Histological Transition From Acute To Chronic Periprosthetic Joint Infection Occurs By Day 14 In A Mouse Arthroplasty Model

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INTRODUCTION: Periprosthetic joint infection (PJI) complicates 2% of primary arthroplasties, constitutes 25% of revisions, and incurs an annual U.S. healthcare cost of $1.6 billion. Accurate staging is critical as DAIR success rates drop from 74% within 30 days to 44% once chronic infection occurs. Currently, staging relies heavily on symptom duration rather than objective tissue-based criteria. The 2018 International Consensus Meeting highlighted the need for objective markers distinguishing acute from chronic PJI. Existing animal studies have inadequately defined intermediate inflammatory transitions. Our study aimed to characterize inflammatory progression and identify clear histological markers of the acute-to-chronic transition using our load-bearing tibial implant mouse model.

METHODS: Twenty 12-week-old C57BL/6 mice underwent unilateral proximal tibial implantation and inoculation with 3×10^4 CFUs of bioluminescent Staphylococcus aureus. Animals were euthanized at 48 hours and days 7, 10, 14, 18, 21, and 28 postoperatively. Radiographs and serum inflammatory markers were assessed. Fixed limb cryosections were stained (haematoxylin-eosin) and semi-quantitatively graded (0–3) for neutrophils, macrophages/lymphocytes, edema/fibrin, and bone necrosis (Figure 1A-B). Acute PJI was defined by neutrophil score ≥2 and macrophage/lymphocyte score ≤1; chronic PJI required macrophage/lymphocyte score ≥2 with fibrosis or bone necrosis score ≥1. All slides were independently reviewed and scored by a US board□certified pathologist.

RESULTS: Peak neutrophil infiltration and edema/fibrin deposition (grade 3) occurred on day 7, coinciding with microabscess formation (1C). By day 14, acute inflammation significantly declined (grades 0–1), while macrophage/lymphocyte infiltration and fibrosis markedly increased (grades 2–3). Bone necrosis appeared after day 18 (1D).

DISCUSSION AND CONCLUSION: Neutrophil-driven acute inflammation peaked by day 7, shifting to macrophage-rich inflammation by day 14. This transition parallels the inflammatory shift described in human periprosthetic membranes7. Thus, the period between postoperative days 7-14 represents a critical acute-to-chronic transition window in this load-bearing mouse model of PJI.

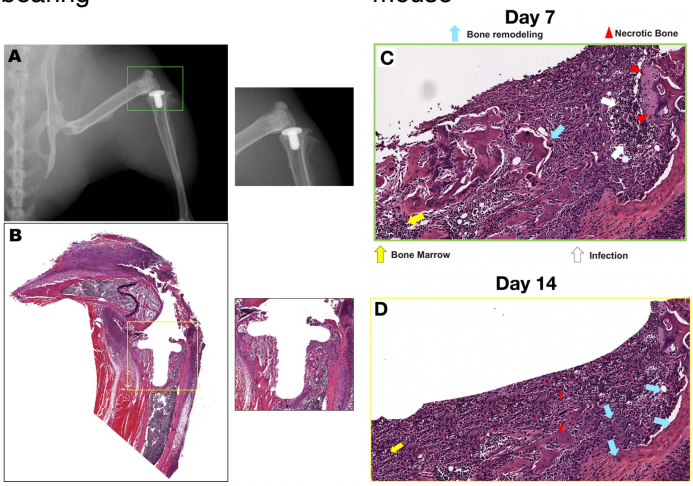

Figure 1. (A) Antero-posterior radiograph of the mouse tibia showing the intramedullary implant (green outline). **(B)** Whole section H&E of the same limb; the yellow box marks the peri-implant region of interest (ROI). **(C)** Day 7 peri-implant ROI: grade 3 neutrophil infiltrate with oedema and micro-abscesses; early bone remodelling (blue arrows), necrotic bone (orange arrowheads), infection front (white arrows) and bone marrow interface (yellow arrow). **(D)** Day 14 peri-implant ROI: neutrophils largely absent, macrophage-rich tissue and woven bone along the implant surface, consistent with progression toward the chronic phase.