Juvenile idiopathic arthritis

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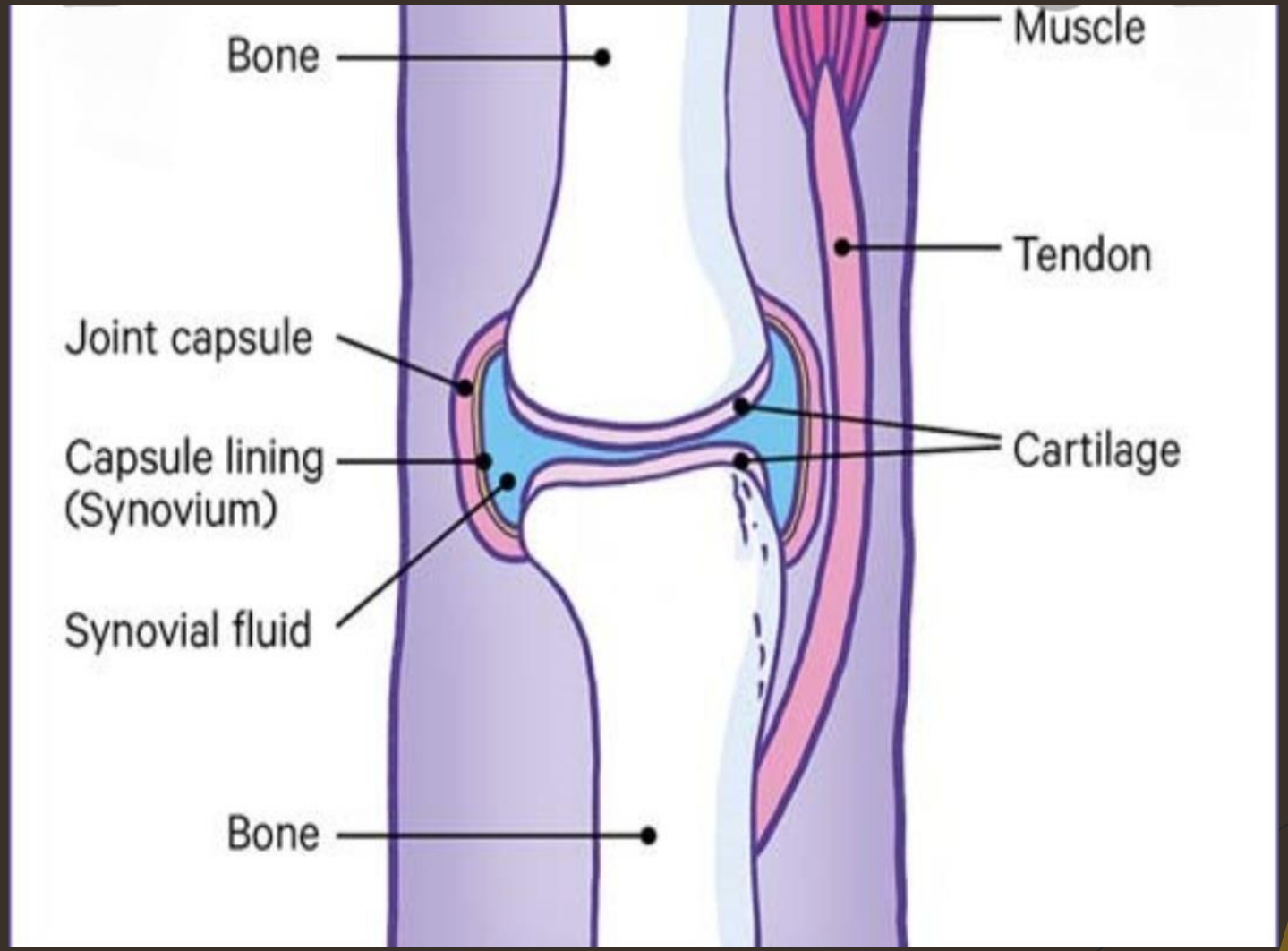
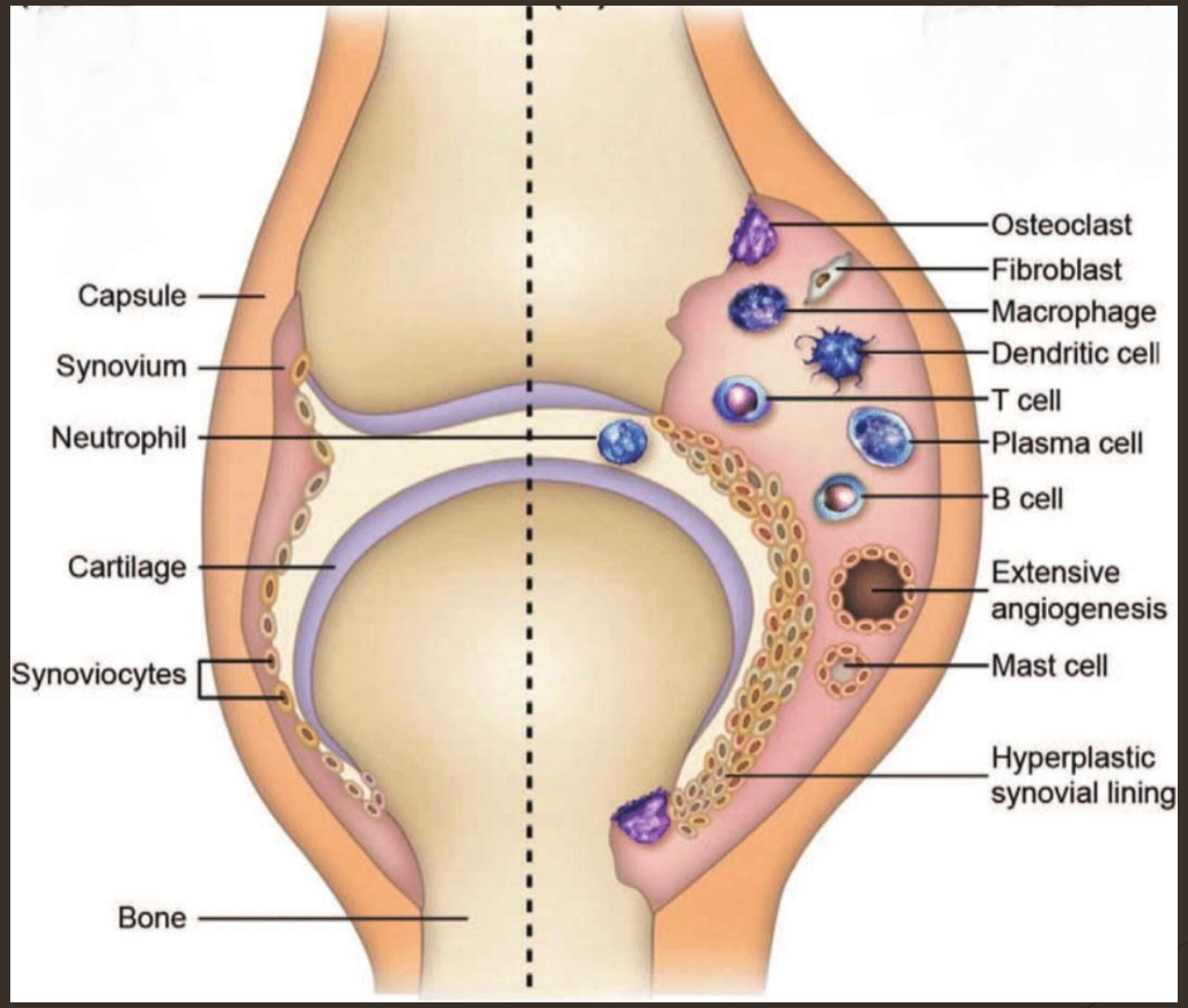
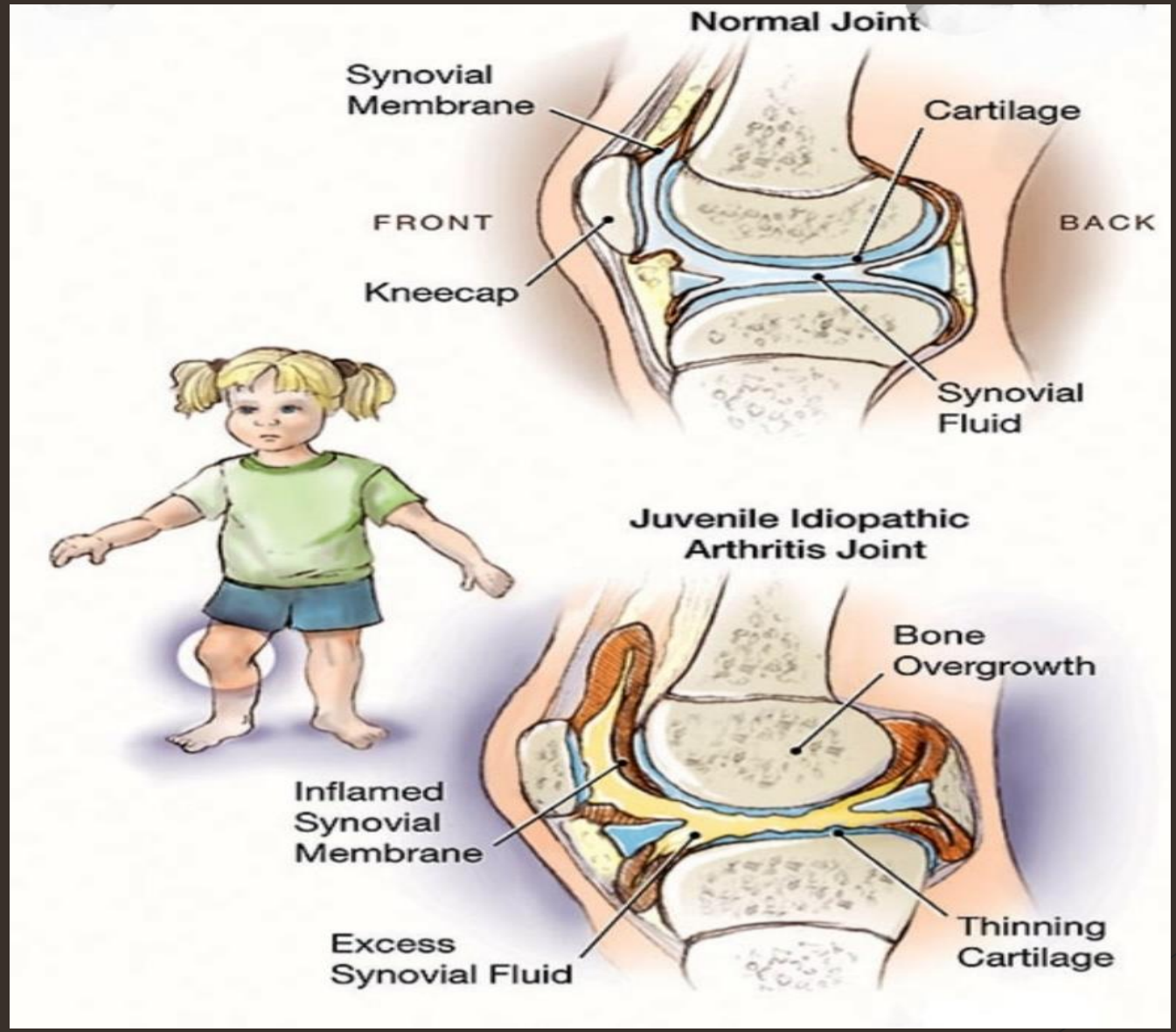
- Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children
- JIA represents a heterogeneous group of disorders sharing the clinical manifestation of arthritis
- The etiology and pathogenesis of JIA are largely unknown and the genetic component is complex, making clear distinction among various subtypes difficult


Bone
Muscle
Tendon
Joint capsule
Capsule lining
(Synovium)
Cartilage
Synovial fluid
Bone


Capsule
Synovium
Neutrophil
Cartilage
Synoviocytes
Bone
Osteoclast
Fibroblast
Macrophage
Dendritic cell
T cell
Plasma cell
B cell
Extensive angiogenesis
Mast cell
Hyperplastic synovial lining


Normal Joint
Synovial Membrane
Cartilage
FRONT
BACK
Kneecap
Synovial Fluid
Juvenile Idiopathic Arthritis Joint
Bone Overgrowth
Inflamed Synovial Membrane
Thinning Cartilage
Excess Synovial Fluid

- The former classification of the American College of Rheumatology (ACR) uses the term juvenile rheumatoid arthritis and categorizes the disease into 3 onset types

- Attempting to standardize nomenclature, the International League of Associations for Rheumatology (ILAR) proposed a different classification using the term juvenile idiopathic arthritis

TABLE 180.1
ADAPTED FROM CASSIDY JT, LEVISON JE, BASS JC, ET AL: A STUDY OF CLASSIFICATION CRITERIA FOR A DIAGNOSIS OF JUVENILE RHEUMATOID ARTHRITIS, *ARTHRITIS RHEUM* 29:174–181, 1986.
CRITERIA FOR THE CLASSIFICATION OF JUVENILE RHEUMATOID ARTHRITIS

Age at onset: <16 yr

Arthritis (swelling or effusion, or the presence of ≥2 of the following signs: limitation of range of motion, tenderness or pain on motion, increased heat) in ≥1 joint

Duration of disease: ≥6 wk

Onset type defined by type of articular involvement in the 1st 6 mo after onset:

- Polyarthritis: ≥5 inflamed joints
- Oligoarthritis: ≤4 inflamed joints
- Systemic-onset disease: arthritis with rash and a characteristic quotidian fever

Exclusion of other forms of juvenile arthritis

BOX 16.3 Classification Criteria for Juvenile Idiopathic Arthritis: Edmonton, 2001

Systemic Arthritis
Oligoarthritis
- a. Persistent
- b. Extended

Polyarthritis (rheumatoid factor negative)
Polyarthritis (rheumatoid factor positive)
Psoriatic arthritis
Enthesitis-related arthritis
Undifferentiated arthritis
- a. Fits no other category
- b. Fits more than one category

Epidemiology

- incidence

from 0.8-22.6 per 100,000 children per year

- prevalence

from 7-401 per 100,000.

- These wide-ranging numbers reflect population differences, particularly environmental exposure and immunogenetic susceptibility, along with variations in diagnostic criteria, difficulty in case ascertainment, and lack of population-based data.
- Oligoarthritis is the most common subtype (40–50%), followed by polyarthritis (25–30%) and systemic JIA (5–15%), ERA JIA (10-20%), psoriatic JIA (5%)

Sex

- no sex predominance in systemic JIA (sJIA)
- more girls than boys are affected in oligoarticular (3 : 1) and polyarticular (5 : 1) JIA
- In ERA male is more affected (3:2)

Age

- peak age at onset is 2-4 yr for oligoarticular disease
- Age of onset has a bimodal distribution in polyarthritis, with peaks at 2-4 yr and 10-14 yr
- sJIA occurs throughout childhood, with a peak at 1-5 yr
- ERA occurs in >6 yr (mean age 12 yr)
- Psoriatic JIA have 2 peaks at 1-5 yr and 12-14 yr

Etiology

- etiology and pathogenesis of JIA are not completely understood, although both immunogenetic susceptibility and an external trigger (infection & thrauma) are considered necessary

Clinical Manifestations

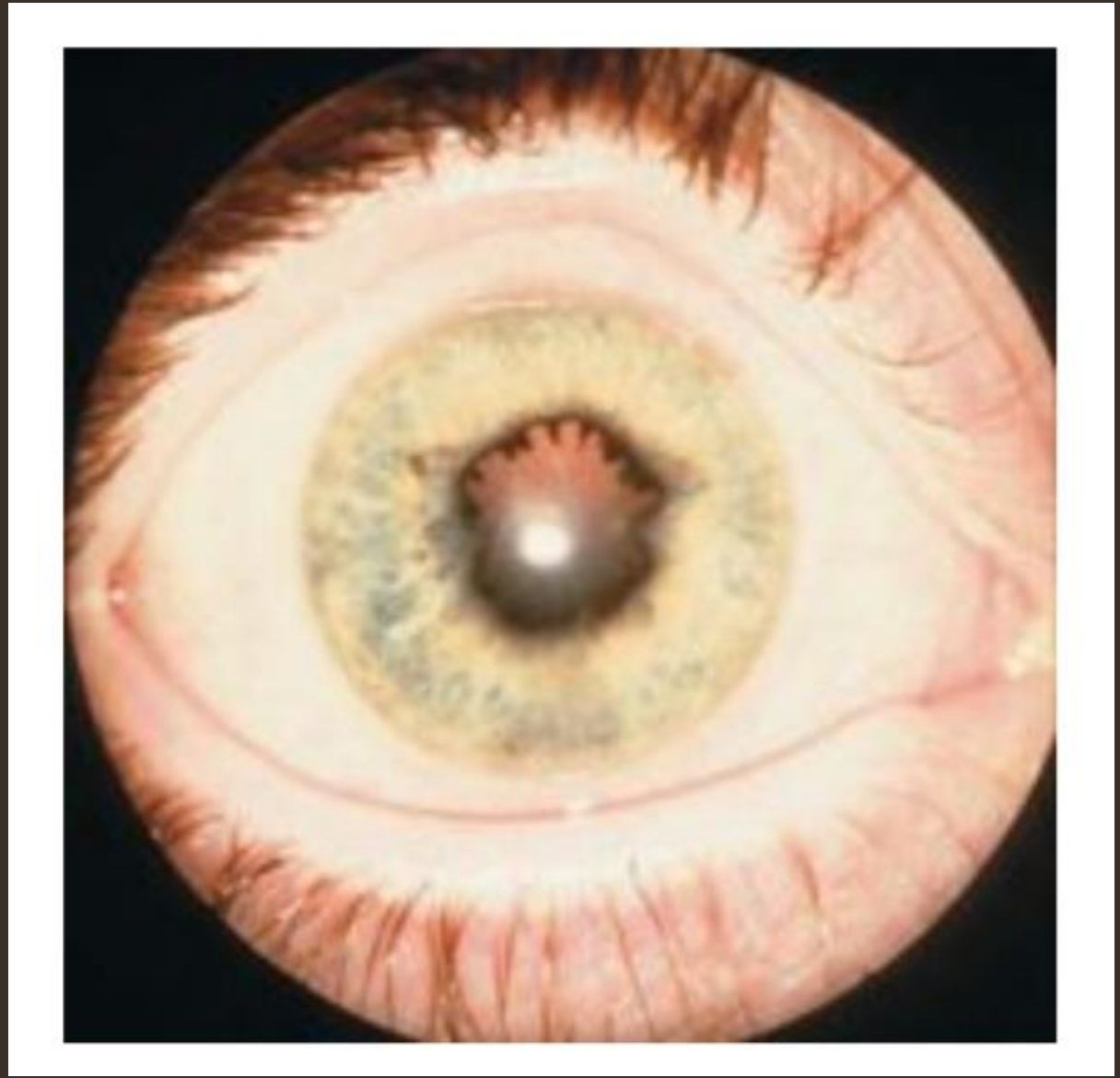
- Arthritis must be present ≥6 wk
- Arthritis is defined by intraarticular swelling or the presence of ≥2 of the following signs:
  - limitation in range of motion (ROM)
  - tenderness or pain on motion
  - warmth
- Initial symptoms may be subtle or acute
- morning stiffness
- gelling after inactivity
- Easy fatigability
- usually are not erythematous
- a discrepancy in limb lengths

Oligoarthiritis JIA

- defined as involving ≤4 joints within the 1st 6 mo of disease onset
- persistent oligoarticular JIA: in <4 joints after 6 months
- extended oligoarticular JIA in >4 joints after 6 mo & associated with a worse prognosis
- often non- symmetric and only a single joint is involved
- predominantly affects large joints & lower extremities, such as knees and ankles
- Isolated involvement of upper-extremity large joints less common
- Isolated involvement of hip almost never a presenting sign and suggests ERA or a nonrheumatic cause
- positive antinuclear antibody (ANA) test confers increased risk for asymptomatic anterior uveitis

ANA positivity may also be correlated with

- younger age at disease onset
- female sex
- asymmetric arthritis
- fewer involved joints over time



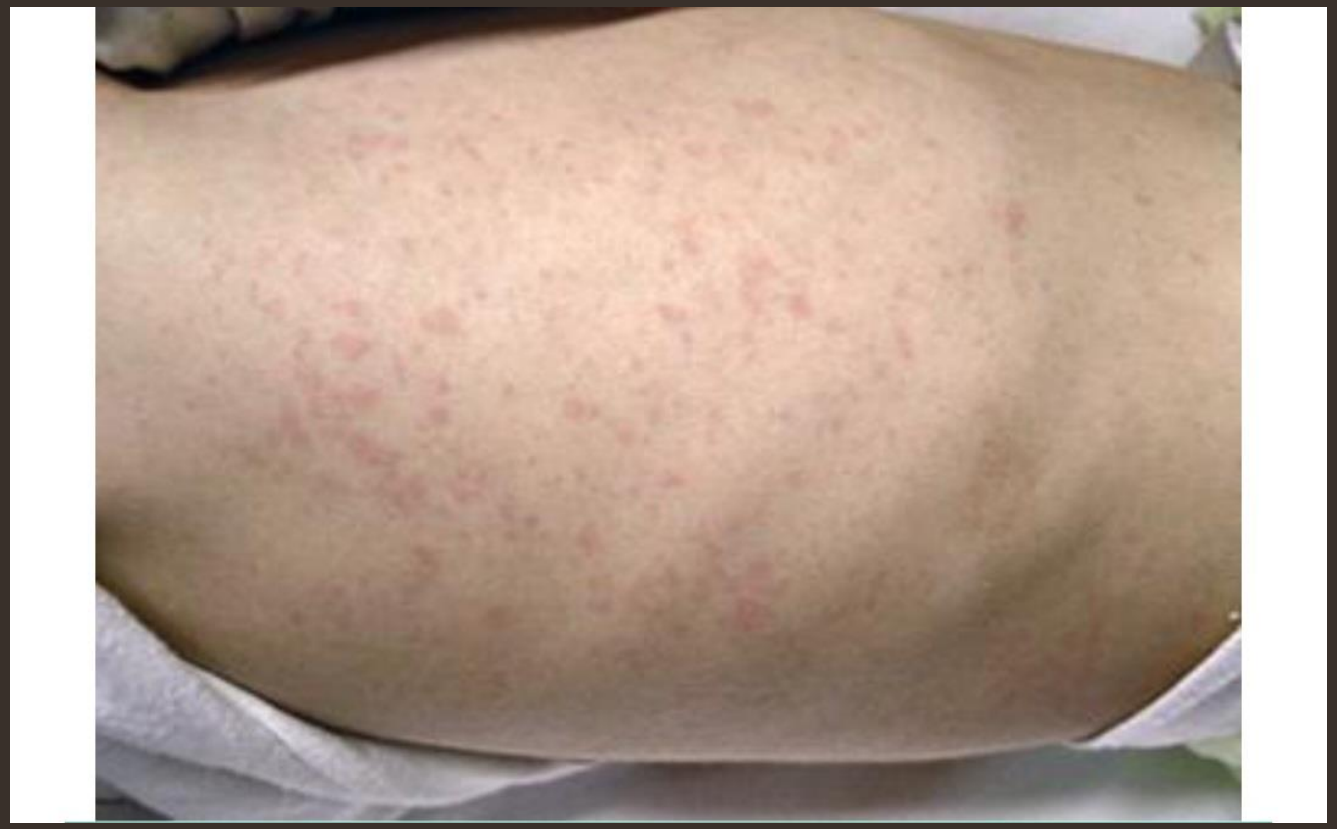
Poliarthritis JIA

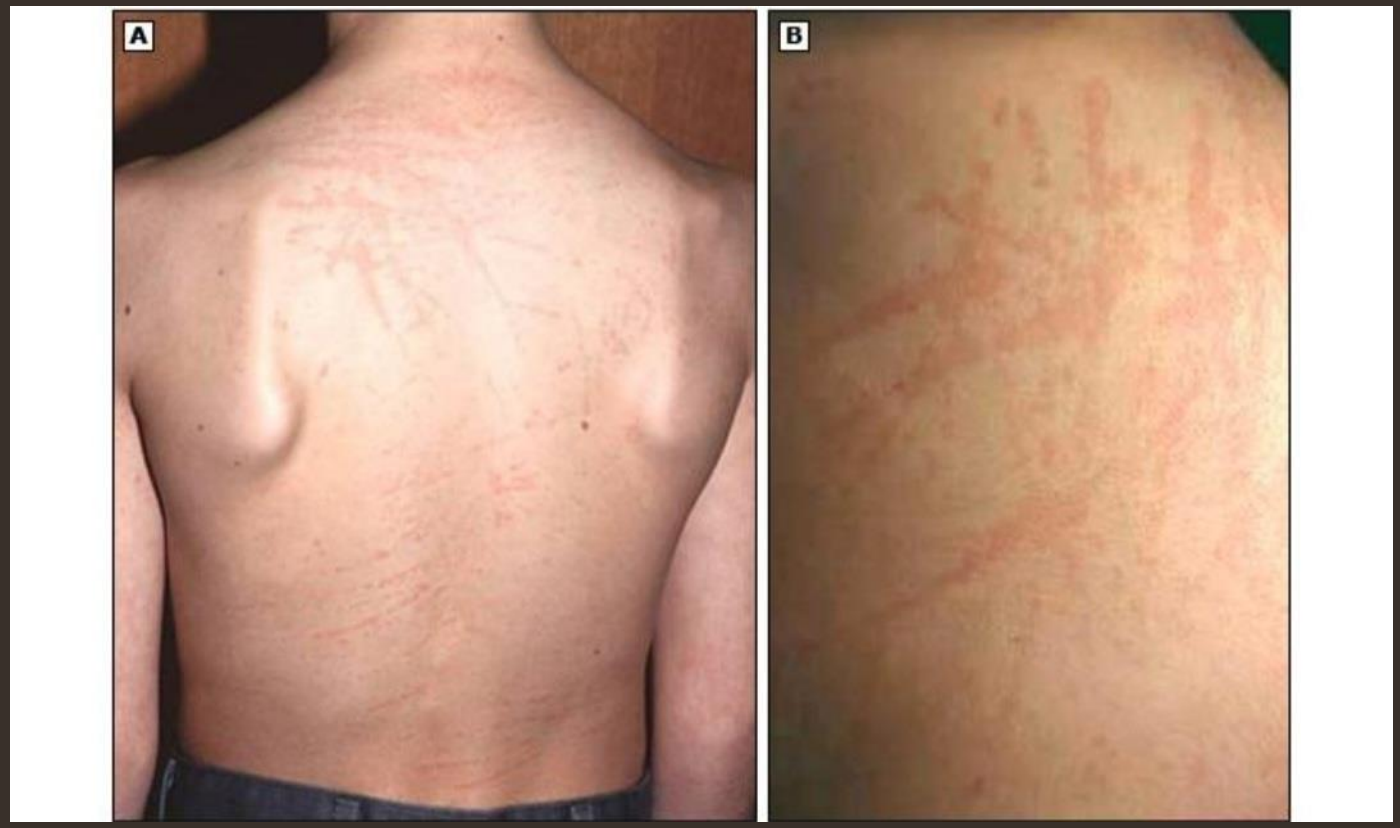
- characterized by inflammation of ≥5 joints in both upper & lower extremities
- Includes 2 types; RF-positive (15%) & RF-negative (85%)
- RF-positive polyarthritis (JRA) resembles the characteristic symmetric presentation of adult rheumatoid arthritis
- Rheumatoid nodules on the extensor surfaces of the elbows, spine and over the Achilles tendons, although unusual, are associated with a more severe course and almost occur in RF-positive individuals
- Micrognathia reflects chronic temporomandibular joint disease
- Cervical spine involvement occurs with a risk of atlantoaxial subluxation and neurologic sequelae

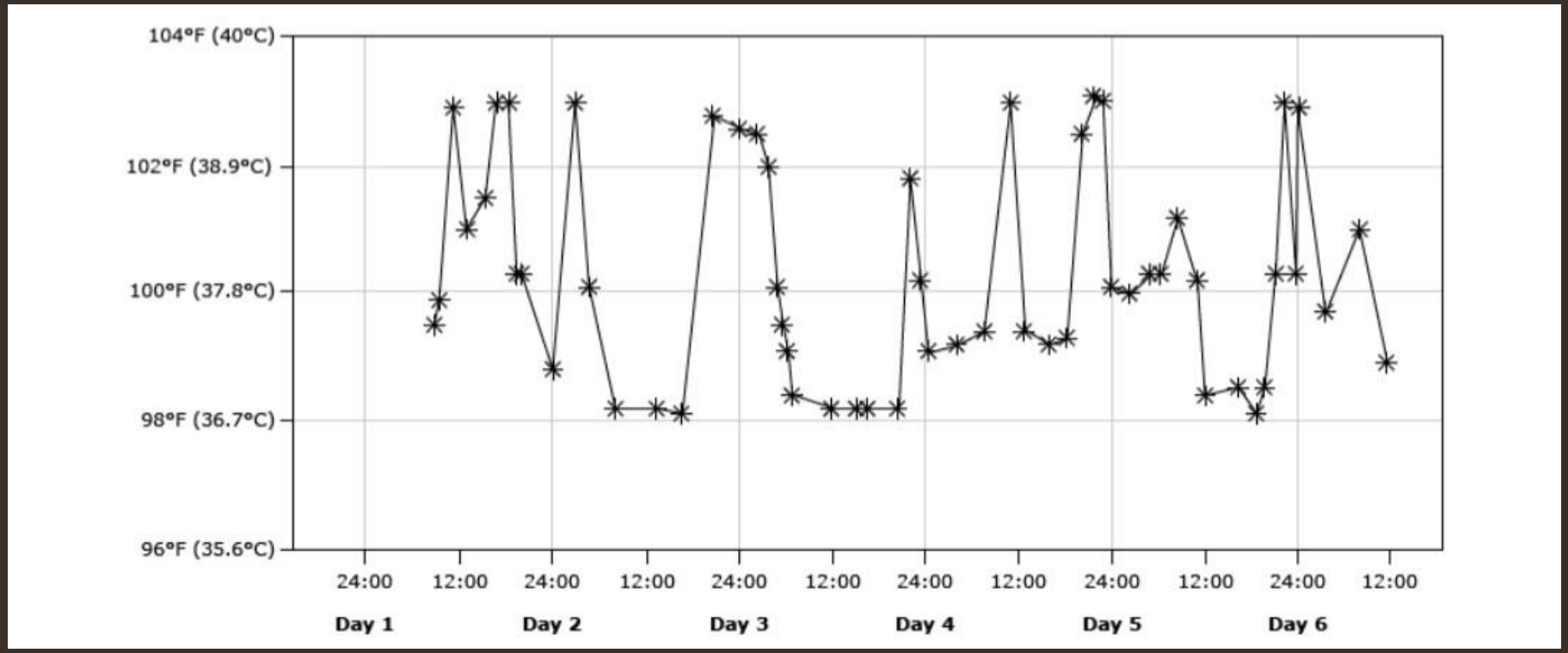
Systemic JIA

- characterized by arthritis, fever and prominent visceral involvement including : rash, hepatosplenomegaly, lymphadenopathy and serositis (pericarditis)
- characteristic fever, defined as spiking temperatures to ≥39°C (102.2°F), occurs on a daily or twice-daily basis for at least 2 wk, with a rapid return to normal or subnormal temperatures
- The fever is often present in the evening and is frequently accompanied by a characteristic faint, erythematous & macular rash

- The evanescent salmon-colored lesions, classic for sJIA, are linear or circular and usually distributed over the trunk and proximal extremities
- The classic rash is nonpruritic and migratory with lesions lasting <1 hr
- Koebner phenomenon , a cutaneous hypersensitivity in which classic lesions are brought on by superficial trauma, is often present. Heat can also evoke rash
- Fever, rash, hepatosplenomegaly, and lymphadenopathy are present in >70% of affected children.
- Arthritis may affect any number of joints, but the course is classically polyarticular, may be very destructive, and can include hip, cervical spine, and temporomandibular joint involvement




A
B


104°F (40°C)
102°F (38.9°C)
100°F (37.8°C)
98°F (36.7°C)
96°F (35.6°C)
24:00
12:00
24:00
12:00
24:00
12:00
24:00
12:00
24:00
12:00
24:00
12:00
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6

MAS(macrophage activation syndrome)

- rare but potentially fatal complication of sJIA that can occur at any time (onset, medication change, active or remission)
- also referred to as secondary hemophagocytic syndrome or hemophagocytic lymphohistiocytosis (HLH)
- There is increasing evidence that sJIA/MAS and HLH share similar functional defects in granule-dependent cytotoxic lymphocyte activity
- MAS classically manifests as acute onset of high-spiking fevers, purpura and mucosal bleeding, lymphadenopathy, hepatosplenomegaly and encephalopathy
- Laboratory evaluation shows thrombocytopenia and leukopenia with elevated liver enzymes, lactate dehydrogenase, ferritin and triglycerides as elevated. fibrin split product values and prolonged prothrombin and partial prothromboplastin times. ESR falls because of hypofibrinogenemia and hepatic dysfunction, a feature useful in distinguishing MAS from a flare of systemic disease

- classification criteria for sJIA-associated MAS, including hyperferritinemia (>684 ng/mL) and any 2 of the following:
  - ✓ thrombocytopenia (≤181 × 10 9 /L)
  - ✓ elevated liver enzymes (aspartate transaminase >48 U/L)
  - ✓ hypertriglyceridemia (>156 mg/dL)
  - ✓ hypofibrinogenemia (≤360 mg/dL)
- These criteria apply to a febrile patient suspected of sJIA and in the absence of disorders such as immune-mediated thrombocytopenia, infectious hepatitis, familial hypertriglyceridemia or visceral leishmaniasis.
- treatment includes high-dose intravenous methylprednisolone, cyclosporine or anakinra

spondyloarthrophay

- The diseases collectively referred to as spondyloarthritides include :
  - ankylosing spondylitis (AS)
  - Enthesitis related arthritis (ERA)
  - arthritis associated inflammatory bowel disease (IBD)
  - Psoriatic arthritis
  - reactive arthritis following gastrointestinal (GI) or genitourinary (GU) infections
- Many children with spondyloarthritis are classified in JIA categories of enthesitis-related arthritis (ERA) or psoriatic arthritis
- Children and adolescents with spondyloarthritis who may not meet JIA criteria include arthritis associated with IBD, JAS and reactive arthritis

Enthesitis Related Arthritis

- accounts for 10–20% of JIA and mean age at onset : 12 yr
- Unlike other JIA categories, males are affected more often than females, accounting for 60% of ERA cases
- These disorders can be familial, largely as a result of the influence of human leukocyte antigen (HLA) -B27 , which is found in 90% of JAS and 50% of ERA patients compared to 7% of healthy individuals
- Children have ERA if they have either arthritis and enthesitis or arthritis or enthesitis, with at least 2 of the following characteristics:
  - (1) sacroiliac joint tenderness or inflammatory lumbosacral pain
  - (2) presence of HLA-B27
  - (3) onset of arthritis in a male older than 6 yr
  - (4) acute anterior uveitis
  - (5) a family history of an HLA-B27–associated disease (ERA, sacroiliitis with IBD, reactive arthritis, or acute anterior uveitis) in a first-degree relative

- During the 1st 6 mo of disease the arthritis is typically asymmetric and involves ≤4 joints. most frequently the knees, ankles and hips
- Inflammation of the small joints of the foot or tarsitis is highly suggestive of ERA
- Enthesitis is typically symmetric and typically affects the lower limbs
- approximately 20% have evidence of sacroiliac joint arthritis at diagnosis. When the sacroiliac or other axial joints are involved, children may experience inflammatory back pain, hip pain and alternating buttock pain. Patients may also experience pain with palpation of the lower back or with pelvic compression
- The risk of sacroiliac joint arthritis is highest in children who are HLA-B27 positive
- Untreated sacroiliitis may, but does not always evolve into AS

Psoriatic arthritis

- approximately 5% of JIA.
- Common clinical features of psoriatic arthritis are nail pitting, onycholysis and dactylitis (sausage-like swelling of fingers or toes)
- Definition is based on arthritis and psoriasis or arthritis and at least 2 of the following:
  - ✓ dactylitis
  - ✓ nail pitting or onycholysis
  - ✓ psoriasis in a first-degree relative
- presence of psoriasis aids in diagnosis but is not required

- Disease onset peaks include :
  - ✓ during the preschool and are more often female, ANA positive and at risk for uveitis
  - ✓ early adolescent years equally common in males and females
- arthritis is asymmetric and affects ≤4 joints at presentation. Large (knees and ankles) and small (fingers and toes) joints may be involved
- Although distal interphalangeal joint involvement is uncommon, highly suggestive of the diagnosis
- Enthesitis is detectable in 20–60% of and seems to be more frequent in those who present at an older age
- Axial (sacroiliac) and root (hip) joints may be affected in up to 30% of children; risk of axial arthritis is highest in HLA-B27 positive

diagnosis

- JIA is a clinical diagnosis without any diagnostic laboratory tests. The meticulous clinical exclusion of other diseases and many mimics is therefore essential. Laboratory studies, including tests for ANA and RF, are only supportive or prognostic and their results may be normal in patients with JIA

Differential diagnosis

- Rheumatic diseases (SLE, JDM, PAN, Scleroderma, HSP, KD,…)
- Infection (bacterial, lyme, fungal, maycobacterial,…)
- Reactive arthritis (Acute rheumatic fever, PSRA, serum sickness, toxic synovitis,…)
- Malignancy (leukemia, neuroblastoma,…)
- Hematologic disorders (sickle cell anemia, hemophilia)
- Immunodeficiency (CVID, IgA deficiency,…)
- Congenital & metabolic disorders (MPS, gout, farber dis, fabry dis, hyper parathyroidism,…)
- Bone & cartilage disorders (trauma, perthes disease, bone tumors,…)
- Neuropathic disorders (peripheral neuropathy, CTS,…)
- Pain syndrome (fibromyalgia, growing pain, somatization, CRPS,…)

treatment

- NSAIDS
- Intra articular corticosteroids injection
- Systemic corticosteroids
  - ✓ Management of severe systemic illness
  - ✓ Bridge therapy wait response to a DMARDS
  - ✓ Control of uveitis
- DMARDS (methotrexate, leflunomide, sulfasalazine, …)
- Biologics (anti TNFa, anti IL1, anti IL6, …)
- Ensure appropriate calcium, Vit D, protein and caloric intake
- Physical therapy and occupational therapy

بیمار دختر ۳ ساله با تورم مفصل زانوی راست و مچ پای چپ از حدود سه ماه گذشته توسط همکار متخصص کودکان به درمانگاه روماتولوژی ارجاع داده شده است. والدین بیمار از لنگش بیمار صبحگاه حین بیدار شدن از خواب شکایت دارند که تا ظهر کاملا برطرف میشود. در ازمایشات همراه نکته خاصی ندارد. تست رایت و کومبس رایت هم انجام شده که منفی است. محتملترین تشخیص ؟

پسر ۲ ساله ای با تب طول کشیده از ۳ هفته گذشته که به گفته مادر تقریبا روزانه بوده در ساعات خاصی از جمله عصرها بیشتر اتفاق می افتد که همزمان بیمار بسیار بیحال و بیقرار میشود. در ازمایشات همراه لکوسیتوزیس ترومبوسیتوز و ESR و CRP بالا دارد. بیمار با این تابلو بستری و تحت مشاوره عفونی قرار میگیرد. پس از w/up کامل عفونی بجز هپاتواسپلنومگالی در سونوگرافی و پریکاردیت در اکوکاردیوگرافی نکته خاص دیگری یافت نشد. محتملترین Dx ؟

- پسر ۱۲ ساله ای با درد کف پاها به ویژه پس از بی حرکتی طولانی و لنگش به دنبال آن از ۲ ماه اخیر مراجعه کرده است. در شرح حال ذکر میکند که سال گذشته به دنبال درد و قرمزی ناگهانی چشم ها و ترس از نور به چشم پزشک مراجعه و مدتی از قطره های موضعی چشمی استفاده کرده است. در ازمایشات همراه بجز ESR بالا نکته خاص دیگری ندارد. از بیمار آزمایشات تکمیلی تر و سونوگرافی هر دو foot درخواست میشود. در سونوگرافی درخواستی تارسیت و افزایش اکو در محل اتصال آشیل گزارش شده است. محتملترین Dx ؟

Thanks