Clin Orthop Relat Res (2015) 473:2236–2237 / DOI 10.1007/s11999-015-4198-9

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

Published online: 18 February 2015

CORR Insights

CORR Insights®: The Alpha-defensin Test for Periprosthetic Joint Infection Responds to a Wide Spectrum of Organisms

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Where Are We Now?

Periprosthetic joint infection (PJI) remains one of the most common and devastating complications following total joint arthroplasty. Despite its prevalence, the diagnosis of infection remains challenging. Many of the tests currently available to diagnose PJI are indirect markers for infection and or inflammation. While they may provide a high sensitivity, they lack specificity in diagnosing PJI. By contrast, tests such as synovial fluid cultures may only identify the infecting organism 40% to 60% of the time. Direct tissue cultures, considered the gold standard for diagnosis, require surgery to obtain appropriate culture and may fail to show growth if not cultured in the appropriate media. Additionally, the results are not available until after treatment has been rendered. All of these factors can lead to confusion and misdiagnosis with both false negatives and false positive results.

Recently, much attention has been given to the role of synovial fluid biomarkers in the diagnosis of PJI. Neutrophils in the synovial fluid secrete specific proteins in the face of infection. These proteins, such as alpha-defensin, appear to be highly sensitive and specific for the diagnosis of PJI. Three current studies [1, 3, 4] have shown sensitivity and specificity above 96% for the diagnosis of PJI.

The present study by Deirmengian et al. aims to now look at the responsiveness of alpha-defensin to a multitude of infecting organisms both in the breadth and magnitude of response. The author demonstrated that all organisms cultured appear to stimulate a positive alpha-defensin response. In addition, various organisms regardless of virulence, stimulate the same magnitude of response eliminating the concern that low virulence organisms may yield false negative results. The results of this study have important implications particularly for fastidious organisms that are difficult to isolate in culture and may stimulate a low or no systemic response.

Where Do We Need To Go?

It is important to keep in mind that no test is 100% sensitive or specific for the diagnosis of PJI. This was the impetus for the Workgroup of the

This CORR Insights® *is a commentary on the article* "The Alpha-defensin Test for Periprosthetic Joint Infection Responds to a Wide Spectrum of Organisms" *by Deirmengian and colleagues available at:* DOI: 10.1007/s11999-015-4152-x.

The author certifies that he, or a member of his immediate family, has no funding or commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

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This *CORR* Insights® comment refers to the article available at DOI: 10.1007/s11999-015-4152-x.

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Musculoskeletal Infection Society's (MSIS) definition of periprosthetic joint infection [2, 5]. By combining many of the indirect tests for detecting PJI, a common method to define and diagnose PJI has been established.

The authors attempted to address concerns that alpha-defensin may not be stimulated or differentially stimulated by different organisms. While the importance of this study should be noted, it is also not without its limitations. Of the 1937 synovial fluid samples analyzed, only 49% had positive cultures. Thus, more than half had no isolation of organisms. Is it possible that if these cultures were positive, the additional organisms may have varied both in response and magnitude? Also, were the culture-negative but alpha-defensin-positive samples a false-positive alpha-defensin test or a false-negative culture result? It would seem unlikely the former is true given the previous published data on the sensitivity and specificity of alpha-defensin test, as well as previous results demonstrating that a positive alpha-defensin test with a negative cultures are in fact infected based on the minor criteria of the MSIS definition of PJI [1, 3, 4]. It would be helpful to know however if these culture-negative infections had a lower magnitude of alpha-defensin response than the culture-positive infections.

How Do We Get There?

The use of synovial-fluid biomarkers appears to be a giant leap forward in the diagnostic evaluation of PJI. Many suspect that this test can and should replace many of the other indirect markers for periprosthetic infection. A test with rapid results that is not open to misinterpretation (positive or negative) result and is at a relatively low cost has mass appeal. This new data also appears to confirm that alpha-defensin is widely applicable regardless of the virulence of the organism. Are we ready to accept this as the gold standard for the diagnosis of PJI for all comers and abandon the current diagnostic criteria? Before we can answer this, more work needs to be done. Keep in mind, there was no clinical data for these patients, so applying a standard definition of PJI such as the MSIS definition was logistically impossible. The role in a wide range of patients, particularly those that are immunocompromised or those awaiting the second stage of a two-stage exchange, is actively being investigated but not clearly elucidated as of yet. Certainly, with the available data, the inclusion of alpha-defensin to the routine diagnostic evaluation of suspected PJI may seem warranted. Large-scale studies comparing our current gold standard to alpha-defensin need to be done, combining laboratory data, improved bacterial identification of organisms and full clinical information.

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