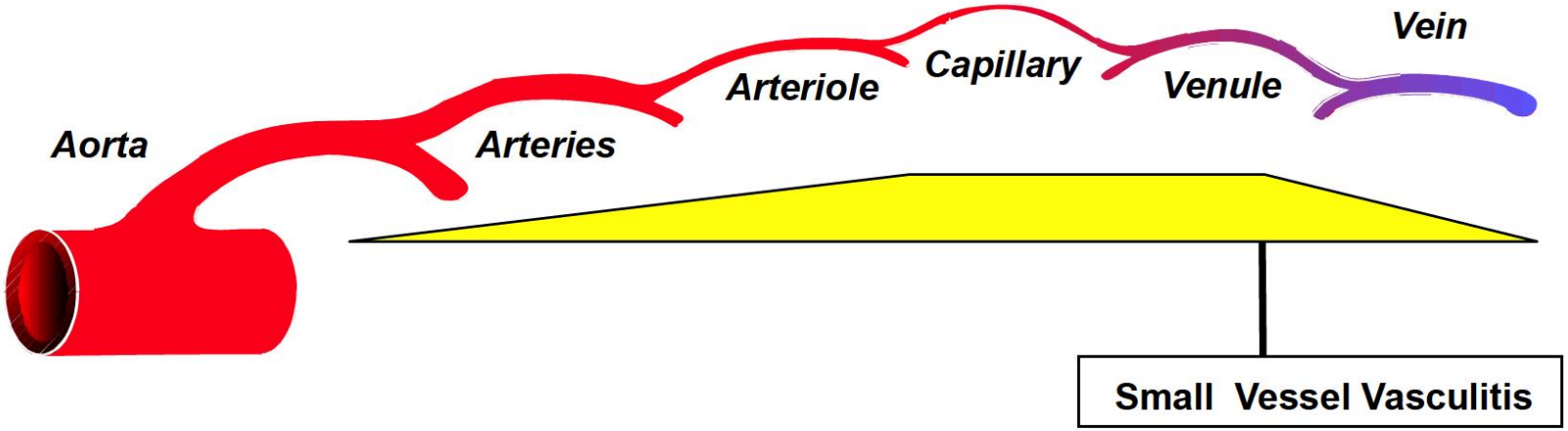




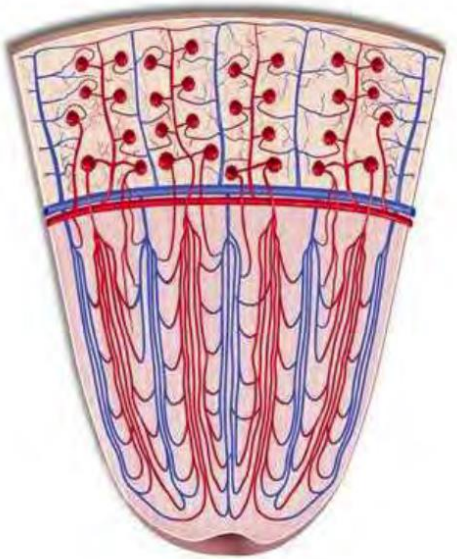




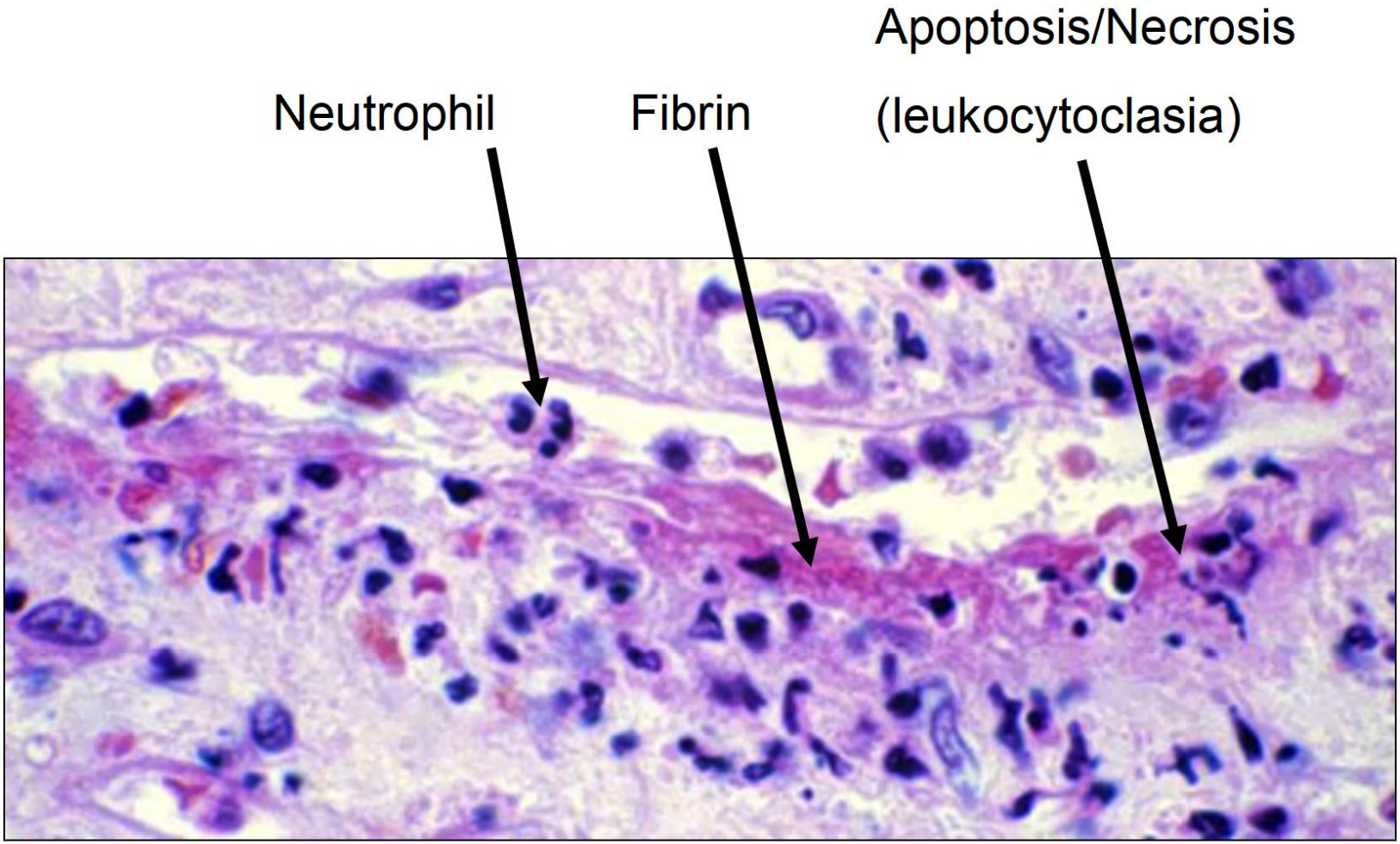
Small Vessel Vasculitis 2012 CHCC Definition



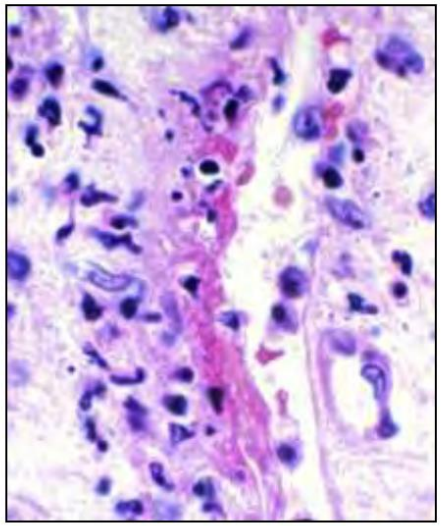
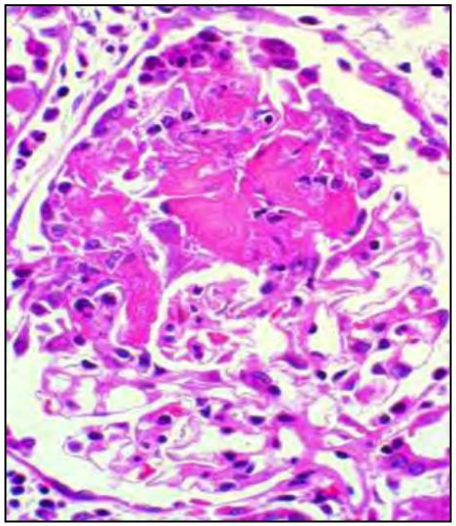
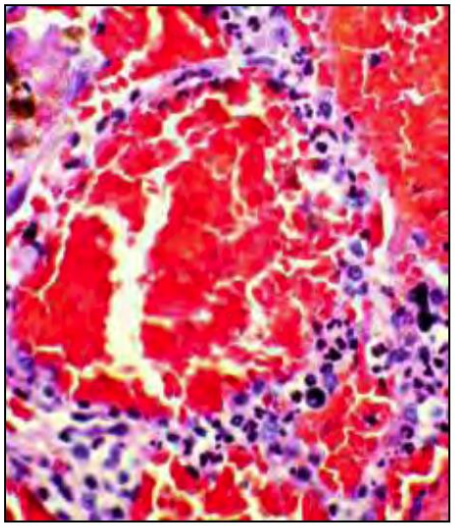
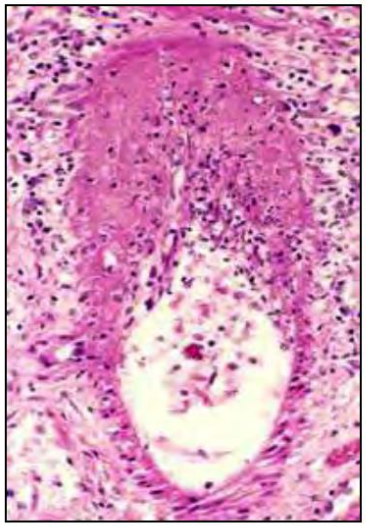
Vasculitis predominantly affecting small vessels, defined as small intraparenchymal arteries, arterioles, capillaries and venules. Medium arteries and veins may be affected.



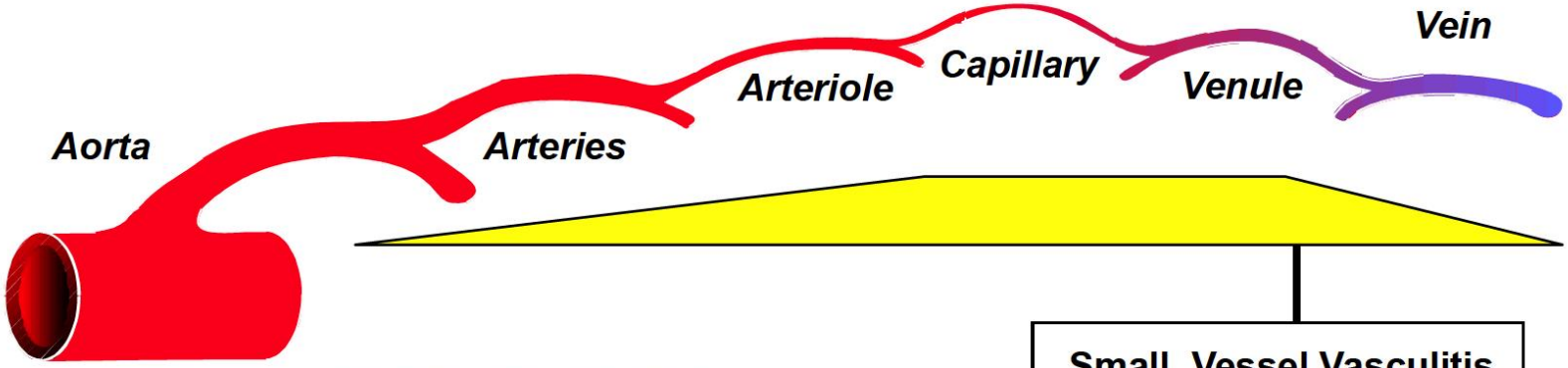
Small vessel vasculitis (leukocytoclastic angiitis)

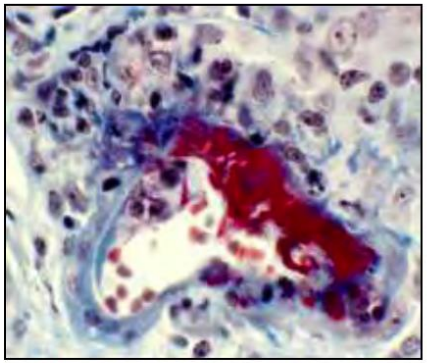


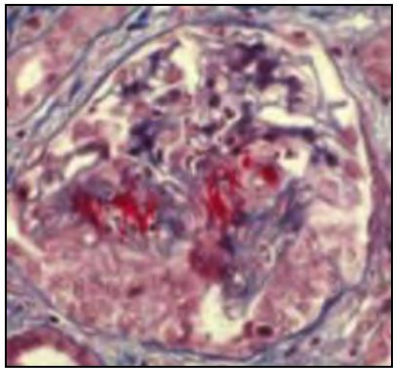
Small vessel vasculitis (necrotizing polyangiitis) often has clinical and pathologic evidence for involvement of capillaries (e.g., glomerulonephritis and pulmonary capillaritis) and venules (e.g., dermal leukocytoclastic venulitis), although arteries may be affected (e.g. epineural arteries causing peripheral neuropathy and intraparenchymal arteries causing abdominal pain).

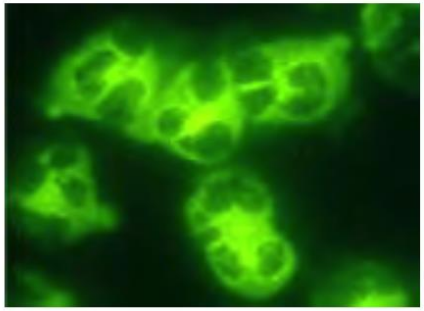





ANCA Associated Vasculitis 2012 CHCC Definition



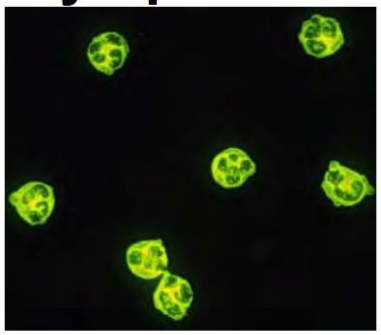
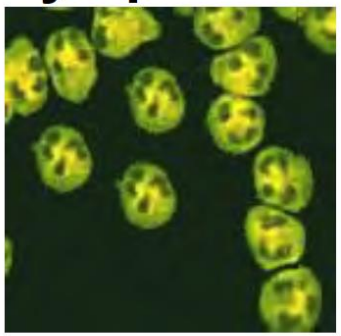
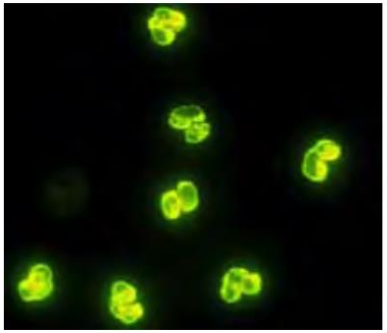
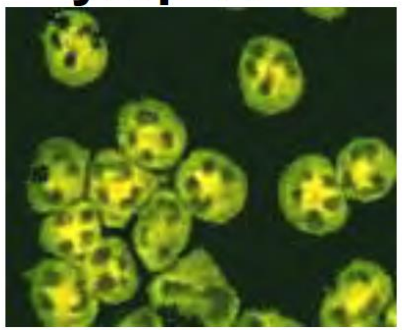




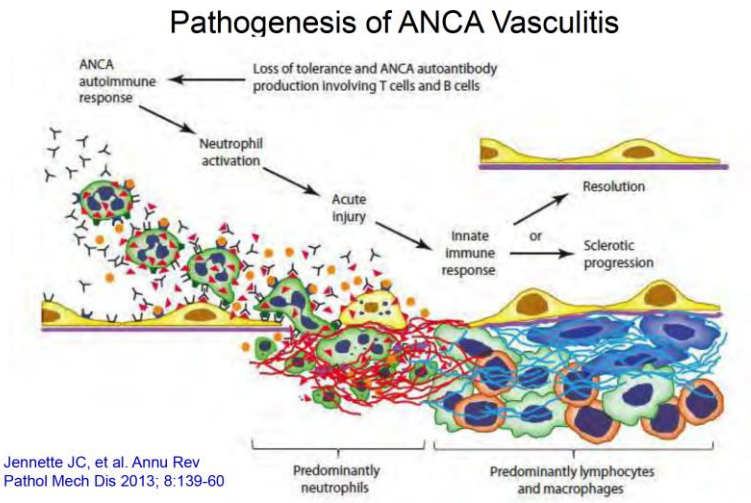


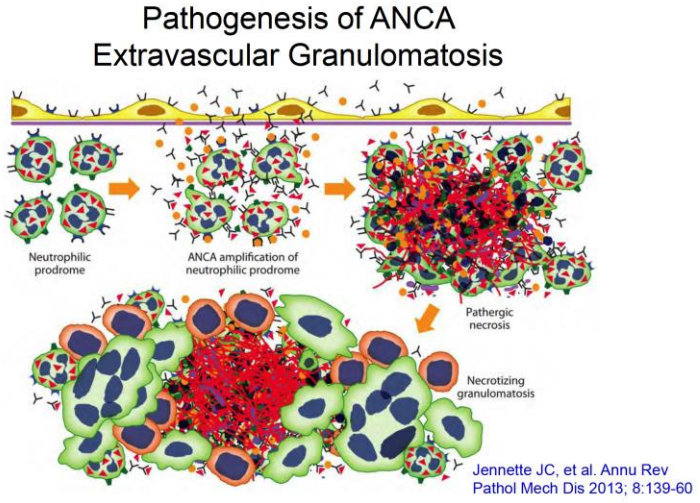
- **Small Vessel Vasculitis**
  - **ANCA Associated Vasculitis**
    - vasculitis with no asthma or granulomas → **Microscopic Polyangiitis** → **MPA**
    - granulomas and no asthma → **Granulomatosis with Polyangiitis (Wegener's)** → **GPA**
    - eosinophilia, asthma and granulomas → **Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss)** → **EGPA**

Anti-neutrophil Cytoplasmic Autoantibodies (ANCA)

	Staining of alcohol-fixed neutrophils	Staining of formalin-fixed neutrophils	Immunoassay antigen specificity
C-ANCA	Cytoplasmic 	Cytoplasmic 	Proteinase 3 (PR3-ANCA), BPI, others
P-ANCA	Perinuclear 	Cytoplasmic 	Myeloperoxidase (MPO-ANCA), elastase, others

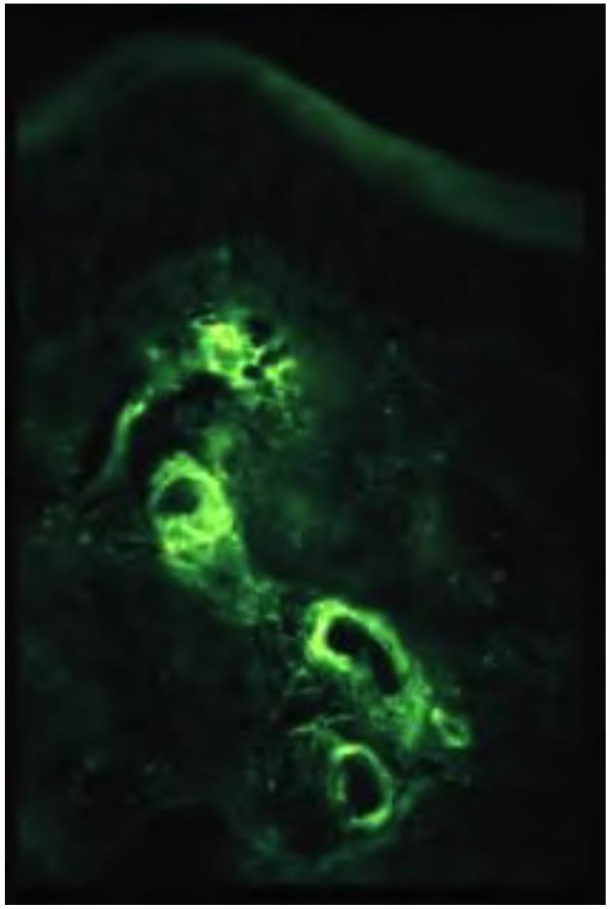
ANCA-mediated Lesions





Immune Complex Vasculitis 2012 CHCC Definition

Vasculitis with moderate to marked vessel wall deposits of immunoglobulin and/or complement components predominantly affecting small vessels (i.e., capillaries, venules, arterioles and small arteries). Glomerulonephritis is frequent.

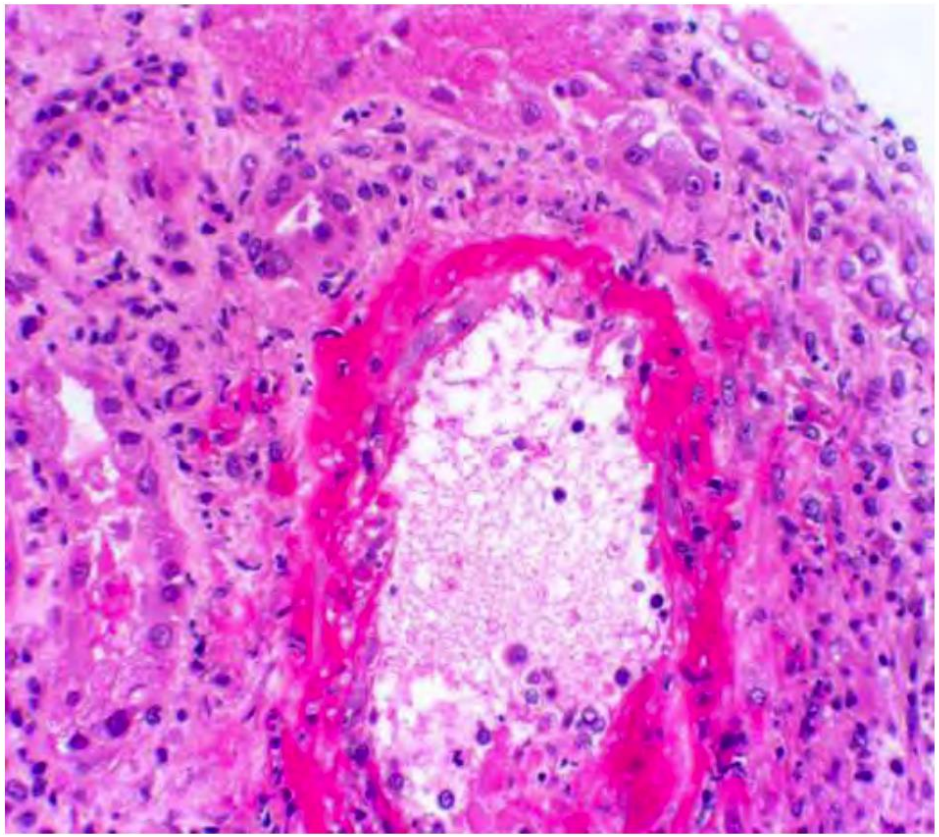


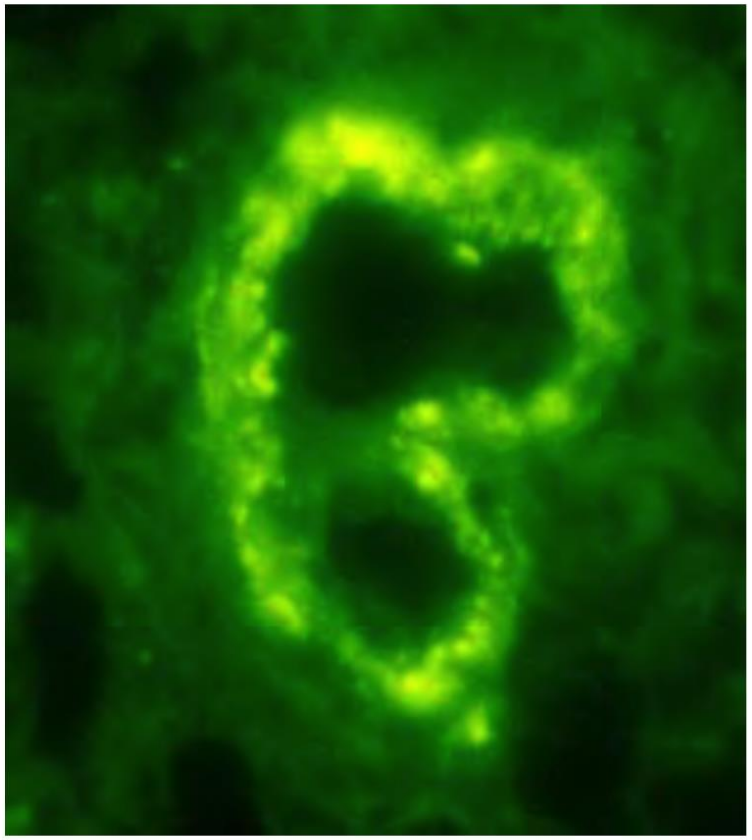
Dermal venules with granular deposits of immunoglobulin

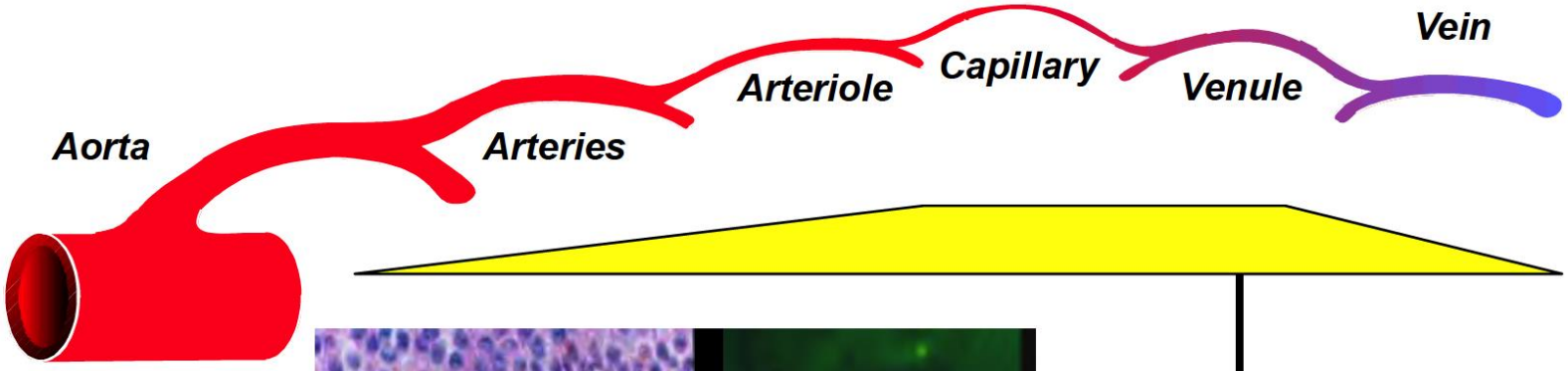
Vasculitis Associated with Systemic Diseases (e.g. Rheumatoid, Lupus, etc.)

Vasculitis Associated with Probable Etiologies (e.g. HBV, HCV, drug, etc.)

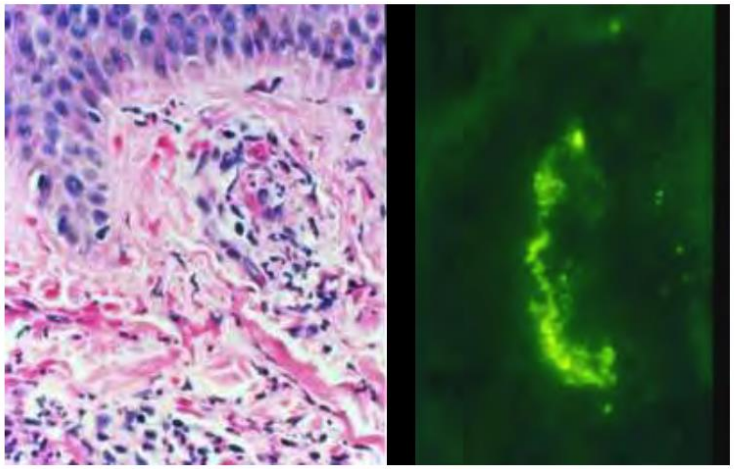
Lupus Arteritis







Immune Complex Vasculitis



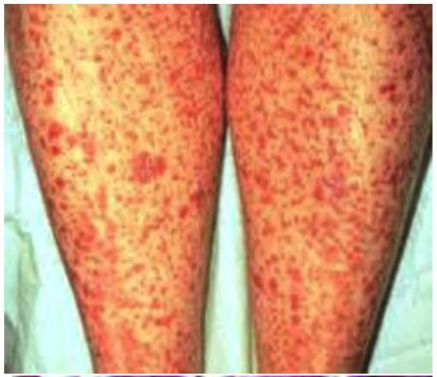
Small Vessel Vasculitis

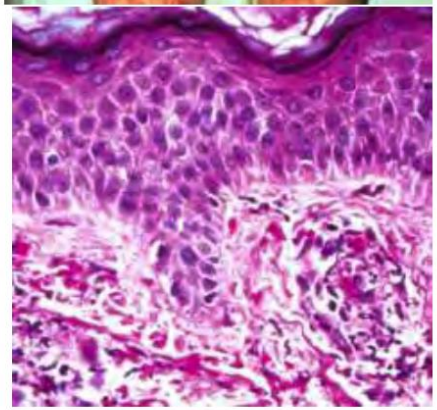
immune complexes in vessels

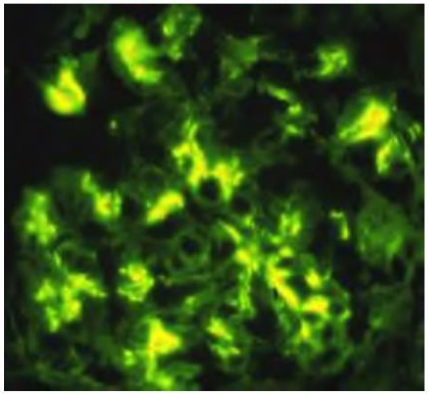
other sources for immune complexes	cryoglobulins in blood and vessels	IgA-dominant vessel wall deposits	SLE or rheumatoid arthritis
Other Im Cx Vasculitis	**Cryoglobulinemic Vasculitis**	**IgAV (HSP)**	**Lupus/Rheumatoid Vasculitis**

IgA Vasculitis (Henoch-Schönlein)
2012 CHCC Definition

Vasculitis, with IgA1-dominant immune deposits, affecting small vessels (predominantly capillaries, venules, or arterioles). Often involves skin and gut, and frequently causes arthritis. Glomerulonephritis indistinguishable from IgA nephropathy may occur.



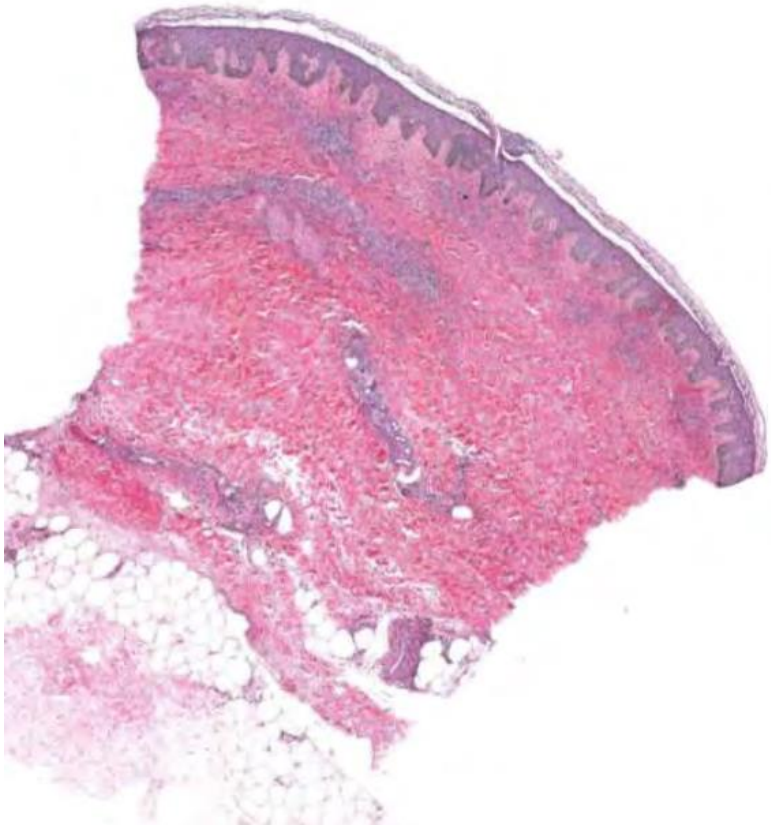


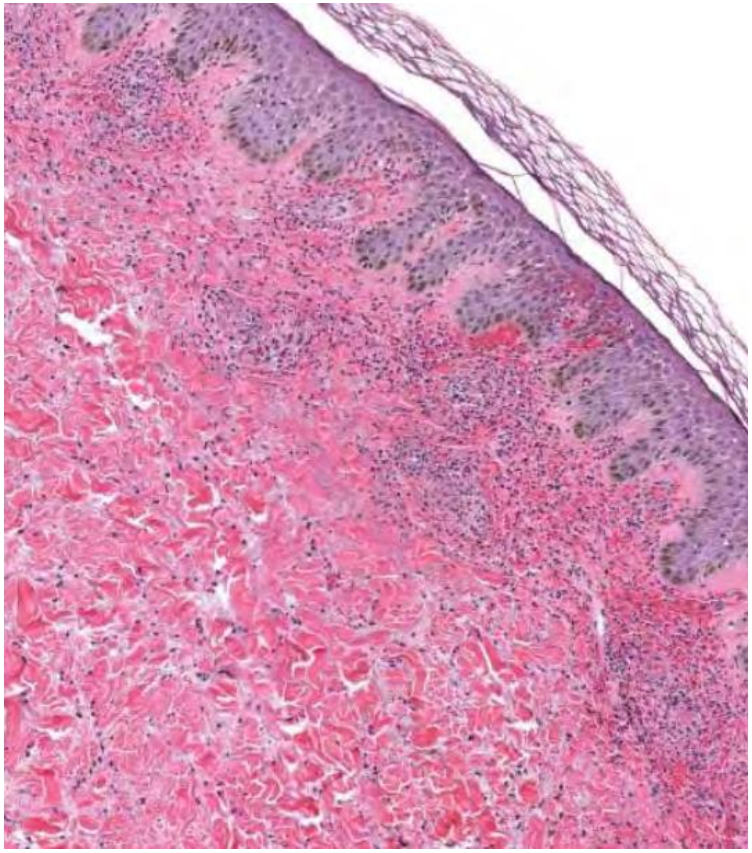


IgA Vasculitis (Henoch-Schönlein purpura)

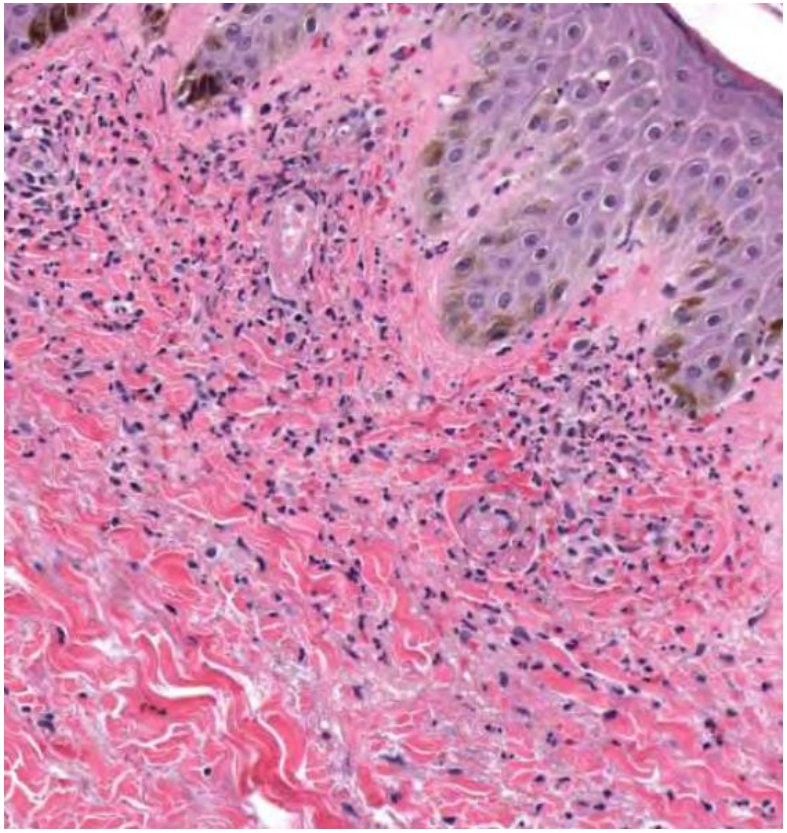
- Most frequent in children, especially children under 10 years old, although it can begin at any age.
- Twice as common in males, and is uncommon in individuals of African descent.
- Onset is most often in the spring and fall, usually at the time of an upper respiratory tract infection.
- Purpura, arthralgias and colicky abdominal pain are the most frequent symptoms.
- Approximately half of the patients have hematuria and proteinuria.
- The lesion in the kidney is indistinguishable from IgA nephropathy although necrosis, crescents and capillary wall deposits are more frequent in HSP nephritis.
- IgA dominant immune deposits occur in renal arterioles and peritubular capillaries in <20%.
- IgA-dominant immune deposits can be identified not only in the kidneys but also in small vessels of the skin and gut; however, this is not of value in differentiating IgAV (HSP) from IgA nephropathy because many IgA nephropathy patients often have IgA in dermal venules.

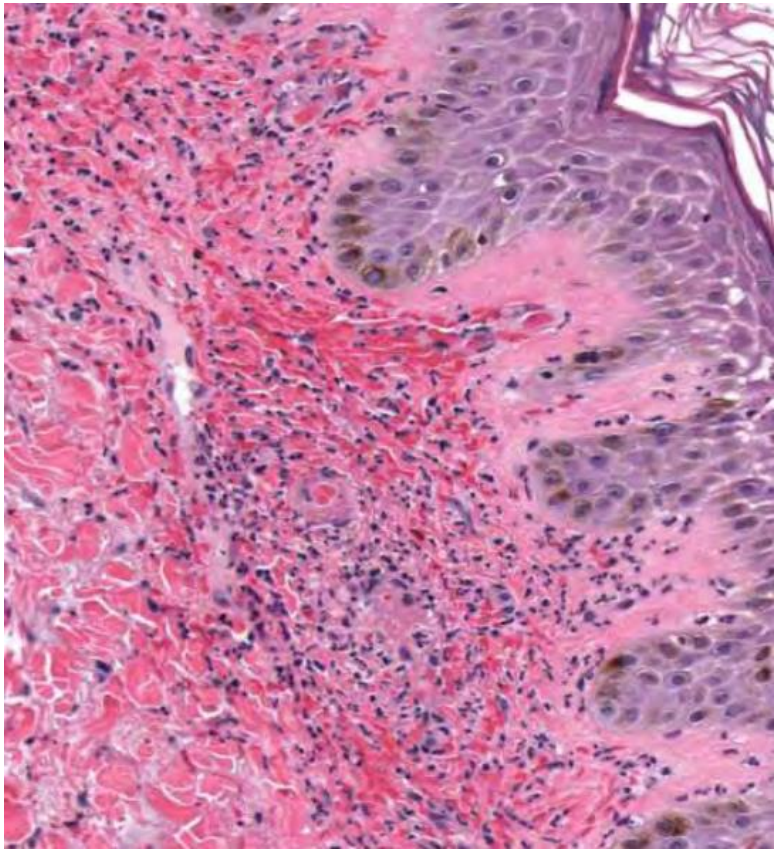
IgA Vasculitis (Henoch-Schönlein purpura)



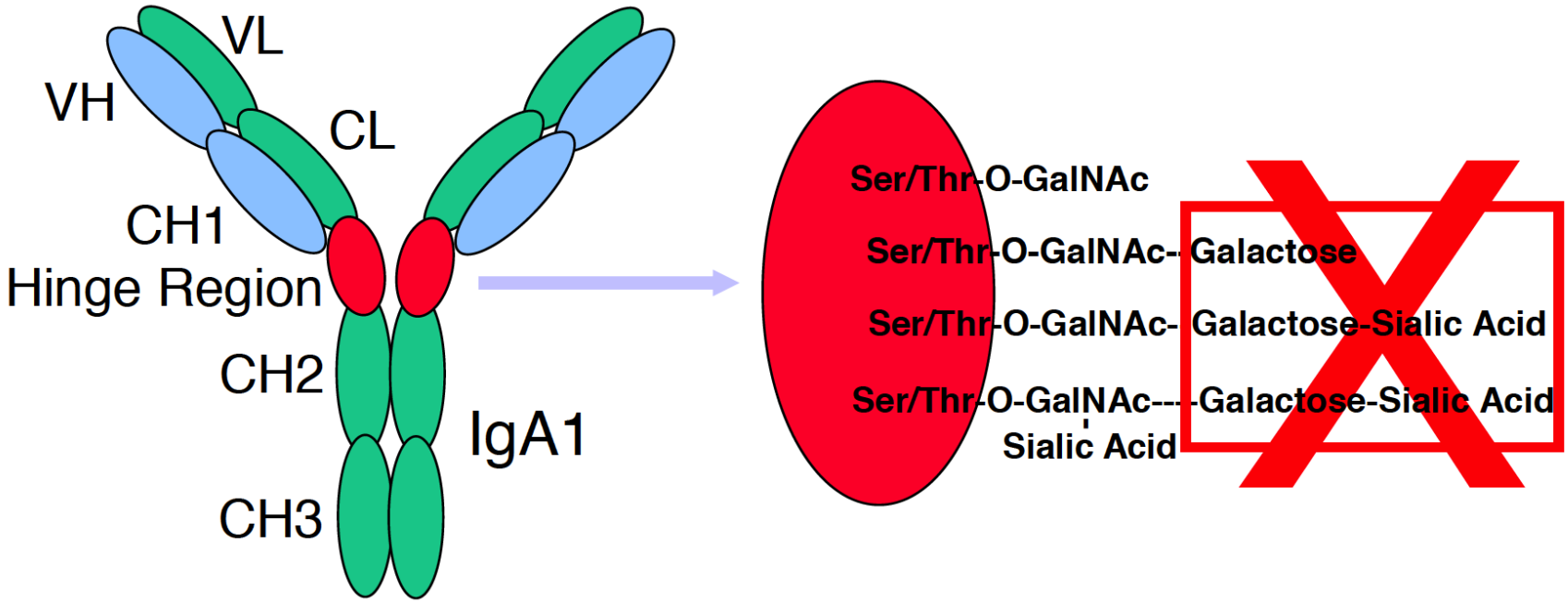


IgA Vasculitis (Henoch-Schönlein purpura)



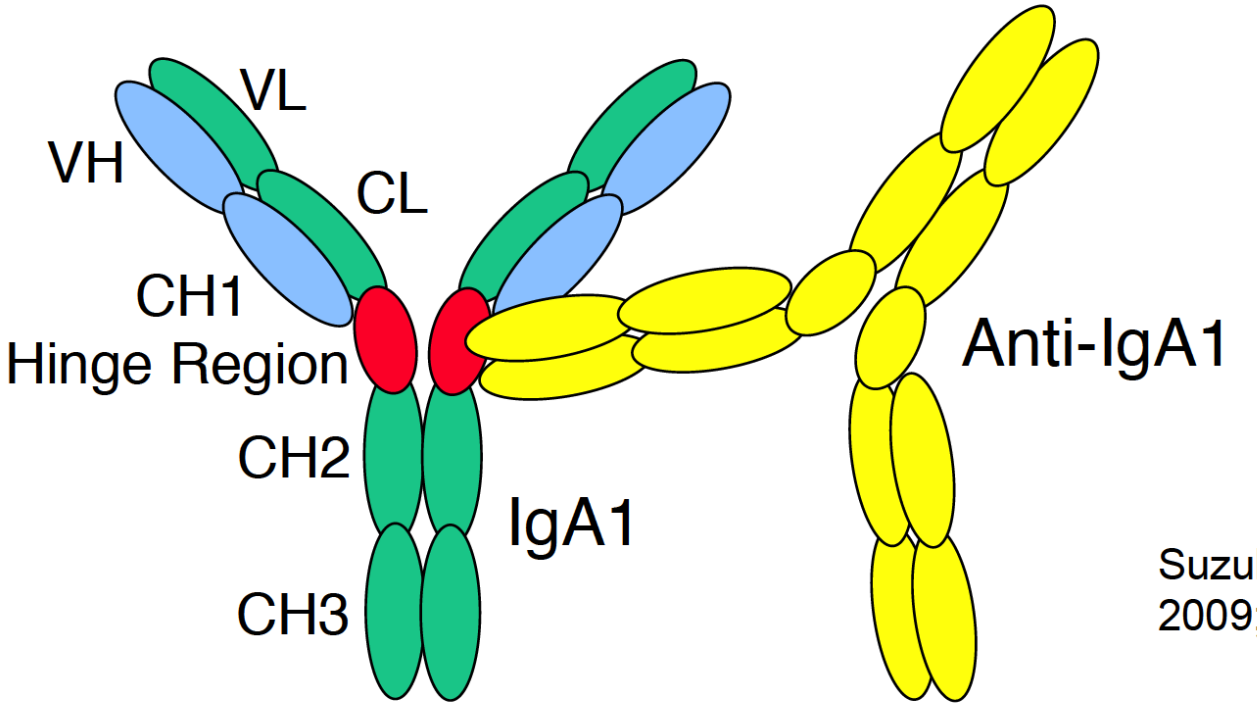


Abnormally reduced glycosylation of the O-linked glycans in the hinge region of IgA1 molecules appear to play a pathogenic role in IgAN and IgAV through a variety of mechanisms



In IgA nephropathy and IgAV, serum IgA1 has reduced terminal galactosylation, resulting in increased exposure of terminal GalNAc, and autoantibody formation against this glycan.

Abnormally reduced glycosylation of the O-linked glycans in the hinge region of IgA1 molecules appear to play a pathogenic role in IgAN and IgAV through a variety of mechanisms



Suzuki H, et al. J Clin Invest. 2009;119:1668-77.

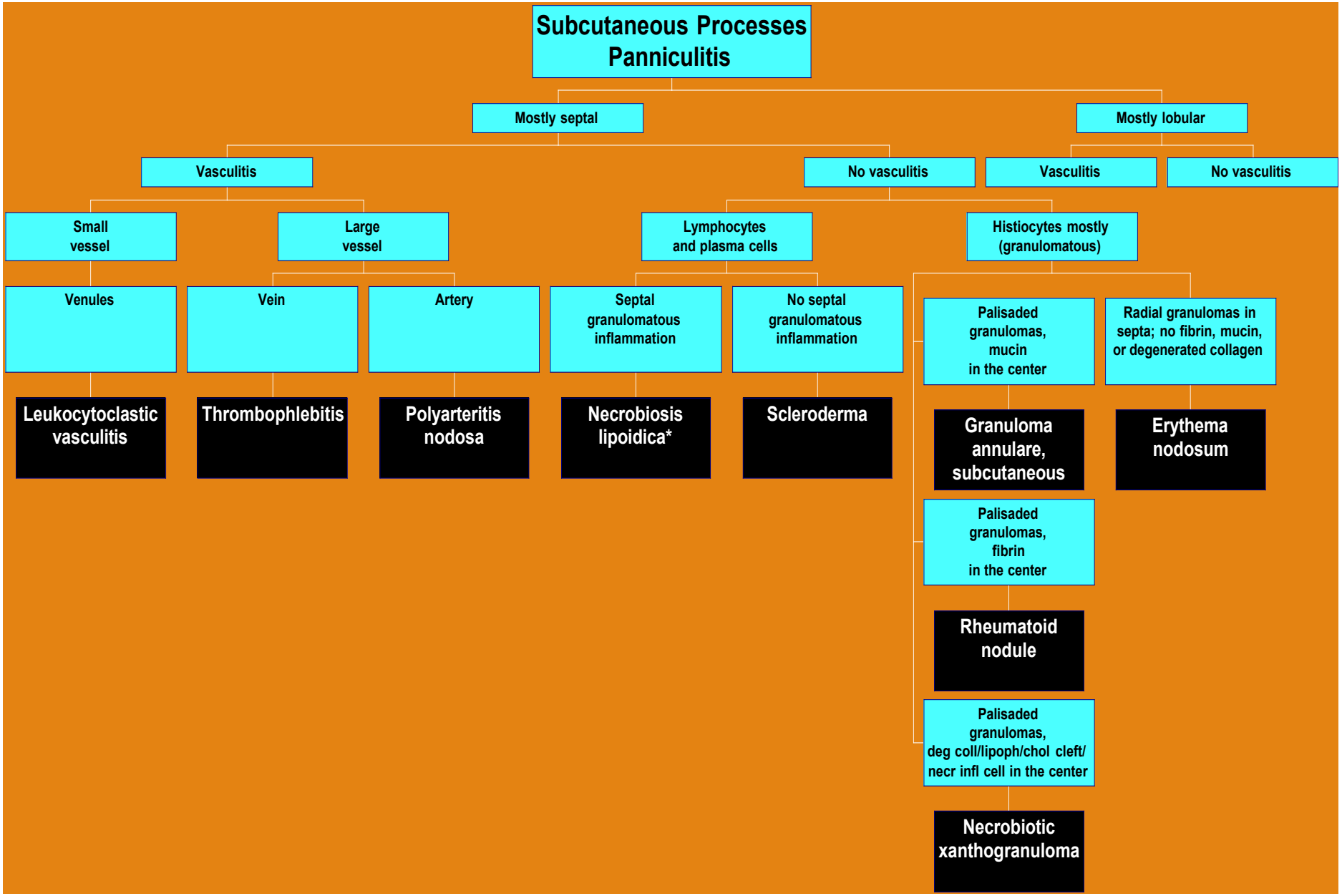
In IgA nephropathy and IgAV, serum IgA1 has reduced terminal galactosylation, resulting in increased exposure of terminal GalNAc, and autoantibody formation against this glycan.

IgA Vasculitis – Mechanisms

- **Abnormally reduced glycosylation of the O-linked glycans in the hinge region of IgA1 molecules may play a pathogenic role in IgAN and IgAV through a variety of mechanisms, e.g.:**
  - **Reduced clearance from the circulation because of lack of receptor engagement by the abnormal IgA**
  - **Development of immune complex-forming autoantibodies directed against the abnormal IgA**
  - **Increased aggregation of IgA in the circulation resulting in mesangial trapping**
  - **Increased affinity of the abnormal IgA for mesangial matrix**
  - **Combinations of these processes.**

Differential Diagnosis of Small Vessel Vasculitis

- **MPA, GPA and EGPA usually have circulating ANCA (AAV) and a pauci-immune vasculitis and glomerulonephritis.**
- **IgA Vasculitis (Henoch-Schönlein) vasculitis has IgA-dominant immune deposits. Soon, serologic demonstration of abnormally glycosylated IgA or antibodies to this abnormal IgA may be used for diagnosis.**
- **Cryoglobulinemic vasculitis has circulating cryoglobulins, hypocomplementemia and usually a type I MPGN.**
- **Lupus vasculitis is presumed in a setting of clinical and serologic evidence for SLE.**
- **Hypocomplementemic urticarial vasculitis has the characteristic urticaria, hypocomplementemia and circulating anti-C1q antibodies.**


Subcutaneous Processes
Panniculitis
Mostly septal
Mostly lobular
Vasculitis
No vasculitis
Vasculitis
No vasculitis
Small vessel
Large vessel
Lymphocytes and plasma cells
Histiocytes mostly (granulomatous)
Venules
Vein
Artery
Septal granulomatous inflammation
No septal granulomatous inflammation
Palisaded granulomas, mucin in the center
Radial granulomas in septa; no fibrin, mucin, or degenerated collagen
Leukocytoclastic vasculitis
Thrombophlebitis
Polyarteritis nodosa
Necrobiosis lipoidica*
Scleroderma
Granuloma annulare, subcutaneous
Erythema nodosum
Palisaded granulomas, fibrin in the center
Rheumatoid nodule
Palisaded granulomas, deg coll/lipoph/chol cleft/ necr infl cell in the center
Necrobiotic xanthogranuloma