

# Juvenile idiopathic arthritisFeedback

**Juvenile idiopathic arthritis** or **juvenile rheumatoid arthritis** is the *most common systemic disease in children*. This disease starts before 16 years of age and must last more than 6 weeks. Classifications of childhood arthritis are different. The latest is the so-called ILAR classification → JIA. Others are: systemic, oligoarthritis, polyarthritis, psoriatic arthritis, arthritis with enthesitis and other arthritis. Knees and other *big joints* are most often affected.

## Epidemiology

It is a common disease, the **incidence' is 2-20/100 000**. *Girls* are affected 2-3 x more often than boys. Juvenile idiopathic arthritis has two peaks - up to 3 years of age and in puberty.

## Etiology and pathogenesis

The disease is relatively unknown, probably multifactorial. There are 2 main **theories**. It is either an **autoimmune disease** characterized by abnormal T-lymphocytes, chronic synovialitis. It is explained by immunogenetic influences that affect antigen presentation (APC) and T-bb, thereby changing the course of the disease. The second possibility is the so-called **Genetic predisposition**, where the part of the short arm of the 6th chromosome, where the HLA system is located, has a controlling role. *Other factors* are stress, hormonal imbalance, infection (mycoplasmas, EBV) or ANS dysregulation.

## Pathological-anatomical picture of joint involvement

There is swelling and hypertrophy of the synovial lining → **pannus** (granulation tissue formed by fibroblasts, blood vessels, round cell infiltration). The vessels are clogged with inflammatory cells and perivascular infiltrates are formed in them. Pannus grows from the area of the osteocartilaginous junction to the cartilage of the articular surfaces and destroys them. Erosion and eventual defects occur. There is involvement of the subchondral bone with the formation of **cysts' and ischemization on the basis of vascular involvement**. There are **deformities** of the articular ends of the articulating bones. The same process takes place periarticularly and leads to wear and tear of the ligaments and joint capsule, which causes instability of the joint.

**Synovial biopsy** is hypertrophy and hyperplasia of the *stratum synoviale*, the subsynovial layer is congested and edematous, there is vascular hyperplasia with T-lymphocyte infiltration and plasmacytes.

## Clinical picture

### Oligoarthritis

Oligoarthritis is a low-intensity inflammatory disorder of 4 or fewer joints. Extra-articular manifestations are rare (with the exception of chronic uveitis). The lower limbs are mainly affected, in 60% it is the knees, then the ankle, or the elbow. Affected joints tend to be swollen, warmer, minimally painful, there is significant limitation of joint mobility (often morning stiffness). **Prognosis** is mostly good.

### Advanced Oligoarthritis

After the first 6 months, the disease affects 5 or more joints. The picture and prognosis are close to polyarthritis. However, flexion contractures and joint deformities are more common.

### Polyarthritis

- According to the immunological evidence of rheumatoid factor (antiglobulin antibody) in the serum, we divide it into:
  1. **polyarthritis RF-negative** (seronegative);
  2. **polyarthritis RF-positive** (seropositive).

The onset is usually gradual, affecting more than 5 joints (mostly more than 8<sup>[1]</sup>) arthritis can be remittent or persistent with a tendency to symmetrically affect mainly the *large joints* (knees, wrists, elbows, ankles), hip joints are affected in ½ cases. Cervical spine and temporomandibular articulation are often affected. In the small joints of the hand, it is a disease mainly of the interphalangeal joint of the thumb, the 2nd and 3rd MCP joints, and the proximal interphalangeal joints of all fingers. They are hot, soaked, rarely reddened. Deformities are divided into: **buttonhole type" (boutonnière, PIP flexion and hyperextension of the DIP joint), where there is flexion contracture of the fingers, and swan neck type** (swan-neck, PIP hyperextension + flexion DIP joint).

**Extra-articular involvement** includes subcutaneous rheumatic nodules, hepatosplenomegaly and lymphadenopathy. '*Seropositive polyarthritis*' **tends to be significantly destructive, corresponding to RA in adults, with seronegative polyarthritis** we note a milder course, where it can even go into permanent remission.

## Systemic form of JIA (Still's disease)

Still's disease is a severe systemic involvement at the onset of JIA in 10% of children. Fever (briefly exceeding 39 °C), tachycardia, macular exanthema around the trunk and upper extremities, hepatosplenomegaly, generalized lymphadenopathy and pericarditis appear.

Joint disorders most often affect the large joints of the limbs and the small joints of the hand. It is important not to forget to examine the TMK and the range of motion of the cervical spine (subluxation in the atlanto-occipital and atlantoaxial levels with compression of nerve structures). The **extra-articular symptoms** include: *abnormalities of the child's growth and overall development, local growth disorders* and *chronic uveitis*. About half of the patients calm down and the further course is under the guise of oligoarthritis, in the 2nd half there is progression and severe involvement of the joints.

## Arthritis with enthesitis (spondyloarthropathy)

Spondyloarthropathy usually begins with the involvement of soft tissues, especially the tendon attachments around the joints.

**SEA syndrome** is a myoskeletal disease with an onset before the age of 16, seronegativity on RF and ANA, enthesitis and arthralgia/arthritis is mostly located outside the axial skeleton.

**Juvenile ankylosing spondylitis** (JAS) is a chronic inflammatory disease of peripheral and axial joints, often associated with enthesitis, seronegativity on RF + ANA, the share of heredity is significant here.

**Etiology and pathogenesis:** the onset of symptoms appears in late childhood and adolescence, 7 x more often boys are affected, there is a close link with the antigen HLA-B27 which is the triggering factor intestinal infection. **Clinical picture:** In the initial stage, arthritis of the peripheral joints appears - mainly on the lower limbs and enthesitis - discrete swelling, pain, inflammatory affection of the SI joint (X-ray: diffuse osteoporosis of the surroundings, rubbing border of the subchondral bone, erosion → widening of the joint space → disappearance of the joint space and sacroiliac fusion), changes on the spine, calcification occurs lig. longitudinale anterius, later to the vertebral synostosis under the "bamboo rod" image.

## Psoriatic arthritis

This is arthritis with psoriasis. The disease is characterized by dactylitis – the finger is sausage-shaped, the so-called "sausage digit") and nail abnormalities, pitting and transverse grooves are observed. The disease occurs mainly in *girls in pre-school age and around 10 years of age. The knee and small joints of the hand and foot are most often affected (typically asymmetrically). The prognosis is worse compared to other forms of JIA.*

## Characteristics of clinical manifestations

- **arthritis** - swelling of a joint with limitation of movement, pain, stiffness, which does not originate from a mechanical disability. The effusion should have a typical cytological finding;
- '*fever*' - daily fevers lasting at least two weeks of a jumping nature with a temperature peak above 39 °C and with a return below 37 °C;
- **serositis** - pericarditis, pleuritis, peritonitis;
- **enthesitis** - swelling and soreness at the point of attachment;
- **psoriatic rash** - to be confirmed by a dermatologist;
- **dactylitis** - swelling of the fingers that extends beyond the edge of the joint (resembles a hot dog);
- **rheumatoid factor positivity, positive ANA** - 2 positive findings in an interval of 3 months are required;
- **uveitis** (rheumatoid eye disease) – it must be confirmed by an ophthalmologist by slit-lamp examination;
- **remission** - no joint symptoms or pain, normal FW during 2 years without treatment;
- **relapse** - return of symptoms after a rest period lasting min. 6 months.

## Diagnosis

Based on the diagnostic criteria, which are numerous:

### ▪ 1. JIA diagnostic criteria:

The disease begins to manifest itself before the age of 16. The patient suffers from arthritis of one or more joints, swelling, effusion, presence of mobility limitation, stiffness during movement, warmer joint. Arthritis lasts 6 weeks and longer. During the first 6 months, a disease such as polyarthritis, oligoarthritis or a systemic form takes place. It is important to rule out other forms of juvenile arthritis.

### ▪ 2. clinical criteria:

Arthritis lasting 3 months or more. Arthritis of the next joint is 3 months. Later, symmetrical involvement of small joints, joint effusions, joint contracture, tendosynovitis or bursitis, muscle hypotrophy and atrophy, joint stiffness, rheumatoid eye involvement and rheumatoid nodules occur.

### ▪ 3. X-ray criteria:

X-rays reveal osteoporosis, microcysts, joint space narrowing, bone growth disorders, and cervical spine involvement.

### ▪ 4. laboratory criteria:

Positive histological evidence from synovial tissue appears. **Blood count** shows signs of inflammation. Active JIA has elevated ferritin, leukocytosis, thrombocytosis, increased sedimentation. The chronic course shows normocytic hypochromic anemia. **Immunological examination** shows ANA (see IgG, positive - high risk of chronic uveitis in girls with oligoarthritis, negative - arthritis with enthesopathy), positive rheumatoid factor (antiglobulin antibodies against the Fc fragment IgG, seropositivity (latex test) indicates a more severe course), HLA-B27 (genetically determined surface antigen of major leukocytes, in most patients with ankylosing spondylitis).

## Conclusion

If the patient has 4 of the listed manifestations with proven arthritis, we are talking about **definite JIA**. If 8 or more criteria are present - **classic JIA**.

This cannot be done in outpatient practice, if a rheumatic disease is suspected, we send the child to a pediatric rheumatologist.

## Zobrazovací vyšetření u JIA

- **RTG** (známky *časné*: otok periartikulárních měkkých tk. a prosáknutí kloubu, *pozdní*: periartikulární osteoporóza, snížení kloubních štěrbin, kostní eroze, akcelerace epifyzárního vyžrávání s časným uzávěrem růstové ploténky a zkratem kosti, hypertrofické konce dlouhých kostí);
- **sonografie** (kvantifikace kloubního výpotku v kyčelním kloubu);
- **MRI** (počínající eroze kloubních chrupavek, podezření na nekrózu hlavičky femuru při chronickém průběhu artritidy, plánování synovektomie);
- scintigrafie, diagnostická artroskopie, synoviální biopsie.

## Imaging examination in JIA

- **RTG** (*early* signs: periarticular soft tissue swelling and joint infiltration, *late*: periarticular osteoporosis, reduction of joint spaces, bone erosion, acceleration of epiphyseal maturation with early closure of the growth plate and shunting of the bone, hypertrophic ends of long bones);
- **sonography** (quantification of joint effusion in the hip joint);
- **MRI** (beginning erosion of articular cartilage, suspicion of necrosis of the femoral head in the chronic course of arthritis, planning synovectomy);
- scintigraphy, diagnostic arthroscopy, synovial biopsy.

## Pharmacological therapy

It can accompany rehabilitation, spa therapy, regimen measures, psychosocial care or rheumatic surgery and prosthetic care.

### Non-steroidal anti-rheumatic drugs

The goal of therapy is to find a drug that blocks more COX-2 (inflammation) than COX-1 (stomach, kidney, platelets). Selective COX-2 are expensive, but they reduce NU (gastropathy, interstitial nephritis, papillary necrosis, bleeding conditions, bronchospasm, etc.). The practitioner can indicate the treatment himself, usually only after consultation with a specialist. The therapy lasts min. 6 weeks before results can be evaluated. The most frequently used therapy is the indication **ibuprofenu**, monitored by KO, liver tests and urine). Diclofenac, tiaprofenic acid and indomethacin *are also indicated, but we do not administer it for more than 3 weeks*.

### Second line of antirheumatic drugs

The second line of anti-rheumatic drugs are slow-acting anti-rheumatic drugs. About 2/3 of children with JIA do not respond to NSAIDs, so we usually treat this group with NSAIDs.

Is part of them:

- **Methotrexate** - a competitive inhibitor of dihydrofolate reductase, leads to a reduction in the supply of pyrimidines and purines to rapidly dividing cells, has an antitumor effect, reduces the activities of neutrophils, lymphocytes and macrophages. The following day we give acid. leaf. Methotrexate is relatively safe in low doses, administered orally (possibly also i.m., s.c.). NÚ - mucosal ulceration, liver damage, changes in KO.
- **Sulfasalazine** - is used, among other things, for non-specific intestinal inflammation. NÚ - skin manifestations, mood changes, hepatotoxicity, KO changes. The effect appears min. in 2-3 months of administration.
- **Antimalarials - hydrochloroquine** (immunomodulation, collagenase inhibition), NÚ - hyperpigmentation, corneal and retinal changes.

## DMARDs

- (Disease-modifying antirheumatic drugs, so-called basal drugs) – if NSAIDs are not enough for therapy of active synovialitis, they have an anti-inflammatory effect by reducing the production of cytokines weeks to months after use.

## Corticoids

The indication of corticoids must be very responsible, the doctor must be aware of the possible consequences. It is administered locally (intra-articularly - a basic element of treatment in the early stage), orally and parenterally. The absolute indication is a systemic form with life-threatening pericarditis and a severe form of uveitis.

## Surgical therapy

In contrast to adults, rheumatic surgery is used less often in children. **Synovectomy is the so-called extirpation of the inflammatory lining of the joint. The soft tissue operations that are performed are called tenotomy and capsulotomy.** *Performances on the skeleton* are usually operations to solve unequal limb lengths after irritating overgrowth of long bones.

## Prognosis

Mortality from JIA is below 1%, permanent arthritis activity occurs in 31-55% of patients, severe functional disability in 9-30%.

## Assessment of disease activity

1. **active'** (the number of joints with active synovialitis unresponsive to therapy is increasing);
2. **stable'** (stable number of joints, corresponding to therapy);
3. **inactive** (no signs of active synovialitis/active extra-articular manifestations);
4. **remission** (no signs of active joint synovitis, extra-articular manifestations, 2 or more years without treatment).

## Evaluation of functional activity of the patient

We divide it into two ratings: **according to Steinbrocker'** and a modified score **according to Lysholm**.

## Links

### Related Articles

- **Rheumatology:** Henoch-Schönlein purpura ■ Kawasaki disease ■ Systemic lupus erythematosus ■ Juvenile dermatomyositis ■ Juvenile idiopathic arthritis ■ Rheumatoid arthritis ■ Psoriatic arthritis ■ 'Ankylosing spondylitis

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