Inflammatory Skin Lesions *(for surgical pathologists)*

Inflammatory Patterns

While not entirely unique, many of the ideas here are modified from "Inflammatory Dermatopathology: A Pathologist's Survival Guide" by Billings and Cotton. A great book if you want more details!

Inflammatory skin diseases often follow one of several "**patterns**" of change, characterized as having primarily ***Epidermal*** vs ***Dermal*** changes.

As a general rule, **epidermal changes overrule dermal changes,** and the dermal patterns lack significant epidermal change. Within the epidermal patterns, the interface/lichenoid pattern overrules the other patterns.

General tips:

Consider the clinical DDX (and address it in your report!).

Dermatologists are advanced consumers of pathology reports. Include a brief (but good) description using appropriate terminology.

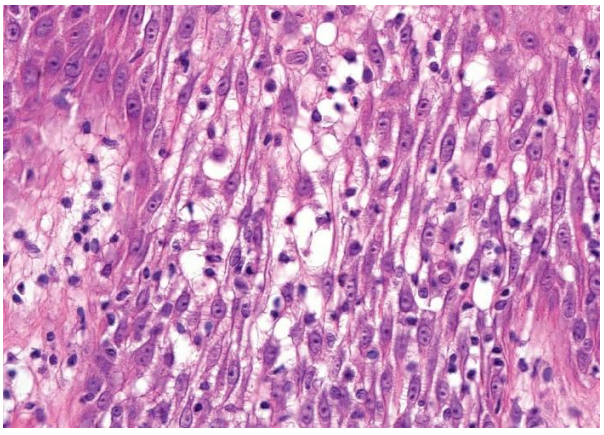
The stratum corneum is normal (basketweave orthokeratosis) in "acute" (quick/recent) processes. With long-standing disease, you get altered stratum corneum, including hyperkeratosis and/or parakeratosis.

Get a PASd stain for fungi, particularly if there are neutrophils in the stratum corneum.

	Basic Pattern	Defining Findings
Epidermal	Spongiotic Dermatitis	Intraepidermal edema
	Interface/Lichenoid Dermatitis	Damage to the basal layer by inflammation, often with keratinocyte destruction
	Psoriasiform Dermatitis	Epidermal hyperplasia
	Vesiculobullous Dermatitis	Acantholysis and blister formation. Subdivided by layer of split.
Dermal	Perivascular Dermatitis	Inflammation predominantly around dermal blood vessels
	Nodular/Diffuse Dermatitis	Dermal inflammation that is *not* vasculocentric
	Granulomatous Dermatitis	Granulomas in dermis
	Sclerosing Dermatitis	Fibrosis of the dermis, often with little inflammation
	Vasculopathic Dermatitis	Vascular changes
	Panniculitis	Inflammation of the adipose tissue

Author's Note: Dermatopathology is a complex and intimidating field with its complex Latin names and clinical correlations. Here, I've tried to include diagnoses that are most common and/or important to know about for general surgical pathologists, and are listed on the ABP content specifications for the Anatomic Pathology exam. However, this is by no means an exhaustive list. I personally have a very low threshold for sharing cases, particularly inflammatory skin cases, with my dermatopathology colleagues.

Spongiotic Dermatitis

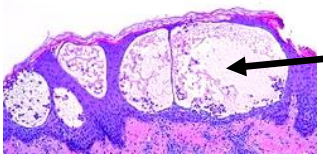


intraepidermal intercellular edema (spongiosis)

- **widened intercellular spaces** between keratinocytes, with elongation of the intercellular bridges

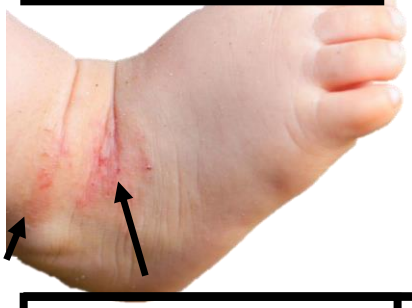
- may be associated inflammation, including in the dermis in a superficial perivascular pattern, often with some Eos.

- with subacute and chronic disease, there can be progressive psoriasiform hyperplasia and parakeratosis, usually accompanied by diminishing spongiosis (*lichenification*)



Intracellular edema can form round microvesicles within the epidermis

Atopic Dermatitis



aka Eczema

Usually presents in ***childhood*** in flexural areas such as the antecubital fossa.
"Atopic Triad:" 1) Atopic dermatitis, 2) Seasonal allergies, 3) Asthma

Acutely→ Edema can form vesicles
Chronically→ Lichenification

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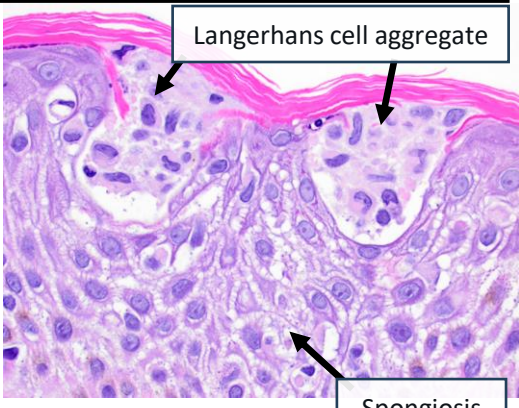
Often positive allergen scratch test or RAST test, elevated serum IgE

Dx: "spongiotic dermatitis consistent with eczematous dermatitis"

Contact Dermatitis

Helpful hint: ***Often localized to area of contact!***
For example, if due to plant contact→ often linear line, corresponding to scratch. If due to Nickel, confined to area of button, jewelry, etc..

Types (below) can appear histologically similar.



Allergic Contact Dermatitis: caused by contact to a previously sensitized *allergen*.
In US, most common is Poison Ivy or Oak. Also, Nickel, cosmetics.
Positive skin patchy test.
Micro: Spongiosis ± lymphs and Eos. Can have superficial perivascular lymph histiocytic dermatitis with eosinophils. Langerhans cell aggregate in epidermis.
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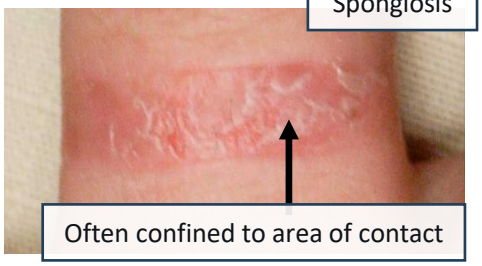

Irritant Contact Dermatitis: caused by *direct toxic effect* of chemical (not immune). Often job-related (e.g., solvents, soaps) or due to diaper. Appears relatively quickly.
If severe enough, can cause epidermal necrosis.
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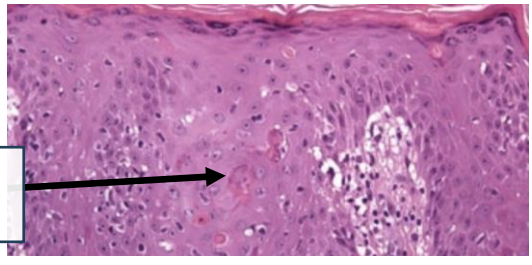
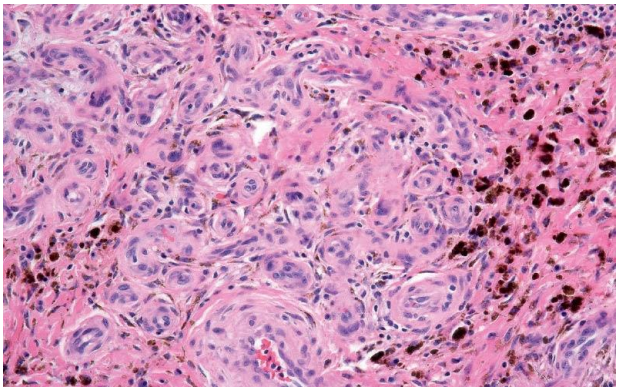


Stasis Dermatitis



Caused be venous insufficiency.
Begins on medial aspect on lower legs but can become circumferential. Clinically mimics cellulitis

Micro: Spongiotic dermatitis, **vascular proliferation** of dilated, thickened blood vessels in papillary dermis, **hemosiderin**, chronic inflammation, **extravasated RBCs**.
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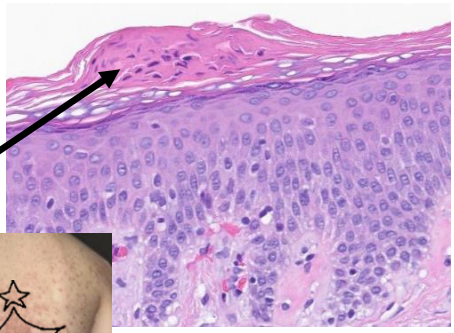
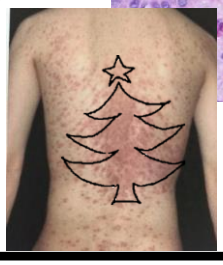
Pityriasis Rosea





Classically, young adults. First finding → salmon "Herald patch"
Followed by secondary lesions 1-2 weeks later, Self-resolving ~1 month
Christmas tree pattern
Clinical DDX: secondary syphilis, cutaneous T cell lymphoma

Micro: Spongiotic dermatitis with **mounds of parakeratosis**.
Extravasated RBCs. Some exocytosis of lymphocytes.
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Other Diseases with Spongiosis:

Often require clinical correlation to diagnose:
Nummular Eczema: coin-shaped (small, round) plaques, mostly on extremities of adults. Frequent acanthosis, so can resemble psoriasis.

Id reaction (Autoeczematization): reaction at a site far away from the primary inflammatory focus. (e.g., stasis dermatitis or tinea pedis on the legs/feet → ezematous dermatitis on arm)

Dyshidrotic Eczema (Pompholyx or Palmoplantar Dermatitis): recurrent, pruritic, often vesicular, eruptions on the soles, palms, or digits. Often related to allergic contact dermatitis. Be sure to exclude dermatophyte infection.

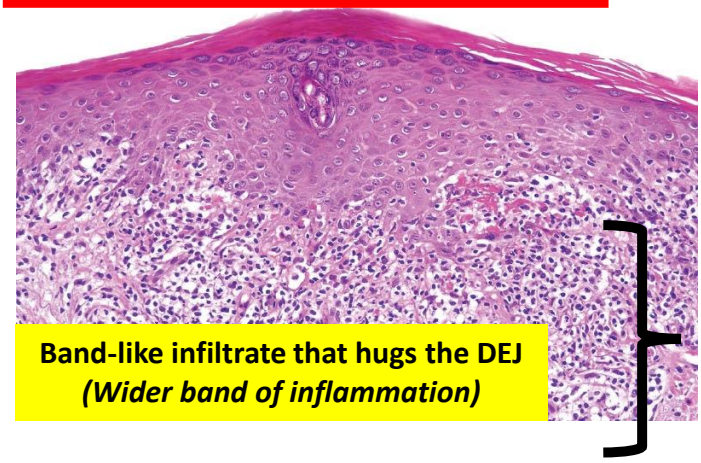
Eczematous Drug Reactions: A minority of drug reactions can appear ezematous.

General comments:
With longstanding spongiotic dermatitis, the epidermal changes increasingly overlap with the psoriasiform pattern.

Spongiotic dermatitis can be secondarily impetiginized, with PMNs in the stratum cornium, resembling a dermatophyte reaction.

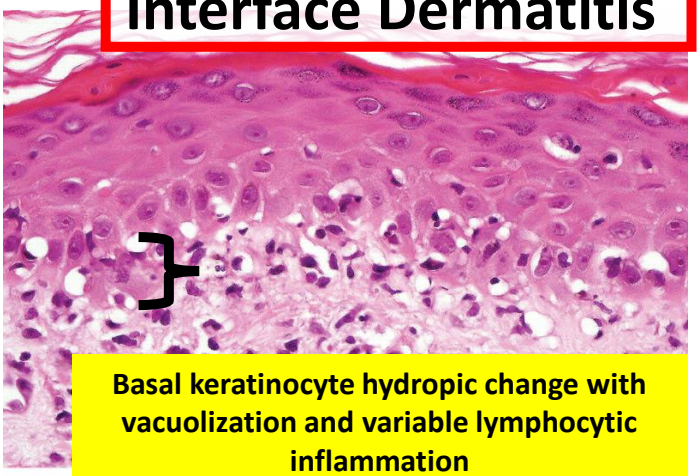
Beware: Mycosis Fungiodes can have some spongiosis, but it should have a disproportionately increased number of lymphocytes for the amount of spongiosis. Lymphocytes have halos and irregular, cerebriform nuclei, and a shift in CD4:CD8 >4-6:1.

Lichenoid Dermatitis



Band-like infiltrate that hugs the DEJ
(Wider band of inflammation)

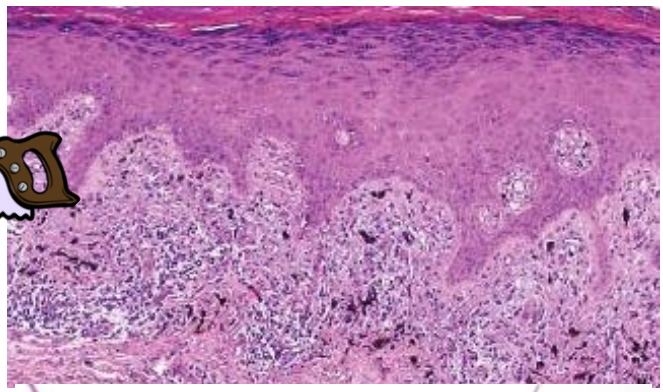
Interface Dermatitis



Basal keratinocyte hydropic change with vacuolization and variable lymphocytic inflammation
(Narrower band of inflammation)

Lichen Planus *"LP"*

5P's: Pruritic, **p**lanar, **p**urple, **p**olygonal **p**apules.
Classically: extensor surfaces of the wrists and ankles.
Oral common too.



Micro: Compact hyperkeratosis (No parakeratosis)
Band-like inflammatory Infiltrate
Civatte bodies (necrotic, pink keratinocytes)
Wedge-shaped hypergranulosis
"Saw-tooth" rete ridges

Epithelium can be hypertrophic (acanthotic) or atrophic (thinner, often with milder changes)

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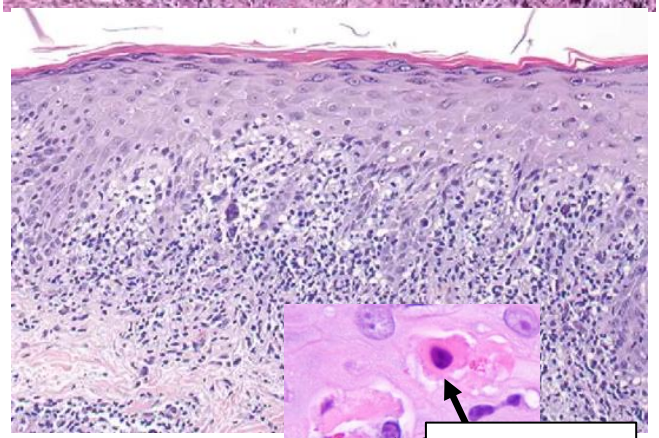


Single lesion on trunk?
Consider **Lichen Planus-like Keratosis (LPLK.)**
(Benign Lichenoid Keratosis)

Lots of Eos? Consider Lichenoid Drug reaction

Top DDX: Lichenoid drug reaction, Secondary syphilis, Pityriasis rosea

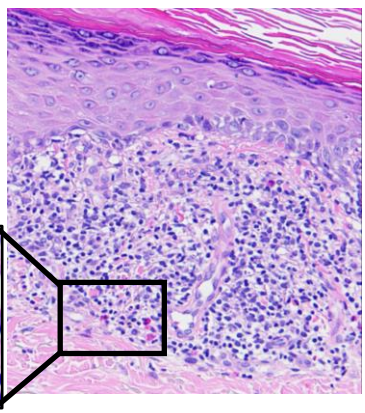
Lichenoid Drug Eruption

Tend to be larger than Lichen planus and located on trunk.

Common inciting drugs: beta blockers, captopril, thiazides, and Lasix.

Like LP: **Band-like inflammatory infiltrate at DEJ.**
Vacuolar change and keratinocyte damage.

***Hint*: look for LP + Eos!**



Different from LP:
Conspicuous eosinophils
Patchy parakeratosis

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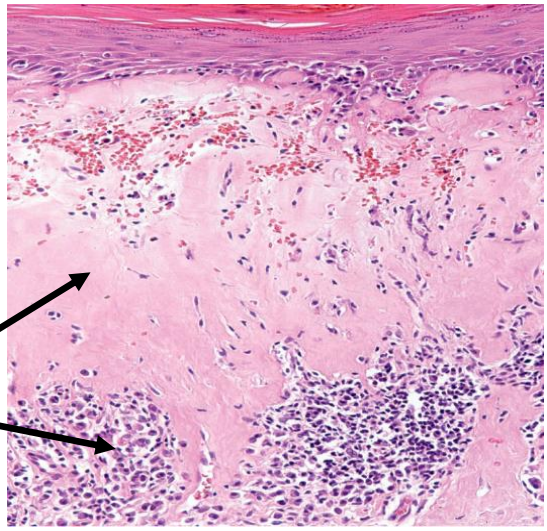
Lichen Sclerosus

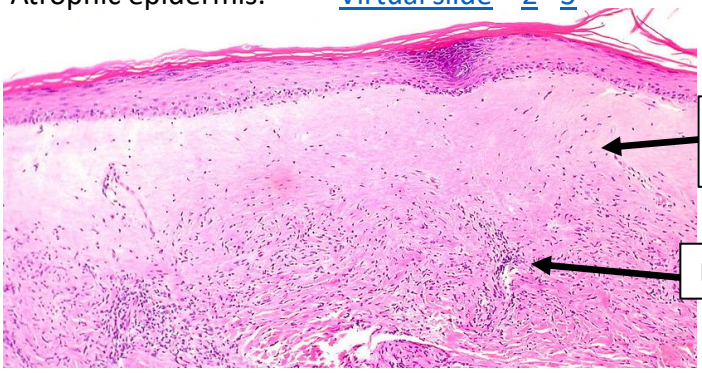
aka "lichen sclerosus et atrophicus"

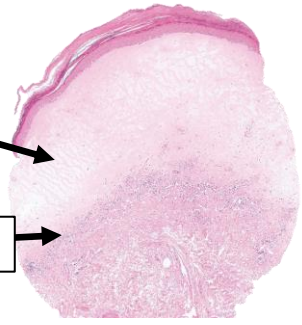
Predilection for **anogenital skin**.
White plaque with epidermal atrophy ("cigarette paper")
Glans penis = "balanitis xerotica obliterans"
Increased risk of SCC (HPV-independent)

Early: Lichenoid inflammation resembling Lichen planus

Late: **Homogenization & sclerosis of dermal collagen**
Variable band of **lymphocytic inflammation** BELOW edema and homogenization. Vacuolar change
Atrophic epidermis. Virtual slide 2 3







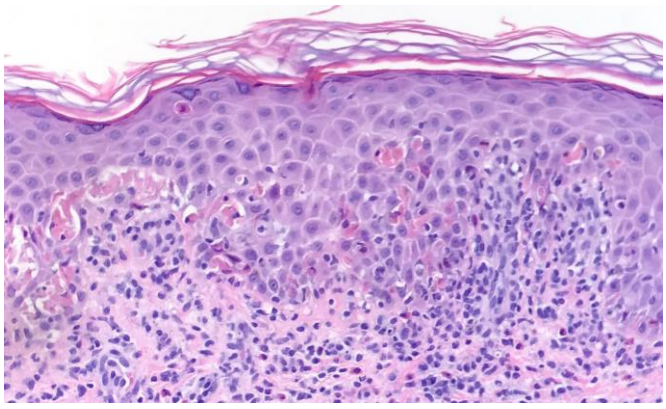
Collagen homogenization & sclerosis

Deep lymphocytic inflammation

Fixed Drug Eruption

Take Drug→ One or few circumscribed, localized erythematous to violaceous/brown plaques, usually on extremities.
Lesions recur **at same site** with rechallenge *("fixed" location)*

Lichenoid inflammation with **Vacuolar change**
Eosinophils, some Neuts
Frequent necrotic keratinocytes
Prominent pigmentary incontinence
Normal basket weave stratum corneum or parakeratosis; no hyperkeratosis



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Dermatomyositis

Inflammatory myopathy with cutaneous findings.
Can be paraneoplastic→ screen for cancer!
Subacute proximal muscle weakness.

Interface dermatitis with hydropic degeneration.
Rare colloidal bodies in papillary dermis.
Often increased dermal mucin.
Histologically often indistinguishable from Lupus!
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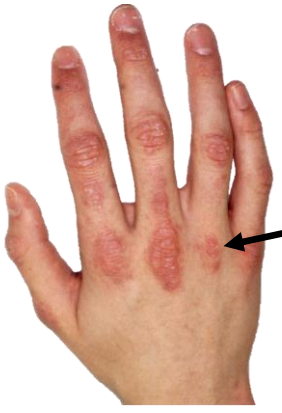
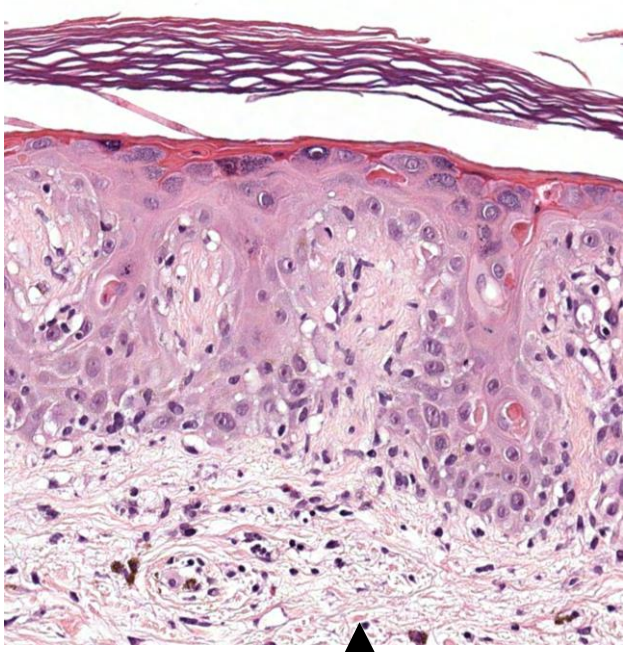


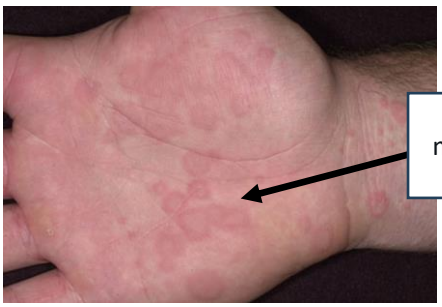
Gottron Papules are pathognomonic skin lesions. Flat, violaceous papules on dorsal IP and MCP joints. Also classic: heliotrope rash around eyes.

Erythema Multiforme *"EM"*



Acute, self-limited disease.
Often reactive (e.g., HSV, Mycoplasma, or **Drug**, esp. Sulfa)
Episodic eruptions of macules, papules, or **targetoid** lesions on the extensor surfaces, palms, soles, and/ or oral mucosa

Vacuolar interface damage with necrosis of keratinocytes, often at all levels of the epidermis
Mild superficial perivascular lymphocytic infiltrate
Inflammation overall sparse (esp. considering damage)
Normal stratum corneum (acute onset)



Targetoid macules on the hand

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Essentially, spectrum of same disease and histologic findings!

Stevens–Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

SJS/TEN are serious, life-threatening with extensive mucosal involvement and epidermal necrosis/sloughing
Often full-thickness necrosis.

Nikolsky's sign: Application of pressure to the skin can cause detachment of the epidermis.

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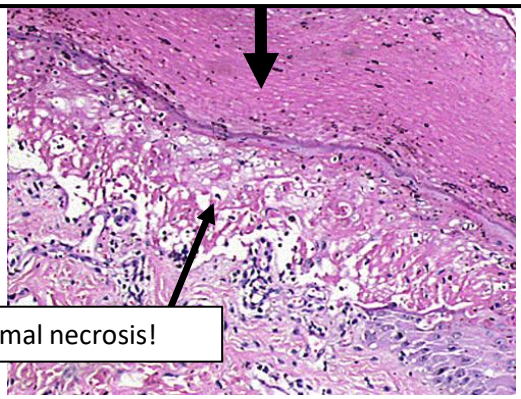
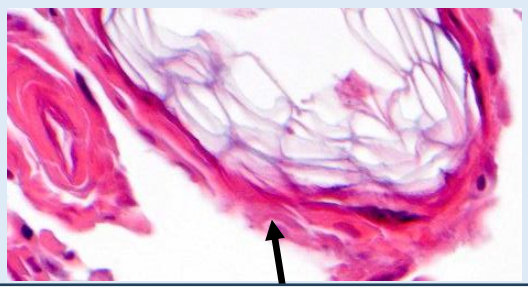


Area of total epidermal necrosis!

Staphylococcal scalded skin syndrome (SSSS)

Clinically resembles SJS/TEN

Bacterial toxin causes a split between the stratum corneum and underlying epidermis.
There is **no** dyskeratosis or interface change



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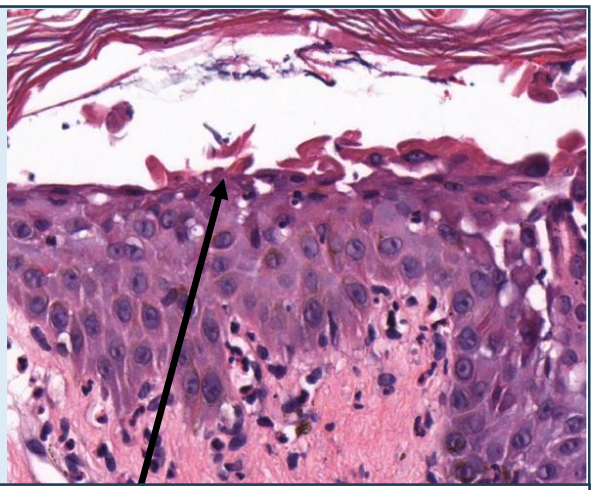
A frozen SSSS peel roll shows: cleavage at granular cell layer, non-inflammatory, no organisms



Superficial acantholysis with subcorneal separation. The intracorneal acanthoslysis can have some PMNs.

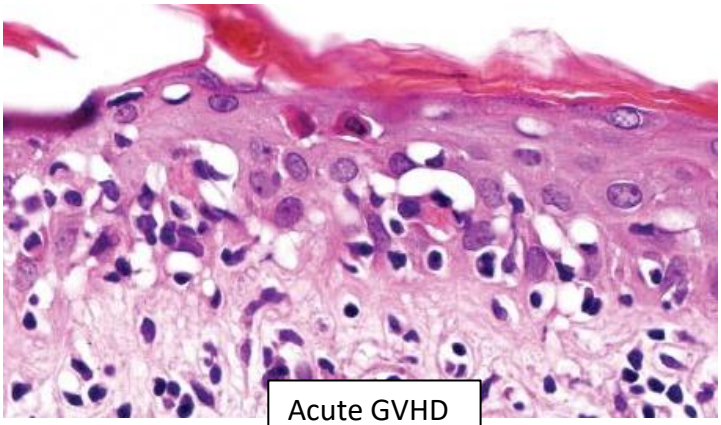
Graft-vs-host Disease (GVHD)

Usually **post-stem cell transplant** (transplanted immunocompetent T-cells attack new host)

Involves skin, liver, GI tract → **rash, ↑LFTs, diarrhea, and vomiting**

Acute GVHD: Interface dermatitis with necrotic/dyskeratotic keratinocytes; "Satellite cell necrosis"- association of lymphs to necrotic keratinocytes *(resembles EM)*

Chronic GVHD: Sclerosis of the dermis, Compact hyperkeratosis, Lichenoid reaction



Acute GVHD

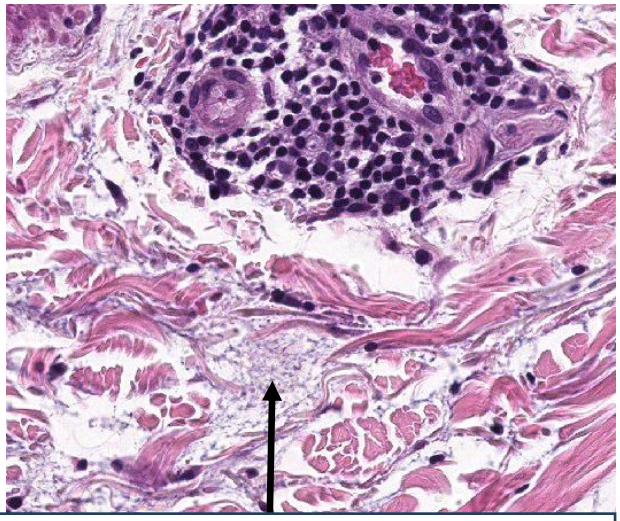
Acute: Virtual slide 2

Lupus Erythematosus *"SLE" or "LE"*

Multisystem autoimmune disorder with several variants that can involve the skin.
Mostly **young women**.
Any form of cutaneous involvement can have systemic involvement. **Photo-distributed** disease
Frequent auto-antibodies: ANA, Anti-dsDNA, anti-smith, etc..

Discoid Subacute

Common findings:
Interface activity with basal vacuolation.
Increased dermal mucin (highlighted by colloidal iron or Alican blue)—appears stringy blue-grey or clear on H&E.
Perivascular lymphocytic infiltrate. Usually no Eos.



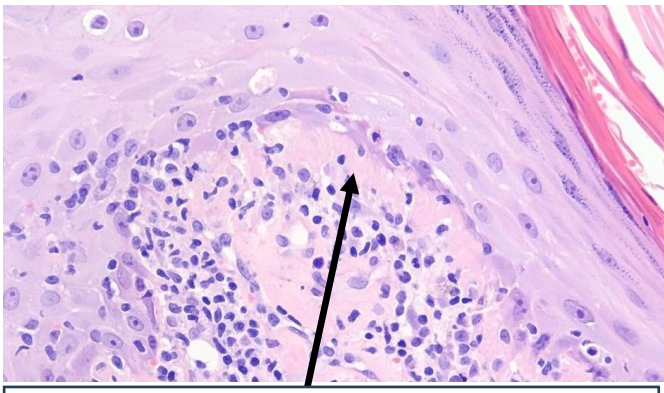
Dermal mucin: On H&E can appear stringy blue-grey

Acute cutaneous lupus:
Most strongly associated with systemic disease.
Erythema with photosensitivity and malar rash.
Frequent anti-dsDNA antibody.

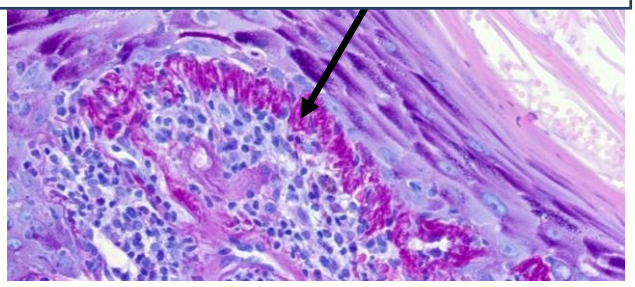
Subacute cutaneous lupus:
Psoriasiform erythematous plaques on sun exposed skin.
Frequent anti-Ro antibody.

Discoid (chronic) lupus:
Indurated, atrophic, hyperpigmented plaques with follicular plugging. Usu. Face/scalp.
Relatively common, but rarely systemic
Thickening of basement membrane (highlighted by PAS)
Hyperkeratosis with **follicular dilation and plugging**.
Thin, atrophic epidermis with flattening of rete ridges.

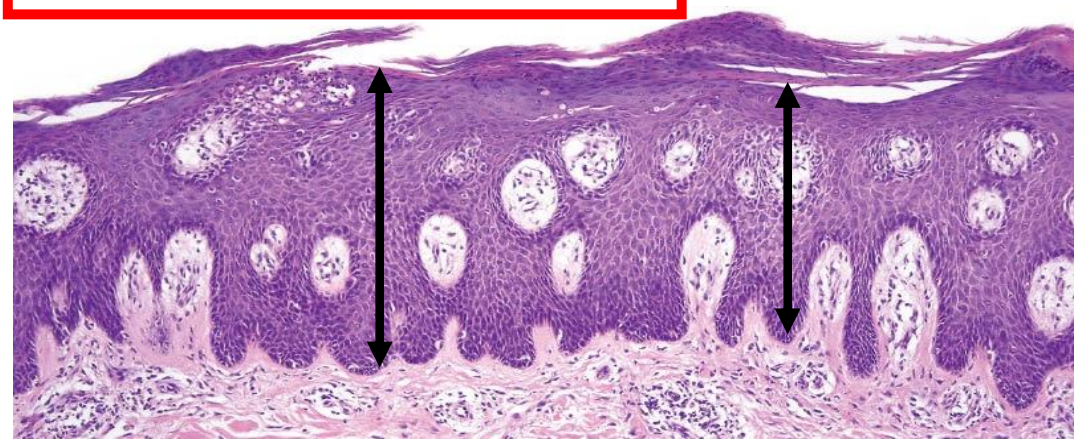
Immunofluorescence: IgM, IgG, C3 → BM deposition



Discoid Lupus with interface activity and thickening of basement membrane (highlighted by PAS, below)



Psoriasiform Dermatitis

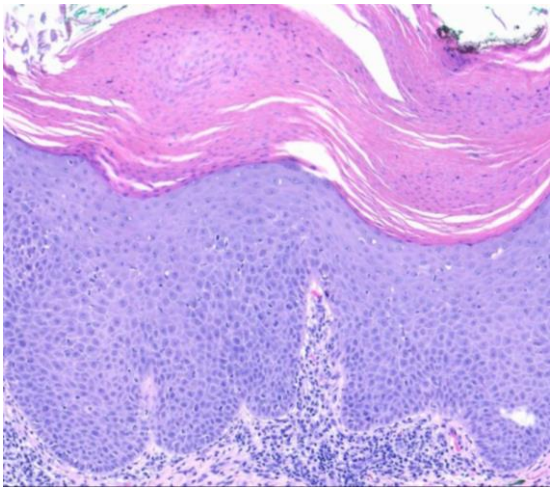


marked, **<u>uniform</u> elongation of the rete ridges**

(acanthosis)

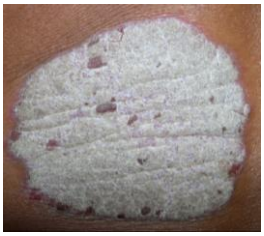
Subacute/chronic spongiotic dermatitis can have overlapping features.

Psoriasis vulgaris



Often referred to as simply "Psoriasis"

<u>Clinical</u>: Usually presents in early adulthood.
Erythematous plaques and silvery white scale
Extensor surfaces, scalp.
Scale is micaceous (oyster-like)



<u>Micro</u>: **Psoriasiform hyperplasia**
<u>Confluent</u> parakeratosis
<u>Hypo</u>granulosis
Neutrophils in the stratum corneum/epidermis
Thinning of supra-papillary plates
Dilated BV in dermal papillae.
<u>No</u> Eos in dermal infilitrate.

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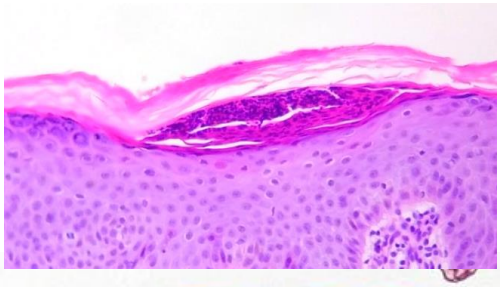
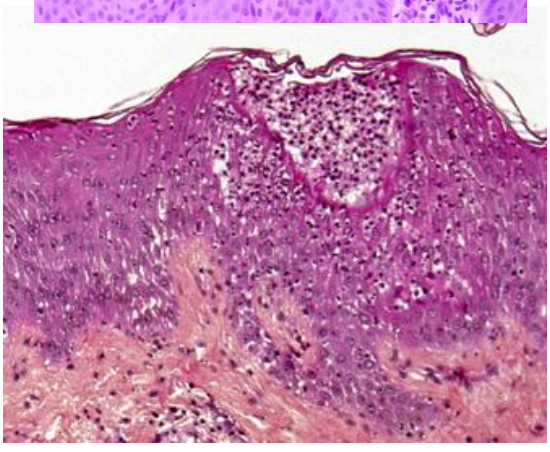
Additional Psoriasiform diseases

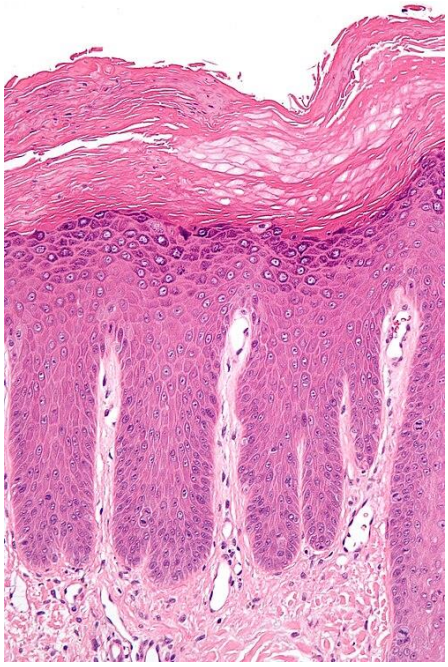
Guttate psoriasis: rapid onset of numerous small plaques. Often a history of (streptococcal) pharyngitis. Less prominent epithelial changes. Discrete mounds of parakeratosis with associated collections of neutrophils overlying the epidermis. Histologically, closely resembles pityriasis rosea.



Pustular psoriasis: widespread rapid onset of numerous pustules. Can be associated with pregnancy or stopping steroids in psoriasis vulgaris. Large collections of neutrophils in the epidermis and/or stratum corneum. No significant acanthosis and the granular layer is only partially diminished or normal (as very rapid). Be sure to rule out infection! Histologic mimic: AGEP



Lichen Simplex Chronicus



Clinical: **result of persistent <u>scratching</u> or rubbing**
Pruritic, scaly plaques

Micro: prominent <u>hyperkeratosis</u> (mostly orthokeratosis)
***<u>Irregular</u>* <u>acanthosis</u>** (different length rete)
± focal parakeratosis, **hypergranulosis**
Often not much inflammation.
Fibrosis of the papillary dermis that is characterized by vertically oriented thick collagen fibers ("vertical streaking")

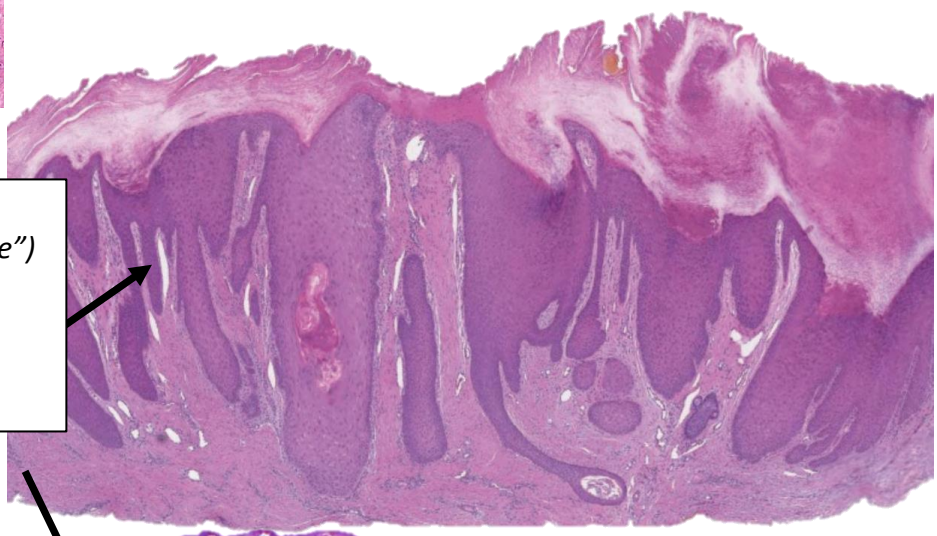
Virtual slide 2 3

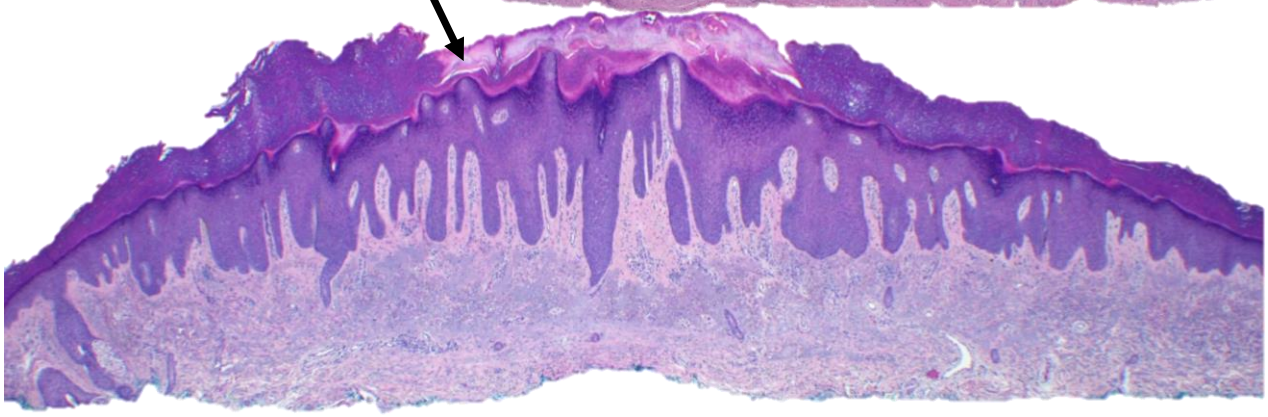
The hyperkeratosis is so striking it makes the skin resemble acral skin, but is usually on hair-bearing skin → "hairy palm sign"

LSC can be superimposed on other lesions. If there is a lot of inflammation→ consider an underlying dermatitis.

Can *mimic* SCC, but in contrast LSC/PN is often **multiple** and **itchy**.

If nodular/discrete nodule →
Prurigo Nodularis *("Picker's nodule")*
more pseudoepitheliomatous appearance or psoriasiform hyperplasia. Cup-shaped.
Virtual Slide

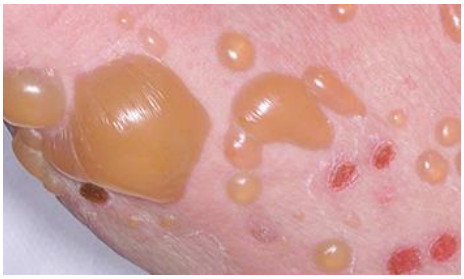




Other disorders that can be psoriasiform:

Reactive arthritis (Reiter's disease)
Pityriasis rubra pilaris
Lichen simplex chronicus/Chronic spong. derm.
Psoriasiform drug eruptions
Herald patch of pityriasis rosea
Secondary syphilis (sometimes)

Vesiculobullous Reaction

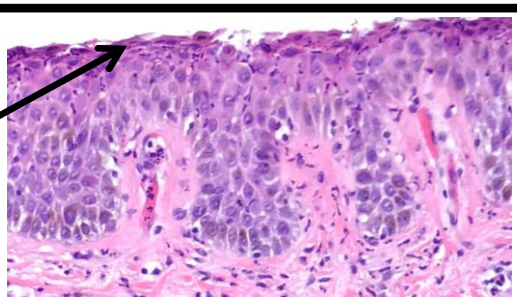


Vesicles or bullae at any level within the epidermis/DEJ.
Acantholysis is due to loss of cell-cell adhesion.
Can be a *secondary* change, so look for other processes.

Specific diagnosis depends on: **1) anatomical level** of the split, **2)** the underlying **mechanism**, **3)**pattern of other **inflammation**.

Biopsies should be perilesional (~1 cm away from blister) and submitted for IF in Michel's solution.

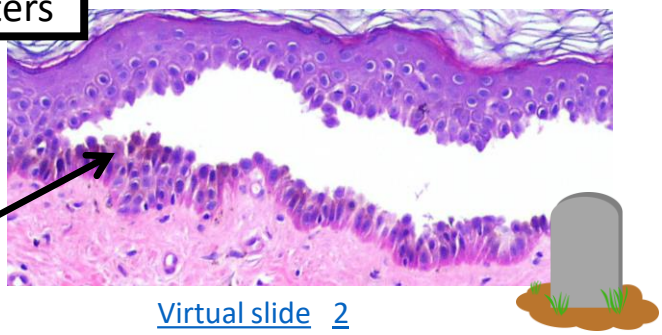
Intracorneal / Subcorneal Blisters



Pemphigus Foliaceus

Most autoantibodies are directed against desmoglein 1 → expressed more in the *upper* epidermis → *superficial* intraepidermal blister formation, often with **loss of the stratum corneum and granular layer.** Virtual slide

Suprabasilar Blisters/Intraepidermal Blisters



Pemphigus Vulgaris

Often older patients with big flaccid bullae
Often involves oral mucosae. **Severe disease!**

Autoantibody to desmosomes (desmoglein 3)
Intraepidermal split→ vesicle
Suprabasilar acantholysis ("tombstoning")
Extends down follicles.

Virtual slide 2

DIF: IgG deposited in the intercellular regions of the epidermis → net-like or chicken wire staining pattern

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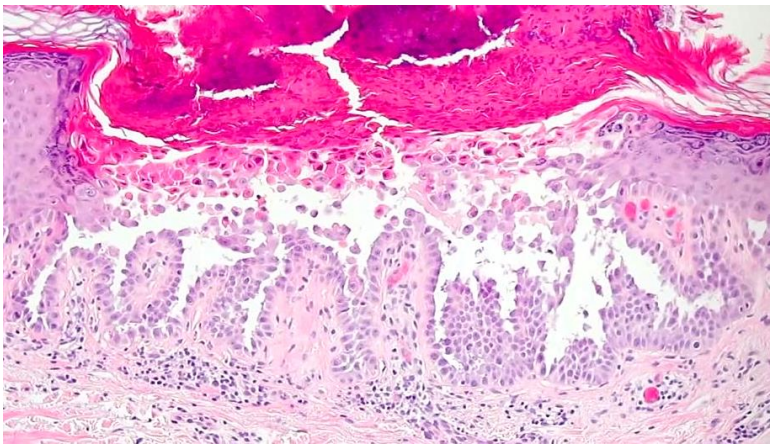
Grover Disease

Transient Acantholytic Dermatosis
Pruritic papulovesicules on the chest and back of older men.



Sharply circumscribed acantholysis
(only a few rete ridges wide!!)
Level of split varies by "pattern" (resembling Hailey-Hailye, et..).
Can be incidental. Often associated SPD.
DIF: Negative Virtual slide 2 3

Darier Disease

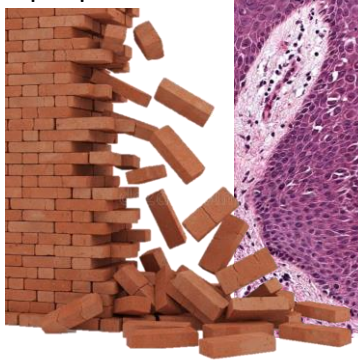
Autosomal dominant genodermatosis (ATP2A2 gene)
Onset late child/teen. Mucous membrane and nail changes. Virtual slide 2 3
Symmetrical crusted brown itchy papules.
Several discrete foci of suprabasilar clefts with acantholytic dyskeratotic cells surrounded by vertical parakeratosis

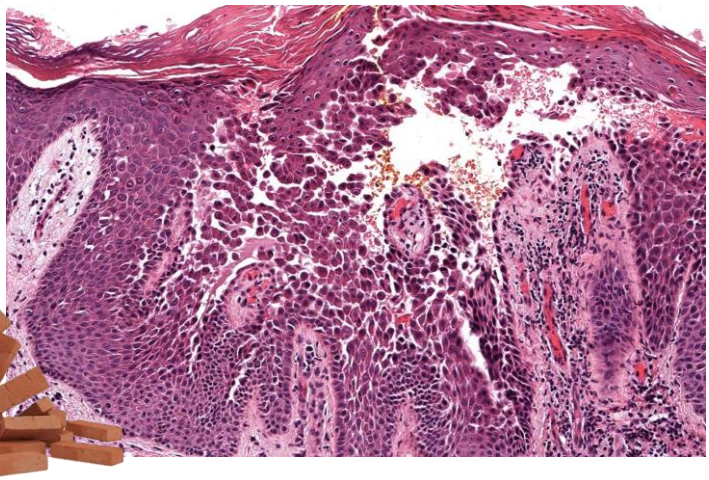
Suprabasilar Blisters/Intraepidermal Blisters *(Continued)*

Hailey-Hailey Disease

Autosomal dominant genodermatosis (AP2C1 gene)
Interiginous zones with malodorous plaques
Extensive epidermal acantholysis
Involves >1/2 epidermis
(suprabasilar → granular layer)
"dilapidated brick wall"
Epidermis hyperplastic

Virtual slide 2 3



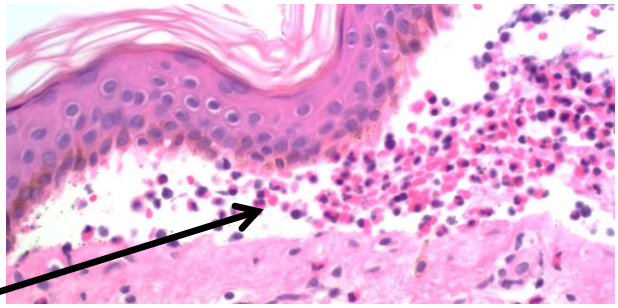


Subepidermal Blisters

Bullous Pemphigoid

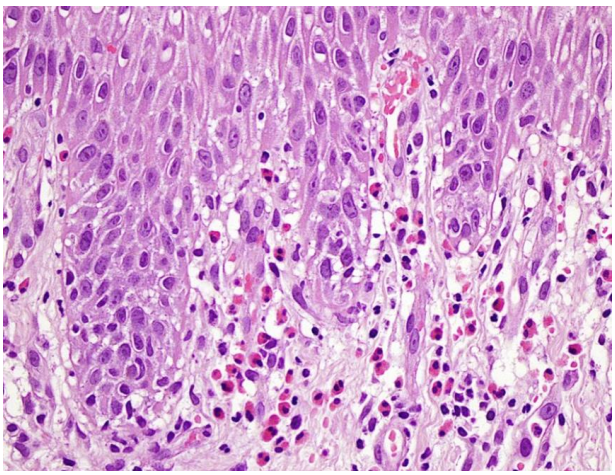
Most common autoimmune blistering disorder
Elderly with tense bullae. Usu. Groin/abdomen.
Chronic disease with remissions/exacerbations.

Autoantibody to hemidesmosomes at DEJ (BPAg1&2)
Subepidermal cleft with abundant **Eosinophils**



DIF: linear deposition of C3 and IgG along DEJ

Virtual slide 2 3



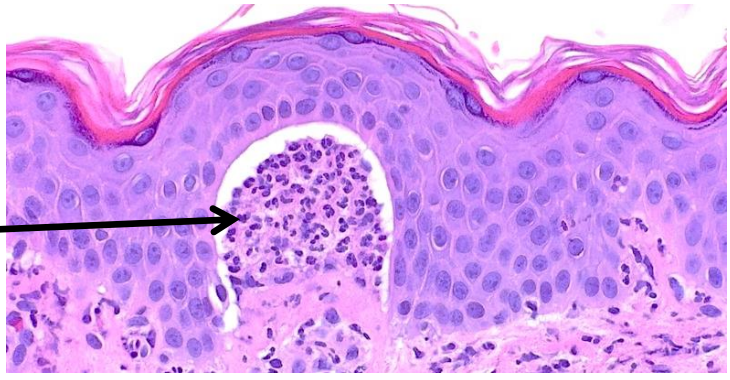
Important variant: ***Urticarial bullous pemphigoid*** is pre-bullous form that shows eosinophilic spongiosis and eosinophils tagging the epidermis along the DEJ and in papillary dermis.

So, "spong derm" with lots of Eos in an old person → consider Urticarial bullous pemphigoid

Dermatitis Herpetiformis

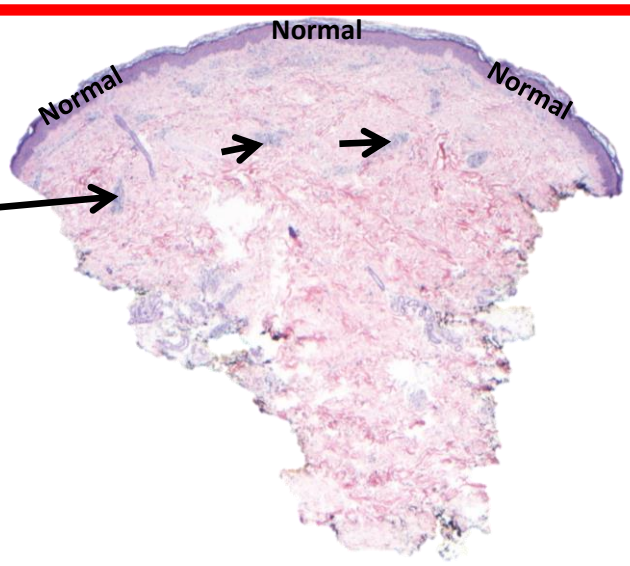
Rare. Very itchy. Papules and vesicles on elbows and knees. Highly associated with **Celiac disease**

Early: subepidermal split with numerous **neutrophils** in dermal papillae (papillary microabscesses).
Late: subepidermal vesiculation with neutrophils
DIF: Granular **IgA** staining



Virtual slide 2 3

Perivascular Dermatitis



***Absence* of significant epidermal changes**

Inflammatory infiltrate that is largely restricted to the around blood vessels.

Classified as to if superficial and/or deep.
e.g., "Superficial perivascular dermatitis" (SPD)

Superficial perivascular dermatitis DDX:

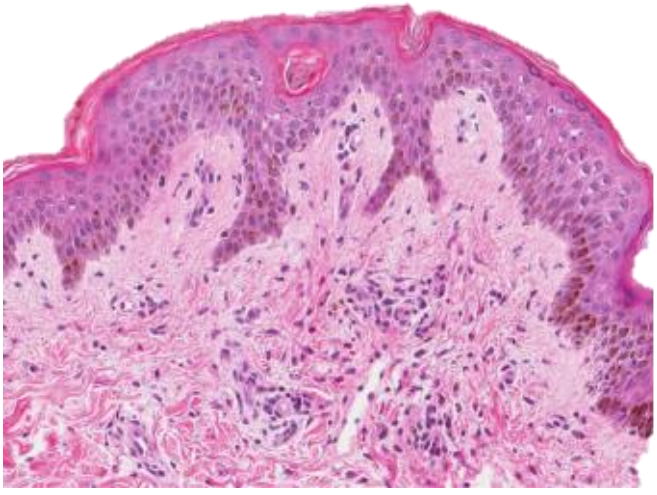
Predominant inflammatory cell	DDX
Lymphocytes	Morbilliform drug eruption
	Viral exanthem
	Chronic urticaria
	Superficial annulare centrifugum (gyrate erythema)
Lymphocytes with extravasated RBCs and/or siderophages	Stasis dermatitis
	Schamberg's disease
Eosinophils	Urticaria
	Urticarial hypersensitivity reaction (arthropod bite or drug)
	Morbilliform drug eruption
Mast cells	Cutaneous mastocytosis

Superficial and deep perivascular dermatitis DDX:

Predominant inflammatory cell	DDX
Lymphocytes	Deep annular erythema (gyrate erythema)
	Polymorphous light eruption
	Perniosis (chilblains)
	Lymphomatoid papulosis
Eosinophils	Dermal hypersensitivity reaction (including arthropod bite reaction or drug)
Plasma cells	Morphea

Modified from "Inflammatory Dermatopathology: A Pathologist's Survival Guide" by Billings and Cotton

Morbilliform Drug Eruption

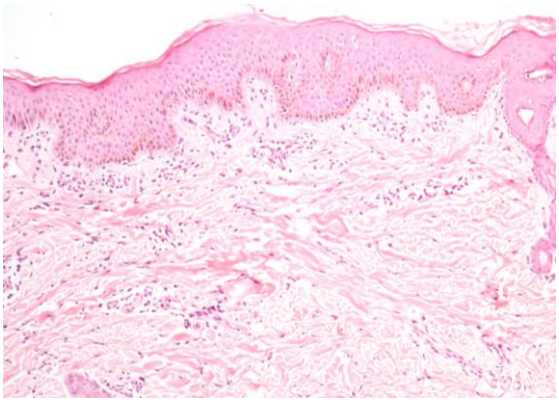


Most common drug rash!
Widespread erythematous macules or papules after taking new drug.
(Morbilliform means "measles-like")

Mild perivascular dermal infiltrate composed of lymphocytes and eosinophils. *("SPD with Eos")*
May see some *mild* interface changes, without many necrotic keratinocytes.

Virtual slide 2 3

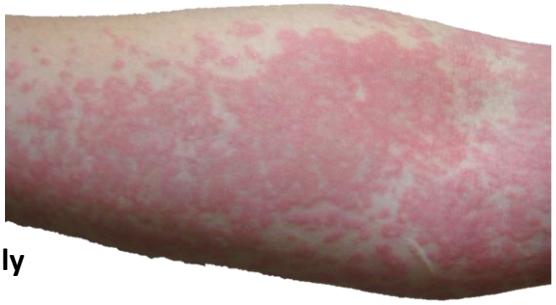
Viral exanthem



Acute, widespread self-limited eruptions of erythematous macules, papules, and vesicles.
Usually systemic symptoms: **fever, malaise,** headache.
More common in **kids**.

Nonspecific superficial perivascular lymphocytic infiltrate.
Eosinophils are usually *not* present.
Can have focal interface.
Virtual slide

Urticaria *"Hives"*

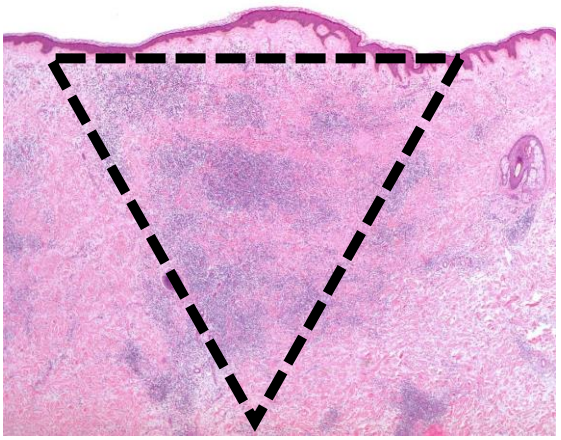


Transient (<24hr) erythematous plaques without scale.

Relatively normal at low power.
Normal epidermis.
Papillary dermis edema.
Mild/sparse perivascular and interstitial mixed infiltrate typically rich in eosinophils. Also often PMNs and lymphs.
May be just superficial or superficial and deep.

Virtual slide 2

Arthropod bite reaction ***"ABR"***



Variable appearance, but often pruritic, excoriated papules, and vesicles.
Can be in a line as insect stopped to have "breakfast, lunch, and dinner."

Various degrees of:
Brisk wedge-shaped perivascular lymphocytic infiltrate with **eosinophils**
Spongiosis, Ulceration, blister formation
Dermal edema, necrosis
Insect tissue fragments may be present

Can have epidermal changes (often spongiosis ±vesicle), especially at site of entry

Spiders → more neutrophils and necrosis

Virtual slide 2

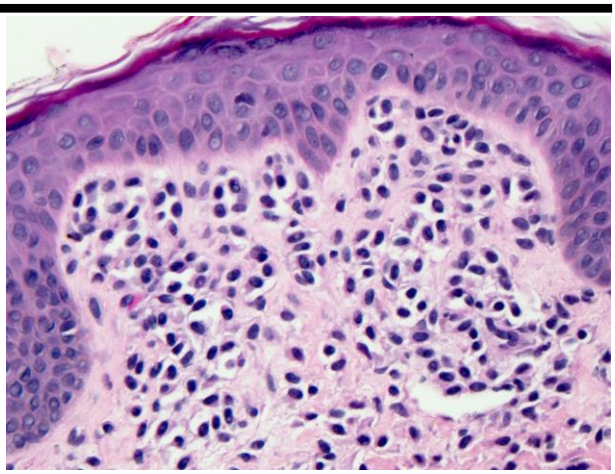
Pro Tip: ABR often has much more severe inflammation than a drug reaction, hives, or viral exanthem.

Common finding: Superficial perivascular dermatitis with eosinophils ("SPD with Eos")

Dx: - Superficial perivascular infiltrate with numerous eosinophils, see comment.

Comment: The epidermis shows minimal changes. There is a mild superficial perivascular mixed inflammatory infiltrate composed of lymphocytes and eosinophils. The histologic features are relatively nonspecific. The differential diagnosis includes dermal hypersensitivity reactions such as a drug eruption or urticaria. An arthropod bite reaction is less likely given the mild nature of the infiltrate. Clinical correlation is recommended. [Edit as necessary]

Cutaneous mastocytosis



Various manifestations, all of which look similar on skin biopsy. Hyperpigmented lesions, wheals with touch (Darier sign).

Moderately dense superficial perivascular infiltrate of mast cells. Often also scattered eosinophils and lymphocytes.
Mast cells amphophilic to basophilic cytoplasm
IHC: (+)CD117 and tryptase

Urticaria pigmentosa Virtual slide (mild) 2
Most common manifestation.
Seen in kids. Low risk of systemic disease.

Single lesion: Mastocytoma

How many mast cells are too many?
A rule of thumb: ***>15 mast cells per HPF*** *suggests mastocytosis*

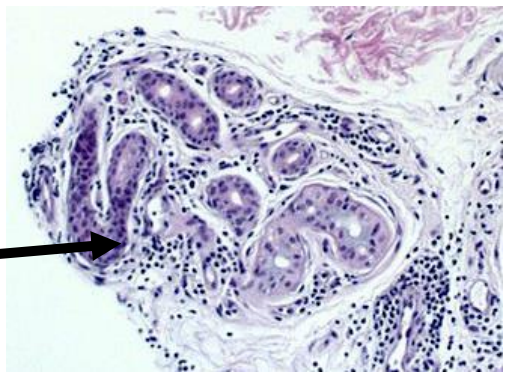
Polymorphous Light Eruption *"PMLE"*

Virtual slide 2

Idiopathic response to ultraviolet light→ sun exposed skin
Usually presents in spring/summer (sun is out!). Relatively quick after exposure.

Superficial and deep dermal perivascular dermal infiltrate composed predominantly of lymphocytes
Prominent subepidermal edema

Perniosis (Chilblains)



Caused by exposure to **cold, damp conditions (winter)**
Painful erythematous nodules on the fingers and/ or toes

Superficial and deep perivascular infiltrate of lymphocytes
Prominent **perieccrine** inflammatory infiltrates
Papillary dermis edema
Lymphocytic vasculitis without necrosis

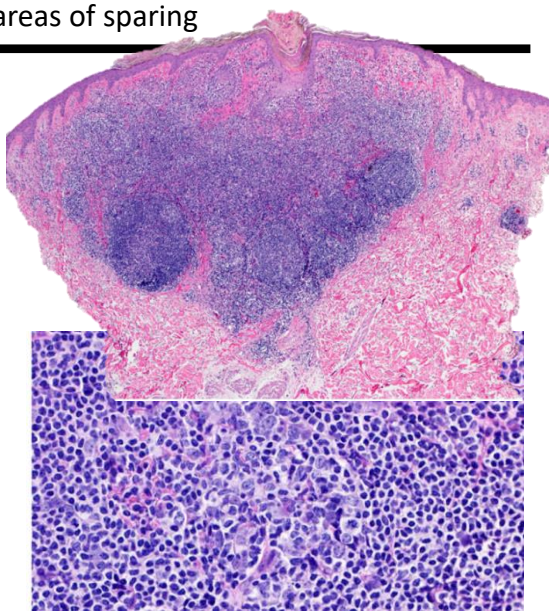
Virtual slide 2

Nodular and Diffuse Dermatitis

Inflammation *not* centered around *just* vessels.

Nodular dermatitis: discrete areas of inflammation, separated by uninvolved areas
Diffuse pattern: dense dermal inflammation without intervening areas of sparing

Reactive Lymphoid Hyperplasia

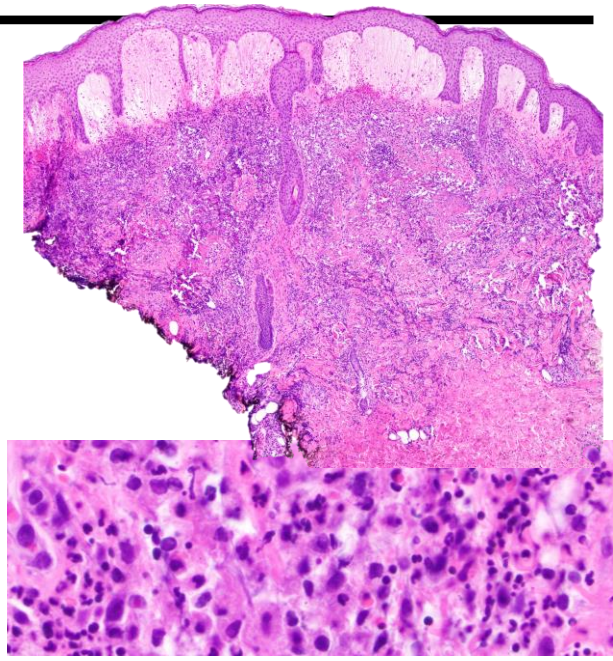


Reactive lymphoid proliferation provoked by chronic antigenic stimulation (arthropod bite, infections, and contact) or certain medications.
Persistent erythematous papules or nodules

Looks like a reactive lymph node: well-demarcated, polarized germinal centers (B cells) with a peripheral cuff of small lymphocytes and central tingibile body macrophages. Surrounding T cells.

Can mimic lymphoma, but no monotypia or clonality.
Often need to do lots of IHC to exclude lymphoma!

Sweet Syndrome



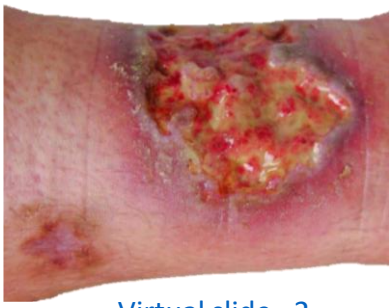
"Acute Febrile Neutrophilic Dermatosis"
Acute onset of fever, malaise, and leukocytosis.
Raised, tender plaques on the extremities and face.
Most often occurs in middle-aged women after a nonspecific respiratory or GI infection. Can be paraneoplastic.

Heavy dermal infiltrate of neutrophils
Variable leukocytoclasis without much vascular damage.
Papillary dermal edema

Important to exclude an infectious etiology by special stains (Gram and fungal) and tissue culture before rendering an unequivocal diagnosis of Sweet Syndrome

Virtual slide 2 3

Pyoderma gangrenosum



Ulcerative lesions with rolled edges.
~1/2 have underlying disease, most commonly IBD
Usually older middle-age. Often trunk and lower extremities

Central deep ulcer with diffuse mixed inflammation
Edge often shows pustule and vasculitis (presumed secondary)
Inflammation usually limited to dermis (not SubQ)

Culture to rule out infection.

Virtual slide 2

Vasculopathic Reaction

Pathological changes in <u>blood vessels</u>
Includes **vasculitis** and **vascular occlusive diseases**

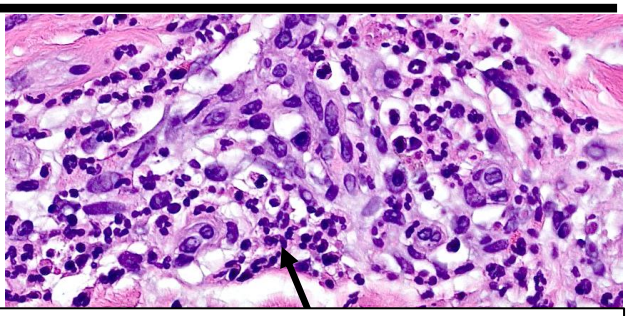
Leukocytoclastic Vasculitis *"LCV"*

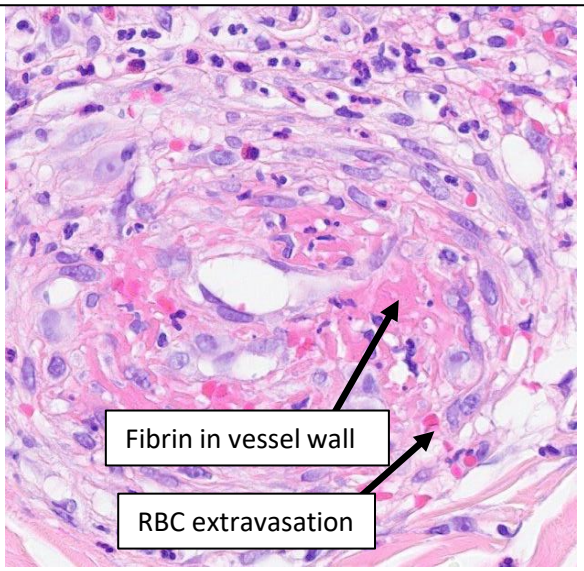
Usually present with **<u>palpable purpura</u>** (non-blanching) on the **lower extremities**.

Histologic reaction pattern due to <u>immune complex deposition</u>. Frequently due to **hypersensitivity** to infection or drug.

Perivascular **neutrophilic** infiltrate
<u>Karyorrhexis</u> (nuclear dust)
Vessel damage
Fibrin deposition in the vessel wall ± fibrinoid necrosis
Endothelial cell swelling
RBC extravasation

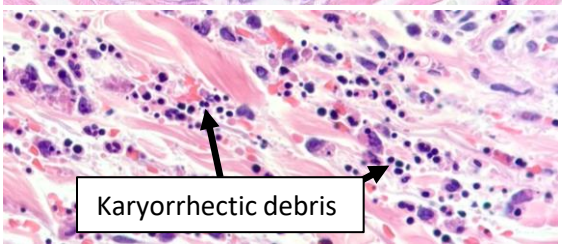
<u>Warning</u>: These changes may be seen *adjacent* to an ulcer and seldom cause ulceration themselves. If there is history of an ulcer, these changes are likely secondary.





<u>Henoch–Schönlein Purpura</u>

Specific type of LCV with IgA-dominant deposits
Vast majority of **pediatric** vasculitis.
Palpable **purpura + arthritis, GI involvement**, and nephritis.
Often **post-infectious** (e.g. URI)
Above LCV findings perivascular deposits of IgA around both involved and uninvolved vessels by immunofluorescence.



Virtual slide 2 3 4 5

Other Vasculitis

See the vascular diseases notes for additional information.

In the skin, most of these just show LCV, but deeper vessels may show more unique changes.

Urticarial Vasculitis: Seen in patients with chronic urticaria. Lesions are present as urticarial plaques. Subtle LCV with only mild/focal vessel damage. Often Eos present.

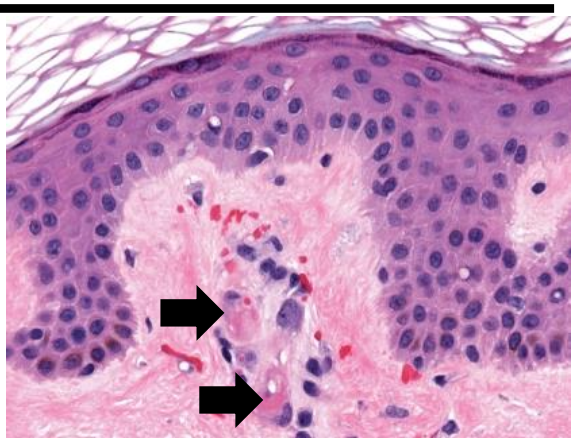
Wegener's granulomatosis: Systemic vasculitis associated with granulomatous inflammation. Frequently impacts the lungs and kidneys. Often c-ANCA antibodies.

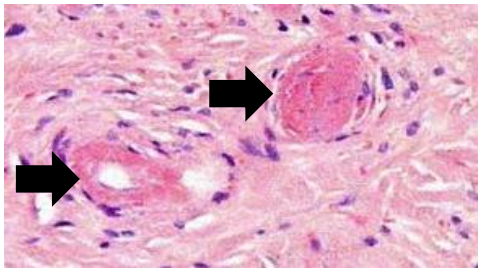
Churg–Strauss Syndrome: Systemic vasculitis with abundant eosinophils. Often also asthma, other allergic symptoms (e.g., allergic rhinitis), and peripheral and tissue eosinophilia.

Microscopic Polyangiitis: Systemic vasculitis with frequent renal involvement. No eosinophils or granulomas. Often p-ANCA antibodies.

Cryoglobulinemia: Systemic vasculitis associated with the presence of cryoglobulins, immunoglobulins that precipitate at colder temperatures, often associated underlying disease such as multiple myeloma.

Thrombotic Vasculopathy





Histologic reaction pattern denoting presence of **<u>non</u>inflammatory** small vessel **<u>fibrin thrombi</u> (→)**

Can have associated hemorrhage, extravasated RBCs, necrosis

Many possible etiologies (e.g., DIC, hypercoagulable state, etc..)

<u>Special types:</u>

Antiphospholipid Antibody Syndrome: autoantibodies directed against phospholipid (common in lupus) → hypercoagulable → recurrent episodes of thrombosis and associated thrombocytopenia and spontaneous abortions. Usually young women.

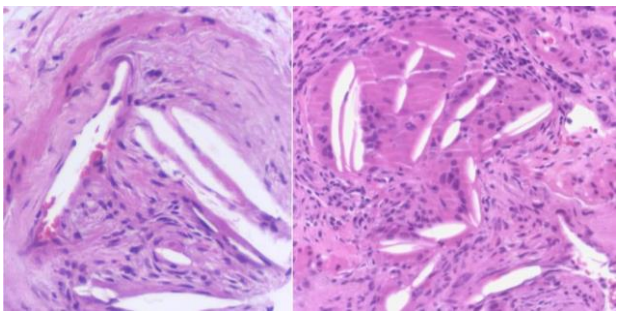
Coumadin necrosis: Lesions begin several days after initiation of therapy with coumadin

Atrophie Blanche (Livedoid Vasculopathy): Most common on distal lower extremities of older women.

Cryoglobinemia: Eosinophilic "hyaline" thrombi that are intensely PAS positive.

Virtual slide 2

Cholesterol Emboli



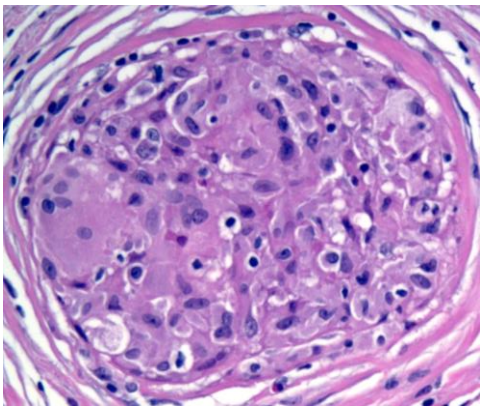
Patients who have significant atheromatous plaques in large vessels, especially the abdominal aorta.
Often recent vascular procedure (e.g., Cath)

Biconvex, needle-shaped clefts in deep dermis/subcutis vessels.

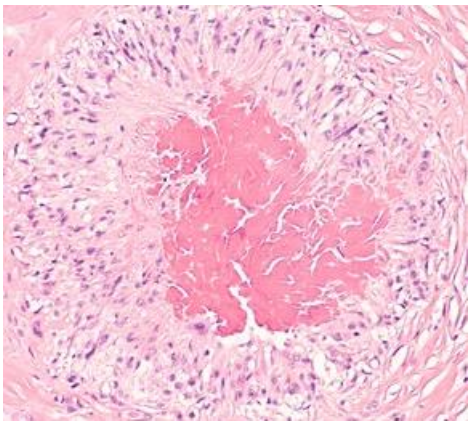
Virtual slide 2

Granulomatous Reaction

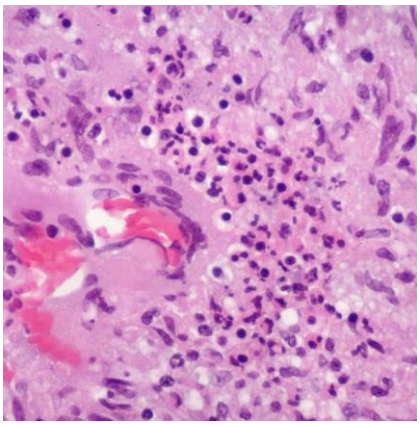
Discrete collections of histiocytes with variable numbers of multinucleated cells and lymphocytes



Sarcoidal Granuloma
Tight, well-formed "non-caseating" granulomas consisting primarily of epithelioid histiocytes, and giant cells, with very little necrosis.



Necrobiotic Palisading Granuloma
central area of degenerated (necrobiotic) collagen surrounded by a rim of histiocytes and giant cells, often forming a "palisaded" (stacked, fence-like) appearance



Suppurative Granulomas
central collection of neutrophils (pus) surrounded by histiocytes and multinucleated giant cells

Sarcoidosis

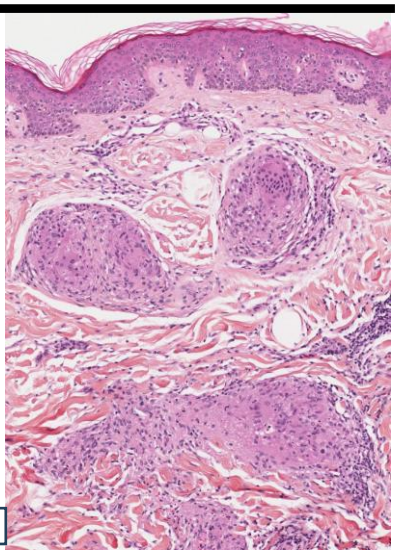
Systemic disease of unknown etiology, defined by the presence of non-caseating granulomata usually affecting multiple organ systems.
Most common in women, esp. African American.

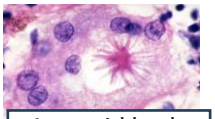
Superficial and deep nodules of non-caseating granulomas
Poorly developed lymphocytic cuff ("naked granulomas").

Nonspecific findings: Asteroid bodies (pink stellate inclusions) and Schaumann bodies (refractile concentric calcium complexes)

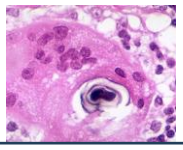
Do bug stains to exclude infection!

Virtual slide 2 3





Asteroid body



Schaumann body

Foreign material reaction

"Foreign body giant cell reaction"

Granulomatous inflammation in response to traumatically introduced "foreign" (non-human) material (e.g., suture, wood, tattoo etc..)

Foreign material often obvious and may be polarizable. Occasionally, levels can be helpful in revealing foreign material.

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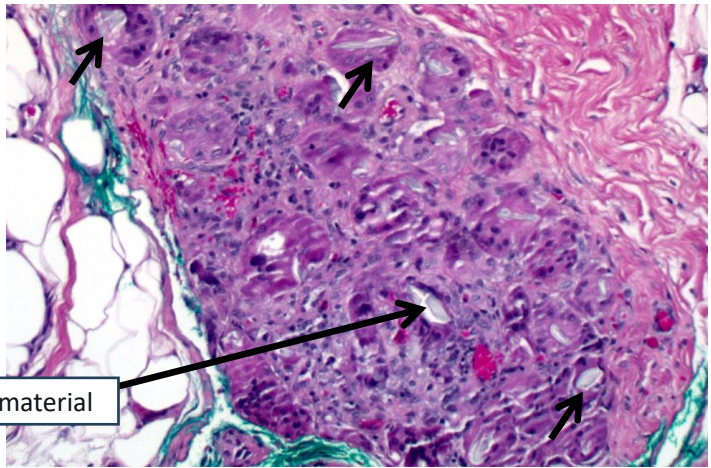
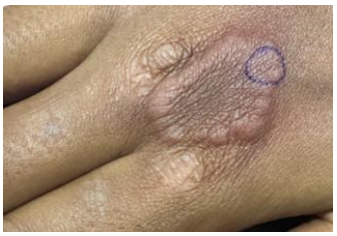


Suture material

Granuloma annulare



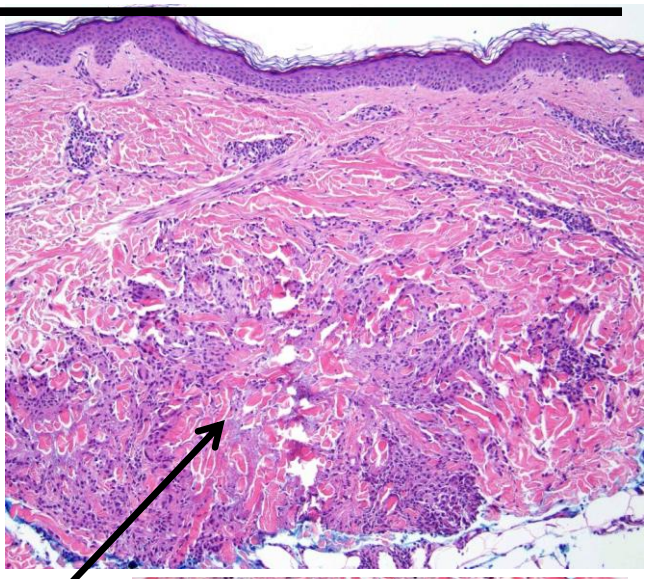
"GA"
Common, asymptomatic.
Often younger women.
Skin-colored circle (annular)

Most commonly located on backs of hands/feet.
Many variants: localized, generalized, deep, etc..

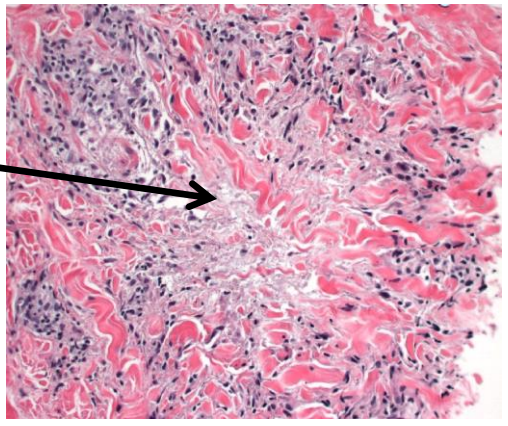
Palisading granuloma: a **palisade of histiocytes** admixed with lymphocytes surrounding a **central zone of altered collagen fibers** ("necrobiotic," often more pink or red), associated with increased dermal mucin.

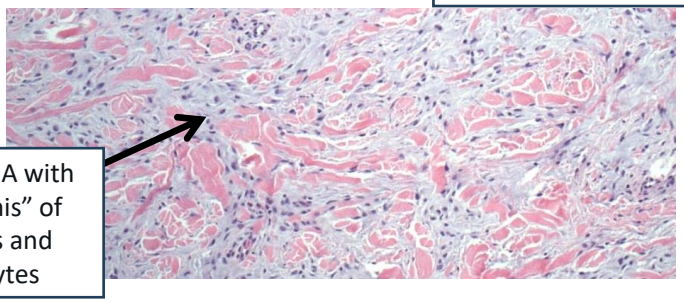
Can be subtle and "interstitial" with a busy dermis of interstitial histocytes and lymphs.

Virtual slide Interstitial Deep



Central necrobiosis and mucin





Interstitial GA with "busy dermis" of histiocytes and lymphocytes

Necrobiosis lipoidica

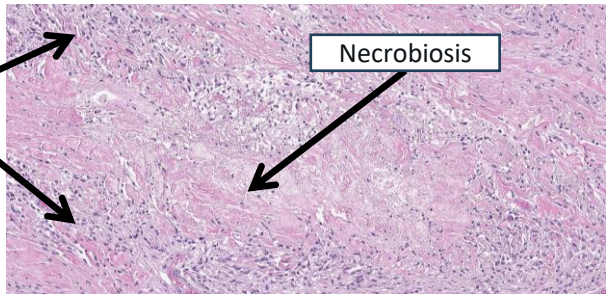
Associated with **diabetes**
(sometimes add "diabeticorum" to name)
Often yellow/brown indurated plaques on **bilateral shins**

Micro: Normal epidermis (unless ulcerated)
Diffuse **dermal involvement.**

Palisading necrobiotic granulomas have a characteristic tiered arrangement of the inflammatory cells alternating with broad zones of necrobiotic collagen that run parallel to the overlying epidermis →**"layer cake" appearance**

Unlike GA: Mucin absent. Frequent plasma cells.
May extend to septae of fat and have lymphoid aggregates.

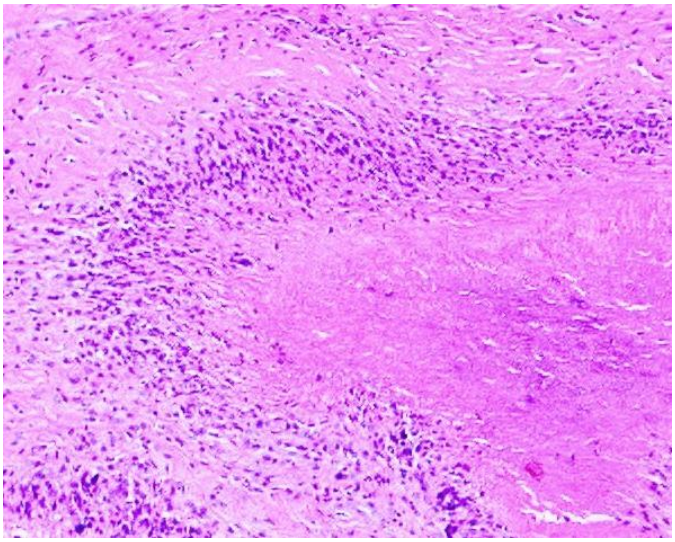
Virtual Slide 2 3



Palisading granulomas

Necrobiosis

Rheumatoid nodule

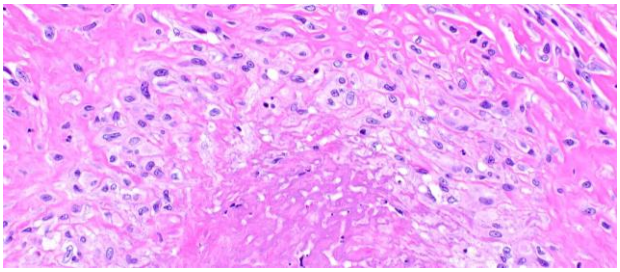


Seen in the setting of **Rheumatoid arthritis**:
Chronic, idiopathic erosive symmetric polyarthropathy.
Serology: Positive Rheumatoid Factor (RF)
Often over bony prominences, especially on **hands**.

Subcutaneous/deep dermal lesions
Central acellular fibrin/necrotic collagen (No mucin)
Surrounded by rim of histiocytes and giant cells in a palisaded pattern.
Often not much associated inflammation

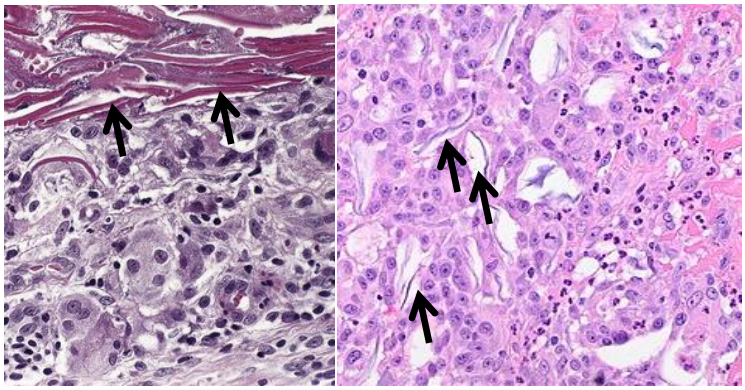
DDX for nodule: Granuloma annulare, infection, and epithelioid sarcoma (CK+, INI1 loss).

Virtual slide 2 3



Be careful diagnosing a RA nodule in someone without a history of RA and consider getting a "screening" CK to exclude epithelioid sarcoma.

Ruptured cysts and follicles

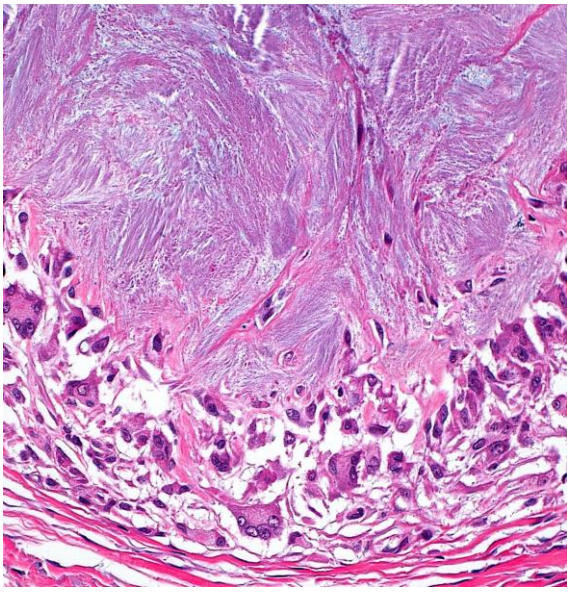


Rupture of an Epidermal Inclusion Cyst (EIC), Follicle, or any structure can induce a response.

Often Foreign body giant cell reaction
± Acute inflammation
± Keratin (→) (Instead of "foreign material")

Virtual slide 2

Gout



Uric acid metabolic disorder: hyperuricemia→ deposit monosodium urate crystals in joint fluid and tissues.

Classically middle-aged males
Most common joint: **1st MTP** (big toe), but can get anywhere
Often get recurring attacks of painful arthritis → eventually chronic gout.

On H&E: See **fluffy, feathery pink deposits** with associated **granulomatous inflammation and giant cells**. Varying associated inflammation. Soft tissue deposits = "**Tophi**"

Virtual Slide 2 3

Sclerosing dermatitis

Dermal sclerosis.
Usually with little inflammation.

Scar/Fibrosis

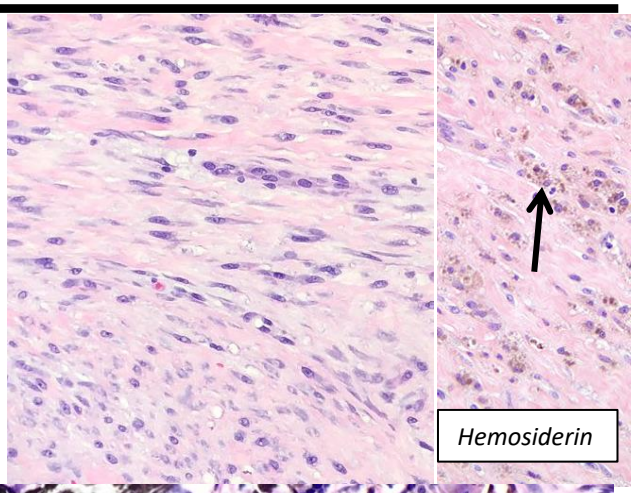
Site of prior trauma or procedure.
Fibroblasts in abundant extracellular collagen

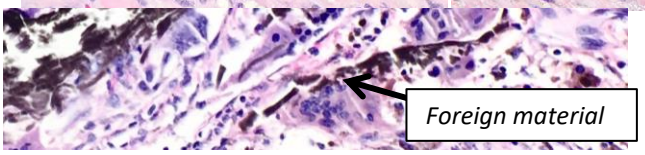
Epidermal atrophy and loss of adnexal structures
Horizontal running fibrosis with **vertically oriented vessels.**

Virtual Slide 2

Frequent inflammatory cells
± Hemosiderin laden macrophages
± Foreign material and/or foreign body giant cells
± Fat necrosis
Variable vascularity, but can be prominent.
Often lots of small capillaries and telangiectatic vessels

"Hypertrophic scars" are raised, but confined to the area of injury.

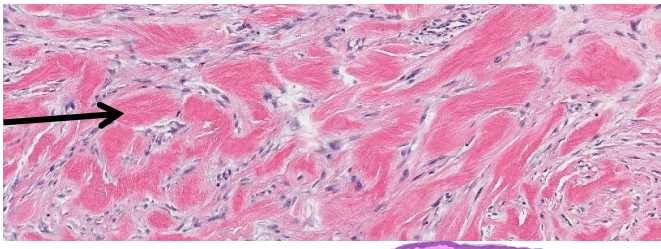




Keloid

Virtual Slide 2 3

Scar + **Prominent thick, eosinophilic bundles of collagen**
Most common in those with African heritage.
Overgrows *beyond* wound. Delayed onset.
Most common site is earlobe (e.g., after piercing)



Morphea/Scleroderma

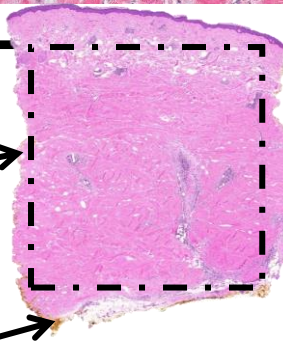
Virtual Slide 2 3

Fibrosing/sclerosing disorder in genetically predisposed individuals. Morphea is the most common variant of scleroderma and is limited to the skin, subcutaneous tissue, muscle, and bone.

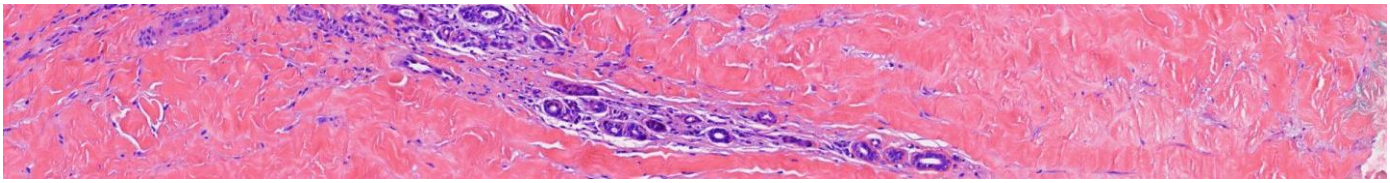
Smooth, indurated plaques.
Early: Superficial and deep perivascular lymphocytic inflammation.

Late: **Obliterative sclerotic dermal collagen bundles**. Hypertrophic collagen replaces fat, entraps/squishes adnexal structures, pushing adnexal structures upward. No space between collagen fibers.

Collagen causes "square" and "cookie cutter" biopsies (straight sides).



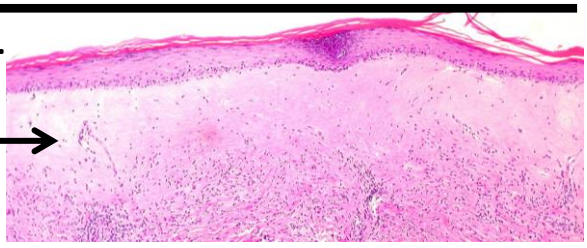
Line/saber sign: straight prominent demarcation/line created at the interface of SubQ fat and sclerotic collagen.



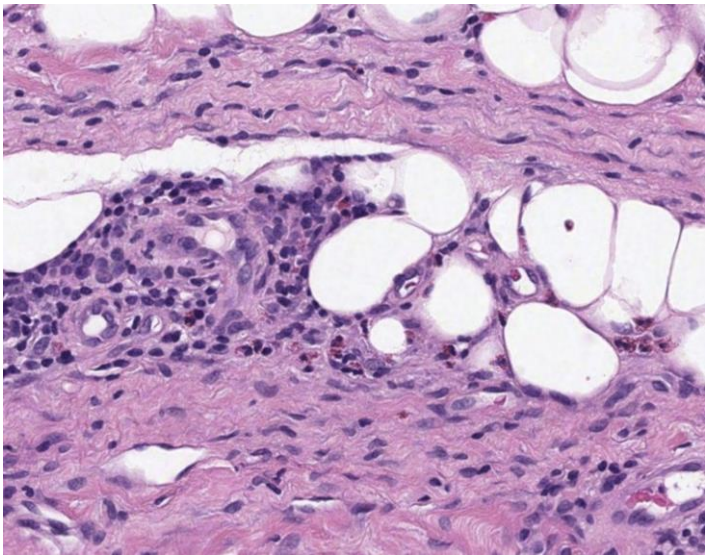
Lichen sclerosus

See Lichenoid section for more info.

Predilection for **anogenital skin**.
Homogenization & sclerosis of dermal collagen
Variable band of **lymphocytic inflammation** BELOW edema and homogenization.



Eosinophilic Fasciitis

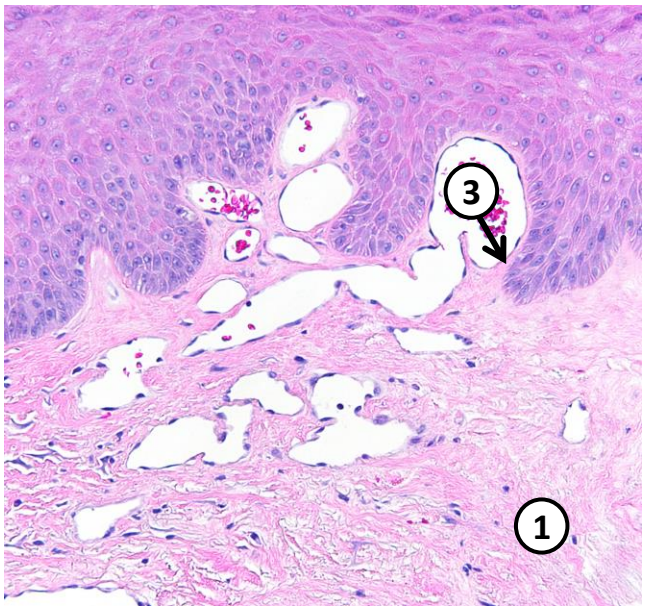


Scleroderma-like disorder: symmetric thickening of fascia with mixed inflammatory infiltrate.
Often middle-age women.
Depressed patches with longitudinal grooves.

Fascial edema and thickening (Deep!)
Mixed infiltrate with eosinophils, lymphocytes, histiocytes, and plasma cells.
(Eos may be focal or prominent)
Thickening of septae in interlobular fascia

Virtual side 2

Radiation Dermatitis

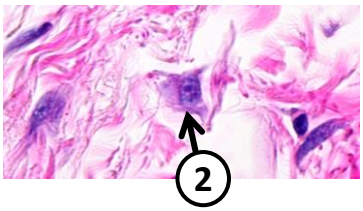


"Radiodermatitis"

Radiation burn caused by irradiation of the skin, usually following **radiation therapy**.

Variable epidermal changes (atrophy or acanthosis)

Chronic changes:
1) Dermal fibrosis
2) *"Radiation fibroblasts"* Atypical stellate fibroblasts
3) Telangiectatic blood vessels with thickened walls and atypical endothelial cells.
Loss of appendages, esp. hair.



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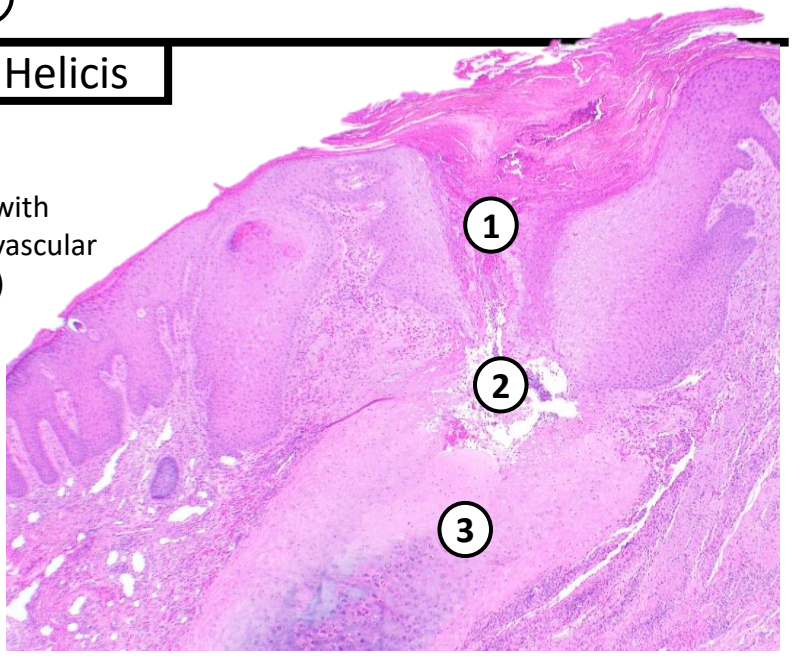
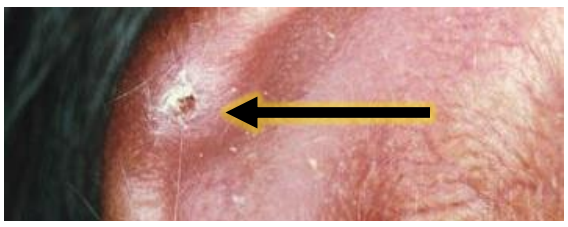
Chondrodermatitis Nodularis Helicis

aka "CNH" Virtual slide 2 3



1) Surface hyperplasia surrounding **ulceration** with **keratin plug,** 2)**Dermal fibrinoid necrosis** and vascular proliferation, and 3)**Necrotic Cartilage** (usually)

Helix or anti-helix of ear
Localized injury. Clinically mistaken for SCC.



Panniculitis

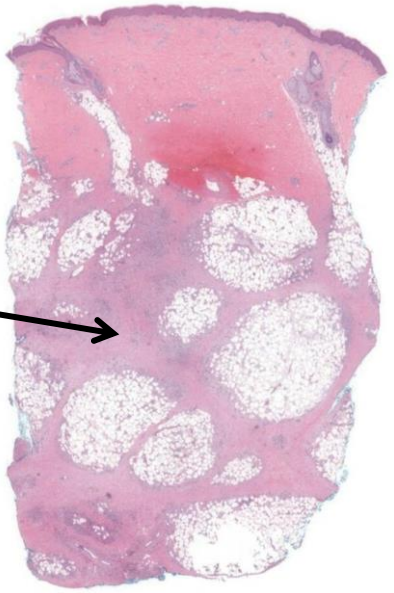
Inflammation of **subcutaneous adipose tissue**
Often classified on if ***predominantly*** involves lobule or septae.
(Most cases have a bit of both, so looking for major pattern).
Also classify by inflammatory cell and vasculitis.

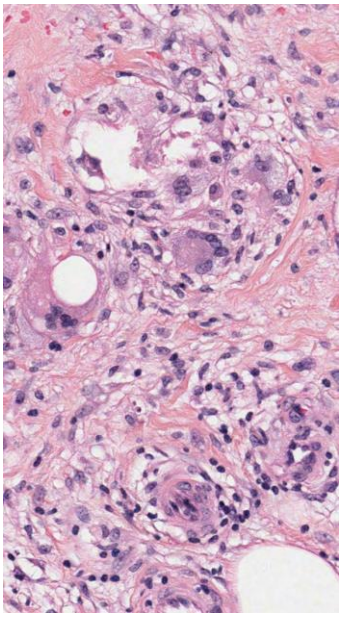
	NO Vasculitis	YES Vasculitis
Septal	**Erythema Nodosum**	**Polyarteritis Nodosa**
Lobular	**Others**: Histiocytic cytophagic panniculitis, α1-antitrypsin deficiency, pancreatic, sclerema neonatorum, subQ fat necrosis of the newborn,	**Erythema Induratum**

Erythema Nodosum

Most common panniculitis.
Usually young adults.
Red, tender nodules, on shins
Associated fever, malaise, arthralgias

Thickening of fibrous septae
Lymphohistiocytic infiltrate
(Early: PMNs and less fibrosis)
Some "spill over" into adjacent fat lobules
NO vasculitis
Multi-nucleate giant cells, granulomas
Miescher's radial granulomas: aggregates of small histiocytes around central cleft





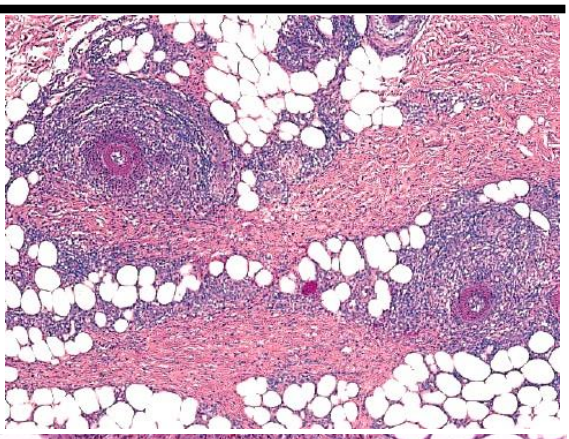
Virtual slide 2 3

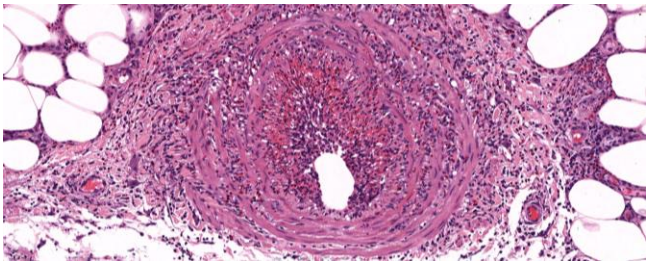
Polyarteritis Nodosa

Systemic vasculitis. Usually middle-age.
Associated with infection and autoimmune conditions.
May be systemic or cutaneous-only

Tender painful nodules on the legs with livedo reticularis.
Systemic symptoms (fever, weight loss, etc…)

Neutrophilic vasculitis of small and medium sized arteries in subcutis.
Overlap with microscopic polyangiitis





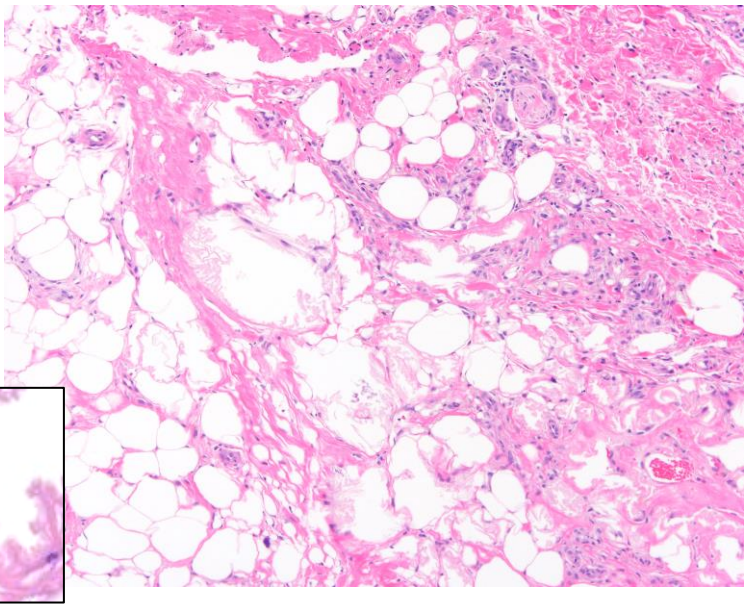
Virtual slide 2 3

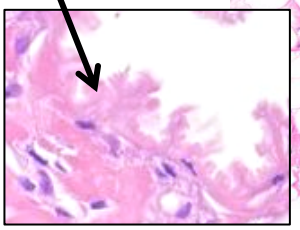
Lipodermatosclerosis

Long-term chronic panniculitis
Indurated plaques on the lower extremities
Usually older women with a history of venous insufficiency and thrombophlebitis.

Little inflammation. Septal and lobular fibrosis.
Fatty microcysts and lipomembranous fat necrosis.
(cystic cavities lined by a feathery hyaline material).
Background stasis dermatitis.

Virtual slide 2 3

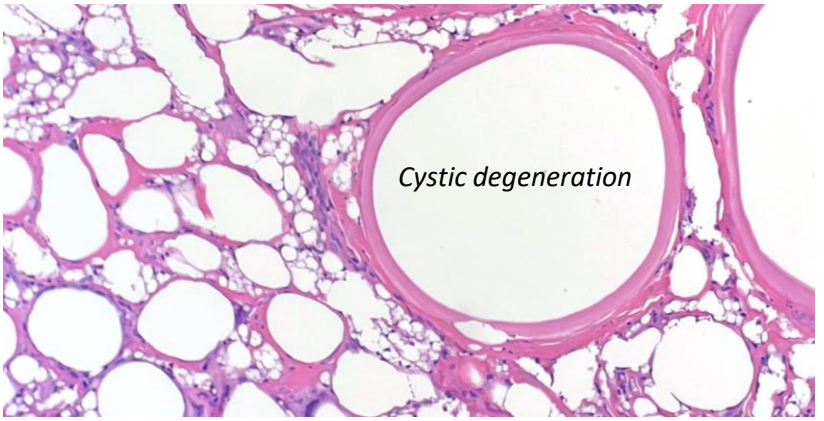




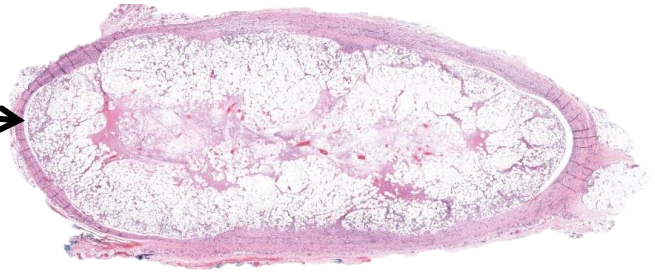
Traumatic Fat Necrosis

From physical or chemical injury
May not remember trauma

Ruptured adipocytes, foam cells, and mixed inflammation
Fat microcysts surrounded by histiocytes
Calcifications



Encapsulated fat necrosis
("mobile encapsulated lipoma")
Fibrous capsule around fat necrosis, often lipomembranous changes (see above)



Other Panniculitis

Factitial panniculitis: Due to patient injection of material. Often done for attention. Suppurative and granulomatous inflammation.

Cold panniculitis: Most often kids on the inside of the cheeks ("popsicle panniculitis"). Crystalline rosettes within lipocytes and surrounding granulomatous response.

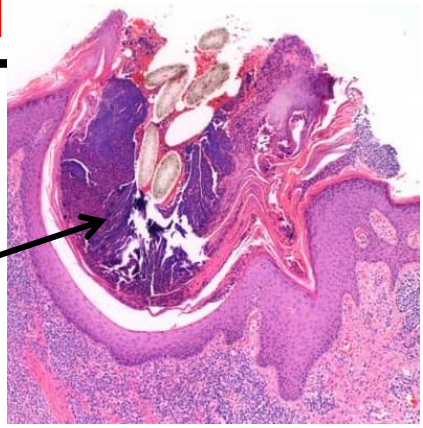
Erythema Induratum: Granulomatous lobular panniculitis with vasculitis. Often younger women on calves as part of a systemic reaction to an infection.

Subcutaneous fat necrosis of the Newborn: Lobular panniculitis in term newborns

Pancreatic panniculitis: Lobular panniculitis associated with pancreatitis and pancreatic carcinoma, presumably from hematogenous dissemination of pancreatic enzymes. Fat necrosis with saponification.

Diseases of Cutaneous Appendages

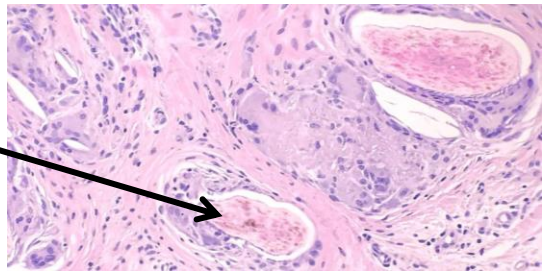
Acne vulgaris



Chronic sebaceous gland-centered inflammation
Multifactorial (genetics, infection, diet, environment)
Worst in teens. Predominantly face, back, chest

Follicular dilation
Filled with laminated keratin, sebum, and bacteria
Perifollicular mixed inflammation. Virtual slide

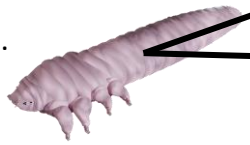
Folliculitis (Acne) Keloidalis Nuchae
Acne variant with Keloid-like scaring on posterior neck and scalp
Hair shafts in dermis in histocytes with chronic inflammation.
Most common in African American men.
Virtual slide 2

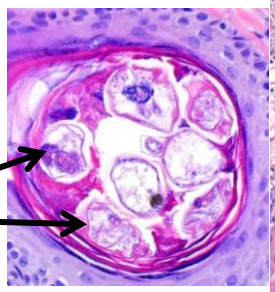


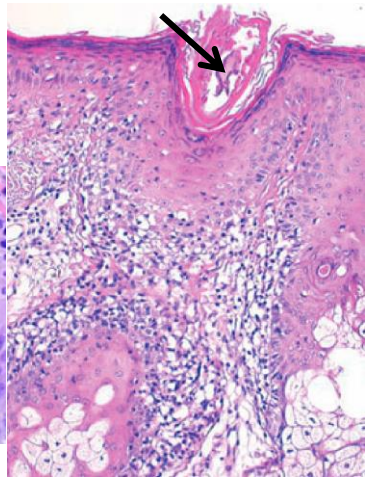
Rosacea

Erythematous eruption in central face.
Esp. around nose. Onset middle-age.
Papules/pustules, ± Telangiectasia

Perivascular and **perifollicular lymphocytic infiltrate**.
May have **granulomatous** inflammation and/or acute inflammation. ± Telangiectasia
May see ***Demodex*** mites in follicle.







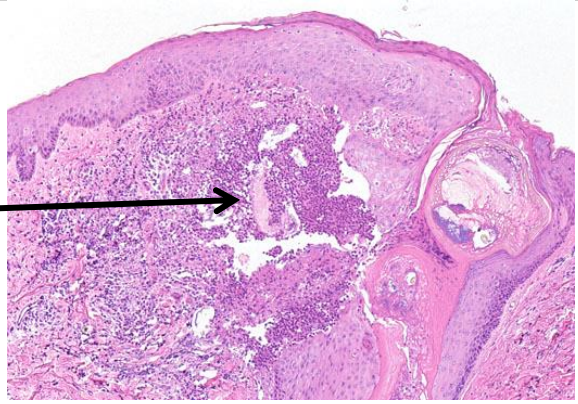
Virtual slide 2 3

Furuncle

Single, painful mass of walled off abscess from a hair follicle. Usually due to *Staphylococcus* species.

Follicular and perifollicular acute inflammation.
Can have hair and keratin material and foreign body reaction. Virtual slide

Multiple furuncles = carbuncle



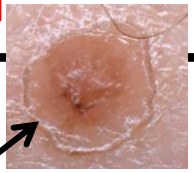
Hidradenitis Suppurativa

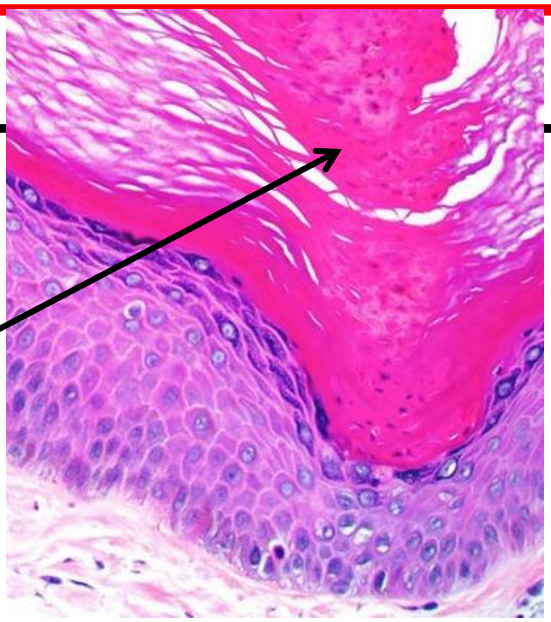
Virtual slide 2

Chronic disease with hyperkeratosis of hair follicle → occlusion of apocrine glands → follicular rupture → abscess → sinus tract & scarring. Interiginous areas, esp. axilla, inguinal, anogenital areas.
Non-specific histology with abscess, mixed inflammation, fibrosis, and granulation tissue

Disorders of Epidermis

Porokeratosis



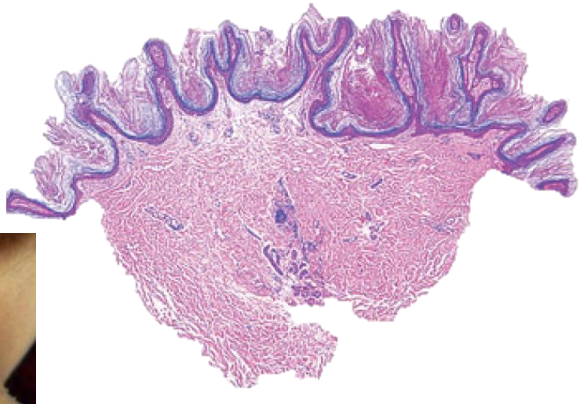


Keratinocyte proliferation (clonal)
Hyperkeratotic plaques with peripheral "cornoid lamella."
Usu. Large, asymptomatic, on arm. Many variants.

Cornoid lamella: angulated, thin, compact column of parakeratosis. Over area of epidermal dysmaturation with granular layer absent/decreased. Dyskeratotic cells present at base. (Not entirely specific for porokeratosis.)

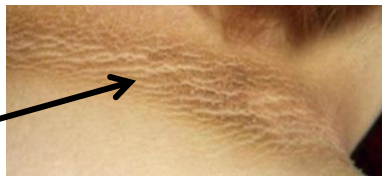
Virtual slide 2 3

Acanthosis nigricans



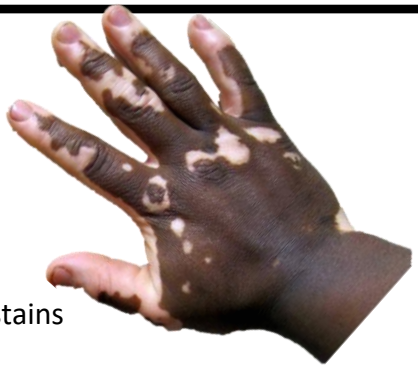
Velvety plaques of brown skin in interiginous areas bilaterally. Esp. Nape of neck, axilla, groin.

Associations: Endocrine disorders (diabetes, Cushing, etc..), Malignancy



Papillomatous epidermis
Hyperkeratosis
Virtual slide 2

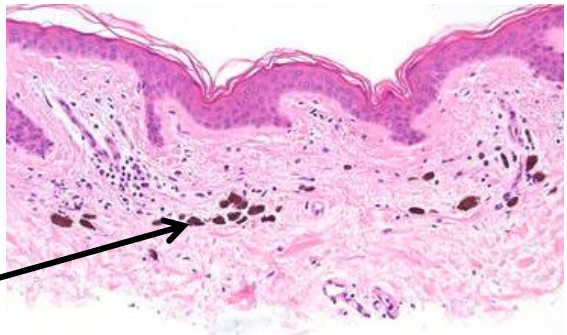
Vitiligo



Acquired progressive destruction of melanocytes.
Unknown pathogenesis. Circumscribed hypopigmented patches.
Often onset in 20s.

Greatly reduced or absence of melanocytes and melanin
(Normal skin: about 1 melanocyte per 7 keratinocytes)
Often requires IHC to confirm! Exclude tinea versicolor with PAS or GMS stains
Virtual slide

Post Inflammatory Pigment Alteration *"PIPA"*



Hyper- or hypopigmented macules after inflammation
Inflammation → damages keratinocytes and melanocytes → leak melanin (pigment incontinence) → phagocytosed by melanophages

Epidermis may show more or less pigment in basal layer.
Mild perivascular lymphocytic infiltrate with melanophages

Virtual slide