Rheumatoid Arthritis in Women

Improving Early Diagnosis, Treatment, and Quality of Life

Robert Bunning, MD
Acknowledgment

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Disclosures

Speaker: Insert disclosures here

Note: Staff and committee disclosures listed in packet
Expert Medical Advisory Committee

• Robert D. Bunning, MD, FACP, FACR, (chair)
• Anne Moore, WHNP/ANP-BC, FAANP
The 2003 Albert Lasker Award
What Is Rheumatoid Arthritis?

- A chronic inflammatory disorder that typically affects small joints in your hands and feet
- RA affects the lining of joints that can result in bone erosion and joint deformity
Learning Objectives

• Recognize symptoms of early rheumatoid arthritis to create a diagnostic and treatment plan or refer to a specialist
• Given a patient with suspected early rheumatoid arthritis, evaluate patient history of common comorbidities, specifically cardiovascular disease, tobacco use, osteoporosis, and bone fractures
Learning Objectives

• Employ a patient-centered approach to counseling
• Assess quality of life issues, thereby improving adherence to treatment protocols for early rheumatoid arthritis
Factors Involved in the Etiology of Rheumatoid Arthritis

Who is Affected by Rheumatoid Arthritis?

Female

- Mean age = 55.5
- 2/3 test + for rheumatoid factor
- Radiographic erosion apparent in first year following Dx
- Current or former cigarette smoker

Risk Factors for Rheumatoid Arthritis

- **Sex**: Women more likely 3:1
- **Age**: Common onset ages 30-50
- **Family history**: Inherit predisposition to RA
- **Smoking**: Long-term use
- **Other**: Oral contraceptive use decreases risk
  Pregnant or breastfeeding women may experience remission

A Note on Pregnancy and Rheumatoid Arthritis

- Effects of pregnancy on RA has been observed for decades
- Results show that RA often improves in women during pregnancy, but no single mechanism explains the improvement
Pathogenesis of Rheumatoid Arthritis: It’s Complicated

• Proliferation of synovial macrophages and fibroblasts
• Lymphocytic infiltration perivascular region
• Endothelial cells proliferate
• Neovascularization occurs
• Irregular growth of inflamed synovial tissue
• Formation of invasive pannus tissue

Pathogenesis of Rheumatoid Arthritis: It’s Complicated (continued)

- Multiple cytokines (ex: TNF), interleukins, proteinases, and growth factors are released.
- Inflamed synovium causes:
  - Damage to cartilage
  - Bone erosion
  - Diminished joint integrity, weakened muscles, ligaments, and tendons surrounding joint

Key Conceptual Points

• Patients will require regular monitoring and evaluation

• Bone damage is thought to occur rapidly and studies show it is often present within the first year
Key Conceptual Points
(continued)

• RA is a systemic autoimmune disease that can affect organs and other areas of the body besides joints
• The systemic nature of RA results in extraarticular manifestations of disease
Rheumatoid Arthritis and Increased Mortality

Ted Pincus, MD

To be added
Typical Presentation: Symptoms of Rheumatoid Arthritis

✓ Pain/stiffness lasting > 30 minutes in morning
✓ Stiffness after prolonged rest (articular gelling)
✓ Tender, warm, swollen joints
✓ Peripheral joints affected in symmetric distribution
✓ Fatigue

Factors Associated with Delay to Diagnosis of Rheumatoid Arthritis

Collaborative Care between Primary Care Providers and Rheumatologists

“...Several healthcare professionals, among whom the PCP plays a pivotal role, should share the management of RA. PCPs should be aware that early detection and prompt referral are of utmost importance...Follow-up can be shared between the PCP and the rheumatologist.”

Comparison of Normal Joint and a Joint Affected by Rheumatoid Arthritis

## Diagnostic Evaluation for Rheumatoid Arthritis

### Assess Medical History

<table>
<thead>
<tr>
<th>Onset and duration of symptoms</th>
<th>Other comorbid conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics of symptoms</td>
<td>Family history</td>
</tr>
</tbody>
</table>

### Perform Physical Examination

| General physical examination | Joint assessment (pain, stiffness, functioning) |

### Conduct Laboratory Evaluations

| Blood tests, urinalysis, stool guaiac, radiographs, joint fluid evaluation |

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Comorbid Health Conditions

- Ischemic heart disease
- Heart failure
- Hypertension
- Cancer
- Infections
- Anemia
- Joint deformities
- Respiratory complications

## Diagnostic Laboratory Evaluations

<table>
<thead>
<tr>
<th>Laboratory Evaluations</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-reactive protein</td>
<td>Typically &gt; 0.7 pg/mL</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>Often &gt; 30 mm/hour</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>Over 2/3 positive</td>
</tr>
<tr>
<td>Anti-CCP antibodies</td>
<td>Over 2/3 positive</td>
</tr>
<tr>
<td>Hemoglobin/hematocrit</td>
<td>Slightly decreased</td>
</tr>
<tr>
<td>AST, ALT, alanine</td>
<td>Normal or slightly elevated</td>
</tr>
<tr>
<td>White blood count</td>
<td>May be elevated</td>
</tr>
<tr>
<td>Platelets</td>
<td>Usually elevated</td>
</tr>
<tr>
<td>Complement levels</td>
<td>Normal or elevated</td>
</tr>
<tr>
<td>Immunoglobulins</td>
<td>Possible elevations in alpha-1 and alpha-2</td>
</tr>
</tbody>
</table>

Sonograms Use in Diagnosing Rheumatoid Arthritis

• Dr. B to insert information re: sonogram use
2010 Rheumatoid Arthritis Classification Criteria

• These criteria reinforce the use of a CCP test
# Differential Diagnosis for Rheumatoid Arthritis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Helpful Distinguishing Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis</td>
<td>RF+ but CCP-; Avoid methotrexate; Plaquenil can help</td>
</tr>
<tr>
<td>Lupus</td>
<td>ANA is usually higher than RF or CCP; more systemic features with lupus: rash, proteinuria, hair loss, sun sensitivity; arthritis of RA is more persistent and (untreated) is additive; lupus arthritis more evanescent; complement may be low</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>Asymmetric knee; Hx of tick exposure or rash; with arthritis, serology is sensitive</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>Spondyloarthopathies and reactive arthritis; more low back symptoms; B27 maybe positive; Sacroiliitis; family history of back problems</td>
</tr>
</tbody>
</table>
# Differential Diagnosis for Rheumatoid Arthritis (continued)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Helpful Distinguishing Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonococcal arthritis</td>
<td>Urethritis; new sexual partner; fever; rash; acute onset</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>MCPs less common; serology negative; worse on weight bearing joints</td>
</tr>
<tr>
<td>Gout</td>
<td>At onset of gout, not much like RA but chronic phase can resemble RA; RA patients can get gout; check uric acid and gout risk factors; may need aspiration</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>Vague abdominal pain; check anti-gliad serology</td>
</tr>
<tr>
<td>Myeloma</td>
<td>High sed rate; polyarthrits renal disease and back pain suggest myeloma; check Immunoglobulins SPEP IPEP</td>
</tr>
</tbody>
</table>

To be added
Treatment Goals for Rheumatoid Arthritis

Supportive Measures
- Eliminate pain, inflammation, progression of joint damage
- Improve quality of life

Drugs
- Methotrexate
- Biologics

Surgery

Simplified Algorithm for Medical Management of Rheumatoid Arthritis

After 6-12 weeks, add TNF AND consider co-management with a rheumatologist.

Methotrexate: Anchor Disease-modifying Anti-Rheumatic Drug

**Dosage**
- 10 to 25 mg orally, IM or SC per week

**Baseline tests**
- CBC, liver transaminases, creatinine, chest x-ray, screen hepatitis B and C for high risk patients

**Vaccinations**
- Pneumococcus, influenza, hepatitis B

**Adverse events**
- Nausea, diarrhea, fatigue, mouth ulcers, alopecia, abnormal liver function tests

Low Dose Pulse Methotrexate Therapy in Rheumatoid Arthritis

ROBERT F. WILLKENS, MARGARET A. WATSON, and CHARLES S. PAXSON

Abstract. Thirty-two patients with definite or classical rheumatoid arthritis were treated with low dose pulse methotrexate (MTX). A therapeutic response was shown in $\frac{2}{3}$ of the patients by statistically significant joint changes and improved global response. Greater than one-half of those who improved demonstrated a drop in sedimentation rate. Eight patients discontinued treatment because of ineffectivity and 2 because of gastrointestinal distress. One patient died of neoplasm. Five liver biopsies performed in patients with abnormal liver enzymes demonstrated no MTX related changes. We conclude that MTX may be an effective alternative to other more toxic immunosuppressive regimens and should undergo future evaluation. (J Rheumatol 7: 501-505, 1980)

The History of Biologics for Rheumatoid Arthritis

1998:
Remicade (Crohn’s)
Enbrel (RA)

2001:
Kineret (RA)

2002:
Enbrel
(Psoriatic Arthritis)
Humira

2003:
Alfacept
(psoriasis)

1999:
Enbrel (JRA)
Remicade (RA)

To be added
Bj to DDH: are there generics available? If none, ok to use trade/brand names

ddmellow, 09/14/2010
### Biologic Response Modifiers

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism of Action</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept/ Enbrel</td>
<td>Binds to and inhibits TNF-α</td>
<td>50 mg SC q w</td>
</tr>
<tr>
<td>Infliximab/ Remicaid</td>
<td>Binds to and inhibits TNF-α</td>
<td>3-10 mg/kg IV + MTX q 4-8 w</td>
</tr>
<tr>
<td>Adalimumab Humira</td>
<td>Binds to and inhibits TNF-α</td>
<td>40 mg SC q 1-2 w</td>
</tr>
<tr>
<td>Golimumumab/ Kenerab or Symponi</td>
<td>Binds to and inhibits TNF-α</td>
<td>50 mg SC q 4 w</td>
</tr>
</tbody>
</table>

what are distinctions between drugs?

ddmellow. 09/14/2010
Rheumatoid Arthritis Impacts Patient Lives, Not Just Their Joints

Case Study: Mary

• 35-yo female, Dx with RA for 6 months and on MTX with fair response
• Presents with complaints of pain and swelling on both her wrists which is impeding her job performance
• Feels depressed but wants to get pregnant
Case Study: Mary
Initial Treatment Plan

- Prescribe other agent for joint pain (ex: low dose prednisone), but consider her interest in preconception
- Referral to an OB/GYN for collaborative preconception care
- If the case becomes difficult, referral to a rheumatologist and/or consider biologics (ex: Plaquenil)
RB: is the consultation talking point correct (re: OB/GYN and Ophtha)
Delysha, 09/12/2010
Adalimumab + MTX: Radiographic Changes at 24 & 52 Weeks

**Joint Erosion**

- MTX alone
- Adalimumab 20 mg weekly + MTX
- Adalimumab 40 mg eow + MTX

* p ≤ 0.001 vs placebo
eow = every other week

Functional and Work Disabilities on Women with Rheumatoid Arthritis

RB: Which is correct statement for the last talking point. "...all drugs [with or without MTX?]..."
Preconception Care

• Refer all women with RA who wish to become pregnant to a rheumatologist
  ▪ MTX cannot be taken during pregnancy because of its teratogenicity
  ▪ Some patients stop taking RA drugs to get pregnant while others use medication alternatives
  ▪ Majority of women with RA who are pregnant have normal births without complications
# CDC Medical Eligibility Criteria for Contraceptive Use 2010

<table>
<thead>
<tr>
<th>Condition</th>
<th>Category 1</th>
<th>Category 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis and on immuno-suppressive therapy</td>
<td>✓Progestin-only pill&lt;br&gt;✓Implant&lt;br&gt;✓LNG-IUD (C)&lt;br&gt;✓Copper-IUD (C)</td>
<td>✓Combined pill, patch, ring&lt;br&gt;✓Injection&lt;br&gt;✓LNG-IUD (I)&lt;br&gt;✓Copper-IUD (I)</td>
</tr>
<tr>
<td>Rheumatoid arthritis and not on immuno-suppressive therapy</td>
<td>✓Progestin-only pill&lt;br&gt;✓Implant&lt;br&gt;✓LNG-IUD&lt;br&gt;✓Copper-IUD</td>
<td>✓Combined pill, patch, ring&lt;br&gt;✓Injection</td>
</tr>
</tbody>
</table>

I = initiation of contraceptive method  
C = continuation of contraceptive method

To be added
Psychological Impact

- Overall reduced quality of life associated with:
  - Depression
  - Anxiety
  - Impaired ability to perform activities of daily living
  - Inability to engage in normal physical activities
  - Impaired social relationships
  - Sleep disturbance
  - Fatigue

Rheumatoid Arthritis Still Affects Women at Older Ages

Case Study: Joanne

• 75 year old grandmother w/MCP swelling, fatigued, thinks osteoarthritis is spreading in shoulders, knees, & wrists
• Former smoker with hypertension
• Mentions MCPs bothering her and is very stiff in the morning
RB: please review case
ddmellow. 09/14/2010
Case Study: Joanne
Initial Treatment Plan

- Order CCP when patients have morning stiffness, additive joints, MCP pain
- For her age, consider myeloma, breast cancer with periostitis, and other differentials
- Tx includes MTX and prednisone for flares, active exercise (balanced with periods of rest), physiotherapy, and use of assistive devices
RB: please review case

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Lifestyle Modifications for Patients with Rheumatoid Arthritis

**Increase:**
- Physical Activity
- Joint Care
- Assistive Devices

**Decrease:**
- Tobacco Use
- Weight
Tobacco Use

- Recommend smoking cessation and develop cessation plan
- Provide ongoing support for cessation
- Pharmacologic interventions

Physical Activity

- Cardiorespiratory aerobic exercise offers many benefits to early stage RA patients
- Older patients with RA should undergo a baseline evaluation prior to initiating physical activity programs

Joint Care

- Patients can improve outcomes by applying:
  - Rest
  - Splints
  - Exercise (ex: hydrotherapy pool)
  - Orthotic devices

Assistive Devices

- Wrist Splint
- Shower Chair
- Reacher
Follow-up Assessments of Disease Activity and Treatment Safety

3-Months
- Degree of joint pain
- Duration of morning stiffness
- Duration of fatigue
- Counts of tender/swollen joints
- Functional limitations

Periodic
- Disease progression
  - Loss of motion
  - Instability
  - Malalignment
  - Deformity
  - Laboratory evaluations
  - Radiographic progression

Other Outcomes
- Physician’s global assessment of disease activity
- Patient’s global assessment of disease activity
- Functional status
- Quality of life

Patient Adherence to Pharmacotherapy for Rheumatoid Arthritis

To be added

FIGURE 2. PROBABILITY OF RA PATIENTS REMAINING ON THERAPY.
Factors Influencing Patient Adherence to Pharmacotherapy

- Forget to take
- Side effects
- No effect
- Financing
  - Cost
  - Reimbursement
  - Insurance

Figure 1. The five dimensions of adherence as suggested by the World Health Organisation
**Case Study: Mary**

**Follow-Up Assessments**

<table>
<thead>
<tr>
<th>3-Months</th>
<th>6-months</th>
<th>Other Outcomes</th>
</tr>
</thead>
</table>
| - Continued pain, functional limitations, and depression | - Mary is pregnant  
- Tx: continue during pregnancy | - Post-natal contraceptive planning          |
| - Tx: addition of biologic for pain (without MTX); consider anti-depressant | | |
RB: please review
ddmellow, 09/14/2010
Case Study: Joanne
Follow-up Assessments

3-months
• Some relief with physiotherapy but signs of progressive disease

4-months
• Additional biologic added to MTX

6-months
• Treat occurrence of flares
• Manage risk of comorbid conditions
RB: please review
ddmellow, 09/14/2010
Key Points for Clinicians

• **Early** diagnosis is critical to prevent joint and bone damage
• Initiate state-of-the-art treatment **early**
• Refer patients to, and collaborate with, rheumatologists and other allied health professionals, to ensure correct diagnosis, optimal treatment, and long-term management
• Be aware RA presents through the lifespan- keep RA as part of Diff Dx

Provider and Patient Resources

- American College of Rheumatology
- Johns Hopkins Arthritis Center
- Mayo Clinic
- Arthritis Foundation
- National Institute of Arthritis and Musculoskeletal and Skin Disease
- WebMD