UMHS Pathology II
Dermatopathology
Quick HY Review Points

Acute Inflammatory Dermatoses (3)

- Urticaria
- Acute Eczematous Dermatitis
- Erythema Multiforme

Urticaria

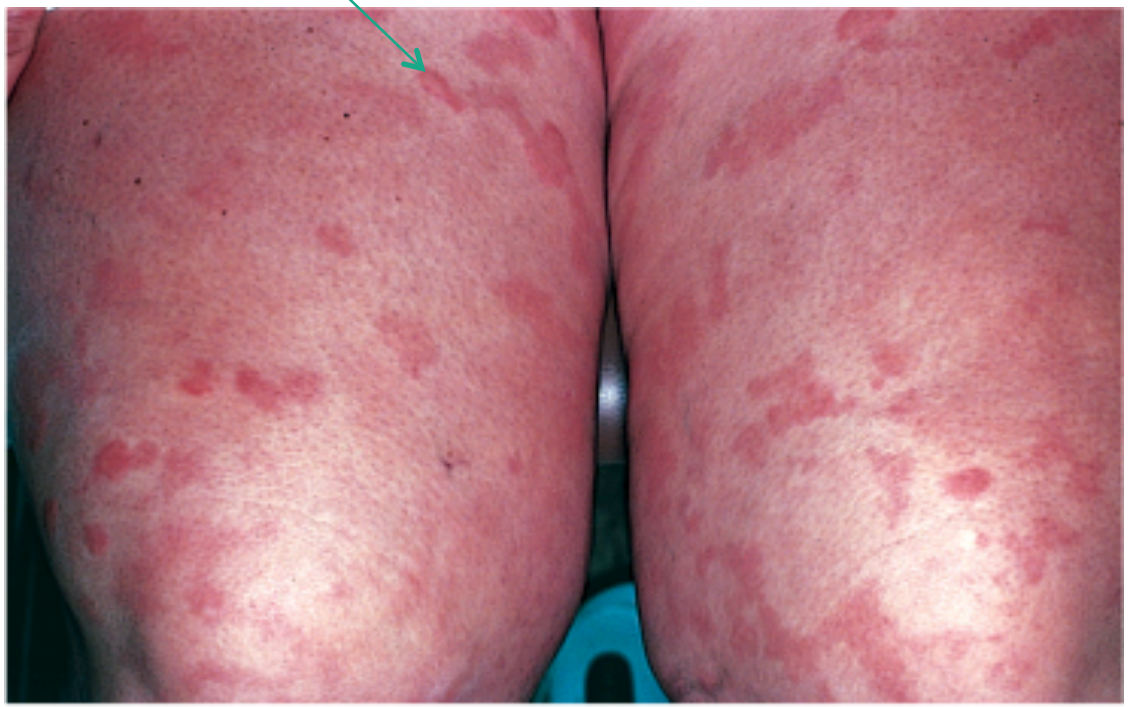
- Raised, itchy lesions due to acute inflammation/ swelling/edema
  - *Edema raises the lesion*
- HSR I: Associated with localized **mast cell** degranulation of mast cells/serotonin → increased vascular permeability & vasodilation
  - *Increased vascular permeability allows for edema & intravasation of neutrophils*
- Ages 20-40 yrs
- IgE dependent or IgE independent

Urticaria

- Involves areas **exposed to pressure**
  - *i.e. wearing tight jeans or a tight watch*
- Characterized by wheals (pruritic edematous plaques), welts and hives
- Morphology: normal skin, sparse superficial perivenular infiltrate consisting of mononuclear cells, superficial dermal edema

Urticaria

Erythematous = red



When you see Eczema, Think → Dry, scaly, flaky

Acute **Eczema**tous Dermatitis

Papule = small, raised lesion
Vesicle = small, bullous lesion or blister (raised w/ fluid)

- Common features include:
  - Early: *papulovesicular*, oozing, crusted lesions, "wheeping"
  - Late: raised, scaling plaques
- Synonym: "**spongiotic dermatitis**"
  - **Spongiosis**-accumulation of edema fluid within the **epidermis** (as opposed to subQ or CT)

Buzz word for boards

Acute Eczematous Dermatitis

- **Contact dermatitis**: cytotoxic-type (HSR IV) hypersensitivity (**poison ivy**)
  - HY for boards - *"I'm going to ask you that."*
  - *Remember*: *main HSR IV for Step to know is Tb*
- Irritant dermatitis: repeated trauma (rubbing)
  - Not very HY, never seen a question about that
- **Atopic dermatitis** (FHx of eczema, hay fever or asthma): type I hypersensitivity
  - Elevated eosinophils – *eosinophils are the cells that cause tissue damage in HSR I via secreted MBP*

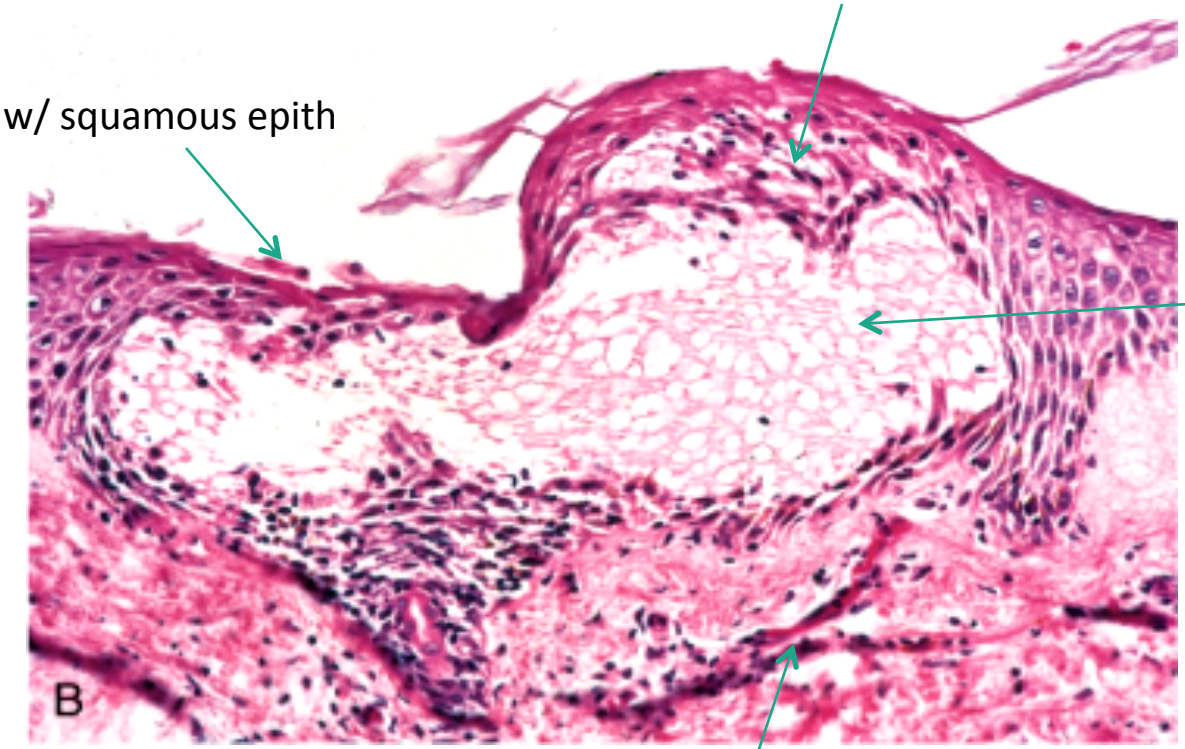
Atopy = predisposition to allergies; have higher levels of IgE & eosinophils in serum
Look for hx of allergies (eczema, Hay Fever, etc.) in patient's families

Acute Allergic Contact Dermatitis

Contact Dermatitis – Hx of using something that was in contact with skin
i.e. new sweater, used new detergent to wash clothes, chain, watch, etc.

Acute Allergic Contact Dermatitis

"Spongiotic Dermatitis"
Individual squamous cells separated by edema fluid in the epidermis
Spaces or holes look like holes of sponge



Erythema = Red *Multiforme = Diff forms or shapes of lesions*

Erythema Multiforme

- Uncommon, *self-limited* disorder
  - Resolves on its own – Don't need any therapy
- **Hypersensitivity** response to certain infections (herpes simplex, mycoplasma) and drugs (**sulfonamides – HY**)
  - Sulfa drugs* used to treat UTI
    - Patient with hx of UTI...
    - Sulfa drugs can cause G6PD
- Also associated with collagen vascular disorders (**SLE**), and malignancy (carcinomas and lymphomas)

Erythema Multiforme

- Clinically presents as "multiform"- various types of lesions including macules (flat), papules (raised), vesicles and bullae (blister), as well as **target lesion**
  - Target Lesions – CLASSIC; HY
- Typically in Adults
- Variants:
  - **Stevens-Johnson Syndrome**: an exaggerated form of erythema multiforme with severe oral, conjunctival and skin lesions
    - Children!
  - Toxic epidermal necrolysis (TEN): simulates extensive burns
    - **Dermatologic Emergency** – Burn-like effect, can lead to infection, BP can bottom out, etc.

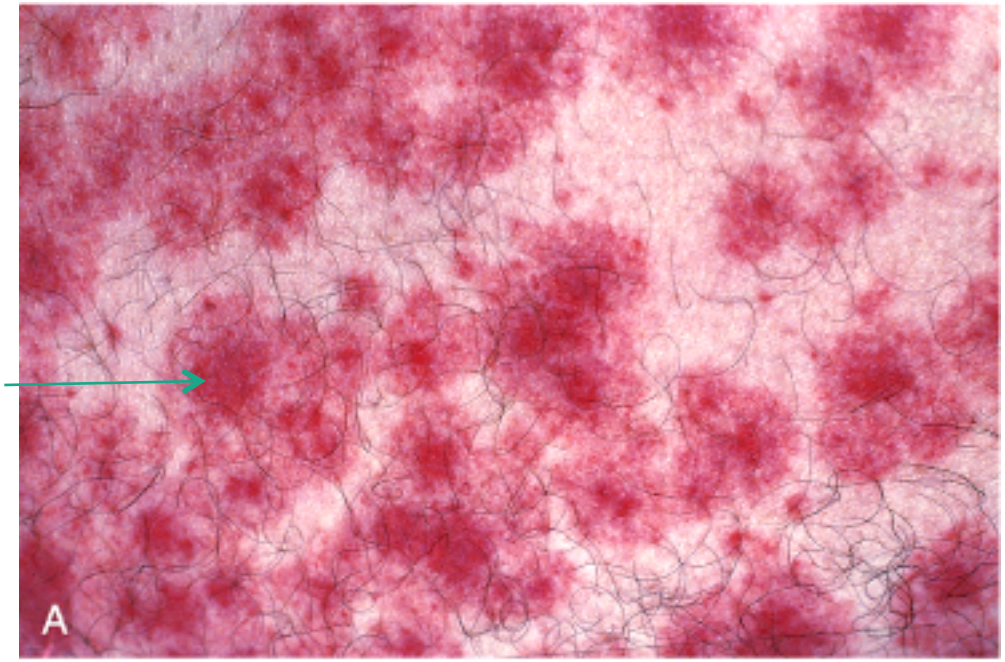
Erythema Multiforme

- Microscopic Features:
  - Superficial perivascular, lymphocytic infiltrate with dermal edema and margination of lymphocytes along the **dermoepidermal** junction
    - Inflammation is where dermis & epidermis meet
  - Associated with degenerating and necrotic keratinocytes
    - Damaging the cells that make up the basal layer of skin → epidermis can separate → bullous lesion
  - **Epidermal necrosis with blister formation**

Erythema Multiforme

Center is more red
"Target"

"Classic Lesion"



Chronic Inflammatory Dermatoses (2)

- Psoriasis
- Lichen Planus

Psoriasis

- **Common**, 1-2 % people in USA affected
- *Immune-based disease, but mechanism is unknown*
- Common sites: extensor surfaces (elbows and knees), palms, scalp, soles and joints
- **Clinically (Gross)**: well-demarcated pink to **salmon**-colored plaques covered by loosely adherent **silver-white** scales
- Remissions and exacerbations typical
  - Chronic problem – lasts weeks/months/years

Psoriasis

Increase in cell #
-plasia = growth

Downward projection of the thickened epidermis into the dermis

- Microscopic Features:
  - Epidermal hyperplasia (**acanthosis**) with **test tube-like** rete pegs
  - **Hyperkeratosis** with parakeratosis
  - Thinned or absent granular layer
  - Accumulation of neutrophils in the **upper epidermis** (**Munro's abscess**) – *if this becomes exacerbated or sever you can get general pustule psoriasis because of these abscesses-911!*

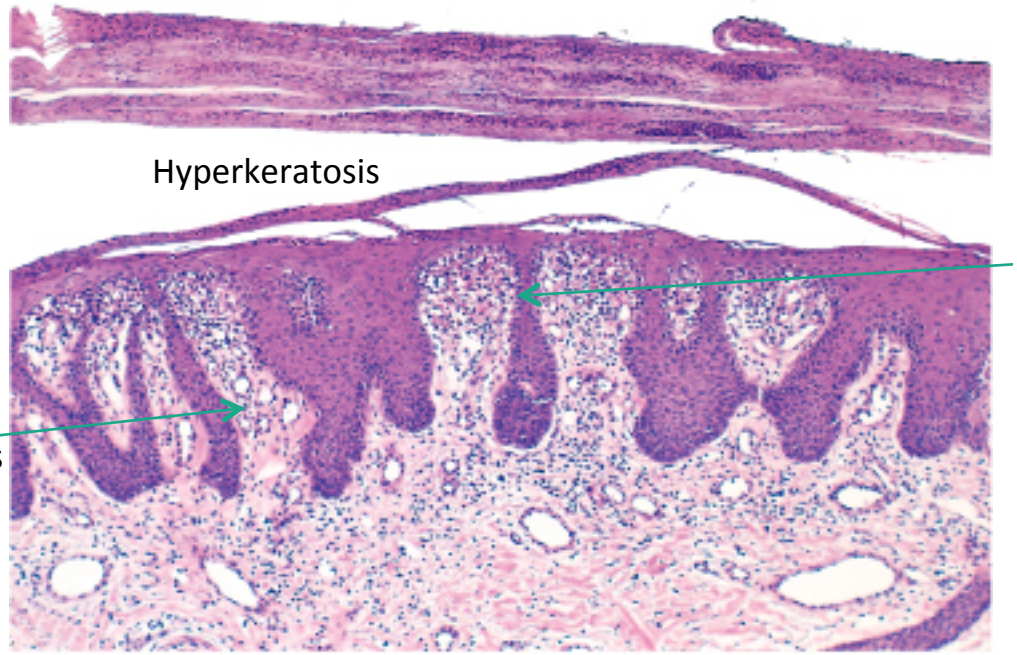
Hyperkeratosis – No nuclei
Parakeratosis – Has nuclei

Psoriasis

- Pathogenesis: not clear, may be immune-mediated
- **Auspitz's Sign**: when scales are lifted from the plaques, multiple bleeding points seen

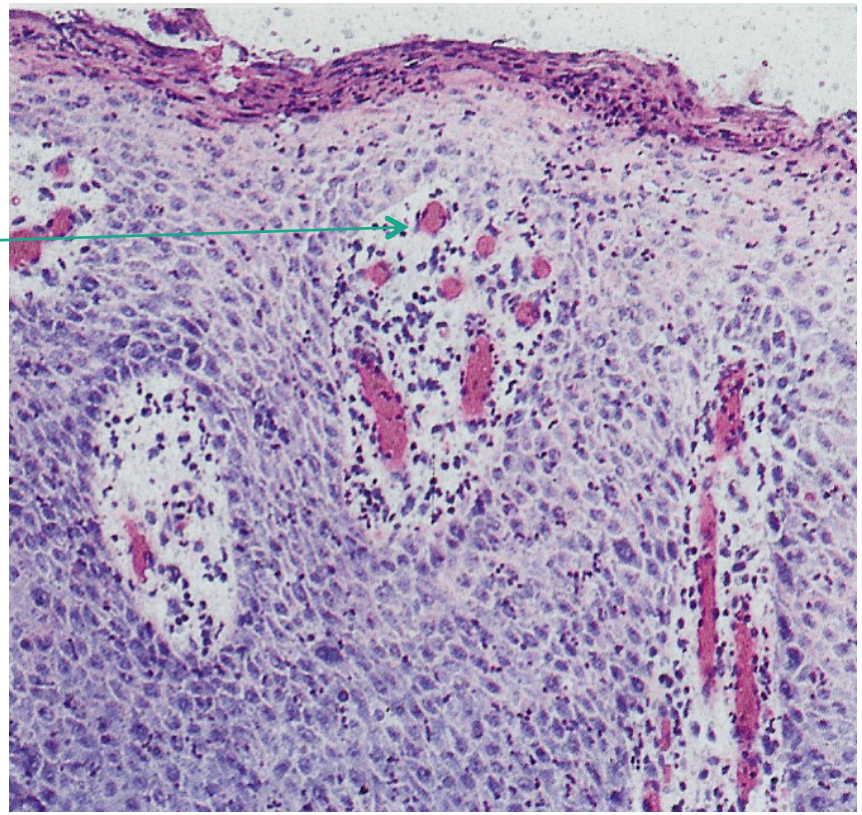
Psoriasis

Psoriasis

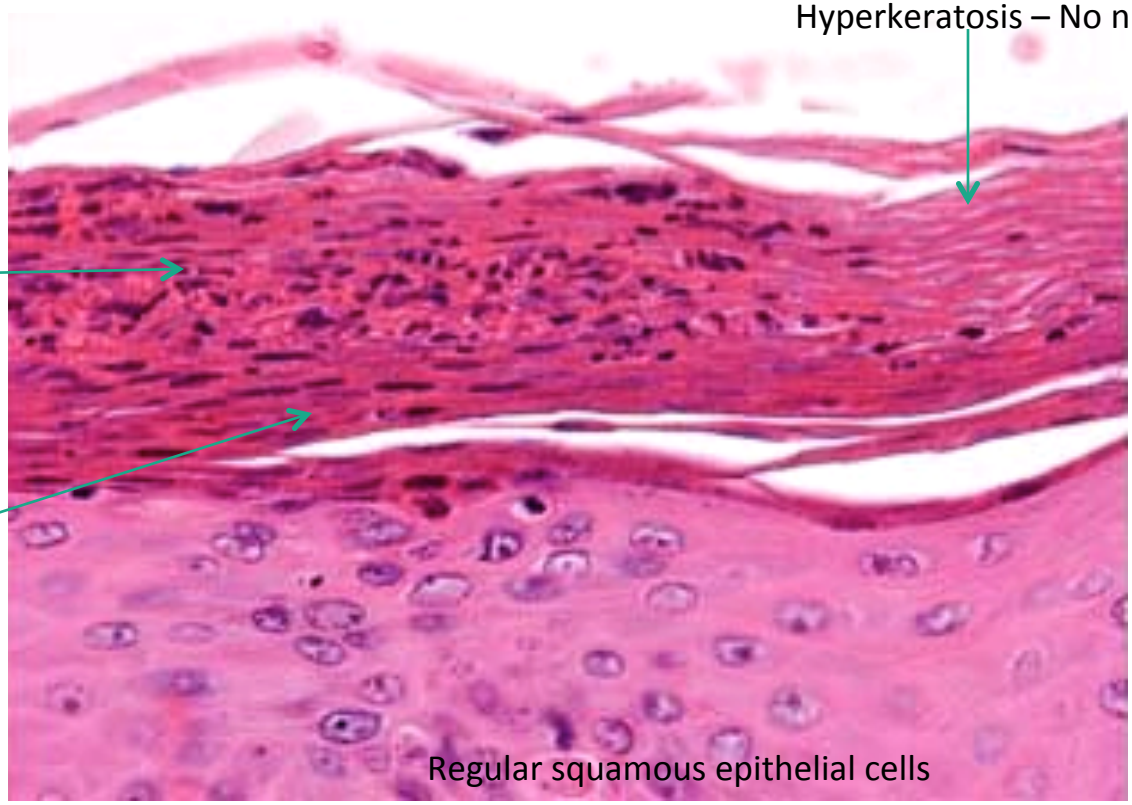

Hyperkeratosis
Inflammatory cells
"Test tubes"
Aconthosis going into dermis
Dermis w/ blood vessels

Psoriasis

Blood vessels in upper dermis
This will rupture when you lift scale
"Auspitz sign"



Psoriasis


Hyperkeratosis – No nuclei
Monroe's Abscess
Elongated nuclei
Parakeratosis
Regular squamous epithelial cells

Lichen Planus

Lichen = "Hairy"

- **Clinically**: Pruritic, purple ("violascious"), polygonal papules of skin (extremities) & membranes (oral mucosa)
- Papules with fine reticulated silver lines (**Wickham's striae**)
  - *Lesions may be **bilateral***
- Self-limiting disease, spontaneous resolution usually occurring in 1-2 years (chronic)
- Pathogenesis unknown

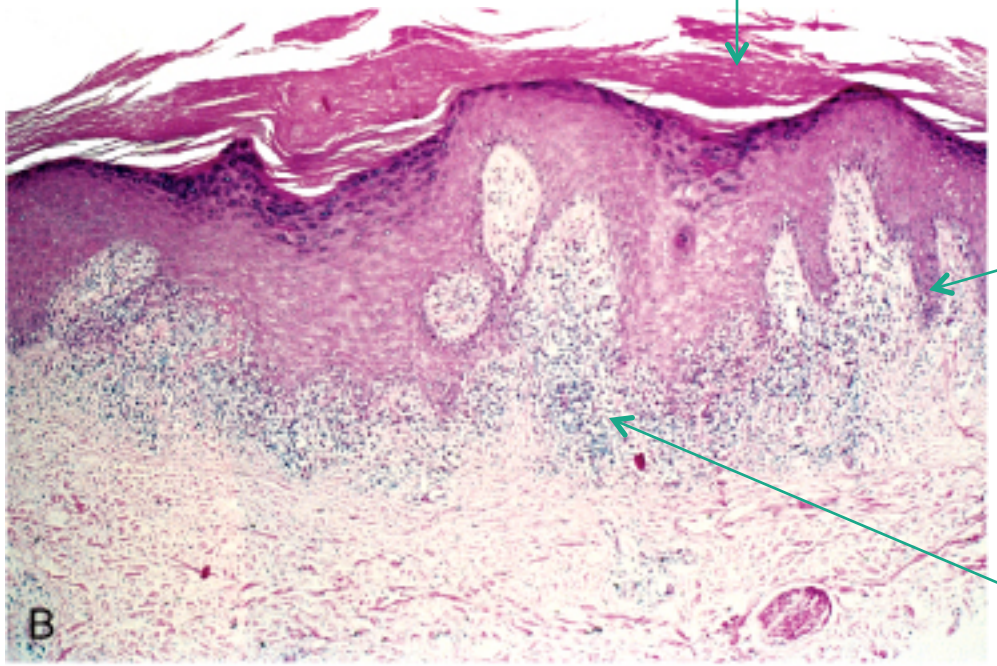
Lichen Planus

- **Microscopic Features (HY):**
  - **Hyperkeratosis** with thickening of the granular layer
  - Liquefaction of the basal cell layer
  - ***Saw-toothed appearance of the rete pegs**
    - *Psoriasis – long, going down, "test tube-like"*
    - *Lichen Planus – short, pointy, saw-tooth*
  - Dense collar of lymphocytes (band of chronic inflammation) & necrosis of basal cells (**colloid** or **civatte bodies**) at **dermoepidermal junction**
    - **Colloid or Civatte Bodies** – **Apoptotic Bodies** because they are individual cells that are dead!

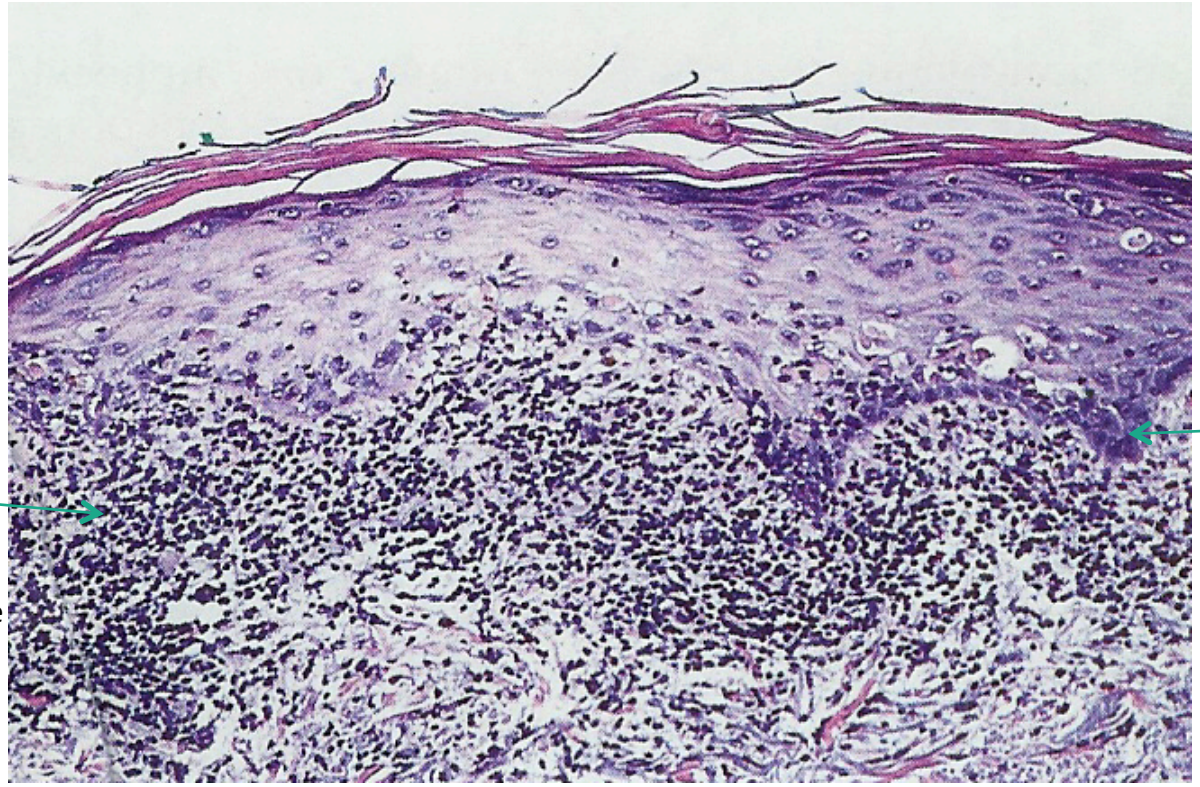
Lichen Planus

Wickman's striae
Light areas

Lichen Planus



Lichen Planus



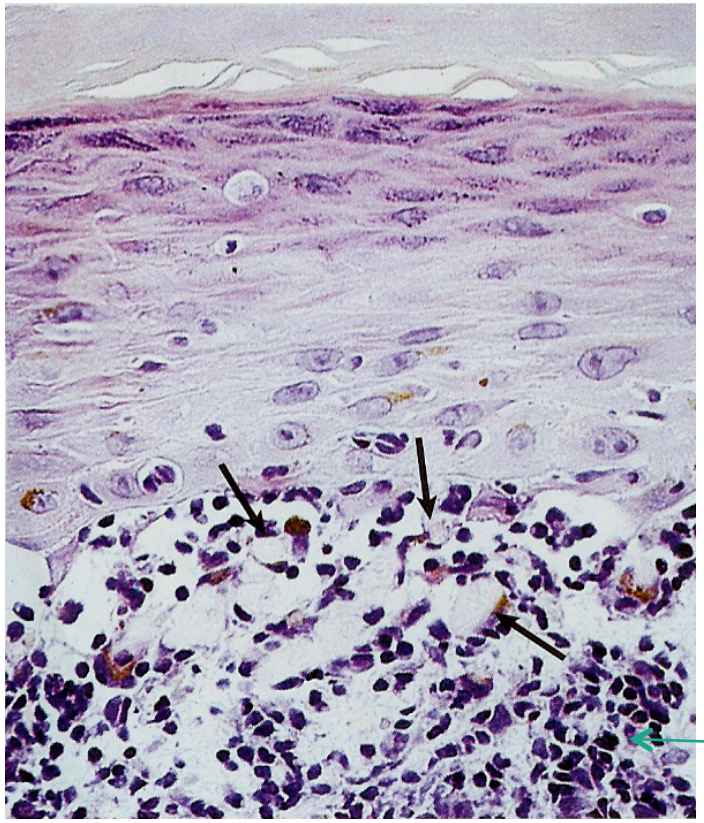
Lymphocytes
Little black dots
w/ scant cytoplasm
Uniform – same size/shape

Vs. neutrophils that are multinucleated & have diff sizes & shapes

"Saw-tooth"

Lichen Planus

Epidermis



Dermis

Arrows = **Colloid or Civatte bodies** (APOPTOSIS) from the basal layer found at the **junction**

Lymphocytes

Blistering (Bullous) Diseases-HY (3)

- Pemphigus
- Bullous Pemphigoid

Differentiate between these 2 on boards

- Dermatitis Herpetiformis

KEY: LOCATION!

Pemphigus

- **Autoimmune** blistering disease; mean age **50**; high prevalence in Jewish people
- *Pemphigus vulgaris: the most common type (80%)*
- Sites: most commonly seen on the scalp, oral mucosa, groin and trunk
- **Lesions**: superficial epidermal vesicles or bullae (**suprabasal** location) that **easily rupture,** leaving bleeding and crusted lesions

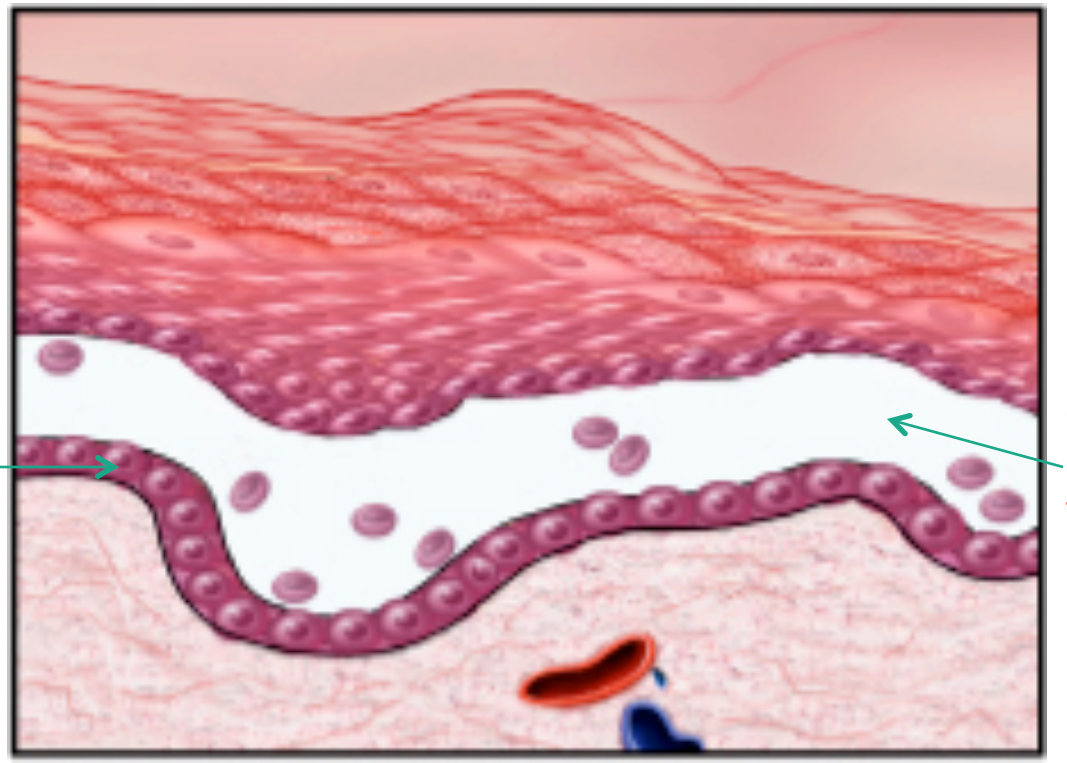
Pemphigus

- **Type II HSR reaction**
  - *Cytotoxic-type hypersensitivity w/ antigen on cell surface*
- **IgG** antibodies to intercellular cement of the keratinocytes
  - *Binds in-between individual squamous cells of epidermis*
- Loss of normal intercellular attachment → **acantholysis** (loss of intercellular connections of keratinocytes) → **suprabasal** blister
  - *Death of basal cell layer must occur for bullous lesion to come to light*
- **Immunofluorescence Test**: **fishnet-like** *(lace-like)* **pattern**

Pemphigus Vulgaris

Already ruptured!

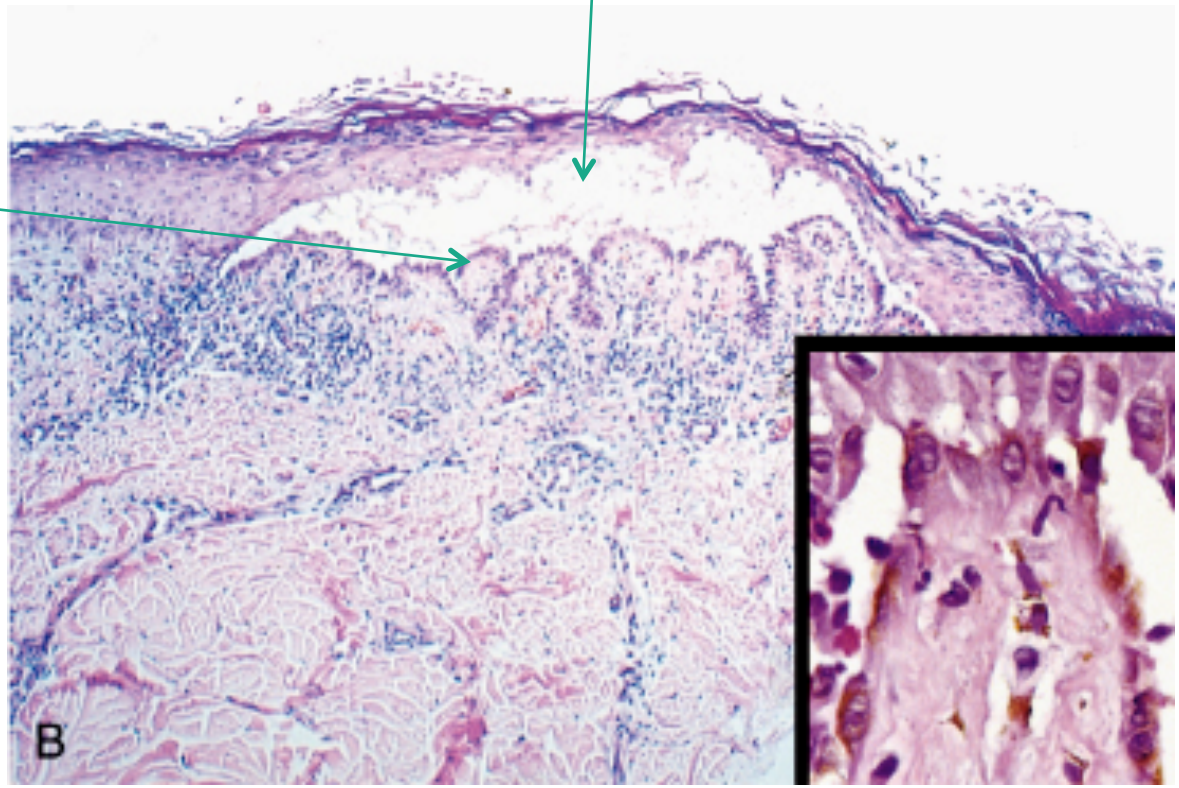
Pemphigus Vulgaris



Pemphigus Vulgaris

Bullous lesion

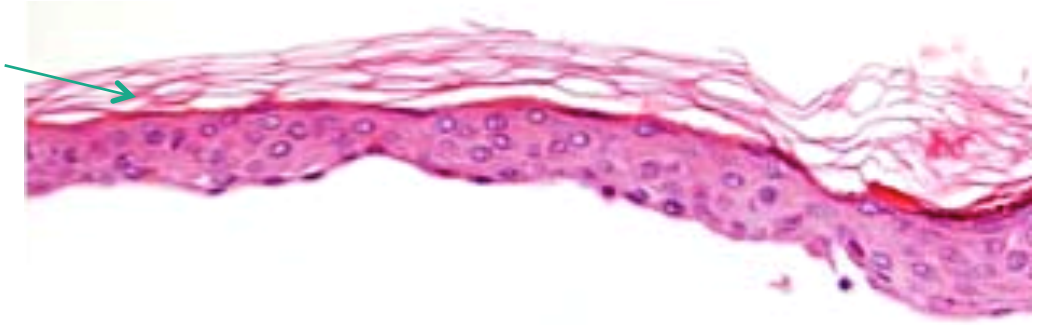
Basal cell layer
attached to dermis



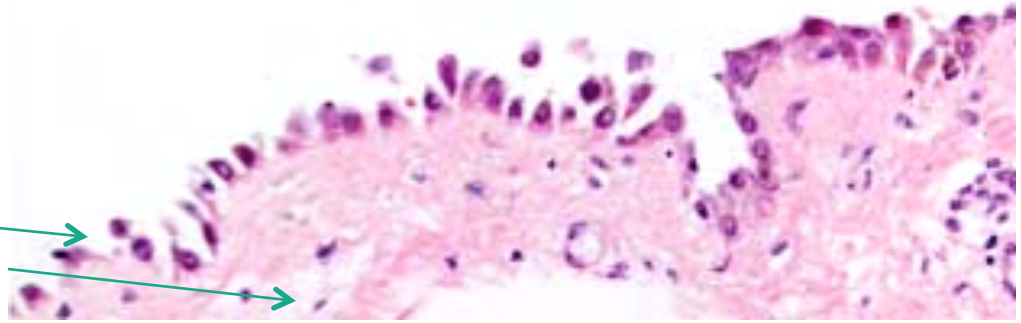
Acontholysis occurs at basal layer

Pemphigus Vulgaris

Hyperkeratosis

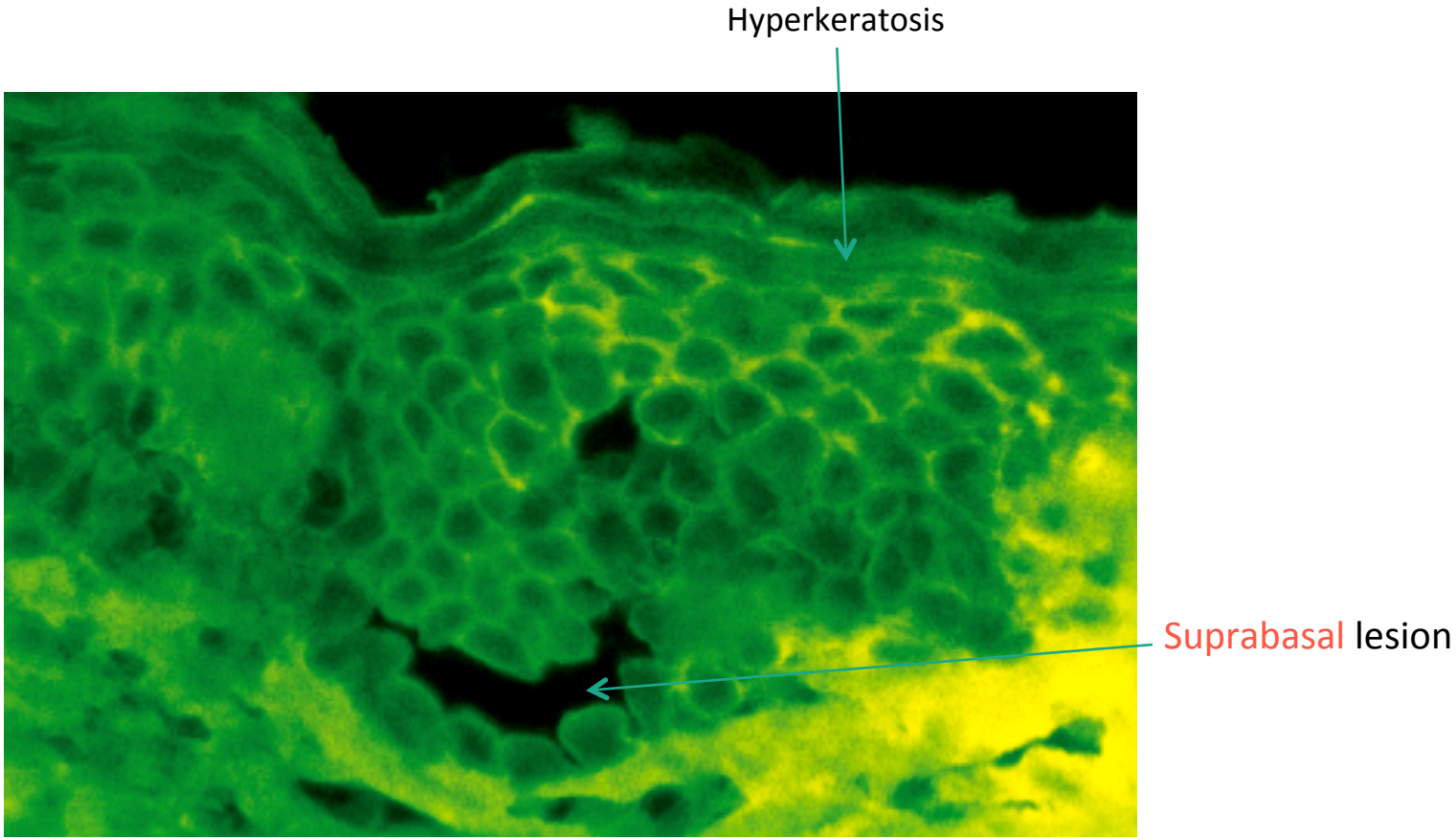


Bullous lesion
Fluid



Basal cell layer
Attached to dermis

Pemphigus Vulgaris



Fish-net or Lace-like Pattern – *outlining individual squamous cell bc Ab goes between them*

Bullous Pemphig**oid**

-oid means "like"

- Type II hypersensitivity (**IgG**)
- Chronic blistering disease due to formation of autoantibodies to skin (epidermal) basement membrane
- Vesicles or bullae: **subepidermal** (below epidermis) without acantholysis
- Clinically resembles that of pemphigus vulgaris
  - *Due to location of lesion, these do not rupture easily like Pemphigus Vulgaris*

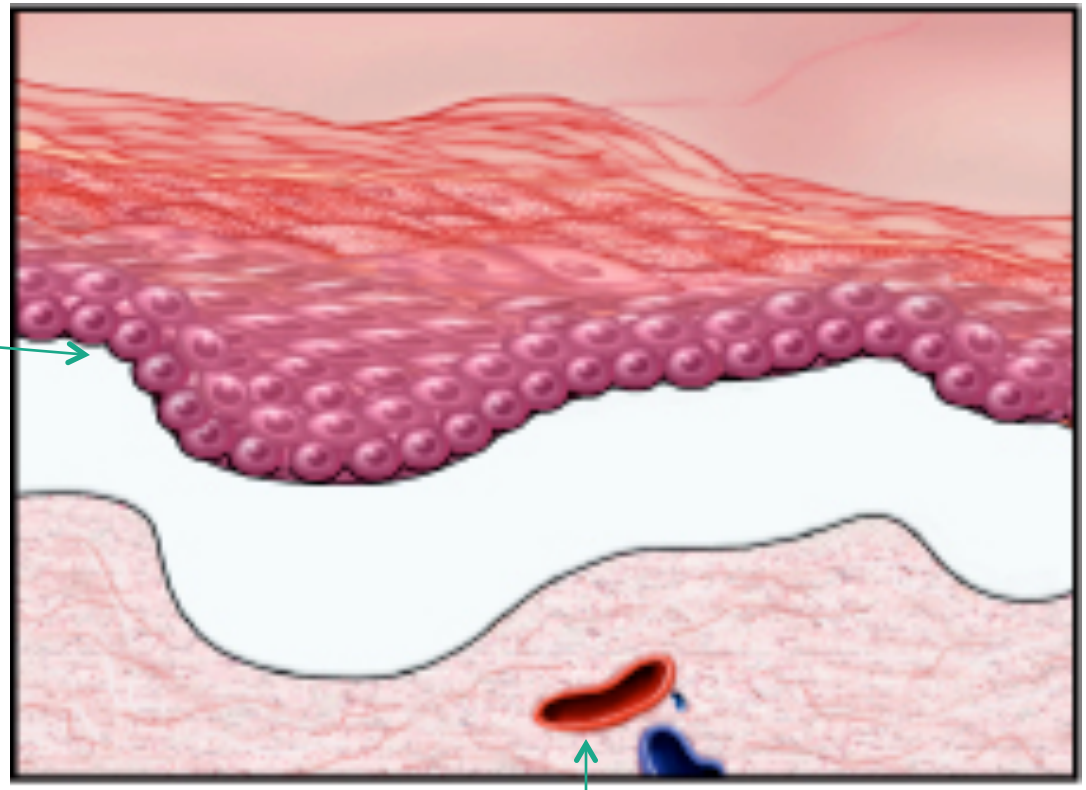
Bullous Pemphigoid

- Sites: inner aspect of thighs, flexor surfaces of forearm
- Oral involvement: present in up to 1/3 of cases
- IF test: **linear** deposits of IgG and C3 in the **basement membrane** zone of the epidermis

Bullous Pemphigoid

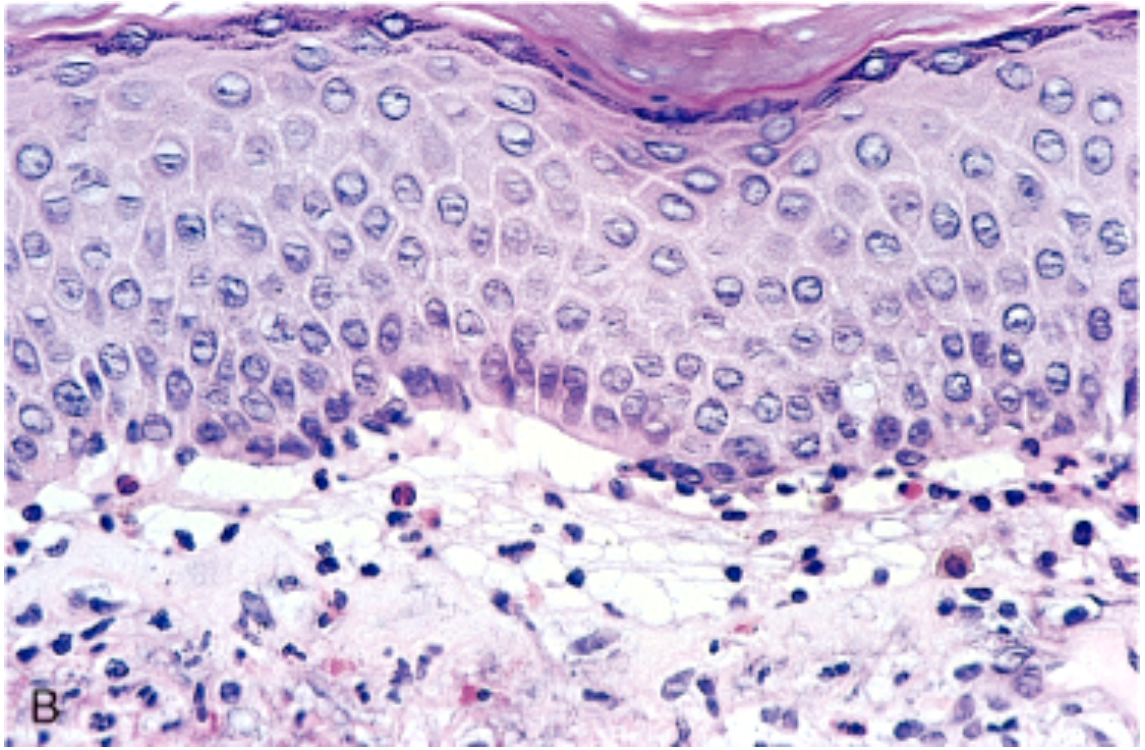
Lesions still **INTACT**
Compared to PV image

Bullous Pemphigoid



Bullous Pemphigoid

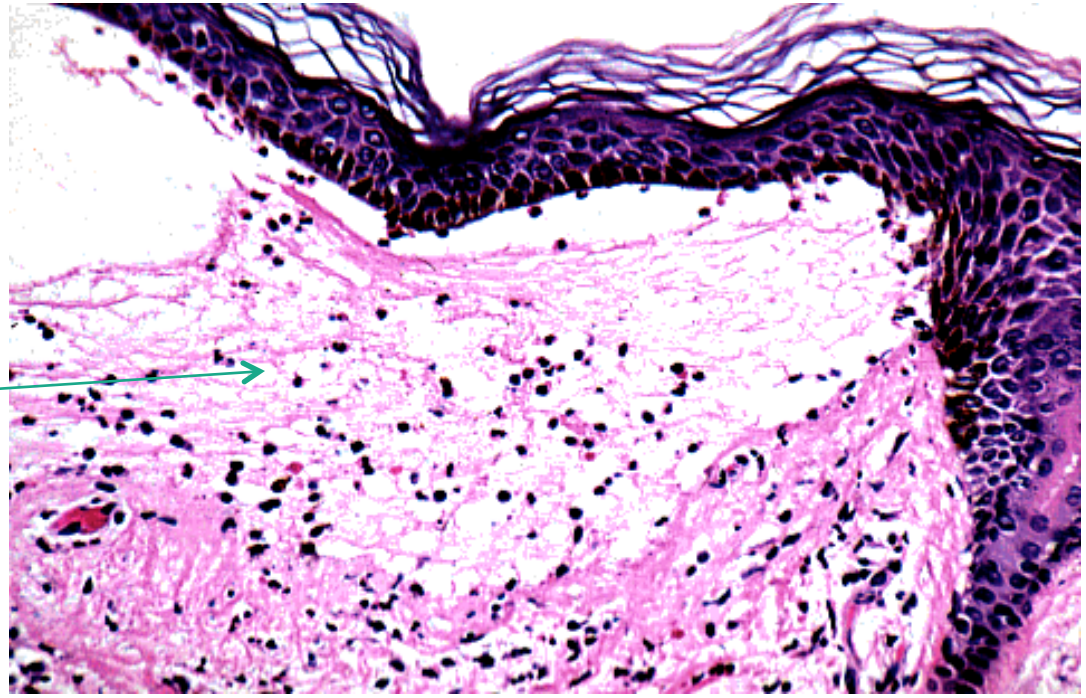
Hyperkeratosis



No acantholysis

Bullous Pemphigoid

Hyperkeratosis

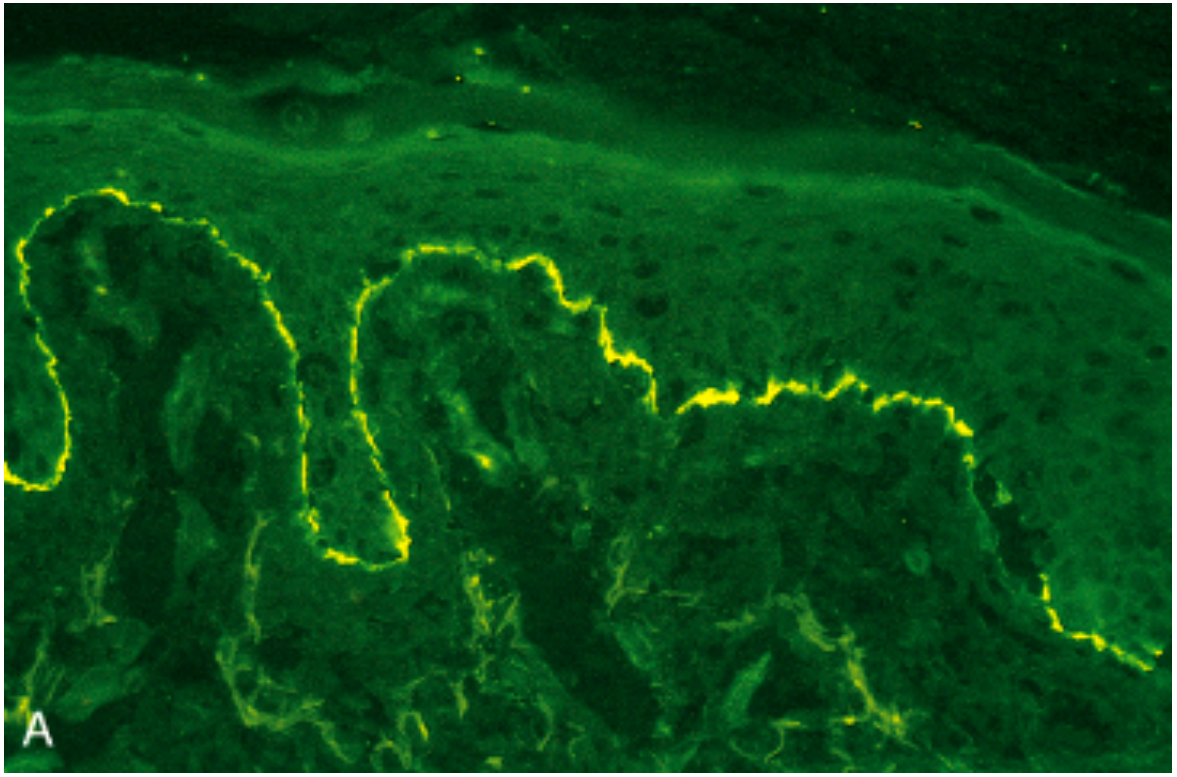


LESION

Dermis w/ no acantholysis

Bullous Pemphigoid

Above the line
Epidermis



Below the line
Dermis

Linear pattern at the basement membrane or dermal-epidermal junction

This lesion is associated with CELIAC DISEASE – *Pt may come in c/o diarrhea & have these lesions*

Lesions look like the vesicles of Herpes
But it is not caused by Herpes

Dermatitis Herpetiformis

- Rare lesion characterized by extremely pruritic urticaria and vesicles
- Bilateral symmetrical groups of lesions commonly occurring over elbows, knees and buttocks
- Age group: **30-40 year olds**

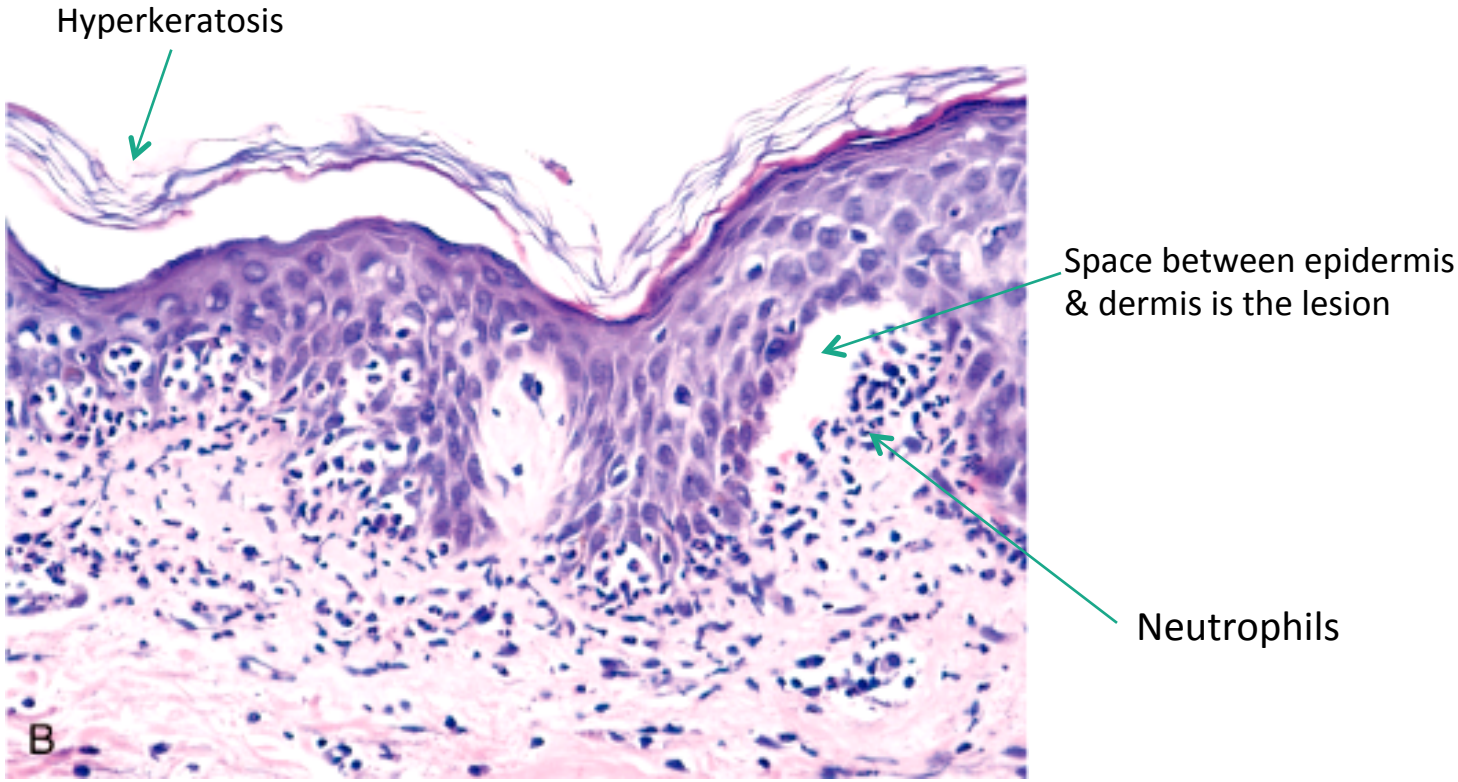
Dermatitis Herpetiformis

- Pathogenesis: associated with **gluten** (gliadin) sensitive enteropathy (**Celiac Disease**)
- **IgA*** antibody reaction with anchoring fibrils of the dermal papillae (at dermoepidermal junction) → vesicle formation and **microabscess formation** (*will see neutrophils)*
  - First, IgA goes to GI tract (small intestine) → atrophy of villi → *Diarrhea*
  - Then, IgA goes to the skin → *Dermatitis Herpetiformis*
- Responds to **gluten-free diet**
  - *Diarrhea goes away & the vesicular lesions should go away*
- *CONNECTION: Beurger's Disease – IgA Nephropathy*
  - *Can also cause these lesions*

Dermatitis Herpetiformis

Small lesions
Look like Herpes

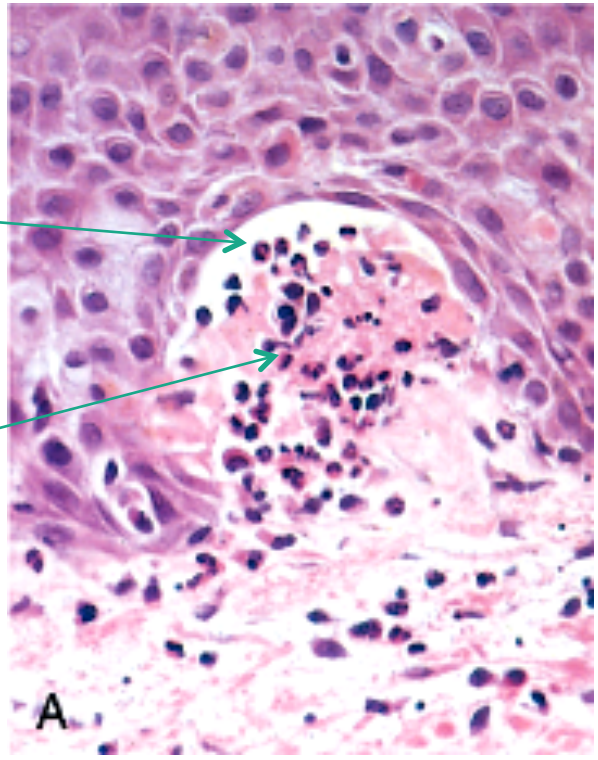
Dermatitis Herpetiformis



Dermatitis Herpetiformis

Small space
Dermal papilla

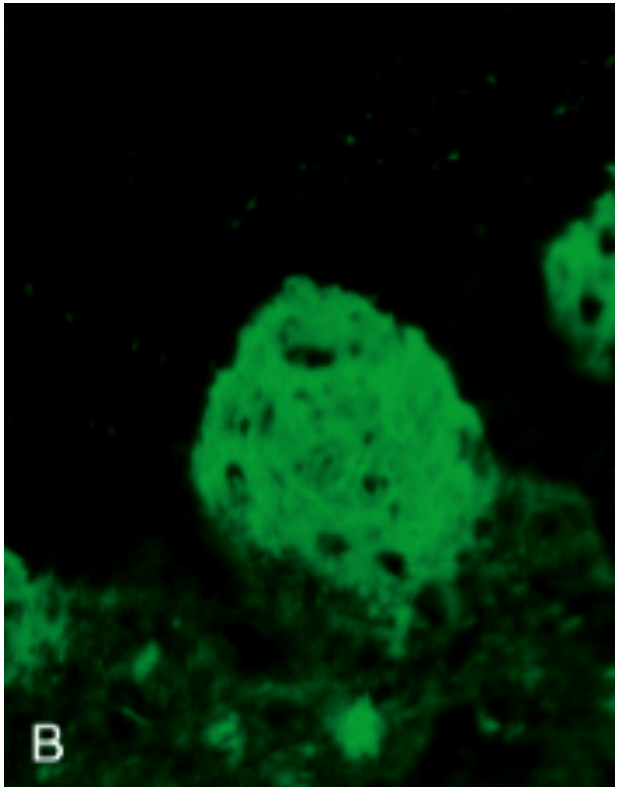
Neutrophils
Microabscess within dermal papillae



Subepidermal location
But smaller in size
& presence of neutrophils
(Compared to Bullous Pemphigoid)

Dermatitis Herpetiformis

Not that HY of boards because it's hard to describe



Seborrheic Keratosis

-osis = "a lot of"

- **Well-circumscribed**, elevated, often pigmented, **scaly**, COIN-like papules or plaques occurring on the *back of the hands, trunk and face* of **elderly persons**

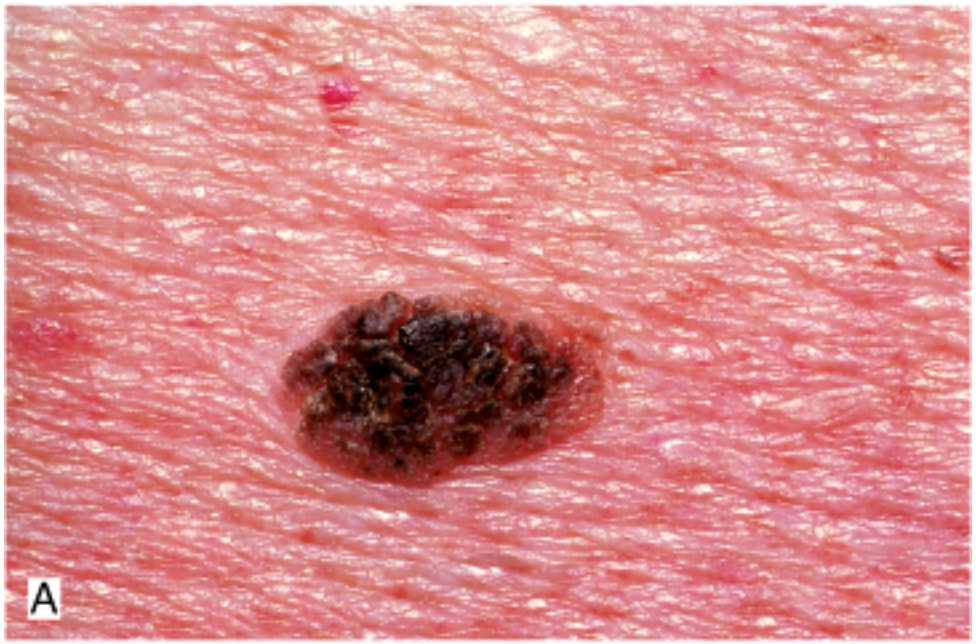
  ***SUN-EXPOSED AREAS**

- Most have 'stuck-on' or 'pasted-on' appearance and waxy texture
- Microscopically: large amounts of keratin, keratin **(horn) cysts**, and **benign** basaloid cell **hyperplasia** with *papillomatosis* (finger-like projections)
  - *Keratin from surface invaginatse down into epidermis & forms horn cysts*

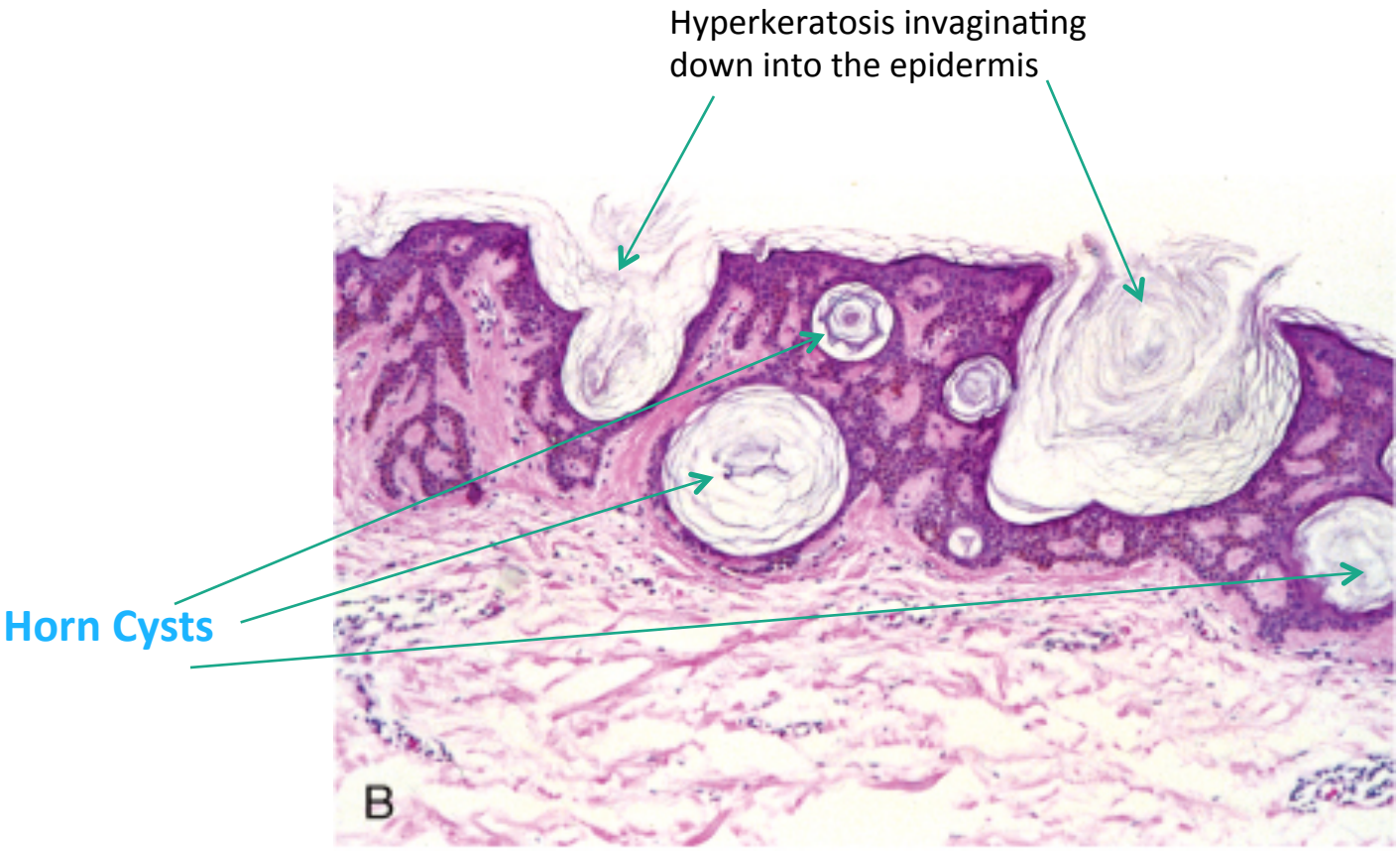
Papillary = Finger-like

Seborrheic Keratosis

Well-defined borders
Pigmented



Seborrheic Keratosis
"Classic Picture"



Cysts = *Fluid-filled* ***lined by epithelial cells***

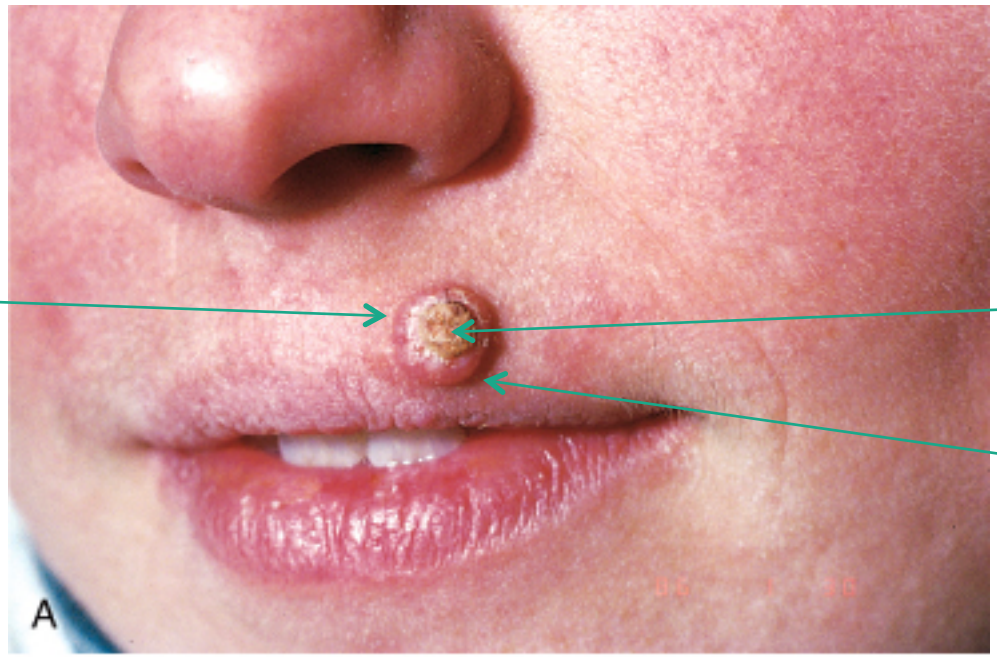
Keratoacanthoma

Lesion w/ keratin + Downward projection of epidermis into dermis

- Arises from hair follicles in **sun-exposed areas** in light-skinned individuals over 50 years of age
- Microscopic: *"Classic presentation"*
  - A dome-shaped crusty lesion with a **central keratin-filled** crater that *mimics a well-differentiated squamous cell carcinoma*
- **Spontaneous regression = Benign**: usually occurs in 3-4 months

Keratoacanthoma

Classic location –
border of the lip



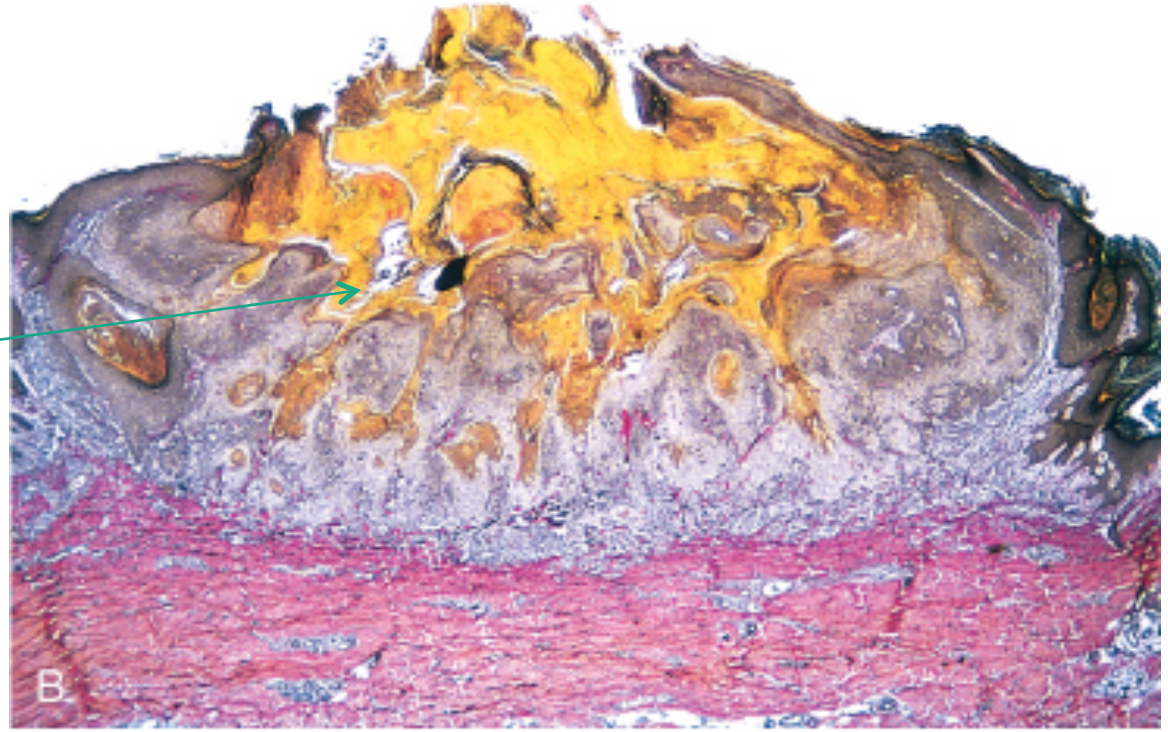
Keratin in middle

Outside area is
Acanthosis

Keratoacanthoma

Yellow = Keratin

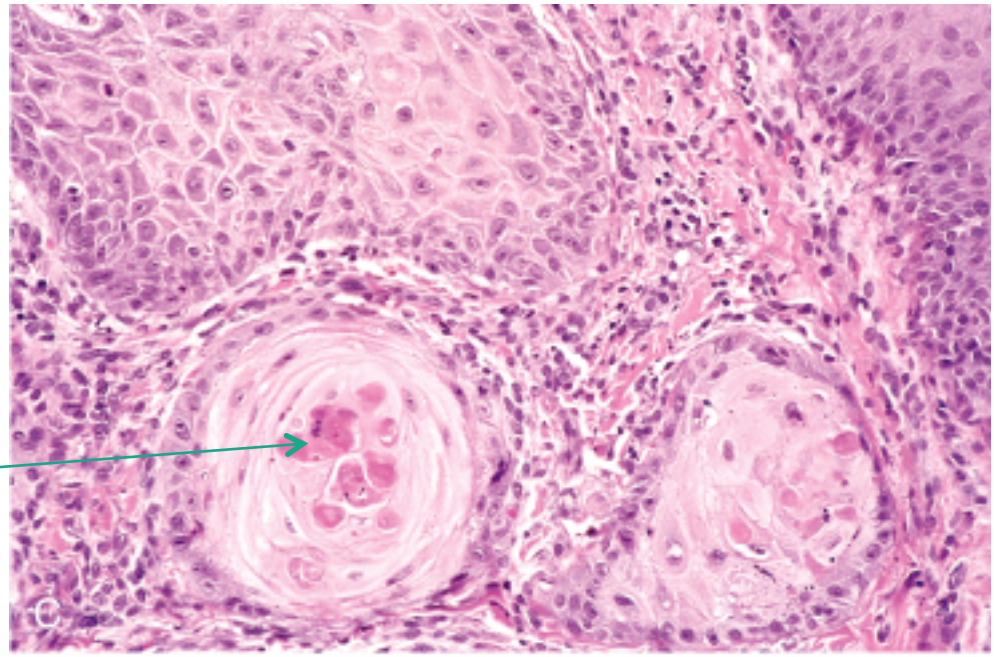
Downward projections into epidermis



Keratoacanthoma

Squamous cells making keratin

Looks like *Keratin Pearls of Squamous Cell Carcinoma*



Verruca = "warty"

Verruca Vulgaris

"Classic Wart"

- Most common sites: Fingers
- Also seen on soles of feet (plantar warts)
- Caused by Human PapillomaViruses (**HPV**)
  - *Typical wart related to condyloma (genital warts) – both caused by HPV*
- Microscopically:
  - **Papillary hyperplasia** with hyperkeratosis and acanthosis
  - Hyperplastic epidermis with many **vacuolated cells** (**koilocytes** – made by HPV)
  - ***Exophilic*** *lesion = growing out of the skin*

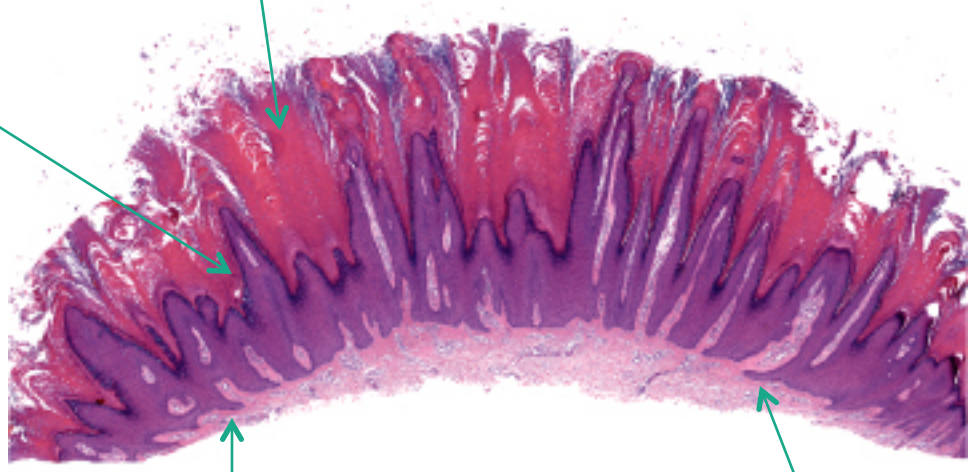
Verruca Vulgaris

Exophilic lesions

Verruca Vulgaris

Red – Hyperkeratosis

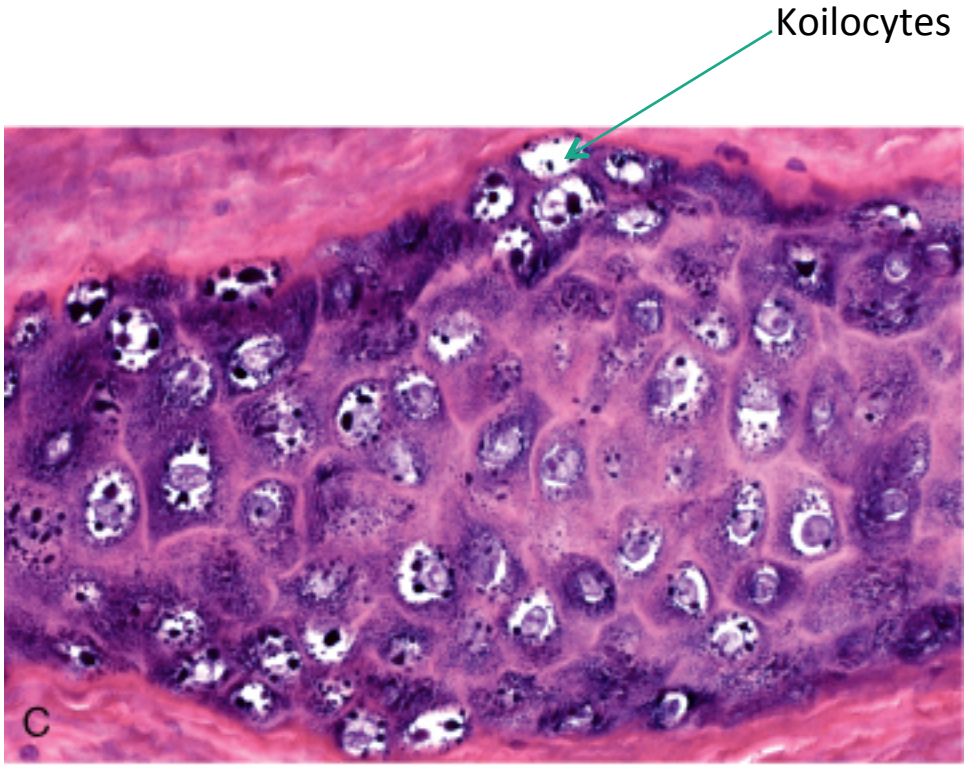
Papillomatosis
Finger-like projections



Acanthosis

Edge of the lesion (acanthosis) curve & point toward the center of the lesion
***Classic for Verruca**

Verruca Vulgaris



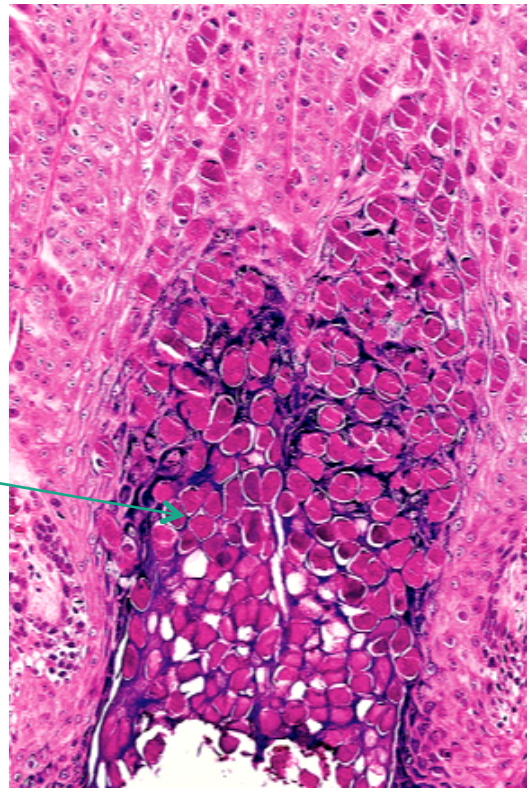
**Differentiate Verruca from Molluscum*

Molluscum Contagiosum

- Common, self-limited disease caused by **Poxvirus***
- Usually found on trunk & *anogenital* areas
- Morphology: cup-like verrucous epidermal hyperplasia with 'mulloscum bodies' of stratum granulosum & corneum
- **Mulloscum Bodies***: clusters of small, round eosinophilic cytoplasmic inclusions
  - HIGH YIELD – *know the descriptions!*

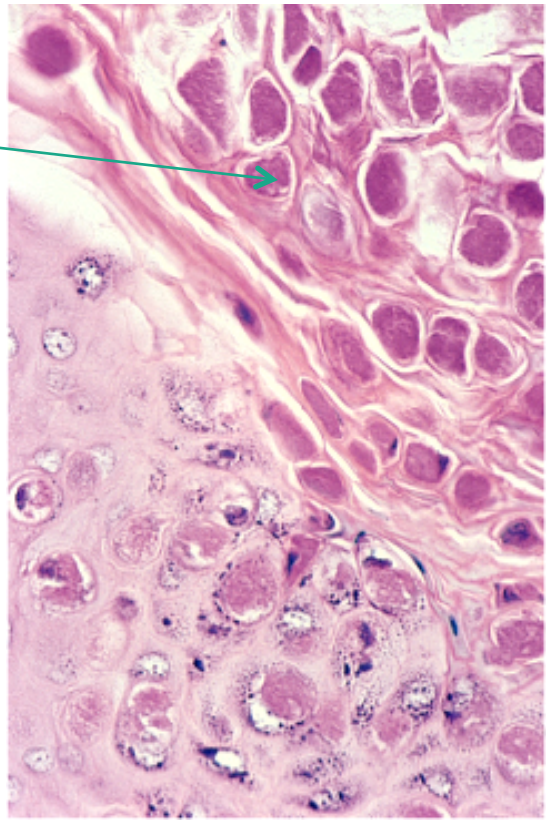
Molluscum Contagiosum

Molluscum Bodies
Round, eosinophilic inclusions
*Key to differentiate from Verruca



Molluscum Contagiosum

Molluscum Bodies
Round, eosinophilic inclusions
*Key to differentiate from Verruca



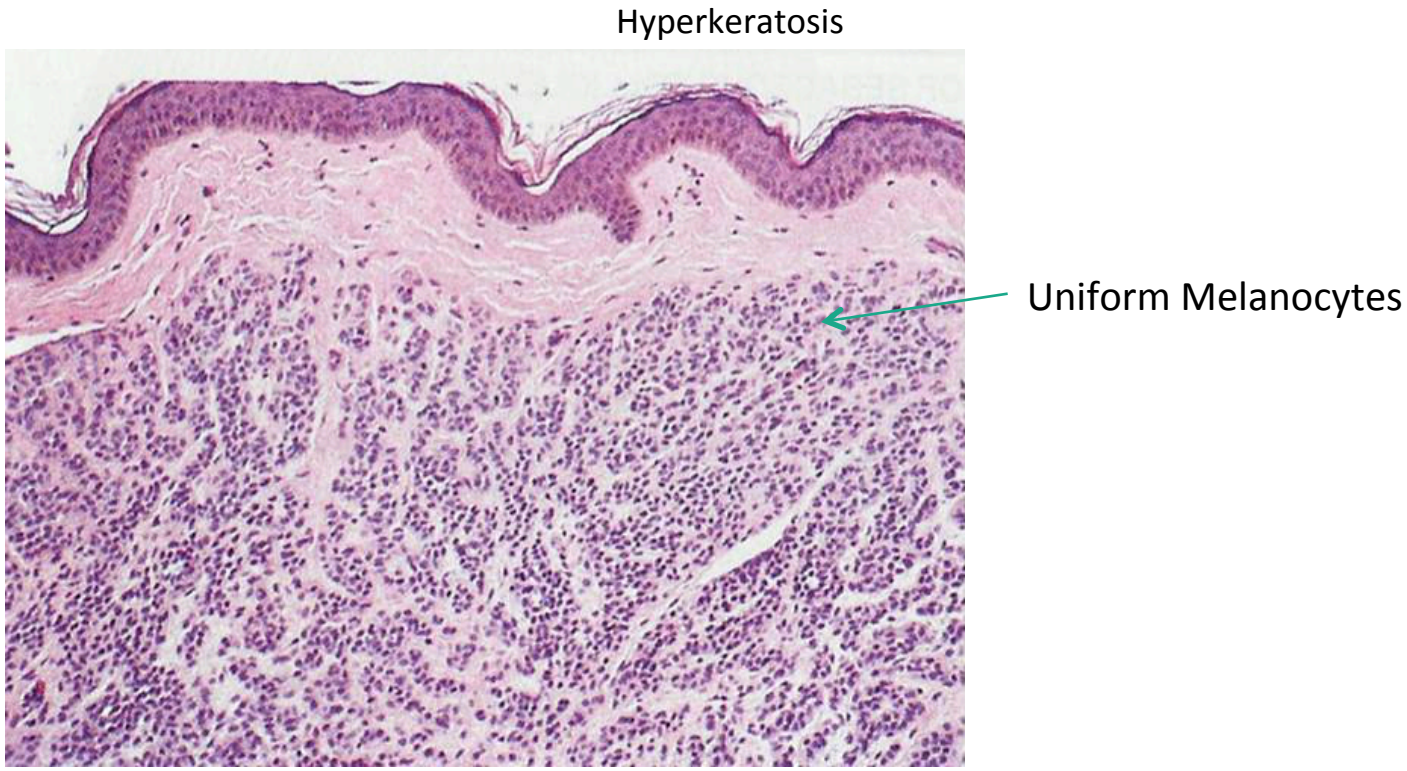
Nevocellular Nevus

- **Benign** neoplasms of melanocytes (nevus cells)
- Tan-to-brown pigmented, small (about 0.5 cm), well-demarcated lesions

Nevocellular Nevus

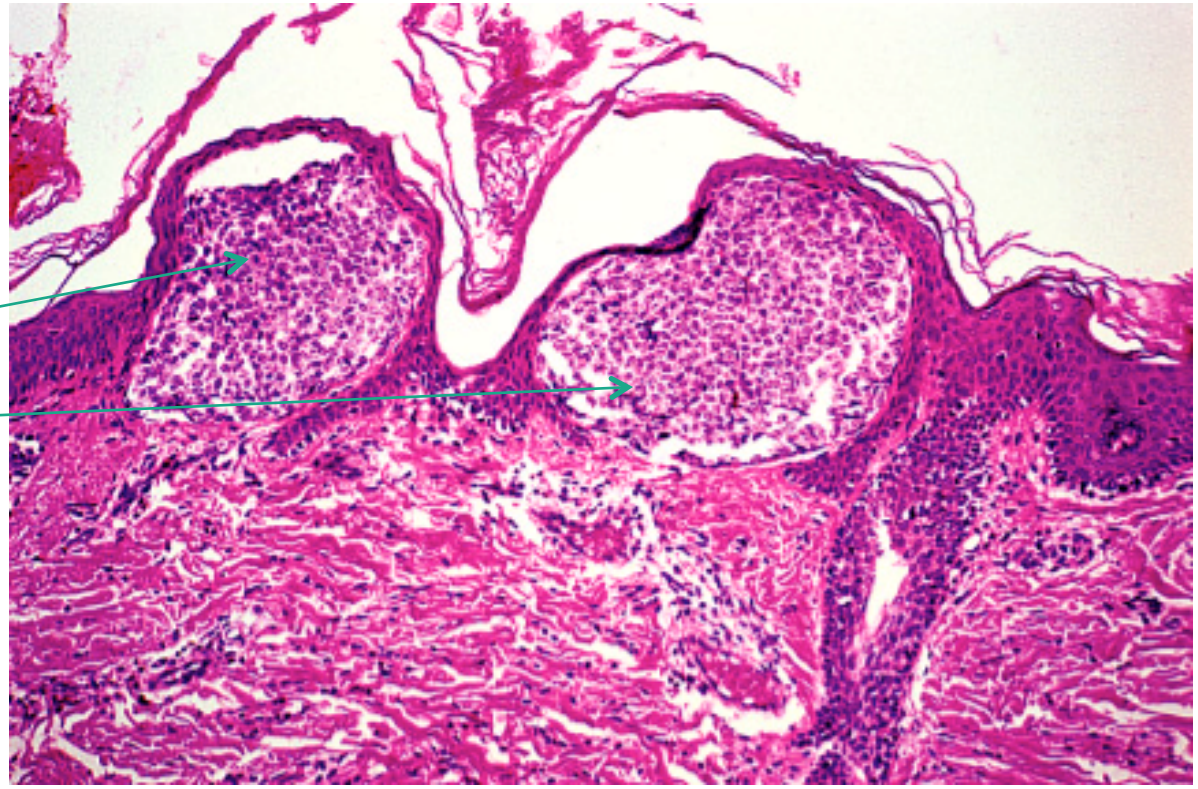
- Types of Nevi***: *Differentiated by LOCATION***
  - **Intradermal Nevi** (elevated, fleshy, slightly to moderately pigmented papules): composed of small *uniform* cell aggregates inside the **dermis**
  - **Junctional Nevi** (flat or slightly raised, brown, tan papules): nests of cells with variable pigmentation present at **dermoepidermal junction**
  - **Compound Nevi**: have both **intradermal and junctional** components; typically all raised
- *All have well-defined borders*

Intradermal Nevus



Junctional Nevus

Hyperkeratosis



2 Nests of Melanocytes at the junction

At the top – raised lesion

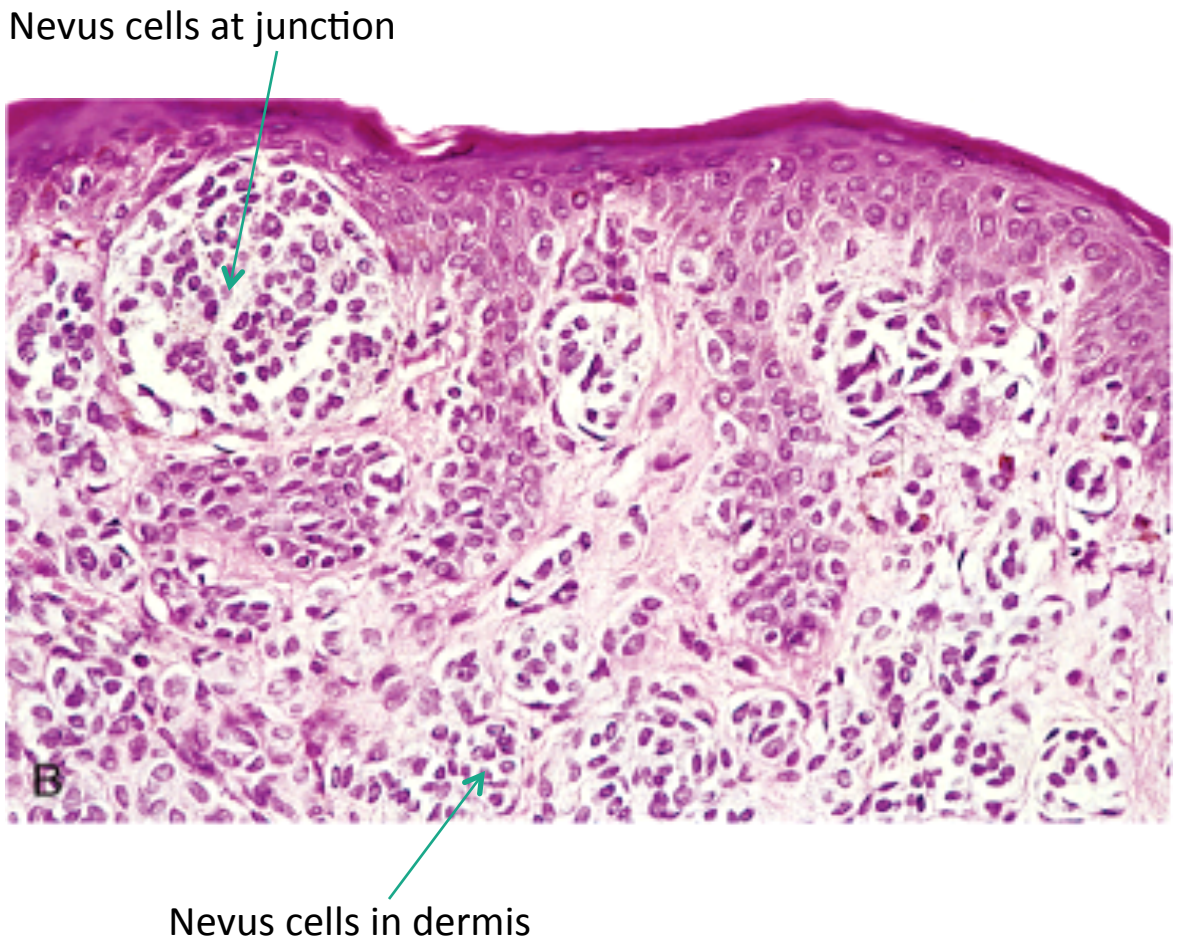
Compound Nevus

"This is important"

Well-defined borders

Homogenous in color

Compound Nevus



Premalignant Skin Lesions (2)

- Actinic Keratosis
  - Premalignant for **Squamous Cell Carcinoma**
- Dysplastic Nevus
  - Premalignant for **Melanoma**

Actinic Keratosis

- Mostly due to ultraviolet radiation damage **to sun-exposed skin**: face, hands and arms
  - *UV light changes or mutates the cells at the basal layer*
- Gross: tan-brown or red colored lesions with a rough yellowish brown adherent scale
  - "**Cutaneous Horn**" due to amount of keratin being produced
- Microscopic:
  - Hyperkeratosis with **atypia** or dysplasia *(loss of orientation or normal architecture of the tissue)* in the **basal layer** of the **epidermis**
    - Eventually it will continue up & become full-thickness dysplasia → cancer
  - Bluish homogenization and inflammatory cellular reaction in the dermis

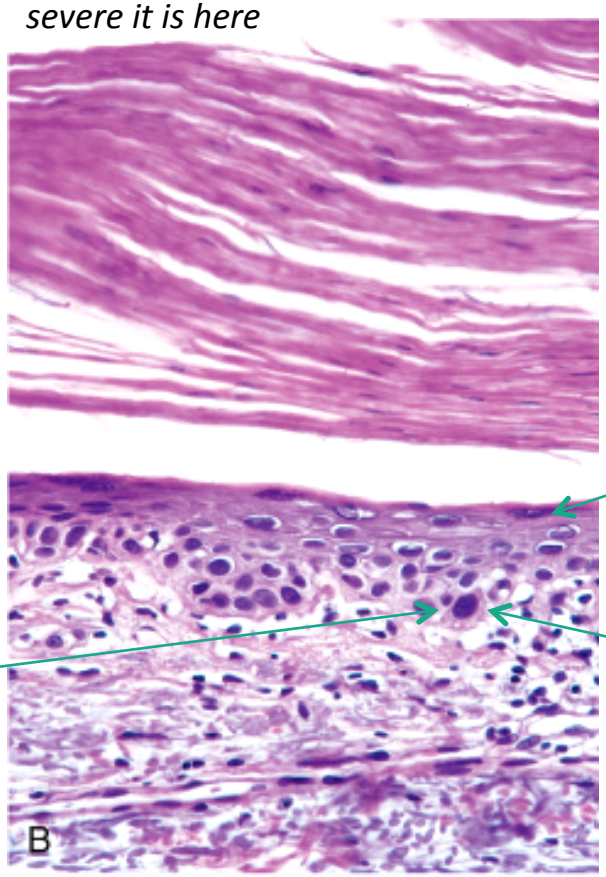
Actinic Keratosis

All of this is keratin
"Cutaneous Horn"

Dysplasia is at the base

Actinic Keratosis

Hyperkeratosis – *Notice how thick & severe it is here*



*Epidermis – Pleomorphic (different sizes & shapes) & Hyperchromatic (about to divide)

Normal cells

Look at this nucleus: It's large & dark

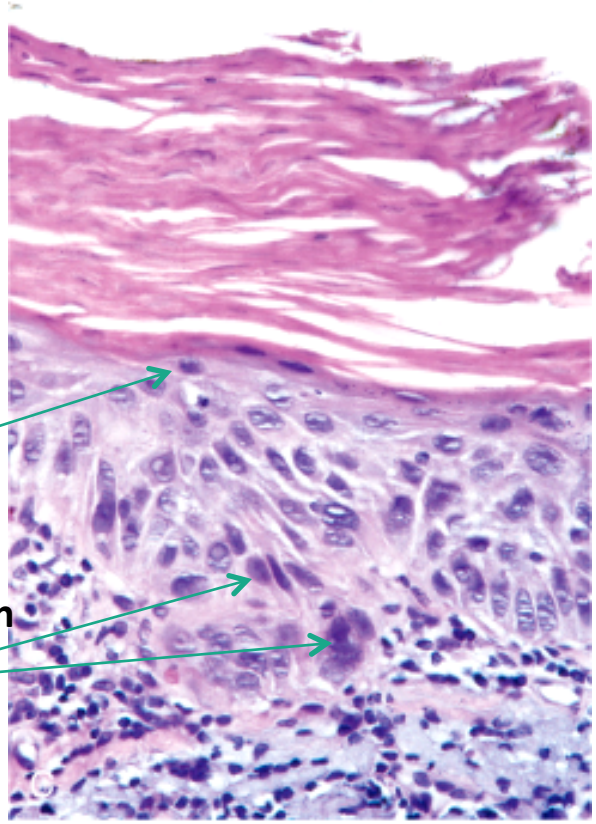
Dysplastic cells – starts at the base & goes toward the surface
**when dysplasia reaches the surface, it is then cancer*

Actinic Keratosis

*Precursor for Squamous Cell Carcinoma

Squamous cells in layers
Horizontal orientation

Dysplastic cells – **vertical orientation**
Pleomorphic + Hyperchromatic



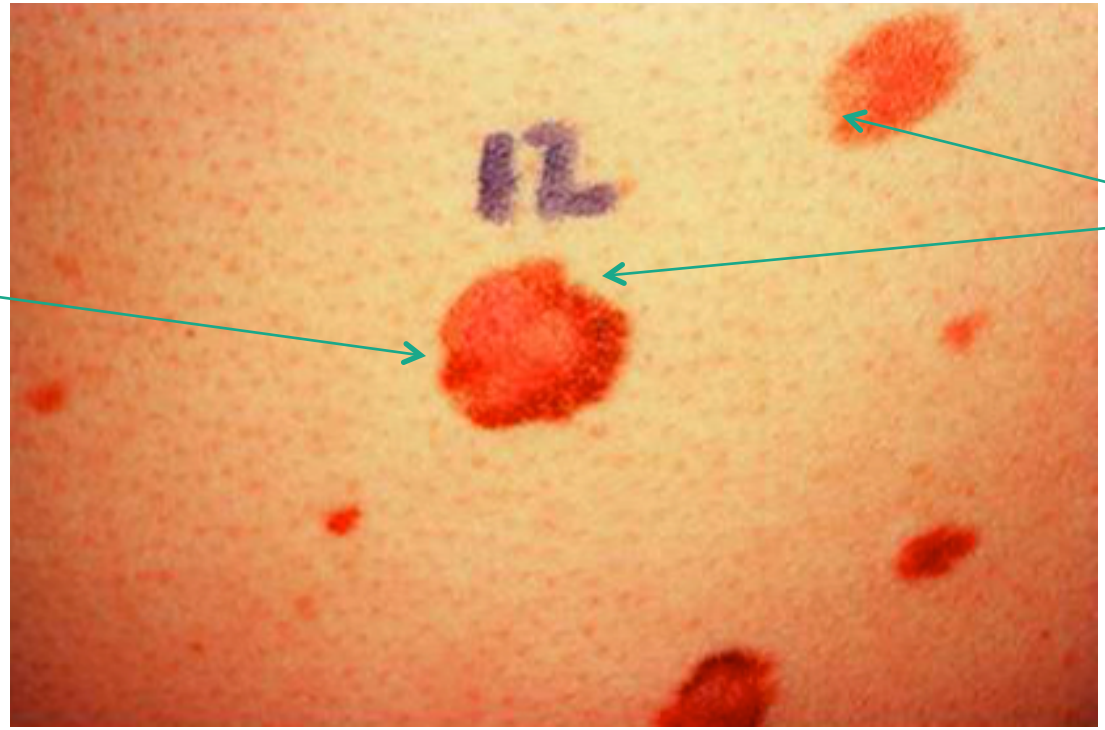
Dysplastic Nevus

- Many lesions *larger than 0.5 cm* (5-15mm) with a *variegated color* and irregular and indistinct margin
  - Malignant vs Benign: large vs small, variegated color vs homogenous, irregular vs well-circumscribed border
- **Microscopically**: single or small clusters of atypical melanocytes with nuclear hyperchromasia found in the **basal zone of the epidermis** (lentiginous hyperplasia)

**Typically found in same areas of Junctional or Compound Nevus*
Uniform cells vs Atypical cells

Dysplastic = Pleomorphic + Hyperchromatic = Atypical Cells

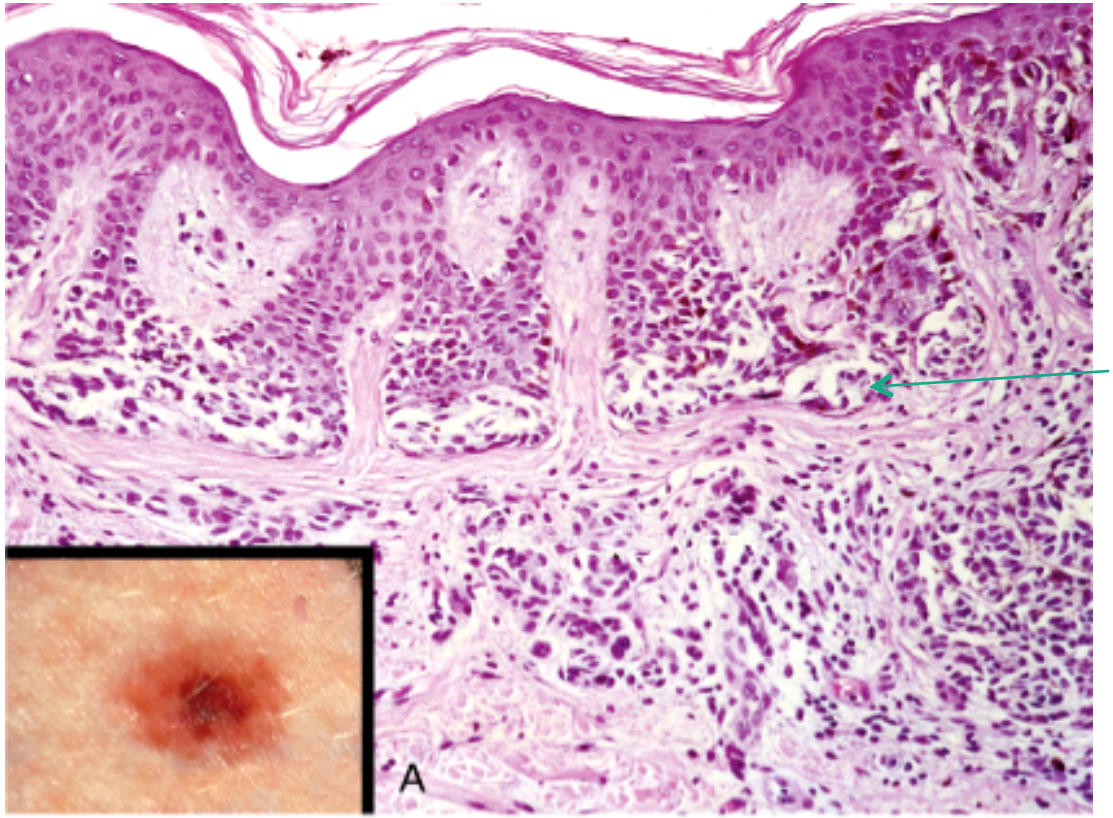
Dysplastic Nevus



Dysplastic Nevus

*Precursor for Melanoma

Hyperkeratosis



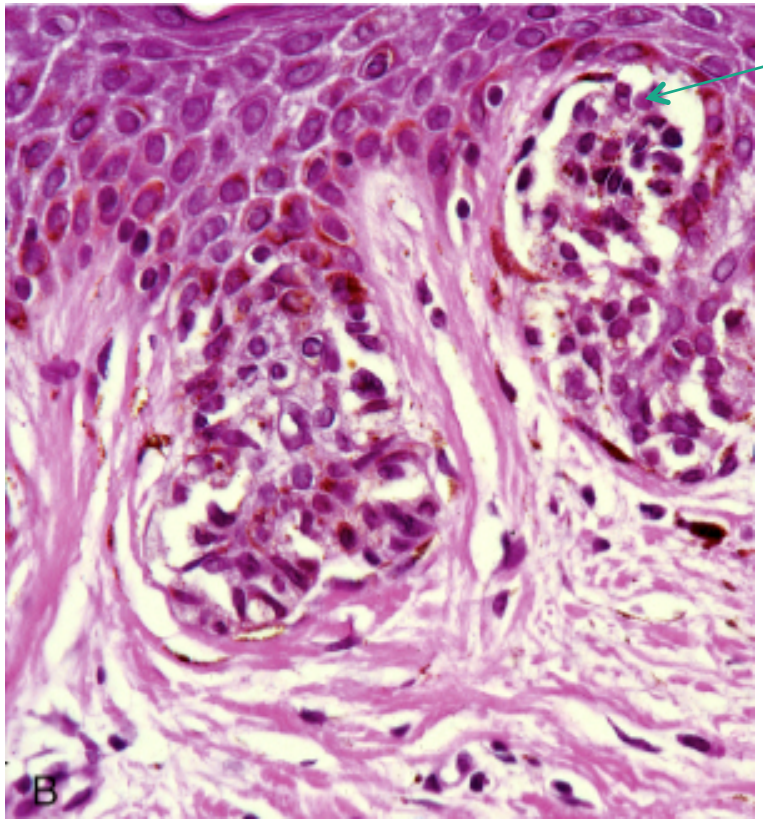
Cells at Basal Layer
Or the **Junction**

***Key:** Hyperchromatic + Pleomorphic by the Junction

Variegation of Color
Indistinct Borders

Dysplastic Nevus

High Magnification



Cells at Basal Layer or the **Junction**

***Key:** Hyperchromatic + Pleomorphic by the Junction = Dysplastic Nevus

Sometimes described as "Junctional activity"

Malignant Epidermal Tumors (3)

- Squamous Cell Carcinoma (SCC)
- Basal Cell Carcinoma – *rarely, if ever, metastasizes*
- Malignant Melanoma

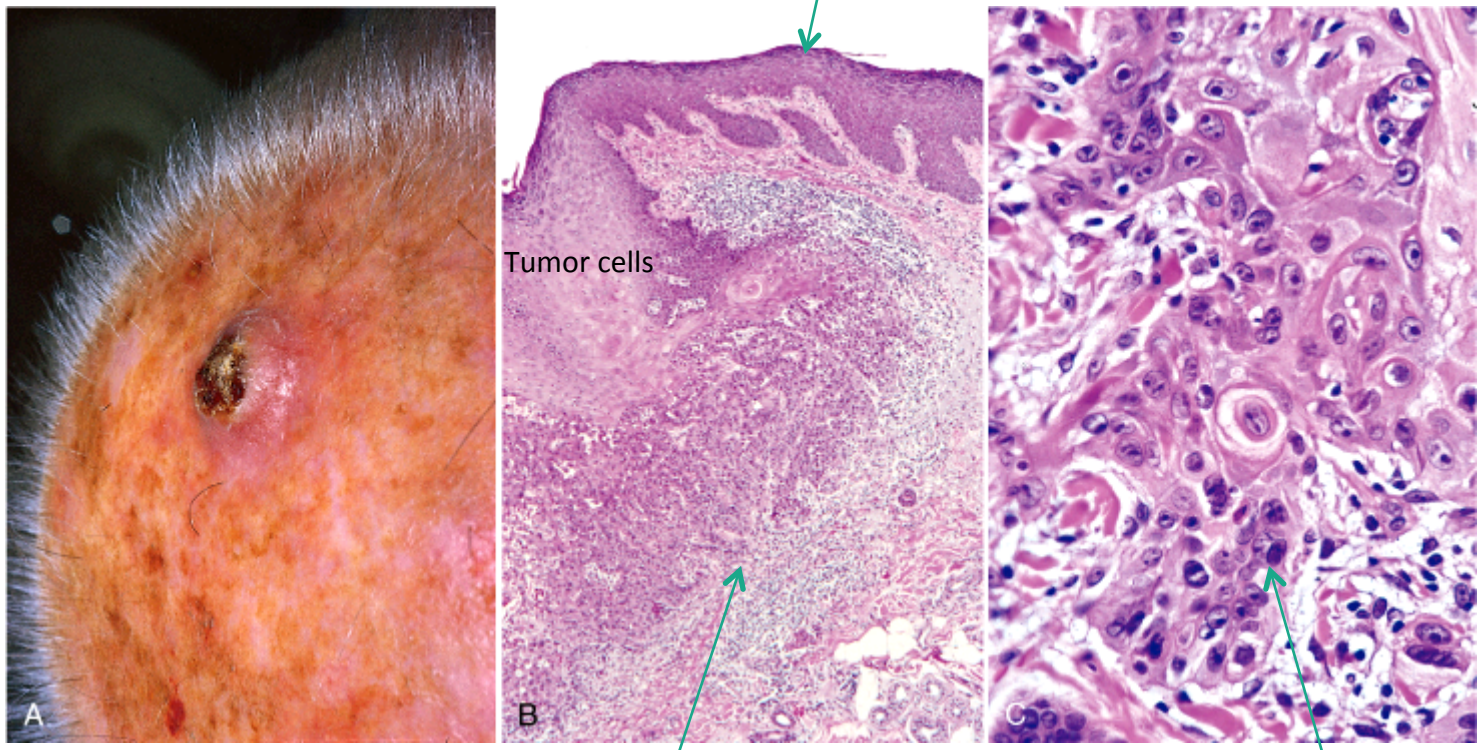
SCC

- *High Risk Factors:*
  - **Actinic** (UV-unrepaired DNA) damage--*most important factor*
  - Ingestion of arsenicals
  - Chronic ulcers and **draining osteomyelitis***
    - HY for boards
    - *Draining sinuses in patient with chronic osteomyelitis (pt w/ sickle cell anemia)*
  - **Xeroderma Pigmentosum**

SCC

- When associated with actinic keratosis, only locally invasive; metastasis not seen
- Microscopic Features:
  - **Keratinous pearls**
    - Key thing you look for in any *well-differentiated* SCC
    - *Poorly-differentiated SCC won't have this*
  - Cell nests and single cells with **hyperchromatic nuclei** and **mitotic figures** *(cells rapidly dividing)* invading the dermis
- Treatment: excision of tumor

SCC


Normal epithelium
Tumor cells
A
B
C
Invasion – Notice the difference in the borders here compared to in the normal epithelium
Hyperchromatic nuclei

Basal Cell Carcinoma

- Skin neoplasm of light-skinned people, occurring on the **sun-exposed areas**, particularly the **face**
- Arises from the basal cells of the epidermis
- Develops locally, though it can invade very deep; never metastasizes
- Tx: excision of tumor

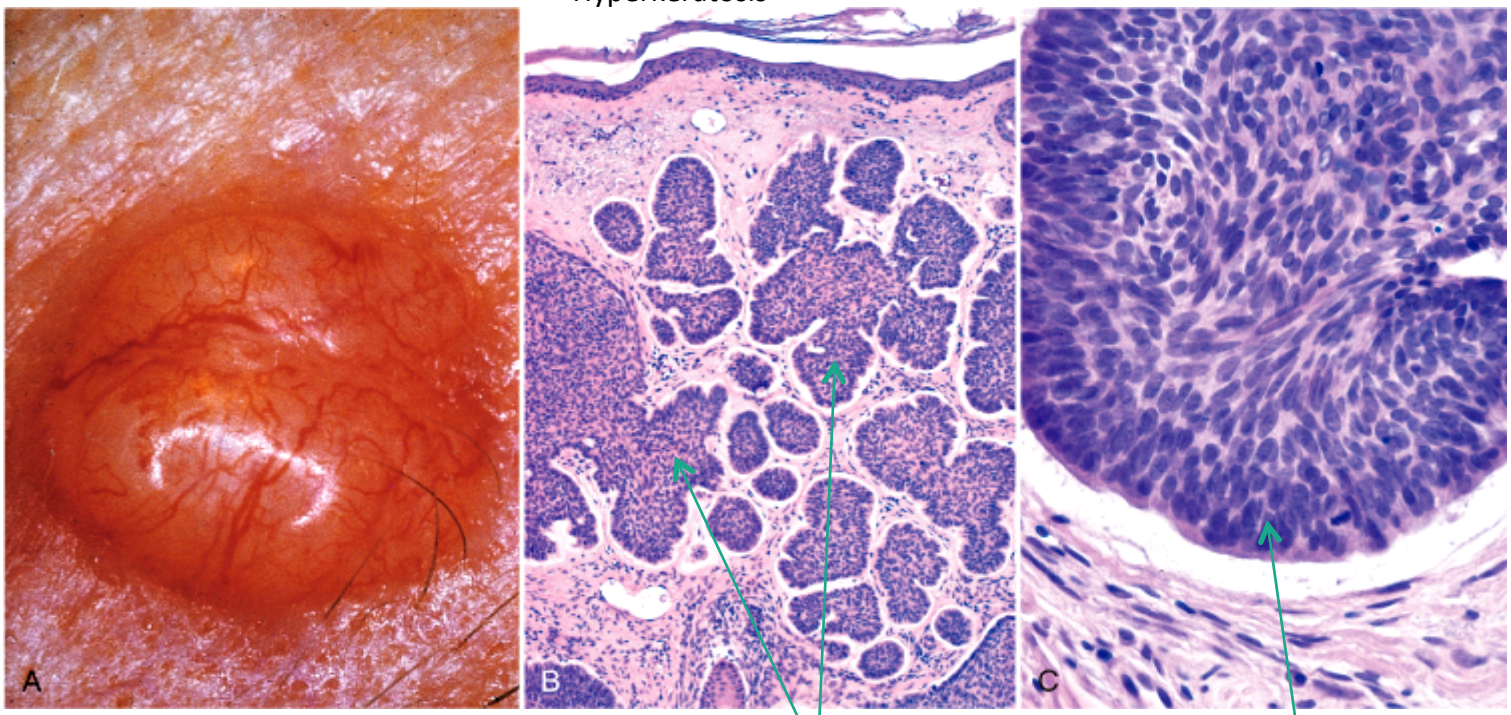
Basal Cell Carcinoma

- **Clinically**: initially pearly white papules or nodules with surface telangiectasia (dilated blood vessels on the surface) *-ectasia = "to dilate"*
- Lesions with ulceration: rodent ulcer

Basal Cell Carcinoma

- Microscopic Features:
  - Usually multifocal – *multiple nests of cells rather than just 1 lesion*
  - Abnormal hyperchromatic basaloid cells in nests, strands, and columns in the **dermis only**
    - *They can eventually grow up to the surface, but not initially*
  - Palisading (round, organized) arrangement of the cells at the **periphery** of the cell nests
    - Line up like a "picket-fence"

Basal Cell Carcinoma



Shiny, pearl-like
Telangiectasia

Nests of cells in the dermis

*Lining up at the periphery of the nests

Malignant Melanoma

- One of the most ***aggressive*** **malignant** neoplasms in the body
- High Risk Factors:
  - Pre-existing dysplastic nevi – *Melanoma growing out of a pre-existing mole is a classic presentation*
  - Excessive (ultraviolet) sunlight exposure
  - Hereditary factors
  - *Increasing in African American & Hispanic populations

Malignant Melanoma

- Most important clinical sign of the disease: change in color in a pigmented lesion
- Gross: variable color changes, depigmentation, uneven and raised surfaces and irregular border

Malignant Melanoma

- Microscopic Features:
  - Very **large** cells
  - Variably pigmented melanoma cells
  - Marked nuclear pleomorphism, high mitotic activity and cellular anaplasia – “Atypical cells”
  - Disproportionately very large nucleoli typically seen in malignant cells

Malignant Melanoma

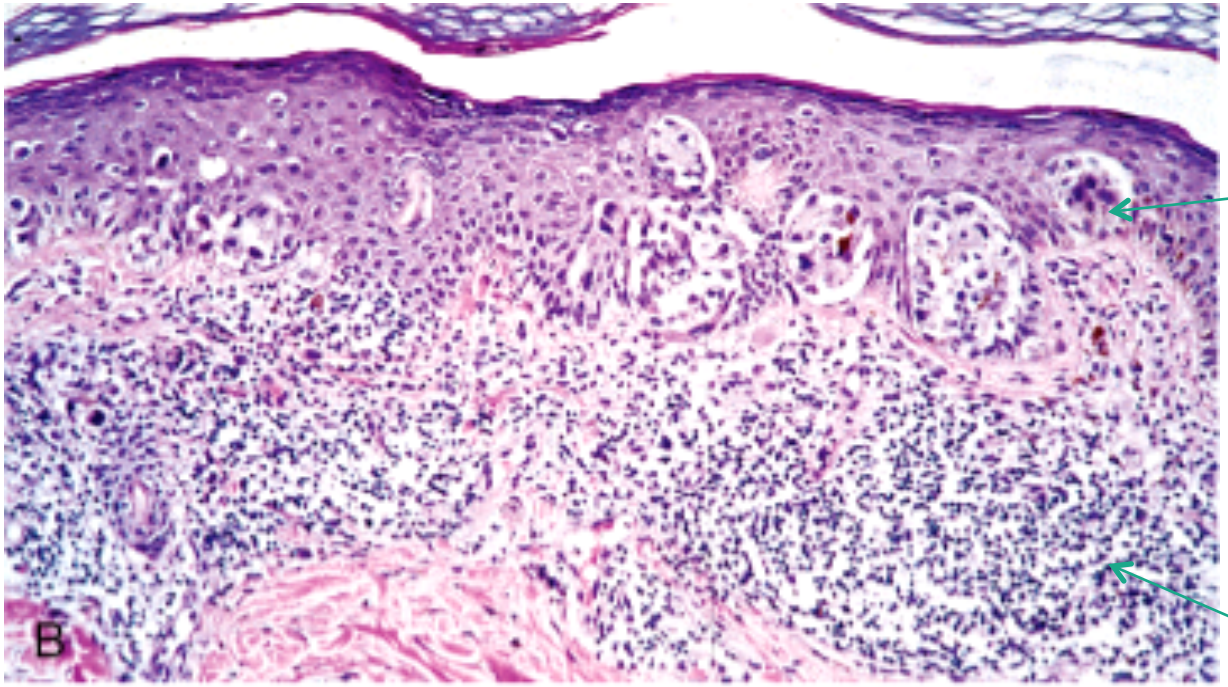
- ***Prognosis**: dependent on the *depth of the invasion* (i.e. the vertical growth phase)
  - HY: Staging > Grading for prognosis
- The horizontal or lateral spread (usually flat lesions) lacks metastatic potential
  - *Spreading out wide does not make for a worse prognosis because it typically will not find a blood vessel large enough to spread to another organ*
- Deeply invasive tumors (usually with **nodular** surface and the depth of penetration more than 1.5 mm): widely metastasizing & carry a poor prognosis

Malignant Melanoma

Can look like Kaposi Sarcoma – but typically are more uniform in color (dark w/ hemorrhagic appearance)

Malignant Melanoma

Hyperkeratosis



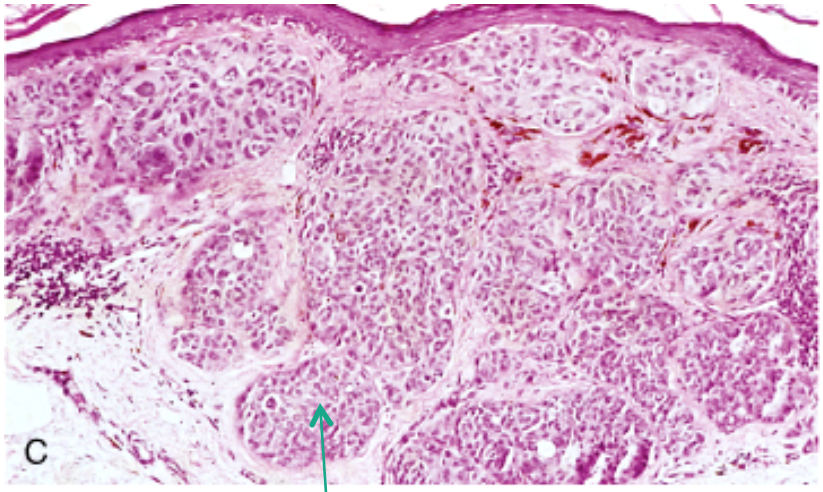
Mainly at the **junction**
May have arisen from dysplastic nevus

Lymphocytes
You can get immune reaction against tumors

**Prognosis here would not be as bad – only radial growth*

Malignant Melanoma

**Poor prognosis due to depth of invasion*

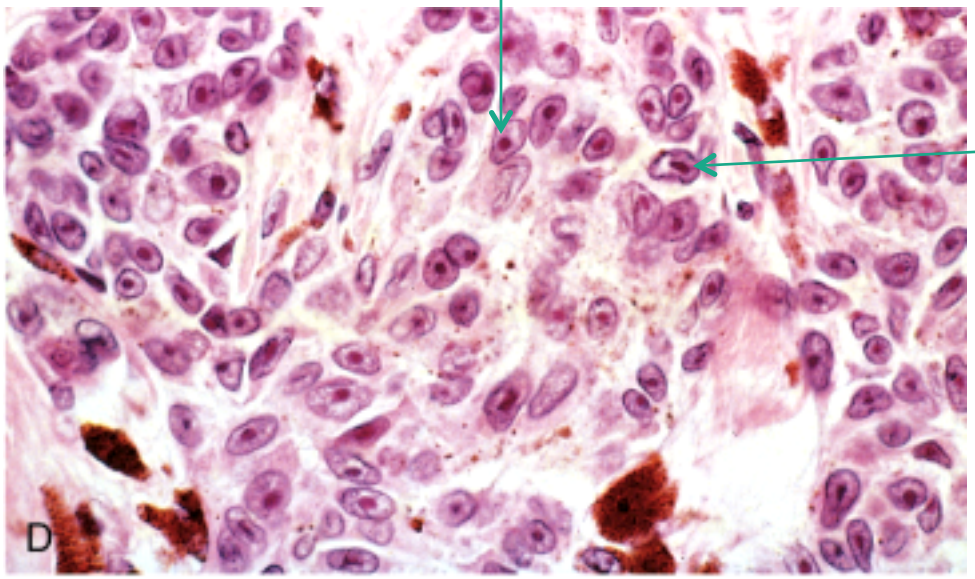


Lesions down into the dermis

Nodular Melanoma

Malignant Melanoma

Prominent nucleoli



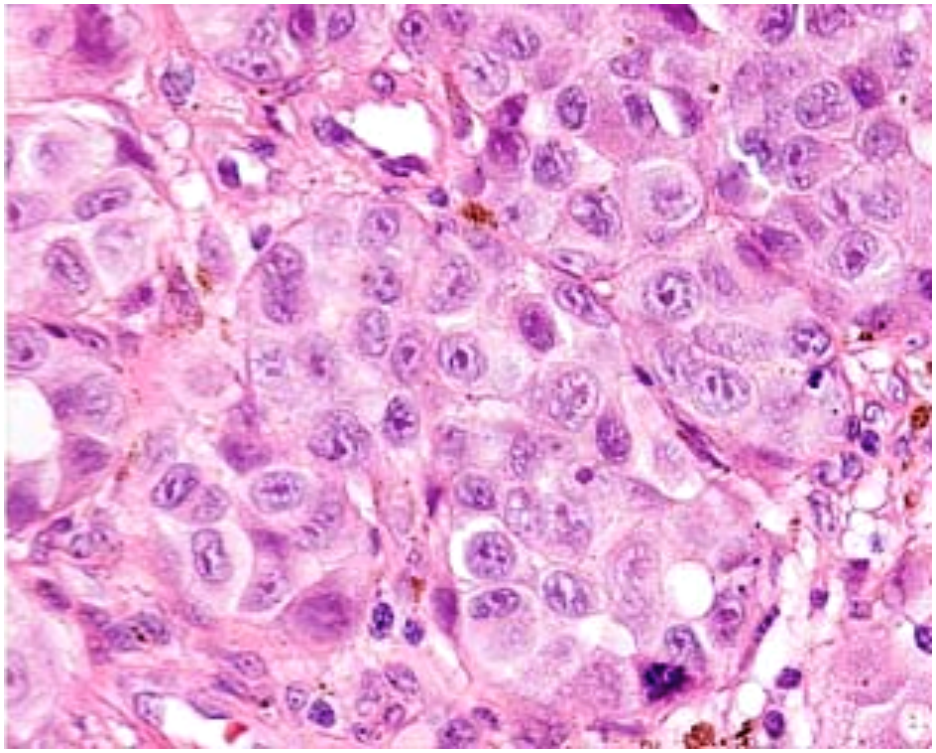
Spindle-shaped nuclei

This is why melanoma can be mistaken for sarcoma

Malignant Melanoma

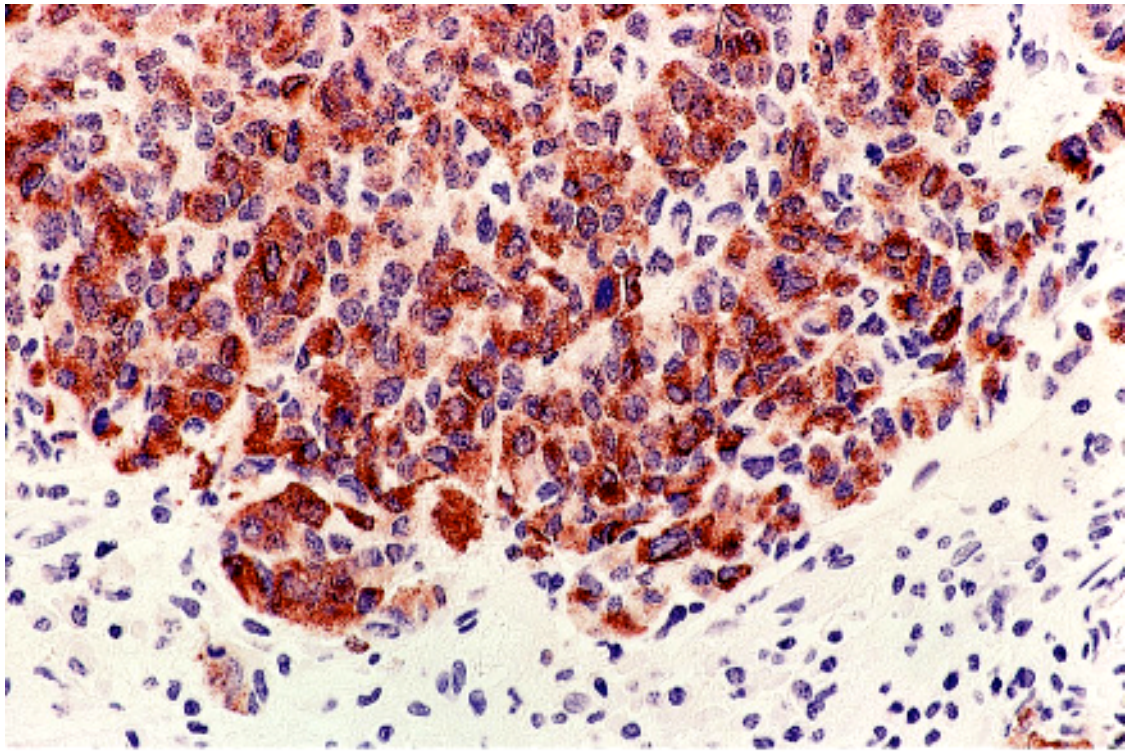
Round-cells

Can also look like a carcinoma

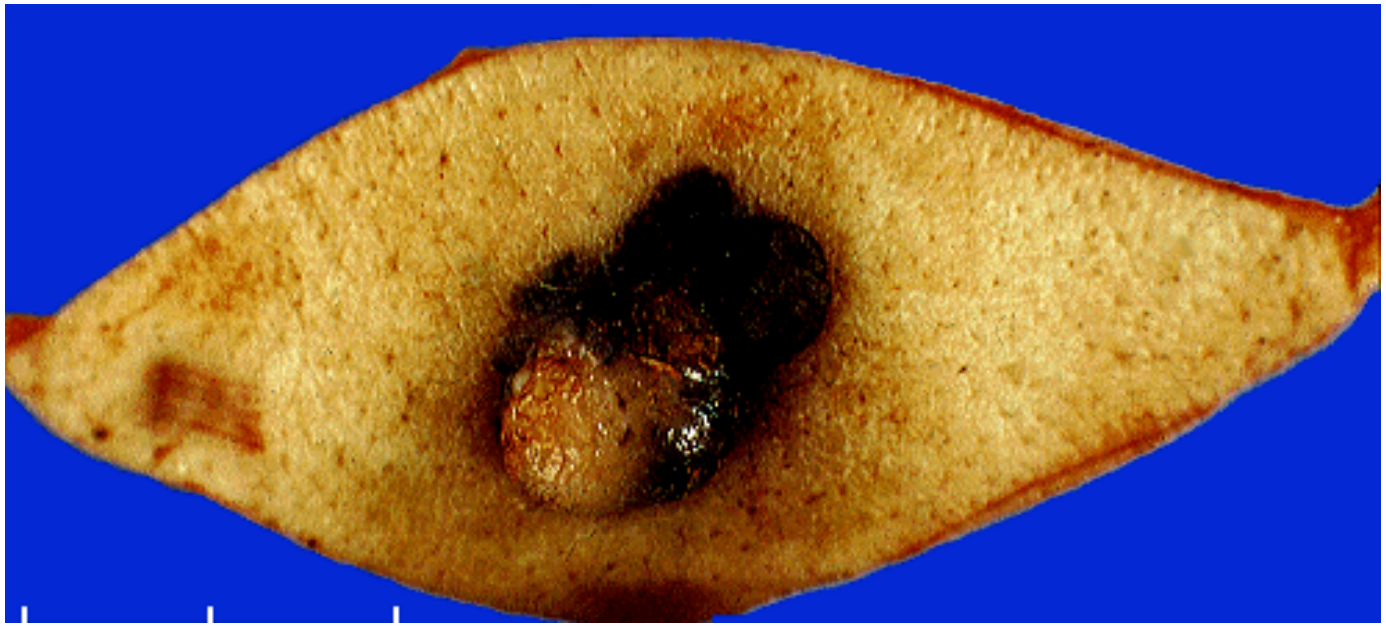


Melanoma – *S100 protein stain (HY)

HMB45 Stain



Malignant Melanoma



Malignant Melanoma

Problem here is location
For excision, you would have to remove his eye, nose, etc.