Polyarticular Arthritis

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Question 1

A 68 year old diabetic female reports a 3-year history of worsening bilateral knee pain. Her knees are stiff for about 15 minutes in the morning. She has difficulty walking and descending stairs because of pain. She has pain with use of the hands. Examination reveals mild swelling of both knees and enlargement of the PIP joints.
Question 1

What is the most likely diagnosis?
1. Rheumatoid arthritis
2. Osteoarthritis
3. Hemochromatosis
4. Sarcoidosis
5. Gout
Polyarticular joint pain

- pain in more than four joints
- diagnostic challenge because of extensive differential diagnosis

History is most important diagnostic tool

**Inflammatory vs Non-inflammatory**

**Inflammatory**
- Rheumatoid arthritis
- Adult-onset Still’s disease
- Spondyloarthopathies
- Lupus
- Rheumatic fever
- Gout
- Viral arthritis
- subacute bacterial endocarditis
- Lyme disease
- Sarcoidosis

**Non-inflammatory**
- Primary Osteoarthritis
- Secondary Osteoarthritis
- Hemochromatosis
- Ochronosis
- Acromegaly
- Hypothyroidism
- Chondromalacia
- Osteonecrosis
Polyarthritis: History

- **Pain** – location, onset, course, duration, other characteristics

- **Stiffness**

- **Other joint symptoms**: swelling, warmth, “locking”, “giving way”

- **Systemic symptoms**: fever, weight loss

**QUESTION 1**

A 68 year old diabetic female reports a 3-year history of worsening bilateral knee pain. Her knees are **stiff for about 15 minutes in the morning**. She has **difficulty walking and descending stairs** because of pain. She has **pain with use** of the hands. Examination reveals mild warmth and swelling of both knees and enlargement of the PIP joints.
**Polyarthritis**

<table>
<thead>
<tr>
<th><strong>Inflammatory</strong></th>
<th><strong>Non-inflammatory</strong></th>
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<tbody>
<tr>
<td>Morning stiffness $&gt; 30$ min</td>
<td>Minimal morning stiffness</td>
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<tr>
<td>Worse at rest / better with activity</td>
<td>Pain during and after use</td>
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<tr>
<td>Prolonged “gel phenomenon”</td>
<td>Minimal “gel phenomenon”</td>
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**Non-inflammatory arthropathy**

**Primary Osteoarthritis**

- **History**
  - Most common symptom is **PAIN**: chronic, worse with activities, may be better with rest
  - Loss of motion and function: Decreased ability to perform daily activities
  - Morning stiffness or gel phenomenon $< 15$ minutes
Primary vs Secondary Osteoarthritis

**PRIMARY:**

- **etiology is unknown**
- most common type
- common sites: spine, DIP, PIP, 1st CMC, hip, knee, 1st MTP, acromioclavicular

**SECONDARY:**

- **Identifiable etiology**
  - crystal-associated arthritis (CPPD / Gout)
  - hemochromatosis, acromegaly, ochronosis, Wilson’s disease
  - hip dislocation: congenital or acquired
  - trauma (chronic joint injuries; surgery)
  - sequelae of hypermobility syndromes
  - inflammatory joint diseases (septic arthritis)

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**Primary Osteoarthritis**

- Examination
  - loss of joint mobility
  - Joints are tender with motion
  - crepitus
  - bony enlargement: fingers and knees
  - little inflammation: small joint effusions
  - Joint deformity / malalignment / instability
Osteoarthritis

Heberden’s nodes

Bouchard’s nodes

Primary Osteoarthritis

**Diagnosis: history and exam**

**Radiographs:** not necessary for diagnosis

→ exclusion of other diseases, assess severity of joint damage, additional diagnostic tool.
  - marginal osteophytes
  - Asymmetric joint space narrowing
  - subchondral bone sclerosis

**Key Point:** *Pain and radiographic findings are poorly correlated:* asymptomatic patients may have radiographic evidence of OA and pts with severe symptoms may have minimal findings of OA on x-ray.
Osteoarthritis: Treatment

Non-pharmacologic

PATIENT EDUCATION

- Physical therapy / exercises
- Weight loss
- Orthotics (insoles, braces, splints)
- Assistive devices (cane)

Pharmacologic

- Analgesics: acetaminophen; nonselective NSAIDs; COX-2 inhibitors
- Glucosamine 1500 mg/day

Intra-articular

- intra-articular corticosteroids
- hyaluronic acid derivatives

Surgical intervention

- osteotomies
- joint replacement (arthroplasty)
Question 2

33 yo woman presents with pain in her elbows, wrists and fingers for several months. Pain is worse in the morning. She had no improvement with tylenol or Ibuprofen. She noticed stiffness and swelling of the fingers in the morning, weight loss of 12 lbs, fatigue and intermittent low grade fever. She works in a day-care facility. Laboratory tests showed mild anemia and negative rheumatoid factor.

What is the most likely diagnosis?
1. SLE
2. Bacterial endocarditis
3. Adult-onset Still’s disease
4. Rheumatoid arthritis
5. Parvovirus B19 infection
What is the most likely diagnosis?

1. SLE
2. Bacterial endocarditis
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5. Parvovirus B19 infection
RA: History

- Morning joint stiffness > 30 min, usually more than one hour.
  - joints feel better with use, worse with rest
  - “gel phenomenon” > 30 min

- Symmetric and polyarticular arthritis

- Joints: PIP, MCP, wrist, elbow, shoulder, C-spine, TMJ, hip, knee, ankle, MTP

- Symptoms of systemic inflammation: low grade fever, weight loss, fatigue, malaise.

RA: Joint exam

- Warmth
- Tenderness
- Synovial proliferation
- Joint effusion
- Loss of motion
- Deformities
- Muscle atrophy around the affected joints
Rheumatoid Arthritis

Rheumatoid Arthritis
Extra-articular RA

Occurrence and severity of extra-articular features generally correlates with disease activity, duration and severity of joint disease.

- Rheumatoid nodules
- Interstitial pneumonitis / Pleural disease
- Pericarditis
- Sjogren’s syndrome: Keratoconjunctivitis sicca
- Scleritis/episcleritis/scleromalacia
  - Vasculitis: association with RF
  - Felty’s syndrome
  - Lower extremity ulcers
  - Amyloidosis

RA: Laboratory

- Increased ESR, CRP

- Mild normocytic normochromic (or hypochromic) anemia

- Eosinophilia

- Thrombocytosis

- Low serum albumin
RA: Laboratory

- Rheumatoid factor: IgM anti-IgG
  - High titers predict more severe disease
  - Sensitivity: 70%  Specificity: 80%
  - Nonspecific: also seen in the elderly, chronic infections, other chronic inflammatory diseases.

- Antibodies to cyclic citrullinated peptide (anti-CCP):
  - Sensitivity about 70% in RA
  - Specificity 95%

RA: Radiographs

- Characteristic joint distribution
- Periarticular osteopenia
- Symmetric joint space narrowing
- Marginal erosions
- May be normal in early disease
QUESTION 3

33 yo woman presents with pain in her elbows, wrists and fingers for several months.

Patient was diagnosed with rheumatoid arthritis and the most appropriate treatment for her is:

1. Daily low dose prednisone
2. Daily Non-steroidal anti-inflammatory drug
3. Weekly methotrexate
4. Infliximab infusion every 2 months
5. Intra-articular steroid injections
RA: treatment

Goals:
- Reduce inflammation / signs and symptoms of disease
- Improve function
- Prevent structural damage

- Early diagnosis and intervention
- Initiate treatment with disease-modifying antirheumatic drugs (DMARDs) to prevent damage.

ADJUNCTIVE DRUG THERAPY:
- Glucocorticoids
- NSAIDs
- Analgesics

DMARDs are the main therapy for RA and all other therapies should be considered adjunctive.
RA: The DMARDs

- Methotrexate
- Leflunomide
- Sulfasalazine
- Hydroxychloroquine

Persistently active disease:
- DMARD Combination therapies
- Biologic therapies – single or combination

Biologics

- Blockers of TNF
  - Etanercept: fusion protein: TNF receptor attached to the Fc region of human IgG
  - Infliximab: chimeric monoclonal antibody
  - Adalimumab: fully human monoclonal antibody
  - Golimumab: fully human monoclonal antibody
Biologics

• **Blockers of IL-1**
  – **Anakinra**: IL-1 receptor antagonist

• **Blockers of costimulation:**
  – **Abatacept**: fusion protein CTLA4-Ig

• **Depletion of B Lymphocytes**
  – **Rituximab**: anti-CD 20 monoclonal antibody

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**Question 4**

33 yo woman presents with pain in her elbows, wrists and fingers for several months. She was treated with methotrexate with initial improvement. 6 months later infliximab was added because of worsening arthritis, and she has complete resolution of symptoms. One year later she presents to her PCP with a 3-month history of low grade fever, abdominal pain and bloating. On exam she had ascitis. Lab tests showed hypochromic, normocytic anemia, WSR 52, normal ALT, AST, Alk Ph. A chest X-ray was normal.
The most appropriate diagnostic approach for this patient is:

1. Liver biopsy to exclude malignancy
2. PPD
3. No tests are necessary, increase therapy for rheumatoid arthritis with extra-articular manifestations.
4. PCR of ascitic fluid
5. No tests are necessary, stop infliximab as abdominal pain is likely a drug side effect.
PCR for *M. tuberculosis complex*

- *Noninvasive* method which can provide the diagnosis of peritoneal TB in most cases.

**Cases of Tuberculosis Associated with Infliximab:**

**Site of TB infection (n)**
- Pulmonary (48)
- Extrapulmonary (59)
- Unknown (23)

**Extrapulmonary TB**
- Peritoneal disease (7)
- Lymph node disease (4)
- Bone or joint (4)

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**Question 5**

- 36 yo male presents to his PCP for evaluation of new bilateral hip pain, left knee pain and swelling. He has a 4-yr history of chronic low back pain that improves with exercise. Since the onset of his illness he had a few acute episodes of red eye, that lasted for about 1 week; treated with topical steroids. You suspect he has a seronegative spondyloarthropathy.
Question 5

The most appropriate test to confirm the diagnosis is:

1. Check HLA-B27
2. Spine and pelvic radiographs
3. Spine and pelvic MRI
4. WSR and c-reactive protein
Spondyloarthropathies

• Related, but different diseases
• Common features
  – sacroiliitis
  – peripheral arthritis: asymmetric; lower extremities
  – enthesopathy: inflammation of tendon insertion
  – inflammatory eye disease (anterior uveitis)
  – Association with HLA-B27
  – Absence of rheumatoid factor
  – Significant familial aggregation

Spondyloarthropathies

• Ankylosing spondylitis
• Psoriatic arthritis
• Reactive arthritis
• Arthropathy of inflammatory bowel disease
• Undifferentiated spondyloarthropathies
• Juvenile-onset ankylosing spondylitis
Ankylosing Spondylitis

Diagnosis based on clinical features, usually supported by radiographic evidence of sacroiliitis.

• Insidious onset of inflammatory back pain and stiffness in late teens or 20s ( < age 40).
• Pain for ≥ 3 months / awakening because of back pain at night
• Family History frequently positive

Ankylosing Spondylitis

Extraskletal manifestations:

• Anterior uveitis or iridocyclitis – most common, usually unilateral
• Osteoporosis – spinal fractures
• Ascending aortitis, aortic valve incompetence, conduction abnormalities, pericarditis
• Lung involvement is rare and late: slowly progressive fibrosis of upper lobes
Question 5: why not MRI?

The most appropriate test to confirm your clinical diagnosis is:
1. Check HLA-B27
2. **Spine and pelvic radiographs**
3. Spine and pelvic MRI
4. WSR and c-reactive protein

Conventional plain spinal pelvic radiographs are still the initial tests for evaluation of the sacroiliac joints in patients with inflammatory back pain.
Ankylosing Spondylitis

• Strong association with HLA-B27
  
  AS – Caucasian: 80-98%  
  – African-american: 50%

  General population: 8%

  However….

  • HLA-B27: **should NOT** be used as a screening or diagnostic test
  • Risk of AS if HLA-B27 positive : only 1-2%

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AS: Treatment

Nonpharmacologic:
• Patient education
• Exercises / Physical therapy

Pharmacologic:
• NSAIDs
• Methotrexate or sulfasalazine – **NOT** effective for spinal arthritis or enthesitis
• **TNF blockers**: Effective for spinal and peripheral arthritis.

There is no evidence that any of the conventional DMARDs, including sulfasalazine and methotrexate, inhibit spinal inflammation or enthesitis in AS.
Question 6

48 yo male presents with a 3-month history of bilateral knee, left ankle, right 1st MTP pain and swelling. On physical exam, in addition to swelling of the painful joints he has diffuse swelling involving the entire left 3rd digit.
The most likely associated feature in this patient is:

1. Pitting of the nails
2. Positive rheumatoid factor
3. Aortic regurgitation
4. Positive HLA-B27
Psoriatic Arthritis

Patient with asymmetric oligoarthritis and one or more additional clinical features: dactylitis, enthesitis or inflammatory back pain.

Psoriasis:
• pre-dates the onset of arthritis – 70%
• presents with arthritis – 15%
• follows the onset of arthritis – 15%

Psoriatic Arthritis

• Clinical presentations
  – Asymmetric oligoarthritis
  – Symmetric polyarthritis: RA-like
  – Predominant DIP arthritis
  – Predominant Spondyloarthritis (sacroiliitis and spondylitis)
  – Destructive (mutilans) arthritis
Psoriatic Arthritis
**Psoriatic Arthritis**

Features that usually help differentiate from RA
- Cutaneous psoriasis
- Nail dystrophy (pitting) – 90%
- DIP involvement
- Enthesitis
- Dactylitis (sausage digit) – > 30%
- Frequent asymmetry of peripheral arthritis
- Spondyloarthropathy – 20 to 40%
- Negative RF

**Psoriatic Arthritis: Treatment**

- NSAIDs
- DMARDs (MTX, leflunomide, SSZ) may have small-moderate effects on peripheral joints, enthesitis, and dactylitis.

Spinal and nail disease do not usually respond.

- TNF inhibitors have been effective in axial and peripheral arthritis, enthesitis, dactylitis, nail disease and skin disease.
A 32 year old male reports pain in the left knee, right ankle and heel. He had one episode of mild diarrhea 2 weeks prior to joint symptoms. The right 4th toe is diffusely swollen, and the right ankle and left knee are warm with pain on range of motion. Urine culture and urethral swab for GC are both negative. What is the most likely diagnosis?

- What is the most likely diagnosis?
  1. Acute gout
  2. Adult-onset Still’s disease
  3. Acute rheumatic fever
  4. Sarcoidosis
  5. Reactive arthritis
Question 7

- **What is the most likely diagnosis?**
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**Reactive arthritis**

- Acute nonpurulent arthritis complicating an infection elsewhere in the body.
  - Genital infection: Chlamydia trachomatis
  - GI infection: yersinia, salmonella, shigella, campylobacter, C. difficile
  - Arthritis 1-4 weeks after exposure
  - HLA-B27 positive in 60-80%. **NOT** a diagnostic test.
  - Young adults

*Triggering infection can be asymptomatic.*
Reactive arthritis

- Classic triad: arthritis, sterile urethritis, conjunctivitis
- **Asymmetric oligoarthritis: large joints of the lower extremities**
- Sacroiliitis and spondylitis
- Keratoderma blenorrhagicum
- Circinate balanitis
- Enthesopathy
  - dactylitis (sausage digit)
  - Achilles tendonitis, plantar fasciitis
Reactive arthritis

- Arthritis
  - often asymmetric, oligoarticular, lower extremities
  - chronic in 15-30% (> 6 months)
  - post-venereal more likely to become chronic
  - Self limiting in the majority of cases but can be erosive and destructive

Arthropathy of inflammatory bowel disease
*Crohn’s disease and ulcerative colitis*

**Peripheral arthritis:** 5-15%
- 2 types: 1 – olygoarthritis and 2 – polyarthritis
- Frequently transient and migratory
- Usually associated with GI symptoms.

**Sacroiliitis and spondylitis:** 10% to 20%
- Axial disease is independent of intestinal disease activity. Symptoms may precede the onset of IBD or appear later.
- Inflammatory back pain
- Tends to be chronic