Laboratory Testing in Rheumatic Disease

Mark A. McQuillan MD FACP
SFHM
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OR...

- “Rule out Collagen/Vascular Syndrome”
- “Rule out Rheumatic Disease”
- “What labs should I order?”
- “What do all these tests mean?”
- “ENA-5 vs ENA-11 vs Rheum-100”
- “HELP!”
Not that we are complaining…

- The Disease Burden of Rheumatic conditions in the US
- 90% of arthritis sufferers never seek medical attention…
- The Role of Rheumatologists
- An underserved population
- Projected numbers of Rheumatologists needed

The Rheumatologist’s Role…

- Diagnosis of Complex Disorders
- Treatment
- Education (patients, community, 3rd parties, government, Medical students and physicians (CME)
- Patient Advocacy (family, work, legal)
- Decision Support for Dx and Rx
- Consultant and sometimes PCP
- Monitoring of Function, RX Response
- Facilitate Timely Surgical Intervention

“Master Diagnosticians” (?)

- John Decker MD NIH NIAMSD quote:
  - “Diagnosing Rheumatic Syndromes is not so hard…See the patient, listen to the history, examine the patient and their joints, order some films and labs, and make a working diagnosis and treat the patient…
  - …then wait two years and see if you were correct or not!”
UMHS Past Presidents of ARA/ACR

- David A. Fox MD
- Giles G. Bole MD
- William N. Kelley MD
- C. William Castor MD
- William Dodd Robinson MD
- Charles E. Fry MD
  - (Rackham Arthritis Research Unit, Ann Arbor)
  - 3rd ARU in US, est. 1937
  - …couldn’t be wrong?

Sources

Primer on Rheumatic Diseases

- Emphasis on Diagnostic Criteria
- Comparison of patient groups
- Utility for diagnosis in a single case has been called into question
  - Exclusionary
  - Cumbersome
  - Others?

The Rheumatologist’s View of the Diagnostic Universe...

- Key algorithm decision points...
  - INFLAMMATION?
  - SYSTEMICALLY ILL?
  - CRYSTALS?
  - INFECTION?
  - NEOPLASM?
  - OVERUSE HISTORY?
  - ENTHESOPATHY?
  - MUSCULAR DISEASE?
  - VASCULITIS?

RHEUMATIC DIAGNOSES

- INFLAMMATION—obvious?
  - Effusion
  - Synovitis
  - Stress Pain
  - Deformity
  - Calor, Rubor, Dolor, Functio Lasse
Not Inflamed…
- STR Soft Tissue Rheumatism
- Overuse
- Repetitive trauma
- Cumulative Trauma Disorders
- CTS Carpal Tunnel Syndrome
- Tendinitis/Tendinosis
- FM Fibromyalgia  RMFPS Regional
- OA Osteoarthritis

Common things are …
- …Most common!
- OA and FM account for 90-95 % of community-based Rheumatology practice
- STR
- CTS
- Parkinsons
- Depression
- Sleep Deprivation
- Conversion Syndromes

SYSTEMICALLY ILL?
- Fever, rash, weight loss, anemia, hypoalbuminemia…
- Neoplasm (lymphoma, leukemia, mets)
- Infection (septic arthritis, osteomyelitis, SBE TB, fungal, Lyme, HIV, leprosy)
- Vasculitis
  - GCA TA PMR Churg-Strauss PAN Wegener’s
- Miscellaneous  (Sarcoid, Eosinophillic, etc)
**OTHERS...**
- Scleroderma
- PM/DM
- SLE
- Amyloid
- EF
- FMF
- JRA/Stills Dx
- "Mixed Connective Tissue Disease"/Overlap

**INFLAMED?**
- Symmetry
- Hands and Wrists
- Rheumatoid Factor
- SI joints, enthesisopathy
- RA vs SSA
- SLE—usually more bland effusions, lack of deformity early, lack of nodules

**Inflammatory Mono/OligoArthritis**
- Infectious (GC, septic, OM, SBE, TB, fungal)
- Crystals
- Neoplastic
- JRA/Stills
- Atypical RA
- AVN/ON
- Hemoglobinopathy (Hgb S-C)
Other Diagnostic Keys...

- RA incidence in Tecumseh MI is 1.0% (US Incidence estimated 0.1 – 1.1%)
- RA:SLE is 200:1

- Remember, OA + FM + RA is 95% plus of community-based Rheumatologic Practice

Seronegative SpondyloArthropathy

- Ankylosing Spondylitis
- Psoriatic Arthritis
- Reactive Arthritis
- Enteropathic Arthritis
- Others
  - Behcet's
  - Whipple's

Pathognomonic?

Q: Are there ANY conditions in Rheumatology that can be definitively diagnosed by the labs?

Possible answers:
- Maybe by polarizing microscopy or culture, but not by Serology
  - Gout
  - GC, SBE, fungal
More Clinical Keys

- I-P-P-A made even easier!
  - No percussion necessary
  - Auscultatory findings rare
    - (tendon rubs such as de Quervain’s or scleroderma)
    - Ophthalmic or temporal artery bruit—VERY rare
- So just inspection and palpation
- ROM active vs. passive
- Resistance testing

Some other clinical key findings...

- “Shoulder pad” sign
- Macroglossia
- Bruisability
- Koebner phenomenon
- Salmon-colored evanescent rash after bathing
- HPO/clubbing
- Pagetic shins

Some other clinical clues...

- OA plus RA
- OA plus gout
- EOA
- “Inflammatory” OA (?)
- OA plus CPPD
- Gout plus CPPD
- RA plus SLE “rhupus”
- MCTD/Overlap syndromes
DISEASE PROFILES (aka “illness scripts”)

- Fibromyalgia:
  - TBA/TBE
  - sleep disturbance
  - trigger points
  - ***ALL LABS ARE NORMAL *** otherwise treat them as FM “suspect”

OA clues

- 10 % may have inflammation
- Erosions
- Surgical specimens
- Wrists, ulnar styloid, elbows spared
- STS vs effusion
- Bony prominences
- ? Coexistent gout and Heberden’s nodes
- Hallux valgus, hallux rigidus, podagra

Elbows and Arthritis

- RA
- SLE
- OA rarely (pneumatic equipment, jack hammers, meat cutters, air guns, riveters)
- Epicondylitis
- Effusions
- Olecranon
- CTD
**Epicondylitis Factors**
- Is it the arrow or the archer?
- Tennis factors
  - Grip,
  - String tension
  - Racquet weight
  - Vibration dampeners
  - Balance point
  - Rotational torque
- TECHNIQUE? (!)

**EPICONDYLITIS**
- TENNIS
- GOLF
- ARCHERY
- HAMMER
- BRIEFCASE
- COOKING
- CANNING
- PAINTING

**TENNIS TECHNIQUE**
- Forehand
- Backhand
- Service
- Overhead
  - "control the collision out front!"
- RX is helped by lessons, arm band, occ. injection
**BASIC LABS—helpful?**
- CBCDP (eos)
- U/A and Cr
- WESR
- CRP
- ALB
- Ca ++
- Alk Phos

**WESR—sick or not sick?**
- Causes of falsely Low WESR
  - Vibration
  - Timing
  - Anemia
  - Hypofibrinogenemia
  - Coagulopathy
  - Hemoglobinopathy
  - Muscle Diseases

**Can you always follow the WESR?**
- Certain diseases classically do not have WESR elevation associated with flares...
  - PM/DM
  - RA
  - OA
  - SD
  - SSA
  - PMR ?
RHEUM SEROLOGIES

- RF
- ANA
- ENA
- Anti-ds DNA
- Coombs
- SPEP
- ACL, APL, CAB, COAGS, mixing studies

ENA

- Sm, Ro, La, RNP
- Centromere
- Histone
- Others

ANA PATTERNS—diffuse, rim, speckled, homogeneous, nucleolar, centromere

?? Significance ??

Anti-CCP

- Antibodies to citrullinated cyclic polypeptides
- Early and sensitive indicator of RA
- Specificity ?
- Confounders:
  - MCTD
  - Other Overlap syndromes

?? Significance ??
Updates in Rheumatology Testing

WESR vs CRP

- Cheap
- Turnaround time
- Sensitivity
- Poor specificity
- False low WESR
- Lab interference
- ? Serial values

- CRP more costly
- More sensitive w IBD
- ?Serial values
- ? Less sensitive vs more sensitive

"ANCA positive Vasculitis"

- MPO
- PR3

Some Conclusions

- History and Physical findings still count
- Pathognomonic lab findings are very few
- Most diagnoses in Rheumatology are:
  - Clinical
  - Laboratory
  - Pathology
VARIOUS

**Table 10-4. Comparison of Rheumatoid Arthritis and Osteoarthritis**

<table>
<thead>
<tr>
<th>Rheumatoid Arthritis</th>
<th>Osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovial fluid: high WBC and low viscosity</td>
<td>Effusions infrequent</td>
</tr>
<tr>
<td>ESR: usually increased</td>
<td>ESR: may be only slightly increased</td>
</tr>
<tr>
<td>RF: usually present</td>
<td>RF: usually absent</td>
</tr>
<tr>
<td>Positive biopsy of subcutaneous rheumatoid nodule and synovium</td>
<td>Rheumatoid changes in flexor aspects</td>
</tr>
</tbody>
</table>

ESR = erythrocyte sedimentation rate, RF = rheumatoid factor, WBC = white blood cell count.
ANKYLOSING SPONDYLITIS

Spondylitis, Ankylosing Rheumatoid (Marie-Strümpell Disease)
- No diagnostic laboratory test exists for this disorder.
- ESR is increased in ≤ 80% of patients.
- Mild to moderate hyperuricemia occurs in ≤ 50% of patients.

PSORIATIC ARTHRITIS

Arthritis Associated with Psoriasis
- Arthritis occurs in ~2% of patients with psoriasis. No correlation is seen between skin activity and joint manifestations; either may precede the other.
- Increased serum uric acid is due to increased turnover of skin cells in psoriasis.
- If serologic tests for RA are negative, should not be classified as RA.
- No characteristic laboratory findings.

REACTIVE ARTHRITIS (formerly Reiter’s Syndrome)

Reiter’s Syndrome
- Triad of arthritis, urethritis, and conjunctivitis has additional features: dermatitis, buccal ulcerations, cervicitis balanitis, and keratitis blennorrhagica. Triad is initially present in only one-third of patients.
- Increased acute-phase reactants
  - Increased ESR parallels the clinical course.
  - Increased CRP
  - WBC is increased (10,000-20,000/cu mm), as is the granulocyte count.
  - Serum globulins are increased in long-standing disease.
- Nongonococcal urethritis, prostatitis, or seminal vesiculitis and subclinical infection of urethra and colon may be found.
ANA patterns

<table>
<thead>
<tr>
<th>Antihistone</th>
<th>Anti-Sm</th>
<th>Anti-RNP</th>
<th>Anti-SSA/Ro</th>
<th>Anti-SSB/La</th>
<th>Anti-Jo1</th>
<th>Anti-PL7</th>
<th>Anti-PL12</th>
<th>Anti-Scl</th>
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SLE

Lupus, Systemic Erythematosus (SLE)

Criteria for Classification of SLE

- Malar rash
- photosensitivity
- Discoid lesions
- Oral ulcers
- Leukopenia (<4.0 x 10^3 cells/mm^3 or 1 standard deviation below normal)
- Arthritis of more than 6 joints
- Renal disease
- Percutaneous Jaccardi index
- Neurologic involvement
- Hematologic involvement
- Thrombocytopenia

Sensitivity Specificity % %
Malar rash 77 66
Photosensitivity 72 39
Discoid lesions 61 64
Oral ulcers 52 59
Leukopenia (<4.0 x 10^3 cells/mm^3 or 1 standard deviation below normal) 48 70
Arthritis of more than 6 joints 54 78
Renal disease 43 62
Percutaneous Jaccardi index 58 79
Neurologic involvement 43 79
Hematologic involvement 41 83
Thrombocytopenia 54 70

Overall 60 60

Sensitivity and specificity of the various clinical features for the diagnosis of SLE are shown in the table above.

After the diagnosis of SLE has been established, patients should be followed closely for long-term complications such as renal disease, pulmonary involvement, and central nervous system involvement.
**SLE CRITERIA**

Lupus, Systemic Erythematosus (SLE)

Criteria for Classification of SLE

- Presence of four or more criteria at some or different times allows the diagnosis of SLE and excludes other disorders.

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**SLE and DRUG-INDUCED SLE**

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