Pediatric Rheumatology: A Cased-Based Approach

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Disclosures

- I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity.
- I am not discussing any off-label uses of medications.
Outline

- Review more common rheumatologic and non-rheumatologic joint disorders
- Review laboratory testing in each disorder
- Discuss therapy for common disorders and the potential complications of that treatment
- See pictures of my kids at Disney
The “Five” Pediatric Rheumatology Disorders

- Juvenile Arthritis
- Systemic Lupus Erythematosus
- Juvenile Dermatomyositis
- Scleroderma (localized and systemic)
- Vasculitis
Case One

- A 14-year-old male presents to the local ER in September with complaints of headache for one week. He also notes some weight loss, rash on his face, and diffuse joint pain.
- Exam reveals a tired-appearing male with a pulse of 122, blood pressure 186/96, resp rate 16, temp 36.7
Case One (continued)

- Facial rash
- Diffuse joint swelling
- UA reveals blood, protein, and red cell casts
Systemic Lupus Erythematosus

- **Incidence/Prevalence**
  - 0.53-0.6 per 100,000 incidence
  - approx 5-10,000 cases in US

- **Approximately 15% present before age 16**
  - rare < 5 years, ↑ in freq through adolescence**

- **Gender**
  - 0-9 years, 4:3 F:M
  - 10-14 yrs, 4:1
  - 15-19 yrs, 5:1
Etiology of SLE

- **Hormonal**
  - Female predominance
  - Role of estrogen
- **Genetic**
  - Twin studies
  - Ethnic/racial predispositions
- **Environmental**
SLE Pathogenesis

- Immune system activation
- Absence of T lymphocytes
- Unchecked B lymphocyte activity
  - Increased polyclonal antibody production
  - Production of pathologic antibodies
- Immune complex formation
- IC trapped in small vessels with subsequent inflammatory response
Clinical Manifestations of SLE**

Mucous Membranes

- Frequency 12%
- Mouth ulcers
- Nasal ulcers

large mouth ulcer
Clinical Manifestation of SLE**

- **Musculoskeletal (72%)**
  - arthralgias/arthritis
  - myalgias/myositis

- **Serositis (30-40%)**
  - pericarditis
  - pleuritis
  - peritonitis

- **Cardiovascular (15%)**
  - raynaud’s phenomenon
  - myocarditis/endocarditis
Clinical Manifestations of SLE**

- Renal (82%)
  - proteinuria
  - casts

- Neurologic (44%)
  - seizures
  - psychosis
  - Depression

- Hematologic (50%)
  - Bleeding/bruising
  - Petechiae
Clinical Manifestations of SLE**

- **Non-specific (100%)**
  - malaise
  - fever
  - weight loss

- **Cutaneous (80-95%)**
  - malar rash
  - discoid LE
  - subacute cutaneous LE
  - photosensitivity
Malar Rash

- Raised, not flat
- Spares nasal-labial fold
- Can occur on nose, forehead, chin, or chest
- Does not scar
Discoid Lupus

- Raised
- Erythematous... inflammatory!
- Causes scarring
- Hyper- or hypo-pigmentation
- Can occur anywhere
- If in scalp, causes permanent alopecia
Discoid Lupus: Histopathology

normal

discoid
Laboratory Testing in SLE**

- Cytopenias
  - hemolytic anemia
  - leukopenia/lymphopenia
  - thrombocytopenia
- Antinuclear antibodies
- Anti-DNA antibodies
- Extractable Nuclear Antibodies (Ro, La, Sm, RNP)
- Complement
Antinuclear Antibodies

- Antibodies directed against nuclear (?) proteins

- Procedure
  - substrate (HEp-2, tissue)
  - indirect immunofluorescence
  - semi-quantitative
  - qualitative by pattern
  - limitations
Antinuclear Antibodies
Specificity of ANAs: Children**

- 1369 children with ANAs performed, 41% positive
- 699 children with known disease, 65% were positive
- at titer of 1:40, screen has sens of 0.63, PPV of 0.33 for predicting rheum disease
- for rheum dz, high sens 0.98, low PPV of 0.10
- ROC curves demonstrated that only titers >1:1280 to be associated with higher frequency of rheum disease

Malleson et al. Arch Dis Child 1997
Antibodies to DNA

- Single stranded versus double stranded
- Procedure
  - Farr (ELISA)
    - can be contaminated with ssDNA
    - higher false positive rate
- Correlation with disease activity**
Complement

- Hypocomplementemia in SLE**
- Qualitative measures: CH50
- Quantitative measures: C3, C4
- Other sources of hypocomplementemia
  - congenital deficiencies
  - chronic antigenemia
    - hepatitis
    - subacute bacterial endocarditis
    - parisitemia
  - glomerulonephritis
Criteria to Diagnose SLE

- 2012 SLICC Criteria versus 1997 ACR criteria
- Require presence of both clinical and immunologic abnormalities
- Both require at least 4 criteria**
  - SLICC includes at least 1 clinical and 1 immunologic
- SLICC includes renal-isolated lupus and more neuro features
ACR Criteria for SLE 1997: Clinical

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulceration
- Arthritis
- Serositis
- Renal
- Neurologic (seizures or psychosis)
- Hematologic (hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia)
ACR Criteria 1997: Laboratory

- Positive ANA
- Positive immunoserology
  - ds DNA antibodies
  - Sm antibody
  - Antiphospholipid Ab

- 4 of 11 criteria sensitivity of 83%, specificity of 96%
SLICC Criteria for SLE 2012: Clinical

- Acute cutaneous lupus
- Chronic cutaneous lupus
- Oral or nasal ulceration
- Non-scarring alopecia
- Synovitis
- Serositis
- Renal
- Neurologic involvement (seizure, psychosis, mononeuritis multiplex, nyelitis, neuropathy, acute confusional state)
- Hemolytic anemia
- Leukopenia or lymphopenia
- Thrombocytopenia
SLICC Criteria 2012: Laboratory

- Positive ANA
- Anti-ds DNA antibodies
- Anti-Sm antibody
- Antiphospholipid Antibodies (lupus anticoagulant, false-positive RPR, anticardiolipin antibodies, anti-beta 2-glycoprotein I)
- Low complement (low C3, low C4, low CH50)
- Positive direct Coombs’ test without a hemolytic anemia

4 of 11 criteria sensitivity of 97%, specificity of 94%
SLE: Treatment**

- Corticosteroids
  - Oral
  - Intravenous
- Hydroxychloroquine (Plaquenil)
- Methotrexate
- Mycophenolate Mofetil
- Cyclophosphamide
- Other
  - Calcium
  - Vitamin D
Complications of Treatment**

- Growth failure
- Fertility/amenorrhea
- Osteoporosis
- Body image
  - weight gain
  - cushingoid appearance
  - acne
Case Two

- An infant is born at 40 weeks EGA to a 32-year-old G1P0-1 female without significant prenatal care.
- The infant has a pulse of 40 and a diffuse, erythematous rash on her face and extremities
- Labs demonstrate a platelet count of 35K and elevated AST and ALT
- Rhythm strip demonstrates the following:
Case Two
NLE: Clinical Manifestations**

- Cutaneous manifestations (50%)
  - resemble SCLE
  - papulosquamous vs annular
  - timing of development, ?photosensitivity
  - typical on face or scalp
  - transient
Placental physiology and Ig

- Placenta able to traffic Ig after week 6
- Levels increase after week 17, rise until delivery
- Heart development recognizable by week 6
- Conduction system by week 8, AV node by week 8
- Conduction system mature by week 16
- Antibodies (Ro/La) cross the placenta and bind to the developing conduction system
NLE: clinical manifestations

- Cardiac: complete heart block (53%)**
  - occurs between 16-24 weeks EGA
  - irreversible
  - most detected on routine prenatal US (81%), but may present after neonatal period
  - incidence 1/15,000 to 1/22,000 live births, NLE approx 90% of cases
NLE: Clinical Manifestations**

- Liver disease (15%)
  - hepatomegaly +/- splenomegaly
  - cholestasis
  - elevated transaminases
  - portal fibrosis

- Hematologic abnormalities (>10%)
  - thrombocytopenia
  - anemia
  - neutropenia
NLE: Clinical Manifestations

➢ Other findings
  ● myelopathy
  ● aseptic meningitis
  ● hypocalcemia
CCHB in NLE: treatment

- **During pregnancy**
  - role of hydroxychloroquine
  - role of corticosteroids
    - if hydrops present
    - 2nd degree heart block
  - role of plasmapheresis
  - intrauterine pacing

- **After pregnancy: cardiac pacing**

- Outcomes depend on cardiac function
Case Three

- A two-year-old female is brought to your office by her mother who reports that the patient was running in the front yard and fell and the mother, upon picking her up, noticed that the right knee was swollen and is worried that “something is broken”
- Exam reveals a large effusion, widening of the surrounding bones, and you are unable to fully extend the knee on range of motion
Basic Questions to Ask

- Acute or Chronic?
- Localized to joints or more systemic features?
- Fever or not?
- Actual arthritis or arthralgias? (i.e., evidence of inflammation?)
- Complaints proportionate to physical findings or not?
Juvenile Idiopathic Arthritis (JIA)
(FKA Juvenile Rheumatoid Arthritis)

- Most common childhood arthritis**
- Occurs in 1:1000 children
- Affects children of all ages, but two peaks, at age 1-2 and age 8-12
JIA: Diagnosis**

Evidence of joints inflammation
- redness
- swelling
- limitation of range of motion
- pain
Duration of Arthritis > 6 weeks
Age at onset < 16 years
JIA: Evidence of Chronicity

- Synovial thickening
- Bony proliferation
- Contracture
- Limb length discrepancy
Classification of JIA

- **Oligoarticular JIA**
  - involvement of <5 joints

- **Polyarticular JIA**
  - involvement of >/= 5 joints
  - RF positive vs. RF negative

- **Systemic JIA**
  - presence of systemic inflammation

- **Juvenile Spondyloarthopathies**
  - Juvenile ankylosing spondylitis
  - Juvenile psoriatic arthritis
  - Inflammatory bowel disease-related arthritis
  - Reactive Arthritis (FKA Reiter’s syndrome)
Oligoarticular JIA: Clinical Features

- Less than 5 joints
- Typically affects medium to large joints
- Asymmetric
Polyarticular JIA: Clinical Features

- 5 or more joints affected
- Typically affects small to medium joints, but can include large joints
- Symmetric
- Other less common joints
Polyarticular JIA: Other Features

Temporomandibular Joint

Cervical Spine Involvement
Systemic JIA (aka Still’s Disease)

- Think of it as a systemic inflammation that **precedes** the onset of arthritis
  - typical fever curve**
    - daily or diurnal temperature spike over 39°C
    - returns quickly to below baseline
    - child feels well between temperature spikes
Systemic JIA (aka Still’s Disease)

- Characteristic rash**
  - occurs frequently at peak of fever
  - erythematous macules on trunk and proximal extremities
  - migratory and evanescent
Still’s rash
Koebner’s Phenomenon (dermatographia)

- Isomorphous reaction in which skin lesions appear at the site of trauma.
Systemic Onset JIA (Cont’d)

- Signs of visceral involvement**
  - hepatomegaly
  - splenomegaly
  - lymphadenopathy
  - serositis
    - pleuritis
    - pericarditis, including pericardial effusions
    - peritonitis
- No peak age of onset
- No gender predilection
Laboratory Testing in JIA**

- Evidence of systemic inflammation
  - white blood cell count
  - red blood cell count
  - platelet count
  - erythrocyte sedimentation rate
  - C reactive protein
  - serum proteins

- Antinuclear antibodies

- Rheumatoid factors
Rheumatoid Factors

- Antibodies directed against the Fc portion of another antibody
- Rheumatoid factors are **negative** in children with JIA
- Rheumatoid factors are **positive** in adolescents and adults with rheumatoid arthritis
- Most common reason for child to make a RF is **infection**.
ANAs in JIA

- Frequency varies from 24-66% overall
- Highest frequency in patients with young (<7yrs), female
- Highest prevalence in patients with oligoarticular JIA and uveitis**
- BUT…up to 20% false positive rate, especially with Hep-2 substrate
Case Four

- 6 year old male presents with several weeks of fever, malaise, bilateral leg pain and refusal to bear weight
- Physical exam shows ill-appearing child with no obvious physical findings, except for significant pain on range of motion of the right leg
- Laboratory testing shows Hgb 7.0, WBC 6.2, and ANA (+) at 1:1280
Laboratory Studies for Critical Exclusions

- Joint fluid analysis
  - if acute presentation, must exclude septic arthritis
- Complete blood count
  - try to exclude hematologic malignancy
- Serologic testing for Lyme
- Radiography
  - may show peri-articular osteopenia
  - may demonstrate other abnormalities, including osteomyelitis or bone cancer
Goals of therapy for JIA**

- Control of pain and inflammation
- Preservation and improvement of function
- Prevention of disability and chronic deformity
Pharmacologic Therapy for JIA**

Anti-inflammatory agents
- NSAIDs
- ASA
- [corticosteroids]

Disease-modifying agents
- hydroxychloroquine
- methotrexate
- sulfasalazine
- biologics (etanercept, infliximab, adalimumab, etc.)
- anakinra
Complications of JIA: Uveitis

- Inflammation of the iris, ciliary body, and choroid
- Tends to be asymptomatic in children
- Screening in required for all children with chronic arthritis
- Number One treatable cause of blindness in children
Acute Uveitis
Complications of JIA**

- Musculoskeletal Deformity
  - Regular stretching program
  - Splinting or bracing
  - Regular physical exercise

- Constitutional Growth Delay

- Macrophage Activation Syndrome (HLH)
Complications of JIA: MAS**

- Massive outpouring of IL-1 leading to uncontrolled activation of T lymphocytes and macrophages
- Leads to cyopenias, liver dysfunction, hepatosplenomegaly, lymphadenopathy, bleeding diathesis
- Labs show ↓ counts, ↑ ferritin, ↑ transaminases, ↑ triglycerides, bone marrow can demonstrate hemophagocytosis
- Treatment: steroids, anakinra (IL-1 RA), cyclosporine
- High morbidity/mortality
Outcome in JIA

- Remission rates 70-85% within 2-5 years**
  - oligoarticular >90%
  - polyarticular ~50%
  - systemic <50%

- After disease, all that’s left is chronic deformities and visual disturbance previously untreated
A Collection of Diseases

- Juvenile Ankylosing Spondylitis (JAS)
- Juvenile Psoriatic Arthritis (JPsa)
- Inflammatory Bowel Disease-related arthritis
- Reactive Arthritis

- Seronegative Enthesopathy Arthropathy Syndrome (SEA)
What’s in a name?

“spondyloarthropathy”
- spondylo = spine
- arthro = joint
- pathy = illness/disease

commonalities
- axial skeletal involvement
- peripheral joint involvement
- extra-articular manifestations
- lack of RF “seronegative”
- familial predilection
Case Five

- A 15-year-old male presents with complaints of back pain for the last several months, particularly when he plays sports and in the mornings.
- Physical exam reveals loss of lumbar lordosis and decreased forward flexion, but no localizing areas of back tenderness. He also has bilateral knee effusions.
Juvenile Ankylosing Spondylitis

- Onset age < 16 years
- Characterized by inflammatory arthritis of peripheral and axial joints**
- Enthesitis
- Hereditary basis (HLA-B27)
- Absence of RF or ANA**
- Extra-articular manifestations**
JAS: Epidemiology

- Incidence and prevalence
  - underdiagnosed in the pediatric age group
  - current estimates about 10% pediatric arthritis (probably low)
  - 10% of adult AS onset < 17 years of age = prevalence of approx 80 per 100,000 (almost equal to JIA)
- Age of onset: 10-16 years**
- Gender predilection: M:F = 7:1
- Genetics: ~90% HLA-B27 (+)
JAS: Clinical Manifestations**

- **Leg/buttock pain**

- **Arthritis**
  - Peripheral arthritis more common than axial arthritis on presentation (82% vs 24%)
  - lower extremity > upper extremity
  - usually oligoarticular

- **Enthesitis**
  - heel pain, foot pain; swelling at insertion site
  - not found in JRA
Enthesitis
JAS: Extra-articular Manifestations**

- **Iritis**
  - red, painful eye with photophobia
  - not associated with disease flare
  - recurrent, non-scarring
  - more common in kids

- **Cardiac (aortic insufficiency) - rare**
JAS: Diagnosis

- Physical Exam
  - peripheral arthritis
  - enthesitis
  - axial skeleton
    - utility of Schober’s exam

- Labs
  - HLA-B27

- Radiography**
  - LS spine
  - dedicated SI joints films
  - MRI
Sacroiliitis
JAS: Prognosis

- Peripheral joint arthritis common, but remitting. Prognosis correlates with persistence of peripheral arthritis
- Eventual axial skeletal involvement in almost 100%
- Tends to be milder than the adult form
Case Six

- A 15-year-old male presents with complaints of back pain for the last several months, particularly when he plays sports and in the mornings.
- Past medical history is unremarkable except for a history of psoriasis diagnosed at age 10.
- Physical exam reveals loss of lumbar lordosis and decreased forward flexion, but no localizing areas of back tenderness. He also has bilateral knee effusions.
Juvenile Psoriatic Arthritis

- Onset age < 16 years
- Characterized by inflammatory arthritis
- Presence of psoriasis before, during, or after onset of arthritis**
JPsa: Epidemiology

- Incidence and prevalence
  - underdiagnosed in the pediatric age group
  - approximately 3% of juvenile chronic arthritis, but may be up to 10%
  - 1-2% of adults develop psoriasis, approx 5% have psoriatic arthritis
- Age of onset: 7-11 years
- Gender predilection: F>M
- Genetic predisposition
JPsa: Clinical Manifestations**

- Arthritis
  - asymmetric oligoarthritis of small and large joints
    - may look just like JIA
    - single isolated small joint JPsA>JIA
  - dactylitis
  - other forms of psoriatic arthritis much less common
Dactylitis
JPsA: Extra-articular Manifestations

- **Skin**
  - onset variable (10% simultaneously, 40% preceding arthritis, 50% following onset of arthritis [up to 14 years])
  - psoriasis vulgaris > guttate > pustular

- **Nails**
  - nail pitting (75%)
  - vertical or horizontal ridging
  - onycholysis

- **Uveitis**
  - chronic anterior uveitis (17%)
JPsa: Diagnosis

- Physical Exam
  - asymmetric arthritis
    - small and large joints
    - first MTP joint or DIP arthritis
  - nails
  - skin

- Labs
  - (+) ANA, no specificity

- Radiography
  - normal or osteopenia
  - erosions rare
JPmA: Diagnostic Criteria

- **Definitive JPsA**
  - Arthritis with typical psoriatic rash \textit{or}
  - Arthritis with 3/4 of following (minor) criteria
    - dactylitis
    - nail pitting (two or more) or onycholysis
    - psoriasis-like rash
    - FH (1st or 2nd degree relative) of psoriasis

- **Probable JPsA**
  - Arthritis with 2/4 of minor criteria
JPswA: Prognosis

- Frequent progression to polyarticular course (66%)
- Relapsing/remitting arthritis
- Not necessarily synchronous with skin disease
Case Seven

- A 15-year-old male presents with a complaint of back pain for the last several months, particularly when he plays sports and in the mornings.
- On review of systems, he has also had a 10-pound weight loss over the last few months and intermittent diarrhea.
- Physical exam reveals loss of lumbar lordosis and decreased forward flexion, but no localizing areas of pain. He also has bilateral knee effusions.
IBD-related Arthritis**

- Onset age < 16 years
- Characterized by non-infectious inflammatory arthritis
- Presence of inflammatory bowel disease before, during, or after onset of arthritis
IBD arthritis: Epidemiology

- Incidence and prevalence
  - occurs in 7-21% of children with IBD
  - no difference in frequency between Crohn’s or UC
- Age of onset: 10-15 years
- Gender predilection: no difference in gender in incidence of arthritis
  - except spondylitis type M>F
IBD arthritis: Genetics

- 15% pts with Crohns and 8% of UC pts have 1st degree relative with IBD
- No specific genetic linkage
- Except in spondylo form---(+) relationship to HLA-B27
IBD arthritis: Clinical Manifestations**

- **Peripheral arthritis**
  - oligoarthritis of small and large joints, but may be polyarticular
  - lower extremity > upper extremity
  - disease fluctuates with IBD activity

- **SI joint arthritis**
  - back pain/stiffness, decreased ROM
  - may have associated enthesitis
  - not related to IBD activity
IBD arthritis: Extra-articular Manifestations**

- **Gastrointestinal**
  - abdominal pain
  - bloody diarrhea
  - weight loss/constitutional symptoms
  - nocturnal defecation

- **Skin**
  - erythema nodosum
  - pyoderma gangrenosum
IBD arthritis: Diagnosis

- **Physical Exam**
  - clinical suspicion!
  - GI involvement
  - arthritis
    - peripheral arthritis
    - sacroiliitis

- **Labs**
  - evidence of inflammation, etc

- **Radiography**
  - SI joint involvement
IBD arthritis: Prognosis

- Peripheral arthritis well controlled with control of disease
- Axial arthritis may progress
- Late hip involvement not uncommon
Case Eight

- An 11-year-old male presents with complaints of ankle, knee, and back pain for the last week.
- His past medical history is unremarkable except for a recent bout of gastroenteritis which affected his entire fifth-grade class.
- Physical exam reveals bilateral ankle and knee arthritis and non-suppurative conjunctivitis.
- UA demonstrates TNTC WBCs.
Reactive Arthritis**

- Any arthritis that follows infection, but not direct infection of the joint itself.

- Features include:
  - Typical causative agents
  - Onset within several days to weeks following infection
  - Symptoms remit within six months (or considered chronic)
  - Distribution similar to other spondyloarthropathies
  - Extra-articular manifestations not uncommon

- Strep-related disease considered separately

- AKA “toxic synovitis”
Reactive Arthritis: Epidemiology

- Incidence and prevalence
  - uncommon in the pediatric population: 0.67% of RA cases
  - occurs in ~0.5-1% of patients following gastroenteritis, 1-4% of patients following urethritis

- Age of onset: usually >16 years

- Gender predilection: M:F 4:1

- Genetics: up to 90% HLA-B27 (+)
Reactive Arthritis: Etiology

- Diarrhea precedes RA in 80% of pediatric pts**
  - shigella flexneri
  - yersinia enterocolitica
  - salmonella enteritidis

- Urethritis-related RA
  - chlamydia trachomatis
  - mycoplasma/ureaplasma
Reactive Arthritis: Clinical Manifestations**

- Constitutional symptoms
- Arthritis (presenting complaint in 25%)
  - oligoarthritis/monarthritis
    - lower extremity > upper extremity
    - may develop new joints over time
  - associated enthesitis
  - axial involvement rare
Reactive Arthritis: Extra-articular Manifestations**

- Urethritis (presenting complaint in 30%)
  - dysuria
  - inflammation of meatus to urethral discharge
- Conjunctivitis (66% at onset)
Conjunctivitis and Uveitis

Conjunctivitis

Hypopion
Reactive Arthritis: Extra-articular Manifestations**

- **Skin**
  - less common in children
  - mucosal ulceration
  - keratoderma blennorrhagicum

- **Nail changes**
Reactive Arthritis: Diagnosis

- **Physical Exam**
  - arthritis
  - genitourinary exam
  - eye exam
  - skin

- **Labs**
  - elevated inflammatory parameters

- **Radiography**
  - usually normal
Reactive Arthritis: Prognosis

- tends to be self-limited in children
Case Nine

- A five-year-old male is brought to your office by his parents for complaints of decreased energy and difficulty performing regular tasks. This has been worsening over the last several weeks. He denies any muscle or joint tenderness. On review of systems, his parents report that he has had eczema on his face for the last several months that has been resistant to any medical therapy.

- Physical exam reveals a cooperative male who is unable to lift his arms above his head or get up from a sitting position. Skin exam reveals a facial rash and red bumps on his fingers.
Juvenile Dermatomyositis (JDM)

- Frequency in population 0.5 per 100,000
- Bimodal peak of age of onset
  - 10-14 years (approx 16-20%)
  - 45-64 years
- Gender predilection: approx 2:1 F:M
Clinical Manifestations of JDM**

- Cutaneous Manifestations
  - JDM rash
  - heliotrope rash
  - Gottron’s papules
  - periungual erythema
  - ulcerative disease
  - [acanthosis nigricans]

- Proximal muscle weakness
  - large muscle groups versus small
  - clues on movement and gait
Clinical Manifestations of JDM

- Evidence of inflammatory myositis**
  - elevated muscle enzymes
  - electromyography
  - muscle biopsy
  - magnetic resonance imaging

- Gastrointestinal
- Respiratory
- Calcinosis
- Lipodystrophy
Laboratory Testing in JDM**

- **Muscle enzymes**
  - AST/SGOT
  - ALT/SGPT
  - CPK
  - aldolase
  - LDH

- **Antibodies**
  - Antinuclear antibodies (frequency 10-80%)
  - PM1, Jo1, etc (<20% in children)
JDM: Differential Diagnosis**

- Dermatomyositis versus polymyositis
- Muscular dystrophy
- Guillain-Barre disease
- Other inflammatory myopathies
JDM: Treatment

- **Immunosuppressive therapy**
  - Prednisone
  - Steroid-sparing agents:
    - methotrexate
    - cyclophosphamide
    - cyclosporine
    - azathioprine
  - Intravenous immunoglobulin
- Stretching to maintain range of motion
- Continuation of other regular activities
JDM: Complications**

- Respiratory impairment
- GI vasculitis
- Steroid-related side effects
- Side effects of steroid-sparing agents
- Calcinosis
- Insulin resistance/lipoatrophy
JDM: Long Term Outcomes

- 70% well and functional
- 20% long term complications
- 10% die
Case Ten

- A 13-year-old female presents with persistent and increasing rash on her left lower extremity. It is red, nontender, and nonpruritic, but is interfering with her ability to extend her leg.

- Physical exam reveals a firm, shiny, erythematous strip of skin extending from the left hip, down the lateral side of her leg, across her knee to the dorsal surface of her foot.
Scleroderma and Relatives**

**Types**
- Localized scleroderma
  - morphea
  - linear scleroderma
- Diffuse scleroderma
  - systemic sclerosis
  - CREST
- Mixed Connective Tissue Disease
- Eosinophilic Fasciitis
Clinical Manifestations of Scleroderma**

- Cutaneous (skin thickening)
- Raynaud’s phenomenon
- Gastrointestinal
- Musculoskeletal
  - Limitation of range of motion
  - Abnormal limb growth
- Pulmonary
- Renal
Laboratory Testing in Scleroderma

- **Antinuclear Antibodies**
  - SCL-70 (DNA-topoisomerase 1) 26% freq
  - anticentromere (kinetochore) 22% freq
  - anti-RNP (100% freq in MCTD)

- **Rheumatoid Factors**

- **Proteinuria/hematuria**

- **Hematologic**
  - anemia
  - eosinophilia
Scleroderma: Treatment**

- Immune modulators/anti-inflammatory therapy
  - Prednisone
  - Methotrexate
  - Cyclophosphamide
- Decrease Collagen cross linking
  - [D-penicillamine]
- Prevention of further organ injury:
  - Ca channel blockers
  - Cold precautions
- Preservation of function:
  - Intensive PT/OT
- General supportive care
Systemic Vasculitis

- Very rare in children**
- Peak age 9-11 yrs, range 3-16 yrs
- Equal incidence male/female
- Most presentations of systemic vasculitis do not follow specific patterns
- Some more common vasculitic syndromes of childhood present as a constellation of otherwise nonspecific symptoms
Classification of Systemic Vasculitis (?)

- Polyarteritis
  - polyarteritis nodosa
  - cutaneous polyarteritis
  - Cogan’s syndrome
  - Kawasaki’s disease
  - Microscopic polyangiitis
- Leukocytoclastic vasculitis
  - Henoch-Schonlein purpura
  - Hypersensitivity vasculitis
- Granulomatous vasculitis
  - Granulomatosis with polyangiitis
  - Churg-Strauss syndrome
  - Primary CNS angiitis
- Giant Cell Arteritis
  - Temporal Arteritis
  - Takayasu’s arteritis
- Other
  - Behcet’s syndrome
  - Mucha-Haberman Disease
Clinical Manifestations of Vasculitis

- **Cutaneous**
  - palpable purpura
  - urticaria
  - dermal necrosis, digital gangrene
  - livedo reticularis

- **Pulmonary**
  - hemoptysis
  - dyspnea
Clinical Manifestation of Vasculitis**

- **Cardiovascular**
- **Gastrointestinal**
  - serositis, abdominal pain
  - GI blood loss
- **Renal**
  - proteinuria/hematuria
  - hypertension
Clinical Manifestations of Vasculitis**

- **Neurologic**
  - seizures
  - psychosis
  - diffuse or focal deficits
  - peripheral neuropathy (mononeuritis multiplex)
  - stroke

- **Non-specific**
  - fever
  - arthralgias/myalgias
  - weight loss
  - night sweats
Laboratory Testing in Vasculitis

- Inflammatory parameters
  - leukocytosis
  - anemia
  - elevated ESR, CRP, immunoglobulins

- no RF or ANA

- Anti-neutrophil cytoplasmic antibodies
  - C-ANCA (PR3) found in 90% pts with GPA
  - P-ANCA (MPO) up to 75% MPA, but many other diseases also

- Tissue
Systemic Vasculitis: Treatment**

- **Corticosteroids**
  - prednisone at 2mg/kg/d

- **Immunosuppressives**
  - Azathioprine 2 mg/kg/d
  - Cyclophosphamide 2 mg/kg/d

- **Biologic Therapy**
  - Rituximab (anti CD-20 monoclonal Ab)
Disease Course and Outcome**

- Highly variable
- Rapid response to steroids good prognosis
- Delayed diagnosis poor prognosis
Case Eleven

- An eight-year-old boy presents to the emergency room with bruising on his lower extremities and abdominal pain.
- Physical exam reveals purpura on both legs, as well as bilateral ankle arthritis. His scrotum is swollen and ecchymotic. Abdominal exam demonstrates normal bowel sounds and no HSM.
Henoch-Schonlein Purpura**

- AKA anaphylactoid purpura
- Second most common vasculitis of childhood
- Most common in children 5-15 years of age, rare in adults
- Male to female 1.5 : 1
- Incidence varies from 0.1 to 13.5 per 100,000
- Seasonal variation: peaks during winter
  - ? Relationship to streptococcus
HSP: Clinical Manifestations

- Cutaneous Manifestations
  - Palpable purpura (100%)
    - most prominent in dependent areas, legs, buttocks
    - range from petechiae to ecchymoses
    - can be preceded by urticaria or MP
  - SQ edema of hands and feet, face, scrotum

- Arthalgias/Arthritis (65-85%)
  - usually involves large joints (knees, ankles)
  - periarticular swelling and tenderness, but usually non-erythematous
  - transient, but not migratory
  - lasts few days to a week
HSP: Clinical Manifestations**

- Gastrointestinal involvement (60-100%)
  - Gut vasculitis
  - colicky abdominal pain
  - heme (+) stools
  - intestinal perforation
  - within one wk to one month of rash

- Renal involvement (20-50%)
  - acute glomerulonephritis
  - hematuria/proteinuria
  - hypertension
  - renal failure
  - within one to three months of rash
HSP: Laboratory Testing

- Pathology: leukocytoclastic vasculitis with IgA deposition
- Must not have thrombocytopenia
- May have elevated inflammatory parameters
- Normochromic normocytic anemia
- Abnormal urinary sediment
- Normal complements
EULAR Consensus Criteria for HSP**

- classical palpable non-thrombocytopenic purpuric rash and any one of the following:
  - Arthritis or arthralgia
  - Abdominal pain and/or GI bleeding
  - Any biopsy with predominant IgA deposition
HSP: Treatment**

- Supportive care
- NSAIDs for arthritis
- Corticosteroids
  - for severe GI disease
  - potentially for renal disease
  - 1 mg/kg/d divided bid
HSP: Disease Course

- Resolves within one month in 66%
- At least 50% will have recurrence, usually of rash or GI symptoms**
  - usually within first 6 wks, but up to 1-2 years
- Don’t forget intussusception**
- Late renal outcome: less than 5% progress to end stage renal disease**
Cohort of pediatric patients

- All referred to one of two pediatric centers with rheumatologic complaints
- 29 patients with assorted suggested diagnoses and complaints
  - musculoskeletal pain (82%)
  - fatigue (50%)
  - weight loss (42%)
  - hepatomegaly (29%)
  - arthritis (25%)
- 6 of 29 with (+) ANA
Their diagnosis: Malignancy

- Red flags:
  - Non-articular bone pain
  - back pain on presentation
  - bone tenderness
  - severe constitutional sxs
  - features atypical of rheum dz
  - abnormal/discrepant labs
  - night sweats
  - ecchymoses/bruising
A 14-year-old boy with refractory oligoarticular JIA of the right knee consents to undergo therapeutic arthrocentesis and corticosteroid injection.

The procedures goes smoothly, but the fluid that is aspirated is reddish-brown and opaque.

Steroids are injected, but the patient has minimal, if any, response.
Tumors Affecting Bone and Joints

- Pigmented Villonodular Synovitis**
- Bone Marrow Expansion
- Primary tumors of bone
  - Osteosarcoma—covered elsewhere
  - Ewing’s sarcoma—covered elsewhere
Pigmented Villonodular Synovitis

- Benign tumor of the synovium characterized by fibrous tissue and hemosiderin deposition
- Peak ages 20-45 years (range 11-70)
- Most common sites are knee and hip
- Insidious onset, can mimic oligoarticular inflammatory arthritis
- Synovial fluid aspiration demonstrates dark brown-reddish fluid
- Radiology (MRI, ultrasound) helpful
Pigmented Villonodular Synovitis
Pigmented Villonodular Synovitis

- Diagnosis made by typical MRI appearance, synovial biopsy, synovial fluid analysis
- Treatment: surgical resection**
- Recurrence rate: up to 45%**
Case Thirteen

- A seven-year-old boy presents to your office with complaints of bilateral calf pain, worse after activity or at the end of the day.
- Physical exam is unremarkable when sitting, but when the patient stands up, you notice collapse of the arch of the midfoot and pronation of both ankles.
Hypermobility

- Laxity of the joints leading to increased range of motion**
- Places abnormal stresses on the joint and risks stability leading to increased risk of injury**
- Can be generalized or local
- Can be isolated or associated with other conditions
Generalized Hypermobility

- Can occur with other conditions
  - Benign Joint Hypermobility Syndrome (BJHS)
  - Ehlers-Danlos Syndrome (EDS)**
  - Marfan Syndrome
  - Stickler Syndrome
  - Williams Syndrome
  - Down Syndrome

- Measured using Beighton’s score
Beighton’s Score for Hypermobility

- Need a score of $\geq 5$
  - Elbow extension beyond $10^\circ$ (1 pt each for right & left)
  - Thumb apposition to forearm (1 pt each for right & left)
  - Extension of 5th finger beyond $90^\circ$ (1 pt each for right & left)
  - Knee extension beyond $10^\circ$ (1 pt each for right & left)
  - Forward flexion of trunk, legs straight, palms touching floor (1 pt)
Generalized Hypermobility

- Incidence up to 20%, F > M
- More common in children between 3-10 years of age

Treatment:
- Reassurance
- Pain control (NSAIDs, acetaminophen)
- Muscle strengthening, especially around affected joints
- Avoid activities that precipitate symptoms

Prognosis:
- May be associated with increased risk of osteoarthritis later in life
Isolated Hypermobility

- Hypermobility at a specific joint or set of joints
- Contributes to symptoms at the joint and surrounding soft tissues
- Common examples
  - Pes planus
  - Genu recurvatum
Pes Planus (Flat Feet)

- Normal in infancy
- Assure no heel cord tightness
- Flexible: medial longitudinal arch decreases with weightbearing**
- Assure foot is supple in non-weightbearing position
- Orthotic only if calf or leg pain**
Genu Recurvatum

- Isolated hypermobility of the knee
- Pain behind knee while standing or walking, improves with rest
- Most common in adolescent girls
- Excessive hyperextension on exam**
- May have small effusions, particularly after exercise
- Treated with repositioning; avoidance of overextension**
Leg positioning
Case Fourteen

- A five-year-old boy is brought to your office by his mother with complaints of bilateral leg pain. She looks exhausted and reports that for the last four months, her son has been awakening at night with leg pain and will not go to sleep again until his legs are massaged. The entire family has not slept in several months.

- The child is running up and down the hallway and his physical exam is unremarkable.
Growing Pains

- Occur in 10-20% of all children
- Peak onset 4-12 years of age
- Deep “aching” pain occurring over long periods of time**
- Can be precipitated by activity, usually occurs late in day or at night
- May be positive family history
- No objective findings on physical exam**
- Treated with stretching and reassurance
Any additional questions?

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