

**A Novel Diagnostic Blood Test for Acute Septic Arthritis: A Prospective Validation Study***Blake J. Schultz, MD; Tim E. Sweeney; Melissa Remmel, MSc; Uros Midic, PhD;**Malcolm DeBaun, MD; Michael J. Gardner, MD**Stanford University, Palo Alto, CA, United States*

**Purpose:** Septic arthritis is an orthopaedic emergency requiring immediate surgical intervention. Current diagnostic standard of care is an invasive joint aspiration. Aspirations provide information about the inflammatory cells in the sample within a few hours, but there is often ambiguity about whether the source is infectious (eg, bacterial) or noninfectious (eg, gout). Cultures can take days to result, so decisions about surgery are often made with incomplete data. Additionally, aspirations carry risk and require technical skill and potentially advanced imaging. Novel diagnostics are thus needed. The ‘Sepsis MetaScore’ (SMS) is an 11-messenger RNA (mRNA) host immune blood signature that can distinguish between infectious and noninfectious acute inflammation. It has been validated in multiple cohorts across heterogeneous clinical settings from outpatient acute infections to patients in ICU suspected of sepsis. Here we studied whether the SMS may hold diagnostic validity in determining if acute arthritis was due to an infectious cause.

**Methods:** We conducted a blinded, prospective, noninterventional clinical study of the SMS. All patients undergoing workup for a septic primary joint at a Level-I trauma center were enrolled. Patients proceeded through the normal standard-of-care pathway, including joint aspiration and inflammatory labs (white blood cells [WBC], erythrocyte sedimentation rate [ESR], and C-reactive protein [CRP]). At the time of the lab draw, venous blood was also drawn into PAXgene RNA-stabilizing tubes and mRNAs were measured using NanoString nCounter. SMS was calculated blinded to clinical results.

**Results:** A total of 19 samples were included, of which 11 were infected based on aspiration or intraoperative cultures. The SMS had an area under the receiver operating characteristic curve (AUROC) of 0.86 for separating infectious from noninfectious conditions. For comparison, the AUROCs for ESR = 0.56, CRP = 0.59, and WBC = 0.58. At 100% sensitivity for infection, the specificity of the SMS was 50%, meaning half of non-septic patients could have been ruled out for further intervention.

**Conclusion:** In this study, the SMS showed a high level of diagnostic accuracy in predicting septic joints compared to other diagnostic biomarkers. This quick blood test could be an important tool for early, accurate identification of acute septic joints and need for emergent surgery, improving clinical care and health-care spending.