Vasculitis and related disorders

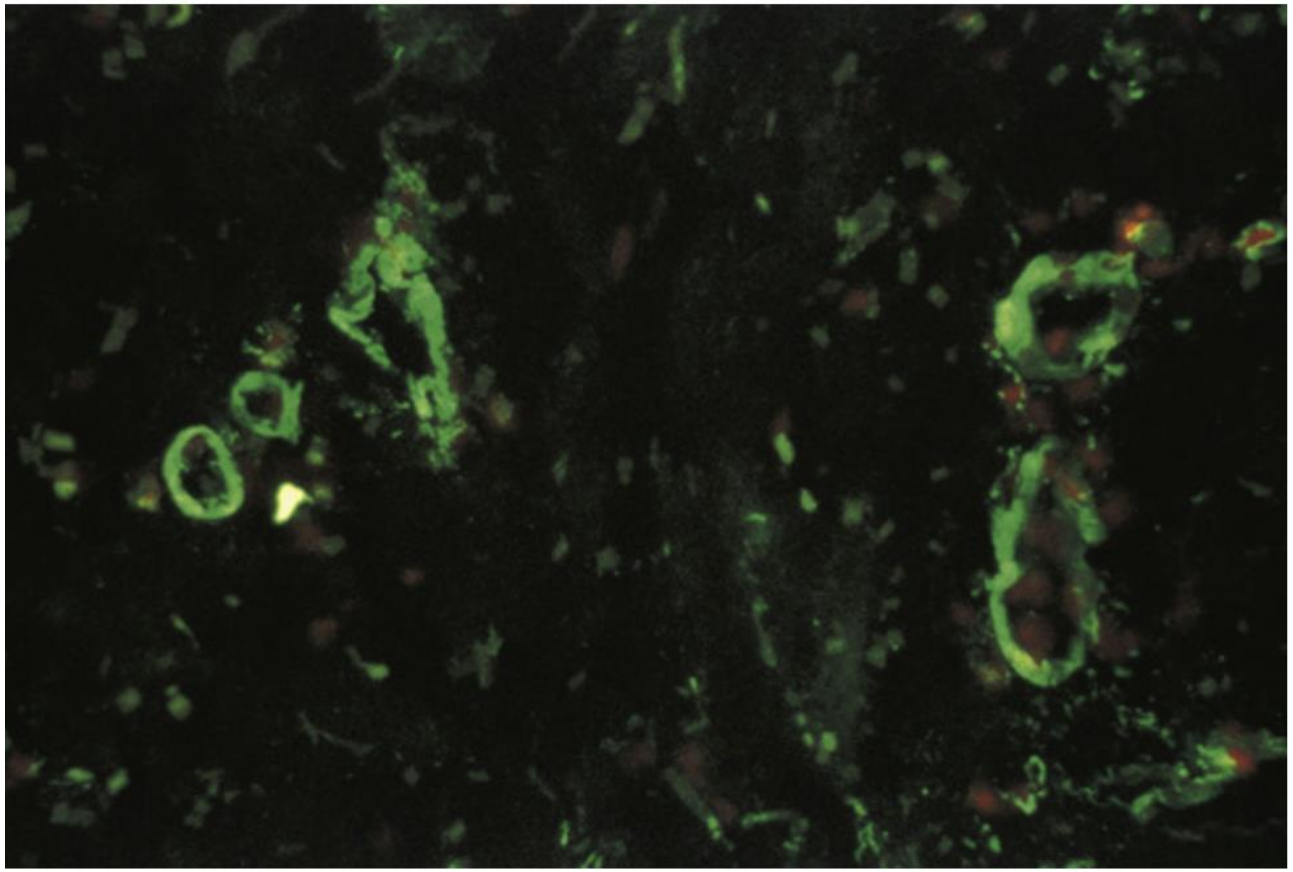
Soheil S Dadras MD-PhD

What is the diagnostic approach to vasculitis?

- Is there vasculitis or vasculopathy?
- Is the process cutaneous or systemic?
- Is the vascular injury primary or secondary?
- What is the size and the type of vessel involved?
  - Small, medium or large?
- What is the composition of the inflammatory infiltrate?
  - Neutrophilic, lymphocytic, eosinophilic, or granulomatous
- What are the associated findings?
  - Infection (special stains and microbial cultures)?
  - Plasma cells (spirochete)?
  - Viral infection (HSV vascular changes)?
  - Suggestion of connective tissue disease (interface dermatitis or dermal mucin)
  - Edema (urticarial reaction)
  - Serologic studies: ANA, ANCAs, RF, cryoglobulins, DIF
  - Clinical context: demographics and presentation, other signs/symptoms

What are the diagnostic tools to make/confirm vasculitis or vascular damage?

- The damage could involve blood vessels in the deep dermis or subcutis
- Histologic evaluation: Perform punch (NOT shave) skin biopsy to include deep reticular dermis and subcutaneous tissue
- Direct immunofluorescence
  - Vascular pattern of immunoglobulins and complements (C3)
- PAS and elastic special stains
- IHC: smooth muscle actin

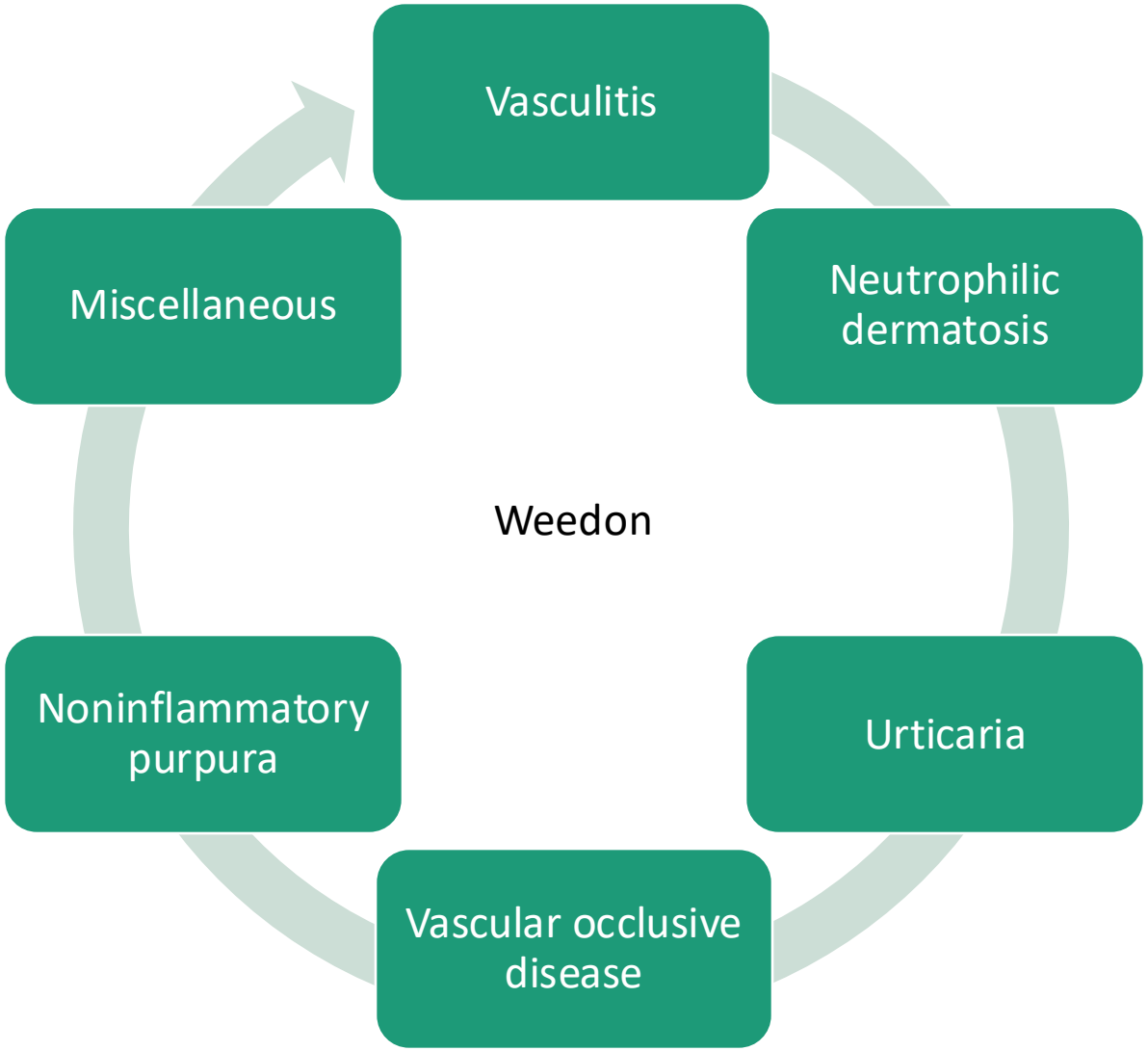


Leukocytoclastic vasculitis: IgM in the luminal surface of blood vessels

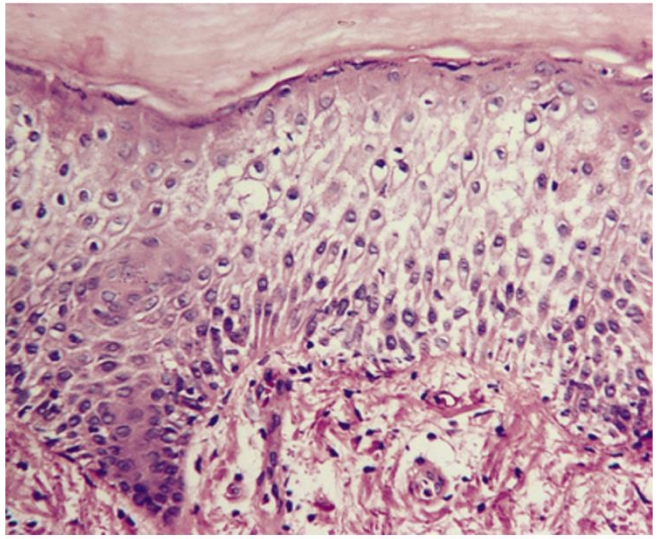
How are the diseases of blood vessels categorized?

Types and definitions of vasculitis

- Adopted by the 2012 Chapel Hill Consensus Conference
- List of clinical criteria and disease nomenclature
- Classified according to the type and size of the vessels
  - e.g., polyarteritis nodosa is under medium vessel vasculitis
- Common denominator: damage to cutaneous blood vessels

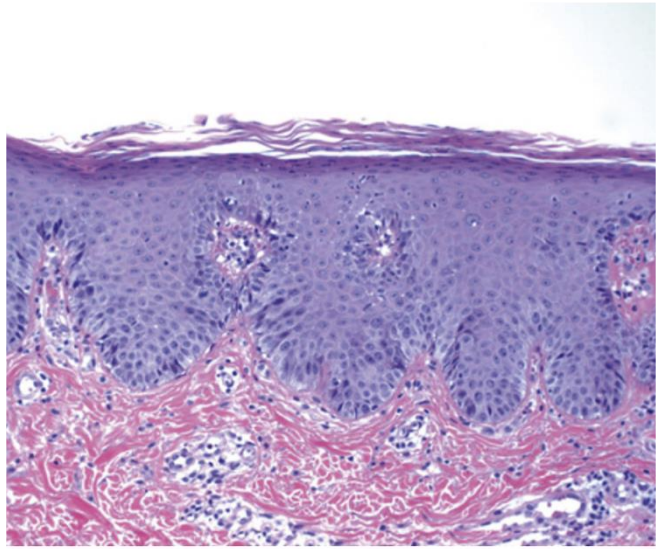


Tissue reaction patterns



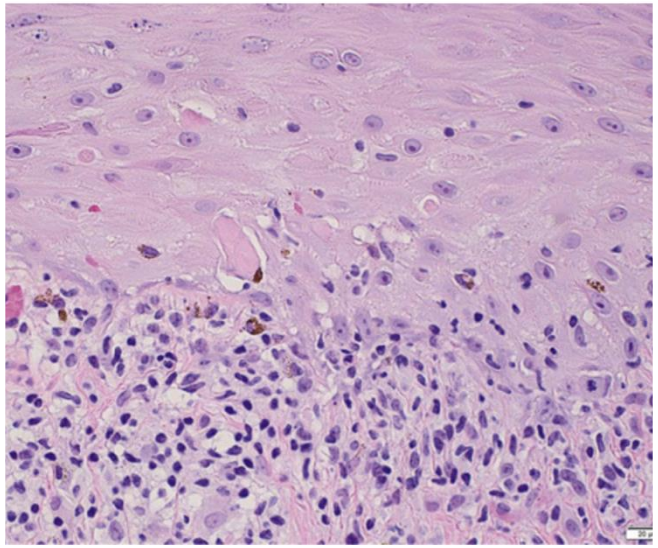
Atopic dermatitis

Spongiotic



Psoriasis

Psoriasiform



Lichen planus

Lichenoid

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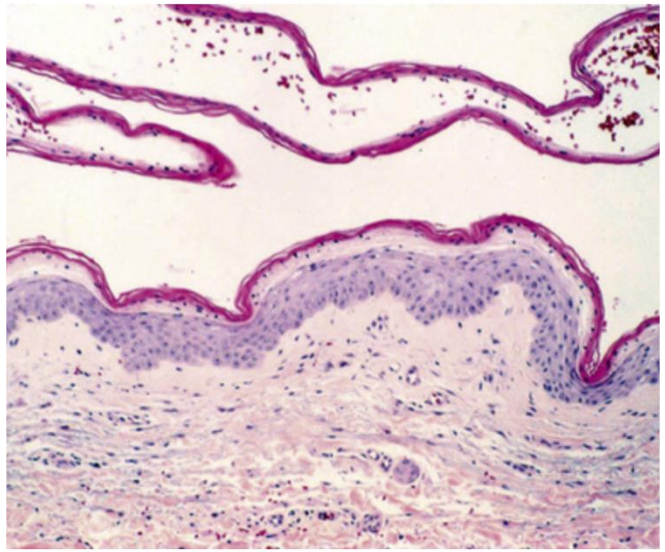
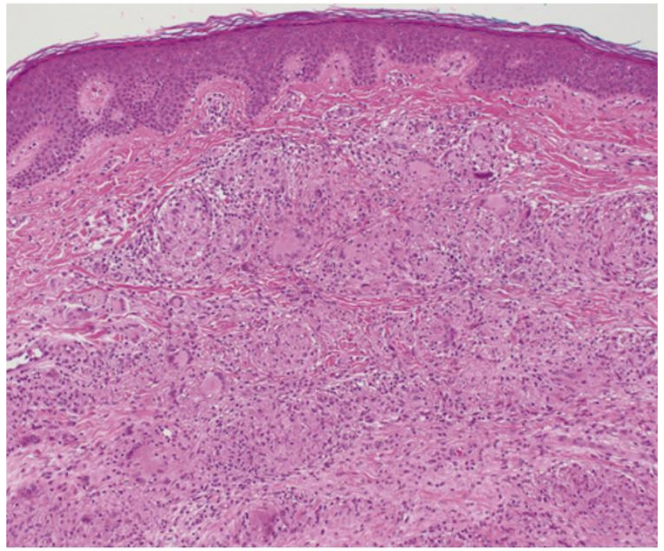
Tissue reaction patterns



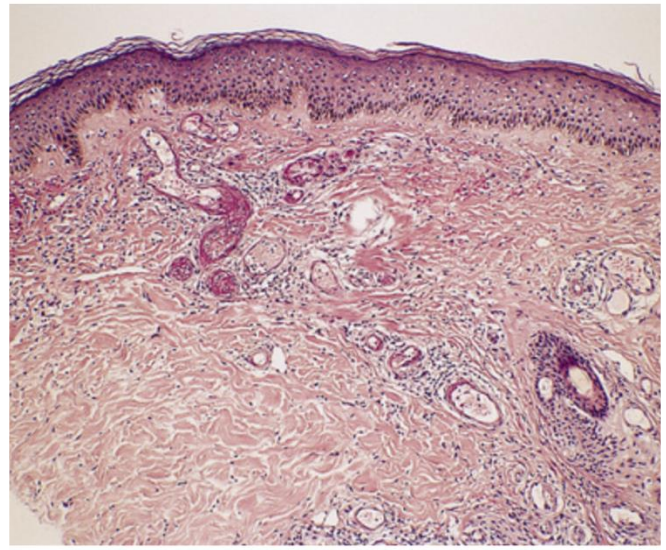
Bullous pemphigoid

Vesiculobullous



Granuloma annulare

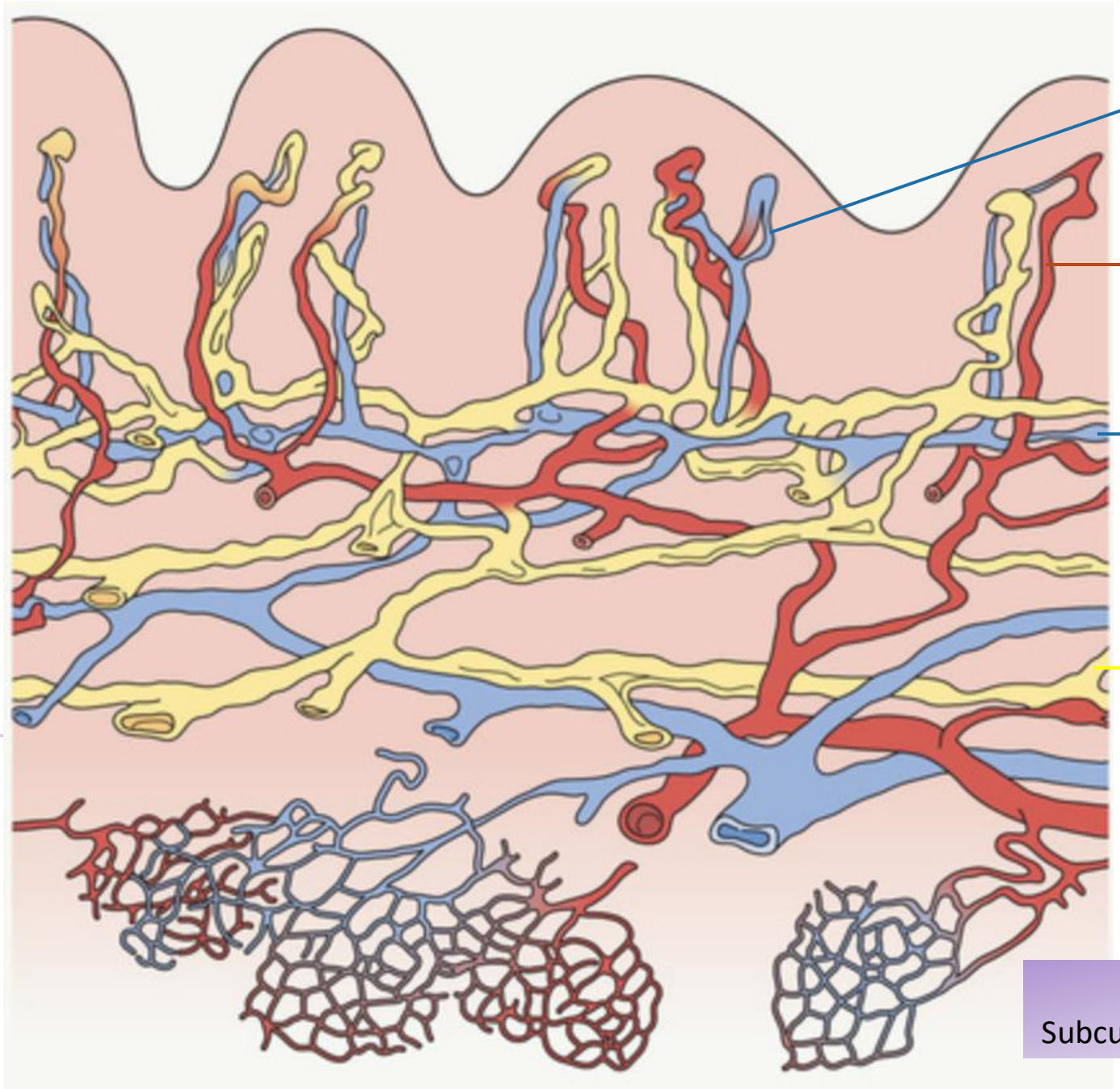
Granulomatous



Atrophie blanche

Vasculopathic

Cutaneous vascular system



Postcapillary venules: Site of vasculitis, permeability, leukocyte recruitment and diapedesis

Arterioles

Venules

Lymphatics

Capillary network
Subcutaneous adipose tissue

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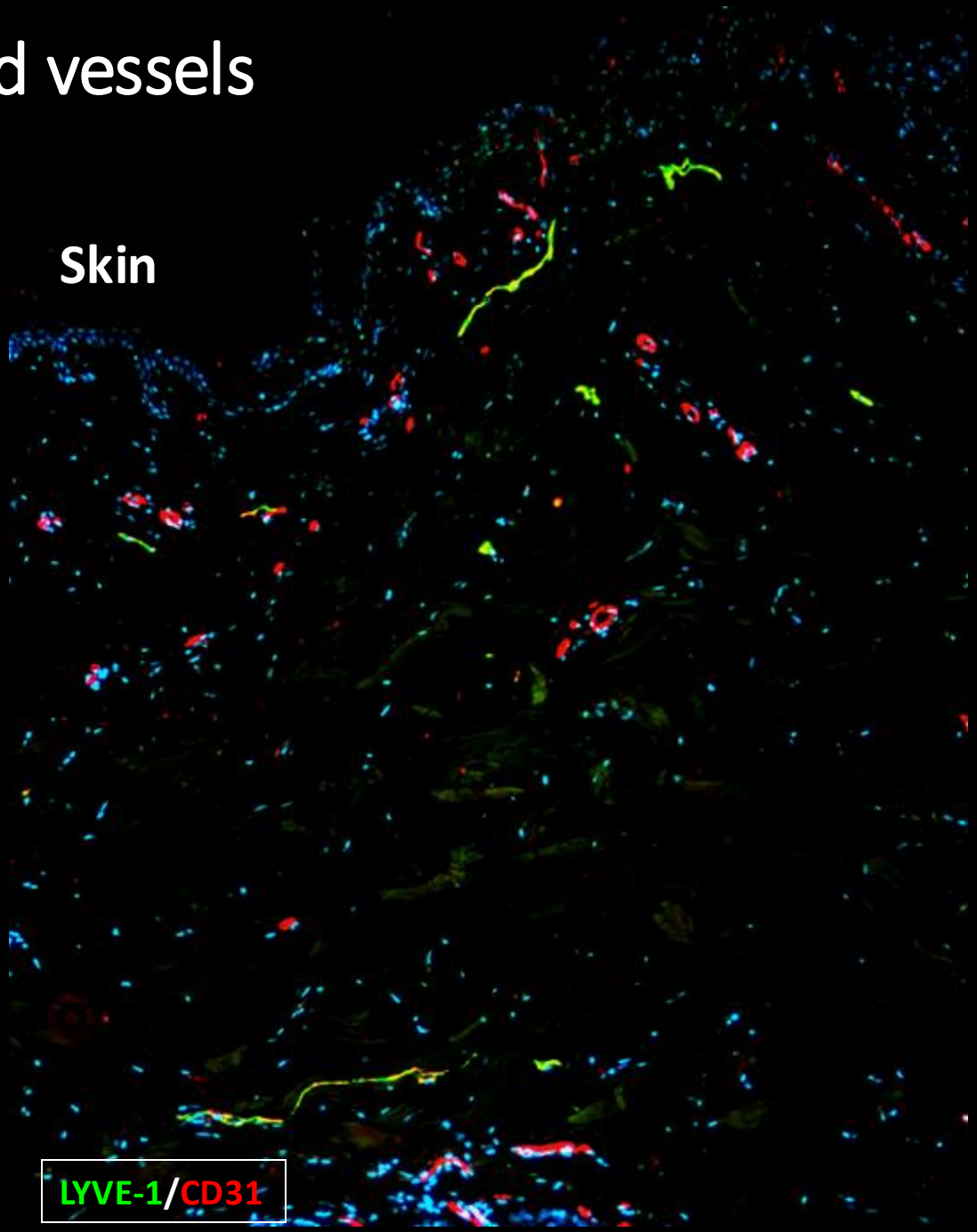
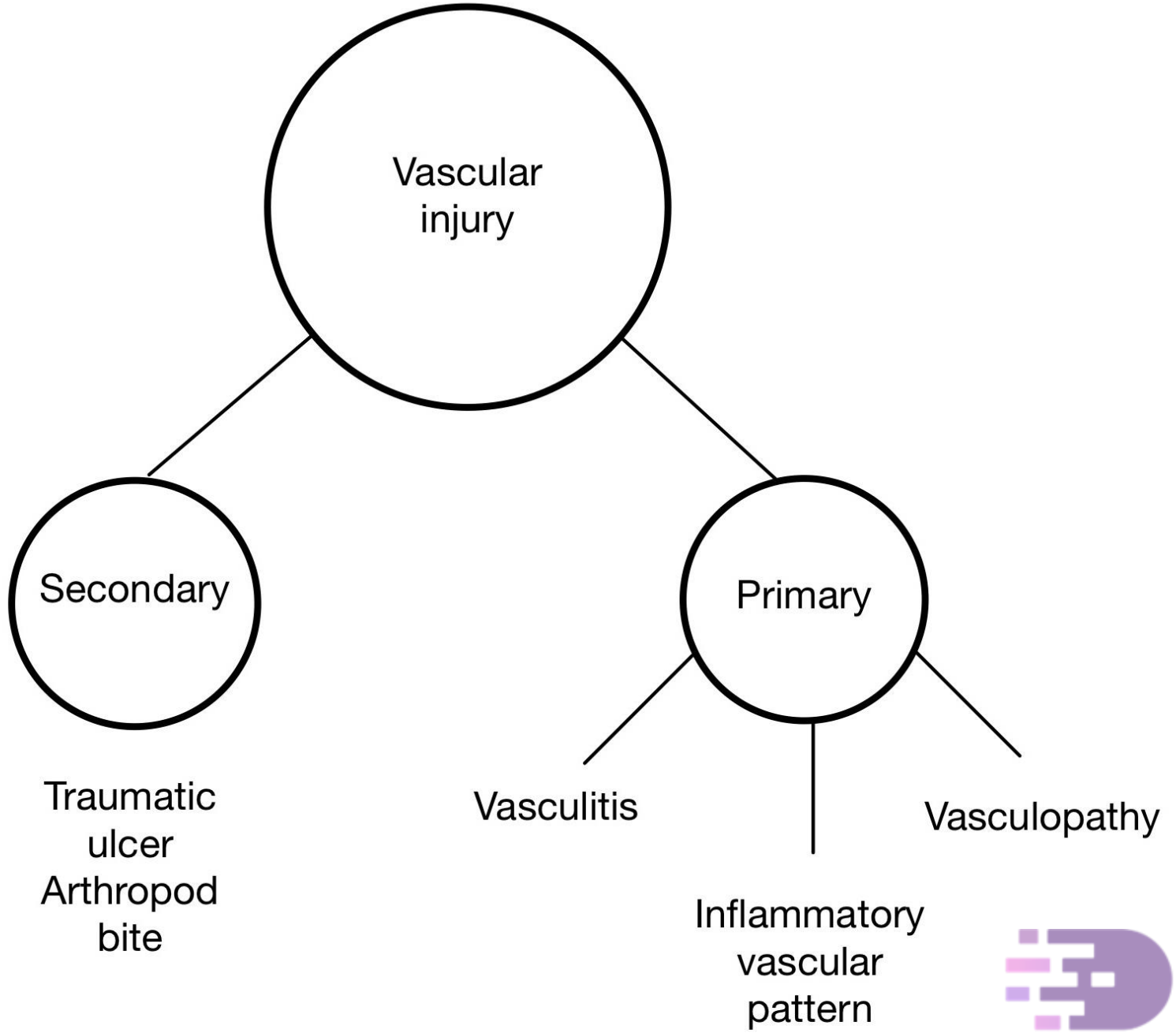
Immunohistochemical markers for blood vessels and lymphatics

Marker	Lymphatic Vessels	Blood Vessels
Blood Vascular Specific		
CD34	-	+
CD44	-	+
PAL-E	-	+
Collagen type IV	-/(+)	+
Collagen type XVIII	-/(+)	+
Laminin	-/(+)	++
Neuropilin-1	-	+
Lymphatic Specific		
VEGFR-3	+	-
Podoplanin	+	-
SLC/CCL21	+	-
LYVE-1	+	-
Prox1	+	-
Panvascular		
CD31 (PECAM-1)	+	++
VEGFR-2	+	+
Factor VIII-related antigen	+	++

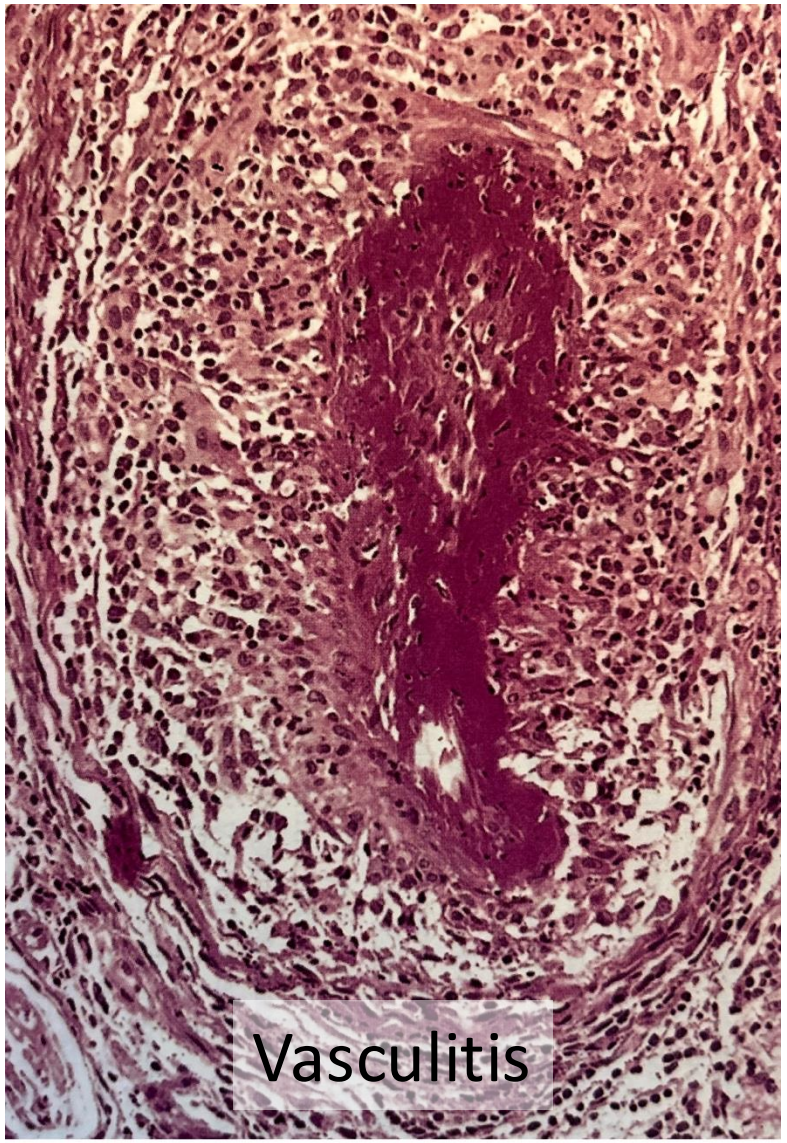
Dadras and Detmar, *Hem. Onc. of North Ame.* 2004

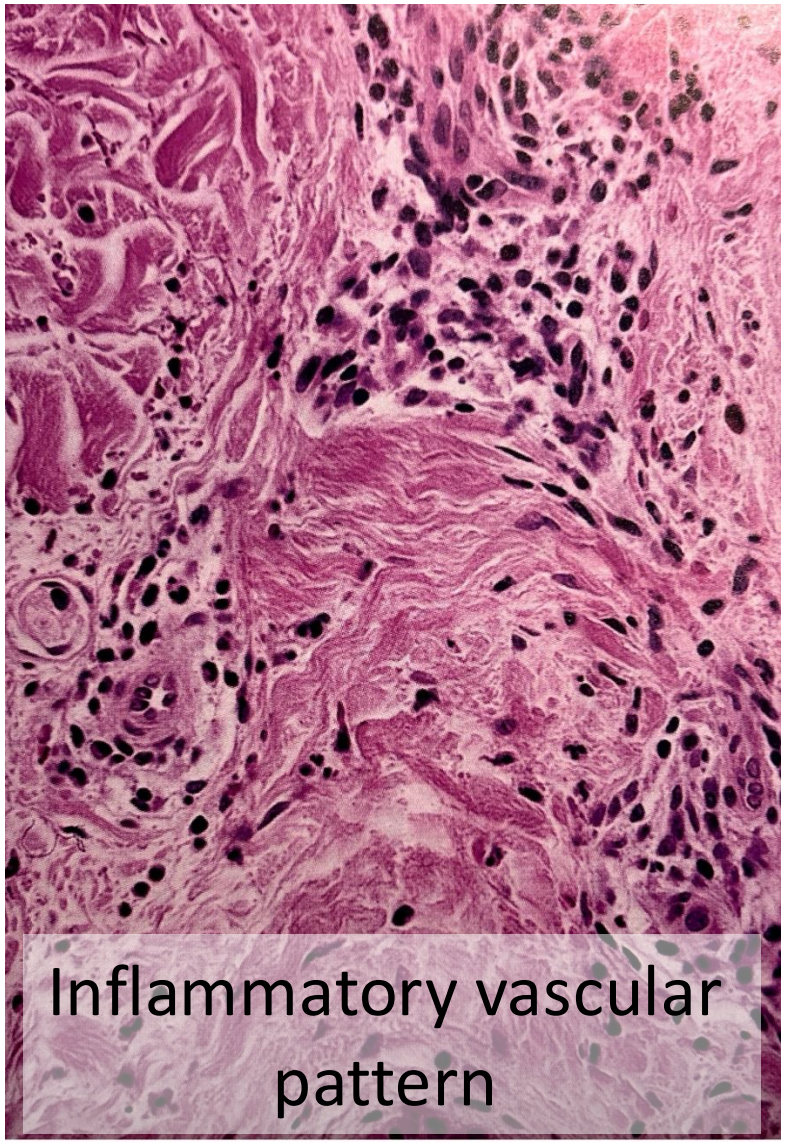


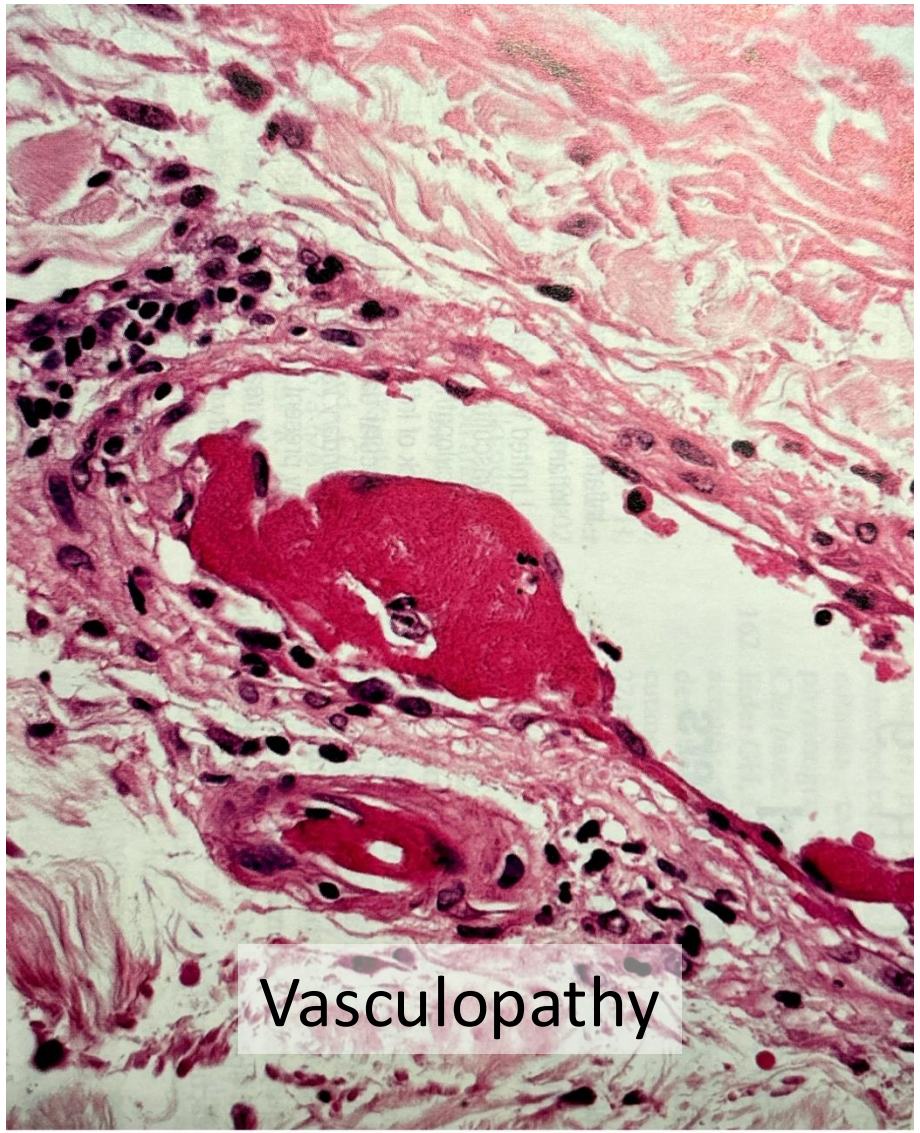
What are the definitions of vascular injury?



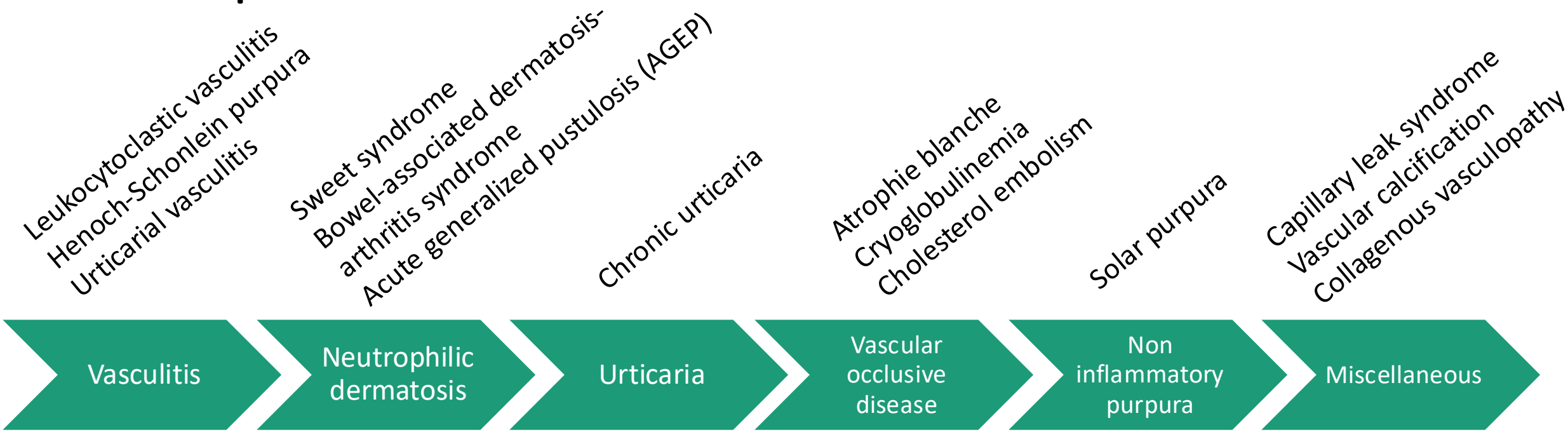
What are the three characteristics of *primary* vascular injury?







Conceptual overview: Vasculitis and related disorders



Fibrinoid necrosis and Inflammation

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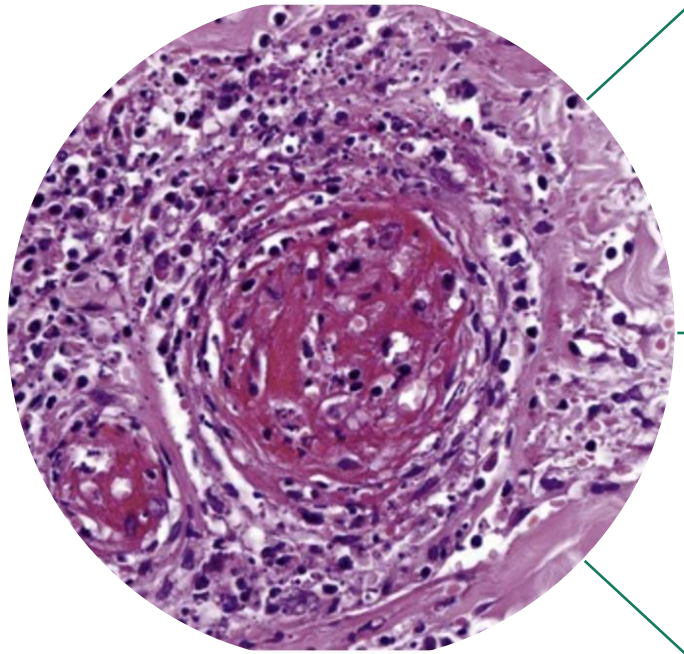
Small-vessel vasculitis



Leukocytoclastic vasculitis

- Bacterial/Rickettsial/fungal/viral
- Immune-complex
  - Henoch-Schoenlein purpura
  - Urticarial vasculitis
- Infection associated
- Drug induced
- Etc.

ANCA Associated vasculitis

- Wegner granulomatosis
- Microscopic polyarteritis
- Churg-Strauss syndrome

Localized fibrosing vasculitis

- Erythema elevatum diutinum
- Granuloma faciale

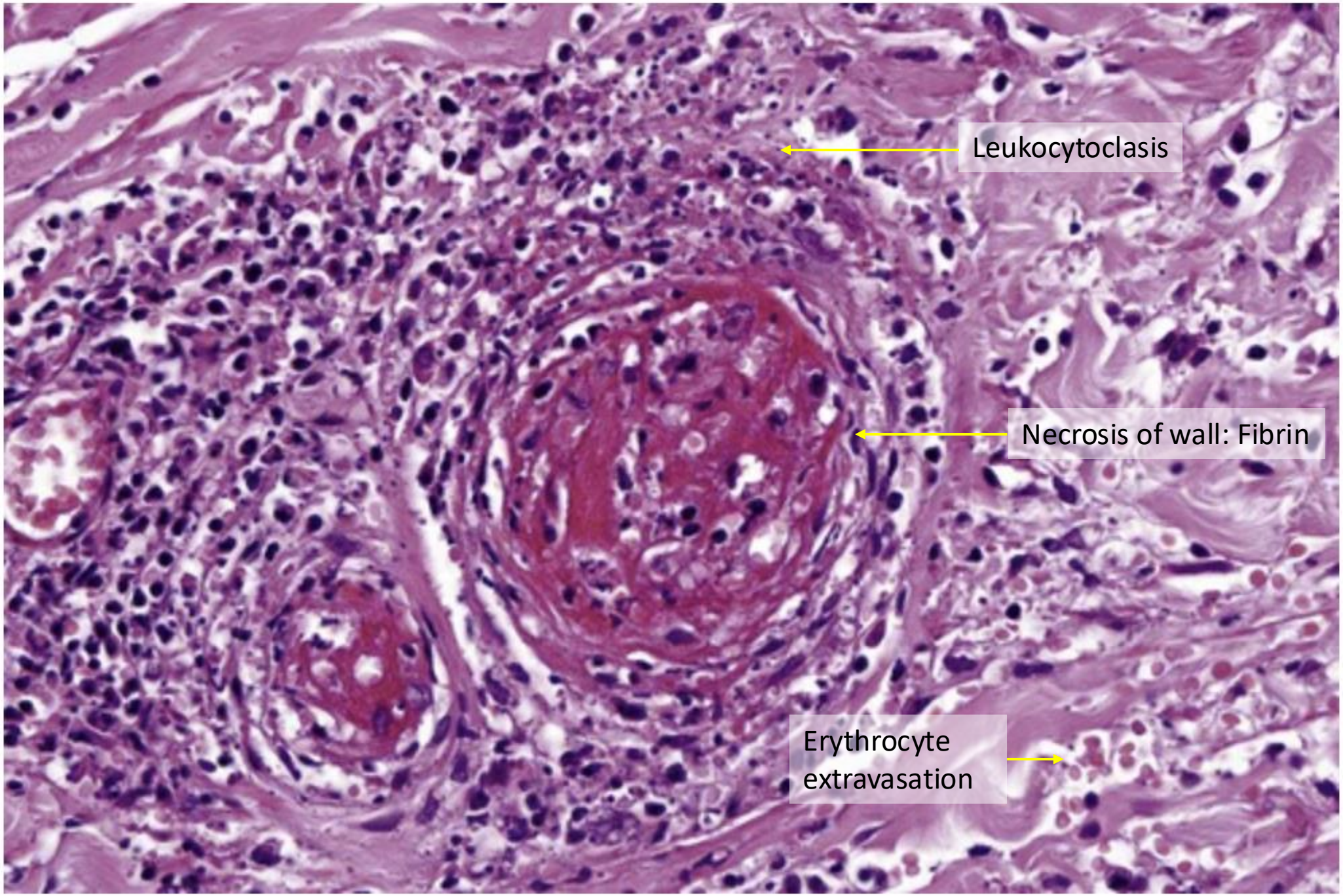
What are the clinical and histologic definitions of leukocytoclastic vasculitis?

Clinical

- Vascular damage:
  - Edema
  - Livedo reticularis (net-like pattern of red-blue skin discoloration)
  - Subcutaneous hemorrhage, or purpura
    - Petechiae, < 3-mm diameter
    - Ecchymoses, larger
    - Palpable purpura (raised, inflammatory infiltrate) [Punch Biopsy]
  - Severe
    - Vascular occlusion --> ischemia --> necrosis --> gangrene --> ulceration

Histologic

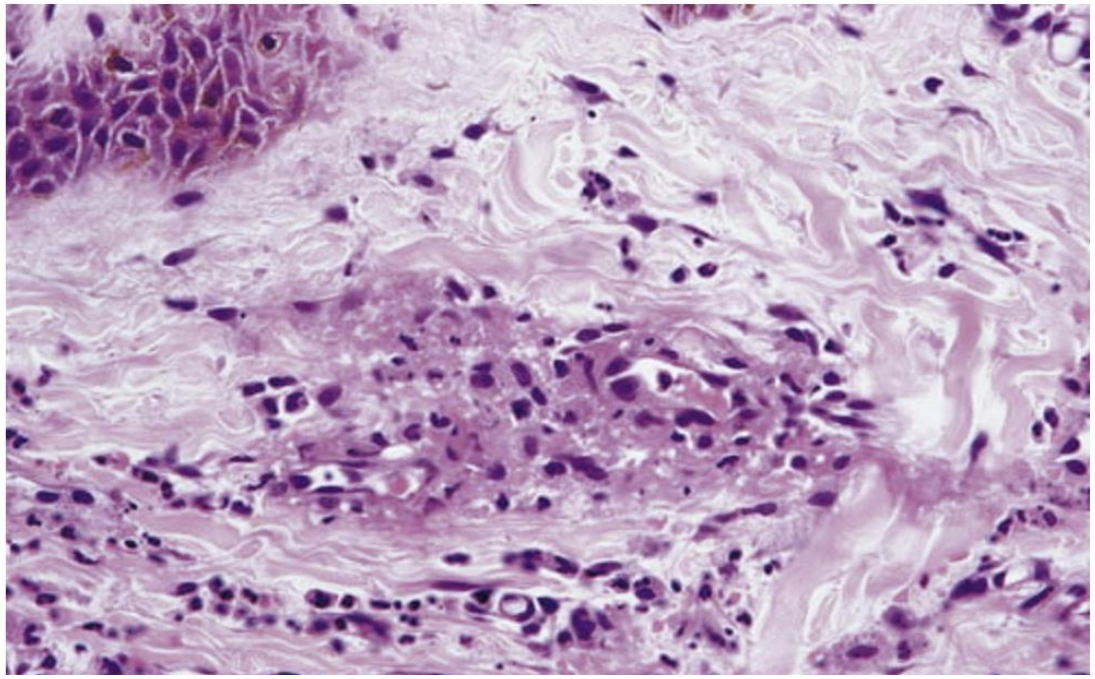
- Necrosis of vessel wall with deposition of fibrinogen material
- Leukocytoclasis (nuclear debris from infiltrating neutrophils)
- Karyorrhexis (nuclear dust)
- Extravasation of erythrocytes
- Endothelial cell swelling
- Luminal thrombosis
- Edema

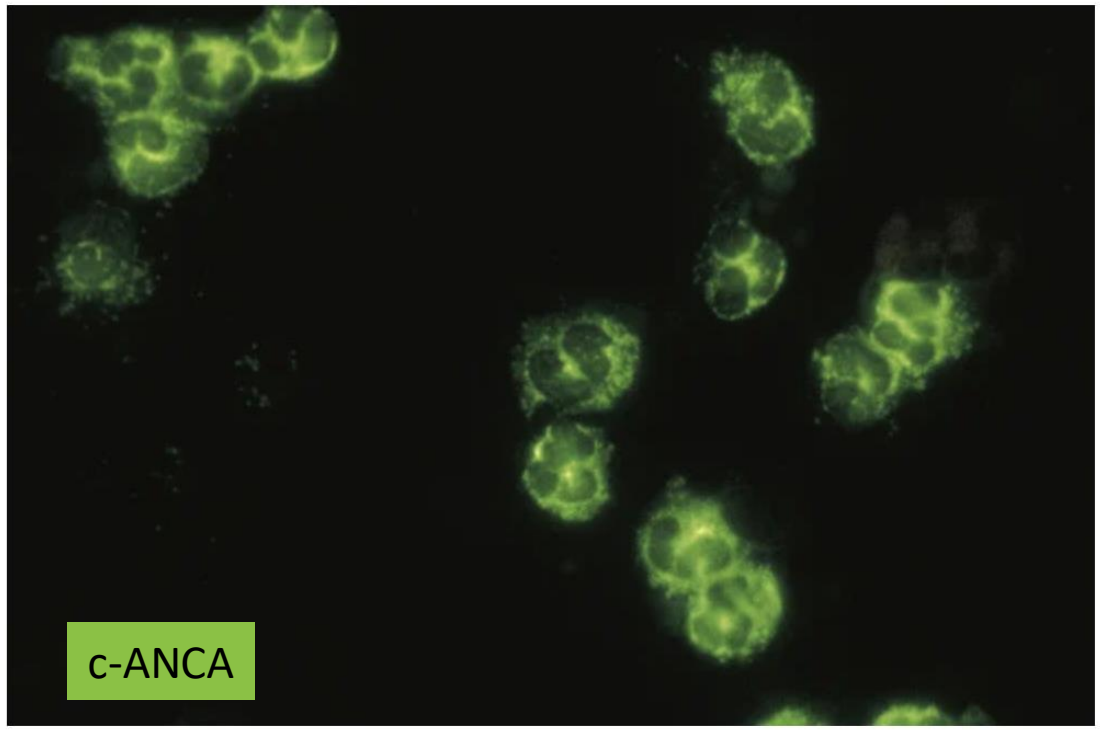

Leukocytoclasis
Necrosis of wall: Fibrin
Erythrocyte extravasation

Antineutrophil cytoplasmic antibodies (ANCA)-associated systemic vasculitis

- Serologic marker to detect specific autoantibody
- Indirect immunofluorescence (IIF) of normal peripheral blood neutrophils
- Followed by enzyme-linked immunosorbent assay (ELISA)
- IIF two patterns:
  - Cytoplasmic (c-ANCA); proteinase 3
  - Perinuclear (p-ANCA); myeloperoxidase

Granulomatosis with polyangiitis (Wegener)

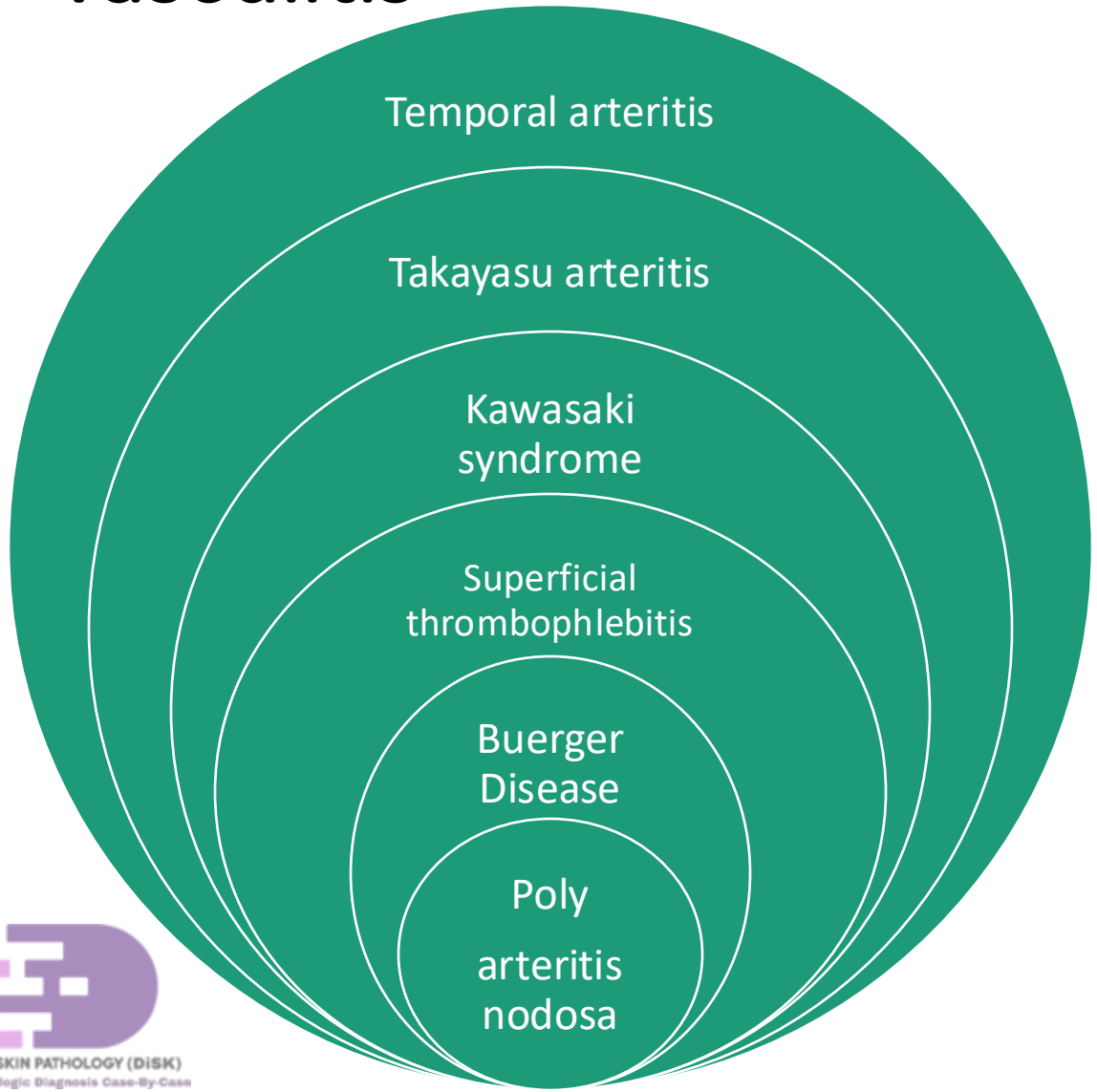


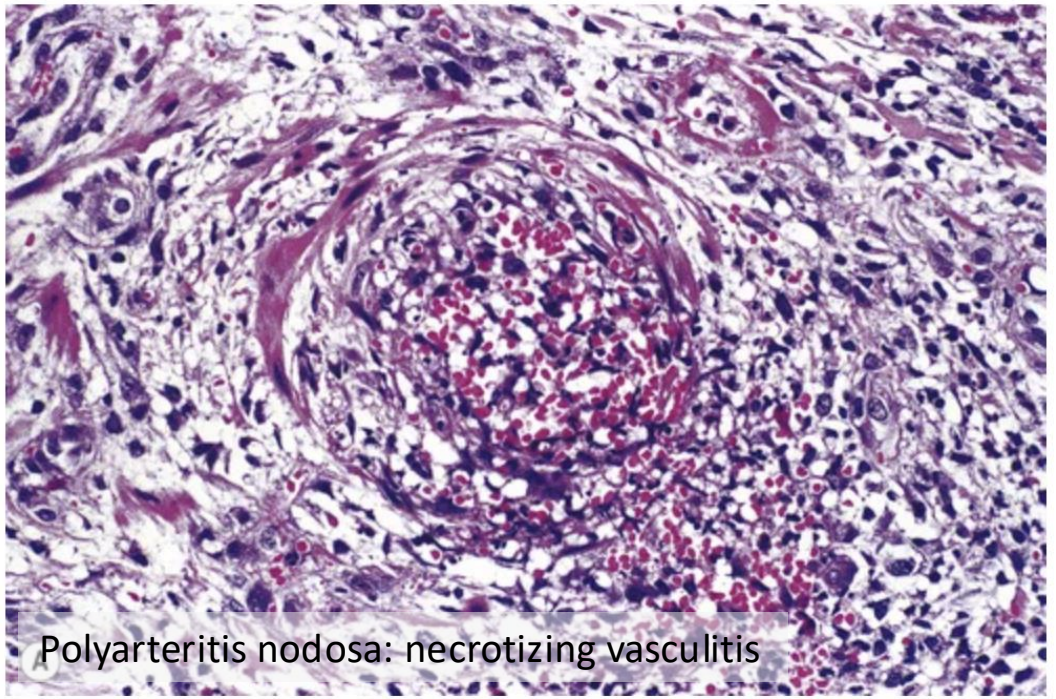


What are ANCA-positive vasculitides?

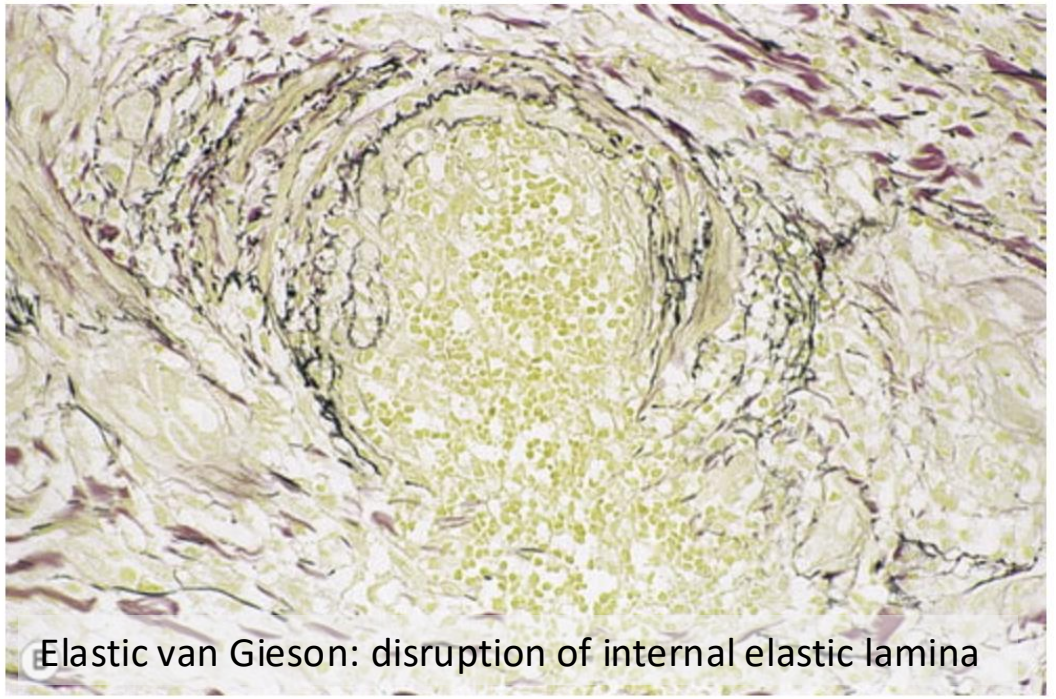
DISEASE PROCESS	ANTI-MYELOPEROXIDASE (pANCA)	ANIT-SERINE PROTEINASE (cANCA)
Wegener granulomatosis	Rare (5%)	Common (80%)
Microscopic polyarteritis	Common (50-60%)	Common (45%)
Churg-Strauss syndrome	Common (70%)	Rare (7%)

Medium and large-seized vasculitis



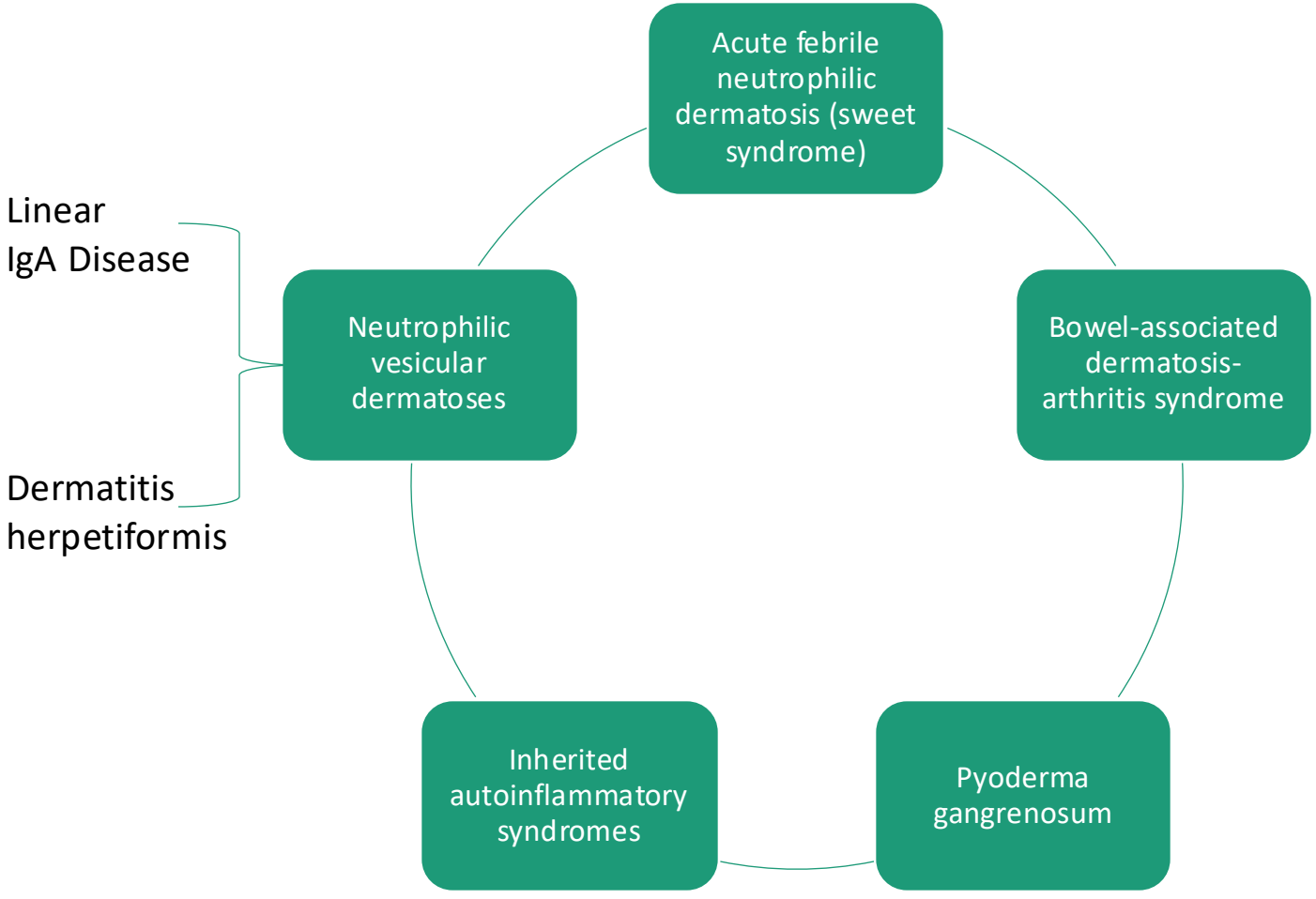


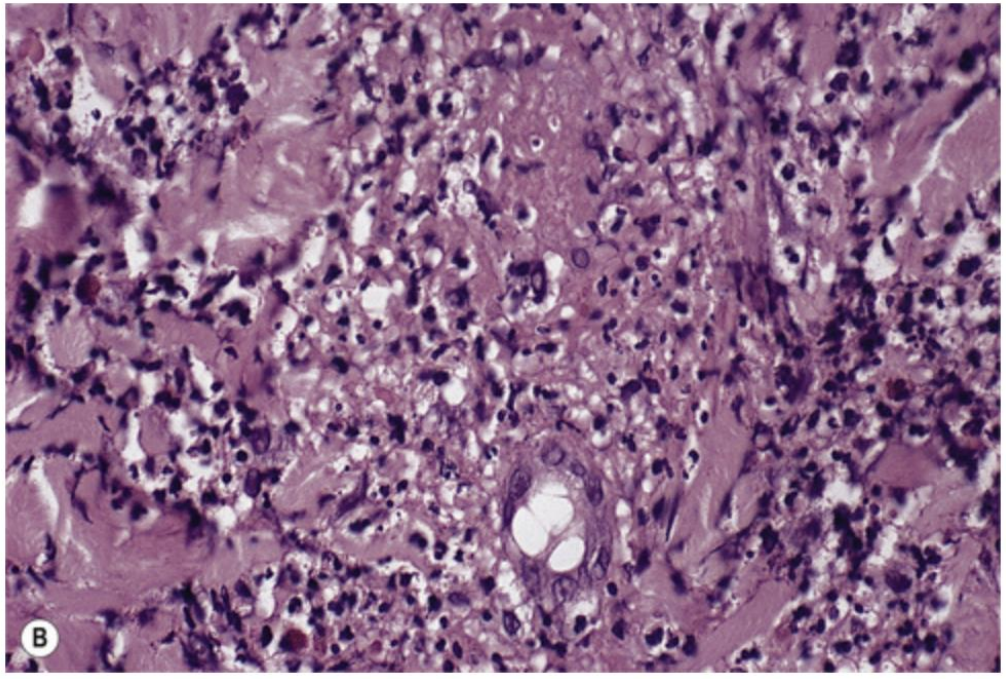
Polyarteritis nodosa: necrotizing vasculitis



Elastic van Gieson: disruption of internal elastic lamina

Neutrophilic dermatoses: Neutrophilic vascular reaction (not necrotizing vasculitis)





Sweet syndrome: numerous neutrophils surrounding blood vessel, no fibrinoid necrosis

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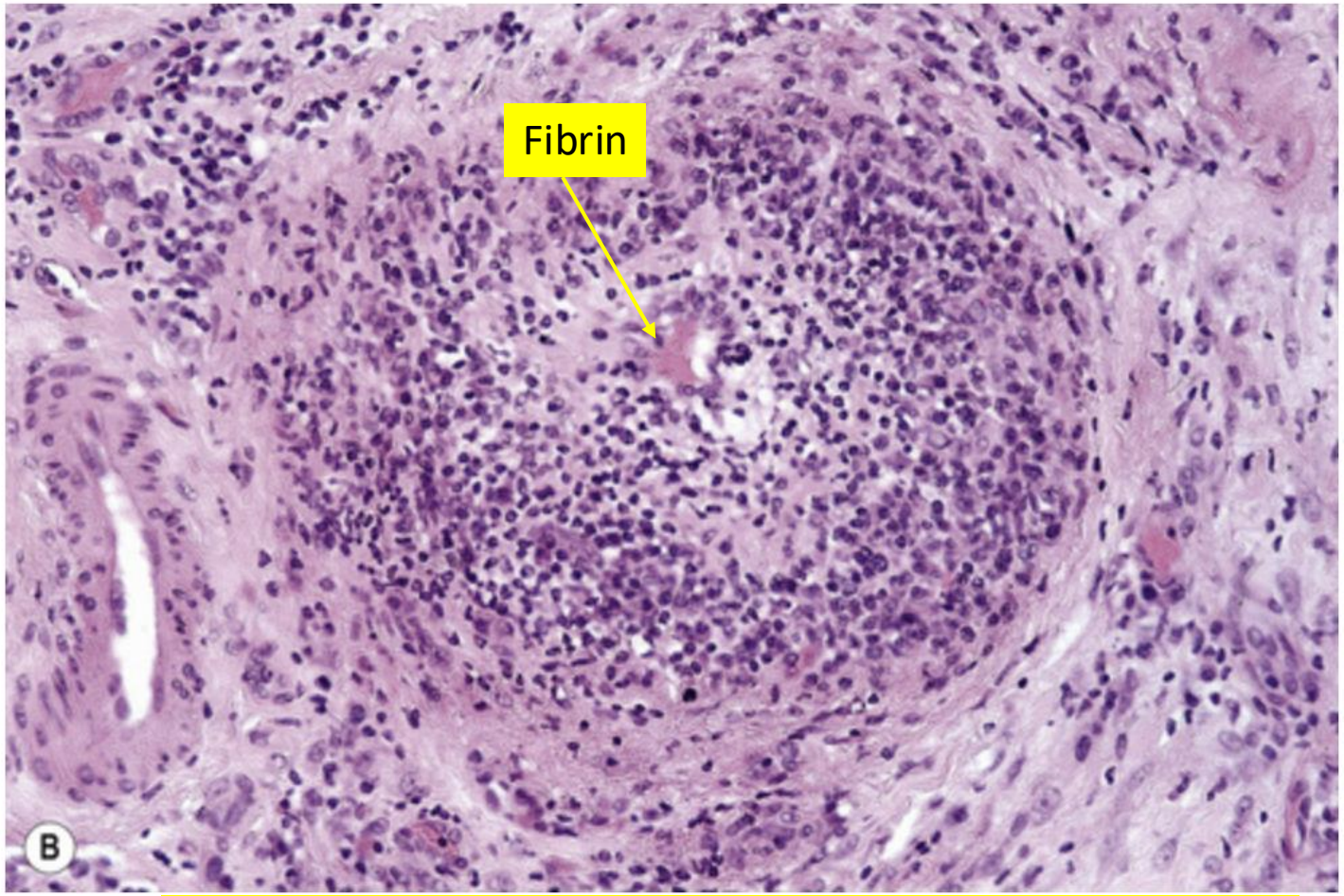
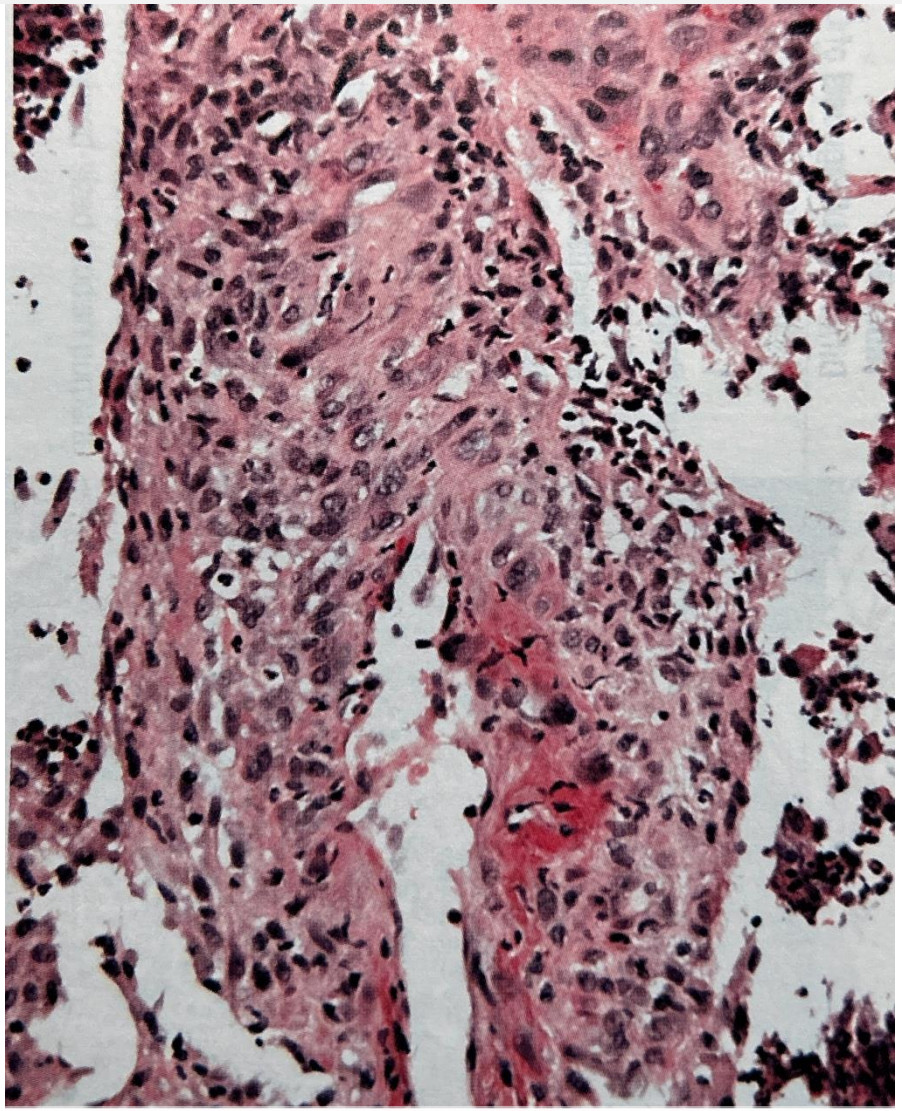
Lymphocytic vasculitis: vascular damage + lymphocytes ± minimal fibrin

- Pernio (chilblains)
- Arthropod bite
- Hypersensitivity reaction
- Connective tissue diorder
- Pigmented purpuric dermatosis
- Lymphomatoid papulosis/lymphoma
- Polymorphous light eruption



Numerous lymphocytes surround a blood vessel; no leukocytoclasis



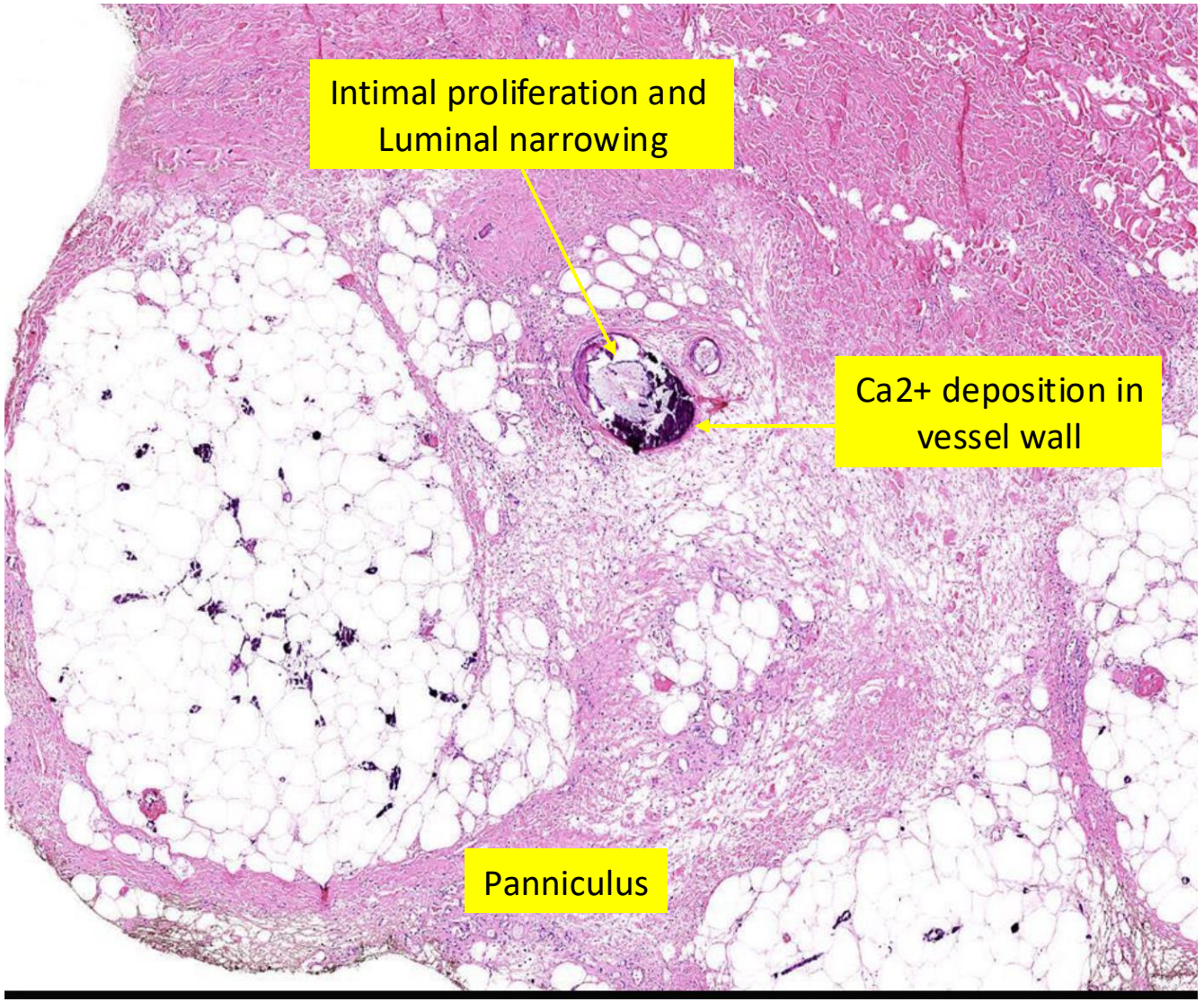
Perivascular histiocytic/granulomatous infiltrate and focal vascular injury

Differential diagnosis of granulomatous vasculitis

Temporal arteritis	Infection	Wegener granulomatosis
Churg-Strauss syndrome	Cutaneous Crohn disease	Drug reaction
Connective tissue disease	Granuloma annulare	Necrobiosis lipoidica
Paraneoplastic phenomena	Angiocentric T-cell lymphoma (lymphomatoid granulomatosis)	Erythema nodosum, and EN-like reactions

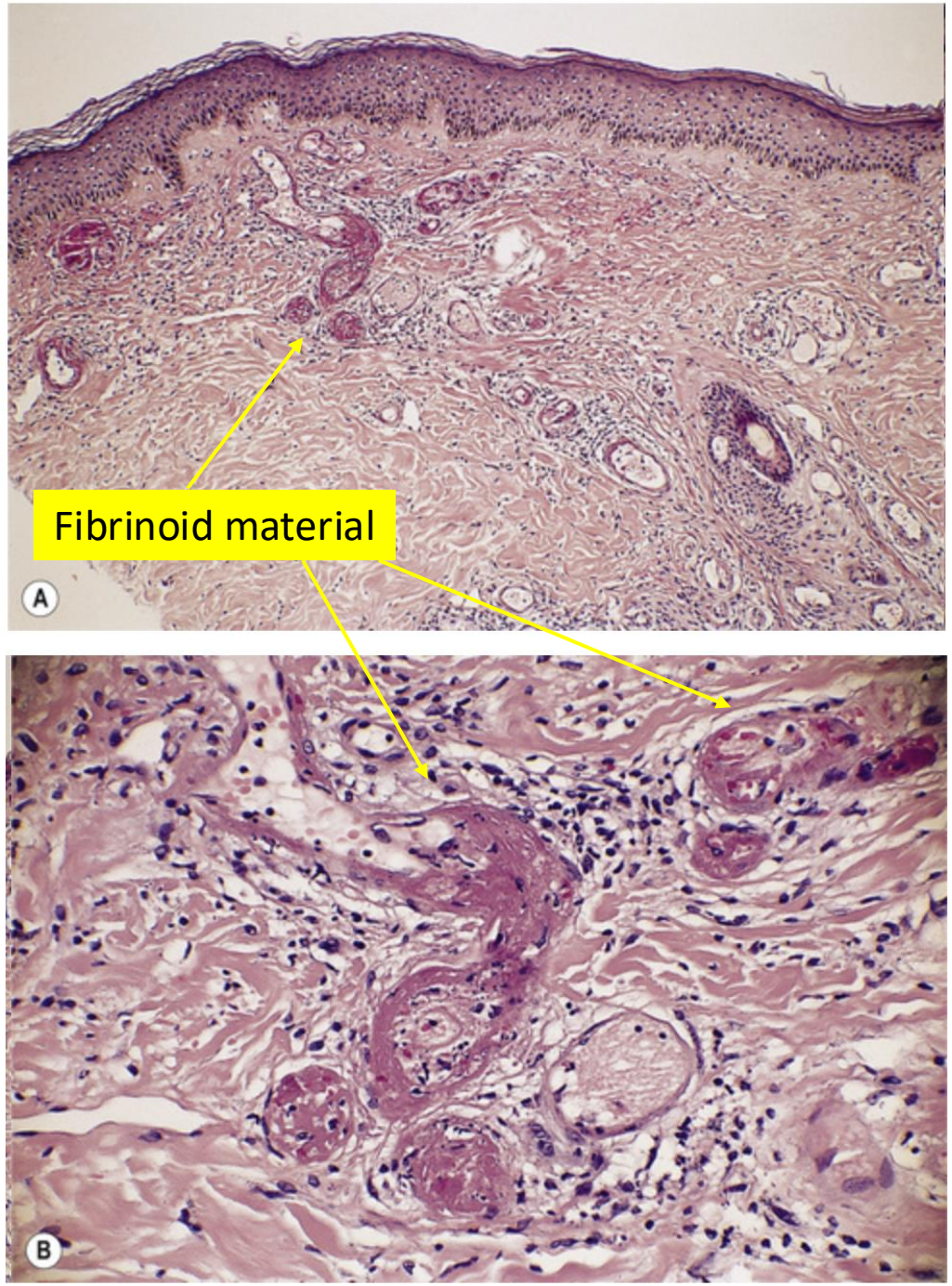
Vascular occlusive disease: vasculopathic reaction and pseudovasculitis

- Cryoglobulinemia
- Cholesterol embolism
- Livedo reticularis
- Atrophie blanche
- Degos syndrome
- Calciphylaxis



Atrophie blanche (livedoid vasculopathy) white atrophy

- Thrombogenic vasculopathy
- Decreased fibrinolytic activity (tissue plasminogen activator release defective)
- “Thrombogenic state” in several conditions
  - Lupus-type anticoagulant
  - Increased anticardiolipin antibody
- Painful, purpuric ulcers with reticular pattern on the lower extremities
- Histopathology:
  - Fibrinoid material
  - Minimal lymphocytic inflammation
  - Necrotic blood vessels
  - No Leukocytoclasis
  - Extravasation of erythrocytes
  - No edema



Unknown cases

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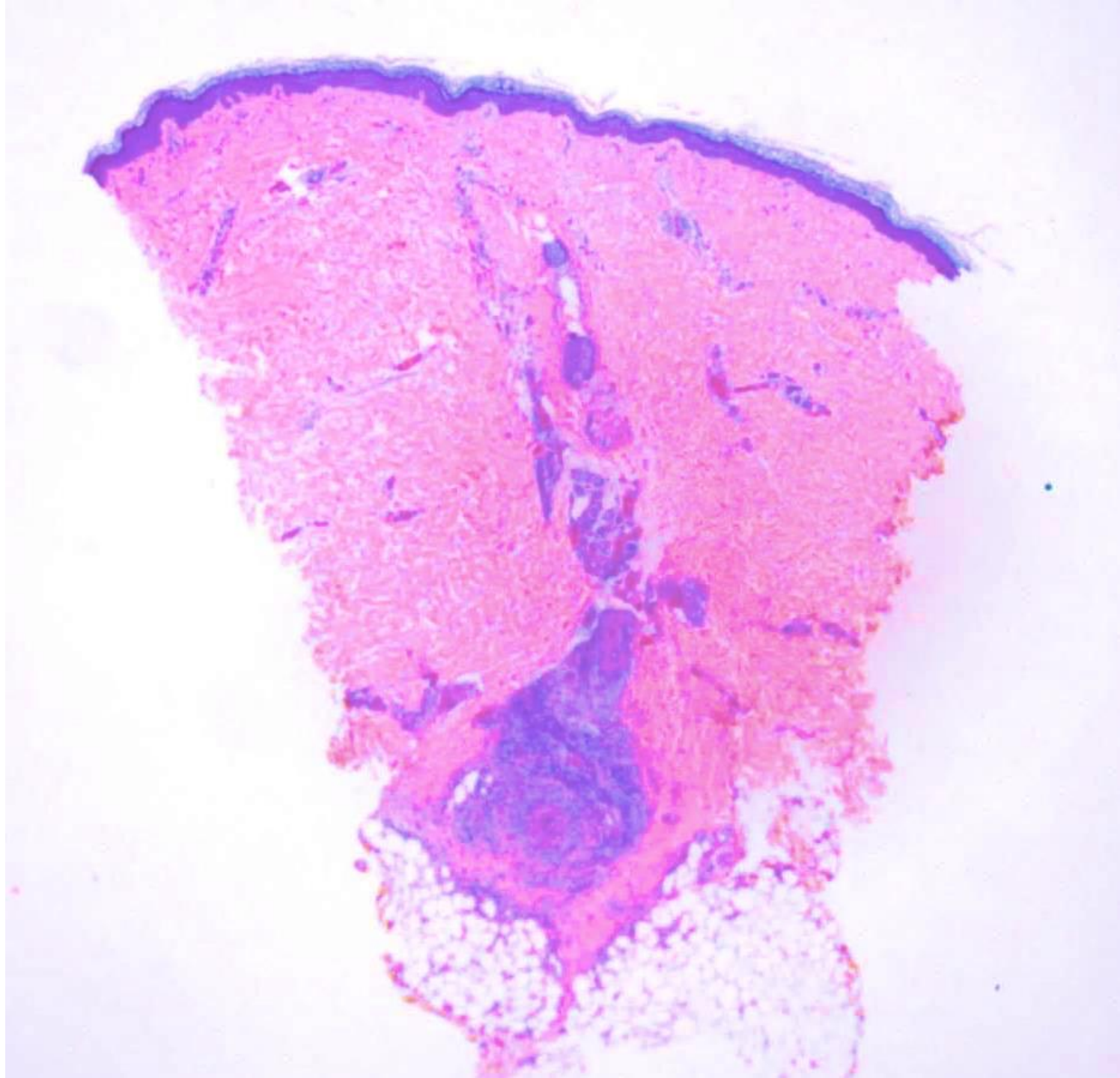

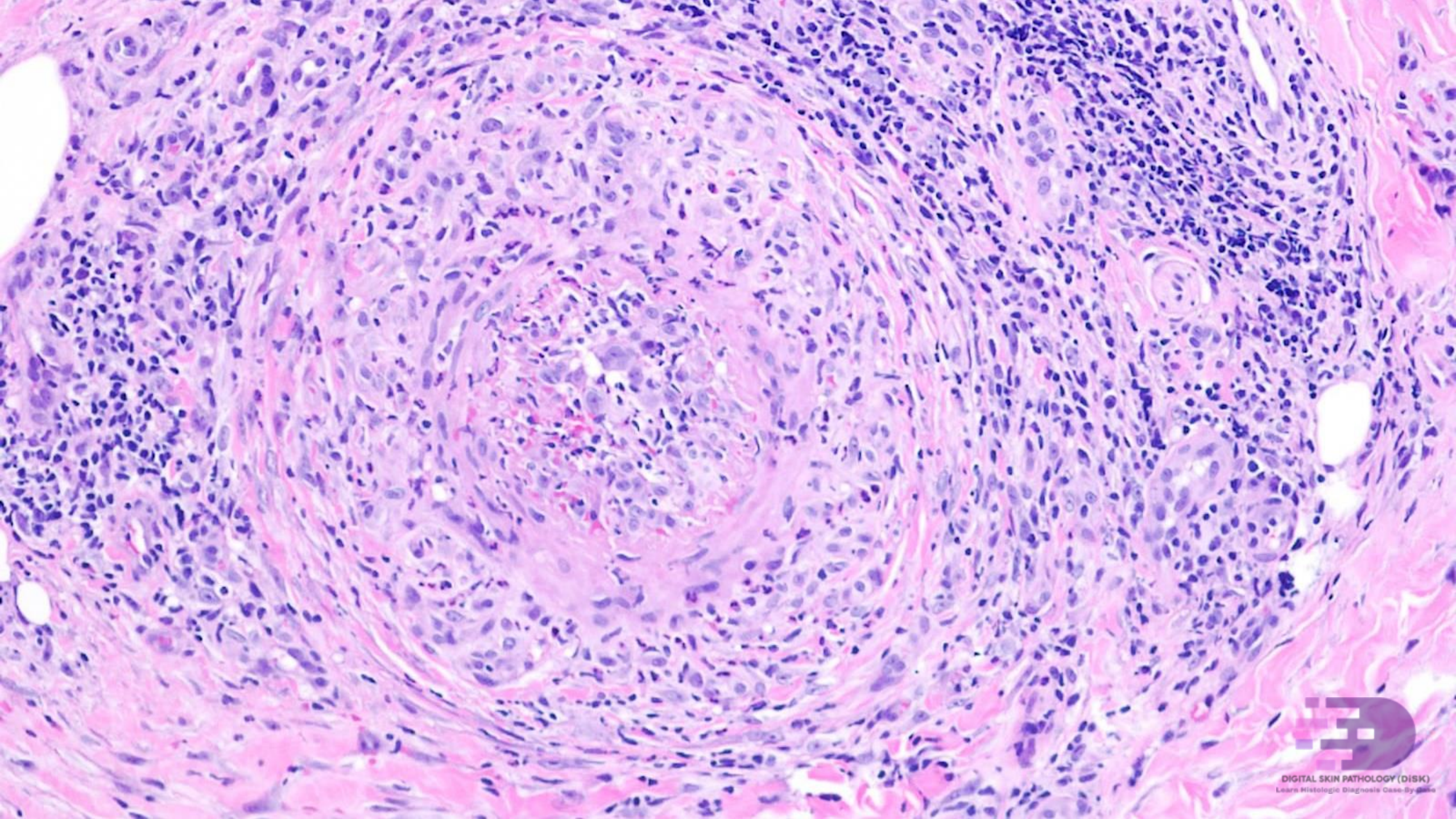
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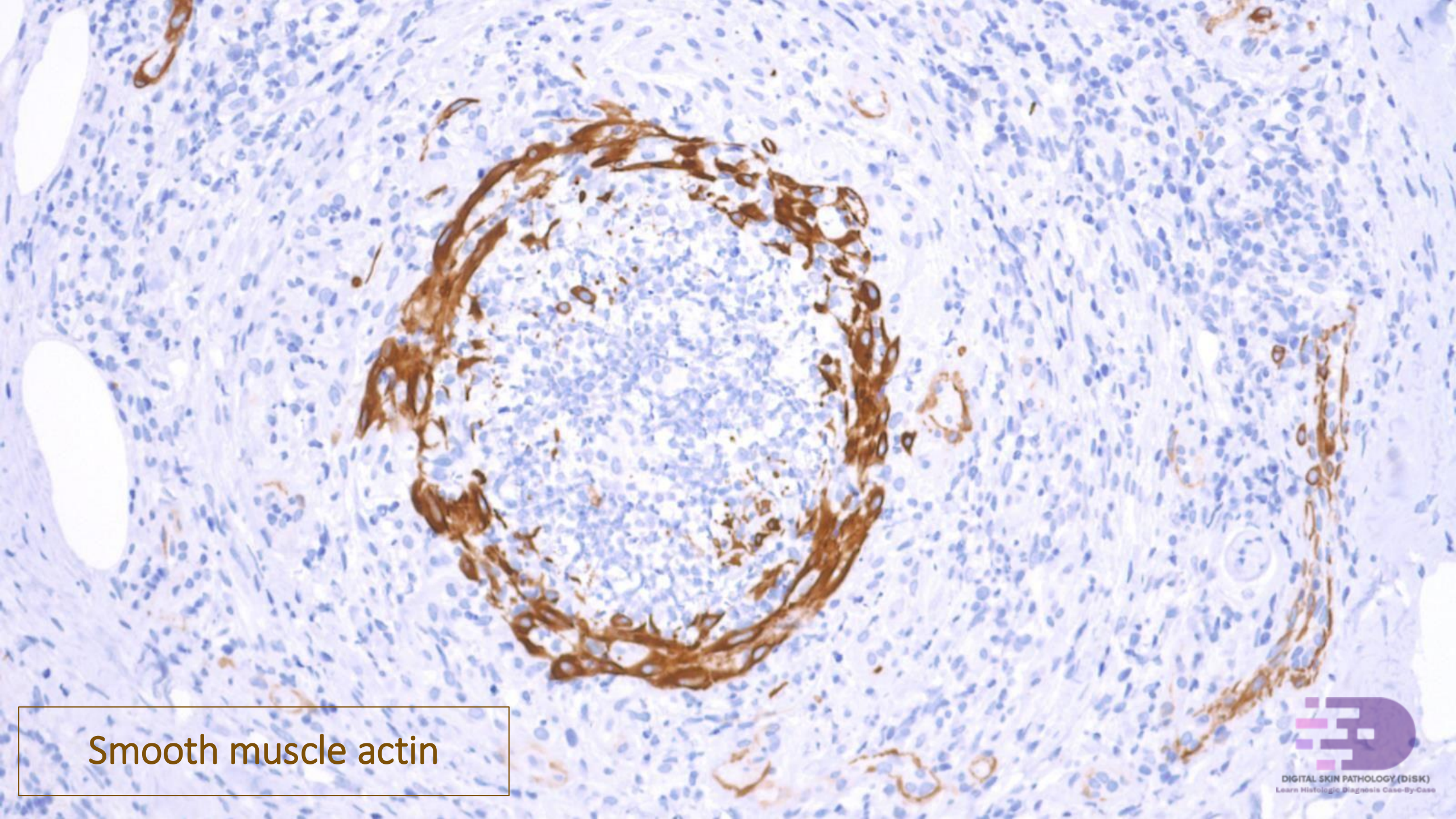
Smooth muscle actin
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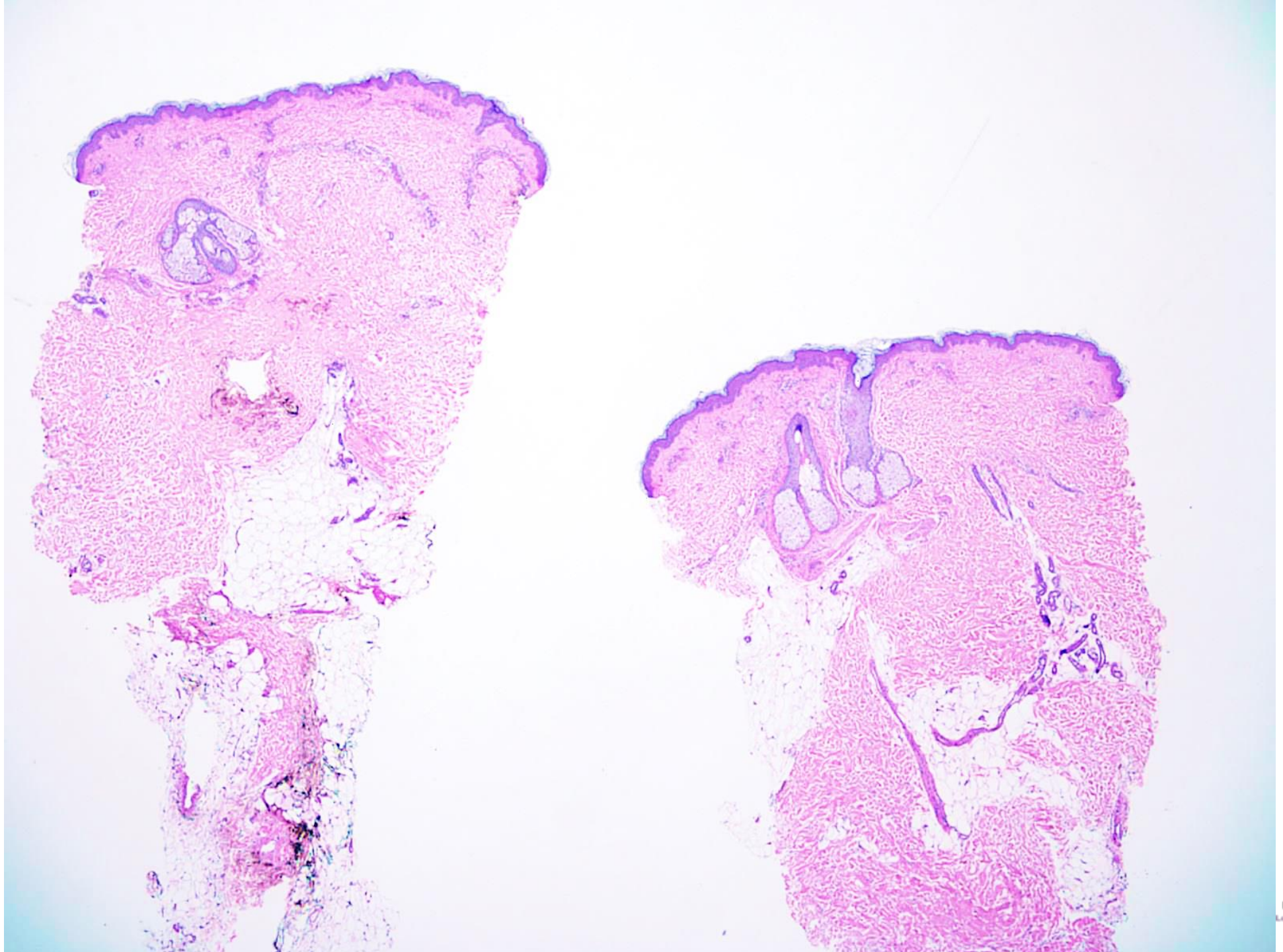
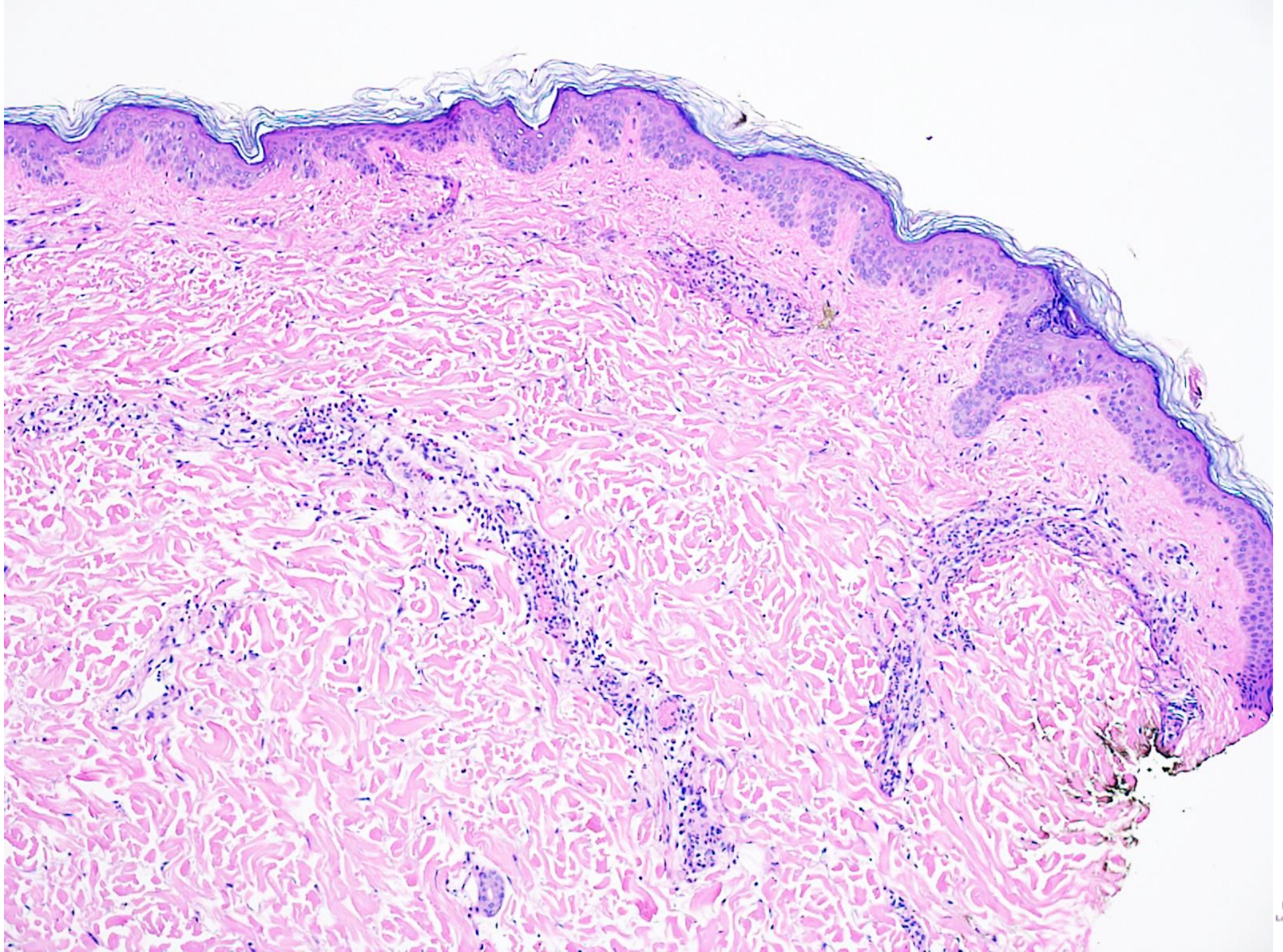
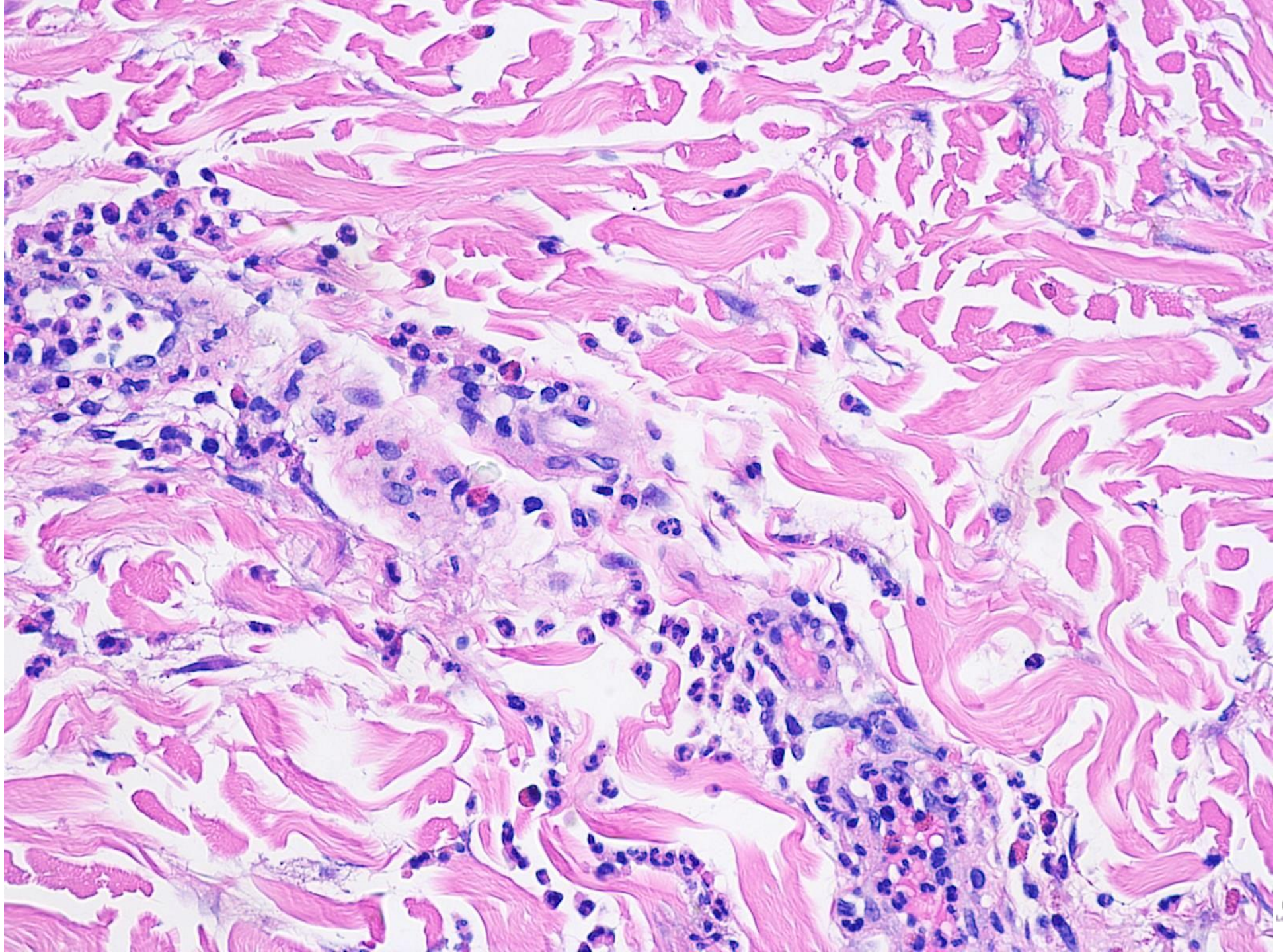
Polyarteritis nodosa

- 64/F LEFT ARM PUNCH with h/o NLD
- The pathology report pertaining to the prior biopsy from right leg/subcutaneous nodule is noted and reviewed (SGS-21-12351).
- The prior biopsy was sent to Dr. at UCSF Dermatopathology Laboratory for second opinion. His diagnosis was palisaded granulomatous dermatitis with focal vasculitis, probably necrobiosis lipoidica.

- LEUKOCYTOCLASTIC VASCULITIS INVOLVING MEDIUM-SIZED MUSCULAR ARTERY IN DEEP DERMIS.
- The current biopsy demonstrates a different histopathology than the prior in that there is no panniculitis. There is only pure leukocytoclastic vasculitis involving medium-sized artery, which can be seen in polyarteritis nodosa. Although necrobiosis lipoidica can demonstrate secondary lymphocytic vasculitis, the current findings are diagnostic for leukocytoclastic vasculitis and do not support necrobiosis lipoidica.



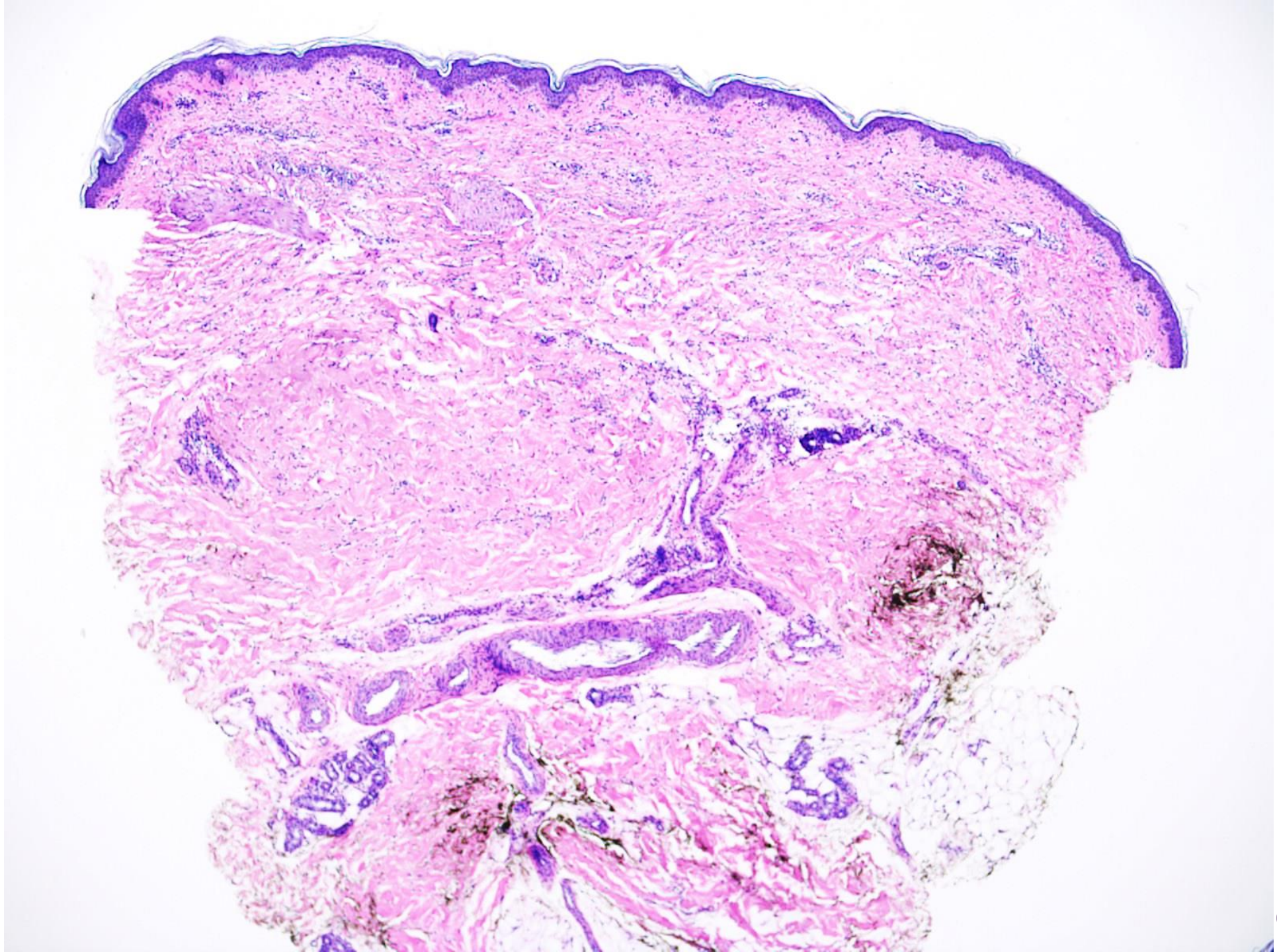


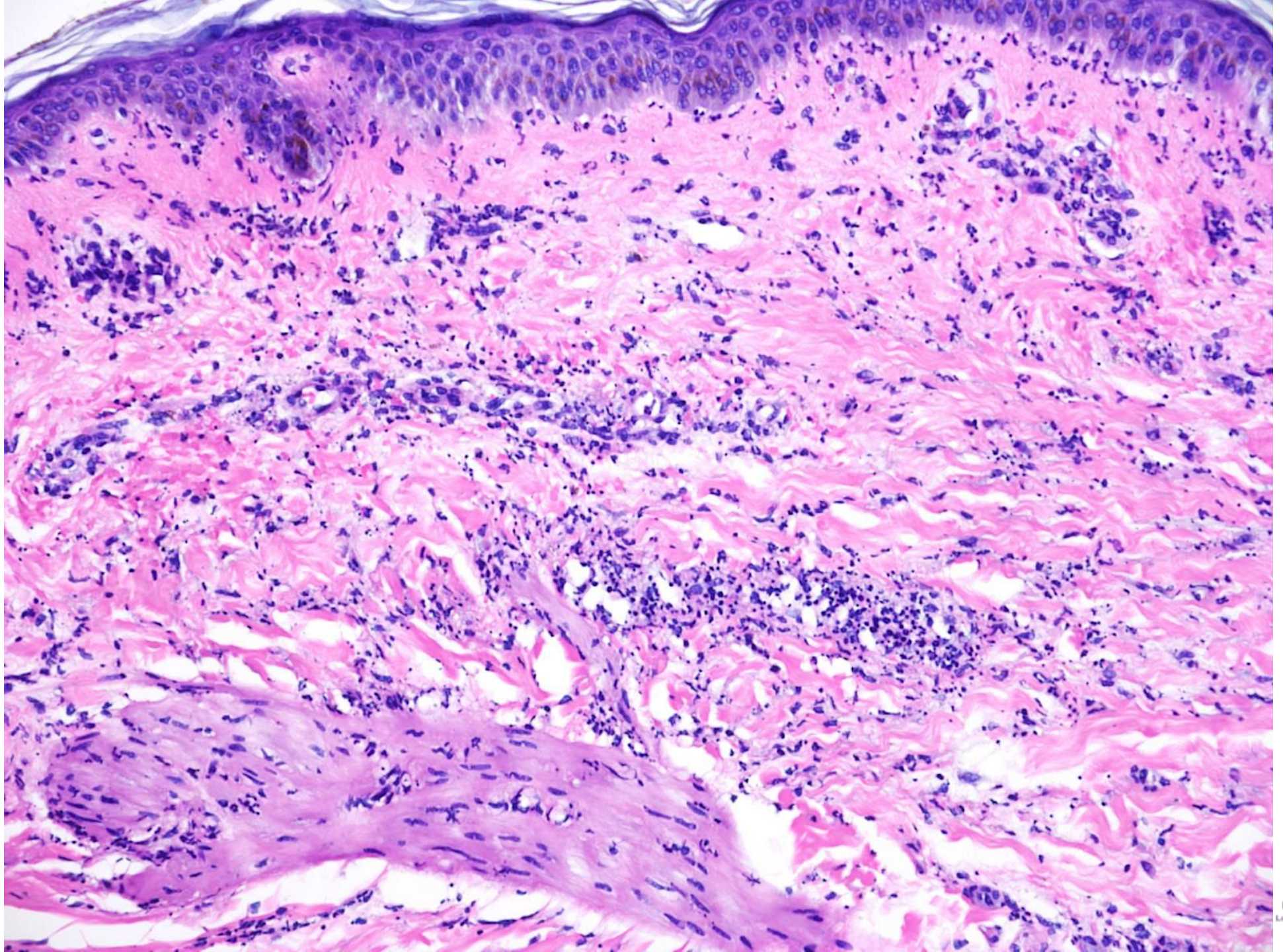


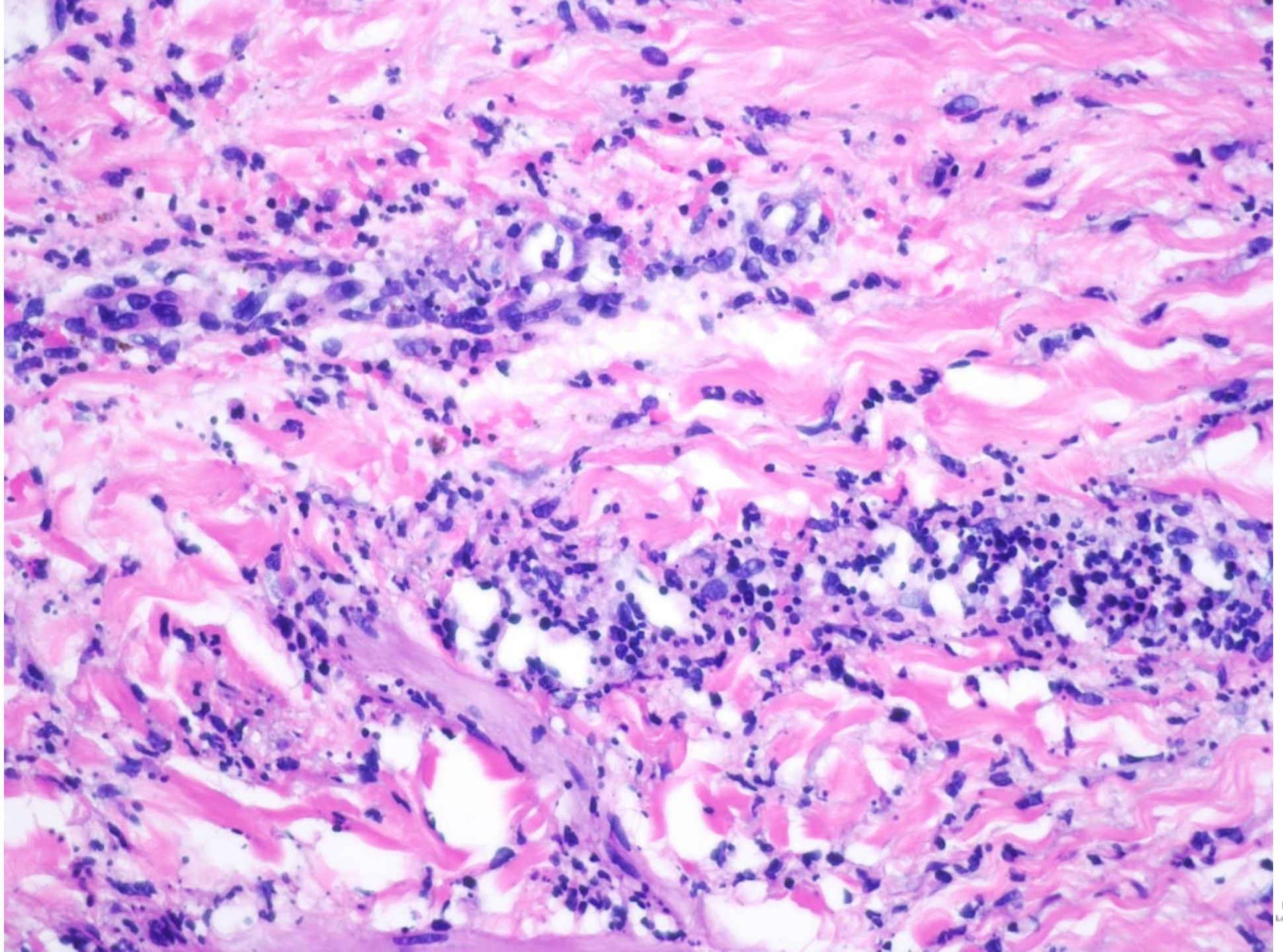
Urticarial Vasculitis

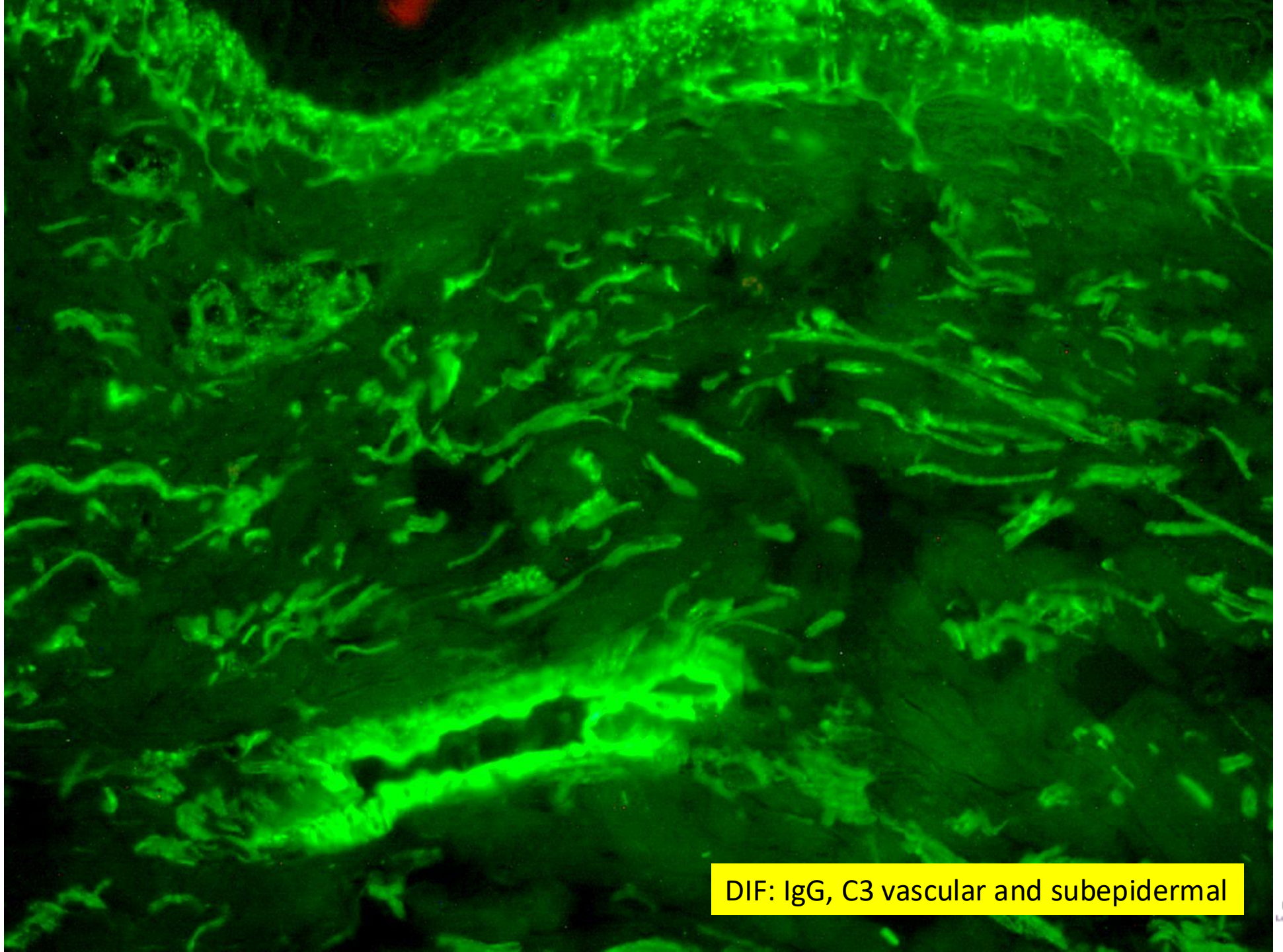
- 34/F RIGHT THIGH PUNCH BIOPSY
- L50.1; DIFFUSE URTICARIAL PAPULES, AREAS OF BRUISING, R/O URTICARIAL VASCULITIS

- COMPATIBLE WITH URTICARIAL VASCULITIS. Overall, the findings support the clinical impression of urticarial vasculitis, early phase. The differential diagnosis includes acute urticaria. Diagnostic features of established leukocytoclastic vasculitis are absent.









LCV in SLE: Lupus vasculitis

- L30.9; 41/F RIGHT THIGH H&E and DIF. PATIENT WITH A HISTORY OF SLE COMPLICATED BY NEPHROTIC SYNDROME AND RHEUMATOID ARTHRITIS WITH AN ACUTE ONSET RASH THAT INCLUDED ARCUATE PLAQUES, EDEMATOUS PAPULES AND PLAQUES ON THE CHEST AND BACK WITH NO MALAR RASH

- LEUKOCYTOCLASTIC VASCULITIS, INVOLVING SMALL-CALIBER BLOOD VESSELS IN SUPERFICIAL-MID DERMIS. The findings of leukocytoclastic vasculitis in this clinical context may represent vasculitis in systemic lupus erythematosus, which can be seen in roughly 11-30% of patients with systemic lupus erythematosus, supported by positive lupus band test and vascular reaction according to the results for DIF.

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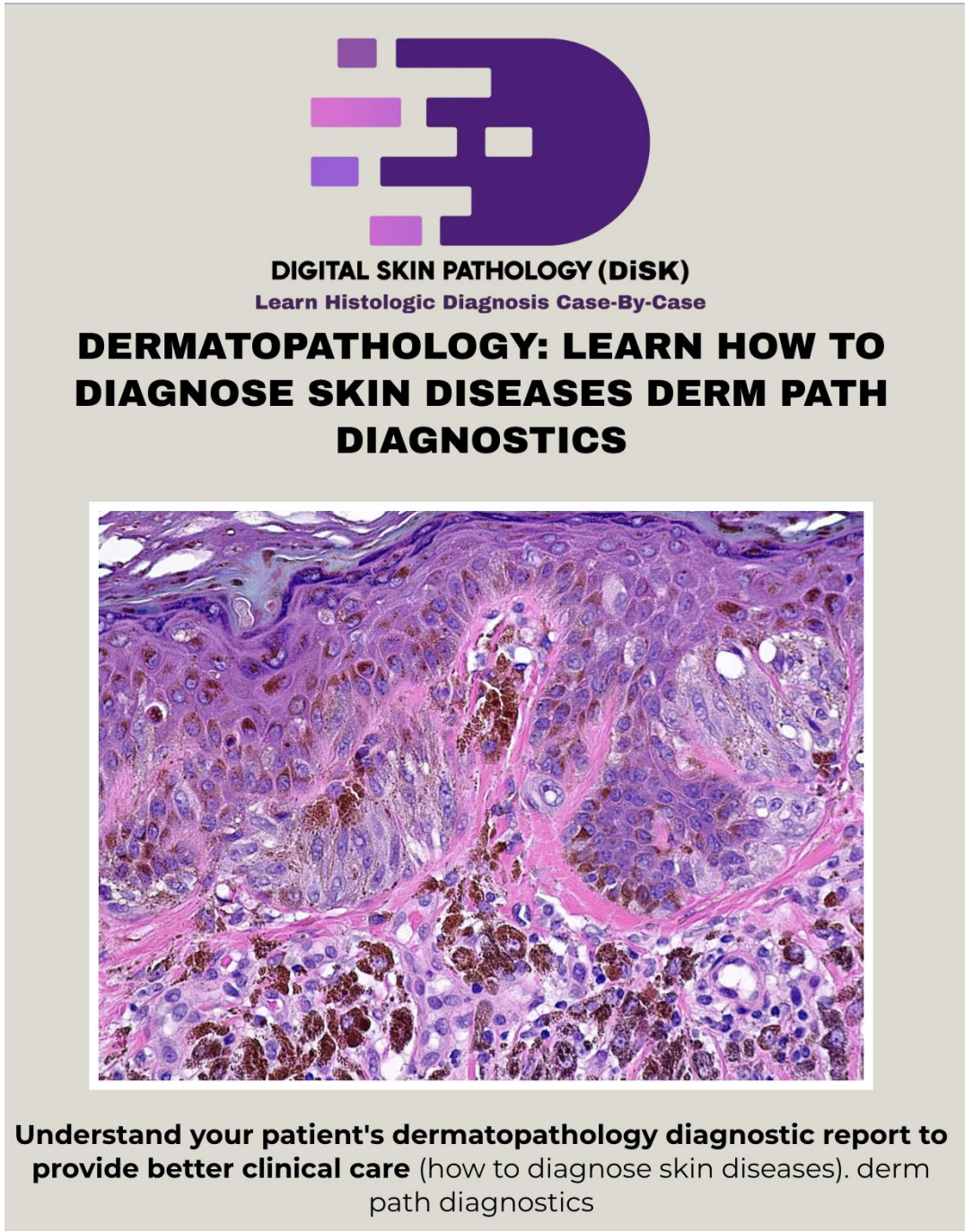

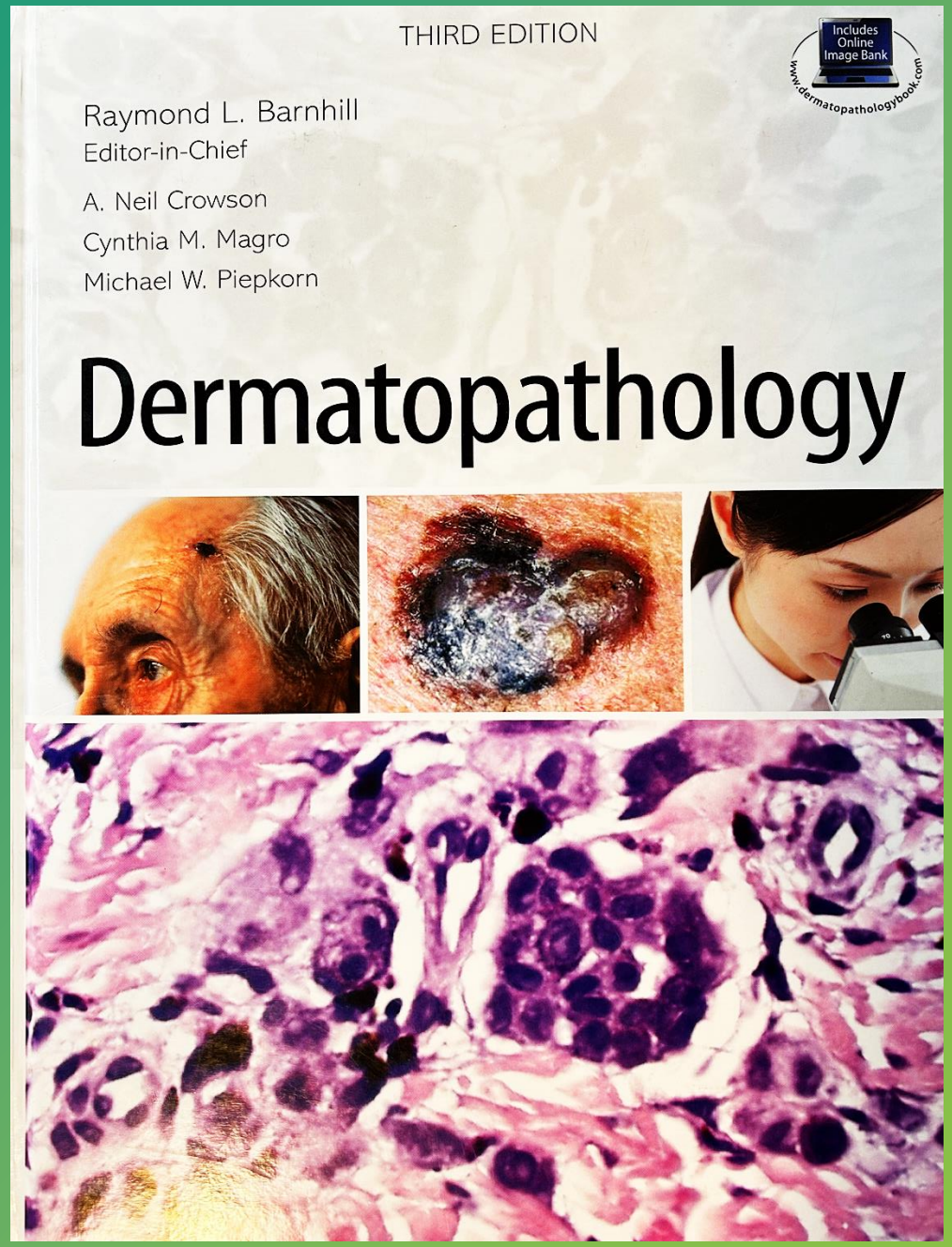

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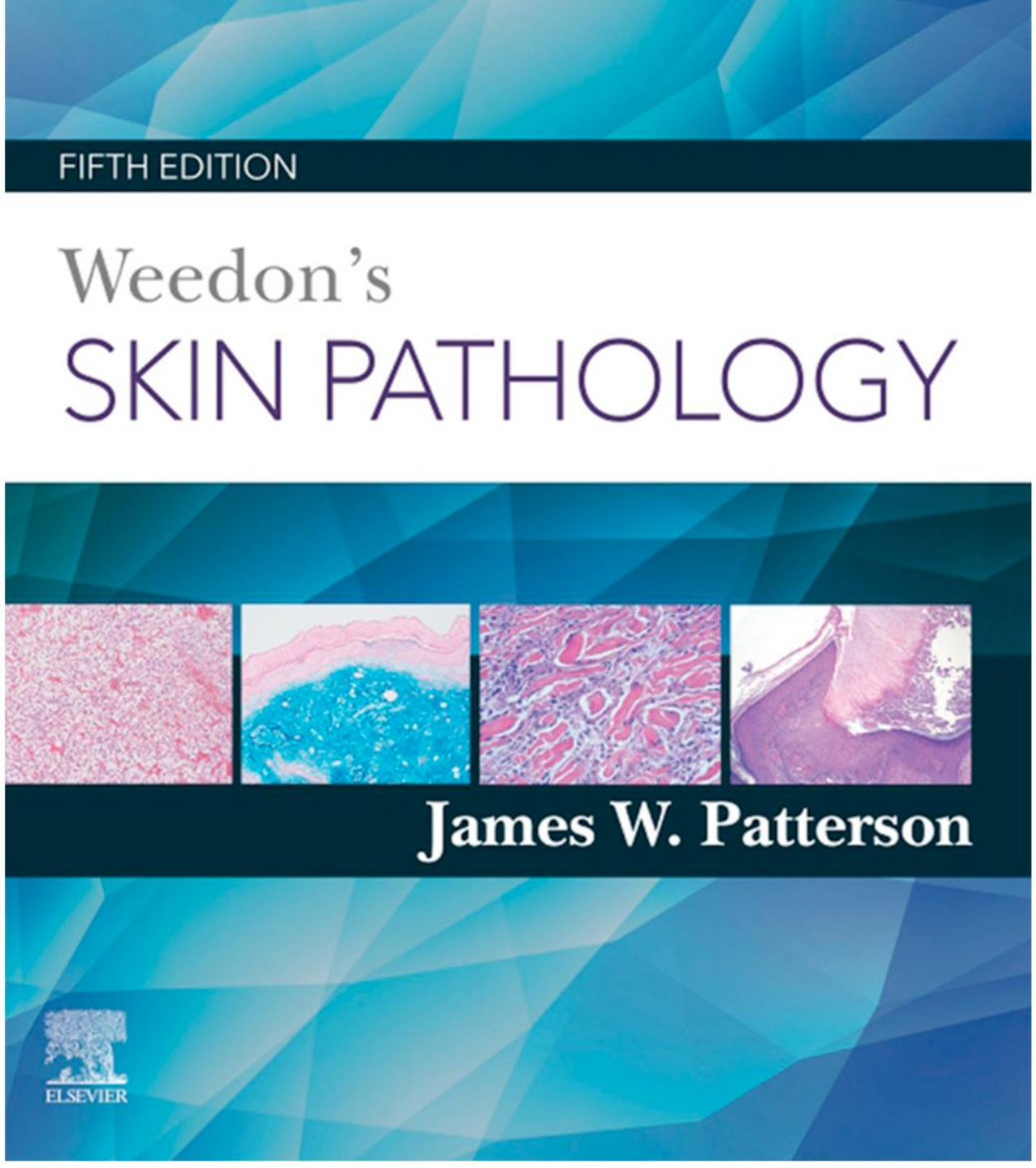
  - A. Neil Crowson
  - Cynthia M Magro
  - Michael W Piepkorn



References

- Weedon's skin pathology
- McKee's pathology of the skin