

Pediatrics TeamWork  
437

# Common Pediatric Rheumatic Diseases

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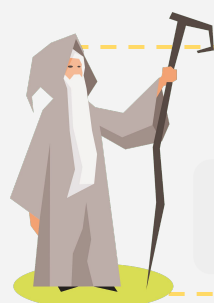
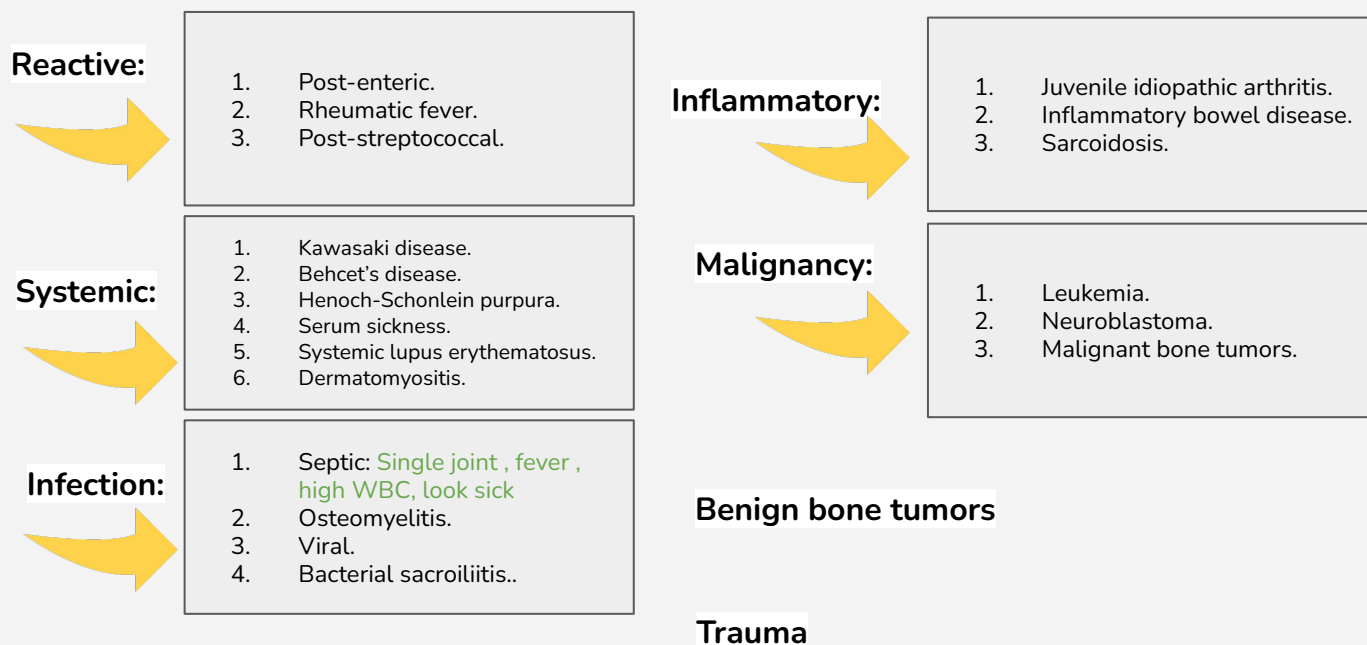
*Kawasaki disease topic  
includes also dr. Mohammed  
alghamdi slides and notes  
from acquired heart disease  
lecture to avoid repeating  
topics!*

# Approach to Arthritis



**Arthritis** (how to know the joint is inflamed): swelling within a joint, or limitation in the range of joint movement with joint pain or tenderness, which **persists for at least 6 weeks**, is observed by a physician, and is not due to primarily mechanical disorders or other identifiable causes.

## Differential diagnosis of arthritis:



-As part of infectious causes don't forget about brucellosis and TB ( ask in Hx ; contact w/ animal ,sick ppl ....)  
-Undifferentiated if it doesn't fit any category

A nice article about Fever evaluation in pediatrics:  
<https://www.aafp.org/afp/2013/0215/afp20130215p254.pdf>

# Juvenile Idiopathic Arthritis



## Overview:

### Old names

Juvenile  
Rheumatoid  
Arthritis

Juvenile  
Chronic  
Arthritis

It is a group of disorders characterized by chronic arthritis (6 wks in duration to diagnose JIA)

It is the **most common chronic rheumatic illness in children**

It is a clinical diagnosis made in a child less than 16 years of age with arthritis

The incidence of JIA ranges from 1 to 22 per 100,000.



## Pathophysiology:

- The pathogenesis of JIA is not understood well
- Substantial evidence suggests that JIA is an autoimmune process.
- Can be triggered by infections or environmental factors
- They usually have other Autoimmune diseases or family history of the disease

## Classification:

International League of Associations for Rheumatology (ILAR)

- 1- Oligoarticular JIA.
- 2- Polyarticular rheumatoid factor positive JIA.
- 3- Polyarticular rheumatoid factor negative JIA.
- 4- Systemic JIA.
- 5- Psoriatic JIA.
- 6- Enthesitis related arthritis(ERA).
- 7- Undifferentiated.

### Oligoarticular (few) JIA:

- **<5 joints** during the **first 6 months of disease**. Large joint : ankle or knees
- At high risk for developing **uveitis** especially **ANA-positive girls** “<7yrs at the onset of illness”
- Persistent & extended oligoarticular JIA.



**Q:** child presented w/ 3 joint involvement in the first 6 months , then after 6 months he came w/ more joint involvement (6-7) what's the type?

**Answer:** Extended Oligoarticular JIA




# Juvenile Idiopathic Arthritis



## Oligoarticular (few) JIA:

- Every single child with oligo JIA should do eye examination. We don't expect them to have symptoms, they may present with asymptomatic uveitis (**anterior uveitis**)

**OCULAR MANIFESTATIONS**

Normal rounded pupil

This is permanent change called synechia

Irregular pupil due to the eye inflammation "uveitis".  
**High risk:** female & ANA +ve  
 Need to be evaluated by ophtha every 10 months

## Polyarticular JIA:

- RF-negative disease (20% to 30% of JIA patients)
- RF-positive disease (5% to 10% of JIA patients).
- Both types affect girls more frequently than boys.
- RF-negative patients often develop polyarthritis in early childhood
- RF-positive disease is like RA in adults "erosion and destruction of joints" . The child may continue to have Sx even as an adult

## Systemic onset juvenile idiopathic arthritis:

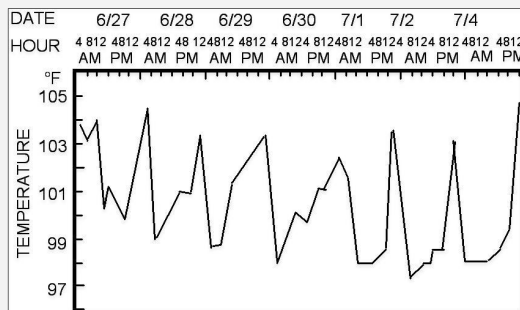
- Undergo extensive investigations to rule out other ddx like: infection or cancer like leukemia , some may need bone marrow aspiration to rule out malignancies. They may present like leukemia!
- No specific age and gender.
- At onset, extra-articular manifestations including rash, fever, lymphadenopathy, hepatosplenomegaly, and serositis predominate.



- The classic rash is evanescent .
- comes and goes
- Stress/ fever or a warm bath may exacerbate the rash.

- Or salmon like rash that disappears within few hours
- If you are on call and a nurse calls you for a pt w/ possible systemic JIA you may not see it but it can come again few hours later

- **Quotidian fever ( 1 or 2 spikes of fever )**
- This chart has 1 spike in day 1 then it's back to normal / subnormal .In the next day there is a 2nd spike



[ Quotidian fever, skin rash, and arthritis this is in favor of systemic JIA ]



**From a paper:** In patients with non-typical JIA and monoarthritis accompanying with intense night pain, highly elevated acute phase reactants, and bone edema in MRI, we believe that bone marrow aspiration should be performed before treatment even if ANA positivity is present.



# Juvenile Idiopathic Arthritis



## Enthesitis-related arthritis:

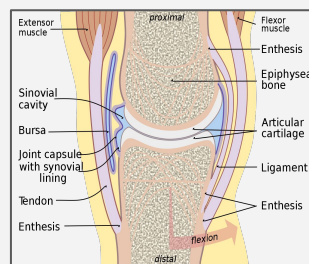
- It is the inflammation of the insertion site of a tendon ,ligament, fascia into bone
- Most common in boys older than 8 years of age.
- It has a strong genetic predisposition.
- The hallmarks of the disease are:

Pain

Stiffness

And eventual loss of mobility of the back

- Like spondyloarthropathy in adults sacroiliac joint involvement, may end up w/ bamboo sign
- Some may present w/ pain in ASIS (anterior superior iliac spine) or below the knee.
- They may have acute eye inflammation not chronic like oligoarticular JIA
- They have genetic predisposition: **HLA-B27** positivity
- Strong family history of inflammatory back pain



Bamboo sign!

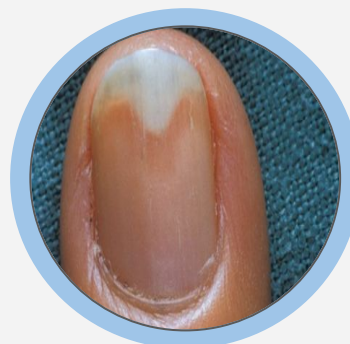
## Psoriatic arthritis:

- Psoriasis + arthritis , but kids may not present w/ typical features of psoriatic arthritis
- A peak age of onset in mid childhood
- **Extra-articular manifestations include:** rash, nail changes (including pitting, onycholysis) and uveitis.+ family history of psoriasis

**Pitting nail**



**Onycholysis**



Inflammation under the nail bed

**Dactylitis**



Dactylitis inflammation of the whole digit

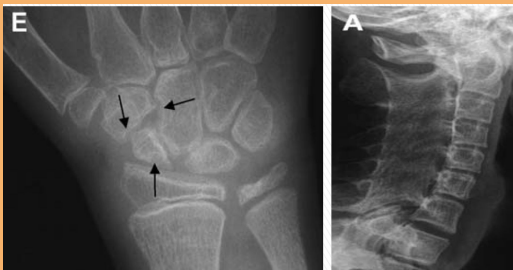
# Juvenile Idiopathic Arthritis



## Investigations:

Dx is mainly clinical

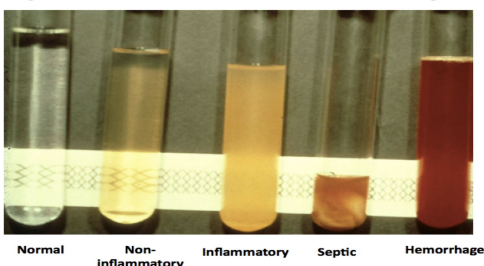
Laboratory	Radiology
<p>- No specific lab. can confirm the diagnosis</p> <p>- Lab. can be used to:</p> <ol style="list-style-type: none"> <li><input type="checkbox"/> Provide evidence of inflammation.</li> <li><input type="checkbox"/> Support the clinical diagnosis.</li> <li><input type="checkbox"/> Monitor treatment toxicity. <b>Monitor liver enzymes and CBC</b></li> </ol> <p>Limited joint disease:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Mild anemia.</li> </ul> <p>Moderate –extensive arthritis:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Normocytic hypochromic anemia or severe anemia.</li> <li><input type="checkbox"/> Iron deficiency anemia.</li> <li><input type="checkbox"/> High WBC count.</li> <li><input type="checkbox"/> High platelets.</li> </ul>	<p><b>Plain x-ray</b></p> <p><b>Early radiological changes:</b></p> <ul style="list-style-type: none"> <li>● Periosteal soft tissue swelling</li> <li>● <input type="checkbox"/> Widening of the joint space</li> <li>● <input type="checkbox"/> Juxta articular osteoporosis</li> <li>● <b>Usually normal X-ray in initial presentation</b></li> </ul>
<p><b>ESR (erythrocyte sedimentation rate):</b></p> <ul style="list-style-type: none"> <li>● <input type="checkbox"/> Useful but not totally reliable measure of active disease. <b>Oligoarticular particularly may be normal</b></li> <li>● Helpful in monitoring the therapeutic efficacy of the medications.</li> </ul> <p><b>CRP (c-reactive protein):</b></p> <ul style="list-style-type: none"> <li>● <input type="checkbox"/> More reliable monitor of inflammation response.</li> </ul>	<p><b>Later changes:</b></p> <ul style="list-style-type: none"> <li>● <input type="checkbox"/> Joint space narrowing</li> <li>● <input type="checkbox"/> Erosions.</li> <li>● <input type="checkbox"/> Subluxation.</li> <li>● <input type="checkbox"/> Ankylosis.</li> <li>● <input type="checkbox"/> Fracture. Specially vertebra</li> </ul>
<p><b>Rheumatoid factor:</b> help in differentiating RF +ve from -ve</p> <ul style="list-style-type: none"> <li>● <input type="checkbox"/> IgM anti IgG.</li> <li>● <input type="checkbox"/> RF positive in: <ul style="list-style-type: none"> <li>○ <input type="checkbox"/> Later childhood polyarthritis.</li> <li>○ <input type="checkbox"/> Subcutaneous nodules.</li> <li>○ <input type="checkbox"/> Articular erosions.</li> </ul> </li> </ul> <p><b>ANA (antinuclear antibody):</b></p> <ul style="list-style-type: none"> <li>● <input type="checkbox"/> More frequent in young girls with oligo JIA</li> <li>● <input type="checkbox"/> Less frequent in older boys with systemic arthritis.</li> </ul>	



**E:** When the chronic inflammation is not treated, there will be Area of erosion (bone eaten up by chronic) osteopenia and osteoporosis and fracture

**A:** Cervical vertebra you expect cervical spine be separated, but it will be ankylosed due to aggressive or chronic inflammation

### Synovial Fluid Color and Clarity



- Joint aspiration not done routinely for JIA unless we want to r/o other ddx (send for culture and cell count). But if the pt has oligo JIA w/ knee **swelling** we may aspirate the joint (therapeutic aspiration) and then inject it w/ steroids (intra-articular).
- **Inflammatory is what we expect in JIA.**



- In **oligo JIA** you might have completely normal labs
- In **systemic JIA** (high WBC, low Hgb, High plts initially but when **MAS develops (pancytopenia)**)

# Juvenile Idiopathic Arthritis



## Management:

### Multidisciplinary approach

### Medications

#### THE AIMS OF MANAGEMENT OF JIA

Controlling pain  
 Controlling inflammation  
 Preserving function  
**Promoting normal growth**  
 Promoting overall development  
 Manage systemic complication

#### NSAIDS

Naproxen or ibuprofen

#### Methotrexate

Specially, for polyarticular JIA

#### Steroids

-Systemic (systemic JIA)  
 -Intraarticular

#### Biologics

Relatively new (we add it when it is NOT responding to treatment. TNF antagonist like humera)

You don't have to know which medication is for which class.

► For oligo JIA we start w/ NSAIDs ; if failed → steroids ( intra-articular)

## Complication:

M

A

S

### EULAR/ACR CLASSIFICATION CRITERIA FOR MAS

A Serious complication of systemic JIA is macrophages activation syndrome (MAS) = Hemophagocytic lymphohistiocytosis (HLH)

Classification of macrophage activation syndrome in systemic juvenile idiopathic arthritis.

A febrile patient with known or suspected systemic juvenile idiopathic arthritis is classified as having macrophage activation syndrome **if the following criteria are met:**

Ferritin >684 ng/ml and any 2 of the following:

Platelet count  $\leq 181 \times 10^9$ /liter

Aspartate aminotransferase >48 units/liter

Triglycerides >156 mg/dl

Fibrinogen  $\leq 360$  mg/dl

Laboratory abnormalities should not be otherwise explained by the patient's condition, such as concomitant immune-mediated thrombocytopenia, infectious hepatitis, visceral leishmaniasis, or familial hyperlipidemia.

Persistent fever (not quotidian), pancytopenia, high liver enzymes and they are very sick. It can be fatal in 40% of pt specially if not detected early

# Systemic Lupus Erythematosus



- SLE is a multisystem autoimmune disease with a great variability in disease presentation and course. **Same as adult, but more complication due to the duration of disease and medication S/E**
- The diagnosis of SLE is based on the clinical and laboratory features consistent with this illness.
- The etiology of systemic lupus erythematosus (SLE) remains unknown and it is **multifactorial**:

Genetics factors	Hormonal factors	Immune abnormalities	Environmental factors
<p>There is a high concordance rate (14 to 57 percent) of SLE in monozygotic twins.</p> <p>Children of mothers with lupus may have a positive test for antinuclear antibodies</p>	<p><b>More in females (4:1)</b></p> <p>The use of estrogen-containing contraceptive agents is associated with a 50 percent increase in risk of developing SLE</p>	<p>SLE is primarily a disease with abnormalities in immune regulation.</p> <p>Immune deficiency is risk factor</p>	<p>Viruses</p> <p>Ultraviolet (UV) light should avoid exposure</p> <p>Allergies to medications anti-TB (isoniazid), anti-HTN ( hydralazine)</p>

## Criteria:



### Old Criteria

SLICC (Systemic Lupus International Collaborating Clinics) Classification Criteria for Systemic Lupus Erythematosus requirements:

- $\geq 4$  criteria (at least 1 clinical and 1 laboratory criteria)
- OR biopsy-proven lupus nephritis with positive ANA or Anti-DNA

Clinical Criteria	Immunological Criteria
<ol style="list-style-type: none"> <li>1.Acute Cutaneous Lupus: malar rash. <b>Sparing nasolabial folds</b></li> <li>2.Subacute cutaneous lupus</li> <li>3.Chronic Cutaneous Lupus: discoid rash.</li> <li>4.Oral Ulcers (<b>painless</b>) OR Nasal Ulcers.</li> <li>5.Non-scarring alopecia. <b>Ask about hair loss</b> - can be early presentation of SLE</li> <li>6.Arthritis involving 2 or more joints (<b>non-erosive</b>)</li> <li>7.Serositis (<b>major</b>): pleural effusions, pericardial effusion, and pericarditis by electrocardiography in the absence of other causes, such as infection, uremia. <b>Peritonitis (abdominal pain)</b></li> <li>8.Renal: urine protein-to-creatinine ratio (or 24-hour urine protein) representing 500 mg protein/24 hours OR red blood cell casts. <b>Imp poor prognostic factor. Even with mild renal involvement sometimes we need renal bx ; why? We expect worse finding in the biopsy compared to the renal symptoms.</b></li> <li>9.Neurologic: seizures, psychosis, mononeuritis multiplex (in the absence of other known causes), myelitis, peripheral or cranial neuropathy (in the absence of other known causes) and acute confusional state (in the absence of other causes). <b>Ask about school performance, renal and CNS involvement affect prognosis</b></li> <li>10.Hemolytic anemia (<b>sudden drop of Hb, jaundice and dark urine</b>)</li> <li>11.Leukopenia (&lt;4000/mm<sup>3</sup>) OR <b>Lymphopenia (&lt;1000/mm<sup>3</sup>)</b>.</li> <li>12.<b>Thrombocytopenia</b> (&lt;100,000/mm<sup>3</sup>) at least once in the absence of other known causes. <b>Pt w/ isolated thrombocytopenia should be followed-up as they may develop lupus in the future.</b></li> </ol>	<ol style="list-style-type: none"> <li>1.ANA level above laboratory reference range. <b>Has to be +ve for Dx of SLE</b></li> <li>2.Anti-dsDNA antibody level above laboratory reference range. <b>specific, renal involvement</b></li> <li>3.Anti-Smith. <b>Also specific</b></li> <li>4.Antiphospholipid antibody. <b>They are prone to secondary (APS)</b> . ask for anticardiolipin, beta-2 glycoprotein I (<math>\beta</math>2GPI), and lupus anticoagulant. Don't bother yourself about names just have an idea</li> <li>5.Low complement (C3, C4, or CH50). If low indicates flare-up. <b>Renal involvement (low C3)</b></li> <li>6.Direct Coombs' test (in the absence of hemolytic anemia)</li> </ol> <p>Antihistone Ab → drug- induced lupus</p>

# Systemic Lupus Erythematosus



Criteria:



## Old Criteria



Malar rash



Subacute Cutaneous Lupus



Discoid rash



Oral ulcer



Non-scarring alopecia



## Updated Criteria

Entry criterion			
Antinuclear antibodies (ANA) at a titer of $\geq 1:80$ on HEp-2 cells or an equivalent positive test (ever)			
↓			
If absent, do not classify as SLE If present, apply additive criteria			
↓			
Additive criteria			
Do not count a criterion if there is a more likely explanation than SLE. Occurrence of a criterion on at least one occasion is sufficient. SLE classification requires at least one clinical criterion and $\geq 10$ points. Criteria need not occur simultaneously.			
Within each domain, only the highest weighted criterion is counted toward the total score.			
Clinical domains and criteria	Weight	Immunology domains and criteria	Weight
<b>Constitutional</b>		<b>Antiphospholipid antibodies</b>	
Fever	2	Anti-cardiolipin antibodies OR	
<b>Hematologic</b>		Anti- $\beta 2$ GP1 antibodies OR	
Leukopenia	3	Lupus anticoagulant	2
Thrombocytopenia	4	<b>Complement proteins</b>	
Autoimmune hemolysis	4	Low C3 OR low C4	3
<b>Neuropsychiatric</b>		Low C3 AND low C4	4
Delirium	2	<b>SLE-specific antibodies</b>	
Psychosis	3	Anti-dsDNA antibody* OR	
Seizure	5	Anti-Smith antibody	6
<b>Mucocutaneous</b>			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
<b>Serosal</b>			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
<b>Musculoskeletal</b>			
Joint involvement	6		
<b>Renal</b>			
Proteinuria $>0.5$ g/24h	4		
Renal biopsy Class II or V lupus nephritis	8		
Renal biopsy Class III or IV lupus nephritis	10		
<b>Total score:</b>			
↓			
Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.			

It must reach  $\geq 10$  points

### Rules:

- 1 from each category
- If you have 2 from the same category, pick the highest weight
- Last one in renal = 10. If present alone w/ +ve ANA, we can diagnose the pt w/ SLE

It's a must to have ANA

Don't remember all the numbers but I want you to have an idea



# Systemic Lupus Erythematosus



## Lupus Nephritis (Notes):

Classification category	Features
Class I: minimal mesangial	Normal/minimal proteinuria, normal creatinine Earliest and mildest form of glomerular involvement
Class II: mesangial proliferative	Microscopic haematuria +/- proteinuria Hypertension uncommon and nephrotic syndrome plus renal insufficiency rarely seen
Class III: focal lupus nephritis	Haematuria, proteinuria, hypertension, reduced eGFR +/- nephrotic syndrome
Class IV: diffuse lupus nephritis	Most common and severe form of lupus nephritis Clinical features as for class III but also significantly low C3 and high dsDNA, especially in active disease
Class V: membranous nephropathy	Nephrotic syndrome, microscopic haematuria, hypertension, normal/high creatinine Can present without other clinical or serological manifestations of SLE but electron microscopy features will distinguish it from the idiopathic form
Class VI: advanced sclerosing lupus	Slowly progressive renal failure with proteinuria and bland urine sediment

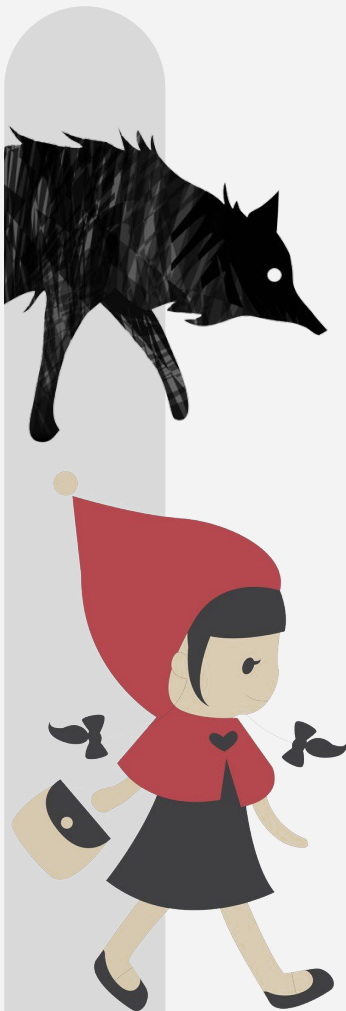
Adapted from Bomback AS, Appel GB. UpToDate: 2018.<sup>12</sup>

Abbreviations: dsDNA = double-stranded DNA; eGFR = estimated glomerular filtration rate; SLE = systemic lupus erythematosus.

## Lupus nephritis

- It has 6 classes
- Class 3,4 - significant renal involvement ( should go for aggressive Tx like cyclophosphamide, MMF or rituximab )
- Class 5 membranous nephritis ( **proteinuria** )
- Class 6 sclerosed kidney ( should go for **dialysis** )

## Treatment :



### General

#### Team approach:

- Counseling
- Education
- Appropriate nutrition
- Use of sun protection
- Immunization
- Prompt management of infection

#### Nonsteroidal Anti-inflammatory

**Hydroxychloroquine** Specially in skin and hematology problems

**Glucocorticoids** The Main treatment specially in the beginning IV in cns, renal and active

**Immunosuppressives** In bad cns or renal

"Red riding hood will help you to remember SLE. Lupus means wolf and erythematosus means red, and in the story the villain is the wolf and the prey is the little girl wearing red hood. SLE = commonly affects woman!"



# Henoch-Schonlein Purpura



- HSP is the most common pediatric vasculitis. Involves small arteries
- Classically presents with the triad of:



Non-thrombocytopenic palpable purpura

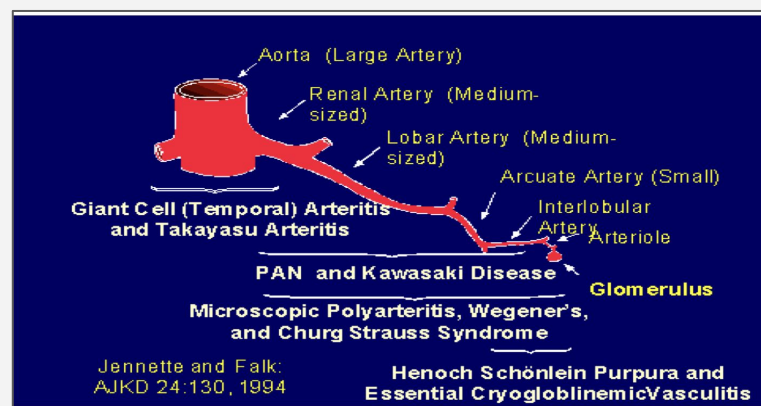


Colicky abdominal pain



Arthritis

Differential diagnoses of Vasculitis (according to vessel size):



## Pathophysiology:

Immunoglobulin A (IgA) immune complexes deposition. This is what you expect to see in skin biopsy

The major cause of morbidity is renal involvement.

3-15 years. if no renal involvement = benign disease

A wide variety of infections may trigger HSP. It's not a must but it could happen

- **Skin involvement (100%)** in HSP may begin as urticaria, but in most cases it progresses to dramatic purple, non-blanching lesions. **Mainly lower limb vasculitis.**
- **Gastrointestinal involvement (75%)** ranges from colicky abdominal pain to profuse bleeding, intussusception.
- **The arthritis of HSP (50%)** is usually transient, and it does not cause chronic joint changes.
- **Renal Disease:** the most serious sequelae of Henoch- Schonlein purpura is renal involvement. This complication occurs in about 25 percent of children



- HSP in ER don't forget the possibility of **intussusception** so we do radiological investigation to rule it out. You may end up with gut gangrene.
- Most common site of intussusception = **ileoileal**. why? GI vasculitis

# Henoch-Schonlein Purpura



Diagnosis: Based on the criteria

Purpura (mandatory criterion):

<b>1</b> Abdominal pain	<b>3</b> Arthritis or arthralgia
<b>2</b> Histopathology; vasculitis with predominant IgA deposit.	<b>4</b> Renal involvement

You can't diagnose HSP w/o skin rash!

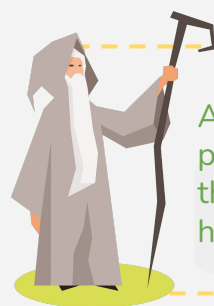
Picture is a histopathology of HSP (EXTRA)

Skin biopsy? If not sure about the Dx

Treatment:

- Therapy of HSP is primarily supportive, aiming for symptomatic relief of arthritis and abdominal pain.
- Use of steroids in children who do not respond to NSAIDs (we usually don't start w/ it b.c of GI upset and renal problems - used if needed ) or in those thought to be at highest risk of developing renal compromise continues to be controversial.
- Indications for steroids from the beginning :

1- renal involvement 2- CNS involvement 3- sever GI bleeding



Adult HSP considered as paraneoplastic syndrome (consider the possibility of malignancy or hepatitis)!!

# Juvenile Dermatomyositis

Triad of : childhood- skin - muscle involvements



Idiopathic inflammatory myopathies (IIMs), collectively known as myositis, are heterogeneous disorders characterized by muscle weakness and muscle inflammation.

The most common subgroups in children, juvenile DM (JDM).

## Incidence:

- In population-based studies, JDM has a reported annual incidence that ranges from two to four cases per one million children. **Not common**
- The peak incidence is from 5 to 10 years of age.

## Etiology & Pathogenesis:

- Cause unknown.
- Likely autoimmune angiopathy.
- Environmental and genetic factors implicated.
  - A history of infection prior to onset is common, 65- 70% of patients have a history of a significant infection during the three months prior to first onset of symptoms.
  - Proposed triggers include various infectious agents, vaccines, medications, UV light.
- Cellular and humoral immunity implicated.
- Complement-mediated injury important.
- Innate immune response: type I interferons and dendritic cells.

## Dermatomyositis (other organ involvement):

1. Gastrointestinal vasculitis: gut wall perforation.
2. Arthritis: common but usually early and mild, non- erosive.
3. Cardiac: inflammation, fibrosis, conduction defects.
4. Renal: glomerular hypercellularity.
5. Pulmonary: fibrosis, pneumothorax. sometimes due to the weakness they might face respiratory problems and need ICU and ventilation .Rash + lung involvement (ILD) → anti-MDA5
6. Central nervous system: behavior changes, seizures.
7. Alopecia.
8. Eyes: exudative vasculitis of retina.
9. Derm: calcinosis, subcutaneous nodules, ulcerations.
10. **Lipodystrophy**. One of the major involvement -> loss of subcutaneous fat

## Differential Diagnosis:

Don't remember the details but I want to tell you that muscle weakness can present in other disease not only JDM

	Condition
<b>Weakness alone</b>	
Muscular dystrophies	Limb-girdle dystrophies, dystrophinopathies, facioscapulohumeral dystrophy, other dystrophies
Metabolic myopathies	Muscle glycogenoses (glycogen-storage diseases), lipid-storage disorders, mitochondrial myopathies
Endocrine myopathies	Hypothyroidism, hyperthyroidism, Cushing's syndrome or exogenous steroid myopathy, diabetes mellitus
Drug-induced myopathy	Consider for patients taking any of the following drugs or biological treatments: statins, interferon $\alpha$ , glucocorticoids, hydroxychloroquine, diuretics, amphotericin b, caine anaesthetics, growth hormone, cimetidine, and vincristine
Neuromuscular transmission disorders	Myasthenia gravis
Motor neuron disorder	Spinal muscular atrophy
<b>Weakness with or without rash</b>	
Viral	Enterovirus, influenza, coxsackievirus, echovirus, parvovirus, poliovirus, hepatitis B, human T-lymphotropic virus 1
Bacterial and parasitic organisms	Staphylococcus, streptococcus, toxoplasmosis, trichinosis, <i>Lyme borreliosis</i>
Other rheumatic conditions	Systemic lupus erythematosus, scleroderma, juvenile idiopathic arthritis, mixed connective-tissue disease, idiopathic vasculitis
Other inflammatory conditions	Inflammatory bowel disease, coeliac disease
Rash without weakness	Psoriasis, eczema, allergy

In many of these conditions, diagnosis is facilitated by muscle biopsy; muscle biopsy should be strongly considered in the absence of rashes of typical juvenile dermatomyositis.

Table 2: Differential diagnosis of childhood idiopathic inflammatory myopathies<sup>43,44</sup>

Bonanza and Peter diagnostic criteria: Old criteria but the popular

<b>A</b>	Proximal and symmetrical muscle weakness of the pelvic and scapular girdle, anterior flexors of the neck, progressing for weeks to months, with or without dysphagia or involvement of respiratory muscles.
<b>B</b>	Elevation of the serum levels of skeletal muscle enzymes: creatine phosphokinase, aspartate aminotransferase, lactate dehydrogenase, and aldolase. <i>AST</i>
<b>C</b>	Electromyography characteristic of myopathy (short and small motor units, fibrillations, positive pointy waves, insertional irritability and repetitive high-frequency firing).
<b>D</b>	Muscle biopsy showing necrosis, phagocytosis, regeneration, perifascicular atrophy, perivascular inflammatory exudate. <i>Muscle biopsy : we don't usually do it. Replaced by MRI</i>
<b>E</b>	Typical cutaneous changes: <ul style="list-style-type: none"> <li>• <b>Heliotrope</b> with periorbital edema and violaceous erythema;</li> <li>• <b>Gottron's sign</b>: vasculitis in the elbow, metacarpophalangeal, and proximal interphalangeal joints.</li> </ul>

Criteria for DM	
Definitive	Three criteria (A, B, C or D) + E
Probable	Two criteria (A, B, C or D) + E
Possible	One criteria (A, B, C or D) + E

Updated criteria

CLASSIFICATION CRITERIA FOR ADULT AND JUVENILE IIM 2275

**Table 2.** The European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIMs)

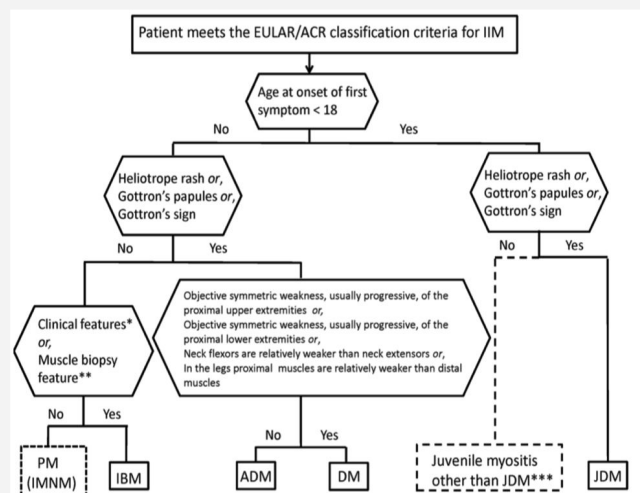
When no better explanation for the symptoms and signs exists, these classification criteria can be used

Variable	Score points		Definition
	Without muscle biopsy	With muscle biopsy	
Age of onset			
Age of onset of first symptom assumed to be related to the disease $\geq 18$ years and $< 40$ years	1.3	1.5	18 $\leq$ age (years) at onset of first symptom assumed to be related to the disease $< 40$
Age of onset of first symptom assumed to be related to the disease $\geq 40$ years	2.1	2.2	Age (years) at onset of first symptom assumed to be related to the disease $\geq 40$
Muscle weakness			
Objective symmetric weakness, usually progressive, of the proximal upper extremities	0.7	0.7	Weakness of proximal upper extremities as defined by manual muscle testing or other objective strength testing, which is present on both sides and is usually progressive over time
Objective symmetric weakness, usually progressive, of the proximal lower extremities	0.8	0.5	Weakness of proximal lower extremities as defined by manual muscle testing or other objective strength testing, which is present on both sides and is usually progressive over time
Neck flexors are relatively weaker than neck extensors	1.9	1.6	Muscle grades for neck flexors are relatively lower than neck extensors as defined by manual muscle testing or other objective strength testing
In the legs, proximal muscles are relatively weaker than distal muscles	0.9	1.2	Muscle grades for proximal muscles in the legs are relatively lower than distal muscles in the legs as defined by manual muscle testing or other objective strength testing
<b>Skin manifestations</b>			
Heliotrope rash	3.1	3.2	Purple, lilac-colored, or erythematous patches over the eyelids or in a periorbital distribution, often associated with periorbital edema
Gottron's papules	2.1	2.7	Erythematous to violaceous papules over the extensor surfaces of joints, which are sometimes scaly. May occur over the finger joints, elbows, knees, malleoli, and toes
Gottron's sign	3.3	3.7	Erythematous to violaceous macules over the extensor surfaces of joints, which are not palpable
Other clinical manifestations			
Dysphagia or esophageal dysmotility	0.7	0.6	Difficulty in swallowing or objective evidence of abnormal motility of the esophagus
Laboratory measurements			
Anti-Jo-1 (anti-histidyl-transfer RNA synthetase) autoantibody present	3.9	3.8	Autoantibody testing in serum performed with standardized and validated test, showing positive result
Elevated serum levels of creatine kinase (CK)* or lactate dehydrogenase (LDH)* or aspartate aminotransferase (ASAT/AST/SGOT)* or alanine aminotransferase (ALAT/ALT/SGPT)*	1.3	1.4	The most abnormal test values during the disease course (highest absolute level of enzyme) above the relevant upper limit of normal
Muscle biopsy features—presence of:			
Endomysial infiltration of mononuclear cells surrounding, but not invading, myofibers	1.7	1.7	Muscle biopsy reveals endomysial mononuclear cells abutting the sarcolemma of otherwise healthy, non-necrotic muscle fibers, but there is no clear invasion of the muscle fibers
Perimysial and/or perivascular infiltration of mononuclear cells		1.2	Mononuclear cells are located in the perimysium and/or located around blood vessels (in either perimysial or endomysial vessels)
Perifascicular atrophy		1.9	Muscle biopsy reveals several rows of muscle fibers, which are smaller in the perifascicular region than fibers more centrally located
Rimmed vacuoles		3.1	Rimmed vacuoles are bluish by hematoxylin and eosin staining and reddish by modified Gomori trichrome stain

\* Serum levels above the upper limit of normal.

Don't bother yourself w/ this criteria ; pt w/ typical skin manifestation of gottron's papule or heliotrope is in favor of dermatomyositis

- Patients with pathognomonic skin rashes (heliotrope rash, Gottron's papules, and/or Gottron's sign) of JDM or DM are accurately classified with the EULAR/ACR classification criteria without including muscle biopsy data.
- For patients without these skin manifestations, muscle biopsy is recommended.
- For DM patients without muscle involvement, a skin biopsy is recommended.
- The EULAR/ACR classification criteria provide a score and a corresponding probability of having IIM.
  - A probable IIM:
    - For a total score of  $\geq 5.5$  and  $\leq 5.7$  for the criteria not including muscle biopsy data, and a score  $\geq 6.7$  and  $\leq 7.6$  when including muscle biopsies.
  - Definite IIM :
    - For a total aggregate score of 7.5 or more without muscle biopsy and 8.7 with muscle biopsy.



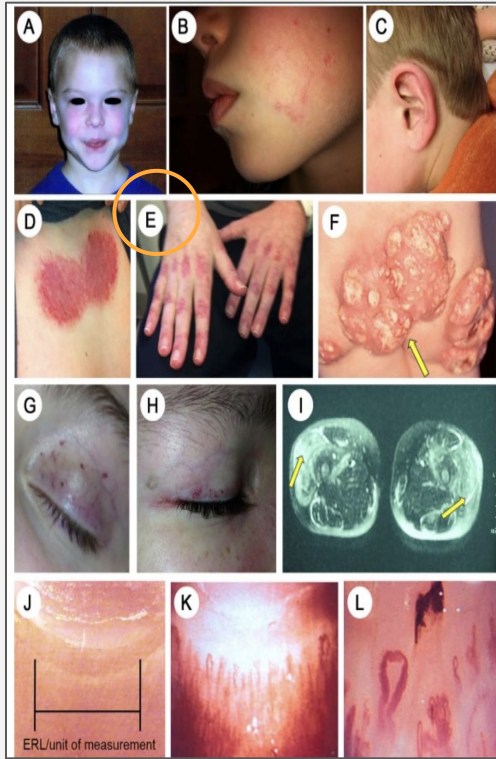
**Figure 2.** Classification tree for subgroups of idiopathic inflammatory myopathies (IIMs). A patient must first meet the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for IIM (probability of IIM  $\geq 55\%$ ). The patient can then be subclassified using the classification tree. The subgroup of polymyositis (PM) patients includes patients with immune-mediated necrotizing myopathy (IMNM). For inclusion body myositis (IBM) classification, one of the following is required for classification: finger flexor weakness and response to treatment: not improved (\*), or muscle biopsy: rimmed vacuoles (\*\*). \*\*\* = Juvenile myositis other than juvenile dermatomyositis (JDM) was developed based on expert opinion. IMNM and hypomyopathic dermatomyositis were too few to allow subclassification. ADM = amyopathic dermatomyositis; DM = dermatomyositis.



# Juvenile Dermatomyositis

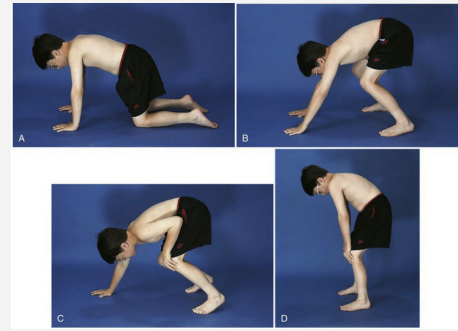


## Clinical Presentations (&Notes):

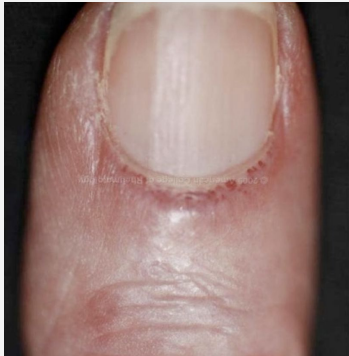


**F:** calcinosis of the skin . hard material or they ooze calcium like pus  
Kids who are diagnosed late or treated late are prone to have it

Calcification of subcutaneous can cause disfiguring oozing



Gower's sign : proximal muscle weakness ( can't stand w/o hand/chair support )



Nail bed changes : capillary loop changes a part of Vasculitis ( hemorrhage due to the inflammation of the vessels and the area w/o blood vessels is called drop out area)



Heliotrope rash: pathognomic . Part of vasculitis . (ask the child to close his eyes )



Shawl sign : skin involvement in exposed area (more lung involvement?)



Gottron's papule: Pathognomic



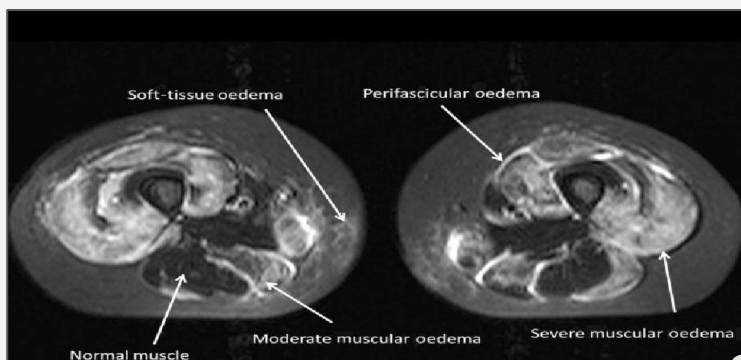
Malar rash ( note: it doesn't spare the nasolabial fold)  
Ddx of malar rash : lupus or JDM

# Juvenile Dermatomyositis

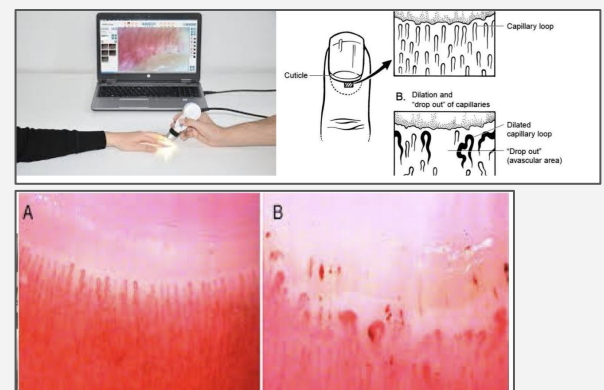


## Investigations:

- Muscle enzymes—including creatinine phosphokinase (CPK), LDH, AST (SGOT), ALT (SGPT), adolase (if available). **Elevated**
- Full blood count and blood film.
- ESR and CRP.
- Myositis-specific and myositis-associated antibodies. **Helpful to know prognosis**  
-**anti-MDA5 bad prognosis**
- Renal function and liver function tests.
- Infection screen (for differential diagnosis).
- Investigations for alternative systemic causes of myopathy including endocrine disorders (especially thyroid function), electrolyte disturbances, vitamin D deficiency.
- Further tests for metabolic/mitochondrial myopathies (especially in the absence of rash/atypical presentation)
- Urine dipstick (with further evaluation if positive for protein)
- Nailfold capillaroscopy
- Echocardiogram and ECG
- Pulmonary function tests (chest X-ray and HRCT if concern)
- MRI of muscles.
- EMG (particularly if suspicion of neuropathy/disorder of neuromuscular junction)
- Muscle biopsy (especially in the absence of rash/atypical presentation)
- MRI brain if neurological involvement suspected.



MRI shows Bright area which is an inflammation of the muscle (hint for proximal muscle weakness) we normally see muscle dark. It involves patchy muscles and bilateral



## Treatment:

Combine both

- Steroid. **Orally**
- Methotrexate (subcutaneous). **Once per week , small dose**
- **Biologics for non responsive cases**



# Kawasaki Disease



## Overview:

- The other name is mucocutaneous lymph node syndrome
- Kawasaki disease mainly affects children of 6 months to 4 or 5 years of age, with a peak at the end of the first year of life.
- **It is the commonest cause of acquired heart disease in children** ( in north america) ( in SA is Acute Rheumatic Fever):

### Cardiac involvement

Dilation and aneurysm formation, thrombus formation, fibrosis and stenosis, myocardial infarction and it may cause myocarditis and endocarditis

- Systemic inflammatory process (Vasculitis: medium size , mainly coronary arteries) with no known etiology
- Maybe infectious etiology
- **More common in children of Japanese and, to a lesser extent, Black-Caribbean ethnicity, than in Caucasians**

## Diagnosis:

**There is no diagnostic test;** instead, the diagnosis is made based on clinical findings alone:

Fever > 5 days



At least **4** of the following:

### 1 Changes in the extremities:

- Erythema and edema of hands and feet (acute phase)
- Subsequent peeling of distal ends of digits (subacute phase)

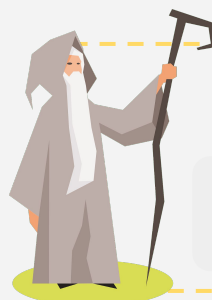
### 2 Polymorphous rash. Any type of skin rash except vesicles and bullae. Check the diaper area

### 3 Non-purulent bilateral conjunctivitis

### 4 Mucosal changes:

- Strawberry tongue
- Red, cracked lips and/or erythema of oral and pharyngeal mucosa

### 5 Cervical lymph node ( $\geq 1.5$ cm in diameter)

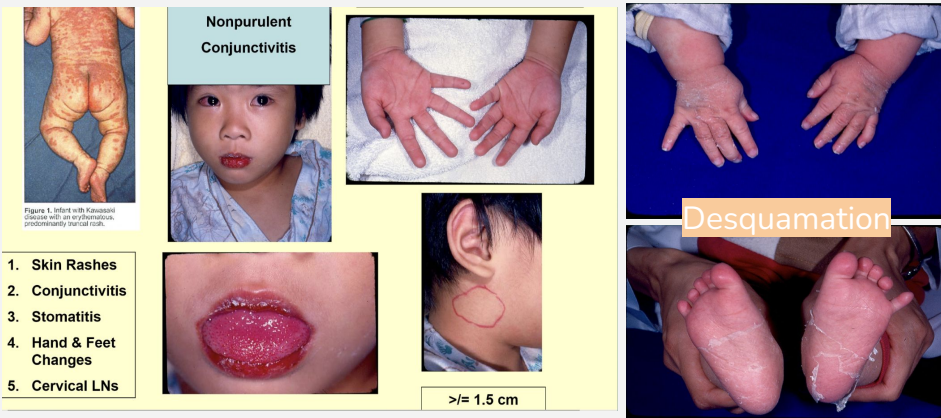


-It is **NOT** a must to have all the clinical features in the same time  
-If you don't ask about red eyes the parents may forget about it (it disappears quickly)  
-Other Ddx of strawberry tongue : scarlet fever  
-Peeling of the skin usually not in the beginning of disease  
-Other medium size arteries: axillary, femoral, iliac and renal arteries

# Kawasaki Disease



## Diagnosis & DDX:

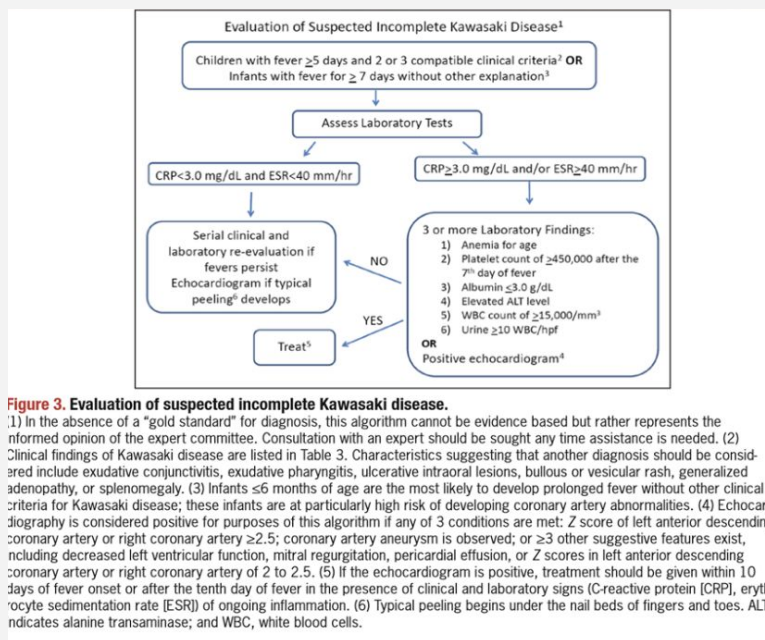


### Differential diagnoses

- Scarlet fever
- EBV infection
- Adenovirus infection
- Staphylococcal scalded skin syndrome
- Drug reactions
- Stevens-Johnson syndrome



Young infants may have 'incomplete' symptoms or diseases, in which not all the cardinal features are present:



For incomplete symptoms, there should remain a high clinical suspicion, particularly for children less than 6 months of age with prolonged fever and these children are more likely to develop coronary artery aneurysms which affected children within the first 6 weeks. It should be treated as complete KD



## Investigations:

- Affected children have **high inflammatory markers** (C-reactive protein, erythrocyte sedimentation rate, white cell count), with a **platelet count that rises typically in the second week of the illness.**
- CBC: Neutropenia, leukocytosis (50%) and nonspecific anemia
- Elevated liver transaminases (40%), low serum albumin level
- Sterile pyuria (33%), aseptic meningitis (up to 50%)
- **Echocardiography should be performed when the diagnosis is first suspected, and at 4–6 weeks to identify coronary artery aneurysms; and it may show a pericardial effusion, myocardial disease (poor contractility), endocardial disease (valve regurgitation), or coronary disease with aneurysm formation, which can be giant ( $\geq 10$  or  $>8$  mm in diameter).**
  - If the coronary arteries are abnormal, angiography or **magnetic resonance imaging (MRI) will be required.**

# Kawasaki Disease

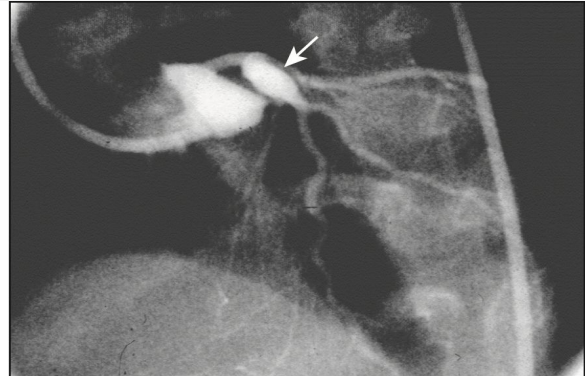


## Management:



### RISK SCORES FOR CORONARY ANEURYSM

1. WBC > 12 000
2. Platelet < 350 000
3. CRP > 3+
4. Hct < 3.5
5. Albumin < 3.5
6. Age <= 12 months
7. Male sex



**Figure 18.22** Kawasaki disease. Angiogram showing coronary artery aneurysm.

## Treatment:

- **Intravenous immunoglobulin (IVIG)**, ideally given within the first 10 days, to lower the risk of coronary artery aneurysms. From 25% to less than 5%
- **Aspirin** to reduce the risk of thrombosis. due to dilation of the coronary even if there is no dilation start aspirin then re-evaluate after 6 wks with another echo If normal → stop aspirin "coronary changes might develop after this period", **decrease** aspirin once afebrile
- **Children with coronary artery aneurysms require long-term low-dose aspirin and lifelong follow-up.**
- Give another anticoagulant if giant aneurysm of CA
- **For resistant Kawasaki disease which presents with fever persists or recurs despite initial treatment: give a second dose of:**
  - intravenous immunoglobulin or,
  - corticosteroids or,
  - infliximab (a monoclonal antibody against tumour necrosis factor- $\alpha$ )



If you find 3/ 6 then treat the pt as Kawasaki disease:  
Anemia for age  
Plt >450  
High WBC count in peripheral blood or in the urine  
Low albumin  
Elevated Na

Even w/o Tx kids w/ Kawasaki most sx will disappear (like: fever ..). But the problem is w/ coronary involvement:

- Stagnation of flow through the coronaries.
- Dilation of the coronaries.
- Coronary aneurysm.

**Whenever you suspect KD or you are not sure, ALWAYS TREAT AS KD!!**

# Book!



## Juvenile Idiopathic Arthritis (JIA)

- Long term, with uncontrolled disease activity, there may be bone expansion from overgrowth, which in the knee may cause **leg lengthening** or **valgus deformity**; in the hands, discrepancy in digit length; and in the wrist, **advancement of bone age**.
- Proteinuria + renal failure = amyloidosis
- However, untreated anterior uveitis is associated with a high risk of developing glaucoma, cataracts, and optic nerve damage.
- **Osteoporosis** is one of the complications and it is multifactorial: diet, reduced weight bearing, systemic corticosteroids and delayed menarche
- Joint injection (steroids) >> first line of treatment for oligoarticular JIA
- STEROIDS injections are used as bridging agent in polyarticular JIA when starting methotrexate

Subtype, typical age of onset and sex ratio (F:M)	Articular pattern	Extra-articular features	Laboratory abnormalities
<b>Oligoarthritis (persistent)</b> (49%) 1-6 years; F:M, 5:1	1-4 (max) joints involved Knee, ankle or wrist	Chronic anterior uveitis – 20% Leg length discrepancy Prognosis: excellent	ANA+/-
<b>Oligoarthritis (extended)</b> (8%) 1-6 years; F:M, 5:1	>4 joints involved after first 6 months. Asymmetrical distribution of large and small joints	Chronic anterior uveitis – 20% Asymmetrical growth Prognosis: moderate	ANA+/-
<b>Polyarthritis (RF negative)</b> (16%) 1-6 years; F:M, 5:1	Symmetrical large and small joint arthritis, often marked finger involvement Cervical spine and temporomandibular joint may be involved	Low-grade fever Chronic anterior uveitis – 5% Late reduction of growth Prognosis: moderate	
<b>Polyarthritis (RF positive)</b> (3%) 10-16 years; F:M, 5:1	Symmetrical large and small joint arthritis, often marked finger involvement	Rheumatoid nodules – 10% Similar to adult rheumatoid arthritis Prognosis: poor	RF+ (long term)
<b>Systemic arthritis</b> (9%) 1-10 years; M:F, 1:1	Oligoarthritis or polyarthritis. May have aches and pains in joints and muscles (arthralgia/myalgia) but initially no arthritis	Acute illness, malaise, high daily fever initially, with salmon-pink macular rash, lymphadenopathy, hepatosplenomegaly, serositis Prognosis: variable to poor	Anaemia, raised neutrophils and platelets, high acute-phase reactants
<b>Psoriatic arthritis</b> (7%) 1-16 years; M:F, 1:1	Usually asymmetrical distribution of large and small joints, dactylitis	Psoriasis, nail pitting or dystrophy Chronic anterior uveitis – 20% Prognosis: moderate	
<b>Enthesitis-related arthritis</b> (7%) 6-16 years; M:F, 1:4	Lower limb, large joint arthritis initially Mild lumbar spine or sacroiliac involvement later	Enthesitis Occasional acute uveitis Prognosis moderate	HLA-B27+

**Fig. 28.18** Classification and clinical features of juvenile idiopathic arthritis (JIA). (ANF: Anti-Nuclear Factor; RF: Rheumatoid Factor. Enthesitis – localized inflammation at insertion of tendons or ligaments into bone, often in feet.)

## Prolonged fever

- Most childhood infections are acute and resolve in a few days. If not, the child needs to be reassessed for prolonged fever is also required for prompt recognition of Kawasaki disease. Causes:

Infective	Non-infective
<ol style="list-style-type: none"> <li>1. Localized infection: e.g. osteomyelitis.</li> <li>2. Bacterial infections: e.g. typhoid, Bartonella henselae (cat scratch disease), Brucella species.</li> <li>3. Deep abscesses: e.g. intra-abdominal retroperitoneal, pelvic.</li> <li>4. Infective endocarditis.</li> <li>5. Tuberculosis.</li> <li>6. Non-tuberculous mycobacterial infections: e.g. Mycobacterium avium complex.</li> <li>7. <b>8. Viral infections: e.g. Epstein-Barr virus, cytomegalovirus, HIV (human immunodeficiency virus).</b></li> <li>9. Parasitic infections: e.g. malaria, toxocariasis, Entamoeba histolytica.</li> </ol>	<ol style="list-style-type: none"> <li>1. <b>Systemic onset juvenile idiopathic arthritis.</b></li> <li>2. <b>Systemic lupus erythematosus.</b></li> <li>3. <b>Vasculitis (including Kawasaki disease).</b></li> <li>4. Inflammatory bowel disease (Crohn disease and ulcerative colitis).</li> <li>5. Sarcoidosis.</li> <li>6. Malignancy: e.g. leukaemia, lymphoma, neuroblastoma, Ewing sarcoma.</li> <li>7. Macrophage activation syndromes: e.g. haemophagocytic lymphohistiocytosis.</li> <li>8. Auto-inflammatory disorders: e.g. familial Mediterranean fever (FMF).</li> <li>9. Drug fever.</li> <li>10. Fabricated or induced illness (including Munchausen syndrome by proxy).</li> </ol>



# Peds Cases !



## JUVENILE IDIOPATHIC ARTHRITIS





### DIAGNOSIS

1. Arthritis in  $\geq 1$  joint for  $\geq 6$  weeks
2.  $< 16$  years old
3. Exclusion of other disease that may cause arthritis

Arthritis  $\Rightarrow$  joint pain, stiffness, decreased range of motion, swelling



### CLINICAL PRESENTATION

TYPE	TYPICAL AGE	AFFECTED JOINTS	JOINT PATTERN	EXTRA-ARTICULAR FEATURES
Oligoarthritis	$< 6y$	1 – 4	Asymmetric Large joints	Asymptomatic uveitis
RF- Polyarthritis	6-7y	$\geq 5$	Symmetric Any sized joints	Asymptomatic uveitis
RF+ Polyarthritis	9-12y	$\geq 5$	Symmetric Any sized joints	Rheumatoid nodules, uveitis
 Systemic Arthritis 	2-4y	$\geq 1$	Any sized joints	Fever, uveitis, lymphadenopathy, rash, serositis, hepatosplenomegaly
Psoriatic Arthritis	7-10y	$\geq 1$	Asymmetric/symmetric Small-medium joints	Dactylitis, nail pitting, psoriasis, uveitis
Enthesitis Related Arthritis	9-12y	N/A	Tendon insertions Lower extremities	Symptomatic uveitis

### INVESTIGATIONS

Diagnosis of JIA is based on clinical findings, investigations are used to rule out other conditions and may help classify type.

- CBC
- ESR/CRP
- RF, ANA
- XR, U/S, MRI, CT

Children presenting with systemic symptoms should be worked up to rule out infection/malignancy.

### DDX

- Infection (septic arthritis, osteomyelitis)
- Malignancy (acute leukemia)
- Growing pains
- Trauma
- Inflammatory Bowel Disease
- Juvenile Dermatomyositis
- Systemic Lupus Erythematosus
- Vasculitis

### MANAGEMENT

PHARMACOLOGIC	NON-PHARMACOLOGIC
<ul style="list-style-type: none"> <li>▪ NSAIDS (ibuprofen, naproxen)</li> <li>▪ Intra-articular steroids</li> <li>▪ Systemic steroids (short course)</li> <li>▪ Disease Modifying Anti-Rheumatic Drugs (methotrexate)</li> <li>▪ Biologics</li> </ul>	<ul style="list-style-type: none"> <li>▪ Regular physical activity</li> <li>▪ Patient education</li> <li>▪ PT/OT</li> <li>▪ Psychotherapy</li> <li>▪ Nutrition</li> </ul>

\*Management is based on type of JIA

### COMPLICATIONS

- Osteoarthritis
- Osteoporosis
- Macrophage activation syndrome
- Growth issues
- Joint erosion
- Functional
- Psychological syndrome



Referral to ophthalmology for regular screening. Untreated uveitis can result in blindness!

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