26th Annual General Pediatric Review & Self-Assessment

Nicklaus Children's Hospital

RHEUMATOLOGY

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Topics You Need to Know

1) Systemic Lupus Erythematosus*
2) Juvenile Idiopathic Arthritis*
3) Vasculitis Syndromes (focus on Kawasaki and HSP)*
4) Dermatomyositis
5) Scleroderma
6) Ankylosing Spondylitis
7) Reactive Arthritis and Post-infectious arthritis
8) Sarcoidosis
9) Hypermobility Syndrome
10) Functional Joint Complaints
11) Marfan's
12) Ehlers-Danlos

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Question 1

A 16-year-old girl comes to your office for a follow-up visit from the emergency department, where she went for the acute onset of knee pain and swelling. The emergency department physician had ordered an antinuclear antibody test, which was positive at 1:320. Further history reveals that she has had intermittent joint pains for several weeks and dark-colored urine. Findings on her physical examination are normal except for an effusion in her right knee. You decide that further evaluation for systemic lupus erythematosus (SLE) is warranted.

Of the following, the MOST specific test in helping you make the diagnosis of SLE is:

a) Lupus anticoagulant
b) Anti double stranded DNA antibody
c) Anti-Ro measurement
d) Complement measurement
e) VDRL (venereal disease research laboratory)

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A 14-year-old girl presents with a 2-month history of joint pain that is responding poorly to over-the-counter anti-inflammatory medications. She reports some sores in her mouth and mild swelling around her eyes and ankles. On physical examination, her temperature is 37.0°C, heart rate is 76 beats/min, respiratory rate is 14 breaths/min, and blood pressure is 130/86 mm Hg. She has oral ulcers, mild periorbital and pretibial edema, and mild swelling of her wrists and knee joints. Laboratory findings include:

- Sodium, 136 mEq/L (136 mmol/L)
- Potassium, 4.8 mEq/L (4.8 mmol/L)
- Chloride, 100 mEq/L (100 mmol/L)
- Bicarbonate, 22 mEq/L (22 mmol/L)
- Blood urea nitrogen, 24.0 mg/dL (8.6 mmol/L)
- Creatinine, 1.3 mg/dL (114.9 mcmol/L)
- Albumin, 2.5 g/dL (25.0 g/L)
- Hemoglobin, 10.1 g/dL (101.0 g/L)
- White blood cell count, 3.0x103/mcL (3.0x109/L)
- Platelet count, 190x103/mcL (190x109/L)
- Urinalysis: 3+ blood, 3+ protein, with 20 to 50 red blood cells/high-power field
- Antinuclear antibody titer: 1:1,280
- Anti-double-stranded DNA titer: 1:640

Of the following, the next BEST step in management is to:

A. Admit the patient for intravenous cyclophosphamide treatment
B. Initiate treatment with ibuprofen
C. order a 24-hour urine for protein collection
D. refer the patient for a renal biopsy
E refer the patient for bone marrow aspiration

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Systemic Lupus Erythematosus

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SYSTEMIC LUPUS ERYTHEMATOSUS

Clinical Manifestations

ACR Criteria (4/11 to meet criteria)

"A RASH POINTs MD"

- Arthritis
- Renal disease
- ANA positive
- Serositis
- Hematologic disorder
- Photosensitivity
- Oral ulcers
- Immunologic disorder
  - (dsDNA, Anti-Sm, Antiphospholipid Ab)
- Neurologic symptoms
- Malar rash
- Discoid rash

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SYSTEMIC LUPUS ERYTHEMATOSUS

Clinical Manifestations: Updated Criteria 2019

New EULAR/ACR criteria for the classification of SLE

Clinical domains	Points
Constitutional domain	
Fever	2
Cutaneous domain	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous or discoid lupus	4
Acute cutaneous lupus	6
Arthritis domain	
Synovitis or tenderness in at least 2 joints	6
Neurologic domain	
Delirium	2
Psychosis	3
Seizure	5
Serositis domain	
Pleural or pericardial effusion	5
Acute pericarditis	6
Hematologic domain	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Renal domain	
Proteinuria > 0.5 g/24 hr	4
Class II or V lupus nephritis	8
Class III or IV lupus nephritis	10

Immunologic domains	Points
Antiphospholipid antibody domain	
Anticardiolipin IgG > 40 GPL *or* anti-β2GP1 IgG > 40 units *or* lupus anticoagulant	2
Complement proteins domain	
Low C3 *or* low C4	3
Low C3 *and* low C4	4
Highly specific antibodies domain	
Anti-dsDNA antibody	6
Anti-Sm antibody	6

REFERENCE: Aringer et al. Abstract #2928. 2018 ACR/ARHP Annual Meeting

- ✓ Classification criteria are not diagnosis criteria
- ✓ All patients classified as having SLE must have ANA ≥ 1:80 (entry criterion)
- ✓ Patients must have ≥ 10 points to be classified as SLE
- ✓ Items can only be counted for classification if there is no more likely cause
- ✓ Only the highest criterion in a given domain counts
- ✓ SLE classification requires points from at least one clinical domain

@Lupusreference

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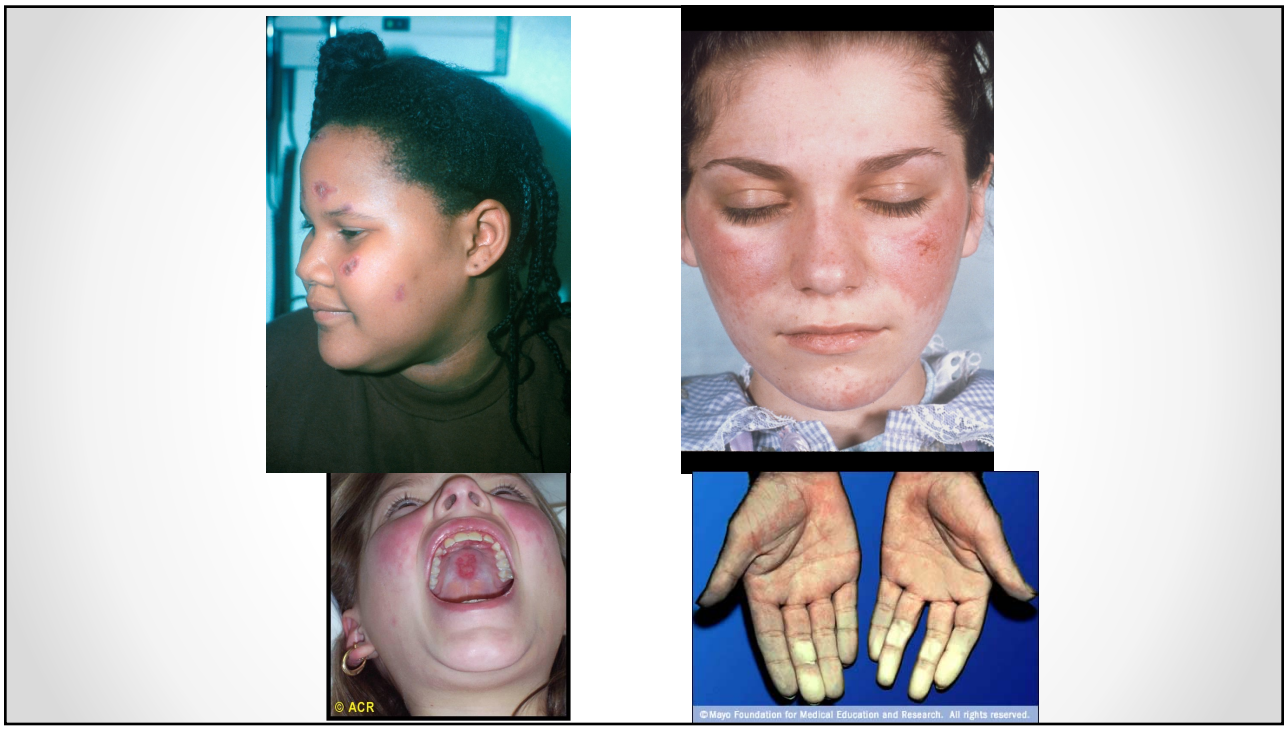

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SYSTEMIC LUPUS ERYTHEMATOSUS

Antinuclear Antibody (ANA) and SLE

- ANA test is almost 100% SENSITIVE, but NOT SPECIFIC
- Approximately 20-30% of healthy children can have positive ANA
- ANA's occur in other autoimmune conditions as well (JIA, scleroderma, Sjogren's, autoimmune thyroid disease)
- Anti dsDNA and Anti Sm tests are **SPECIFIC** for SLE

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SYSTEMIC LUPUS ERYTHEMATOSUS

Course and Complications

- Wide spectrum of severity based on organs involved
- Lupus nephritis is a common complication
  - Spectrum of severity
  - Multiple Classes of lupus nephritis (I-VI)
- Renal and Neurologic involvement tend to lead to the most morbidity
- Immunosuppression occurs from disease and medications
- Following anti-dsDNA and complement levels is helpful in disease management
  - C3 and C4 levels drop in active disease
- Treatment (immunosuppression) is based on systems involved and severity of disease
  - Hydroxychloroquine for essentially all patients
  - Prednisone +/- additional immunosuppressive meds based on severity

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NEONATAL LUPUS

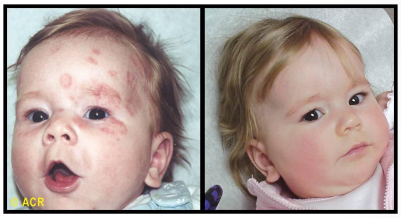
Maternal Anti-Ro (SSA), Anti- La (SSB)

↓

Cross placenta (IgG)

↓

Lead to inflammation/scarring

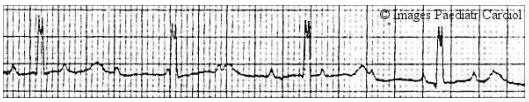


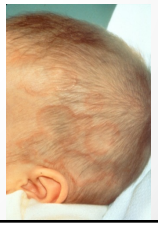
Clinical Manifestations:

Rash

Thrombocytopenia

Heart Block





Treatment:

Rash and Thrombocytopenia self resolve

Cardiac pacing for complete heart block

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You treat a 15-year-old girl in your practice who has juvenile idiopathic arthritis (JIA). She is brought in by her mother today with complaints of a low-grade fever and diffuse pain. On physical examination, she has a temperature of 38.0°C and a heart rate of 100 beats/minute. As she sits on the examination table, she leans forward. During auscultation of her lungs, she complains of pain with deep inspiration.

Of the following, the MOST likely explanation for her symptoms is:

a) Costochondritis
b) Gastritis
c) Pericarditis
d) Pneumonia
e) Pulmonary Embolism

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Juvenile Idiopathic Arthritis

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Juvenile Idiopathic Arthritis

Definition

- Arthritis of UNKNOWN ETIOLOGY
- Lasting 6 weeks or more
- Occurring in child <16
- Other causes investigated and ruled out

Differential Diagnosis

- Infectious arthritis
  - Septic Arthritis
  - Viral Arthritis
- Post infectious reactive arthritis
  - Acute Rheumatic Fever
  - Post Strep Reactive Arthritis
  - Reactive Arthritis (formerly "Reiters")
- Lyme disease
- Malignancy
  - Leukemia
  - Neuroblastoma
- Hemophilia
- Mucopolysaccaroidosis

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Juvenile Idiopathic Arthritis

TABLE 4
Synovial Fluid Findings

Findings	*Normal*	*Noninflammatory*	*Inflammatory*	*Septic*
Color	Clear	Yellow	Yellow to green	Yellow
Clarity	Transparent	Transparent	Opaque	Opaque
Viscosity	High	High	Low	Variable
WBC per mm^3	< 200	200 to 2,000	2,000 to 150,000	15,000 to 200,000
PMNs	< 25%	< 25%	> 50%	> 75%
Mucin clot	Good	Good	Good to poor	Poor

WBC = white blood cells; PMNs = polymorphonuclear cells.

Adapted with permission from McGahan JP, Shoji H. Knee effusions. J Fam Practice 1977;4:141–4.

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Juvenile Idiopathic Arthritis

JIA SUBTYPE	# joints involved	Distinguishing features
Systemic	any	Fever, rash, adenopathy, serositis, splenomegaly, cytopenias
Oligoarticular	4 or fewer	Younger age, female predominance, highest **UVEITIS** risk
Polyarticular	5 or greater	Slightly older age
Enthesitis Related	any	Male predominance, HLA B27 positivity, included ankylosing spondylitis, relationship with IBD
Psoriatic	Any	+/- psoriasis, dactylitis, spondylitis
Undifferentiated	any	Satisfies none or multiple categories

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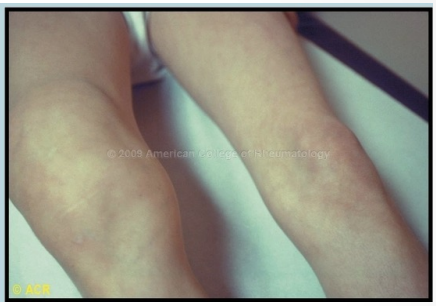
Other important causes of arthritis

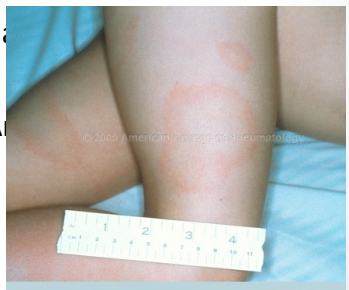
Lyme Arthritis

- **ALWAYS** on the differential of m
- Most commonly affects the kne
- Late manifestation of lyme disea
- Most likely will never have notic
- Understand early vs. late manife



Diagnosis based on serology with confirma

Treatment: 4 weeks antibiotics (Doxy or A



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Other important causes of arthritis

Acute Rheumatic Fever vs. Post Strep Reactive Arthritis

- Know JONES criteria!
- Very painful arthritis, can mimic septic arthritis
- VERY responsive to NSAIDs
- No debate about the importance of penicillin prohpylaxis

- Doesn't meet JONES criteria
- Less painful arthritis, more persistent, non-migratory
- NOT really responsive to NSAIDs
- Most people prophylax for some period of time

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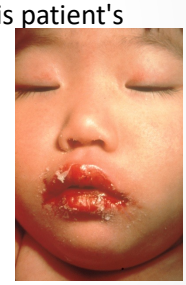
- An 18-month-old boy is brought to [illegible] irritability. His mother explains tha[illegible] week and a red rash on his extrem[illegible] has a temperature of 39.2°C; he is [illegible] without discharge (Item Q197A); and his lips are dry, red, and cracked (Item Q197B). All other findings are within normal limits.

Of the following, the MOST appropriate next step in this patient's care is to



A) administer intravenous antibiotics
B) administer intravenous gamma globulin
C) obtain blood cultures
D) obtain electrocardiography
E) perform a lumbar puncture and culture the cerebrospinal fluid

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Vasculitis

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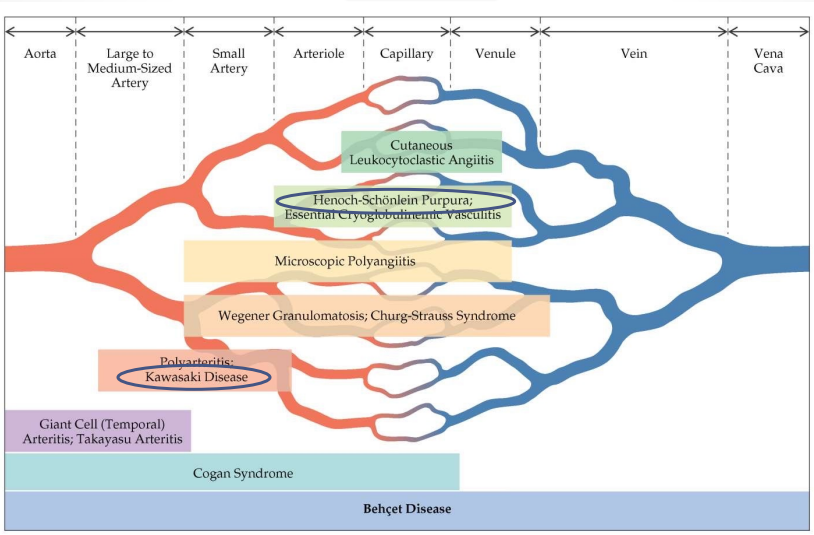
Vasculitis



HSP and Kawasaki:
-most common vasculitides in childood
-usually acute, self limited illnesses

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Kawasaki Disease

Clinical Manifestations:

Most commonly young child (toddler age)

Must have at least **5 days** of fever + 4/5:

- Cervical adenopathy (≥1.5cm)
- Mucous membrane changes (dry, cracked lips or "strawberry tongue")
- Conjunctivitis ("limbic sparing")
- Rash (basically any type)
- Extremity changes (edema, desquamation)

Lab findings:

- sterile pyuria
- Elevated acute phase reactants (can remain high for weeks)
- Thrombocytosis
- Leukocytsosis

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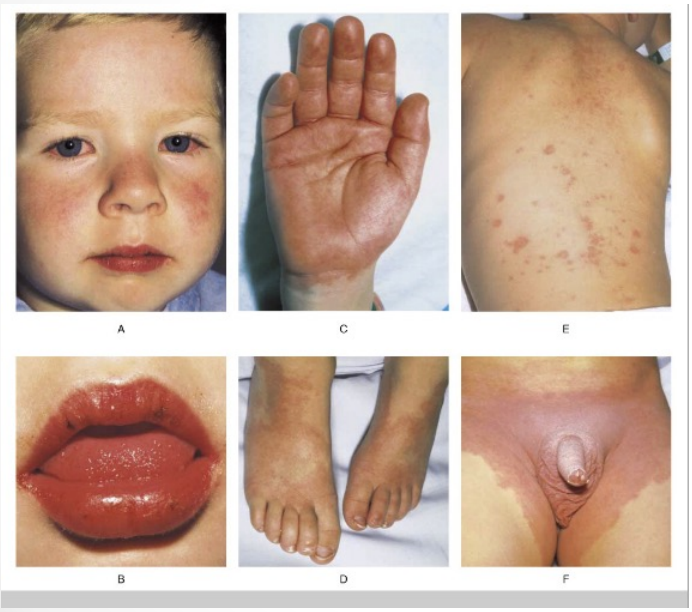
Kawasaki Disease



DDX:

- Infection
- Systemic JIA
- Immune/Drug reaction
- Serum Sickness
- Other vasculitis (PAN)

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Kawasaki Disease

Treatment:

Goals: avoid cardiac complications and calm ongoing inflammation
Don't need definitive diagnosis to start treatment
Ideally IVIG + Aspirin before within first 10 days of illness

- IVIG: 2mg/kg (can give repeat dose)
- Aspirin 80-100mg/kg/day for 24-48 hours
- Low dose aspirin (3-5mg/kg/day until ESR&CRP normalize)

Lifetime aspirin if coronary aneurysm present

ECHO: Baseline
Follow up at 2-3 weeks
Follow up at 6-8 weeks

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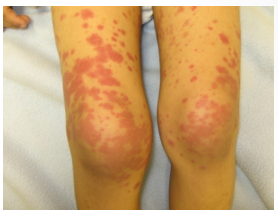
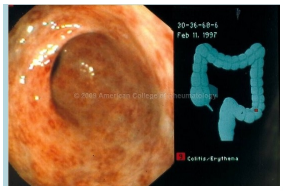
Henoch-Schonlein Pupura (HSP)

Clinical Manifestations:

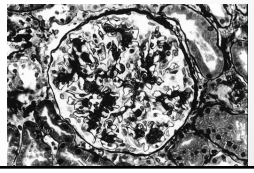


Skin:
- palpable purpura
- rash 1st feature only ¾ patients
- Lower legs/buttock mostly (dependent area)

Joints:
- Arthritis
- Arthralgia
- Periarticular swelling
- May refuse to ambulate, especially young kids



GI Tract:
- Abdominal pain*
- Intussusception: **ileo-ileal**
- Guaiac positive stool common



Renal:
- Microscopic hematuria +/- proteinuria
- Gross hematuria and nephrotic range proteinuria less common

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Henoch-Schonlein Pupura (HSP)

Diagnosis

- Usually clinical
- Skin biopsy
  - usually reserved for atypical presentation
  - IgA deposition in post-capillary venules
  - Pathology described as "leukocytoclastic vasculitis"

Treatment and Prognosis

- Mostly supportive care
- Hospitalization: severe abdominal pain or PO intolerance, severe joint involvement, intussusception or GI bleeding, severe renal involvement
- NSAIDs for pain control (unless severe GI or Renal involvement)
- Steroids reserved for significant abdominal pain (doesn't prevent renal disease
- Prognosis generally very good
- Small % patient go on to long term kidney disease
- Monthly BP checks and U/A for 6 month after diagnosis!

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Dermatomyositis

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Dermatomyosits

Clinical Manifestations:

- Typically school age child
- Skin findings:
  - Heliotrope rash "violacious rash to eyelids or face"
  - Gottron's papules "erythematous papules on extensor surfaces"
  - Nailfold changes
  - Lipodystrophy
- Proximal muscle weakness
  - Difficulty with stairs, brushing hair, getting on the bus
- Voice changes or dysphagia***
  - These are worrisome signs of pharyngeal muscle involvement
  - Risk of aspiration
- Calcinosis
  - Deposition of calcium substances in soft tissues

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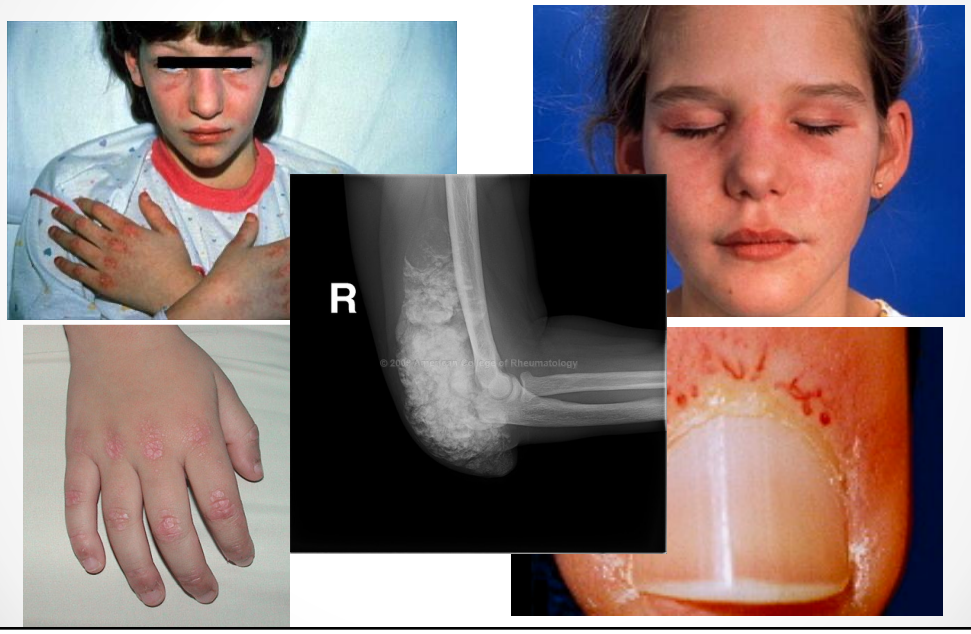
Dermatomyositis



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Dermatomyositis

Treatment:

- High dose steroids
- IVIG
- Methotrexate

Polymyositis vs Dermatomyositis : NO RASH in PM
Muscle sx very similar
PM super rare in kids

No increased risk of malignancy in juvenile dermatomyositis (like there is in adults)

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Scleroderma

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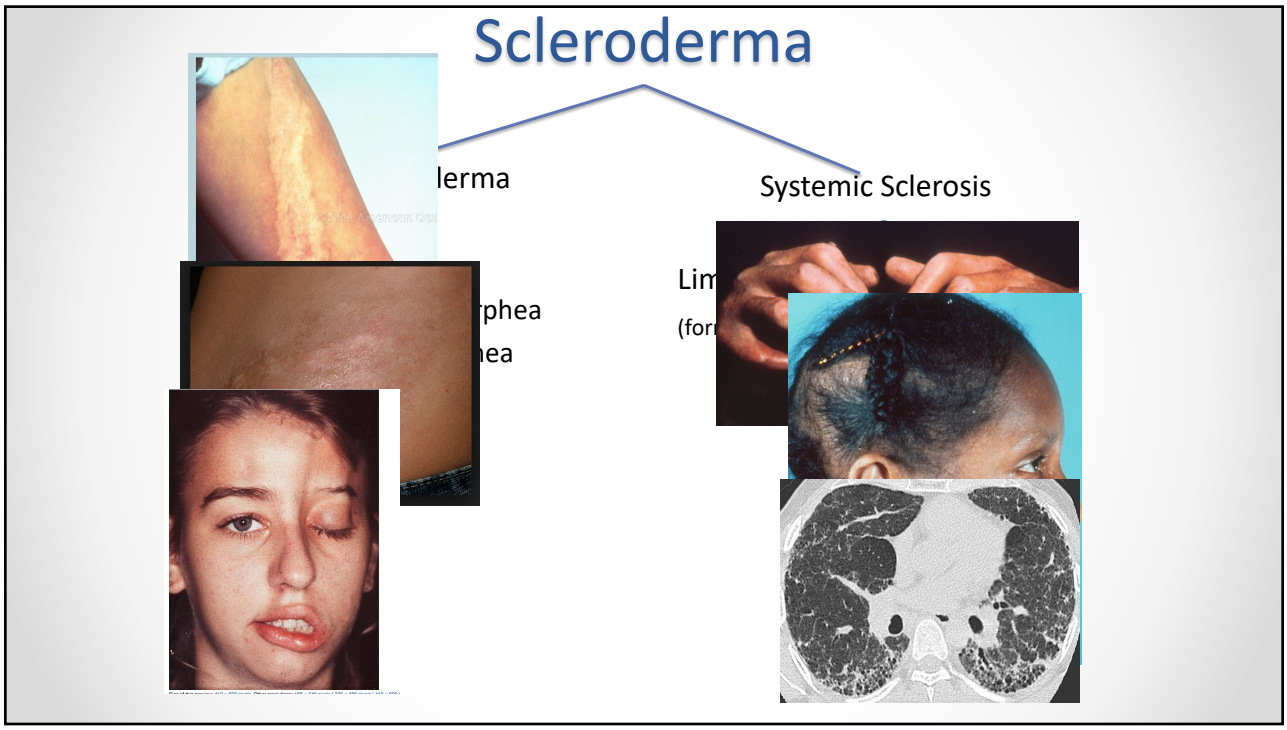

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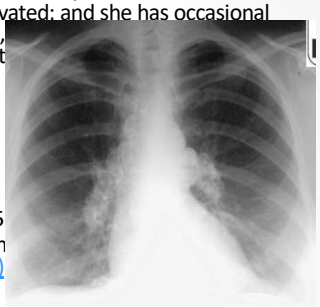
A previously healthy 11-year-old girl has had a dry hacking cough for 3 months associated with fatigue, occasional fevers (temperature of 38.4°C), and a 4-kg weight loss. On physical examination, the tired-appearing child has multiple firm, non-tender posterior cervical, axillary, and inguinal nodes; her respiratory rate is slightly elevated; and she has occasional wheezes. Small nodules are visible along the iris-pupil margin, recently diagnosed anterior uveitis. Laboratory findings of not



Hemoglobin, 10.9 g/dL (109 g/L)
White blood cell count, 16.0x103/mcL (16.0x109/L)
Erythrocyte sedimentation rate, 32 mm/hr
Calcium, 12.3 mg/dL (3.1 mmol/L)
Serum angiotensin converting enzyme, 110 units/L (normal, 5
A purified protein derivative test is negative. Chest radiograph adenopathy but no obvious parenchymal disease (Item Q227)

Of the following, the MOST useful test(s) for establishing the diagnosis is(are):

A) ANA and Rheumatoid Factor
B) Bone marrow biopsy
C) EBV serology
D) Immunofluorescence and ELISA for mycoplasma pneumonia
E) Lymph node biopsy

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Sarcoidosis

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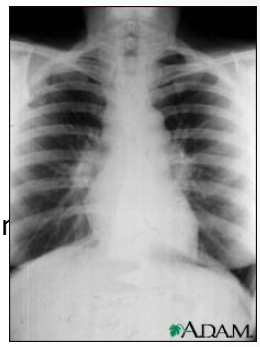
Sarcoidosis

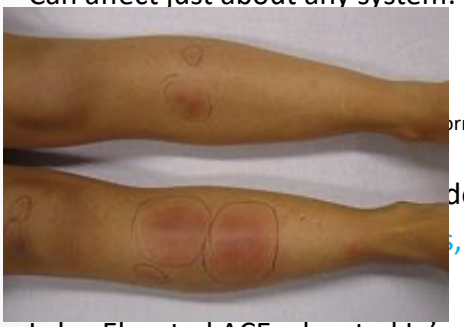
Systemic granulomatous disease

- Non-caseating granulomas

More common in African Americans

Can affect just about any system: Most commo



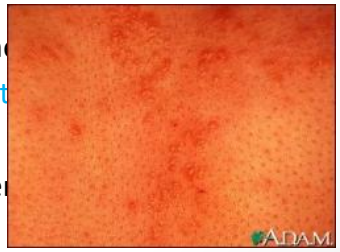


rmal PFT's

docrin

, uveit

Labs: Elevated ACE, elevated Ig's, hype



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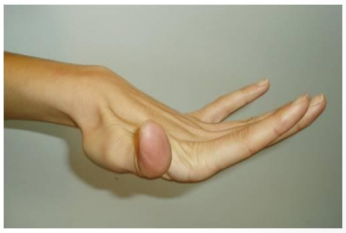
A 3-year-old boy is brought to the clinic by his parents due to concerns about how easily he bruises. They say that since he began walking at 18 months, he frequently has large, purple bruises that appear with no known history of trauma. They do not believe that he falls more frequently than other children his age, and they deny a family history of easy bruising. On physical examination, the normally grown child has prominent eyes, a delicate and narrow nose, and numerous bruises in various stages of healing, primarily overlying his shins but also scattered elsewhere on his body. He has translucent skin over the chest, with prominent vascular markings, and his fingers are slender and hypermobile (Item Q39B).

Of the following, the condition that is MOST consistent with this boy's features is

A) Ehlers Danlos
B) Hemophilia A
C) Von Wilibrand disease
D) Stickler's
E) Marfan's



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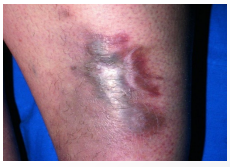
Ehlers Danlos

- Multiple subtypes
- Etiology: genetic defects in collagen or collagen modifier genes
- Clinical Features:
  - Joint hypermobility
  - Skin extensibility
  - Wide atrophic scars ("cigarette paper scars")
  - Easy bruising

- Diagnosis
  - Genetic testing
  - Collagen analysis (skin biopsy)



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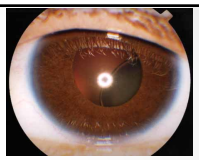
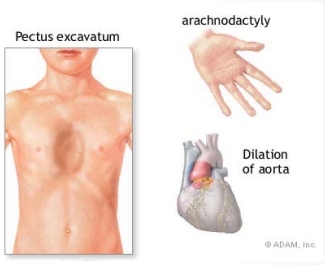
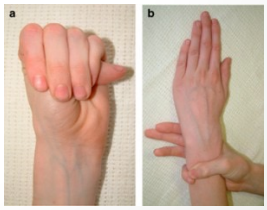
Marfan Syndrome



- Variable severity
- Etiology: genetic defects in Fibrillin 1 gene
  - Fibrillin 1 expressed in skin, heart, muscle, cornea, bone, lungs, kidney and vasculature
- Clinical Features:
  - Tall stature
  - Joint hypermobility
  - Kyphoscoliosis
  - High arched palate
  - Lens dislocation (ectopia lentis)
  - Pectus carinatum or excavatum
  - *Cardiac*: aortic root dilation, MV prolapse, conduction defects
  - Skin: striae
- Diagnosis:
  - clinical scoring system
  - genetic testing





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A 6-year-old boy complains of achy pain in his lower legs about 1-2 times per night per week that is relieved with massage and heat. He has had no fever, rash, fatigue, joint swelling, weight loss, or other systemic symptoms. The pain is always better in the morning, and he remains very active. He has had no unusual or compulsive leg movements associated with the pain. Findings on physical examination, including thorough joint, muscle, and neurologic evaluation, are normal.

Of the following, the MOST appropriate next step in the care of this child is to:

A) Obtain a bone scan
B) Obtain CBC,ESR,RF
C) Prescribe Calcium and Vit D
D) Prescribe muscle stretching, analgesia and warmth
E) Refer to orthopedist

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What if the question said he gets pain in one leg, worse at night that sometimes wakes him from sleep and is always relieved with an NSAID?

Think osteoid osteoma

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Benign Causes of Joint Pain

- Joint complaints are very common in childhood
- 85% of children asked at a well visit will say they have joint pain
- Always look for red flags: night waking, unilateral pain, no relief with simple measure, growth disturbance

Think of:

- Hypermobility syndrome
- "Benign joint pains"
- Growing pains

Usually reassurance to child and parent that it will improve with time if sufficient treatment. PRN NSAID ok too.

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