

# IMPLANT INFECTIONS- A HEAVEN FOR OPPORTUNISTIC BACTERIA

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**INTRODUCTION:** In the US approximately 2 million nosocomial infections cost nearly \$ 11 billion annually. Exposure to invasive medical devices represents one of the most important risk factors<sup>1</sup>. Devices predispose to infection by damaging or invading epithelial or mucosal barriers, and by supporting growth of microorganisms thus serving as reservoirs. Invasive medical devices impede host defence mechanisms, and, when contaminated, directly infect patients. These deficiencies, which can result in resistant infection, chronic inflammations or tissue necrosis and are the major objection to extended use of implant devices<sup>2</sup>. Hybrid materials slowly delivering antimicrobial drugs may reduce implant infections effectively as second-generation materials in the future.

**METHODS:** Prevention of colonization of foreign-body surfaces by continuous release of bactericidal, highly biocompatible antibiotics incorporated or adsorbed to the materials has been investigated as a new promising approach. Antimicrobial coated silicone and polyurethane materials were investigated by HPLC-measurement and different antimicrobial assays.

**RESULTS:** Perfect sink conditions were used to determine controlled release of antibiotics. The release rate of each of used antimicrobials showed two significant periods. The initial release rate, the so-called "burst effect", depends on the mass, distribution and solubility of superficial located antibiotics. The delivery rate was nearly constant after the burst effect in a range of about 3-5 µg/cm segments. Antimicrobial delivery exceeded 21 days for both polyurethanes and more than 100 days for silicone materials. Controlled drug delivery governed by the physico-chemical mass transfer from the bulk provided a long-term release of the antimicrobial substances from the material. The effectiveness of modified silicone and polyurethanes containing antimicrobial drugs were proved in the stationary adhesion assay against *S.aureus 5aW 1136*. Sterility was achieved after 48 hours in contrast to the conventional catheters.

**DISCUSSION & CONCLUSIONS:** Successful tissue integration or implant infection is the result of the race for the surface between host macromolecules, bacteria and tissue cells. Bacteria

find their way into the host independently of technique and sterility of the environment. Pathogenic bacteria such as *S.aureus* could be recovered from about 90 percent of clean wounds at the time of closure. It is impossible to create a predictable sterile wound, even under laminar air conditions. Despite adherence to hygienic guidelines, a significant number of implant infections occur "physiologically"<sup>1,2</sup>. The coupling of antimicrobial substances to biomaterials may reduce infection susceptibility to low bacterial counts and warrants pursuit investigation. In our drug delivery concept we could show, that the long period of antimicrobial slow release was chosen in order to ensure protection over the whole indwelling period of the implant materials. Attempts to decrease the concentration of antimicrobials led to a failure of protection for the target period<sup>3</sup>. The in vitro and in vivo results of our coating techniques are encouraging<sup>4</sup> therefore we hope, that the antimicrobial modifications with a long-lasting efficacy may fulfil clinically the comment made by Dennis Maki<sup>5</sup>: "Binding of a non-toxic antimicrobial drug to the catheter surface or incorporation of the substance into the catheter material itself may ultimately prove to be the most effective technological innovation for reducing the risk of device-related infections".

## REFERENCES:

- <sup>1</sup> W.E. Stamm, (1978) Infections related to medical devices. *Ann. Int. Med.* **89** (2), 764-769.
- <sup>2</sup> A.G. Gristina, (1987). Biomaterial-centered infection: microbial adhesion versus tissue integration. *Science* **237**, 1588-1595.
- <sup>3</sup> J.M.Schierholz, R.Lefering, E.Neugebauer, J.Beuth, D.P. König, G. Pulverer (2000 ). Central venous catheters and bloodstream infection. *JAMA* **26**;283(4):477-9.
- <sup>4</sup> J.M. Schierholz, C. Fleck, J. Beuth, G. Pulverer (2000) The antimicrobial efficacy of a new central venous catheter with a long-term broad-spectrum activity, *JAC*, 46(1), 45-50
- <sup>5</sup> D.G. Maki, L Cobb, J.K. Garman, J.M. Shapiro, M. Ringer, R.B. Helgerson (1988). An attachable silver-impregnated cuff for prevention of infection with central venous catheters: a prospective randomised multicenter trial. *JAMA* **85**, 307 - 316.