Antinuclear antibody (ANA) testing for pediatric rheumatology referrals

What are antibodies?

Antibodies are proteins produced by white blood cells that circulate in the bloodstream. They play a crucial role in the immune system by helping to defend the body against diseases and infections. However, not all antibodies function correctly. Antinuclear antibodies (ANA) are a type of antibody that mistakenly target the body's own healthy cells, rather than harmful invaders like bacteria or viruses. This misdirected immune response is often associated with autoimmune disorders.

What is the ANA test?

An **antinuclear antibody (ANA) test** is a blood test used to measure the level of antinuclear antibodies in the bloodstream. While a positive ANA test can support the diagnosis of an autoimmune disorder, it is not specific and can also be found in healthy individuals. In fact, 15–30% of healthy children may have a positive ANA result without having any autoimmune condition. Because of this, a positive ANA test alone is not typically indicative of systemic lupus erythematosus (SLE) or other autoimmune diseases in children. To illustrate, for every child diagnosed with juvenile idiopathic arthritis (JIA) or systemic lupus erythematosus (SLE), approximately 400 children with a positive ANA test will not have a rheumatic disease.

When should an ANA test be ordered?

The antinuclear antibody (ANA) test is often overused in the pediatric population. It is not recommended as a screening tool in either children or adults, in alignment with guidance from the **American College of Rheumatology** and the **AAP Choosing Wisely Campaign.**

Importantly, the ANA test should not be used alone to diagnose any rheumatic or autoimmune disease due to several key limitations:

- A low-titer positive ANA (less than 1:160) can be seen in up to 25% of healthy children and adults.
- False positives are common and can be triggered by viral infections, recent vaccinations, family history of autoimmune disease, medications, as well as thyroid, gastrointestinal, liver diseases, and even cancer.
- The ANA test is also costly, with prices ranging from $100 to $1,000, depending on the laboratory.

Additionally, ANA testing has no diagnostic role in conditions such as juvenile idiopathic arthritis (JIA) in children or rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis in adults. Once performed, ANA testing does not need to be repeated, regardless of the result.

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That said, the ANA test can be useful in evaluating suspected systemic lupus erythematosus (SLE) when clinical symptoms support the diagnosis. Signs and symptoms of lupus may include:
- Persistent or prolonged fever
- A butterfly-shaped facial rash
- Joint pain, stiffness, and swelling
- Muscle aches
- Fatigue
- Renal or neurological involvement

Ultimately, the decision to order an ANA test should be based on clinical suspicion and not used as a general screening tool. Appropriate use of this test helps reduce unnecessary anxiety, costs, and follow-up procedures.

How to interpret an ANA test?

An ANA test detects the level, or titer, of ANA and identifies the staining pattern, if ANA is present. The titer is reported as a ratio with most labs considering a titer of 1:160 as positive. A titer of 1:320 or 1:640 has a strong clinical correlation with Lupus. The patterns of ANA are not specific to any one disease and do not have clinical significance in pediatrics.

Concerns about lupus or a lupus-like disease?

If there is clinical concern or suspicion for systemic lupus erythematosus (SLE) or a lupus-like autoimmune condition, additional laboratory evaluation is necessary to guide diagnosis and management.

Recommended additional laboratory tests:
- Complete blood count (CBC) with differential
- Erythrocyte sedimentation rate (ESR)
- C-reactive protein (CRP)
- Comprehensive metabolic panel (CMP)
- Complement levels (C3 and C4)
- Urinalysis (UA)
- Urine protein-to-creatinine ratio
- Extractable nuclear antigen (ENA) panel

Next steps based on test results

If the results indicate a high likelihood of lupus, the Pediatric Rheumatology team at Manning Family Children's will review the findings and expedite an appointment to ensure timely diagnosis and early, effective treatment.

If the additional lab results are largely normal, but symptoms persist, the patient may benefit from referral to another specialty depending on their clinical presentation.