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Introduction for the *Journal of Orthopaedic Research* Special Issue on Musculoskeletal Infection

Edward M. Schwarz^{1,*}, J. J. Chris Arts^{2,3}, Antonia F. Chen⁴

¹Department of Orthopaedics, University of Rochester, Rochester, NY, USA

²Department of Orthopaedic Surgery, Maastricht University Medical Center, Maastricht, the Netherlands

³Department Orthopaedic Biomechanics, Faculty Biomedical Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands

⁴Department of Orthopaedic Surgery, Harvard Medical School, Boston, MA, USA

Osteomyelitis is one of the oldest diseases in history¹, and while major advances in research have led to a vast array of new and improved bone and joint treatments over the last 50-years, musculoskeletal infections (MSKI) remain a bane within orthopaedic surgery². An example of this dichotomy is elective total joint replacement (TJR), which was hailed as the most successful medical procedure developed in the 20th century that has now expanded to more than 1.5 million TJRs being performed each year^{3–6}, yet the most rigorous prophylaxis and aseptic surgical techniques cannot reduced infection rates below 0.5–2%^{7–10}. Treating established MSKI remains extremely challenging, as current rates of recurrent or persistent infection following revision surgery are still as high as 33%^{10–12}. Overall, the incidences of infection for all orthopaedic subspecialties ranges from 0.1%–30%, at a cost of \$17,000–\$150,000 per patient¹⁰.

Remarkably, it has been over 200 years since Sir Benjamin Brodie described MSKI abscesses¹³, and >40 years since Dr. William Costerton proposed the biofilm hypothesis of chronic MSKI¹⁴. Based on these fundamentals, a standard of care treatment for implant-associated osteomyelitis, most notably prosthetic joint infection (PJI), was developed in the 1970s, and reports in the 1980s claimed 5-year success (survival) rates of 77%¹⁵. Unfortunately, the results from the 2018 International Consensus Meeting (ICM) on MSKI show no changes in: PJI infection rates, the primary pathogen involved, treatment algorithm, and poor outcomes, since the original standards of care were established^{10; 16; 17}. However, the great need for better treatments for our patients, punitive healthcare reforms for MSKI complications, and transformative public-private efforts that facilitated development of COVID-19 vaccines from concept through FDA-approval in less than 1-year, have reinvigorated MSKI clinicians, scientists and regulators to find cost-effective solutions for this grievous illness. Evidence of a new era in MSKI research can be found from the outcomes of Consensus Articles, which are new to the *Journal of Orthopaedic*

*To whom correspondence should be addressed Dr. Edward Schwarz, University of Rochester Medical Center, 601 Elmwood Ave., Box 665, Rochester, NY 14642, Phone: 585-275-3063, FAX: (585) 276-2177, Edward_Schwarz@URMC.Rochester.edu.

Research^{18–20}, and the new MSKI Research Interest Group that commenced at the 2020 Annual Meeting of the Orthopaedic Research Society (<https://www.ors.org/2020-rigs/>), and has its 2nd meeting scheduled for February 13, 2021 (<https://www.ors.org/2021-rigs/>).

Based on this momentum, we were invited to generate this *JOR* Special Issue on MSKI as Guest Editors. The initial call for submission of Consensus Articles, Perspectives, Reviews and Research Articles went out in May 2020, all of the papers were received by September, and the peer review process was completed by December 11, 2020. Of note, we received so many additional outstanding manuscripts that those accepted for publication in *JOR* will be published in regular issues due to space limits in the Special Issue. Most of these papers are research articles of equivalent quality and importance to the research articles selected, and warrant similar attention.

The following *JOR* Special Issue on MSKI was designed to emphasize new paradigms on the use of antibiotic-loaded bone cement, the host microbiome, bacterial toxins, and antimicrobial biomaterials. We also aimed to have balance between novel findings with diagnostics and clinical outcome studies, and pre-clinical innovations with antimicrobials, drug delivery systems, and imaging technologies to study microbial pathogenesis in bone. We trust that the intended audience will find this Special Issue to be informative and thought provoking, and that the impact of these articles will lead to further research to end musculoskeletal infection as a plague in orthopaedics.

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