**Pharmacologic Therapy:**

- **Lot**: Exercise but avoid overexertion, Quit smoking now.
- **Exercise**: Moderate to prompt physical activity, monitor and adjust.

**Non-Pharmacologic Therapy**: Avoid the Sun – Use Sunscreen (SPF>30). Have a balanced diet with hella VitD, Rest a lot, Exercise but avoid overexertion, Quit smoking now, Vaccinate early and treat your infections early.

**Pharmacologic Therapy**: Choose therapy based on organ system involved and activity/severity of the disease. Therapy is specific to each patient.

- **FDA Approved Therapies**: Limited to ASA, Pred, HCQ, and Belimumab… though these others are still “Standard of Care”. Why? Because insurance companies are a buncha assholes.

**Goals of Treatment**

- Prevent disease flares and involvement of other organs (CONFINE LUPUS)
- Achieve lowest possible disease activity to prevent organ damage
- Improve QoL and Ensure long-term survival

**Non-Pharmacologic Therapy**

<table>
<thead>
<tr>
<th>Severity</th>
<th>MILD</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Involves</strong></td>
<td>Skin, Joint, a little muscle. Some constitutional Sx.</td>
<td>Significant Constitutional, Musculoskeletal, Hematological, but not life-threatening</td>
<td>Life-threatening, Renal or CNS involvement</td>
</tr>
<tr>
<td><strong>Preferred Tx</strong></td>
<td>HCQ ± NSAIDs ± Pred-(Low/Short-term)</td>
<td>HCQ ± Pred-(Med/Short-term)</td>
<td>Induction: High IV Roids + MMF (6mo)</td>
</tr>
</tbody>
</table>

**NSAIDs**: *First-line (combo) for arthritis, musculoskeletal sx, fever, serositis (inflammation of organ lining)*

- Low Dose ASA. Especially in patients with aPL, will decrease risk of clots
- Risks: Renal function, may increase cardiac events, risk of bleeding, ulcers, bronchospasms
- **Corticosteroids**: First-line (combo) for disease flares and to maintain low disease activity
  - I-say-'Roids-you-think-Taper: use lowest effective dose to maintain low disease activity. If opportune, use steroid-sparing medications to eliminate steroids, except for as needed for flares.
  - AE: Insomnia, HT, Dyslipidemia, Hyperglycemia/DM, Cataracts, Infection, Myopathy, Stroke
    - Avoid live vaccines in Pred > 20mg/Qdaily

- **Hydroxychloroquine (HCQ)**: All patients should take HCQ unless ContraX
  - Function: Anti-inflammatory, Immunomodulatory, Antithrombotic effects
  - AE: Insomnia, HT, Dyslipidemia, Hyperglycemia/DM, Cataracts, Infection, Myopathy, Stroke

- **Methotrexate (MTX)**: Used primarily for Arthritis and Skin, May not come into play until late moderate.
  - Dose: Starting dose PO 10mg/Qweekly. Once you hit 25mg/Qweekly, this is the max absorbable, may need to do SubQ if you want to bypass GI disturbances or dose higher.
  - AE: Hematologic (bone marrow suppression) – decreased CBC. Hepatotoxic: No boozing
  - Cautions: Renal/Hepatic: Monitor organ function, Renal impairment prolongs half-life, ↓dose.
  - Avoid Live vaccines when dose > 3mg/kg AZA

- **Azathioprine (AZA)**: Inhibits DNA synthesis, decreases immune cell proliferation. Check Enzyme activity
  - TPMT Assay: Low enzyme activity increases the risk of myelosuppression and hepatotoxicity
  - Xanthine Oxidase: Avoid XO inhibitors (Allopurinol), otherwise risk myelosuppression/hepatotoxicity
  - AE: N/V/D, take with food or divide doses
  - Serious Caution:
    - Hepatotoxicity: Monitor LFT↑, Bilirubin. May be sx of Hepatosplenic T cell lymphomas
    - Hematologic Toxicity: Dose-related, monitor CBC and Hg
    - PML, Pericarditis, Malignancy, Infections,, yea this is bad
    - Avoid live vaccines when dose > 3mg/kg AZA

- **Mycophenolate (MMF)** - Considered to be not as effective for joints as AZA or MTX. Hella AE
  - MoA: Inhibits inosine monophosphate dehydrogenase (IMPDH), thereby inhibiting de novo synthesis of guanosine nucleotides, ↓proliferation/differentiation of T and B cells
  - Induces activated T cell apoptosis, Inhibits adhesion molecule expression
  - Dosing: Depends on their tolerance
  - AE: Potentially severe N/V/D, Hematologic-Neutropenia, Hepatotoxic, Malignancies, Infections
    - Avoid live vaccines.

- **Belimumab (Benlysta)**: Anti-BLyS human mAb
  - MoA: Binds to soluble BLYS (B-lymphyocyte stimulatory) thus inhibiting its action at BCR. This will increase the apoptosis of B cells (especially auto-reactive B cells), decrease their differentiation, Ig production, and production of the autoantibodies.
  - Place in Therapy: Treats active SLE Ab+ (ANA or Anti-dsDNA) on standard therapy (excluding cyclophosphamide and rituximab)
  - Dosing: LD then once monthly IV infusion.
    - Prior to Initiation: Labs – CBC, TB, HepB+C
  - AE: Most common are mood changes, depression, suicidal ideation. Must assess patient beforehand for predisposing conditions. Otherwise, N/D, Fever, Insomnia, HA
    - Severe: Infection, PML, Malignancy, Infusion Rxns
  - ContraX: CNS Lupus or Lupus Nephritis (Severe+Active)
  - Avoid Live vaccines

- **Rituximab (Rituxan)**: Anti-CD20 Chimeric mAb
  - MoA: Target B cells by binding to CD20, depleting them.
  - AE: Common are fever, chills, weakness, N, HA, Rhinitis, Pharyngitis
    - Severe Infusion rxn, especially on 1st infusion – Urticaria, Hypotension, Hypoxia, Cardiogenic shock, Death. → Premedicate with [DPH, Medrol, APAP]
    - Cardiac Risk – Cardiac Arrhthmias
    - Nephrotoic, Cytopenic, PML, SJS, TEN
  - Monitoring: Check HepB+C before starting therapy
  - Special: No need to monitor TB, this is the therapy of choice for patients treated for cancer < 5y
- **Cyclophosphamide** (Cytoxan, CYC) Cytotoxic Alkylating Agent – Inhibits DNA synthesis
  - Dosing: IV is preferred (PO available). Must prophylactically dose with Zofran for severe Nausea
    - Prior to Dosing, Check: Renal function, CBC, UA
  - AE: Hemorrhagic Cystitis (Stay hydrated), Sterility (harvest them eggs!), Malignancy, Cardiac toxicity, Leukopenia, Thrombocytopenia
  - I see no reason why we would give this medication.

**Treatment Considerations**
- Immunizations: Lupus patients are more susceptible to HPV, they do not clear the virus well → So we should vaccinate, though it will raise the risk of Thromboembolic events - especially when aPL
- Treat Comorbidities: Such as HT, Depression
- Treat SLE Sequelae: Raynaud’s, APLS

**Cutaneous Lupus (CL):** 3 types, of which they are most often found on the head/neck, upper trunk, arms.
- Treatment: If lifestyle modifications or topical therapies are ineffective, change to prescription
  - Lifestyle Modifications: Avoid the sun, use sunscreen (SPF >30)
  - Topical Therapies: Corticosteroids, CNI

**CNS Lupus:** To properly treat this condition, must identify the source and nature of the problem. Treatment will be based on neurologic manifestations, often requiring symptomatic therapy (anticonvulsants, antidepressants)
  - If it is Inflammatory: steroids ± immunosuppression
  - Find Thrombosis or titers of aPL: Use anticoags ± inhibitors of platelet aggregation

**Lupus Nephritis (LN):** Must biopsy all patients with evidence of active LN, and all patients will receive HCQ
  - ACR Treatment Guidelines: Classifies LN, where I, II are not bad, VI means game over, your kidneys are fucked
    - I,II: No immunosuppression required. This is called minimal mesangial LN
    - III,IV: Induction therapy (for 6mo) using MMF, then low dose maintenance
    - V: MMF + Pred
      - Improve? Switch Pred to AZA-
      - Not improve? Switch CYC to MMF, keep Pred, add GC pulse
  - If LDL > 100mg/dL → Add statin therapy

**Managing Pregnancy in SLE:** Major goal of this lecture. Pregnant women have a much higher rate of developing lupus.
- Mortality Risk: There is a high risk of developing Lupus and increased maternal morality.
- Flares: SLE often flares during pregnancy/post-partum, though it is less likely if SLE is in remission at the time of conception, moreso if stable for ≥6mo.
  - APLS: Clot off placenta and lose baby.
- Want to get pregnant?
  - Wait until it is ≥6mo from a severe flare.
  - d/c teratogenic drugs at least 3mo prior to conception (MTX, MMF, CYC)
  - d/c biologics 3-6mo prior to pregnancy
  - Use low dose ASA to decrease the risk of preeclampsia and feta loss [Consider low MW Heparin]
  - May continue to use HCQ as it reduces the incidence of flares
  - If needed, roids can be used, use the lowest effective dose otherwise predisposing self to DM
  - If immunosuppression is needed, use AZA

**Antiphospholipid Ab Syndrome (APLS):** 40% of SLE pt have aPL, though not all will have APLS.
- **Dx:** Must meet 1 lab criteria and experience at least 1 clinical event. Secondly, the lab criteria and clinical event must be >12w apart but <5years. The guys who made these guidelines smoked crack, but I bet there’s some logic
  - Lab Criteria: Lupus anticoag, anticardiolipin Ab, Anti-β2glycoprotein (x2, q12w)
  - Clinical Events: Arterial or Venous Thrombosis, CVA, PE, Pregnancy complications (fetal death)
- **Tx:** Give low dose ASA for pt without hx of arterial or venous thrombosis
  - Have a TE event: Give warfarin with an INR goal of 2-3, they’ll be long-term anticoagas.

**Drug-Induced Lupus:** ~common, presents as constitutional symptoms (rash, myalgia, arthralgia, weight¹, fever)
- **Dx:** Antibody to histones is an excellent indicator (>96%), though oddly, low incidence of anti-dsDNA.
- **Pathogenesis:** Drug triggers immune response in a pt w/o hx of SLE
  - Implicated drugs: **Isoniazid, Penicillamine**
- **Tx:** d/c offending med, Sx usually resolve.