Psoriatic Arthritis
PSORIATIC ARTHRITIS (PsA)

- Chronic inflammatory arthropathy associated with psoriasis
- Etiology and genotype unclear
- 1-5% of US population has Psoriasis: 5-42% of these will develop psoriatic arthritis (skin usually precedes joints)
  - Frequency of PsA increases with disease severity and duration
- Nail changes: pitting, dystrophy, onycholysis
- Course: chronic, destructive arthritis in 30-50%
# Epidemiology of Psoriatic Arthritis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak age (years)</td>
<td>20–40</td>
</tr>
<tr>
<td>Sex distribution (F:M)</td>
<td>1:1 Overall</td>
</tr>
<tr>
<td></td>
<td>spinal involvement M&gt;F</td>
</tr>
<tr>
<td></td>
<td>DIP only M&gt;F</td>
</tr>
<tr>
<td></td>
<td>symmetrical polyarthritis F&gt;M</td>
</tr>
<tr>
<td>Prevalence rate (per 100,000)</td>
<td>50–100</td>
</tr>
<tr>
<td>Race and geography</td>
<td>Psoriasis prevalent in North European and North American Whites, uncommon in Asians</td>
</tr>
<tr>
<td>Genetic associations</td>
<td>B38 (RR52=59)</td>
</tr>
<tr>
<td></td>
<td>Peripheral arthritis</td>
</tr>
<tr>
<td></td>
<td>B39 (RR58=6)</td>
</tr>
<tr>
<td></td>
<td>Symmetrical polyarthritis</td>
</tr>
<tr>
<td></td>
<td>DR4 (RR53=7)</td>
</tr>
<tr>
<td></td>
<td>Spinal arthritis</td>
</tr>
<tr>
<td></td>
<td>B27 (RR53=5)</td>
</tr>
<tr>
<td></td>
<td>Juvenile psoriatic arthritis</td>
</tr>
<tr>
<td></td>
<td>A2 (RR53=02)</td>
</tr>
</tbody>
</table>
• Key cell: Ly Th1

• CK: INFγ, TNFα, IL1

• Activation: Mo/Mf

• CK: TNFα, IL1

• Stimulation secretion:
  - pro-inflammatory mediators
  - Metalloproteases: collagenase, stromelisine
Key Actions of TNFα in Psoriasis and PsA

- **T- Lymphocytes**
  - Pro-inflammatory cytokines and chemokines (IL-1, IL-6, IL-8)
  - Adhesion molecules

- **Macrophages**

- **Endothelium**
  - Vascular endothelial growth factor (VEGF)

- **Hepatocytes**

- **Epidermis**
  - Keratinocyte hyperproliferation

- **Synoviocytes**
  - Metalloproteinase synthesis

- **Increased inflammation**
- **Increased cell infiltration**
- **Increased angiogenesis**
- **Increased CRP in serum**
- **Skin plaques**
- **Articular cartilage degradation**

*Colloque Interface 10 Mai 2005*
JUIN IN VOLUME IN PSORIATIC ARTHRITIS
**CIASSification criteria for Psoriatic Arthritis (CASPAr)**

**Established inflammatory musculoskeletal disease**  
(joint, spine, or entheseseal)

With 3 or more points from (*scores 2):

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
</table>
| 1. Psoriasis  
(one of a, b, c) | (a) Current psoriasis * | Psoriatic skin or scalp disease present today as judged by a rheumatologist or dermatologist |
|   | (b) Personal history of psoriasis | A history of psoriasis that may be obtained from patient, family doctor, dermatologist or rheumatologist |
|   | (c) Family history of psoriasis | A history of psoriasis in a first or second degree relative according to patient report |
| 2. Psoriatic nail dystrophy |   | Typical psoriatic nail dystrophy including onycholysis, pitting and hyperkeratosis observed on current physical examination |
| 3. A negative test for rheumatoid factor |   | By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range |
| 4. Dactylitis  
(one of a, b) | (a) Current dactylitis | Swelling of an entire digit |
|   | (b) History of dactylitis | A history of dactylitis recorded by a rheumatologist |
| 5. Radiological evidence of juxta-articular new bone formation |   | Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain x-rays of hand or foot |

Clinical Findings

• 1. Skin and nail changes
• 2. Articular involvement
• 3. Dactylitis
• 4. Enthesitis
• 5. Extra-articular manifestation
• Affected skin is painful, itchy, often bleeds, and is debilitating when involving the face, genitals, palms, or soles

• Under the microscope, affected skin is thickened, has increased blood vessels, and contains numerous white blood cells
CLASSIC ANATOMIC LOCATIONS FOR PSORIASIS

- Scalp (80%)
- Elbows (78%)
- Legs (74%)
- Knees (57%)
- Nails (10-55%)
- Gluteal cleft
- Palms/soles (12%)
CLINICAL VARIANTS

- Chronic plaque psoriasis
- Guttate psoriasis
- Erythrodermic psoriasis
- Generalized pustular psoriasis (von Zumbusch)
- Localized pustular psoriasis
  - Palmaris and plantaris
  - Acrodermatitis continua
- Inverse psoriasis
Psoriatic skin and nail changes
Guttate psoriasis with widespread small red scaly papules.
PSORIATIC NAIL CHANGES

- Onycholysis
- “Oil drops”
- “Salmon patches”
- Pitting
- Subungual debris
- Onychodystrophy
- Splinter hemorrhages
Nail involvement with psoriasis. Note pitting, onycholysis (a) and hyperkeratosis (b).
<table>
<thead>
<tr>
<th>TABLE 110.4 THE MOLL AND WRIGHT CLASSIFICATION OF PSORIATIC ARTHRITIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Arthritis with distal interphalangeal joint involvement predominant</td>
</tr>
<tr>
<td>● Arthritis mutilans</td>
</tr>
<tr>
<td>● Symmetric polyarthritis – indistinguishable from RA</td>
</tr>
<tr>
<td>● Asymmetric oligoarticular arthritis</td>
</tr>
<tr>
<td>● Predominant spondylitis</td>
</tr>
</tbody>
</table>

© www.rheumtext.com - Hochberg et al (eds)
## Classification of Psoriatic Arthritis

<table>
<thead>
<tr>
<th>Type</th>
<th>Key Clinical Features</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Asymmetric polyarthritis or oligoarthritis</td>
<td>Morning stiffness, DIP and PIP involvement, nail disease, ≤ 4 joints involved</td>
<td>40%</td>
</tr>
<tr>
<td>2. Symmetric polyarthritis</td>
<td>Symmetric polyarthritis, RA-like distribution, but RF negative</td>
<td>25%</td>
</tr>
<tr>
<td>3. Ankylosing spondylitis</td>
<td>Inflammatory low back pain, sacroilitis, axial involvement, 50% HLA-B27+</td>
<td>20%</td>
</tr>
<tr>
<td>4. Distal interphalangeal joint disease</td>
<td>Nail changes, often bilateral joint involvement</td>
<td>15%</td>
</tr>
<tr>
<td>5. Arthritis mutilans</td>
<td>Destructive form of arthritis, telescoping digits, joint lysis, typically in phalanges and metacarpals</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>
Monoarthropathy associated with psoriasis vulgaris.
Distal interphalangeal joint involvement
Psoriatic arthritis with predominant involvement of the DIP joints
Involvement of the joint and adjacent nail. (a) In the right hand. (b) In the foot. Note the lack of involvement of the right 4th finger and nail.
Symmetric polyarthritis resembling RA
Arthritis mutilans. Note shortening of the thumbs and left index finger (the right 5th finger has been amputated).
Dactylitis of the second toe
Dactylitis

[Images of affected fingers and toes]
Enthesitis involving the insertion of the right Achilles tendon
Laboratory findings

- Inflammatory syndrom: ESR, CRP
- Hyperuricemia: 20% patients
- RF usually negative
- Synovial fluid analysis reveals inflammatory fluid, white blood cell counts 5000-50000/mm range
Radiographic findings

- Asymmetric proliferative erosions with ill-defined margins
- Periosteal reaction
- Soft tissue swelling
- “Pencil-in-cup” deformity
- Resorption of distal phalangeal tufts
- Subluxation
- Axial manifestations: sacroiliitis, spondylitis
Psoriatic arthritis
Radiograph of the hands, showing erosive changes at the DIP and PIP joints, with sparing of the MCP joints and wrists.
**Arthritis mutilans.** Marked osteolysis and 'pencilling', resulting in complete disorganization of the metatarsophalangeal (MTP) joints. There is also a 'pencil-in-cup' deformity of the right 5th MTP joint (b).
Asymmetric involvement of the hands. Soft tissue swelling and periosteal reaction in the right 2nd and 3rd fingers in the typical 'ray' distribution.
Examples of periosteal reactions. (a) Along the shaft of the proximal phalanx. (b) Adjacent to a large erosion, producing 'whiskering'.
Whiskering in the terminal interphalangeal joint of the great toe.
Whittling.
asymmetric sacroiliitis, with erosion and sclerosis of the left sacroiliac joint
Osteolysis.
Pencil-in-cup appearance.
Bony changes observed in degenerative disc disease (osteophytes), AS (syndesmophytes), and psoriatic spondylitis (nonmarginal syndesmophytes and paraspinal ossification)
Asymmetrical syndesmophytes and large other-than-marginal syndesmophytes
Non-marginal 'chunky' syndesmophytes
Asymmetrical sacroiliitis.
'Whiskering' is present at the insertion of the Achilles tendon, and plantar fascia, periostitis can be seen along the inferior and posterior aspects of the calcaneus.
Imaging of inflammatory changes. (a) MRI of the sacroiliac joints. (b) Bilateral inflammatory changes visualized by gadolinium enhancement (5 minutes after gadolinium injection). (c) MRI subtraction evaluation; enhancement of synovial part of sacroiliac joints and juxta-articular bone (reflecting inflammatory changes in the bone, the so called 'bone edema') are clearly visible.
<table>
<thead>
<tr>
<th>Author</th>
<th>Disease duration (years)</th>
<th>DIP predominant</th>
<th>Oligoarticular</th>
<th>Polyarticular</th>
<th>Spondyloarthropathy</th>
<th>Arthritis mutilans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones et al.</td>
<td>Onset</td>
<td>2*</td>
<td>63†</td>
<td>25</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Veale et al.</td>
<td>4 (median)</td>
<td>16</td>
<td>43</td>
<td>33</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Gladman et al</td>
<td>9 (mean)</td>
<td>12</td>
<td>14</td>
<td>40</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Jones et al.</td>
<td>12 (mean)</td>
<td>1*</td>
<td>26</td>
<td>63</td>
<td>6</td>
<td>4</td>
</tr>
</tbody>
</table>

* Defined as DIP only, in this series. † Includes mono- and oligoarticular onset. ‡ The balance in this series had overlapping patterns.

Findings of selected clinic series are displayed according to disease duration of the cohort studied. (Note: Jones et al. described patterns at onset and follow-up.)
<table>
<thead>
<tr>
<th>Feature</th>
<th>Psoriatic arthritis</th>
<th>Rheumatoid arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex M:F</td>
<td>1.1</td>
<td>2:1</td>
</tr>
<tr>
<td>RF</td>
<td>&lt;10%</td>
<td>80%</td>
</tr>
<tr>
<td>DIP joints</td>
<td>30–50%</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Pattern of joint involvement</td>
<td>Asymmetric ‘Ray’ pattern</td>
<td>Symmetric ‘Row’ pattern</td>
</tr>
<tr>
<td>Sacroiliac joints/axial spine</td>
<td>35% – any level</td>
<td>Cervical spine in late disease</td>
</tr>
<tr>
<td>Other musculoskeletal</td>
<td>Enthesitis, Dactylitis, Periarticular erythema</td>
<td></td>
</tr>
<tr>
<td>Extra-articular</td>
<td>Skin, Nail dystrophy</td>
<td>Nodules, Sicca, Vasculitis</td>
</tr>
<tr>
<td>Radiology</td>
<td>Erosion (DIP joints)</td>
<td>Periarticular osteopenia</td>
</tr>
<tr>
<td></td>
<td>Periostitis/bony proliferation</td>
<td>Erosion (wrists)</td>
</tr>
<tr>
<td>Feature</td>
<td>Psoriatic arthritis</td>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>Sex M:F</td>
<td>1:1</td>
<td>9:1</td>
</tr>
<tr>
<td>Sacroiliac joints/axial spine</td>
<td>35%</td>
<td>100%</td>
</tr>
<tr>
<td>Spinal movements</td>
<td>↓</td>
<td>↓↓</td>
</tr>
<tr>
<td>Peripheral joint involvement</td>
<td>90–95%</td>
<td>40%</td>
</tr>
<tr>
<td>Peripheral joint pattern</td>
<td>Upper and lower limbs, Large and small joints</td>
<td>Lower limbs, Large joints</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>10–25%</td>
<td>90%</td>
</tr>
<tr>
<td>Spinal radiology</td>
<td>Random distribution, Asymmetric, ‘Chunky’ syndesmophytes</td>
<td>Contiguous involvement, Symmetric, Classic syndesmophytes</td>
</tr>
</tbody>
</table>
### TABLE 112.4 PSORIATIC ARTHRITIS: RISK FACTORS FOR A POOR PROGNOSIS

- Juvenile onset
- Young adult onset
- Extensive skin involvement
- Polyarticular involvement
- Failed response to non-steroidal anti-inflammatory drugs
- Association with HIV infection
- Association with certain HLA antigens
  - HLA-B27, correlates with spondolytic involvement
  - HLA-B27, -B39 and -DQw3 correlate with progressive disease
  - HLA-DR3, -DR4 correlate with erosive disease.

Recognition of these risk factors associated with disease severity allows better and prompt planning of an early and aggressive therapeutic program.
<table>
<thead>
<tr>
<th>Therapeutic Management of Psoriatic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient education</strong></td>
</tr>
</tbody>
</table>
| **Rehabilitation and physical therapy**      | Early and aggressive active and passive physical therapy  
                                           | Dynamic strengthening exercises  
                                           | Preservation of a normal upright posture  
                                           | Avoidance of contact sports and heavy physical activity |
| **Pharmacologic measures**                   | Non-steroidal anti-inflammatory drugs  
                                           | Selective COX-2 inhibitors  
                                           | Disease-modifying drugs |
| **Dermatologic measures**                    | Photochemotherapy with psoralen  
                                           | Steroids |
| **Surgical measures**                        | Synovectomy  
                                           | Joint arthroplasty |

Early institution of an aggressive comprehensive medical management program may prevent the development of serious joint deformity and disability.
<table>
<thead>
<tr>
<th>TABLE 112.2 DISEASE-MODIFYING DRUGS IN PSORIATIC ARTHRITIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Methotrexate</td>
</tr>
<tr>
<td>- Sulfasalazine</td>
</tr>
<tr>
<td>- Cyclosporin A</td>
</tr>
<tr>
<td>- Azathioprine</td>
</tr>
<tr>
<td>- Leflunomide</td>
</tr>
<tr>
<td>- Biological agents</td>
</tr>
<tr>
<td>- Etanercept (Enbrel)</td>
</tr>
<tr>
<td>- Infliximab (Remicade)</td>
</tr>
<tr>
<td>- Alefacept</td>
</tr>
<tr>
<td>- Gold compounds</td>
</tr>
<tr>
<td>- Retinoid treatment</td>
</tr>
<tr>
<td>- Corticosteroids</td>
</tr>
<tr>
<td>- Colchicine</td>
</tr>
</tbody>
</table>

The most common agents used in treatment of psoriatic arthritis – alone or in combination
GRAPPA Treatment Guidelines for Psoriatic-Arthritis

Peripheral Arthritis
- Therapy
  - NSAID
  - IA Steroids
  - DMARD (MTX, CsA, SSZ, LEF)
  - Biologicals (Anti-TNF)

Skin and Nail Disease
- Therapy
  - Topicals
  - PUVA/UVB
  - Systemics (MTX, CsA)
  - Biologicals (Anti-TNF)

Axial Disease
- Therapy
  - NSAID
  - Physiother.
  - Biologicals (Anti-TNF)

Dactylitis
- Therapy
  - NSAID
  - Steroid Injections
  - Biologicals (Anti-TNF)

Enthesitis
- Therapy
  - NSAID
  - Steroid Injections
  - Biologicals (Anti-TNF)

Reassess Response to Therapy and Toxicity

Kavanaugh et al, J Rheumatol, 2006; 33:1417-21
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HUMIRA™ (adalimumab)</th>
<th>ENBREL® (etanercept)</th>
<th>REMICADE® (infliximab)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class</strong></td>
<td>TNF-α mAb</td>
<td>sTNFR</td>
<td>TNF-α mAb</td>
</tr>
<tr>
<td><strong>Construct</strong></td>
<td>Recombinant human mAb</td>
<td>Recombinant fusion protein</td>
<td>Chimeric mAb</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>10–20 days</td>
<td>4 days</td>
<td>8–10 days</td>
</tr>
<tr>
<td><strong>Binding target</strong></td>
<td>TNF-α</td>
<td>TNF-α/LT-α</td>
<td>TNF-α</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>40 mg SC Every other week*</td>
<td>25 mg SC Twice weekly</td>
<td>3–10 mg/kg IV with MTX Every 4–8 weeks</td>
</tr>
</tbody>
</table>

*May be administered weekly (ie, 40 mg SC without concomitant MTX).
IV = intravenous; LT = lymphotoxin; mAb = monoclonal antibody; SC = subcutaneous; sTNFR = soluble TNF receptor-human IgG complex.
Guidelines for the use of anti-TNFα therapy in Psoriatic Arthritis

1. Active Psoriatic Arthritis
   ≥3 tender and ≥3 swollen joints on 2 separate occasions 1 month apart.

2. Failure of standard therapy
   Adequate therapeutic trial of at least 2 standard DMARDs (Sulfasalazine, Methotrexate, Ciclosporin or Leflunomide). An adequate therapeutic trial is defined as:
   - Treatment for at least 6 months, with at least 2 months at standard target dose (SZP 2g/day, MTX 20mg/week, CYS 3-5mg/kg/day, LEF 20mg/day) unless significant toxicity limits the dose.
   - Treatment for < 2 months, where treatment is withdrawn because of drug intolerance or toxicity. When treatment is withdrawn after > 2 months, at least 2 months should have been at therapeutic doses (SZP 1-2g/day, MTX 7.5mg/week, CYS 3mg/kg/day, LEF 10mg/day).

Infliximab: FDA and EMEA approved for Psoriatic Arthritis, PSO (EMEA)

- Anti-TNFα mAb
- Mouse (Binding Site for TNFα)
- Human (IgG1)

- Chimeric (mouse/human) IgG1 monoclonal antibody
- Binds to TNFα with high:
  - Specificity
  - Affinity
  - Avidity
- ↓ signs and symptoms
- ↓ X-ray progression
- ↓ dactylitis and enthesopathy
INFLIXIMAB (REMICADE®)

- IMPACT-the Infliximab Multinational Psoriatic Arthritis Controlled Trial

  - dose: 5 mg/kg body weight, in perfusion, in weeks So, S2, S6 and later at 8 weeks.

  - Insufficient response:
    - the dose is risen up to maximum 10 mg/kg body weight or
    - the dosing interval can be diminished to 4-6 weeks
ADALIMUMAB (HUMIRA®)

Adalimumab

- **Structure:**
  - Fully human monoclonal antibody

- **Mechanisms:**
  - High affinity (Kd=0.07 nM) and selectivity for TNF
  - No binding to lymphotoxins
  - Potent neutralization of TNF (IC50 < 0.20 nM)
  - Long half-life (10-20 days)

- **Indications:**
  - Rheumatoid arthritis
  - Psoriatic arthritis
  - Ankylosing spondylitis

ADALIMUMAB (HUMIRA®)

ADEPT study – the Adalimumab Effectiveness in Psoriatic Arthritis Trial

- **dose:** 40 mg, subcutaneously, every 2 weeks

- administrated in monotherapy or in combined therapy (+MTX)
Etanercept: FDA/EMEA-approved for Psoriatic Arthritis and Psoriasis

- Soluble receptor tumor necrosis factor (TNF) antagonist
- FDA approved for PSA
  - ↓ signs and symptoms
  - ↓ X-ray progression
  - ↑ physical function
- FDA approved for psoriasis
ETANERCEPT (ENBREX®)

- **dose**: 50mg/week, subcutaneously

- in monotherapy or in combined therapy (+MTX)
ANTI-TNF-α – BIOLOGICAL THERAPY

• Before of the beginning of the treatment it is obligatory to:
  – Screen for tuberculosis: tuberculin test (PPD) and chest X-ray
  – Screen for viral infection: B and C hepatitis, HIV
  – Exclusion of neoplasia and demyelination diseases
  – Exclusion of asocate autoimmune phenomena (anti ds DNA antibodies)
BIOLOGICAL THERAPY
MAIN EXCLUSION CRITERIA/CONTRAINDICATIONS

- Pregnancy /breast-feeding
- Autoimmune diseases associated : systemic lupus erythematosus and multiple sclerosis
- Severe chronic heart failure (class III/IV NYHA)
- Demyelinating diseases
- Optical Neuritis
- Tuberculosis: active infection or a history of tuberculosis or positive PPD test
- Cancer, personal history of neoplasia (except neoplasia without recurrence for ≥ 10 years)
- Active/chronic/recurrent infections (infection with HBV, HCV, HIV)
- Septic arthritis (≤ 12 months)
- Infection of joint prostheses (≤ 12 months-if the prosthesis is extracted or is on an indefinite period - if the prosthesis remains in situ)
BIOLOGICAL THERAPY - MAIN SIDE EFFECTS

- Acute side effects of intravenous perfusion: fever, headache, pruritus, urticaria, hypotension, dyspnoea - infliximab;
- Infections - tuberculosis relapse - all anti-TNF-α biological agents;
- Hypersensitivity of delayed type: myalgia, arthralgia, erythema, oedema;
- Autoimmune Phenomena: human antichimeric antibodies (HACA), antinuclear antibodies (ANAs), anti-double-stranded DNA autoantibodies (lupus-like phenomena) - infliximab;
- Cardio-vascular events: worsening of heart failure, arrhythmias;
- Digestive manifestations: nausea, diarrhea;
- Neurological manifestations: demyelinating syndromes;
- Hematological manifestations: leucopenia, anemia, thrombocytopenia;
- Neoplasias, lymphomas.
Reactive Arthritis

• “Reactive Arthritis (ReA) is an infectious induced systemic illness characterized by an aseptic inflammatory joint involvement occurring in a genetically predisposed patient with a bacterial infection localized in a distant organ/system”.
REACTIVE ARTHRITIS

- Acute inflammatory arthritis occurring 1-3 weeks after infectious event (GU, GI, idiopathic)
- TRIAD: arthritis + urethritis (vaginitis) + conjunctivitis (classic triad found in < one-third of patients)
- Usually asymmetric oligoarticular + extraarticular manifestations
  - Arthritis recurrent in 15-30%, more in chlamydial arthritis patients.
- HLA-B27+ in 75-80% Caucasians
- Post-venereal onset: more common; Sex 5:1 M:F
- Post-dysenteric: less, equal M=F
- Course: self limiting (< 6 months), chronic, intermittent
- Complications: Acute anterior uveitis 5%, carditis, fasciitis
Infectious Triggers for Reactive Arthritis

COMMON PATHOGENS

• Enteric Infections
  – Shigella flexneri, serotype 2a, 1b
  – Salmonella typhimurium, S. enteritidis
  – Yersinia enterocololitica (serotypes 0:3, 0:8, 0:9; SCANDINAVIA)
  – Campylobacter jejuni

• Urogenital Infections
  – Chlamydia trachomatis, C.Pneumoniae
  – Ureaplasma Urealyticum
UNCOMMON Infectious Triggers

  - Y. pseudotuberculosis (outside of Scandinavia)
  - C. fetus
  - Vibrio parahemolyticus
  - C. psittaci
  - Streptococcal (Group A,G G)
  - Clostridium difficile
  - Propionibacterium Corynebacterium Acne
  - Staphylococcus aureus (Toxic shock arthritis)

- **Spirochetal**: Borrelia burgdorferi

- **Mycobacterium** tuberculosis and avium intracellulare (Poncet's disease)

- **Parasitic**: Giardia lamblia, Strongyloides stercoralis, Cryptosporidium, Ascaris lumbricoides, Taenia saginata, Filaria

- **Immunotherapy/Immunization Related**
  - Bacillus Calmette-Guerin : intravesical injection
  - Hepatitis A vaccine
Chlamydial Arthritis

- More than 50% of Reiter’s patients have Abs to Chlamydia
- Chlamydial Ags by RNA or DNA probes found in joints
- May account for up to 10% of all EARLY Arthritis patients
- C. Trachomatis > C. psittaci or C. Pneumoniae (erythema nodosum, pneumonia, myocarditis)
- Manifestations similar to Reiters, < 50% B27+; and ~15% have no urogenital sxs.
- Dx: Sxs + serology or PCR probe
- Rx: doxycycline or lymecycline > 3 mos. to eradicate infx and decrease sequellae
Post-Dysenteric Outbreaks of Reiters

• Epidemics of known arthritogenic bacteria
  – < 20% of HLA-B27(+) persons develop incomplete Reiters
  – Fewer develop Complete Reiters syndrome

• Shigellosis: 0.2-2% of patients develop reactive arthritis
  – often diarrhea resolves before arthritis appears

• Salmonella: 1-3% develop reactive arthritis (6-12% seen?)
  – Like Shigella, arthritis more likely in HLA-B27 or HLA-B7 (+)
    • Other cross reactive Ags: Bw22, B40, B42, or B60
HIV and Reactive Arthritis

- 1st described 1987, after immunosuppression HIV → AIDS
- B27+ HIV+ patients may manifest a severe form of:
  - Reactive arthritis; Psoriatic arthritis; Spondyloarthropathy
  - Common: asymmetric poly- or oligoarthritis, lower extremity arthritis, dactylitis, enthesitis, fasciitis, conjunctivitis, urethritis
- Anti-Viral Therapy as resulted in these being less common in the USA and more common in sub-Saharan Africa
- DOES NOT OCCUR → anklylosing spondylitis OR uveitis
- Epidemiologic studies DID NOT show increased incidence of Reiters in HIV+ populations
- Notes on Rx: poor NSAID response; progression of AIDS w/ immunosuppressive Rx
Clinical Findings

- In patients with postchlamydial disease, urethritis is usually mild, painless and nonpurulent.
- Conjunctivitis is usually observed very early, before the onset of arthritis, uveitis is less common but occurs in 15% of patients with chronic persistent disease.
- Skin manifestations include: *Keratoderma blenorrhagica*, *Circinate balanitis* and oral ulcers.
- Less common patients can develop valvulitis, rhythm disturbances.
CLINICAL MANIFESTATIONS OF REACTIVE ARTHRITIS

- Arthritis
- Uveitis, conjunctivitis
- Nephritis
- Carditis
- Osteitis, hyperostosis
- Enthesopathy
- Gut inflammation
- Urethritis, cervicitis, prostatitis, balanitis
- Skin, nail, mucous membrane involvement
Reactive arthritis of the knee.
KERATODERMA BLENORRHAGICUM
Keratoderma blenorrhagicum
Keratoderma blenorrhagicum of the palm in a patient with reactive arthritis.
Circinate balanitis in a man with reactive arthritis
Genito-urinar involvement

- Urethritis
- Prostatitis
- Orchitis
- Balanitis
- Vaginitis
- Cervicitis

Sausage Digits
= periostitis + enthesitis + synovitis.
INVESTIGATION OF REACTIVE ARTHRITIS

- ESR
- C-Reactive protein
- Blood cell count
- Liver function tests, e.g. ALAT, GT
- Kidney function tests, e.g. serum creatinine or blood urea nitrogen
- Rheumatoid factor tests
- Urinalysis
- ECG
- Joint fluid sample with analysis of:
  - Cell count
  - Exclusion of crystals
  - Gram stain
  - Bacterial culture
- Bacterial culture of:
  - Feces
  - Urine or urethral swab
  - Cervical sample
  - Throat
- Blood culture (not always necessary)
- Antibody determination at admission
- HLA-B27 antigen (or HLA typing) after 2–4 weeks
- X-Ray of affected joints
- Ophthalmological examination if eye symptoms present
TREATMENT OF ACUTE REACTIVE ARTHRITIS

- Antibiotics if infection is still present
- Rest
- Nonsteroidal anti-inflammatory drugs
- Intra-articular corticosteroid
- Systemic corticosteroids
- Rarely, second-line antirheumatic drugs
Reactive Arthritis

**Treatment:**
- NSAIDS are the first line of treatment.
- In patients with frequent recurrences or chronic arthritis benefit from DMARDS such as sulfasalazine or methotrexate.
- If there is axial involvement they will benefit from TNF-alpha blockers.
- Topical steroids are indicated in conjunctivitis and uveitis.
- In monoarthritis steroid injections could be beneficial.
Enteropathic arthritis

- Ulcerative colitis
- Crohn’s disease
- Whipple disease
- Coeliac disease
- Intestinal bypass surgery
ENTEROPATHIC ARTHRITIS

• 5-20% of IBD patients (Crohn's disease or Ulcerative colitis) will develop inflammatory arthritis

• Risk increases with extent of colonic disease and presence of other extraintestinal manifestations: abscesses, E. Nodosum, uveitis, pyoderma gangrenosum

• Gut disease may be asymptomatic for years

• Subsets:
  – Asymmetric oligoarthritis (intermittent or chronic)
  – Seronegative RA-like polyarthritis 20% of IBD pts
  – Spondylitis 10-15% (may be misdiagnosed as AS)

• Peripheral arthritis parallels the gut! NOT THE SPINE!
SAPHO Syndrome

• Synovitis, Acne, Pustolosis, Hyperostosis, Osteitis
• (Pustular Skin Disease + Osteitis or Arthritis)
• Rare form of reactive
• Most reports from Japan > Scandinavia > France > USA
• Arthritis of Amphiarthroses (Saddle joints): AC, SC, Manubriosternal
• Imaging: erosions, osteitis, ~30% sacroiliitis
• Therapy: Rx of pustular skin disease
  – +/- response to Abx, NSAIDs, Steroids, SSZ, colchicine
  – Good response to TNF inhibitors