ARTHRITIS

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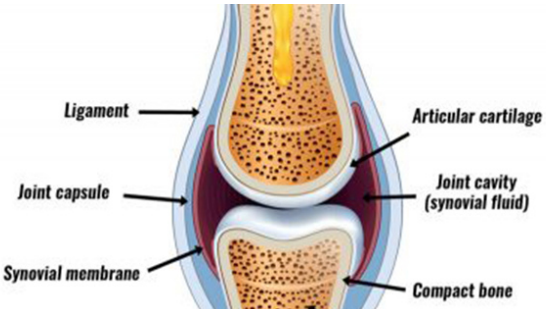
Joints Classification

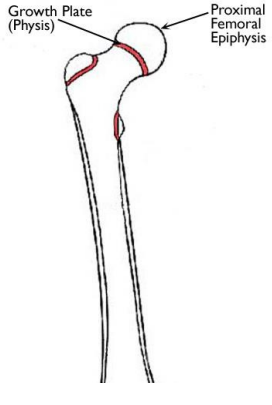
- There are many ways to classify joints, one of them is according to movement limitation:
- [ ] Synarthrosis: joints with limited movement (e.g. sutures in skull or symphysis pubis).
- [ ] Diarthrosis: Joints that are freely movable.
- Another way to classify joints:
- [ ] Fibrous joints – sutures of the skull
- [ ] Cartilaginous joints- symphysis pubis
- [ ] Synovial joints – separated by fluid filled cavity (less than 1 ml present)

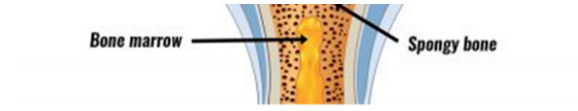
→ Our focus will be on synovial joints, since most of the diseases discussed involve this type of joints.

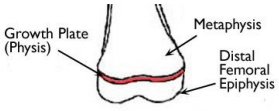
Structures of Synovial Joints

- **Outer ligament**, **joint capsule**, **synovial membrane** (made up of synoviocytes, part of these cells are responsible for the inflammation and act as if they are part of the immune system (act like macrophages), while the rest of cells are responsible for the production of collagen and the protein components of the joint).
- **Synovial fluid**: acts as a lubricant to decrease the amount of friction between the two joints.
- When an inflammation occurs, it would involve the synovial membrane which leads to the proliferation of cells, and the blood vessels will increase in permeability leading to leakage of protein, fluid and cells into the synovial fluid. Proliferation and vascularization occur as a result of the reaction of the tissue itself or due to the effects of **cytokines**.
- One of the things we fear in arthritis in children is the presence of a cartilaginous growth plate between the epiphysis and metaphasis, which may be damaged in chronic inflammation or septic arthritis. It is either destroyed which causes the affected leg to become shorter than the other one or due to the proliferation of blood vessels overgrowth occurs so the affected leg would become taller than the other leg. Either way, the child may present with **painless limping.**









Synovitis & Arthritis

- When the inflammation occurs the permeability increases, so blood vessels will leak proteins and WBCs. If the infection is bacterial then neutrophils will be the highest in the exudate. CRP will release to stimulate the liver to produce more proteins and fibrinogen so the protein levels increase in the serum.
- The synovial fluid is an ultrafiltrate of the plasma (like the CSF and pleural fluid), it has the same components of the plasma but in lesser amounts, unless there is an inflammation in which the amounts increase.
- If a child came with a painful joint or limping, the first thing that should come to your mind is if this condition is inflammatory or non-inflammatory. Then if it is infectious or non-infectious.

Causes of "Joint Pain"

1. **Inflammatory arthritis:**
- **Infectious (septic) arthritis**
- **Non-infectious arthritis:**
  a. Reactive arthritis
  b. JIA
  c. Other rheumatic disorders
2. **Non-inflammatory joint pain:** (not arthritis, but considered from differentials since they are very similar in presentation):
- **Legg-Calve-Perthes disease**
- **Slipped capital femoral epiphysis (SCFE)**

Inflammatory Arthritis

- **Infectious**: acute 2-3 days for onset of symptoms, does not self-resolve, may have systemic symptoms (H. influnazae may be accompanied by a low grade fever only and non-prominent systemic manifestations while with other bacteria such as staph. aureus the patient would be febrile and ill looking).
- Ask about systemic symptoms.
- you should notice any hotness/redness/tenderness in the joint since the symptoms only accompany septic arthritis and are not due to rheumatologic causes of arthritis.
- If unable to know the type of arthritis, fluid is aspirated from the joint. We may first do some imaging tests to make sure if this is a soft tissue inflammation or not since the patient may have cellulitis.

- The hip, unlike other joints, is a deep joint surrounded by muscles, so both redness and hotness cannot be assessed, you can only assess pain and limitations in the range of movements.
- The **hip** is the only joint where the blood supply **enters the capsule**, so if it is inflamed and the pressure increased it would compress the blood supply leading to **necrosis of the femoral head** which is an emergency.

	Appearance	WBC/mm3	Neutrophils%	Glucose
Normal	clear	0 - 200	less than 10%	same as serum
Infectious	turbid	10,000 - 250,000	more than 90%	low, 50-90 mg/dl different from serum glucose
Inflammatory	turbid/cloudy	250 - 80,000	more than 70%	mild low, 30 mg/dl different from serum glucose

- When comparing the levels of a certain entity to that of the serum, the serum level measurement should be done at the same time.
- Why does turbidity occur in infection/inflammation? It indicates the presence of high numbers of proteins and cells.
- So as a rule, if the WBCs are more than 100,000 suspect septic arthritis and less than that it might or might not be septic.
- In non-infectious arthritis patients don't present with acute joint pain, they would have suffered from 4-6 weeks with on and off limping and on the last week would have a constant limping, so it has an insidious (gradual) onset.
- Systemic symptoms usually not present but even if present it would be mild (e.g. low grade fever).
- Septic arthritis is usually preceded by URTI since its route is hematogenous from the infection site to the joint. While JIA is an autoimmune process so the patient would have a very long history with subtle systemic manifestations.
- Synovial fluid aspiration is rarely done, unless we are suspecting septic arthritis or we want to give intraarticular steroid injection or if the symptoms occur in the hip joint where the cause is hard to differentiate, while in other joints MRI and history are usually adequate.

Septic Arthritis (Suppurative Arthritis)

- More common in children <5 years & adolescents.
- They hypothesize that at these two ages there is increased activity, so the trauma may predispose to turbulence of the blood flow around the joint and eventually septic arthritis might occur.
- It is usually monoarticular, except in an adolescent with gonococcal disease, **Neisseria gonorrhea** causes symmetrical, multiple joint arthritis and it is very similar to JIA but has a more acute picture of redness and hotness, so it is the only cause of **polyarticular septic arthritis** and usually comes with a picture of previous urethritis.
- It has an acute-onset, and the patient presents with one or more of the following:

☐ Fever, redness, swelling, hotness, tenderness, decreased range of motion, limping, inability to bear weight, pain upon joint movement with diaper change.

- Limping and inability to bear weight should be noticed by the physician, a child should be able to bear weight after 6 months if you hold him.
- Involved joints: knees (40%) > hip (20%) > ankle (14%)•
- Hip held in flexion and external rotation, knee and ankle held in flexion. The child would hold the joints at these positions to decrease the pressure applied to them and refuses to walk.
- Hematogenous spread (from blood) of bacterial organisms usually and it could be directly spread from surrounding tissues but its less likley.
- Causative organisms depending on the patients age:
  - <2 months: GBS, Staph aureus, E.coli, Klebsiella pneumoniae
  - 2mo-maturity: Staph.aureus , Strep pneumoniae, GAS, Kingella kingae, N.gonorrhea (late disease, sterile culture of joint aspirate), Borrelia burgdorferi (Lyme disease)

Investigations

1. Synovial fluid analysis
2. Gram stain & culture
3. If the culture is negative do PCR for Kingella
   - Kingella is a fastidious organism, so it might not grow in a normal culture and may have nearly normal inflammatory markers.
4. CBC:
   - In the CBC if WBCs are elevated → CRP and ESR
5. In adolescents check for N. gonorrhea by urethral, cervical, rectal and pharyngeal cultures or NAAT (Nucleic Acid Amplification Test)

- **Imaging**:
  - if the picture of septic arthritis is clear, we don't do imaging.
  - US → effusion
  - X ray → increased joint space (only shows bone, not soft tissue so not very useful unless there is a very large amount of fluid that caused the two joints to be further apart).
  - MRI **with** contrast → synovitis **(Gold standard)**.

***Contrast is used to visualize symptoms of inflammation and in order to detect abscess formation or synovitis.**

Treatment

- We treat depending on: age, organism, gram stain, culture.
    - **<2 months:**
    - GBS → Ampicillin & aminoglycoside
    - Staph aureus → Nafcillin, Oxacillin, Cefazolin, Clindamycin, Vancomycin (usually used to cover MRSA)
    - E.coli / Klebsiella → Cefotaxime +/- aminoglycoside

    - **2months-maturity:**
    - Staph. aureus (QUEEN OF SEPTIC ARTHRITIS AND OSTEOMYLITIS) → Nafcillin, Oxacillin, Cefazolin, Clindamycin, Vancomycin
    - Strep. pneumoniae → Ampicillin, Cefotaxime, Ceftriaxone, Vancomycin
    - GAS → Penicillin G
    - Kingella kingae → Amoxicillin, Ampicillin, Cefotaxime
    - N.gonorrhea (late disease, sterile culture of joint aspirate) → Ceftriaxone

*In late disease **Neisseria** itself goes to the joint and causes septic arthritis (multiple symmetrical joints), while in early disease when the patient has urethritis, **reactive arthritis** occurs (hip joint or 2 joints max).

Clinical Tips

- Septic arthritis of the hip is an EMERGENCY, needs incision and drainage.
- The duration of treatment is 2-3 weeks on average, Depending on clinical response and labs (ESR, CRP).
- We could switch to oral antibiotic for the rest of the duration of treatment, in case there is a good response & if the organism is susceptible to the available oral agents.

Reactive Arthritis

- Immune-mediated synovial inflammation "following" bacterial or viral infection.
- Reactive arthritis is asymmetric and polyarticular.
- Following gastroenteritis, urethritis, URI.
- **"Toxic synovitis"**: is a reactive arthritis of the hip in children 3-6 years of age.
- **Treatment**: NSAIDs until the symptoms resolve.
- **Common organisms**:
    - Yersinia enterocolicia || Campylobacter jenuni => Gastroenteritis
    - Shigella flexneri
    - Chlamydia trachomatis => UTI
    - Salmonella
    - GAS

- Neisseria meningitidis (early disease)

Chronic Arthritis

- Could be due to:
  - juvenile idiopathic arthritis (JIA)
  - or other rheumatic disorders (SLE, systemic sclerosis, MCTD, etc.)
- Chronic = lasting for 6 weeks or more.
- Insidious onset.
- Pain, swelling, limited range of motion.
- The pain worsens in the morning and gets better as the day goes on.
- Children would have swelling but can move normally, though movement is hard in the morning and gets better as the day goes on.
- Not moving the joint for more than 20 mins then having stiffness is a characteristic feature of chronic arthritis in many cases.
- Pain is disproportional with swelling.
- Morning stiffness & gelling.

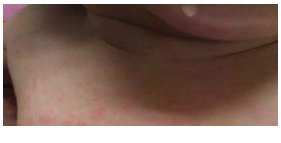
Juvenile Idiopathic Arthritis (JIA)

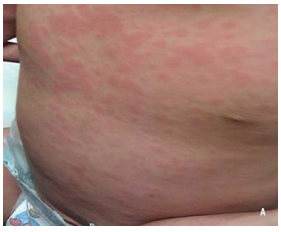
- One of the most common chronic diseases in children.
- **Arthritis, for ≥ 6 weeks, in a child <16 years of age, excluding other forms of arthritis.**
- ILAR (International league of associations for rheumatology) classified JIA into 7 subtypes according to the number of involved joints:

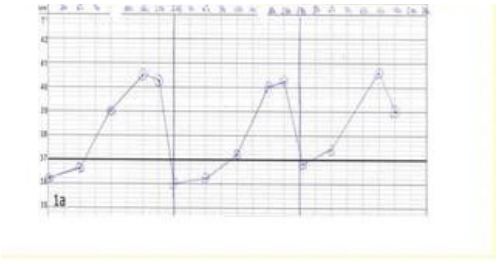
1. Oligoarthritis: 4 joints or less
2. Polyarthritis: 5 or more joints (**two types**)
   - Polyarthritis with positive Rheumatoid factor
   - Polyarthritis with negative rheumatoid factor
3. Systemic onset JIA
4. Psoriatic related arthritis
5. Enthesitis related arthritis (ERA)
6. Undifferentiated arthritis

Systemic Onset JIA

- Childhood, F = M
- Arthritis of ≥ 1 joint **AND**
- Fever daily for ≥ 3d/week for ≥ 2 weeks **AND**
- ≥ 1 of 4: Rash, lymphadenopathy, HSM, serositis
- Autoinflammatory not autoimmune, there is a problem with the innate System so there is no rheumatoid factor present, and the ANA is negative (no antibodies).







Oligoarticular JIA

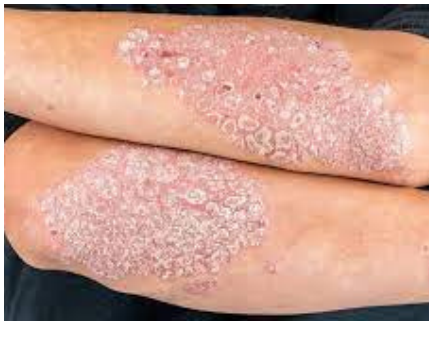
- Early childhood; 2-4 yrs
- F > M
- Arthritis of ≤ 4 joints in the first 6 months of disease
- After 6 months of the disease:
  - If still ≤ 4 joints → persistent
  - If ≥ 5 joints → extended

Polyarticular JIA

- F > M
- Arthritis of ≥ 5 joints in the first 6 months of the disease
- RF-negative: (biphasic: 2-4 yrs & 6-12 yrs)
- RF-positive (+ve RF on ≥2 occasions - 3 months apart): (late childhood or adolescence)

Psoriatic Arthritis

- Biphasic: 2-4 yrs & 9-11 yrs
- F > M
- Arthritis + psoriasis **OR**
- Arthritis + ≥ 2 of 3: nail pitting, dactylitis, family history of psoriasis in 1st degree relative.



Enthesitis Related Arthritis

- A late childhood or adolescence arthritis

- M > F = 7 : 1
- Arthritis **OR** Enthesitis **AND**
- ≥ 2 of 5: male > 6yrs, sacroiliac pain or tenderness, HLA-B27 positive, FH of first degree relative with HLA-B27 associated diseases, at onset, acute anterior uveitis
- It is the pediatric version of **ankylosing spondylitis** but here there is inflammation of the tendons.
- MRI is useful
- Enthesitis related and Psoriatic related arthritis affect the sacroiliac joint causing axial arthropathies usually, while the other forms cause peripheral arthropathies.

Undifferentiated Arthritis

Arthritis not fulfilling specific category's criteria.

Inflammatory Bowel Disease - Related Arthritis

- NOT a subtype of JIA but associated with arthritis
- 7-21 % of children with IBD develop arthritis before or during the course of IBD
- 32% with Crohn's disease > 22% with ulcerative colitis
- Arthritis is of two patterns:
  a. Peripheral (more common, related to the IBD disease activity) if IBD managed gets better.
  b. Axial (SI joint, less, course unrelated to IBD disease activity) treated as if one the subtypes of JIA since only controlling the IBD will not treat it.

Workup for a patient with suspected JIA

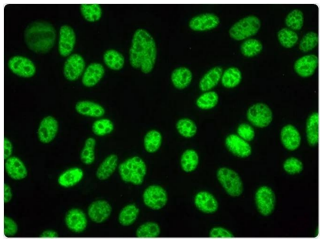
- Ophthalmologic exam for uveitis (especially in oligo and ANA positive subtypes)
- Labs
- Imaging (MRI with contrast is preferred)

LABs:

CBC	Kidneys	Liver	Inflammatory Markers
Could be normal in JIA	BUN, Creatinine	ALT, AST	Are not always elevated in JIA
Anemia of chronic disease	UA for blood and protein		

- **Renal and liver tests:**
  - because medications given affect the kidneys (non-steroids) and the liver (methotrexate) so we need base line functions to know if the patient can tolerate them or not.

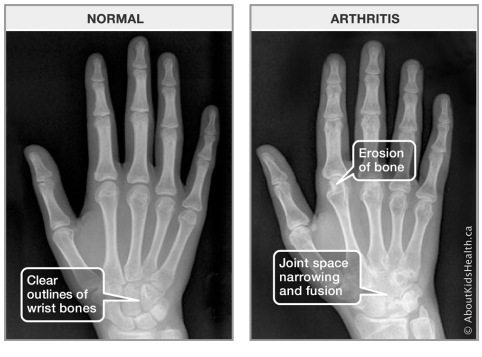
- Labs might be normal but this would not rule out JIA, the diagnosis is **clinically assisted** and MRI imaging might help.
- **ANA**:
  - is not a general screening tool.
  - Could be false positive with infections or malignancy (transient).
  - Could be positive in 15-30% of healthy children (do not predispose for future rheumatic disease).
  - Positivity in JIA reflects the risk of uveitis and dictates the interval for regular uveitis checks.



- **Rheumatoid Factor (RF):** In pediatrics rheumatology is not diagnostic and is not significant except for:
  - polyarticular JIA → prognosis worse for RF positive poly-JIA
- **Genetic testing:**
  - **HLA-B27** should only be tested in symptomatic children for diagnostic purposes.

IMAGING:

- **Plain X-ray Films:**
  - Can only show bones, not active arthritis or inflamed synovium.
  - Do X-ray to check for fractures.
  - MRI with Gadolinum is best.
  - Arthritis does not lead to abnormal "bone/joint" X rays until late stages when erosions appear.
  - Normal SI joint X rays does not rule out sacroiliitis.

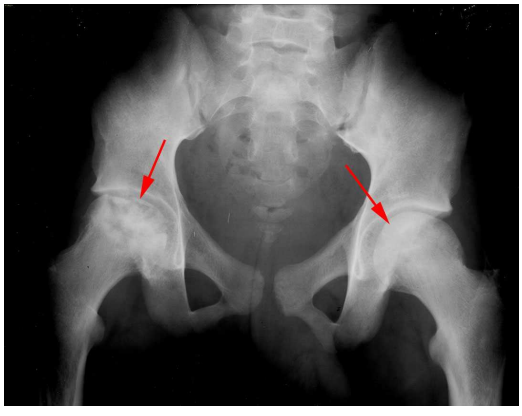


Non-Inflammatory Joint Pain

- Some DDx of arthritis of the hip are non-inflammatory conditions:
  - Legg-Calve-Perthes disease
  - Slipped capital femoral epiphysis

Legg-Calve-Perthes disease

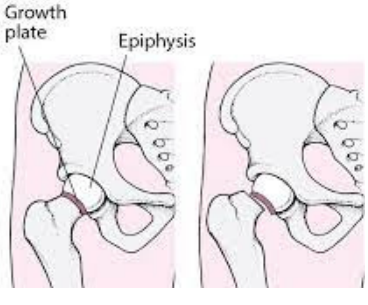
- 3-10 years of age
- Avascular necrosis of the hip (may present insidiously or acutely)
- Presents with painless limping
- Diagnosed by X ray → flattened/ fragmented femoral head
- Management: refer to Orthopedics, treated by traction or external fixation, etc.

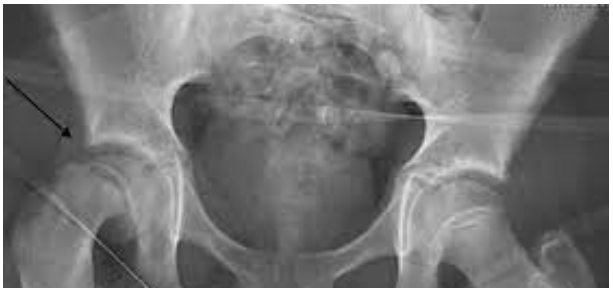


Chronic steroid usage may also lead to this picture, so if a pt is being treated for JIA and remained on steroids for a long time, then developed limping you have to suspect this rather than thinking that it is a flare up of the JIA they already have. Also it is common in SLE pts who are on chronic steroids so the cause of **avascular necrosis** would be iatrogenic, they may need joint replacement.

Slipped Capital Femoral Epiphysis (SCFE)

- Teenage years (10-16 years)
- The epiphysis (head of the femur) slips downwards & backwards off the neck at the growth plate (weak area)
- Boys, overweight, family history of SCFE, endocrine (hyperthyroidism) = risk factors
- Sudden onset after trauma or gradual over weeks (less than 6)
- **Exam** shows limited range of motion (especially internal rotation)
- **X ray** confirms the diagnosis
- **Treatment** is surgical → refer to Orthopedics





- On x-ray notice that there is no neck, as if the greater trochanter is placed directly over the femoral head.
- Usually the scenario is: an obese child who carried out a certain movement that applied extra pressure on the head of the femur which caused its displacement at the growth-plate area.

- **Problems:**

1. When a fracture happens, it would occur at the area of the growth plate since it is a weak area.
2. If the growth plate has a fracture it will no longer grow, so growth discrepancy occurs in the legs.
3. Since the growth plate is cartilaginous, so the blood supply will come from the bone and angulates at this area so the blood flow becomes turbulent and slow at this area causing an increased risk of osteomyelitis in children leading to septic arthritis.