Preventing Pain in RA

Gail S. Kerr, MD, FRCP(Edin)
Chief Rheumatology
VAMC and Howard University Hospital
Professor of Medicine
Georgetown and Howard University Hospitals, Washington, DC
Clinical Professor of Medicine,
Uniformed Services University of the Health Sciences, Bethesda, MD
Disclosures

- Abbott
- Amgen
- Ardea
- Genentech
- Savient
- Astra-Zeneca

• Pfizer
• BMS
• GlaxoSmithKline
• Pfizer
• Eli-Lilly
• American College of Rheumatology
RA Hand Radiograph
Notes

- Vital signs – (maybe)
- “…No complaints, doing well”
- “…Continue meds”
  - NSAID
  - Gold
  - Prednisone
- “..Follow up in 6 months..”
The patient

• 32 yr-old teacher
• **Pain**, swelling, hands, wrists x 3 weeks
• Morning stiffness “most of the day”
• Fatigue, no fever, rash, alopecia
• Full ADL’s, but “spotty work attendance”
• ROS: smoker, mild HTN, mild obesity
• FH: + CVD
Clinical Evaluation

• MDHAQ = 1.2
• Pain = 50mm
• Patient global = 75mm

• Weight = 184, Height = 5’4’’; BMI = 32kg/m²
• General exam normal, including BP
• Musculoskeletal exam
  – Tender/Swollen R 2nd, MCP, PIP, L 3rd MCP
  – Tender both wrists
    • Tender Joint Count (TJC) = 6
    • Swollen Joint Count (SJC) = 3
• MD global = 80mm
• No nodules, rash, sicca symptoms
### One-Page Patient Self-Report Form

#### Global Assessment
- Morning Stiffness
- Quality of Sleep
- Medical History
- Joint Pain
- Comorbidities
- Pain
- Activities of Daily Living

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**Welcome to the Arthritis Center.** Answer below by writing in the space provided or placing a circle/mark for each question. This survey will help your doctor to evaluate you.

### Since last visit, I'm doing:
- (circle): Very Good
- Good
- Fair
- Poor
- Very Poor
- Better
- Worse

#### What bothers you most today?
- How long is your AM Stiffness? None: <10min, 15min, 30min, 45min, 1hr, 2hr, 4hr, All day
- Describe your night-time Sleep: Great, Normal, Fair, Poor, Very Poor, Can't fall asleep, Can't stay asleep, Wakes early, Snoring, Restless legs, Night pain

#### Since last visit I've had:
- Stomach Ulcers
- Accidents or Falls
- Infection
- Heart or Lung Problem
- Eye problems
- New Diagnosis
- New Symptom
- New Procedure

#### DO YOU NOW HAVE?
- Dry mouth/eyes
- Sore throat
- Sore in mouth
- "Cold"/stuffy nose
- Smells
- Ear
- Breath
- Itching
- Hives
- Diarrhea
- Constipation
- Nosebleeds

#### Any New Medicines you've started/changed?

#### In the PAST WEEK, how much pain have you had?
- (circle number or mark thru the line below)

#### TODAY ARE YOU ABLE TO:
- Dress yourself, including laces & buttons?
- Get in and out of bed?
- Lift a full cup or glass to your mouth?
- Walk outdoors on flat ground?
- Wash and dry your entire body?
- Bend down & pick up clothing from floor?
- Turn regular faucets on and off?
- Get in and out of a car?
- How do you pay for medication?
- Insurance
- Co-Pay
- Mos Mail-away
- Medicaid
- Cash
- Are you? Working Full-time
- Part-time
- Homemaker
- School
- Disabled
- Applying for disability
- Date of Annual Physical Exam?
- Your Primary Care Doctor?
- Do you need refills today? Yes

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*Courtesy of Theodore Pincus, MD.*
5-Year Survival in 206 Patients With RA
1985 – 1990

Rheumatoid Factor

mHAQ Score

Survival of Patients With Severe Rheumatoid Arthritis*

Rheumatoid Arthritis (joint count)
- ≤10 joints
- 11-20 joints
- 21-30 joints
- >30 joints

Coronary Artery Disease
- 1-vessel disease
- 2-vessel disease
- Left main disease
- 3-vessel disease

Hodgkin's Disease
- Stage I
- Stage II
- All cases, all stages
- Stage III
- Stage IV

*Defined as >20 actively inflamed joints.
Adapted with permission from Pincus et al. Ann Intern Med. 1999;131:768.
Figure 2. Long-term systemic complications of rheumatoid arthritis. Inflammatory mediators produce effects in multiple organ systems that result in increased rates of metabolic syndrome, osteoporosis, cardiovascular disease & increased mortality that are not explained by traditional risk factors. Implicated cytokines include TNF-α, IL-1, IL-6 & complement immune complexes. (Adapted from McInnes & Schett, 2011).
Comorbidities in RA

• Cardiovascular disease
  – HTN
  – DM
  – Lipids
• BMI
• Osteoporosis
• Periodontal
Periodontal disease

- ↑ RA vs OA
- ↑ in +ACPA, RF
- ↑ SJC, ↑DAS28,
- ↑ Sharpe scores
- ↑ Porphyromonas gingivalis Ab in RF and ACPA + patients
- ↑ seropositive RA independent of P. gingivalis infection
- ? Role of other microbes
  - Fusobacterium nucleatum

Cooles, Current Opinion in Rheumatology 2011
Dissick, J. Periodontology, 2010
Mikuls, Arthritis Rheumatology, 2014
Arvikar, Arthritis Res Ther, 2013
The Progression of RA

Photo: Copyright © American College of Rheumatology.
American College of Rheumatology (ACR) Classification Criteria for RA

At least 4 of the following criteria:

1. Morning stiffness \( \geq 1 \) hour
2. Arthritis of \( \geq 3 \) joint areas
3. Arthritis of hand joints
4. Symmetric arthritis
5. Rheumatoid nodules
6. Serum RF
7. Radiographic changes*

Criteria 1 through 4 must be present for at least 6 weeks; criteria 2 and 5 must be observed by a physician.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>1987 Criteria</th>
<th>2010 Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning stiffness</td>
<td>In and around joints, for at least 1 hour</td>
<td>Clinical synovitis/swelling in at least 1 joint not explained by another disease</td>
</tr>
<tr>
<td>Joint involvement</td>
<td>Physician observed soft tissue swelling or fluid in 3 of 14 possible joints</td>
<td>1 large joint</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-10 large joints</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-3 small joints (with or without large joint)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4-10 small joints (with or without large joint)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;10 joints (at least 1 small)</td>
</tr>
<tr>
<td>Arthritis of hand joints</td>
<td>At least 1 swollen hand or wrist area</td>
<td>NA</td>
</tr>
<tr>
<td>Symmetric arthritis</td>
<td>Simultaneous bilateral involvement</td>
<td>NA</td>
</tr>
<tr>
<td>Rheumatoid nodules</td>
<td>Subcutaneous nodules over bony prominences, extensor surfaces, or in juxtaarticular regions observed by physician</td>
<td>NA</td>
</tr>
<tr>
<td>Serology</td>
<td>Positive RF serum test</td>
<td>Negative RF and negative ACPA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low-positive RF or ACPA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-positive RF or ACPA</td>
</tr>
<tr>
<td>Radiographic changes</td>
<td>Erosions or unequivocal bony decalcification in or adjacent to the involved joints, but not consistent with osteoarthritis</td>
<td>NA</td>
</tr>
<tr>
<td>Acute phase reactants</td>
<td>CRP and ESR</td>
<td>Normal CRP and ESR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abnormal CRP or ESR</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>First 4 criteria must be present for at least 6 weeks</td>
<td>&lt;6 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥6 weeks</td>
</tr>
<tr>
<td>Criteria score required</td>
<td>≥4/7</td>
<td>≥6/10</td>
</tr>
</tbody>
</table>

ACPA indicates anti-citrullinated protein antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NA, not applicable; RF, rheumatoid factor.
RA Management

• Treatment
  – Early
  – “Aggressive”
Start of DMARD therapy

Presentation to rheumatologist

Start of symptoms

Start of damage

Natural course

Treated late

Treated early

Ideal course

Time
Measures used in Clinical Trials

- **Patient Self-Report Questionnaire (PRO’s)**
  - HAQ

- **Composite Disease Activity Measures**
  - ACR 20, 50, 70
  - DAS28, DAS44
  - CDAI, SDAI, **RAPID-3** *(pain, patient global, pain)*
  - EULAR response criteria

- **Imaging**
  - Plain Xray
    - Sharp Scoring – van der Heijde modified
    - (Genant, Larsen)

- **Work Productivity**
RA Treatment Approach

ACR/EULAR 2010 positive

Rx
- MTX 10-15 mg/wk,
- ↑20 mg/wk after 4-8 wk if laboratory test results okay*
- Prednisone 15-60 mg/d, taper to 5 mg/d by 8 wk
- Folic acid 1 mg/d

*Substitute LEF if MTX intolerance

3-Month follow-up

Target:
- Low disease activity
  - SDAI ≤11 (CDAI ≤10)

Target attained

Target not attained

Continue Rx

Moderate disease activity
  - SDAI 11 to ≤26 (CDAI 10 to ≤22)
  - Modify Rx
  - Options:
    - ↑MTX 25 mg/wk
    - Switch to SC MTX
    - Add SSZ + HCQ
    - Add LEF

High disease activity
  - SDAI >26 (CDAI >22)
  - Modify Rx
  - Options:
    - Add SSZ + HCQ
    - Switch to SC MTX
    - Add TNF inhibitor
    - Add CTLA4:1g
Mean Change in Total Sharp Score 52 weeks Early (≤2 Years) vs Established RA (>2 Years)

BeST Study

Treatment Strategies in Early Rheumatoid Arthritis: Clinical and Radiological Outcomes After 2-year Follow-Up

- Seq. mono n=126
- Step-up combo n=121
- Initial combo w/prednisone n=133
- Initial combo w/IFX n=128

TSS change from baseline
Healing erosion in RA patient
Abatacept - Mean change from baseline in the individual subscales of the SF-36 at 2 years

Genovese, Ann Rheum Dis, 2007
Challenges in RA Treatments

• Urban
• Longer disease duration, lower SES and educational level
• RA poor prognosticicators
• Access to specialty, RA treatments
• Comorbidities
Ethnic Minority Rheumatoid Arthritis Consortium

USA
1. Detroit (Mosley-Williams, VAMC)
2. New York (Yazici, NYU)
3. Washington, DC (Kerr, HUH)
4. St. Louis, MO (Ince, PP)
5. Greenville, NC (Treadwell, ECU)
6. New Orleans, (Espinoza, LSU)
7. Fort Lauderdale (Sherrer, PP)
8. Atlanta, GA (Lawrence-Ford, PP)

International
1. Garcia-Valladares (Mexico)
2. Perez-Alamino (Argentina)

VAMC Veterans Affairs Medical Center
NYU New York University
ECU East Carolina University
LSU Louisiana State University
PP Private Practice

Statistician, database manager, programmer:
Christopher Swearingen
Lessons from EMRAC

• African Americans have less years of Education and longer disease duration ACR 2011

• Hispanics have greater discordance in Patient vs Physician Global Scores, higher disease activity ACR 2012

• Use of biologic agents is greater in Caucasians than non-Caucasians ACR 2011

• Less than 5% of Ethnic Minorities meet Inclusion Criteria for Randomized Controlled Trials EULAR 2013

• Double Sero-Positivity is more prevalent in Ethnic Minorities, but associated with Clinical Response ACR 2014

• Educational level and not Ethnicity is an important determinant of RA disease progression ACR 2014

• African Americans and Hispanics achieve a minimal clinical response at 6 and 12 months of RA treatment (despite less use of biologic agents) ACR 2014
RA Treatments of Ethnic Subsets by Cohort (VARA and EMRAC)

* P values are from Chi-square tests of independence

- Prednisone Use:
  - Caucasian: 39%, VARA 27%, EMRAC 36%
  - Non-Caucasian: 33%, VARA 36%, EMRAC 33%
- DMARD Use:
  - Caucasian: 71%, VARA 62%, EMRAC 69%
  - Non-Caucasian: 68%, VARA 69%, EMRAC 68%
- Biologic Use:
  - Caucasian: 21%, VARA 45%, EMRAC 45%
  - Non-Caucasian: 22%, VARA 33%, EMRAC 33%

†P=0.006
‡P<0.001
Potential Analyses - Pain

• Impact of Pain on PRO
• Source of pain in RA
  – Central vs peripheral
  – Inflammatory vs non-inflammatory
• Intervention for pain management
  – Ethnic response
Pain in RA

- RA disease “flares”
  - Define
  - Differential diagnosis
  - Systemic vs local treatments

- Confounders
  - Comorbidities
  - Secondary OA
  - Mental illness

- Fibromyalgia

Avoid Narcotics, not a DMARD!!!
- Smokers, Psychiatric history, PTSH, FH substance abuse
Treating Chronic Pain

- Use measurement tools to assess scope of the problem
  - eg PHQ-9, GAD, ORT
- **Primary treatments** for chronic pain
  i. Motivation/activation/self-help
  ii. Counseling
- **Secondary treatments for chronic pain**
  i. Low risk analgesics (eg gabapentin)
  ii. Psych meds for depression/anxiety/PTSD

**Narcotic use**

**BENEFIT**
- Intractable pain-producing disease
- Goal is comfort

**RISK**
- Substance abuse Hx
- Family Hx sub abuse
- Childhood sexual abuse
- PTSD
- Anxiety
- Depression
- Other MHD

*Courtesy of Dr. Ballantine*

Triple Arthrodesis - Joints that are fused

- Talonavicular Joint
- Subtalar Joint
- Calcaneo-cuboid Joint
The Way It Was
The Way It Should Be