Juvenile rheumatoid arthritis (JRA) / Juvenile chronic arthritis (JCA)

JRA/RA = 1/20

JRA is a group of diseases (5 subgroups)

Etiology
- Unknown.
- Precipitating or aggravating factors: infection, trauma, stress
- Endocrine influences (high female prevalence)
- Systemic type: HLA-B35
- Pauciarticular type: HLA-DR5
- Seropositive JRA: HLA-DR4 (as in adult JRA)

Pathogenesis and pathology
- Similar to adult RA, but only 20% is RF positive (adult: over 66%)
- Agammaglobulinaemia and IgA deficiency are associated with chronic polyarthritis

Classification of JRA

Systemic-onset JRA (20%) Febrile form of Still’s disease
- Both boys and girls under 5, but can be adult-onset Still disease
- High fever (40 °C), macular pink rash on trunk and upper arm
- Generalized lymphadenopathy, hepatosplenomegaly (leukemia? neuroblastoma?)
- Pleuritis, pericarditis
- Arthralgia, muscle spasm, morning stiffness, but no true synovitis
- Febrile episodes subside after 1-2 years, but the arthritis remains
- RF, ANA: neg.
- Remission rate: 50%

Polyarticular (RF-positive) JRA (10%)
- Resembles adult-onset RA
- Preadolescent girls
- Systemic and polyarticular involvement of both large and small joints (fingers)
• Cervical spine involvement (pain, torticollis, limited motion
• Subluxation of the atlantoaxial joint may be fatal during anesthesia!
• Temporomandibular joint involvement: ear pain, pain during eating, inability to open the mouth, micrognathia
• Low grade fever, weight loss, anemia, growth retardation, morning stiffness, rheumatoid nodules
• RF: 100%, ANA: 75%

Polyarticular (RF-negative) JRA (30%)
• Mostly girls are affected
• Clinically similar to the seropositive polyarticular group, but: RF is absent, ANA 5% pos. Onset is common at any age. Prognosis is more favorable. No vasculitis. Erosions are less common

Oligoarticular (pauciarticular) JRA (type 1) (25%)
• Girls under 5 are affected
• Chronic iridocyclitis: before, during, after arthritis. unilateral, starts insidiously – eye watering, photophobia. Slit-lamp examination: every 3 months. If not treated early → blindness!
• Arthritis: 4 or less joints are affected during the first 6 months
• ANA pos. in 50% → high rate for iridocyclitis!

Knee involvement in JRA : common in oligoarticular form

Oligoarticular (pauciarticular) JRA (type 2) (15%)
• Mostly in preadolescent boys
• RF, ANA neg.
• HLA-B27 in 75% → spondylitis ankylopoetica or Reiter’s syndrome will develop
• iridocyclitis – mainly acute
• Remission rate: 15-20% (50% of these is permanent)

Laboratory findings
• ↑ESR
• Mild to moderate anemia, leukocytosis (up to 50,000/μl)
• Thrombocytosis → poor prognosis
• Acute phase reactants: ↑CRP, ↑C3, ↑haptoglobin,
• RF, ANA may be positive
• Synovial fluid analysis: cloudy appearance: ↑WBC, up to 100,000/μl, mostly PMN-s, glucose normal, cultures are negative, ↓C3, ↓C4

Roentgenographic findings
• Early: swelling of soft tissues, effusion, periostitis
• Late: osteoporosis, accelerated bone growth
• Chronic: narrowing of joint space, bone destruction, fusion
• Temporomandibular joint: erosion, flattening, rarefaction of the condyle. Shallow glenoid fossa.

Differential diagnosis of JRA
• Systemic: infections, leukemia, neuroblastoma
• Polyarticular: acute rheumatic fever, gonococcal arthritis/dermatitis, PSS
• **Monarticular:** infectious arthritis, aseptic necrosis, pigmented villonodular synovitis
• **Pauciarticular:** ankylosing spondylitis, Reiter’s syndrome, inflammatory bowel disease, Lyme disease

**Management of JRA**
Since the prognosis is relatively good, the aims are:

1. To treat with drugs less dangerous than is the disease
2. To preserve joint function
3. Patient and family education
   • Bed rest – only if pericarditis is present
   • Local rest – splints if severe inflammation is present

**Drugs:**
- Acetylosalicylic acid, other NSAIDs.
- Systemic corticosteroids only for pericarditis, resistant systemic JRA, severe iridocyclitis
- Local steroids in eye drops of intraarticularly

**Simple measures:**
- Sleeping bag, warm tub baths, cycling, swimming
- Temporomandibular joint: liquid fluids with straw; chewing gum
- Orthopedic surgery: mainly to release contractures

**Iridocyclitis: urgent!**
- All children: slit-lamp examination yearly
- Pauciarticular: every 3 months, later every 6 months

**Prognosis**
- Good for most patients
- Mild to moderate deformities: 15%
- Severe deformities: < 5%
- Mortality rate: < 1%
- Worse in the systemic and polyarticular seropositive forms
Reiter's syndrome

Described by Hans Reiter in 1916.

**Definition**
A triad of polyarthritis, conjunctivitis, urethritis + mucosal ulcerations, keratoderma blenorrhagicum, balanitis circinata

**Pathogenesis and pathophysiology**
- Reactive changes in genetically susceptible individuals:
  - HLA-B27 positivity in more than 75%
  - **Postinfectious variant**: reactive arthritis after Shigella (mainly flexneri), Salmonella, Yersinia and Campylobacter infections
  - **Venereal variant**: M/F: 50/1: after Mycoplasma, Chlamydia trachomatis, Ureaplasma urealyticum infections
- Arthritis: synovitis without pannus formation.
- HIV positive patients develop exceptionally severe symptoms.

**Clinical manifestations**
Mainly young men are affected. Non-gonococcal urethritis after sex. Arthritis, conjunctivitis develop simultaneously or 2-6 weeks later. Fatigue, weight loss, hectic fever, anorexia, lymphadenopathy, splenomegaly
- Arthritis in Reiter’s syndrome: Acute, asymmetric, pauciarticular (small joints of feet, ankles, knees), sacroilieitis (mainly unilateral)
- Enthesitides, Achilles tendinitis, calcaneal bursitis (lover's heel), plantar fasciitis
- Keratoderma blenorrhagicum: serpiginous, macular hyperkeratotic, scaling lesions on hands, soles and scalp

**Oral lesions** occur in 85%, are painless
- Red papular lesions of 1 mm - 1 cm diam. asymptomatic mucosal ulcerations of the buccal or mucosa, gingiva and lips (10%)
- Geographic tongue with superficial erosion
- Palatal mucosa: small, bright red macules, later darken
- Small, opaque vesicles, glistening erythema with a granular surface
- Histologically: parakeratosis, acanthosis, intraepithelial microabscesses with PMN infiltration

Balanitis circinata: weeping or dry ulcerations, erosive plaques on the scrotum

Conjunctivitis occurs in at least 1/3 of cases, later iritis. May progress to iridocyclitis. Episcleritis can also occur.

**Other clinical manifestations**
- Urethritis: frankly purulent or watery discharge. Prostatic massage yields pus. Can be sterile in enteral variant.
- Other: polyneuritis, cardiac conduction defects, aortic insufficiency

**Cutaneous lesions resembling psoriasis**
- psoriasiform lesions on the abdomen and buttocks
- subungual lesions resembling psoriasis, may lead to onycholysis
- exfoliative dermatitis (rarely)

Differential diagnosis
- Erythema multiforme (greater involvement of the lips and target lesions on the skin)
- Behcet’s syndrome
- Gonococcal and staphylococcal infection: pathogens recoverable in synovial fluid
- Other reactive arthritides: Crohn’s disease, ulcerous colitis, Whipple’s disease
- Psoriatic arthritis: skin lesions, DIP-s are affected

Therapy
- Bed rest
- With marked systemic component: NSAID-s (aspirin or indomethacine) for arthritis
- Sulfasalazine, up to 3 g/d
- Enthesitis, tendinitis: intralesional corticosteroids
- Uveitis: aggressive corticosteroid treatment
- in debilitating cases: azathioprine 1-2 kg/kg, MTX 7.5-15 mg/wk
- in HIV positive patients: AZT
- Skin lesions: tar and topical steroids
- Physical therapy
- Dental management
- Topical analgesic mouth rinses (Benadryl) or ointments (5% lidocaine)
- Mouth rinse with neutral solutions (sodium bicarbonate, calcium bicarbonate, peroxide)
- Tetracycline ointment or solution, fluorinated steroids
- Supplementation of vitamin B12, folate, iron

Course and prognosis
Variable course: one shub; relapses; persisting symptoms. Prognosis: good, no joint deformity. 10% transforms to SPA.
Behçet's syndrome

Classic triad of oral ulcers, genital ulcers, eye inflammation, + recurrent multisystem sings and symptoms involving the skin, mucous membranes, vessels and joints. Most frequent in Japan (1/10 000), Turkey, Mideastern countries. M/F: 5/1

Pathology

- Etiology: unknown
- Weak association with HLA-B5, HLA-B12,
- Vasculitis
- Autoimmune mechanism: increase in total complement and C9
- C3, C9 deposition in blood vessel walls, C9 in basement membranes
- Lymphocyte cytotoxicity against oral mucosal homogenate

Clinical features

- **Major:** recurrent aphthous stomatitis, recurrent genital ulcerations, ocular involvement (uveitis, chorioretinitis) (1-4)
- **Minor:** arthralgia, intestinal ulcers

1. Oral ulcerations (90%)

Occur on non-bone bound tissues. Recurrent, painful, aphthouslike ulcerations of the oral mucosa, lips and pharynx. Small lesions of recurring aphthous stomatitis, or large, scarring, disabling lesions (Sutton’s disease)

2. Genital ulcerations

Small, punched out, painful ulcerations of the male genitalia or painless ulcerations of the female vulva and vaginal mucosa

3. Eye lesions

Iritis (80%), often associated with other signs of ocular inflammation (photophobia, conjunctivitis, uveitis, neuritis, episcleritis, hypopyon, vitreous opacification, retinal changes). May be reversible or lead to blindness

4. Skin lesions (80%)

Pyoderma, erythema nodosum, or pustule formation at the site of a needle puncture (pathergic sign)

4. Neurologic manifestations (25%)

Organic confusional states, cranial nerve damage, spinal cord involvement, meningeal and spinal encephalitis, psychologic changes, hemiparesis, paralysis, death

5. A variety of other lesions

- vasculitis, colitis (ulcers, vomiting, flatulence, diarrhea or constipation)
- seronegative arthritis (60%), arthralgia, swelling, synovitis in the knee and ankle (in more than 50%), no disability
- migrating thrombophlebitis (20-65%), Budd-Chiari syndrome

Laboratory findings

No specific test. Elevated ESR during the attack
Diagnosis
if 4 major criteria are present

Differential diagnosis
Reiter’s syndrome (ulcers are not painful), SLE, Stevens-Johnson syndrome, aphthous ulcers

Therapy
Fibrinolytic agents, steroids, whole blood transfusion, transfer factor

Dental management

- minor oral ulcers: topical or intralesional corticosteroid, tetracycline, chlorhexidine
- severe disease: systemic steroids (Prednisone 4-60 mg/die), azathioprine, chlorambucil, colchicine, cyclosporin A
- soft toothbrush, and toothpaste, baking soda