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Does C6 Represent a “C” Change For Diagnosis of Lyme Arthritis?

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Among children with acute arthritis who present to clinics and emergency departments in Lyme endemic regions, Lyme disease is substantially more common than septic arthritis.

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Among children with acute arthritis who present to clinics and emergency departments in Lyme endemic regions, Lyme disease is substantially more common than septic arthritis. However, because septic arthritis may be associated with significant morbidity if operative treatment is delayed, clinicians are faced with the conundrum of differentiating Lyme arthritis from septic arthritis. Unfortunately, clinical signs and laboratory abnormalities can overlap between children with Lyme and septic arthritis. Even when a diagnostic arthrocentesis is performed for diagnosis, synovial fluid white blood counts similarly overlap in Lyme and septic arthritis and less than half of the children with septic arthritis have a positive synovial fluid Gram stain. Therefore, clinicians must make treatment decisions before definitive two-tiered Lyme serology and synovial fluid culture results are available in 24 to 48 hours. There are risks on both sides of this decision: unnecessary operative treatment of children with Lyme arthritis vs. delay in treatment for children with septic arthritis.

Enter the serum C6 enzyme immunoassay (EIA). With first-tier test results in available in a few hours, C6 EIA could impact clinical decision-making in real-time. For this issue of *Pediatrics*, Nigrovic et al (10.1542/peds.2019-0593) conducted a 6-center prospective cohort study that reported the following test characteristics of the C6 EIA for diagnosis of Lyme arthritis: 100% sensitivity, 94% specificity, 100% negative predictive value, and 84% positive predictive value. Although the specificity and positive predictive value were not 100%, these reported test characteristics are higher when compared with the whole cell EIA. Furthermore, none of the 11 children with septic arthritis had a positive C6 EIA, and nearly 11% of children with a positive C6 EIA underwent an operative washout. With a higher specificity and positive predictive value, and results available at the time of clinical decision-making, the C6 EIA could reduce unnecessary operative management, hospitalization, and intravenous antimicrobial therapy for children with positive first-tier testing who are unlikely to have septic arthritis.

However, in an accompanying commentary (10.1542/peds.2019-1998), Shapiro and Oliveira address several limitations to the study. Specifically, the commentary writers point out that a positive first-tier C6 EIA result was included in the definition of Lyme arthritis, and thereby the sensitivity of the C6 EIA had to be 100%. They also raised the question of whether some of the children with joint pain, but not effusion, had false positive C6 EIA testing, which would lower the reported specificity and positive predictive value.

So, do the results of this multicenter study support a “C” change when it comes to Lyme testing for children with acute arthritis? The C6 EIA is certainly promising for more rapid identification of children with Lyme vs. septic arthritis, when used in the appropriate clinical context. Please “C” for yourself and take a read through the article as well as the accompanying commentary.

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