Rheumatoid Arthritis: Key Features

- Symptoms >6 weeks’ duration
  - Often lasts the remainder of the patient’s life
- Inflammatory synovitis
  - Palpable synovial swelling
  - Morning stiffness >1 hour, fatigue
- Symmetrical and polyarticular (>3 joints)
  - Typically involves wrists, MCP, and PIP joints
  - Typically spares certain joints
    - Thoracolumbar spine
    - DIPs of the fingers and IPs of the toes

Rheumatoid Arthritis: Key Features (cont’d)

- May have nodules: subcutaneous or periosteal at pressure points
- Rheumatoid factor
  - 45% positive in first 6 months
  - 85% positive with established disease
  - Not specific for RA, high titer early is a bad sign
- Marginal erosions and joint space narrowing on x-ray

Rheumatoid Arthritis: PIP Swelling

- Swelling is confined to the area of the joint capsule
- Synovial thickening feels like a firm sponge

Rheumatoid Arthritis: Ulnar Deviation and MCP Swelling

- An across-the-room diagnosis
- Prominent ulnar deviation in the right hand
- MCP and PIP swelling in both hands
- Synovitis of left wrist

Clinical Course of RA

Type 1 = Self-limited—5% to 20%
Type 2 = Minimally progressive—5% to 20%
Type 3 = Progressive—60% to 90%

Rheumatoid Arthritis: Typical Course

- Damage occurs early in most patients
  - 50% show joint space narrowing or erosions in the first 2 years
  - By 10 years, 50% of young working patients are disabled
- Death comes early
  - Multiple causes
  - Compared to general population
    - Women lose 10 years, men lose 4 years

Rheumatoid Arthritis

- Key points:
  - The sicker they are and the faster they get that way, the worse the future will be
  - Early intervention can make a difference
  - Essential to establish a treatment plan early in the disease

Rheumatoid Arthritis: Treatment Principles

- Confirm the diagnosis
- Determine where the patient stands in the spectrum of disease
- When damage begins early, start aggressive treatment early
- Use the safest treatment plan that matches the aggressiveness of the disease
- Monitor treatment for adverse effects
- Monitor disease activity, revise Rx as needed
Critical Elements of a Treatment Plan: Assessment

- Assess current activity
  - Morning stiffness, synovitis, fatigue, ESR
- Document the degree of damage
  - ROM and deformities
  - Joint space narrowing and erosions on x-ray
  - Functional status
- Document extra-articular manifestations
  - Nodules, pulmonary fibrosis, vasculitis
- Assess prior Rx responses and side effects

Critical Elements of a Treatment Plan: Therapy

- Education
  - Build a cooperative long-term relationship
  - Use materials from the Arthritis Foundation and the ACR
  - Assistive devices
- Exercise
  - ROM, conditioning, and strengthening exercises
- Medications
  - Analgesic and/or anti-inflammatory
  - Immunosuppressive, cytotoxic, and biologic
  - Balance efficacy and safety with activity

Rheumatoid Arthritis: Drug Treatment Options

- NSAIDs
  - Symptomatic relief, improved function
  - No change in disease progression
- Low-dose prednisone (≤10 mg qd)
  - May substitute for NSAID
  - Used as bridge therapy
  - If used long term, consider prophylactic treatment for osteoporosis
- Intra-articular steroids
  - Useful for flares
Rheumatoid Arthritis: Treatment Options

- Disease modifying drugs (DMARDs)
  - Minocycline
    - Modest effect, may work best early
  - Sulfasalazine, hydroxychloroquine
    - Moderate effect, low cost
  - Intramuscular gold
    - Slow onset, decreases progression, rare remission
    - Requires close monitoring


Rheumatoid Arthritis: Treatment Options (cont’d)

- Immunosuppressive drugs
  - Methotrexate
    - Most effective single DMARD
    - Good benefit-to-risk ratio
  - Azathioprine
    - Slow onset, reasonably effective
  - Cyclophosphamide
    - Effective for vasculitis, less so for arthritis
  - Cyclosporine
    - Superior to placebo, renal toxicity


Rheumatoid Arthritis: Treatment New Options—Combinations

- Methotrexate, hydroxychloroquine, and sulfasalazine
- Superior to any one or two alone for ACR 50% improvement response and maintenance of the response
- Side effects no greater

2-Year Outcome

- Percent with 50% ACR Response
- Treble RX
- SSZ+HCO
- MTX

Percent with 50% ACR Response

0 10 20 30 40 50 60 70 80

Triple RX SSZ+HCO MTX
Rheumatoid Arthritis: Treatment
New Options—Combinations (cont’d)

- Step-down prednisone with sulfasalazine and low-dose methotrexate*
  - Superior to sulfasalazine in early disease*
- Methotrexate + hydroxychloroquine or methotrexate + cyclosporine†
  - May have additive beneficial effects †


Rheumatoid Arthritis: Treatment
Options—New DMARDs

- Leflunomide
  - Pyrimidine inhibitor
  - Effect and side effects similar to those of MTX
- Etanercept
  - Soluble TNF receptor, blocks TNF
  - Rapid onset, quite effective in refractory patients in short-term trials and in combination with MTX
  - Injection site reactions, long-term effects unknown, expensive


Rheumatoid Arthritis: Monitoring
Treatment With DMARDs

- These drugs need frequent monitoring
- Blood, liver, lung, and kidney are frequent sites of adverse effects
- Interval of laboratory testing varies with the drug
  - 4- to 8-week intervals are commonly needed
- Most patients need to be seen 3 to 6 times a year
Rheumatoid Arthritis: Case 1

- 34-year-old woman with 5-year history of RA
- Morning stiffness = 30 minutes
- Synovitis: 1+ swelling of MCP, PIP, wrist, and MTP joints
- Normal joint alignment
- Rheumatoid factor positive
- No erosions seen on x-rays
**Rheumatoid Arthritis: Case 1 (cont’d)**

- **Assessment**
  - Current activity — mild
  - No sign of damage after 5 years
  - Type 2 minimally progressive course

- **Treatment**
  - NSAID + safer, less potent drugs, eg,
    - Hydroxychloroquine, minocycline, or sulfasalazine
  - Education + ROM, conditioning, and strengthening exercises

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**Rheumatoid Arthritis: Case 2**

- 34-year-old woman with 1-year history of RA
- Morning stiffness = 90 minutes
- Synovitis: 1+ to 2+ swelling of MCP, PIP, wrist, knee, and MTP joints
- Normal joint alignment
- RF positive
- Small erosions of the right wrist and two MCP joints seen on x-rays

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**Rheumatoid Arthritis: Case 2 (cont’d)**

Early erosion at the tip of the ulnar styloid
Rheumatoid Arthritis: Case 2 (cont’d)

1. Soft-tissue swelling, no erosions
2. Thinning of the cortex on the radial side and minimal joint space narrowing
3. Marginal erosion at the radial side of the metacarpal head with joint space narrowing

How fast is joint damage progressing?

Assessment of case 2
- Moderate disease activity
- Many joints involved
- Clear radiologic signs of joint destruction early in disease course
- Type 3 progressive course
- Treatment should be more aggressive
  - NSAID, MTX, SSZ, and hydroxychloroquine would be a good choice

Rheumatoid Arthritis: Case 3

- 34-year-old woman with 3-year history of RA
- Morning stiffness = 3 hours
- 2 to 3+ swelling of MCP, PIP, wrist, elbow, knee, and MTP joints
- Ulnar deviation, swan neck deformities, decreased ROM at wrists, nodules on elbows
- RF positive, x-rays show erosions of wrists and MCP joints bilaterally
- Currently on low-dose prednisone + MTX, SSZ, and hydroxychloroquine
Rheumatoid Arthritis: Case 3 (cont’d)

- **Assessment**
  - Very active disease in spite of aggressive combination therapy
  - Evidence of extensive joint destruction
- **Treatment options are many**
  - Step-down oral prednisone, 60 mg qd tapered to 10 mg qd over 5 weeks, can be used for immediate relief of symptoms
  - Use other cytotoxics or cyclosporine
  - Consider TNF inhibitor or leflunomide

**Rheumatoid Arthritis: Treatment Plan Summary**

- A variety of treatment options are available
- Treatment plan should match
  - The current disease activity
  - The documented and anticipated pace of joint destruction
- Consider a rheumatology consult to help design a treatment plan

**High Impact Rheumatology**

**Rheumatoid Arthritis**

*Potential Complications*
RA: Unknown Case 1

- 68-year-old woman with 3-year history of RA is squeezed into your schedule as a new patient
- She presents with 4 weeks of increasing fatigue, dizziness, dyspnea, and anorexia
- Her joint pain and stiffness are mild and unchanged
- Managed with ibuprofen and hydroxychloroquine until 4 months ago, when a flare caused a switch to piroxicam and prednisone

RA: Unknown Case 1 (cont’d)

- Past history: Peptic ulcer 10 years ago and mild hypertension
- Exam shows a thin, pale apathetic woman with Temp 98.4ºF, BP 110/65, pulse 110 bpm
- Symmetrical 1+ synovitis of the wrist, MCP, PIP, and MTP joints
- Exam of the heart, lungs, and abdomen is unremarkable

RA: Unknown Case 1 (cont’d)

- You are falling behind in your schedule
- What system must you inquire more about today?
  - A. Cardiovascular
  - B. Neuropsychological
  - C. Endocrine
  - D. Gastrointestinal
RA: Unknown Case 1 (cont’d)

- Don’t Miss It
- NSAID gastropathy is sneaky and can be fatal

RA: Unknown Case 1 (cont’d)

- Clues of impending disaster
  - High risk for NSAID gastropathy
  - Presentation suggestive of blood loss
    - Pale, dizzy, weak
    - Tachycardia, low blood pressure
  - No evidence of flare in RA to explain recent symptoms of increased fatigue

NSAID Gastropathy

- Gastric ulcers are more common than duodenal ulcers
- No reliable warning signs
- 80% of serious events occur without prior symptoms
- Risk of hospitalization for NSAID ulcers in RA is 2.5 to 5.5 times higher than general population
- 107,000 patients are hospitalized and 16,000 deaths occur annually in the US because of NSAID-induced gastrointestinal complications

Key Point: Know the Risk Factors for NSAID Ulcers

- Older age
- Prior history of peptic ulcer or GI symptoms with NSAIDs
- Concomitant use of prednisone
- NSAID dose: More prostaglandin suppression = greater risk of serious events
- Disability level: The sicker the patient the higher the risk


NSAID Gastropathy: Treatment

- Acute bleed or perforation
  - Stop NSAID
  - Endoscopy or surgery
  - Start omeprazole
- Ulcer without bleed or perforation, and needs or wants continued NSAID
  - Omeprazole 20 mg qd—76% healed
  - Misoprostol 200 µg qid—71% healed

NSAID Gastropathy: Prevention

- Avoid the problem
- Stop the NSAID and use alternative treatment
  - Low-dose prednisone
  - Acetaminophen
  - Nonacetylated salicylates
- Use a selective cyclooxygenase-2 inhibitor
Differential Expression of COX-1 and COX-2

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Selective COX-2 Suppression: A Potentially Elegant Solution

- Traditional NSAIDs at full therapeutic doses inhibit both enzymes
  - Most have greater effect on COX-1 than COX-2
- The new drugs are highly selective for COX-2
  - >300-fold more effective against COX-2
  - This difference allows
    - Major reduction in COX-2 production of proinflammatory PGs
    - Sparing of COX-1–produced housekeeping PGs


NSAID Gastropathy: Prevention

- Short-term (1 to 4 weeks) clinical studies with COX-2 inhibitor in patients with OA and RA*
  - Significant control of arthritis symptoms
  - Fewer endoscopic ulcers
  - No effect on platelet aggregation or bleeding time
  - Insufficient data to determine risk of serious events or safety in high-risk populations
- Celecoxib and rofecoxib have been approved; meloxicam and other selective inhibitors are currently in clinical trials

*Celecoxib.
NSAID Gastropathy: Prevention (cont’d)
- Counteract the problem
  - Misoprostol
    - Reduction of serious events by 40%
    - Results best with 200 µg qid
    - Side effects: diarrhea and uterine cramps
    - Avoid if pregnancy risk is present
  - Omeprazole
    - Recent studies show 72% to 78% reduction in all ulcers when used for primary prevention at 20 mg qd

NSAID Gastropathy: Key Points
- Keep it in mind
- Know the risk factors
- The best way to treat it is to prevent it
  - Avoid it: Use acetaminophen, salsalate, or a selective COX-2 inhibitor
  - Counteract it: Omeprazole or misoprostol
  - Antacids and H2 blockers are not the answer
    - May mask symptoms but do not prevent serious events

Rheumatoid Arthritis: Unknown Case 2
- You are doing a preop physical for a routine cholecystectomy on a 43-year-old woman with RA since age 20. PMH includes bilateral THAs and left TKA. No other medical problems.
  - Current meds: NSAID, low-dose prednisone, MTX, and HCQ
  - General physical exam normal
  - MS exam, extensive deformities, mild synovitis
  - In addition to routine tests, what test should be ordered before surgery?
Subluxation of C1 on C2

Don't Miss It

RA can cause asymptomatic instability of the neck
Manipulation under anesthesia can cause spinal cord injury

Clues for C1-C2 Subluxation

- Long-standing rheumatoid arthritis or JRA
- May have NO symptoms
- C2-C3 radicular pain in the neck and occiput
- Spinal cord compression
  - Quadriparesis or paraparesis
  - Sphincter dysfunction
  - Sensory deficits
  - TIA as secondary to compromise of the vertebral arteries


Rheumatoid Arthritis: Special Considerations on Preop Exam

- C1-C2 subluxation
- Cricoarytenoid arthritis with adductor spasm of the vocal cords and a narrow airway
- Pulmonary fibrosis
- Risk for GI bleeding
- Need for stress steroid coverage
- Discontinue NSAIDs several days preop
- Discontinue methotrexate 1 to 2 weeks preop
  - Cover with analgesic meds or if necessary short-term, low-dose steroid if RA flares
Rheumatoid Arthritis: Unknown Case 3

- 52-year-old man with destructive RA treated with NSAID and low-dose prednisone. MTX started 4 months ago, now 15 mg/wk
- Presents with 3-week history of fever, dry cough, and increasing shortness of breath
- Exam: Low-grade fever, fine rales in both lungs, normal CBC and liver enzymes, low albumin, diffuse interstitial infiltrates on chest x-ray

RA: Unknown Case 3 (cont’d)

- What would you do?
  - A. Culture, treat with antibiotic for bacterial pneumonia
  - B. Culture, give cough suppressant for viral pneumonia and watch
  - C. Give oral steroid for hypersensitivity pneumonitis and stop methotrexate
  - D. Give a high-dose oral pulse of steroid and increase methotrexate for rheumatoid lung

DMARDs Have a Dark Side

DMARDs have a dark side
Methotrexate may cause serious problems
- Lung
- Liver
- Bone marrow
Be on the look out for toxicity with all the DMARDs
Methotrexate Lung

- Dry cough, shortness of breath, fever
- Most often seen in the first 6 months of MTX treatment
- Diffuse interstitial pattern on x-ray
  - Bronchoalveolar lavage may be needed to rule out infection
- Acute mortality = 17%; 50% to 60% recur with retreatment, which carries the same mortality
- Risk factors: older age, RA lung, prior use of DMARD, low albumin, diabetes


Rheumatoid Arthritis: Summary

- Joint damage begins early
- Effective treatment should begin early in most patients
- Aggressive treatment can make a difference
- Assess severity of patient’s disease
  - Current activity
  - Damage
  - Pace

Rheumatoid Arthritis: Summary (cont’d)

- Choose a treatment plan with enough power to match the disease
  - If in doubt, get some help
  - Rheumatologists can be a bargain
  - New classes of drugs and biologics offer new opportunities
- Do no harm
  - Monitor for drug toxicity—high index of suspicion and routine monitoring
  - Alter the treatment based on changes in disease activity