The McMaster *at night* Pediatric Curriculum

John, J & Chandran, L. “Arthritis in Children and Adolescents”. Pediatrics in Review 32 (11). 2011.

Objectives

- Identify the common and joint-threatening causes of arthritis in children and adolescents
- Develop a broad differential for pediatric arthritis
- Recognize and manage a patient with septic arthritis
- Discuss the diagnostic and management approach to a variety of causes of pediatric arthritis

Background

- Arthritis is defined simply as inflammation of a joint, while arthralgia is pain without inflammation (warmth, erythema, tenderness, edema)
- The history and physical exam are the most important diagnostic tools which can help direct a clinician to joint-saving intervention
- The number of joints involved has important diagnostic implications
  - Monoarthritis: single joint
  - Oligoarthritis: 4 joints or fewer
  - Polyarthritis: 5 joints or more

The Case

- A 6-year-old boy presents to the emergency department with a 24h history of fever and swelling of the left knee
- He is in severe pain and refusing to weight bear
- He fell down on at school two days ago but his knee seemed fine at the time
- He has no significant past medical history and his immunizations are up-to-date

History

What would you ask?

History

- Characterize the pain in terms of onset, duration, timing, locations, severity and character
  - Is it constant or does it occur primarily in the morning or evening?
  - Which joints are involved?
  - Is the pain migratory or persistent?

- Ask if the pain is associated with stiffness, limited range of motion, limp, or refusal to move the joint or weight bear

- Ask about constitutional and other associated symptoms such as fever, rash, eye and GI symptoms

History

- Ask about antecedents such as trauma, recent infections, travel, and sexual history
- Perform a thorough past medical history, including immunization status and systemic illness
- Family history of arthritis and autoimmunity
- Social history should focus on impact of pain on function (adolescents require a full HEADSSS exam)
- Complete review of systems

Physical Exam

What would you look for?

Physical Exam

- Does the child appear ill or toxic? Is there a fever?
- Evaluate each joint for inflammation (warmth, tenderness, edema)
  - Keep in mind that the hip joint is less amenable to direct examination
- Observe the position at rest, and attempt active and passive range of motion
- Palpate for crepitus and effusions

Physical Exam

- Examination of the skin can be very revealing; findings may include generalized rash, malar or discoid rash, erythema migrans, or subcutaneous nodules
- Careful examination of the oral cavity and eye including fundoscopic exam
- Systemic exam including abdominal exam as well as cardiac exam for murmurs and signs of failure
- Depending on history, pelvic and bimanual exams may be required

Workup

What would you order?

Workup

- Arthrocentesis is the gold standard and must be performed whenever septic-arthritis is strongly considered (gram stain, WBC count, culture)
- If gonorrhea is suspected in sexually active patients, obtain pelvic, urethral, throat and rectal cultures as well
- CBC, ESR, CRP are non-specific markers of an inflammatory or infectious process
- ANA, RF and auto-antibodies should be obtained if autoimmune disease is suspected

Workup

- Toxic-appearing children or those in whom septic arthritis, osteomyelitis or rheumatic fever are suspected should also have blood cultures drawn
- Consider lyme serology and coagulation studies
- Plain radiographs
  - Diagnose solid tumors, avascular necrosis of the hip and SCFE
  - Show widened joint space, tissue edema, and eventually subchondral changes in septic arthritis
  - Show erosive changes in advanced autoimmune disease

Workup

- Ultrasound is a rapid means of detecting joint effusions especially in the hip
- MRI is the best test for suspected osteomyelitis
- Suspicion of acute rheumatic fever merits echocardiography as well as confirmation of GAS infection (throat swab, ASOT, rapid antigen test)
- Consult ophthalmology for reactive arthritis and autoimmune disorders especially if ANA-positive

Differential Diagnosis

Single Joint	
Infectious	Autoimmune
Septic arthritis Gram positives Gonococcal arthritis	Juvenile idiopathic arthritis Oligoarticular
	Systemic Lupus Erythematosus
Toxic/transient synovitis	Orthopedic
Osteomyelitis adjacent to joint	Trauma
Reactive arthritis	Overuse syndromes
Neoplastic	Slipped capital femoral epiphysis
Osteoid osteoma adjacent to joint	Legg-Calve-Perthes disease
Osteosarcoma adjacent to joint	Hematological
Ewing's sarcoma adjacent to joint	Hemarthrosis
Leukemia	

Differential Diagnosis

Multiple Joints	
Infectious	Auto-immune
Disseminated gonorrhea	Juvenile idiopathic arthritis Oligoarticular Polyarticular RF negative Polyarticular RF positive Systemic Enthesitis-related arthritis Psoriatic arthritis
Lyme disease	
Reactive arthritis	
Rheumatic fever	
Streptococcal-associated polyarthritis	
Other	Systemic lupus erythematosus
Kawasaki disease	Inflammatory bowel disease
Henoch-Schonlein purpura	Connective tissue disorders
	Behcet's disease

Septic Arthritis

- Bacterial invasion of the synovium and joint space
- S. *aureus* is the most common pathogen; others include GAS and S. *pneumoniae*
- H. *influenzae* B is no longer an important cause, but be on alert for MRSA and N. *gonorrheae*, which require a change to the usual empiric therapy
- For neonates, suspect GBS and E. coli as well
- In sickle cell disease, consider salmonella

Septic Arthritis

- Hematogenous seeding is the most common method of infection in children, but arthritis may also result from spread from soft tissue or bone
- The most commonly affected joint in children is the knee and in infants is the hip
- Patients may present with localized symptoms alone, or generalized fever, malaise and toxic appearance
- Involved joints are kept immobile, flexed, and in the case of the hip abducted and externally rotated

Septic Arthritis

- Arthrocentesis is mandatory, while CBC, ESR and CRP and radiographs are supportive
- Ultrasound is useful for delineating effusion prior to arthrocentesis of the hip
- MRI is definitive but takes time; MRI is useful for identifying erosive sequelae

Test Your Knowledge

- You discover that your 6-year-old patient with left knee septic arthritis has parents who are medical residents and a prior history of skin boils. What empiric therapy would you choose?

    A. Clindamycin
    B. Cefazolin and vancomycin
    C. Trimethoprim-Sulfamethoxazole
    D. Cefoxatime and gentamycin

The Answer

- Age and risk factors guide empiric therapy which must cover gram+ skin organisms at minimum
  - Child: cefazolin or clindamycin
  - Neonate: cefotaxime and gentamycin
  - MRSA risk: add vancomycin
    - Gonorrhea risk: ceftriaxone
    - Sickle cell: 3rd gen cephalosporin
    - IV drug user: pseudomonal coverage

- MRSA resistance patterns to clindamycin are variable
- TMP/SMX is usually an oral antibiotic

Septic Arthritis

- Therapy should continue for 2-6 weeks depending on organism and response to treatment, with the at least the first week being parenteral
- Timely diagnosis and treatment prevents lifelong morbidity

Reactive Arthritis

- Arthritis associated with infection at a distant site
- 3:1 male:female ratio, and associated with HLA-B27
- Most commonly associated with C. trachomatis, but also caused by GI infections (Shigella, Salmonella, Campylobacter, Yersinia) and respiratory pathogens (GAS)
- Commonly presents with mono or oligo-arthritis of the lower limbs
- Reiter's includes urethritis and conjunctivitis

Reactive Arthritis

- Primarily a clinical diagnosis once other etiologies are ruled out
- Positive chlamydia or stool culture is supportive, along with elevated inflammatory markers
- Treatment is supportive with NSAIDs, rest, and treatment of underlying infection
- Symptoms persist weeks to months and in 4-19% of patients become chronic (> 6 months)

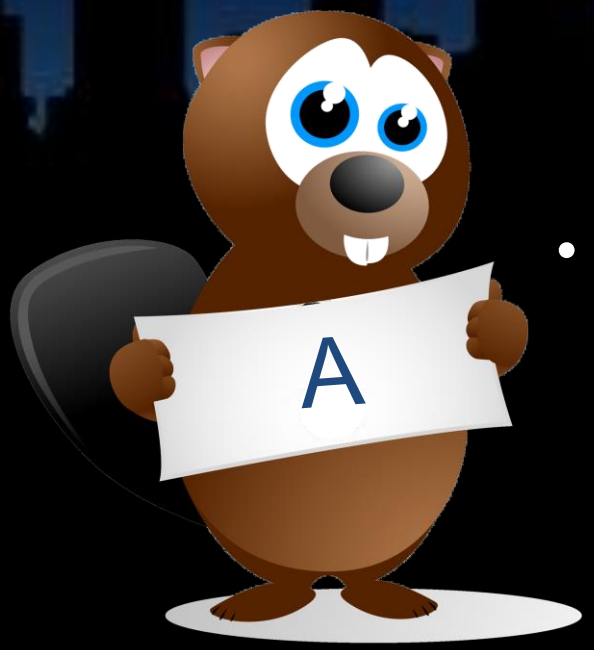
Test Your Knowledge

- Which of the following is *not* a major criterion for acute rheumatic fever?

A. Fever
B. Erythema marginatum
C. Polyarthritis
D. Subcutaneous nodules

The Answer

- The major Jones criteria in decreasing frequency are polyarthritis (60-80%), carditis (50-60%), chorea (10-15%), erythema marginatum, and subcutaneous nodules



- Minor criteria are fever, arthralgia, elevated ESR or CRP, and prolonged PR interval
- The diagnosis is made with 2 major or 1 major and 2 minor criteria, plus confirmation of antecedent GAS infection

Acute Rheumatic Fever

- Multisystem process 1-3 weeks following acute infection with Group A Streptococcus
- Peaks at 5-15 years
- Rare in North America, but small outbreaks persist
- Group A Streptococcus infection is confirmed by
  - Positive throat culture
  - Positive rapid antigen test
  - High or rapid rise in ASOT

Acute Rheumatic Fever

- Polyarthritis: first clinical feature, migratory, responds dramatically to ASA
- Carditis: tachycardia, systolic murmur of mitral insufficiency, may involve pericarditis, acute heart failure occurs in 5%
- Chorea: symmetric choreatic movements, halting or explosive speech, 1-6 month latency
- Erythema marginatum: evanescent, serpiginous
- Nodules: painless, > 1cm, over bony prominences

Acute Rheumatic Fever

- Treatment for all cases consists of 10 days of oral penicillin V or a single IM dose of penicillin G
- For carditis and arthritis, high dose ASA for 4 weeks
- Treat chorea with anticonvulsants or antipsychotics
- Secondary prophylaxis is accomplished with po penicillin bid or monthly IM penicillin for:
  - 5 years without carditis
  - 10 years or age 21 with no residual heart disease
  - 10 years or age 40 with residual heart disease

Lyme Disease

- Caused by B. *burgdorferi* spirochete in deer ticks
- Suspect lyme disease in any patient who has been to a lyme endemic area, regardless of recollection of tick bite or erythema migrans
- Stage I: circular rash, malaise and asymmetric mono- or oligo-arthralgias
- Stage II: early disseminated disease with neurological and MSK symptoms +/- cardiac
- Stage III: progressive neuropathy/encephalopathy

Lyme Disease

- Serology confirms the diagnosis but has limitations
- Treat early uncomplicated disease with 10-14 days of doxycyline (>8 years) or amoxicillin (<8 years)
- Morbidity relates to fixed neurological deficits and treatment-resistant arthritis in cases that are not treated early
- Prevent lyme disease with long pants and sleeves, light clothing, DEET, and careful tick checks in endemic areas

Juvenile Idiopathic Arthritis

- Arthritis of unknown etiology starting before the 16th birthday and persisting for > 6 weeks

Subtype	Description
Oligoarticular	Most common subtype, best prognosis Arthritis in 1-4 joints Most often knees, followed by ankles, wrists and elbows ANA positive in 60-80% (associated with higher risk of uveitis) Treat with NSAIDS +/- intra-articular corticosteroids
Poltarticular RF negative	5 or more joints Symmetrical arthritis of large and small joints 25% ANA positive Younger age and better prognosis than RF positive
Polyarticular RF positive	Symmetric arthritis of small joints 75% ANA positive Difficult to treat, worse prognosis, joint damage likely Usually adolescent girls

Juvenile Idiopathic Arthritis

Subtype	Description
Systemic	Arthritis is usually oligoarticular with hips and spine involved 2 weeks of fever with quotidian pattern for at least 3 days Evanescent, salmon-coloured rash Generalized lymphadenopathy, hepatosplenomegaly Serositis
Enthesitis-related arthritis	Arthritis and enthesitis OR Arthritis or enthesitis with at least 2 of: back pain, SI joint pain, HLA-B27, male >6y, uveitis, family hx
Psoriatic arthritis	Arthritis and psoriasis OR Arthritis and at least 2 of: dactylitis, nail pitting or oncholysis, family hx of psoriasis
NOS	Criteria not met for the other 6 subtypes

- Treat with NSAIDs, intra-articular steroids (not systemic), methotrexate, and biologic DMARDS

Test Your Knowledge

- The parents of your 12-year-old patient with systemic JIA have requested urgent follow-up. She is treated with methotrexate and has had compliance issues in the past. For the past 24h she has been feeling extremely unwell with unremitting fever > 40C. She presents with pallor, tachycardia, and HSM. What is the most likely cause?

A. Missed methotrexate
B. Methotrexate overdose
C. Bacterial sepsis
D. Macrophage activation syndrome

The Answer

- MAS is a life-threatening complication of systemic JIA occurring in 5-10%, characterized by high fever, pancytopenia, lymphadenopathy, coagulopathy, and HSM
  - MAS may be brought on by infection or disease flare-up
  - Bacterial sepsis is a consideration in immunosuppressed patients but HSM is not a typical feature
  - Methotrexate causes hepatotoxicity and neurotoxicity but not fever

Summary

- Arthritis can be a manifestation of multiple disease processes; therefore, consider a broad differential keeping in mind those with serious consequences
- Use a complete history and physical exam to determine diagnosis and need for investigations
- Prevention of debilitating consequences requires prompt diagnosis and appropriate management
- Patients with chronic diseases benefit from a multidisciplinary approach and long-term follow-up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