

Culture-Negative Infection After Traumatic Injury*I Leah Gitajn, MD¹; Marilyn Heng, MD¹; Michael Weaver, MD; Mitchel Harris, MD²;**¹Massachusetts General Hospital, Boston, Massachusetts, USA;**²The Brigham & Women's Hospital, Boston, Massachusetts, USA*

Background/Purpose: The diagnosis and treatment of infection associated with orthopaedic implants is a challenge. Clinicians make these diagnoses based on a combination of clinical presentation, laboratory studies and bacterial culture. Identification of the primary pathogen directs antibiotic regimen. Definitive culture growth is the primary method by which we determine the pathogen. However, this traditional approach often results in false positives (contaminants, but not pathogens) or false negatives (either previous treatment with antimicrobials or fastidious pathogens), both of which result in a clinical dilemma. False negatives are particularly problematic in patients with clear clinical signs of infection. This relatively common clinical scenario is the impetus to our study question: do culture-negative infections behave differently than infections with an identifiable pathogen? The purpose of this study was to compare outcomes of patients with culture-negative infections to those with culture-positive infections. Furthermore, we sought to identify the incidence and describe the common characteristics of culture-negative infections in patients who sustained traumatic injuries that required surgical stabilization/fixation.

Methods: Patients treated for surgical site infection at two Level I trauma centers were retrospectively identified. 392 patients between January 2007 and December 2013 met inclusion criteria. Inclusion criteria consisted of patients who underwent operative irrigation and debridement (I&D) for a surgical site infection after having undergone fixation of an open or closed fracture. Patients who underwent arthroplasty for primary fracture treatment were excluded. Infection was defined as erythema and/or purulent drainage presenting after definitive wound closure necessitating return to the operating room for I&D, as indicated by the responsible surgeon. The primary outcome measures were successful eradication of infection and time to fracture union. Secondary outcome measures included need for subsequent operative procedures. Cultures were taken at the time of index I&D. Antibiotic therapy was initiated with consultation by an infectious disease specialist.

Results: The overall rate of culture negative infection was 9% (34 of 392). An additional 8% (31 of 392) grew positive bacterial culture from broth only, which may represent contaminants rather than infecting pathogens. There were no significant differences between the two groups with regard to treatment failure, time to union, and need for subsequent procedure. 34% of culture-positive infections were treatment failures and 38% of culture-negative infections were treatment failures ($P = 0.13$). Time to union among culture-positive infection was 22 weeks and among culture-negative infection was 24 weeks ($P = 0.185$). 30% of patients with culture-positive infection required subsequent procedure (including amputation, arthrodesis, arthroplasty, girdlestone, soft-tissue reconstruction) and 35% of patients with culture-negative infection required similar secondary procedures ($P = 0.6608$).

Conclusion: To our knowledge, this is the first study evaluating culture-negative infection in the orthopaedic trauma literature. This remains a treatment dilemma that is encountered frequently, in nearly 10% of infections in this study, but has been poorly addressed in the

literature. This study found no difference between patients with positive intraoperative cultures and those with negative intraoperative cultures with regard to success of treatment, need for subsequent procedure, or time to union. This suggests that current empiric therapy for negative intraoperative cultures is as effective as microbe-specific therapy.

The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or medical device he or she wishes to use in clinical practice.