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Rheumatology Serologic Testing

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Evidence Based Statements

- Laboratory testing should not be undertaken in the absence of a careful history and physical exam, establishing the pretest probability of disease – B
- Osteoarthritis can be diagnosed on clinical grounds alone – B
- 30% of patients with rheumatoid arthritis are seronegative for RF – A
- Ordering anti-CCP antibody along with the RF increases the sensitivity of detecting early RA – A

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Evidence Based Statements (cont.)

- Low level ANA titers greater than or equal to 1:40 are seen in up to 20-30% of healthy individuals and this increases with age – A
- ANA titers with specific antibodies should be measured only when ANA related diseases are highly suspected on clinical grounds - B
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**Rheumatoid Factor**

- Low sensitivity (26-60%) and specificity (85%)
- Found positive in significant amounts in RA, lupus, scleroderma, Sjögren's, tuberculosis, hepatitis, sarcoidosis, interstitial lung disease and COPD.
- May be positive in 5-40% of healthy individuals, and prevalence increases with age.
- Found in only 70% of patients with RA.
- When used as a screen PPV for RA is 24% and 34% for other rheumatic disease.
- If used in a population with inflammatory arthritis, PPV increases to 80%.

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**Anti-Cyclic Citrulinated Peptide**

- High sensitivity (50-75%) and specificity (>90%).
- Measurement is helpful in workup of inflammatory arthritis and increases the prognostic significance of RF positivity.

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**Anti-Nuclear Antibodies**

- Positive in non-rheumatologic conditions: aging, autoimmune thyroiditis, PBC, ITP, IBD, infections, GN, malignancy, pregnancy, relative of patients with CVD, drugs and MS.
- Positive ANA tests are much more prevalent than collagen vascular disease; most abnormal results are false positives.
- ANA testing should only be ordered in the context of clinical signs that correlate with related diseases.
- Helpful in the diagnosis of lupus, scleroderma, MCTD, Sjögren's and polymyositis.
- Serial ANA testing is rarely useful.
ANA testing in the real world

232 referrals over 3 years for positive ANA (17.7% of entire referral volume)
9.1% ended up having an ANA associated rheumatic disease
9.1% had isolated autoimmune thyroid antibodies
Positive predictive value of the positive ANA was 2.2% for lupus.
For an ANA titer less than 1:160 the positive predictive value was 0.8%

Choosing Wisely
**Take Home Points**

- Using serologic testing as a screening tool in nonspecific musculoskeletal pain will result in a large amount of false positive results
- Advising patients who test positive for RF and ANA that they have RA or lupus is premature
- Using history and physical to increase pretest probability will dramatically improve predictive value
- Obtaining an anti-CCP antibody concomitantly with a rheumatoid factor increases the utility of the test result

**Take Home Points (cont.)**

- Low titer ANAs are more likely to be false positives compared to ANAs > 1:160
- For positive ANA screens, obtaining a full ANA profile (profile 224 in quest) which includes disease specific antibodies can improve diagnostic accuracy
- If a patient requires a workup for CVD and already has a diagnosis of an ANA related disease, consider skipping the ANA screen and start with a full ANA profile.