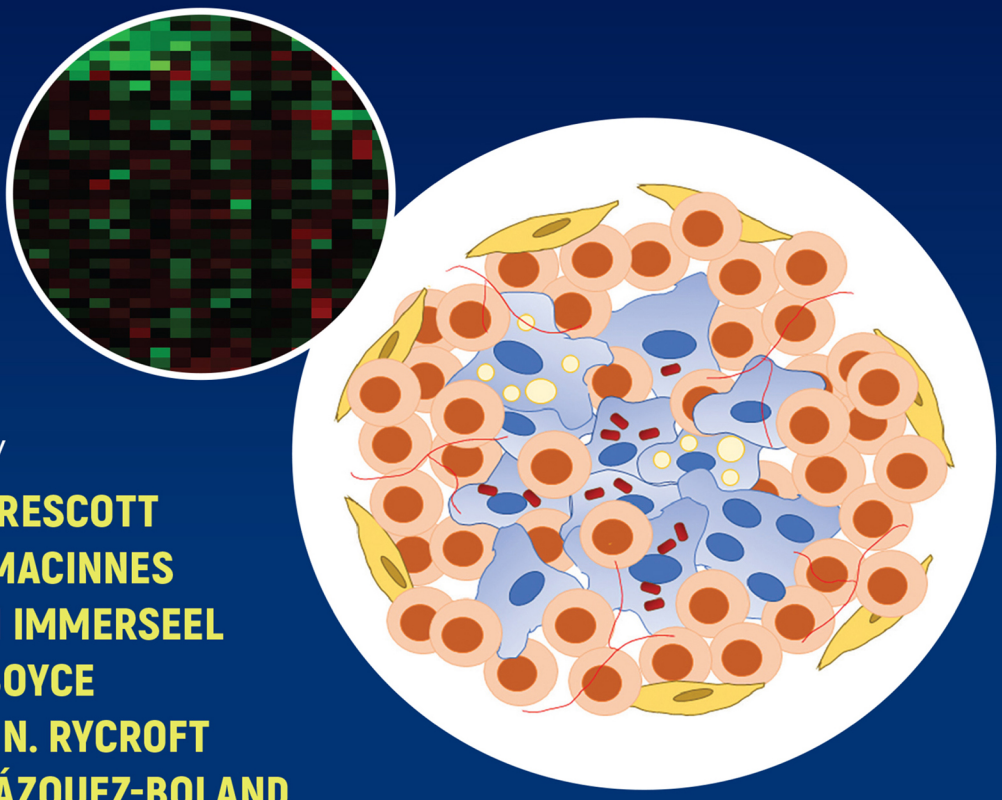
FIFTH EDITION

PATHOGENESIS OF BACTERIAL INFECTIONS IN ANIMALS



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WILEY Blackwell

Pathogenesis of Bacterial Infections in Animals

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Preface

The fifth edition of *Pathogenesis of Bacterial Infections in Animals* tries to capture the many fascinating and rapid developments in our understanding of how major bacterial pathogens of animals cause disease. It is the product of the efforts of 87 experts from 14 countries: Australia, Brazil, Belgium, Canada, China, France, Germany, Mexico, New Caledonia, Spain, Switzerland, the United Kingdom, the United States, and Uruguay. We thank them all.

Although molecular pathogenesis is a major aspect in almost every chapter, the authors have been careful to place pathogens in their broader context. As in the previous editions, we have presented the disease process at both the herd/flock and cellular/molecular levels. The details vary from one organism to another, partly because bacterial diseases develop under widely varying circumstances, and partly because the extent of knowledge varies considerably.

Since the last edition, we have added introductory material on pathogenesis and bioinformatics (Chapter 3), on experimental approaches to understanding pathogenesis (Chapter 4) as well as on pathogenesis-based strategies to combating bacterial infections (Chapter 6). To accommodate the expanding importance genera such as *Avibacterium*, *Glaesserella*, and *Gallibacterium*, we have an expanded description of these organisms in Chapter 13, Other Pasteurellaceae. In this fifth edition, *Brachyspira* and *Helicobacter* also get their own chapters (Chapters 24 and 19, respectively), and we have added *Coxiella* to the chapter on *Chlamydia* (Chapter 20).

In addition to these new chapters, a major change in the fifth edition has been a focus on the wealth of new information that has been generated by the recent genomics revolution with its application to pathogenesis as well as to understanding the evolution of pathogens. We have therefore included "pathogenomics" and "evolution" within new section headings in the pathogen chapters. Although pathogenesis is always full of surprises, the last section in the pathogen chapters, "Gaps in knowledge and anticipated directions," provides a glimpse into where the experts think the research is heading.

Understanding how bacterial pathogens cause disease is invariably challenging and their study of requires multidimensional and multidisciplinary approaches. To help the reader get a rapid overview, authors of the pathogen chapters have produced figures that integrate the major elements in pathogenesis. We have also added regulation of virulence as a new section heading, since this complex topic is a critical integrating element. There is admittedly a long way to go before we have a well-integrated understanding of bacterial pathogenesis of many organisms, but with at least some pathogens, our understanding has been much improved.

The past two decades have seen the emergence of the antimicrobial resistance crisis in both human and veterinary medicine, which demonstrates the extraordinary ability of

bacteria to adapt to different pressures, often remarkably rapidly. This adaptability is also evident in the markedly enhanced virulence seen in some bacterial pathogens of food animal, apparently in response to changes in animal management.

One interesting emerging theme in this book is the adaptation of what used to be regarded as relatively broad host-range pathogens to specific animal species, such that the usually considerable knowledge of the pathogenesis of human bacterial pathogens may not be immediately applicable to the pathogen that has adapted to animals.

Although we all look back to the heroes of the microbiological revolution, personified by Louis Pasteur and Robert Koch, and many veterinary microbiologists from that era, we are convinced that the golden age of microbiology is the present and also continues to lie ahead. If we can understand the pathogenesis of important veterinary pathogens at a fundamental level, we should be able to use this understanding to develop novel strategies for prevention, treatment, and control of serious pathogens.

This book is based on the work of hundreds of researchers, whose ideas, innovation, and research skills have produced the body of knowledge on which we draw. The authors have presented captivating stories of bacterial pathogenesis based on their own work and that of their scientific colleagues. One of the challenges in preparing the book was the question of adequate attribution of research findings. While trying to acknowledge key contributions, we have had to limit the number of references, recognizing with regret that not all researchers who made important contributions to the literature will be recognized.

The new editorial team owes a great debt of thanks to the previous editors of this book: Carlton L. Gyles, J. Glenn Songer, and Charles (Chuck) O. Thoen. Most of all, we would like to acknowledge Carlton Gyles, who had the original inspiration for this book and who carried much of the load in assembling earlier editions. Carlton has made inestimable contributions to the field of veterinary bacteriology and the continuation of this book into a new edition is a tribute to his work. The chapter by John Fairbrother and Carlton Gyles on *Escherichia coli* in this book is a masterpiece.

Finally, we thank our publishers who have been extremely helpful in transforming the writings of so many individuals into a beautiful book. Special thanks go to Merryl Le Roux, the managing editor; Susan Engelken, editorial program coordinator; and Erica Judisch, executive editor.

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About the Companion Website

This book is accompanied by a companion website:

www.wiley.com/go/prescott/pathogenesis

The website includes:

- PowerPoint of all figures from the book for downloading
- References from book

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Themes in Bacterial Pathogenesis

John F. Prescott

Introduction

The speed of progress in understanding how bacteria cause disease is providing novel insights and perspectives on pathogens and the pathogenesis of bacterial infections at an almost overwhelming rate. As the tsunami of antimicrobial resistance threatens our long-standing expectation that we can successfully treat bacterial infections with existing antimicrobial drugs, understanding how bacterial pathogens of animals cause disease is of fundamental value in designing new and better ways to counter infections. Combined with rapid diagnosis of specific infections, novel antimicrobial treatments based on understanding the unique weaknesses of pathogens, such as those discussed in Chapter 6, can be targeted in ways that could overcome the inherently highly untargeted and resistance-enhancing nature of most current antimicrobial therapies.

Although an overview of the basic themes in bacterial pathogenesis provides a conceptual skeleton for the extensive details of individual pathogens and their interaction with the host given in later chapters, understanding of virulence and pathogenicity is changing rapidly. The fundamental concepts have withstood the test of time, but new knowledge has brought the complexities of host–pathogen interactions into sharper focus and has identified both important broad new topics as well as nuances not recognized previously. Although more is understood about bacteria, especially through the application of genome sequencing and related technologies such as RNAseq (Chapters 3, 4), bacterial infections seem to be increasing and changing, especially those associated with increased antibiotic resistance, driven both by exposure to increasingly powerful antibiotics and by changes in affected patient populations. Numerous anthropogenic activities, including antibiotic use at both therapeutic and subtherapeutic concentrations, may be driving bacterial evolution and the selection of pathogens adapted to changed circumstances (Chapter 2). Against the background of stunning advances in technologies, there is increasing recognition of the poor general application of well-established simple infection control techniques, such as hand washing to reduce the transmission of infection in people and in animals in clinical settings. The fight against bacterial infections requires the disciplined use of hard-earned knowledge, not simply the development and application of new technology.

The Basic Elements of Bacterial Pathogenesis

The basic elements in the establishment of infection by a bacterial pathogen (Figure 1.1) are well established. These are:

1. *Association* (colonization, invasion, or other ways of entry into the body).

Pathogenesis of Bacterial Infections in Animals, Fifth Edition.
Edited by John F. Prescott, Janet I. MacInnes, Filip Van Immerseel, John D. Boyce, Andrew N. Rycroft, and José A. Vázquez-Boland.

Companion Website: www.wiley.com/go/prescott/pathogenesis

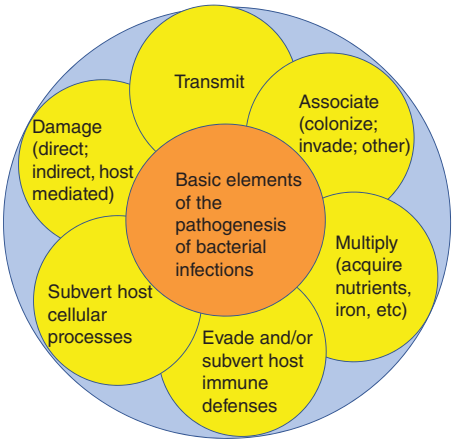

Figure 1.1 Basic processes in the pathogenesis of bacterial infections. The processes are more stages than steps, occurring often simultaneously, but also progressively and dynamically, integrated by regulatory processes responsive to signals provided by the host and environment. "Regulation" is shown in the sea of blue in which the processes are embedded. For highly virulent, destructive pathogens, "subversion of host cellular processes" does not occur, whereas it is critical for intracellular pathogens.

2. *Multiplication* (after nutrient, iron, etc. acquisition) to significant numbers at the site of infection and/or spread to other sites.
3. *Evasion* of host innate, sometimes acquired, immune defenses.
4. *Damage* to the host, either directly through subversion of cellular processes, or indirectly through host responses to the pathogen or its products.
5. *Transmission* from the infected animal to other susceptible animals, so that the infection cycle can continue.

As would be expected for carefully regulated systems, the infection process is a dynamic continuum rather than a clear series of steps, but breaking it down into progressive steps allows ease of understanding.

Pathogen Association with the Host

Successful colonization of the skin or a mucosal surface of the host is usually the first prerequisite of the infectious process. Some organisms need to employ motility and chemotaxis as well as resistance to acid and bile to reach their target host cells. Initial contact between bacterial pathogen and host cell is usually mediated by fimbrial or non-fimbrial adhesins on the bacterial surface. Binding may result either in extracellular colonization or in internalization of the pathogen. The adhesins bind to specific host cell surface receptors, and both host and organ specificity of infection are determined by differences among animals in cellular receptors for the bacterial adhesins. For example, the *Listeria monocytogenes* adhesion molecule internalin A (InlA) promotes uptake of the bacterium into intestinal epithelial cells by binding to E-cadherin. InlA binds to human and rabbit E-cadherin and causes disease in these species; however, it fails to bind to mouse E-cadherin and so does not readily cause disease in mice. Interestingly, Wollert et al. (2007) showed that by making two substitutions in InlA, they could increase the binding affinity to mouse E-cadherin by 10 000-fold and thereby establish experimental infection in mice. New host adaptations of different infections arise by similar naturally occurring mutations.

As many receptors are developmentally regulated, age specificity may also be determined by the receptor that a pathogen binds to. Well-established examples are known in K99 (F5) pili of porcine and bovine enterotoxigenic *Escherichia coli* (ETEC), which bind to the intestinal epithelium of neonatal animals, and in F18 pili of porcine ETEC, which bind to the intestinal epithelium of recently weaned pigs.

Bacterial pathogens, including those associated with wound infections, may bind to extracellular matrix molecules such as fibronectin, collagen, laminin, or other proteins possessing RGD (Arg-Gly-Asp, arginine-glycine-aspartic acid) sequences for binding of eukaryotic cell membrane integrins. Bacteria may use "invasins" to mediate their uptake into non-professional phagocytic host cells