Introduction to Pediatric Rheumatology

Dina Kafisheh, MD
Pediatric Rheumatologist
University of Jordan- 5th year lecture.

A few pearls

Pediatric rheumatology:

- Diagnoses and treats autoinflammatory and autoimmune conditions. Some of these include:
    - Juvenile Idiopathic Arthritis
    - Systemic Lupus Erythematosis
    - Systemic Vasculitis
    - Idiopathic inflammatory myopathies
    - Scleroderma
    - Autoinflammatory diseases
    - Uveitis
- Conditions often involve many organ systems; wide range of clinical manifestations
- Most rheumatologic conditions lack a definitive diagnostic test, therefore, **clinical history and physical exam are essential.**

How common are rheumatologic conditions in pediatrics?

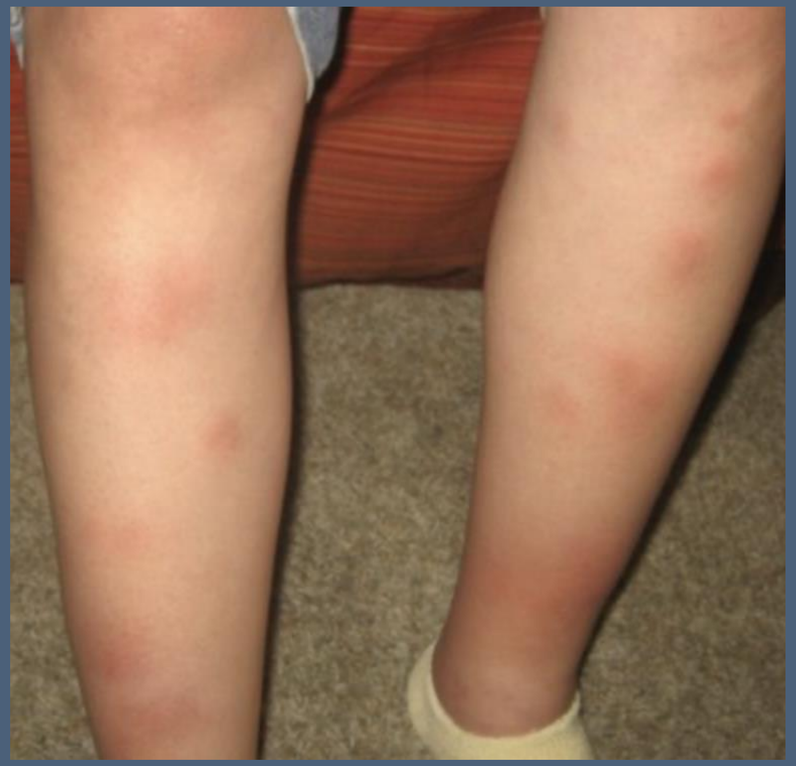
- Musculoskeletal (MSK) problems in children are common~ 1:8
  - causes range from benign (e.g., hypermobility) to serious (e.g., inflammatory arthritis, SLE) or **life threatening** (e.g., malignancy, infection or non-accidental injury).

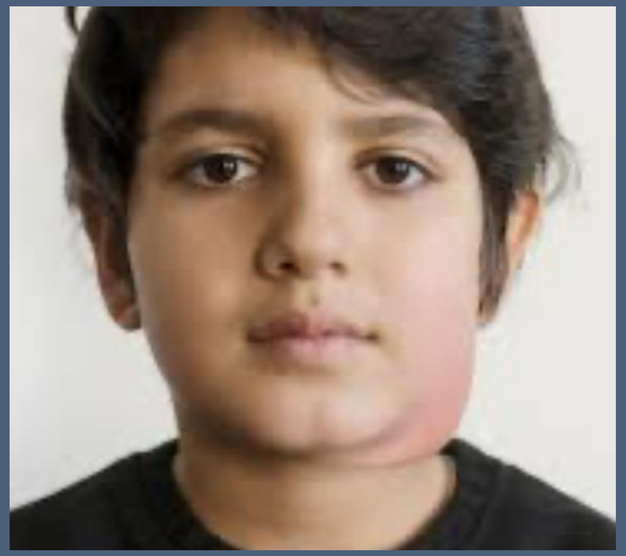
- Incidence of rheumatic conditions is variable:
  - The most common chronic rheumatic illness is Juvenile Idiopathic Arthritis;
    - The global prevalence ranges from 3.8-400/100,000. Incidence 1.6-23/100,000.
  - SLE incidence varies 0.36 to 2.5 per 100,000
  - Juvenile Dermatomyositis 2.5-4 per million

Common complaints/ presentations

How to approach them?

- Joint pain
- Back pain
- Muscle weakness
- Fevers
- Lymphadenopathy
- Erythema Nodosum
- Recurrent parotitis
- Stroke-like presentations





Clinical assessment

History and physical exam

- Thorough history and complete review of systems.
- Red flags in history
- Distinguish Inflammatory from Mechanical Features

Distinguish Inflammatory from Mechanical Features

	Inflammatory	Mechanical	Muscle
Pain	*Yes, but may not be verbally expressed, particularly in younger children (below 4 years). May manifest as change of mood or avoidance of activities.*	*Usually a predominant feature.*	*Rarely, pain in calves.*
Relationship to activity	*Movement may ease symptoms, inactivity may cause gelling.*	*Usually worse with and after activity.*	*Reduced endurance, may complain of pain in legs after activity.*
Morning stiffness	*Present. Important to ask about self-care (e.g., dressing), behaviour and activities in the mornings. Stiffness may manifest as 'gelling' after periods of rest (e.g., difficulty getting up from sitting on the floor).*	*Usually absent.*	*Absent.*
Swelling	*Yes, and usually persistent for several days to weeks, waxing and waning over months.*	*Usually worse with, and after activity.*	*Calf hypertrophy (overdeveloped calf muscles, out of proportion with rest of body).*
Locking	*Usually absent.*	*May be present.*	*Absent.*
Giving way	*Usually absent.*	*May be present.*	*May be present.*
Worst time of day	*Usually mornings.*	*Often after school or evening.*	*Mornings can be worse after activity.*
Restriction of movement	*Often present, can be profound.*	*May be present.*	*May have ankle tightness.*
Systemic features	*Fever, anorexia, weight loss may occur with inflammatory disease (and autoinflammatory or multisystem diseases in particular) but infection (including Tuberculosis) and malignancy need to be excluded. A travel history or awareness of infections in endemic areas is important.*	*Not present.*	*May be present.*

Physical exam

- Complete physical exam

- pGALS (pediatric Gait, Arms, Legs and Spine):
  - A simple quick MSK tool
  - Validated in school-aged children
  - Facilitate early recognition of joint problems and prompt referral to specialist teams to optimize clinical outcomes.

https://www.youtube.com/watch?v=ENiuZoSD33o

The pGALS musculoskeletal screen

Screening questions

- Do you (or does your child) have any pain or stiffness in your (their) joints, muscles or back?
- Do you (or does your child) have any difficulty getting yourself (him/herself) dressed without any help?
- Do you (or does your child) have any problem going up and down stairs?

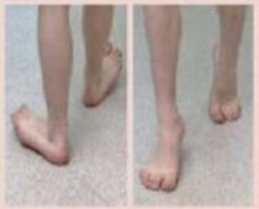
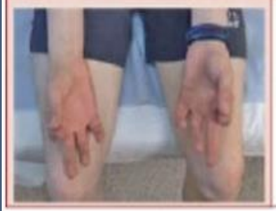
FIGURE	SCREENING MANOEUVRES (Note the manoeuvres in bold are additional to those in adult GALS[1])	WHAT IS BEING ASSESSED?
	Observe the child standing (from front, back and sides)	• Posture and habitus • Skin rashes – e.g. psoriasis • Deformity – e.g. leg length inequality, leg alignment (valgus, varus at the knee or ankle), scoliosis, joint swelling, muscle wasting, flat feet
	Observe the child walking and **'Walk on your heels' and 'Walk on your tiptoes'**	• Ankles, subtalar, midtarsal and small joints of feet and toes • Foot posture (note if presence of normal longitudinal arches of feet when on tiptoes)
	'Hold your hands out straight in front of you'	• Forward flexion of shoulders • Elbow extension • Wrist extension • Extension of small joints of fingers
	'Turn your hands over and make a fist'	• Wrist supination • Elbow supination • Flexion of small joints of fingers
	'Pinch your index finger and thumb together'	• Manual dexterity • Coordination of small joints of index finger and thumb and functional key grip

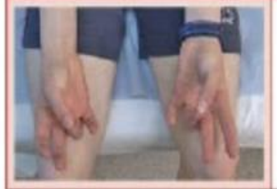
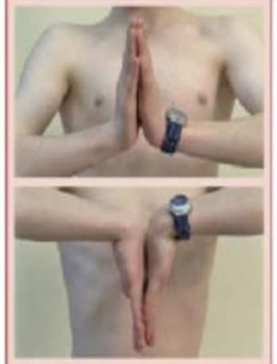
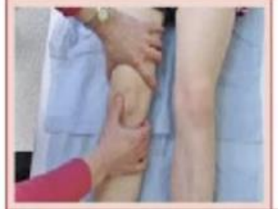
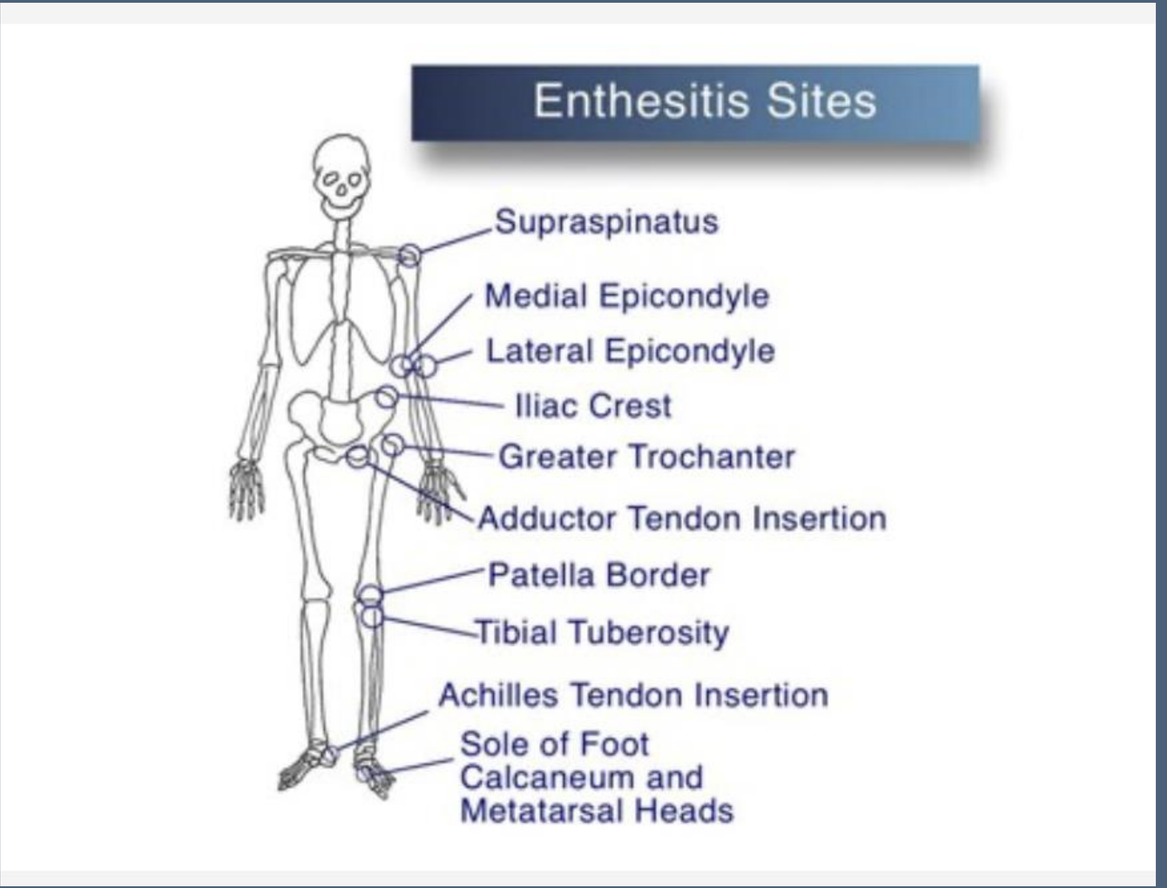
FIGURE	SCREENING MANOEUVRES	WHAT IS BEING ASSESSED?
	'Touch the tips of your fingers'	• Manual dexterity • Coordination of small joints of fingers and thumbs
	Squeeze the metacarpo-phalangeal joints for tenderness	• Metacarpophalangeal joints
	**'Put your hands together palm to palm' and 'Put your hands together back to back'**	• Extension of small joints of fingers • Wrist extension • Elbow flexion
	**'Reach up, "touch the sky"' and 'Look at the ceiling'**	• Elbow extension • Wrist extension • Shoulder abduction • Neck extension
	'Put your hands behind your neck'	• Shoulder abduction • External rotation of shoulders • Elbow flexion

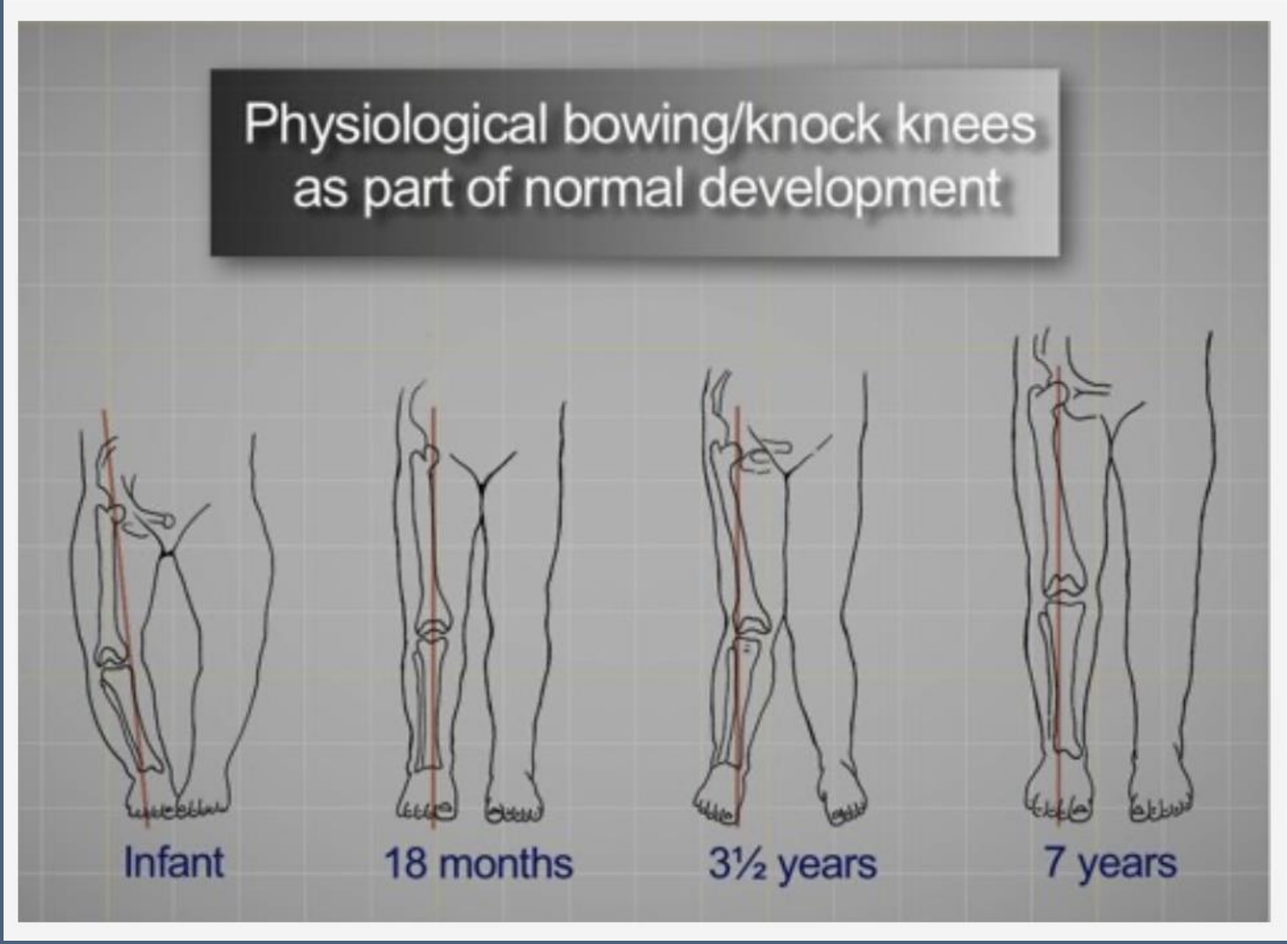
FIGURE	SCREENING MANOEUVRES	WHAT IS BEING ASSESSED?
	'Try and touch your shoulder with your ear'	• Cervical spine lateral flexion
	**'Open wide and put three (*child's own*) fingers in your mouth'**	• Temporomandibular joints (and check for deviation of jaw movement)
	Feel for effusion at the knee (patella tap, or cross-fluctuation)	• Knee effusion (small effusion may be missed by patella tap alone)
	Active movement of knees (flexion and extension) and feel for crepitus	• Knee flexion • Knee extension
	Passive movement of hip (knee flexed to 90°, and internal rotation of hip)	• Hip flexion and internal rotation
	'Bend forwards and touch your toes?'	• Forward flexion of thoraco-lumbar spine (and check for scoliosis)

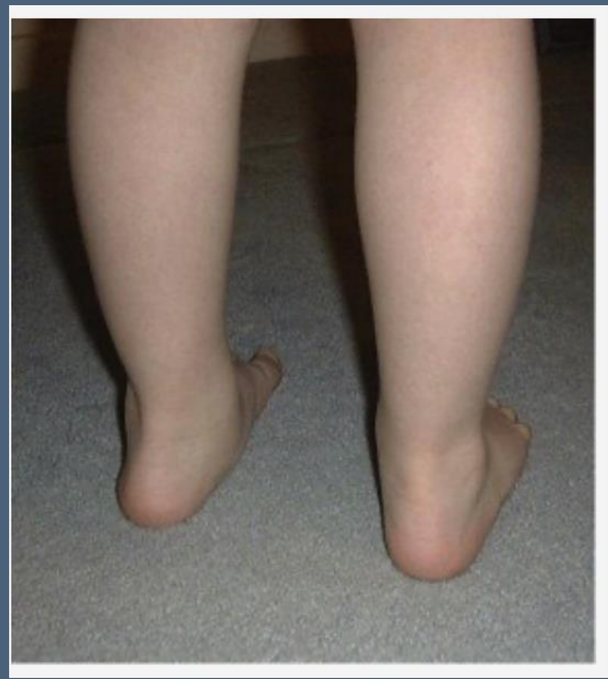
Terminology

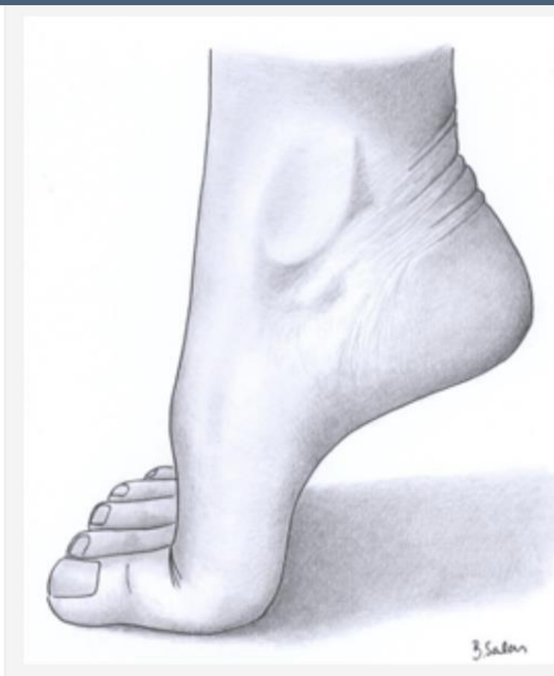
- **Arthritis**
- **Enthesitis**
- **Arthralgia**
- **Myalgia-** pain, no tenderness or weakness
- **Myositis**



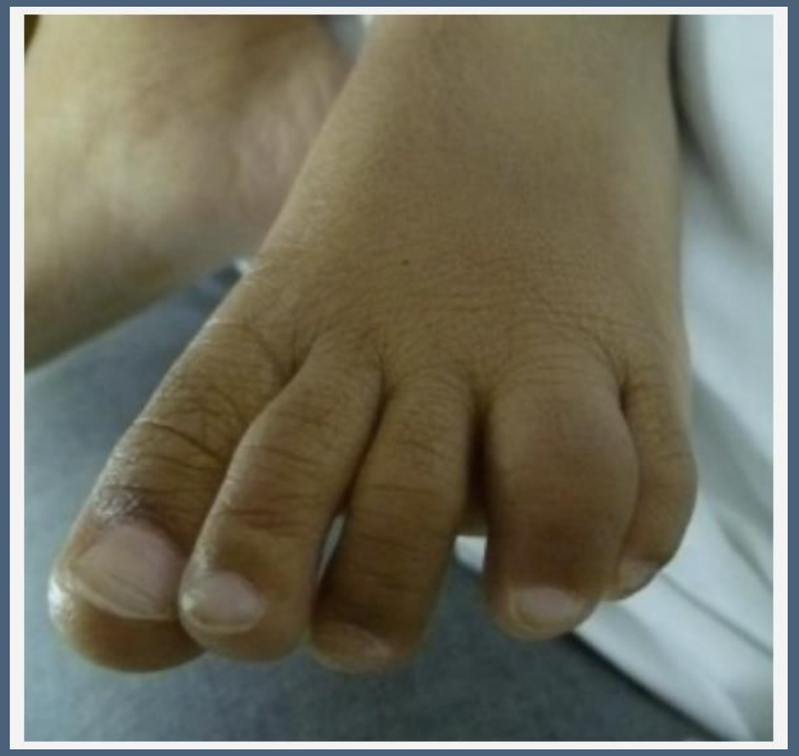
Normal MSK variants

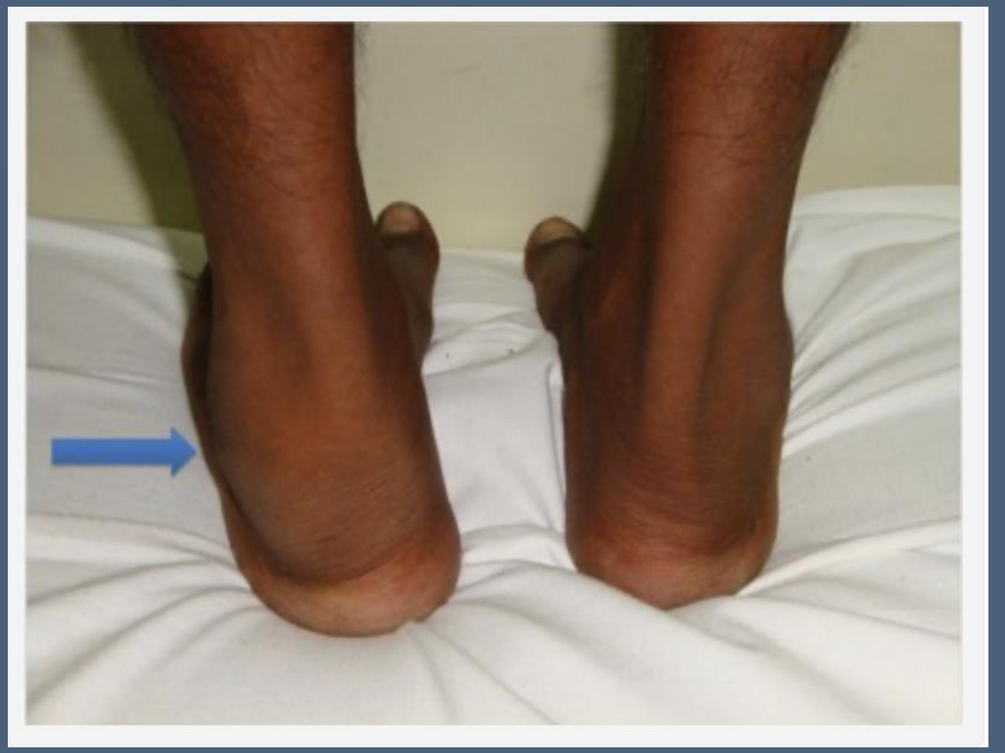


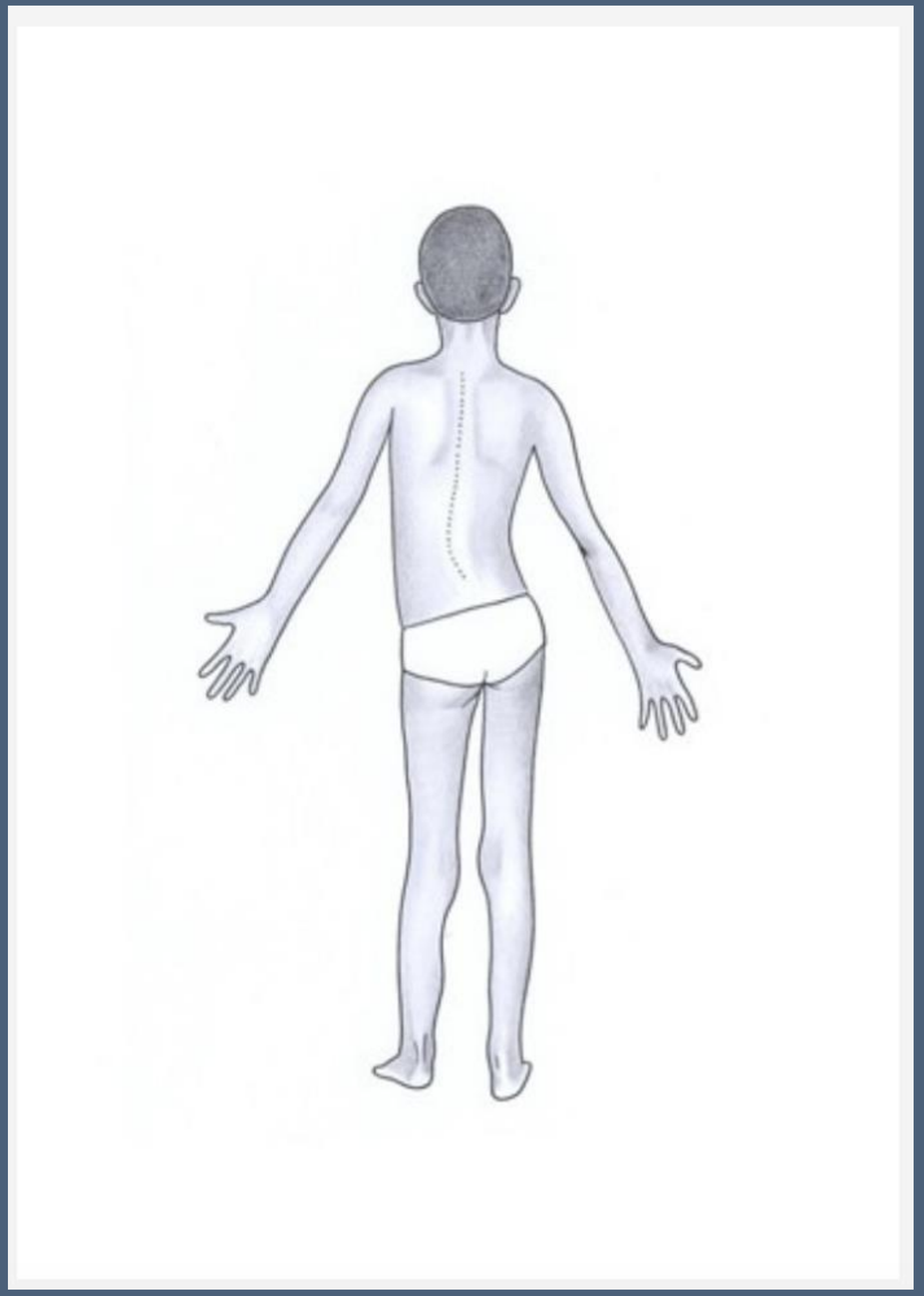




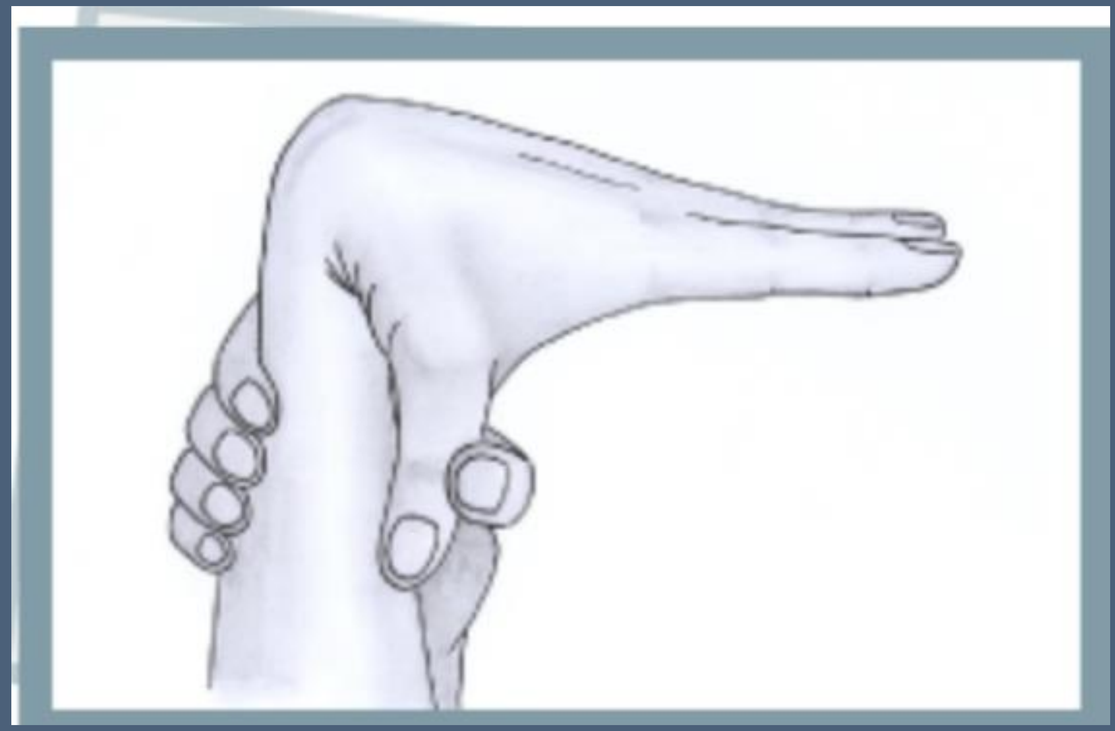
Name the findings?







- Right ankle swelling
- Calf wasting; sign of chronicity >6w



Hypermobility of the thumb.

May cause discomfort with handwriting

Case 1

A 3 year old limping child

- Mom brings Sarah to your clinic. She has been limping at daycare for 2 days. Her mom is concerned that the limp is getting worse.

- Keys points in the history:

  Onset, pattern

  - Trauma?
  - Pain history
  - Joint swelling
  - Diurnal variation
  - Morning stiffness
  - Systemic features (exclude red flags)
  - Preceding illness/infections
  - Previous episodes

History

Sarah's mom tells you:

She has limped for 2 days

Happens all day, worse in the evenings

Has still been playing but is much quieter than normal.

She is happiest when sitting

No history of recent injury, but she had a sore throat a week ago without any fever.

On exam:

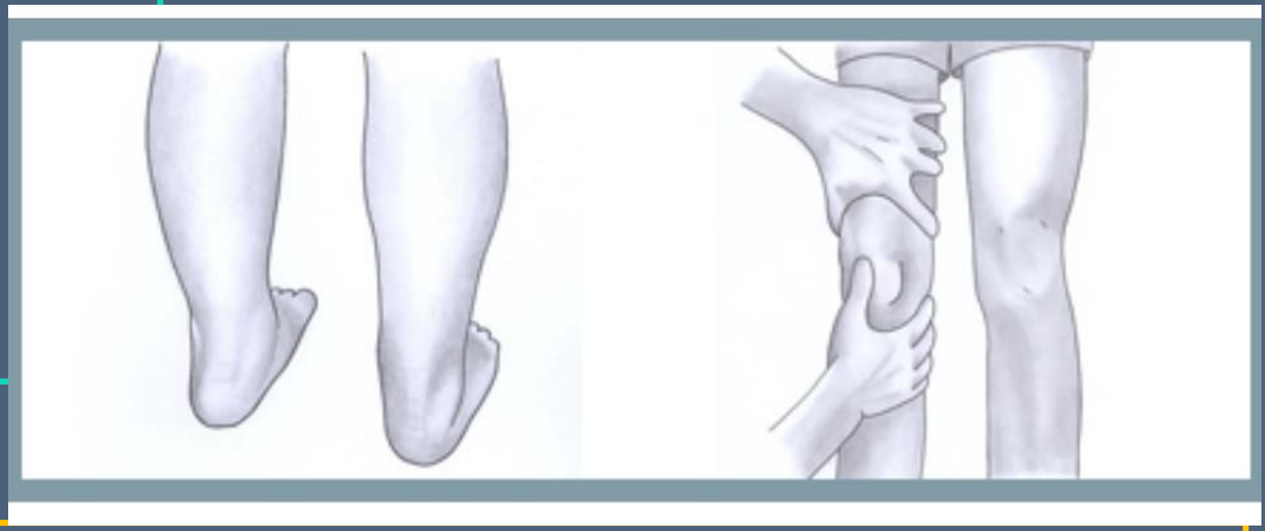
Sarah is quiet. Temp 37.5

Observations are otherwise normal

She has a runny nose and a red throat

Exam key points:

- In the clinic room and while the child is at play- limping?
- General exam and vitals
- Rash? LAD?
- MSK exam: pGALS, more detailed exam in any obvious areas of abnormality
- Other systems: chest, abdominal, ..etc



Sarah's assessment:

A 3 y.o girl with a 2-day history of limping associated with rhinorrhea and a red throat. Her pGALS revealed she was flat footed and generally hypermobile. She was limping and her right knee was swollen, but not hot or red.

Sarah most likely has reactive arthritis.

It is important to re-evaluate in 2-4 weeks.

Instruct family to return in case high fever, persistent pain/limping/ swelling occur.

Follow up in 2 weeks:

Sarah is happily running around your clinic room. Her mom reports she is no longer limping. Her knee swelling resolved

Repeat pGALS shows that she is flat footed and hypermobile, no other abnormalities

Key learning points

Reactive arthritis

- is common following a viral illness
- Joint swelling with or without pain
- Can persist for 2-3 weeks
- Can be recurrent

Septic arthritis:

- Typically presents with high fever, hot swollen joint
- Investigations: CBC, inflammatory markers, imaging, and joint aspiration may be needed to confirm.
- Treatment with IV antibiotics

Juvenile Idiopathic Arthritis (JIA):

- Should be on the differential if joint swelling persists beyond 6 weeks.
- Joint stiffness, swelling, change in function- not pain

Investigations?

Labs and imaging

- May not be indicated
- When needed to support or rule out a diagnosis;
  - Blood tests
    - CBC, blood film, inflammatory markers,
    - Vitamin D, thyroid function, CK, muscle enzymes
    - KFT, LFT, Urine analysis
    - Autoantibodies: ANA, RF, CCP, anti-dsDNA
    - Complement levels

Imaging

- Xray
- Ultrasound
- MRI
- CT and bone scan

Case 3

Widespread Pain

- A 10 year old girl presents with her mother with a 4 week history of aches in her legs, especially around her knees after exercise.

Otherwise she is well and not limited by her symptoms.

Her GP notes that she looks well and has some bruising to her shins. She has hypermobile joints noted on pGALS examination. She has some scars over her knees from mild injuries in the past but these have healed normally.

Otherwise examination was normal with no lymphadenopathy, and her abdomen is soft and non-tender.

The differential diagnosis:

- Must exclude malignancy
- Metabolic cause (hypothyroidism, osteomalacia) and,
- Inflammatory muscle disease.

Investigations include:

- Blood tests and acute phase reactants (all normal).
- Muscle enzymes, thyroid function and bone chemistry and vitamin D levels (all normal).

The likely diagnosis is hypermobility related pain. No features to suggest inherited collagen disorders such as Marfan's syndrome.

Management includes:

- Reassurance and advice about hypermobility
- Advice on footwear and onward referral to Orthotics/Podiatry if appropriate
- Referral to physiotherapy for pain management strategies, and strengthening exercises.

Juvenile Idiopathic Arthritis

Definition of JIA

- Arthritis in one or more joints for at least 6 weeks.
- Onset children <16 y.o
- Clinical diagnosis. A diagnosis of exclusion.
- Is the most common rheumatic condition in children
- The global prevalence ranges from 3.8-400/100,000. Incidence 1.6-23/100,000.

Classification

The International League of Associations for Rheumatology (ILAR, 2001):

1. Oligoarthritis; the most common subtype
2. RF-negative polyarthritis
3. RF-positive polyarthritis
4. Systemic arthritis
5. Psoriatic arthritis
6. Enthesitis related arthritis
7. Undifferentiated arthritis

Case 1

A 4-year-old girl is brought in by her mother for evaluation of left knee swelling and decreased activity. Her mother first noticed that the child avoided playing tag with her friends about 7 weeks ago. About a month later, the mother noticed that the patient began to limp. On physical examination, the child is afebrile and appears to be well. There is left knee swelling and a small effusion. Labs show a positive antinuclear antibody (ANA+), negative rheumatoid factor (RF–), and a normal erythrocyte sedimentation rate. Plain radiographs of the left knee are normal.

What is this child at risk of developing?

Oligoarticular JIA

- Typically affects females, 1-3 y.o
- 4 or less joints
- Usually medium-large joints (knee, ankle, ..)
- Present with:
  - Stiffness; refuse to play, decreased activity, slow in the morning, need help with daily activities
  - Joint pain, only 25%
- On exam:
  - Asymmetric arthritis
  - Leg-length discrepancy
  - Flexion contracture
  - Growth disturbance
  - No fever

Labs:

- Usually normal inflammatory markers
- ANA positive (up tp 70%)
- RF/ CCP/ HLA-B27 negative

If ANA + risk for chronic uveitis

- Need frequent eye screening (slit lamp exam)
- Chronic uveitis: asymptomatic, may complain of photophobia, decreased vision, irregular pupil shape

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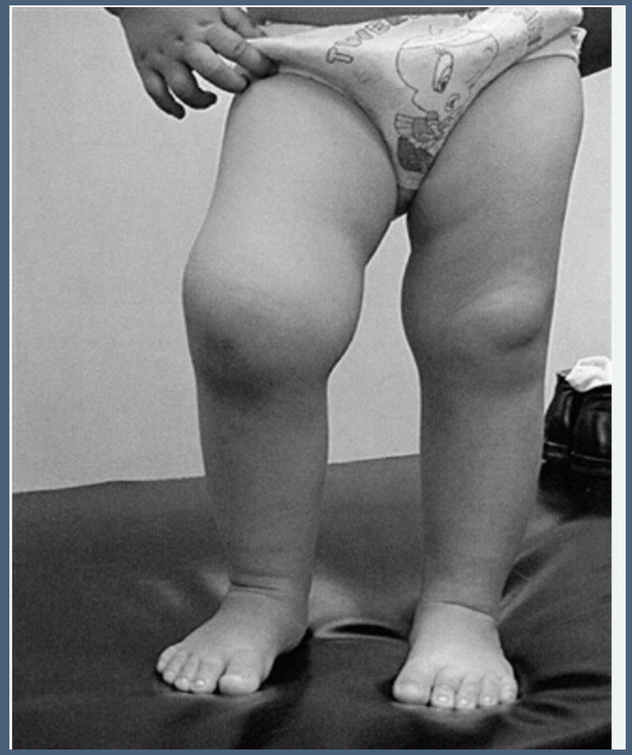


A. Macrophage activation syndrome

B. Chronic, symmetric arthritis

C. Uveitis.

D. Oral ulcers.

E. Osteosarcoma

Case 2

A 13-year-old girl is seen in the office with complaints of joint pains for several months. Her mother reports that she has difficulty arising from bed in the morning due to stiffness. She denies any fevers, weight loss, change in appetite, visual problems, or rashes. Physical exam is remarkable for multiple small- and large-joint swelling and painful range of movement (ROM) bilaterally. The rest of the exam is unremarkable. The anti-CCP (anti-cyclic citrullinated peptide) antibody, rheumatoid factor (RF), and anti-nuclear antibody (ANA) tests are pending.

Which of the following is true regarding her disease?

A. She has juvenile psoriatic arthritis. She is likely to have a negative ANA, RF, and anti-CCP tests.

B. She has systemic juvenile idiopathic arthritis. Her ANA, RF, and anti-CCP tests will likely be positive.

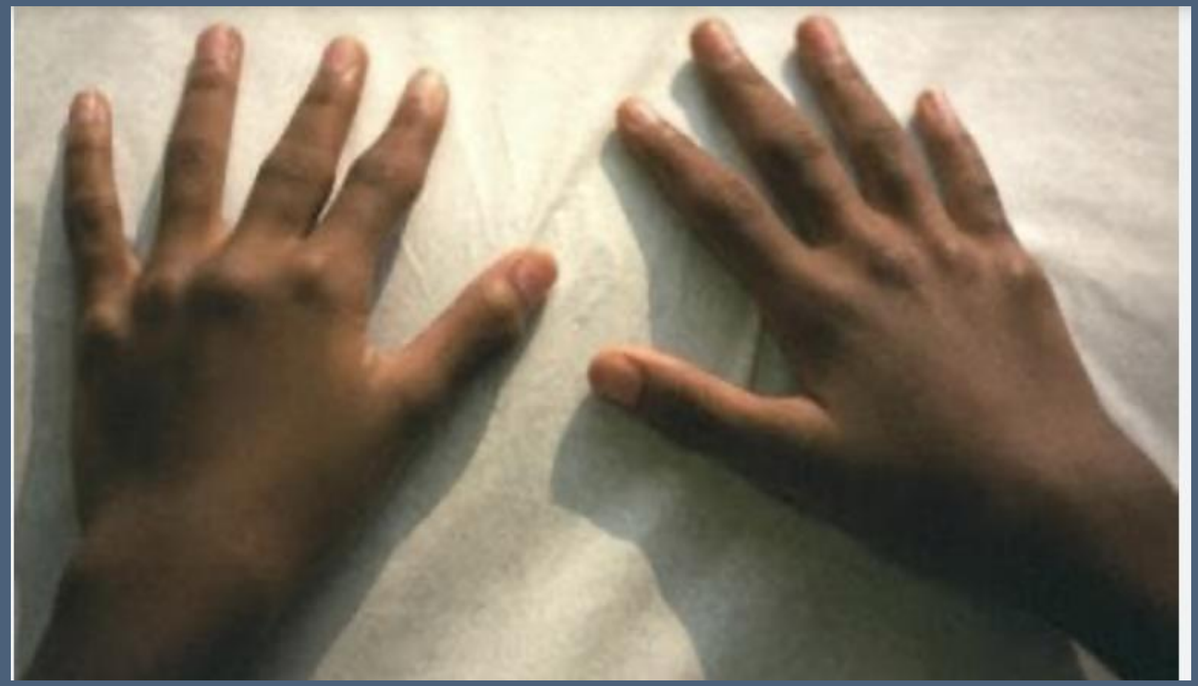
C. She has oligoarticular juvenile idiopathic arthritis. If the ANA, RF, and anti-CCP tests are negative, she will likely have more aggressive disease.

D. She has polyarticular juvenile idiopathic arthritis. If the ANA, RF, and anti-CCP tests are positive, she will likely have more aggressive disease.

E. She has enthesitis-related arthritis. She is likely to have a negative ANA, RF, and anti-CCP tests.

Polyarticular JIA

- >/= 5 joints
- Large & small
- C-spine, shoulders, hips, fingers, TMJ common
- Not DIP (if DIP involved, think psoriatic)
- More common in girls (3:1)



Polyarticular subtype

RF negative:

- Age: biphasic
- F>M
- ANA +ve in ~ 50%
- Potential complications: uveitis, growth disturbance
- Poor prognostic factors: involvement of hip or c-spine. Radiographic damage to joints

RF positive:

- Age: 9-11
- F>M
- Labs:
  - +ve RF
  - +ve anti-CCP (~60%)
  - +ve ANA (~50%)
- Poor prognostic factors: CCP Ab, erosive disease

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E. She has enthesitis-related arthritis. She is likely to have a negative ANA, RF, and anti-CCP tests.

Case 3

A 16-year-old boy presents for the third time in the last 8 months with right knee pain and swelling. He is a soccer player at his school team but does not recall a specific injury. Both previous episodes of knee pain were thought to be related to physical activity and responded to rest and physical therapy. He denies any history of rash, malaise, photosensitivity, or eye pain. On physical examination, the right knee is swollen. There is no associated warmth. Tenderness over areas of ligamentous insertion is noted not only in the involved knee, but in the contralateral knee and left ankle. Results of laboratory evaluation include a positive HLA-B27.

- **Which of the following is likely to be identified during additional evaluation of this patient?**

A. Fusion of hypoplastic cervical vertebra on plain radiograph
B. Bilateral fragmentation, loss of height, and angular deformity of the medial portion of the proximal tibia on plain radiograph
C. Erosive symmetrical polyarthritis
D. Limited anterior forward flexion of the lumbosacral spine
E. Syndactyly

Enthesitis related arthritis

- Enthesitis & arthritis

OR

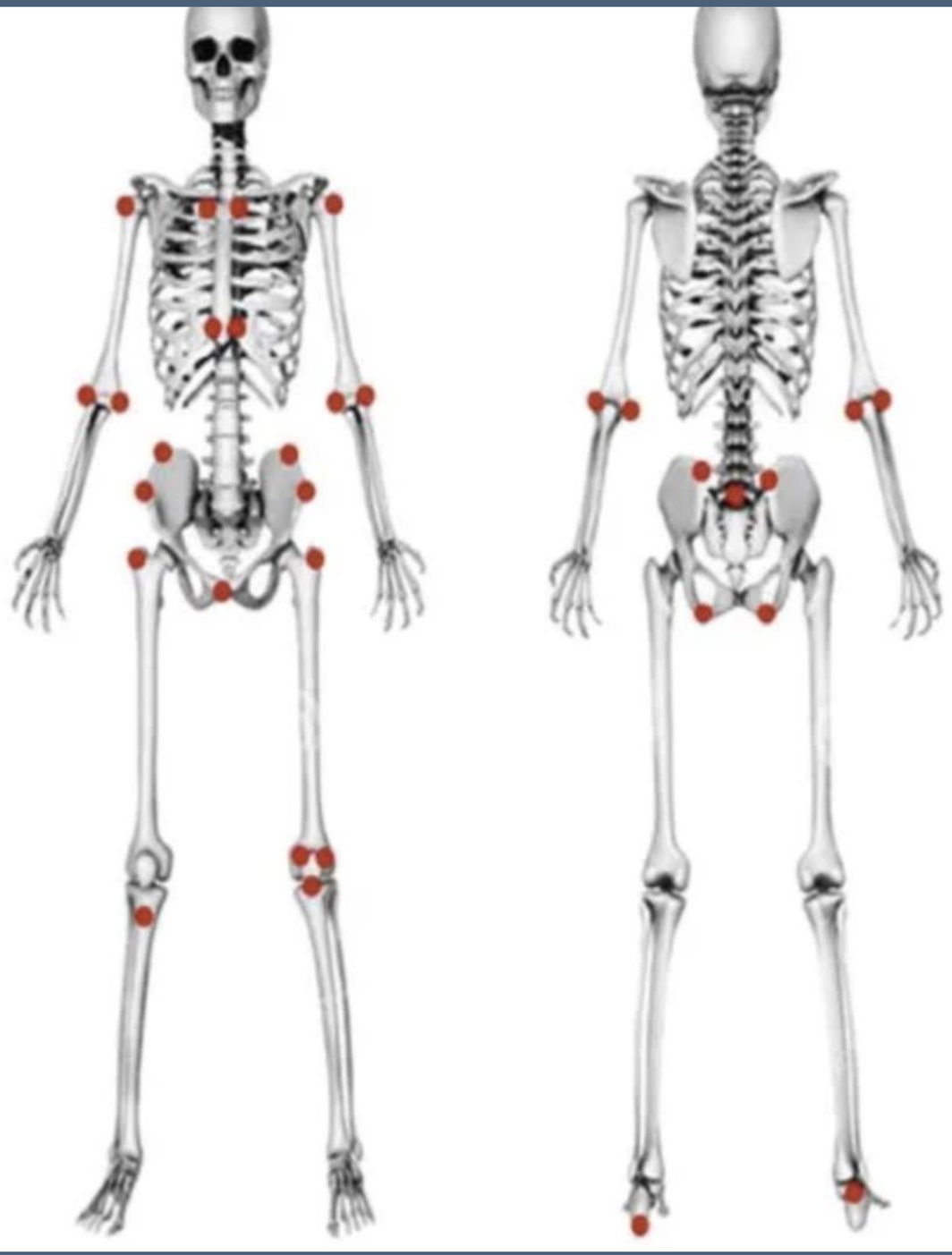
- Either enthesitis or arthritis PLUS at least 2 of the following:

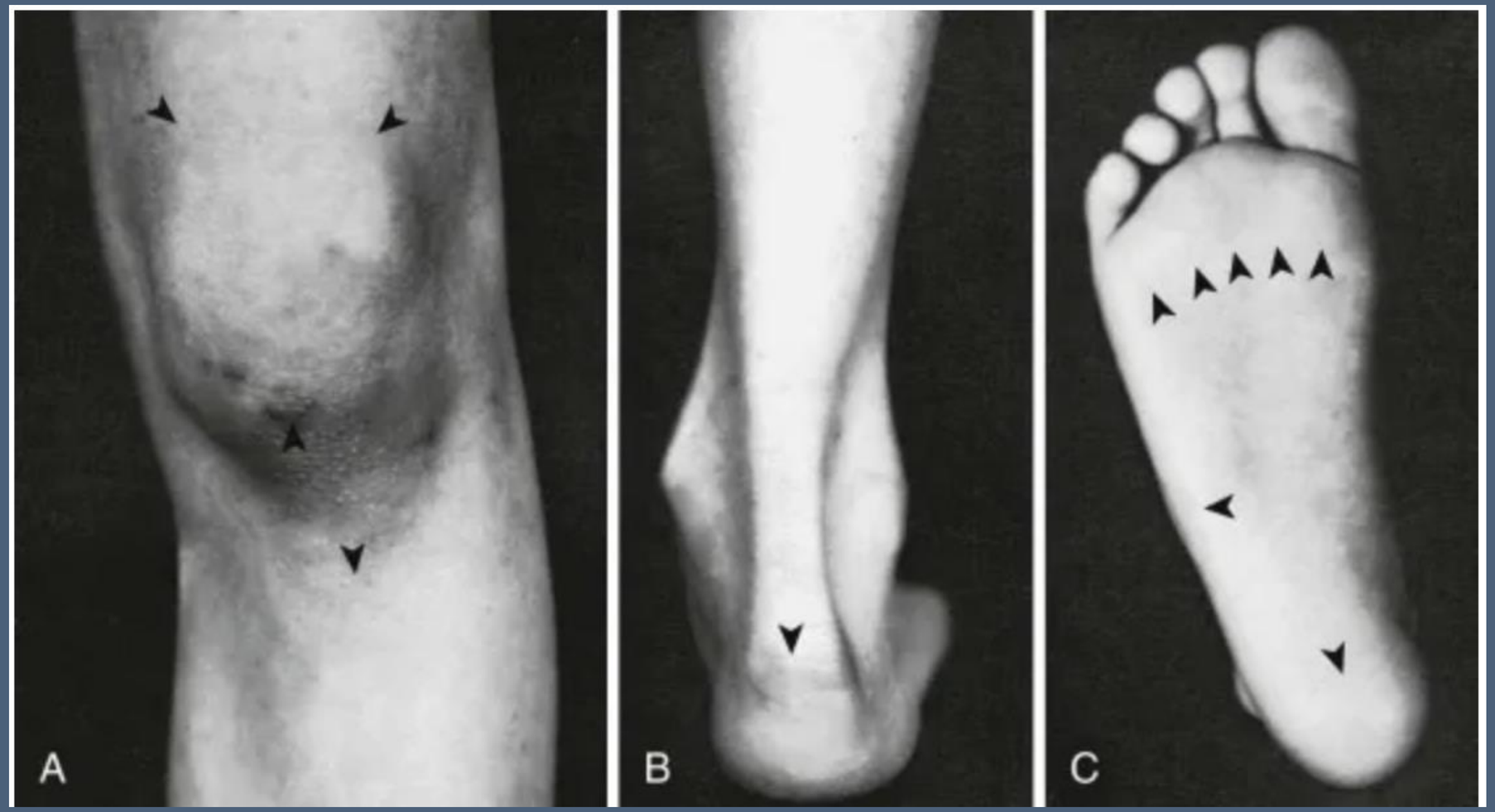
1. SIJ tenderness and/or inflammatory lumbosacral pain
2. HLA-B27+
3. Onset of arthritis in a male > 6 years of age
4. Acute symptomatic uveitis
5. First degree relative with AS, ERA, sacroiliitis with IBD, or ReA.

Exclusion:

- Psoriasis in patient or first degree relative
- +ve RF at least 2 occasions 3 months apart
- Systemic JIA

Anatomic region	Enthesitis exam
Foot and ankle	Achilles tendon insertion to calcaneus Plantar fascia insertion to calcaneus Plantar fascia insertion to metatarsal heads Plantar fascia insertion to base of fifth metatarsal
Knee	Quadriceps tendon insertion to patella (2 and 10 o'clock) Infrapatellar ligament insertion to patella (6 o'clock) and tibial tuberosity
Pelvis	Hip extensor insertion at greater trochanter of femur Sartorius insertion at anterior superior iliac spine Posterior superior iliac spine Abdominal muscle insertions to iliac crest Gracilis and adduction insertion to pubis symphysis Hamstrings insertion to ischial tuberosity
Spine	5th lumbar spinous process
Upper extremity	Common flexor insertion at medial epicondyle of humerus Common extensor insertion at lateral epicondyle of humerus Supraspinatus insertion into greater tuberosity of humerus
Chest	Costosternal junctions (1st and 7th)




A
B
C

A **16-year-old boy** presents for the third time in the last *8 months* with **right knee pain** and swelling. He is a standout player on his high school soccer team but *does not recall a specific injury*. Both previous episodes of knee pain were thought to be related to physical activity and responded to rest and physical therapy. He denies any history of rash, malaise, photosensitivity, or eye pain. On physical examination, the right knee is swollen. There is no associated warmth. *Tenderness* over areas of **ligamentous insertion** is noted not only in the involved knee, but in the **contralateral knee** and left ankle. Results of laboratory evaluation include a **positive HLA-B27**.

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- C. Erosive symmetrical polyarthritis
- D. Limited anterior forward flexion of the lumbosacral spine. ***-Sacroilitis, ERA (JAS)***
- E. Syndactyly

Case 4

A 12-year-old girl presents with arthritis of her left knee and hand. On physical exam, you note dactylitis and pitting of her nails. The distal interphalangeal joint (DIP) joints of her hand are most severely affected by the arthritis. An antinuclear antibody (ANA) test returns positive.

- **Which of the following is the most likely diagnosis?**

A. Polyarticular juvenile idiopathic arthritis
B. Juvenile psoriatic arthritis
C. Mixed connective tissue disease
D. Juvenile enthesitis-related arthritis
E. Systemic lupus erythematosus

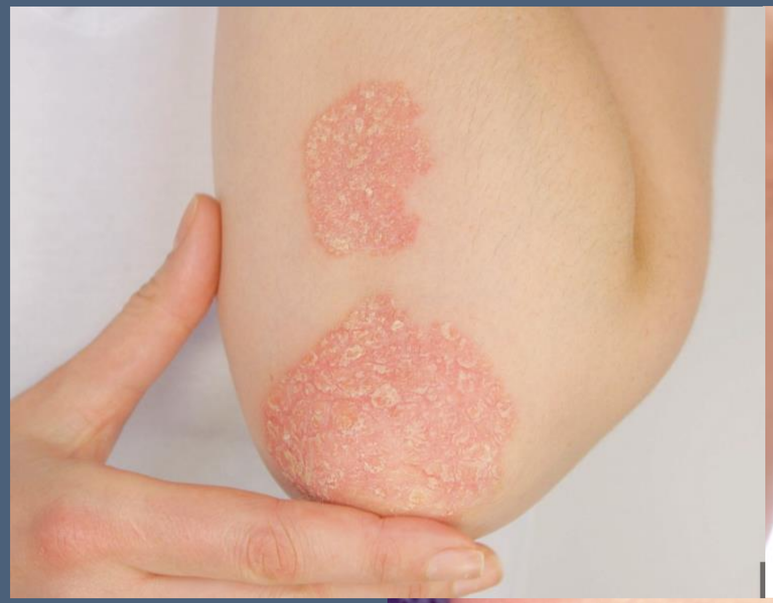
Psoriatic JIA

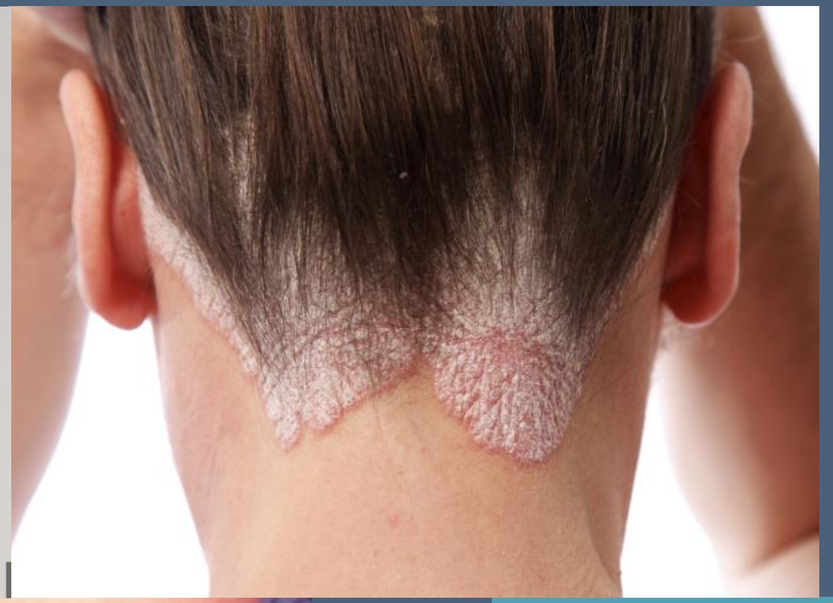
Diagnostic criteria

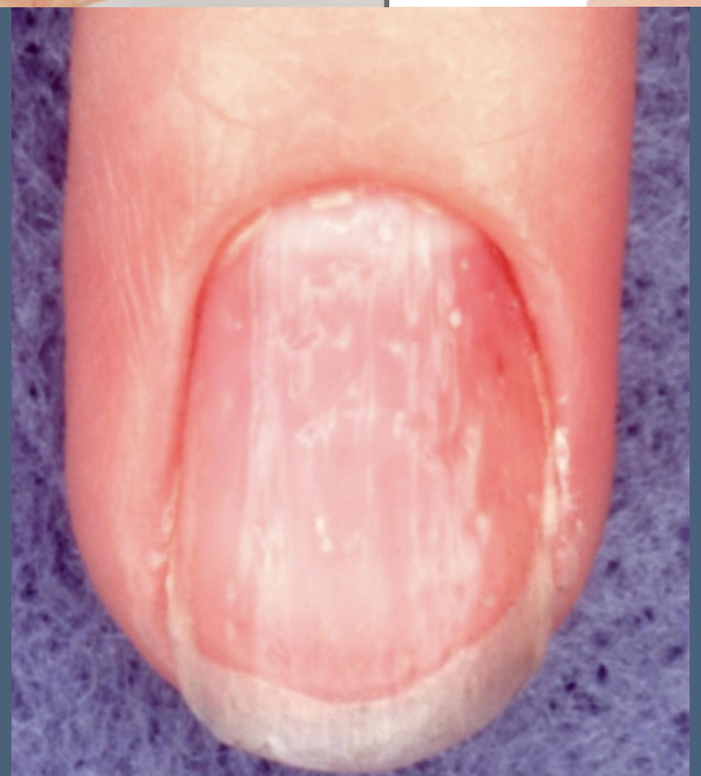
1. Arthritis with an onset < 16 y.o, lasts for at least 6 weeks
2. With either:
    - Psoriasis, or
    - Two minor criteria:
        - Dactylitis
        - Nail pitting or onycholysis
        - Psoriasis in a first degree relative

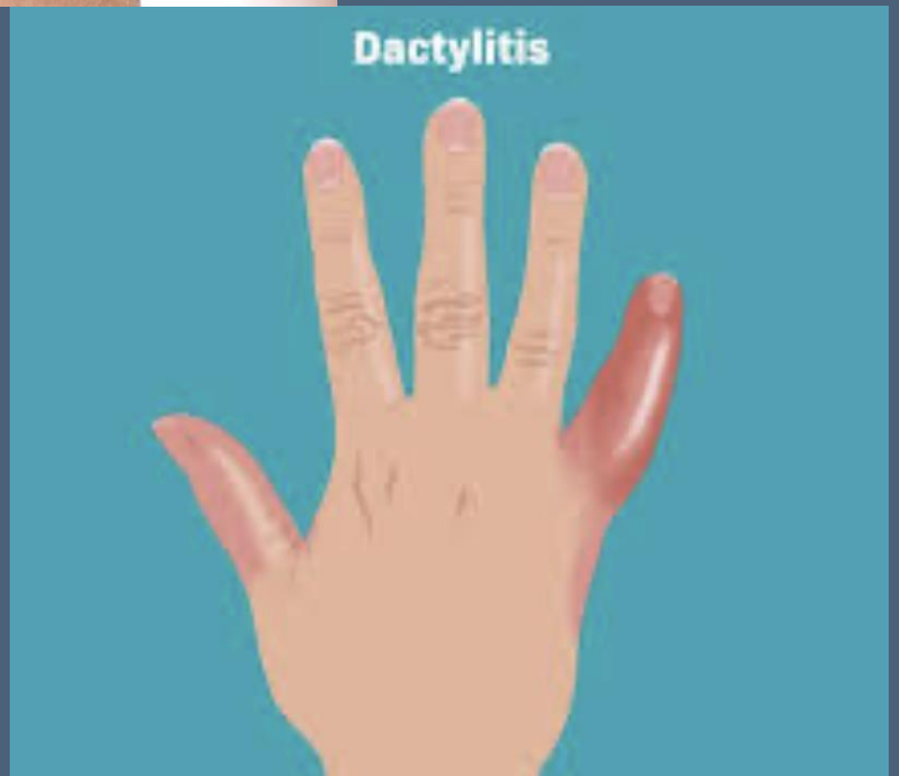
Exclusion criteria:

- +ve RF on 2 occasions.
- First degree family hxt of HLA-B27 associated disease
- Onset of arthrtis in a male >6y.o with HLA-B27+ve
- Features of systemic JIA)








Dactylitis

A 12-year-old girl presents with **arthritis** of her left **knee** and hand. On physical exam, you note **dactylitis** and **pitting** of her nails. The distal interphalangeal joint **(DIP) joints** of her hand are most severely affected by the arthritis. An antinuclear antibody **(ANA)** test returns positive.

- **Which of the following is the most likely diagnosis?**

A. Polyarticular juvenile idiopathic arthritis.
B. Juvenile psoriatic arthritis
C. Mixed connective tissue disease
D. Juvenile enthesitis-related arthritis
E. Systemic lupus erythematosus

Systemic juvenile idiopathic arthritis (Still disease)

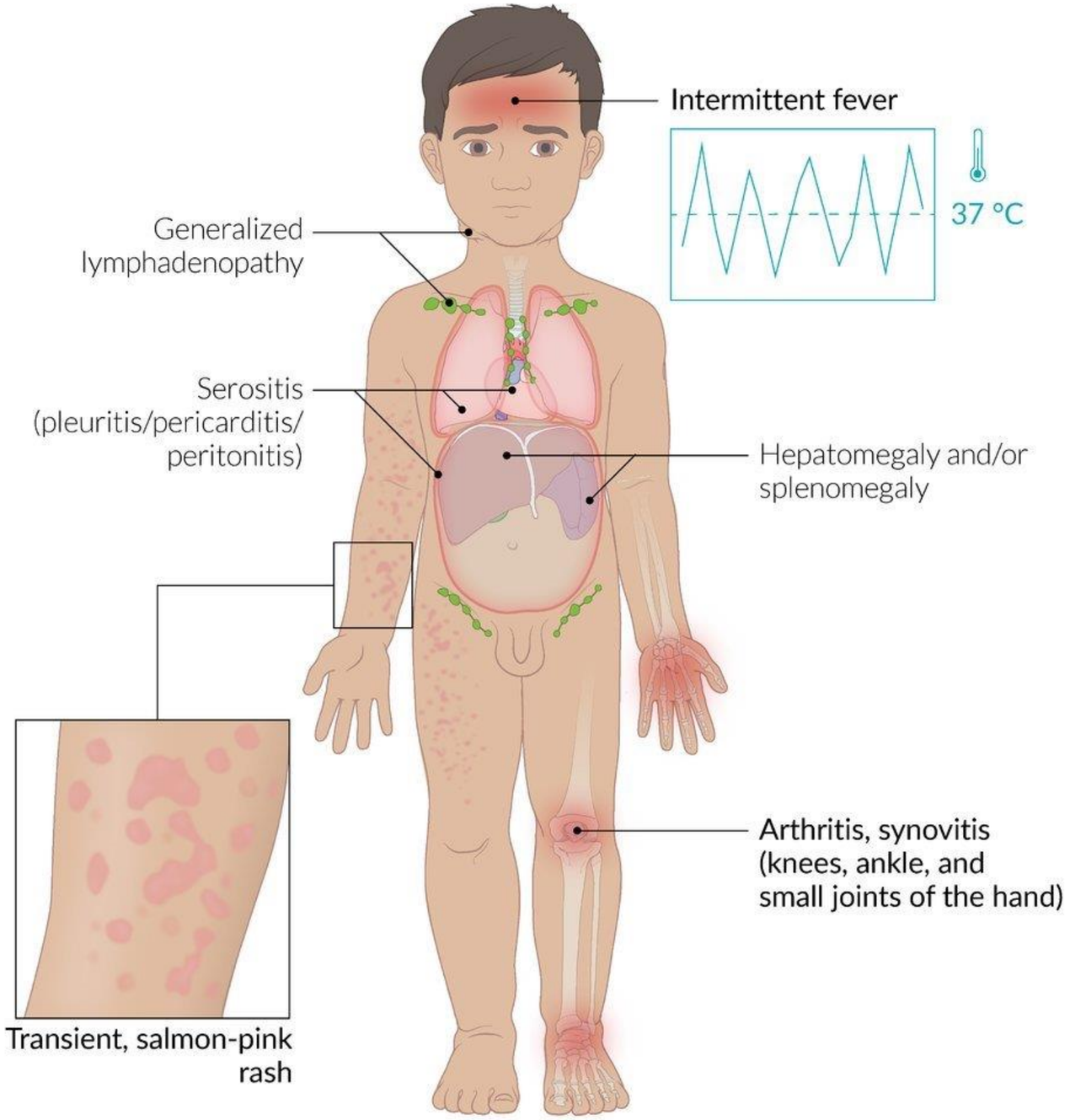
Etiology
Idiopathic

Epidemiology
♀ = ♂
Peak age of onset: 2–4 years

Serology
Typically negative for autoantibodies

Laboratory studies
Anemia, leukocytosis, thrombocytosis

Complications
Macrophage activation syndrome (MAS)



Systemic JIA

- **Quotidian fever**
  - 1-2x/day; spiking; often at night
  - Fever associated with rash

- **Rash**
  - Salmon colored
  - Migratory, evanescent
  - Dermatographism

- **Joints:**
  - Poly>oligo
  - May occur later (fever & rash first)

- **Organs**
  - HSM
  - LAD
  - Pericardial effusion

- **Labs**
  - Very high ESR,CRP
  - Inflammatory CBC
  - Elevated ferritin & fibrinogen

- **MAS**
  - Hemophagocytosis on BMBx
  - Persistent fever
  - Elevated ferritin & CRP
  - ***Low/dropping ESR, fibrinogen***
  - Coagulopathy (d-dimers, PT)
  - ***Evolving/relative cytopenia***
  - Elevated TG
  - Transaminitis (AST, ALT, LDH)

- **Differentiate from**
  - Malignancy; esp if MAS
  - Infection
  - Kawasaki
  - Periodic fever syndrome- pattern is cyclical vs quotidian

Case 5

- A 3-year-old girl presents to the hospital with complaints of progressive malaise, fevers, and joint pains for several weeks. Her parents state she has a history of arthritis for the past year. She presents now with spiking fevers, especially in the evenings, associated with a salmon-pink evanescent rash. Her current medications are ibuprofen and a multivitamin. There is no history of headaches, ocular changes, chest pain, abdominal pain, seizures, night sweats, or weight loss. No recent travel or outdoor activities, such as camping or hiking in the woods, have occurred. There are no sick contacts.

- Physical exam: temperature 38.3°C (101°F), BP 100/60 mmHg, pulse 90 bpm, and RR 14 and nonlabored. Skin reveals an erythematous morbilliform rash on the trunk. HEENT exam reveals no conjunctivitis, uveitis, or glossitis. Neck has cervical lymphadenopathy. Lungs are clear to auscultation bilaterally. Cardiac exam reveals no murmurs, rubs, or gallops. Abdomen demonstrates hepatosplenomegaly. Extremities demonstrate synovitis at the wrists, knees, and ankles bilaterally. Motor strength is intact at 5/5 for upper and lower extremities bilaterally. Neurologic exam reveals 2+ deep-tendon reflexes (DTRs) and is nonfocal without any deficits.

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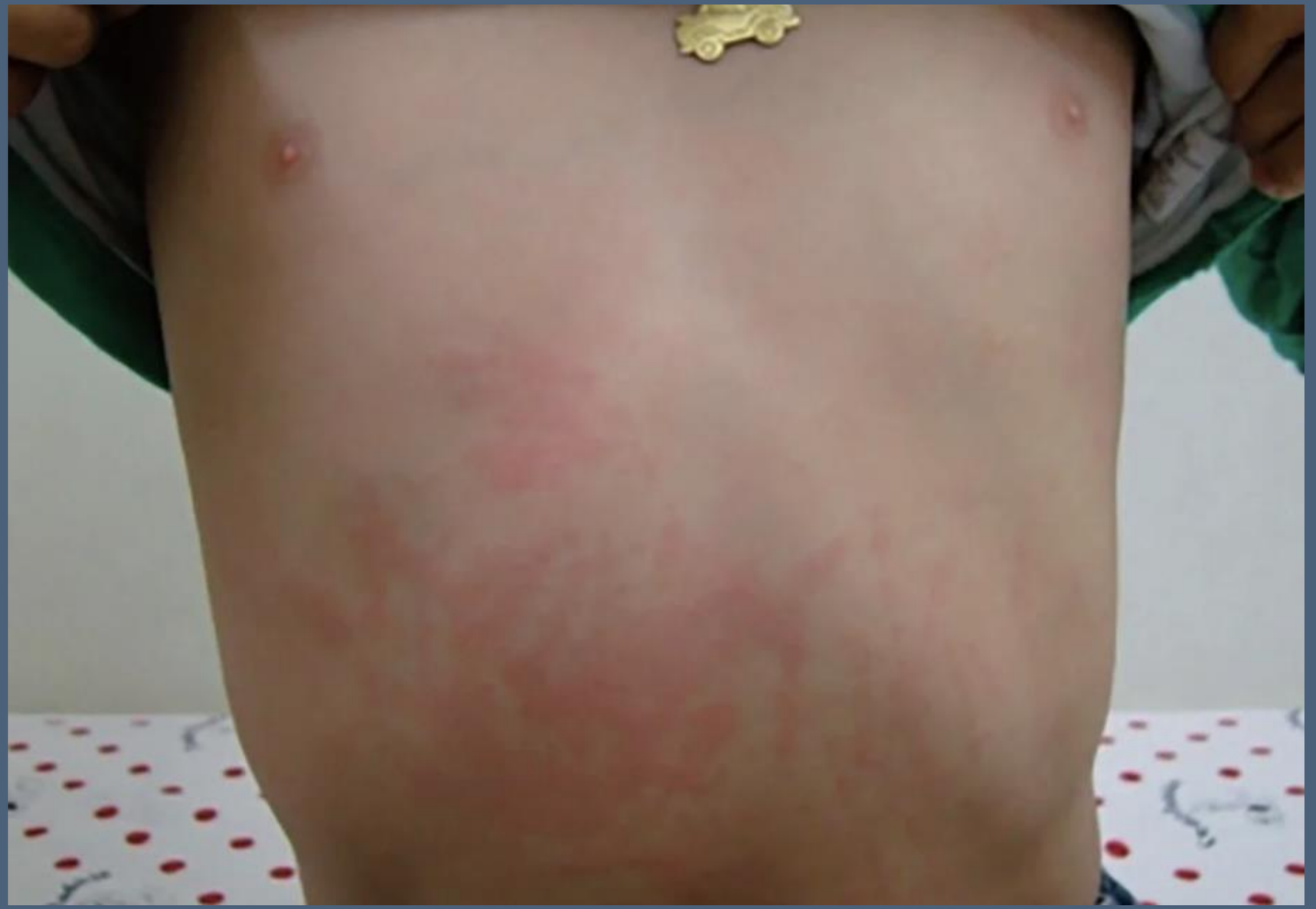

- Labs: WBC count is 4,000 cells/μL, Hgb is 8 g/dL, and platelets are 100,000 cells/μL. Complete metabolic panel reveals elevated liver transaminases. Erythrocyte sedimentation rate (ESR) and C-reactive protein levels are low. Prothrombin time and partial thromboplastin time are prolonged with low fibrinogen levels. Serum ferritin levels are elevated at 16,000 ng/mL. ANA titer is < 1:40 (negative). Rheumatoid factor and anti-CCP antibodies are negative. Serum IgG, IgM, IgD, IgA, and IgE levels are normal.
- Plain films of the wrists, knees, and ankles reveal **juxtaarticular** osteopenia and small erosions.
- A bone marrow aspirate and biopsy demonstrate hemophagocytosis by histiocytes.

- **Which of the following is the most likely diagnosis in this patient?**
  A. Familial Mediterranean fever
  B. Systemic lupus erythematosus
  C. Macrophage activation syndrome
  D. Hyperimmunoglobulin D syndrome
  E. Cryopyrin-associated periodic syndromes

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Questions?