INFLAMMATORY DISEASES OF THE SKIN

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Normal Anatomy

notice the 3 layers: epidermis, dermis and subcutaneous tissue

- Epidermis
- Stratum corneum
- Dermis
- Subcutaneous tissue
- Hair follicle
- Sebaceous gland
- Blood vessels
- Nerve fiber
Normal Anatomy

dermis (pink because it is collagen)

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

epidermis
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.

keratinocytes die here.

stratum corneum

spinosum-desmosomes look like spines. form most of the epidermis.

stratum spinosum (Lamellar granules)

filagrin is the glue that keeps keratinocytes together.

stratum granulosum (Filaggrin)

base: keratinocytes that divide and will give origin to keratinocytes at the top.

stratum basalis
EPIDERMIS

KERATINOCYTES

LANGERHANS CELLS

Langerhans cells = immune system. APC cells of epidermis.

MERKEL CELLS

Merkel cells = neuroendocrine component. role not well known.

MELANOCYTES

"guys with the white cytoplasm". produce melanin "your natural sunscreen"
Normal Anatomy

DERMIS

collagenous tissue
SUBCUTANEOUS TISSUE

Fat, divided into lobules and septae. Inflammation can include either lobules or septae.
ADNEXAL STRUCTURES

Normal Anatomy

- 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
FUNCTIONS

• External organ protection:
  – Impermeable
  – Melanin

• Temperature control

• Vitamin D

The skin is a very active layer: it protects, helps in temp. control and even produces things!
Describing lesions:
Macule
a. Change in skin color
b. No elevation or depression
c. Nonpalpable

MACULE: Coloration, circumscribed
Elevated lesions: plaques, papules and nodules.

- **PLAQUE**: Elevated, > 10mm (surface larger than height)
- **PAPULE**: Elevated, < 5mm
- **NODULE**: Elevated, > 5mm
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 hypeplastic and becomes rough (where you scratch a lot, for instance)
ACANTHOSIS

thickening of the epidermis.

normal thickness is shown here.

ATROPHY

thinning of the epidermis.
MICROSCOPIC TERMS (II)

HYPERKERATOSIS
Orthokeratosis: normal keratin
Parakeratosis: nuclei Stratum corneum

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

1. Hyperkeratosis = increased stratum corneum

ulcer - loss of epidermis.

abnormal keratinocytes.
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
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

• **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.

PSORIASIFORM DERMATITIS
increased thickening of the epidermis

PERIVASCULAR DERMATITIS
inflammation around vessels

INTERFACE- LICHENOID DERMATITIS
inflammation between epidermis/dermis. "band-like"
DERMATITIS PATTERNS:

**PANNICULITIS**

Inflammation in subcutaneous tissue. Classify as lobular or septal.

**VASCUITIS**

Inflammation that targets vessels.
ALLERGIC CONTACT DERMATITIS

• Morbidity
• Leading occupational disease
• Mostly irritant mechanisms
• Type IV immune-reaction:
  – Sensitization
  – Elicitation
• Langerhans cells
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)
PSORIASIS

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

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

raised and surface larger than height-plaque!
PSORIASIS

stratum corneum
ERYTHEMA MULTIFORME

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

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

**Example of target lesion.**

**Target lesions = erythema multiforme**

MEDICAL EMERGENCY!!!! Treat with steroids.

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

*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

Pathogenesis:

Etiology:
- Infection (HSV, mycoplasm)
- Medications (sulfa, NAIDS)
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
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

VASCULITIS

palpable purpura - red palpable lesions on skin.

when inflammation hits vessels in the dermis.
LUPUS ERYTHEMATOSUS

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

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

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

- Epidermal atrophy.
- Inflammation often involves adnexal structures.
- Immunologic system attacks keratinocytes, leading to vacuolar changes.
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:** hair follicle is dilated and obstructed. If opened, the sebum (fat) is oxidized and we get blackheads.
- **Papule/pustule/nodules/cysts**
  - If pus
  - If more than 5mm
hair follicle gets plugged with sebum and dilates.

you break and the sebum and keratinocytes get out, leading to inflammation.

finally, you get a scar.
ACNE: HISTOLOGY

ruptured hair follicle with inflammation.
ERYTHEMA NODOSUM

- Panniculitis
- Bilateral painful/tender
- Erythematous/violaceous nodules
- Lower legs
- Arthralgias

- 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
ERYTHEMA NODOSUM

inflammation in SEPTAE

acute edema and neutrophiles.

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**
  - Note linear pattern- means that he probably touched something.
Description of lesion:

- Diffuse redness and areas of elevation (nodules) across the lower leg
  - 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**.
  - 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 propioinibacteria, 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