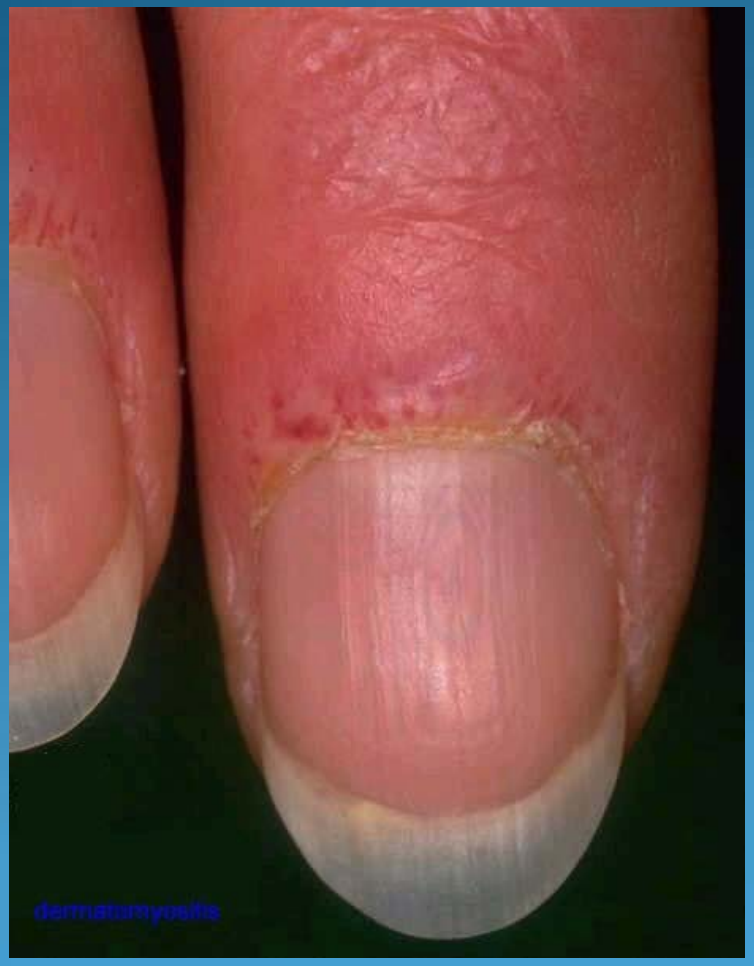
Gastrointestinal Disease and Dermatopathology

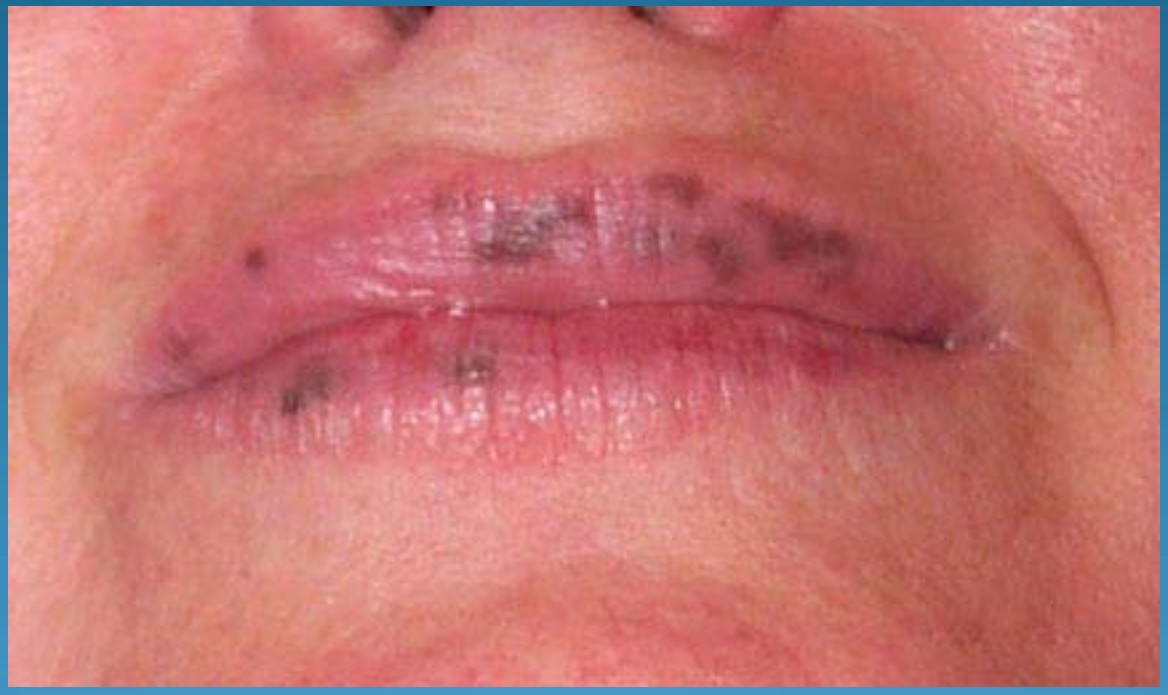
Paul K. Shitabata, M.D.
Dermatopathology Institute

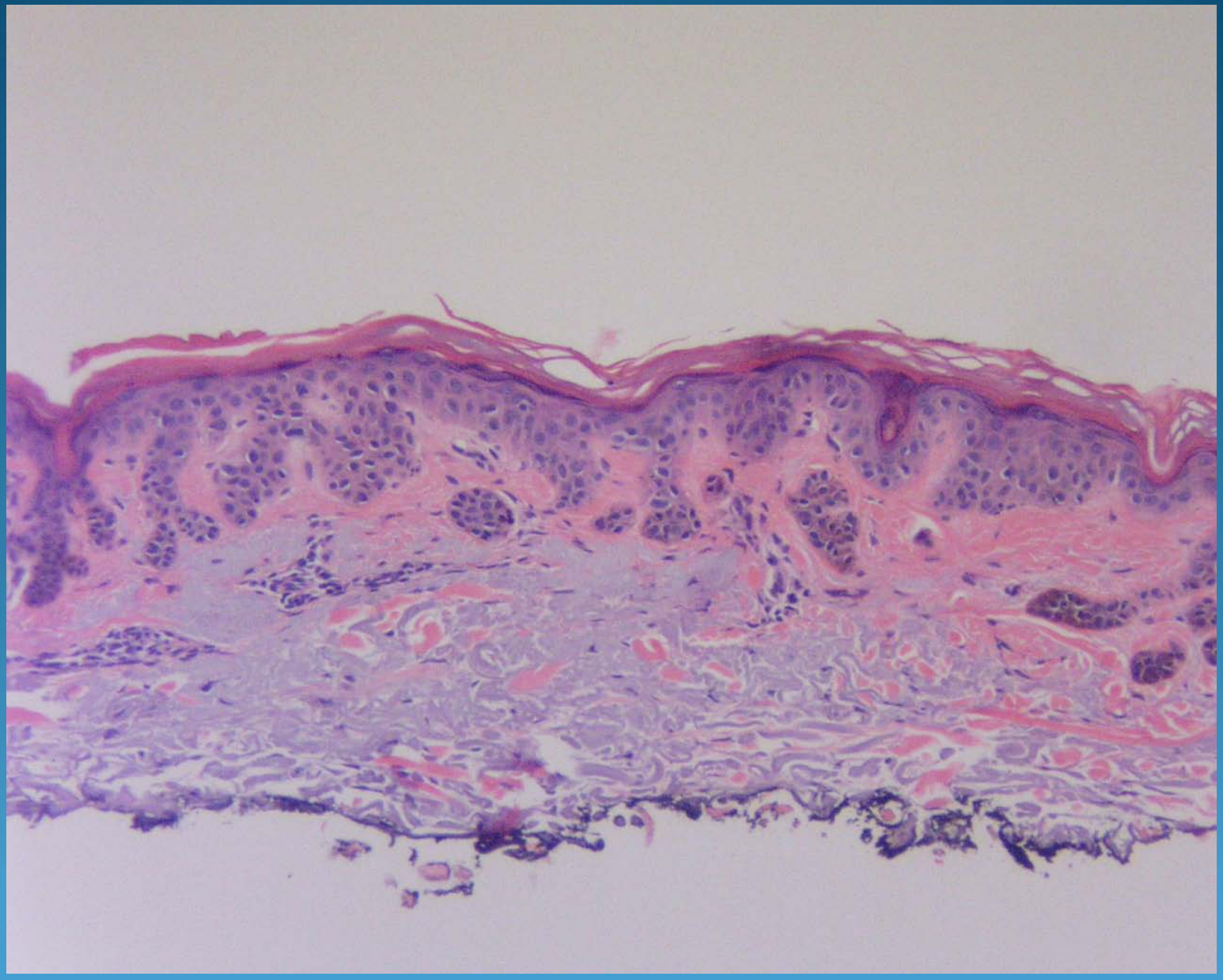
Key Points

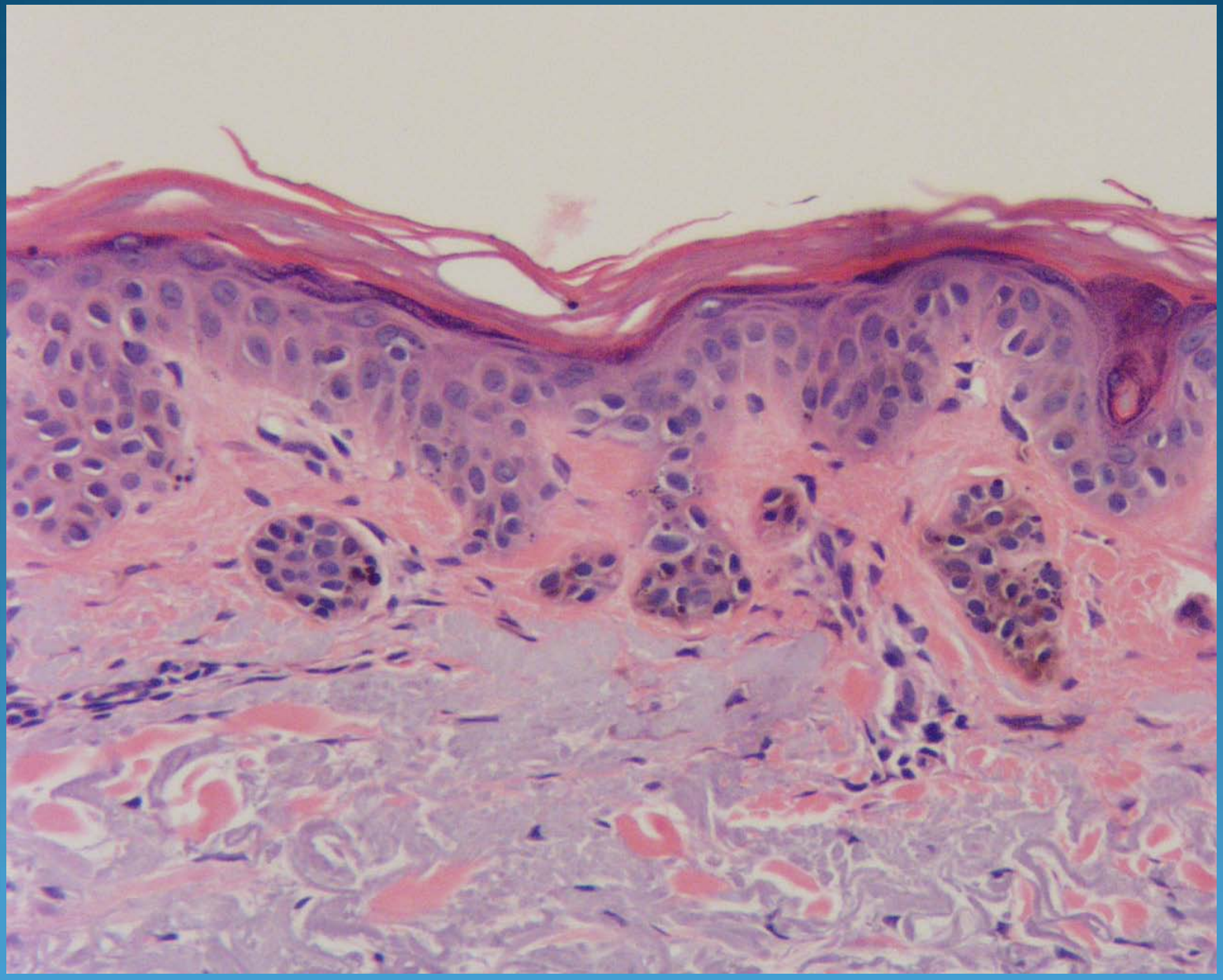


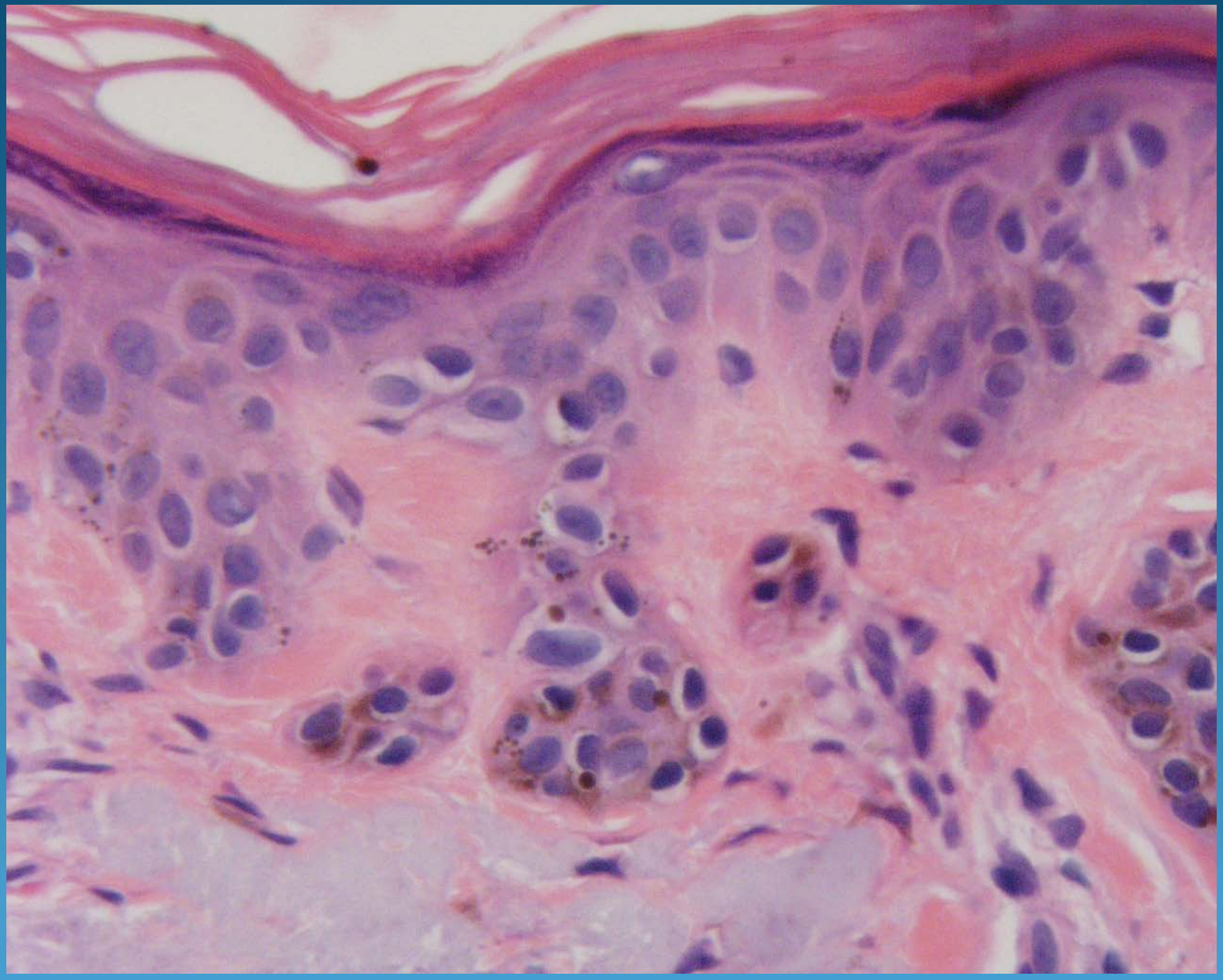
- Subtle dermatologic signs may suggest significant gastrointestinal and systemic disease
- Check family history
- Several dermatologic disorders may be present

24 y.o. Male
Perioral spotting



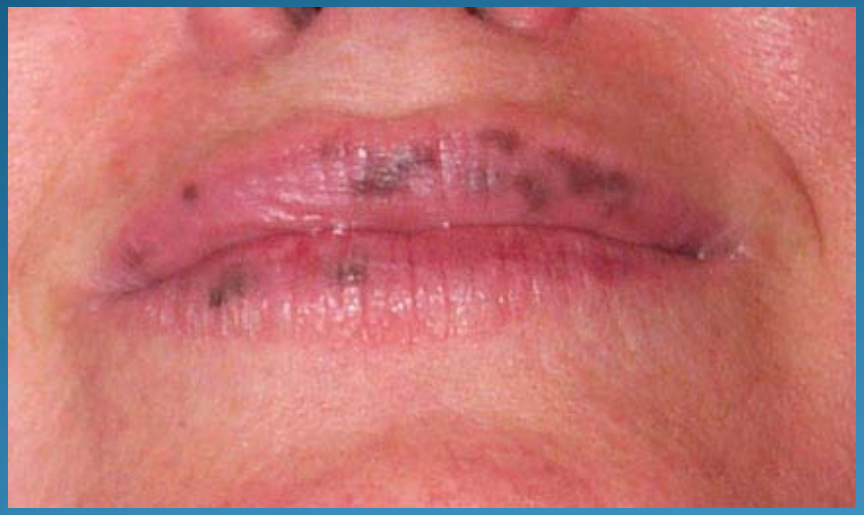






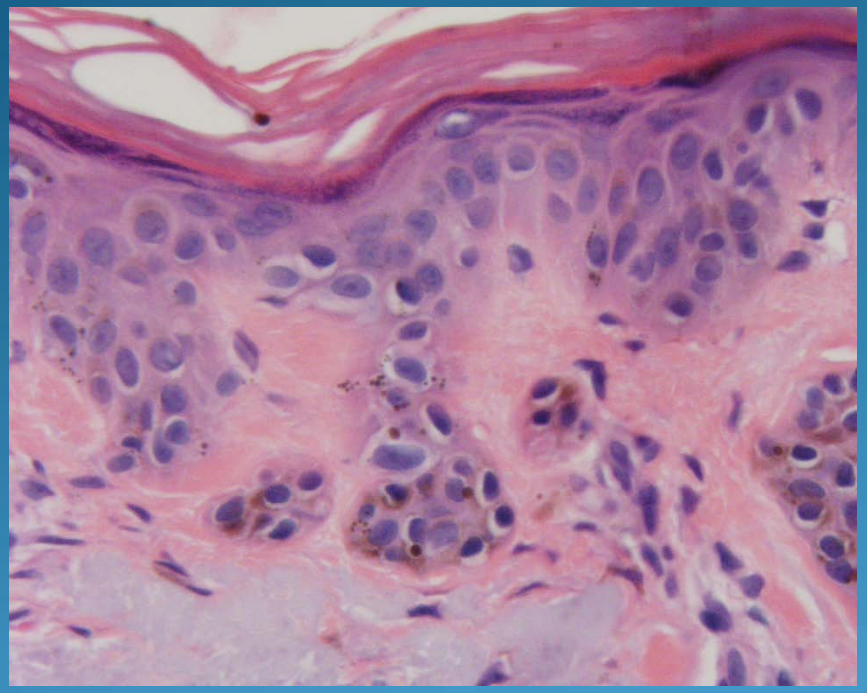
Peutz-Jegher Disease

Cutaneous Changes



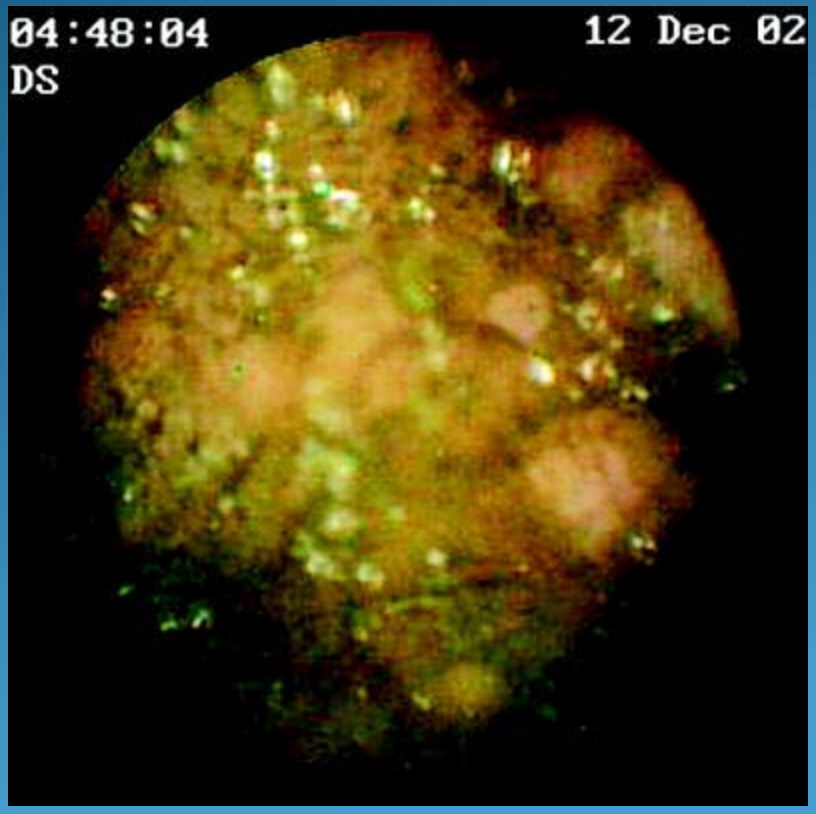
- Excessive freckling or spots on the skin
- Sites
  - Inner lining of the mouth, gums, the lips, around the mouth
  - Around the eyes
  - Fingers or toes
  - Genitalia

Cutaneous Changes



- Oral lesions remains through adulthood
- Bluish black to dark brown to blue
- > 95% of pts.
- No correlation with GI symptoms

GI Disease

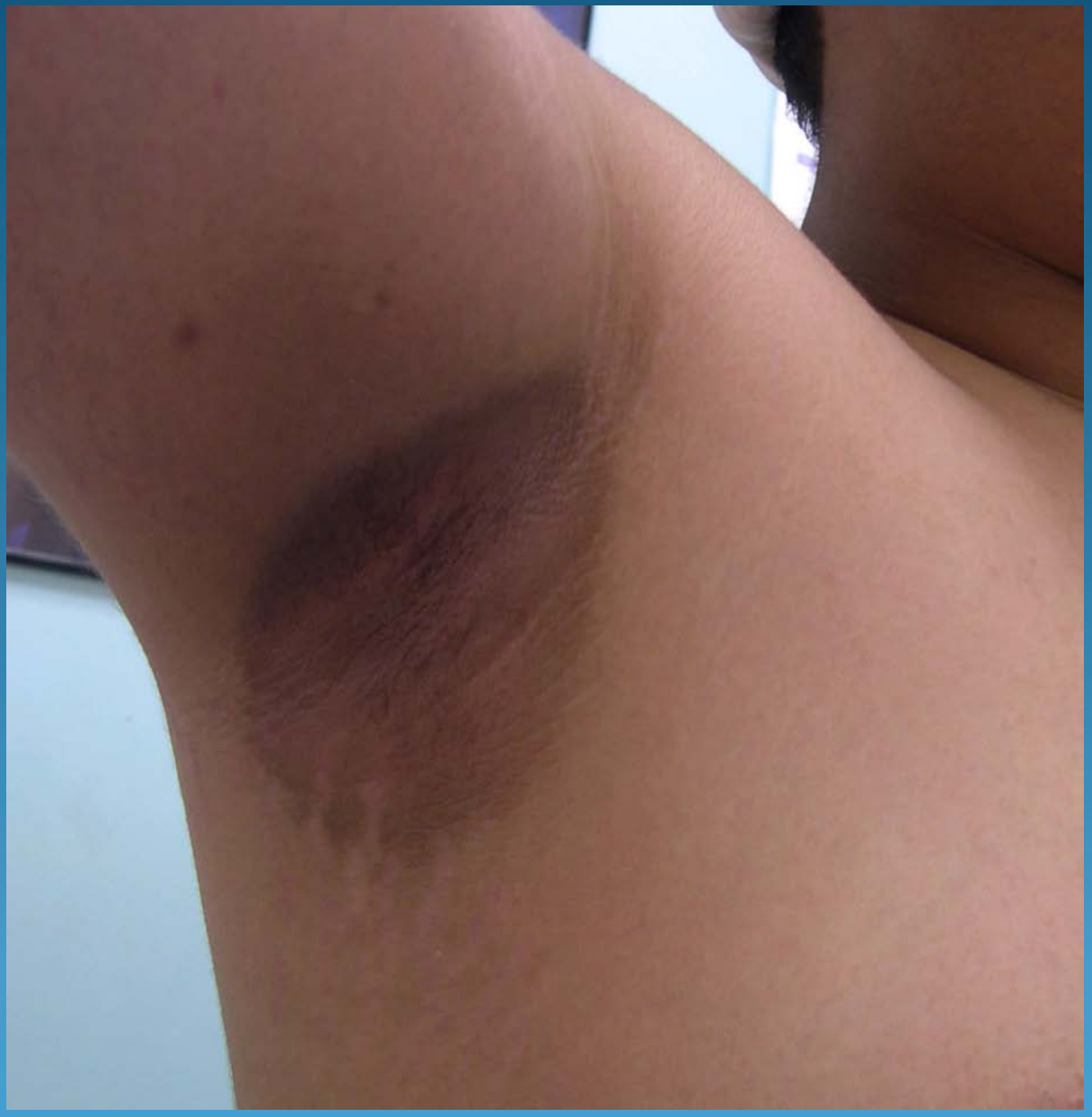


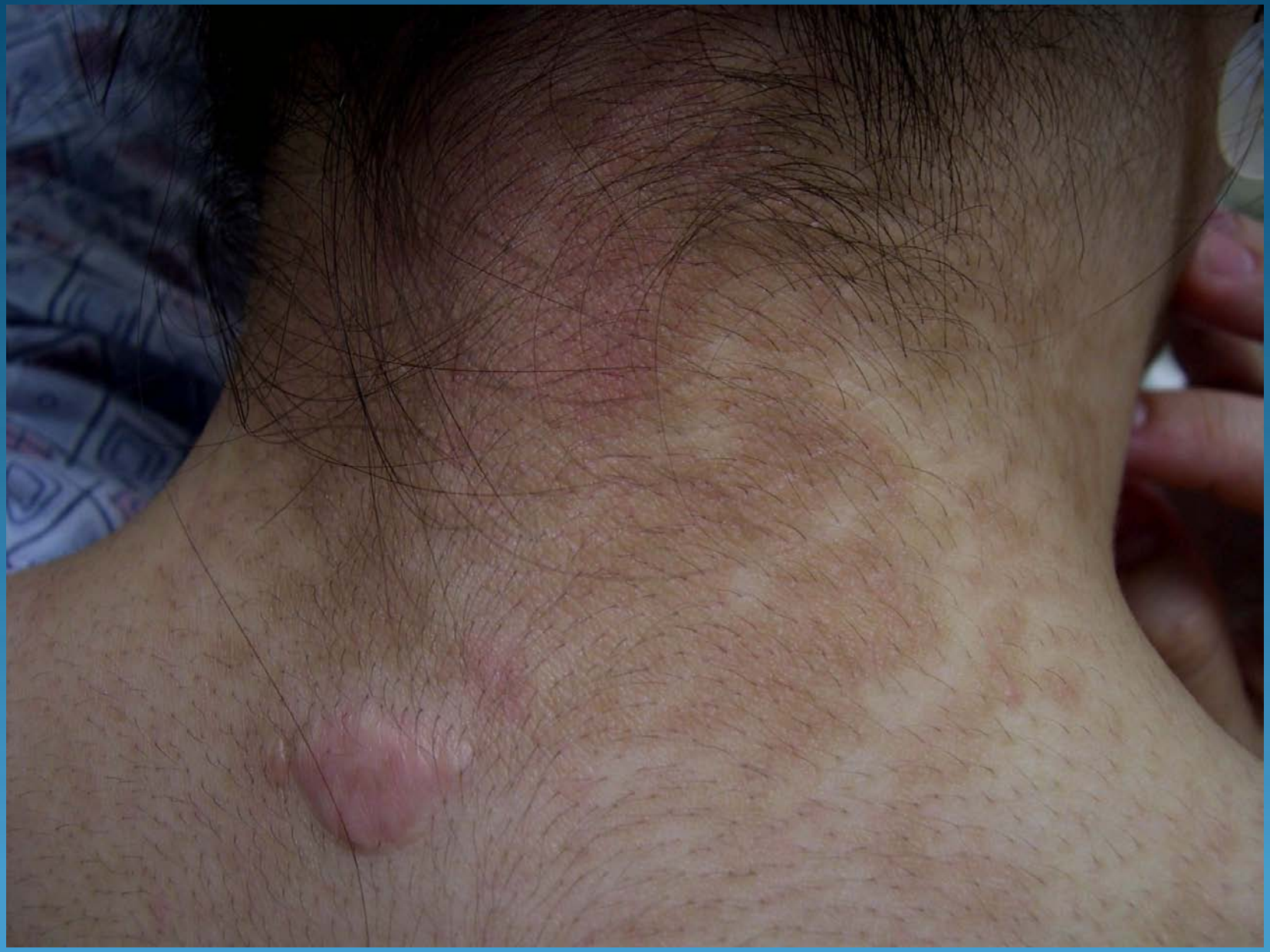
- Numerous hamartomatous polyps in stomach and intestines
- Variant of FAP a genetic defect on the APC gene (5q21)
- 500-2500 colonic adenomas with a minimum of 100 needed for diagnosis

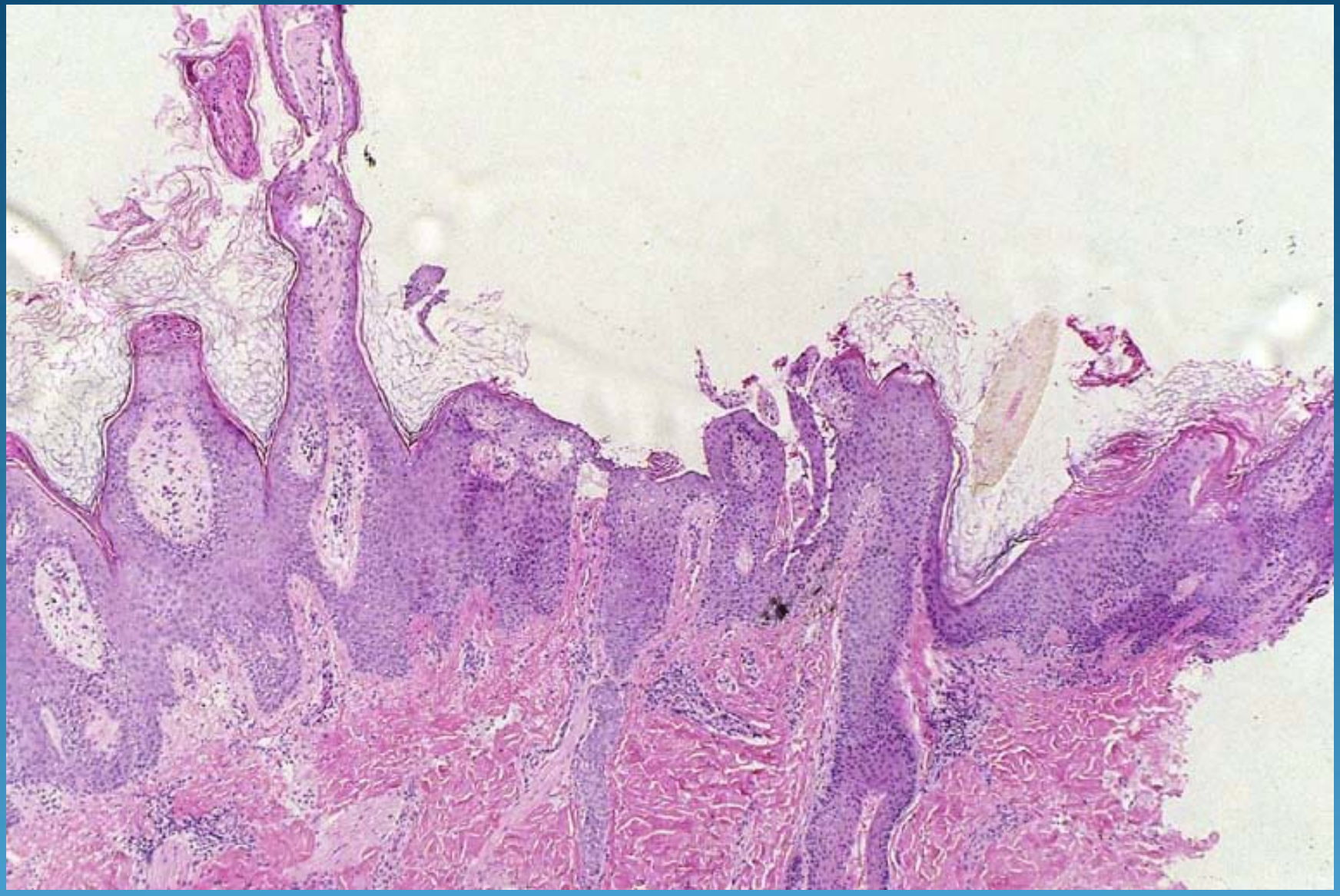
DDX

Syndrome	Characteristics
FAP	Genetic defect on the APC gene (5q21) 500-2500 colonic adenomas with a minimum of 100 needed for diagnosis
Gardner Syndrome	Variant of FAP Colonic adenomas, osteomas of the bone, epidermal cysts, thyroid cancer, and fibromatosis
Turcot Syndrome	Adenomatous colon polyps and tumors of the central nervous system (usually gliomas) Polyps arise from 10-20 yrs, cancer follows after 10-15 yrs

44 y.o. F
Diabetes mellitus x15 yrs
Complaining of dirty neck and armpits

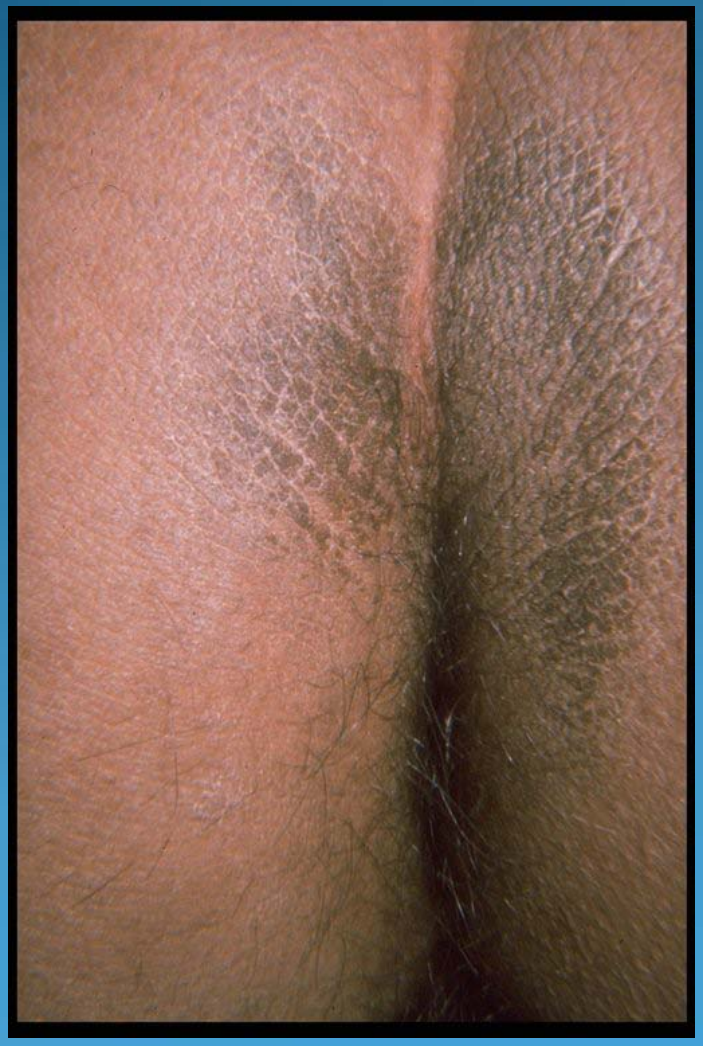






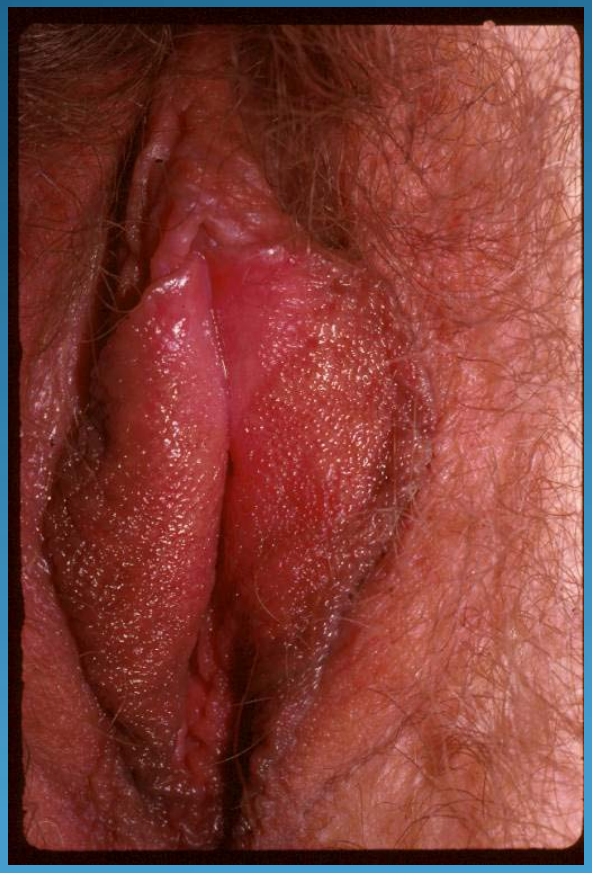
Acanthosis Nigricans

Clinical Appearance



- Symmetrical, hyperpigmented, velvety plaques
- Intertriginous areas (axilla, groin, posterior neck)
- Posterior neck common in children

Clinical Appearance



- Vulva in obese hyperandrogenic females
- Acrochordons (skin tags) in affected area
- Nail changes rare

Clinical Variants

Obesity associated

Syndromic

Acral

Unilateral

Familial

Drug induced

Malignant

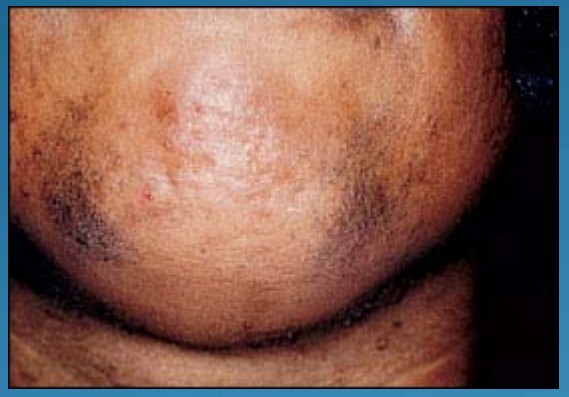
HAIR-AN SYNDROME

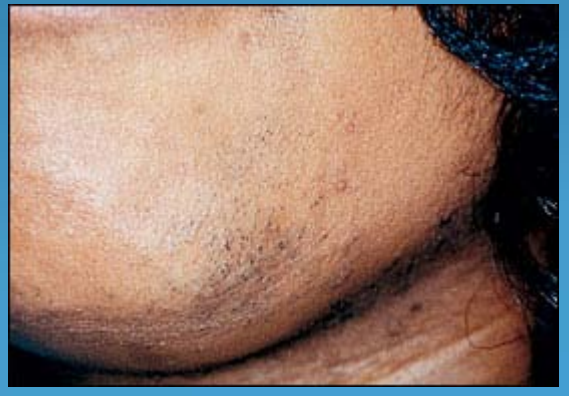
Hyperandrogenemia

Insulin resistance

Acanthosis nigricans syndrome

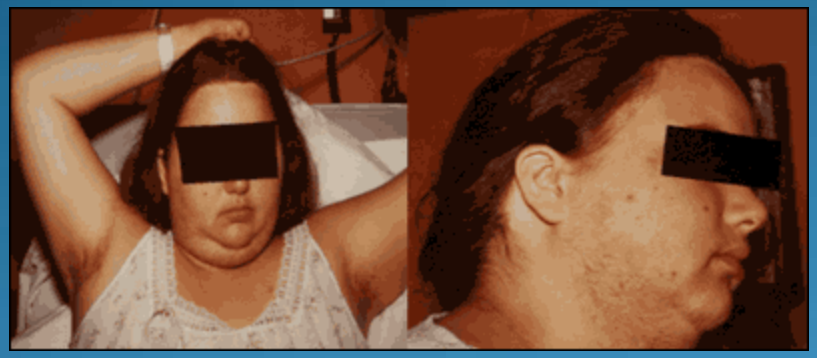
HAIR-AN Syndrome-Type A





- Familial, affecting primarily young women
- Polycystic ovaries
- Signs of virilization (eg, hirsutism, clitoral hypertrophy)
- High plasma testosterone levels
- Infancy with progression

HAIR-AN Syndrome-Type B

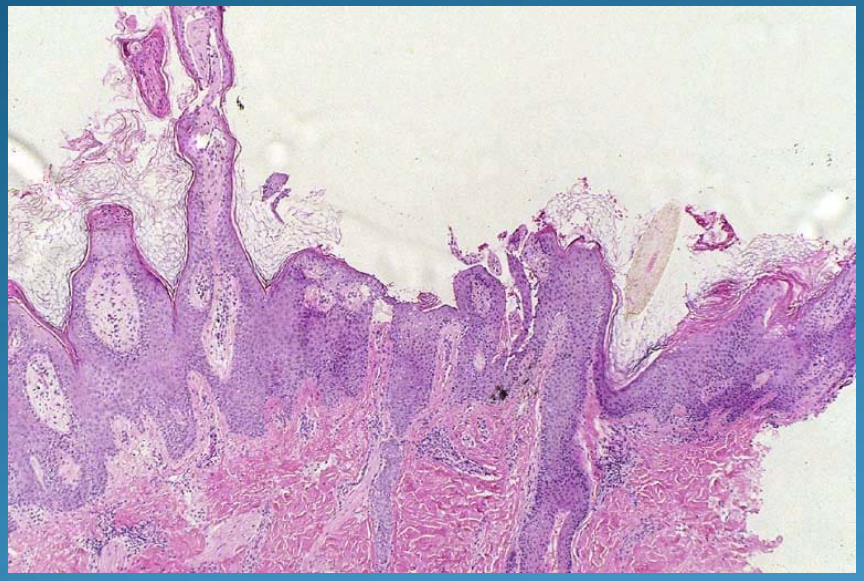


- **Uncontrolled diabetes mellitus**
- **Ovarian hyperandrogenism**
- **Autoimmune disease-Ab to insulin**
- **Circulating antibodies to the insulin receptor**
- **Varying symptomatology**

Malignant

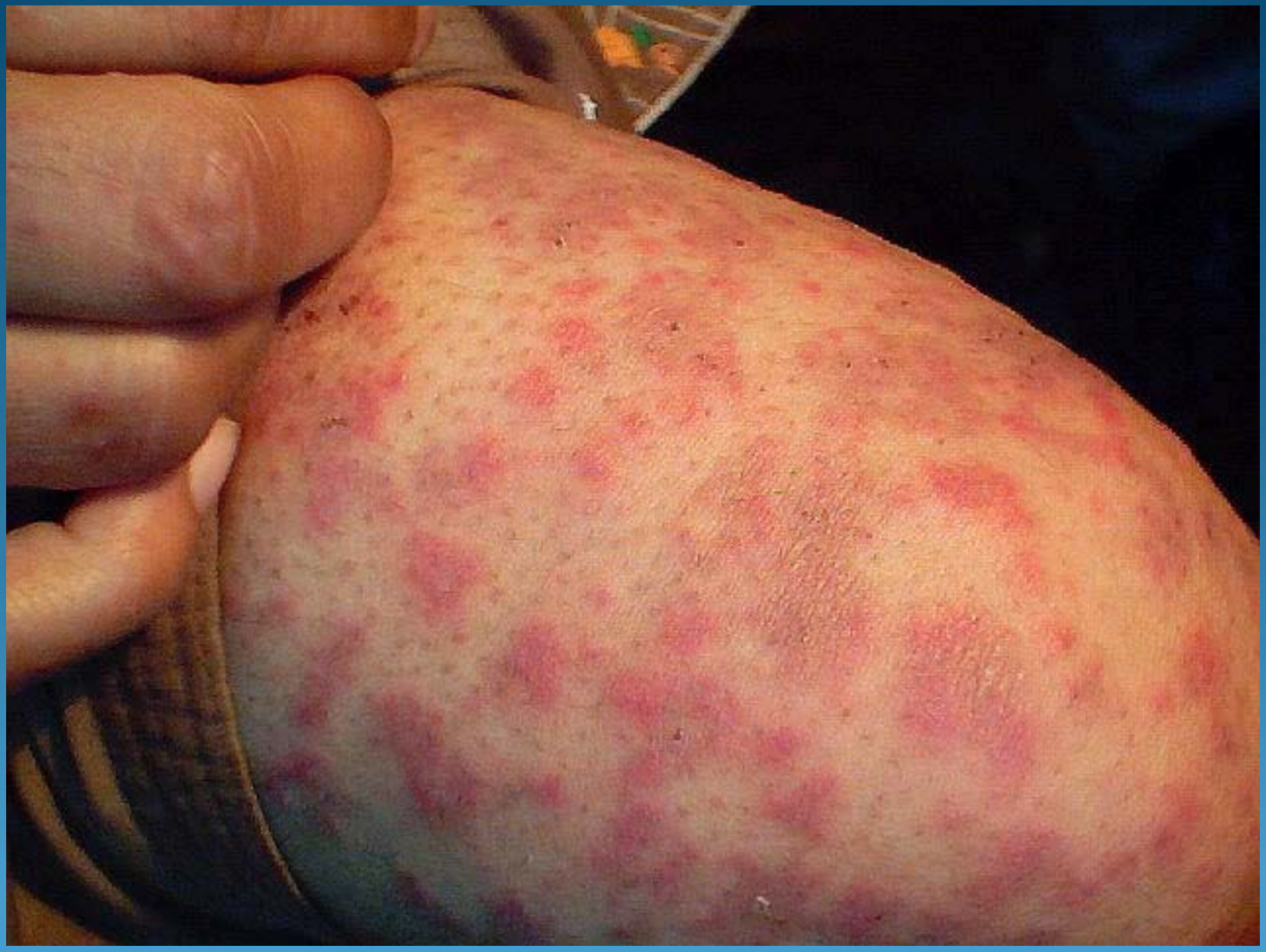
Cancer Type	Percentage
Gastric	69-90%
Oral (tongue, lips)	25-50%

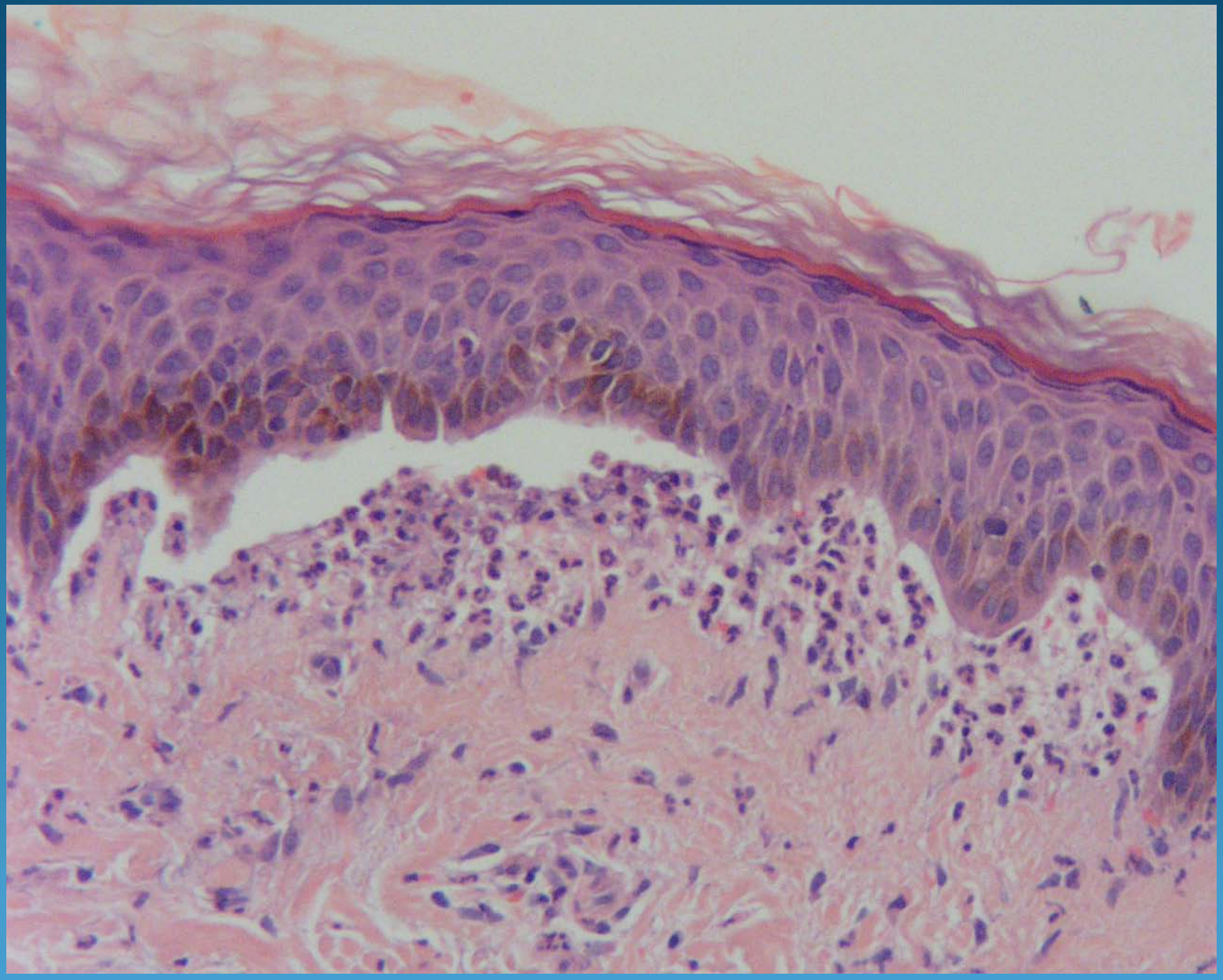
Histopathology

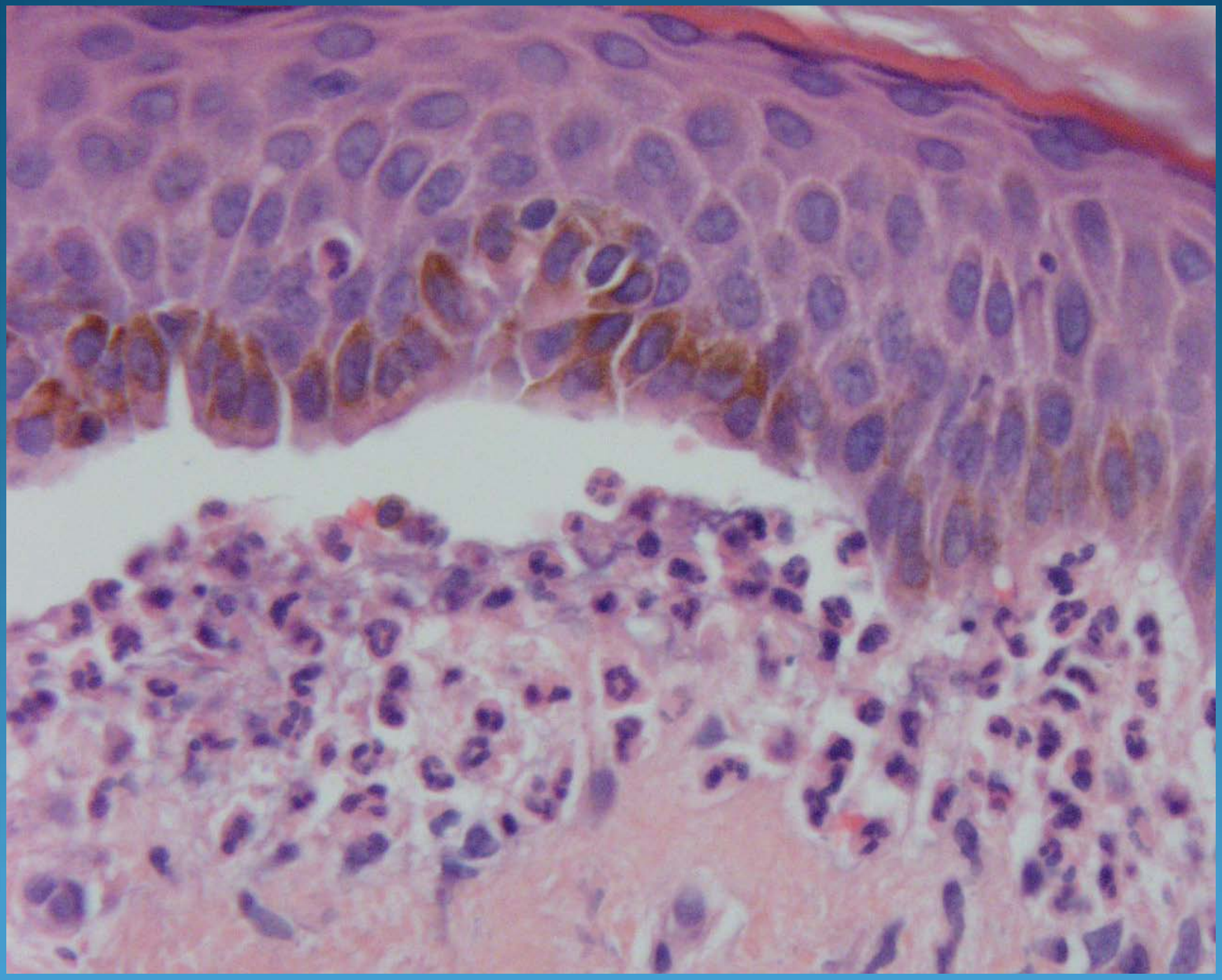


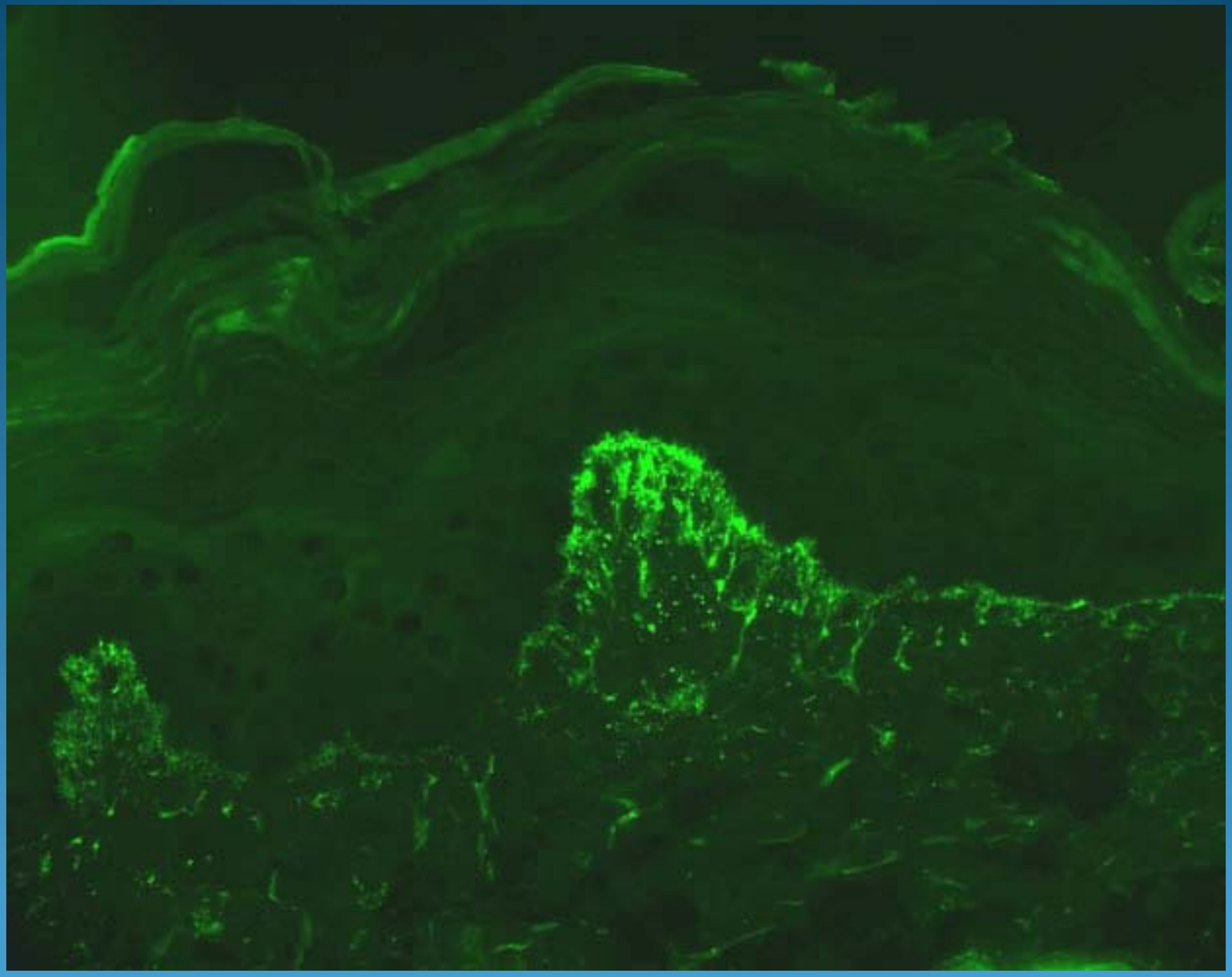
- Slight papillomatosis
- Minimal basal melanin pigment
- Hyperkeratosis
- Horn pseudo-cysts
- DDX: SK, lentigo

35 y.o. F
Watery stools
Weight loss for 3 months
Rash on trunk and extremities



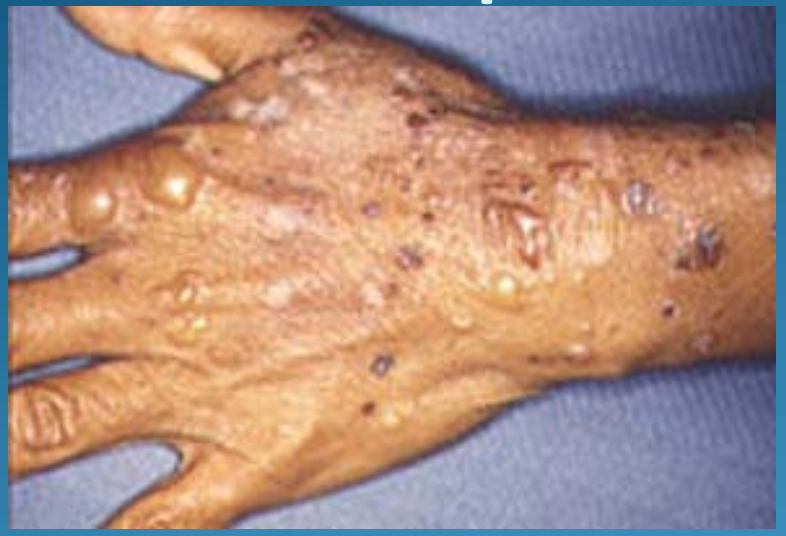


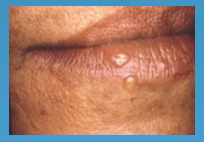




Dermatitis Herpetiformis with Celiac Sprue

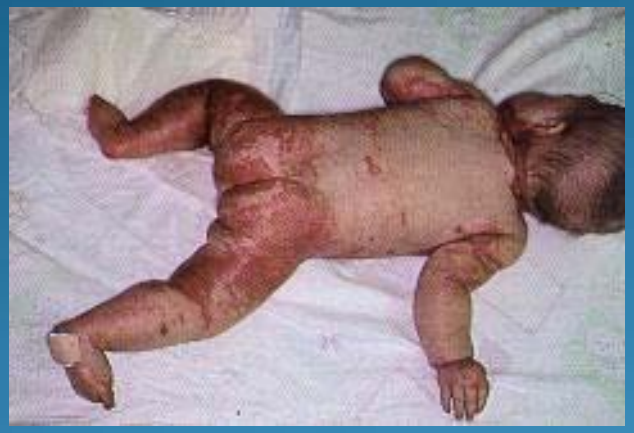
Malabsorption and Skin Disease

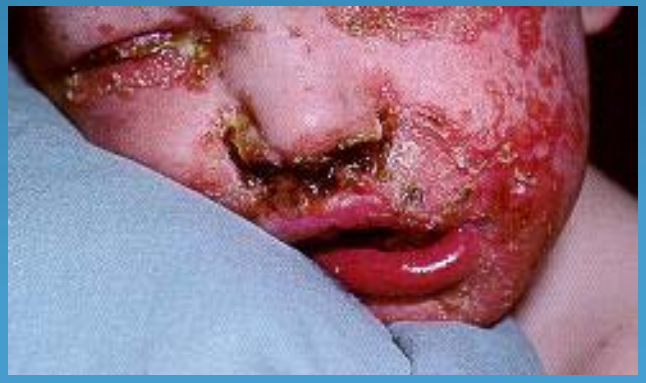




- Ichthyosis and pruritis
- Hair and nail changes
- Hyperpigmentation
- Skin texture and elasticity
- Eczematous and psoriatic rashes

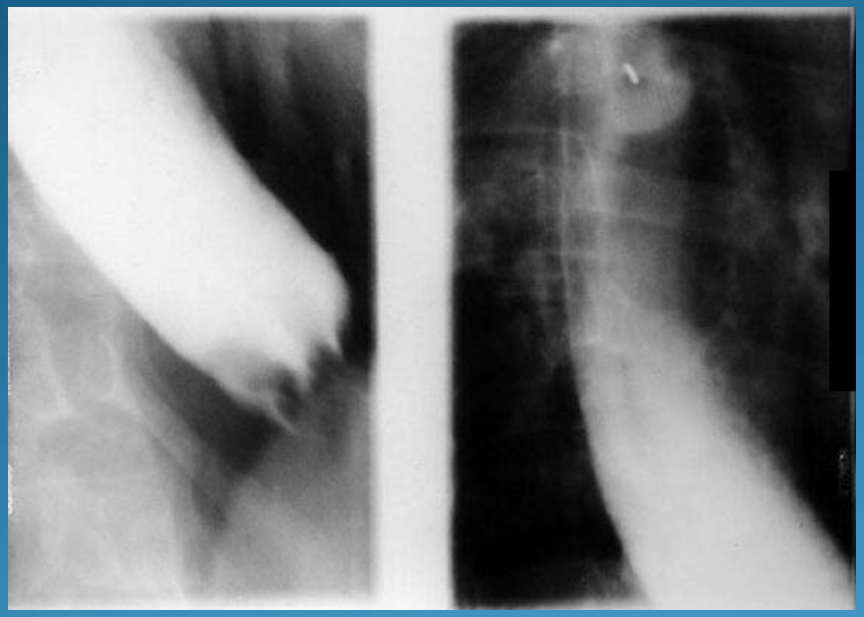
Malabsorption and Skin Disease





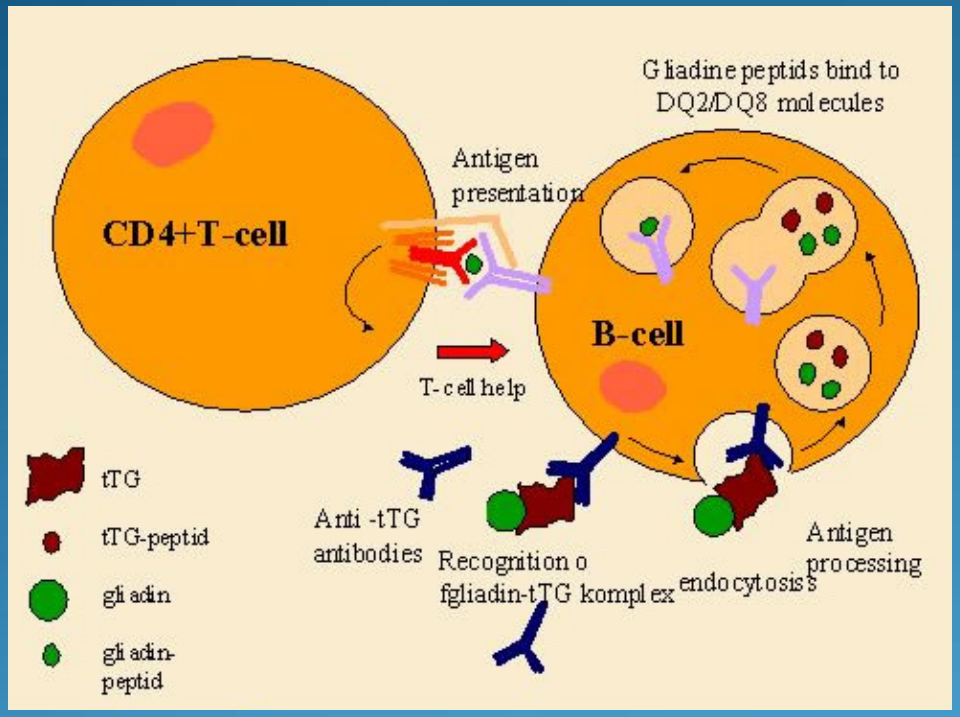
- Zinc
- Essential fatty acids
- Vitamins

Malabsorption and Skin Disease



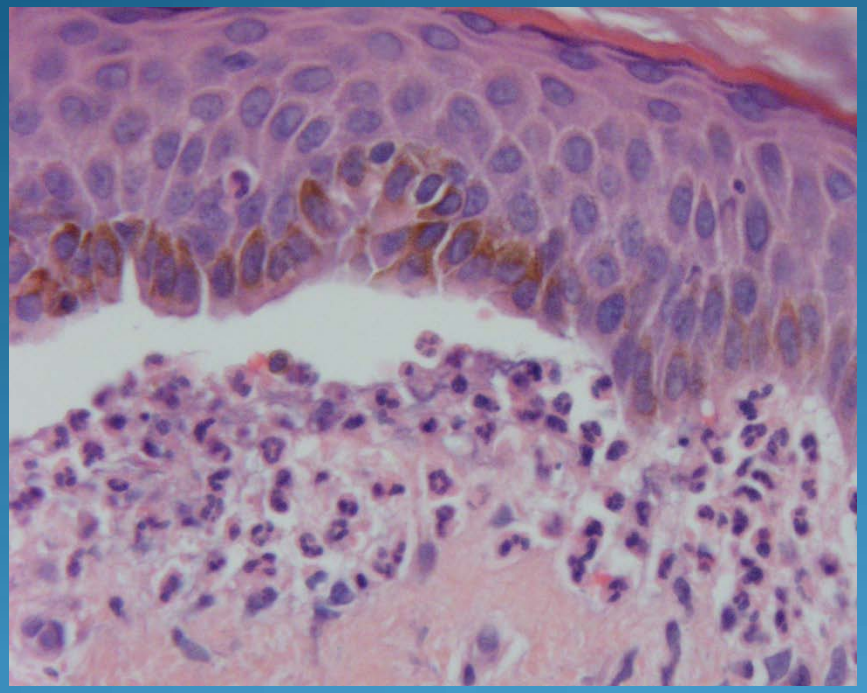
- Collagen vascular disease
- DH and celiac disease

Laboratory Evaluation



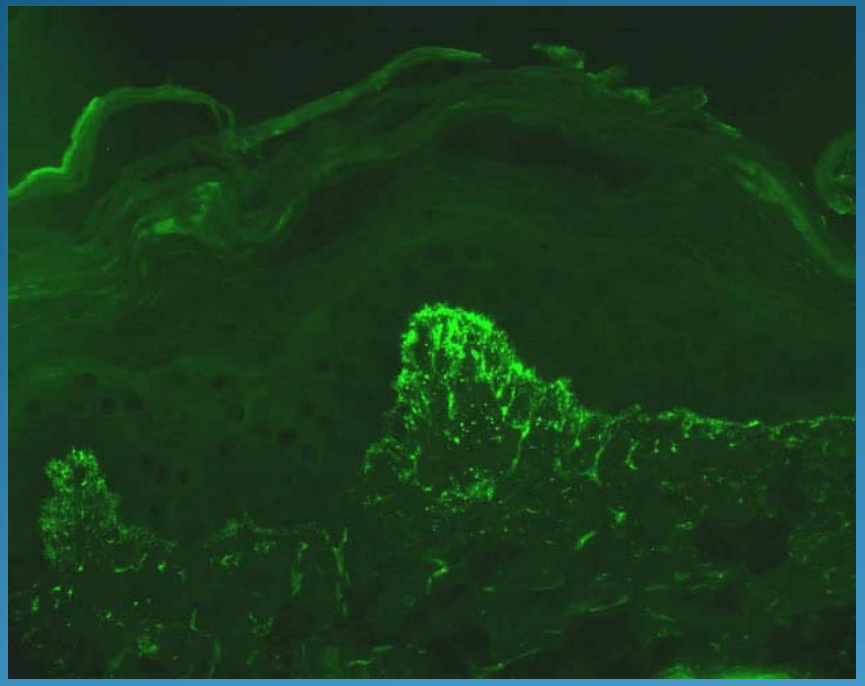
- IgA Tissue transglutaminase Antibodies
- IgA Anti-Endomysium Antibodies
- Anti-Gliadin Antibodies

Histopathology



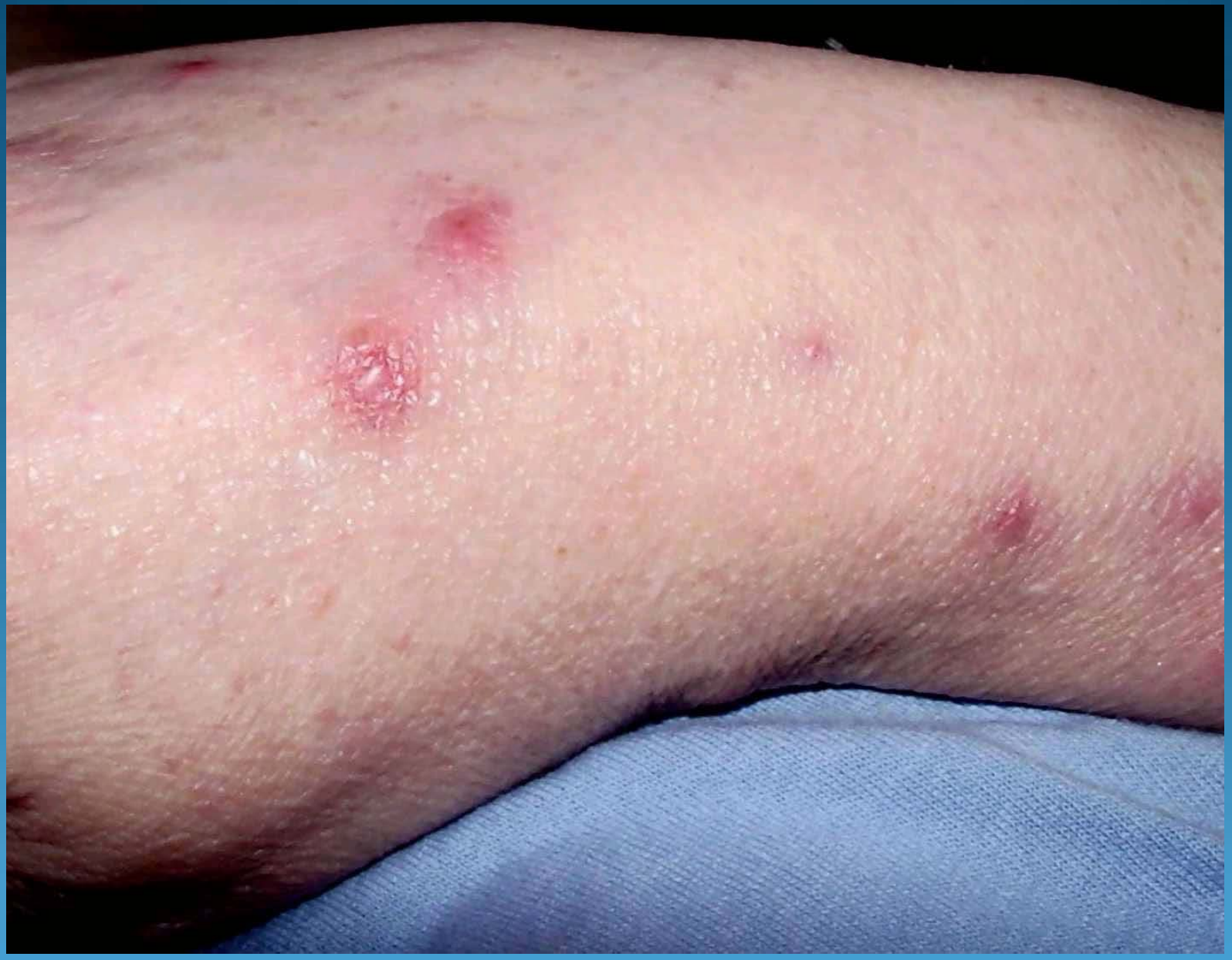
- Subepithelial collections of neutrophils with vesicle
- Tips of papillary dermal papillae
- Minimal eosinophils
- DDX: Linear IgA disease

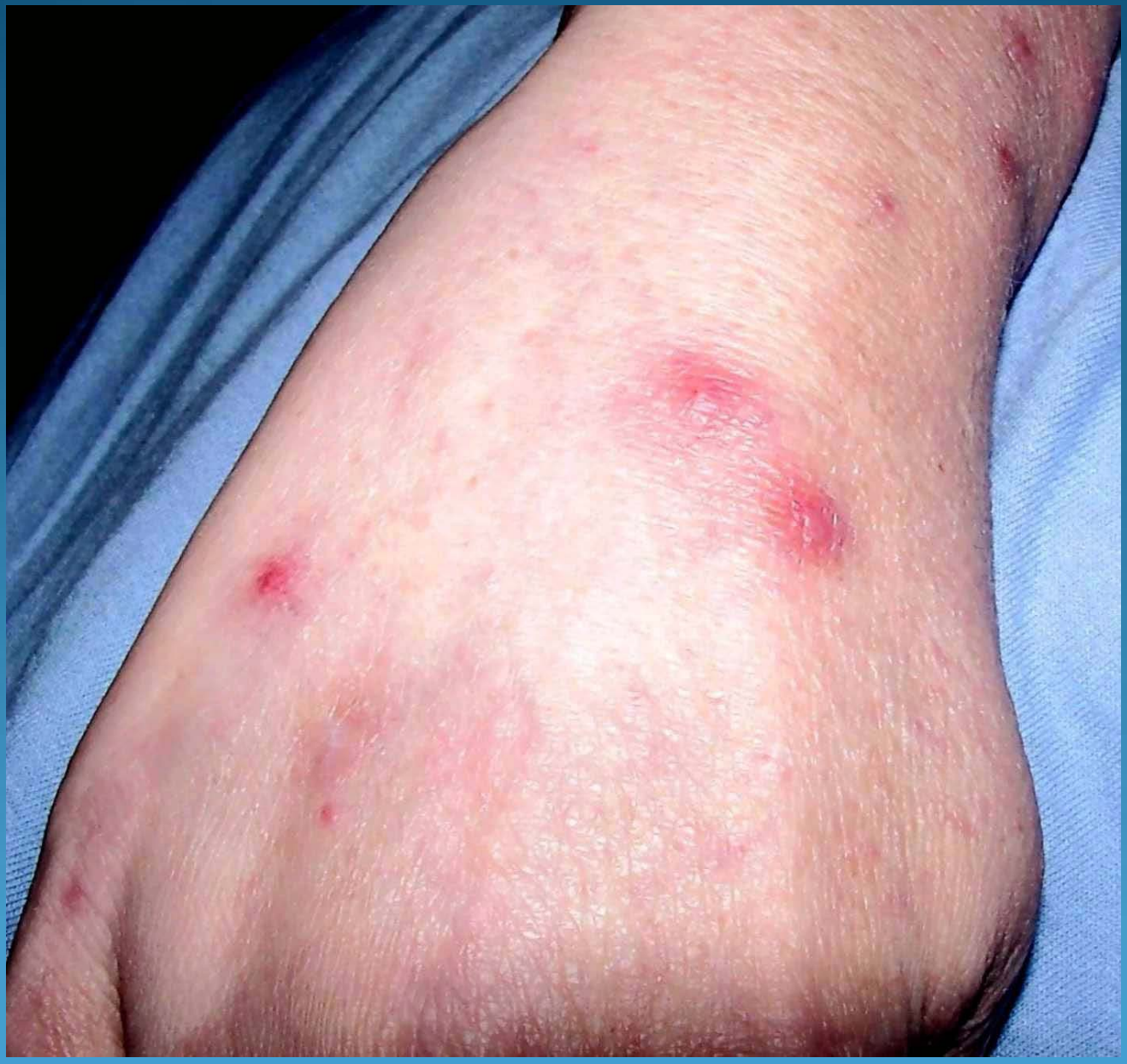
DIF

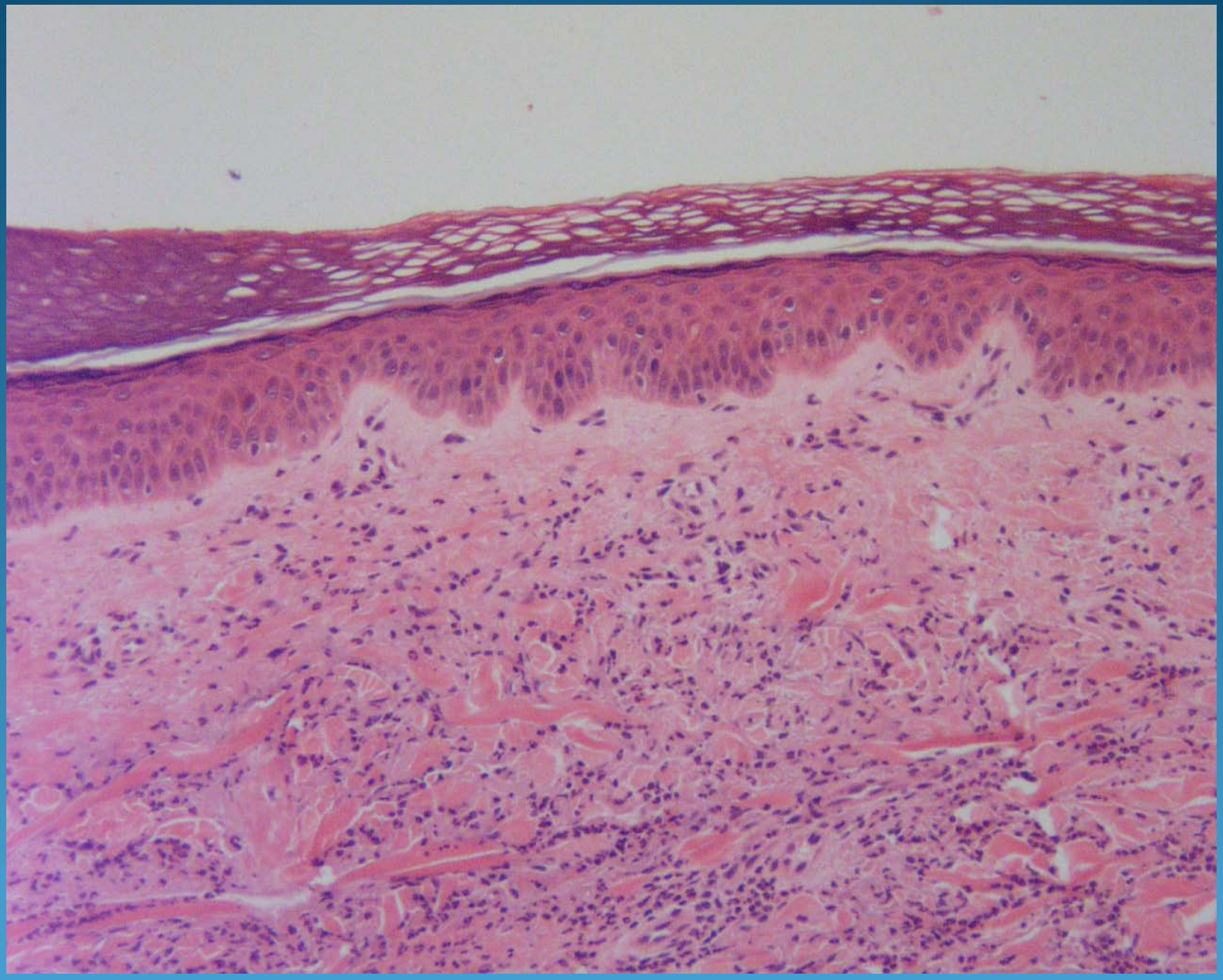


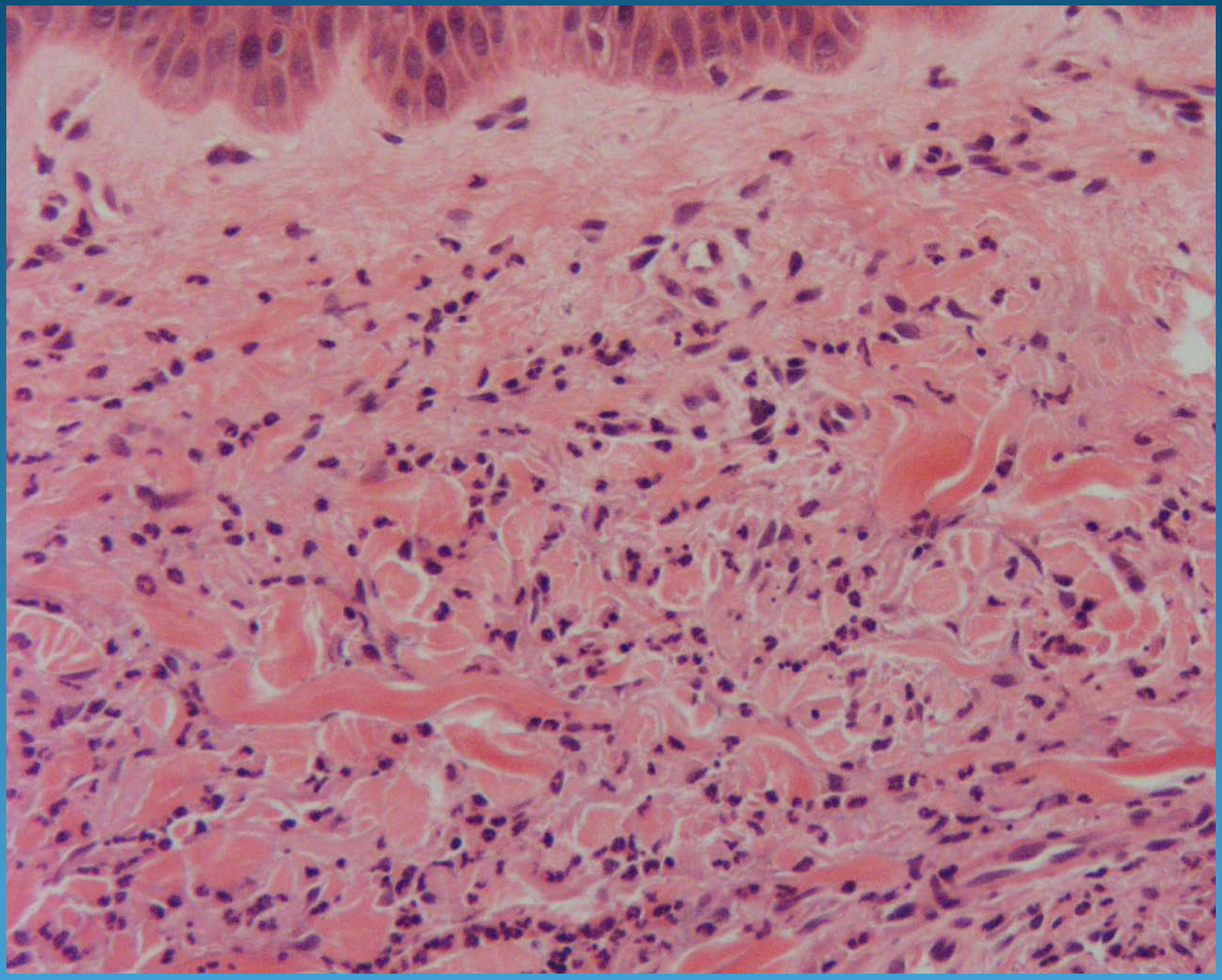
- Subepidermal granular collection of IgA
- DDX: Linear IgA disease

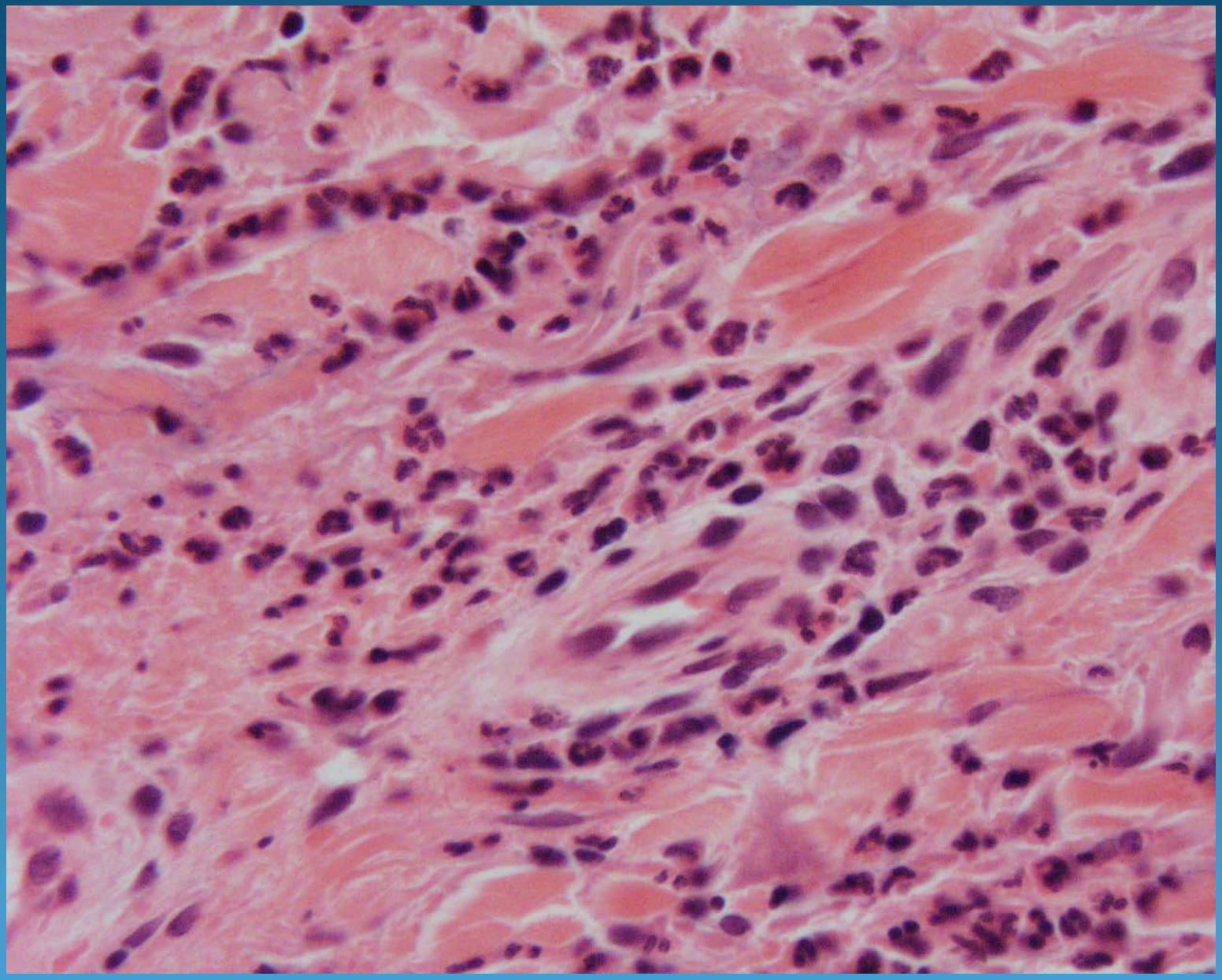
57 y.o F
S/P Roux-en-Y for PUD





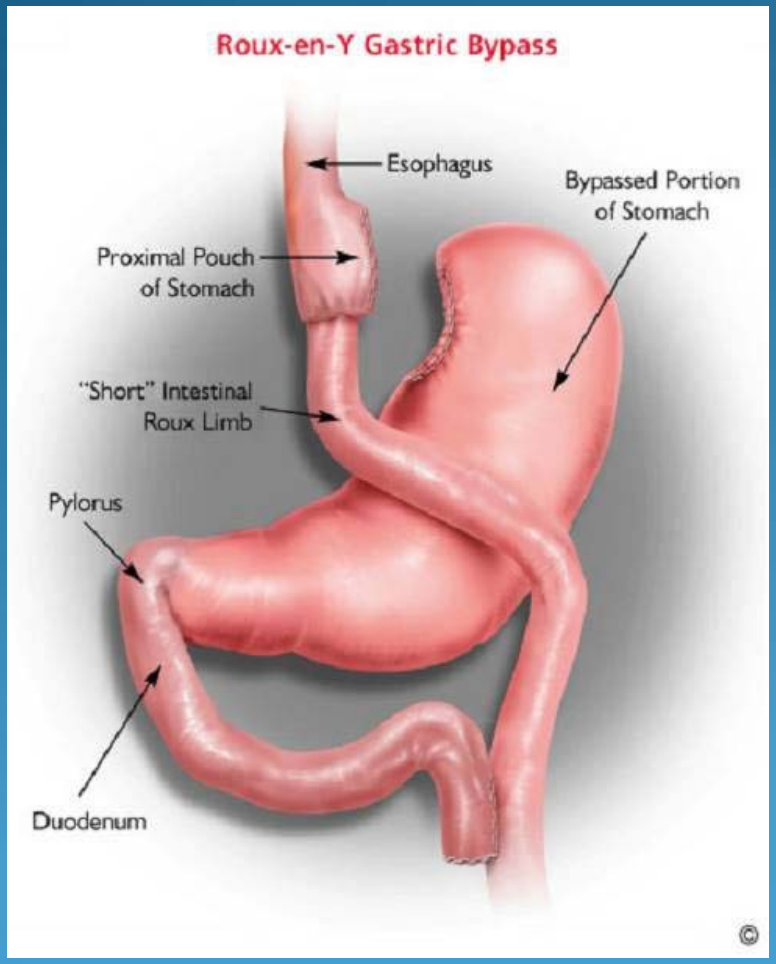






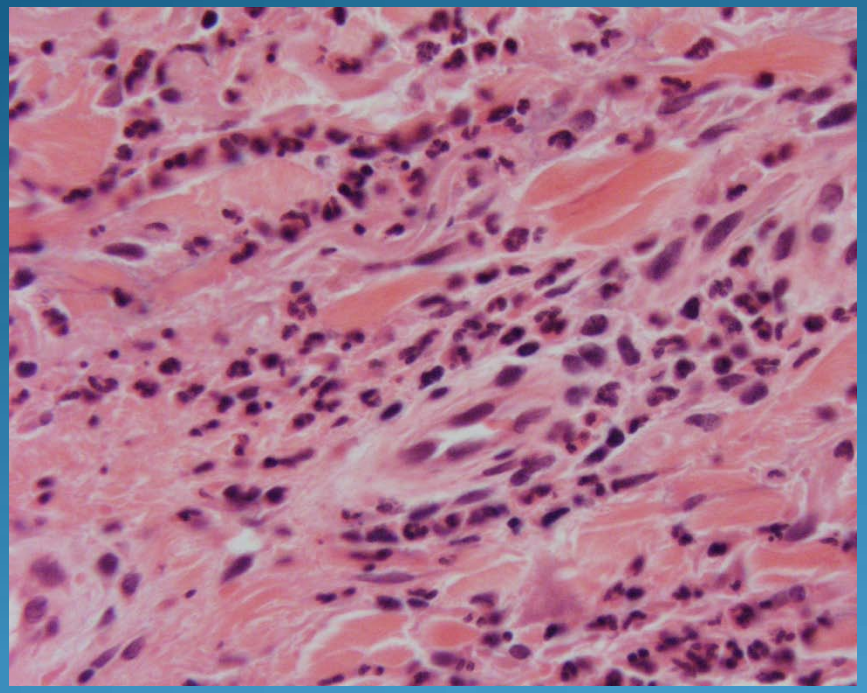
Bowel Bypass Associated Arthritis and Dermatosis

Quick Facts



- Blind loop
- Pts. with bowel bypass surgery, inflammatory bowel disease, and ulcer surgery
- Resolves with correction of the bowel anatomy
- Tetracycline or metronidazole

Histopathology

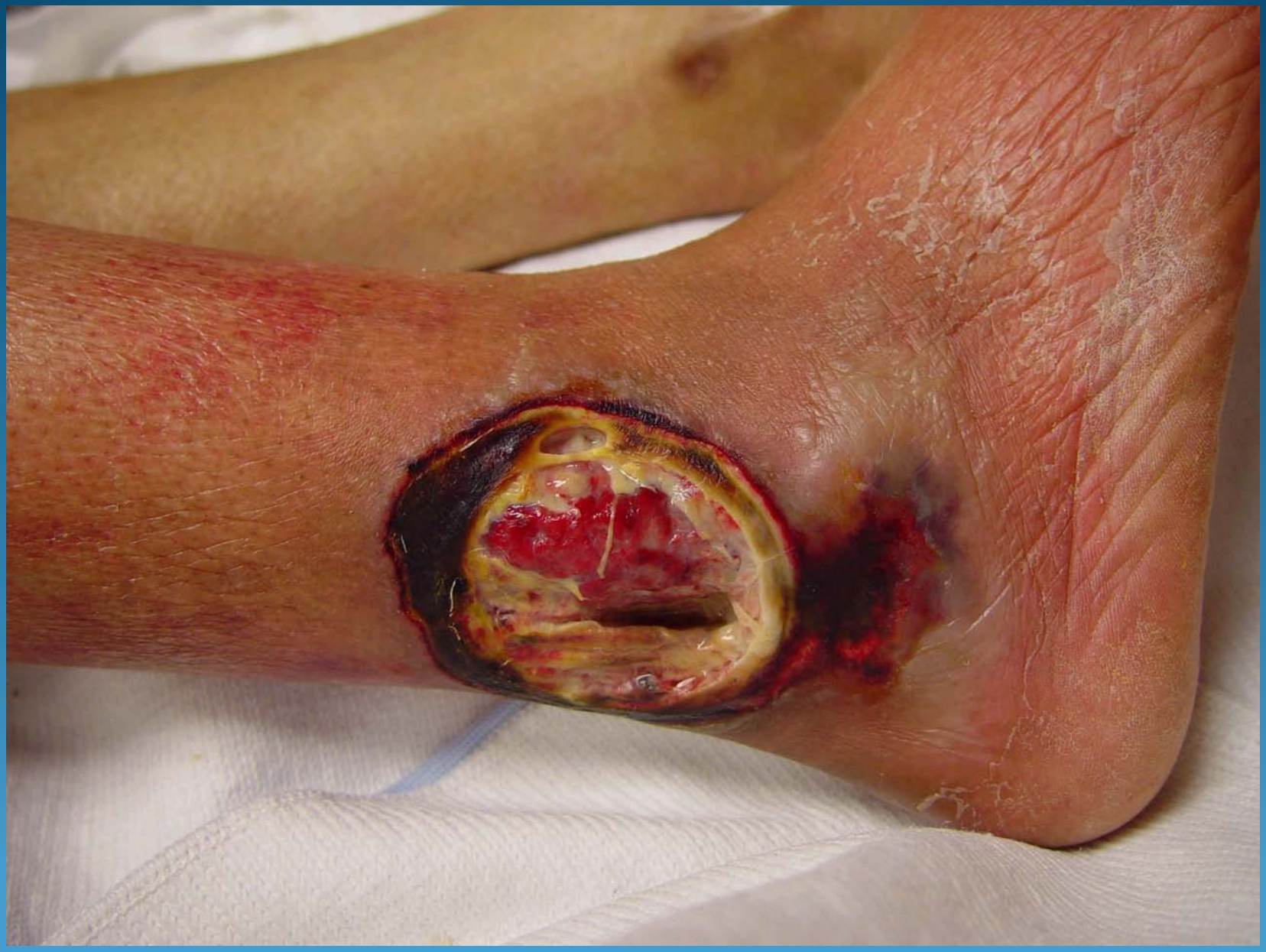


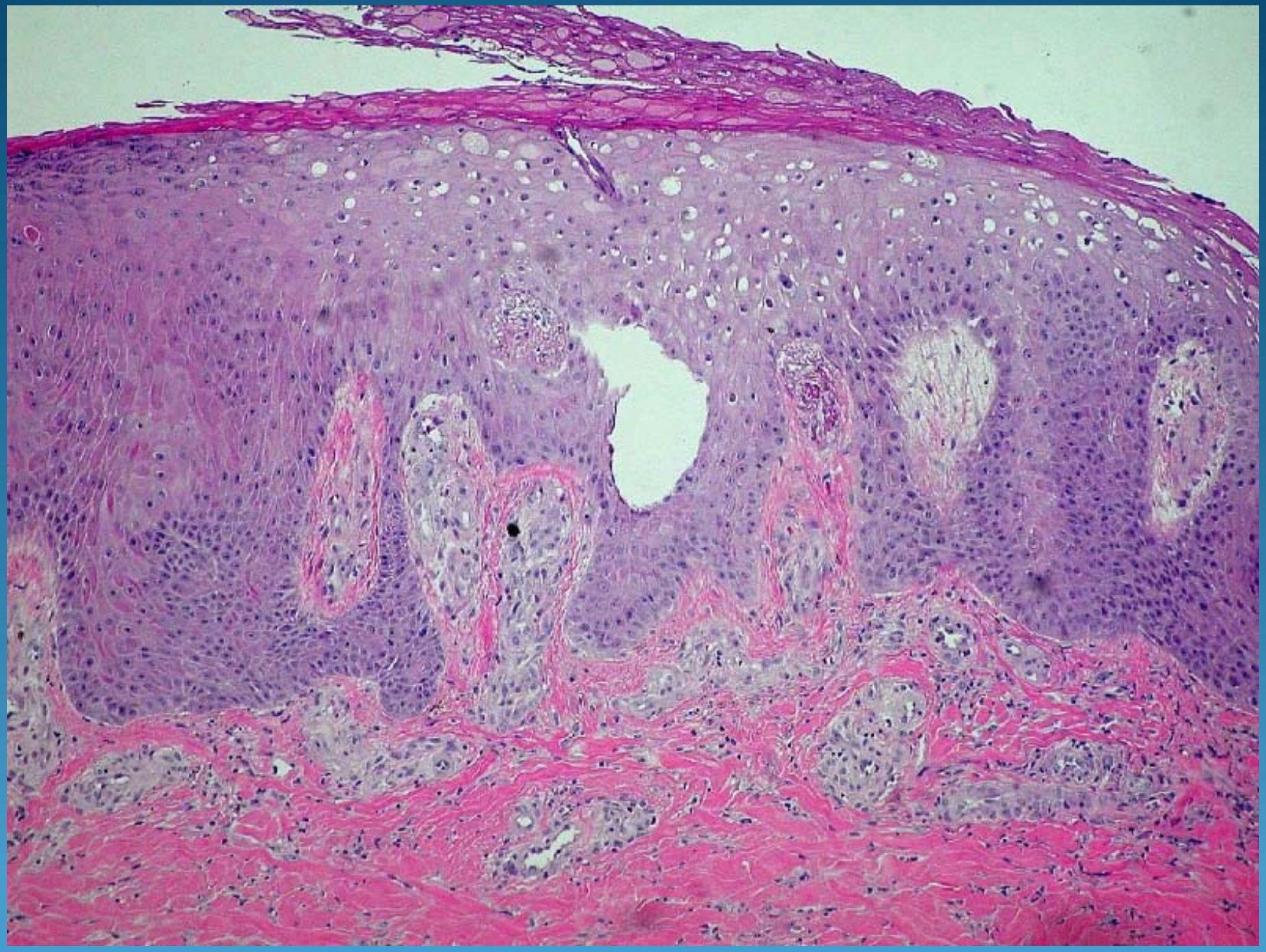
- Neutrophilic dermatosis
- DDX: Sweet's, LCV

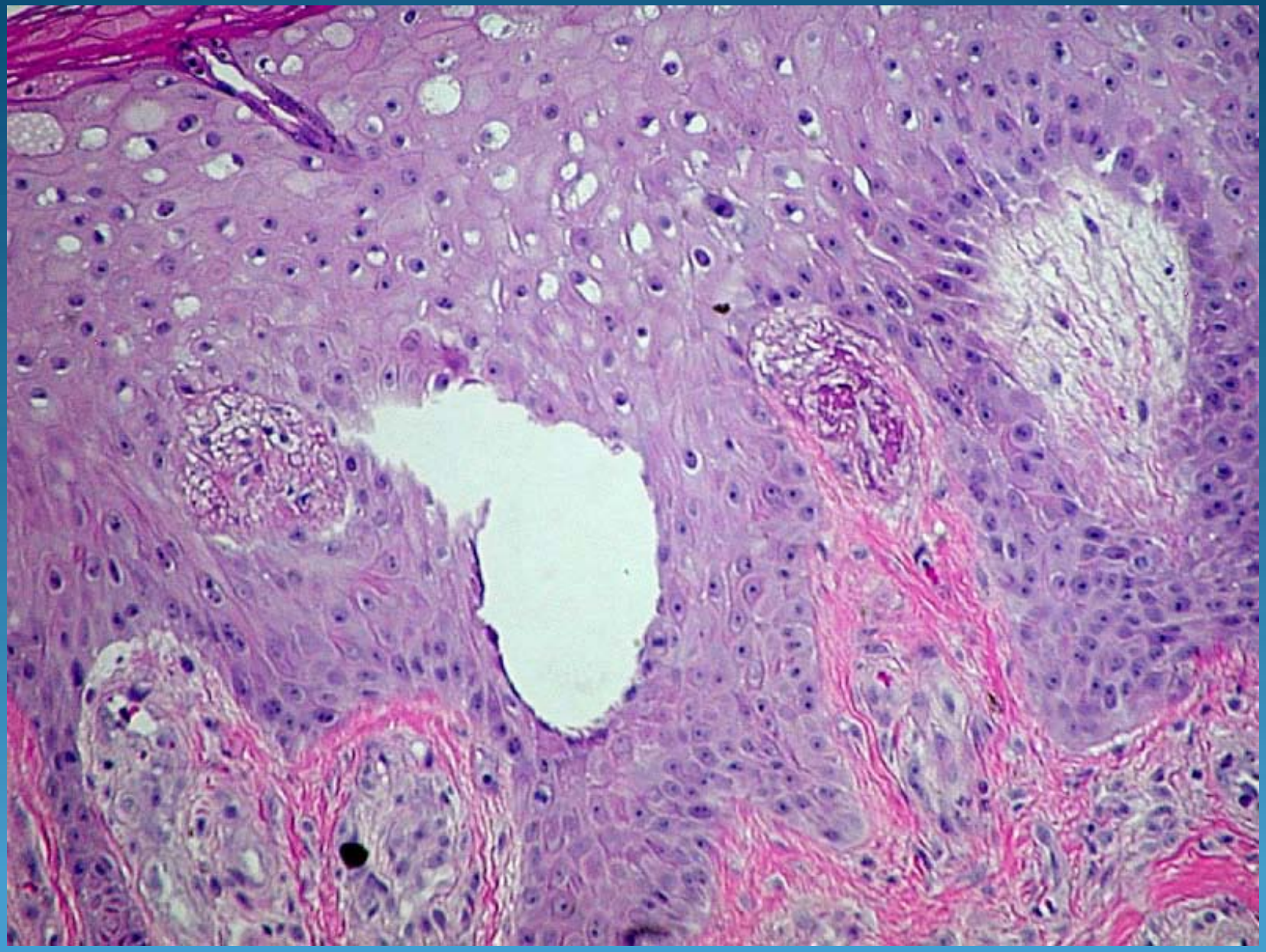
37 y.o. F

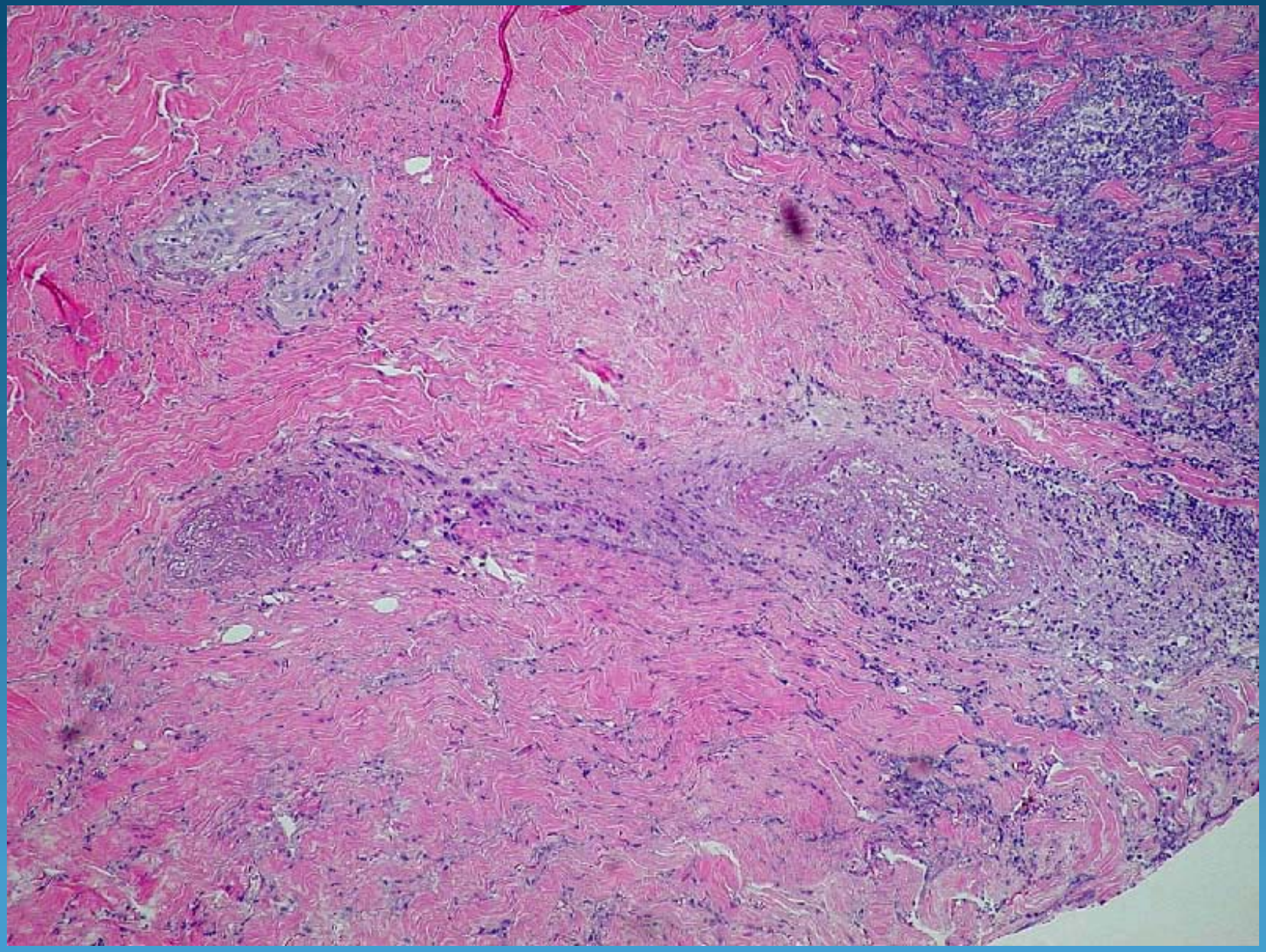
Persistent diarrhea, occ. bloody

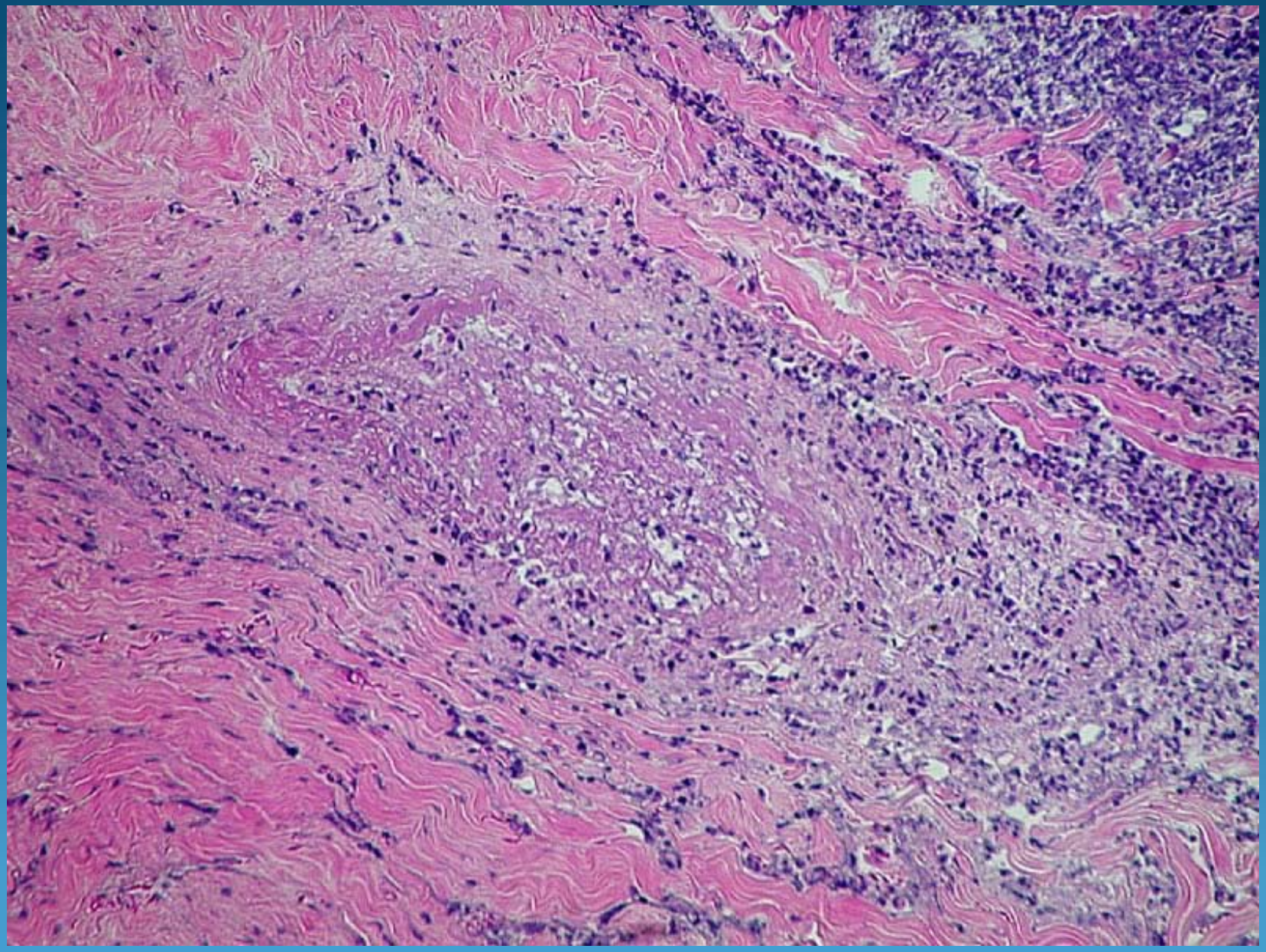
Ulcerative lesion on ankle





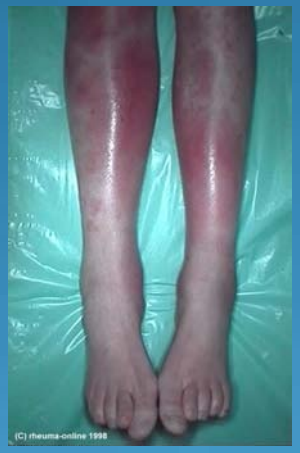






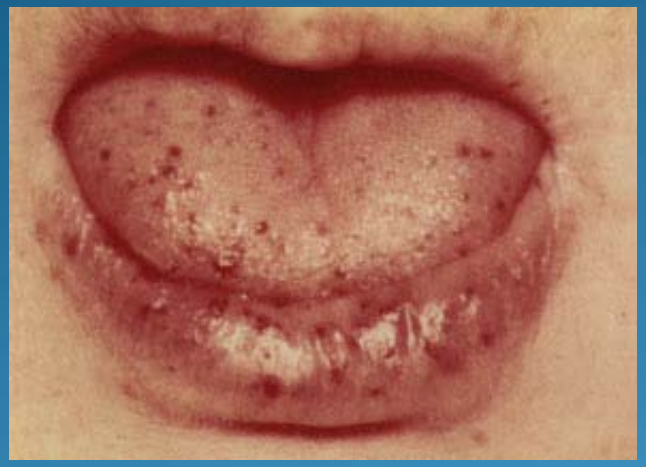
Pyoderma Gangrenosum arising in patient with Ulcerative Colitis

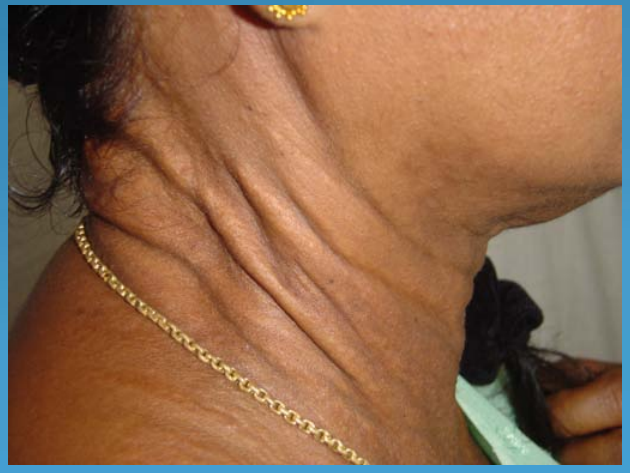
Skin Lesions in IBD



- Pyoderma gangrenosum
- Granulomas
- Erythema nodosum
- Aphthous ulcers
- Malnutrition
- Erythemas, lichen planus, and vascular thrombosis
- Rashes at ileostomy and colostomy sites

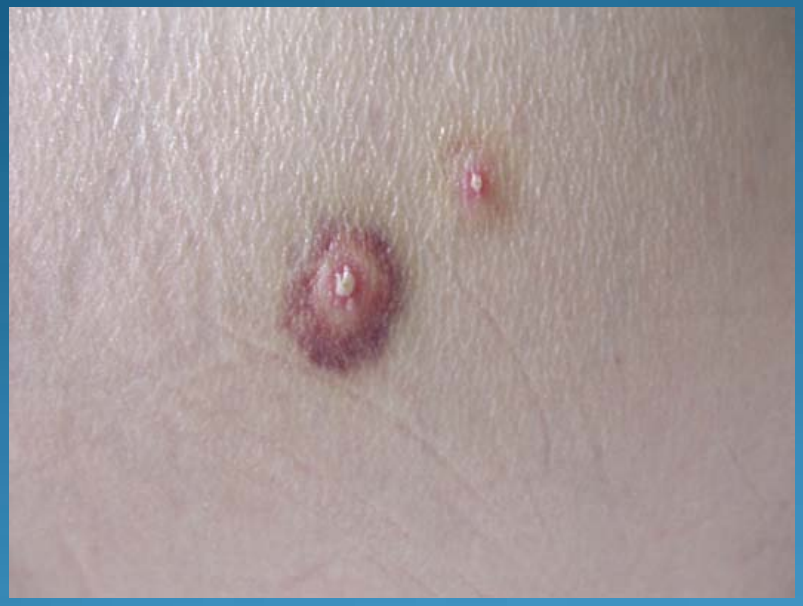
GI Bleeding and Skin Disease





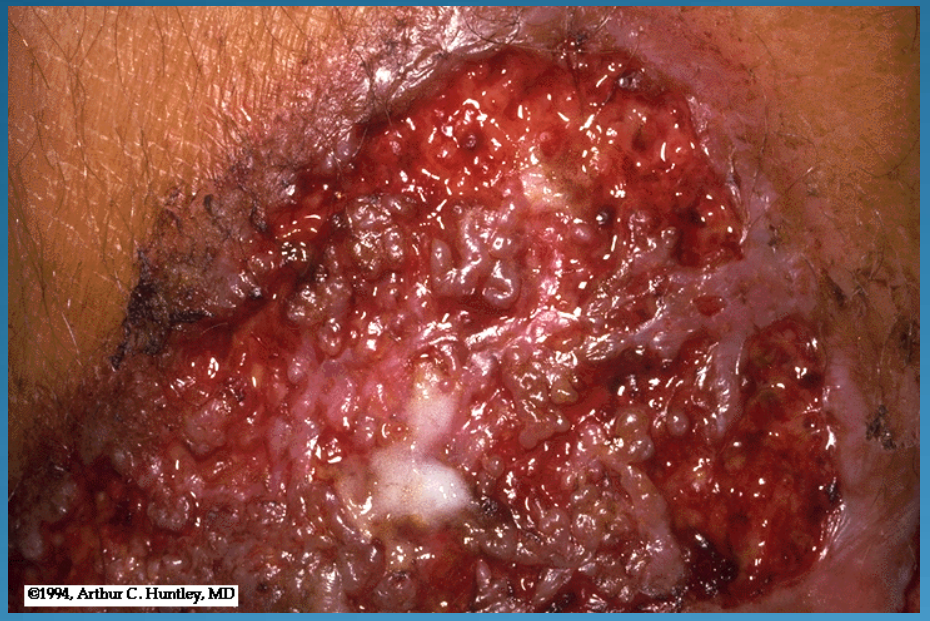
- Hereditary hemorrhagic telangiectasia
- Ehlers-Danlos syndrome
- Pseudoxanthoma elasticum
- Kaposi's sarcoma
- Vasculitis
- Polyposis
- IBD
- Tumors

Pyoderma Gangrenosum



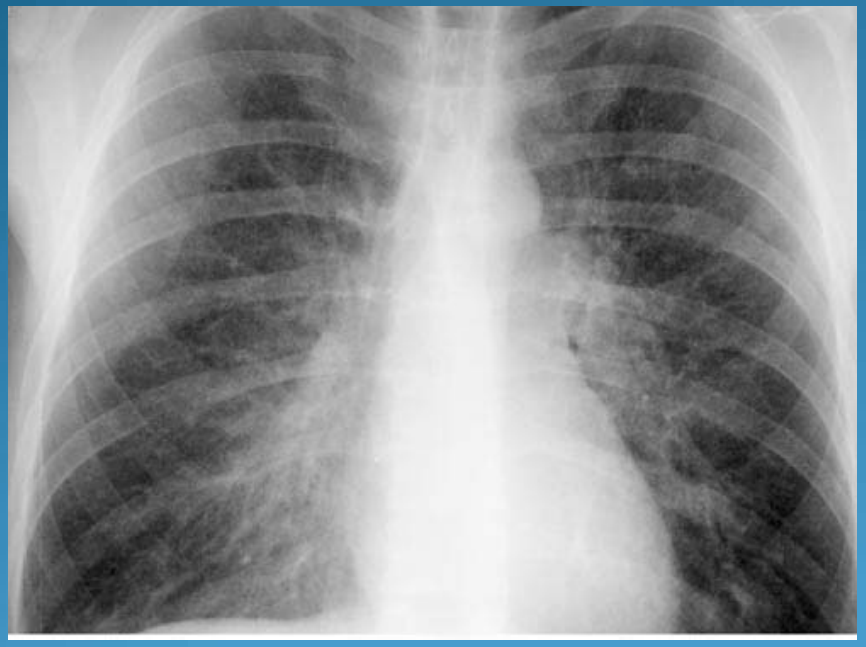
- Systemic diseases in 50%
- Diagnosis of exclusion
- Pathergy

Clinical Variants



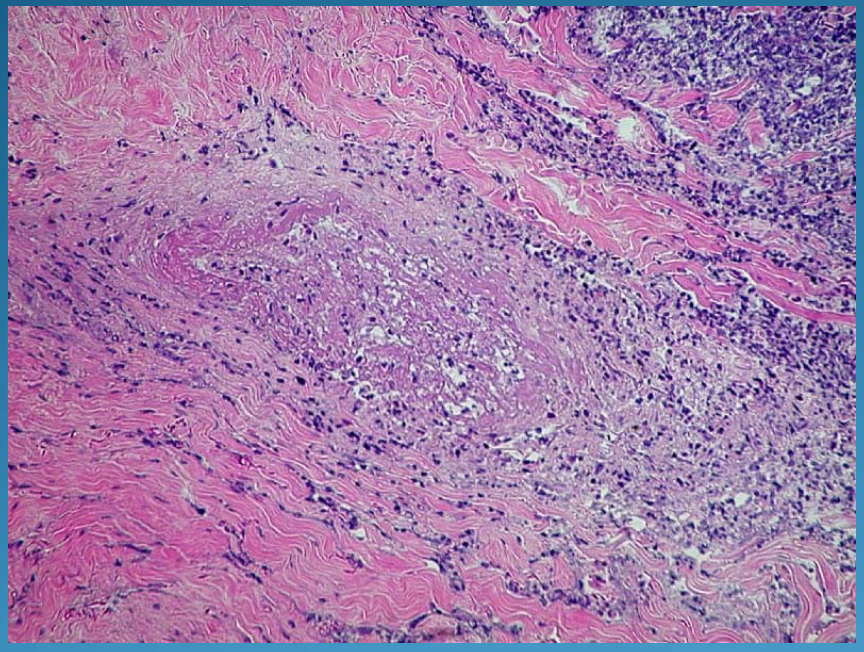
- Two primary variants of PG exist
  - Classic ulceration on legs
  - Superficial (Atypical PG) on hands
- Prognosis good
- Recurrences may occur, and residual scarring is common

Clinical Variant



- **Extracutaneous changes**
  - **Culture-negative pulmonary infiltrates**
- **Overall-NSAIDS, corticosteroids, immunosuppressive agents**

Histopathology

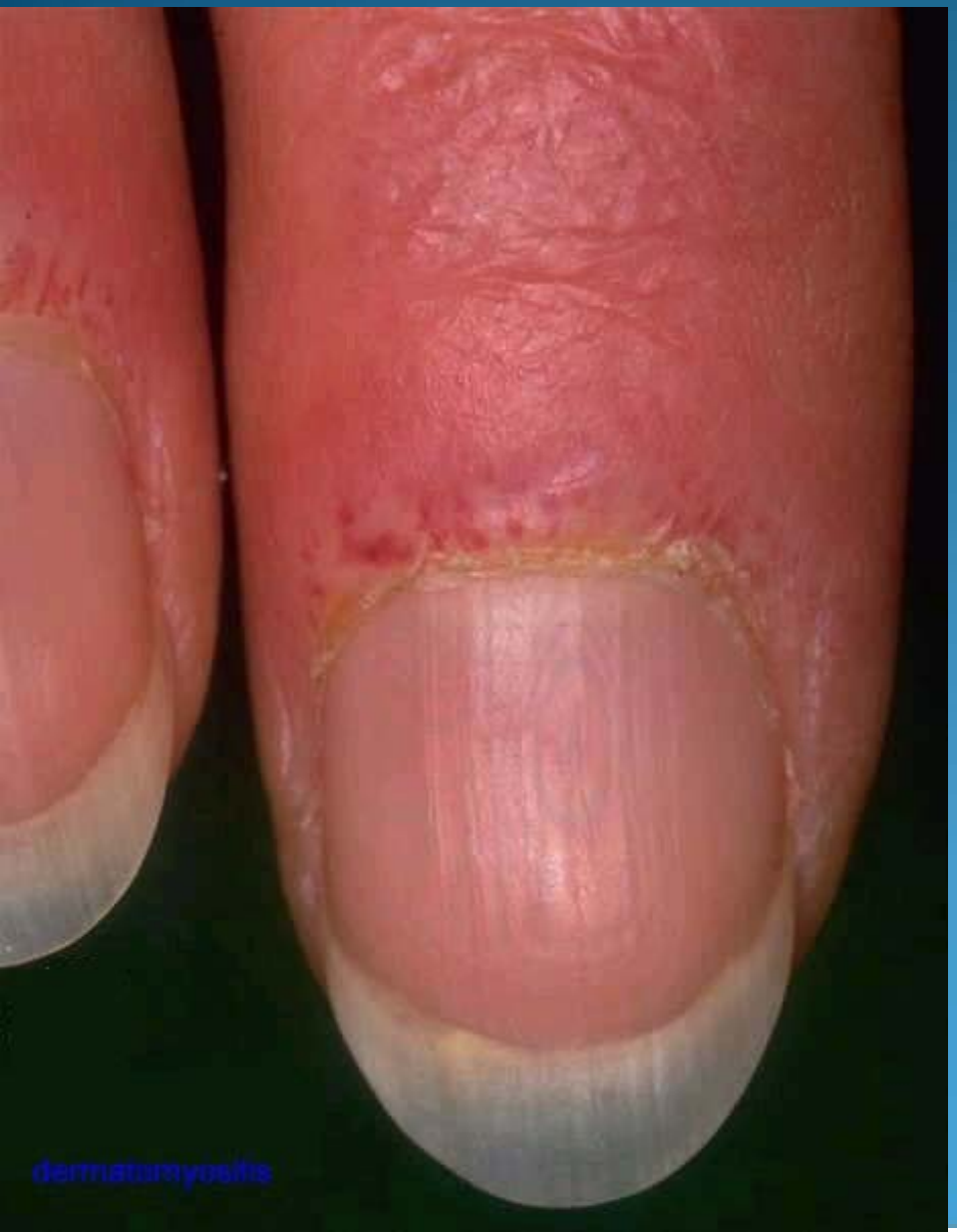


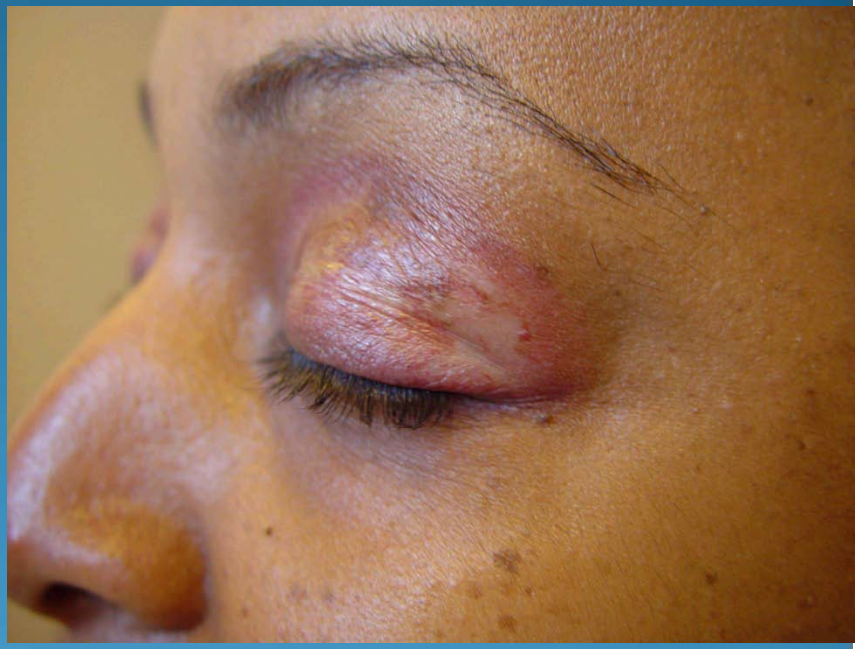
- Neutrophilic dermatosis
- Diagnosis of exclusion

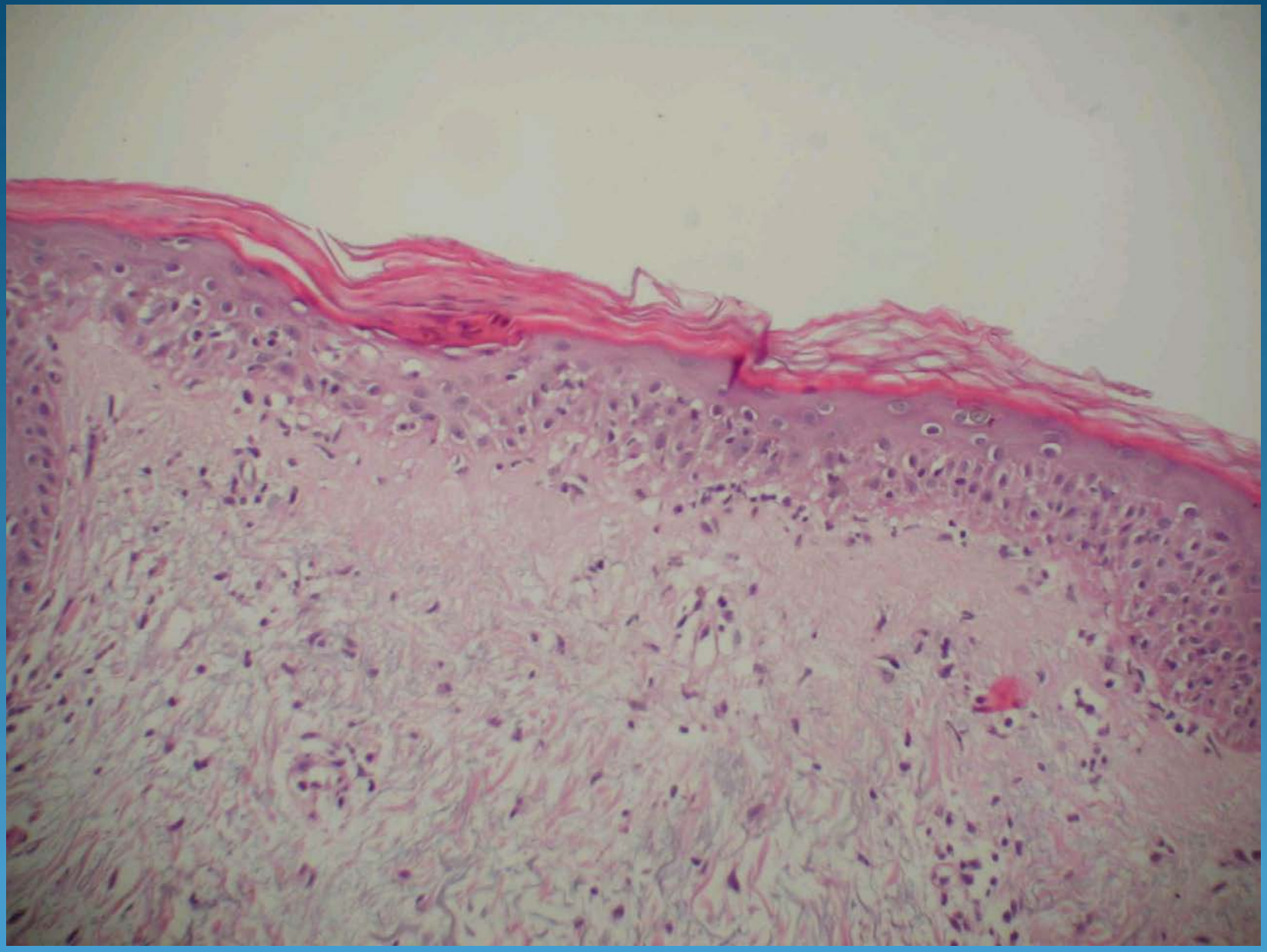
54 F

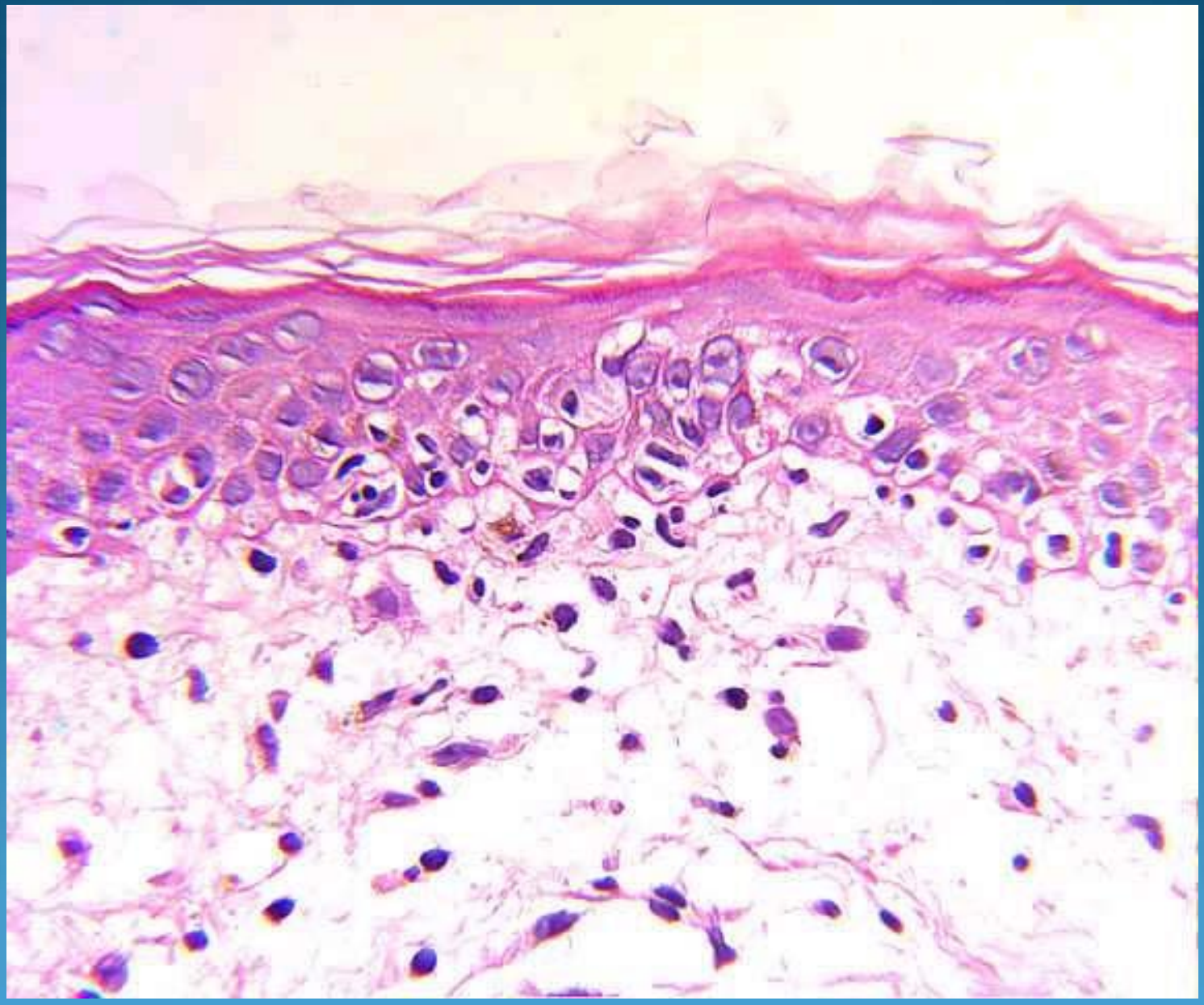
BRBPR

BE with tumor at SC


dermatomyositis





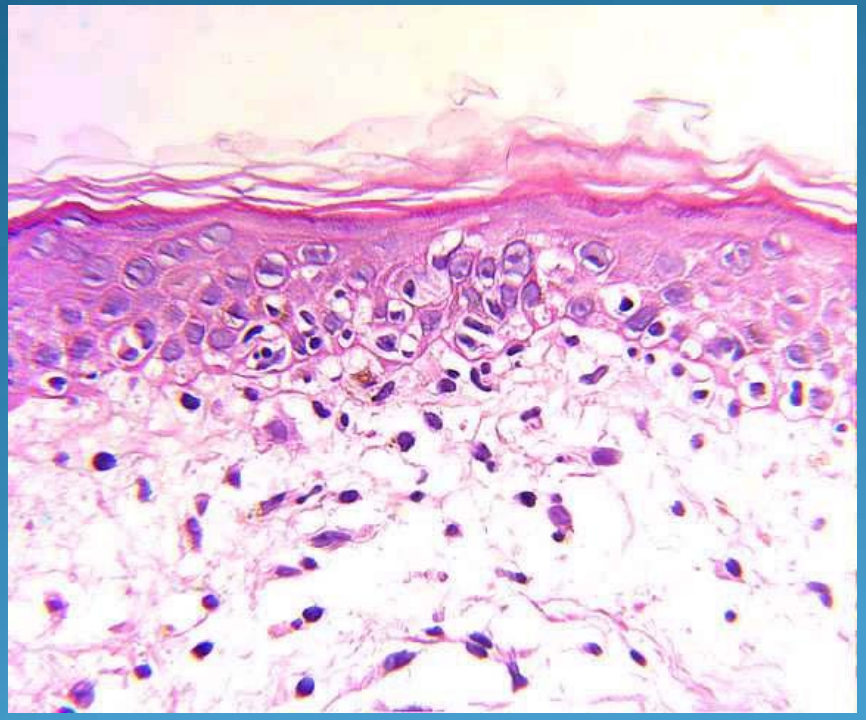


Dermatomyositis

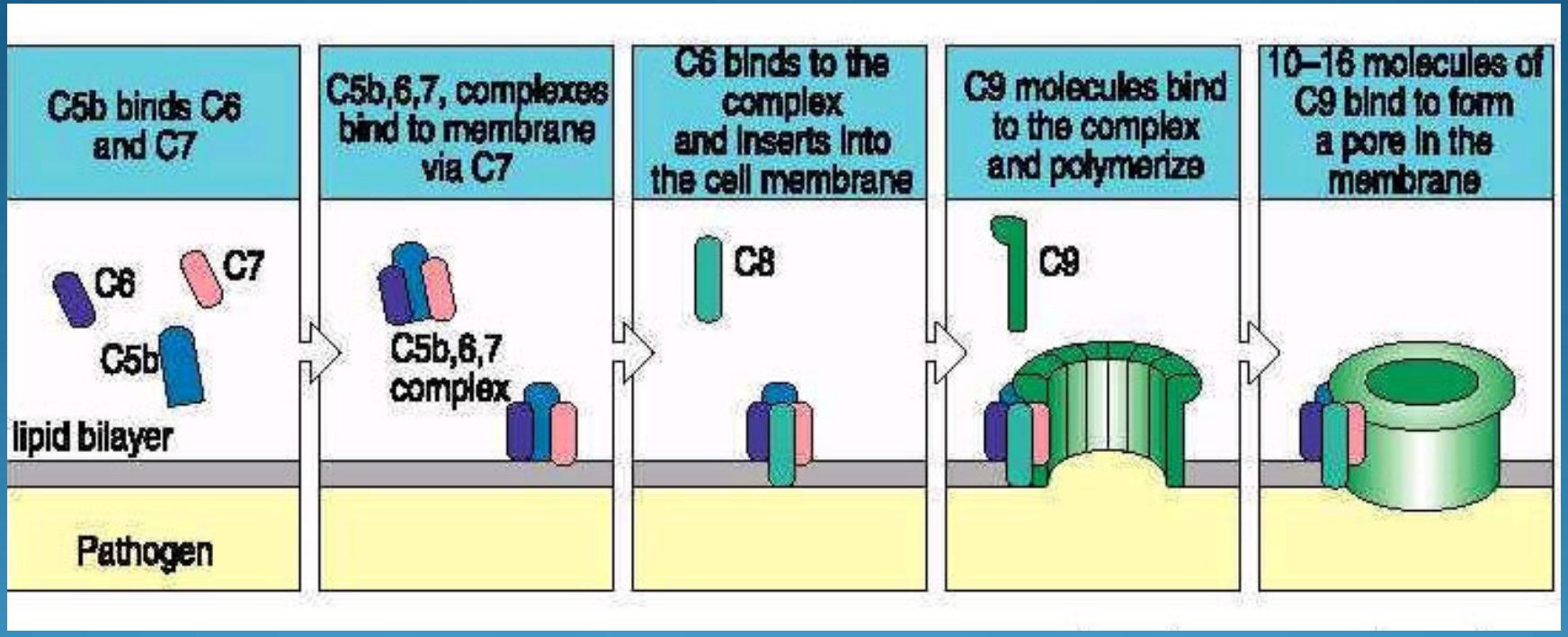
Dermatomyositis and Malignancy

Study	Pts	Malignancy
Sparsa A etal.	33	39% (13/33)
Stockton D etal.	705 with DM or PM	7% (50 DM and 40 PM)
Buchbinder R etal	537 with biopsy proven myositis	116 malignancies in 104 pts Highest risk in DM pts

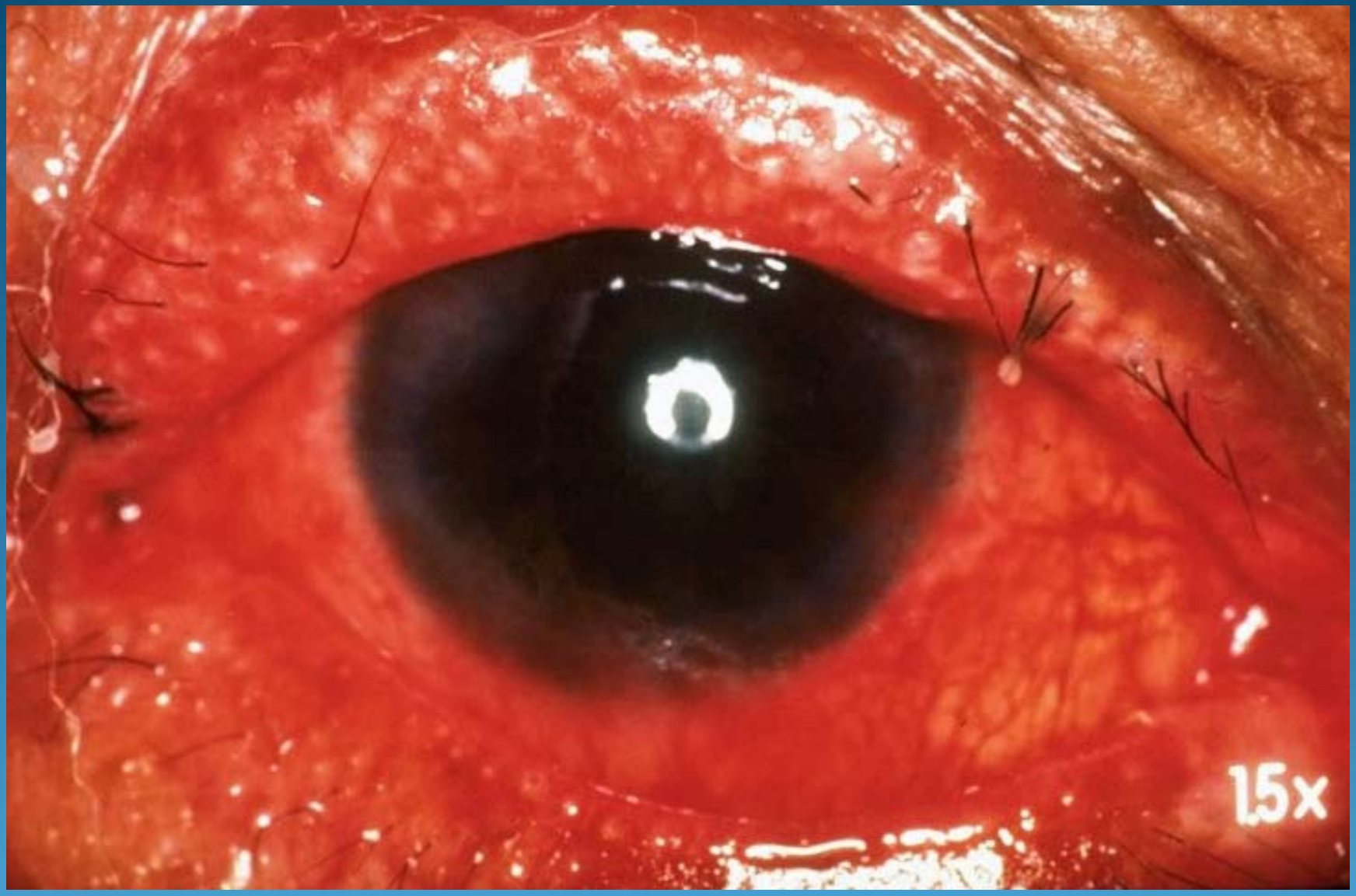
Histopathology

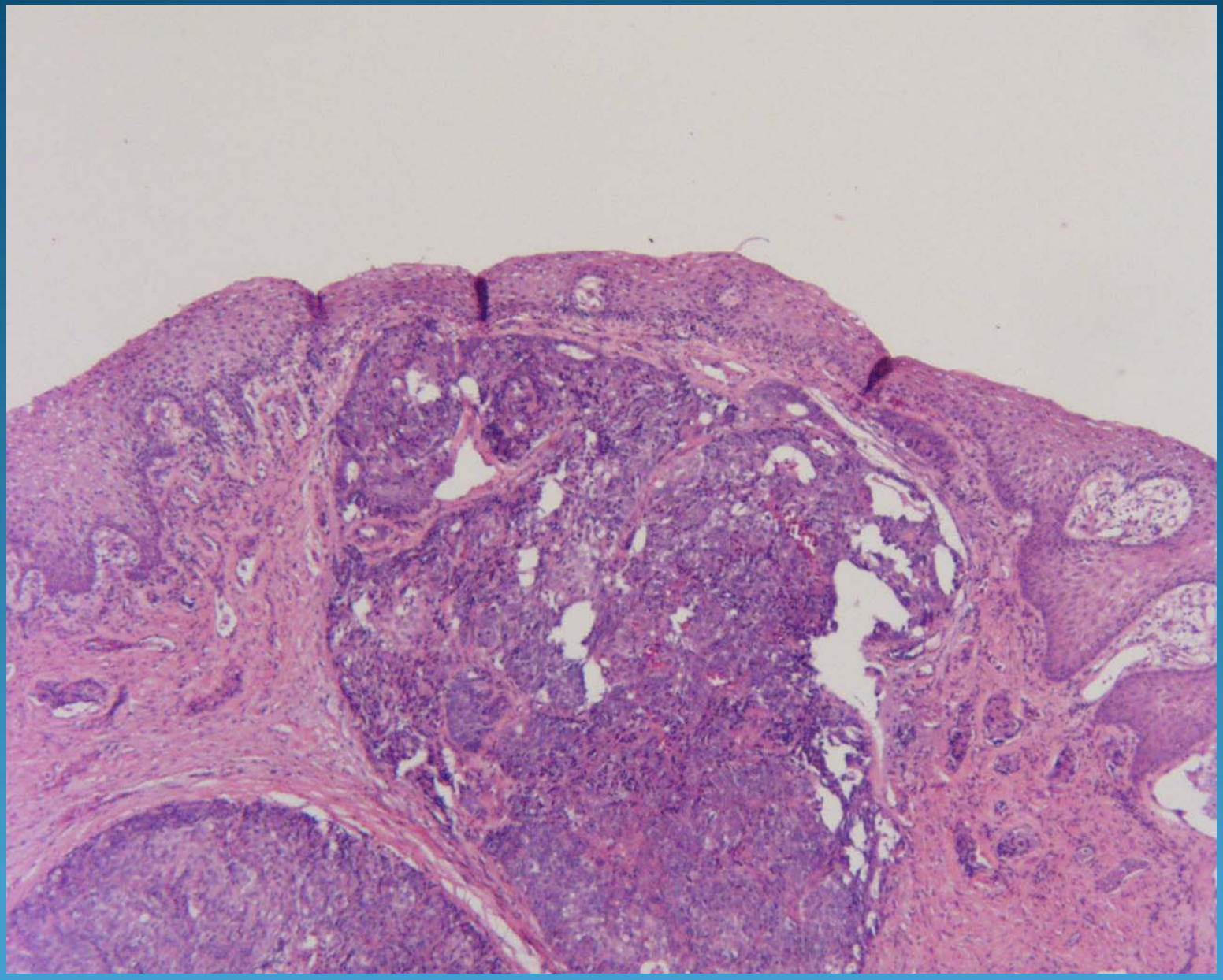


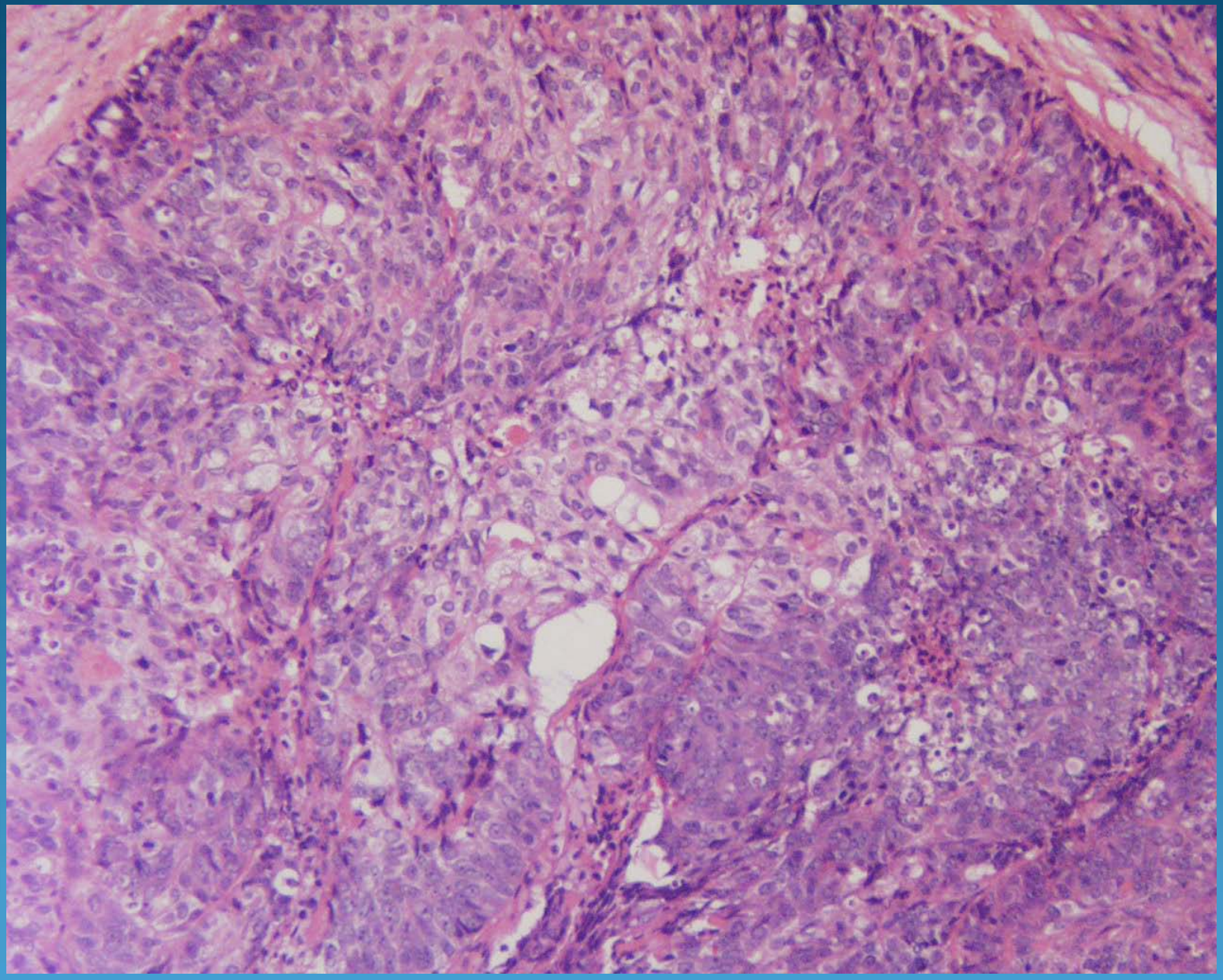
- Cell poor lichenoid interface dermatitis
- Orthokeratosis
- Dermal mucinosis
- DIF for C5b-9 at DEJ and endothelial cells

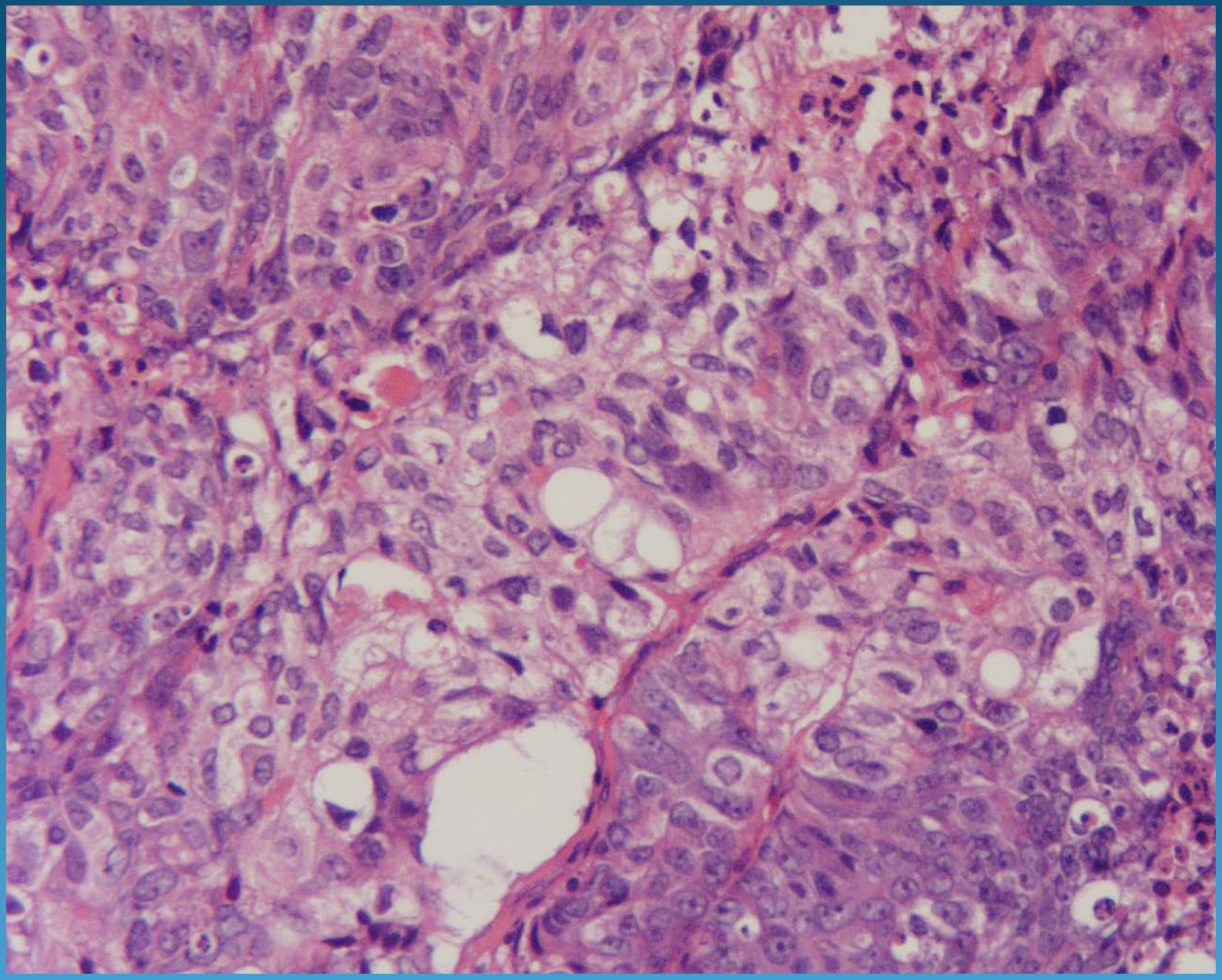

C5b binds C6 and C7
C6
C7
C5b
lipid bilayer
Pathogen
C5b,6,7, complexes bind to membrane via C7
C5b,6,7 complex
C6 binds to the complex and inserts into the cell membrane
C8
C9 molecules bind to the complex and polymerize
C9
10–16 molecules of C9 bind to form a pore in the membrane

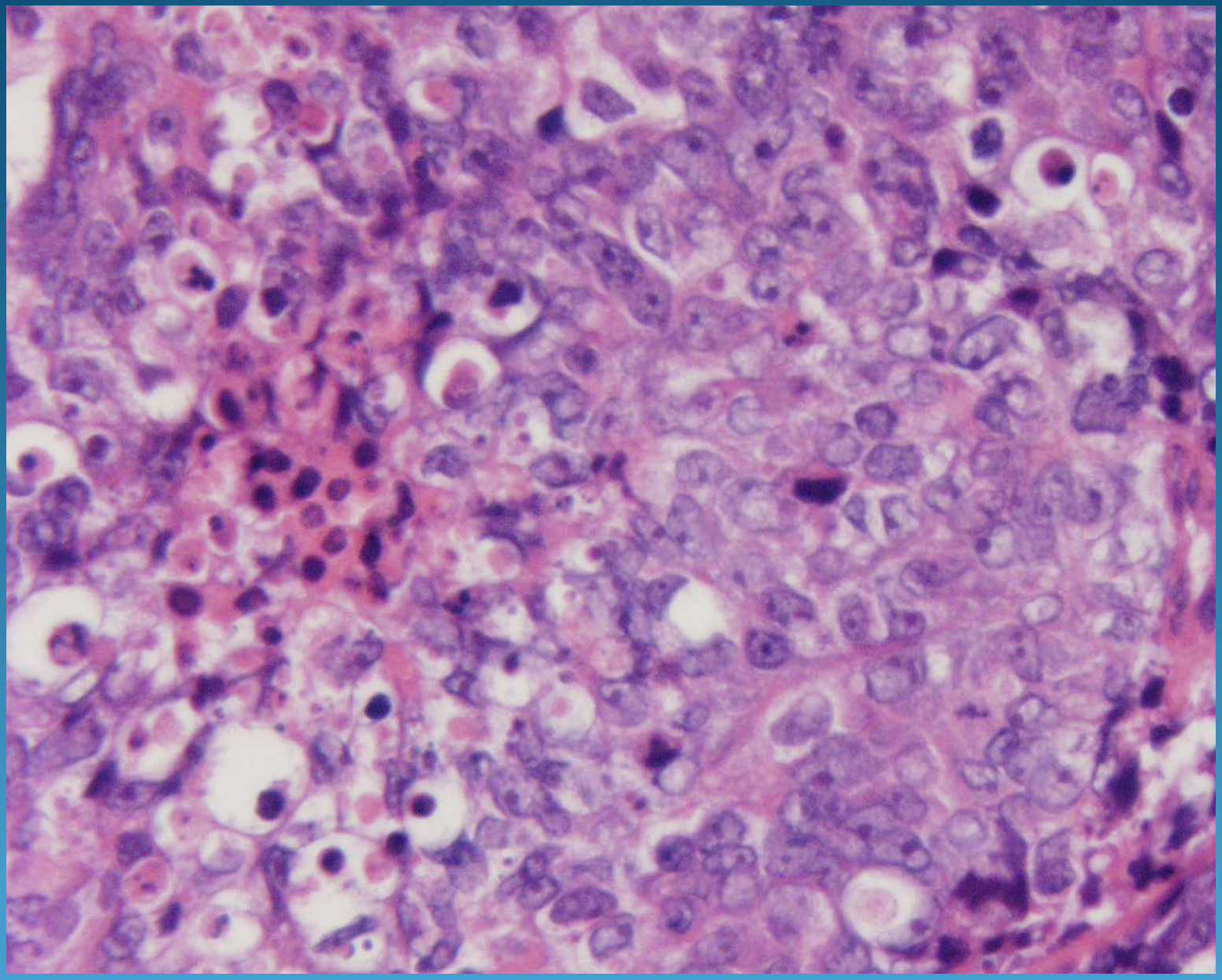
41 y.o. M
S/P Colectomy for Dukes B2 cancer

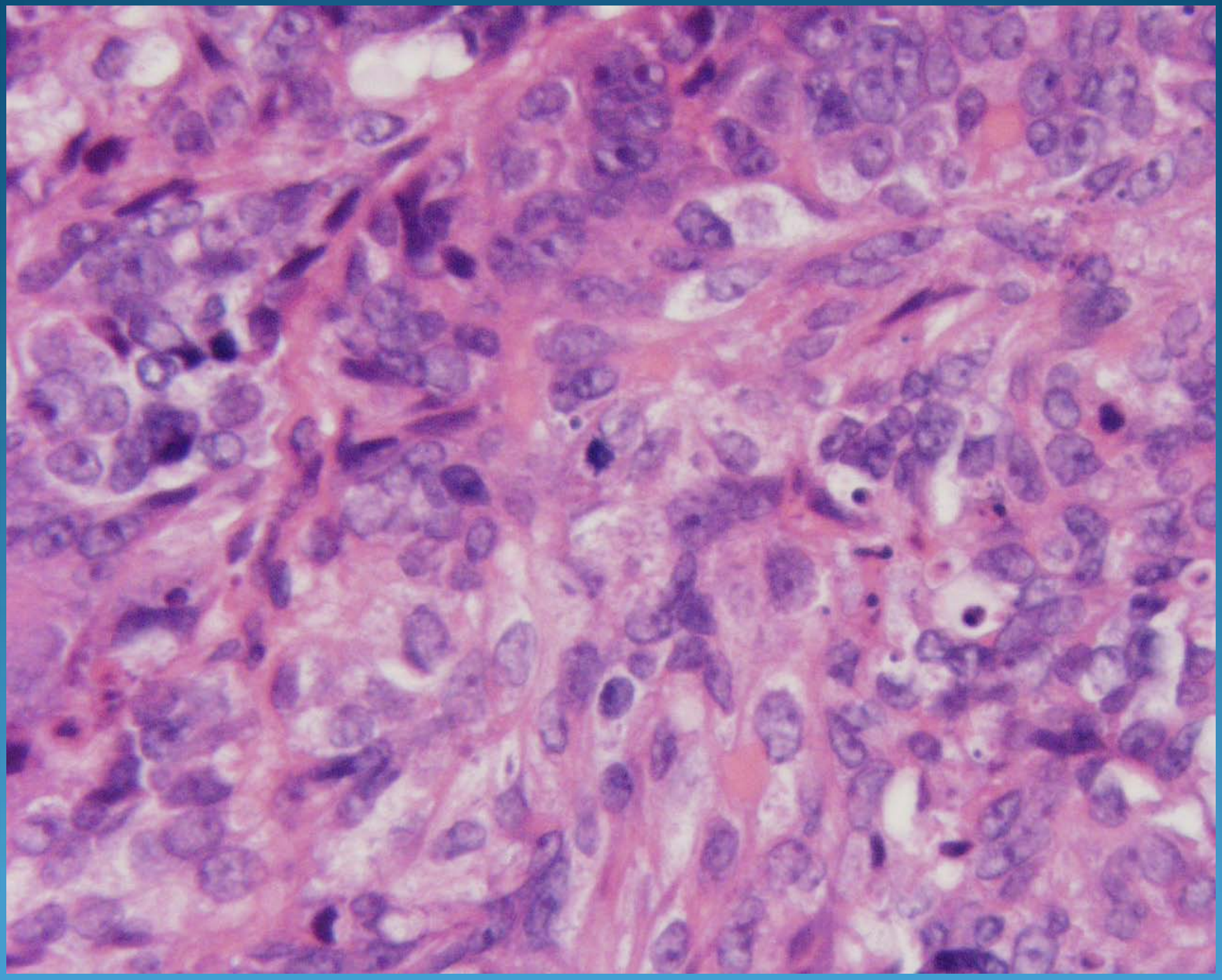

1.5x

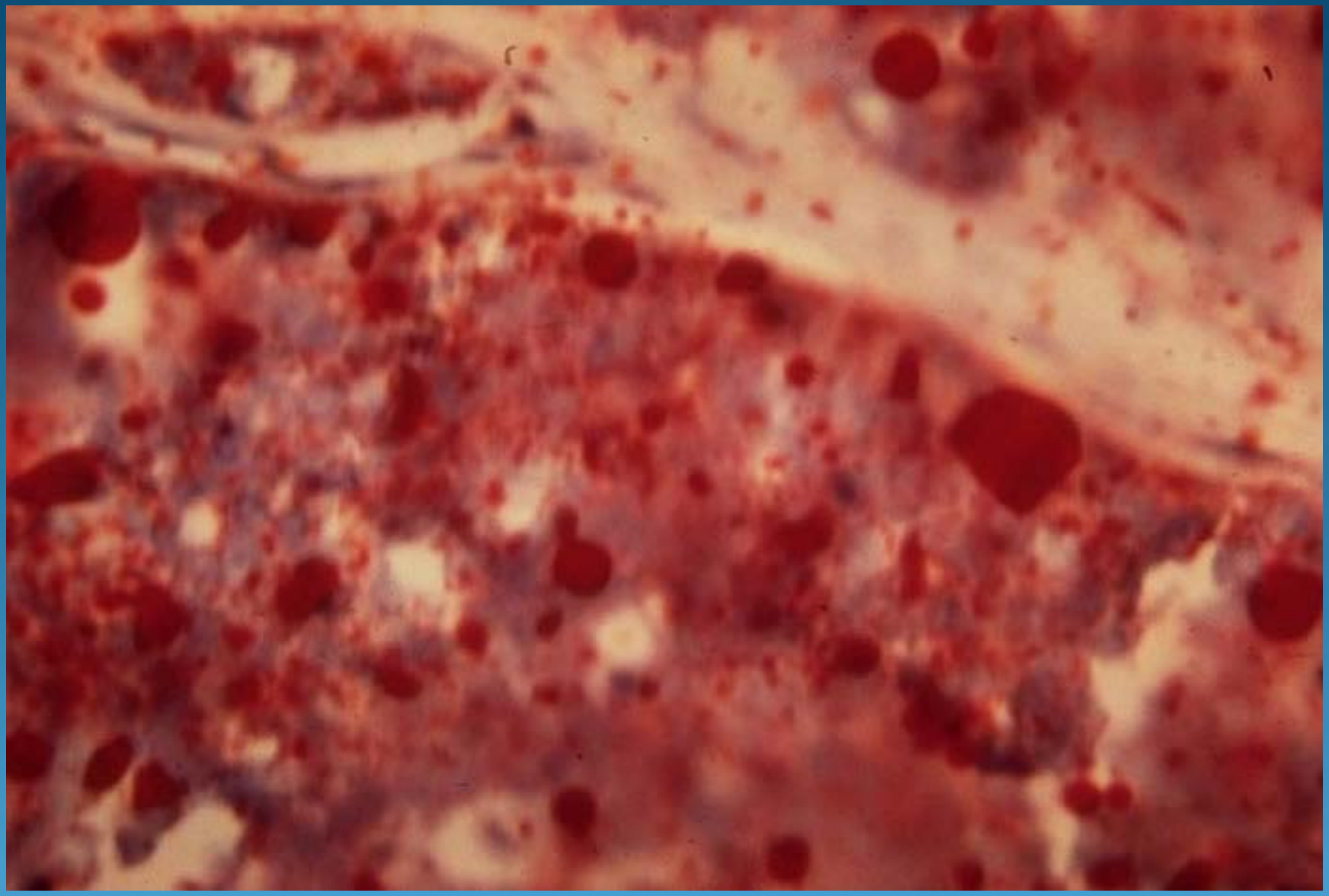






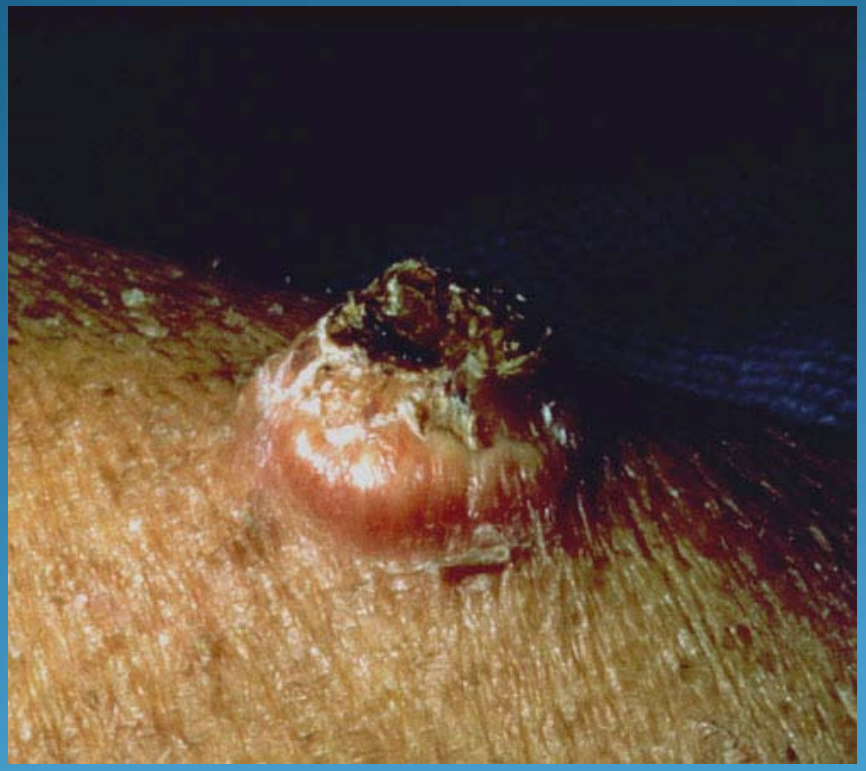






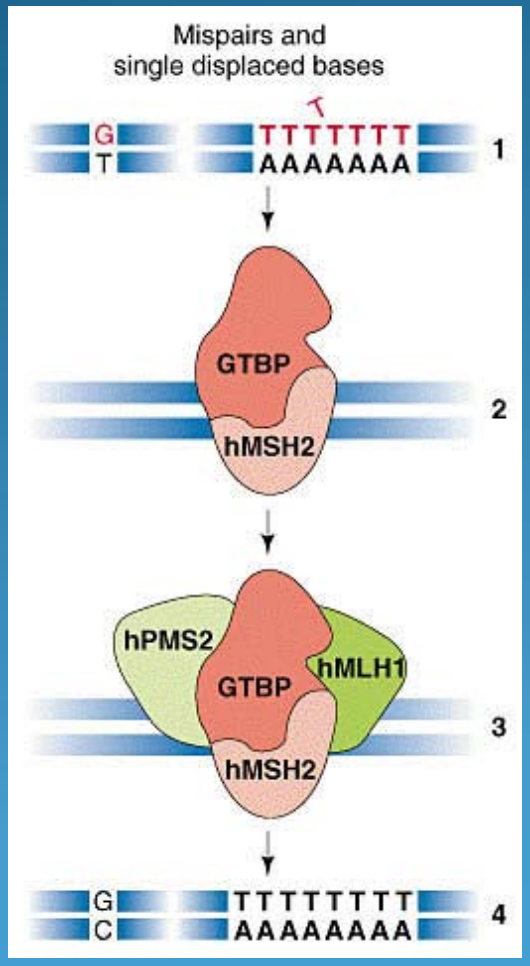
Sebaceous Carcinoma occuring with Muir-Torre Syndrome

Quick Facts



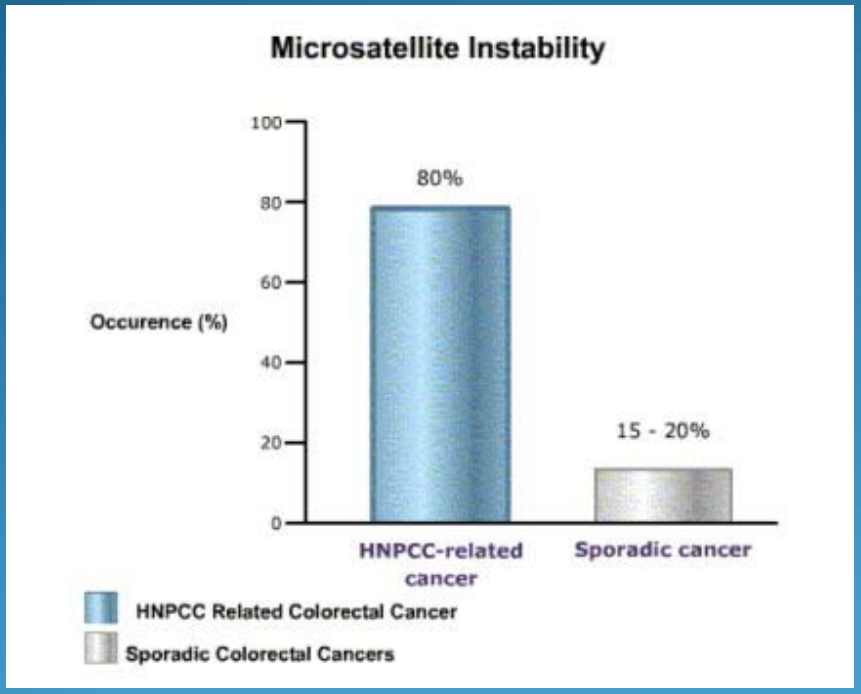
- Keratoacanthomas, sebaceous neoplasms including sebaceous carcinoma
- Internal visceral malignancies particularly of the gynecological and gastrointestinal tract
- Autosomal dominant

Pathogenesis



- LOH in the chromosomal regions containing hMSH2 and hMLH1 Mismatch repair genes
- hMSH2 > hMLH1

Hereditary nonpolyposis colorectal cancer syndrome (HNPCC)



- Two HNPCC-related cancers
  - Synchronous and metachronous colorectal cancers or associated extracolonic cancers (endometrial, ovarian, gastric, hepatobiliary, or small bowel cancer or transitional cell carcinoma of the renal pelvis or ureter)
- Colorectal cancer and a first degree relative with colorectal cancer or HNPCC-related extracolonic cancer or colorectal adenoma
  - One diagnosed <45 years and adenoma diagnosed <45 years

HNPCC-Criteria cont.

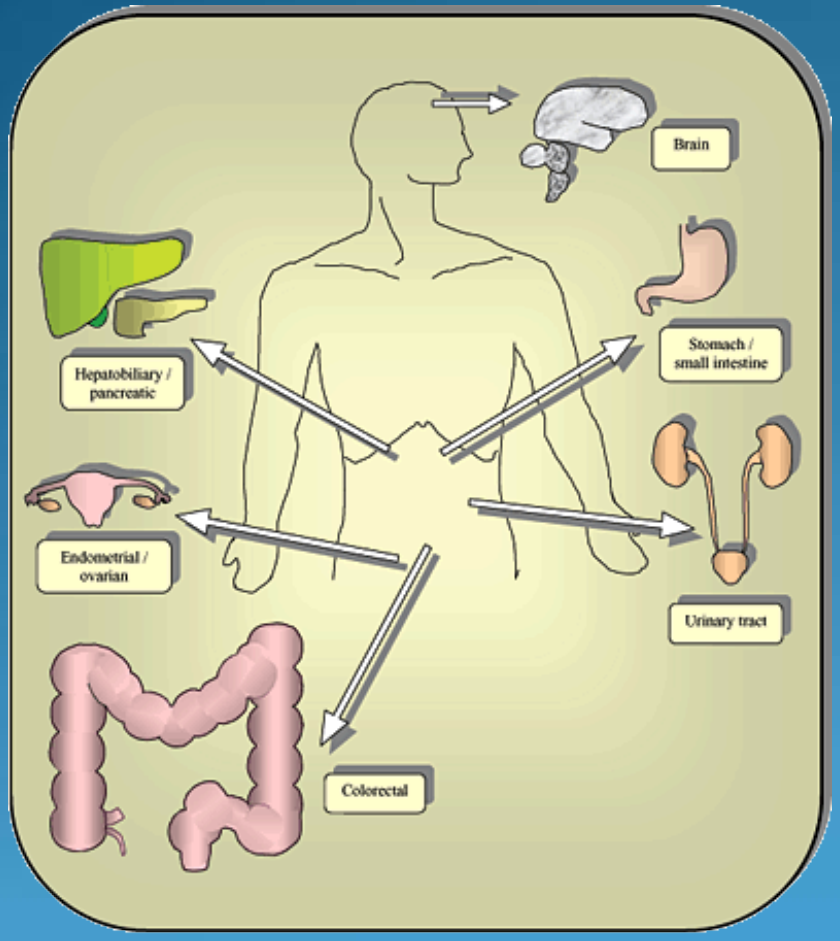


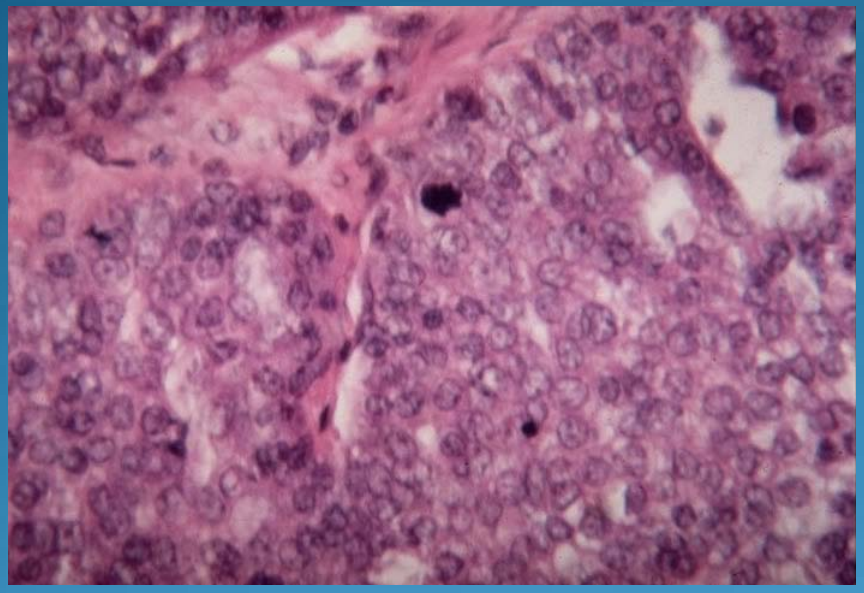
Figure 2. Colon and extracolonic cancers associated with HNPCC

- Colorectal cancer or endometrial cancer <45 years
- Right-sided colorectal cancer with an undifferentiated pattern (solid/cribriform) on histopathology age <45 years
- Signet-ring-cell-type colorectal cancer diagnosed <45 years (>50% signet ring cells)
- Colorectal adenomas diagnosed at age <40 years

Studies

Study	Patients	Results
Mathiak M, etal.	28 skin lesions from 17 MT pts	15/18 tumors with known MSH2 mutations in pt.
Machin P, etal.	10 skin lesions and 11 visceral tumors from 6 MT pts	All cases with MI 5 pts. Neg for MSH2 1 pt neg. MHL1, pos. for MSH2

Histopathology



- Sebaceous cells in varying stages of maturation
- Lack peripheral palisading
- ORO positive
- EMA+, CD15+?

Key Points

- Subtle dermatologic signs may suggest significant gastrointestinal and systemic disease
- Check family history
- Several dermatologic disorders may be present