

# **Springer Series on Biofilms**

Volume 3

Series Editor: J. William Costerton

Los Angeles, USA

Mark Shirtliff • Jeff G. Leid  
Editors

# The Role of Biofilms in Device-Related Infections

 Springer

*Editors*

Dr. Mark Shirliff  
Department of Biomedical Sciences  
University of Maryland  
School of Medicine  
655 W. Baltimore Street  
Baltimore MD 21201  
USA

Dr. Jeff G. Leid  
Department of Biological Sciences  
Northern Arizona University  
Box 5640  
Flagstaff, AZ 86011  
USA

*Series Editor*

J. William Costerton  
Director, Center for Biofilms,  
School of Dentistry  
University of Southern California  
925 West 34th Street  
Los Angeles, CA 90089  
USA

ISBN 978-3-540-68113-7      e-ISBN 978-3-540-68119-9  
DOI: 10.1007/978-3-540-68119-9

Library of Congress Control Number: 2008940067

© 2009 Springer-Verlag Berlin Heidelberg

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer. Violations are liable to prosecution under the German Copyright Law.

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

*Cover design:* SPi Publisher Services

Printed on acid-free paper

9 8 7 6 5 4 3 2 1 0

springer.com

# Preface

*The Role of Biofilms on Indwelling Medical Devices* is the third volume in the continuing Springer Series on Biofilms. In this volume, we explore biofilm infections of indwelling medical devices from the point of view of both the host and the infecting pathogen. We begin this volume with an analysis of the primary source of indwelling medical device fouling, namely the host microbial skin flora. Then, each major form of indwelling medical device infection, including orthopaedic implants, biofilms on ventilators, dental implant infections, urinary tract infections due to catheters, intravenous catheter fouling, and endophthalmitis infections, will be described. Not only will the general properties of the infection be discussed, but also the relationship and balance between the host and the infecting microbial species. The final two contributions take into account the biofilm phenotype to evaluate and describe both the specifics of the host response to biofilm infections and novel methods of diagnosis.

Device-related biofilm infections increase hospital stays and add over one billion dollars/year to U.S. hospitalization costs. As the use and the types of indwelling medical devices commonly used in modern healthcare are continuously expanding, especially with an aging population, the incidence of biofilm infections will also continue to rise. The central problem with microbial biofilm infections of foreign bodies is their propensity to resist clearance by the host immune system and all antimicrobial agents tested to date. In fact, compared to their free floating, planktonic counterparts, microbes within a biofilm are 50–500 times more resistant to antimicrobial agents. Therefore, achieving therapeutic and non-lethal dosing regimens within the human host is impossible. The end result is a conversion from an acute infection to one that is persistent, chronic, and recurrent, most often requiring device removal to eliminate the infection. This text will describe the major types of device-related infections, and will explain the host, the pathogen(s), and the unique properties of their interactions to gain a better understanding of these recalcitrant infections.

Chronic diseases such as AIDS, cancer, or diabetes are first understood as a collection of seemingly individual and anecdotal reports of symptoms. However, the link between the disparate signs and symptoms and the causal factor had to be made to make the first steps towards diagnosis, treatment, prevention and/or research towards a cure. While the causal factors of these maladies are recognized as a “disease”,

such is not the case for biofilm diseases. The commonalities of chronic infection, tissue damage, recalcitrance to antimicrobial therapy, and resistance to clearance by the host immune system, are the symptoms of biofilm disease. It has been assumed that an understanding of the disease process can be obtained while ignoring the biofilm mode of growth from the host and microbiological standpoint. This approach has generally left us with two options: longterm, non-curative antibiotic therapy or surgical removal of the nidus of infection.

These chronic bacterial and fungal infections are not only difficult to treat, but in some cases impossible. In fact, 56% of all infections are due to biofilms, according to the Centers for Disease Control and that equates to approximately half a million deaths annually in the United States alone. The sheer number of infections and diseases related to the biofilm phenotype is clearly the number one cause of medical morbidity in the United States. Extrapolated to a global perspective, biofilm disease can be viewed as the major disease plaguing the human population. Until there is a greater realization of the role of biofilms in chronic diseases in humans and fitting directed research, the appropriate paradigm shift will not occur and in turn, the cost, treatment and morbidity and mortality associated with these diseases will not improve.

This book is meant to provide insight into the role of biofilms in implant-mediated infections. The authors and chapters have been focused on the most common types of implant infections, the most common pathogens associated with each infection, and in some cases, how the human host responds to the presence of these microbial communities. Although biofilm infections in humans are found outside the realm of medical devices, it is clear that the enormous increase in the clinical usage of medical devices presents a major challenge to health care not only in the United States, but across the globe. Hopefully this book and the chapters contained herein help to shed light on these issues and lead to further research that directly and positively impacts patient health.

October 2008

Mark Shirtliff  
Jeff Leid

# Contents

<b>Microbial Ecology of Human Skin and Wounds</b> .....	1
G. James, E. Swogger, and E. deLancey-Pulcini	
<b>Infections of Orthopaedic Implants and Devices</b> .....	15
Rebecca A. Brady, Jason H. Calhoun, Jeff G. Leid, and Mark E. Shirtliff	
<b>Biofilms and Aseptic Loosening</b> .....	57
Mark S. Smeltzer, Carl L. Nelson, and Richard P. Evans	
<b>Biofilms and Ventilation</b> .....	75
J.G. Thomas, L. Corum , and K. Miller	
<b>Biofilm Formation on Natural Teeth and Dental Implants: What is the Difference?</b> .....	109
Debora Armellini, Mark A. Reynolds, Janette M. Harro, and Liene Molly	
<b>Complicated Urinary Tract Infections due to Catheters</b> .....	123
G.A. O’May, S.M. Jacobsen, D.J. Stickler, H.L.T. Mobley, and M.E. Shirtliff	
<b>Biofilms in Hemodialysis</b> .....	167
Mark Pasmore and Karine Marion	
<b>Bacterial Endophthalmitis Following Cataract Surgery</b> .....	193
M.E. Zegans, C.M. Toutain-Kidd, and M.S. Gilmore	
<b>Use of Immunodiagnostics for the Early Detection of Biofilm Infections</b> .....	219
Laura Selan, Jennifer Kofonow, Gian Luca Scoarughi, Tim Vail, Jeff G. Leid, and Marco Artini	

**Immune Responses to Indwelling Medical Devices** ..... 239  
M. Nymer, E. Cope, R. Brady, M.E. Shirtliff, and J.G. Leid

**Index**..... 265

# Contributors

## **Debora Armellini**

Endodontics, Prosthodontics and Operative Dentistry, Dental School, University of Maryland-Baltimore, 650 W. Baltimore Street, Baltimore, MA 21201, USA

## **Marco Artini**

Department of Public Health Sciences, University “La Sapienza”, P. le Aldo Moro 5, 00185 Rome, Italy

## **Rebecca A. Brady**

Department of Biomedical Sciences, Dental School, University of Maryland-Baltimore, 666 W. Baltimore Street, Baltimore, MA 21201 USA

## **Jason H. Calhoun**

Department of Biomedical Sciences, Dental School, University of Maryland-Baltimore, 666 W. Baltimore Street, Baltimore, MA 21201, USA

## **Emily Cope**

Department of Biological Sciences, Northern Arizona University, 21 S. Beaver Street, BLDG 21, Flagstaff, AZ 86011, USA

## **Linda Corum**

Department of Pathology, Proteomics, West Virginia University, Morgantown, WV 26506, USA

lcorum@hsc.wvu.edu

## **Elinor DeLancey-Pulcini**

Center for Biofilm Engineering, Montana State University, Bozeman, USA

## **Richard P. Evans**

Department of Microbiology and Immunology, University of Arkansas for Medical Sciences, Little Rock, AR 72205

## **Michael S. Gilmore**

Schepens Eye Research Institute, Harvard Medical School, Boston, MA, USA  
michael.gilmore@schepens.harvard.edu



**Janette M. Harro**

Department of Microbial Pathogenesis, University of Maryland – Baltimore,  
Dental School, 650 West Baltimore Street, Baltimore, MD 21201, USA  
jharro@umaryland.edu

**S.M. Jacobsen**

Department of Microbial Pathogenesis, University of Maryland – Baltimore,  
Dental School, 650 West Baltimore Street, Baltimore, MD 21201, USA

**Garth James**

Center for Biofilm Engineering, Montana State University, Bozeman, USA  
GJames@erc.montana.edu

**Jennifer Kofonow**

Department of Otorhinolaryngology, Hospital of the University of Pennsylvania,  
Philadelphia VA Medical Center Room A215, 3900 Woodland Avenue,  
Philadelphia, PA 19104  
jenk@mail.med.upenn.edu

**Jeff G. Leid**

Center for Microbial Genetics and Genomics, Department of Biological Sciences,  
Northern Arizona University, 21 S. Beaver Street, BLDG 21, Flagstaff,  
AZ 86011, USA  
Jeff.Leid@nau.edu

**Karine Marion**

Universite Lyon1, Faculte de Pharmacie, Laboratoire de Microbiologie,  
Lyon, France

**Karla Miller**

Pharm D, Health Corporation of America, Clinical Services Group,  
One Park Plaza, Bldg.II, 4W, Nashville, TN 37203, USA  
Karla.Miller@HCAhealthcare.com

**H.L.T. Mobley**

Department of Microbiology and Immunology, University of Michigan  
Medical School, Ann Arbor, MI 48109, USA

**Liene Molly**

Department of Periodontics, Dental School, University of Maryland-Baltimore,  
650 W. Baltimore Street, Baltimore, MA 21201, USA  
lmolly@yahoo.com

**Carl L. Nelson**

Department of Microbiology and Immunology, University of Arkansas  
for Medical Sciences, Little Rock, AR 72205

**Matt Nymer**

Department of Biological Sciences, Northern Arizona University, 21 S. Beaver Street, BLDG 21, Flagstaff, AZ 86011, USA

**G.A. O'May**

Department of Microbial Pathogenesis, University of Maryland – Baltimore, Dental School, 650 West Baltimore Street, Baltimore, MD 21201

**Mark A. Reynolds**

Department of Periodontics, Dental School, University of Maryland-Baltimore, 650 W. Baltimore Street, Baltimore, MA 21201, USA

**Mark Pasmore**

Sr. Principal Engineer, Sterility Assurance Technology Resources, Baxter Healthcare Corporation, 25212 W IL Rocete 120, Round lake, IL 60073, USA

**Gian Luca Scaorughi**

Department of Public Health Sciences, University “La Sapienza”, P. le Aldo Moro 5, 00185 Rome, Italy

**Laura Selan**

Department of Public Health Sciences, University “La Sapienza”, P. le Aldo Moro 5, 00185 Rome, Italy  
laura.selan@uniroma1.it

**Mark E. Shirliff**

Department of Microbial Pathogenesis, University of Maryland – Baltimore, Dental School, 650 West Baltimore Street, Baltimore, MD 21201, USA  
mshirliff@umaryland.edu

**Mark S. Smeltzer**

Department of Microbiology and Immunology, University of Arkansas for Medical Sciences, Little Rock, AR 72205  
smeltzermarks@uams.edu

**D.J. Stickler**

Cardiff School of Biosciences, Cardiff University, Cardiff, Wales, CF10 3TL, UK

**Ellen Swogger**

Center for Biofilm Engineering, Montana State University, Bozeman, USA

**John G. Thomas**

Department of Pathology, West Virginia University School of Medicine, Morgantown, WV 26506, USA  
jthomas@hsc.wvu.edu

**Christine M. Toutain-Kidd**

Department of Surgery (Ophthalmology) and Department of Microbiology and Immunology, Dartmouth Medical School, Hanover, NH, USA

**Tim Vail**

Department of Chemistry and Biochemistry, P.O. Box 5698, South Beaver and Ellery Sts., Northern Arizona University, Flagstaff, AZ 86011  
Timothy.Vail@nau.edu

**Michael E. Zegans**

Department of Surgery (Ophthalmology) and Department of Microbiology and Immunology, Dartmouth Medical School, Hanover, NH, USA