



## EXPERIMENTALLY INDUCED DISEASE

# Suppurative Inflammation and Local Tissue Destruction Reduce the Penetration of Cefuroxime to Infected Bone Implant Cavities

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## Summary

Treatment of post-traumatic and implant-associated osteomyelitis (IAO) includes surgical debridement, removal of implants and long-term antibiotic therapy. The success of antibiotic therapy relies not only on activity towards the infecting pathogen, but also on sufficient penetration of the target site. The aim of the present study was to characterize the local pathological changes associated with reduced penetration of cefuroxime to infected bone implant cavities. Previously, reduced penetration of systemically administered cefuroxime was demonstrated in the implant cavity of 10 pigs with *Staphylococcus aureus* IAO present for 5 days. In the present study, a comprehensive histopathological characterization of the peri-implant bone tissue was performed and correlated with the reduced penetration of cefuroxime. In two pigs, the levels of oxygen, pyruvate and lactate was estimated in the implant cavity. A peri-implant pathological bone area (PIBA) developed with a width of 1.2 up to 3.8 mm. PIBAs included: (1) suppuration, resulting in destruction of the implant cavity contour, and (2) a non-vascular zone of primarily necrotic bone tissue. A strong negative correlation was seen between PIBA width and cefuroxime area under the concentration time curves ( $AUC_{[0-last]}$ ) and peak concentration of cefuroxime ( $C_{max}$ ). All metabolic measurements demonstrated hypoxia. In conclusion, subacute suppurative bone inflammation with local tissue destruction can result in decreased penetration of antibiotics and insufficient oxygen supply.

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## Introduction

Post-traumatic and implant-associated osteomyelitis (IAO), including periprosthetic infections, are among the most severe orthopaedic conditions (Kapadia *et al.*, 2016). Treatment of IAO includes surgical debridement, removal of implants and long-term antibiotic therapy (Kapadia *et al.*, 2016). The success of antibiotic therapy relies not only on activity towards the infecting pathogen, but also on sufficient

penetration of the target site (Landersdorf *et al.*, 2015). Consequently, knowledge of antibiotic penetration of bone following systemic administration is important in order to improve treatment of IAO (Landersdorf *et al.*, 2015). For osteomyelitis systemic post-operative antibiotic treatment is normally recommended for 4–6 weeks (Waldvogel *et al.*, 1970; Norden *et al.*, 1986; Sia and Berbari, 2006; Haidar *et al.*, 2010).

Numerous clinical studies have been conducted in order to quantify antibiotic concentrations in non-infected bones rather than in bones from patients

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