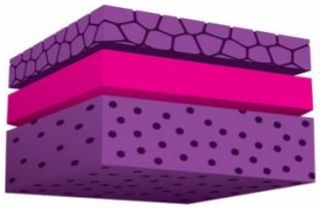

THE GRENZ ZONE℠

DISSECTING DERMATOLOGY DIFFERENTLY

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Contents

1 – Intro/Anatomy of skin, hair and nails

Vital Functions

- Sensation, barrier, immune surveillance, UV protection, thermoregulation

Fun facts

- The skin is the largest human organ, 15% of a person's body weight
- Skin ***cancer*** = most common cancer worldwide; affects 1 in 5 people
- Our skin is constantly being renewed, with the epidermis turning over q40-56 days, results in average person shedding **9 lbs** of skin yearly

Skin thickness varies based on….

- **Location**: epidermis is thickest on palms/soles at ~ 1.5mm (thickness of a penny), thinnest on eyelid/postauricular at ~ 0.05mm (paper)
- **Age**: Skin is relatively thin in children, thickens up until our 30's or 40's, and then thins out thereafter.
- **Sex:** Male skin is generally thicker than female skin in all locations

Overall Anatomy

- Epidermis
- Dermoepidermal junction (DEJ)
- Subcutaneous tissue

The Epidermis

Layers

- **Stratum corneum** (most superficial)
  - Serves as a **barrier**, helping to keep the good stuff in (such as water) and the bad stuff out such as bacteria and allergens.
  - Structure is analogous to bricks and mortar (corneocytes=bricks which are embedded in the mortar of lipids such as ceramides)
  - Not present on mucosal sites
- **Stratum lucidum**
  - Only present on the palms/soles, appears clear on H&E
- **Stratum granulosum**
  - Produces the cornified cell envelope (composed of lipids and proteins; helps skin function as a mechanical and water barrier)
  - Not present on mucosal sites
- **Stratum spinosum**
  - Superficial to stratum basale, named for spiny-appearing desmosomes between cells
  - Keratins 1 and 10 are expressed in this layer and are mutated in epidermolytic hyperkeratosis (aka bullous congenital ichthyosiform erythroderma)
- **Stratum basale**
  - Located just above the basement membrane, is composed of 10% stem cells
  - Keratins 5 and 14 are expressed in the basal layer and are mutated in patients with epidermolysis bullosa simplex (EBS)

Major CELL TYPES of the epidermis

1. **Keratinocytes** (KC) ("squamous cells", "epidermal cells")
   - Make up most of epidermis, produce keratin
2. **Melanocytes** (MC)
   - Neural-crest derived
   - Normally present in ratio of 1 MC : 10 KC's
   - Synthesize and secrete pigment granules called **melanosomes**
   - *** Different races and skin types actually have the ***same*** **amount of melanoCYTES** but differ in the number, size, type, and distribution of melanoSOMES, with fairer skin types having more lighter-colored **pheo**melanin and darker skin types having more of the dark **eu**melanin.
3. **Langerhans Cells**
   - Consist of 3-5% of the cells in the stratum spinosum, are derived from bone marrow, function as antigen-presenting cells
   - Stain with S-100, CD1a, vimentin, Langerin, peanut agglutinin ○ Contain Birbeck granules, which appear on electron microscopy as tennis racket-shaped organelles
   - **Ultraviolet radiation decreases the number of Langerhans cells**, which may explain the mechanism of PUVA/narrow-band UVB in

decreasing inflammation in psoriasis

4. **Merkel Cells**
    - Located just above the basal cell layer of the epidermis and in the bulge region of hair follicles
    - Believed to function as slow-adapting touch receptors
    - Give rise to Merkel cell carcinomas, which are rare, aggressive skin cancers on the head and neck of elderly Caucasian patients

The DERMOEPIDERMAL JUNCTION (DEJ) – to be discussed in the vesiculobullous podcasts

The Dermis

Papillary dermis (superficial)

- Appears wavy in 2D on biopsy specimens, as papillary dermis interdigitates with downward projections of epidermis ("rete ridges")
- Contains the **sub-papillary plexus**, which contains arterioles, capillaries, venules, lymphatics, and nerves
- Contains Meissner corpuscles which sense touch and pressure.

Reticular dermis (deeper)

- Has its own plexus but contains larger blood vessels.
- Clinical correlation: **Clark's levels for melanoma staging**
    - Level 1 = in situ in the epidermis
    - Level 2 = tumor reaches papillary dermis
    - Level 3 = tumor fills papillary dermis
    - Level 4 = tumor reaches reticular dermis
    - Level 5 = Tumor invades subcutaneous tissue

Breslow's depth: measures tumor depth in mm's from the granular layer or base of an ulcerated melanoma to the bottom of the tumor

Dermal Cell Types

- **Fibroblasts** - produce collagen, elastin, and ground substance.
    - **Collagen** - 70% of the dry weight of skin, important in wound healing (Type III fetal collagen ❼stronger type I collagen)
        - **COLLAGEN 1 AND 3 SYNTHESIS IS DOWNREGULATED BY CORTICOSTEROIDS (❼ATROPHY) AND UV LIGHT (❼HOTOAGING). UPREGULATED BY RETINOIC ACID.**
    - **Elastic fibers** – help skin elasticity
        - Decrease in number with aging and are also defective in Marfan's syndrome due to fibrillin-1 mutations.
    - **Ground substance** – glycosaminoglycans (GAGs) and mucopolysaccharides
        - E.g. hyaluronic acid ❼maintains water within the dermis and is often used in many cosmetic fillers
- **Adnexa** – hair follicles, sebaceous and apocrine glands, eccrine glands
- Other cells/tissues: blood vessels, lymphatics, and nerves

THE SUBCUTANEOUS TISSUE ("Sub-Q")

- is composed of lipocytes and fibrous septa containing collagen and larger blood vessels and nerves.
- Functions as an **energy store**, an **insulator** that protects underlying muscles and bones, and as an **endocrine organ** where aromatase converts androstenedione to estrone (possible link between obesity and breast cancer)

THE ADNEXA (skin appendages)

Eccrine Glands

- Release **sweat** to help regulate body temperature by cooling the skin when the sweat evaporates.
- Located nearly everywhere on the skin except for the lips, the external auditory canal, the glans penis, and the labia minora and clitoris.
- The total mass of eccrine glands in our body is about the same as one kidney and can make up to 1.8 liters of sweat in an hour!
- NOT associated with the hair follicle
- Have **muscarinic acetylcholine receptors** which bind acetylcholine released from sympathetic nerves, which explains why we sweat when we're nervous
    - Nervous situation ❼sympathetic nerves are activated ❼release acetylcholine ❼binds receptors on our eccrine sweat glands ❼sweat is released ❼you're a hot mess
    - Explains why botulinum toxin injections, which block acetylcholine release, are effective for hyperhidrosis patients.

Apocrine Glands

- Locations ("4 A's") - the axilla, areola of the nipple, the anogenital region, and the auditory canal where they contribute to cerumen (earwax) formation
    - Also make up the Moll's glands of the eyelids (not to be confused with Meibomian glands, which are of sebaceous origin)
- Secrete odorless variety of proteins, carbohydrates, ammonia, lipids, and iron ➡digested by bacteria that create odorous byproducts ➡body odor
- Apocrine glands begin to function at puberty and are mainly stimulated by *sympathetic* adrenergic stimuli.

Sebaceous Glands

- Associated with hair follicles (unlike eccrine glands)
- Located everywhere except the palms and soles (which are hairless)
- Secrete sebum (composed mostly of triglycerides, wax esters, squalene, and free fatty acids)
- Under **hormonal** influence rather than neurologic influence as is seen with eccrine and apocrine glands

Hair follicles

- Fun facts
    - Humans contain 5 million hairs on average
    - On average, people have 100,000 hairs on the scalp and lose 100 scalp hairs daily.
        - Blondes have thicker hair (~120k), red heads have ~80k
        - Hair on the scalp grows roughly 1 cm/month
    - Hair color depends on melanocytes in the hair bulb transferring melanosomes, which are pigment granules, to the keratinocytes in the bulb matrix.
    - **Darker** hair has mostly **eu**melanin, whereas **blonde** or **red** hair has more **pheo**melanin.
- *Add diagram of hair anatomy?

Hair anatomy

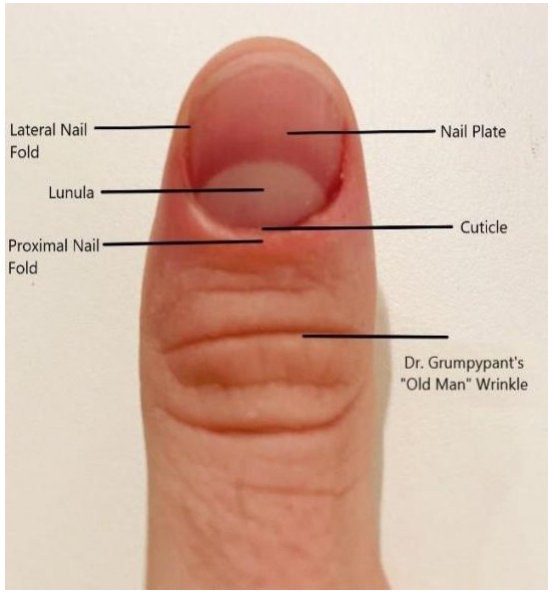
- 3 zones: infundibulum, isthmus, and inferior segment
- **Infundibulum**: from surface down to sebaceous gland insertion
    - **A**pocrine gland insertion is **A**bove sebaceous gland insertion
    - Location of inflammation in lichen planopilaris
- **Isthmus**: from sebaceous insertion down to the Hair **bulge** (location of **arrector pili insertion)**
    - Location of inflammation in discoid lupus (**D**iscoid = **D**eeper)
- **Inferior segment** – everything inferior to hair bulge
- Hair bulb
    - Located in deep dermis or superficial sub-Q for anagen hairs
        - ✦ Want to undermine beneath this plane in surgery, otherwise risk permanent hair loss (e.g. beard, scalp)
- Layers of hair from outside to in…
    - Glassy membrane (outermost)
    - Outer root sheath
    - Inner root sheath – itself has 3 layers…
        1. Henle's layer (outermost)
        2. Huxley's layer ("Henle hugs Huxley")
        3. Cuticle (innermost)
    - Hair shaft – also with 3 layers
        - Cuticle (outermost) – gives hair its shine after using conditioner
        - Cortex
        - Medulla

Hair growth

- Anagen phase (active growth)
    - Normally 85-90% of scalp hairs are in anagen phase; lasts 2-6 years on average.
    - Fractured by chemotherapy in anagen effluvium
- Catagen phase (involution phase)
    - < 1% of scalp hairs are in catagen phase at any given time due to its short length of approximately 2 weeks.
- Telogen phase (resting phase)
    - Lasts 3-5 months and thus 10-15% of hairs are in telogen phase in a normal patient.
    - Telogen effluvium = early cessation of anagen phase so that >20% of hairs are in telogen phase.

- Occurs approximately 3-5 months after a trigger such as an emotionally stressful event, severe illness, or pregnancy (prolonged anagen phase until delivery).

Nails



- Helpful in dermatology because specific nail changes are caused by a variety of conditions including psoriasis, alopecia areata, renal disease, and liver disease, amongst others

- Fingernails grow 2-3 mm per month on average and take 4-6 months to regrow its entire length.
- Toenails grow approximately 1 mm per month and take 12 to 18 months to regrow.
- **Nail plate** – hard part of the nail
- **Lateral nail fold** – the skin abutting the lateral sides of the nail plate
- **Proxima nail fold** – skin proximal to cuticle
- **Cuticle (eponychium)** - cornified epithelium overlying the lunula -
  Lunula - white crescent-shaped region under the proximal nail plate - that represents the distal nail matrix.
- **Nail matrix** - underneath the cuticle and proximal nail fold.
  - The proximal matrix forms the top or dorsal nail plate, while the distal matrix forms the bottom or ventral nail plate.
  - Contains melanocytes, therefore melanomas can form in this location.
- **Nail bed** - underneath the nail plate, is distal to the lunula, and does not contain melanocytes.

Basic Histology Terminology

- **Acanthosis** - hyperplasia or thickening of the epidermis and is seen in hyperproliferative conditions such as psoriasis.

- **Spongiosis** - swelling and edema of the epidermis.
  - Spiny desmosomes between cells are visible.

- **Parakeratosis** - represents thickened stratum corneum *with* nuclei present
- **Hyperkeratosis** - thickened stratum corneum *without* nuclei present.

- **Hypergranulosis** - thickening of the granular layer and may be seen in lichen planus.

- **Papillomatosis** refers to multiple finger-like warty projections of the epidermis
  Atrophy thinning of a layer of skin, such as epidermal atrophy seen in lichen sclerosis.

2 – The Dermatology Exam

Important to form good habits for thorough dermatologic H&P

Primary lesions

- Flat lesions
    - Macule (<1cm) – e.g. freckles
    - Patch (>1cm) – e.g. vitiligo
- Raised lesions
    - Papule (<1cm) – e.g. acne papule
    - Plaque (flat and >1cm) – e.g. psoriasis
    - Nodule (rounded and >1cm) – e.g. epidermal inclusion cyst
- Fluid-filled
    - Vesicle (<1cm) – e.g. herpes zoster
    - Bullae (>1cm) – e.g. bullous pemphigoid
    - Nikolsky sign – lateral pressure on unblistered skin causes shearing of epidermis
    - Asboe-Hansen sign – vertical pressure on bullae causes lateral spread; seen with deep bullae
- Purulent lesions
    - Pustules
    - Furuncles ("boil")
    - Carbuncle – coalescing furuncles
- Wheal (hives) – fleshy plaques 2/2 dermal edema

Secondary lesions (when primary lesion is traumatized)

- Excoriations – linear scratch or punctate lesions
- Fissure – crack that reaches dermis
- Erosion – part of epidermis lost (e.g. ruptured vesicle)
- Ulcers – excavations that reach dermis
- Crusts – dry blood, pus, or serum ("scab")

Vascular lesions

- Telangiectasias – small, discrete bv's, blanch with pressure
- Petechiae – **nonblanching** red-brown macules <5mm
- Purpura – nonblanching, >5mm

- If palpable, think about inflammation of lesions
    - Ecchymosis (i.e. bruise)

Other terms

- Scale – pathology in epidermis
- Reticulate = lacy pattern
- Lichenification – accentuated skin lines

Describing rashes (LES T CABS) – adopted from *Derm Notes: Dermatology Clinical Pocket Guide by Anatoli Freiman and Benjamin Barankin)*

- **L**ocation (area of body, flexors/extensors, sun-exposed, symmetrical, lateralized, dermatomal)
- **E**rythema (pink, red, red-brown, violaceous, near black)
- **S**urface (smooth, rough, warty, crusted, scaly)
- **T**ype of lesion (patch, papule, etc)
- **C**olor – also includes hypopigmented or depigmented
- **A**rrangement – how lesions are arranged in relation to one another (e.g. grouped, generalized, unilateral, linear)
- **B**order/shape (well circumscribed vs poorly defined, circular, oval, polycyclic)
- **S**pecial sites (mouth, genitalia, nails, hair)

Get a good history

- HPI of rash/lesion (OPQRST's)
    - Onset
    - Previous episodes

    - Progression of disease since onset
    - Palliating factors (what makes it better)
    - Provoking factors (what makes it worse)
    - Quality of symptoms (itching, burning)
    - Radiation of symptoms
    - Severity of symptoms ("how itchy are you on scale of 1-10")
    - Treatments tried
- PMH
    - Atopic triad (atopic dermatitis, asthma, seasonal allergies)
    - Diabetes – predisposed to infection
- PSH
- Allergies
- Medications
    - Rx, OTC, herbals/supplements, when meds were started, recent dosing changes, changes between generics/brand names
    - Bleeding time affected by: 5 G's (garlic, ginsing, ginger, green tea, gingko), fish oil, vitamin E, saw palmetto, St. John's wort
- FH
- SH
    - Occupation, hobbies, pets, recent travel (hiking),
- Physical
    - Pick a routine for your FBSE and do it the same each time ○ Head to Toe (scalp, ears, face, hands, arms, neck, chest, abdomen, back, top of legs, feet, have pt stand up to examine buttocks, groin, and back of legs)
    - Don't forget to look in mouth
    - Palpate areas where AK's are common (explain to patient why you do this)
    - Always get permission to examine sensitive areas (breasts, groin)
    - Nails/nailfolds if worried for CTDZ

3 – Intro to Reaction Patterns

- Please refer to Dr. Gropper's paper for further details….
    - Gropper, C.A., 2001. An approach to clinical dermatologic diagnosis based on morphologic reaction patterns. *Clinical cornerstone*, *4*(1), pp.1-14.

5 Reaction patterns

1. **Papulosquamous**
    a. Psoriasiform – psoriasis, seborrheic dermatitis, parapsoriasis, mycosis fungoides
    b. Pityriasiform – pityriasis rosea, tinea versicolor, secondary syphilis
    c. Lichenoid – lichen planus, lichenoid drug eruptions
    d. Annular – SCLE, EAC, tinea
    e. Erythroderma – papulosquamous causes (psoriasis, PRP), dermatitis (atopic, ACD, seborrheic, chronic actinic dermatitis), drug reactions, CTCL (Sezary, erythrodermic MF), infections (viral exanthem, Norwegian scabies, SSSS), autoimmune (e.g. BP), physical (e.g. burns)
2. **Eczematous**
    a. Acute – e.g. contact dermatitis
    b. Subacute – e.g. stasis dermatitis
    c. Chronic – e.g. atopic dermatitis
3. **Vascular**
    a. Erythema multiforme
    b. Toxic erythema – viral exanthems, drug eruptions (SJS/TEN)
    c. Scarlatiniform – scarlet fever, SSSS, TSS, Kawasaki DZ
    d. Figurate erythema – EAC, erythema gyratum repens, erythema migrans, erythema marginatum
    e. Urticaria (hives)
    f. Vasculitis
    g. Vasculopathy
    h. Retiform purpura
    i. Vascular growths
4. **Dermal disorders**
    a. Type of inflammatory cells
        i. Histiocytic – sarcoid, GA, NL, leprosy, TB

ii. Lymphocytic – leukemia, lymphoma, lupus, PMLE
iii. Neutrophilic – Sweet's, pyoderma gangrenosum, EED
iv. Eosinophilic – Well's syndrome, eosinophilic pustular follicultiis
v. Mast cell – urticaria pigmentosa

b. Depositional – amyloidosis, calcium, urate, mucin (e.g. myxedema), lipids (e.g. xanthomas)

5. Vesiculobullous

a. Superficial
   i. Subcorneal pustular dermatosis
b. Intraepidermal
   i. Pemphigus vulgaris
   ii. Pemphigus vegetans
   iii. Pemphigus erythematosus
   iv. H-H
c. Subepidermal
   i. BP
   ii. Herpes gestationis
   iii. DH iv. EBA
   v. Darier's DZ
   vi. Grover's DZ

4/5 – Psoriasis

Epidemiology/Pathogenesis

- Bimodal onset (3rd and 6th decade; 75% start <40 yo) but may present at any age
- Caused by environmental triggers in genetically predisposed pt's
  - Triggers **SICK LAB**
    - **S**tress/Smoking
    - **I**nfection (Group A Step, URI)
    - hypo**C**alcemia
    - **K**oebnerization – 25% of pt's, takes 2-6 weeks
    - **L**ithium
    - **A**ntimalarials/ACEI/alcohol
    - **B**eta blockers
    - Others
      - CCB's, NSAIDS, TNF-alpha inhibitors
  - Genetic predisposition
    - PSORS1
    - HLA-Cw6 - a/w 90% of early onset, 50% late onset cases
    - HLA-B27 – associated with sacroiliitis-assoc Pso, PsA, pustular Pso
    - Remember what HLA types encode….
      - HLA A,B,C encode MHC class 1 on Nu cells
      - HLA-DR,DP,DQ encode MHC class 2 on APC's
    - 1 parent affected = 15% risk; both parents = 40% risk

Clinical presentation

- Classically presents with **erythematous plaques** with **silvery scale** on **extensor elbows/knees, trunk/scalp/umbilicus/sacrum**
- Variants
  - **Guttate psoriasis** – raindrop-shaped papules/plaques in younger patients 2-3 weeks after Strep infxn or URI
  - **Palmoplantar** – chronic, thick, painful plaques and fissures on p/s
  - **Inverse** – intertriginous areas

    - **Erythrodermic** – affects >80-90% BSA
    - **Pustular**
        - Impetigo herpetiformis (occurs in pregnancy)
        - Von Zumbusch (generalized, rapid onset, associated with systemic steroid withdrawal)
- Nail psoriasis
    - Seen in 10-80% of patients; a/w PsA (psoriatic arthritis)
    - **Onycholysis, irregular pitting, oil spots, splinter hemorrhages, subungual hyperkeratosis**
- Psoriatic arthritis (PsA)
    - **More likely if nails and scalp affected**; often with am stiffness >30-45 minutes
    - 5 types
        - Oligoarthritis with swelling and tenosynovitis of hands - 6070% of cases.
        - Asymmetric DIP with nail damage
        - Rheumatoid arthritis-like
        - Arthritis mutilans - rarest and most severe.
        - Ankylosing spondylitis, which is associated with HLA-B27.
    - Pearls vs other forms of arthritis on hands
        - **Psoriasis** – affects PIP's, DIP's, usually **spares MCP's**
        - **RA** – affects MCP's, PIP's, **spares DIP's**
        - **OA** – can affect **any joint**
- Enthesitis – inflammation at tendon insertion sites ○ Occurs in 20% of patients, classically affects achilles
- Dactylitis – swelling of finger(s) ("sausage digit"), seen in 15-30% of patients

History/ROS

- Get HPI of lesions using OPQRST's
- Assess for triggers (SICK LAB)
    - Look over patient's medications!
- Do you have joint pain? If yes, do you have morning stiffness and for how long?
- Do you have tendon pain, such as your achilles or elbow?
- How has your mood been? (depression screen)
- Discuss diet/exercise
- Perform FBSE, look in scalp for unidentified psoriasis
- Assess oral mucosa if diagnosis unclear (e.g. Wickham's striae of LP)
- Assess nails for psoriatic nail changes
- Assess finger joints for obvious deformity, point tenderness, limitations in flexion/extension
- Evaluate genitalia if concern for involvement
- Take note of BSA
    - Patient's palm (including fingers) = 1% BSA
    - Rule of 9's for burns

Histology:

- Confluent **parakeratosis**
- **Munro's microabscesses** – collections of **neutrophils** in **stratum corneum**, aka "neuts in the horn"
- **Decreased** or **absent granular layer**
- **Regular acanthosis** with **thinning over dermal papilla**, which contain **dilated capillaries**

Immunology overview

- APC's present antigens to naïve T cells in lymph nodes, which differentiate into Th1 cells for cell-mediated immunity (CMI) or Th2 cells for humoral immunity
- Th1 cells: stimulated by IL-12 and promote CD8 T cells to produce IFN-gamma, IL-2, IL-6, IL-8, IL-12
    - IFN-gamma – activates macrophages to secrete TNF-α, IL-23, and other inflammatory cytokines
    - IL-2 – generates CTL's and NK cells
    - IL-6 – activates acute phase proteins
    - IL-8 – recruits neutrophils
- Th17 cells: stimulated by IL-12 and IL-23 and themselves release IL-17, IL-22, and TNF-α
    - Ustekinumab (Stelara) blocks p40 subunit common to IL-12 and IL-23
    - IL-17 and IL-22 are proinflammatory and increase KC proliferation
    - TNF-α - proinflammatory
- Th2 cells: stimulated by IL-4 and produce IL-10 (anti-inflammatory cytokine which inhibits Th1 cells)

Treatment

Topicals

- **Topical corticosteroids** (TCS) – decrease pro-inflammatory cytokines like TNF-α and increase IL-10
    - Different strengths and formulations (ex. cream, ointment, foams) depending on severity/location
        - SE: atrophy, telangiectasias, striae (permanent)
- **Calcipotriene** – vitamin D analog, decreased KC proliferation and blocks IL-2, IL-6, IFN-gamma
- Others: tazarotene, topical calcineurin inhibitors (TCI's)

UV treatment

- nb-UVB ("narrow band", 311-313 nm)
    - Typically 2-3 tx's/week, >20 treatments usually needed
- bb-UVB ("broad band")
- PUVA (psoralen + UVA)
- Excimer laser (308 nm) – great for scalp

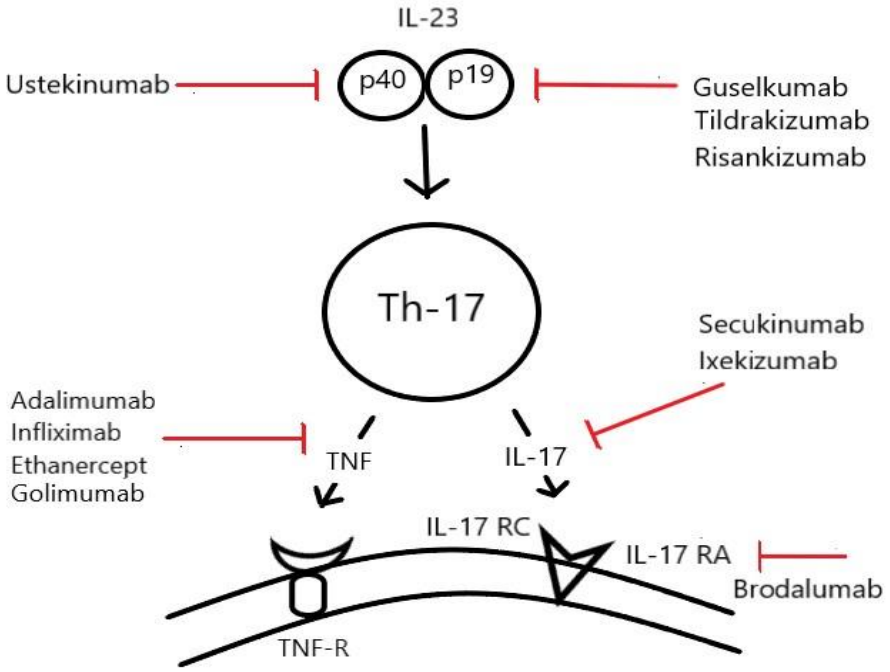
Oral agents – MTX, CsA, Acitretin, apremilast

- **Methotrexate**
    - MOA: inhibits **dihydrofolate reductase** (DHFR) ❼inhibits purine synthesis in **S phase**; since T cells have no purine salvage pathway, they cannot synthesize DNA/survive
    - Dosed 2.5 – 25mg po once weekly; may divide in 2-3 doses q12 hours
    - Give folic acid 1mg daily on days not taking MTX
    - Contra: pregnancy, active infections, liver disease, renal disease, cytopenias
    - SE: GI issues (N/V/D), infections, bone marrow suppression, rarely interstitial pneumonitis
    - Screen: CBC, CMP, hep panel, pregnancy test, HIV (if RF's)
    - Monitor: CBC week 2 and 4, LFT's mo 1 and 2, CBC/CMP q3 mo
        - Liver biopsy at 1.5 – 4g
- **Cyclosporine (CsA)**
    - MOA: complexes with cyclophilin to inhibit calcineurin and reduce IL-2 production
    - Dose: usually started 2.5 mg/kg/day (divided in BID dosing)
    - Contra: impaired renal function, uncontrolled HTN, malignancy, serious infections
    - SE: nephrotoxicity, HTN, GI issues, headache, vertigo, hypertrichosis, gingival hyperplasia, lab changes (BULK up; low Mg)
        - "BULK up" – hyper**B**ilirubinemia, hyper**U**ricemia (❼gout), hyper**L**ipidemia, hyperkalemia
    - Screen: CBC, CMP, hep panel, pregnancy test, quant gold, Mg, uric acid, fasting lipids, urinalysis, blood pressure
    - Monitor: CBC, CMP, lipids, UA, Mg, BP monthly x2 mo then q3mo
    - If Cr increases 30% over baseline, decrease dose
- **Acitretin (Soriatane)**
    - Especially useful for pustular, palmoplantar, erythrodermic Pso
    - Dose: 25-50mg/d
    - Contra: pregnant patients, childbearing age not on contraception, severe liver or kidney DZ, excess ETOH use
    - SE: dry eyes, decreased night vision, dry lips, elevated LFT's, teratogenicity
    - Screen: CBC, CMP, lipid panel, pregnancy test
        - Monitor: same labs at 1 month then q3 month
- **Apremilast (Otezla)**
    - MOA: inhibits phosphodiesterase type 4 (PDE4), leading to **increase in cAMP** levels which **inhibit TNF-α, IL-17, and IL-23**
    - No lab monitoring required, however may want to screen for renal disease if suspected (due to renal dosing)
    - SE: N/D/weight loss, association with depression

PASI (psoriasis area and severity index)

- Score 0-72 based on BSA and 0-4 score for lesion erythema, induration, and desquamation/scale
- PASI-75 = 75% reduction in PASI score (e.g. 40 ❼10)
    - Can calculate easily using Grappa app

Biologics



- Screen patients for hepatitis, TB, malignancy, +/- HIV

TNF-alpha inhibitors

- Additional screening: CHF, demyelinating disease (multiple sclerosis, Guillain-Barre syndrome)
- **Etanercept (Enbrel)**
    - MOA: fully human fusion of TNF receptor linked to Fc portion of IgG, binds soluble and membrane-bound TNF
    - Dose 50mg SQ twice weekly x3 months then weekly thereafter
-
    - Approved for chronic-severe Pso patients age 4+
- **Infliximab (Remicade)**
    - MOA: chimeric mouse-human IgG that binds TNF only
    - Dose: 5 mg/kg **IV** week 0, 2, 6, then q8 weeks
- **Adalimumab (Humira)**
    - MOA: fully human monoclonal IgG Ab against transmembrane TNF receptor
    - Dose: 80mg SQ week 0, 40mg week 1, then 40mg q2 weeks
        - Note: different from dosing for hidradenitis suppurativa (160mg SQ day 1, 80mg day 15, then 40mg weekly starting day 29)
- **Certolizumab pegol (Cimzia)**
    - Dose: 400mg week 0, 2, 4, then q4 weeks
    - Minimal to no placental transfer of drug

IL-17 inhibitors

- **Work quickly**
- Additional screening: IBD, depression (brodalumab)
    - No increased risk for CHF, neurologic disorders (MS), lymphoma
- **Ixekizumab (Taltz)** – inhibits IL-17a
    - Dose: 160mg SQ week 0, then 80mg q2 weeks until week 12, then q4 weeks thereafter
- **Secukinumab (Cosentyx)** – inhibits IL-17a
    - Dose: 300mg SQ weekly x5 weeks then 300mg monthly
- **Brodalumab (Siliq)** – inhibits IL-17 receptor
    - Dose: 210mg week 0, 1, 2, then q2 weeks thereafter

Biologics affecting IL-23

- **Ustekinumab (Stelara)**
    - MOA: blocks p40 subunit common to IL-12 and IL-23

    - Weight based dosing: <100kg patients receive 45mg dose while >100kg patients receive 90mg doses
    - Dose: SQ injection day 0, month 1, then q-3 mo
- **Guselkumab (Tremfya)**
    - MOA: blocks p19 subunit on IL-23 only
    - Dose: 100mg SQ week 0, 4, then q8 weeks
- **Tildrakizumab (Ilumya)**
    - MOA: blocks p19 subunit on IL-23 only
    - Dose: 100mg SQ week 0, 4, then q12 weeks
- **Risankizumab (Skyrizi)**
    - MOA: blocks p19 subunit on IL-23 only
    - Dose: 150mg SQ week 0, 4, then q12 weeks

6-Seborrheic Dermatitis

Epidemiology:

- All ages, typically **post-puberty ages 30-50 y/o**
- On average, 1 in 20 of people affected.

Background:

- Lipophilic commensal yeast**, malassezia furfur** (Pityrosporum ovale)
- Those affected have **higher** levels of **triglycerides** and **cholesterol** and **low** levels of **squalene and FAs** in their sebum
    - Lower levels of P.acnes (converts triglycerides to Free FAs which are antimicrobial to malassezia species)
- Triggers: **Stress, Immunosuppression, Sun Exposure, Heat, Fever**

PEARL: If you see severe seborrheic dermatitis in a pt what are some associated disorders? **Neurologic dz** (e.g. Parkinson's or Epilepsy) & **HIV/AIDs**

Clinical Presentation:

- **Symmetric erythematous patches** with overlying **greasy-yellow scale** affecting the **seborrheic areas (scalp, face, chest, & intertriginous)**. Itching and burning may be present.
    - Adults: M>F, onset in 30s-50s
    - Infants (**"cradle cap"**): one week after birth. Classic erythematous, **itchy patches** with **greasy yellow scale** that **resolve** by **4 months involving face**, **post-auricular, sternum, & intertriginous areas**
- Spectrum of dz
    - **Mild**: dandruff on the scalp w/out erythema
    - **Moderate**: typical clinical picture above with thickening plaques (sebopsoriasis)
    - **Severe**: erythroderma covering 90% of BSA

Differential

- **Scalp (Adult)**
    - **Psoriasis**: more circumscribed thick silvery plaques that are less itchy. Additional lesions elsewhere on body! LOOK for NAIL changes! + FH of Pso, + Pso triggers (SICK LAB)
    - **Tinea Capitis**: younger population (3-7 y/o). broken hairs to go along with erythema as well as posterior lymphadenopathy
    - **Chronic Contact Dermatitis**: >itchy. New hygiene products? Shampoo**.**
- **Face (Adult)**
    - **Rosacea**
    - **Actinic Keratosis**: scale are less yellow/greasy
    - **Lupus**: malar rash spares nasolabial folds vs seb derm involving this location
    - **Dermatomyositis**: heliotrope rash is more violaceous
    - **Tinea faciei**: more annular asymmetrically distributed on check
- **Face (Infant)**
    - **Atopic Dermatitis**: onset later at 1-16 weeks vs seb derm at 1 week. Location on face & flexor surfaces. Look for family hx of atopic triad (atopic derm, allergic rhinitis, asthma). More pruritic and inflammatory
    - **Psoriasis**: uncommon and more adherent scales
    - **Tinea capitis**: look for broken hairs and posterior lymphadenopathy

Diagnosis:

- **KOH Prep** ("**spaghetti & meatballs**"; hyphae & spores)
- **Biopsy –** if diagnosis unclear
- HIV testing – if severe/refractory to treatment

Histology:

- **Regular acanthosis** (regular rete ridge depth + thickened epidermis), **spongiosis, shoulder parakeratosis**

Treatment:

- Scalp: Topical anti-inflammatory + Topical antifungals
    - **Selenium Sulfide (Selsun Blue), Ketoconazole shampoo,** ciclopirox, salicylic acid, or tar shampoo
        - 2-3 x weekly- 5 to 30 minutes
- Face: Topical Antifungals
    - **Ketoconazole vs ciclopirox + 2.5 % hydrocortisone**
- Infants: **Conservative approach w/ no tear shampoo ❼Selenium Sulfide**
- Patient Education:
    - Chronic nature of seb derm: **control** not necessarily cure
    - Maintenance therapy once flare controlled
        - Selenium sulfide vs ketoconazole on weekend
        - Calcineurin inhibitor (tacrolimus & pimecrolimus)

7-Mycosis Fungoides

Epidemiology:

- Most common **~ 50-60 y/o**, but may be younger/older
- Incidence = 1 in 300,000

Background:

- Although lymphoma usually originate in the lymph nodes they can also arise from the skin **❼primary cutaneous lymphoma** (PCL)
-

- 1) Hodgkin's vs 2) non-Hodgkin's
    - **Most common** PCL being **non-Hodgkin's cutaneous lymphoma**
        - **80%** T-cell origin = **CTCL**
        - **20%** B-cell origin = **CBCL**
        - Note: primary cutaneous Hodgkin's lymphoma is very rare
    - CTCL (Cutaneous T-Cell Lymphoma)
        - 1) **65% Mycosis fungoides,** including variant **Sezary Syndrome**
            - Other variants: Folliculotropic, pagetoid reticulosis, granulomatous slack skin
        - 2) **25% CD30+ Lymphoproliferative disorders**
            - Lymphomatoid papulosis (LyP)
            - Cutaneous anaplastic large cell lymphoma (cALCL)
        - 3) 10%
            - 1) Adult T-cell leukemia/lymphoma
            - 2) Subcutaneous panniculitis-like T-cell lymphoma
            - 3) Extranodal NK/T-cell lymphoma nasal type
                - 4) Epidermotropic CD8+ CTCL
            - 5) Cutaneous Gamma-Delta t-cell lymphoma
            - 6) Cutaneous CD4+ small/medium t-cell lymphoproliferative disorder
            - 7) Primary Cutaneous Acral CD8+ T-cell lymphoma
            - 8) Peripheral T-cell Lymphoma

Clinical Presentation:

- **Erythematous**, occasionally pruritic, **oval** scaly **patch** in **sun-protected "bathing suit"** distribution. Classically **slow progression through 3 stages.**

Important to note that not all lesions progress in the following manner and can skip this order!

- 3 Stages
  - **Patch ➐Plaque➐Tumor**
  - **Patch**: round or oval patches 1-5 cm in width and may be annular or polycyclic. Itchy and appear on sun-protected areas (e.g. upper thighs and buttocks) in a "bathing suit" distribution
  - **Plaque**: well-demarcated indurated scaly plaques that take on a variety of shapes with a violaceous to red-brown color
  - **Tumor**: rapidly enlarging nodules that develop within patches or within plaques of MF

PEARL: What should you think about when you see psoriasis in a sun-exposed area? Think Mycosis Fungoides!

Diagnosis:

- **Skin biopsy**:
  - Will need **multiple biopsies** to reach definitive diagnosis
  - If clinical suspicion is high, don't be afraid to repeat the biopsy
  - **Broad shave biopsy** instead of punch = give pathologist **more epidermis** to catch **epidermotropism**
- Patch & Plaque MF **w/out palpable lymphadenopathy** does NOT need further staging work-up e.g. CT scan, lymph node biopsy
- **Immunohistochemical** Staining:
  - **CD3+, CD4+, CD8-, CD30-**
    - Exception for **hypopigmented** variant of MF favoring children and darkly pigmented pt: CD4-, **CD8+**
  - **Loss of CD7** (most common, least specific)
  - **Loss of CD5 & CD2** (less common, more specific)
    - Note: CD7, CD5, and CD2 are T cell markers
  - **Ratio of CD4:CD8 increases as MF progresses**
    - Normally 1:1 in other inflammatory dz
    - <4:1 = less progression = longer survival
    - <10:1 worse prognosis (seen in Sezary Syndrome)

Histology:

- **Patch: band-like distribution of atypical lymphocytes @ DEJ**
  - Presence of **Epidermotropism**: atypical lymphocytes seen in epidermis (where they shouldn't be)
  - Minimal spongiosis
  - Look for **Pautrier's microabscess**, atypical lymphocytes with large hypochromatic nuclei that appear in clusters
  - **Papillary dermal fibrosis**
- **Plaque**: similar histo findings to patch stage, but *more dense band-like infiltrate* in the upper dermis + *more epidermotropism*
- **Tumor: increase in depth and density** of **atypical lymphocytes.** Important to note **epidermotropism** may be **diminished** or gone in this stage!

Treatment:

- **Patch** & **Plaque Stage MF**
  - Skin Directed therapy
    - **Clobetasol** -60% remission
    - **Nitrogen Mustard** -60% remission
    - Narrow band **UVB** – 75% remission
    - Psoralen + PUVA
    - Radiation therapy
  - Systemic Therapy: (refractory cases)
    - **Interferon-alpha**
    - **Oral retinoids** (bexarotene… SE = central hypothyroidism)
  - Systemic Therapy (rapidly progressive or lymph node/visceral involvement)
    - Chemotherapy: **"CHOP"**
      - **C**yclophosphamide
      - **H**ydroxydaunorubicin (Doxorubicin)
      - **O**ncovin (Vincristine)
      - **P**rednisone

8-Parapsoriasis

Background:

- Uncommon chronic idiopathic rash mimicking psoriasis

Epidemiology:

- Onset ~40 y/o. Males>female (M:F) 3:1 **Clinical Presentation:**

- **Small Plaque Parapsoriasis (SPP):**
  - **Scaly patches < 5 cm**
  - Wax and wane in course and then either resolve spontaneously or w/ treatment after several years
  - **"Bathing suit"** distribution
  - **NO association** w/ **cutaneous lymphoma**
  - Variant: *digitate dermatosis*: long finger-like patches along cleavage lines on the flanks

- **Large Plaque Parapsoriasis (LPP):**
  - **Scaly patches > 5cm**
  - **"Bathing suit"** distribution
  - **May progress to MF!**
    - **10-35% in 6-10 years**
  - Variant: *retiform parapsoriasis*. Wide-spread erythematous scaly patches in a net-like distribution.
    - Almost all cases progress to MF

Diagnosis:

- **Biopsy**: **interstitial infiltrate** of **CD4+ T-cells**

Histology:

- Both SPP and LPP have **parakeratosis**, corresponds to the scale seen clinically.
- Mild **acanthosis** and **spongiosis**.

-

- Mild **lymphocytic infiltrate** at the **DEJ** predominantly **CD4+** and may have **Tcell clonality**, especially LPP

Treatment:

- **Topical corticosteroids** & various **phototherapies** like narrow band UVB

8-Pityriasis Rubra Pilaris

Epidemiology: acquired w/ bimodal onset in childhood/adolescence or in patients' 50's

Clinical Presentation:

- May begin with **scalp erythema** with scale❼**Red/brown follicular papules** with **central keratotic plug** having a "**nutmeg** grater" appearance affecting the **neck**, **head**, **trunk**, **extensor extremities**, and **dorsal fingers** ❼Eventually coalescing to **scaly plaques** w/ a **salmon to red orange color** that are **diffuse** and **symmetric** with **islands of sparing** (patches of normal skin within affected areas)
- Look for **keratoderma ("PRP sandals"**: thick hyperkeratosis of the skin of palms and soles
- Thickened yellow brittle nails, **NO PITTING** (vs. pitting seen in psoriasis)

PEARL: What are the 6 types of PRP?

- **Type 1) Classical Adult (55%):**
  - Rapid onset of clinical findings w/ good clinical prognosis.
    - 80% cases resolving over 3 years.
- **Type 2) Atypical Adult (5%)**
  - Chronic course of ichthyotic leg lesions, keratoderma, alopecia
- **Type 3) Classical Juvenile (10%)**
  - Clinical picture of classical adult but presenting in < 2 y/o
- **Type 4) Localized/Circumscribed Juvenile (25%)**
  - Symmetric keratotic follicular papules and erythematous plaques on extensor fingers, elbows, and knee
  - Most common type of PRP in children

- **Type 5) Atypical Juvenile (5%)**
    - Chronic follicular hyperkeratosis and erythema + *scleroderma-like* tightening of hands and feet
- **Type 6) HIV associated PRP (1%)**
    - Associated follicular spines, acne conglobata, hidradenitis suppurativa

Diagnosis:

Biopsy

Histology:

- "**Checkerboard**" pattern: **alternating orthokeratosis** and **parakeratosis** w/ hyper and hypogranulosis
    - Looks like a "checkerboard" because you have orthokeratosis (without nuclei) sitting above purple hypergranulosis alternating with parakeratosis (has purple nuclei) sitting above hypogranulosis
- **Follicular plugging** (also seen in lichen sclerosis & discoid lupus)
- **Shoulder parakeratosis** (also seen in seb derm)
- **Irregular acanthosis**

Treatment:

- **Systemic Retinoids:** acitretin or **isotretinoin (1mg/kg per day)** may clear PRP in 6 months
- Methotrexate
- TNF-alpha
- Cyclosporine
- Azathioprine
- Phototherapy
- Note: topical corticosteroids are typically not that helpful

9-Pityriasiform Disorders

Pityriasis Rosea

Background:

- Bug or Drugs: **Viral associations** prior to onset of rash (HHV 6 & 7), **bacterial infections** (Strep), **ACE**-i, **NSAIDs**, **beta blockers**, gold

Epidemiology:

- Ages **10-40 y/o**

Clinical Presentation:

- Begins w/ **herald patch** 7 hours to weeks later = **diffuse eruption** of smaller **salmon colored oval** and slightly **scaly macules**, **patches** and **plaques** in a "**Christmas tree**" pattern on the **trunk** and **proximal** extremities along lines of **skin cleavage**
    - Look for a **trailing scale** (scale does not reach the leading edge of the erythematous lesion) and mild **itching**
    - **Herald patch**: present in **70**% of cases.
- Atypical forms:
    - Papular Pityriasis rosea: African American children and immunosuppressed. May involve face & scalp.
    - Inverse Pityriasis rosea: intertriginous areas
    - Oral Pityriasis Rosea: aphthous-like ulcers

PEARL: What other conditions have a trailing scale? Erythema annulare centrifugum

Diagnosis:

- Biopsy

Histology:

- **Thin mounds** of **parakeratosis**, **spongiosis**, **perivascular lymphohistiocytic infiltrate** and **extravasated RBCs**

PEARL: What other disorder shows mounds of parakeratosis? (think "PEGS") – **P**ityriasis rosea, **E**rythema annulare centrifugum, **G**uttate psoriasis, **S**mall plaque Parapsoriasis

Treatment:

- **Self-limited condition & Supportive: Resolves** on its own **in 3-8 weeks**
    - **If pruritic ❼Mild topical steroids**, **oral anti-histamines**, UVB, oral erythromycin (250 mg x4 daily for 2 week duration)

Secondary Syphilis

Background:

- Gram-Negative Spirochete: *Treponema pallidum*
- Congenital, Primary, Secondary, and tertiary forms

Clinical Presentation:

- **Rule of 3s**:
    - **~3 weeks** for **1^0 chancre** to develop after inoculation (painless, indurated ulcer w/ associated inguinal lymphadenopathy)
        - Range: 10-90 days
    - **Chancre** lasts **~3 weeks**
    - **~3 weeks** (range 3-10 weeks) after **1^0 chancre** appearance, **2^0 syphilis rash develops**, lasting **3**-12 weeks = pityriasiform, papulosquamous rash
    - If untreated, latency period lasting months to years before tertiary syphilis appears w/ gummas, cardiovascular, and neurological changes

PEARL: Secondary Syphilis vs PR: How to tell the difference? 1) Lesions = **Darker copper color** compared salmon colored of PR 2) **NO** herald patch 3) Can affect **palms & soles** 4) Prodromal of fatigue, fever, and arthralgia as well as **generalized lymphadenopathy**, **moth eaten alopecia**, **condyloma lata lesions** in the **mouth** and **genitals**

-

Diagnosis:

- **Screen with + RPR** or **VDRL ❼FTA-abs** for confirmation ○ **RPR & VDRL correlate** w/ **disease activity** = helpful for assessing tx response. Repeat @ 6 & 12 months.
- **Biopsy**
- Chlamydia, gonorrhea, & HIV testing co-testing

Histology:

Acanthosis w/ **long thin "phallic" rete ridges**, **vacuolar interface** dermatitis, **neutrophils** in **stratum corneum**, **plasma** cells in **dermal infiltrate**

Treatment:

- **Benzathine Penicillin** IM x1 dose @ 2.4 million units
    - If penicillin **allergy** → **Doxycycline** 100 mg BID 14 days
    - Adverse effect: **Jarisch-Herxheimer rxn**-systemic inflammatory response occurring in **first 24 hrs after penicillin** tx. Presents w/ fever, headache, myalgias due to **body's inflammatory rxn** to **dead spirochetes**
    - Patient Education:
        - Safe sex practice
        - Sexual partners should be assessed and treated as well

Tinea Versicolor

Background:

- Caused by *Malassezia furfur & globosa*

Clinical Presentation:

- **Scattered**, **hypopigmented papules** and **patches** on **upper trunk** and **proximal extremities** w/ **scale**
- Occurs in sunny more humid climates when patients skin tends to be oilier

PEARL: Why are these lesions hypopigmented? Malassezia yeast digest oils on the skin into azelaic acid which inhibits melanocyte melanin production = no pigment. However, TV isn't always hypopigmented – it often appears that way because sun exposure tans the surrounding skin! W/o sun exposure, TV will be tan to red macules patches and plaques w/ scale.

Diagnosis:

- KOH Prep: "**Spaghetti & Meatballs**" = Hyphae and spores

Treatment:

- OTC **Selenium Sulfide** (Selsun Blue) or **zinc pyrithione** used as **body washes**. Keep on skin for >5 minutes prior to rinsing.
- **Topical Antifungals**: **Terbinafine**, **ciclopirox**, **ketoconazole** for 2 week course w/ ~80% cure rate

- Oral therapy fluconazole x2 300 mg one week apart
- Patient Education:
    - Recurrent nature of dz
    - Hypopigmented lesions can take months to repigment after tx
    - Maintenance therapy, especially during summer months using OTC body wash x1 every 2-4 week

10-Lichenoid Disorders

Lichen Planus

Background:

- 1% population
- Pt's usually >20 y/o w/ peak onset in **40-70s**
- Inflammatory disease that affects the **skin**, **mucous membranes**, hair and nails
- Unknown cause: pt may be predisposed to certain HLA subtypes + triggers (meds or virus) → alternate antigens on basal keratinocytes → targeted by TCells causing inflammation and lesions

Clinical Presentation:

- Remember the **6 Ps**!
    - **Pruritic**, **purple**, **polygonal**, **planar**, **papules**, and **plaques**
    - Skin manifestations: **anterior forearms** and **wrists**, hands, shins, neck, sacrum, genitals, and generalized
    - Look for **wickham striae** (fine grey-white dots or a net-like pattern overlying lesions)
    - Look for **koebnerization** = new lesions in the area of trauma (e.g. pt **scratching** → **new lesions in linear arrangement**)

PEARL: Most common location to see wickham striae is the oral mucosa. However, only 10% of patients w/ oral lichen planus go on to manifest the stereotypical skin findings.

- LP Variants: Location vs. Appearance vs. Cause
    - **Location: Genital LP, Mucosal LP, Nail LP, Inverse LP, Palmoplantar LP, Lichen Planopilaris**
        - *Genital*: 50% women & 25% men with cutaneous LP
        - *Mucosal*: 50% pts with cutaneous LP. Reticular wickham striae w/ asymptomatic lacy lines on the inside of the check. Can be caused by dental fillings, **amalgam** (mercury).
        - *Nail*: 10% of pts w/ cutaneous LP. Look for **lateral thinning, longitudinal ridges, pitting**, trachyonychia, dorsal pterygium
        - *Inverse*: **Intertriginous** areas of axilla, inguinal, and inframammary fold

- *Palmoplantar*: pain ulcerations on the sole
- *Lichen Planopilaris*: erythema and **perifollicular** scale around the **hair follicle** on the scalp and can **lead** to **scaring alopecia**.

PEARL: LPP vs Discoid Lupus: LPP has more superficial inflammation at the infundibulum vs **D**iscoid Lupus that is **D**eeper at the isthmus

PEARL: Clinical findings of **Graham-Little-Piccardi-Lasseur Syndrome**? Scarring alopecia of the scalp caused by LPP, non-scarring hair loss at the pubic and axillary lesions, follicular papules that appear as keratosis pilaris and classic LP lesions of the skin and the mucosa

- **<u>Appearance</u>: Classic, Annular, Atrophic, Hypertrophic, Ulcerative, Linear, and Bullous, Pemphigoids, Pigmentosus**
  - *Classic*: 6 Ps!
  - *Acute*: classic LP w/ rapid onset of diffuse lesions that resolve more quickly over course of 3-9 months vs >1 year for classic LP
  - *Annular:* **ring-like** and typically affect the **penis** or **axilla**
  - *Atrophic:* **depressed** or hyperpigmented lesions on the **legs**
  - *Ulcerative:* affects the palmoplantar surfaces. Chronic ulcers are at > risk for SCC transformation
  - *Hypertrophic:* thick scaly **plaques** on the **shins** and dorsal **feet** that are often **symmetric** really **itchy** and can be confused with pickers nodules. SCC or KA develop in chronic LP.
  - *Bullous:* **blisters** that arise *within* **chronic** LP lesions
  - *Pemphigoides*: blisters arise mostly on *uninvolved skin*; 2/2 IgG auto-antibodies targeting BP antigen 2 of basement membrane (also targeted in bullous pemphigoid and herpes gestationis)
  - *Pigmentosus*: grey brown macules w/out prior erythema on the **sun exposed areas** of the **face** and **neck** w/ darker Fitzpatrick **skin types 3, 4.**
    - Typically older age of onset ~30-40 y/o (vs ashy dermatosis teens-20s)

-

- **<u>Cause</u>: Actinic, Drug-induced**
  - *Actinic:* young **middle-eastern** adults and presents as **red/brown** plaques on the **sun-exposed** areas of the face, neck, and extremities
  - **Drug-induced**: 60 y/o w/ generalized lesions**, more eczematous, photo-distributed**, **NO** wickham striae, **spares** the **mouth** and **genitals**
    - **Delayed** rxn up to 1 year!
    - Look for **eosinophils** on path
    - **ACE-I, BB,** NSAIDs**,** gold**, HCTZ,** antimalarials**,** TNFalpha inhibitors

Diagnosis:

- Biopsy

Histology:

- **Compact hyperkeratosis** w/out **parakeratosis**
- **Hypergranulosis** (opposite to psoriasis which typically has hypogranulosis)
- **Irregular acanthosis** w/ **sawtooth rete ridges**
- Dense **lichenoid lymphocytic** infiltrate leading to development of **civatte** bodies **(apoptotic keratinocytes)** or **Max-Joseph spaces (separation between dermis and epidermis**)
- **Eosinophils**? Think **drug**-induced LP

PEARL: Think of classic LP as the strict parent that does not let parakeratosis or eosinophils around!

Treatment:

- **Classic LP: topical corticosteroids**
- **Oral or genital LP**: topical **calcineurin** inhibitors (pimecrolimus or tacrolimus)
- **Hypertrophic** lesions: **intralesional Kenalog**:
- **Generalized LP: Prednisone 20 mg multiple weeks** w/ **taper**, **Intramuscular kenolog, low dose methotrexate, metronidazole 500mg BID, phototherapy (UVB or PUVA)**
  - **Acitretin** or **cyclosporine** as **last resort**

11-Annular Disorders

Tinea

Background:

- Fungi: Can be classified as **molds**, yeasts, dimorphic fungi
    - **Molds**: **filamentous fungi** that weave together and form **mycelium**
    - Acquired via direct contact with animals, other infected humans, fomites
    - Ex: aspergillus, **tinea** infections
- Yeast: round, unicellular organisms that reproduce by budding
    - Ex: *Cryptococcus, Candida, Malassezia furfur*
- Dimorphic: "molds in the cold" (outside the body @ 25^0C) and "yeast in the beast" (in host tissue at 37^0C)
    - Ex: *Coccidiomycosis, Paracoccidiomycosis, Histoplasmosis, Blastomycosis*

Clinical Presentation

- **Expanding erythematous annular patches** or **plaques** that classically have an **inflamed** or **scaly leading border**
- Small **vesicles** or **pustules** at the **leading edge**
- Pruritic

PEARL: Name tinea infections based on their location!

- **Scalp, eyebrows, eyelashes**: **Tinea Capitis**
    - *Trichophyton tonsurans* (MC cause in U.S.)
        - Causes an endothrix, *within* the hair shaft
    - *Microsporum canis* (MC cause worldwide)
        - Causes an ectothrix, *outside* the hair shaft
- **Beard**: **Tinea Barbae**
- **Face**: **Tinea Faciei**
- **Torso**: **Tinea Corporis**
- **Arms & Legs**: **Tinea Corporis**
- **Groin**: **Tinea Cruris** (*remember if scrotum affected think candida, not tinea*)
- **Feet**: **Tinea Pedis**
- **Nails**: **Tinea unguium** or **onychomycosis**
- **Hair Follicles outside scalp**: **Majocchi granuloma**

Diagnosis:

- **KOH Prep: Branching hyphae** and **mycelium** (Candida: yeast and pseudohyphae)
- **Biopsy**

PEARL: What is the difference between hyphae and pseudohyphae? Hyphae are long branching filaments that are partitioned by septa w/out constrictions between the cells. Pseudohyphae are chains or budding cells that can look similar to hyphae but have constrictions between the cells that makes them look like sausage links!

Histology:

- Look for **hyphae** in the **stratum corneum**
- Highlighted by PAS stains

Treatment:

- Tinea Corporis:
    - **Topical Antifungals** (terbinafine, ketoconazole, clotrimazole, econazole, ciclopirox, tolnaftate, naftifine)
    - **Oral Antifungals** for **extensive lesions** and **hair follicle** involvement (terbinafine, fluconazole)

PEARL: Name superficial tinea infections that require oral therapy? Tinea Capitis, Tinea faciei, Majocchi granuloma. Oral treatments needed due to the fact that topical tx cannot penetrate to the hair follicle in the deep dermis!

Subacute Cutaneous Lupus Erythematosus

Background:

- **Chronic** cutaneous lupus: discoid lupus, hypertrophic lupus, lupus panniculitis, tumid lupus, mucosal lupus
- **Acute** cutaneous lupus: strong association w/ SLE presenting with malar rash and photosensitive eruptions
- **Subacute** cutaneous lupus erythematosus (SCLE) **Rule of 50s**

- **Rule** of **50s**: ~ ½ + ANA, ~ ½ meet criteria for SLE, ~ ½ photosensitive,
  ~ ½ + Direct immunofluorescent findings

Clinical Presentation:

- **Papulosquamous SCLE**: mimics psoriasis but has a photo distribution
- **Annular SCLE**: polycyclic annular plaques occurring on the sun-exposed areas of the face, neck and upper back

Diagnosis:

- **Biopsy**
- **Anti-Ro** (anti-SSA) & **Anti-La** (anti-SSB)
  - + in SCLE, Sjogren syndrome, neonatal Lupus
- 50-80% + ANA
- Leukopenia on CBC

PEARL: Drug induced SCLE (anti-Ro) vs Drug-induces SLE (anti-histone)

- **Drug-induced Systemic LE (SLE)**: ↓ **cutaneous changes,** arthralgias, serositis, malar rash; **+ anti-histone Ab's**
  - **"My HIPP"** – **M**inocycline (+p-ANCA), **H**ydralazine, **I**soniazid, **P**rocainamide, **P**enicillamine
- **Drug Induced Subacute LE (SCLE)**: ↑ **cutaneous changes** w/ minimal systemic involvement; + **anti-Ro (SS-A)**
  - "**THANG**": **T**erbinafine, **H**CTZ, **A**CE-I, **N**SAIDs, **G**riseofulvin

Histology:

- **Vacuolar interface** (degenerate changes at DEJ looking like bubbles) w/ prominent **lymphocytic infiltrate**, **thickening** of the **basement membrane**, **mucin** deposition, **perivascular** and **peri-adnexal lymphoid aggregates**

Treatment:

- Antimalarials: hydroxychloroquine
- Sun Protection
- Topical steroids
- Stop/switch possible causative medications

Erythema annulare centrifugum

Background:

- Type of hypersensitivity due to long list of possible triggers
  - **Infections**: Tinea
  - **Medications**: penicillin, plaquenil, cimetidine, HCTZ, amitriptyline
  - **Foods**: blue cheese, tomatoes
  - Autoimmune: SLE, hashimotos thyroiditis, pemphigus vulgaris
  - Cancer: leukemia, lymphoma, breast, lung, GI, and prostate cancer

Clinical Presentation:

- **Superficial EAC** vs **Deep EAC**
  - **Superficial**: Single or multiple annular, erythematous scaling plaques that are slow growing and occasionally pruritic w/ trailing scale
  - **Deep**: Dermal process so no scale on lesions

PEARL: Other dz w/ trailing scale? Pityriasis rosea or resolving pustules/furuncles

Diagnosis:

- **KOH: negative**
- **Biopsy**

Histology:

- Classic "**coat-sleeve**" **infiltrate** (densely packed lymphocytes around the blood vessels) w/ **diagonal cut**

Treatment:

- Address Triggers
- Topical steroids, calcineurin inhibitors, UV treatments

12-Erythroderma

Background:

- Aka exfoliative dermatitis, pts who have **erythema** and **scaling affecting > 80-90% BSA** regardless of cause
    - At least 50% caused by pre-existing rashes that worsen
    - Children: May also be 2/2 immunodeficiency (e.g. OMENN syndrome)
- **Main Causes (7)**
    - **Papulosquamous**: psoriasis, pityriasis rubra pilaris
        - Psoriasis is the most common cause of erythroderma (~ 20% of cases)
            - Caused by withdrawal of steroids/cyclosporine/methotrexate vs triggers ("SICK LAB"❼Smoking/Stress, Infections, Hypocalcemia, Koebnerization, Lithium, Antimalarial/ACE-I, BB…also alcohol, obesity, NSAIDs, terbinafine, TNF-alpha inhibitors)
    - **Dermatitis**: atopic, allergic contact, seborrheic, chronic actinic dermatitis, stasis derm
        - *Atopic Derm*: hx of ≥1 features of atopic triad: atopic derm, hay fever, asthma. More severe itching. Look for ↑ IgE + eosinophilia on labs
        - *Allergic Contact*: (e.g. *Parthenian* plant in India.)
        - *Seborrheic*: think of neurologic conditions (Parkinson's) or HIV
        - *Chronic Actinic*: men >50 caused by UVA, UVB, and visible light. ↑CD8:CD4 .
        - *Stasis derm with profound Id reaction*: very rare cause of erythroderma
    - **Drug Rxn:** SJS, TEN, DRESS syndrome, drug rash
        - SJS triggers: Allopurinol, sulfa drugs (Bactrim), phenytoin, HIV pt w/ antiretroviral therapy
    - **CTCL**: erythrodermic MF, Sezary syndrome
        - Erythrodermic MF: pre-existing patches or plaques of MF then progress to erythroderma
        - Sezary Triad: Diffuse lymphadenopathy, malignant T-cells, erythroderma. Also look for alopecia, nail changes, leonine facies.
            - 1000 Sezary cell per microliter or ↑ CD4:CD8 >10, ↑CD4 (CD7/26-)
    - **Infections**: Viral exanthems, Norwegian Scabies, Staph Scalded Skin syndrome
    - **Auto-immune conditions** such as Lupus, GVHD, bullous pemphigoid
    - **Physical causes:** e.g. Burns

- PEARL: Differential for leonine facies? "PALMS" **P**aget's disease of the bone, **A**myloidosis, **L**epromatous Leprosy, **L**ymphoma, **L**eishmaniasis, **M**ycosis fungoides, **S**arcoidosis, **S**cleromyxedema

Clinical Presentation:

- Very scaly rash!
- **Skin vasodilation** = ↓ **peripheral resistance** may lead to **tachycardia**, **high output cardiac failure,** and **edema**
- Extra blood flow in skin can **disrupt thermoregulation** leading to hyper or hypothermia. CC: **Chills**!
- **ROS:**
    - **Severe pruritis**: **atopic dermatitis** or **Sezary**
    - **Joint pain**: **psoriasis**
    - Fever: argues against psoriasis
- **Hints on Physical Exam (suggestive findings):**
    - **Rash** affecting the **face** = argues against **psoriasis**
    - **Facial edema** = **drug rxn** or **DRESS**
    - **Mucosal** Inflammation = **SJS/TEN**
    - **Waxy keratoderma** = **pityriasis rubra pilaris**
    - **Nail changes** (**pitting**, onycholysis, oil spotting) = **psoriasis**
    - **Violaceous** rash = **CTCL**
    - **Salmon** rash = **pityriasis rubra pilaris**
    - **Blisters** = **bullous pemphigoid**
    - **Follicular plugging** w/ **islands** of **sparing** on **dorsal fingers** and **knees** = **pityriasis rubra pilaris**

- **Larger** areas of **peeling** = **acute drug rxn** (vs **Fine scale** = **atopic dermatitis** or **generalized tinea**)
- **Lymph nodes** = malignancy (**Sezary**)
  - Note: lymphadenopathy is not uncommon in erythroderma regardless of cause

Diagnosis (suggestive findings):

- CBC: eosinophilia ➡ drug rxn or atopic derm
- CMP: Electrolyte Imbalances & LFT elevations – DRESS syndrome
- Blood Culture & Viral Cultures
- IgE: atopic derm
- ANA: Lupus and dermatomyositis
- Peripheral blood smear & Flow Cytometry: Sezary cells Flow; ↑ CD4:CD8 >10:1
- Multiple Biopsy: may be non-specific in 1/3 of patients; *still a crucial part of workup!
- KOH study if rash is scaly to r/o generalized tinea
- Lymph node biopsy vs PET CT if lymphadenopathy + concern for Sezary syndrome

Treatment:

- **Diffuse scaling**: **Emollients diffusely** w/ **class IV-XI topical steroid**
- If **2^0 infection** present? **Topical antibiotics** like **mupirocin** or bleach baths
- **Pruritis**: **Wet dressings** & **sedating anti-histamines** (**Benadryl**, **hydroxyzine**), consider **prednisone**, cyclosporine, or methotrexate depending on etiology and severity

13-Contact Dermatitis

Background

- Eczematous reaction patterns include
  - Acute: Ex. **Irritant** vs **Allergic Contact Dermatitis**
  - Subacute: Ex. Stasis Dermatitis
  - Chronic**:** Ex. Atopic Dermatitis
  - Note: Any of these forms of dermatitis can present in an acute, subacute, or chronic fashion. Above are the more common presentations for each

- **Irritant** (80% of cases): chemical that **directly damages** the **skin** barrier **with minimal immune system involvement** (via innate immunity)
  - Variants: Acneiform, sensory, airborne, plant-derived
    - Acneiform: exposure to metal or metal like fluids
    - Sensory: Burning sensation w/out skin changes
    - Airborne: dust or fiberglass
    - Plant-derived
  - Can affect **anyone** with **enough contact** w/ **substance**
  - Can occur in hours of contact since there is no need to recruit memory cells
  - Acid vs **Base**: **Bases** are **more damaging**! Denature proteins in skin and also disrupts lipids in stratum corneum
    - Bases: Detergents, soaps, bleaches, cleaning products
    - Acids: Sulfuric, hydrochloric, nitric acids
- **Allergic** (20%): mediated by **immune system**, **Type IV hypersensitivity** to allergen
  - Only affects **small %** of pts exposed to **allergen**
  - 1st exposure: (APCs + allergen) ➡ **sensitization** (primed + CD8 T-cells)
  - 2nd exposure: Primed Memory CD8 T-cells + allergen ➡ inflammatory response w/in 1-2 days
- **7 Main Causes of allergic contact dermatitis (ACD)**:
  - *Topical medications*: **Nitrogen Mustard**, triple antibiotic ointments, **Oxybenzone (sunscreen ingredient)**, **procaine**, **topical steroids**, lanolin, propylene glycol, ethylenediamine, propolis, urushiol oil

PEARL: Which ingredients in antibiotic ointment cause allergic contact dermatitis? "**BNP**": bacitracin, neomycin, polymyxin B

- *Plants*: **urushiol oil** (ivy, oak, sumac) ❼"**rhus**" **dermatitis**

PEARL: Poison ivy, oak, sumac ❼toxicodendron, anacardiaceae family

- *Metals*: **nickel** (earrings, belt-buckle), **chromates** (leather, cement, green felt on pool tables), **cobalt**, gold, mercury
- *Cosmetic Products*: **Fragrance**, **Balsam of Peru**, **paraphenylenediamine** (hair dye, henna tattoos)

PEARL: Cross Rxn w/ **para-phenylenediamine** "PASTA": Paraben, Para-aminobenzoic acid (PABA), Azo dyes, sulfonamides, thiazides, anesthetics –

- Preservatives: **formaldehyde**

PEARL: What causes allergic contact dermatitis on baby's buttocks? Methyl-isothiazolinone used in baby wipes

- Adhesives: **cyanoacrylates**, **methacrylate (artificial nails)**, epoxy resin
- Rubber: **latex**, neoprene in wetsuits, **mercaptobenzothiazole** (shoe dermatitis)

PEARL: What does latex cross-react with? "BACK PASSION": Bananas, Avocados, Chestnuts, Kiwi, Passionfruit

Clinical Presentation:

- **Acute**:
  - **Inflamed lesions, weeping fluid,** w/ **vesicles** & **bulla** w/in **hours** to **days**
- **Subacute**:
  - **Progressive acute** lesions that may have **scale**
- **Chronic:**
  - Lasting months to years
  - Look for **lichenification**: thickened skin w/ accentuated skin lines
- ROS:
  - Ask about **new personal care products**/**clothing**: make-up, chap sticks, lotions, laundry-detergents, jewelry, shoes
  - If **chronic**, ask the pt. if the rash gets **better** on **vacation**
- Physical Exam:
  - **Earlobes**: **Nickel** from earrings
  - **Neck**: **Fragrances**, **Perfumes** such as Balsam of peru
  - **Hands**: **Latex** gloves or **poison ivy**
  - **Arms**: **Poison ivy**
  - **Wrist**: **Nickel** in watches, **chromates** in leather on wristband
  - **Foot**: **mercaptobenzothiazole** in rubber or **chromates** in leather shoe
  - **Armpits**: **Fragrance** or **propylene glycol** in deodorants
  - **Abdomen**: **Nickel** in belt buckles or **rubber** in elastic waistbands
  - **Lower Legs**: **bacitracin** or **neomycin** used for stasis dermatitis
  - **Lips**: **propolis** in natural chap sticks or those that contain sunscreen w/ **oxybenzone**
  - **Eyelids**: **tosylamide** in nail polish w/ pt rubbing eyes, mascara, eyeshadow rubber sponge
  - **Penis**: **latex** or **rubber**, **poison ivy**
  - **Anus**: **methylisothiazolinone** in wet wipes

Diagnosis:

- **Patch Testing**: TRUE test (most common)
  - 3 panels w/ 12 test spots for allergens = **35 allergens** + **1 control**
  - **Location**: typically **Upper Back**
  - **Procedure**: Apply TRUE test ❼return in 2 days for patch removal + 1st reading ❼return 2-5 days for 2nd reading
    - Ideally: Apply Monday, Remove Wednesday, Read Friday/Monday
    - **Rules**:
      - Don't apply to inflamed skin where pt may have acne or sunburns
      - No topical steroids on site w/in a week or systemic steroids w/in 1-2 weeks
      - No showering or vigorous exercise for initial 2 days while patches on (may dislodge them)
  - **Results**:
    - - = no rxn
    - +/- =doubtful pink rxn

- 1+ = weak red rxn
- 2+ = vesicular rxn
- 3+ = bullous rxn

PEARL: If rxn improves in 2nd reading, it's likely irritant contact. If rxn, progressively gets worse at 2nd reading, it's likely allergic contact.

-**Biopsy**

Histology: Hallmark is "**spongiosis**" ➡edema in epidermis

- Acute: **swelling** can be abrupt, forming **vesicles** and **bulla**
- Chronic: **acanthosis** (thickening of epidermis)

PEARL: Allergic vs Irritant? **Allergic** will have **more spongiosis** and **inflammation** in dermis compared w/ irritant. **Irritant** will also have more "**dead-red"** keratinocytes

Treatment:

- **Avoid irritants** and **allergens**
- **Topical steroids** – **mild**
- **Systemic steroids** -**moderate/severe**
- Topical Calcineurin inhibitors on face and intertriginous

14- Stasis Dermatitis/Red Leg Differential

Stasis Dermatitis

Background:

- Seen on lower legs of pt w/ chronic venous insufficiency
- **Pathogenesis: Venous insufficiency** ➡venous HTN and extravasation of fluid and RBCs out of vessels into interstitium ➡edema, hemosiderin deposition, and inflammation in the skin
- Differential**: Lipodermatosclerosis, Contact Dermatitis, Cellulitis, DVT, Necrotizing Fasciitis**

Clinical Presentation:

- **Subacute eczema** w/ **erythematous** slight **scaly patches** and **plaques** on the **lower legs**, especially the *medial* side of the lower leg
- Associated **pitting edema**
- **Typically bilateral** (can be unilateral if pt has had trauma, prior cellulitis, or surgery e.g. vein harvest for CABG)
- Also can have **acute** or **chronic presentations**:
    - **Acute**: **bright red, warm, tender patches** or **plaques** that may have **vesicles** or **serous weeping fluid**

PEARL: Ask the patient if they were standing for an extended period of time! (Standing for long periods ➡acute flare of stasis derm)

- **Chronic**: more **scale** and **hyperpigmentation** due to hemosiderin deposition

PEARL: Name other complications that can occur in stasis dermatitis?

- Contact sensitization (**allergic contact dermatitis):** Higher rate ➡due to pts using **triple abx ointment** on rash since they think it is infected, impaired skin barrier, ↑ presence of inflammatory cells
- Auto-sensitization (**id rxn): immune mediated eczematous** or **papulovesicular** lesions that occur at **distant sites** from primary rash

- **Secondary infections**: altered skin barrier + poor circulation = predisposition for super-infection from *Staph* or *Strep*

Physical Exam:

- **Unilateral vs bilateral:**
  - Unilateral suggests cellulitis but stasis dermatitis can also be unilateral
- **Look for an entry for skin infections:**
  - Tinea pedis or skin maceration between toes
- **Look for scale** on rash itself (takes time to develop!)
  - Argues against cellulitis, suggests stasis dermatitis
- **Palpate the affected skin**
  - Exquisite pain or crepitus, think necrotizing fasciitis
  - Unilateral pitting edema + Homans, think DVT
- **Elevate the leg for 30 seconds**
  - Erythema improves, think stasis dermatitis
- **If thinking cellulitis, outline erythema on legs**
  - Helps to monitor for improvement w/ antibiotic regimen

PEARL: Swollen Leg? What do you ask your patient?

- Is the rash **painful**? Suggests **cellulitis**
- **Itchy**? Suggests **Stasis** or **Contact Dermatitis**
- **Extended time on your feet** (Trip to Disney)? **Stasis Dermatitis**
- Significant time **immobilized** (Plane or Post Surgery)? **DVT**
- **One sided**? **Cellulitis**
- **Bilateral**? **Stasis Dermatitis**
- **Risk factors** for **infection** (**Diabetes**, **immunosuppressants**, recently **hospitalized**)? **Cellulitis**
- **Topicals** on the rash (Antibiotic ointment)? **Allergic Contact Dermatitis**

Diagnosis = CLINICAL!

- Biopsy: **May not be helpful**; pt already has poor circulation and likely will not heal well

Histology:

- **Spongiosis** correlating w/ dermatitis seen clinically, **increase proliferation** of **capillaries below DEJ** (reactive to the relative anoxia), **extravasated RBCs** w/ **hemosiderin deposits**, and possibly **dermal fibrosis** at later stages

Treatment:

- **Compression** & **Elevation**
  - Compression stockings (>20 mmHg)
  - Severe: Serial Unna Boots or prednisone
  - Elevate above level of heart as much as possible
- **Topical** corticosteroids + Mupirocin for dermatitis
- Patient education
  - No cure, only control with above measures; may have another case of stasis dermatitis in future
  - Empower pt to use compression + elevation

Cellulitis

Clinical Presentation:

- Look for the 4 Cardinal Signs of Inflammation: **Red**, **Hot**, **Swollen**, **Tender**
- Systemic Changes: **Fever** & **Fatigue**
- **+/- Mild ↑ WBC** count
- Moderate to Severe: +/- Vesicles vs bullae, bruising, petechiae

Asteatotic Eczema

Background:

- Extreme form of xerosis affecting pt > 60 y/o
- Also known as Eczema Craquele

Clinical Presentation:

- Diffuse **xerosis** w/ **fine scaling** that **progresses** to **inflammation** and **cracking** of the **skin** (resembling cracked porcelain)
- Pt experiences pruritis and can be painful when cracking of skin is deep enough to cause **fissures**
- Weeping, crusting, bleeding on occasion

PEARL: What can exacerbate xerosis to cause eczema craquele?

- **Low Humidity**
- **Harsh soaps**
- **Prolonged or frequent hot showers**
- **Heating w/ wood stoves**
- Hypothyroidism, renal failure, liver DZ, malnutrition, HIV, Sjogren's

Diagnosis:

- Clinical diagnosis typically sufficient w/out biopsy
- If no improvement w/ treatment, consider Labs for Thyroid (TSH), Liver & Renal DZ (CMP), HIV, Zinc levels, ANA w/ reflex

Treatment:

- **Avoid Triggers**
- Apply **moisturizer**
    - Vanicream, Cetaphil, Cerave, Vaseline **w/in 3 minutes** after shower **while skin is damp** to hold moisture
- Topical corticosteroids + antihistamines for itching

15- Atopic Dermatitis

Background:

- Form of eczema that is often the first presentation of the "**atopic triad**" **(Atopic Dermatitis, Asthma, & Allergic Rhinitis)**
    - Can occur simultaneously or in succession (the atopic march)
- 60% rule: **60% begin by age 1; 60% resolve by 12 y/o**

Pathogenesis:

- Due to several genetic and environmental factors
    - 1 parent atopic = >50% chance child will be atopic
    - Mutations in the **filaggrin** gene: **fil**ament **agg**regating prote**in** ❼ natural moisturization factor
    - Deficient in several types of **ceramides:** sphingolipids ("mortar" that holds corneocytes ("bricks") together in stratum corneum)

PEARL: What type of inflammatory response is present in **acute** atopic derm vs **chronic** atopic derm? **Acute** atopic derm has overactive **Th2** w/ ↑ IL4, 5, 13 vs **chronic** atopic derm has **Th1** response w/ IFN-g and IL-12

PEARL: What are some of the major triggers for atopic dermatitis? Think **FADS**!

F: Fragrances (laundry detergents or perfume), fabrics (wool or polyester), food allergies (wheat, eggs, milk, peanuts) **A:** Allergens (pet dander, dust mites)

D: dry environments, detergents

S: stress, smoking, sweating, soaps, showering (too long or too hot)

Clinical Presentation:

- **Infantile** (2 months – 2 yrs)
    - **Erythema** and **scale** on the **cheeks**, **scalp**, and **neck** along w/ **extensor arms** and **legs**
    - Very itchy and inflamed
    - Can develop exudative plaques w/ *Staph aureus* colonization

- Up to 90% of atopic derm pts are colonized with *Staph aureus* b/c their skin has ↓ antimicrobial peptides (vs psoriatic plaques having ↑ antimicrobial peptides = less likely to get infected)

- **Childhood** (2 -12 yrs)
  - "The itch that rashes"
  - Antecubital fossa (**flexures**) becomes itchy; pt's tend to scratch leading to classic excoriated lesions and lichenified plaques
  - Acute flare: ↑ erythema, pruritus, vesicles, and oozing

PEARL: What are some other features of atopic dermatitis in children that can help your diagnosis? Eyes: **Dennie-Morgan lines & allergic shiners**; Face & Neck: **Pityriasis alba & hyperlinear neck folds**; Extremities: **hyperlinear palms**, keratosis pilaris

- **Adolescent**/**Adult** (12-60 yrs)
  - Similar presentation to adolescents w/ ↑ **hand eczema**
- **Senile** (60+ yrs)
  - Xerosis triggered by sweating or stress

Diagnosis:

- **Clinical Diagnosis** consisting of **three essential features**: **1) pruritus, 2) eczematous rash, 3) chronic relapsing course**
  - Other less common important features include: early age of onset, xerosis, atopy
  - Associated features include: atypical vascular response (facial pallor), keratosis pilaris, pityriasis alba, hyperlinear palms, ichthyosis, periorbital changes (Dennie-Morgan lines), lichenification
- Allergen specific IgE tests:
  - **RAST Test** ("immunoassay"): detect antigen-specific IgE in blood to various foods, insect venoms, medicine (penicillin), environmental allergen (pollen or dust mites), & work allergens (latex)
  - Skin Tests (**Skin Prick** or **patch testing**): detect allergen-specific IgE that activates mast cells in skin ❼wheals or contact dermatitis respectively

Histology:

- Acute: **spongiosis**, perivascular lymphocytes and histiocytes w/ occasional eosinophils
- Subacute: ↓ **spongiosis** and ↑ **acanthosis**
- Chronic: ↓↓ **spongiosis,** ↑↑ **acanthosis** (mimicking psoriasiform DZ) dermal fibrosis, hyperkeratosis

Treatment:

- **Avoid Triggers** (FADS)
- **Moisturizing** skin daily w/ in few minutes of exiting shower (use bland emollients or petroleum)
- First try, **low-mid potency topical steroids** (e.g. fluocinolone, triamcinolone) or topical **Calcineurin** inhibitors (pimecrolimus or tacrolimus)
- Non-sedating **antihistamines** (loratidine) in morning then sedating antihistamines (diphenhydramine, hydroxyzine) at night
- Then systemic therapy if needed, narrow-band **UVB**, then **prednisone**, **cyclosporine**, **azathioprine**, mycophenolate mofetil, methotrexate, dupilumab

Glossary of abbreviations

- 2/2 = secondary to
- ACEI – ACE inhibitors
- APC – antigen presenting cells
- BP – bullous pemphigoid
- BSA – body surface area
- BV = blood vessel(s)
- CCB – calcium channel blocker
- CMI – cell mediated immunity
- Contra - contraindications
- CsA – cyclosporine A (regular cyclosporine 😊)
- CTDZ – connective tissue disease
- CTL – cytotoxic T lymphocyte
- DEJ – dermoepidermal junction
- DIP - distal interphalangeal joint
- DZ – disease
- EBA – epidermolysis bullosa acquisita
- EED – erythema elevatum diutinum
- FBSE – full body skin exam
- FH – family history
- GA – granuloma annulare
- H-H – Hailey Haily disease
- Infxn - infection
- KC - keratinocyte
- MC – melanocyte
- MTX - methotrexate
- MCP – metacarpophalangeal joint
- MOA – mechanism of action
- NL – necrobiosis lipoidica
- Nu – nucleus, nucleated
- p/s – palms and soles
- PIP – proximal interphalangeal joint
- PMLE – polymorphous light eruption
- Pt – patient
- Pso – psoriasis
- PsA – psoriatic arthritis
- RF – risk factors
- SE – side effects
- SH – social history
- SJS – Stevens Johnson Syndrome
- SSSS – staphylococcus scalded skin syndrome
- TB – tuberculosis`
- TCI – topical calcineurin inhibitor - TCS – topical corticosteroids
- TEN – Toxic epidermal necrolysis