

Implant Healing in Experimental Animal Models of Diabetes

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Abstract

Diabetes mellitus is becoming increasingly prevalent worldwide. Additionally, there is an increasing number of patients receiving implantable devices such as glucose sensors and orthopedic implants. Thus, it is likely that the number of diabetic patients receiving these devices will also increase. Even though implantable medical devices are considered biocompatible by the Food and Drug Administration, the adverse tissue healing that occurs adjacent to these foreign objects is a leading cause of their failure. This foreign body response leads to fibrosis, encapsulation of the device, and a reduction or cessation of device performance. A second adverse event is microbial infection of implanted devices, which can lead to persistent local and systemic infections and also exacerbates the fibrotic response. Nearly half of all nosocomial infections are associated with the presence of an indwelling medical device. Events associated with both the foreign body response and implant infection can necessitate device removal and may lead to amputation, which is associated with significant morbidity and cost. Diabetes mellitus is generally indicated as a risk factor for the infection of a variety of implants such as prosthetic joints, pacemakers, implantable cardioverter defibrillators, penile implants, and urinary catheters. Implant infection rates in diabetic patients vary depending upon the implant and the microorganism, however, for example, diabetes was found to be a significant variable associated with a nearly 7.2% infection rate for implantable cardioverter defibrillators by the microorganism *Candida albicans*. While research has elucidated many of the altered mechanisms of diabetic cutaneous wound healing, the internal healing adjacent to indwelling medical devices in a diabetic model has rarely been studied. Understanding this healing process is crucial to facilitating improved device design. The purpose of this article is to summarize the physiologic factors that influence wound healing and infection in diabetic patients, to review research concerning diabetes and biomedical implants and device infection, and to critically analyze which diabetic animal model might be advantageous for assessing internal healing adjacent to implanted devices.

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Abbreviations: (BB) biobreeding, (ECM) extracellular matrix, (eNOS) endothelial nitric oxide synthase, (EPC) endothelial progenitor cell, (FGF) fibroblast growth factor, (GK) Goto-Kakizaki, (IL) interleukin, (KK) Kyoji Kondo, (MCP-1) monocyte chemotactic protein 1, (MHC) major histocompatibility complex, (MIP-2) macrophage inflammatory protein 2, (MMP) matrix metalloproteinase, (NO) nitric oxide, (NOD) nonobese diabetic, (PDGF) platelet-derived growth factor, (PMNL) polymorphonuclear leukocyte, (TGF- β) transforming growth factor β , (TNF- α) tumor necrosis factor α , (VEGF) vascular endothelial growth factor

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