Idiopathic Connective Tissue Diseases (Autoimmune Dermatitis)

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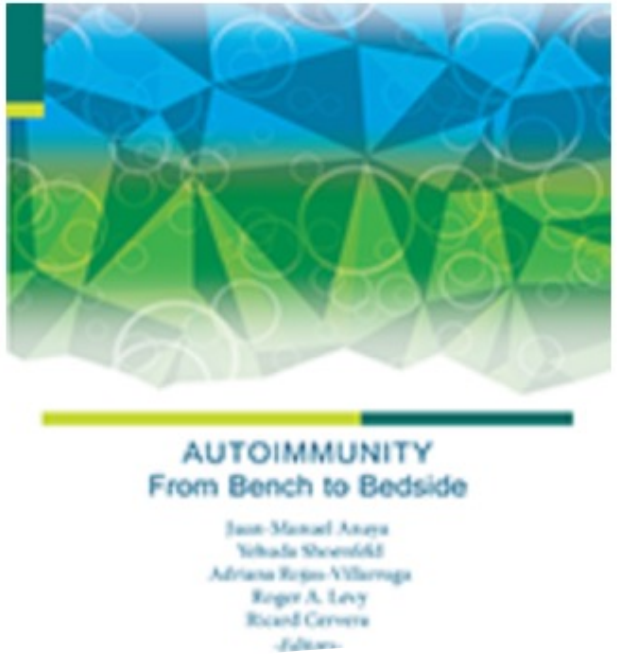

Autoimmunity

National Library of Medicine Bookshelf

From Bench to Bedside

Editors: Juan-Manuel Anaya, MD, PhD, Yehuda Shoenfeld, MD, FRCP (UK), Adriana Rojas-Villarraga, MD, Roger A. Levy, MD, PhD, and Ricard Cervera, MD, PhD, FRCP (UK).

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Introduction: how to define dermatological autoimmune diseases?

Classification system that provides for five types of diseases as follows: 1) monogenic autoimmune diseases, 2) polygenic diseases exhibiting a prominent autoimmune component, 3) monogenic autoinflammatory diseases, 4) polygenic disease exhibiting a prominent autoinflammatory component, and 5) mixed pattern diseases.

Most autoimmune skin diseases belong to the second category, as is the case for autoimmune bullous disease (pemphigus and pemphigoid), and one example of autoinflammatory skin disease is psoriasis.

How to define dermatological autoimmune diseases?

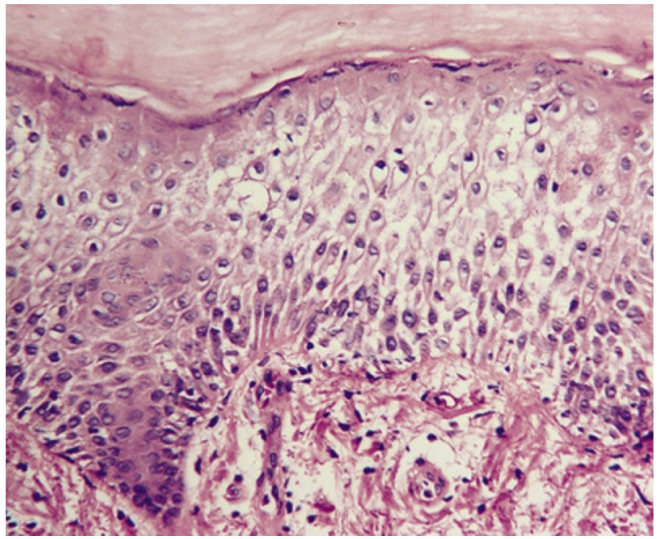
Autoimmunity

- A self-directed inflammation caused by aberrant dendritic cells and T and B cell behaviors that disrupt tolerance, resulting in an adaptive immune response that plays a central role in the phenotypical clinical expression of autoimmune diseases.
- Pemphigus, pemphigoid, dermatitis hepetiformis, and vitiligo

Autoinflammation

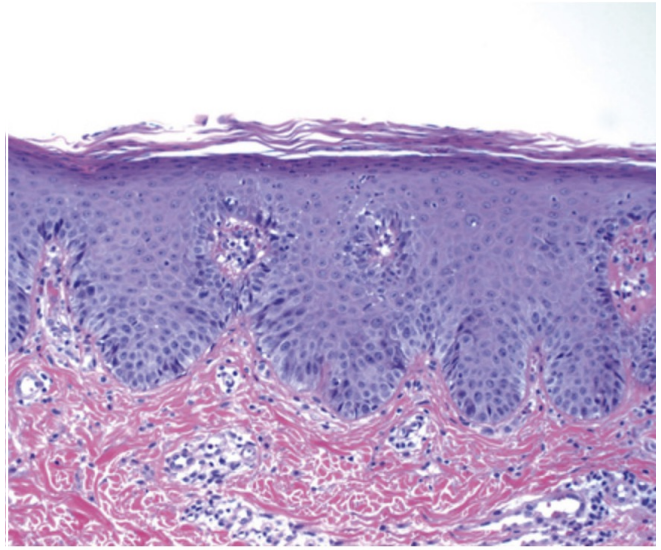
- Leads to the activation of the innate immunity and may result in tissue damage through the alteration of cytokine cascades, which induce site-specific inflammation and is independent of the adaptive immune response.
- Psoriasis: common autoinflammatory disease

Tissue reaction patterns



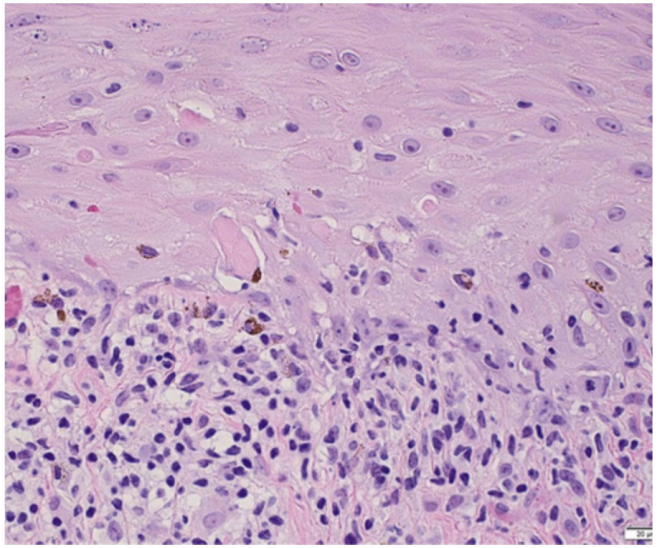
Atopic dermatitis

Spongiotic



Psoriasis

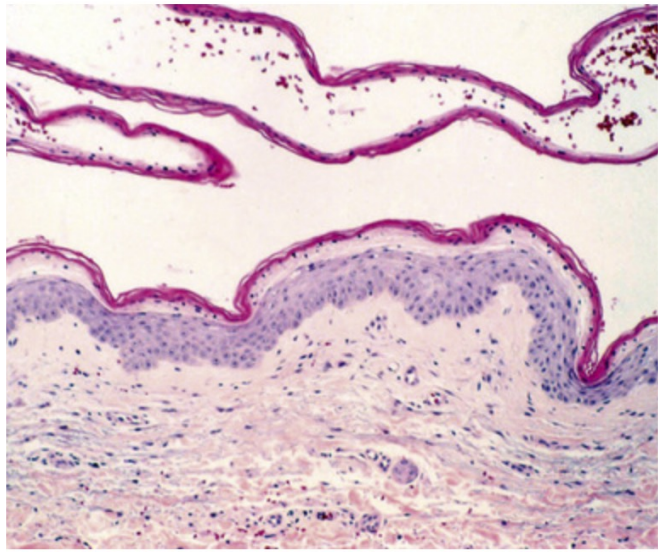
Psoriasiform



Lichen planus

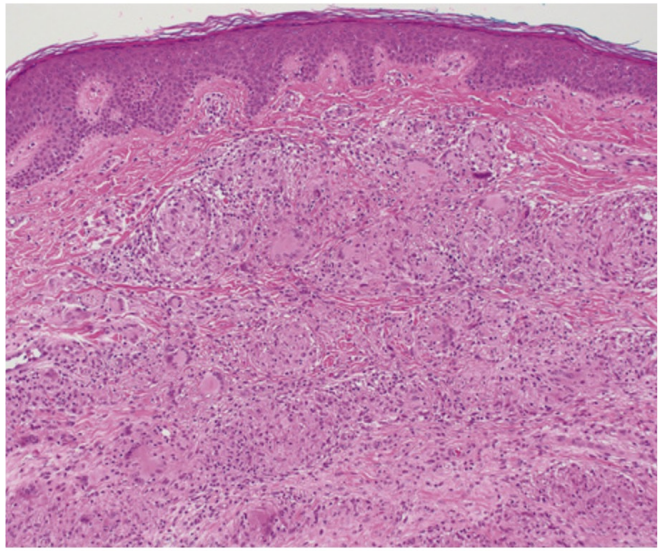
Lichenoid

Tissue reaction patterns



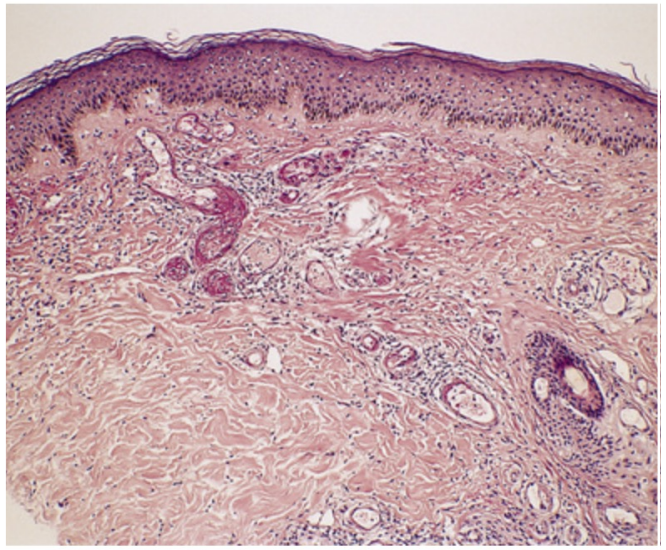
Bullous pemphigoid

Vesiculobullous



Granuloma annulare

Granulomatous



Atrophie blanche

Vasculopathic

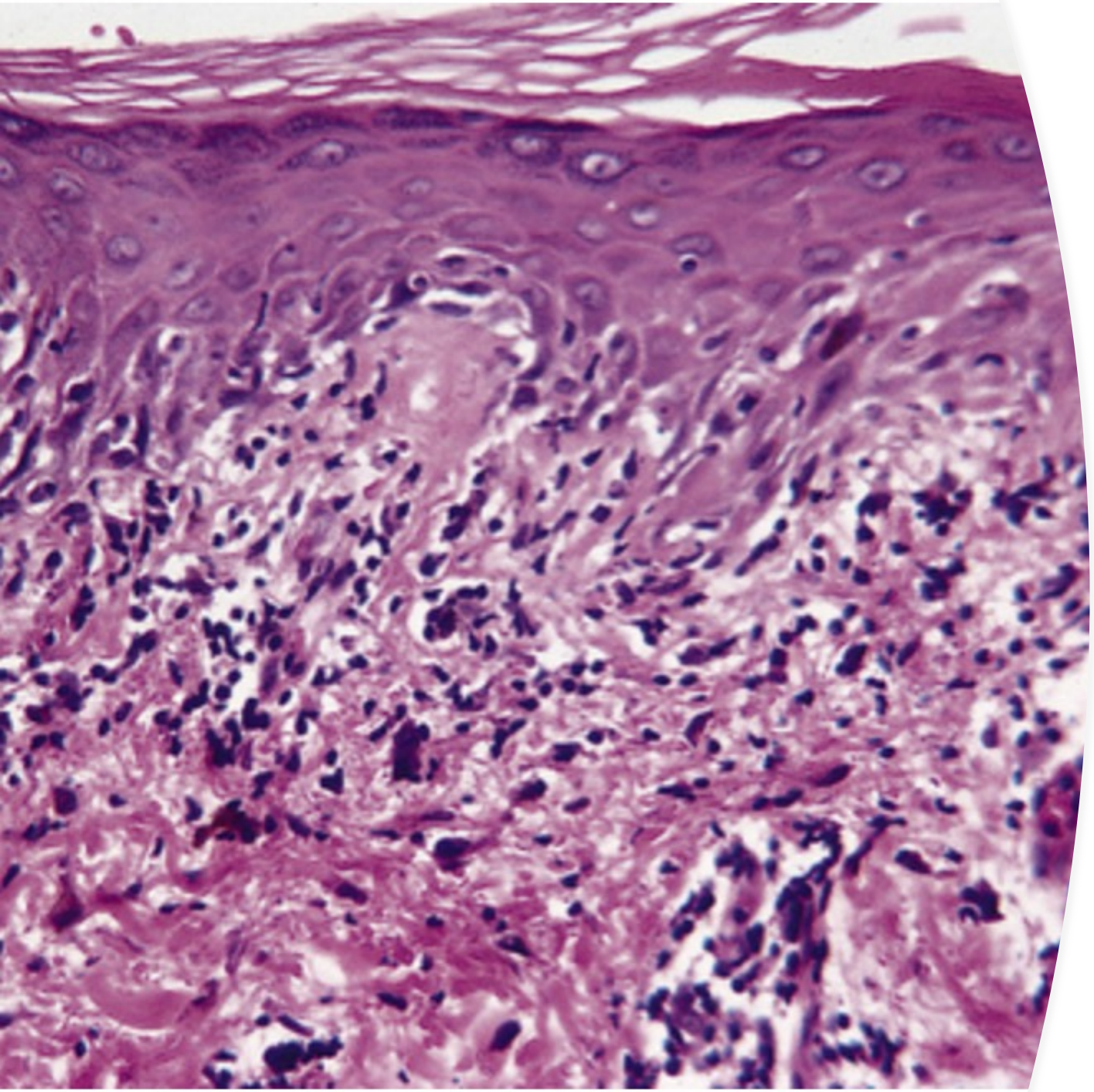
Idiopathic Connective Tissue Diseases

Disorders of Collagen

1. **Scleroderma**
   - **Localized, e.g., morphea**
   - **Systemic, e.g., diffuse systemic scleroderma**
2. Sclerodermoid disorders
3. Hypertrophyic collagenoses
4. Atrophic collagenoses
5. Perforating collagenoses
6. Variable collagen changes
7. Syndromes of premature aging

Lichenoid reaction pattern ('interface dermatitis')

1. Lichen planus and others
2. Lichenoid drug eruption
3. Fixed drug reactions
4. Erythema multiforme
5. Graft-vs-host disease
6. **Lupus erythematosus**
7. **Dermatomyositis**
8. Poikiloderma
9. Pityriasis lichenoides
10. Paranneoplastic pemphigus



Lupus Erythematosus

- Chronic inflammatory disease of unknown etiology
- Middle-aged women
- Clinical variants:
  - Chronic discoid lupus erythematosus, (skin only)
  - Systemic lupus erythematosus (multisystem disease)
  - Subacute lupus erythematosus (skin and mild systemic illness).
- Histopathology: lichenoid reaction pattern (interface dermatitis)
  - Absent in tumid lupus and lupus profundus

Discoid lupus erythematosus

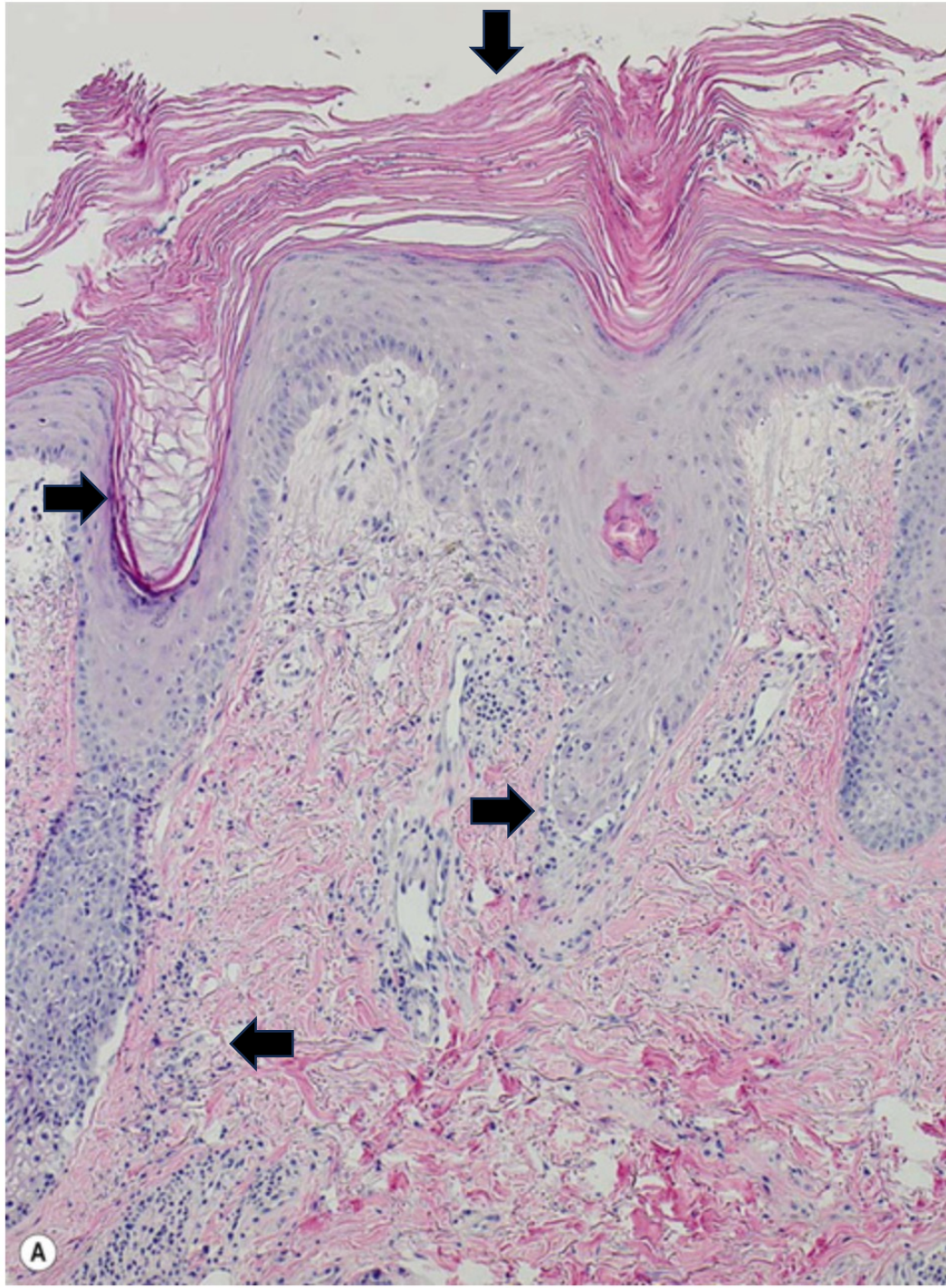
Sharply demarcated, erythematous, scaly patches with follicular plugging

- Involving the skin of the face: butterfly distribution on the cheeks and bridge of the nose

Lichenoid reaction pattern (interface dermatitis): vacuolar change (“liquefaction degeneration”)

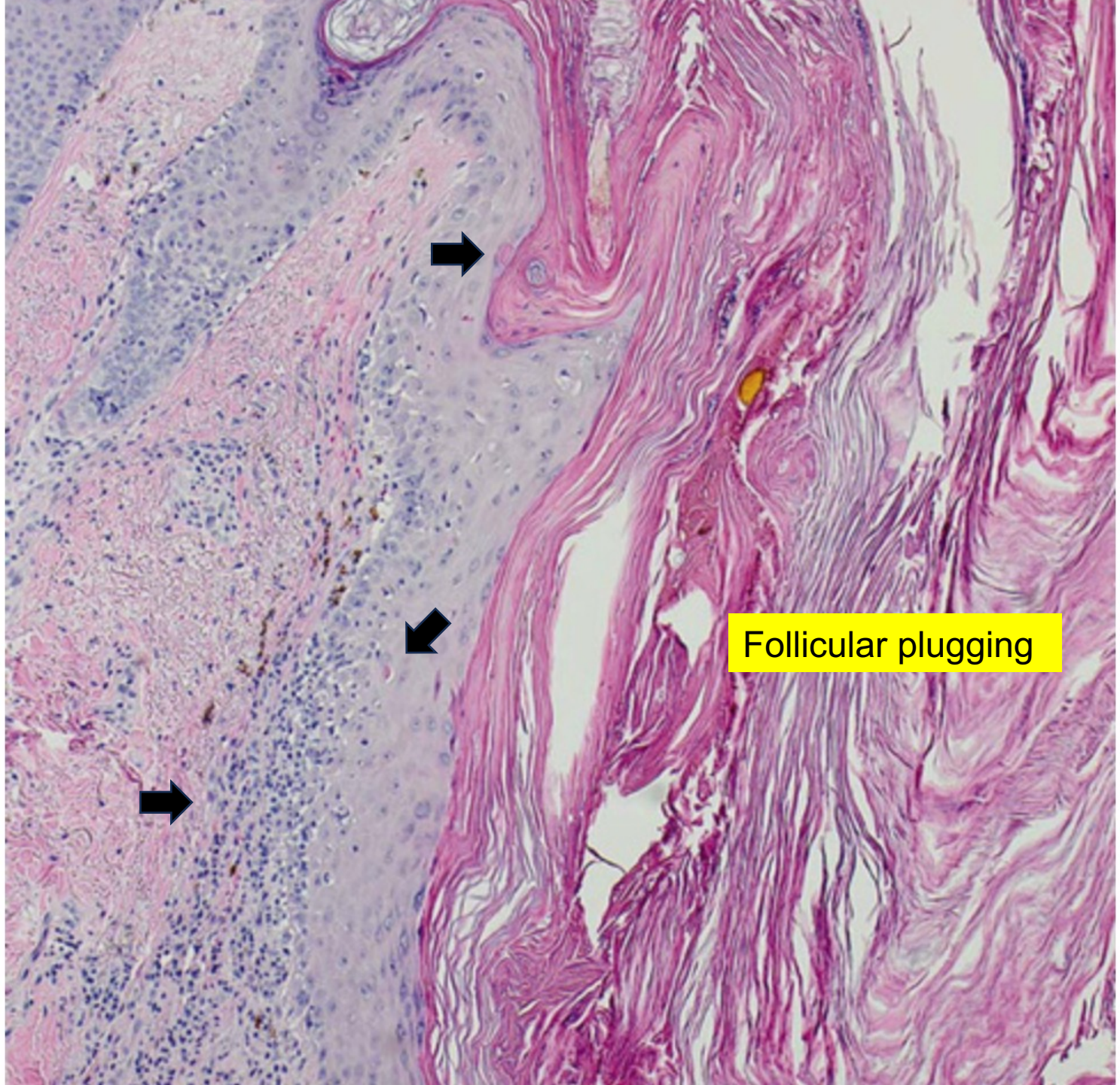
- Scattered Civatte bodies (apoptotic keratinocytes)
- Progressive thickening of the basement membrane (PAS)

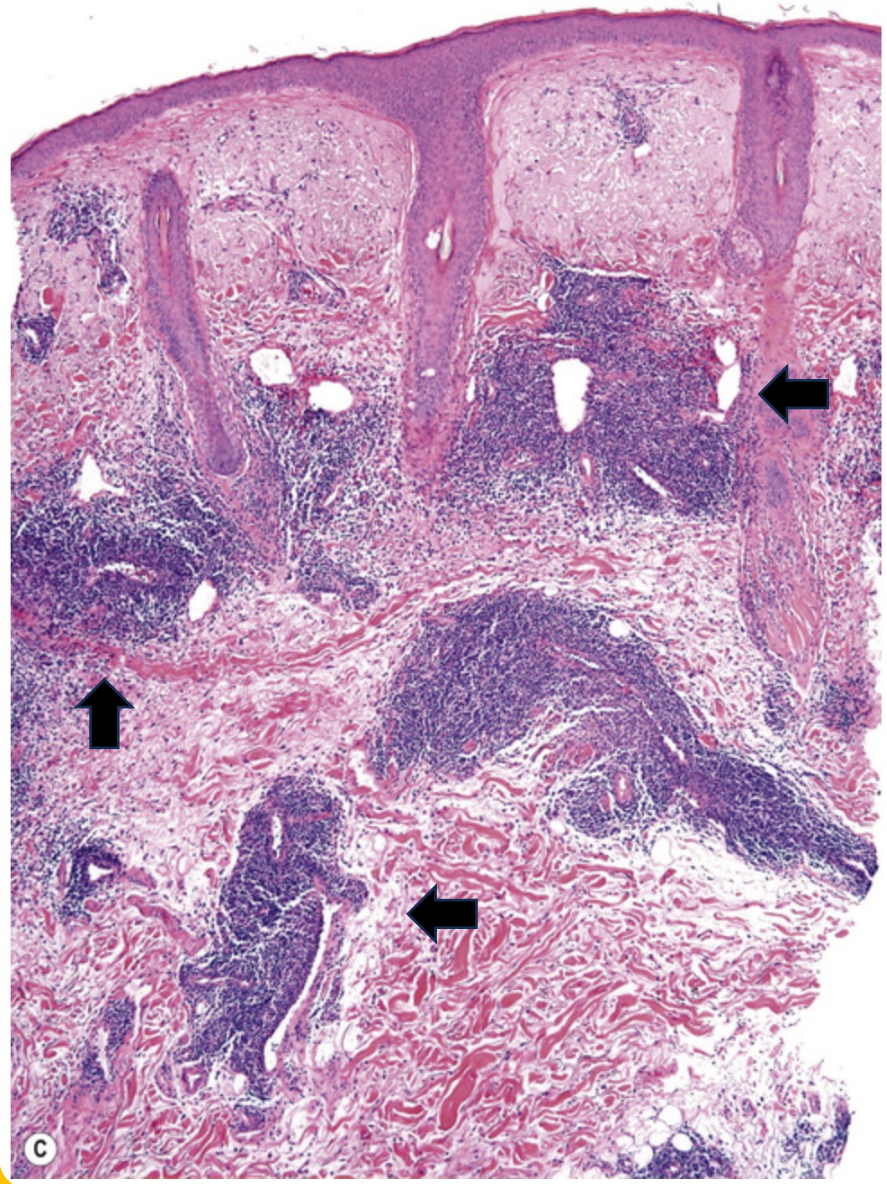
Other epidermal changes: hyperkeratosis, keratotic follicular plugging, and epidermal atrophy



Discoid lupus erythematosus

- Lichenoid lymphocytic inflammation
- Vacuolar change (holes in basilar keratinocytes)
- Lymphocytic inflammation involving the basilar layer of the outer root sheath
  - Superficial and deep dermal hugging the pilosebaceous follicles
    - Dermal CD4+>>CD8+ T-cells
- Melanin incontinence
- Dyskeratosis



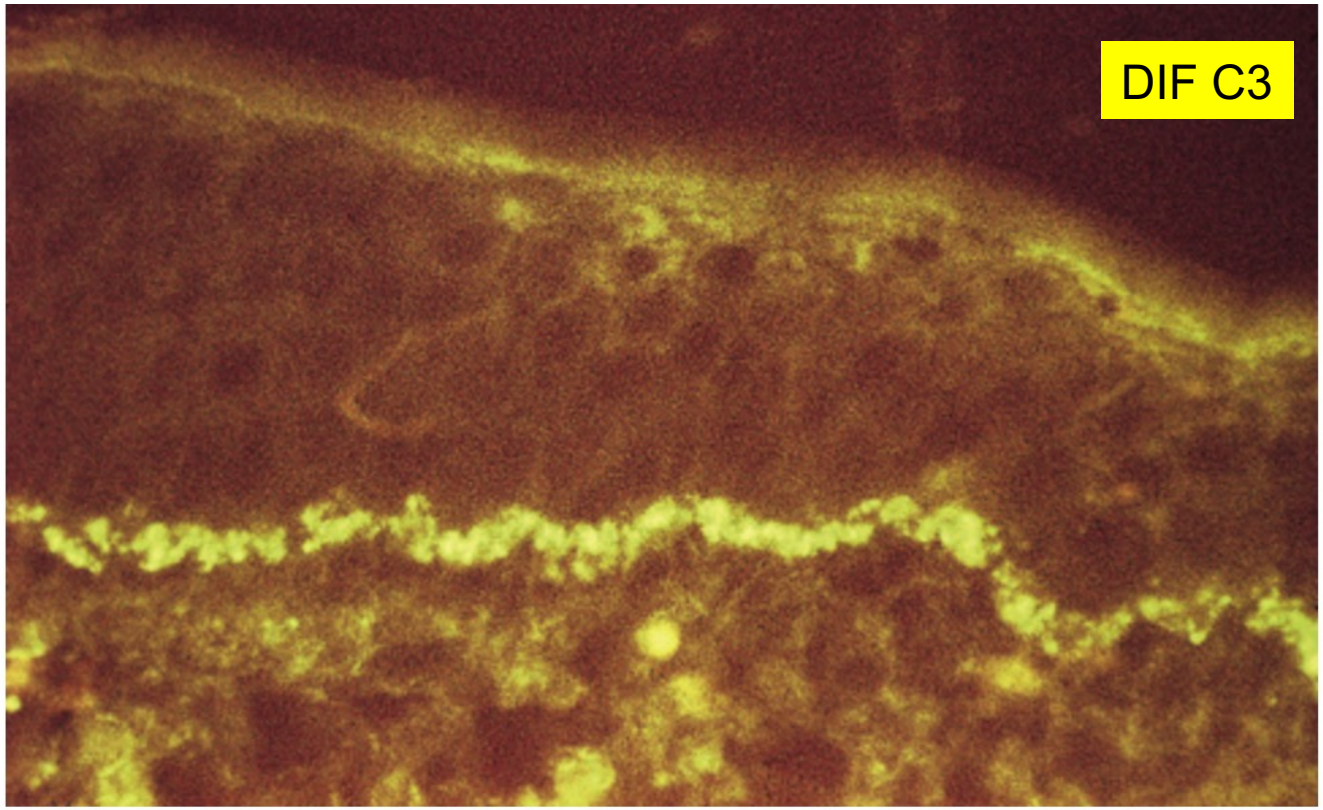


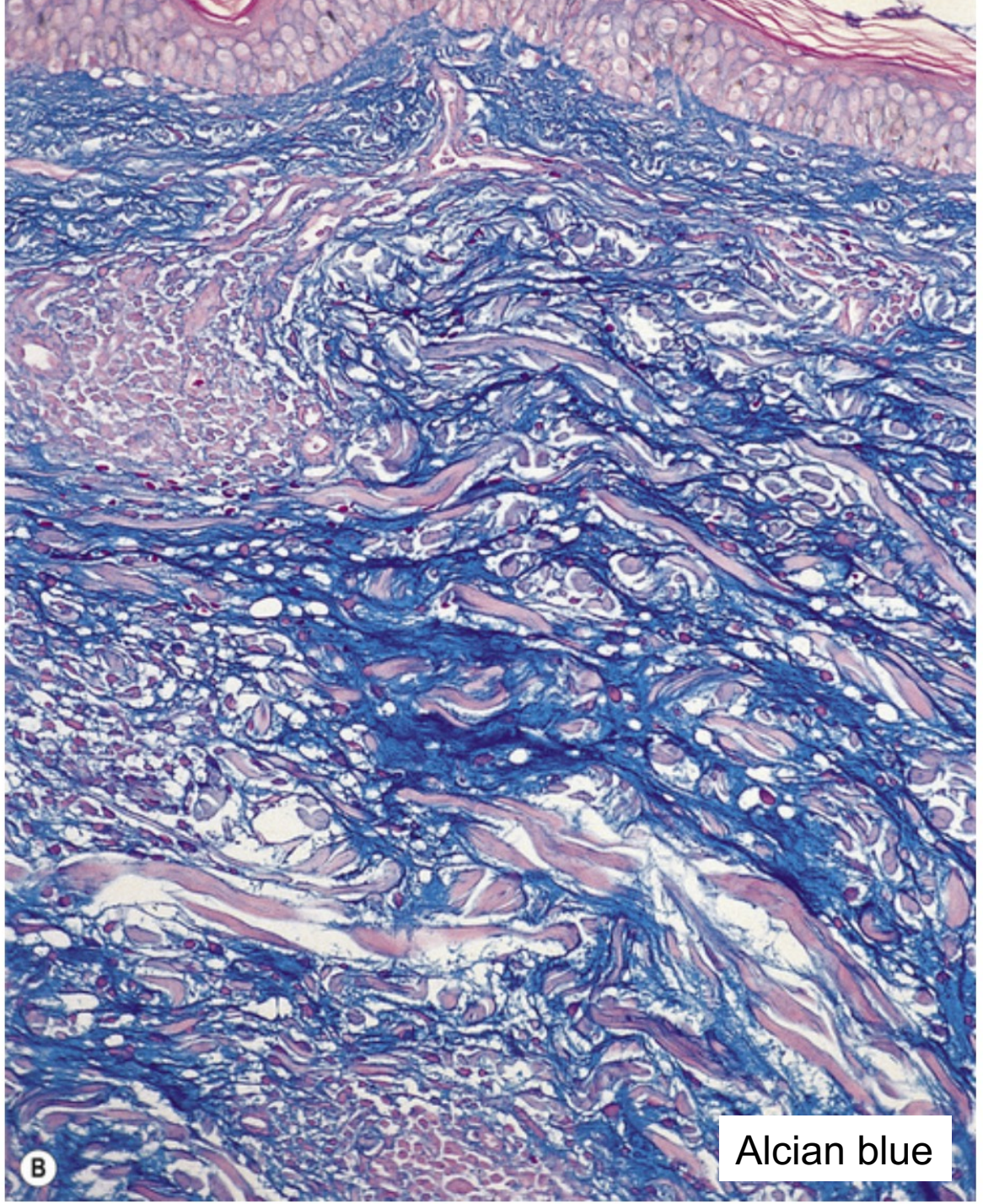
Tumid lupus erythematosus

- Face, neck, and upper trunk:
  - Erythematous, urticaria-like, nonscarring plaques/papules
  - Sun-exposed areas
- Occurs in a setting of DLE, but sometimes SLE has been present or rarely develops subsequently.
- Lymphocytic infiltration of the skin (of Jessner and Kanof) is now regarded as a variant of DLE
- Histopathology: need to perform a punch biopsy (indurated lesion with substance)
  - Superficial-deep periadnexal and perivascular dense infiltrate of lymphocytes
  - Lymphocytes forming dermal nodules
  - Background solar elastosis
  - Subepidermal edema

Tumid lupus erythematosus

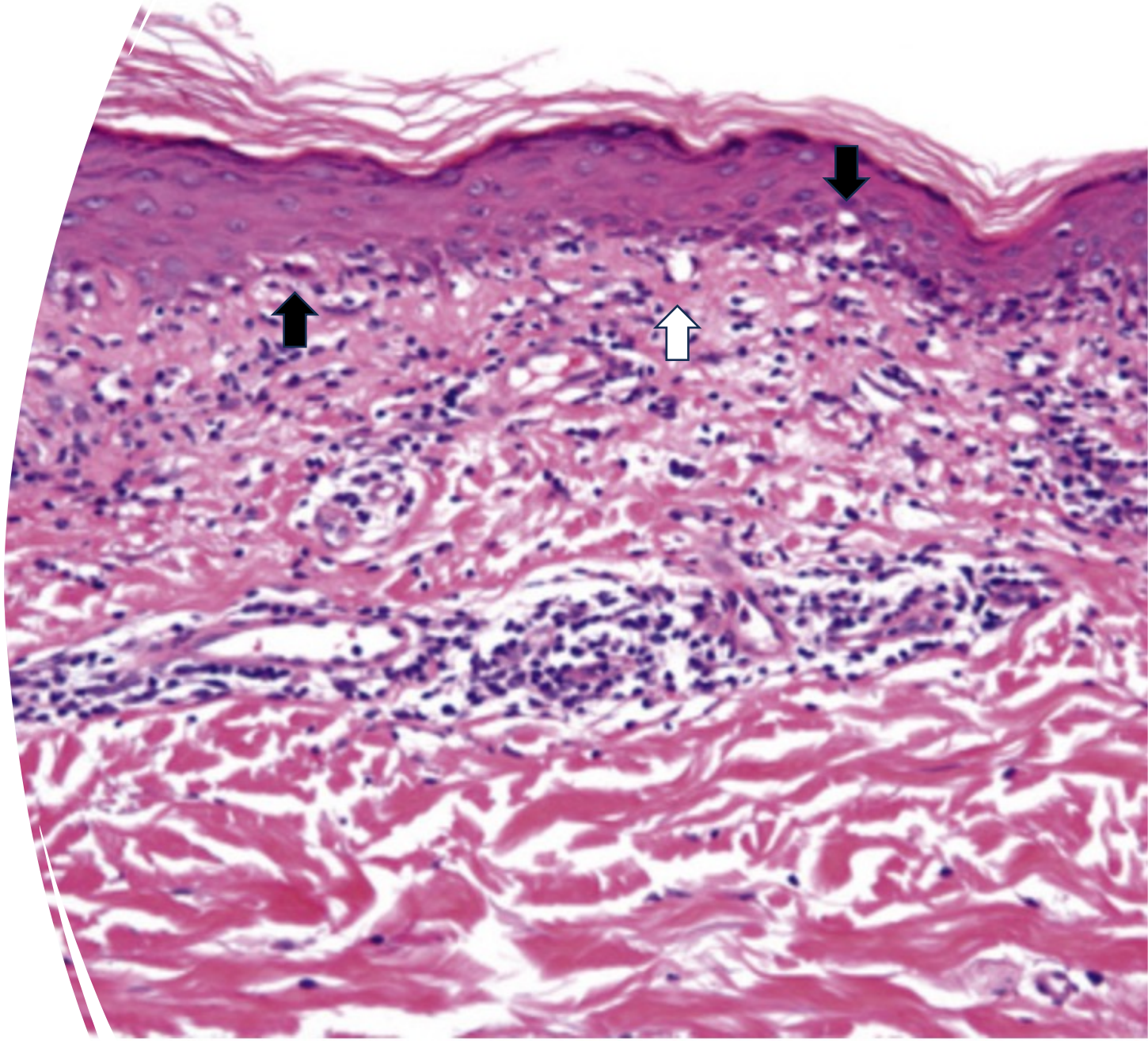
- Increased dermal mucin on special stains: Alcian blue & Colloidal iron
- DIF: Linear IgG and IgM (along the basement membrane zone) in 50% to 90% of cases
- Lupus band test positive less often, need CPC





Subacute lupus erythematosus

- Recurring, photosensitive, nonscarring annular or papulosquamous lesions
- Face, neck, upper trunk, and extensor surfaces of the arms
- Mild systemic illness with musculoskeletal complaints and serological abnormalities (16% renal involvement)
- Histopathological features differ only in degree from those seen in discoid lupus
  - Pauci-inflammatory, vacuolar, lymphocytic interface dermatitis.
  - Apoptotic keratinocytes (Civatte bodies) are prominent (resembling erythema multiforme)

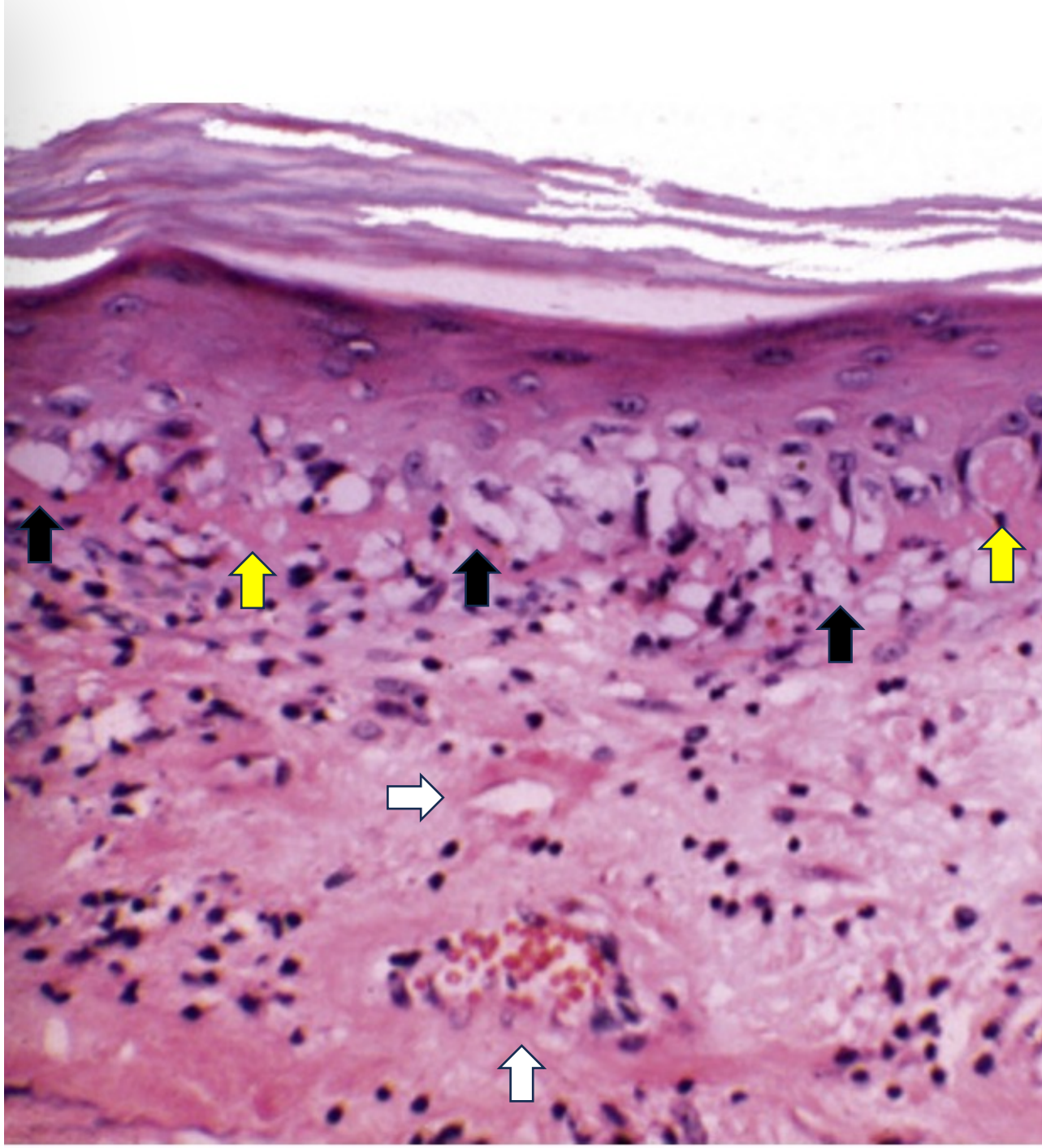


Histologic comparison: DLE vs. SLE

Discoid lupus erythematosus	Subacute lupus erythematosus
• Less basal vacuolar change, epidermal atrophy, and dermal edema and superficial mucin	• More basal vacuolar change, epidermal atrophy, and dermal edema and superficial mucin
• More hyperkeratosis, pilosebaceous atrophy, follicular plugging, basement membrane thickening, and cellular infiltrate	• Less hyperkeratosis, pilosebaceous atrophy, follicular plugging, basement membrane thickening, and cellular infiltrate
• Lupus band test: thick, intense	• Lupus band test: thin, dim • dust-like particles of IgG (a speckled pattern)

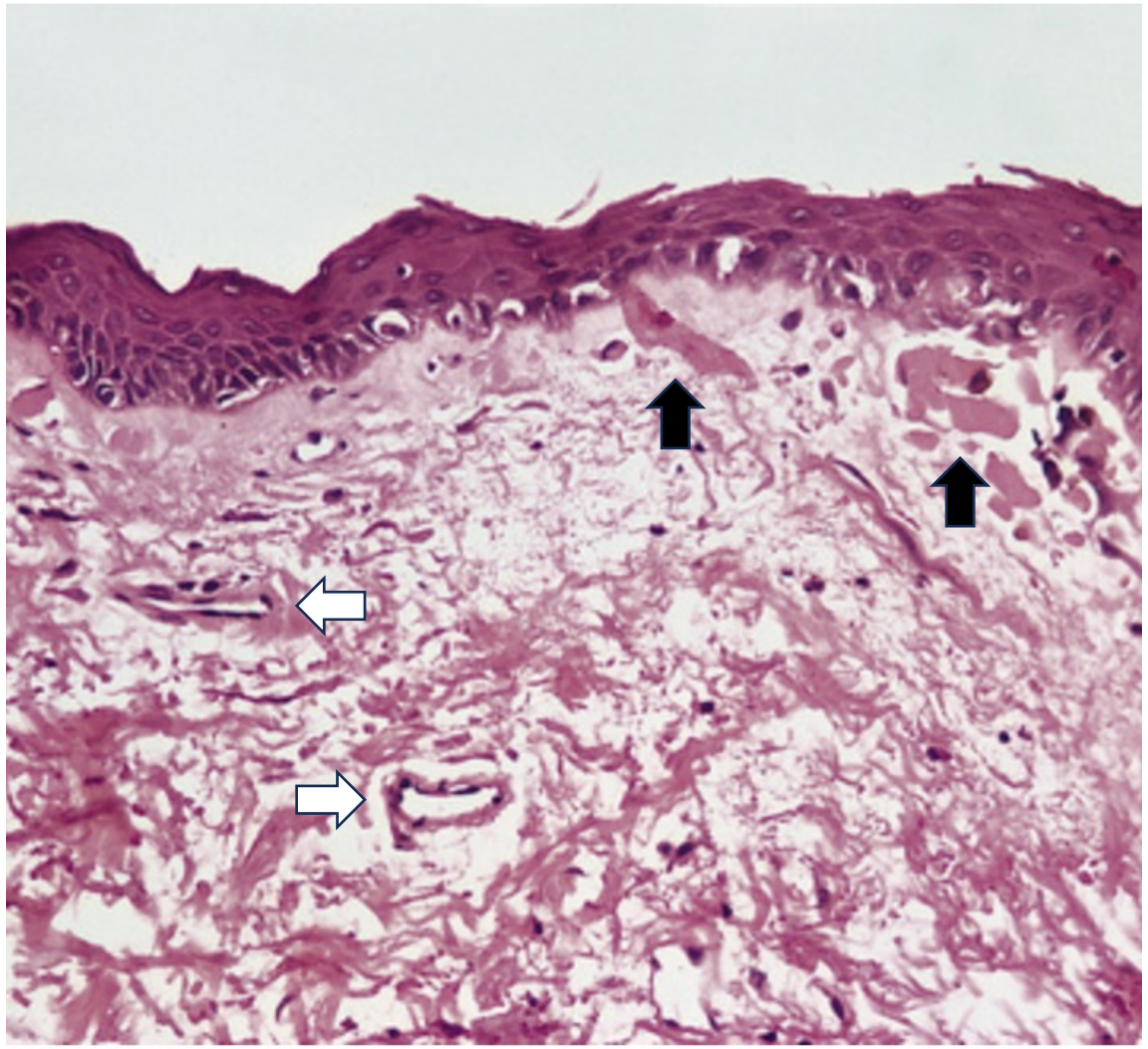
Systemic lupus erythematosus

- Skin lesions, renal involvement, joint involvement, and serositis
- Skin malar areas: erythematous, slightly indurated patches with only a little scale
- More extensive, less defined than DLE
- Microvascular injury: chilblain (perniotic) lupus
- Histopathology:
  - Prominent basilar vacuolar change
  - Civatte body not a feature
  - Thickening of the basement membrane zone
  - Upper dermis: edema, small hemorrhages, and a mild infiltrate of lymphocytes
  - Eosinophils (drug-induced cases and in urticarial lesions)
  - Fibrinoid material: around capillary blood vessels, on collagen, and in the interstitium
  - +/- Vasculitis +/- thrombosis



Differential diagnosis for lupus erythematosus

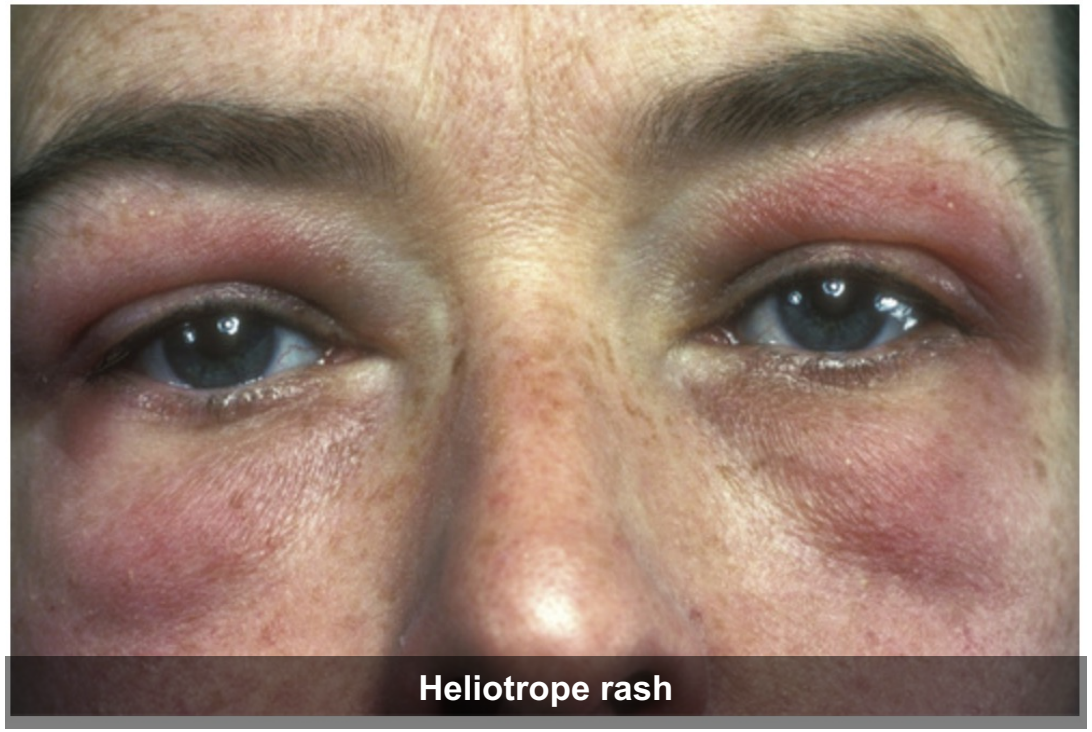
- Lichen planus, hypertrophic variant
  - Lichen planopilaris
  - DIF: IgM positive Civatte bodies in papillary dermis
- Other connective tissue diseases
  - Dermatomyositis
  - Morphea/scleroderma
- Poikiloderma atrophicans vasculare
- Patch stage mycosis fungoides
- SDPVLD: secondary syphilis, polymorphous light eruption, lymphoma, CLH (pseudolymphoma), reticular erythematous mucinosis, and lymphocytic infiltration of Jessner



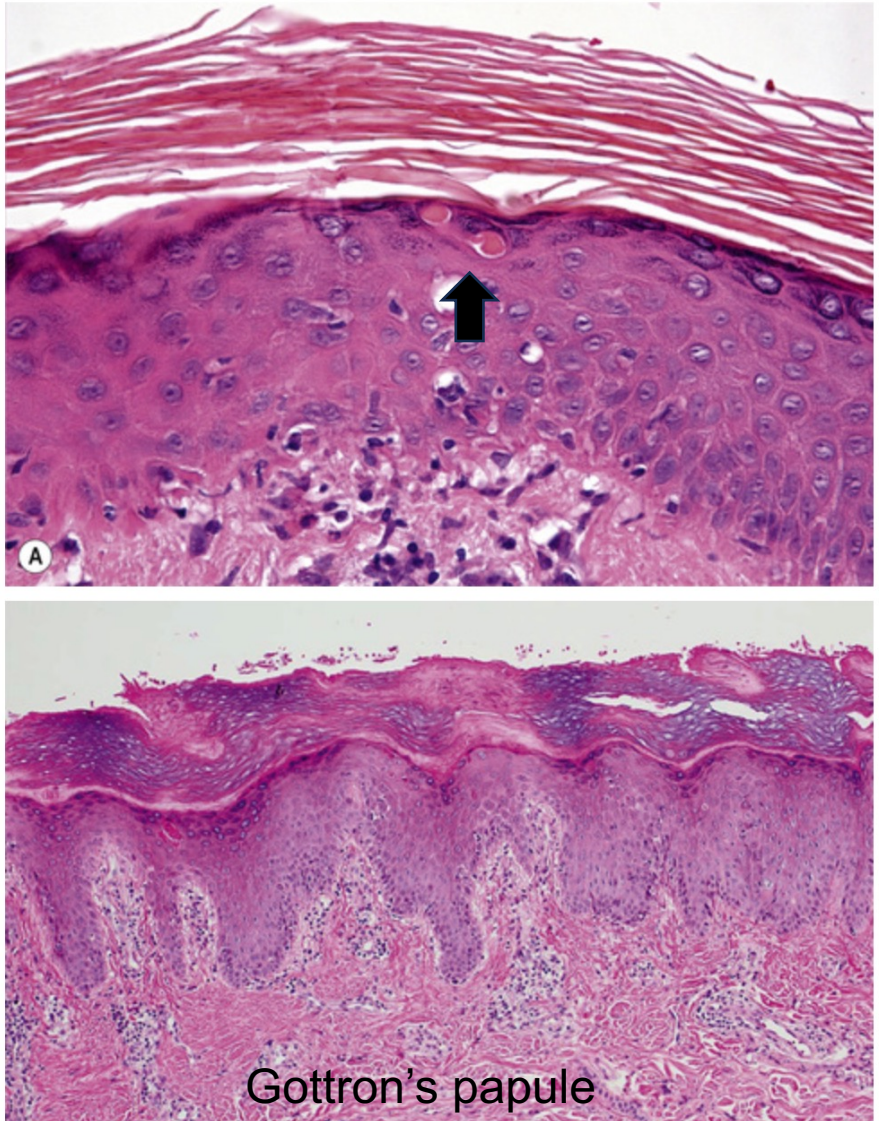
Dermatomyositis

Dermatomyositis

- Coexistence of a nonsuppurative myositis (polymyositis) and inflammatory dermatosis
- Cutaneous lesions may precede muscle involvement by up to 2 years
- Violaceous or erythematous scaly lesions: face, shoulders, the extensor surfaces of the forearms, and the lateral thighs or hips (the “holster” sign)
- Purplish discoloration and edema of the periorbital tissues (heliotrope rash), and atrophic papules or plaques over the knuckles (Gottron's papules).



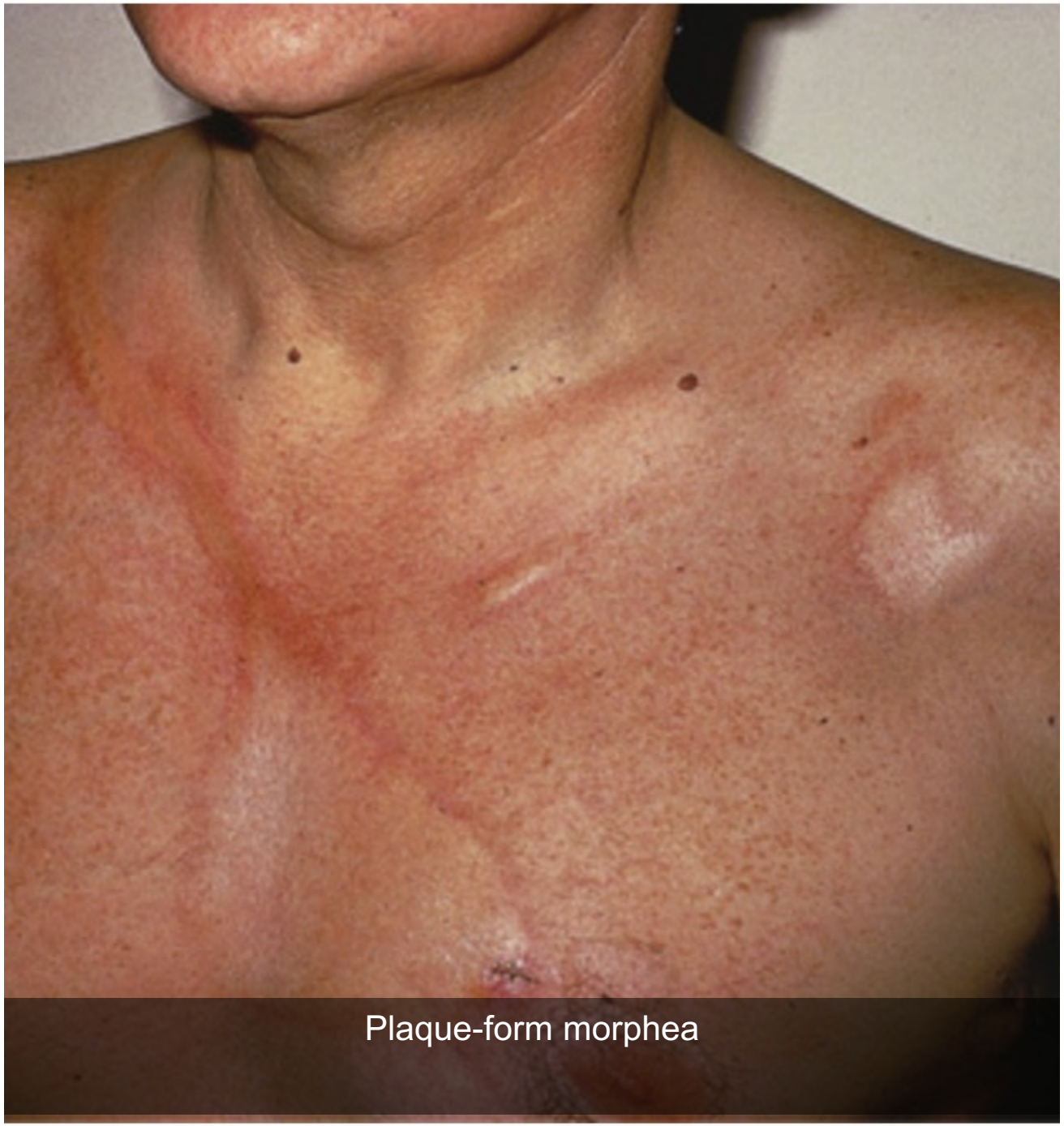
Heliotrope rash



Gottron’s papule

Dermatomyositis

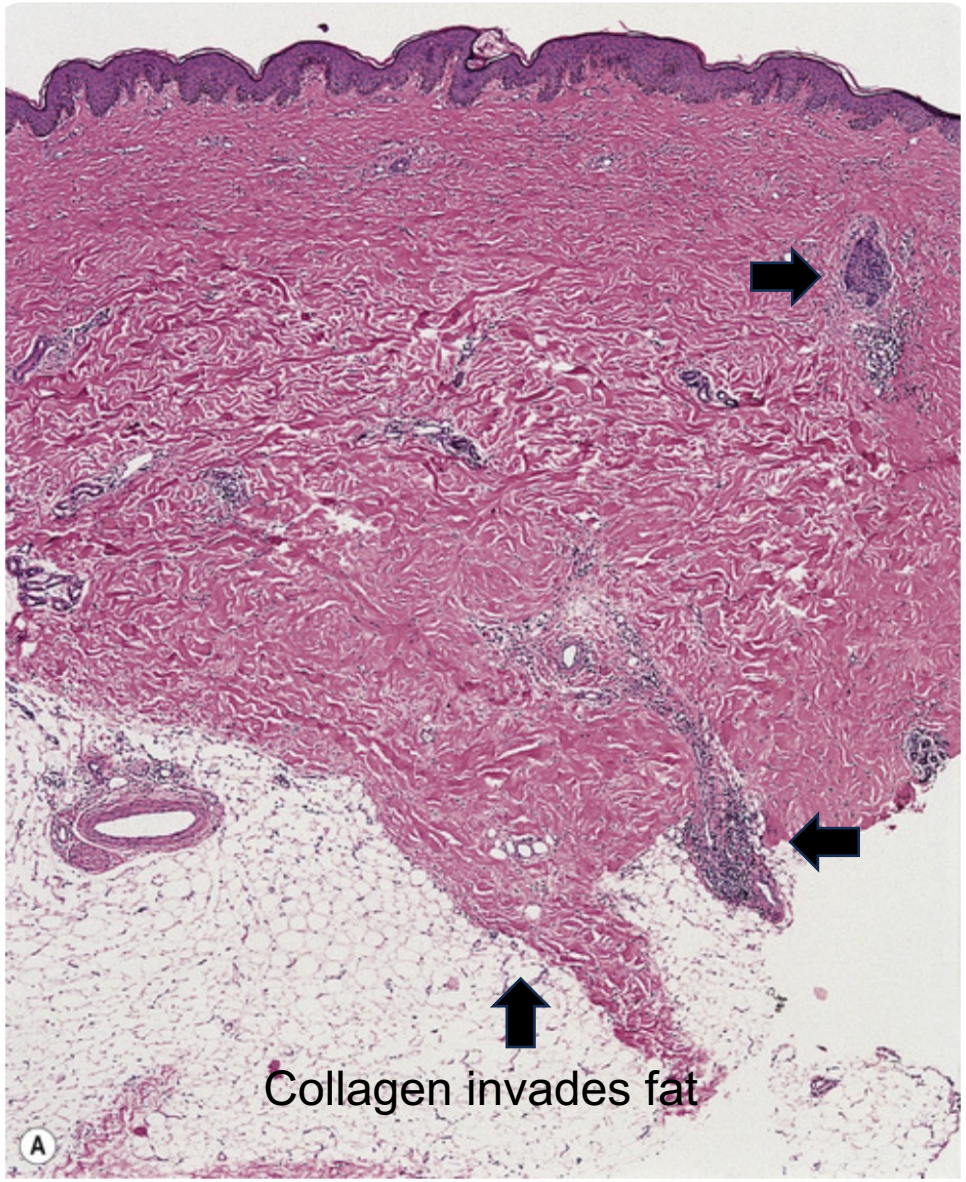
- Histologic features are variable
- Subtle: sparse superficial perivascular infiltrate of lymphocytes, with variable edema and mucinous change
- Lichenoid tissue reaction: basal layer vacuolar change
- Occasional apoptotic keratinocytes
- Gottron’s papule: subtle, ill-defined lichenoid lymphocytic infiltrate, irregular acanthosis, and hyperkeratosis (lacks interface)



Plaque-form morphea

Disorders of Collagen

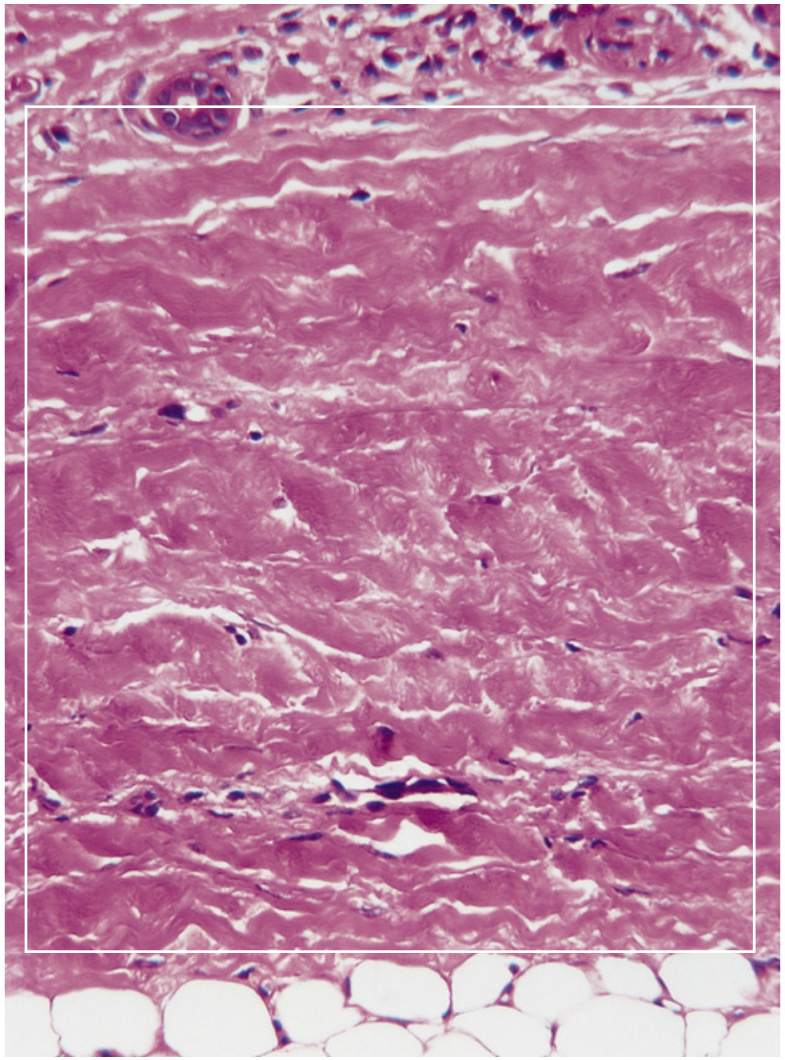
- Localized scleroderma
  - Morphea (most common)
  - Linear scleroderma
- Systemic scleroderma
- Mixed connective tissue disease
- Eosinophilic fasciitis
- Atrophoderma



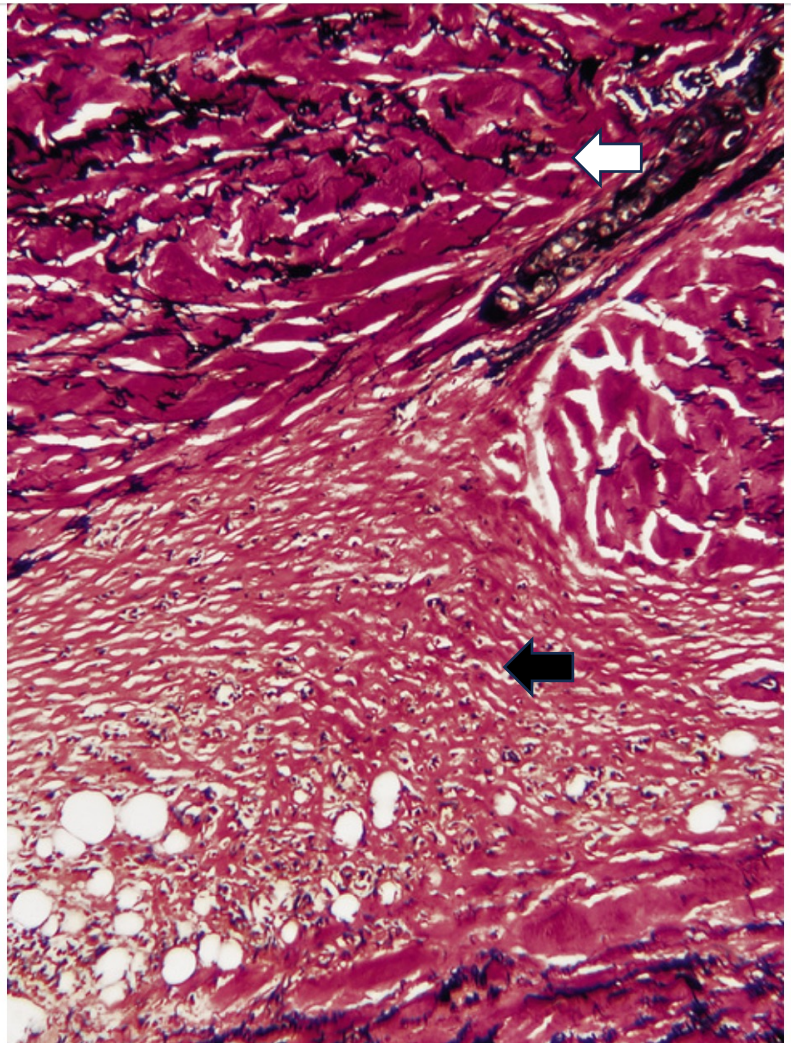
Localized scleroderma (morphea)

- Children and young adults, female preponderance
- No visceral involvement or Raynaud's phenomenon, self-limiting course
- Trunk or extremities indurated plaques with an ivory center and a violaceous border (the “lilac ring”)
- Histopathology:
    1. Deposition of collagen in the dermis and subcutis
    2. Vascular changes
    3. Inflammatory cell infiltrate (early lesions)

Morphea



H & E

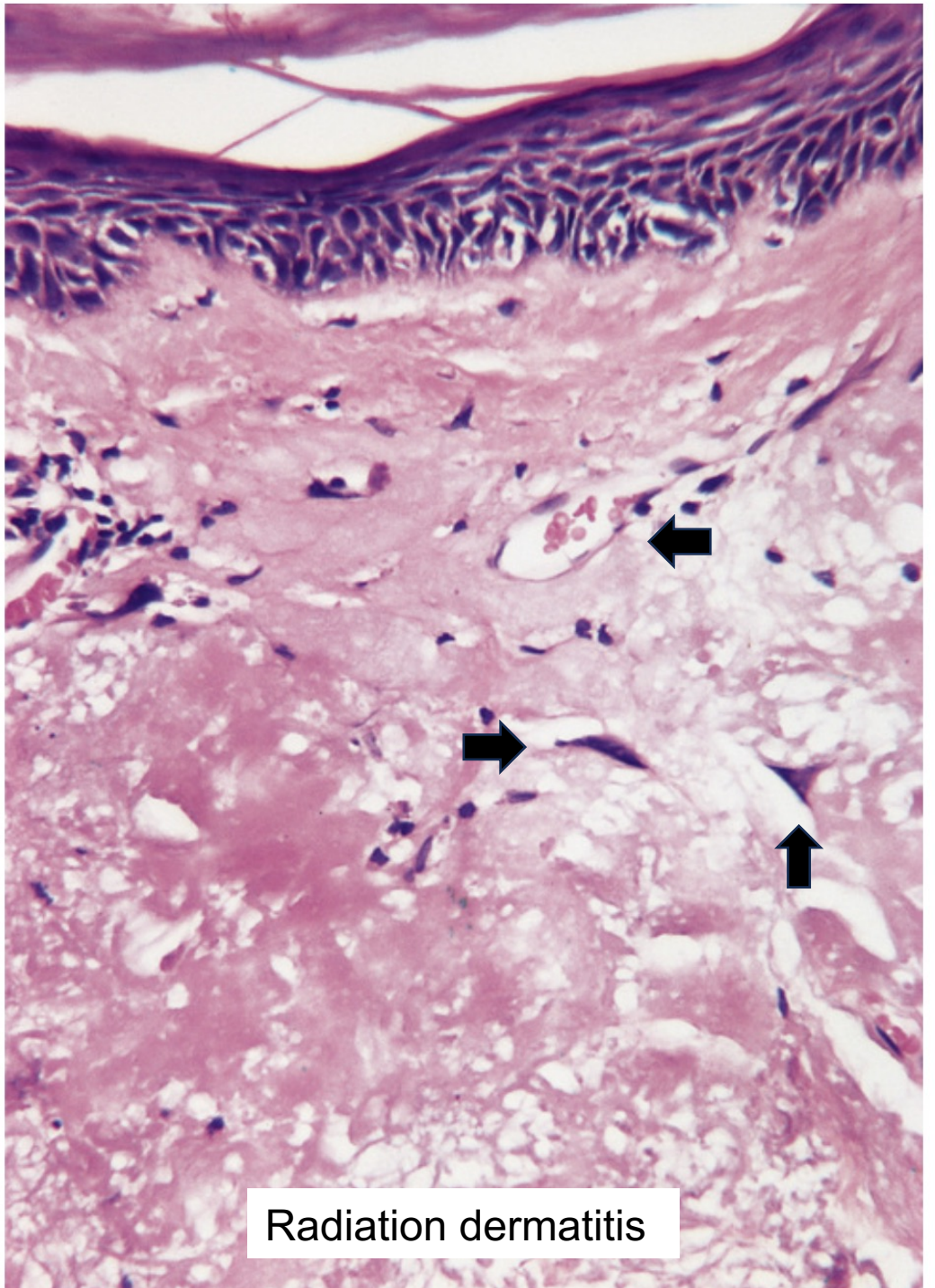


Verhoeff-van Gieson: Devoid of elastic fibers

- Thickened dermis: broad sclerotic collagen bundles (trichrome positive)
  - Mid-deep reticular dermis
  - Replaces fat around sweat glands
  - Extends into the subcutis
- Atrophy of adnexa
- Thickened blood vessels
- Lymphocytes

Differential diagnosis for morphea

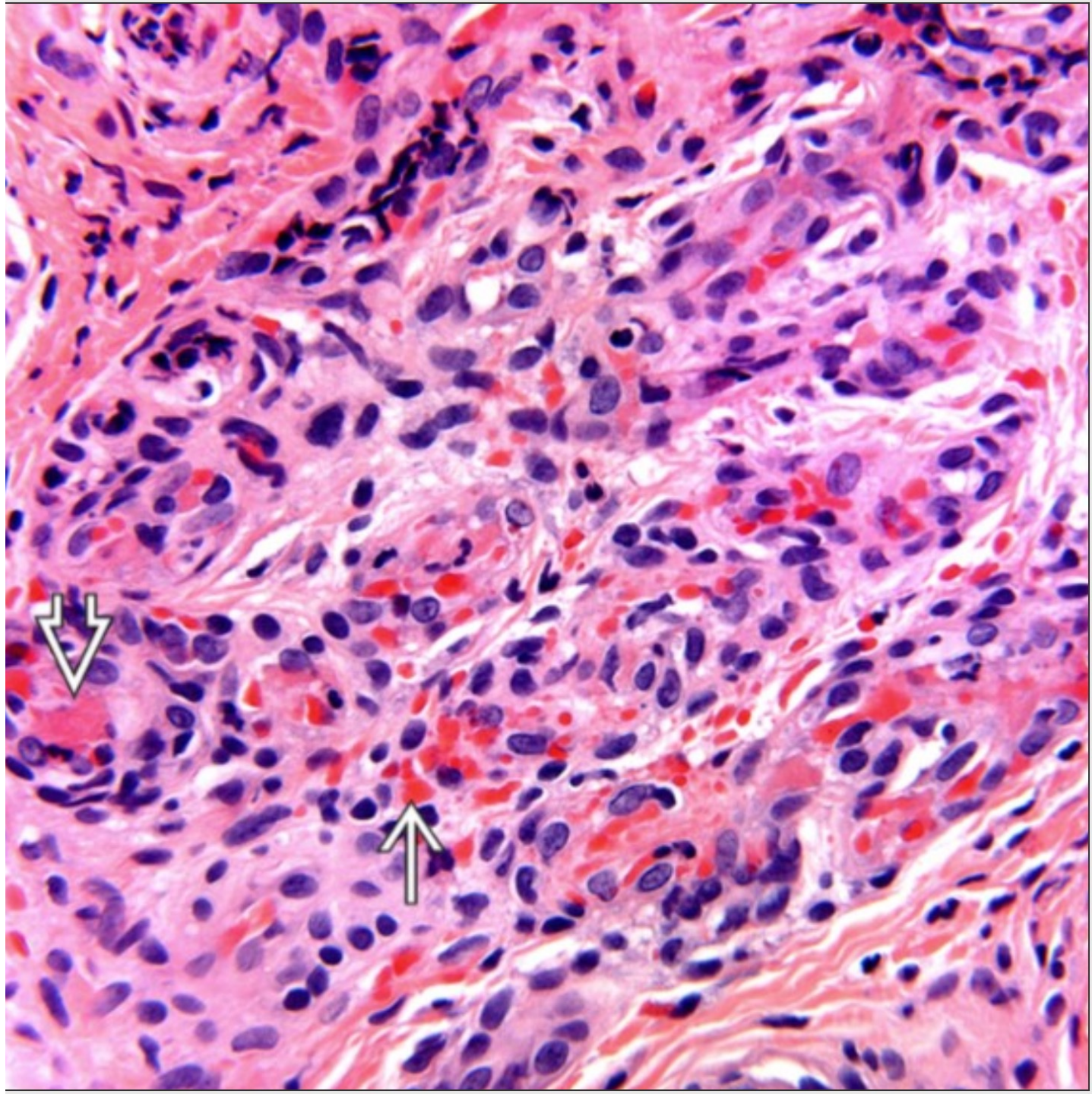
- Normal back skin
- Systemic sclerosis (less inflamed, more collagenous)
- Lichen sclerosus
- Hypertrophic scar/keloid
- Late-stage radiation dermatitis (radiation fibroblasts)
- Ischemic changes
  - vessel occlusion, calciphylaxis, prolonged pressure, and/or ingestion of drugs such as barbiturates
- Nephrogenic systemic fibrosis



Radiation dermatitis

Antiphospholipid antibody syndrome (anticardiolipin or antilupus anticoagulant)

- 10% to 15% of SLE patients with recurrent thromboses or pregnancy morbidity
- Circulating anticoagulant known as the antiphospholipid antibody is associated with paradoxical thrombosis, spontaneous abortion, premature labor, intrauterine death, labile hypertension, cutaneous necrosis, gangrene, ecchymoses, purpura, leg ulcers, atrophie blanche, livedo reticularis, and false-positive syphilis serology – the lupus anticoagulant syndrome
- Young adult women, it has been documented in children as well as the elderly.
- Histopathology: vascular occlusion of arterioles and arteries with a fibrinoid plug
  - Minimal or no inflammation of the blood vessel wall or surrounding tissue.
  - Marked dermal necrosis



Digital Skin Pathology

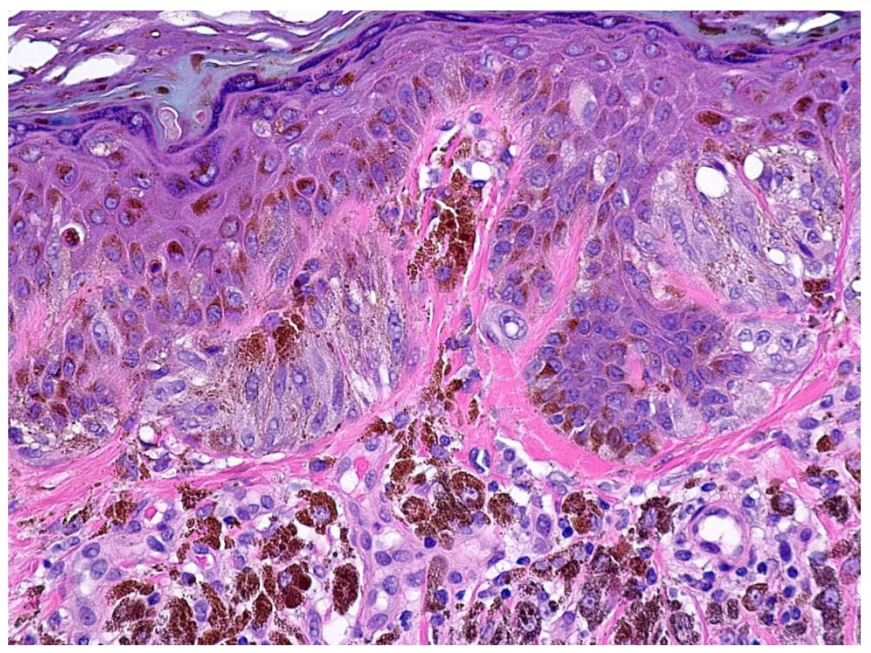
https://digitalskinpathology.com/

- Meet the challenges of the growing needs for dermatopathology knowledge
- Learn Dermatopathology based on actual real-life cases
- Dermatology PAs and NPs
- Primary MDs and general surgeons
- Residents of Dermatology and Pathology
- https://digitalskinpathology.com/

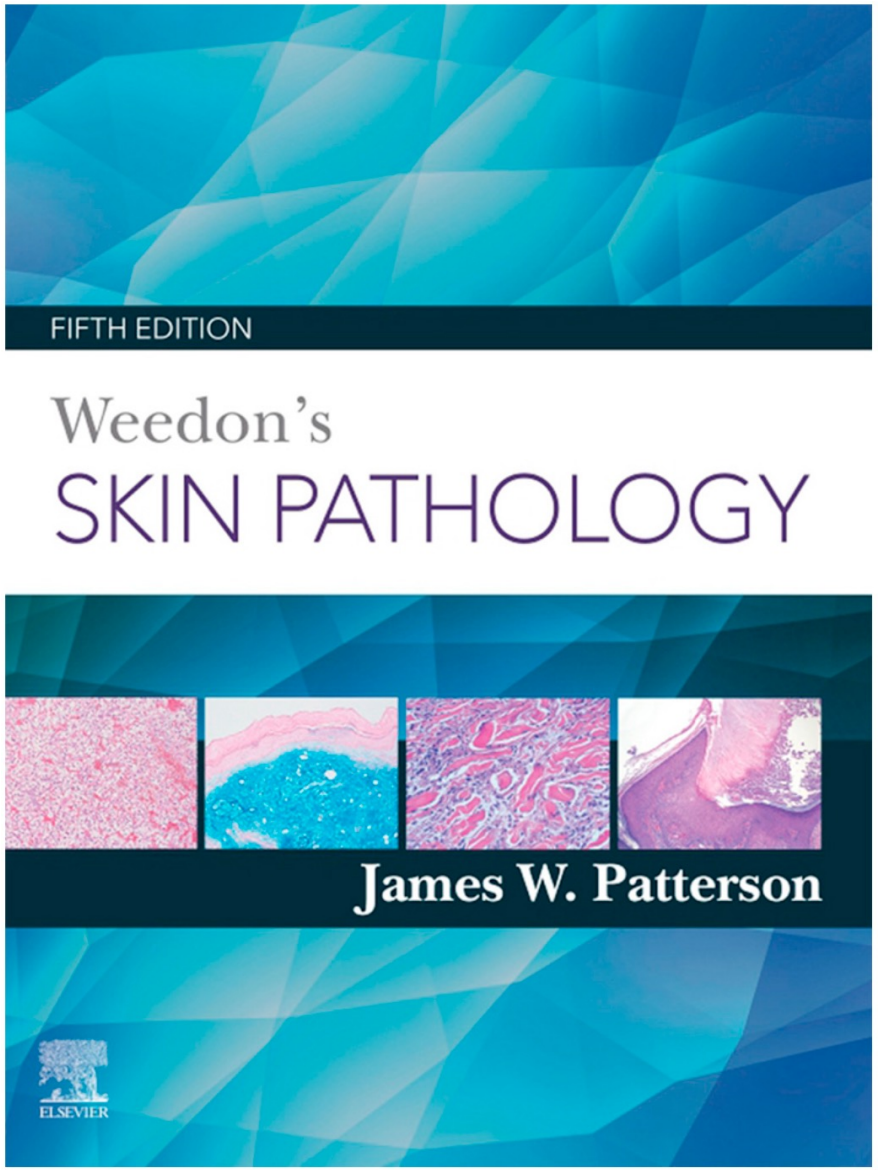
DIGITAL SKIN PATHOLOGY (DiSK)

Learn Histologic Diagnosis Case-By-Case

DERMATOPATHOLOGY: LEARN HOW TO DIAGNOSE SKIN DISEASES DERM PATH DIAGNOSTICS



Understand your patient's dermatopathology diagnostic report to provide better clinical care (how to diagnose skin diseases). derm path diagnostics



References

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