Is It a Rheumatological Disease?

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Vice Dean for Clinical Education

**IS IT A RHEUMATOLOGICAL DISEASE?**

**MONARTICULAR**
- Crystal
- Septic-Arth.
- RA
- Psoriatic

**POLYARTICULAR**
- CTD
- Gout
- Septic Arth.
- RA
- Psoriatic
- Vasculitis

**NON-ARTICULAR**
- Endocrine & Metabolic
- Degenerative

**ENDOCRINE & METABOLIC**
- Thyroid
- Cystoid

**DEGENERATIVE**
- Primary
- Secondary

**METABOLIC BONE DISEASE**
- Osteoporosis
- Paget’s
- Hyperparathyroidism

**CLINICAL CLASSIFICATION OF THE RHEUMATIC DISEASES**

POFPS 40th Annual CME Symposium
August 7-9, 2015
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**APPROACH TO THE PATIENT WITH JOINT PAIN**

- History
- Physical Examination
- Laboratory Data
- X-ray
- Tissue Diagnosis

**PATTERNS OF JOINT INVOLVEMENT IN THE RHEUMATIC DISEASES**

- Number of Joints
  - Monarticular
  - Oligoarticular
  - Polyaarticular
- Symmetry vs. Asymmetry
- Distribution

**HISTORY IN RHEUMATIC DISEASES**

- AGE
- SEX
- A.M. Stiffness
- Pattern of Joint Involvement
- Extra-articular Symptoms
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NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

• Largest class of pharmaceutical agents used worldwide
• Cornerstone agents in the pharmacologic therapy of arthritis
• Effective in relieving pain, inflammation, and stiffness in arthritis patients
• Enhance function and improve quality of life in arthritis patients
• Good safety profile when prescribed and monitored appropriately

REvised Criteria for SLE

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral Ulcers
5. Arthritis
6. Serositis - (a) (b)
7. Renal Disorder - (a) (b)
8. Neurologic Disorder - (a) (b)
9. Hematologic Disorder - (a) (b) (c) (d)
10. Immunologic Disorder - (a) (b) (c) (d)
11. ANA

Joint Pain

Clinician must differentiate ARTHRITIS from ARTHRALGIA
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CRYSTAL-INDUCED ARTHRITIS
-Characteristic Features-
Acutely painful
Monoarticular
May Remit Spontaneously
(Intermittent)

INFECTIOUS ARTHRITIS
-CHARACTERISTIC FEATURES-
Monoarticular
- May be Oligo or Poly Syndromes
Sign(s) of Infection Elsewhere
“Primary” Septic Arthritis
MONOARTICULAR ARTHRITIS

[ Most Common]
Gout
Pseudogout
Septic Arthritis
Traumatic Arthritis
Mechanical Derangement
Bursitis/Tendinitis
SERONEGATIVE SPONDYLOARTHROPATHIES

Ankylosing Spondylitis
Reiter’s Syndrome
Psoriatic Arthritis
Enteropathic Arthritis
Yersinia Enterocolitis

SERONEGATIVE SPONDYLOARTHROPATHIES

-Characteristic Features-

- Usually Oligoarticular, Asymmetrical
- Lower Extremities (or upper)
- Low Back Stiffness
- Enthesopathy → Heel Pain
- Costochondritis
- HLA-B27
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CHARACTERISTIC FEATURES OF CTD

POLYARTHRITIS (Arthralgia)

TRIAD

SYSTEMIC SIGN(S) OF DISEASE

MULTIPLE AUTOANTIBODIES

CONNECTIVE TISSUE DISORDERS

- RHEUMATOID ARTHRITIS
- SYSTEMIC LUPUS ERYTHEMATOSUS
- SYSTEMIC SCLEROSIS
- POLY/DERMATOMYOSITIS
- VASCULITIS
- SJÖGREN’S SYNDROME
- OVERLAP (MCTD)
- UNDIFFERENTIATED CTD
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**LAB TESTING DEFINES THE DISEASE?**

A) Joint Aspiration  
“When in doubt, TAP!”

B) Serological Testing  
Sensitivity vs. Specificity

C) Screening Tests  
“The Big Six”

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**Principles of Rheumatological Testing**

A) Order a test only if it will establish a DX. and/or Change therapy

B) Order a test only after performing a careful Rheumatologic H&P

C) Order a “Panel” only after screening has been positive Cost containment

D) Remember: The lab supports your clinical impression

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SYNOVIAL FLUID ANALYSIS

- WBC with differential
- Gram Stain, C & S
- Glucose
- Crystal Analysis
  - *Protein
  - *Complement
- Mucin Clot
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LABORATORY SCREENING TESTS FOR CTD

CBC  ANA
UA   RA-Latex
CMP  ESR
ANTINUCLEAR ANTIBODY (ANA)

1. Indirect immunofluorescence
2. Positive Titer
3. Significant Titer
4. Disease Associations

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pulmonary Fibrosis</th>
<th>Burns</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE</td>
<td>COPD</td>
<td></td>
</tr>
<tr>
<td>Other CTD</td>
<td>CAH</td>
<td>Myasthenia</td>
</tr>
<tr>
<td>Drugs</td>
<td>Herpes</td>
<td>CUC</td>
</tr>
<tr>
<td>Age</td>
<td>AIDS</td>
<td>Malaria</td>
</tr>
</tbody>
</table>

POSITIVE ANA (HIGH TITER) FURTHER TESTING MAY INCLUDE

- Anti-DS DNA
- RPR (VDRL)
- RNP
- SMITH
- RO (SS-A)
- LA (SS-B)
- Anti-ENA
- Complement (CH50)
- Anti-Histone
**Antibodies associated with Rheumatic Diseases: Percentages of Patients Affected**

<table>
<thead>
<tr>
<th>Antibodies to...</th>
<th>Percentages of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native DNA</td>
<td>SLE: 50% - 60%</td>
</tr>
<tr>
<td>Sm antigen</td>
<td>SLE: 30%</td>
</tr>
<tr>
<td>Histones</td>
<td>Drug-induced SLE: 95%</td>
</tr>
<tr>
<td></td>
<td>SLE: ≤ 40%</td>
</tr>
<tr>
<td></td>
<td>Rheumatoid arthritis: 20%</td>
</tr>
<tr>
<td>SS-A</td>
<td>Sjogren’s syndrome: 70%</td>
</tr>
<tr>
<td></td>
<td>SLE: 30% - 40%</td>
</tr>
<tr>
<td></td>
<td>Rheumatoid arthritis and mixed connective tissue disease: frequency and titer low</td>
</tr>
<tr>
<td>SS-B</td>
<td>Sjogren’s syndrome: 60%</td>
</tr>
<tr>
<td></td>
<td>SLE: 15%</td>
</tr>
</tbody>
</table>


**Antibodies associated with Rheumatic Diseases: Percentages of Patients Affected (continued)**

<table>
<thead>
<tr>
<th>Antibodies to...</th>
<th>Percentages of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNP</td>
<td>Mixed connective tissue disease: 95% - 100%</td>
</tr>
<tr>
<td>Scl-70</td>
<td>SLE: 30% at low titers</td>
</tr>
<tr>
<td></td>
<td>Scleroderma: low frequency and titer</td>
</tr>
<tr>
<td></td>
<td>Scleroderma: 10% - 20%</td>
</tr>
<tr>
<td>Nucleolar antigens</td>
<td>Scleroderma: 40% - 50%</td>
</tr>
<tr>
<td>Centromere antigens</td>
<td>CREST: 80% - 90%</td>
</tr>
<tr>
<td>RANA</td>
<td>Rheumatoid arthritis: 85% - 95%</td>
</tr>
<tr>
<td>PM-1</td>
<td>Polymyositis: 50%</td>
</tr>
<tr>
<td></td>
<td>Dermatomyositis: 10%</td>
</tr>
</tbody>
</table>

**LAB ASSESSMENT OF ACTIVITY OF SLE**

**Clinical Signs:**

- Anti-ds DNA
- Complement
- Hematocrit
- (UA)
- (S. Creatinine)
- (Creatinine Clearance)
HELPFUL SEROLOGIES IN SLE

1. Most Sensitive: ANA
2. Most Specific: Anti-Smith
3. Subset Markers: Anti-ds DNA — Renal
Anti-RNP — Overlap
Anti-Ro — Skin
Anti-Histone — Drug LE

Anti-Cyclic Citrullinated Peptide Ab (Anti-CCP)

-Citrulline is a non-standard amino acid resulting from deamination of arginine

-Citrullinated Peptides are autoantigenic targets locally produced in synovial joint

-Actual Epitope recognized in Anti-Keratin (1979), Anti-Perinuclear Factor (1964), and Anti-Filaggrin
Anti-Cyclic Citrullinated Peptide Ab (Anti-CCP)

- Detected by Elisa technique
- As sensitive as (47-80%) but more specific (97%) than IgM rheumatoid factor
- Marker of erosive disease
- In undifferentiated CTD-(UCTD) may predict RA
- Detected in “Healthy” population years before clinical RA
- Found in 40% “Seronegative RA”
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**ANCA (Anti-neutrophil cytoplasmic Ab)**

Sensitive Assay for
- Wegener's Granulomatosis
- Systemic Vasculitis
- Renal Vasculitis

Indirect Immunofluorescent Technique
- a. Perinuclear --> Renal-limited
- b. Cytoplasmic --> Pulmonary involvement

Titers Vary
- Extent of Disease
- Therapy

**ANCA IN VASCULITIS**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>C-ANCA (Anti-proteinase-3)</th>
<th>P-ANCA (Anti-myeloperoxidase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wegener's</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>Crescentic GN</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>PAN</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Temporal Arteritis</td>
<td>0</td>
<td>+/-</td>
</tr>
<tr>
<td>Churg-Strauss</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>SLE Vasculitis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HSP</td>
<td>0</td>
<td>+/-</td>
</tr>
</tbody>
</table>

Ref: Nephron 19, 1994