Learning Objectives

1. Cite a systematic approach to the diagnosis of arthritic and autoimmune disorders.
2. Identify indications and use of disease-modifying, anti-rheumatic drugs.
3. Know how to diagnose & treat PMR and temporal arthritis.

1. A 28 yo HISP F c/o 8-mo Hx of painful, swollen joints
   + AM stiffness; several joints in hands & arm involved, bilaterally; + fatigue; no wgt loss, fever
   PE WNL except joints:
   Swollen, tender left wrist, 3 MCPs & 2 PIPs; Tender right wrist, left ankle & other MCPs

What type of arthritis does she have?

A. Monoarticular
B. Crystal-induced
C. Symmetric polyarticular
D. Asymmetric polyarticular

An Approach to Rheumatoid Articular Disease

• Look for the Pattern: 1 of 3 patterns
  – Monoarticular
  – Symmetric Polyarticular
  – Asymmetric Polyarticular
### Monoarticular
- Septic
- Gout
- CPPD
- Tumor
- Trauma
- Viral

### Symmetric Polyarthritis
- RA
- SLE
- Psoriatic
- Osteoarthritis
- Scleroderma
- Lyme
- Rheumatic fever
- Gout
- CPPD
- Hepatic

### Asymmetric Polyarthritis
- HLA-B-27 dz: Psoriatic, ankylosing spondylitis, reactive arth, IBD
- Gout
- CPPD
- Lyme
- Viral

2. Which of the following findings is most specifically diagnostic of classic RA?

   - A. High ESR
   - B. Positive ANA
   - C. Rheumatoid joint erosions
   - D. Rheumatoid factor

**ANSWER**
- C. Rheumatoid Joint Erosions
- All of the others are associated with RA, but only joint erosions are seen only in classic RA
3. To diagnose RA, one needs which of the following?

A. 3/6 criteria fulfilled
B. 5 points total
C. 6 points total
D. 4/6 criteria fulfilled
E. 5/8 criteria fulfilled

New Criteria for RA

• Every patient with points > 6 is unequivocally classified as an RA patient
• Provided he has synovitis in ≥ one joint and given that there is no other diagnosis better explaining the synovitis.
• 4 areas are covered in the diagnosis

1. Involvement of

• 1 large joint = 0 points
• 2-10 large joints = 1 point
• 1-3 small joints (with or without involvement of large joints) = 2 points
• 4-10 small joints (with or without involvement of large joints) = 3 points
• > 10 joints (with involvement of at least 1 small joint) = 5 points

2. Serological Parameters – Including RF & "ACPA" (Anti-citrullinated Protein Antibody)

• Negative RF and negative ACPA gives 0 points
• Low-positive RF or low-positive ACPA gives 2 points
• High-positive RF or high-positive ACPA gives 3 points

1st Area

• Joint involvement: designating the metacarpophalangeal joints, proximal interphalangeal joints, the interphalangeal joint of the thumb, second through third metatarsophalangeal joint and wrist as small joints
• Elbows, hip joints and knees as large joints
3. Acute Phase Reactants:
- 1 point for elevated erythrocyte sedimentation rate (ESR), or elevated CRP value (c-reactive protein)

4. Duration of arthritis:
- 1 point for symptoms lasting six weeks or longer

4. To diagnose SLE, one needs the following # of criteria fulfilled?
- A. 4/7
- B. 5/7
- C. 3/9
- D. 3/11
- E. 4/11

Diagnosis of SLE
- Malar rash
- Photosensitivity*
- Arthritis
- Renal dz
- Heme disorder*
- Immunologic disorder (antibody)
- Discoid rash
- Oral ulcers*
- Serositis
- Neuro dz*
- ANA abn

3/11 = probable; 4/11 = definite

5. In treating RA, DMARDs should be started when?
- A. As soon as the diagnosis is made
- B. After 3 months of therapy with NSAIDs
- C. Only after NSAIDs have failed
- D. Only by a rheumatologist
5. In treating RA, DMARDs should be started when?

- A. As soon as the diagnosis is made (71%)
- B. After 3 months of therapy with NSAIDs (8%)
- C. Only after NSAIDs have failed (21%)
- D. Only by a rheumatologist (3%)

### Treatment of Rheumatoid Dz

- **DMARDs** should be started as early as possible to delay disease progression; A Rec
- Use NSAIDs in lowest dose for relief & cut back when DMARDs work; A Rec
- No regimen of monotherapy is clearly superior to any other; A Rec, AHRQ, 2007
- Exercise is effective in improving function & reducing bone loss; A Rec, Cochrane, 2009
- Alt/Comp med therapies have NO evidence; A Rec, Cochrane: Diet, U/S, balneotherapy, acupuncture

### DMARDs
- Disease-modifying anti-rheumatic drug
- Immunosuppressants
- Anti-Malarials
- TNF
- Cytokine Inhibitors
- D-penicillamine: High toxicity
- Gold: Limited by adverse effects
- Steroids: Assoc with increased CV Risk. Used today only as an adjunct; systemic or intra-articular
- Use with contraception
- TNF inhibitors: Increase in skin cancer & opportunistic infections
- Biologics are TNFI, T-cell I, B-cell Modulators and Interleukin Modifiers

### DMARDs
- TNF-a Inhibitors may be the most powerful DMARDs for overall efficacy in RA, JRA*, Ankylosing Spondylitis, & Behcet’s
- Reduce disease activity, retard progression & improve QOL
- But watch for adverse effects

### DMARDs
- Antimalarials can improve survival in SLE pts B Rec
- Mortality fell from 3.85/1000 person-years in non-users to 0.54 in users > 2yrs
DMARDs

- Etanercept & adalimumab are more effective than anakinra in RA
- Etanercept is better tolerated than adalimumab, anakinra, & infliximab
- A Rec, Cochrane

Don’t Forget About Associated Issues

- Neuropsych issues in SLE
  - Occur in 80% of all SLE patients
  - Can occur early, in absence of systemic Dz
  - HAs, seizures, psychosis, cognitive dysfxn
  - Mortality is increased 2-3x

- Insulin Resistance in both RA & SLE
  - 50%-60% IN RA
  - 30% in SLE
  - CV risk = that of diabetics; A Rec, Am Coll Rheum, 2008
  - Folate does protect vs. MTX G.I. side effects: Cochrane, 2009

6. A 67 yo WF c/o 1 mo of fatigue, wgt loss, & aching/stiffness in upper back & shoulders
Which of the following is the next most appropriate diagnostic study?

A. X-rays
B. ESR
C. Febrile agglutins
D. ANA

7. A 70 yo WF c/o fever, neck, shoulder and arms ache & HA evolving over 5 weeks
The most important Dx test is:

A. EMG
B. CPK
C. Muscle biopsy
D. Temporal artery biopsy
7. A 70 yo WF c/o fever, neck, shoulder and arms ache & HA evolving over 5 weeks
   The most important Dx test is:

   A. EMG 1%
   B. CPK 22%
   C. Muscle biopsy 10%
   D. Temporal artery biopsy 68%

Polymyalgia Rheumatica & Temporal Arteritis*

- Closely related inflammatory conditions
- PMR more common, TA more dangerous
- Both have high ESRs
- Both occur usually in age > 50
- *TA also called cranial arteritis & giant cell arteritis

Dx of PMR

- Clinical syndrome of:
  - Fever
  - Nonspecific somatic complaints
  - Pain & stiffness in shoulder &/or pelvic girdle (proximal muscle groups)
  - Elevated ESR

Treatment of PMR

- Corticosteroids: 5-20 mg/day.
- Response is dramatic within 48 hrs
- < 1% patients need > 15 mg/day
- Relapses increase if dose = 10 mg/day
- Adverse effects increase @ > 15 mg/day with NO additional benefit

Treatment of PMR

New Evidence

- Adding methotrexate @ 10 mg/week to steroids decreased steroid use and relapse rates
- Infliximab added to steroids: NO benefit
- Azathioprine to steroids: ???
- NSAIDs: Do not use long-term

Treatment of PMR
New Evidence

- After Sx resolution, taper by 2.5 mg q 2-4 weeks to 10 mg/day
- Then taper @ < 1mg q 4-8 weeks to 5 mg/day
- Then lengthen taper over total of 18-24 months

8. The most specific symptom of Giant Cell Arteritis is:
A. High ESR
B. Temporal headache
C. Jaw claudication
D. Vision changes

Dx of Temporal Arteritis

- Presents with many of findings in PMR
- High ESR
- HA
- Tender scalp
- Jaw claudication*
- Vision changes
- Arterial biopsy

Rx of Temporal Arteritis

- Corticosteroids (quickly)
- Don’t wait for Bx, but get Bx within 72 hrs or lose sensitivity
- W/o visual Sx, 40-60 mg/day
- With visual Sx, 250 mg solu-medrol q 6 hrs x 3-5 days, then switch to po

TA Rx

- Sx resolve & ESR normal within 2-4 weeks
- Then begin taper: ≤ 10% daily dosage q 2 weeks
- Monitor for Sx or ESR increase; if + stop taper & await resolution, then restart taper
- Further taper is same as for PMR
Treatment of PMR & TA

• Watch for osteoporosis
• Bisphosphonates are recommended in elderly women on steroids

Summary

• Diagnostic approach to rheumatologic Dz
• Rheumatoid arthritis
• Systemic lupus
• DMARDs
• Review of PMR & TA

Bibliography

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Answers

1. C
2. C
3. C
4. E
5. A
6. B
7. D
8. C
9. B

Disease Specific ANAs

Disease  | ANA Assoc
---------|-------------------
SLE  | Anti-Smith
RA  | RF
Scleroderma  | Anti-centromere
MCTD  | Anti-U1RNP
Polymyositis  | Anti-Jo-1
Sjogren  | Anti-SSA & anti-SSB
gener  | c-ANCA & p-ANCA

Rheumatologic Remission

• Clinical vs. Radiologic
• Can have clinical w/o radiologic
• TNF’s may be the best meds to achieve either
• The earlier meds begun, the better the chances of remission: ergo, the new criteria
Rheumatoid Factor

- Lacks both Sens & Spec
- Useful in RA for severity & extra Sx, But NOT following dz
- Testing appropriate when suspect
  - RA: 50%-90%
  - Sjogren: 75%-95%
  - Cryoglobulinemia: 40%-100%
  - MCTD: 50%-60%
- Doesn’t rule out; can support Dx

ANA

- Reported as titers: > 1:320 more likely to be true dz
- Titers of ≤ 1:40 unlikely to have a rheumatologic dz
- ANA pattern is more specific for dz
- Best for SLE, drug-induced lupus, Sjogren, scleroderma & MCTD

Chromatin Antibodies

- Anti-dsDNA: Rule in SLE
- Anti-histone: Rule out drug-induced lupus
- Anti-Smith: R/I SLE
- Anti-Ro: Assoc with Sjogren
- Anti-centromere: Assoc with scleroderma
- c-ANCA: Sens & Spec for Wegener

HLA-B27

- Assoc with Spondyloarthropathies:
  - AS: 95% Sens
  - Reiter’s: 80% Sens
  - Psoriatic: 70% Sens
  - IBD: 50% Sens
- Testing rarely useful
- Only when above are suspected

ESR

- Low Specificity
- Correlates with clinical activity in RA
- Best when used for
  - PMR: Sens = 80%
  - TA: Sens = 95%
- Usually quite high vs elevated (NOT 20-50)

Giant Cell Arteritis

- If biopsy of 1 side is negative, but suspicion is still high, biopsy the other side.
- Remember: this disease can be in any cranial artery, not just the temporal