Enterohemorrhagic

*Escherichia coli*

and Other Shiga Toxin-Producing *E. coli*
Enterohemorrhagic
*Escherichia coli*

and Other Shiga Toxin-Producing *E. coli*

EDITED BY

**Vanessa Sperandio**
Department of Microbiology
University of Texas
Dallas, TX 75390

and

**Carolyn J. Hovde**
School of Food Science
Idaho INBRE Program
Moscow, ID 83844-3025

ASM PRESS
Washington, DC
## Contents

**Contributors**  ix  
**Preface**  xv  

### OVERVIEW

1. **Overview and Historical Perspectives**  3  
   James B. Kaper and Alison D. O’Brien

### MICROBIOLOGY

2. **Taxonomy Meets Public Health: The Case of Shiga Toxin-Producing *Escherichia coli***  17  
   Flemming Scheutz

3. **Shiga Toxin (Stx) Classification, Structure, and Function**  37  
   Angela R. Melton-Celsa

4. **Enterohemorrhagic *Escherichia coli* Genomics: Past, Present, and Future**  55  
   Shah M. Sadiq, Tracy H. Hazen, David A. Rasko, and Mark Eppinger

### PATHOGENESIS

5. **Role of Shiga/Vero Toxins in Pathogenesis**  75  
   Fumiko Obata and Thomas Obrig

6. **The Locus of Enterocyte Effacement and Associated Virulence Factors of Enterohemorrhagic *Escherichia coli***  97  
   Mark P. Stevens and Gad M. Frankel

7. **Enterohemorrhagic *Escherichia coli* Adhesins**  131  
   Brian D. McWilliams and Alfredo G. Torres

8. **Animal Models of Enterohemorrhagic *Escherichia coli* Infection**  157  
   Jennifer M. Ritchie

9. **Enterohemorrhagic *Escherichia coli* Virulence Gene Regulation**  175  
   Jay L. Mellies and Emily Lorenzen

### INCIDENCE, EPIDEMIOLOGY, AND ECOLOGY

10. **Shiga Toxin (Verotoxin)-Producing *Escherichia coli* in Japan**  199  
    Jun Terajima, Sunao Iyoda, Makoto Ohnishi, and Haruo Watanabe
11 Animal Reservoirs of Shiga Toxin-Producing *Escherichia coli* 211
   Anil K. Persad and Jeffrey T. LeJeune

12 Shiga Toxin-Producing *Escherichia coli* in Fresh Produce: A Food Safety Dilemma 231
   Peter Feng

13 Public Health Microbiology of Shiga Toxin-Producing *Escherichia coli* 245
   Alfredo Caprioli, Gaia Scavia, and Stefano Morabito

**DIAGNOSIS, DETECTION, AND STRAIN CHARACTERIZATION**

14 Detection of Shiga Toxin-Producing *Escherichia coli* from Nonhuman Sources and Strain Typing 263
   Lothar Beutin and Patrick Fach

**CLINICAL, PATHOLOGICAL, AND PATHOPHYSIOLOGICAL ASPECTS**

15 Shiga Toxin/Verocytotoxin-Producing *Escherichia coli* Infections: Practical Clinical Perspectives 299
   T. Keefe Davis, Nicole C. A. J. van de Kar, and Phillip I. Tarr

16 The Inflammatory Response during Enterohemorrhagic *Escherichia coli* Infection 321
   Jaclyn S. Pearson and Elizabeth L. Hartland

17 New Therapeutic Developments against Shiga Toxin-Producing *Escherichia coli* 341
   Angela R. Melton-Celsa and Alison D. O’Brien

**HOST DETERMINANTS OF DISEASE AND HOST RESPONSE**

18 Risk Factors for Shiga Toxin-Producing *Escherichia coli*-Associated Human Diseases 361
   Marta Rivas, Isabel Chinen, Elizabeth Miliwebsky, and Marcelo Masana

19 Enterohemorrhagic *Escherichia coli* Pathogenesis and the Host Response 381
   Diana Karpman and Anne-lie Ståhl

20 The Interplay between the Microbiota and Enterohemorrhagic *Escherichia coli* 403
   Reed Pifer and Vanessa Sperandio

**PREVENTION AND CONTROL STRATEGIES**

21 “Preharvest” Food Safety for *Escherichia coli* O157 and Other Pathogenic Shiga Toxin-Producing Strains 421
   Thomas E. Besser, Carrie E. Schmidt, Devendra H. Shah, and Smriti Shringi
22 Peri- and Postharvest Factors in the Control of Shiga Toxin-Producing Escherichia coli in Beef 437
Rodney A. Moxley and Gary R. Acuff

23 Veterinary Public Health Approach to Managing Pathogenic Verocytotoxigenic Escherichia coli in the Agri-Food Chain 457
Geraldine Duffy and Evonne McCabe

24 Clinical Studies of Escherichia coli O157:H7 Conjugate Vaccines in Adults and Young Children 477
Shousun Chen Szu and Amina Ahmed

25 Vaccination of Cattle against Escherichia coli O157:H7 487
David R. Smith

ESCHERICHIA COLI O104:H4

26 Escherichia coli O104:H4 Pathogenesis: An Enteraggregative E. coli/Shiga Toxin-Producing E. coli Explosive Cocktail of High Virulence 505
Fernando Navarro-Garcia

THE WAY FORWARD

27 The Way Forward 533
Vanessa Sperandio

Index 541
About the Editors 553
Contributors

Gary R. Acuff
Department of Animal Science, 2471 TAMU, Texas A&M University,
College Station, TX 77843-2471

Amina Ahmed
Levine Children’s Specialty Center - Pediatric Infectious Disease,
Carolina Medical Centers, Charlotte, NC 28203

Thomas E. Besser
Veterinary Microbiology and Pathology, Washington State University, Pullman,
WA 99164

Lothar Beutin
National Reference Laboratory for Escherichia coli, Department of Biological
Safety, Federal Institute for Risk Assessment (BfR), Diererdorfer Weg 1,
D-12277 Berlin, Germany

Alfredo Caprioli
EU Reference Laboratory for E. coli, Dipartimento di Sanità Pubblica
Veterinaria e Sicurezza Alimentare, Istituto Superiore di Sanità,
Viale Regina Elena 299, 00161 Rome, Italy

Isabel Chinen
Servicio Fisiopatogenia, Instituto Nacional de Enfermedades Infecciosas –
ANLIS “Dr. C. G. Malbrán,” (1281) Buenos Aires, Argentina

T. Keefe Davis
Division of Nephrology, Department of Pediatrics, Washington University
School of Medicine, St. Louis, MO 63110

Geraldine Duffy
Teagasc Food Research Centre, Ashtown, Dublin 15, Ireland

Mark Eppinger
Department of Biology and South Texas Center for Emerging Infectious
Diseases, University of Texas at San Antonio, San Antonio, TX 78249

Patrick Fach
Food Safety Laboratory, ANSES (French Agency for Food, Environmental
and Occupational Health and Safety), Fr-94706 Maisons-Alfort, France
Peter Feng  
Division of Microbiology, U.S. Food and Drug Administration,  
College Park, MD 20740–3835

Gad M. Frankel  
MRC Centre for Molecular Bacteriology & Infection, Department of Life  
Sciences, Imperial College London, London, SW7 2AZ, United Kingdom

Elizabeth L. Hartland  
Department of Microbiology and Immunology, University of Melbourne,  
Victoria 3010, and Murdoch Children’s Research Institute, Royal Children's  
Hospital, Parkville, Victoria 3052, Australia

Tracy H. Hazen  
Institute for Genome Sciences, Department of Microbiology and Immunology,  
University of Maryland School of Medicine, Baltimore, MD 21201

Sunao Iyoda  
Department of Bacteriology, National Institute of Infectious Diseases, 1-23-1  
Toyama, Shinjuku-ku, Tokyo 162-8640, Japan

James B. Kaper  
Department of Microbiology & Immunology, University of Maryland School of  
Medicine, Baltimore, MD 21122

Diana Karpman  
Department of Pediatrics, Clinical Sciences, Lund University, 22185 Lund,  
Sweden

Jeffrey T. LeJeune  
Food Animal Health Research Program, Ohio Agricultural Research and  
Development Center, The Ohio State University, Wooster, OH 4491

Emily Lorenzen  
Laboratory of Chemical Biology and Signal Transduction, The Rockefeller  
University, 1230 York Avenue, New York, NY 10065

Marcelo Masana  
Instituto Tecnología de Alimentos, Centro de Investigación de Agroindustria,  
Instituto Nacional de Tecnología Agropecuaria, INTA, (B1708WAB) Morón,  
Pcia. De Buenos Aires, Argentina

Evonne McCabe  
Teagasc Food Research Centre, Ashtown, Dublin 15, Ireland

Brian D. McWilliams  
Department of Microbiology and Immunology, University of Texas  
Medical Branch, Galveston, TX 77555

Jay L. Mellies  
Department of Biology, Reed College, 3203 SE Woodstock Blvd.,  
Portland, OR 97202
Angela R. Melton-Celsa  
Department of Microbiology & Immunology, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814

Elizabeth Miliwebsky  
Servicio Fisiopatogenia, Instituto Nacional de Enfermedades Infecciosas – ANLIS “Dr. C. G. Malbrán,” (1281) Buenos Aires, Argentina

Stefano Morabito  
EU Reference Laboratory for E. coli, Dipartimento di Sanità Pubblica Veterinaria e Sicurezza Alimentare, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy

Rodney A. Moxley  
School of Veterinary Medicine and Biomedical Sciences, University of Nebraska-Lincoln, Lincoln, NE 68685-0905

Fernando Navarro-Garcia  
Department of Cell Biology, Centro de Investigación y de Estudios Avanzados del IPN (CINVESTAV-IPN), México DF, Mexico

Fumiko Obata  
University of Maryland School of Medicine, 685 W. Baltimore St., HSF-1 Suite 380, Baltimore, MD 21201

Alison D. O’Brien  
Department of Microbiology & Immunology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814

Thomas Obrig  
University of Maryland School of Medicine, 685 W. Baltimore St., HSF-1 Suite 380, Baltimore, MD 21201

Makoto Ohnishi  
Department of Bacteriology, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8640, Japan

Jaclyn S. Pearson  
Department of Microbiology and Immunology, University of Melbourne, Victoria 3010, Australia

Anil K. Persad  
Food Animal Health Research Program, Ohio Agricultural Research and Development Center, The Ohio State University, Wooster, OH 4491

Reed Pifer  
Department of Microbiology and Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas, TX 75390

David A. Rasko  
Institute for Genome Sciences, Department of Microbiology and Immunology, University of Maryland School of Medicine, Baltimore, MD 21201
Jennifer M. Ritchie
School of Biosciences and Medicine, University of Surrey, Guildford GU27XH, United Kingdom

Marta Rivas
Servicio Fisiopatogenia, Instituto Nacional de Enfermedades Infecciosas – ANLIS “Dr. C. G. Malbrán,” (1281) Buenos Aires, Argentina

Shah M. Sadiq
Department of Biology and South Texas Center for Emerging Infectious Diseases, University of Texas at San Antonio, San Antonio, TX 78249

Gaia Scavia
EU Reference Laboratory for E. coli, Dipartimento di Sanità Pubblica Veterinaria e Sicurezza Alimentare, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy

Flemming Scheutz
WHO Collaborating Centre for Reference and Research on Escherichia and Klebsiella, Department of Microbiology and Infection Control, Statens Serum Institut, DK-2300 Copenhagen S, Denmark

Carrie E. Schmidt
Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164

Devendra H. Shah
Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164

Smriti Shringi
Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164

David R. Smith
College of Veterinary Medicine, Mississippi State University, Mississippi State, MS 39762-6100

Vanessa Sperandio
Department of Microbiology and Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas, TX 75390

Anne-lie Ståhl
Department of Pediatrics, Clinical Sciences, Lund University, 22185 Lund, Sweden

Mark P. Stevens
The Roslin Institute & Royal (Dick) School of Veterinary Studies, University of Edinburgh, Midlothian, EH25 9RG, United Kingdom

Shousun Chen Szu
Eunice Kennedy Shriver National Institute of Child Health & Human Development, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892
Phillip I. Tarr
Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, and Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, MO 63110

Jun Terajima
Department of Microbiology, National Institute of Health Sciences, Kamiyoga 1-18-1, Setagaya-ku, Tokyo 158-8501, Japan

Alfredo G. Torres
Department of Pathology and Sealy Center for Vaccine Development, University of Texas Medical Branch, Galveston, TX 77555

Nicole C. A. J. van de Kar
Division of Nephrology, Department of Pediatrics, Radboud University Medical Centre, Nijmegen, The Netherlands

Haruo Watanabe
Director, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8640, Japan
Preface

This book is an exceptional compilation of our current worldwide understanding of the enterohemorrhagic *E. coli* (EHEC) and other Shiga toxin-producing *E. coli*. It spans diverse topics including microbial pathogenesis, pathophysiology of the disease, food safety, genetic analysis, veterinary microbiology, epidemiology, and environmental microbiology. It was compiled as an introduction, review, and critical overview of the pertinent areas of knowledge and brings the previous edition (Kaper JB, O’Brien AD [ed], *Escherichia coli* O157:H7 and Other Shiga Toxin-Producing *E. coli* Strains, ASM Press, 1998) up to date with the current literature.

The style and content are intended to make this volume of interest and value as a resource for research scientists, clinicians, students, health professionals, policy makers, and those in industry. In addition, we believe the text could be used for advanced courses in microbiology, food safety, infectious disease, or microbial pathogenesis.

The book contributors come from many and diverse research disciplines. Its breadth demonstrates the complexity of the problem of EHEC and Shiga toxin-producing *E. coli*. For rapid and timely dissemination, each chapter previously appeared in *Microbiology Spectrum* and is available online, but they are assembled here as a convenient hardbound reference volume. The book begins with a broad overview and historical perspective, followed by eight sections that organize information into subtopics. The text concludes with the traditional “look to the future” in chapter 27, titled “The Way Forward,” which was not previously published.

We gratefully acknowledge the outstanding skill and organizational work of all those at ASM Press who made this book possible. It was a pleasure working with Greg Payne, Ellie Tupper, Kenneth April, Courtenay Brown, and Cathy Balogh.

Both of us have devoted our professional careers to understanding the EHEC in hopes of contributing to effective interventions to improve human health. As editors, we are humbled by the exceptional work done by our colleagues, the chapter authors. They brought their full and thoughtful expertise and knowledge to their writing and fueled our excitement for the book. We hope that you, as a reader, will find the topics covered to be relevant and that their depth will bring new insights to your own work.

Vanessa Sperandio
Carolyn J. Hovde
December 2014