

“Screening” for Autoimmune Disease

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Objectives

- Identify when to “screen” for autoimmune disease
- Explain ANA testing
- Review common symptoms, physical findings and laboratory abnormalities associated with autoimmune diseases

Case #1

- 45 year-old male patient presents to your office with c/o generalized fatigue, diffuse arthralgias and diffuse myalgias
- PMHx/PSHx: HTN, PTSD, appendectomy
- FHx: Mother age 65 with "some kind of arthritis" affecting her hands and knees
- SocHx: Recently divorced. No children. Construction worker – recently unemployed. Smokes 1-2 ppd for 25 years. Drinks 2 beers each night, more on weekends. No IVDA.

Case #2

- 32 year-female patient presents with complaints of a new rash on her face, fatigue and hand pain. She states she hasn't been able to get her rings on and off easily. Her knuckles feel swollen & stiff.
- PMHx/PSHx: G2P2. C-section x2
- FHx: Sister with RA.
- SocHx: Married. SAHM. 2 children ages 3 and 6. Smokes on the weekends socially, but not daily. ETOH on weekends: 2-4 beers. No IVDA.

Case #3

- 55 year-female patient presents with complaints of her fingers turning white and blue with cold exposure.
- PMHx/PSHx: GERD
- FHx: Unremarkable.
- SocHx: Divorced. Lab tech. No children. Smokes 1-2ppd for 20+ years. Denies routine ETOH. No IVDA.

Overview

- Complaints of chronically low energy, arthralgias and myalgias are common
- Fact:
 - Few of these pts will have lupus or other CTD
 - Many will be diagnosed with Fibromyalgia (FMS)
- Autoantibody testing is best reserved for pts whose pretest odds of an autoimmune disease are high
- All rheum lab tests must be interpreted in the context of the history and physical exam

Demographics

- Lupus is not a common disease
 - US prevalence:
 - white women 10-50/100,000
 - black women 4-5 x's higher
- FMS is common
 - US prevalence: 1% in women 18-29 years old; 7% in women over age 59
 - At least 20 x's more prevalent than lupus in white women

ANA

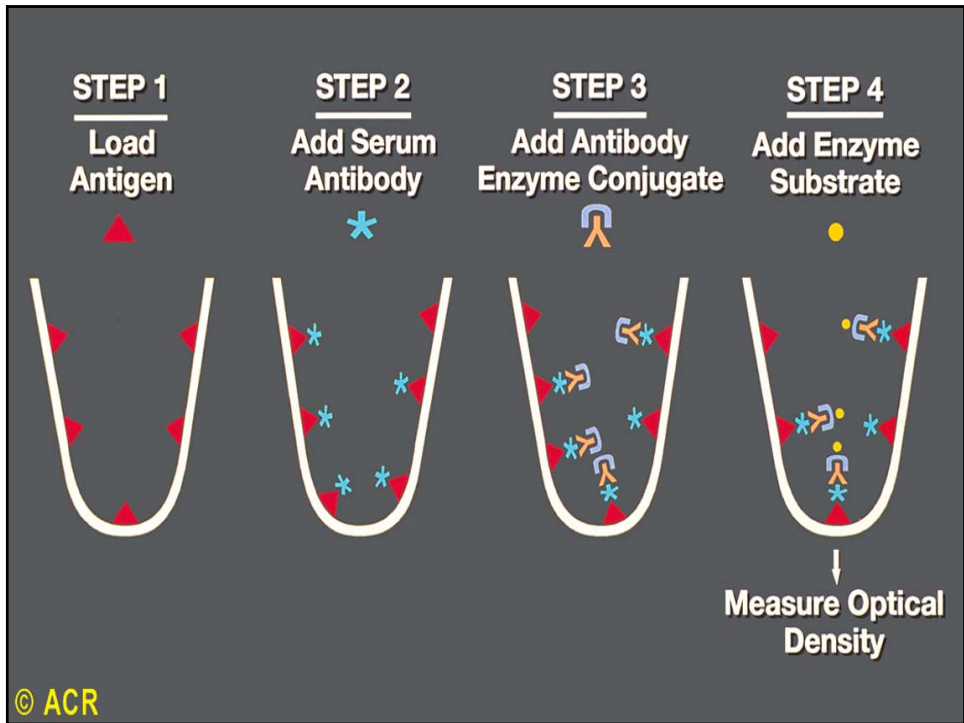
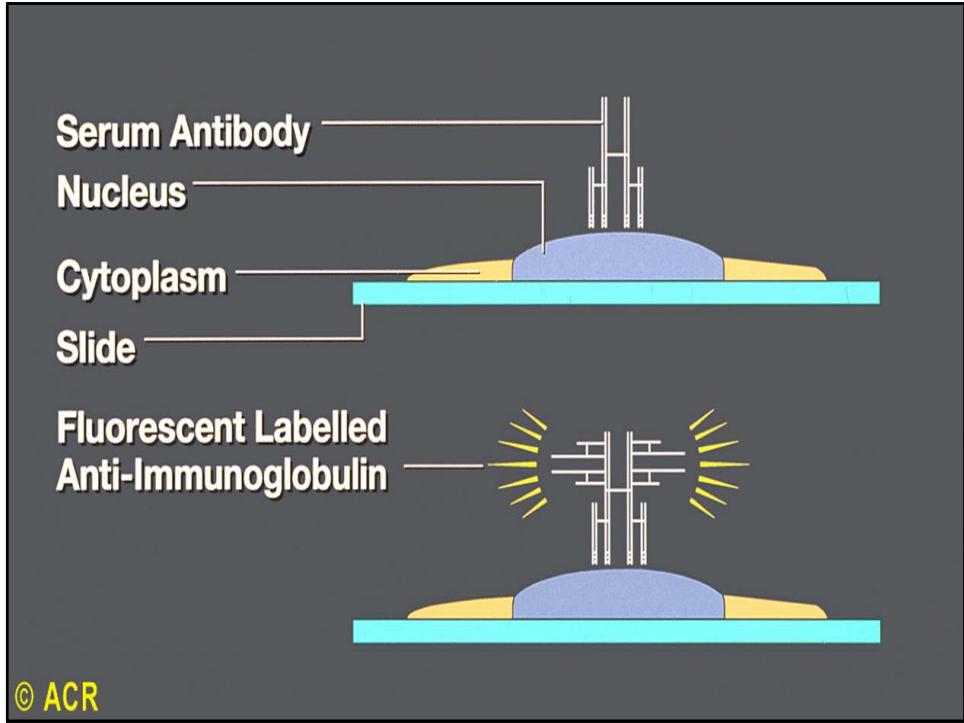
- Short for "anti-nuclear antibody"
- Positive ANAs are commonly found in the normal population
- False positive ANAs (ie, ANAs in the absence of autoimmune disease or known antigenic stimuli) are more commonly seen in women and in elderly patients. The majority of these are present in low titer.

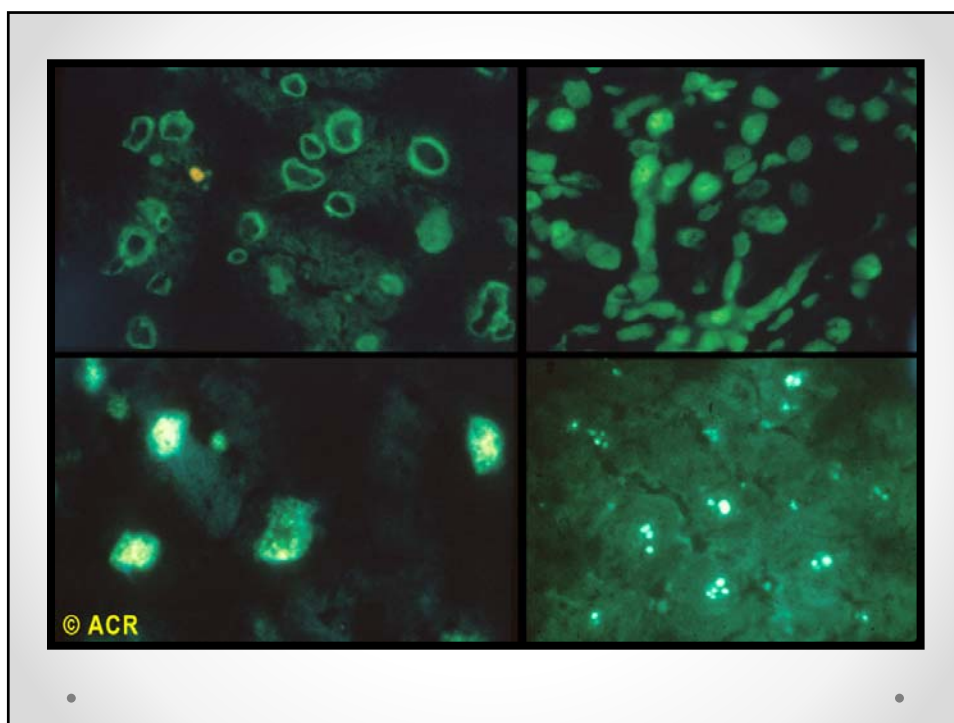
How common are they?

- DeVlam et al looked at healthy blood donors
 - 20% of women & 7% of men studied had a positive ANA
 - Women >40 years old - 31% ANA+
- Tan et al studied healthy adults ages 20-60
 - 32% 1:40, 13% 1:80, 3% 1:160
 - 39% of pts with "soft tissue rheumatism" 1:40, 23% 1:80
- Slater et al reviewed 1010 ANA results
 - False positive rate was 72% in pts <65; 90% in >65 group
 - Even ANAs 1:320 or greater were more likely to be falsely positive (55%) than indicative of rheumatic disease (45%)

Methods of Detection

- FANA – standard method
 - Sera incubated with substrate cells that have been fixed with acetone
 - Bound antibodies are detected by fluorescein-conjugated anti-human IgG
 - Viewed through fluorescence microscope, antibodies bound to nuclear antigens produce a nuclear pattern
 - Dilution at which nuclear fluorescence disappears = titer
 - Results: pattern and titer
- Others:
 - Immunodiffusion
 - Counterimmunoelectrophoresis (CIE)
 - Immunoprecipitation
 - Immunoblot
 - Enzyme Immunosay (ELISA)





Complicating factor

- Laboratory methods differ and are constantly changing
 - Often have extensive data on tests no longer in use & limited data on those currently available
 - Traditional: ANA by direct immunofluorescence (DIF) after incubation of sera with fixed Hep-2 cells
 - Newer: ELISA
- Emlen and O'Neill compared FANA to ELISA
 - 88% of known SLE pts had positive ANA by FANA
 - ELISA ranged 62-90%

H&P is the key

- Advances in diagnostic testing have not supplanted a carefully performed H&P
- History & ROS should seek clues of autoimmune disease and also evidence of FMS
- When a lab test (eg, ANA) is not very specific, it is essential to determine the pre-test likelihood of the disease

Symptoms of ANA positive Rheumatic diseases

- Sjogren's
 - Dry eyes
 - Dry mouth
 - Vaginal dryness
 - Parotid swelling
 - Accelerated dental caries or gingivitis
- Lupus
 - Alopecia
 - Oral or nasal ulcers
 - Malar rash
 - Photosensitivity
 - Raynaud's
 - Pleuritic chest pain
 - Joint pain and stiffness
 - Unexplained fever
 - Unexplained weight loss
 - Unexplained LAD

Symptoms of ANA positive Rheumatic diseases

- Scleroderma/CREST
 - Hand stiffness
 - Raynaud's
 - Digital infarcts
 - Calcinosis
 - Telangiectasias
 - Heartburn
 - Dysphagia
 - Dyspnea
- Myositis
 - Insidious proximal muscle weakness
 - Rash
 - Dyspnea

2010 ACR/EULAR Classification Criteria for RA

JOINT DISTRIBUTION (0-5)	
1 large joint	0
2-10 large joints	1
1-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
SEROLOGY (0-3)	
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
SYMPTOM DURATION (0-1)	
<6 weeks	0
≥6 weeks	1
ACUTE PHASE REACTANTS (0-1)	
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1

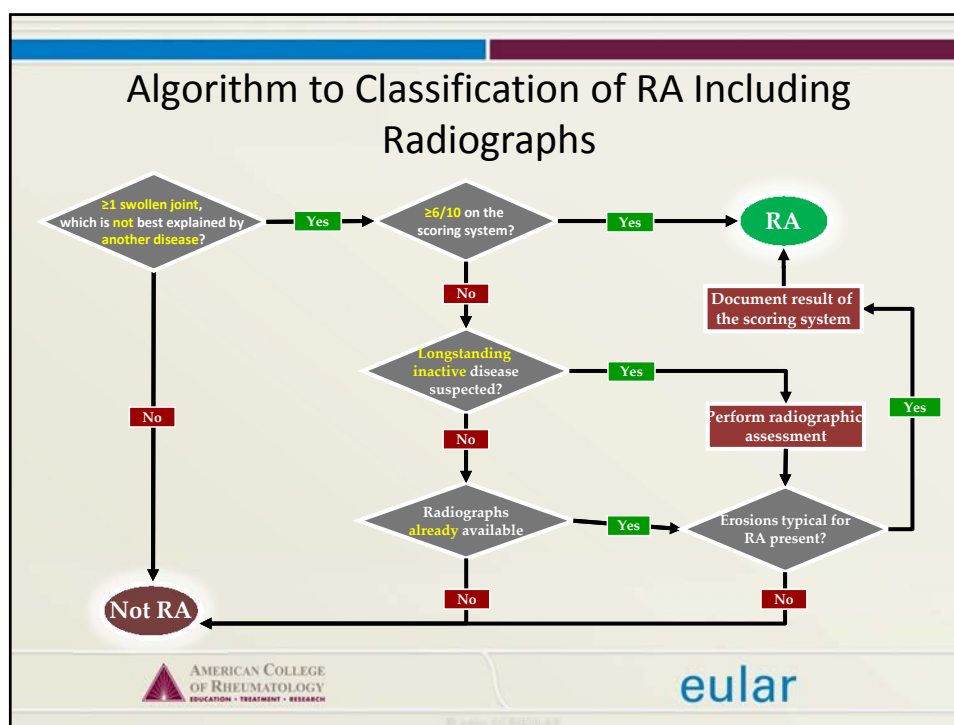
≥6 = definite RA

What if the score is <6?

Patient might fulfill the criteria...

→ **Prospectively** over time
(cumulatively)

→ **Retrospectively** if data on all
four domains have been
adequately recorded in the past



SLE: Diagnostic criteria

- D: discoid rash. Erythematous raised lesions.
- O: oral and nasal ulcers.
- P: photosensitivity
- A: arthritis. (nonerosive, 2+ jts, symm)
- M: malar rash. Fixed erythema over malar eminences.
- I: immunologic. Anti-dsDNA, anti-Sm, or APL abs.
- N: neuropsych (sz or psychosis)
- R: renal. Proteinuria or cellular casts.
- A: +ANA
- S: serositis. Pleurisy or pericarditis
- H: hematologic. (hemolytic anemia, ↓ WBCs, ↓ plts)

• (Any 4 or more of the 11 criteria present, serially or simultaneously, during any interval of observation) •

SLE: rash, face and neck



SLE: butterfly rash, discoid type





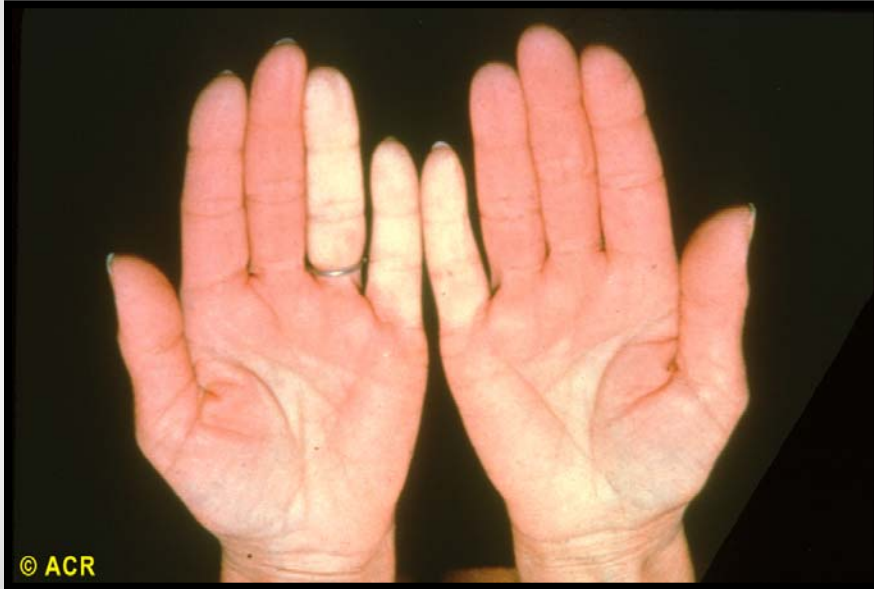
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SLE: bullous lesions, palate



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Raynaud's phenomenon, blanching of hands



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Raynaud's phenomenon: hands



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Raynaud's phenomenon: cyanosis of the hands



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Fusiform swelling, hand



Jaccoud's arthropathy (clinical and radiograph)



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Photosensitivity, face and neck



Laboratory abnormalities in lupus

- Serum Chemistry
 - Elevated Cr
 - Low albumin
 - Polyclonal hyperglobulinemia
 - Elevated CPK
- UA
 - Proteinuria
 - Microscopic hematuria
 - RBC or hyaline casts
- CBC
 - Leukopenia: usually lymphopenia, occ neutropenia
 - Anemia: chronic disease, hemolytic
 - Thrombocytopenia

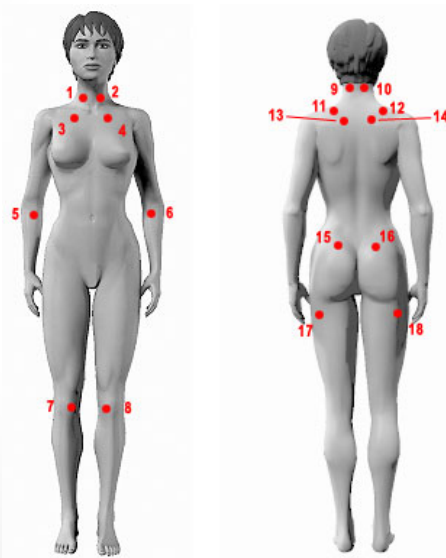
History & Physical Exam

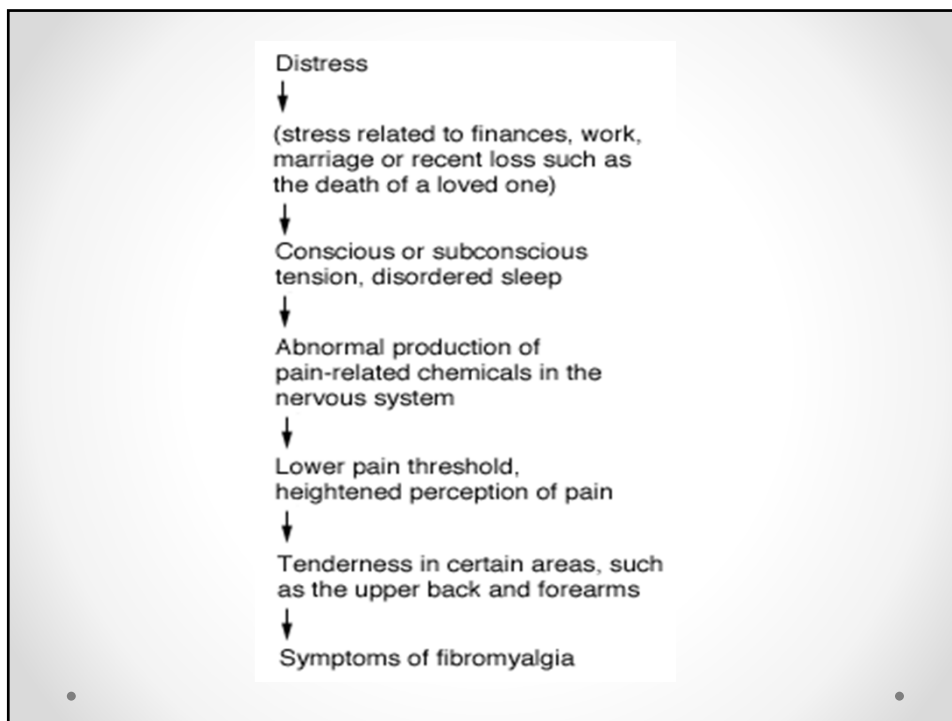
- Differentiating lupus from FMS by history alone can sometimes be difficult
 - Fatigue, arthralgia, morning stiffness, cold intolerance, chest wall pain and subjective deficits in memory and concentration
 - The likelihood of lupus increases if the pt gives a convincing history of lupus that would not ordinarily occur in FMS
- While excluding lupus, look for fibromyalgia

Fibromyalgia

- Not merely a diagnosis of exclusion
- Often occurs in a setting of stress, depression, anxiety, lack of sleep, lack of exercise, and traumatic life experiences
- Related symptoms:
 - Chronic headaches, memory loss, loss of concentration, paresthesias of the extremities, irritable bowel or bladder
- Normal lab values: CBC, CMP, UA
- When the history, PE, and routine lab testing supports a diagnosis of FMS, autoantibody testing is not necessary

Fibromyalgia Tender Points





Case #1

- 45 year-old male patient presents to your office with complaints of generalized fatigue, diffuse arthralgias and diffuse myalgias
- PMHx is significant for HTN, PTSD
- PSHx: vasectomy
- FHx: Mother age 65 with "some kind of arthritis" affecting her hands and knees
- SocHx: Recently divorced. No children. Construction worker – recently unemployed. Smokes 1-2 ppd for 25 years. Drinks 2 beers each night, more on weekends. No IVDA.

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QUESTIONS?



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