Rady Children's Hospital San Diego

Myths and Misconceptions in Pediatric Rheumatology

Johanna Chang, MD

Division of Allergy, Immunology, and Rheumatology

Rady Children's Specialists of San Diego

Disclosures

- None

Case 1:

From Epic inbox: “Hi, Johanna. I have a 2 yo patient whose parents have noted that she has been limping for the past few weeks. Her right knee is a little swollen but it doesn’t seem to bother her. I was thinking of sending her to orthopedics but was wondering if you might want to see her also. If so, what labs would you want? Thanks, ____”

Case 1:

From Epic inbox: “Hi, Johanna. I have a **2 yo** patient whose parents have noted that she has been **limping for the past few weeks**. Her **right knee is a little swollen but it doesn’t seem to bother her**. I was thinking of sending her to **see orthopedics** but was wondering if you might want to see her also. If so, what **labs** would you want? Thanks, ____”

Juvenile Idiopathic Arthritis (JIA)

- Defined as arthritis in a child < 16 yrs of age with a duration of disease of 6 weeks or longer with exclusion of other forms of juvenile arthritis
- Arthritis is defined as
  - Swelling/effusion OR
  - Painful limitation of range of motion (Wallace et al., 2004)
- Incidence of JIA in the US may be as high as 1/1000 (Peterson et al., 1996)
- Estimated 1.7-8.4 million children in the world with juvenile arthritis (Petty and Cassidy, 2011)

ILAR classification of JIA (Petty et al, 2004)

- Most recent classification system in which JIA is divided into 7 subtypes

1. Oligoarticular: 1-4 joints during first 6 months of disease
   a. Persistent: <=4 joints
   b. Extended: >4 joints after first 6 months
2. RF neg polyarticular: >4 joints in first 6 months of disease AND RF neg
3. RF pos polyarticular: >4 joints in first 6 months of disease AND RF pos x 2
4. Psoriatic
   - Arthritis and psoriasis OR
   - Arthritis and 2 of the following: dactylitis, nail pitting/oncholysis, psoriasis in 1st degree family member

ILAR classification of JIA (Petty et al, 2004)

5. Systemic: Arthritis and preceding or concurrent fever x 2 weeks with at least 3 consecutive days of quotidian fever plus 1 of the following: red, evanescent rash, generalized lymphadenopathy, hepatomegaly, serositis
6. Enthesitis-related
   - Arthritis and enthesitis OR
   - Arthritis or enthesitis plus 2 of the following: presence or history of SI tenderness , HLA-B27+, onset in male >6 yrs, acute anterior arthritis, history of AS, ERA, sacroiliitis with IBD, Reiters, or uveitis in a 1st- degree relative
7. Undifferentiated: Does not fit any of the above categories or fits in 2 or more of the above categories

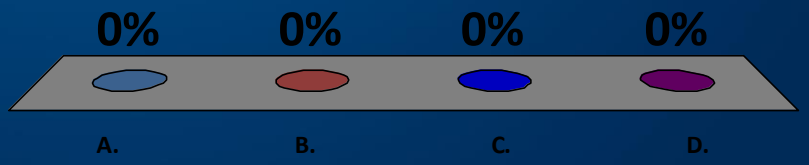
Case 1:

From Epic inbox: “Hi, Johanna. I have a 2 yo patient whose parents have noted that she has been limping for the past few weeks. Her right knee is a little swollen but it doesn’t seem to bother her. I was thinking of sending her to orthopedics but was wondering if you might want to see her also. If so, what labs would you want? Thanks, ____”

Question 1

Based on the description of the child in Case 1, this patient most likely has

A. Systemic JIA
B. Oligoarticular JIA
C. Polyarticular JIA
D. Undifferentiated JIA



Question 1

Based on the description of the child in Case 1, this patient most likely has

A. Systemic JIA
B. Oligoarticular JIA
C. Polyarticular JIA
D. Undifferentiated JIA

Oligoarticular JIA

- This is the MOST COMMON type of JIA
  - 50-80% of all chronic arthritis (Petty and Cassidy, 2011)
  - 20% of all peds rheum referrals to the US (Bowyer et al., 1996)
- Peak incidence 1-2 years of age
- Female to male 3:1
- Ddx of monoarthritis
  - Infectious arthritis
  - Malignancy
  - Hemophilia
  - Trauma
  - PVNS, pseudoarthritis

Oligoarticular JIA

- Clinically, affected joint is swollen and may be warm but **IS USUALLY NOT VERY PAINFUL OR TENDER**
- No red joints

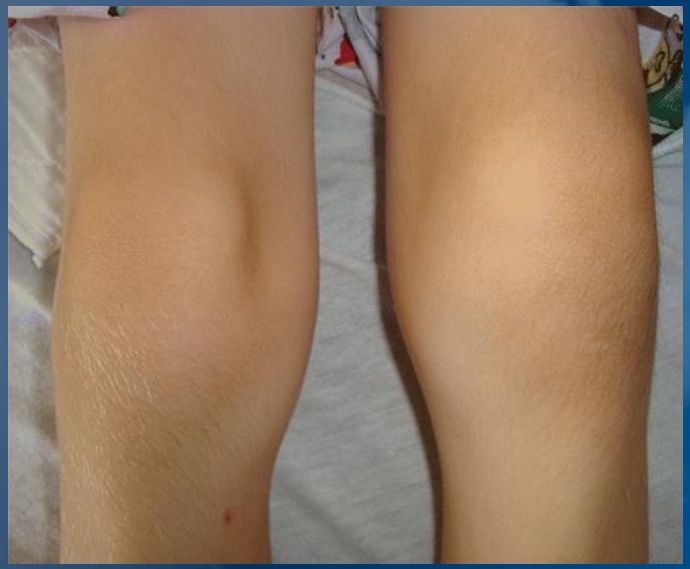
- **MYTH #1: ARTHRITIS IS ALWAYS PAINFUL**

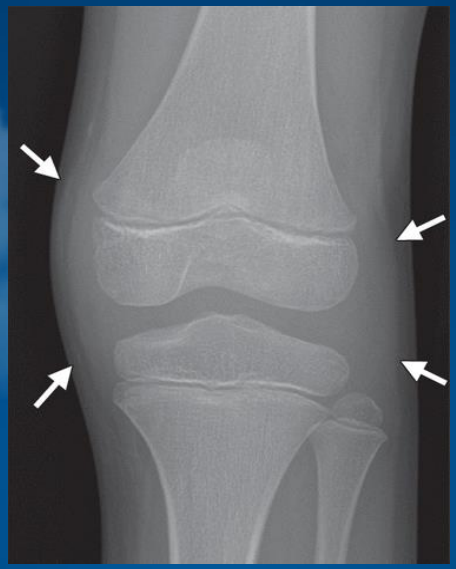
Work-up and management

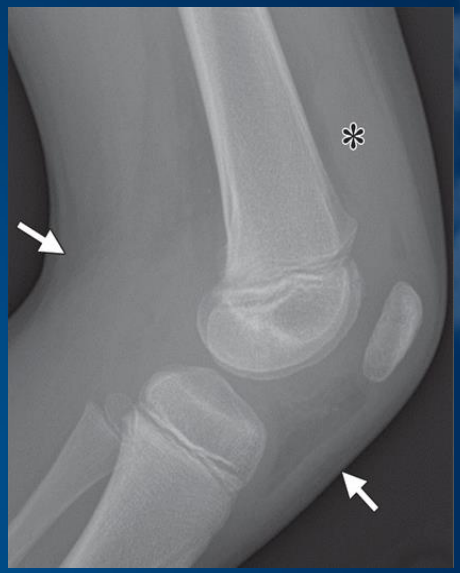
- NO LABS TO START
  - Usually normal ESR and CRP
  - However, if needing lab draw for some other reason or for suspicion of other causes of arthritis, I would recommend CBCD, CMP, ESR, CRP, UA, (ANA, RF, CCP)
- Xray of affected joint to document baseline
  - Usually with normal radiograph
  - May show soft tissue swelling
  - With poly JIA or long-standing arthritis may show osteopenia or joint space narrowing

Xray findings in JIA

Images from Sheybani et al., 2013







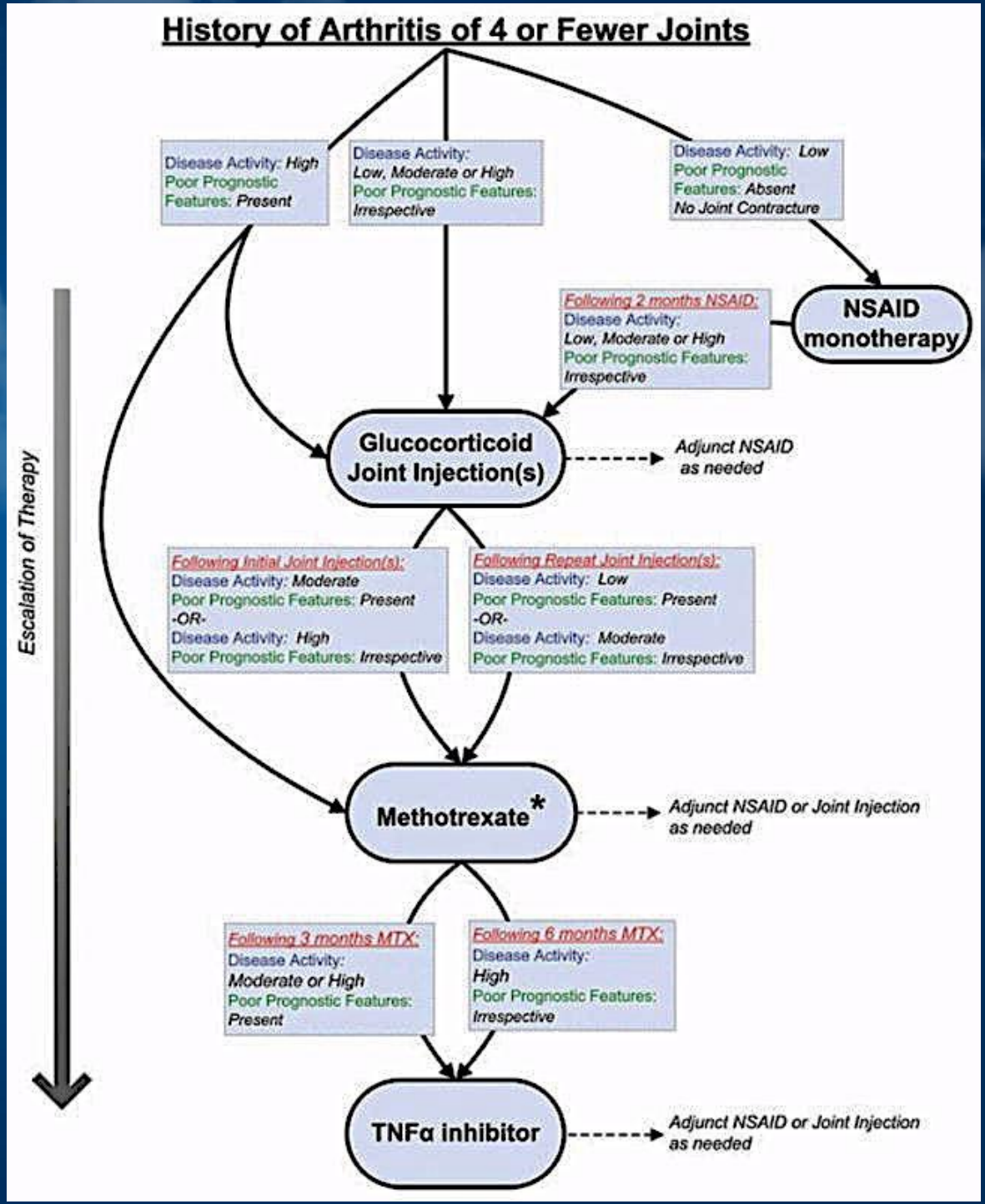
- Xrays only show soft tissue swelling but do show lack of bony trauma
- Joint space narrowing is present in only 5% early disease (15% 6 yrs after disease)
- Erosions in only 10% early disease (25% 6 yrs later)
- Bone overgrowth in 20% early disease – most commonly at the knees (Oen et al. 2003)

Work-up and management

- No need to refer to orthopedics unless suspected trauma
- Please refer to ophthalmology!
  - Presence of uveitis will affect management
  - Subacute chronic uveitis is diagnosed in 50% of JIA patients around time of arthritis diagnosis (Petty and Rosenbaum, 2011); 5% present with uveitis 1st
    - Most common in oligo JIA and RF-negative poly JIA
      - Prevalence 17-26% and 4-25%
      - ANA+, <6 yrs at onset, female sex, and oligo subtype are highest risk factors

Treatment

ACR 2011 Recommendations for treatment of arthritis
Beukelman et al., 2011



Rady Children's Specialists of San Diego

Prognosis

- 70-90% without serious disability
- Mortality <0.3%
  - Infection and cardiac dysfunction, secondary amyloidosis (Hull, 1988)
- Risk of decreased growth, leg-length discrepancy, and complications of uveitis
  - 1/3 JIA with complications from chronic uveitis (Saurenmann et al. 2007)
- Systematic review of prognosis in JIA (2014):
  - Poly JIA with worse prognosis
  - Diagnostic delay and systemic JIA highest risk for continued active disease
- May have significant physical/psychosocial impact
  - Peterson et al.: higher disability, more body pain, lower personal health perception, and decreased physical functioning compared to controls.

Prognosis of oligo JIA

- Persistent oligo: 68% clinical remission off medication
- Extended oligo: 31% clinical remission off medication
- High risk of flares: 47% persistent oligo and 67% extended oligo 2 yrs off medication
- Only 6% remain in remission > 5 yrs

  Wallace et al., 2005

Case 2:

15 yo female has been complaining of diffuse, intermittent body pains and fatigue. Her thyroid function tests are normal. She has normal cell counts and metabolic panel. Inflammatory markers normal. She has a +ANA. She has a normal physical exam apart from vague complaints of tenderness throughout the exam.

Case 2:

15 yo female has been complaining of diffuse, intermittent body pains and fatigue. Her thyroid function tests are normal. She has normal cell counts and metabolic panel. Inflammatory markers normal. She has a +ANA. She has a normal physical exam apart from vague complaints of tenderness throughout the exam.

The infamous antinuclear antibody (ANA)

- Immunoglobulins directed against structures within the cell (i.e. DNA, ribonuclear proteins, histones, and centromere)
- Immunofluorescent assay incubates patient's serum with mouse/rat liver nuclear substrate. If ANA is present, they will bind to the nuclear antigens and stain. Titer preformed by serial dilution.
- ELISA method not recommended by ACR
- Pattern of staining = NOT USEFUL.
- Titer of ANA may have some prognostic value.



Rady Children's Hospital San Diego

The infamous antinuclear antibody (ANA)

- Approximately 15% of healthy, asymptomatic population has a positive low titer ANA (<=1:160)
- As one ages, ANA titers increase (40% with low positive ANA by age > 60 yrs)
- Low titers (<= 1:160) found in:
  - Infections
  - Drugs
  - Neoplasias
- High titers (>1:320) found in variety of autoimmune disease

The infamous antinuclear antibody (ANA)

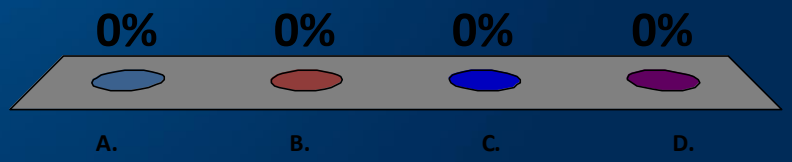
- +ANA is not diagnostic and does not correlate with disease activity
  - Cabral et al., 1992: +ANA in 24/108 kids with musculoskeletal pain but thought unlikely due to autoimmune disease. None developed autoimmune disease over 5 yr follow-up period
  - Deane et al., 1996: +ANA in 113/500 children referred to peds rheum. 31 kids (27%) had no rheum condition at initial visit and followed over 3 years; by end of follow up, 25 patients had resolution of complaints, 5 had significant improvement, 1 autoimmune hepatitis
- Best used as a screening test for suspected lupus and to help evaluate risk of uveitis in patient with JIA

Case 2:

15 yo female has been complaining of diffuse, intermittent body pains and fatigue. Her thyroid function tests are normal. She has normal cell counts and metabolic panel. Inflammatory markers normal. She has a normal physical exam apart from vague complaints of tenderness throughout the exam. She has a +ANA.

This patient most likely has:

A. Juvenile arthritis
B. Systemic lupus erythematosus
C. A pain syndrome
D. I don't know but it's probably autoimmune since she has a +ANA



Question 2

This patient most likely has

A. Juvenile arthritis
B. Systemic lupus erythematosus
C. A pain syndrome
D. I don't know but it's probably autoimmune since she has a +ANA

Myth #2: ANA = rheumatologic illness

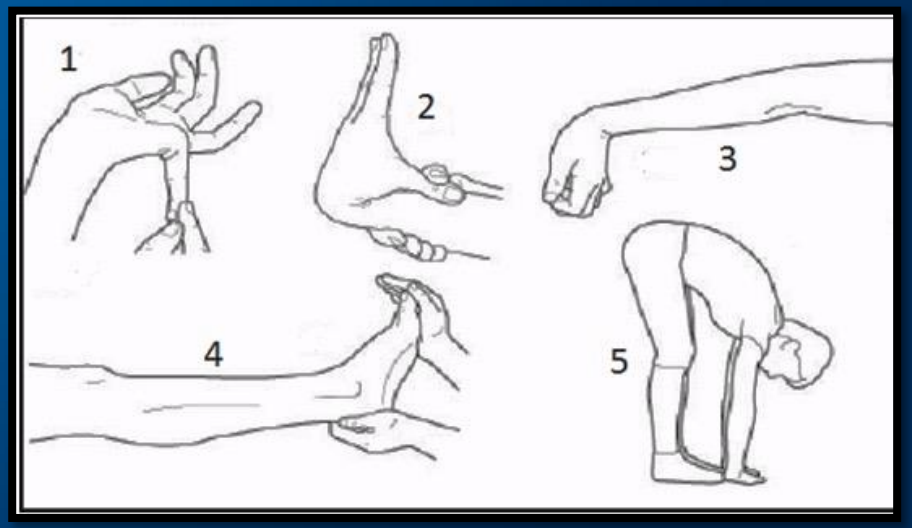
Chronic pain syndromes

Can be divided into 2 groups:

1. Mechanical/orthopedic
   - Generalized hypermobility
   - Overuse injuries
   - Osteochondroses
   - Spondylolysis/spondylolithesis
   - Scheurmann disease
   - Growing pains
2. Pain amplification syndromes
   - Aka complex regional pain syndrome, fibromyalgia

Generalized hypermobility

- Beighton scale or Carter-Wilkinson criteria
- Make sure no other findings concerning for syndromes with hypermobility (Marfan, Stickler, etc)
- 20% of the Caucasian population and likely higher in Asians
- Peak ages 3-10; F>M
- Usually FH of “flexibility”
- May have pes planus (mobile flat foot)
- Treatment is supportive



Growing pains

- Aka “benign nocturnal pains of childhood”
- 4-12 yrs, M=F
- Tends to be cramping pain in thigh or calf that occurs later in the day and resolves by morning; responds to massage and mild analgesia
- Normal physical exam
- Treatment is supportive
  - In children with frequent attacks, oral analgesia in the evening may be preventive
  - May benefit from treatment of any underlying mechanical abnormalities

LeBlanc and Houghton, 2011

Pain amplification

- Largely defined as pain out of proportion in the absence of concerning physical exam, labs, or imaging
- Various subsets of chronic pain syndromes
  - CRPS – edema, changes in blood flow in painful area
  - Fibromyalgia – widespread pain for 3 months with pain on digital palpation in 11/18 sites
  - Diffuse idiopathic pain - >=3 sites for >=3 months
  - Localized idiopathic pain – pain in 1 limb
- Up to 10% of new patients presenting to US pediatric rheumatology centers have a chronic pain syndrome

Sherry, 2011

Pain amplification – Work up

- Labs – usually not necessary but would include CMP, CBCD, CRP, ESR, UA
  - The most common abnormal test is a low +ANA
  - High risk of false positives
- Imaging – again, not usually necessary
  - Some studies suggest that bone scans are most useful study if diagnosis is in doubt (Laxer et al, 1985; Goldsmith et al., 1989)
  - MRI in localized pain amplification can show bone marrow edema

Pain amplification – Treatment

- Goal is restoration of function and relief of pain
- Treatment team is multi-disciplinary and often consists of anesthesiologist or rehab physician, psychologist/psychiatrist, and physical therapist
  - Few pediatric rheumatologists are actively involved in management of chronic pain disorders
- The vast majority of publications focus on PT and OT to reverse immobility and increase function
- Drug treatment (including use of antidepressants and anti-epileptics) is off-label and not well-supported in medical literature as to efficacy
- Psychological support is important
  - Role of guided imagery and muscle relaxation, CBT, traditional psychotherapy

The evolving world of rheumatology

Myth #3: Pediatric rheumatologists treat all autoimmune disease

"So what is it you do again?"

We do it!

Juvenile idiopathic arthritis
Reactive arthritis
Lupus
Juvenile dermatomyositis
Vasculitis

- Leukocytoclastic (refractory HSP)
- Wegeners (shared with pulm and renal)
- MPA (shared with renal)
- PAN

Sjogren's
Scleroderma (systemic and limited)
Sarcoidosis
Behcet

Not so much (*institution-dependent)

Genetic connective tissues disorders (Ehlers-danlos, Marfan's)
Immunodeficiency
Urticaria
Abnormal rash
Autoimmune hepatitis
*Kawasaki disease
*Periodic fever syndromes

Our Team

Robert Sheets, MD
- Rady Main
- Escondido
- Murrieta

Peter Chiraseveenuprapund, MD, MS
- Rady Main
- Escondido
- Murrieta

Suhas Radhakrishna, MD
- Rady Main
- Encinitas
- Oceanside

Rady Children's Specialists of San Diego

RNs: Esther Ford, Donna Douglas, Sheryl Hayes
Admin: Priscilla Mendoza Contact: 858-966-8082

Rady Children's Hospital San Diego

Thank You!

Johanna Chang, MD
jchang@rchsd.org
858-966-8082