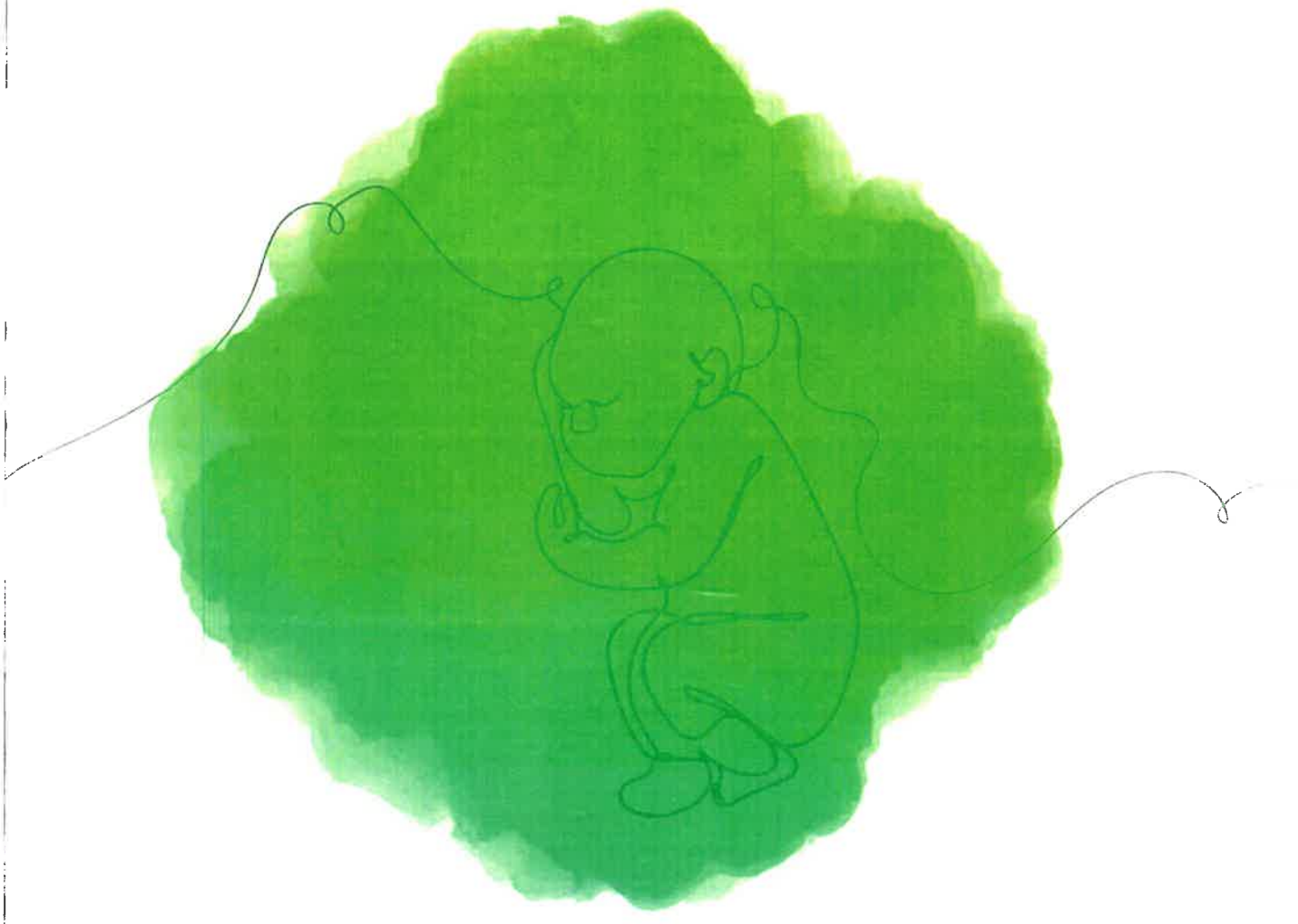
VOLUME 2

PrepLadder



PEDIATRICS

NEET SS VERSION 4.0

PREFACE

Dear Dreamer,

Pat your back and reward yourself, today you've taken an important step towards reaching your dream. Mark Twain said, "the secret of getting ahead is getting started". You have started in the right direction.

The next few months until your targeted exam or exams are crucial. Every moment counts and each step you take now, will help you reach your goal, your dream.

PrepLadder is your partner in this journey. We are in this together. So, don't worry, do not stress. Just focus on your preparation and stay positive. Set daily targets, achievable and realistic ones. If you pass the target, celebrate. However, if you miss a daily target, forgive yourself, move on and do better the next day.

Always remember that you are special and unique. Do not compare your preparation, your speed, your abilities with others. Believe us, it doesn't help.

Practice a lot. Solve the QBank. Take Grand Tests. Review your performance. But don't let ranks and results drag you down. Rather use them as a guiding light to know your strengths and weaknesses, to increase your speed and accuracy, and to get yourself ready for the exam day.

If you have a doubt or a question, ask us. We are here.

Lastly and most importantly. take care of yourself. You and your health are precious. So, keep up with exercise, eat healthy, get enough sleep and care for yourself.

We're behind you, cheering you on to the finish line. You might be feeling stressed, overwhelmed, and so tired, but you're nearly there. Give it everything you've got, and know that whatever happens next, you've got what it takes for the life you want. You are a Champion.

Own Your Dream
Team PrepLadder

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PEDIATRIC RHEUMATOLOGY AND VASCULITIS

1 PEDIATRIC VASCULITIS CLASSIFICATION AND HSP

The International Chapel Hill Consensus Conference Nomenclature classification 00:01:29

	Type of vasculitis	Diseases included
Primary Vasculitis	Large vessel vasculitis	• Takayasu arteritis • Giant cell arteritis
	Medium vessel vasculitis	• PAN • Kawasaki disease
	Small vessel vasculitis	**A.** ANCA - associated • Microscopic polyangiitis • GPA (Wegener's granulomatosis) • Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) **B.** Immune complex • Anti - GBM disease • IgA vasculitis (HSP) • Cryoglobulinemic • Hypocomplementemic urticarial vasculitis (Anti-C1q vasculitis)
	Variable vessel vasculitis	• Behcet Disease • Cogan Syndrome
	Single-organ vasculitis	• Cutaneous arteritis, Primary CNS vasculitis, isolated aortitis, etc.
Secondary vasculitis	Vasculitis associated with systemic disease	• Lupus vasculitis, Rheumatoid vasculitis, Sarcoid vasculitis
	Other/Associated Etiology	• HBV / HCV associated • Syphilis associated • Drug associated • Cancer-associated

EULAR/PRES Classification of Pediatric Vasculitis 00:04:00

- **Predominantly large vessel vasculitis**
  - Takayasu arteritis
- **Predominantly medium vessel vasculitis**
  - Kawasaki disease
  - Childhood PAN
- **Predominantly small vessel vasculitis**
  - Granulomatous: GPA and EGP
  - Non-granulomatous: Microscopic polyangiitis, HSP, Hypocomplementemic urticarial vasculitis, and isolated cutaneous leukocytoclastic vasculitis.
- **Others**
  - Behcet's disease, vasculitis secondary to an infection, and Cogan's syndrome.

Henoch-Schoenlein Purpura 00:05:45

- It is also known as IgA vasculitis.
- It is the most common pediatric vasculitis overall.
- It is usually mild vasculitis in children.
- The peak age is 3-10 years.
- It can occur in children less than three years old or children more than 10 years old.

- Rarely occurs in adults; if it occurs, it is chronic and more severe.
- It is more common in males as compared to females (ratio 1.5:1).

Etiopathogenesis of HSP

- The cause of HSP is still unclear.

An infectious trigger (Upper respiratory tract, or rarely GIT)

↓

Leads to increased production of IgA (particularly IgA1 and sometimes abnormal glycosylated IgA1 is formed).

↓

The antigen-antibody immune complexes are formed

↓

Which gets deposited in various organs and produce manifestations.

What's New?

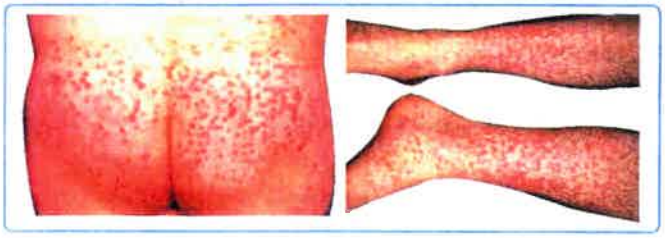
- HLA-B34 and HLA-DRB1*01 alleles have been linked to an increased risk of HSP nephritis.
- Patients with familial Mediterranean fever, hereditary periodic fever syndromes, and complement deficiencies are at increased risk for developing HSP, suggesting that genetically determined immune dysregulation may contribute.

Clinical Features 00:14:00

Infection
↓1-3 weeks
Onset of HSP Tetrad

90-100% skin involvement (hallmark)	Renal involvement in 30% of cases	Joint involvement in 75% of cases	GIT involvement in 80% of cases
Rash: Palpable purpura • Gravity-dependent parts: Lower limb, Buttocks • B/L symmetrical • Subcutaneous Edema may be present • The rash is never associated with thrombocytopenia.	Glomerulonephritis • Hematuria • Proteinuria • ± Edema • ± HTN	Arthritis or Arthralgia • Non - deforming • Large joints - knee, ankle • Lasts 2 weeks and then disappears.	Colicky abdominal pain Others • Malena • Intussusception • Vomiting

- CNS involvement is not a part of the classic tetrad, but it is common.
  - CNS manifestations may be in the form of:
    → Headache
    → Raised intracranial pressure
    → Seizures
    → Altered sensorium



Points to Remember about the Rash in HSP

- Rash may
  - Show recurrence up to 4 months.
  - It usually lasts 3-10 days.
  - It may be associated with subcutaneous edema of the dorsum of hands and feet, periorbital region, lips, scrotum, and scalp.

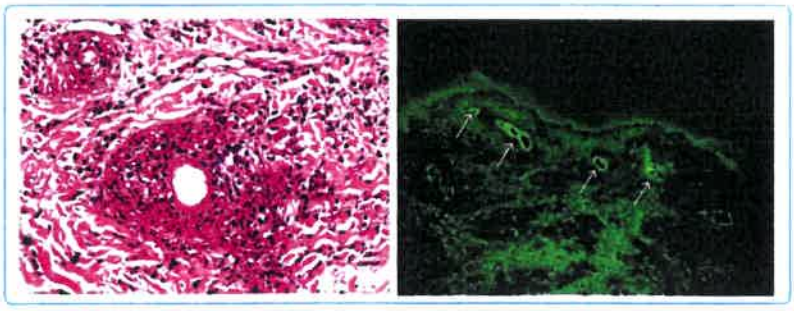
Diagnosis: EULAR Criteria

00:26:50

Criterion	Description
Mandatory criterion	• Purpura or petechiae with lower limb predominance (with no evidence of coagulopathy or thrombocytopenia)
Minimum 1 out of 4 criteria	• Diffuse abdominal pain with acute onset. • Histopathology showing leukocytoclastic vasculitis or proliferative glomerulonephritis, with predominant immunoglobulin (IgA) deposits. • Arthritis or Arthralgia of acute onset. • Renal involvement in the form of proteinuria or haematuria.

Investigations

- Increased ESR can be seen.
- Increased CRP can be seen.
- Platelet count is usually normal.
- Increased levels of total serum IgA can be seen (Not considered to be diagnostic)
- A skin biopsy or kidney biopsy are investigations of choice.
  - Skin will show Leukocytoclastic vasculitis.
  - Kidneys will show Mesangial deposits of IgA.
    → It may also be associated with C3, IgM deposition, and fibrin deposition.
    → Mesangial deposits may take the form of Focal deposits with endocapillary proliferation OR Crescent formation (Rare in children)



Treatment

00:32:30

- Over 90% of children spontaneously improve with conservative management within 4 weeks.
- Corticosteroids (Oral prednisolone 1-2 mg/kg/day for 1-3 weeks) are indicated only in severe GIT involvement.
- Giving steroids
  - Does not alter the natural course of illness or
  - Decrease the risk of HSP nephritis.
- If a patient develops HSP nephritis:
  - Mild to moderate cases are managed conservatively.
  - Severe cases associated with crescent formation will require immunosuppressive agents (I.V. Methylprednisolone) with or without other drugs.

Important Information

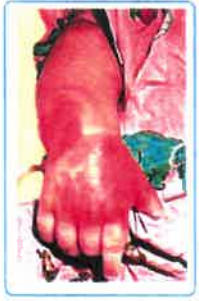
- The most common long-term complication of HSP is Chronic renal disease (more common in adults than in children). Chronic renal disease can progress to end-stage renal disease (ESRD).
- The risk of development of CRD in children is 1 to 3 %, and among that, only 5% are likely to develop ESRD.

Differential Diagnosis of HSP

00:38:12

Infantile Acute Hemorrhagic Enema (AHE)

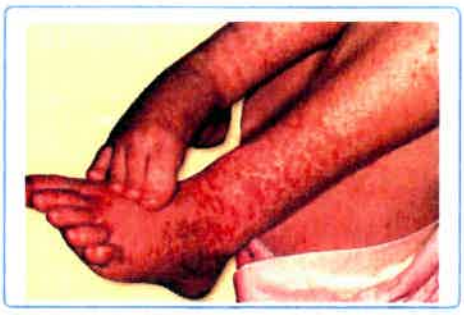
- AHE is an isolated cutaneous leukocytoclastic vasculitis that affects infants < 2 years of age and resembles HSP clinically.
- It manifests as fever, tender edema of the face, scrotum, hands, and feet, and ecchymosis (usually larger than the purpura of HSP) on the face and extremities.
- How to distinguish from HSP?
  - Younger age
  - The rash shows a different pattern



- No other organ system is involved
- The biopsy can easily distinguish

Quick Summary for Exams

- When to suspect HSP?



- When a Child of 3-10 years gets an upper respiratory infection and 1-3 weeks later develops rashes along with proteinuria/ haematuria / recent joint pain/ abdominal pain, it is a possible case of HSP.

2 KAWASAKI DISEASE

- Kawasaki disease is based on the name of Prof. Tomisaku Kawasaki (1925 – 2020).
- Another name for Kawasaki disease
  - Acute mucocutaneous lymph node syndrome of childhood.
  - Infantile PAN. (Not in use now)
- An acute, multisystem febrile illness is affecting medium-sized arteries.
- It is the 2nd most common vasculitis in India
- Most common vasculitis in the world.
- A most common cause of acquired heart disease in children in developed countries.
- Most common serious vasculitis in children.

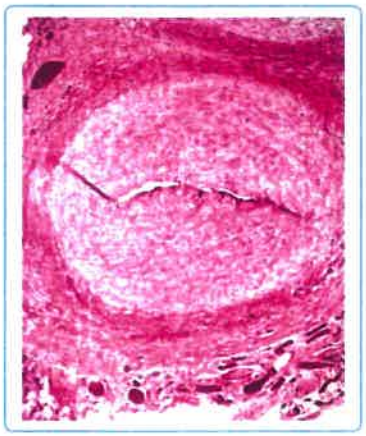
Etiopathogenesis 00:03:30

- The exact cause of the disease is unknown.
- Sex: It is more common in males than in females.
- Age: It mostly occurs in young children.
  - It is never seen in adults (MCQ).
  - 80% of children below 5 years of age are affected.
  - The Peak age at which the disease is more common is 18-24 months.
- High risk is seen in Asians, especially in Japanese.
- The genes implicated are:
  - ITPKC (A T-cell Regulator, Increased risk of Coronary Artery Aneurysms, Increased Resistance to IVIg)
  - CASP-3
  - BLK
  - FCGR2A
- Single nucleotide polymorphism (SNPs) in HLA class 2 antigen.

Important Information

- **Anti-endothelial cell antibodies are found to be increased in some children with Kawasaki disease**

Pathology 00:06:12



Histopathology shows 3 phases

- 1st phase: Neutrophilic necrotizing arteritis.
- 2nd phase: Subacute/chronic arteritis.
- 3rd phase: Myofibroblast proliferates, which causes stenosis / obstruction.

Clinical Features 00:07:30

- Mnemonic: "**Face CREAM**"
  - F – Fever: High grade, remittent, lasts for ≥ 5 days, unresponsive to antibiotics
  - C – Conjunctivitis: Bilateral, non-purulent
  - R – Rash: Polymorphous, does not have vesicles, bullae, or ulcerative lesions on the skin.
  - E - Extremities: Acute changes lead to manifestations like edema and erythema of fingers/toes.
  - Whereas subacute changes lead to desquamation of tips of fingers and toes.
  - A – Adenopathy: Cervical lymphadenopathy, size > 1.5 cm, unilateral.
  - M – Mucosal: Oral and tongue regions are affected, but the classic feature is "Strawberry Tongue". The tongue is swollen, red in color and looks like Hypertrophied.

Other clinical features

- Gallbladder hydrops
- Perianal desquamation
- Beau's lines on the nail
- Irritability
- Joint pains

Diagnosis of KD 00:15:05

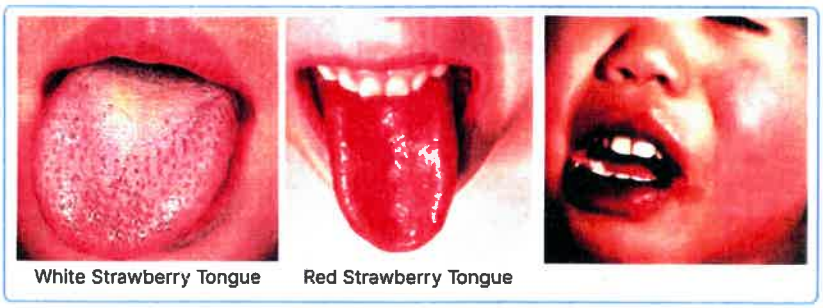
- Kawasaki disease is diagnosed when there are symptoms like fever and any 4 out of 5 criteria **(CREAM).**
- **Incomplete Kawasaki Disease**: When there is fever, and only 2 or 3 criteria are fulfilled.
- **Atypical Kawasaki**: When there is fever and unusual/ atypical organ failure, e.g., renal involvement, pulmonary involvement
- The terms atypical KD and incomplete KD are interchangeably used, but recent consensus is to use atypical KD in patients who have unusual clinical features and complications of KD.

Side Note

- Fever + 3 criteria + echocardiography shows any cardiac abnormality. The patient is treated for Kawasaki disease.

Oral Mucosal changes in Kawasaki Disease

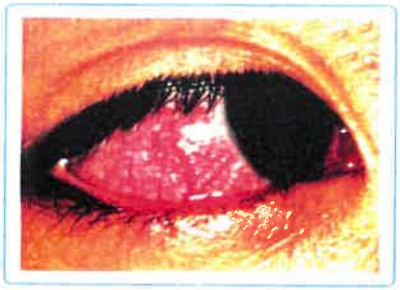
- Two types of tongue are described in the Kawasaki Disease:
  - White strawberry tongue
  - Red Strawberry tongue
- Red strawberry tongue more commonly seen in: Kawasaki Disease
- White strawberry tongue mc seen in Scarlet fever
- Red Strawberry tongue is also seen in case of Scarlet Fever.



White Strawberry Tongue Red Strawberry Tongue

- When not specifically mentioned, it refers to red strawberry tongue.
- White strawberry tongue:
  - Tongue has a white coating
  - Exudates are covering the surface of the tongue
  - Hypertrophic papillae which are pink coloured are projecting out of the surface of the white coating.
  - Is seen in the early stages of Kawasaki Disease.
  - Also seen in patients with scarlet fever.
- Oral mucosal changes: Swollen lips, cracking fissures in the lips causing bleeding is also a feature of Kawasaki disease

Bilateral, Non-Purulent Conjunctivitis



- Intense inflammation in the eyes without any puss discharge.
- A term which is also used for this condition is "Conjunctival Injection"

Natural history of Kawasaki Disease 00:21:07

- **Acute Phase**
  - Lasts 1 to 2 week
  - Fever and other signs
- **Subacute Phase**
  - Lasts around 3 weeks
  - Desquamation
  - Increased platelet count.
  - Coronary artery aneurysm.
  - Most dangerous phase.
- **Convalescent Phase**
  - Occurs 6 to 8 weeks after onset
  - Fever resolves
  - ESR normalizes.

New markers in Kawasaki disease

- Serum procalcitonin
  - It is average in Kawasaki disease but elevated in risk of coronary aneurysms.
  - It is normally normal in Kawasaki Disease.
- Serum pro-BNP and serum NT-BNP.
  - Helpful to differentiate from infection.

Investigations 00:23:11

- Increased ESR
- Increased CRP: Sensitive to monitor disease activity.
- Increased neutrophils.
- Platelet count is normal or Increased in the subacute phase. Subacute phase normalizes in 6 weeks.

Side Note

- Thrombocytopenia is usually not seen in Kawasaki disease normally.
- If it occurs, there is a high risk of coronary artery aneurysm, and it becomes resistant to treatment.

How frequently should one repeat Echo in a child with KD?

- At diagnosis.
- Uncomplicated patients: 1-2 weeks and also 4-6 weeks after treatment. This is because dilatation is unusual beyond 6 weeks. Normal coronaries may be discharged from cardiology care after 12 months but the medical records should permanently mention the diagnosis of KD.
- For significant and evolving coronary abnormalities. At least twice per week till luminal dimensions stabilize and we should look specifically for thrombus. After that at 2 weeks, 4-6 weeks, 3 months and then every 6-12 months till parameters normalize.

Pearls and One-Liners

- The late clinical manifestation is Desquamation.
- Kawasaki disease can have atypical complications such as aseptic arthritis, aseptic meningitis, and macrophage activation syndrome.

Complications 00:29:34

- The most common cardiac complication is myocarditis (can present in 1st week of illness), seen in 50-70%, and can be asymptomatic or can presents as features of CCF.
- 2nd most common is coronary artery aneurysms:
  - Seen in the subacute phase.
  - If Kawasaki is untreated, the risk of CAA is 20-25%. If treated, risk of CAA is <5%.
  - If left untreated, this can also lead to death. The cause of death can be thrombosis (most common cause), obstruction, and rupture.
- Kawasaki disease shock syndrome
- Mitral regurgitation.
- Increased risk of asymptomatic pericardial effusion.

Treatment 00:33:15

The drug of choice is

- IVIG
  - A single dose of 2g/kg is given.
  - Infusion is done over 12 hrs.
  - Give within 7-10 days of onset.
  - It can be useful even in presentations beyond 10 days if the patient has high ESR, CRP, and CAA.

Side Note

- Regimen: IVIG (Single dose, once) + Daily Aspirin (50 mg/kg/day) high dose is given till the patient is afebrile for more than 48 hours.
- Then aspirin is shifted to a low dose (3-5/mg/kg/day) and given for 6 to 8 weeks, and then echocardiography is done.
- If the results are normal, then aspirin doses are stopped.
- If the findings are in resolving conditions, the aspirin is continued for 1 year.
- If the conditions are persistent, then anticoagulation treatment is considered. (Target INR 2-2.5 and Warfarin/LMWH should be used).

IVIG - Resistant KD and its management 00:38:11

IVIG resistant KD

- When fever persists ≥36 hrs after IVIG infusion is completed.
- Seen in 15% cases
- High risk of CAAs

Treatment

- Repeat the dose of IVIG and oral prednisolone(2g/day).
- If there is no response, consider anti-TNF alpha agents (infliximab).
- After that, consider cyclosporine and plasma exchange.

Differential Diagnosis 00:40:16

- If there is no fever or mild fever, the differential diagnosis of Kawasaki disease is Steven Johnson syndrome and toxic epidermal necrolysis.
- Another one is scarlet fever.
  - Fever < 5 days, responds to Beta-Lactam Antibiotics

- Tender lymphadenopathy which can be bilateral or unilateral
- Pharyngitis
- Evidence of streptococcal infection
- Little to no cardiac manifestations. This can be used to distinguish scarlet fever over Kawasaki disease.

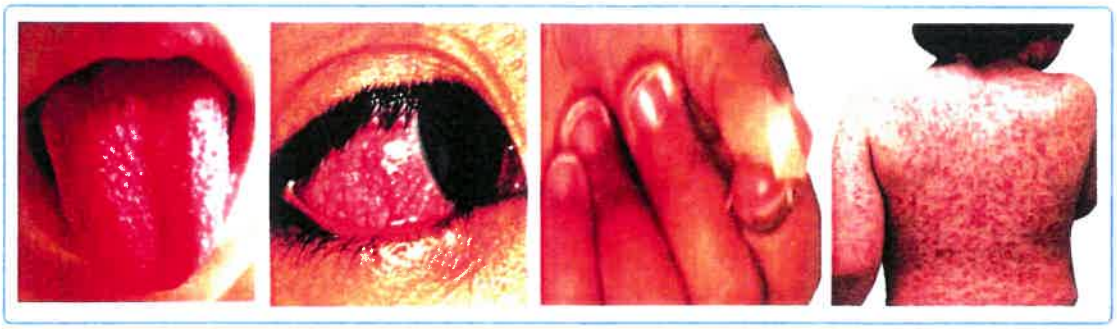
Clinical Question

Q. What happens to fever if you do not give IVIG?
Ans. If untreated, fever continues for 1-3 weeks and resolves spontaneously by 3-4 weeks, the mean duration of fever being 11 days.

Q. What are the most common manifestations of KD?
Ans. Fever

Q. What is the least common manifestation of KD?
Ans. Cervical lymphadenopathy.

High Yield Concept



- MAS can develop in KD as a rare complication. How will you suspect and confirm?
- In severe Kawasaki disease, there is increased ESR and CRP.
- Whereas in Kawasaki with MAS, ESR is normal to increase slightly, and CRP is increased.
- A useful marker is serum ferritin which is elevated in MAS and is normal in Kawasaki disease.

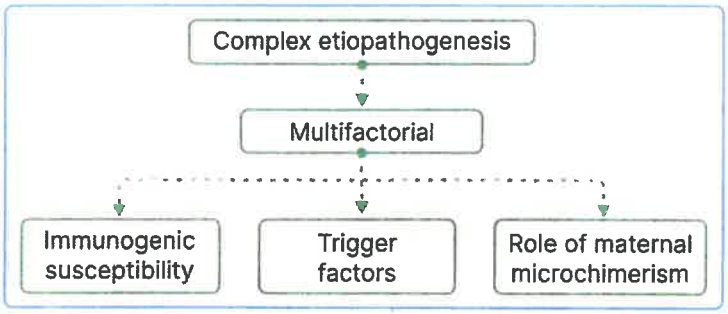
3 JUVENILE DERMATOMYOSITIS

Epidemiology 00:00:52

- It is the most common inflammatory myositis in children.
- Incidence of JDM worldwide: 3 cases/1 million children/year
- The peak age at the onset of the disease is around 4-10 years.
- Females > Males (2:1)
- Increased familial association of other autoimmune diseases.

Etiopathogenesis 00:02:27

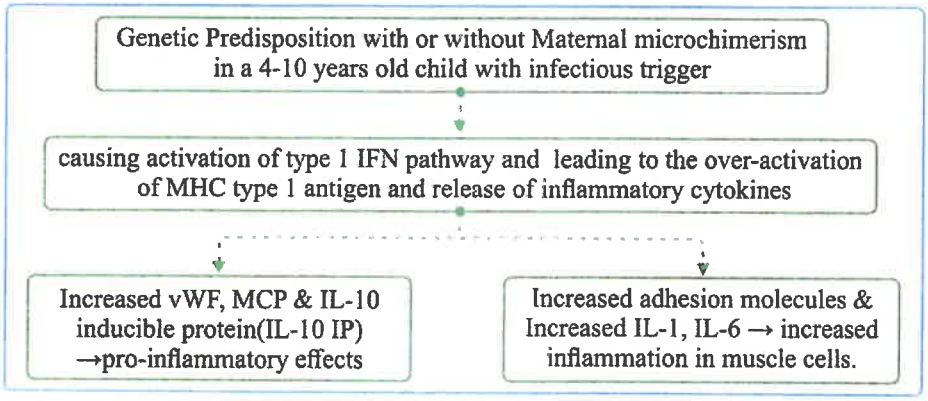
- Role of maternal micro chimerism: Maternal cells appear in a postnatal child and can happen in utero, during childbirth, or during lactation.
- Genetic predisposition
  - HLA with increased risk: B8, DRB1 0301, DQA1 0501 & DQA1 0301
  - Polymorphism in TNF-α promoter region & VNTRs in IL-1R antagonism
- **Role of maternal microchimerism**
  - Maternal cells in children may contain antigens (not self), produce GVHD, or induce autoimmune phenomena leading to disease.



Infectious Triggers in JDM 00:06:22

- History of preceding infection for last 3 months before JDM onset.
  - 2/3rd → Upper respiratory infection.
  - 1/3rd → Gastrointestinal infection.
- Agents: Group A streptococcus (commonly), Enteroviruses, Coxsackie-B, Parvo B19, and rarely mycoplasma.

Pathogenesis



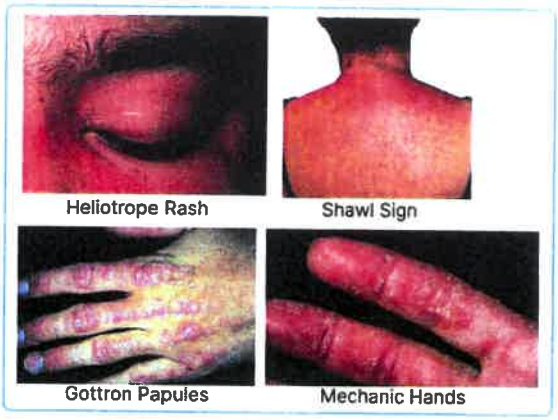
- The number of T cells, natural killer cells, and plasmacytoid dendritic cells has increased.

Clinical Features of JDM 00:11:08

A. Dermatological manifestations: 85-100%

- 1st symptom in 50% Rash
- In 25% of rashes come with myopathy

- Heliotrope rash: Violet pink discoloration, present on eyelids +/– periorbital edema
- The photosensitive rash occurs in an erythematous form on photo-exposed parts like the neck and upper back. It is also known as the shawl sign.
- Malar rash/erythema on the face involves Nasolabial Folds whereas in SLE spares the Nasolabial Folds
- Gottron papules: Atrophic or hypertrophic papules or patches seen on knuckles (PIP/DIP), elbow, knee, and tarsal joint.
- Mechanic hands: Scaly plaques or rash on palm/ soles/ fingers (especially along flexor tendons)
  - Strongly associated with anti-Jo-1 antibodies.



B. Myositis: Insidious onset, gradually progressive & proximal myopathy (shoulder & hip girdle)

- Initially: Lethargy
- Later: Inability to comb hair, inability to climb stairs
- Gower sign positive
- Associated with muscle tenderness in > 50% of cases
  - Rarely, involvement of esophageal muscles leads to dysphagia, increased risk of aspiration
  - Respiratory muscle involvement: progressive respiratory paralysis.

MCQ Points- Nelson 21st Ed

- Respiratory muscle weakness causes respiratory failure in JDM → There is no increased work of breathing (no retraction) and no hypoxemia; instead, hypercarbia is a clue.

Other features

- Fever
- Raynaud's phenomena
- Periungual capillary changes
- Calcinosis
- Lipodystrophy
- Arthralgia & arthritis
- Joint contractures
- Restrictive lung disease

Variant of JDM

00:24:28

Amyopathic JDM / Dermatomyositis Sine Myositis

- Prominent dermatological features but no/clinically silent myositis

Diagnosis Test

00:25:40

Classic rash	Heliotrope rash of the eyelids Gottron papules
Plus 3 of the following:	
Weakness	Symmetric Proximal
Muscle enzyme elevation (1)	Creatine kinase, Aspartate transaminase Lactate dehydrogenase, Aldolase
Electromyographic changes	Short, small polyphasic motor unit potentials Fibrillations Positive sharp wave, Insertional irritability Bizarre, high-frequency repetitive discharges
Muscle biopsy	Necrosis, Inflammation

Key points related to investigations in JDM

- AST elevation is seen before other muscle enzymes rise in JDM
- ESR is usually normal, and RF is negative
- ANA is + in > 80% cases

Autoantibodies in JDM

Autoantibodies in JDM	
Myositis-Associated Antibodies (MAA)	**Myositis Specific Antibodies (MSAs)**
• SS-A • SS-B • Anti-Smith Antigen • Anti-RNP • Anti-dsDNA ○ If present in JDM → there is an increased risk of overlap/MCTD	• Anti-Jo-1 • Anti-Mi-2 • Anti-p155/140 (Anti-TIF-1γ) • Anti-NXP2 (Anti-MJ) • Anti-MDA5

Specific Associations of MSAs

- Anti-p155/140 (Anti-TIF-1γ) are seen in 23-30% of children with JDM - Associated with photosensitive rashes, ulceration, and lipodystrophy. (In adults, it is associated with malignancy, and in children, it is associated with JDM)
- Anti-MJ (Anti-NXP2) is seen in 12-23% of children with JDM and is associated with cramps, muscle atrophy, contractures, and dysphonia.
- Anti-MDA5 is seen in 7-33% of children with JDM - associated with ILD
- Anti-Jo-1 associated with mechanic hands

Role of other investigations

- T2-Weighed MRI is useful for identifying sites of muscle biopsy
- Contrast swallow study may be done in suspected palatal dysfunction and risk of aspiration
- PFT: Restrictive lung disease, reduced DLCO may be seen in fibrosis

Complications in JDM 00:32:55

- Risk of aspiration: Associated with either esophageal or palatal palsy
- Respiratory failure
- GIT vasculitis: Colicky abdominal pain +/– occult blood losses.
  - Often diffuse in nature, no role of surgical management
  - Increased risk of massive bleeding & GIT perforation
- Cardiac involvement: Pericarditis or myocarditis → systolic & diastolic dysfunction
- ILD
- Calcinosis cutis: in 40% of patients, the risk is increased in prolonged disease.
  - Calcium Phosphate (hydroxyapatite) crystals are deposited in the skin, subcutaneous tissue & muscles.
  - Ulcerative skin lesions show crystals in discharge
  - Increased risk of developing cellulitis
  - If in proximity to bone, it can produce osteomyelitis.
  - Polymorph of TNF-α 308
  - The risk is particularly high in JDM patients with TNF-α genetic polymorphism.
- Lipodystrophy: in 10-40%
  - Loss of fat on face & buttock region
  - Associated with: PCOS, Metabolic syndrome like insulin resistance, acanthosis nigricans, obesity with dyslipidemia
- Side effects related to steroid toxicity:
  - Cushing's syndrome: HTN, cushingoid facies, posterior lenticular opacities, peptic ulcers, rickets, and steroid-related psychosis.

Treatment of JDM

00:39:45

- Mainstay → Steroids ~ (> 50-70%)

Oral Prednisolone – (2 mg/ kg/ day)
↓ slow tapering
Over 1 year

- Severe myositis esophageal/ respiratory muscle involvement → I.V. methylprednisolone (30 mg/kg/d) × 3 days → Switch to oral prednisolone
- Steroid toxicity/ less response → Steroid sparing agents (Methotrexate → 15 mg/m^2/ week S.C)
- Some studies show → Steroids + Methotrexate – Effective where monotherapy has failed.
- Hydroxychloroquine
  - Orally 4-6 mg/kg/day
  - Maintenance agent → Good add on effect
    → S/E: Cutaneous toxicity/hemolysis in G6PD individuals
- Rituximab
- IVIG → Salvage Therapy → (2g/kg infusion every 2 weekly) × 3 doses, followed by every 4 monthly.

Supportive Therapy

- Physiotherapy and Occupational therapy
- Feeding → Risk of aspiration → Gastrostomy or NG Tube feeding
- Sun protection → Cover/ use sunscreens with high Sun Protection Factor (SPF 30 or more)
- Calcium and Vitamin D supplementation is given to all patients.

Mortality rate

- Previously - 30-50%
- Today - 1%
  - Left with problems like vasculitis

4 JIA & OTHER MSK DISORDERS IN CHILDREN

Pediatric JIA and Other MSK Disorders in Children

00:00:31

- JIA stands for juvenile idiopathic arthritis, one of the common rheumatological disorders affecting joints and children.

Arthritis

- According to Nelson, 21st Ed as well as standard textbooks.
- Arthritis is defined by the presence of
  - Intra-articular swelling OR
  - Two or more of the following:
    - → Pain on Motion
    - → Loss / Restriction in the movement
    - → Erythema or redness
    - → Heat

Important Information

- Nelson's 21st Edition states that joint pain or tenderness is a single point, not two separate points.

Classification of Arthritis in Children

Acute (<2 weeks)	Subacute (2-6 weeks)	Chronic (> 6 weeks)
• Acute Rheumatic Fever • Transient/ Toxic synovitis • Arthritis in HSP • Septic arthritis	• Reactive arthritis • Juvenile Dermatomyositis • SLE, Hypogammaglobulinemia • Arthritis in Malignancy / Sickle Cell Disease	• JIA • Ankylosing spondylitis • TB Arthritis • Legg-Calve-Perthes Disease

Juvenile Idiopathic Arthritis (JIA)

- Most common Arthritis of rheumatological origin in children.
- Juvenile idiopathic arthritis is characterized as chronic arthritis.
- JRA juvenile rheumatoid arthritis given by ACR is now discarded.
- Now, ILAR is used, where ILAR stands for International League of Association for Rheumatology.
  - Gave the term - JIA

Criteria to define JIA

- Four criteria are used to define JIA, according to ILAR:
  1. The age at the onset - less than 16 years.
  2. The duration of arthritis - equal to or more than 6 weeks.
  3. Arthritis affecting one or more joints.
  4. Other causes: For example, infections and connective tissue disorders should be ruled out.

Types of JIA

00:07:21

A. Oligoarthritis

- Up to four or fewer joints are involved in JIA, called Oligoarthritis (overall most common variety).
- Oligoarthritis is further subdivided into two parts:
  - Persistent
  - Extended

B. Polyarthritis / Polyarticular JIA

- 5 or more joints are involved.
- Polyarthritis two types:
  - Rheumatoid Factor positive and rheumatoid factor negative

C. Systemic onset JIA (SOJIA)

- There is a prominent system with features like rash, fever, hepatosplenomegaly lymphadenopathy, and pruritic pericarditis.
- It is a very strong systemic component, along with arthritis.

D. Psoriatic JIA

E. Enthesitis-related JIA

- Enthesitis refers to inflammation at the point where the tendons and ligaments are attached to the bones.
- It is related to Ankylosing Spondylitis and inflammatory bowel disease.

F. Unclassified JIA

- If any JIA cannot be placed in any of these five categories, it should be placed in a heterogeneous category called unclassified JIA.

Epidemiology of JIA Arthritis 00:10:28

- Worldwide incidence: 0.8 and 22.6/1 lakh children per year.
- Estimated prevalence: 0.4 and 1.3 per thousand children < 16 years.
- Most common type - Oligoarthritis (50-60%) > Polyarthritis (30-35%) > SOJIA (10-15%)
- Sex predilection
  - JIA is more common in females than males.
  - In the Indian population, the female preponderance tends to become diluted.
  - Generally, both oligoarthritis and polyarthritis are more common in females compared to males by a ratio ranging between 3:1 to 5:1
  - SOJIA is equally prevalent in both sexes
- Peak age at onset
  - Periarticular: Between 2-4 years
  - Polyarticular: Bimodal- 1st peak at 2-4 years, 2nd peak at 10-14 years
  - SOJIA: No peak, occurs throughout childhood.

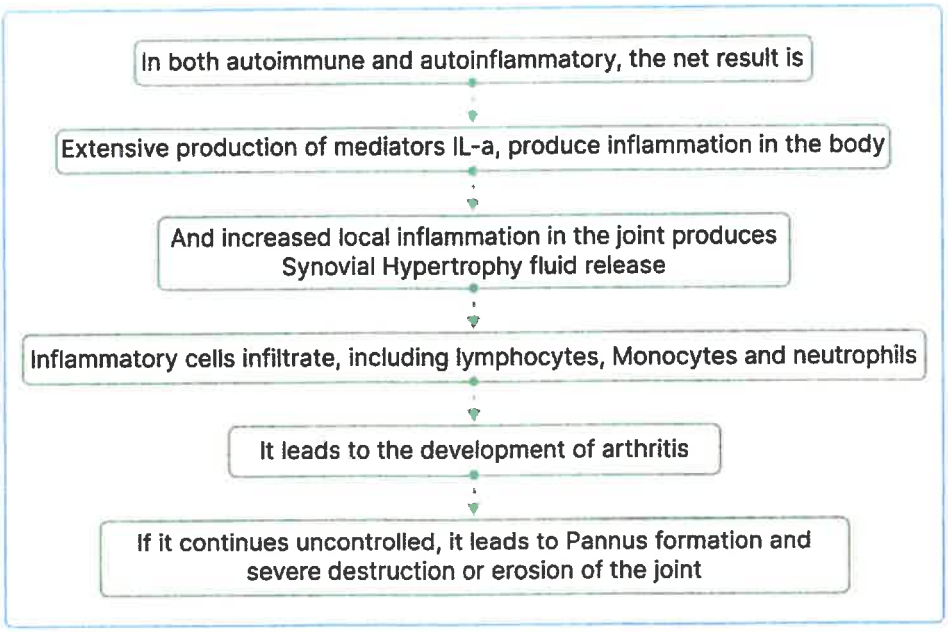
Etiopathogenesis 00:14:41

2 key factors implicated in JIA	
Immuno-genetic predisposition	**Trigger Factors**
• HLA-DR5 and DR8: Early-onset Oligoarthritis • HLA-B27: Enthesitis-related JIA, Late-onset Oligoarthritis • HLA-DR4, Dw4, DR1: RF + Polyarthritis • Polymorphisms in PTPN-22, TNF-α, MIF, IL-6, IL-1 α	• Infections: Parvo B19, Rubella, TB, EBV, Mycoplasma pneumoniae • Physical or joint Trauma • Severe mental stress • Abnormal hormonal status

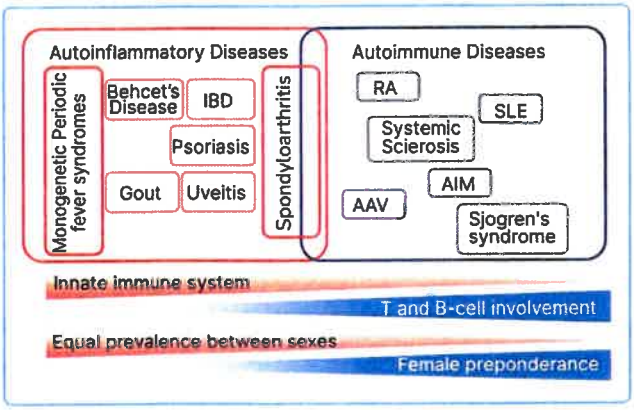
Mechanism Implicated 00:17:33

2 varieties of JIA	
Autoimmune	**Autoinflammatory**

• Adaptive immunity is dysregulated.
• Adaptive immunity dysregulation produces autoreactive T-cells and the production of autoantibodies.
• Children with oligoarthritis, polyarthritis, and other forms of JIA.
  ○ All were found to be autoimmune.
  ○ They show T cell Dysfunction (Upregulation of the TH_1 pathway, with increased production of IL-1, TNF α, and IL-6).
	• Innate immunity is dysregulated.
	• Lack of autoantibodies, regulatory T-cells, and autoreactive T-cells.
	• SOJIA: Shows autoinflammatory mechanism.
	• Some varieties of enthesitis are related to JIA.



Summary 00:22:54

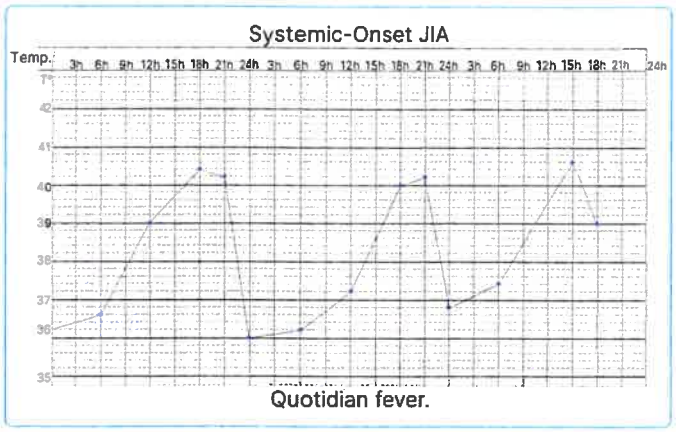


Individual Subtypes of JIA 00:24:04

Systemic-Onset JIA

- Arthritis affects one or more joints
- Age less than 16 years
- Onset - more than six weeks
- Fever lasts 2 weeks or longer
  - Type of fever - quotidian fever
  - Quotidian fever reaches a Peak of at least 39°C in 24 hours, and within 24 hours after the peak, it spontaneously comes down and becomes normal, coming to 37°C or below. (multiple peaks returning to baseline within 24 hours).
  - Quotidian fever is commonly associated with malaria-like falciparum malaria but is also a feature of systemic onset JIA (Still's disease).
- One or more of the followings
- Rash
  - **Type** - Macular, Maculopapular rash.
  - The rash is evanescent transient (fever comes, the rash appears, stays for some time, and then fades away by itself).
  - Salman's pink color.
  - Most commonly appears on trunks > proximal extremities.
  - It shows Koebner's phenomenon.

- Hepatosplenomegaly
  - There may be either liver enlargement / spleen enlargement, or both.
- Generalized lymphadenopathy
- Serositis (pericarditis or pleuritis or peritonitis, or a combination of these).

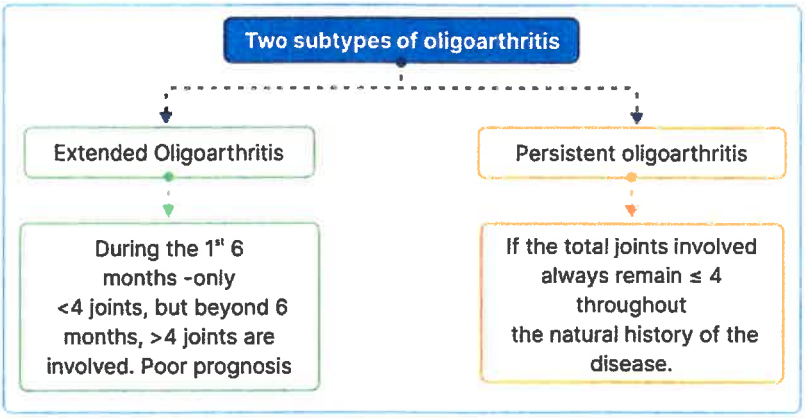


Important Information

- Nelson says that Arthritis is any joint in the body that can be involved in systemic onset JIA, but the joint involvement is usually severe, and large joints like the hip joint, cervical spine, and temporomandibular joint are frequently implicated in many patients of systemic onset JIA.

Oligoarthritis 00:31:07

- Overall, it is the most common variety of JIA worldwide.
- 4 joints are involved in the 1st 6 months of the disease.
- It is more common in females > than males.
- Associated with asymmetric large joint involvement, including knee and ankle joints.
- Develop Chronic uveitis (Iridocyclitis)
  - Risk increases if they are found to be ANA positive.
- Swelling in the joint is more than the pain in the joint.

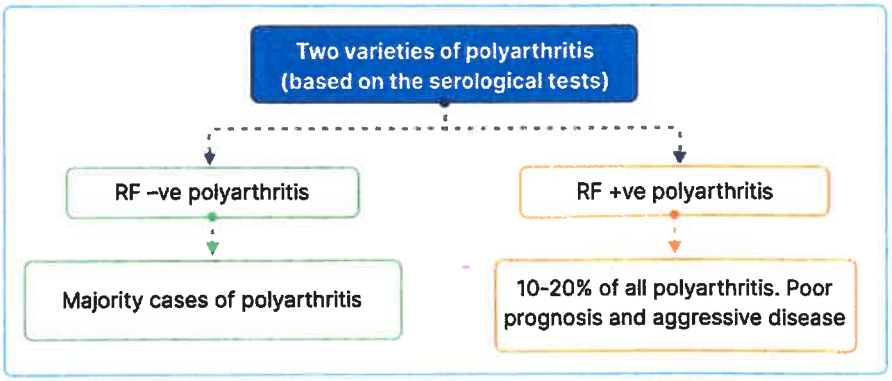


MCQ Point: ANA-Positivity in JIA It is associated with

- Less joint involvement
- Asymmetrical joint involvement
- Female sex
- Younger age at onset
- High risk of developing uveitis/iridocyclitis

Polyarthritis 00:35:45

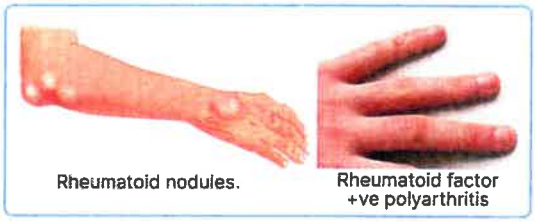
- When 5 joints are affected in JIA.
- Polyarthritis is more common in females compared to males.
- Pain is significantly more than swelling of the joints.



Differences Between RF+ve and RF –ve Polyarthritis

Feature	RF + Polyarthritis	RF- Polyarthritis
Age	Late childhood or early adolescence	Any age
Severity	More severe	Less severe
Joint involves	Symmetrical	Asymmetrical
Joint affected	• MCP, PIP • Cervical spine • TMJ	• Knee, wrist • Hip • Ankle
Rheumatoid Nodules	+	-
Deformities	+	-

- Micrognathism - due to severe TMJ involvement.
  - Affects young children
- Rheumatoid nodules
  - The common site is the wrist, back of the hands, and elbow.
- This is the patient with the JIA, and nodules are seen below.



Rheumatoid nodules. Rheumatoid factor +ve polyarthritis

Psoriatic JIA

00:40:32

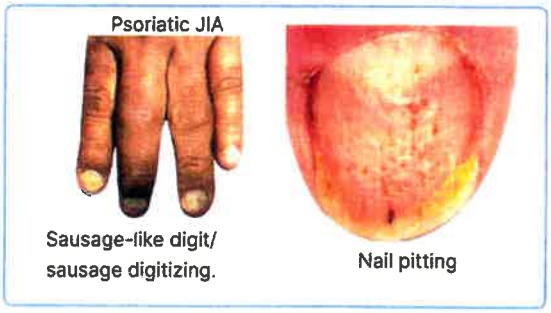
- Associated with psoriasis
- If any JIA is associated with clinical psoriasis, the typical skin disease, it is diagnosed as psoriatic JIA.

OR

- JIA is associated with any two of the following:
  - Dactylitis (sausage digits) is swelling of the middle part of the digits of the hands and feet.
  - Nail pitting / Onchyocolysis.
  - First-degree relative with clinical psoriasis.
- If arthritis is present with two of these three features, the patient has psoriasis JIA.
- Subclinical form of psoriasis - is very common in all parts of the world, including India, especially in the northern and western parts of India.

Important Information

- Nelson 21st Edition: Although distal interphalangeal joint involvement (DIP) joint involvement is uncommon in psoriatic Arthritis, if it is present, it is highly suggestive of the diagnosis.



Sausage-like digit/ sausage digitizing. Nail pitting

Enthesitis-Related JIA (ERA)

- It comprises 10-20% of all JIA; in India, it comprises 35 % of all cases.
- Mean age at onset: 12 years.
- Males > Females. Especially above 8 years of age.
- Asymmetrical large joint involvement in the knee, ankle joints, and sometimes hip joint.
  - The hip is never involved in an isolated form. It is always associated with the knee and Ankle joint.
- Strong association with HLA B-27.
- Self-limited iritis (Acute) but doesn't progress to severe chronic iridocyclitis.
- Inflammation of the foot's small joints, or tarsitis, is highly suggestive of ERA.
- Most ERA adolescents tend to develop ankylosing spondylitis in later life.
- Once this Ankylosing Spondylitis develops, the hallmark of the feature is sacroiliitis, which develops an inflammatory back pain.

Features of inflammatory back pain

- Pain at night with morning stiffness and improvement on arising.

- No improvement of back pain with rest.
- Improvement with exercise
- Good response to NSAIDS

Q. What is different in ERA?

- HLA-B27 is prone to misfolding. Forms abnormal cell surface structures and triggers inflammation.
- Altered gut microbiota and an abnormal immune response to normal microbiota.
- Inflammation directed towards joints and entheses > GI tract.
- Inflamed joints and entheses in spondylarthritis contain T and B cells, macrophages, osteoclasts, proliferating fibroblasts, and osteoblasts with IL-17/IL-23 pathway activation.
- Bone loss and osteoproliferation in and around the vertebral bodies and facet joints in long-standing Ankylosing Spondylitis contribute to significant morbidity.
- Adult Ankylosing Spondylitis - Bamboo spines.

Criteria to diagnose ERA

- Either
  - Arthritis + enthesitis.

    or
  - Arthritis + enthesitis + 2 of the following:
    → Sacroiliac joint tenderness or inflammatory lumbosacral pain.
    → HLA-B27 positivity
    → Male patient > 6 years
    → Acute anterior uveitis
    → A positive family history of HLA-B27-related disease

Investigation in JIA 00:50:50

- CBC - TLC is elevated
  - Neutrophilia (Increase in SOJIA)
- Platelet count - elevated. Thrombocytosis is part of the acute inflammatory response.
- Inflammatory markers are:
  - ESR
  - CRP
    → CRP indicates disease severity.
    → Used to monitor response to therapy.
- Anti-nuclear antibody (ANA) positivity.
  - Maximally seen in oligoarticular JIA > polyarticular JIA.
  - If ANA positivity is seen, it increases the risk of iridocyclitis.
- Rheumatoid factor and anti-CCP (Cyclic citrullinated peptide) → positive in RF +ve variety of polyarticular JIA.
- X-rays of the affected joints -Baseline and then at each follow-up visit.
- Active: Joint Swelling → ↑ Joint Space
- Periarticular osteopenia (MRI / CT better than plain)

  ↓

  Subchondral erosions, cartilage damage
- Role of synovial aspiration
  - Normal: Not done
  - Indicated
    → Monoarthritis
    → Suspecting underlying malignancy/transient synovitis

Complication in JIA 00:56:42

- Anemia
  - Microcytic hypochromic
  - Anemia of chronic disease
  - Decreased oral intake
  - Increased GI occult blood loss due to the use of non-steroidal anti-inflammatory drugs initially forms the mainstay of therapy, but long courses in high doses are sometimes needed up to 6 weeks or even 8-12 weeks.
- Growth disturbances
  - Short stature is common in JIA
- Limb length discrepancies
  - Common in asymmetric types of JIA
- Joint contractures
  - Particularly fixed flexion type of joint
- Involvement of cervical spine
  - Fusion of C2 and C3 Lamina produces difficulty in neck movement, and sometimes it can also produce torticollis.
- Chronic TMJ involvement:
  - Difficulty in opening the mouth → affect speaking and oral intake.
  - Rarely, Micrognathiasm
- Secondary Amyloidosis (Rare)
  - Hypoalbuminemia
  - Proteinuria
- Chronic anterior uveitis/Iridocyclitis
  - Clinically silent and potentially blinding complication.
  - This is seen in young females who are ANA+ and < 6 years in oligoarthritis > polyarthritis.

Screening Protocol

- All JIA patients should be referred for ocular examination.
- Symptomatic patients need to be seen within 1 week of referral.
- Asymptomatic patients need to be seen within 6 weeks of referral.
- All patients need 2 monthly visits initially.
- Then, 3-4 monthly screening.

Time duration for which 3-4 monthly screening is to be done

- All Oligo, PsA, and ERA patients < 11 years, irrespective of ANA status.
- Polyarthritis if ANA+ve

Age at onset (yr.)	Length of screening (yr.)
<3	8
3-4	6
5-8	3
9-10	1

Age at onset (yr.)	Length of screening (yr.)
<6	5
6-9	2

- Polyarthritis if ANA –ve onset < 7 years: only 5 yearly screenings needed.
- SOJIA or rheumatoid factor positive polyarthritis: Low risk of uveitis; only initial screening is needed.
- All types where onset is >11 years: one year of screening.
- After stopping immunosuppression: 2 monthly screenings in the first six months, then as above.