Juvenile Idiopathic Arthritis

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Juvenile idiopathic arthritis (JIA)

- Formerly called juvenile rheumatoid arthritis(JIA)
- Is a broad term used to describe several different forms of chronic arthritis in children
- The most common chronic rheumatological disease of childhood
- Without appropriate and early aggressive treatment, JIA may result in significant morbidity, such as leg-length discrepancy, joint contractures, permanent joint destruction, or blindness from chronic uveitis.

Definition

- Arthritis is defined as joint effusion with the presence of : limitation of range of motion, tenderness, and hotness
- JIA is defined as arthritis of one or more joints occurring for at least 6 weeks in a child younger than 16 years of age
- JIA is a diagnosis of exclusion. A number of conditions, such as infections, malignancy, trauma, reactive arthritis, and connective tissue diseases such (SLE), must be excluded before a diagnosis of JIA can be made

Etiology

- The etiology is not completely understood
- multifactorial, (genetic and environmental factors)
- siblings of those affected by JIA have a prevalence that is 15-30 fold higher than the general population.
- Other factors : psychological stress, trauma, hormonal abnormalities, and infectious triggers

Epidemiology

- JIA is one of the more frequent chronic diseases of childhood
- prevalence of 1 : 1,000 children.
- has two peaks, one at 1-3 years and one at 8-12 years, but it can occur at any age.
- Girls are affected more commonly than boys

Pathology

- Cell-mediated and humoral immunity play a role in the pathogenesis of JIA
- The common underlying manifestation is the presence of chronic synovitis.
- The synovium becomes thickened and hyper vascular with infiltration by lymphocytes, along with inflammatory cytokines such as: (TNF-a), (IL-6), IL-1 and IL-17.
- The role of humoral immunity in is supported by the increased level of autoantibodies, such as antinuclear antibodies (ANAs), and by the presence of circulating immune complexes

Clinical Features

All subtypes of JIA, share common symptoms:

1- Joint swelling .

2- morning stiffness .

3- pain, and limited movement of a joint.

4- Limping or problems using a limb.

5- Spiking fevers

6- Rash

7- Eye involvement : uveitits , iritis . (Red eyes)

8- Unspecific symptoms like : lethargy, reduced physical activity, and poor appetite .

There are five types of juvenile arthritis:

1- Oligoarthritis

2- Polyarthritis

3- Systemic-onset JIA

4- Psoriatic arthritis

5- Enthesitis related arthritis

Oligoarthritis

-The **most common** type
-presents in **young children**, with a peak at **2 to 4 years** .
-It's **often mild**
-female > male (3:1)

Oligoarthritis

-Arthritis affecting 1-4 joints during 1st 6 mo of disease.
-The arthritis is found **in medium-sized to large joints**
-Asymmetrical pattern
-Large, weight-bearing joints (knee and ankle) are usually affected.

Oligoarthritis

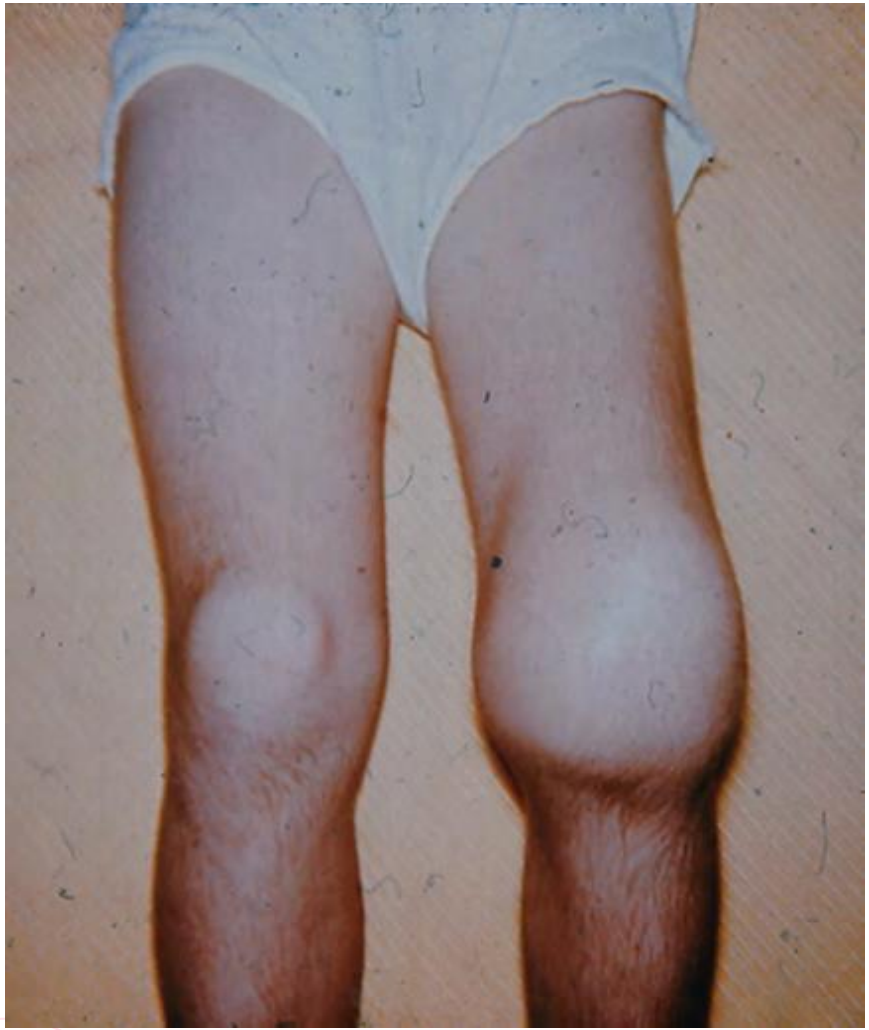
-Extra-articular manifestations :

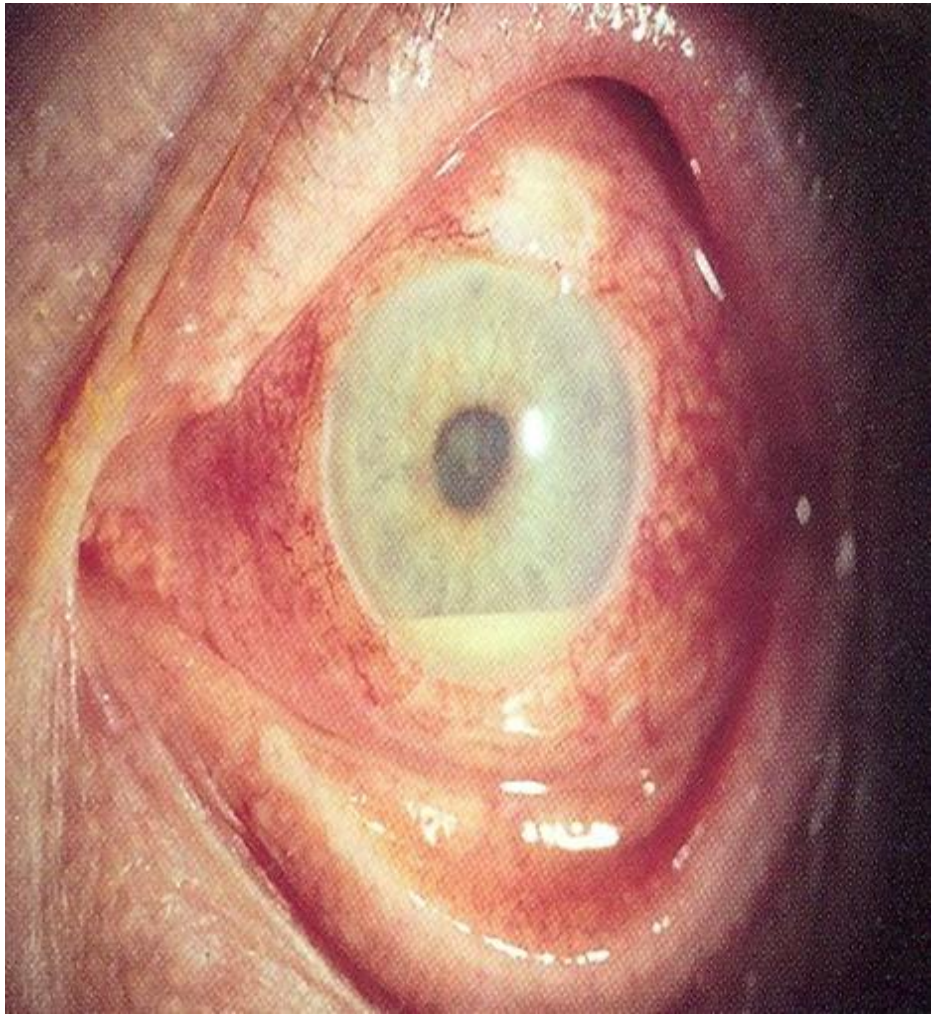
***Most likely type to cause chronic anterior uveitis (with an incidence of 80%)**

*The incidence of anterior uveitis increases when antinuclear antibodies (ANA) are present

-Prognosis :

- **Mostly good**
- 10% of cases may progress to symmetric polyarthritis, which has an unfavorable prognosis





Polyarthritis

-Also called **polyarticular juvenile idiopathic arthritis** (pJIA)

-The **second most common** type of JIA.

-In this type (40%), children present with arthritis **in five or more joints** within the first 6 months of diagnosis.

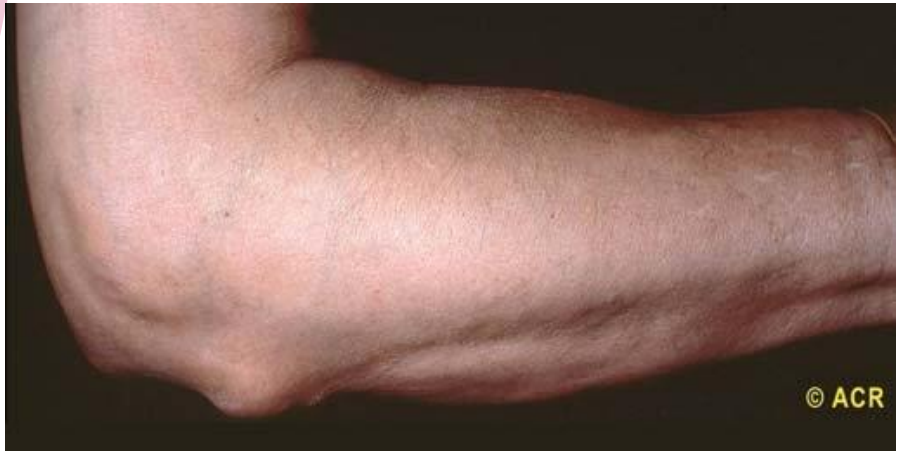
Children who develop polyarticular disease after oligoarthritis called extended oligoarthritis

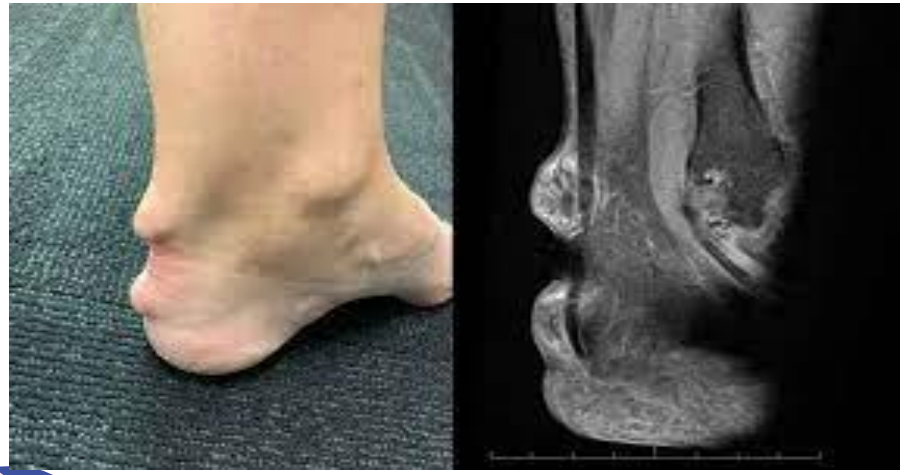
Polyarthritis

classification depends on RF

1. Seronegative polyarticular JIA :

-most common
-RF negative
-Symmetrical or asymmetrical
-Peak incidence : 1–4 years and 6–12 years (bimodal incidence)
-Female > male
-moderate risk of chronic uveitis





Polyarthritis

2. Seropositive polyarticular JIA :

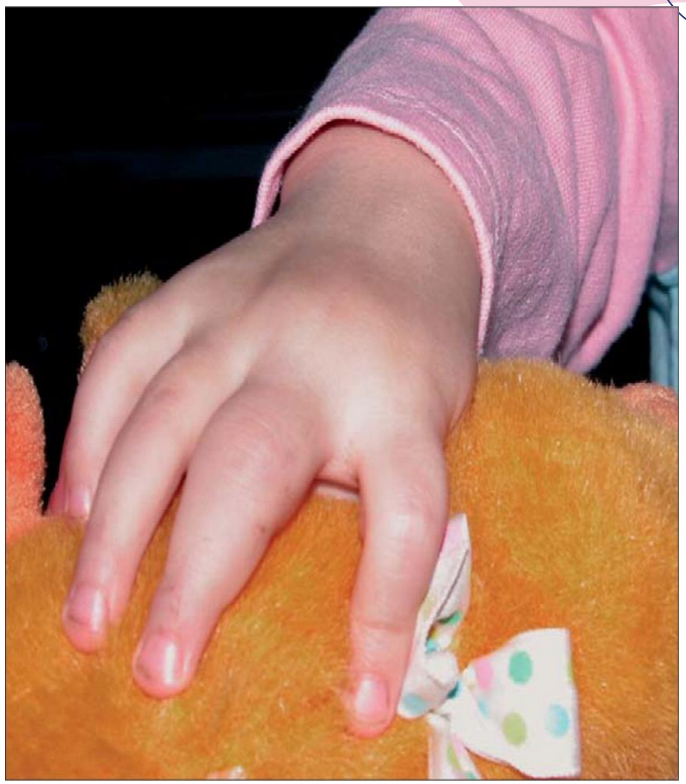
-< 10% of cases
-RF positive
-Symmetrical
-Peak incidence : 9-12 years
-Female > male (10:1)
-Extra-articular manifestations : Rheumatoid nodules on the extensor surface of elbows and the Achilles tendon (~ 30% of cases)

- Evidence of systemic inflammation is more common in ployarthritis than oligoarthritis .(including malaise , low grade fever , anemia of chronic disease and elevated inflammatory markers ESR , CRP)

- Patient can present with chronic uveitis and its complication

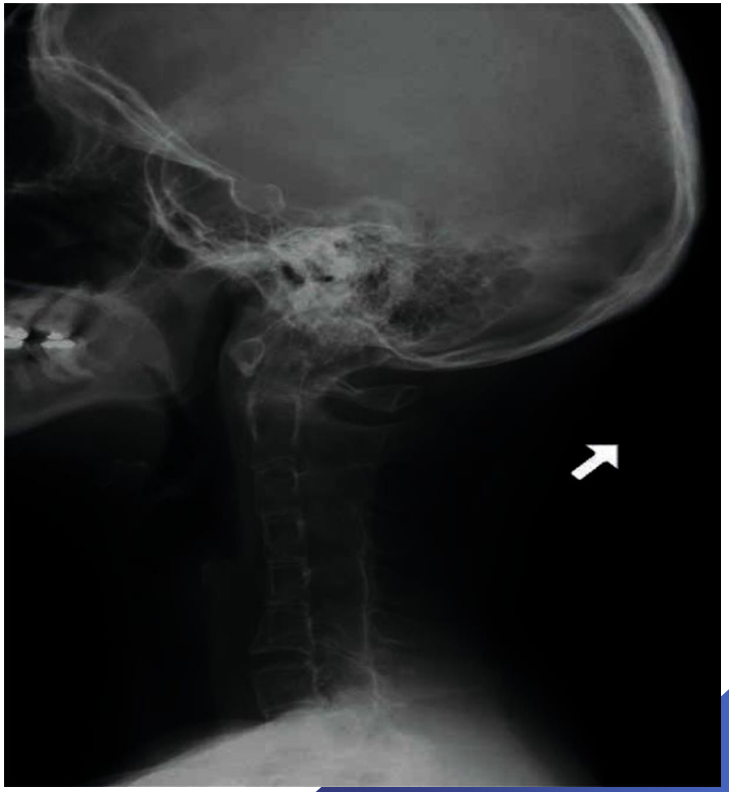
- Sausage finger (Dactylitis)

- DDX:
- psoriasis
- Sickle cell disease
- Various form of arthritis

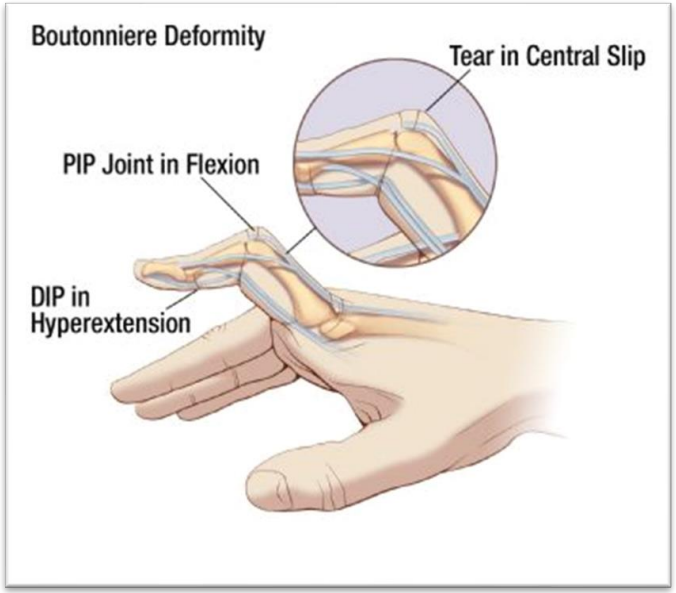


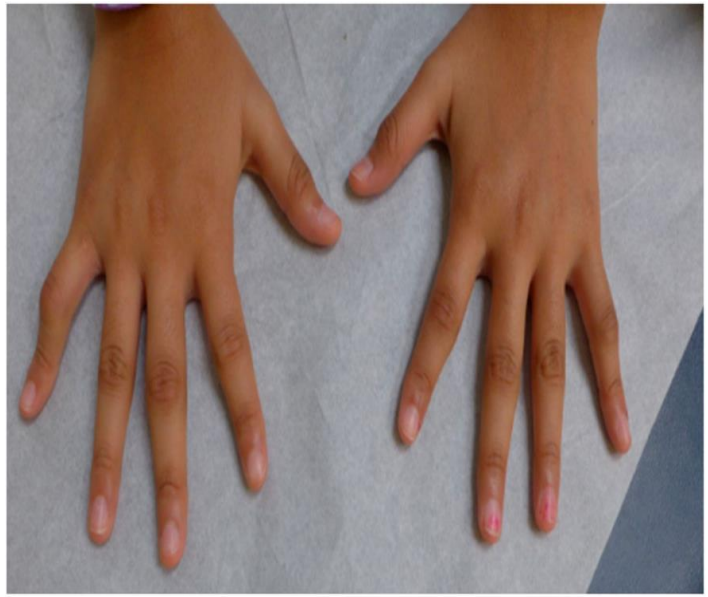
- Long term complication :cervical spine involvement through subluxation and fusion with loss of lordosis and limited extension

FIG. 180.9 Radiograph of the cervical spine of a patient with active juvenile idiopathic arthritis, showing fusion of the neural arch between joints C2 and C3, narrowing and erosion of the remaining neural arch joints, obliteration of the apophyseal space, and loss of the normal lordosis.



- long term complication : Boutonnière finger
- (flexion at PIP , extension DIP)





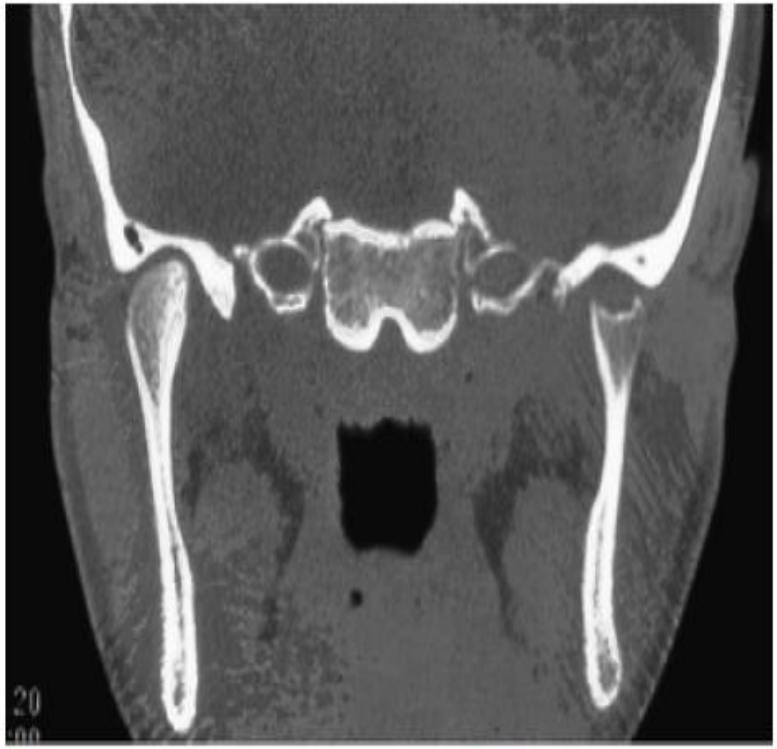


FIG. 180.8 CT scan of the temporomandibular joint of a patient with juvenile idiopathic arthritis exhibiting destruction on the right.

TM joint involvement may lead to micrograthia (undersized jaw)

TM involvement + loss of lordosis
May lead to intubation and anaesthetic difficulty

Systemic onset JIA

- Or also **called juvenile form of Still's disease**
- - In this type (10%) patients do not present with onset of arthritis but rather with **preceding systemic inflammation**.
- - The arthritis of JIA follows the systemic inflammation by 6 weeks to 6 months. The arthritis is typically polyarticular nature and can be extensive and resistant to treatment
- - Peak incidence : 2–4 years
- - Females = males

Systemic onset JIA

- Typical**, intermittent spiking fever** (up to 39), once or twice per day, of at least 2 weeks' duration.

Extra- articular manifestations :

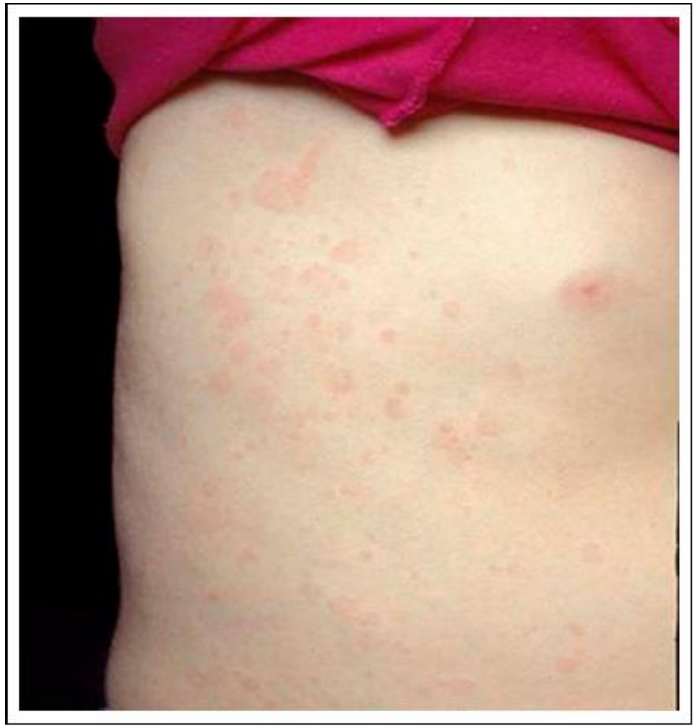
1- Salmon-pink macules of different sizes accompanies febrile periods seen on trunk and proximal extremities or over pressure areas. Rarely to pruritic.

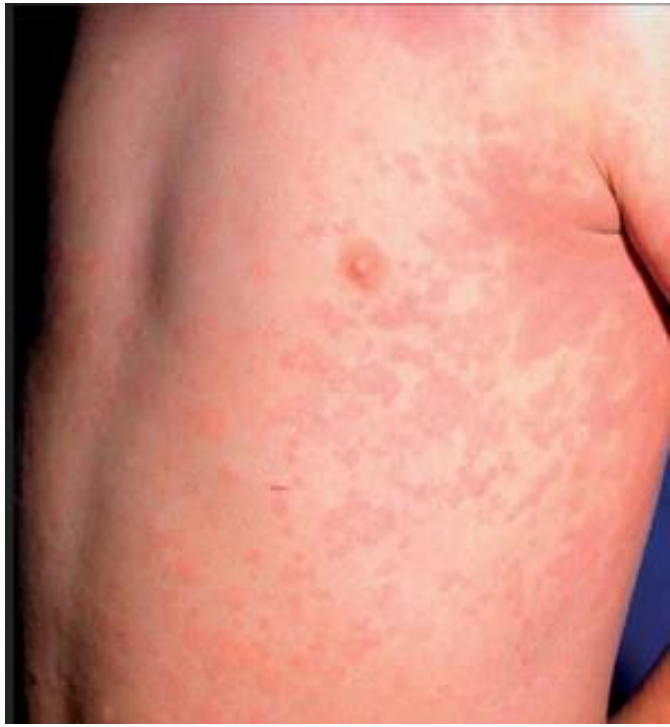
2- Hepatosplenomegaly occurs in 70% of children.

3- Generalized lymphadenopathy .

4- Serositis, such as pleuritis and pericarditis , occurs in 50% of children

salmon-pink macules





Diagnosis & prognosis

Diagnosed by exclusion

Lab findings:

Systemic inflammatory features include : anemia of chronic disease, leukocytosis, thrombocytosis, elevated acute phase reactants(ESR, CRP, ferritin)

-The prognosis of systemic JIA depends on the severity of the arthritis

-Most systemic symptoms resolve over months to years, and mortality, which is < 0.3% in North America, is associated mainly with Macrophage Activation Syndrome (MAS) and infections secondary to immune suppression.

Macrophage Activation Syndrome

- - Occurring in more than 10% of sJIA patients.
- - MAS can be seen in the context of overwhelming inflammation which leads to activation of proliferation of T lymphocytes and macrophages
- resulting in overwhelming release of proinflammatory cytokines.
- - The patient develops high fevers, **liver insufficiency** hepatosplenomegaly, neurological abnormalities, and bleeding diathesis.
- - There is evidence of disseminated intravascular coagulation,

Table 3. Macrophage Activation Syndrome

Physical findings	Bruising, purpura, mucosal bleeding
	Enlarged lymph nodes, enlarged liver and spleen
Laboratory findings	Elevated: AST, ALT, PT, PTT, fibrin degradation products, ferritin, triglycerides
	Decreased: white blood cell and platelet counts, erythrocyte sedimentation rate, fibrinogen, clotting factors
Bone marrow	Active phagocytosis by macrophages and histiocytes
Treatment	Intravenous glucocorticoid, cyclosporine

MAS

Bone marrow sampling may identify mature macrophages displaying hemophagocytic activity

Laboratory abnormalities include pancytopenia, prolongation of the PT and PPT and elevated levels of D-dimer, and ferritin

Because MAS carries a significant mortality early recognition and treatment of MAS with corticosteroids or cyclosporine is important to prevent multisystem organ failure

Psoriatic arthritis

Defined by arthritis together with either a psoriatic rash or two of the following:
-dactylitis (sausage-like fingers)
-nail pitting
-onycholysis (painless detachment of the nail from the nail bed)
-psoriasis in a first-degree relative

Dactylitis

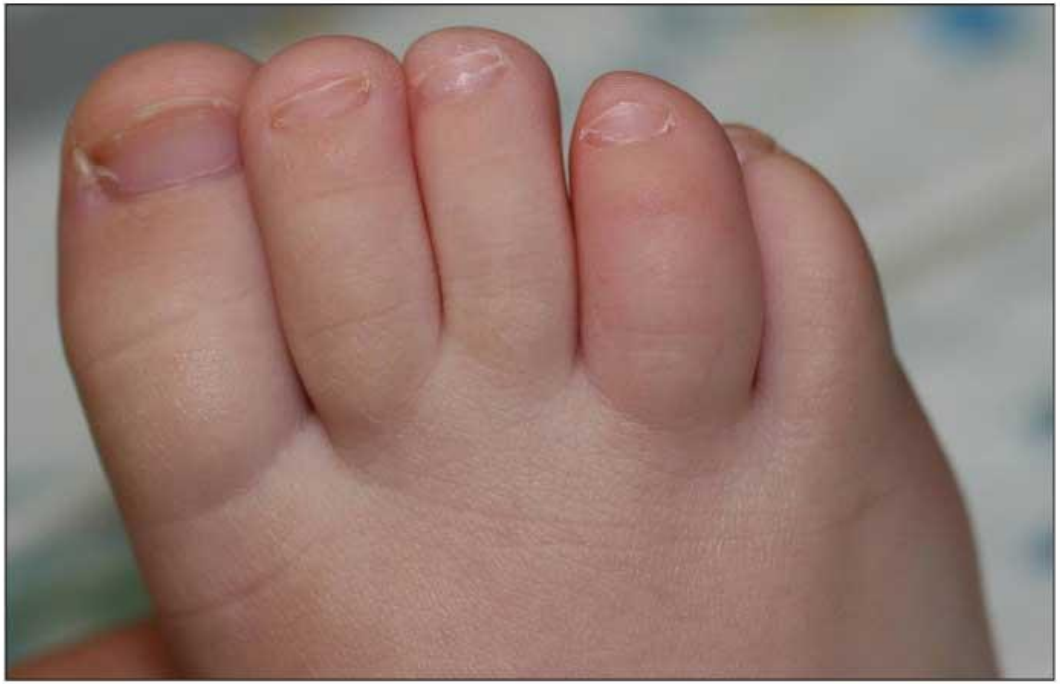


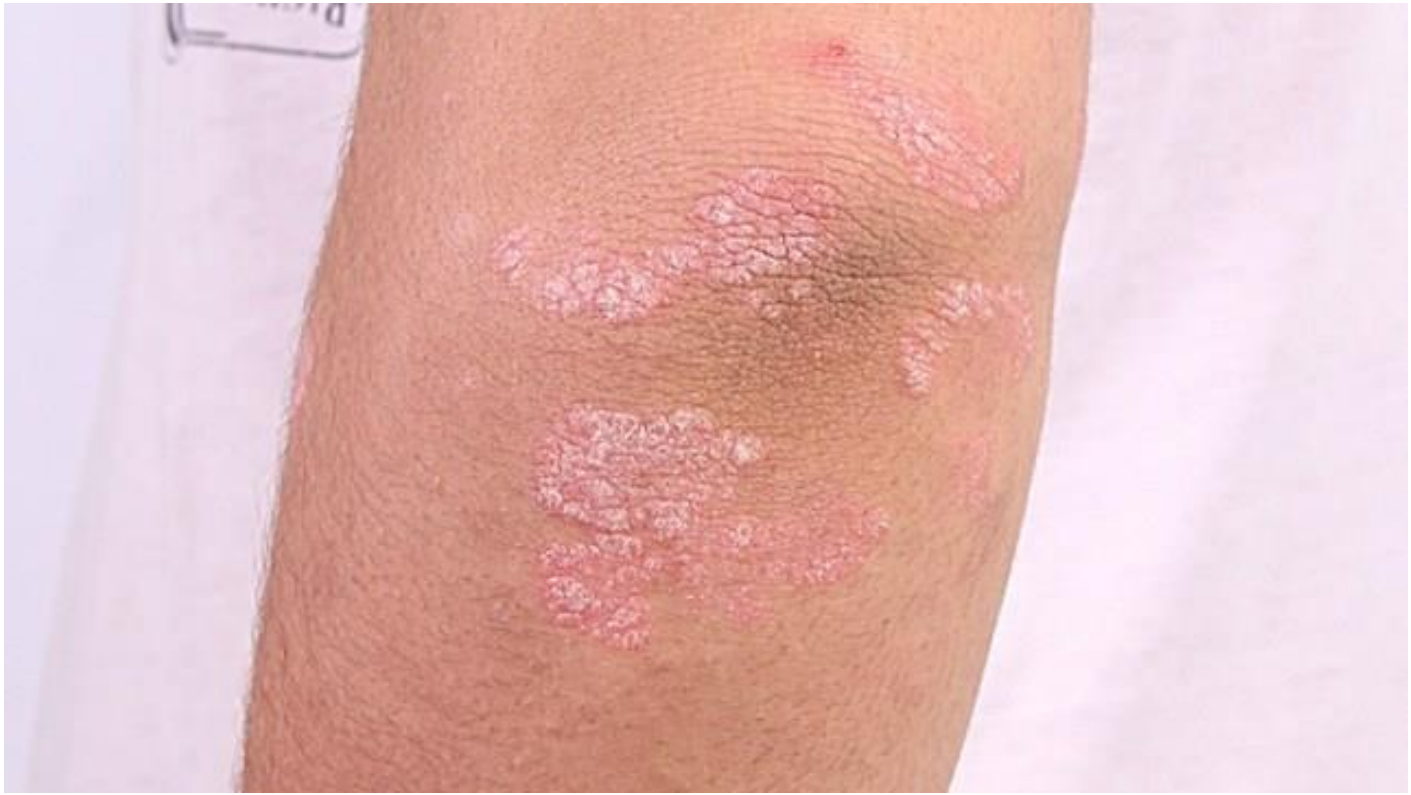
Figure 2 – *Dactylitis, or "sausage digit," is seen in the toes of a child with psoriatic juvenile idiopathic arthritis.*

-Juvenile psoriatic arthritis most often appears between the ages of 11 and 12 .

-Girls are more likely to develop it when they are younger and boys when they are older.

-Typically, psoriatic plaques are seen on the extensor sides of joints, haired skin, the umbilicus and the perineum

psoriatic plaques



Enthesitis Related Arthritis

-Enthesitis is defined as tenderness at the insertion of a tendon, ligament, joint capsule, or fascia to bone.

-This form occurs most often in boys older than 6 years and is linked to ankylosing spondylitis and inflammatory bowel disease.

The main characteristics of the patients include:

1. RF and ANA negativity
2. HLA B27 positivity is reported in 65-80 % of patients
3. Asymmetric arthritis of the lower extremities
4. The Achilles tendon is the most commonly affected site

Other characteristics :

1. Presence of or history of sacroiliac joint tenderness or inflammatory lumbosacral pain, or both.

2. Acute (symptomatic) anterior uveitis.

3. History of ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with IBD or acute anterior uveitis in first degree relative

Undifferentiated arthritis

Arthritis that fulfills criteria in no category or in ≥2 of the above categories.

Table 89-1 Features of Juvenile Idiopathic Arthritis Subgroups

FEATURE	OLIGOARTICULAR	POLYARTICULAR	SYSTEMIC ONSET
No. joints	<5	≥5	Varies, usually ≥5
Types of joints	Medium to large (also small in extended oligoarthritis)	Small to medium	Small to medium
Gender predominance	F > M (especially in younger children)	F > M	F = M
Systemic features	None	Some constitutional	Prominent
Eye disease	+++ (uveitis)	++ (uveitis)	+ (uveitis)
Extra-articular manifestations	None	None	Systemic features
ANA positivity	++	+	—
RF positivity		+ (in older children with early-onset RA)	
Outcomes	Excellent, >90% complete remission	Good, >50% complete remission, some risk of disability	Variable, depends on extent of arthritis

COMPLICATIONS of JIA :

Complications with JIA result primarily from :
the loss of function of an involved joint secondary to contractures, bony fusion, or loss of joint space.

More serious complications stem from associated **uveitis**; if left untreated, it can lead to serious visual loss or blindness.

Long-term Complications:

1. Anemia of chronic diseases
2. Permanent joint damage
3. Decreased Growth
4. Disproportionate limbs
5. Pericarditis, pleuritis

Differential diagnosis

The diagnosis of JIA is established by the presence of arthritis, the duration of the disease for at least 6 weeks, and exclusion of other possible diagnoses.

Table – Differential diagnosis of childhood arthritis

Reactive: postviral, reactive arthritis, rheumatic fever, poststreptococcal arthritis
Inflammatory: juvenile idiopathic arthritis, inflammatory bowel disease, sarcoidosis
Infection: septic, osteomyelitis, Lyme disease, viral, bacterial sacroiliitis, diskitis
Systemic: Kawasaki disease, Behçet disease, Henoch-Schönlein purpura, serum sickness, systemic lupus erythematosus, dermatomyositis, progressive systemic sclerosis
Malignancy: leukemia, neuroblastoma, malignant bone tumors (osteosarcoma, Ewing sarcoma, rhabdosarcoma), benign bone tumors (osteoid osteoma, osteoblastoma)
Trauma: accidental, nonaccidental, foreign-body synovitis

Important notes

-The diagnosis of (JIA) is based on the history and physical examination findings.

-No laboratory studies are diagnostic for JIA, and indeed, all laboratory study findings may be normal in children with this disorder.

-Testing can be used to monitor the condition, its potential complications, response to treatment, and to monitor for potential side effects associated with some treatments

LABORATORY AND IMAGING STUDIES

Usual Lab Test workup

- CBC
- ESR & CRP
- ANA
- RF
- HLA-B27
- Synovial fluid analysis

CBC

Children with polyarticular and systemic disease commonly show anemia of chronic disease, Leukocytosis and thrombocytosis

-Most children with oligoarticular JIA have no laboratory abnormalities.

ESR & CRP

-(ESR) or (CRP) level is usually elevated in children with systemic-onset JIA .

-May be elevated in those with polyarticular disease.

-It is often within the reference range in those with oligoarticular disease.

-When elevated, inflammatory markers can be used to monitor disease activity

ANA & RF

-70% of children with oligoarticular JIA have positive ANA.
-Positive ANA should also raise suspicion of (SLE).
-A positive ANA is a marker for increased risk of anterior uveitis.

-Patients with seropositive polyarticular disease should have a rheumatoid factor(RF)

-Anti-cyclic citrullinated peptide (anti-CCP) antibody performed to identify children with early onset adult rheumatoid arthritis(indicate a poor prognosis).

Synovial fluid analysis

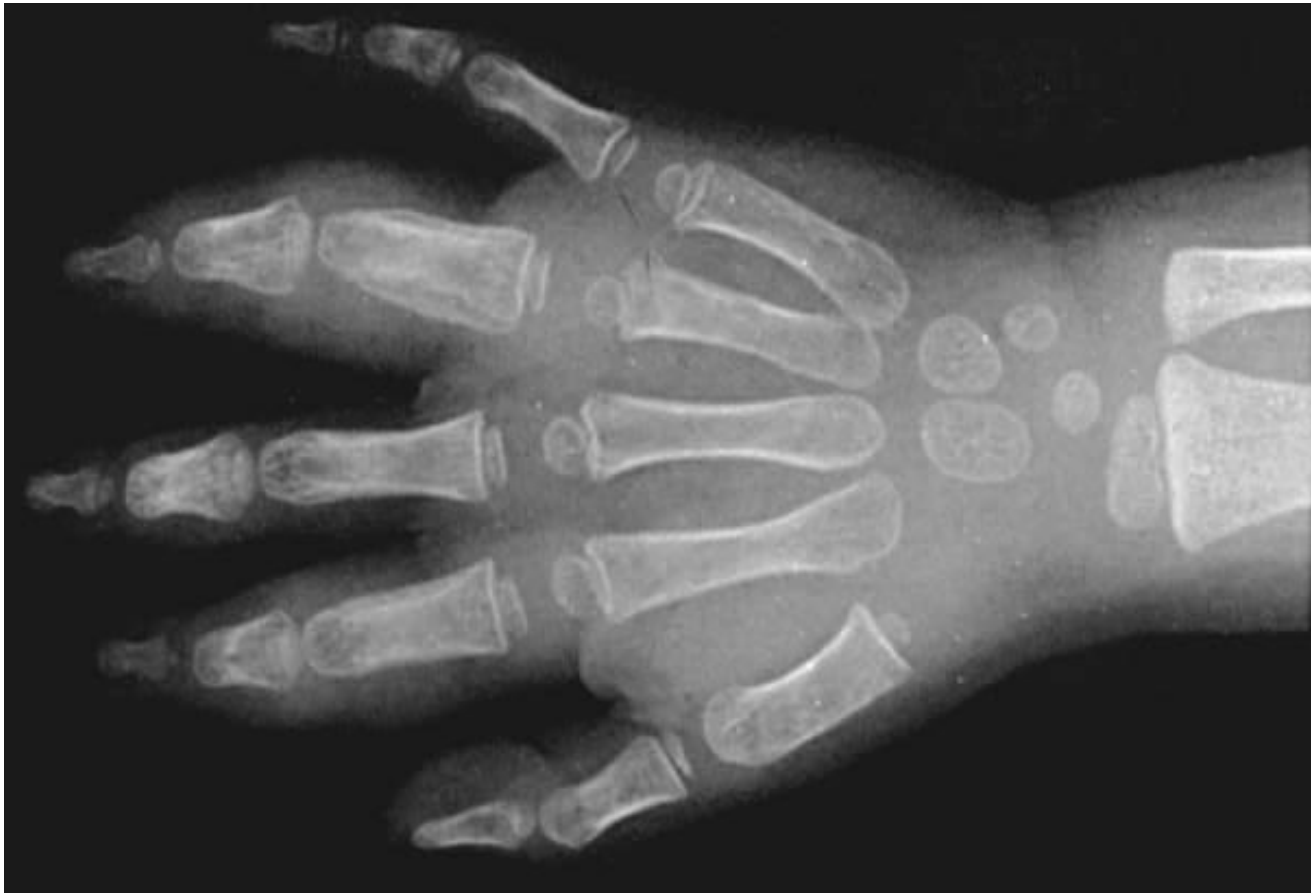
Diagnostic arthrocentesis may be necessary to exclude suppurative arthritis in children who present with acute onset of monarticular symptoms.

The synovial fluid white blood cell count is typically less than 50,000 to 100,000/mm3 and should be predominantly lymphocytes, rather than neutrophils seen with suppurative arthritis. Gram stain, PCR, and culture should be negative.

Radiology

Early radiographic changes include:

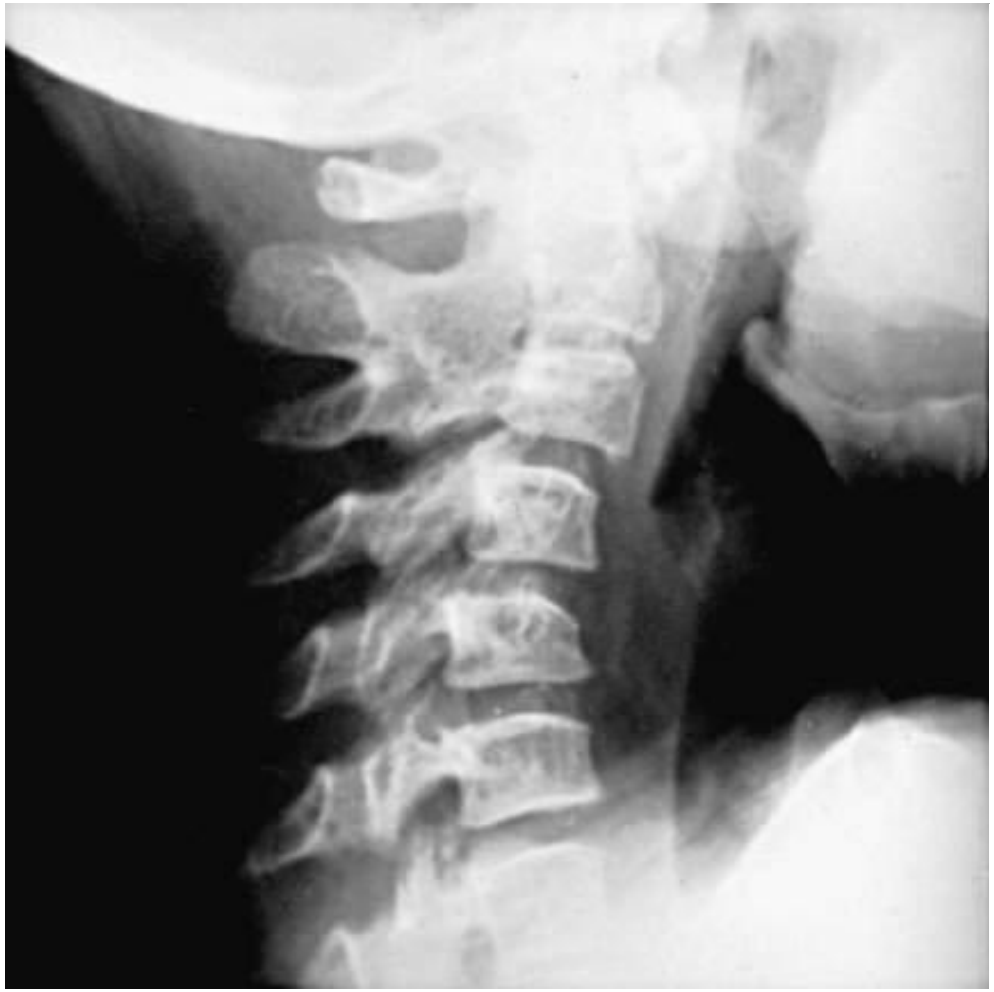
-Soft tissue swelling
-Periarticular osteopenia
-periosteal new-bone formation around affected joints
-Erosions of bony articular surfaces may be a late finding.



Early(6mo duration) radiographic changes of JIA. Soft-tissue swelling and periosteal new bone formation appear adjacent to the 2nd and 4th proximal interphalangeal joints.

Continued active disease may lead to :

-subchondral erosions
-loss of cartilage
-with varying degrees of bony destruction, and fusion.



Radiograph of the cervical spine of a patient with active JIA, showing:
1- fusion of the neural arch between
joints C2 and C3,
2- narrowing and erosion of the remaining neural arch joints,
3- obliteration of the apophyseal space, and loss of the normal lordosis

TREATMENT

The treatment of JIA focuses on suppressing inflammation, preserving and maximizing function, preventing deformity, and preventing blindness.

Nonsteroidal anti-inflammatory drugs :(NSAIDs) are the first choice in the treatment of JIA. Naproxen, ibuprofen, indomethacin, and others have been used successfully.

Second-line medications : disease-modifying antirheumatic drug(DMARD) such as :

- **Hydroxychloroquine** and **sulfasalazine**
have been used in patients whose arthritis is not completely controlled with NSAIDs alone.

- **Methotrexate**, has become the drug of choice for polyarticular and systemic-onset JIA, which may not respond to baseline agents alone.

- Methotrexate can cause bone marrow suppression and hepatotoxicity; regular monitoring can minimize these risks.

Biologic agents that inhibit TNF-α and block the inflammatory cascade, including : etanercept, infliximab, and adalimumab, are effective in the treatment of JIA.

The risks of these agents are greater, include serious infection and, possibly, increased risk of malignancy.

Anakinra, an interleukin-1receptor antagonist, is very beneficial in the treatment of the systemic features of systemic-onset JIA

Systemic corticosteroid medications, such as prednisone and prednisolone, should be **avoided** in all but the most extreme circumstances, such as for severe systemic-onset JIA with internal organ involvement or for significant active arthritis leading to the inability to ambulate.

In this circumstance, the corticosteroids are used as **bridging therapy** until other medications take effect.
For patients with a few isolated inflamed joints, i**ntra-articular** corticosteroids may be helpful.

Non-pharmacological interventions :

Rehabilitation of the involved joints :

interventions such as dynamic exercises , occupational therapy and hydrotherapy can be applied as treatment adjunct to pharmaceutical interventions in patients with early arthritis.

- **American College of Rheumatology (ACR) criteria for complete remission are as follows :**

- No inflammatory joint pain
- No morning stiffness
- No fatigue
- No synovitis
- No progression of damage, as determined in sequential radiographic examinations
- No elevation of the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels

Thank you