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 - 60-70% 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) → inhibits 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 (→ gout), 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

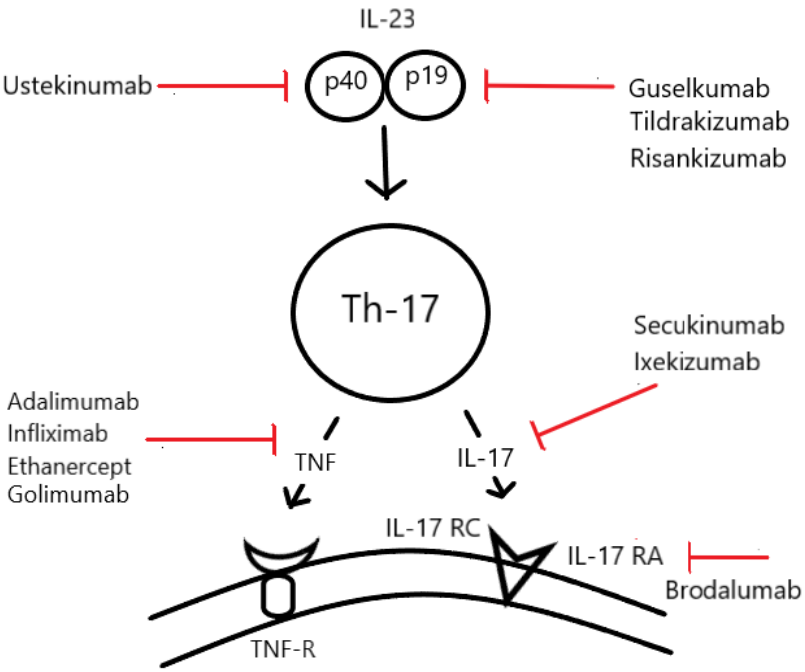
PASI (psoriasis area and severity index)

- 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 → 10)
    - 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