Clin Orthop Relat Res (2015) 473:204–205 / DOI 10.1007/s11999-014-3794-4

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

Published online: 16 July 2014

CORR Insights

CORR Insights®: The Alpha-defensin Test for Periprosthetic Joint Infection Outperforms the Leukocyte Esterase Test Strip

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Where Are We Now?

The diagnosis and treatment of prosthetic joint infection (PJI) is common enough to be disconcerting, seldom easy to make, and always hard on our patients. While we have myriad of implants and spacers to treat it, we lack good diagnostic tools to detect and confirm the presence of PJI. Arthroplasty surgeons should familiarize themselves with the modification of the Musculoskeletal Infection Society's definition as formulated by the international consensus meeting on PJI in 2013 [1, 4].

The Erythrocyte Sedimentation Rate and C-Reactive Protein screening tests, while useful as a screening mechanism, suffer poor specificity in patients with inflammatory conditions or infections elsewhere in their bodies. Synovial fluid white cell count and percentage polymorphonuclear leukocytes both are established markers of PJI; however both can be abnormally elevated in patients with aseptic failures. Histological analysis of polymorphonuclear leukocytes in tissues is useful, but there is a lack of consensus as to where to set the threshold for the number of polymorphonuclear leukocytes per high powered field that defines an infection diagnosis. Purulence was previously considered pathognomonic of PJI, but even this is difficult to interpret in patients with local tissue reactions associated with metal-on-metal bearings.

Parvizi et al. [3] previously reported their utilization of the leukocyte esterase strip with a high success rate. Encouraged by these results, they have pioneered the alpha defensin immunoassay to enable surgeons to accurately diagnose PJI. The correct treatment of PJI is predicated on exact diagnosis. This work is an important step in that direction.

Where Do We Need To Go?

When Gristina [2] coined the phrase, "the race for the surface" to reflect biofilm growth, he incited a paradigm shift in scientific direction with regard to infection. Perhaps a novel test is what we need to redirect our efforts in the diagnosis of these planktonic and sessile biofilms responsible for PJI.

Deirmengian et al. attempt to compare an existing recognized modality of PJI diagnosis, namely the urinary dipstik leukocyte esterase, with a

This CORR *Insights*® *is a commentary on the article "The Alpha-defensin Test for Periprosthetic Joint Infection Outperforms the Leukocyte Esterase Test Strip" by Deirmengian and colleagues available at:* DOI: 10.1007/s11999-014-3722-7.

The author certifies that he, or any 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/s11999-014-3722-7.

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newly developed immunoassay for alpha defensin. Alpha defensin is a naturally occurring peptide produced in an infection-triggered cascade by neutrophils. One can understand the drawbacks of using leukocyte esterase reagent strips, primarily the subjectivity of readings coupled with the blood prone contamination of joint samples. In the current study, Deirmengian and colleagues banked and analyzed samples of fluid aspirates. Interestingly, all samples, including those from patients having had antibiotics prior to aspiration, were included. Patients with inflammatory conditions were also included. This would be an accurate reflection of current practice comorbidities. The average increase in an alpha defensin test was 31 times normal. The alpha defensin assay certainly does outperform the leukocyte esterase test strip.

The perfect test for PJI would have 100% sensitivity and 100% specificity. In this initial study, Deirmengian et al. appeared to achieve that high standard with the alpha defensin test. Only time will tell whether others will reproduce these groundbreaking results. Any definitive test for PJI will be simple to use, relatively quick, inexpensive, and fully reliable. Will alpha defensin become the orthopaedic PJI mirror of the hugely successful (and now ubiquitous) Human Chorionic Gonadotropin test for pregnancy? Unlike confirming a pregnancy, confirming PJI currently requires a host of tests, biopsies, cultures, and expensive diagnostic modalities, each with shortcomings. Is the alpha defensin assay the test we have been waiting for?

How Do We Get There?

The alpha defensin immunoassay is performed in a laboratory by trained staff. In order to be considered commercially viable, the test needs to be user friendly and easy to use. Surgeons need a rapid "on the spot", reliable diagnosis in the operating room. Further studies are also warranted to perhaps correlate organisms with specific levels of positivity. In other words, could the test be used to determine the species of organism colonizing? Does the alpha defensin level correlate with organism quantity or do certain species produce a more intense response, such as MRSA/Gram negatives? Propionibacterium acnes infections commonly are underdiagnosed commensals responsible for PJI. Does the alpha defensin test reliably diagnose organisms like P acnes? Can it diagnose fungal infections?

The diagnosis of native joint infection may be another use for this new test. Prospective studies confirming its accuracy against current diagnostic criteria for septic arthritis should be performed. For these and other avenues of inquiry, we need further prospective studies to corroborate the findings of this study. Deirmengian et al. have created a simple test based on a peptide released during PJI by our natural defense mechanisms. We await with interest future studies of this exciting line of research. Complexity is not something we desire in orthopedics. Simplicity after all, is the ultimate sophistication.

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