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

Investigations

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

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

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
  - GIB/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

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)

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

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

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

System	Timing	Consequence
CNS	Acute	Insomnia → psychosis
HEENT	Chronic	Cataracts, glaucoma
CVS	Acute	Hypertension
	Chronic	Atherosclerosis
Endocrine	Acute	Hyperglycemia
	Chronic	Adrenal cortex suppression, weight gain
Immunologic	Chronic	Suppression, leukopenia, infections
Skeletal	Chronic	Osteoporosis, avascular necrosis
Muscular	Chronic	Myopathy, weakness
Neurologic	Chronic	Neuropathy
Skin	Chronic	"Cushinghoid appearance", acne, hirsutism, edema, thinning

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
  - Brought intracellular by folate receptors
  - Inhibits dihydrofolate reductase (inhibits purine synthesis)
  - Affects rapidly dividing undifferentiated cells
  - Increases adenosine release into blood
- Immunosuppression
  - Delayed onset of anti-inflammatory effects
  - Inhibits new cell synthesis
  - 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

Routine screening prior to starting

- CBC with differential
- Liver enzymes
- SCr, urea
- Hep B & C, HIV, TB
- Anti-nuclear antibody (autoimmune)

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