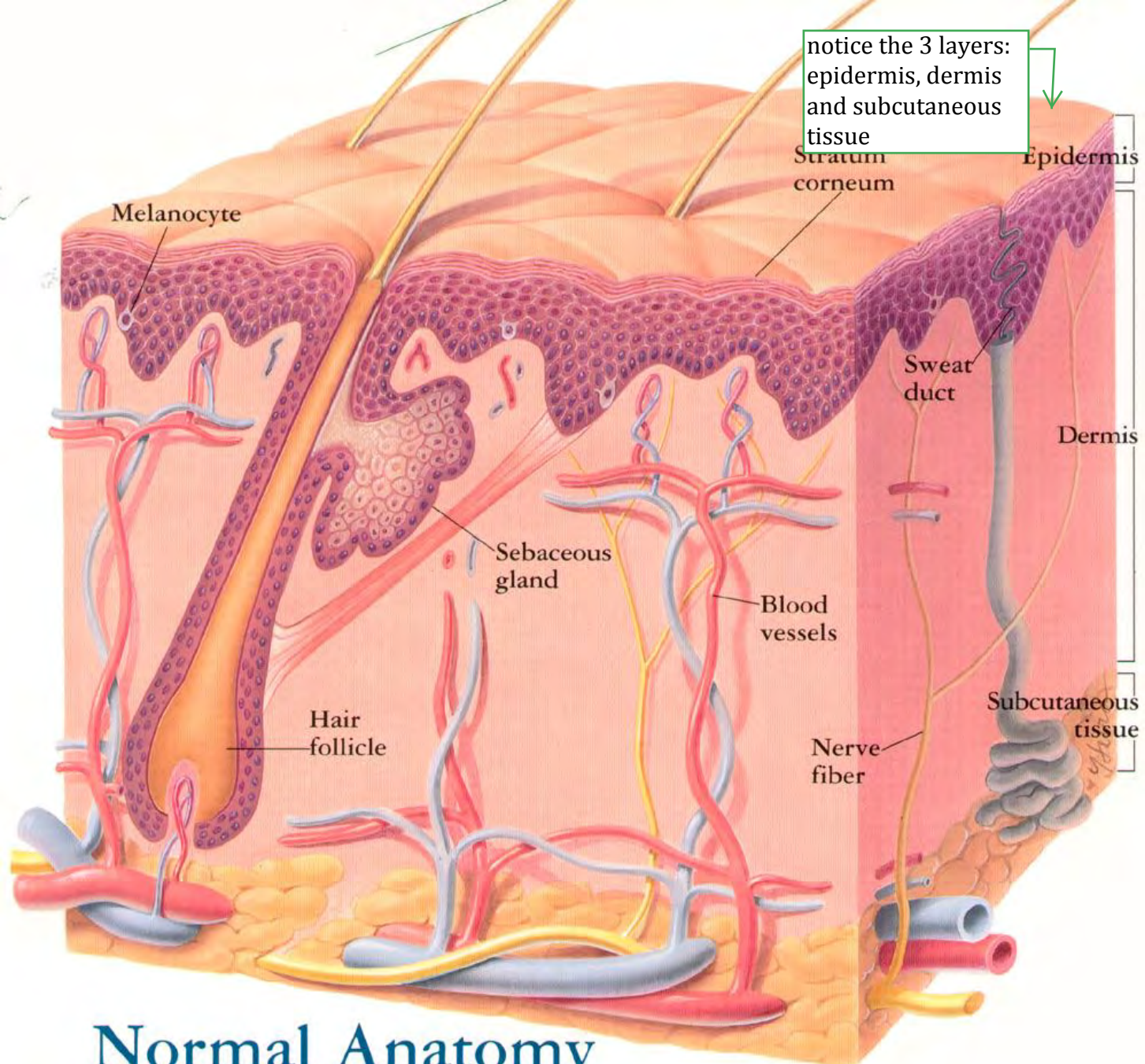


# INFLAMMATORY DISEASES OF THE SKIN

**APPROVED**

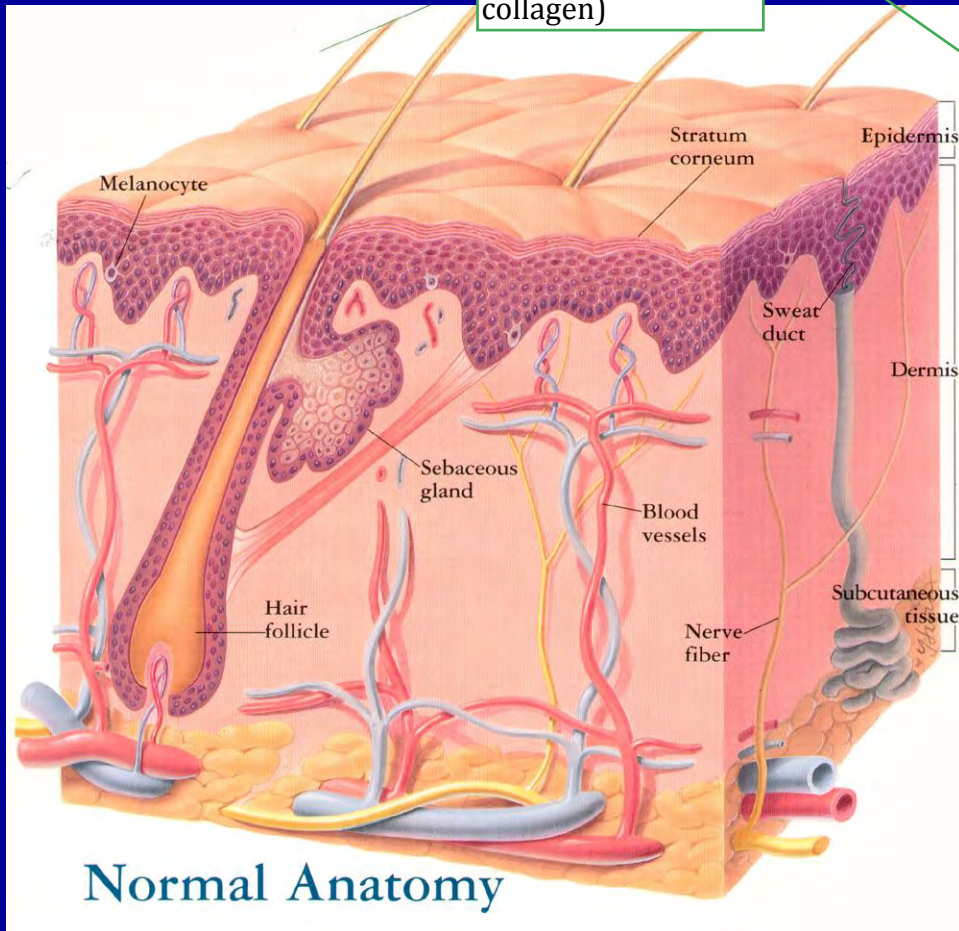
*M. Angelica Selim, M.D.  
Dermatopathology Unit  
Pathology Department*



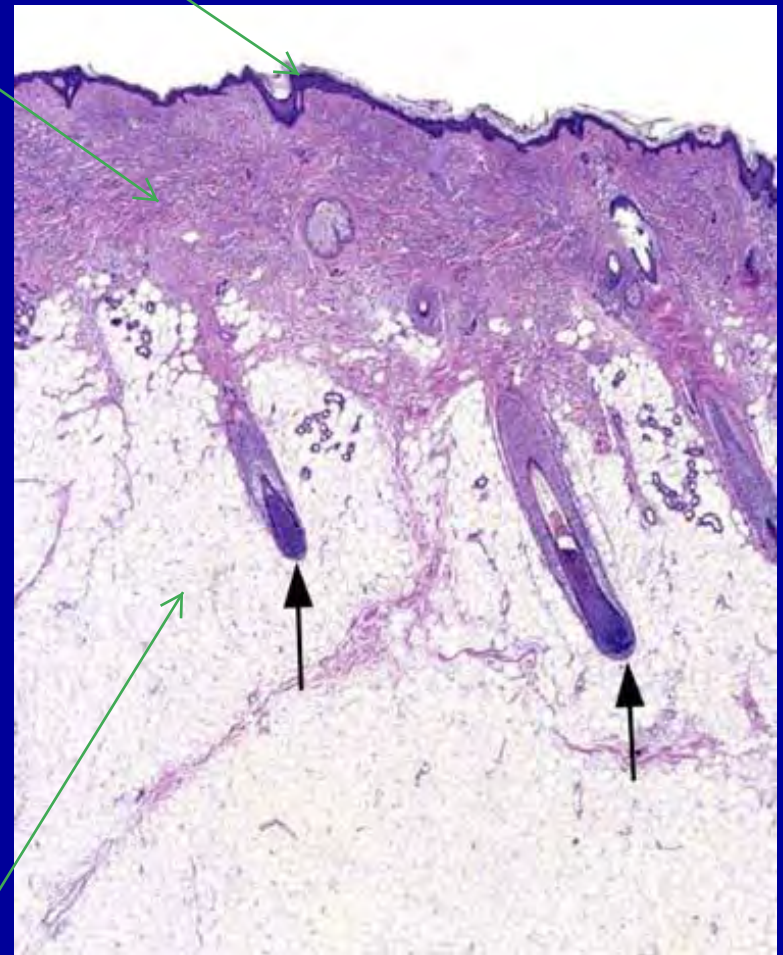
Normal Anatomy



dermis (pink  
because it is  
collagen)



epidermis



fat (why white?  
lipids are dissolved  
when alcohol is  
added to the slide)

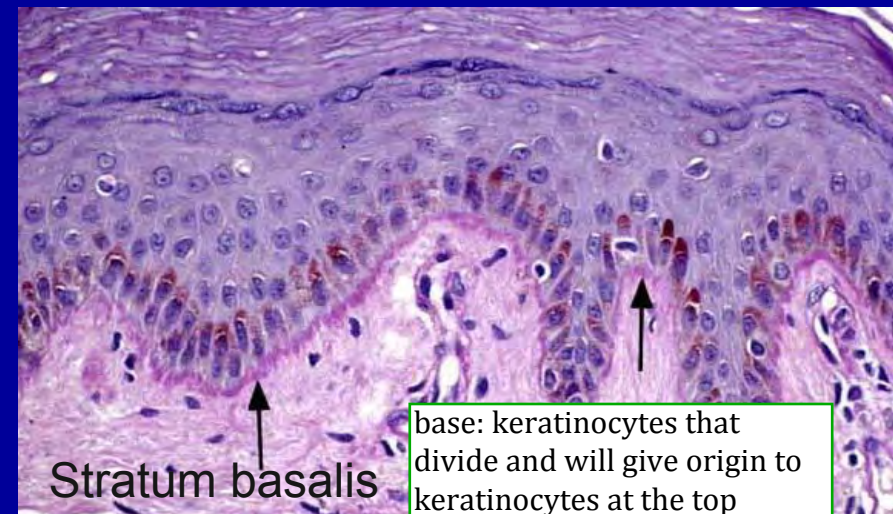
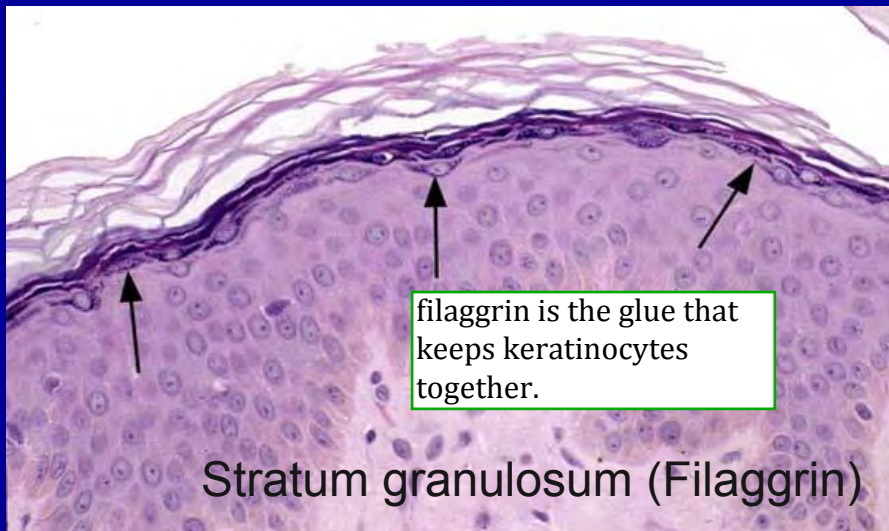
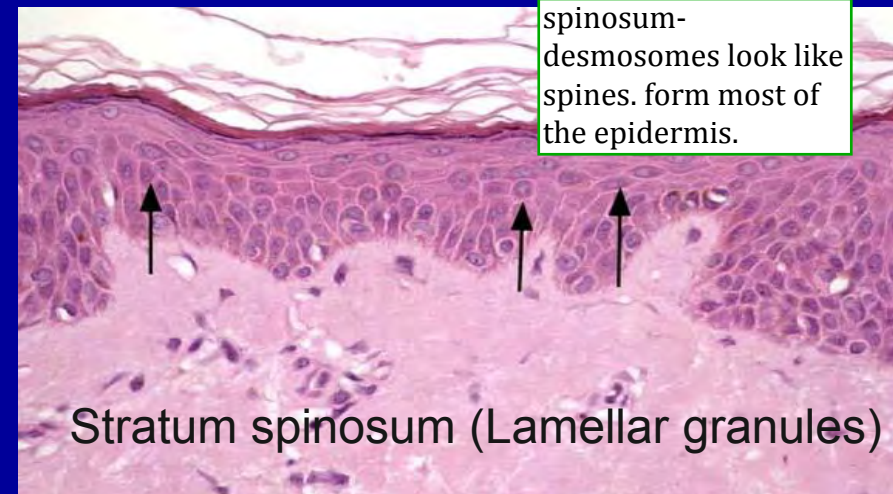
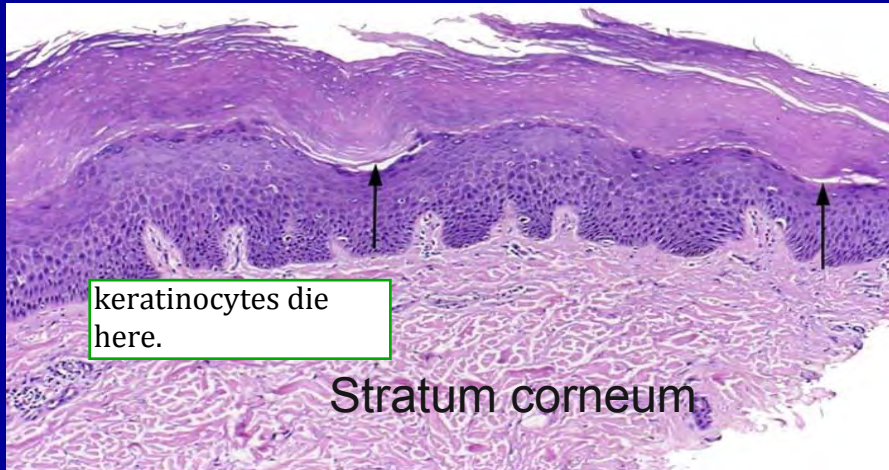
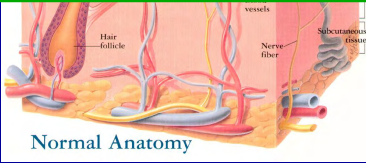


4 layers from bottom to top:

- stratum basalis
- stratum spinosum
- stratum granulosum
- stratum corneum

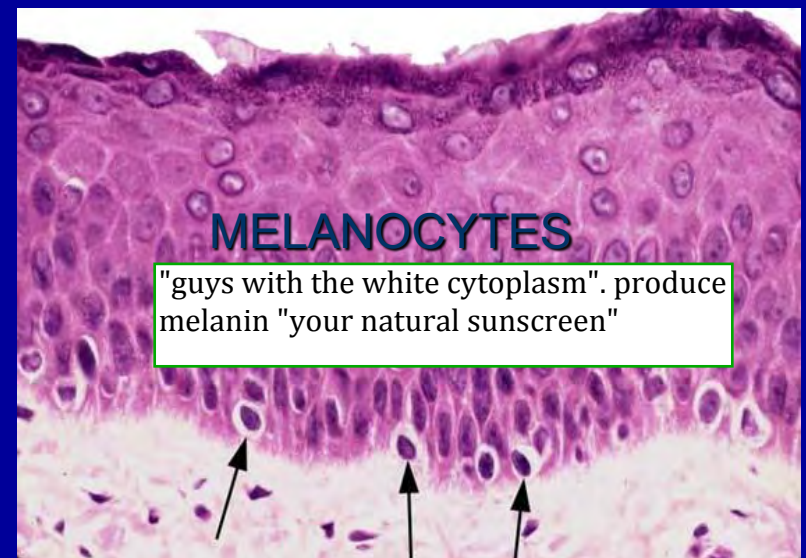
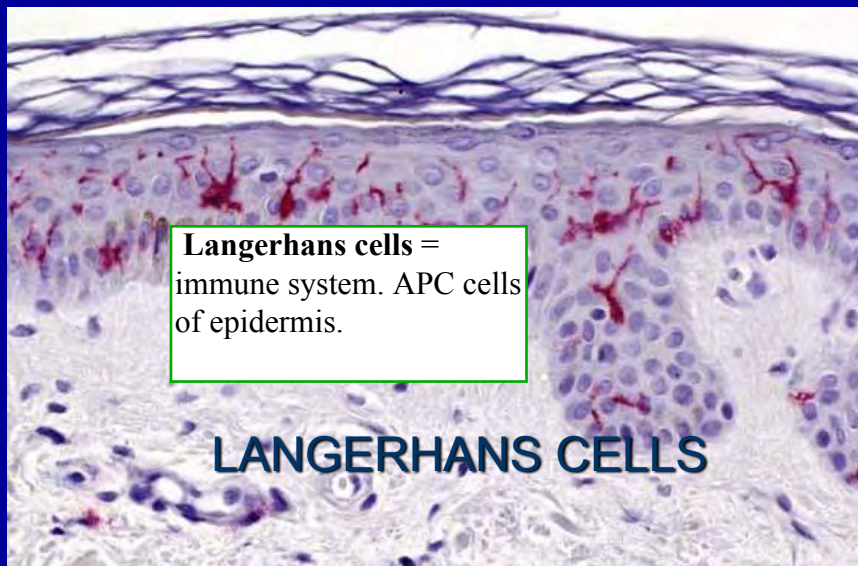
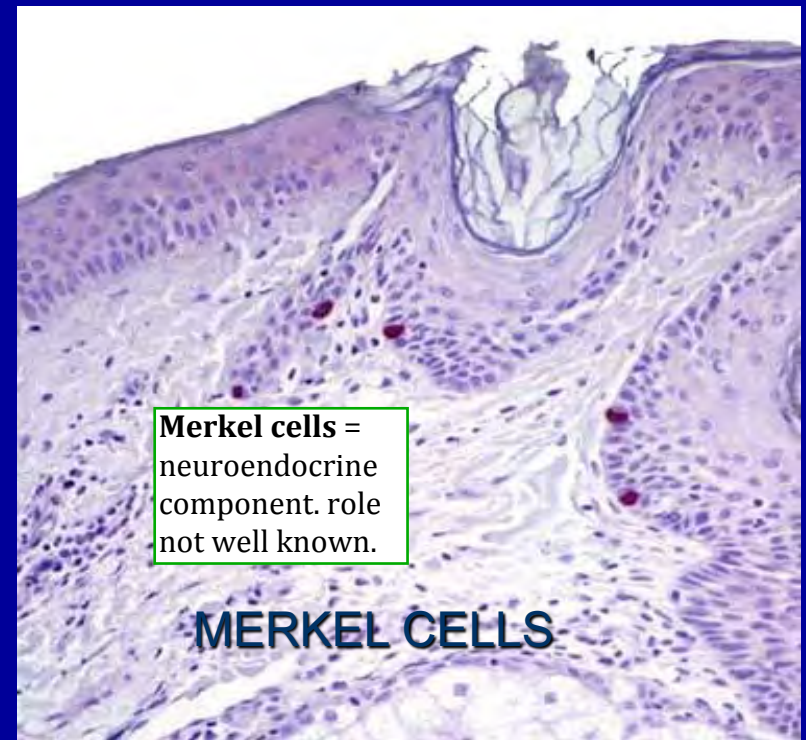
# EPIDERMIS

epidermis is like a wall with bricks. the bricks are the keratinocytes.





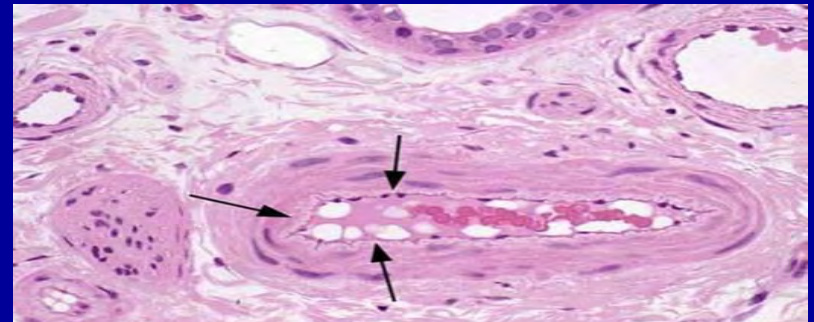
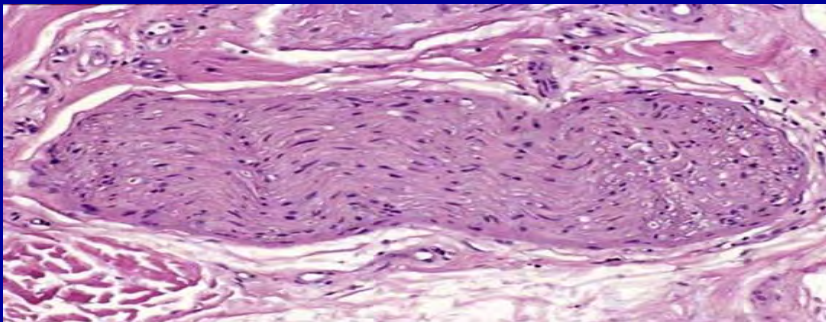
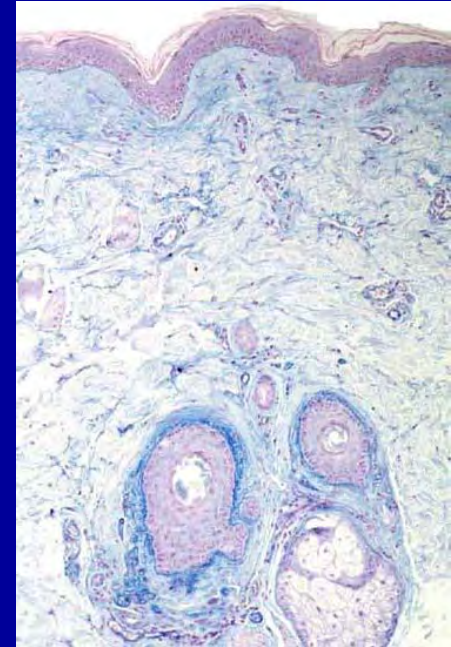
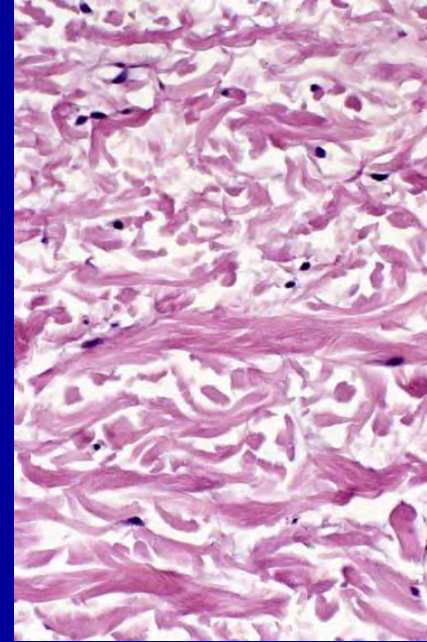
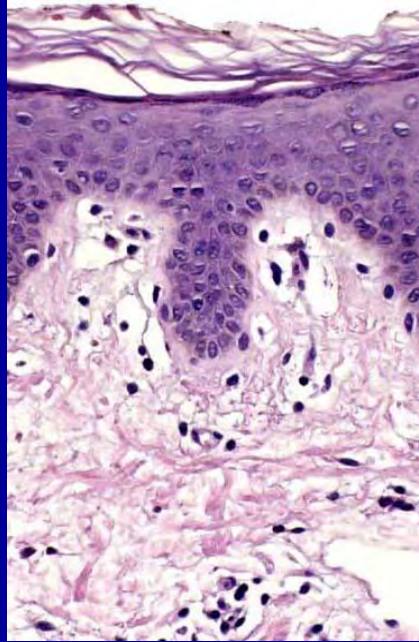
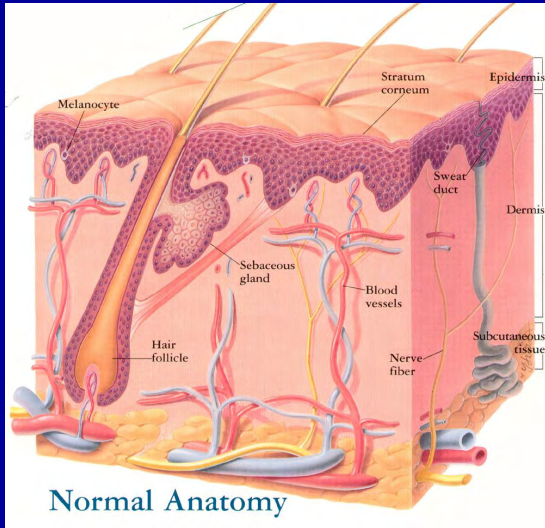
# EPIDERMIS





# DERMIS

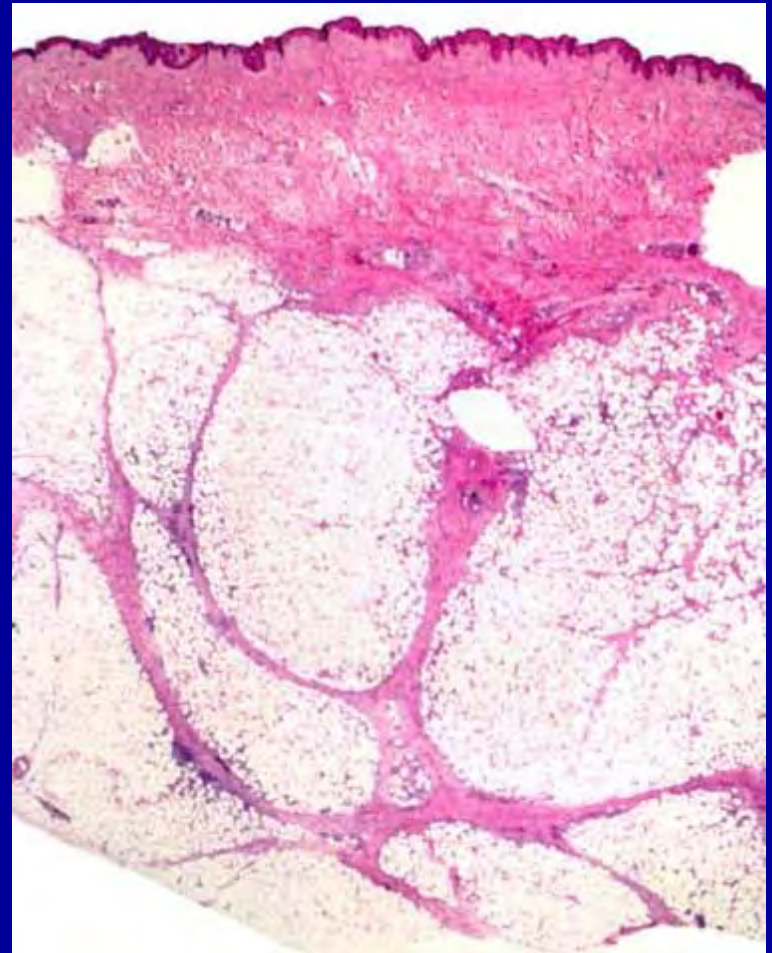
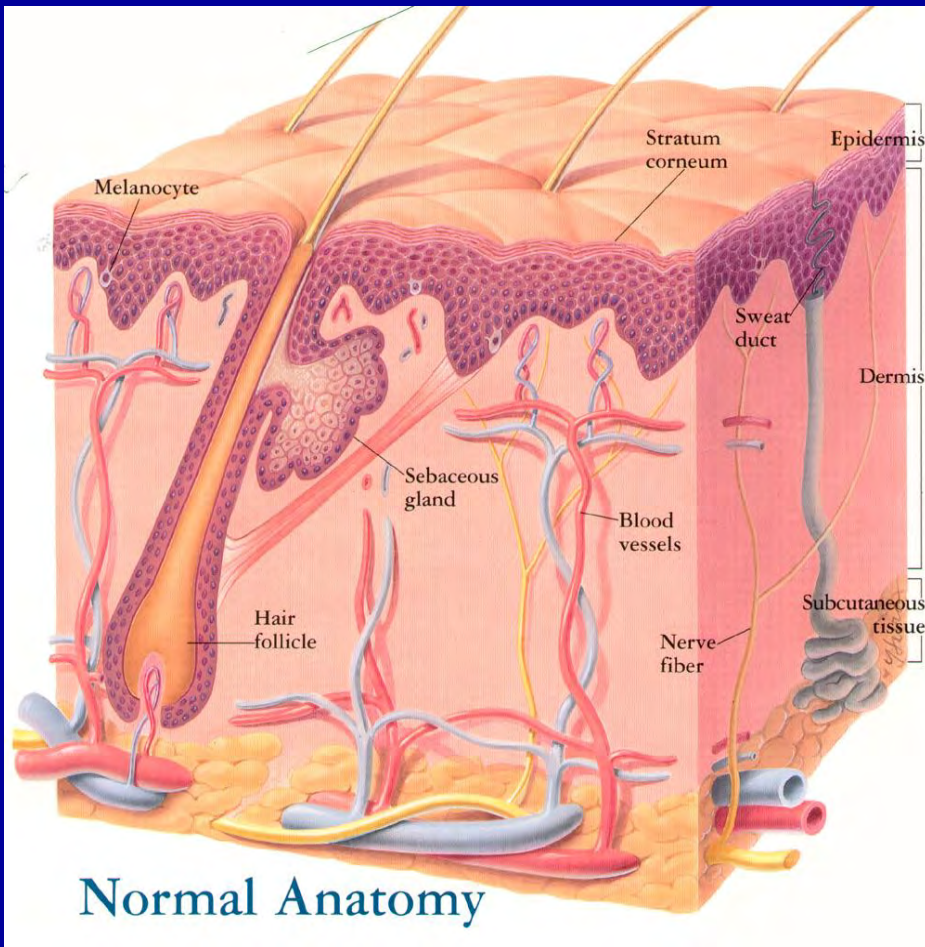
collagenous tissue





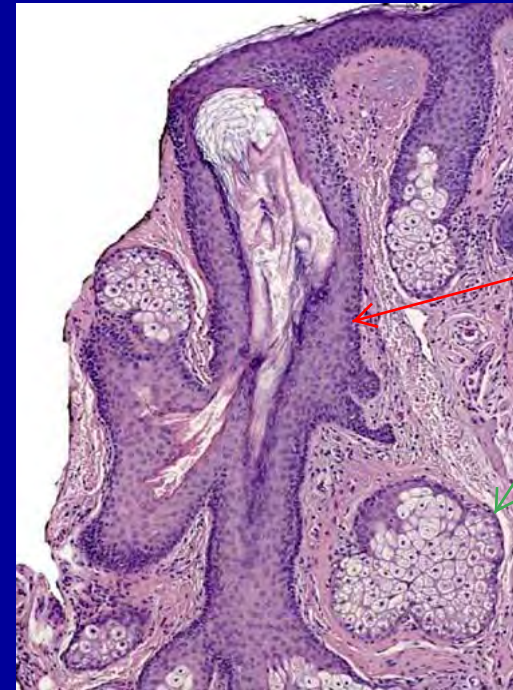
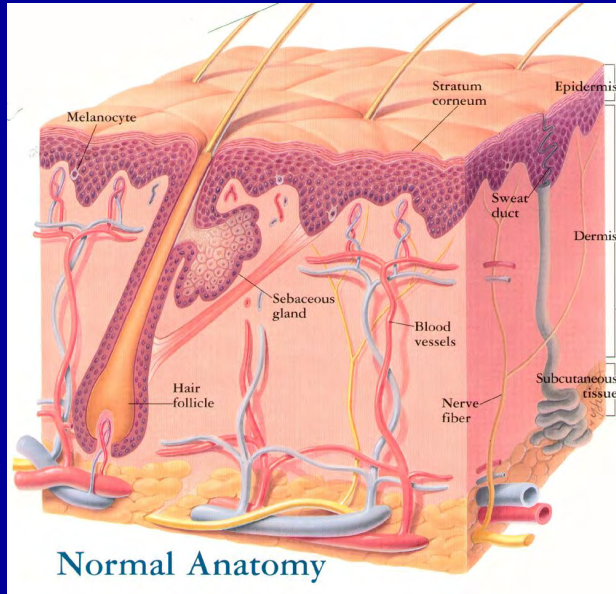
# SUBCUTANEOUS TISSUE

fat. divided into lobules and septae. inflammation can include either lobules or septae.





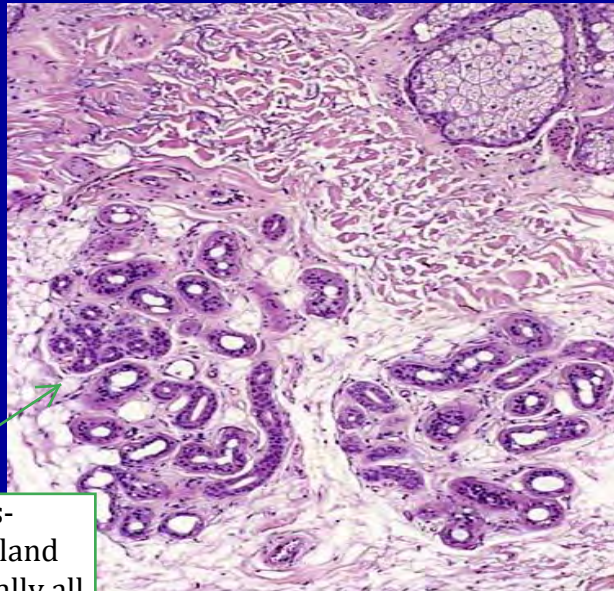
# ADNEXAL STRUCTURES



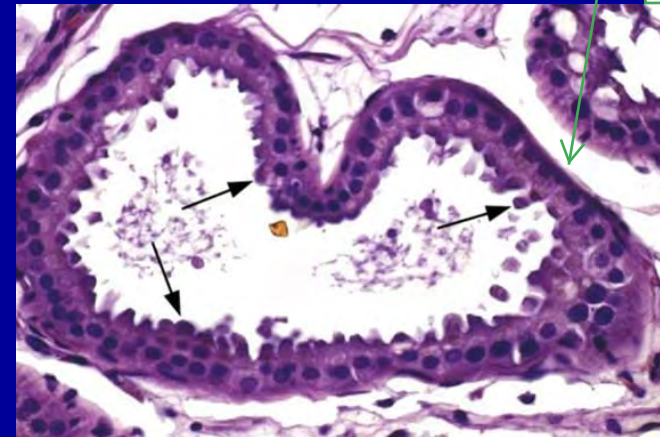
hair follicles with sebaceous glands hydrate and protect your hair shaft.

sebaceous gland

apocrine gland- "body odors" found in axilla for example



eccrine glands- major sweat gland found in virtually all skin





the skin is a very active layer: it protects, helps in temp. control and even produces things!

# FUNCTIONS

- External organ **protection:**
  - **Impermeable**
  - **Melanin**
- **Temperature control**
- Vitamin D

you can even produce things!

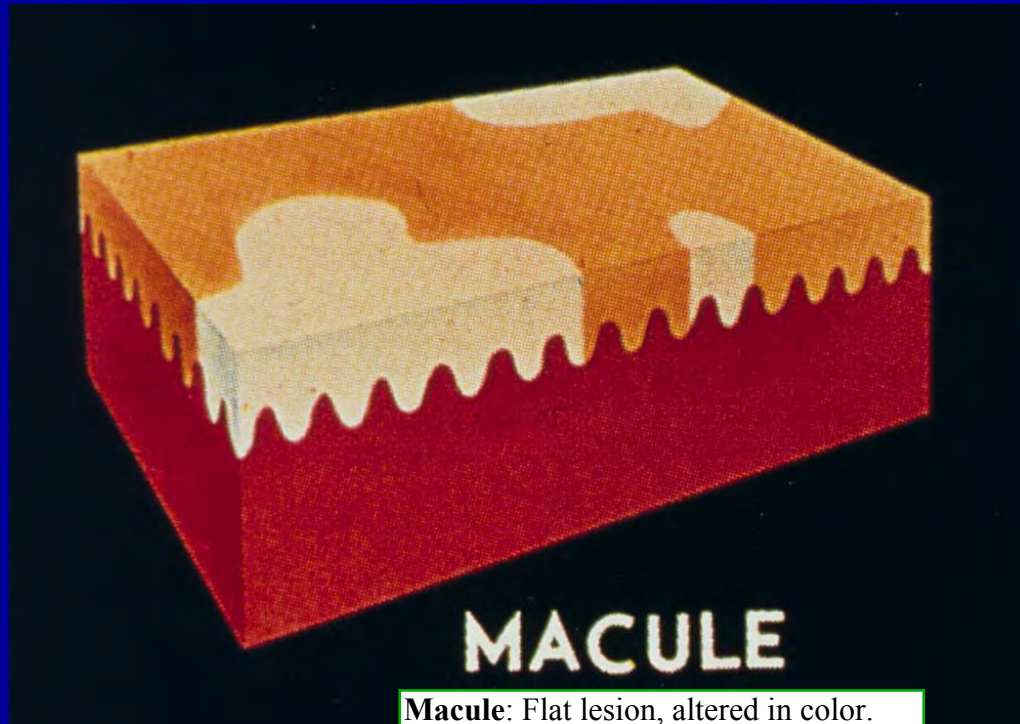
sweat glands help you control temperature

Describing lesions:

Macule

- a. Change in skin color
- b. No elevation or depression
- c. Nonpalpable

PTION



**Macule:** Flat lesion, altered in color.

➤ **MACULE:** Coloration, circumscribed



Elevated lesions: plaques, papules and nodules.

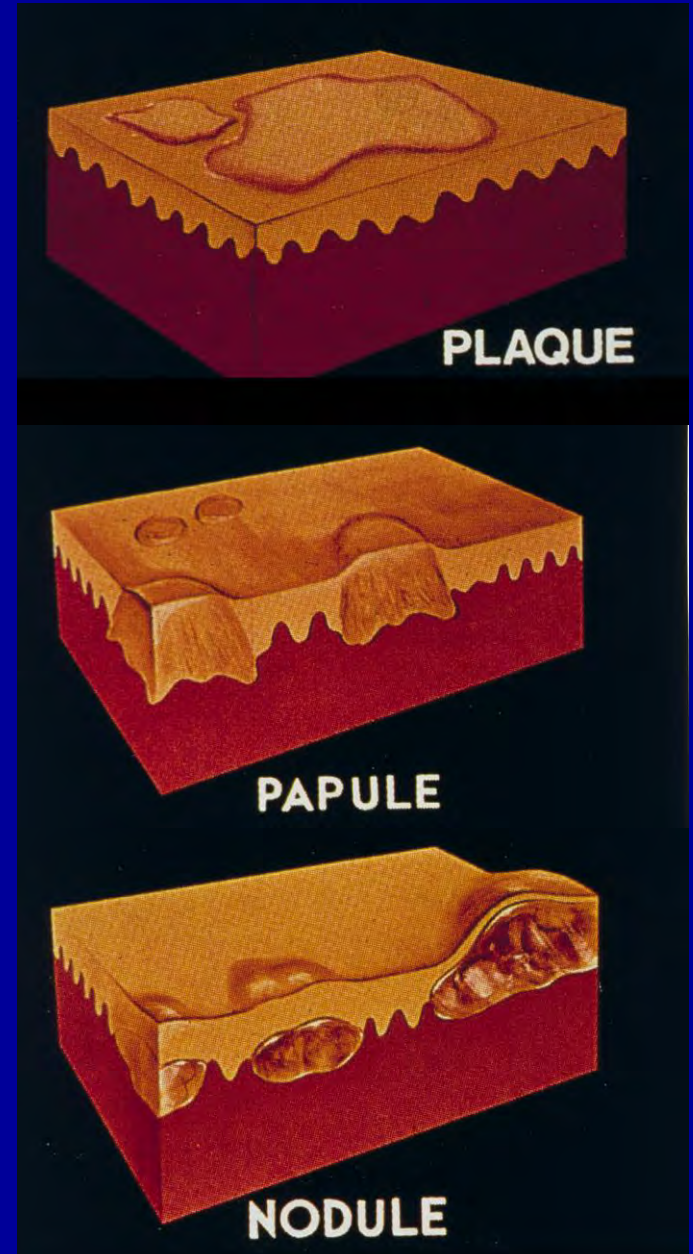
➤ **PLAQUE**: Elevated,  $> 10\text{mm}$  (surface plaque- surface larger than height  
larger than height)

papule- tiny elevations  
less than 5mm

➤ **PAPULE**: Elevated,  $< 5\text{mm}$

nodule- circumscribed but  
higher (greater than 5mm)

➤ **NODULE**: Elevated,  $> 5\text{mm}$



Creating spaces in epidermis: wheal, blisters and pustules

➤ **WHEAL:** Pale papule, plaque, evanescent  
urticaria- comes and goes.

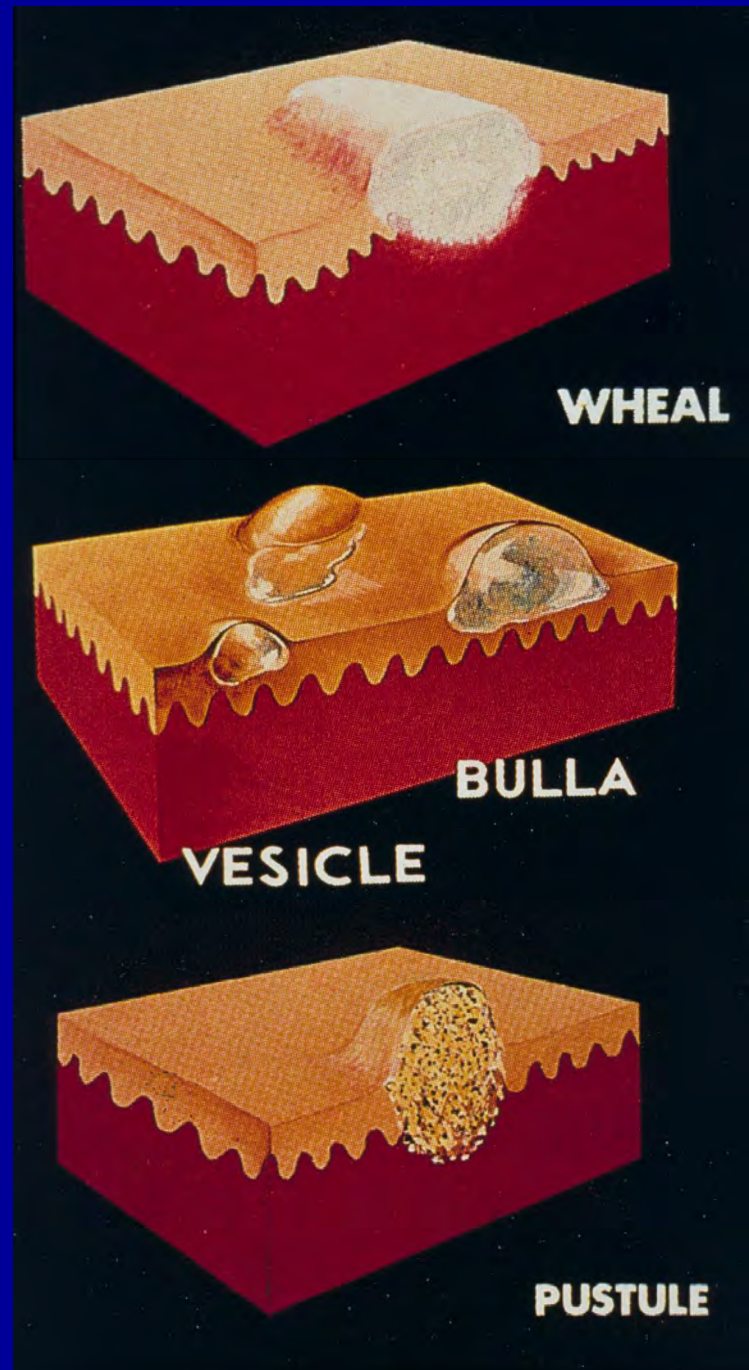
➤ **BLISTER:** space in the epidermis  
classified by its size:

➤ **VESICLE:** Fluid, <10 mm

➤ **BULLA:** Fluid, > 10mm

➤ **PUSTULE:** Pus-filled blister

pustule- pus





➤ **CRUST:** Serous, purulent exudates

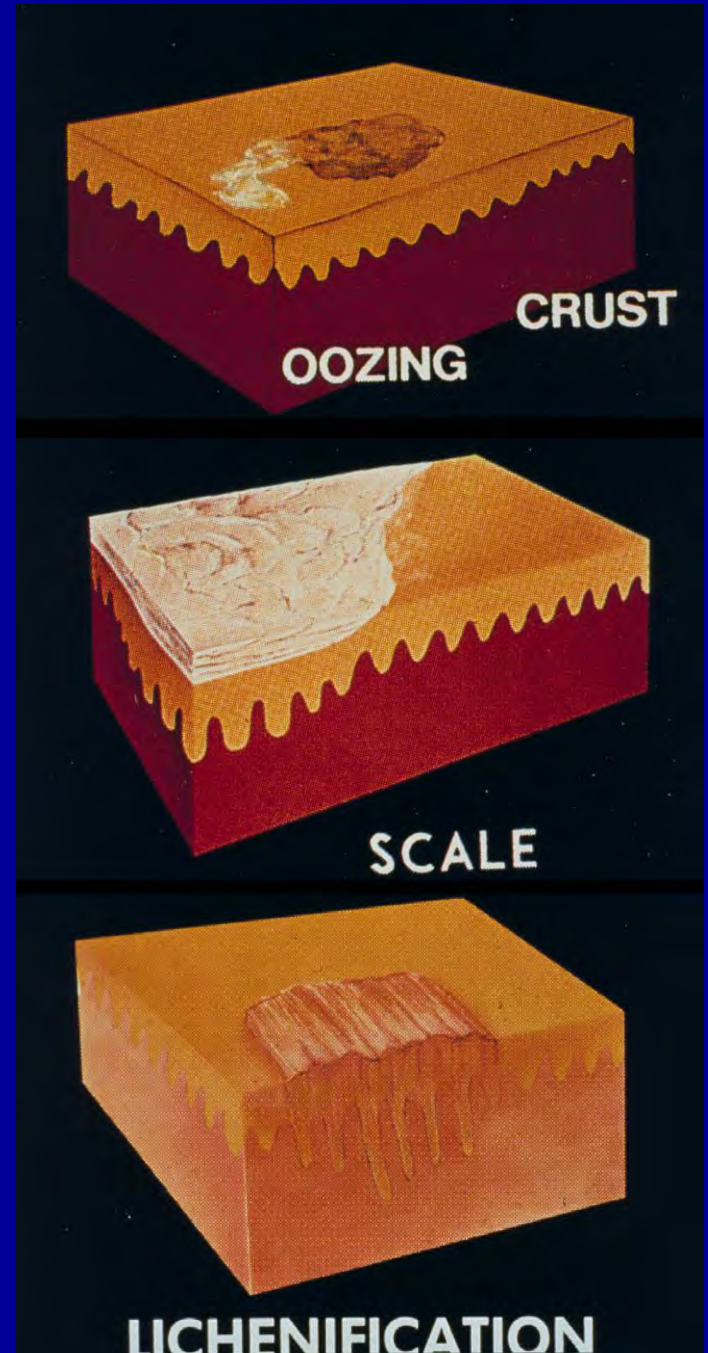
can also be a scab.

➤ **SCALE:** Dry, plate-like excrescence

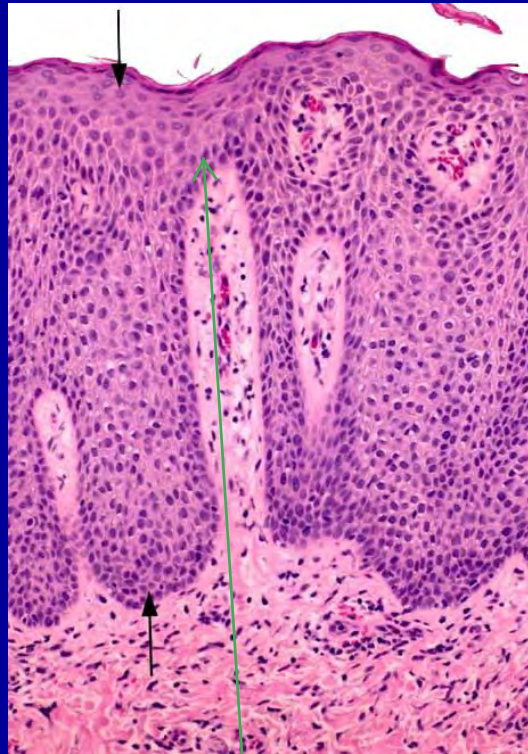
scale- classic of psoriasis

➤ **LICHENIFICATION:** Thickened, rough

skin marks are very obvious because epidermis gets hyperplastic and becomes rough (where you scratch a lot, for instance)



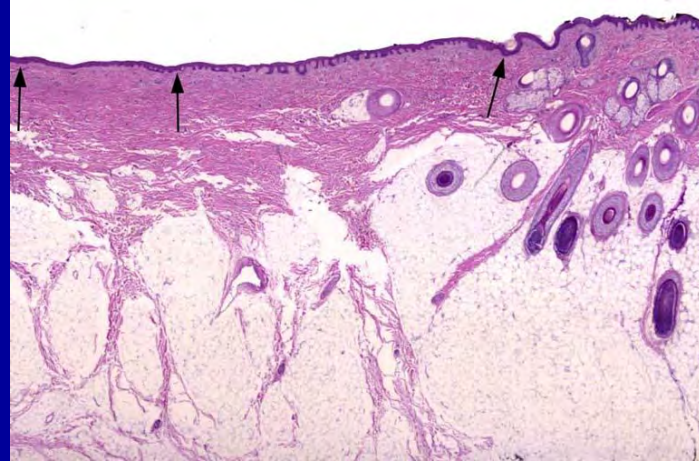
# MICROSCOPIC TERMS (I)



normal thickness is shown here.

## ACANTHOSIS

thickening of the epidermis.

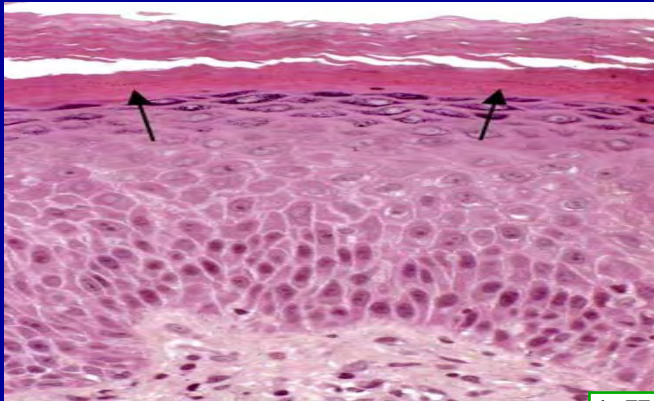


## ATROPHY

thinning of the epidermis.



# MICROSCOPIC TERMS (II)



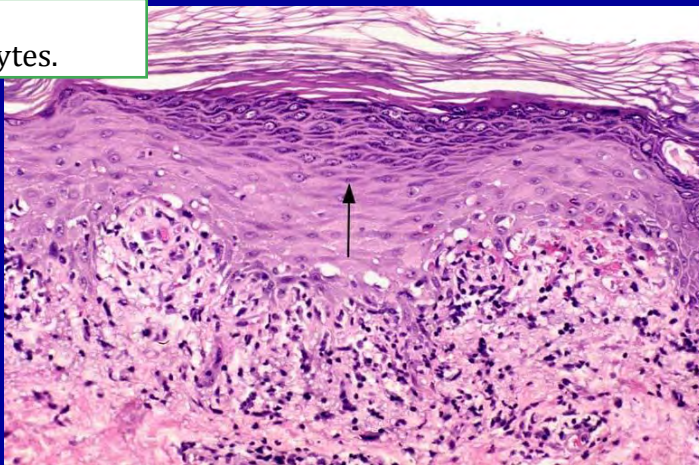
1. **Hyperkeratosis** = increased stratum corneum

## HYPERKERATOSIS

Orthokeratosis: **normal** keratin

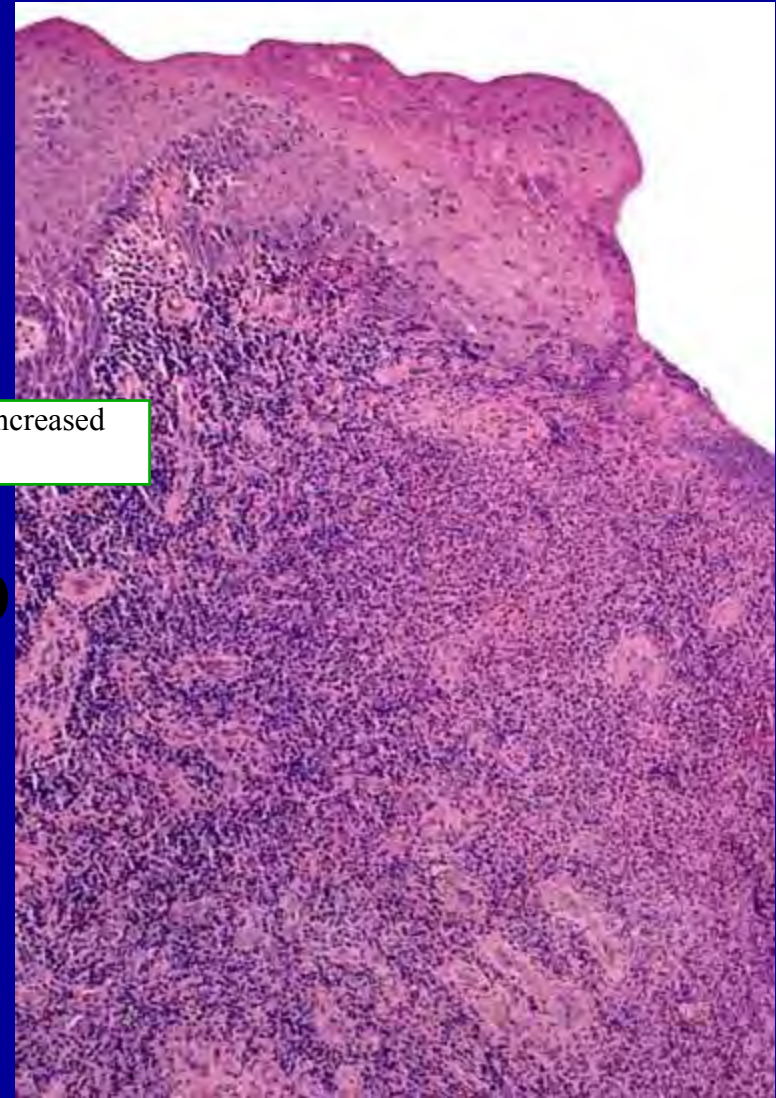
Parakeratosis: **nuclei Stratum corneum**

abnormal  
keratinocytes.



## HYPERGRANULOSIS

**Hypergranulosis** = increased stratum granulosum layer (topmost layer before keratin)



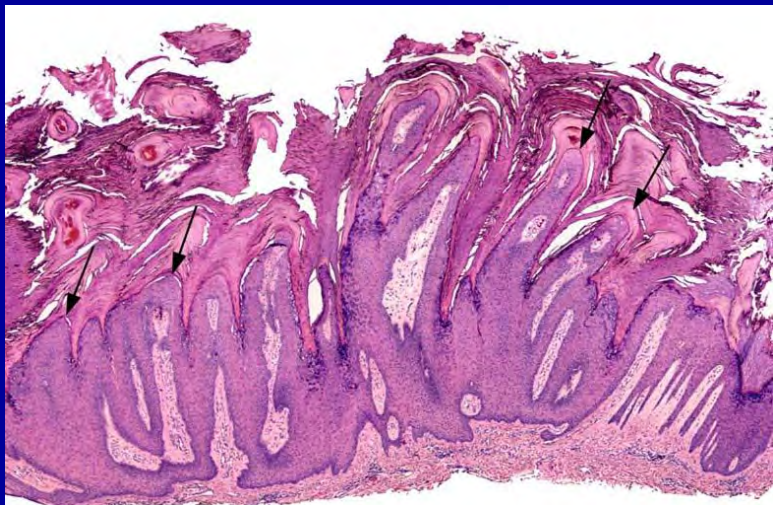
## ULCER

**ulcer**- loss of epidermis.



You can go up  
or down.

# MICROSCOPIC TERMS (III)



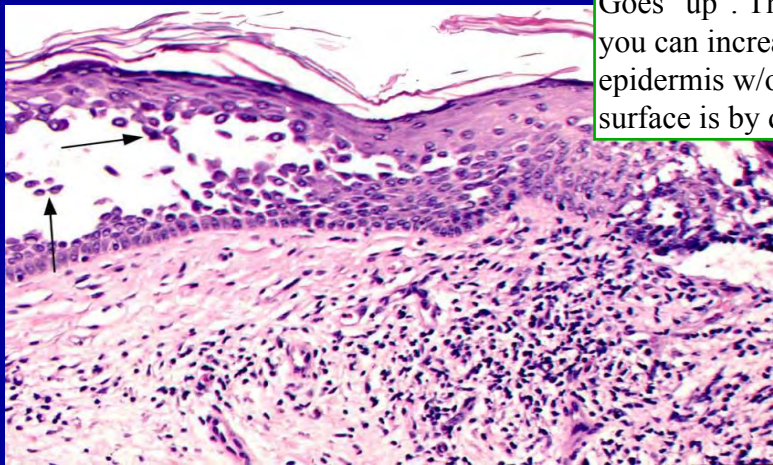
**PAPILLOMATOSIS**

**Papillomatosis** = hyperplasia of dermal papillae cause wrinkling: Goes "up". The only way you can increase epidermis w/o increasing surface is by doing this.



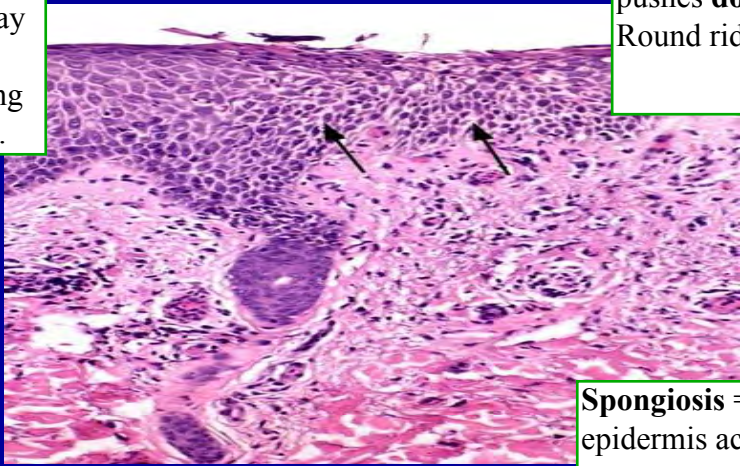
**PSORIASIFORM**

**Psoriasiform** = too much epidermis but pushes **down**. Round ridges.



**ACANTHOLYSIS**

**Acantholysis** = loss of intercellular connections. Epidermis "can't keep it together"



**SPONGIOSIS**

**Spongiosis** = epidermis acts as a sponge and begins to absorb fluid



need to know where the disease is in order to decide the type of biopsy.

# TYPES OF BIOPSY:

- Shave superficial lesion.
- Punch
- Ellipse cut off the whole lesion.
- Major excision if you are worried about various levels. can cut down to the
- ALWAYS CAREFUL !!!!

# INDICATIONS FOR BIOPSY

Why do we biopsy?  
- unknown diagnosis  
- systemic disease

- Unknown diagnosis:
  - Inflammatory disease
  - Neoplastic
- Systemic disease:
  - Vasculitis
  - Amyloidosis



# TECHNIQUES

- Hematoxylin and eosin
- Histochemistry
- Immunohistochemistry
- Electron microscopy

routine- what we will see today

do i have infection?

use antibody antigen interactions.

ultrastructure.

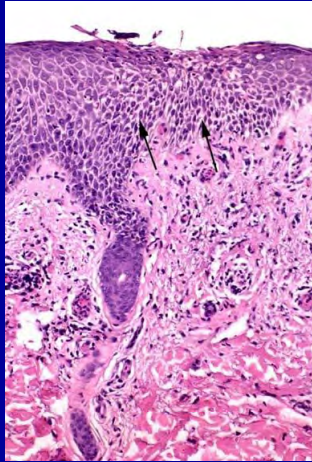
# DERMATITIS (PATTERNS)

Classify by:

- Location
- Superficial/deep
- Cellularity

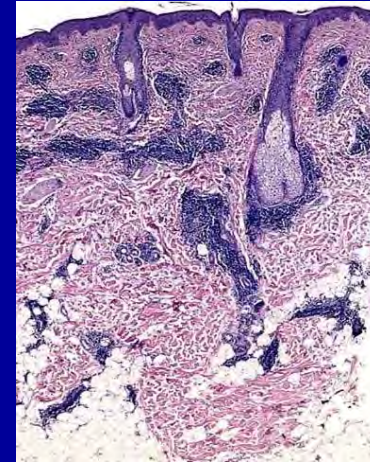


# DERMATITIS PATTERNS



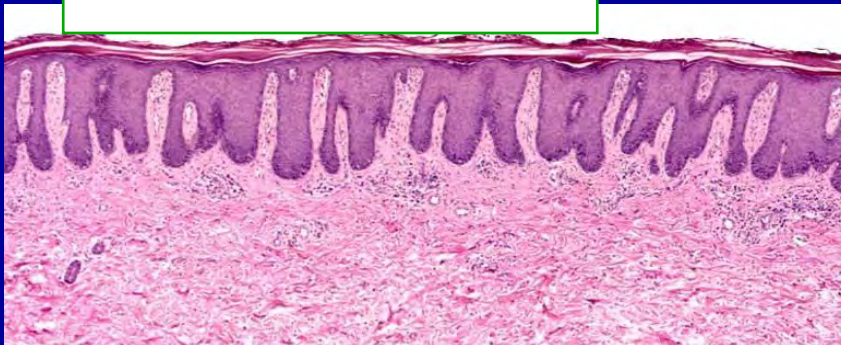
## SPONGIOTIC DERMATITIS

eczema: what happens in a basic inflammatory disorder. collect fluid.



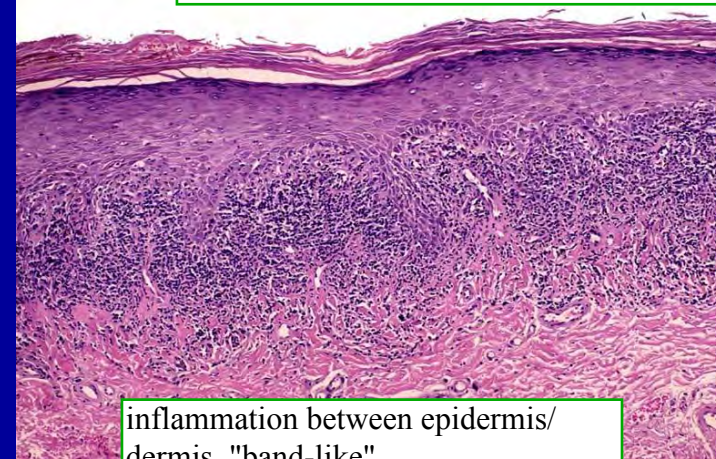
## PERIVASCULAR DERMATITIS

inflammation around vessels



## PSORIASIFORM DERMATITIS

increased thickening of the epidermis

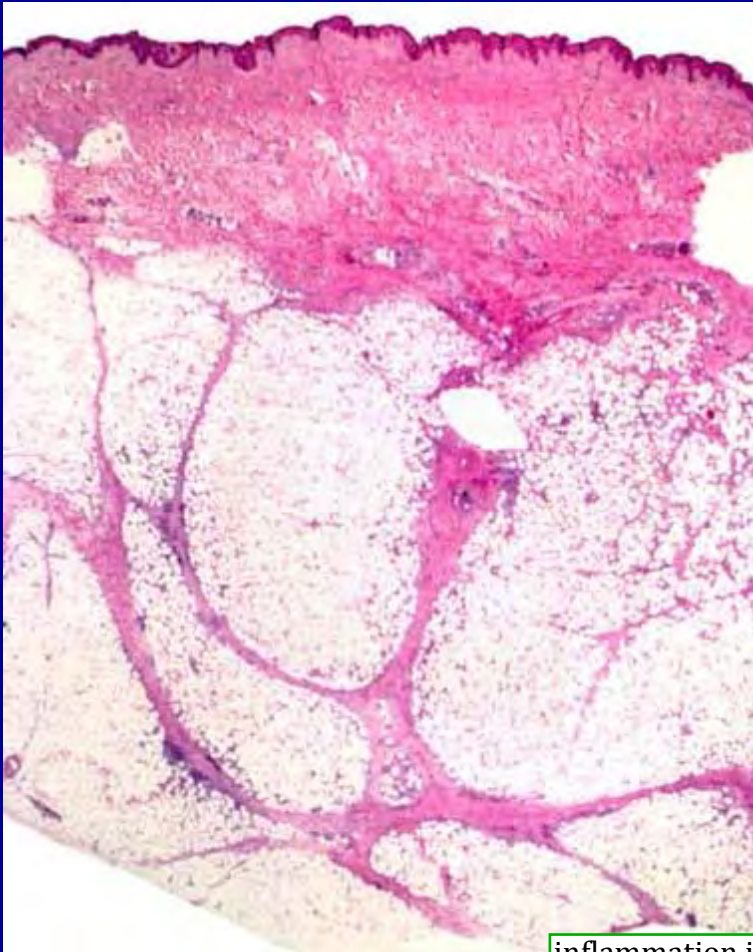


inflammation between epidermis/dermis. "band-like"

## INTERFACE-**LICHENOID** DERMATITIS

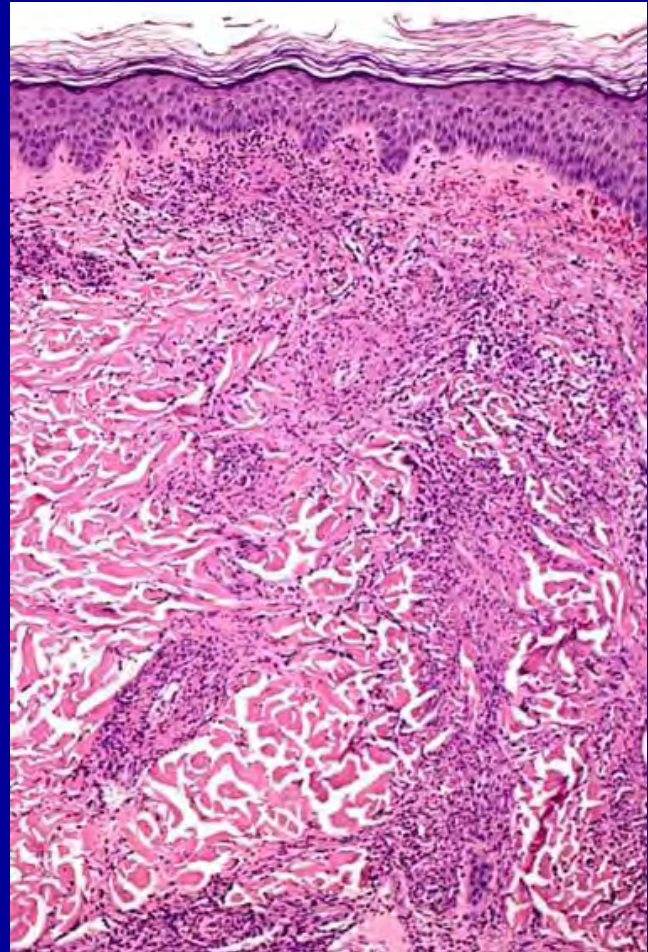


# DERMATITIS PATTERNS:



**PANNICULITIS**

inflammation in  
subcutaneous tissue.  
classify as lobular or  
septal.



**VASCULITIS**

inflammation that  
targets vessels.



# ALLERGIC CONTACT DERMATITIS

eczema.

- Morbidity very bothersome. example of not doing dishes because soap gives you contact dermatitis.
- Leading occupational disease
- Mostly irritant mechanisms
- Type IV immune-reaction:
  - Sensitization Type IV hypersensitivity reaction via Langerhans cells
  - Elicitation
- Langerhans cells 1st exposure to poison ivy -> body creates memory through langerhans cells -> reaction upon second exposure.

# ALLERGIC CONTACT DERMATITIS: MORPHOLOGY

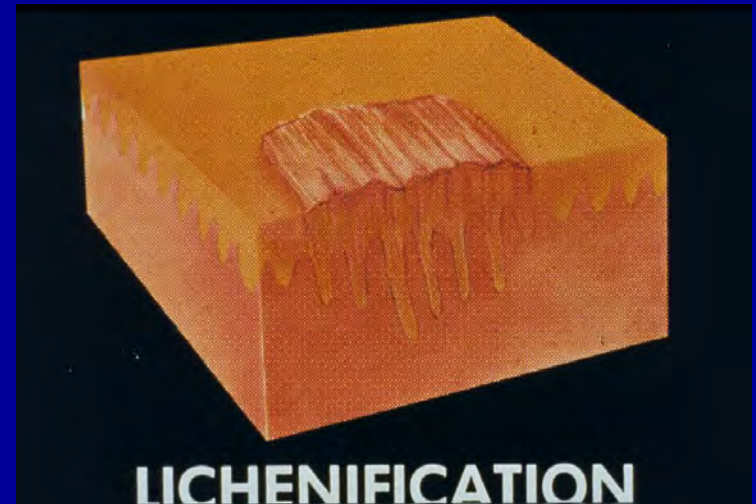
- ACUTE:
  - Erythematous macules
  - Papules and vesicles

**Acute** see macules (**flat**) and some papules (**small**) and vesicles (**fluid**)



- CHRONIC:
  - Erythema
  - Scale
  - Lichenification

**Chronic** see more scaling and lichenification



# ALLERGIC CONTACT DERMATITIS:HISTOLOGY

- Spongiosis
- Eosinophils
- Psoriasiform hyperplasia
- Parakeratosis

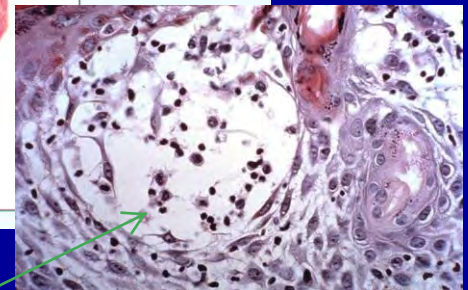
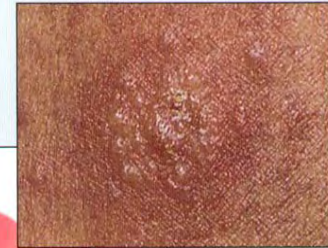
Over time get **psoriasiform hyperplasia** (pushes down) and parakeratosis (increase in stratum corneum- gets very scaly over time)

fluid collects and creates vesicles.

acute inflammation-eosinophils

Contact Dermatitis


keratinocytes separated by fluid





# PSORIASIS

- 1-2 %population in USA
- Scalp, acral, extensor surfaces (elbows/knees)
- Nails (pits)
- Arthritis



likes to develop in areas of trauma (elbows and knees)

# PSORIASIS

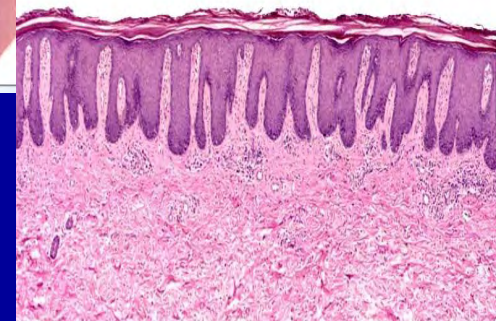
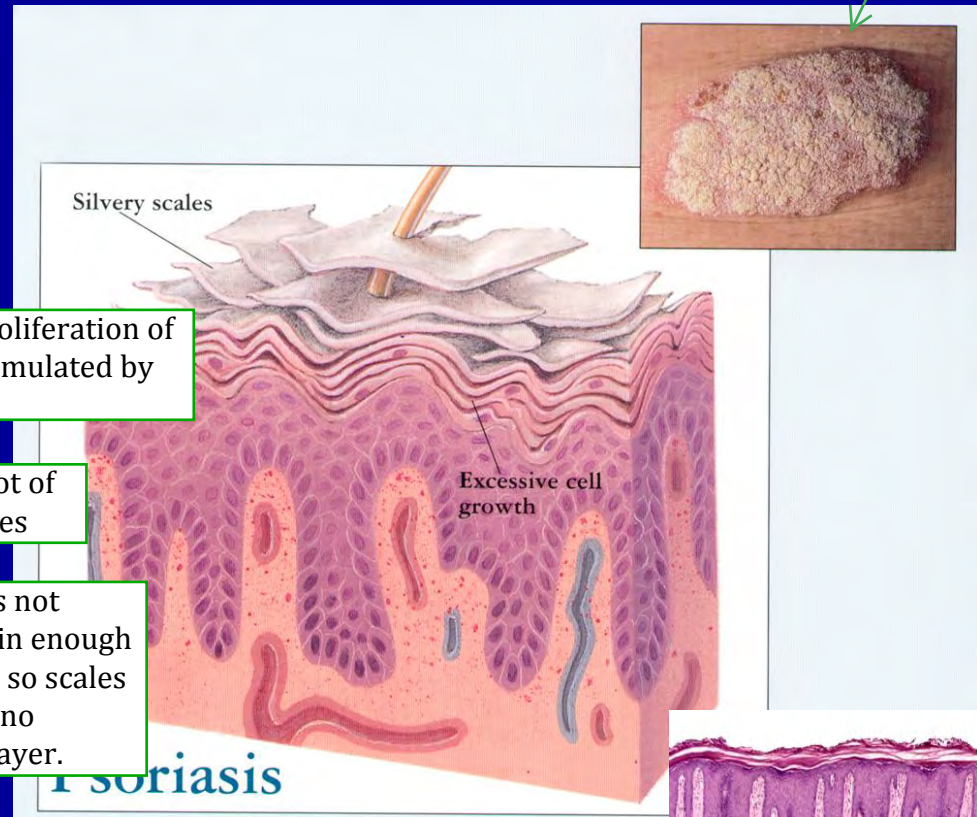
raised and surface  
larger than height-  
plaque!

- Scaly erythematous plaques
- Histology
  - Psoriasiform hyperplasia
  - Hyperkeratosis
  - Hypogranulosis
  - **Mitotic figures**
  - **Microabscesses** (Munro/Kogoj)

out of control proliferation of keratinocytes stimulated by T-cells

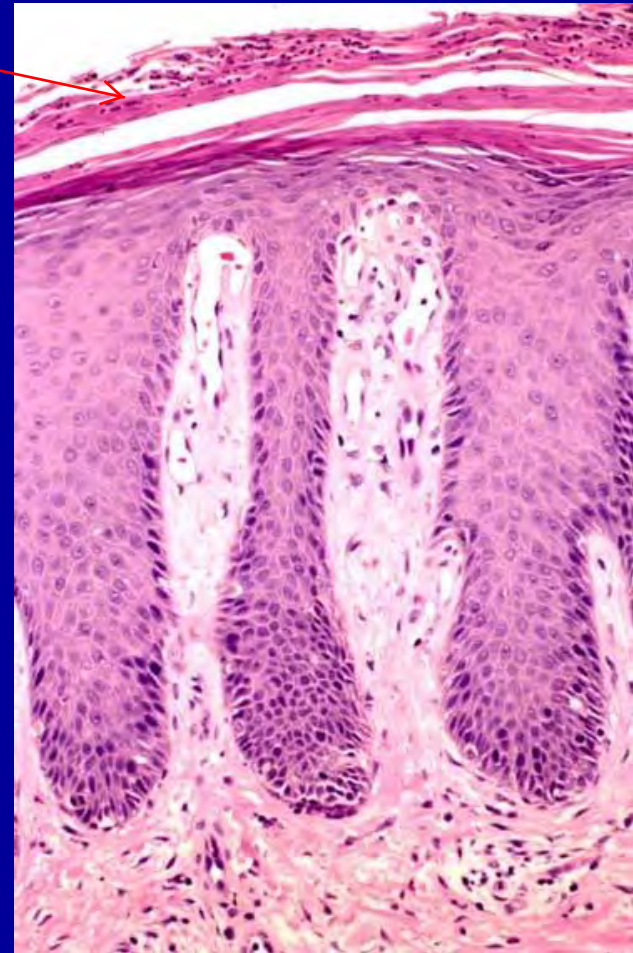
produce a lot of keratinocytes

filaggrin is not produced in enough quantities so scales are loose. no granular layer.



# PSORIASIS

stratum corneum





# ERYTHEMA MULTIFORME

MEDICAL EMERGENCY!!!! Treat with steroids.

immune system is reacting against you and is out of control.

- Children and young adults
- Emergency
- Pruritic/painful macules
- Papules/plaques
- Target lesions:
  - Dusky center (epidermal necrosis)
  - Red ring (erythema)
  - Pale ring (edema)

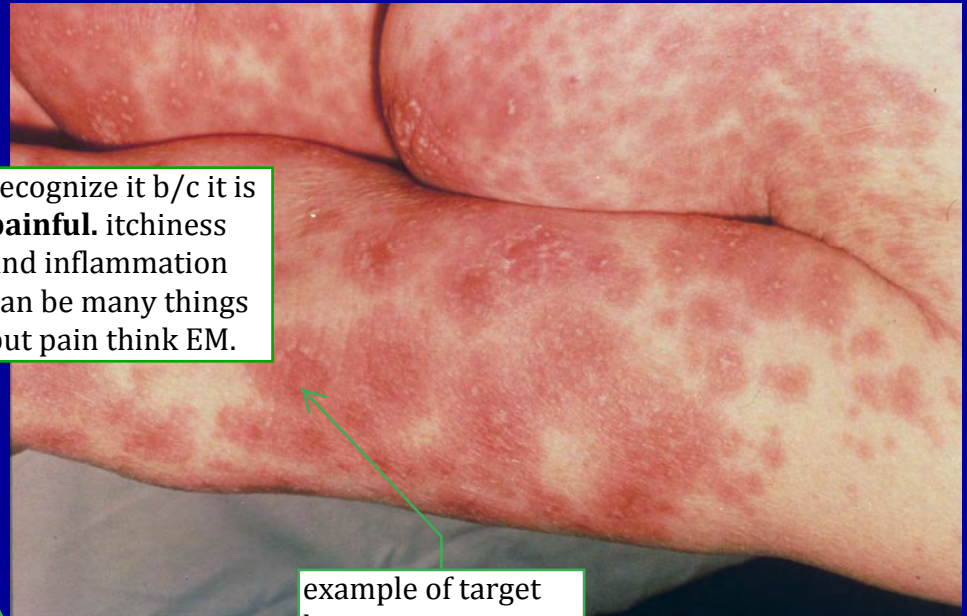
target lesions = erythema multiforme

recognize it b/c it is **painful**. itchiness and inflammation can be many things but pain think EM.

example of target lesion.

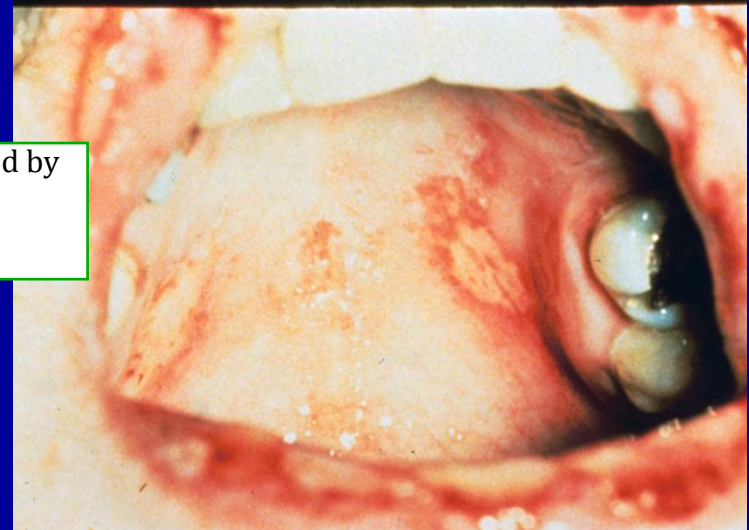
multiforme because you can get a variety of lesions.

if you don't stop this you might end up in a burn unit because your skin will continue to die and peel off.



# ERYTHEMA MULTIFORME

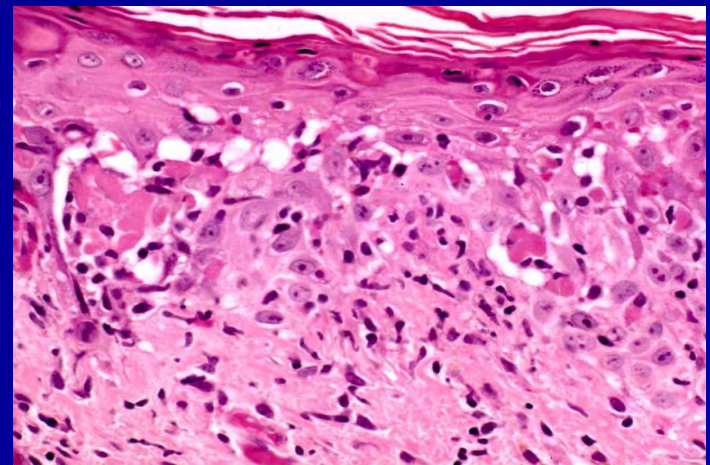
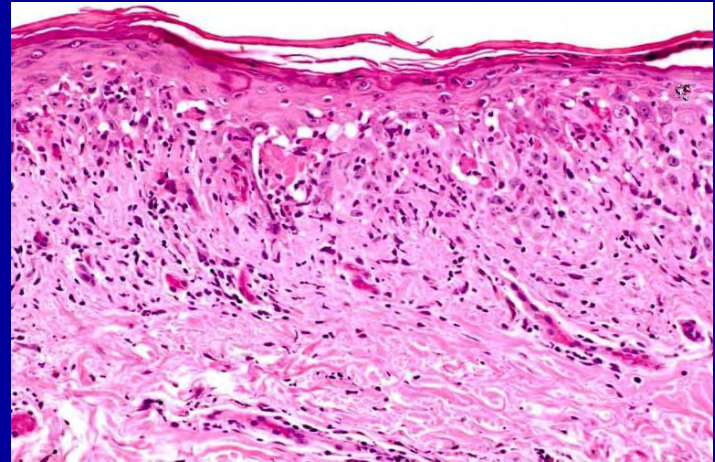
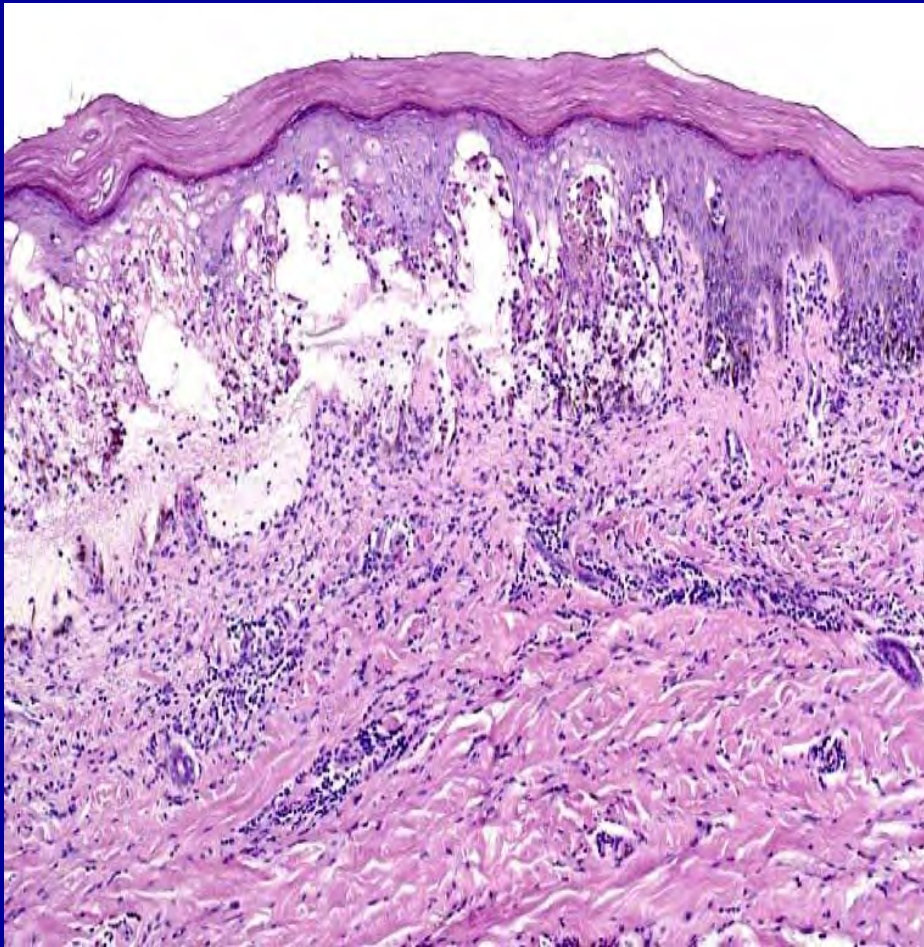
- Steven-Johnson  
(Mucosa)
- Toxic epidermal necrolysis entire epidermis is killed.
- Pathogenesis:
- Etiology:
  - Infection (HSV, mycoplasma)
  - Medications (sulfa, NAIDS)



usually caused by infection or medication.



# ERYTHEMA MULTIFORME



lymphocytes everywhere and associated with degenerating, necrotic keratinocytes.

# DRUG REACTIONS:

- 2 % of inpatients
- 3/1000 Rx
- Within 1 week
- Amoxicillin, bactrim, ampicillin
- Penicillin, barbiturates, benzodiazepines, thiazides

Happen to 2% of inpatients, within one week of giving a variety of drugs. Can lead to any type of dermatitis. ALWAYS keep it at the back of your mind.



Pathogenesis includes  
hypersensitivity types I-IV  
Also includes non-immune causes  
(overdose, photosensitivity, etc.)

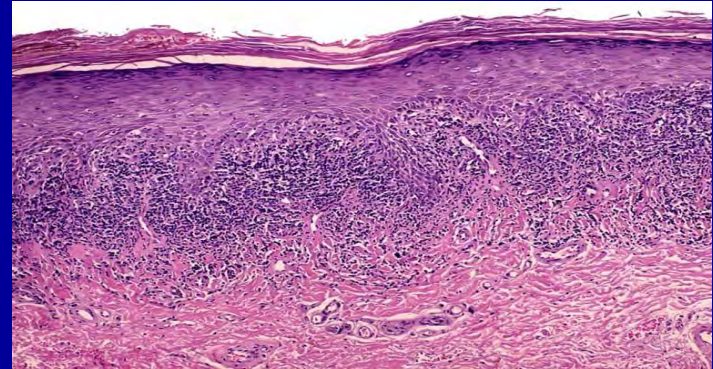
# DRUG REACTIONS PATHOGENESIS

- Immune:
  - I: IgE (penicillin)
  - II: cytotoxic
  - III: immune-complex (vasculitis)
  - IV: cell mediated (vitamin K)
- Non-immune:
  - Activation (mast cell degranulation)
  - Overdose
  - Side effects (alopecia/ChemoRx)
  - Photosensitivity (tetracycline)
  - Others

# DRUG REACTIONS MORPHOLOGY

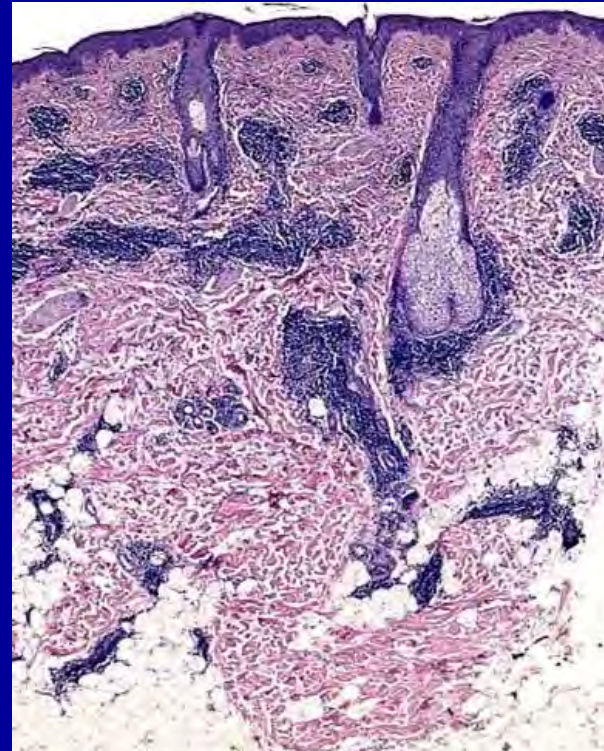
- Lichenoid

Typically get **vasculitis**, lichenoid



- Superficial and deep perivascular

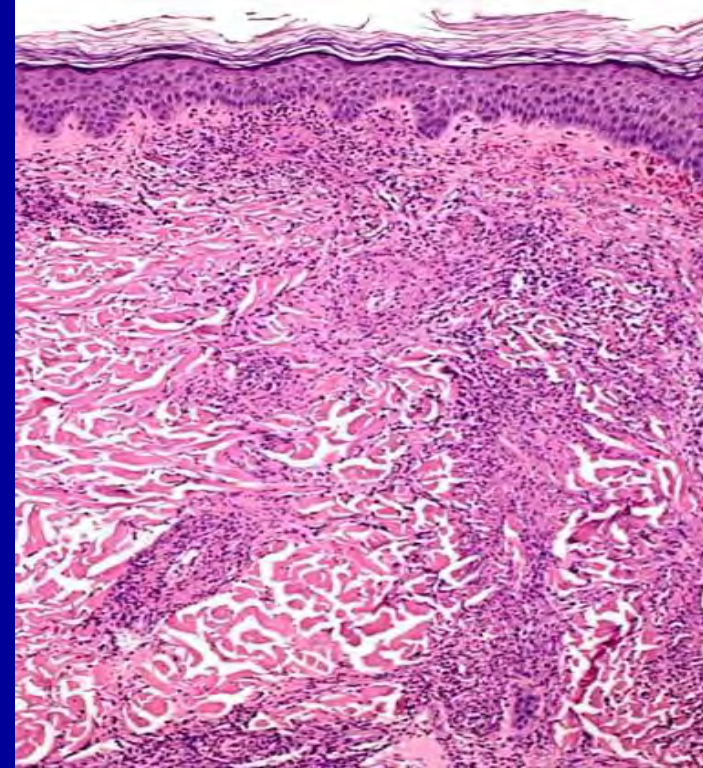
Again, we can look at any pattern of inflammation and it can be caused by a drug.



# DRUG REACTIONS MORPHOLOGY



palpable purpura- red  
palpable lesions on skin.



## VASCULITIS

when inflammation hits vessels in  
the dermis.



READ:

# LUPUS ERYTHEMATOSUS

classic connective tissue disease.

- Multiple organs
- **Cutaneous or systemic**
- Diagnosis:
  - Clinical
  - Histologic
  - Biochemical
- Pathogenesis:
  - HLA
  - Medications (hydralazine, procainamine, D-penicillamine)
  - Hormonal
  - Autoimmunity

diagnosis supported by histology.

# LUPUS ERYTHEMATOSUS

- Chronic:
  - Sun exposed (malar)
  - Well demarcated
  - Erythematous
  - Round (“discoid”)
  - Scale and atrophy

"discoid lupus"  
skin lesions look  
like disks.



## Chronic (discoid) Lupus:

- Can be cutaneous or systemic
- Preferentially attacks sun exposed skin
- Well demarcated, round rashes
- **atrophic epidermis, interface dermatitis, inflammation** around skin structures like hair follicles (can lead to alopecia)



# LUPUS ERYTHEMATOSUS

- Subacute:
  - Erythematous
  - Symmetrical
  - Trunk and arms
  - Systemic involvement

they can have systemic involvement vs discoid that usually does not evolve.

looks same in both sides.

key: systemic involvement.





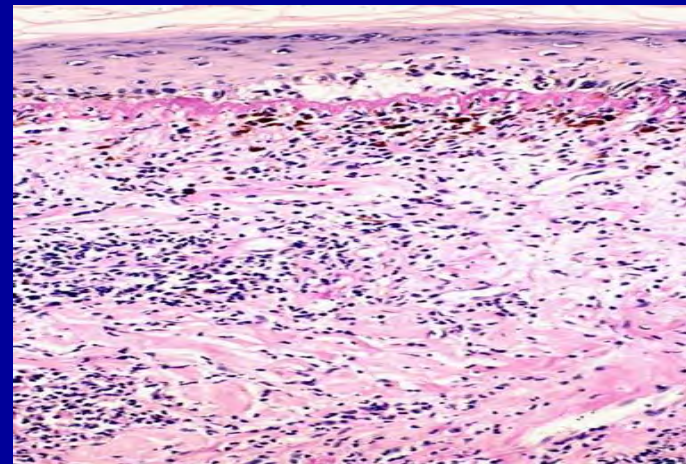
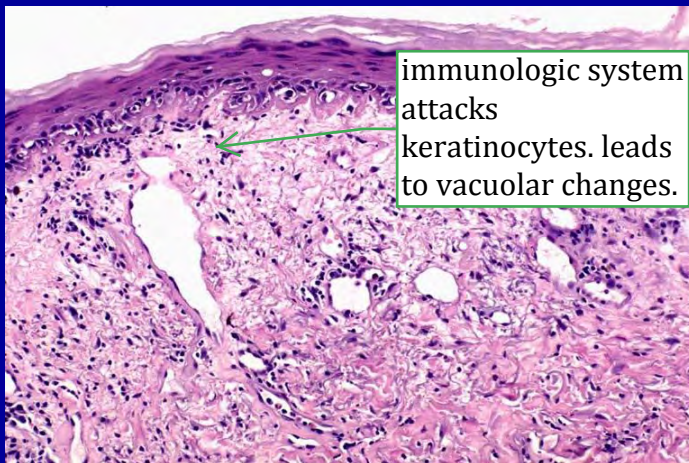
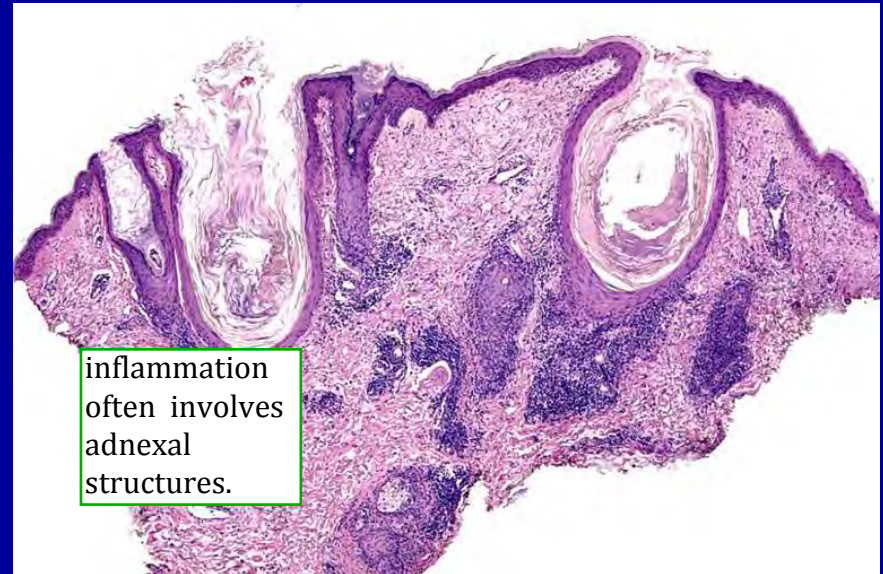
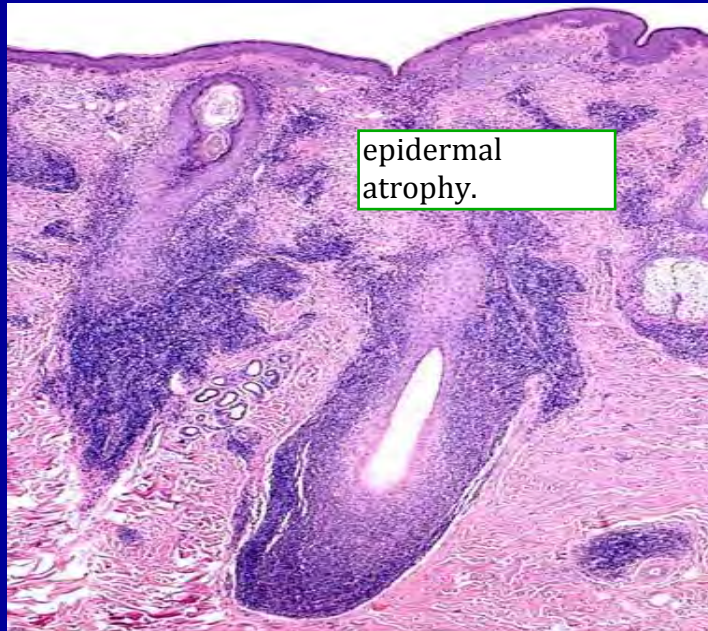
# LUPUS ERYTHEMATOSUS

- Systemic

typical patient comes with kidney issues with a story of just coming back from the beach with a butterfly rash.



# LUPUS ERYTHEMATOSUS: HISTOLOGY



# ACNE

- Disorder of the pilosebaceous unit
- Face, neck, back
- Onset:
  - Puberty
  - Neonatal
- Etiology:
  - Propionibacterium acnes (acids)
  - Occlusion
  - Stress
  - Hormones

Causes include propionibacteria, occlusion, stress, hormones. We honestly don't know what really causes it.



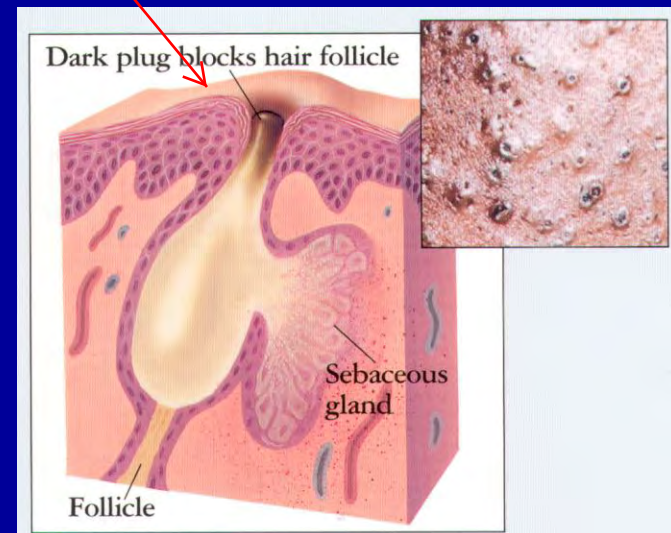
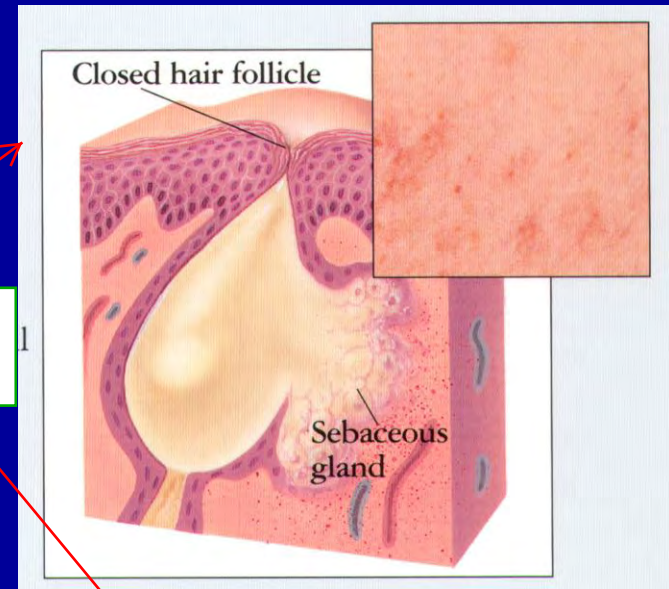
# ACNE

- Morphology:
- Comedo
- Papule/pustule/nodules/  
cysts

hair follicle is dilated and obstructed. can be closed. if opened the sebum (fat) is oxidized and we get blackheads.

if pus

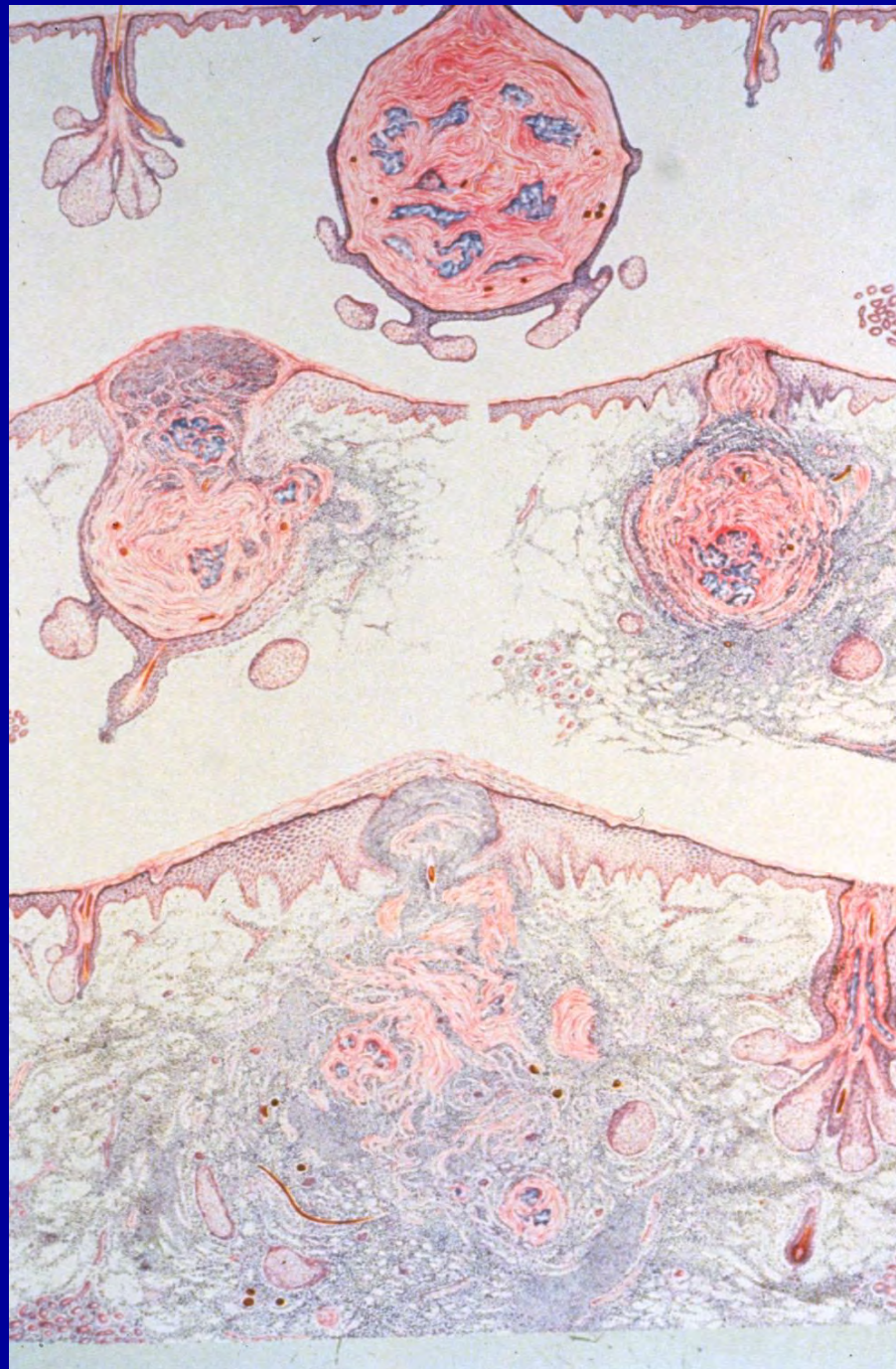
if more than 5mm



hair follicle gets  
plugged with  
sebum and dilates.

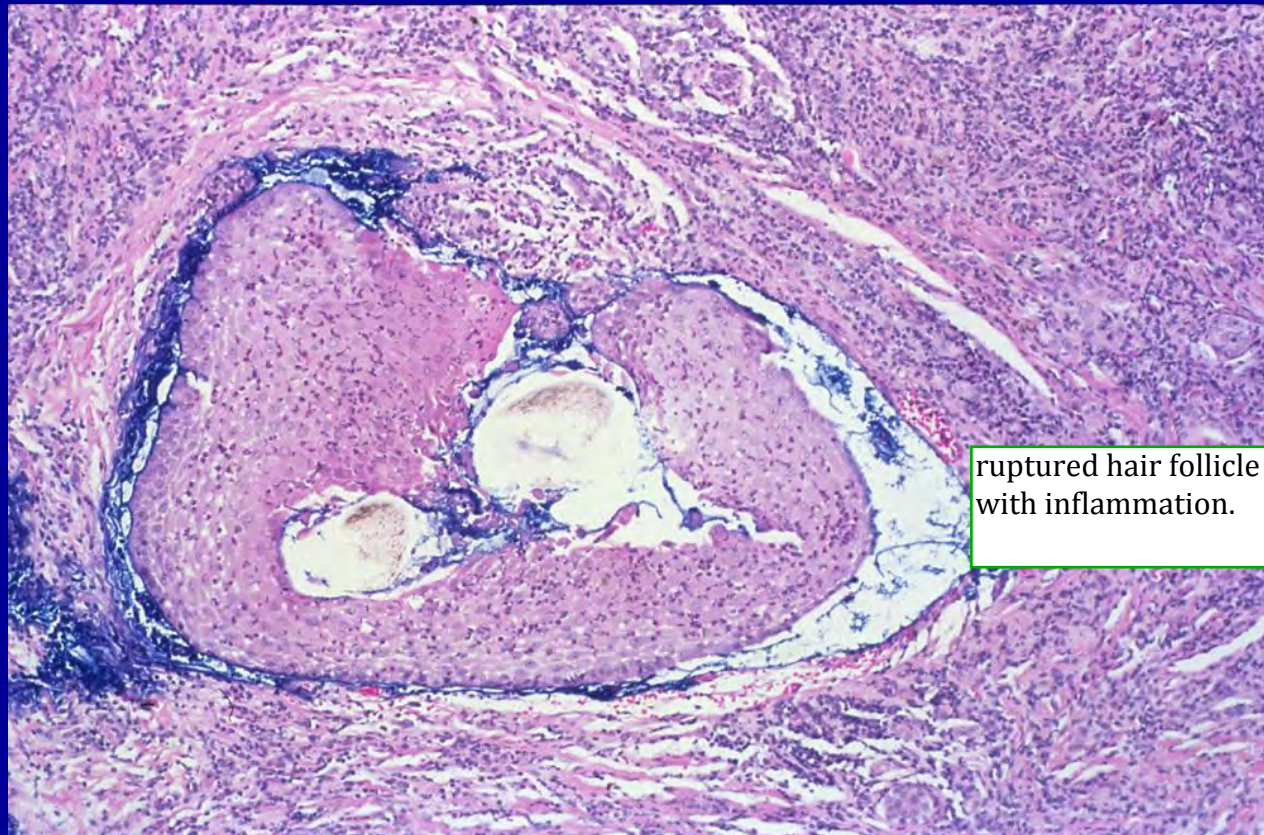
they break and  
the sebum and  
keratinocytes get  
out, leading to  
inflammation

finally, you get  
a scar.





# ACNE: HISTOLOGY





# ERYTHEMA NODOSUM

- Panniculitis inflammation in subcutaneous tissue
- Bilateral painful/tender painful nodules in legs.
- Erythematous/violaceous nodules
- Lower legs
- Arthralgias important because it can be the manifestation of a systemic disease like sarcoidosis and lymphoma.



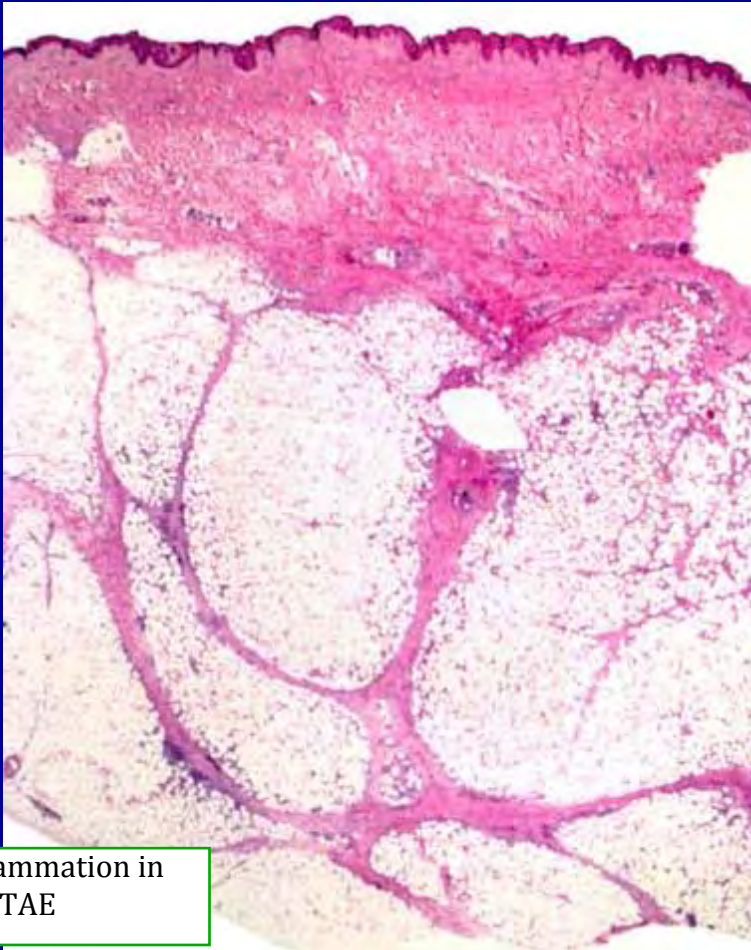
**- Inflammation of the subcutaneous fat**  
- Tend to see it in the lower legs (both sides)  
- Erythema nodosum is an indication something more systemic is wrong (sarcoid, Hodgkin, viral, bacteria, etc.)

# ERYTHEMA NODOSUM

- Association:
  - Bacterial (TB, leprosy)
  - Fungal (histoplasma)
  - Viral
  - Medications (contraceptives, sulfas)
  - IBD
  - Sarcoidosis
  - Hodgkin disease

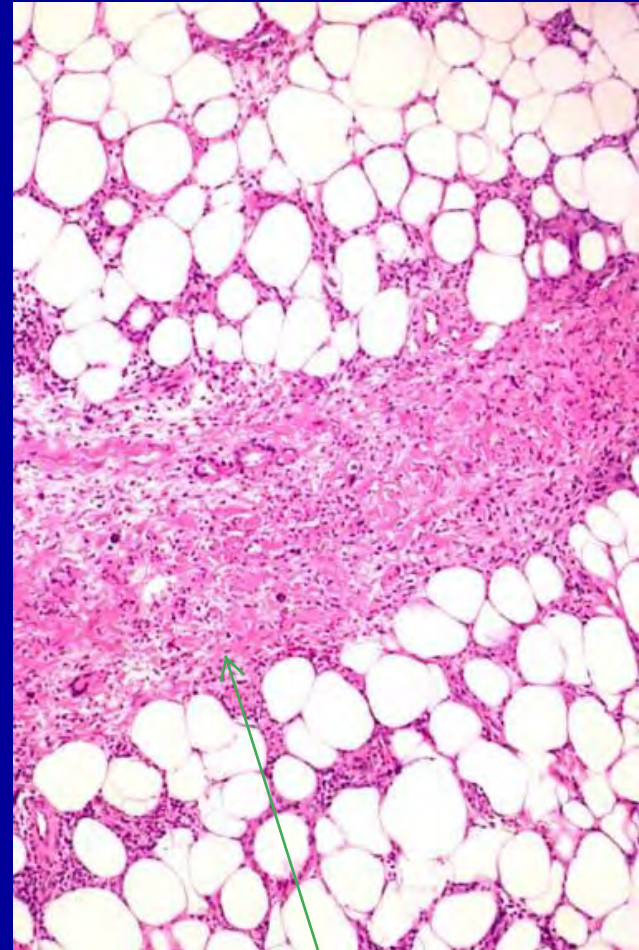
She just read the list and said: if pathologist says erythema nodosum you go back to the patient and figure out what s/he has.

# ERYTHEMA NODOSUM



inflammation in  
SEPTAE

acute edema and  
neutrophils.



chronic- fibrosis.





Description of lesion:

- Arm
- Erythematous macules- Some areas are flat with redness
- Vesicles- blistering of the skin
- Is the patient in pain? Uncomfortable but not in pain
- Are there systemic findings? No, but he might be camping recently around a lot of trees.
- Diagnosis: **acute contact dermatitis**
  - o Note linear pattern- means that he probably touched something.



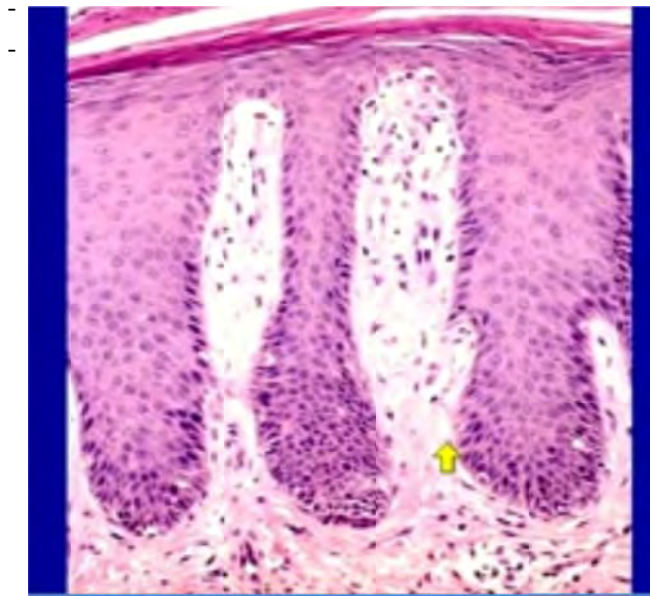
Description of lesion:

- Diffuse redness and areas of elevation (nodules) across the lower leg
  - o The rash is in both legs.
- Patient is complaining of pain. Can't sit because of pain.
- Does the patient have bloody diarrhea? Not to Matt's knowledge.
- Diagnosis- **erythema nodosum**.
  - o Need to find what is wrong with the patient! Probably something systemic going on.



Description:

- Localization- elbows, superficial
- Kind- plaque, erythematous, scaly
- Look at the whole patient- may have pits on the nails
- Diagnosis- psoriasis
- Histology- psoriasiform hyperplasia



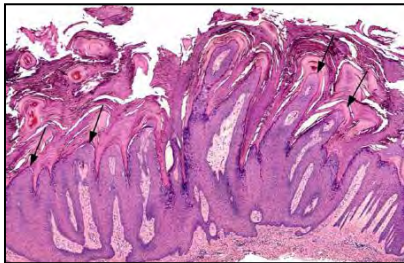


### Describing Lesions:

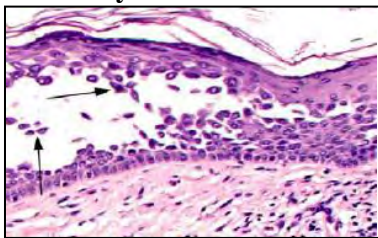
1. **Macule:**
  - a. Change in skin color
  - b. No elevation or depression
  - c. Nonpalpable
2. **Elevated lesions:**
  - a. **Papule** = elevated lesion under 5 mm in diameter
  - b. **Nodule** = elevated lesion over 5 mm in diameter
  - c. **Plaque** = less elevated but surface greater than 1 cm in diameter
3. **Wheal** = pale (white color) papule or plaque that comes and goes
4. **Blisters:**
  - a. **Vesicle** = fluid filled and under 10 mm
  - b. **Bulla** = fluid filled and greater than 10 mm
5. **Pustule** = blister filled with pus
6. **Crust** = serous, purulent exudate oozing out of a lesion
7. **Scale** = dry, plate-like scales coming off
8. **Lichenification** = thickened, rough

### Microanatomy:

1. **Acanthosis** = thickening of epidermis
2. **Atrophy** = thinning of epidermis
3. **Hyperkeratosis** = increased stratum corneum
4. **Hypergranulosis** = increased stratum granulosum layer (topmost layer before keratin)
5. **Papillomatosis** = hyperplasia of dermal papillae cause wrinkling:



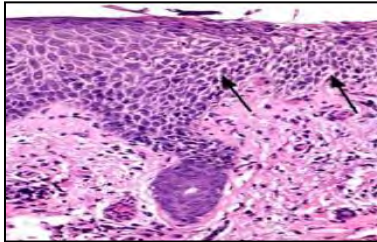
6. **Acantholysis** = loss of intercellular connections:



7. **Psoriasiform** = too much epidermis but pushes **down**:



8. **Spongiosis** = epidermis begins to absorb fluid:

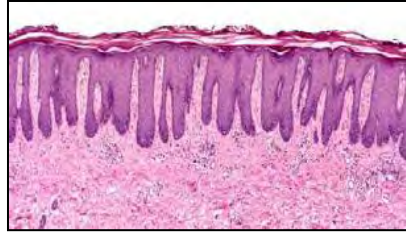


#### Biopsy:

1. **Reasons to biopsy:**
  - a. **Unknown diagnosis** (inflammatory disease, neoplasm)
  - b. **Systemic disease** (vasculitis, amyloidosis → skin biopsy easier than bronchus)
2. **Types of biopsy:**
  - a. **Shave** (epidermis and some dermis)
  - b. **Punch** (gets all layers but small area)
  - c. **Ellipse** (cuts off the whole lesion)
  - d. **Major excision** (goes all the way to muscle)

#### Diseases:

1. **Dermatitis:**
  - a. Need to know location, superficial vs. deep, and cellularity
  - b. **Types** [see slide 25]:
    - i. **Spongiotic** = eczema
    - ii. **Perivascular** = inflammation around vessels
    - iii. **Psoriasiform** = psoriasis
    - iv. **Interface-lichenoid** = inflammation between epidermis/dermis
    - v. Panniculitis = inflammation of dermis (mainly lobules vs. septa)
  - c. **Allergic contact dermatitis:**
    - i. Type IV hypersensitivity reaction via Langerhans cells
    - ii. **Acute** see macules (**flat**) and some papules (**small**) and vesicles (**fluid**)
    - iii. **Chronic** see more scaling and **lichenification**
    - iv. Over time get **psoriasiform hyperplasia** and parakeratosis
2. **Psoriasis:**
  - a. Affects 1-2% of population
  - b. Main areas are scalp, nails, and extensor surfaces (elbows/knees)
  - c. Get **scaly erythematous plaques**
  - d. Histology: **psoriasiform hyperplasia**, hyperkeratinosis, hypogranulosis



3. **Erythema multiforme:**
  - a. **Medical emergency**, typically affects **children**/young adults
  - b. Get multiform papules and plaques
  - c. Lesions have red ring/pale ring with dusky centers
  - d. **Causes:**
    - i. **Infection** (HSV, mycoplasma)
    - ii. **Medications** (sulfa, NSAIDs)
  - e. Mainly due to immune complex and lymphocytes invading everywhere
4. **Lupus erythematosus:**
  - a. Can be cutaneous or systemic
  - b. Preferentially attacks sun exposed skin
  - c. Well demarcated, round rashes
  - d. Histology: **atrophic epidermis, interface dermatitis, inflammation** around skin structures like hair follicles
5. **Acne:**
  - a. Causes include propionibacteria, occlusion, stress, hormones
  - b. **Comedo** = dilated hair follicle (black head)
  - c. Pustule is when closed hair follicle fills with neutrophils → turns into nodule
6. **Erythema nodosum:**
  - a. **Inflammation of the subcutaneous fat**
  - b. Tend to see it in the lower legs (both sides)
  - c. Erythema nodosum is an indication something more systemic is wrong (sarcoid, Hodgkin, viral, bacteria, etc.)
7. **Drug reactions:**
  - a. Happen to 2% of inpatients, within one week of giving a variety of drugs
  - b. Pathogenesis includes hypersensitivity types I-IV
  - c. Also includes non-immune causes (overdose, photosensitivity, etc.)
  - d. Typically get **vasculitis**, lichenoid