The Infected Implant in Orthopaedic Reconstruction: An Update on the Clinical and Molecular Approaches to Prevention and Diagnosis

(Organized by the Musculoskeletal Tumor Society (MSTS) and ORS)

Organizers:

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Speakers:

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Carlos A. Higuera Rueda
Nicholas Bernthal, MD
Introduction:
Implant related infections in joint reconstruction are among the most devastating complications in orthopaedic surgery. The cost to the healthcare system and the patient associated morbidity demand ardent focus on the prevention and early diagnosis of these infections. This workshop focuses on three key areas of prevention and diagnosis. First, an update on the clinical evidence for systemic antibiotic prophylaxis is presented with surprising data that does not support routine current clinical practice guidelines. Second, the latest data on serum and synovial biomarkers for the diagnosis of peri-prosthetic joint infection are provided. Finally, an in vivo model of antimicrobial implant coating and bioluminescent imaging provides insight into a unique and novel approach to infection prophylaxis. Overall, this workshop combines clinical, cellular and molecular updates on this critical area of orthopaedic care.

Speaker 1: Dr. Michelle Ghert
Antibiotic prophylaxis in tumor and joint reconstruction: Where does the evidence lead us?

Take Home Points:

In total joint arthroplasty:
- Peri-operative antibiotics are effective at reducing surgical site infections (SSIs)
- Guidelines recommend 24 -36 hours post-operative duration (Table 1)
- Currently the evidence does not support post-operative antibiotics (Figure 1)
- A well-designed multi-center randomized controlled trial can clarify if any post-op antibiotics are required for efficacy

Tumor/Endoprosthetic Reconstruction:
- Many surgeons prolong antibiotic duration
- There is no evidence at this time to support longer duration
- The multi-center international Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) trial will provide evidence for practice

Antibiotic stewardship is critical in the face of the worldwide antibiotic resistance crisis.

Table 1: Guideline Recommendations
<table>
<thead>
<tr>
<th>Organization</th>
<th>Key Recommendations</th>
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<tbody>
<tr>
<td>American Academy of Orthopaedic Surgeons (AAOS)</td>
<td>Duration of prophylactic antibiotic administration should not exceed the 24-hour post-operative period</td>
</tr>
<tr>
<td>British Orthopaedic Association (BOA)</td>
<td>All patients should receive, intravenously, an antibiotic at induction of anesthesia and for the first 24-hours after the operation</td>
</tr>
<tr>
<td>New Zealand Orthopaedic Association (NZOA)</td>
<td>All patients should receive an IV broad-spectrum antibiotic at induction of anesthesia and for the first 24-36 hours after the operation</td>
</tr>
</tbody>
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**Figure 1: Forest plot showing no risk difference between post-op antibiotics and no post-op antibiotics for surgical site infection**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Post-op antibiotics</th>
<th>No post-op antibiotics</th>
<th>Risk Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Heydemann 1986</td>
<td>0</td>
<td>108</td>
<td>0</td>
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<tr>
<td>Kaneliakopoulou 2009</td>
<td>11</td>
<td>338</td>
<td>2</td>
</tr>
<tr>
<td>Ritter 1989</td>
<td>0</td>
<td>98</td>
<td>0</td>
</tr>
<tr>
<td>Wymenga 1981</td>
<td>52</td>
<td>1511</td>
<td>43</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>63</strong></td>
<td><strong>2055</strong></td>
<td><strong>45</strong></td>
</tr>
<tr>
<td></td>
<td>Total events</td>
<td>63</td>
<td>45</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00$, $\text{Chi}^2 = 4.04$, df = 3 ($P = 0.26$); $I^2 = 26\%$

Test for overall effect: $Z = 1.33$ ($P = 0.19$)
Speaker 2: Dr. Carlos A. Higuera Rueda

New Techniques on the Cellular and Molecular Diagnosis of the Infected Joint.

Despite all the refinements in the diagnosis and treatment of periprosthetic joint infection (PJI), the burden of this condition is still dramatic. The cost of treatment of PJI has surpassed $1 billion per year just in the United States. The main areas where future prospects and challenges of PJI diagnosis are discussed. The accuracy of the current diagnostic criteria is not optimal, especially during the re plantation of a 2-stage revision. Improved diagnosis accuracy with the use of synovial fluid biomarkers such as alfa-defensin and IL-6 may outcast these. Often, a joint aspiration may be a dry tap and the lack of availability of synovial fluid cell count and cultures may mislead the treatment. Therefore, either a point of care testing or serum and/or blood biomarkers may be the most appropriate diagnostic tools in such setting. Identification of bacteria using improved PCR techniques may also improve the tailoring of antibiotic treatment. The use of such techniques may facilitate the diagnosis of PJI and potentially decrease the burden of such condition when treatment is delayed.

Summary: Improved diagnostic tools such as synovial fluid alfa-defensin and IL-6 in addition to future prospects of serum/blood biomarkers are discussed. Current PCR techniques to identify bacteria are also discussed. These tools may lead the way for the diagnosis of PJI in the future.
Speaker 3: Dr. Nicholas Bernthal

Novel molecular implant modifications directed at infection prophylaxis

The concept of antimicrobial coatings has been suggested as a method to protect implant surfaces from bacterial colonization as well as deliver drug locally at high concentrations. However, technical and regulatory challenges have stymied scientific progress and widespread adoption. Utilizing a novel animal model that longitudinally tracks infection and immune response over time, we now have an assay that allows accurate and efficient assessment of efficacy and safety. This tool has encouraged a series of breakthroughs and modifications that leave us at the precipice of game-changing technologies in the prevention of implant infection.

Summary: Accurate and efficient pre-clinical animal models of implant infection have encouraged scientific discovery in the field. Novel techniques of surface modification and “smart” implant coatings may soon be available to prevent this dreaded complication.