Common Pediatric Rheumatologic Diseases

objectives:

- Perform a proper history for a patient with arthralgia / arthritis
- Discuss (Definition and classification, etiology, epidemiology, clinical manifestation, laboratory and radiology findings, differential diagnosis, treatment, and prognosis) for the following:
  - Juvenile idiopathic arthritis.
  - Systemic lupus erythematosus.
  - Juvenile dermatomyositis.
  - Henoch-Schönlein Purpura.
  - Kawasaki disease.

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Special thanks to team 437 & Faisal alsaif

Notes

Important

Book

Approach to Arthritis

Arthritis: 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.

DDx of arthritis:

Reactive:

- Post-enteric.
- Rheumatic fever.
- Post-streptococcal.

Systemic:

- Kawasaki disease.
- Behcet's disease.
- Henoch-Schonlein purpura.
- Serum sickness.
- Systemic lupus erythematosus.
- Dermatomyositis.

Infection:

- Septic: Single joint, fever, high WBC, looks sick.
- Osteomyelitis.
- Viral.
- Bacterial sacroiliitis.
- TB, Brucellosis: ask about contact with animals, sick patients in Hx.

Inflammatory:

- Juvenile idiopathic arthritis.
- Inflammatory bowel disease.
- Sarcoidosis.

Malignancy:

- Leukemia.
- Neuroblastoma.
- Malignant bone tumors.

Trauma

Benign bone tumors

Juvenile Idiopathic Arthritis

Overview of JIA:

- It is a group of disorders characterized by chronic arthritis.
- 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.

Juvenile Idiopathic Arthritis

Classification (ILAR):

- Oligoarticular JIA.
- Polyarticular rheumatoid factor positive JIA.
- Polyarticular rheumatoid factor negative JIA.
- Systemic JIA.
- Psoriatic JIA.
- Enthesitis related arthritis(ERA).
- Undifferentiated.

Table II. Epidemiological characteristics of the different ILAR categories of JIA[1,11]

	Frequency	*Gender*	*Age*
Systemic	5-15%	F = M	Any age
Oligoarthritis	30-60%	F >>> M	Early childhood (peak 2-4 years)
RF negative polyarthritis	20-25%	F >> M	Biphasic distribution (2-4 years and 6-12 years)
RF positive polyarthritis	2-5%	F >> M	Late childhood or adolescence
Enthesitis-related arthritis	10-15%	M >> F	Late childhood or adolescence
Psoriatic	5-10%	F > M	Biphasic distribution (2-4 years and 9-11 years)
Undifferentiated	10-20%	–	

JIA: juvenile idiopathic arthritis; F: female; RF: rheumatoid factor; ILAR: International League of Associations for Rheumatology; M: male.

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. So if a child presented with 3 joint involvement and after 6 months he came with 6-7 joints involvement, what's the type? the answer: Extended Oligoarticular 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)

Polyarticular JIA:

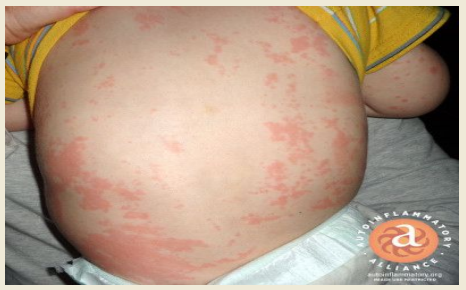
- RF-negative disease (20% to 30% of JIA patients).
- RF-positive disease (5% to 10% of JIA patients).
- Both types affect girls more frequently than boys.
- RF-negative patients often develop polyarthritis in early childhood.
- RF-positive disease is like RA in adults "erosion and destruction of joints"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

Juvenile Idiopathic Arthritis

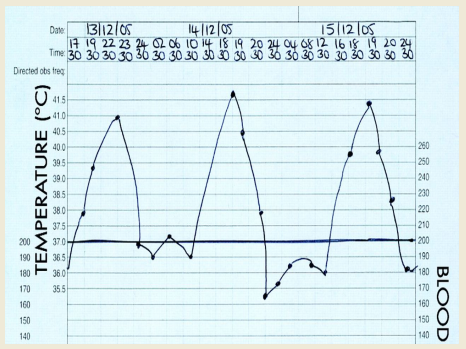
Systemic onset JIA:

- Undergo extensive investigations to rule out other ddx like: infection or cancer like leukemia , some may need bone marrow aspiration to r/o 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. 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)



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



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

Macrophage activation syndrome (MAS)

- The most serious complication of systemic JIA is macrophage activation syndrome (MAS), which occurs in 4%–13%.
- Presentation is acute, with continuous fever ,reduction in erythrocytes, leukocytes and platelets, abnormal clotting and multiple organ failure.
- Without early recognition and prompt treatment, it is life-threatening. (Treatment is high doses of steroids for 3-5 days).

EULAR/ACR CLASSIFICATION CRITERIA FOR MAS 7

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:

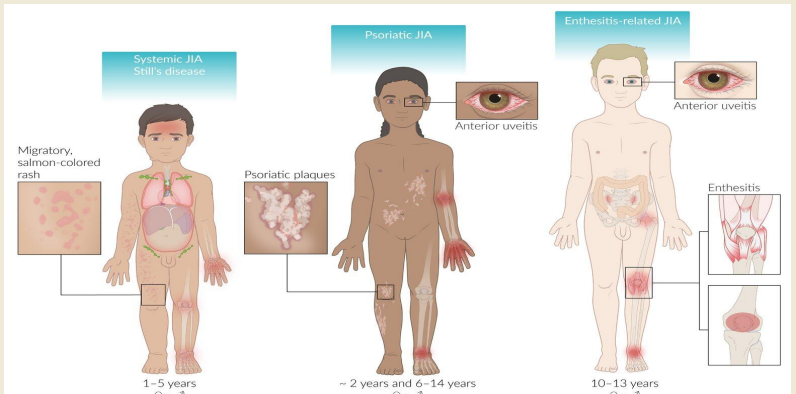
Ferritin >684 ng/ml
and any 2 of the following:
Platelet count ≤181 x 10^9/liter
Aspartate aminotransferase >48 units/liter
Triglycerides >156 mg/dl
Fibrinogen ≤360 mg/dl

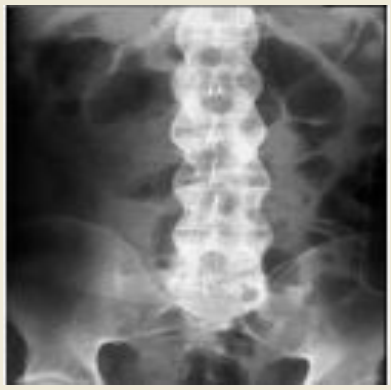
Figure 2. Criteria for the classification of macrophage activation syndrome in patients with systemic juvenile idiopathic arthritis. Laboratory abnormalities should not be otherwise explained by the patient's condition, such as concomitant immune-mediated thrombocytopenia, infectious hepatitis, visceral leishmaniasis, or familial hyperlipidemia.

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 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.

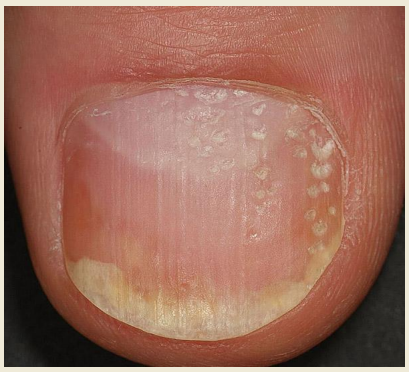




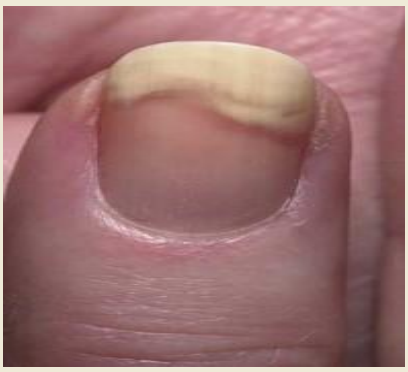
Bambo Sign

Psoriatic arthritis:

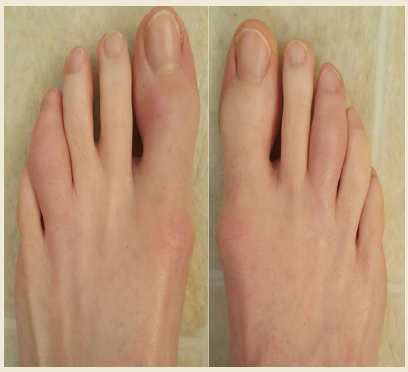
- Psoriasis + arthritis , but kids may not present w/ typical features of psoriatic arthritis.
- A peak age of onset in mid childhood.
- **Extra-articular manifestations include**: rash, nail changes (including pitting, onycholysis) and uveitis.+ family history of psoriasis



Nail pitting



Onycholysis



Dactylitis

Juvenile Idiopathic Arthritis

Differential diagnosis of arthritis: Before labeling JIA we have to search for the causes

- **Reactive:**
  - Post-enteric.
  - Rheumatic fever.
  - Post-streptococcal.
- **Inflammatory:**
  - Juvenile idiopathic arthritis.
  - Inflammatory bowel disease.
  - Sarcoidosis.
- **Malignancy:**
  - Leukemia.
  - Neuroblastoma.
  - Malignant bone tumors.
- **Systemic:**
  - Kawasaki disease.
  - Behcet's disease.
  - Henoch-Schonlein purpura.
  - Serum sickness.
  - Systemic lupus erythematosus.
  - Dermatomyositis.
- **Infection:**
  - Septic.
  - Osteomyelitis.
  - Viral.
  - Bacterial sacroiliitis.
- **Benign bone tumors.**
- **Trauma.**

Investigations:

Laboratory

- No specific lab. can confirm the diagnosis
- Lab. can be used to:
  1. Provide evidence of inflammation.
  2. Support the clinical diagnosis.
  3. Monitor treatment toxicity. Monitor liver enzymes and CBC

Limited joint disease:

- Mild anemia.

Moderate –extensive arthritis:

- Normocystic hypochromic anemia or severe anemia.
- Iron deficiency anemia.
- High WBC count.
- High platelets.

ESR (erythrocyte sedimentation rate):

- Useful but not totally reliable measure of active disease. Oligoarticular particularly may be normal
- Helpful in monitoring the therapeutic efficacy of the medications.

CRP (c –reactive protein):

- More reliable monitor of inflammation response.

Rheumatoid factor: help in differentiating RF +ve from -ve

- IgM anti IgG.
- RF positive in:
  - Later childhood polyarthritis.
  - Subcutaneous nodules.
  - Articular erosions.

ANA (antinuclear antibody):

- More frequent in young girls with oligo JIA
- Less frequent in older boys with systemic arthritis.

Radiology

Plain x-ray

Early radiological changes:

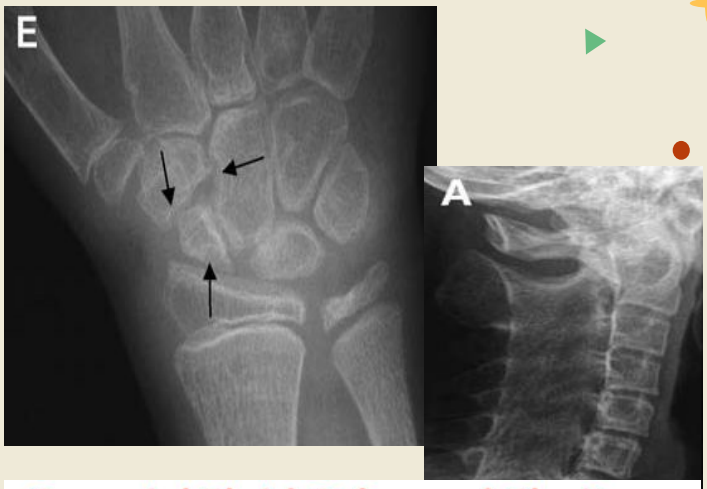
- Periosteal soft tissue swelling
- Widening of the joint space
- Juxta articular osteoporosis
- Usually normal X-ray in initial presentation

Later changes:

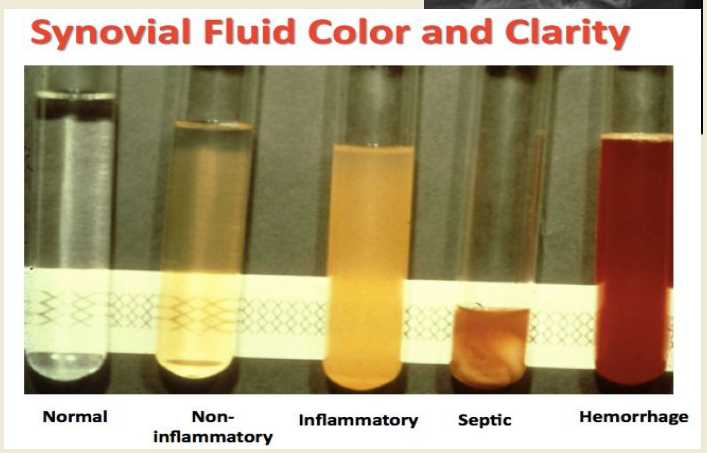
- Joint space narrowing
- Erosions.
- Subluxation.
- Ankylosis.
- Fracture. Specially vertebra

Juvenile Idiopathic Arthritis

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 .



- 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.



Management:

Multidisciplinary approach	Medications:
The aim of management of JIA include: ● Controlling pain. ● Controlling inflammation. ● Preserving function. ● Promoting normal growth. ● Promoting overall development. ● Manage systemic complication.	● NSAIDS: Naproxen. ● Methotrexate: Specifically for Polyarticular JIA. or extended oligo JIA. less effective for systemic manifestations of JIA. ● Steroids: Systemic or intra-articular (intra articular is For pts with few joint involvement. 1st line for oligo JIA ● steroids Can be used in polyarticular JIA as a bridge when starting MTX ● Biologics: Relatively new. (we add it when it is NOT responding to treatment. TNF antagonist like humera)

- For oligo JIA we start w/ NSAIDs ; if failed → steroids (intra-articular)
- Systemic JIA start them on systemic steroids + biologics

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

Criteria:

Old criteria

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

- ➢ ≥ 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
1.Acute Cutaneous Lupus: malar rash. Sparing nasolabial folds 2.Subacute cutaneous lupus 3.Chronic Cutaneous Lupus: discoid rash. 4.Oral Ulcers (painless) **OR** Nasal Ulcers. 5.Non-scarring alopecia. Ask about hair loss - can be early presentation of SLE 6.Arthritis involving 2 or more joints (non-erosive) 7.Serositis (major): pleural effusions, pericardial effusion, and pericarditis by electrocardiography in the absence of other causes, such as infection, uremia. Peritonitis (abdominal pain) 8.Renal: urine protein–to-creatinine ratio (or 24-hour urine protein) representing 500 mg protein/24 hours **OR** red blood cell casts. 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. 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). Ask about school performance, renal and CNS involvement affect prognosis 10.Hemolytic anemia (sudden drop of Hb, jaundice and dark urine) 11.Leukopenia (<4000/mm3) **OR** **Lymphopenia (<1000/mm3)**. 12.**Thrombocytopenia** (<100,000/mm3) at least once in the absence of other known causes. Pt w/ isolated thrombocytopenia should be followed-up as they may develop lupus in the future.	1.ANA level above laboratory reference range. Has to be +ve for Dx of SLE 2.Anti-dsDNA antibody level above laboratory reference range. specific, renal involvement 3.Anti-Smith. Also specific 4.Antiphospholipid antibody. They are prone to secondary (APS) . ask for anticardiolipin, beta-2 glycoprotein I (β2GPI), and lupus anticoagulant. Don't bother yourself about names just have an idea 5.Low complement (C3, C4, or CH50). If low indicates flare-up. Renal involvement (low C3) 6.Direct Coombs' test (in the absence of hemolytic anemia) Antihistone Ab → drug- induced lupus

Systemic Lupus Erythematosus

Updated criteria:

- ❖ It must reach ≥ 10 points.
- ❖ Rules:
- ➢ One from each category.
- ➢ If you have 2 from the same category, pick the one with the highest number
- ➢ 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.

Entry criterion
Antinuclear antibodies (ANA) at a titer of ≥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 ≥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
Constitutional		***Antiphospholipid antibodies***	
Fever	2	Anti-cardiolipin antibodies OR	
Hematologic		Anti-β2GP1 antibodies OR	
Leukopenia	3	Lupus anticoagulant	2
Thrombocytopenia	4	***Complement proteins***	
Autoimmune hemolysis	4	Low C3 OR low C4	3
Neuropsychiatric		Low C3 AND low C4	4
Delirium	2	***SLE-specific antibodies***	
Psychosis	3	Anti-dsDNA antibody* OR	
Seizure	5	Anti-Smith antibody	6
Mucocutaneous			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		
Renal			
Proteinuria >0.5g/24h	4		
Renal biopsy Class II or V lupus nephritis	8		
Renal biopsy Class III or IV lupus nephritis	10		

Total score:

↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

Figure 2 Classification criteria for systemic lupus erythematosus.
§Additional criteria items within the same domain will not be counted.
*Note: In an assay with at least 90% specificity against relevant disease

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

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)

Complications:

- Arthritis involving 2 or more joints (usually not destructive)
- Serositis, pleural effusions, pericardial effusion, pericarditis by electrocardiography In the absence of other causes, such as infection, uremia.
- Renal: Proteinuria, hematuria or renal failure, RBC casts. (Renal involvement is an important prognostic factor, pts with renal involvement have bad prognosis compared to those who don't have it)
- CNS: Seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial involvement, acute confusional state (in the absence of other known causes) CNS manifestations are bad prognostic factors for lupus
- Hemolytic anemia
- Pancytopenia: Leukopenia (<4000/mm3) or **Lymphopenia** (<1000/mm3) Thrombocytopenia (<100,000/mm3)
- Immunology:
  - ANA levels above lab. reference range. (no lupus patient has -ve ANA, but it's not specific)
  - Anti-dsDNA, Anti-smith (Specific, not sensitive)
  - Antiphospholipid antibody (secondary antiphospholipid syndrome) Ask for : anticardiolipin, beta-2 glycoprotein I (β2GPI), and lupus anticoagulant. Thrombosis anywhere (brain, lung, legs) & must investigate every single patient with lupus for antiphospholipid syndrome
  - Low complement (C3, C4, CH50. Specially in renal involvement.)
  - Direct Coomb's test (in the absence of hemolytic anemia, it indicates a flare up)
  - Anti-Histone antibody > Drug induced lupus.

Systemic Lupus Erythematosus

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

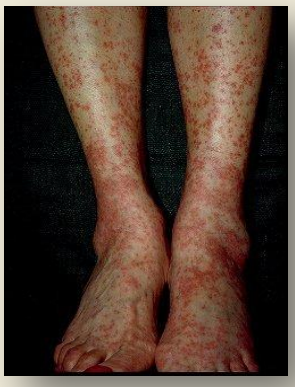
Glucocorticoids The Main treatment specially in the beginning IV in cns, renal and active

Immunosuppressives In bad cns or renal

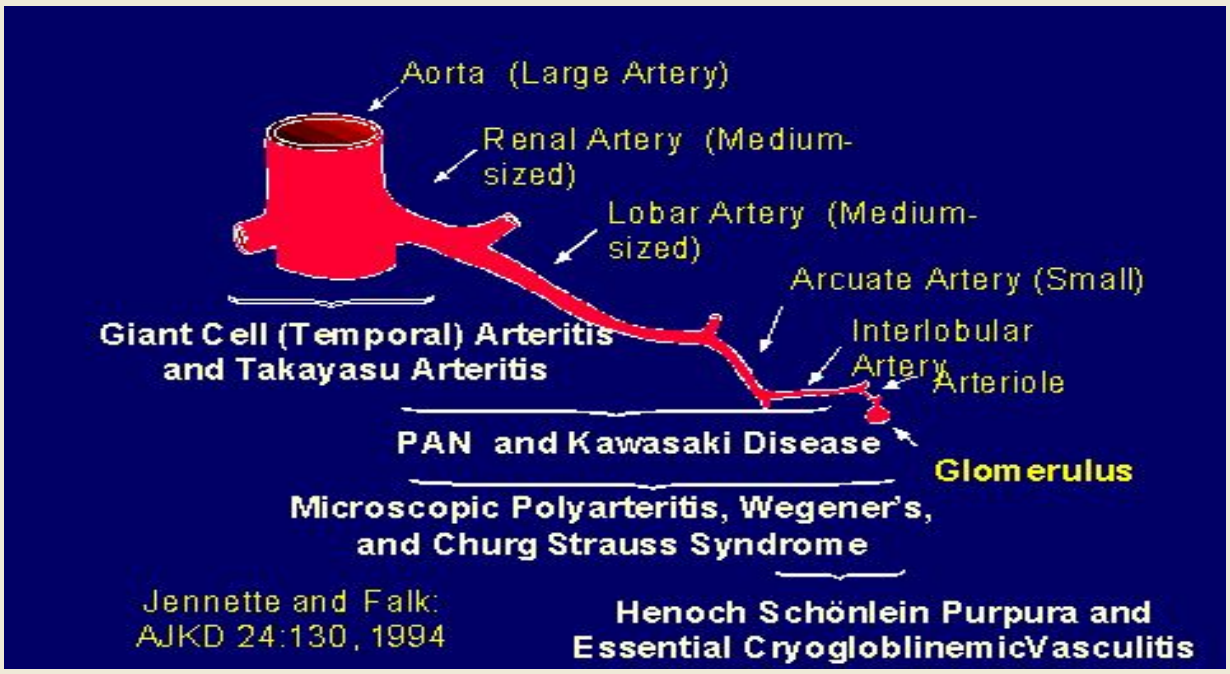
"Red riding hood will help you to remember SLE. Lupus means wolf and erythematosus means red, and in the story the villain is the wolf and the prey is the little girl wearing red hood. SLE = commonly affects woman!"

Henoch-Schonlein Purpura

- HSP is the most common pediatric vasculitis. Involves small arteries
- Classically presents with the triad of:
- Nonthrombocytopenic palpable purpura.
- Colicky abdominal pain.
- Arthritis.



Differential diagnosis 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. if no renal involvement = benign disease
- Usually present at 3-15 years.
- A wide variety of infections may trigger HSP. It's not a must but it could happen

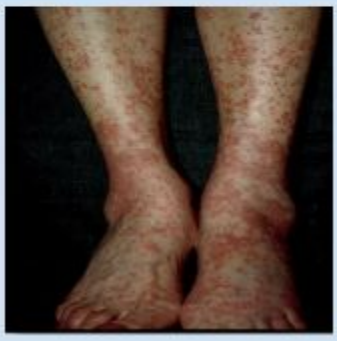
- Skin involvement (100%) in HSP may begin as urticaria, but in most cases it progresses to dramatic purple, non-blanching lesions . Mainly lower limb vasculitis.
- Gastrointestinal involvement (75%) ranges from colicky abdominal pain to profuse bleeding, intussusception.
- The arthritis of HSP (50%) 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

Henoch-Schonlein Purpura

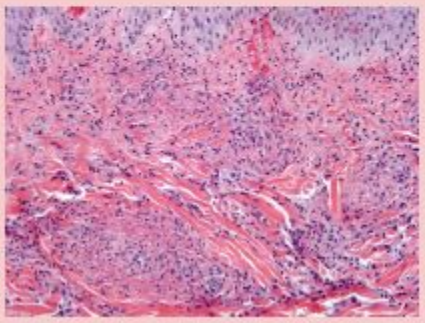
Diagnosis: Based on the criteria

Purpura (mandatory criterion):

1. Abdominal pain
2. Histopathology; vasculitis with predominant IgA deposit.
3. Arthritis or arthralgia
4. 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 : Renal involvement - CNS involvement - Severe GI Bleeding

- 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

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

Juvenile Dermatomyositis

- ❖ 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 l 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

Differential Diagnosis of Juvenile Idiopathic Inflammatory Myopathies

	Condition
Weakness alone	
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 α, glucocorticoids, hydroxychloroquine, diuretics, amphotericin b, caine anaesthetics, growth hormone, cimetidine, and vincristine
Neuromuscular transmission disorders	Myasthenia gravis
Motor neuron disorder	Spinal muscular atrophy
Weakness with or without rash	
Viral	Enterovirus, influenza, coxsackievirus, echovirus, parvovirus, poliovirus, hepatitis B, human T-lymphotropic virus 1
Bacterial and parasitic organisms	Staphylococcus, streptococcus, toxoplasmosis, trichinosis, *Lyme borreliosis*
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.

Feldman et al, Lancet 2008; 371, 2201-12

Juvenile Dermatomyositis

Criteria:

Bohan and Peter diagnostic criteria: Old criteria but the popular

A	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	Elevation of the serum levels of skeletal muscle enzymes: creatine phosphokinase, aspartate aminotransferase, lactate dehydrogenase, and aldolase. AST
C	Electromyography characteristic of myopathy (short and small motor units, fibrillations, positive pointy waves, insertional irritability and repetitive high-frequency firing).
D	Muscle biopsy showing necrosis, phagocytosis, regeneration, perifascicular atrophy, perivascular inflammatory exudate. Muscle biopsy : we don't usually do it. Replaced by MRI
E	Typical cutaneous changes: • Heliotrope with periorbital edema and violaceous erythema; • Gottron's sign: vasculitis in the elbow, metacarpophalangeal, and proximal interphalangeal joints.

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

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: Without muscle biopsy	Score points: With muscle biopsy	Definition
Age of onset			
Age of onset of first symptom assumed to be related to the disease ≥18 years and <40 years	1.3	1.5	18 ≤ 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 ≥40 years	2.1	2.2	Age (years) at onset of first symptom assumed to be related to the disease ≥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
Skin manifestations			
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 pulpable
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	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 ≥5.5 and ≤5.7) for the criteria not including muscle biopsy data, and a score ≥6.7 and ≤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.

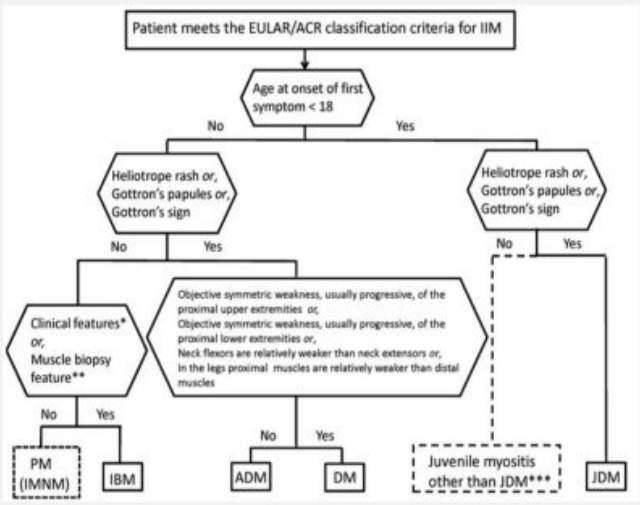
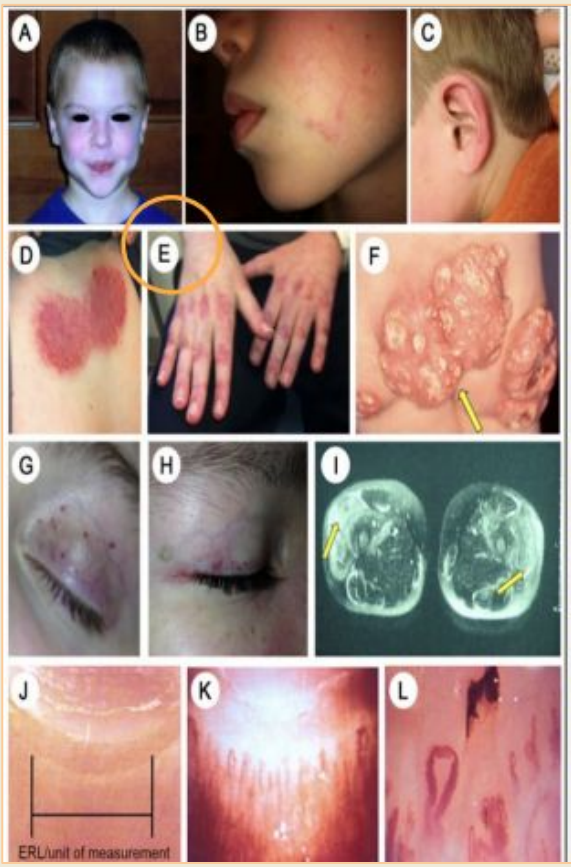


Figure 2. Classification tree for subgroups of idiopathic inflammatory myopathies (IIMs). A patient must first meet the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for IIM (probability of IIM ≥55%). The patient can then be subclassified using 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.

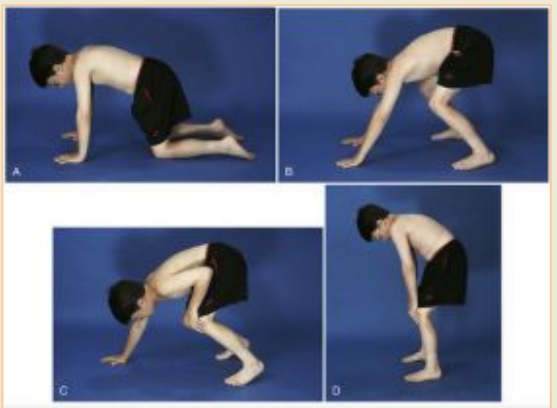
Juvenile Dermatomyositis

Clinical Presentations (Notes):

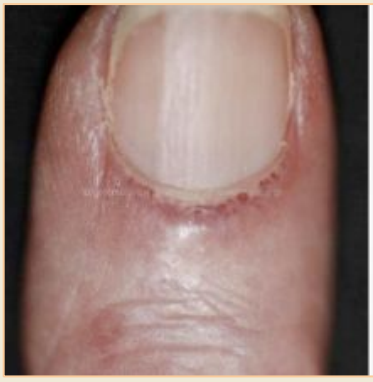


F: calcinosis of the skin . hard material or they ooze calcium like pus
Kids who are diagnosed late or treated late are prone to have it

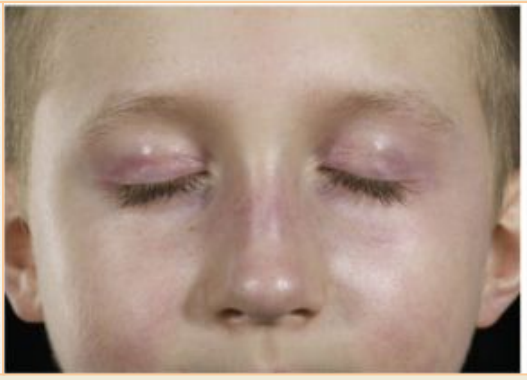
Calcification of subcutaneous can cause disfiguring oozing



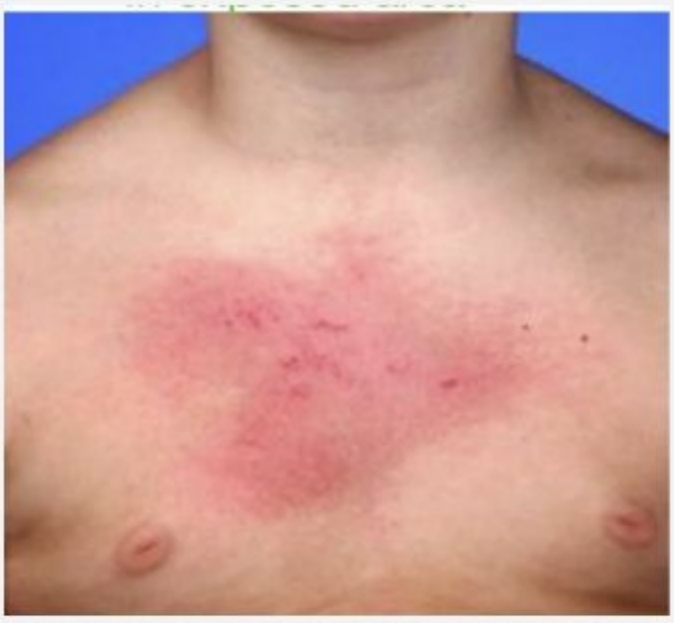
Gower's sign : proximal muscle weakness (can't stand w/o hand/chair support)



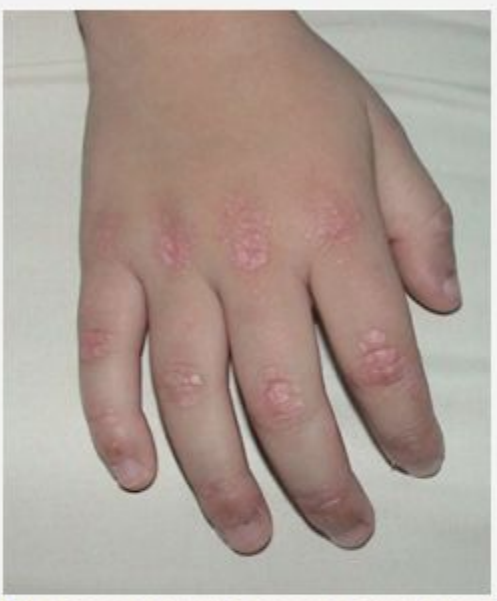
Nail bed changes : capillary loop changes a part of Vasculitis (hemorrhage due to the inflammation of the vessels and the area w/o blood vessels is called drop out area)



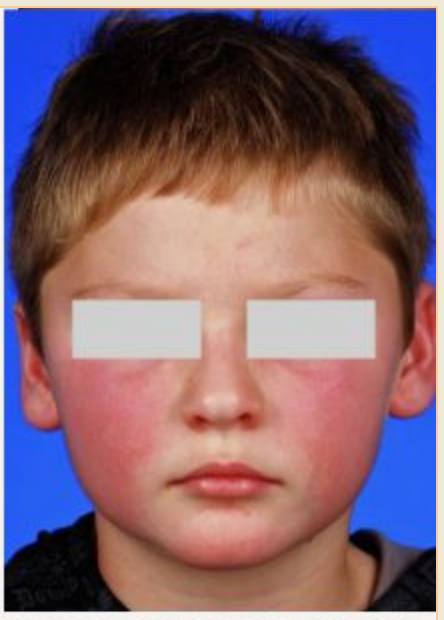
Heliotrope rash: pathognomic . Part of vasculitis . (ask the child to close his eyes)



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



Gottron's papule: Pathognomic

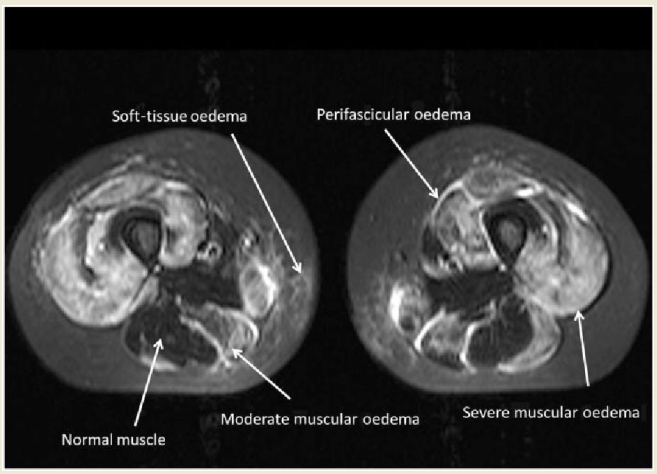


Malar rash (note: it doesn't spare the nasolabial fold)
Ddx of malar rash : lupus or JDM

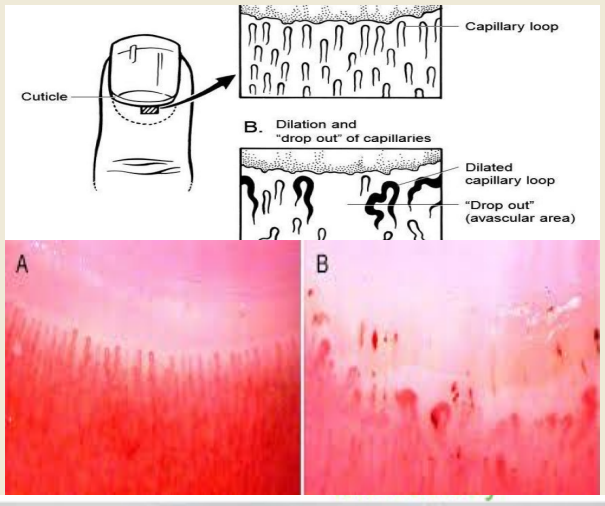
Juvenile Dermatomyositis

Investigations:

- Muscle enzymes—including creatinine phosphokinase (CPK), LDH, AST (SGOT), ALT (SGPT), aldolase (if available). Elevated
- Full blood count and blood film.
- ESR and CRP.
- Myositis-specific and myositis-associated antibodies. Helpful to know prognosis
  -anti-MDA5 have 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



capillaroscopy

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 KSA is Acute Rheumatic Fever).
- 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

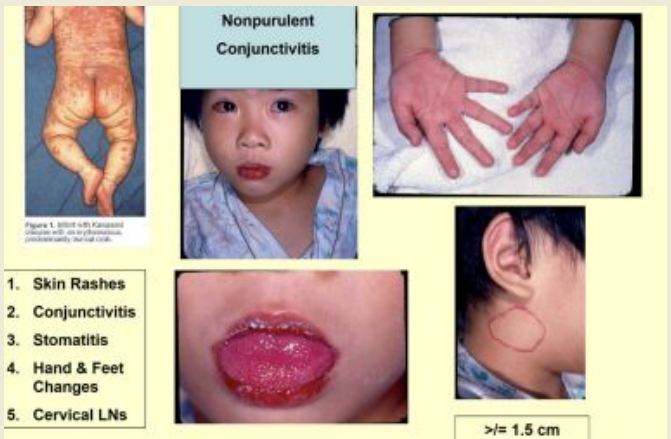
Diagnosis:

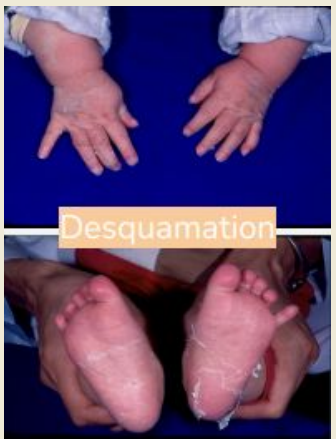
The diagnosis is made based on clinical findings alone:

❖ Fever > 5 days + at least 4 of the following:

1-Changes in the extremities:	2-Polymorphous rash.	3-Non-purulent bilateral conjunctivitis	4-Mucosal changes:	5- Cervical lymph node
- Erythema and edema of hands and feet (acute phase). - Subsequent peeling of distal ends of digits (subacute phase).	- Any type of skin rash except vesicles and bullae. Check the diaper area		- Strawberry tongue. - Red, cracked lips and/or erythema of oral and pharyngeal mucosa.	unilateral (>= 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

Differential diagnoses

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

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**

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

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 (>/= 10 or >8 mm in diameter).
    - If the coronary arteries are abnormal, angiography or **magnetic resonance imaging (MRI) will be required.**

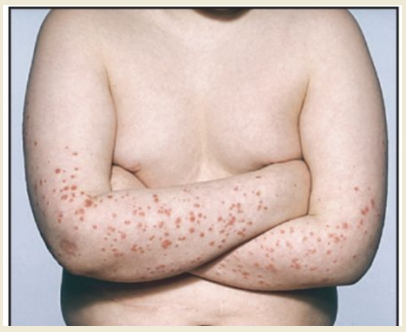
Treatment:

- **Intravenous immunoglobulin, 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-α)

Questions

1- Karen, aged 5 years, presents to her general practitioner. She has been unwell for 2 weeks with lethargy, fever and painful wrists and knees. On examination she has a temperature of 38.5°C and a subtle erythematous rash on her trunk.
You identify that several joints are swollen, warm, and painful to move, including the wrists, her right elbow, the knees, her left ankle and left hip. She has some cervical lymphadenopathy and her spleen is palpable. She has no previous medical problems and her mother has been giving her paracetamol. You perform some blood tests and get the following results:
• Hb (haemoglobin), 85 g/L; WBC (white blood count), 17 × 109/L; neutrophils, 10.4 × 109/L; platelets, 366 × 109/L • blood film: normal, no atypical lymphocytes • ESR (erythrocyte sedimentation rate): 70 mm/hour • ANA (antinuclear antibody): negative • double-stranded DNA: negative • antistreptolysin O titre: normal.
What is the most likely diagnosis?
A. Acute lymphoblastic leukaemia
B. Epstein–Barr virus infection
C. Post-streptococcal arthritis
D. (SLE)
E. Systemic-onset juvenile idiopathic arthritis

2- William is an 8-year-old boy who presents with joint pain. His mother reports that since yesterday he has been refusing to walk, as his legs are so painful. On examination his temperature is 37°C and his heart rate is 100 beats/min. He is settled at rest and playing a computer game on his iPad. On further examination you notice a rash over his lower limbs, buttocks, and forearms (Fig. 28.2). The rash comprises some large (5–15 mm), red, raised lesions, and multiple pin-point lesions, which do not blanch on pressure. His peripheries are warm and he has a good pulse volume with a normal capillary refill time. There is some generalized swelling around his knees and ankles. He has pain on passive movement of both knees and ankles.
What is the most likely diagnosis?
A. Henoch–Schönlein purpura
B. Immune thrombocytopenic purpura
C. Meningococcal septicaemia
D. Reactive arthritis (transient synovitis)
E. Systemic-onset juvenile idiopathic arthritis



3- Dominika is a 3-year-old girl. She presents with an acute onset limp which was not present on the previous day. Her mother reports that she was unwell 2 weeks ago with a coryzal illness. The pain is in her right leg and is present only on walking. On examination she has a temperature of 37°C. The hip and leg look normal but on passive movement of her right hip, there is decreased external rotation.
What is the most likely diagnosis from the list below?
A. Bone tumour
B. Perthes disease
C. Reactive arthritis (transient synovitis)
D. Septic arthritis
E. Slipped capital femoral epiphysis

Answers

1- E
2- A
3- C