THERAPY in RHEUMATOLOGY

- RA
- OA
- AS
- Systemic diseases
  - SLE
  - Dermatomyositis
  - Scleroderma
- Gout
- Rheumatic fever
- Lyme disease
RHEUMATOID ARTHRITIS

- **Education**
  - Build a cooperative long-term relationship
  - Use materials from the Arthritis Foundation and the ACR
  - Assistent devices

- **Exercise**
  - ROM, conditioning, and strengthening exercises

- **Medications**
  - Analgesic and/or anti-inflammatory
  - Immunosuppressive, cytotoxic, and biologic
  - Balance efficacy and safety with activity
Rheumatoid Arthritis: Drug Treatment Options

- **NSAIDs**
  - Symptomatic relief, improved function
  - No change in disease progression
- **Low-dose prednisone (≤10 mg qd)**
  - May substitute for NSAID
  - Used as bridge therapy
  - If used long term, consider prophylactic treatment for osteoporosis
- **Intra-articular steroids**
  - Useful for flares
Rheumatoid Arthritis: Drug Treatment Options

- Disease modifying drugs (DMARDs)
  - Minocycline
    - Modest effect, may work best early
  - Sulfasalazine, hydroxychloroquine
    - Moderate effect, low cost
  - Intramuscular gold
    - Slow onset, decreases progression, rare remission
    - Requires close monitoring
Rheumatoid Arthritis: Drug Treatment Options

- **Immunosuppressive drugs**
  - Methotrexate
    - Most effective single DMARD
    - Good benefit-to-risk ratio
  - Azathioprine
    - Slow onset, reasonably effective
  - Cyclophosphamide
    - Effective for vasculitis, less so for arthritis
  - Cyclosporine
    - Superior to placebo, renal toxicity
Combinations therapy

- Methotrexate, hydroxychloroquin, and sulfasalazine
- Superior to any one or two alone for ACR 50% improvement response and maintenance of the response
- Side effects no greater
Combinations

- **Step-down prednisone with sulfasalazine and low-dose methotrexate**
  - Superior to sulfasalazine in early disease
- **Methotrexate + hydroxychloroquine or methotrexate + cyclosporine**
  - May have additive beneficial effects

New drugs

- **Leflunomide**
  - Pyrimidine inhibitor
  - Effect and side effects similar to those of MTX

- **Etanercept**
  - Soluble TNF receptor, blocks TNF
  - Rapid onset, quite effective in refractory patients in short-term trials and in combination with MTX
  - Injection site reactions, long-term effects unknown, expensive

- **Infliximab**
  - Anti TNF chimeric monoclonal antibody
  - Effective in refractorz patients in comb. With MTX
  - I.v. (9x /y)
Rheumatoid Arthritis: Monitoring Treatment With DMARDs

- These drugs need frequent monitoring
- Blood, liver, lung, and kidney are frequent sites of adverse effects
- Interval of laboratory testing varies with the drug
  - 4- to 8-week intervals are commonly needed
- Most patients need to be seen 3 to 6 times a year
## Rheumatoid Arthritis: Adverse Effects of DMARDs

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*Long-term data not available.

DMARDs Have a Dark Side

• DMARDs have a dark side
• Methotrexate may cause serious problems
  – Lung
  – Liver
  – Bone marrow
• Be on the look out for toxicity with all the DMARDs
Methotrexate Lung

- Dry cough, shortness of breath, fever
- Most often seen in the first 6 months of MTX treatment
- Diffuse interstitial pattern on x-ray
  - Bronchoalveolar lavage may be needed to rule out infection
- Acute mortality = 17%; 50% to 60% recur with retreatment, which carries the same mortality
- Risk factors: older age, RA lung, prior use of DMARD, low albumin, diabetes
Cyclooxygenase (COX) enzymes are a key step in prostaglandin production.

<table>
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<th>COX-1</th>
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<td>platelets</td>
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</tr>
<tr>
<td>Inducible</td>
<td>Housekeeping</td>
</tr>
<tr>
<td>macrophages</td>
<td>brain, kidney</td>
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</table>
Selective COX-2 Suppression: A Potentially Elegant Solution

- Traditional NSAIDs at full therapeutic doses inhibit both enzymes
  - Most have greater effect on COX-1 than COX-2
- The new drugs are highly selective for COX-2
  - >300-fold more effective against COX-2
  - This difference allows
    - Major reduction in COX-2 production of proinflammatory PGs
    - Sparing of COX-1–produced housekeeping PGs
NSAID Gastropathy: Prevention

- Short-term (1 to 4 weeks) clinical studies with COX-2 inhibitor in patients with OA and RA*
  - Significant control of arthritis symptoms
  - Fewer endoscopic ulcers
  - No effect on platelet aggregation or bleeding time
  - Insufficient data to determine risk of serious events or safety in high-risk populations

- Celecoxib has been approved; rofecoxib, meloxicam, and other selective inhibitors are currently in clinical trials
**NSAID Gastropathy: Prevention (cont’d)**

- **Counteract the problem**
- **Misoprostol**
  - Reduction of serious events by 40%
  - Results best with 200 µg qid
  - Side effects: diarrhea and uterine cramps
    - Avoid if pregnancy risk is present
- **Omeprazole**
  - Recent studies show 72% to 78% reduction in all ulcers when used for primary prevention at 20 mg qd
NSAID Gastropathy: Key Points

- Keep it in mind
- Know the risk factors
- The best way to treat it is to prevent it
  - Avoid it: Use acetaminophen, salsalate, or a selective COX-2 inhibitor
  - Counteract it: Omeprazole or misoprostol
- Antacids and H2 blockers are not the answer
  - May mask symptoms but do not prevent serious events
Therapy OA I.

- **Initial stages, intermittent, exercise pain**
  - Non pharmacological therapy
  - Local therapy (NSAIDs, capsaicin)
  - Analgetics (paracetamol)
  - NSAIDs

- **Less to moderate**
  - see A
  - SYSADOA (hyaluronic acid, glucosaminosulfate, chondroitinsulfate)
  - intraarticular corticosteroid

- **Advanced AO**
  - NSAIDs full dose
  - Opioids (tramadol)
  - Protetické pomůcky
  - Orthesis
  - Surgery
Terapy OA II.

- **acute flare**
  - Rest in bed
  - Physical therapy
  - Full dose NSAIDs
  - intrarticular corticosteroids
  - Radio-active synovectomy
  - surgery
- **OA with minimal progression**
  - x-ray in 2 years
- **OA with progression over 1mm/y with progressive pain**
  - X-ray every year
  - Prostetics
Therapy of AS

- **Regime therapy**
- **Rehabilitation therapy**
- **Pharmacological therapy**
  - NSAIDS
  - SAS (AZA, MTX)
  - intraarticular corticosteroids
  - Radio-synovectomy
- **Balneotherapy**
  - Newly diagnosed from I.st.
  - Higher stages from II.st. 1x y
- **Surgical treatment**
  - synovectomie
  - TEP
  - vertebral osteotomy
SLE – Therapy

1. **Diagnosis of SLE**
   - yes
     - **Immunisupression needed?**
       - yes
         - corticosteroid in high dose
       - no
         - alternative aproaches
           - anticoagulation
           - splenectomy
           - psycho-pharmacs
     - no
       - conservative aproach
         - analgetics
         - NSAIDs
         - antimalarials
   - no
     - Quality of life
     - acceptable
     - dose tapering
     - cytotoxic therapy
       - AZA, CFA, MTX
       - CyA
     - clinical response and toxicity
     - dose tapering
     - experimental therapy
   - Not acceptable
     - coricosteroid in small dose
     - without change
     - Life threatening condition ?
     - yes
     - Quality of life
   - Not acceptable
   - acceptable

Acceptable

Not acceptable
SLE-Therapy

• Corticosteroids
• Antimalarials
• Azathioprine
• Cyclophosphamide (nephritis)
• Cyclosporin A (nephritis)
• Methotrexate
Dermatomyositis

- Corticosteroids in high dose
- Azathioprine
- MTX
- Cyclosporin A
- Cyclophosphamide
- Ig
Scleroderma

- Vasodilation in Raynaud’s syndrome
  - Ca-blockers, pentoxyphyllin, prostavasin
- ACE inhibitor in hypertension and renal involvement
- Corticosteroids in lung fibrosis
- D-penicillamin in peripheral sclerosis
- Cyclophosphamide in lung fibrosis
Therapy of gout
non-pharmacological Th

• Diet
• Reduction of weight
• Drugs leading to hyperurikemia
• Cold water
Therapy of acute gout

- **Colchicin 1mg, then 0.5mg every 2 hours (to 6mg/day)**
- **NSAIDs (Indomethacin, Diclofenac, Ibuprofen)**
- **Corticosteroids intraarticular or per os (20-60mg)**
Therapy of gout in the intermittent or chronic stage

- Inhibitors xantinoxidase- alopurinol 200mg/day
- Urikosurics (probenecid, benzbromaron)
- NSAIDs
- Colchicin
- Diet and regime
Principals of gout therapy

Gout attack
- Colchicin
- Effect: yes → Cease the therapy
- Effect: no → further evaluation

Intermitent phase
- Diet

Chronic gout
- Inhibitors of xantinoxidase uricosurics
- NSAIDs
- Gout attacks
  - Colchicin as profylaxy
Therapy of acute rheumatic fever

- **ATB-penicillin 10 days**
- **Antiinflammatory therapy**
  - General approach
  - Salicylates 80mg/kg in 4 doses 2 weeks, then 60mg/kg another 6 weeks
  - Corticosteroids in carditis prednison 2mg/kg (2-4 w.)
  - Th. of chorea (diazepam, phenobarbital, chlorpromazin)
  - Profylaxy Penicillin G 250,000 2x d., or benzatin penicillin 1.2 mil. IU 3.-4. w for 5 y.
Lyme disease - ATB

- 1.st. Deoxymycoin, TTC, Amyxycillin (Erytromycin) 10-21 d.
- 2. and 3.st. Ceftriaxon 2g/24 h, Cefotaxim, 14-21 d.
- In arthritis try prolonged p.o. therapy (Deoxymycoin)
- neuroborreliosis, carditis are indicated to i.v. ATB therapy
- **Asymptomatic seropositivity is no indication to therapy!**