Risk factors: female (3x), smoking (2x), alcohol use, coffee intake, oral contraceptive use, low SE status

Inflammatory arthritis
- PRISH
- Dull, aching pain along joint line
- Prolonged morning stiffness (>60 mins)
- Improvement with movement
- Spontaneously fluctuating course
- Rheumatoid nodules: 20% of patients
- Fatigability, anorexia, weight loss, fever, night sweats
- Inflammatory markers: ESR, CRP, thrombocytopenia, anemia, leukocytosis

Pathology: several disease subsets ongoing (central immunological + joint space etiology)
- Inflammation
  - Overproduction of TNF-α & IL-6
  - Activates T & B lymphocytes, fibroblasts & macrophages
- Synovial cells & cartilage cells
  - Invaded by lymphocytes
  - Fibrosis from chronic inflammation
- Autoantibodies
  - IgM and IgA rheumatoid factors
  - ACPA (citrullinated peptides)

Investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Diagnostic Value</th>
<th>Disease Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR/CRP</td>
<td>Very low specificity</td>
<td>Disease activity &amp; response with txt</td>
</tr>
<tr>
<td>Rheumatoid Factor (RF)</td>
<td>Low sensitivity but +ve in severe RA</td>
<td>No value</td>
</tr>
<tr>
<td>Antinuclear antibody (ANA)</td>
<td>Not very specific but +ve in severe RA</td>
<td>No value</td>
</tr>
<tr>
<td>X-rays</td>
<td>Diagnostic joint erosions in disease &gt; 3 mo</td>
<td>Serial x-rays may show progression</td>
</tr>
<tr>
<td>Joint aspiration</td>
<td>Rule out infection or gout</td>
<td>No value</td>
</tr>
</tbody>
</table>

Goals of therapy
- Improve or maintain functional status
- Improve quality of life
- Achieve disease remission
- Control disease activity & joint pain
- Educate patient on disease state & medication use

Therapeutic approach
- Rapid control of sx: lowest effective dose of NSAID or short-term glucocorticoids
- Treat with DMARDs in active disease ASAP: Methotrexate 1st line
- Refractory disease: use biologics +/- MTX

Juvenile rheumatoid arthritis
- Age <16 years at onset
- No known etiology
- Follows same pattern of inflammation as RA → treated similar to Ra
- Commonly associated with ankylosing spondylitis, psoriatic arthritis

Non-pharmacological treatment
- Rest
- Occupational therapy
- Physical therapy
- Use of assistive devices
- Weight reduction
- Arthroplasty

Analgesia: “offer to ppl with RA whose pain control is not adequate... use lowest effective dose for shortest possible time period”
- NSAIDS: all equally effective; select based on comorbidities
  - CVD: naproxen 250 – 500 mg q12h
  - GI/B/renal: celecoxib 100 – 200 mg q12h
- Opioids: use combination of regular dosing interval or long-acting formulations with PRN doses
  - Codeine 15 mg q4h +/- APAP
  - Oxycodone 5 mg po q4h +/- APAP
  - Morphine 5 mg po q4h
  - Hydromorphone 1 mg po q4h
**Glucocorticoids**

**Bridging therapy**
- Control pain & synovitis when DMARD is initiated
- High dose bursts for 2 wks to treat disease flares

**Maintenance therapy**
- Frequent flares in inflammation despite DMARD/biologic
- Benefit outweighs risk of long-term use

**MOA:** anti-inflammatory & immunosuppressive
- Interferes with antigen presenting T lymphocytes
- Inhibits prostaglandin and leukotriene synthesis
- Inhibits neutrophil activity
- Impairs immune cell migration

**Dosing**
- Methylprednisolone succinate 40 mg IV daily
- Prednisone 1 mg/kg (up to 50 mg) po daily
- Methylprednisolone acetate 10-80 mg IA every 1-4 wk PRN
- Triamcinolone 10-80 mg IA every q1-4 wk PRN

**Adverse effects**

<table>
<thead>
<tr>
<th>System</th>
<th>Timing</th>
<th>Consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Acute</td>
<td>Insomnia → psychosis</td>
</tr>
<tr>
<td>HEENT</td>
<td>Chronic</td>
<td>Cataracts, glaucoma</td>
</tr>
<tr>
<td>CVS</td>
<td>Acute</td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Acute</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td>Adrenal cortex suppression, weight gain</td>
</tr>
<tr>
<td>Immunologic</td>
<td>Chronic</td>
<td>Suppression, leukopenia, infections</td>
</tr>
<tr>
<td>Skeletal</td>
<td>Chronic</td>
<td>Osteoporosis, avascular necrosis</td>
</tr>
<tr>
<td>Muscular</td>
<td>Chronic</td>
<td>Myopathy, weakness</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Chronic</td>
<td>Neuropathy</td>
</tr>
<tr>
<td>Skin</td>
<td>Chronic</td>
<td>“Cushingoid appearance”, acne, hirsutism, edema, thinning</td>
</tr>
</tbody>
</table>

**DMARDs:** should be started as soon as diagnosis of RA is made; goal of therapy is disease remission
⇒ if not achieved with 3 DMARDs +/- prednisone, consider biologic

**Dosing**
- Methotrexate 7.5 – 15 mg po/IM weekly (max 30 mg/week)
- Leflunomide 100 mg po daily x 3/7, then 10 mg po daily
- Sulfasalazine 500 mg po TID, up to 1 g TID
- Gold 10 mg IM initial, then 25 – 50 mg IM weekly-monthly
- MTX initial regimen, then add 2nd agent

**MOA:** folate analogue
- Cellular
  o Brought intracellular by folate receptors
  o Inhibits dihydrofolate reductase (inhibits purine synthesis)
  o Affects rapidly dividing undifferentiated cells
  o Increases adenosine release into blood
- Immunosuppression
  o Delayed onset of anti-inflammatory effects
  o Inhibits new cell synthesis
  o Adenosine inhibits IL-8, IL-6, monocyte & neutrophil synthesis and invasion into synovial fluid

**AEs:** GI upset, ↑ liver enzymes, alopecia, cytopenia, lung fibrosis

**Folate deficiency:** in patients treated with MTX ⇒ GI SEs & liver toxicity = administer Vitamin B9 (converted to folate)
# Biologics

## Principles of biologics
- Targeted therapy with monoclonal antibody
  - TNF-α, IL-6, CD-20, T-lymphocyte antigen 4
- Expensive and parenteral administration only
- Studied mostly with MTX as co-therapy
  - Patients that failed combo DMARDs
- Pharmacare Special Authority
  - Patients that have failed MTX & 2 other DMARDs with 1 trial of combination DMARDs

## Guidelines
- **Anti-TNF** as initial biologic after DMARD failure
- Abatacept (anti-T cell) recommended after inadequate response to anti-TNF
- Rituximab (anti-B cell) recommended with RF-positive after inadequate response to DMARD and anti-TNF
- MTX co-prescription recommended with biologics for improved efficacy

## Toxicities
- Infusion/injection reactions
  - Common, typically first dose monitored in dr clinic or hospital
  - Pre-medication common
- Infections
  - Greatest risk in first 6 mo
  - TNF inhibitors greatest risk
  - TB and hepatitis reactivation may require prophylaxis
- Cancer: possibly increase risk of solid tumors

## Routine screening prior to starting
- CBC with differential
- Liver enzymes
- SCr, urea
- Hep B & C, HIV, TB
- Anti-nuclear antibody (autoimmune)