Effective Health Care Program

Muscle, Bone, and Joint Conditions
Juvenile Idiopathic Arthritis

Antinuclear Antibody, Rheumatoid Factor, and Cyclic-Citrullinated Peptide Tests for Evaluating Musculoskeletal Complaints in Children

Research Focus for Clinicians

In response to a request from the public, a systematic review assessed the test performances of antinuclear antibody (ANA), rheumatoid factor (RF), and cyclic-citrullinated peptide (CCP) for pediatric systemic lupus erythematosus (pSLE) and juvenile idiopathic arthritis (JIA) among children (≤18 years) with undiagnosed musculoskeletal (MSK) pain. The systematic review included 28 clinical studies published from January 1960 to January 2010 and also characterized the prevalence and etiology of MSK pain in children. This summary is provided to inform discussions of options with patients and to assist in decisionmaking along with consideration of the values and preferences of patients and their caregivers; it should not be construed to represent clinical recommendations or guidelines. The full report is available at www.effectivehealthcare.ahrq.gov/anatest.cfm.

Background

MSK pain is common in children and can affect physical, psychological, and social functions. MSK pain is often nonspecific, which can confound an accurate diagnosis. MSK pain may be due to nonrheumatic or rheumatic causes. Nonrheumatic causes are far more common, generally benign, and most often attributable to trauma, overuse, and normal bone growth. Rheumatic causes such as inflammatory arthritis are infrequent but generally chronic, thus requiring timely diagnosis and effective intervention to prevent progression and long-term damage. Rheumatic causes of childhood MSK pain may include JIA and pSLE. In childhood, the prevalences of JIA and pSLE are 100 in 100,000 and 3.3 to 8.8 per 100,000, respectively.

A complete patient history and physical examination is generally considered the best way to diagnose a rheumatic cause of MSK pain. For patients suspected of having inflammatory arthritis, some physicians also request serological tests such as ANA, RF, and CCP, despite the fact that the diagnostic performance, usefulness, and proper interpretation of these tests remain uncertain in pediatric populations.

Conclusions

Nearly all MSK pain in children (97%) results from noninflammatory causes (see prevalence and etiology on back page). There is low-strength evidence for the utility of RF in diagnosing JIA in children with undiagnosed MSK pain (sensitivity = 4.8%; specificity = 98%). The low sensitivity suggests diagnosing JIA should not rely on serological tests alone but may be combined with thorough clinical assessment that suggests the presence of inflammatory arthritis. The use of ANA and CCP tests to diagnose JIA or pSLE remains unsupported due to the methodological limitations of existing studies that prevent assessment of sensitivity and specificity. The low prevelance of these two diseases in the pediatric population also limits the diagnostic value of these tests.

Clinical Bottom Line

One retrospective cohort study examined records of 437 pediatric hospital patients with MSK pain who had an RF test. They found very limited utility of the RF test for diagnosing JIA with a positive predictive value of 45 percent and a negative predictive value of 77 percent (sensitivity = 4.8%; specificity = 98%). ●○○

The evidence is insufficient to evaluate the sensitivity and specificity of most test-disease combinations. Thus, the diagnostic performances of these tests remain unknown. ○○○

Strength of Evidence Scale

High:	●●●	There are consistent results from good-quality studies. Further research is very unlikely to change the conclusions.
Moderate:	●●○	Findings are supported, but further research could change the conclusions.
Low:	●○○	There are very few studies, or existing studies are flawed.
Insufficient:	○○○	Research is either unavailable or does not permit estimation of a treatment effect.

Glossary

- Sensitivity—known as the "true-positive rate" or the ability of a test to correctly identify people with a condition.
- Specificity—known as the "true-negative rate" or the ability of a test to correctly identify people without a condition.
- Positive Predictive Value—indicates the likelihood that a person with a positive test result will have the condition for which the test is used. The higher the positive predictive value (e.g., 90% is considered a high value), the more useful the test is for predicting that the person has the condition.
- Negative Predictive Value—indicates the likelihood that a person with a negative test result does not have a condition. The higher the negative predictive value (e.g., 99% is considered a high value), the more useful the test is for predicting that a person does not have the condition.

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Findings on Prevalence and Etiology of MSK Pain and Serological Tests in Healthy Children

The systematic review included a literature search to evaluate the prevalence of MSK pain in children and adolescents who do not have JIA and pSLE and to determine the prevalence of positive ANA, RF, and CCP test results among healthy patients.

Prevalence of Undiagnosed MSK Pain in Children

- The prevalence of MSK pain ranged from 2 percent in 12-year-olds to 52 percent in 18-year-olds.
  - Up to 30 percent of children reported having chronic pain (including MSK pain) lasting more than 6 months.
- Recurrence rates of pediatric MSK pain are high.

Etiology of Undiagnosed MSK Pain in Children

- According to 1 retrospective chart review, 97 percent of MSK pain in children was of noninflammatory origin.
  - The most common cause is physical trauma (44%).
  - Other causes include overuse (24%), osteochondroses (10.3%), hypermobility (3.3%), growing pain (3.5%), and viral infection (4.5%).
  - The prevalence of these etiologies varies with age.
- Of the 3 percent of pediatric cases of MSK pain that result from inflammatory causes:
  - 2.5 percent result from toxic synovitis (also known as transient synovitis).
  - 0.8 percent result from inflammatory arthritides.

Test Positivity in Healthy Children

- The prevalences of positive ANA, RF, and CCP test results in healthy children were as follows:
  - ANA: 0–18 percent
  - RF: approximately 3 percent
  - CCP: 0–0.6 percent

Gaps in Knowledge

- No studies examined clinically important outcomes—such as the impact of the test results on referrals, ordering additional tests, patient management, and patient and parent anxiety levels—which can affect quality of life and psychological well-being.
- No studies addressed the patient or clinical characteristics that could modify the accuracy of these serological tests including age, sex, race, history of recent infections, and presence of other characteristics other than MSK pain.

What To Discuss With Your Patients

- That MSK pain is common and may recur
- That inflammatory causes are found in only 3 percent of children
- The important role of a complete patient history and physical examination in diagnosing a rheumatic cause of MSK pain
- When ANA, RF, or CCP serological testing is useful
- Reasonable expectations of a positive or negative serological test result when taking the clinical diagnosis into account

Ordering Information

For electronic copies of this clinician research summary and the full systematic review, visit www.effectivehealthcare.ahrq.gov/anatest.cfm. To order free print copies of this clinician research summary, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

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