Antinuclear Antibodies


Key Points:
- These tests should only be ordered in patients for whom you have a reasonable pre-test probability
- ANA results (titer and pattern) are subjective and depend on laboratory experience
- There are six patterns of staining in ANA with their own disease associations

Categories of autoantibodies
- Plasma membrane (antiphospholipid)
- Cytoplasm (antimitochondrial)
- Nucleus (anti DS DNA)
- Nucleolus (anti topoisomerase I)
- Neutrophilic cytoplasm (anti-proteinase 3 or C-ANCA)

ANA
- Only order when high enough pre-test probability (remember that PPV depends on test characteristics and prevalence)
- Indirect immunofluorescence assay: Hep-2 cells on a glass slide are coated with patient’s serum, washed, then stained with fluorescent labeled antibodies to human serum
- For certain specific antibodies, additional immunoblotting, Western blotting, immunodiffusion, ELISA
- 95% sensitive for SLE
- Low specificity
  - Autoimmune thyroid disease
  - Other CTD
  - Infections: virus, SBE, TB
  - Malignancy
  - Healthy controls (5%)
- Titer and pattern are subjective and not always reliable / reproducible
- <1:80 less significant
- Does not correlate with disease activity

Six patterns of ANA and disease associations
- Homogenous pattern
  - Anti dsDNA
    - Specificity for SLE 95% - false positive in some hepatitis
    - Sensitivity 40-60% in SLE
    - One of 11 criteria for SLE
    - Predicts flares: may predate nephritis
  - Anti-Histone
    - Drug-induced lupus (procainamide, hydralazine, aldomet, dilantin, INH, tegretol)
    - Best for negative predictive value

- Speckled pattern (ENA or acid extractable nuclear antigens)
  - Anti-Smith
    - 99% specific, 20% sensitive for SLE
  - Anti U1-RNP
    - 30-40% sensitive for SLE (associated with Raynaud’s and less severe clinical course)
    - Mixed connective tissue disease:
      - Nearly 100% sensitive
      - SLE, Raynaud’s, myositis, non-erosive arthritis, puffy hands, esophageal dysmotility, sicca, scleroderma-like
      - Other CTD: 2-5% scleroderma, 24% PM/scleroderma overlap, 4-17% PM/DM
  - Anti Ro (SSA) and La (SSB)
    - In primary Sjogren’s: Anti-SSA 88-96% and Anti SSB 71-87%
      - Associated with increased severity (vasculitis, hypergammaglobulinemia, lympho/leukopenia)
    - SLE: SSA 25%, SSB 10%
    - Neonatal lupus: 90%
NR Dec-03

- Nucleolar (RNA-associated antigens)
  - Anti SCL-70 (Topoisomerase I)
    - 95% of patients with scleroderma – predicts more subacute, progressive, systemic disease
    - Diffuse scleroderma: 25-75% sensitivity, 93% specificity
    - CREST 13%
  - Anti PM-SCL: polymyositis/scleroderma overlap syndromes

- Centromere
  - Limited scleroderma: 60-80%
  - Isolated Raynaud’s: 25% - may predict risk of CREST
  - Primary biliary cirrhosis
  - Normal: nearly 1% of female blood donors

- Peripheral - antibodies to nuclear envelope, seen with staining for dsDNA in older systems

- Cytoplasmic
  - Mitochondrial pattern: primary biliary cirrhosis, autoimmune hepatitis, IBD, scleroderma
  - Anti Jo-1 (speckled cytoplasmic)
    - 20-40% of patients with dermatomyositis, polymyositis, mixed PM/DM
    - Higher prevalence of ILD (20-25%)

Test characteristics from UpToDate

<table>
<thead>
<tr>
<th>SLE</th>
<th>ds DNA</th>
<th>Histone</th>
<th>Smith</th>
<th>RNP</th>
<th>SSA</th>
<th>SSB</th>
<th>SCL-70</th>
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<tr>
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<tr>
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<td>Moderate</td>
<td>97%</td>
<td>46-85%</td>
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<td>14-60%</td>
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