A Guide to

Infection Control in the Hospital

Fifth Edition

Bearman

Stevens

Edmond

Wenzel

A Guide to

Infection Control in the Hospital

An official publication of the International Society for Infectious Diseases (ISID)

Fifth Edition

Bearman

Stevens

Edmond

Wenzel

2014
International Society for Infectious Diseases
Boston, MA • USA

International Society for Infectious Diseases
9 Babcock Street, Unit 3
Brookline, MA 02446 • USA
Phone: (617) 277-0551
Fax: (617) 278-9113
E-mail: info@isid.org
Web site: http://www.isid.org

ISBN 0-9749031-0-8

Printed in the United States of America

Sales and Distribution

Worldwide

International Society for Infectious Diseases
9 Babcock Street, Unit 3
Brookline, MA 02446 • USA
Phone: (617) 277-0551
Fax: (617) 278-9113
E-mail: info@isid.org
Web site: http://www.isid.org

Editors

Gonzalo M.L. Bearman, MD, MPH
Professor of Medicine
Associate Hospital Epidemiologist
Department of Medicine
Virginia Commonwealth University
School of Medicine
Richmond, Virginia, USA

Michael Stevens, MD, MPH
Assistant Professor of Medicine/
Division of Infectious Diseases
Associate Hospital Epidemiologist
Director, Antimicrobial
Stewardship Program
Director, Travel & Tropical
Medicine Clinic
Virginia Commonwealth University
Health System
Richmond, Virginia, USA

Michael B. Edmond, MD, MPH, MPA
Professor of Internal Medicine
Chief Quality Officer
University of Iowa
Iowa City, Iowa, USA

Richard P. Wenzel, MD, MSc
Professor and Former Chairman
Department of Internal Medicine
Medical College of Virginia Campus
Virginia Commonwealth University
Richmond, Virginia, USA

List of Contributors

Awa Aidara Kane, PhD
Department of Food Safety
and Zoonoses
WHO
Geneva, Switzerland

Paul R. Allyn, MD
Fellow, Division of Infectious
Diseases
University of California,
Los Angeles
Los Angeles, California, USA

Susan Assanasen, MD
Division of Infectious Diseases,
Department of Medicine,
Siriraj Hospital
Mahidol University
Bangkok, Thailand

Gonzalo M.L. Bearman, MD, MPH
Professor of Medicine
Associate Hospital Epidemiologist
Department of Medicine
Virginia Commonwealth University
School of Medicine
Richmond, Virginia, USA

Mohamed Benbachir, PhD
Quality Consultant
Casablanca, Morocco

Frederick James Bolton, PhD,
FRCPath
Regional Health Protection Agency
Laboratory
Manchester Royal Infirmary
Manchester, United Kingdom

Timothy F. Brewer, MD,
MPH, FACP
Vice Provost, Interdisciplinary
and Cross-Campus Affairs
Professor of Medicine
University of California,
Los Angeles
Los Angeles, California, USA

Melanie Brown, MD
Division of Infectious Diseases
Virginia Commonwealth University
Health System
Richmond, Virginia, USA

Anne Dediste, MD
University Hospitals St. Pierre
Brugmann, and Queen Fabiola
Brussels, Belgium

Patrick De Mol, MD, PhD
Department of Microbiology, Sart
Tilman University Hospital
Liège, Belgium

Summer Donovan, DO
Pediatric Infectious Diseases Fellow
Virginia Commonwealth University
Health System
Richmond, Virginia, USA

Herbert L. DuPont, MD
University of Texas
School of Public Health
Baylor St. Luke's Medical Center
Houston, Texas, USA

Adriano G. Duse, MT, MBBCh (Rand), DTM&H, MMed (Microbiology), FCPath SA (Microbiology)
Chief Specialist, Chair and Academic Head, Department of Clinical Microbiology and Infectious Diseases (CMID)
School of Pathology of the NHLS and Faculty of Health Sciences, University of the Witwatersrand
Johannesburg, South Africa

Michael B. Edmond, MD, MPH, MPA
Professor of Internal Medicine
Chief Quality Officer
University of Iowa
Iowa City, Iowa, USA

Javier Ena, MD, MPH
Consultant
Department of Internal Medicine
Hospital Marina Baixa
Alicante, Spain

Betty A. Forbes, PhD
Professor of Pathology
Director of Clinical Microbiology
Department of Pathology
Virginia Commonwealth University
Richmond, Virginia, USA

Patricia Pecora Fulco, PharmD, BCPS, FASHP, AAHIVP
Clinical Pharmacy Specialist
Internal Medicine/HIV
Clinical Associate Professor of Pharmacy
Clinical Assistant Professor
Internal Medicine/
Division of Infectious Diseases
Virginia Commonwealth University Medical Center
Richmond, Virginia, USA

Michèle Gerard, MD
Department of Infectiology
Saint-Pierre University Hospital
Brussels, Belgium

Helen Giamarellou, MD
Professor Internal Medicine
Infectious Disease Department
Athens University Medical School
Athens, Greece

Ravindra Gopaul, MD, MPH, MBA
VCU Combined EM/IM Residency Program
Department of Emergency Medicine
Virginia Commonwealth University Medical Center
Richmond, Virginia, USA

Bart Gordts, MD, MBA
Clinical Microbiology and Infection Control
Hospital Network Antwerp (ZNA)
Antwerp, Belgium

Imma Grau, MD
Hospital Bellvitge
University of Barcelona
Barcelona, Spain

Jonathan Grein, MD
Associate Director, Hospital Epidemiology
Cedars-Sinai Medical Center
Los Angeles, California, USA

T. D. Healing, MSc, PhD
London, United Kingdom

Peter Hoffman, BSc, Hon DipHIC
Consultant Clinical Scientist
Antimicrobial Resistance and Healthcare Associated Infection Reference Unit
Public Health England
London, United Kingdom

Claudia D. Jarrin Tejada, MD
Infectious Disease Fellow
Virginia Commonwealth University Health System
Richmond, Virginia, USA

Jan Kluytmans, MD, PhD
Consultant Microbiologist
Amphia Hospital Breda/Oosterhout, Sint Elisabeth Hospital and Twee Steden Hospital, Tilburg
Professor of Medical Microbiology and Infection Control
VU University Medical Center, Amsterdam
Amsterdam, The Netherlands

Eva-Birgitta Kruse, MD
Laboratoriumsmedzin Köln
Cologne, Germany

Caroline Landelle, PharmD, PhD
Infection Control Program and WHO Collaborating Centre on Patient Safety
University of Geneva Hospitals and Faculty of Medicine
Geneva, Switzerland

Surbhi Leekha, MBBS, MPH
Assistant Professor, Departments of Epidemiology and Public Health and Medicine
University of Maryland School of Medicine
Associate Hospital Epidemiologist
University of Maryland Medical Center
Baltimore, Maryland, USA

Sebastiano Leone, MD
Division of Infectious Diseases
San Gerardo Hospital
Monza, Italy

Philippe Lepage, MD, PhD
Head, Department of Pediatrics
Hôpital Universitaire des Enfants Reine Fabiola
Université Libre de Bruxelles
Brussels, Belgium

Jack Levy MD, PhD
Head, Department of Pediatrics
CHU Saint-Pierre
Professor of Pediatrics
Université Libre de Bruxelles
Brussels, Belgium

Denise K. Lowe, PharmD, BCPS
Director, Drug Information Services
Virginia Commonwealth University Health System
Clinical Associate Professor
Virginia Commonwealth University School of Pharmacy
Richmond, Virginia, USA

Alejandro Macias, MD, MSc
Specialist in Internal Medicine and Infectious Diseases
Professor and Head, Infection Control
University of Guanajuato and National Institute of Medical Sciences and Nutrition
Mexico City, Mexico

J. Daniel Markley, DO
Virginia Commonwealth University Medical Center
Richmond, Virginia, USA

Alexandre R. Marra, MD
Hospital Israelita Albert Einstein
São Paulo, Brazil

Tawana McNair, MD
Clinical Infectious Diseases Fellow
Department of Medicine
Division of Infectious Diseases
Virginia Commonwealth University
Richmond, Virginia, USA

Véronique Y. Miendje Deyi, PharmD, PhD
Brugmann University Hospital Microbiology Lab
Brussels, Belgium

Rebekah W. Moehring, MD, MPH
Assistant Professor of Medicine
Division of Infectious Diseases
Duke University Medical Center
Durham, North Carolina, USA

Rekha Murthy, MD
Director, Hospital Epidemiology, Professor of Medicine, Cedars-Sinai Medical Center
Professor of Clinical Medicine, UCLA David Geffen School of Medicine
Los Angeles, California, USA

Emanuele Nicastri, MD, PhD
Epidemiologist
National Institute for Infectious Diseases
L. Spallanzani IRCCS
Rome, Italy

Belinda Ostrowsky, MD, MPH
Director Antimicrobial Stewardship and Associate Professor
Montefiore Medical Center & Albert Einstein College of Medicine
Bronx, USA

Amy L. Pakyz, PharmD, MS
Assistant Professor
Virginia Commonwealth University School of Pharmacy
Medical College of Virginia Campus
Richmond, Virginia, USA

Roman Pallares, MD
Hospital Bellvitge
University of Barcelona
Barcelona, Spain

Tara Palmore, MD, FACP
Deputy Hospital Epidemiologist
National Institutes of Health Clinical Center
National Institutes of Health
Bethesda, Maryland, USA

Didier Pittet, MD, MS
Infection Control Program and WHO Collaborating Centre on Patient Safety
University of Geneva Hospitals and Faculty of Medicine
Geneva, Switzerland

Samuel R. Ponce de León, MD, MSc
Division of Hospital Epidemiology and Quality Care
Instiuto Nacional de la Nutrición Salvador Zubirán
Mexico City, Mexico

M. Sigfrido Rangel-Frausto, MD, MSc, MQ
Infectious Diseases Department
Hospital Medica Sur
Mexico City, Mexico

Marie-Claude Roy, MD, MSc
Microbiology and Infectious Diseases
Hôpital de l'Enfant-Jésus
Québec City, Québec, Canada

William A. Rutala, MS, MPH, PhD
Professor of Medicine, UNC School of Medicine
Director, Statewide Program for Infection Control and Epidemiology
Director, Hospital Epidemiology, Occupational Health and Safety Program, UNC Health Care
Chapel Hill, North Carolina, USA

Harald Seifert, MD
Professor of Medical Microbiology and Hygiene
Institute for Medical Microbiology, Immunology and Hygiene
University of Cologne
Cologne, Germany

Michael Stevens, MD, MPH
Assistant Professor of Medicine/ Division of Infectious Diseases
Associate Hospital Epidemiologist
Director, Antimicrobial Stewardship Program
Director, Travel & Tropical Medicine Clinic
Virginia Commonwealth University Health System
Richmond, Virginia, USA

Andrew J. Stewardson, MBBS
Infection Control Program and WHO Collaborating Centre on Patient Safety
University of Geneva Hospitals and Faculty of Medicine
Geneva, Switzerland

Marc Struelens, MD, PhD
Department of Microbiology
Erasme University Hospital
Brussels, Belgium

Pawan Suri, MD
Chair, Division of Observation Medicine, Department of Emergency Medicine
Program Director, Combined EM/IM Residency Program
VCU School of Medicine
Assistant Professor in Emergency Medicine and Internal Medicine
Virginia Commonwealth University Medical Center
Richmond, Virginia, USA

Made Sutjita, MD, PhD
Loma Linda University
Infectious Disease Section
Riverside County Regional Medical Center
Moreno Valley, California, USA

C.M.A. Swanink, MD, PhD
Rijnstate Hospital
Department of Medical Microbiology and Immunology
Arnhem, The Netherlands

Antoni Trilla, MD, MSc
Chief, Preventive Medicine and Hospital Epidemiology Unit
Professor of Public Health
Hospital Clinic-University of Barcelona
Barcelona, Spain

Philippe Van de Perre, MD, PhD
Professor of Virology, University Montpellier 1
Head of Dept Bacteriology-Virology, University Teaching Hospital
Director of INSERM U 1058, Université Montpellier 1
Montpellier, France

Olivier Vandenberg, MD, PhD
Infectious Disease Epidemiological Unit
Department of Environmental Health
Public Health School
Université Libre de Bruxelles
Brussels, Belgium

Jacobien Veenemans, MD, PhD
Medical Microbiologist in Training
Laboratory for Microbiology and Infection Control
Amphia Hospital, Breda
Breda, The Netherlands

Heike von Baum, MD
Division of Clinical Hygiene
Institute for Microbiology and Hygiene
Ulm, Germany

Margreet C. Vos, MD, PhD
Professor in Health Care Related Infections
Medical Microbiologist
Dept of Medical Microbiology and Infectious Diseases,
Erasmus MC
Rotterdam, The Netherlands

Andreas Voss, MD. PhD
Professor of Medical Microbiology and Infection Control
Radboud University Medical Center
Departement of Medical Microbiology
Nijmegen, The Netherlands

Constanze Wendt, MD, MS
Dr. Limbach and Colleagues Medical Diagnostic Laboratory
Heidelberg, Germany

Joshua A. White, MD
Clinical Infectious Disease Fellow
Virginia Commonwealth University
Richmond, Virginia, USA

David J. Weber, MD, MPH
Professor of Medicine, Pediatrics and Epidemiology
UNC Schools of Medicine and Public Health
Medical Director, Hospital Epidemiology and Occupational Health, UNC Health Care
Chapel Hill, North Carolina, USA

Richard P. Wenzel, MD, MSc
Professor and Former Chairman
Department of Internal Medicine
Medical College of Virginia Campus
Virginia Commonwealth University
Richmond, Virginia, USA

Sergio B. Wey, MD, PhD.
Infectious Diseases Division
Federal University of São Paulo
São Paulo, Brazil

Andreas F. Widmer, MD, MS
Professor of Medicine and Infectious Diseases
Division of Infectious Diseases and Hospital Epidemiology
Head, Division of Hospital Epidemiology
University Hospitals
Basel, Switerland

Hilmar Wisplinghoff, MD
Institute for Medical Microbiology, Immunology and Hygiene
Cologne, Germany

Mireille Wulf, MD, PhD
Viecuri Medical Center
Dept. Clinical microbiology
Venlo, The Netherlands

S.E.J. Young, FRCP
Retired
London, United Kingdom

Introduction

The field of infection prevention has grown in importance over the last 30 years. The science of infection prevention, like others, is in constant evolution. With the collaboration of international leaders and front line practitioners in infection prevention, we summarize the most up to date principles, interventions, and strategies for maximizing the reduction of healthcare associated infections. The chapters herein are intended to improve quality of care, minimize risk, save lives, and reduce costs.

As our intention is to publish an up-to-date guide every 5 years, we welcome your comments and thoughts as we proceed with future editions.

Remarks may be sent to:
Dr. Gonzalo Bearman
International Society for Infectious Diseases
9 Babcock Street, Unit 3
Brookline, MA 02446 USA
Fax: (617) 278-9113
E-mail: info@isid.org

We wish to thank all our colleagues and friends for their contributions.

Table of Contents

CHAPTER 1

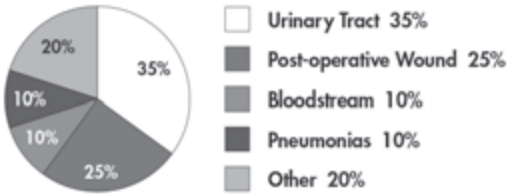
Importance of Infection Control

Richard P. Wenzel, MD, MSc

Health is a high priority for any society, and infections remain a leading cause of disease globally. Those infections which occur among patients in hospitals and become manifest only after 48 hours of stay are called "nosocomial." Some prefer the term "health care associated" infections. Such nosocomial or hospital acquired infections lead to significant morbidity, mortality and economic burden beyond those expected from the patients' underlying diseases alone. In this text we will use the term health care associated most of the time

In the Western world the health care associated infection rate is 5–10% or 5–10 infections per 100 patient admissions. In the developing world the rate can be 25% or more. Some hospitals prefer to measure the number of infected people per 100 admissions. Others prefer to add up the total hospital stay in days for all patients over a period of time and report the number of infections per 1000 patient days.

The distribution of infections by anatomic site in acute care hospitals in the developed world is shown below:



Proportion of all health care associated infections by anatomic area

In developing countries the distribution may be different, with fewer bloodstream infections since fewer devices are used, more gastrointestinal infections, and a higher proportion of post-operative wound infections.

Mortality

Bloodstream and pulmonary infections carry the highest mortality rates, approximately 25–30% in developed countries. It has been shown that health care associated infections are equivalent to the 8th leading cause of death in the U.S., even if one examines only health care associated bloodstream infections. There should be low mortality rates or no deaths following urinary tract or postoperative wound infections. These rates might be expected to be higher for developing nations because of limited resources to manage them, including limited critical care availability.

Importantly, when a patient with a health care associated infection dies prematurely, there are also years of life lost (YLL) directly due to the infection. For example, if a 40 year old woman whose life expectancy is 60 years dies from a health care associated infection, her death contributes 20 years of life lost. If 100 similar patients died over a period of one year, then there would be 20 years x 100 patients or 2000 YLL lost due to health care associated infections that year. In the U.S. it has been estimated that health care associated bloodstream infections each year lead to 260,000 YLL.

Morbidity

Few studies have examined morbidity directly related to health care associated infections. However, one thinks of pain, stress, depression or "suffering" when one considers morbidity. With psychological instruments one could systematically measure the days of each, even consider giving a score for each parameter such as scoring pain on a 1–5 scale.

One could also imagine measuring the quality of life, days before return to school or job, or number of doses of pain medication as measures of morbidity. However, little has been done in this area.

Costs

Almost all studies of the economic burden of health care associated infections have examined only the *direct* costs of additional hospital stay. For example, in developed countries, patients with health care associated bloodstream infections stay an extra 10–14 days, presumably for additional therapy. From a hospital administrator's perspective, there are fixed and variable costs. The fixed costs include those for heat, air conditioning, lighting,

etc. The variable costs are those that increase for each additional day of hospitalization. For example, additional nursing care may be required as the census increases. If the incremental cost of stay—the variable cost above the expected fixed cost of stay—averages $500/day, the additional economic burden is $5,000 to $7,000 for each infection.

Patients with post operative wound infections stay in the hospital twice as long as matched controls without a wound infection. This leads to considerably additional costs. It is generally thought that health care associated urinary tract infections add 1–3 additional days in the hospital, and health care associated pneumonias add approximately 9 days to the expected stay compared to matched controls without a health care associated pneumonia.

There are also "indirect" costs, such as the costs of rehabilitation after hospitalization, the costs of outpatient medications, and costs of followup appointments. Depending on a country's healthcare reimbursement system, a great deal of the indirect costs might be borne by the patients themselves.

Table 1.1 below summarizes the ways to measure the impact of health care associated infections:

Table 1.1 Measures of the Impact of Health Care Associated Infections

Impact of Health Care Associated Infections:	
Mortality —	Number of Deaths per 100 infected Years of Life Lost (YLL) from health care associated infections per 100 admissions
Morbidity —	Pain and suffering days resulting from an infection
Costs —	Direct costs of extra hospital days per 100 admissions Number of **extra** hospital days from health care associated infections

A Quality Issue

An important point is that many view infection control as a key issue in quality of care. In fact, in the developed countries it is the first "success" story in the use of intervention measures to improve patient care in hospitals. Thus, those who espouse quality care should begin with infection control, in part because the outcomes are so serious without control and in part because successful interventions have been developed.

Individual Commitment

In the developed world, it is likely that at least 20% of all health care associated infections can be prevented. More could be prevented in the developing world. Most of the interventions are simple and behavioral and relate to the individual healthcare worker: careful hand washing, appropriate isolation and use of gloves where appropriate, and proper use of devices such as the insertion and care of foley bladder catheters. Thus, the link between individual commitment to quality and improved outcomes can be demonstrated for infection control.

System Issues

There are also system issues that need to be addressed for infection control. For example, soap and water have to be available at all times for healthcare workers and placed in convenient locations for easy access. There needs to be a system by which surgical patients receive preoperative antibiotics in the 1–2 hours before the incision, not greater than two hours and never delayed to one after the incision. A system has to be in place to isolate some patients with communicable disease. Very recently the importance of team-based prevention of health care associated infections has been shown to be valuable when the team utilized evidence-based interventions such as proper hand hygiene, barrier precautions and subclavian site as the preferred one for a central line. The implication of the team approach is that any member of the team of healthcare professionals—physicians or nurses—can ask the physician to restart a bedside procedures if there is a break in sterile technique.

A Societal Issue

Lastly, I would return to the beginning to emphasize that a healthier community can contribute more to its citizens. With fewer infections and their complications, a well society is better able to work, to educate, to contribute to the arts, and to provide a myriad of services that are unavailable to a more ill society. Infection control is a key ingredient to and an essential component of a better functioning and happier society. In the end, proper infection control can make a significant contribution to improving the human condition.

References

Book

Prevention and Control of Nosocomial Infections (4th Edition), Wenzel RP (Ed). Baltimore: Lippincott Williams & Wilkins, 2003.

On Line Resources.

Decision Support In Medicine.Com: Program—Hospital Infection Control. Wenzel RP, Bearman G (Eds) 2013. Available at: http://www.decisionsupportinmedicine.com

Manuscripts

Wenzel RP, Edmond MB. The Impact of Hospital Acquired Bloodstream Infections. *Emerg Infect Dis*. 2001. 7:174–7.

Pronovost P, Needham D, Berenholtz S, et al. An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. *N Engl J Med*. 2006. 355:2725–2732.

Wenzel RP. Healthcare Associated Infections: Major Issues in the Early Years of the 21st Century. *Clin Infect Dis*. 2007. 45(Suppl 1):585–8.

Wenzel RP, Edmond MB. Team-Based Prevention of Catheter-Related Infections. *N Engl J Med*. 2006. 355:2781–3.

Wenzel RP. Minimizing Surgical Site Infections. *N Engl J Med*. 2009. 326:75–7.

Wenzel RP. Infection Control: The Case for Horizontal Rather than Vertical Interventional Programs. *Internat J Infect Dis*. 2010. 14, Supp 4:53–5.

Edmond MB, Wenzel RP. Screening Inpatients for MRSA—Case Closed. *N Engl J Med*. 2013. 368:2314–5.

CHAPTER 2

Organization

Richard P. Wenzel, MD, MSc

A necessary feature for a successful program in infection control is dedicated leadership that creates a culture for excellence. Without leaders, there are no followers among the management team. Some important attributes of the management team that support the culture for excellence include a knowledge of microbiology, excellent communication skills, and an understanding of the key discipline of epidemiology. Some ability to gather data and perform basic analyses is extremely useful.

Ideally, a trained infectious diseases specialist with some training in infection control would lead the hospital's program. Such individuals have complementary clinical, microbiological, and epidemiological skills useful in providing the vision and oversight of a high performance team. Since energy and commitment are so critical to success, a hospital may begin with candidates that have these two attributes and select someone with most but not all of the other skills listed above.

Leadership and management are distinct but overlapping skills, useful for any program. The leader is charged with creating the vision, the day-to-day culture, the energy, the ideals and the ethics of a program. The manager is charged with carrying out the vision, making the components of a complex organization function well while meeting all financial budget restrictions. Some leaders have management skills, but the key role of the hospital epidemiologist is to lead!

The team members supporting the hospital epidemiologist may in fact be leaders in their respective fields of nursing epidemiology, microbiology, pharmacy, employee health, biostatistics and epidemiology, and computer support. However, each has a responsibility as a manager in their area of expertise and oversight. They are charged with making the system work. In small hospitals and those with limited resources, a single individual may be charged with more than one of these tasks.

Table 2.1 The Infection Control Team

Role	*Team Member*	*Ideal Skills*
Leader	Hospital Epidemiologist	Infectious Diseases, microbiology, and infection control communication
Manager(s)	Microbiologist	Microbiology, interpretation of antibiotic resistance
	Nurse Epidemiologist (infection control practitioner)	Nursing & Epidemiology including surveillance skills, communication
	Pharmacist	Pharmacokinetics and Pharmacodynamics of drugs, especially antibiotics. Education
	Employee Health Director	Infection Control, Vaccine Use
	Biostatistician	Inference statistics and modeling skills
	Computer Technician	Design data base and search features

Functions

The starting point of a good program for infection control is basic surveillance by which rates of infection can be calculated after valid case finding. Most experts prefer prospective surveillance rather than retrospective surveys because of the greater accuracy of the former. Although hospital-wide surveillance is the ideal, with limited resources a program may wish to focus only on health care associated bloodstream infections because of the high associated mortality and the relative ease with which to identify nonpathogens from pathogens in blood cultures. One could begin surveillance in the microbiology laboratory, and after ruling out all of the contaminants, the physician or nurse epidemiologist could gather clinical data from the infected patients' charts to be used later in epidemiological analyses.

Alternatively, with limited resources a decision could be made to survey only post-operative (incisional) wound infections because of their high frequency, significant morbidity, and high costs. One could survey all surgical patients only for a fixed period of time after the operation, seeking evidence of infection (pus at the incision site).

The number of infections or infected patients is included in the numerator, and one has various options for the denominator.

Thus, various rates can be calculated:

- The number of infections/100 admissions.
- The number of infected patients/100 admissions.
- The number of infections/1000 patient-days.

The critical point is that for calculation of a rate, the denominator must include the total number of patients at risk. If one is surveying only for post operative wound infections, each month the population at risk, the denominator, would be all patients undergoing operations during that time.

Some of the key functions of an effective infection control program are shown in the *Table 2.2* below:

Table 2.2 Functions of an Infection Control Program

- Surveillance
- Education and feedback to clinicians using surveillance data and antibiogram data by anatomic site
- Management of proper isolation techniques
- Provision of either hand washing materials or alcohol-based (waterless) hand cleansing materials
- Development of standards for management of proper insertion and maintenance of medical devices
- Monthly meeting of the infection control team

Most of the roles indicated in *Table 2.2* rely on excellent education of various members of the healthcare team. Thus, communication skills, and teaching skills specifically, greatly enhance the value of the infection control team.

A key function of the organization that is necessary for its optimal functioning is the monthly infection control meeting. The goals of the monthly meeting are few in number but very important:

- Brief review of surveillance data.
- Summary of any epidemic workup.
- Review of antibiogram data, listing resistance rates for important antibiotics such as methicillin resistant *S. aureus*, vancomycin-resistant *E. faecium*, and third generation cephalosporin antibiotic-resistant gram-negative rods.

- Review and passage of one new policy or procedure each month. This may sound simple and easy to perform, but it is the most difficult goal for any team, requiring homework, background political work and bold decision making.

Summary

The effective infection control program needs a designated leader supported by a team with special skills. Although ideal leadership and management skills are listed above, a hospital with limited resources will need to accommodate the program with interested and dedicated personnel possessing most of the desired skills. The role of surveillance is to provide local data, especially important in education. A monthly infection control meeting for the continued review and development of policies is especially important.

References

Book

Katzenbach JR, Smith DK. *The Wisdom of Teams*. New York: Harper Business, 1994.

Manuscripts

Wenzel RP. Leadership, Management and Politics: Issues for Healthcare Epidemiology *in* Decision Support In Medicine.Com: Programs—Hospital Infection Control. Wenzel RP, Bearman G (Eds) 2013.

Wenzel RP. Leadership and Management for Healthcare Epidemiology *in* Prevention and Control of Nosocomial Infections (4th Edition), Wenzel RP (Ed). Baltimore: Lippincott Williams & Wilkins, 2003. Pgs. 609–16.

Wenzel RP. The Hospital Epidemiologist: Practical Ideas. *Infect Control Hosp Epidemiol*. 1995.

CHAPTER 3

Role of the Microbiology Laboratory in Infection Control

Mohamed Benbachir, PhD

Key Issue

The microbiology laboratory plays an important role in the surveillance, treatment options, control and prevention of health care associated infections. The microbiologist is a permanent member of the infection control committee (ICC).

Known Facts

The first task of the microbiology laboratory is accurately, consistently and rapidly to identify the responsible agents to species level and identify their antimicrobial resistance patterns. This has been made easier because of the important progress made in the fields of instruments, reagents and techniques. The quality of the microbiology results is directly linked to the quality of the specimens. Specimens that are not collected and transported properly may lead to misleading results. Since the ICC programms rely on microbiological results, quality assurance is an important issue.

The microbiology laboratory is a surveillance and early warning system. Laboratory based surveillance is an essential part of the hospital wide surveillance in concert with surveillance based on patient units (e.g., ICU, haematology) and on specific sites of infection (e.g., blood, surgical site). Routine surveillance of health care associated infections is based both on daily review and on periodic reports of microbiology records. The microbiology laboratory is also a sentinel system. Prompt notification to clinical wards and to ICC initiate epidemiological investigation which may lead to preventive measures to halt the spread of causative microorganisms.

The microbiology laboratory is also involved in the detection and investigation of outbreaks. Comparison ("typing" or "fingerprinting") of epidemiologically related isolates helps to

determine whether these organisms are related or not and thus essential to confirm the existence of an outbreak. The laboratory must collaborate with the ICC in the investigation of outbreaks. Typing of isolates is also useful during outbreaks to determine the prevalence and mode of spread of strains and to identify reservoirs and carriers.

Antibiotic resistance levels vary widely depending on geographic location and even among hospitals from the same country. Hospital antibiotic policies can be generated only when local information is available. Monitoring the antibiotic susceptibilities of bacteria generates a database which is consulted when writing hospital antibiotic policies. On the other hand the evolution of antibiotic resistance levels is a marker of the quality of infection control in a hospital.

Controversial Issues

Laboratory based surveillance is efficient but incomplete because of the lack of clinical and epidemiological data available in the laboratory and because specimens are not always collected from all cases of health care associated infections.

The counterpart to the improvement of laboratory performances (detection and typing) is the extra investment needed. A special budget to participate in infection control activities is not always available, especially in developing countries.

Reference typing techniques (e.g., PFGE) are costly, labor-intensive and require interpretation skills. Alternative methods (e.g., Arbitrarily Primed-PCR) lack reproducibility and standardized interpretative criteria. Whether to fingerprint the isolates locally or to send the strains to reference laboratories depends on laboratory staffing and skills, the number of isolates and available budget.

Suggested Practice

A representative of the microbiology laboratory staff must be an active member of the ICC. In many hospitals, the ICC is chaired by a microbiologist, and a key function is to improve collaboration between clinical, laboratory and ICC personnel. If necessary, the microbiologist gives training in basic microbiology to ICC members and provides expertise (e.g., ready to use microbiological strategies to deal with each specific infection control situation, evaluation of resources needed, interpretation of culture results).

The microbiology laboratory staff should implement external and internal quality controls, and participate in continuous education and training to detect recognized, unusual and new phenotypes of resistance. The quality of specimens collection and transport should be maintained in collaboration with clinicians and nursing staff through seminars and procedure books. On the other hand a minimum of epidemiological (e.g., date of hospitalization) and clinical data should accompany the culture orders.

Laboratory records are an important source of information for the ICC. Storage and analysis of information are usually computerized. For laboratories with limited resources, the WHONET software from WHO is a powerful tool which is free of charge, user friendly and can be customized to each laboratory needs.

The microbiology laboratory is responsible for dissemination of this information. All significant laboratory results should be reported as quickly as possible to the clinicians and to the ICC. Some of these results (isolation of *Salmonella*, *Shigella* or *Neisseria meningitidis*, smears showing acid fast bacilli, cultures with multi-resistant bacteria) have a high priority and should be notified immediately by phone.

The microbiology laboratory must issue daily reports of significant microbiology results. This report includes patient's identification, date of hospitalization, type and date of collection of specimen and culture results. Reports that focus on selected pathogens (e.g., methicillin resistant *Staphylococcus aureus*, vancomycine resistant *Enterococcus*, extended spectrum ß-lactamase producing Enterobacteriaceae, carbapenem resistant *Acinetobacter baumannii* can also be issued. The list of selected pathogens which include bacteria with known epidemic potential and multi-resistant bacteria is established by the ICC and is revised periodically following the epidemiological situation at the institution.

Periodic reports are also useful in that they monitor trends. Data from various time periods should be analysed to study the patterns of infections.

The microbiology laboratory is responsible for the early detection of clusters of microorganisms with the same phenotypic characteristics. Laboratory and epidemiological studies

of suspected outbreaks should be conducted in parallel. During outbreaks the microbiology laboratory collaborates with the ICC to choose the specimens to collect, the isolates to fingerprint, and the relevant isolates to store. In some situations, cultures of samples from carriers, from healthcare workers and the environment will be considered. All this work should be done timely.

Surveys of hospital personnel and environment should not be conducted routinely but only to address specific situations.

Biotyping and antibiotic resistance phenotypes are not reliable epidemiological markers. Molecular biology techniques are more discriminatory than phenotypic methods. The use of chromosomal restriction patterns by pulsed field gel electrophoresis is considered the reference technique for typing most bacterial species.

Data on antimicrobial resistance should be periodically available to the medical staff, at least annually. The data should be summarized for each ward or clinical specialty and by anatomic site of infection or type of pathogen. These data are helpful for generating hospital treatment guidelines, which are useful in situations where empirical therapy is often given before the microbiology results are available.

References

McGowan JE, Weinstein RA. The role of the laboratory in control of nosocomial infection *in* Hospital infections (4th Edition). Bennett JV, Brachman PS (Eds). Philadelphia. Lippincott-Raven, 1998. Pgs. 143–164.

Pfaller MA, Herwalt LA. The clinical microbiology laboratory and infection control: Emerging pathogens, antimicrobial resistance and new technology. *Clin Infect Dis*. 1997. 25:858–870.

Tenover FC, Arbeit RD, Goering RV and the Molecular Typing Working Group of the Society for Healthcare Epidemiology of America. How to select and interpret molecular strain typing methods for epidemiological studies of bacterial infections: A review for healthcare epidemiologists. *Infect Control Hosp Epidemiol*. 1997. 18:426–439.

Wilson MP, Spencer RC. Laboratory role in the management of hospital acquired infections. *J Hosp Infect*. 1999. 42:1–6.

Espy MJ, Uhl JR, Sloan LM, et al. Real Time PCR in Clinical Microbiology: Applications for Routine Laboratory Tests. *Clin Microbiol*. 2006. 19:165–256.

CHAPTER 4

Antibiotic Resistance Challenges

Richard P. Wenzel, MD, MSc

Key Issue

Begun in the 1940s, the antibiotic era is under 80 years' duration, yet now is challenged by the worldwide increase in the incidence of resistance by microorganisms.

Known Facts

- In the community, penicillin-resistant pneumococci and multidrug-resistant tuberculosis are major public health problems. These organisms also have become significant health care associated pathogens. A more recent issue is the emergence of community-acquired methicillin resistant *S. aureus* (CA-MRSA). A more virulent strain of *C. difficile* with higher than usual toxin production has caused epidemics in Canada and the U.S.
- In hospitals throughout the world, there are special problems with methicillin resistant *Staphylococcus aureus*—both health care associated and the new strains of CA-MRSA.
- The explosion of infections with vancomycin-resistant *Enterococcus faecium* in hospitals in the United States has been remarkable. Much lower rates have been reported from Europe.
- Resistance of gram-negative rods to quinolones and third generation cephalosporins continues to increase.
- Those strains resistant to Ceftriaxone are called ESBLs because they carry extended spectrum βeta Lactamases enabling the bacteria to resist most βeta Lactam antibiotics. Such strains are usually susceptible to carbapenems such as imipenem and meropenem.
- With increasing use of carbapenems there has been the emergence of bacteria harboring carbapenemases, βeta Lactamases that inactivate imipenem and meropenem. Some such strains are susceptible only to colistin.

- The emergence of strains of *S.aureus* with intermediate levels of resistance to vancomycin (VISA) has been noted in several countries. These have MICs of 4 or 8 μg/ml, making therapy a challenge with vancomycin. Furthermore, strains with full resistance to vancomycin have been recovered (VRSA). In 2002, two strains of *S.aureus* with high levels of resistance to vancomycin (VRSA) were reported in the United States. These strains have MICs ≥16μg/ml. As of November 2013, 13 patients in the U.S. have been identified with infections due to VRSA.

Unless we pay attention to the problem of antibiotic resistance, we will quickly run out of effective therapy. Unfortunately, the problem of resistance comes at a time when fewer pharmaceutical companies are in the business of developing new antimicrobials. Thus, the pipeline of new drugs is limited.

Controversial Issues

- The causes of antibiotic resistance are not clearly known, but surely **unnecessary use of antibiotics** is important. Such high use leads to the selection of resistant organisms. Once a patient has a resistant organism, then the possibility exists for transmission to other patients. The initiating problem is the selection of a resistant isolate under the "pressure" of antibiotic usage.
- A second issue is excellent **infection control**—isolation and hand washing—to minimize spread of antibiotic resistant isolates. Exactly what proportion of the level of resistance stems from poor infection control is unclear, but is thought to be higher for Gram positive than Gram negative organisms.
- The third issue relates to the **influx of patients** harboring resistant strains on admission to the hospital. Thus, the issue is a need for quickly identifying patients and isolating them on admission. This requires labeling the charts of patients previously known to be infected with or carriers of antibiotic-resistant pathogen. When the patient enters the hospital, he or she should be automatically placed in appropriate isolation. It remains unclear at what level of resistance it is no longer cost effective to maintain a program of isolation on admission. However, there are some data suggesting its usefulness in controlling the rates of MRSA.

The level of resistance in hospitals to antibiotics can be considered to be influenced by three major parameters: how much enters in institution, how much is selected *de novo* or afterwards, and how much spread as a result of poor infection control. Imagine that one wanted to know what contributed to the current rate of MRSA: It is mostly related to infection control, influenced by the incoming burden of MRSA positive cases, but less so by the quantity of methicillin used. In contrast, the level of resistant gram-negative rods is very much influenced by antibiotic pressure and the incoming burden of resistant gram-negative rods.

Suggested Practice

Three areas for control of this problem are as follows:

1. Minimize the use of antibiotics to limit the selection and emergence of a resistant clone.
2. Maximize good hand washing and isolation practices to limit transmission of any antibiotic-resistant organisms that may emerge in the hospital to enter with a new patient.
3. Develop systems to identify quickly and isolate immediately all new patients who might be carrying an important antibiotic-resistant pathogen. This may be accomplished by marking the charts of patients previously known to be carriers or by isolating all patients coming from another facility known to have a high number of antibiotic-resistant organisms.
4. Begin to develop policies for changes in both empiral therapy and perioperative prophylaxis should health care associated strains of CA-MRSA become more prevalent.

References

Wenzel RP, Edmond, MB. Managing Antibiotic Resistance. *N Engl J Med*. 2000. 343:1961–3.

Wenzel RP, The antibiotic pipeline: challenges, costs and values. *N Engl J Med*. 2004. 351:523–5.

Wenzel RP, Bearman G, Edmond MB. Community Acquired MRSA: New issues for infection control. *Int J Antimicrob Agents*. 2007. 30:210–2.

Bouchet HW, Talbot GH, Benjamin DK, Jr., et al. 10x'20 Progress—Development of New Drugs Active Against Gram-Negative Bacilli: An Update From the Infectious Diseases Society of America. *Clin Infec Dis*. 2013. 56:1685–94.

CHAPTER 5

Waste Management

Tawana McNair, MD and Gonzalo Bearman MD, MPH

Key Issue

Waste is generated in the health care setting. The key step in waste management is to distinguish between infectious and noninfectious waste. Infectious waste has the potential to transmit disease and should be collected, transferred, and disposed of in a manner that decreases the risk of injury to healthcare workers, waste management workers, patients, and the community.

Known Facts

- There are many materials/equipment components used in hospitals for the diagnosis and treatment of patients. These materials have come in contact with blood, bodily fluids, and tissues of patients and may contain infectious microorganisms. These materials have the potential to transmit disease and thus require proper management and disposal following use. Prior to disposal, these materials need to be classified into infectious and noninfectious waste.
- The definition of infectious waste is not concrete or universal. However, the general idea is that infectious medical waste has the potential to transmit microorganisms. There are many factors which facilitate the progression of an infectious exposure to an infectious disease. These factors include the size of the inoculum, the virulence of the microorganism, and the susceptibility of the person in contact with the infectious waste. Currently, there is no method to determine the risk of disease as these factors are usually unknown prior to exposure. This limitation and the ambiguous definition of infectious waste, highlight the need to correctly identify infectious waste from noninfectious waste in order to decrease the risk of disease transmission. Strict protocols should be in place to ensure compliance.

- Exposure to infectious wastes can occur in many settings, including outpatient/clinic settings, however, the majority of accidents and exposures to infectious waste occur in the hospital setting. The waste products from sharps (e.g. needles, vials, surgical equipment) and cultures concentrated with microorganisms have the highest potential for disease transmission; however, disease transmission has also resulted from exposure to blood, bodily fluids, tissue from infected patients or laboratory animals, and material from microbiology and pathology laboratories.

Controversial Issues

- There is no set protocol or strict criteria to determine which type of medical waste has the potential to cause disease in susceptible hosts. However, there are categories of medical waste that have a greater potential for transmitting disease. Three questions should be considered when deciding if medical waste has the potential to transmit pathogens. An infection control practitioner should be consulted for questions and guidance.

1. Does the medical waste contain blood, body fluids, or tissue with pathogenic microorganisms in sufficient quantity to produce disease?

- Patients with known infections are likely to generate waste containing a large amount of microorganisms. The supersaturated gauze covering a draining wound, the sputum of a patient with known TB, the syringe used on a patient with known HIV or Hepatitis, a diaper with the stool of a baby admitted with diarrhea, are all examples of infectious waste with the potential to transmit disease. All blood and body fluids, organs, and microbiology laboratory specimens should be considered infectious waste regardless of the patient's diagnosis.

2. Does the waste contain viable and pathogenic microorganisms?

- Clinical microbiology laboratories handle a large number of microorganisms daily. These organisms are cultured from blood, sputum, stool, and other body fluids and

should therefore be treated as infectious while in the laboratory and once disposed. Infectious waste in the clinical microbiologic laboratory also includes material used for isolation and identification of the microorganisms (e.g. slides, pipettes, and tubes).

- Consideration should also be made outside of the microbiology laboratory pertaining to blood and body fluid samples sent for general evaluation such as the clinical chemistry laboratory. These samples should also be considered infectious waste given their potential to contain pathogenic organisms.

3. Can the waste create a portal of entry for pathogenic organisms into a susceptible host?

- Sharps are the single most frequent cause of occupationally acquired blood-borne disease in health care workers and should always be considered infectious waste. Sharps include needles, scalpel blades or other sharp instruments, IV catheters, broken glass (vials), and razor blades (no longer used for trimming hair given significant risk for infection). The health status of a patient is not always readily available, therefore, sharps containing blood should be classified as infectious because they provide a portal of entry for microorganisms.
- Sharps that do not contain blood (e.g., broken glass) are still dangerous because they may cause puncture injuries to healthcare workers and waste management workers that can produce a portal of entry for pathogenic microorganisms.

Suggested Practice

- The key step in waste management is to distinguish between infectious and non-infectious waste. The definition and regulation of "infectious waste" varies by state. Each hospital should develop written procedures for waste management on the basis of national and regional regulations, the prevalence of infectious diseases that can potentially contaminate medical waste and the local infrastructure for processing infectious waste. Hospital staff should receive training for correctly segregating all medical waste and regulation of the written procedure must be strictly enforced.

- In a waste management program, biologic waste should first be separated from non-biologic waste (paper, glass, plastic). Biologic waste should then be separated into infectious and non-infectious waste. Non-infectious waste can be collected in regular black bags and treated as residential waste.
- Sharp infectious waste must be placed in rigid, puncture proof and impermeable containers that bear the universal biologic hazard symbol and should be removed from use and discarded when the container is ¾ full. Incineration is the preferred treatment method for sharps as it eliminates microorganisms and any possibility of puncture wounds. Other methods for treatment of infectious waste include steam sterilization and chemical treatment.
- Non-sharp infectious waste should be collected in leak-resistant biohazard bags and sent for incineration. Alternatively, it can be decontaminated on site and subsequently discarded as non-infectious waste. On-site decontamination of microbiology laboratory waste is preferred, as this reduces the potential of exposure during the handling and transportation of infectious materials. Identification of live cultures and stocks should be made in efforts to avoid aerosolization of infectious microorganisms.
- Disposal equipment including sharps containers, garbage bags and bins should be readily available and easily accessible throughout all patient areas. Infectious waste should be transported within the hospital in wheeled trolleys or carts through specially designed routes and at low volume times of the day. These routes should avoid patient care areas as well as areas where food is prepared, stored, or transported whenever possible.
- Infectious waste should be treated soon after discarding. If transport for off-site incineration is required, it should be temporarily stored in a secure and completely closed storage room.

Summary

Although the risk of acquiring disease from infectious waste is low, the consequences can be significant. As a result, all hospitals need to develop a waste management program. The program should be jointly designed and coordinated by the infection control department, the hospital engineering staff, and municipal authorities. Medical waste should be classified as infectious when it contains a sufficient quantity of pathogenic microorganisms to produce disease and there is a potential within the waste management setting to create a portal of entry into a susceptible host.

References

Hedrick ER. Infectious waste management—will science prevail? Agency for Toxic Substances and Disease Registry. The public health implications of medical waste: A report to Congress. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. *Infect Control Hosp Epidemiol*. 1988. 9:488–90.

Pruess A, Giroult E, Rushbrook P. Safe Management of Wastes from Healthcare Activities. World Health Organization. Geneva. 1999.

Rutala WA, Mayhall CG. SHEA position paper: Medical Waste. *Infect Control Hosp Epidemiol*. 1992. 13:38–48.

Sehulster LM, Chinn RYW, Arduino MJ, Carpenter J, Donlan R, Ashford D, Besser R, Fields B, McNeil MM, Whitney C, Wong S, Juranek D, Cleveland J. Guidelines for Environmental Infection Control in Healthcare Facilities. Recommendations from CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Chicago IL. American Society for Healthcare Engineering/American Hospital Association. 2004.

Zaidi M, Wenzel RP. Disinfection, Sterilization, and Control of Hospital Waste *in* Principles and Practice of Infectious Diseases (5th Edition), Mandell GL, Bennett JE, Dolin R. (Eds). Philadelphia: Churchill Livingstone, 2000. Pgs. 2995–3005.

Zaidi, M. Waste Management. A Guide to Infection Control in the Hospital. An Official Publication of the International Society for Infectious Diseases (ISID) (4th Edition), Wenzel RP, Bearman G, Brewer T, and Butzler J-P. (Eds). Boston, 2008. 5:22–25.

CHAPTER 6

Hand Hygiene

Andrew J. Stewardson, MBBS, and Didier Pittet, MD, MS

Keywords
Hand hygiene, hand washing, hand antisepsis, hand disinfection, alcohol-based handrub, epidemiology, healthcare workers, patient safety.

Key Issues

- Hand hygiene is the cornerstone of infection prevention.
- Multimodal promotion can improve healthcare worker hand hygiene compliance.
- Enhanced compliance is associated with decreased cross-transmission and reduced infection rates.

Known Facts

- Appropriate hand hygiene is considered the leading measure to reduce the transmission of health care associated pathogens in healthcare settings. Its impact on infectious and resistant organisms' cross-transmission risk is recognized in hospitals, schools, and day care centers, as well as in community settings.
- Inappropriate hand hygiene practice has been identified as a significant contributor to numerous outbreaks.
- Several studies have shown the impact of improved hand hygiene on the risk of health care associated infection and multiresistant pathogen cross-transmission. To date, most studies have focused on methicillin resistant *Staphylococcus aureus*.
- Bacteria present on human skin can be considered as belonging to one of two groups: resident and transient flora. Transient flora colonizes the superficial layers of the skin. It has a short-term persistence on skin, but a high pathogenic potential. It is usually acquired by healthcare workers during direct contact with patients or contaminated environmental surfaces adjacent to the patient, and is responsible for most health care

associated infections and spread of antimicrobial resistance resulting from cross-transmission. Resident flora is attached to deeper skin layers and has a low pathogenic potential unless introduced into the body by invasive devices. It is also more difficult to remove mechanically. Hand hygiene decreases colonization with transient flora and can be achieved either through handwashing or hand antisepsis.

- *Hand hygiene* is a general term that includes the appropriate use of handwashing, antiseptic handwashing, and antiseptic handrubbing. *Handwashing* refers to the action of washing hands with plain (non-antimicrobial) soap and water. *Antiseptic handwashing* refers to washing hands with water and soap or other detergents containing an antiseptic agent. *Antiseptic handrubbing* refers to the application of an antiseptic handrub (usually an alcohol-based formulation) to the hands to reduce or inhibit the growth of microorganisms.
- *Hand antisepsis* refers to either antiseptic handwashing or antiseptic handrubbing. *Hand disinfection* is a similar concept, but may cause confusion because disinfection usually refers to environmental decontamination. *Surgical hand preparation* refers to the procedure recommended to clean hands performing surgery; it is, however, not discussed in this chapter.
- The WHO 'My Five Moments for Hand Hygiene' is based on a conceptual model of microbial transmission and can be used for teaching, monitoring and reporting hand hygiene compliance. It defines five *indications* for hand hygiene in healthcare (*see Table 6.1*). A period of time during which one or more of these indications for hand hygiene exists is called an *opportunity*. Hand hygiene compliance is calculated by dividing the number of hand hygiene actions performed when an opportunity exists by the total number of hand hygiene opportunities.
- Major risk factors for noncompliance are healthcare worker profession (physicians are usually less compliant than nurses), workload (compliance is inversely related to workload), indication (compliance is worse before patient contact than after), poor access to hand hygiene materials (sinks, dispensers), and the absence of multimodal hand hygiene promotion (*see page 25, first bullet*).

- Among all identified risk factors for noncompliance, time constraint is the most important. In other words, the higher the demand for hand hygiene, the lower the compliance. Thus, access to hand hygiene products at the point of care and the use of a fast-acting agent both facilitate improved compliance.
- The ideal technique for hand hygiene should be quick to perform at the point of care, reduce hand contamination to the lowest possible level, and be free from significant side-effects on the HCWs' skin.
- Alcohols are currently the preferred agent for routine hand hygiene. They have excellent activity and the most rapid bactericidal action of all antiseptics. Of importance from a workflow perspective, alcohols dry very rapidly, allowing for fast antisepsis at the point of care. In addition, alcohols are more convenient for hygienic handrub than aqueous solutions given their excellent spreading quality and rapid evaporation. Furthermore, there is no antibacterial resistance to alcohols. Importantly, however, visibly-soiled hands should be washed with soap and water.
- When evaluating hand hygiene products for use in the healthcare setting, important factors include their relative efficacy against pathogens, rapidity of action, acceptance and tolerance by HCWs, convenience of use, accessibility, and cost. With alcohol-based agents, the time required for drying may affect efficacy and user acceptance. Alcohol-based antiseptics intended for hand hygiene in healthcare are available in rinse, gel, and foam formulations. At equal concentrations, n-propanol is the most effective alcohol, and ethanol the least.
- Alcohol-based handrubs (whether isopropyl, ethyl, or n-propanol, in 60–90% vol/vol), when containing appropriate emollients such as glycerol (1 to 3%) or other skin-conditioning agents, are less irritant to healthcare workers' hands than soap and water. Soaps and detergents are damaging substances when applied to the skin on a regular basis by increasing skin pH, reducing lipid content, increasing transepidermal water loss, and even enhancing microbial shedding.

- Multimodal promotion strategies are the most effective means of improving hand hygiene compliance. The WHO multimodal hand hygiene strategy includes: 1) system change, including alcohol-based handrub at the point of care; 2) education and training; 3) observation and performance feedback; 4) reminders in the workplace; and 5) patient safety climate (an implementation guide and suite of tools are available at www.who.int/gpsc/5may/en/). The WHO Hand Hygiene Self-Assessment Framework is a self-administered questionnaire that can be used to provide a situation analysis of hand hygiene resources, promotion, and practices within healthcare facilities, and to develop an action plan for future interventions.
- The cost-effectiveness of hand hygiene promotion has been demonstrated in several studies.

Controversial Issues

- The central challenge for hand hygiene in healthcare involves translating recommendations into HCW behavior change. The most widely implemented and successful model is the multimodal promotion strategy recommended by WHO, which has been used and adapted to various healthcare systems, cultures and resources worldwide. However, the most influential components of multimodal intervention strategies for hand hygiene promotion remain to be determined.
- While multimodal promotion is known to be the most effective way to improve hand hygiene compliance, the key determinants of long-lasting improvement requires further investigation. In addition, there is a need for effective strategies to improve hand hygiene compliance amongst physicians, a group that is generally less sensitive to standard multimodal promotion.
- Direct observation using the WHO 'My Five Moments for Hand Hygiene' technique is currently considered the optimal method to monitor hand hygiene compliance. Advantages include provision of a meaningful denominator (e.g. when hand hygiene is indicated), capacity to stratify results (e.g. by profession or indication), and the behavior change

benefit of immediate performance feedback. Key limitations, however, are the relatively small proportion of total actions that are monitored, and the resource-intensive nature of this activity. Other options include monitoring product consumption (such as alcohol-based handrub), self-reporting, patient observers, and automated systems. These alternatives are likely to be the focus of intensive research given the increasing focus on hand hygiene compliance as a quality/performance indicator.

- Some encouraging data exist to support a role for patient participation in hand hygiene promotion. In its most active form, this involves inviting patients to remind healthcare workers to perform hand hygiene. But this strategy remains challenging to implement and should be introduced cautiously and only with the support of all stakeholders. A gradual change in culture should be expected. Generally more acceptable is education of patients and their visitors about when they themselves should perform hand hygiene. The impact of this latter strategy in terms of infection rate reduction remains, however, to be determined.
- Most antiseptics, including alcohols, have very poor or no activity against bacterial spores. Handwashing is preferred over hand rubbing when spore contact is likely because of the mechanical action involved. However, initial concern that widespread use of alcohol-based handrubs could result in increased transmission of *Clostridium difficile* has not been borne out in practice.
- Methods used to assess the antimicrobial efficacy of products differ among studies and countries, including whether or not the efficacy of the agent is to be tested against viral pathogens. The correlation between laboratory-based standards and effectiveness in clinical practice has been questioned. Further studies should be conducted at the bedside using standardized protocols to obtain more realistic views of microbial colonization and the risk of bacterial transfer and cross-transmission. Moreover, further evidence is required regarding the relative efficacy of foam formulations.

- The role of gloves in healthcare is in evolution, with recent evidence indicating that gloves can be associated both with lower hand hygiene compliance and reductions in cross-transmission under certain circumstances.

Suggested Practice

Guidelines for hand hygiene in healthcare settings have been developed by the CDC/HICPAC, SHEA, APIC, and IDSA in 2002 (available at www.cdc.gov/ncidod/hip/hhguide.htm), and WHO in 2009 (available at www.who.int/gpsc/5may/tools/9789241597906/en/). Each recommendation was classified in 4 categories. The guidelines include indications for hand hygiene (*see Table 6.1*), surgical hand preparation, selection of hand hygiene agents, healthcare worker skin care and education, strategies for motivational programs, administrative measures, and recommended outcome or process measurements.

Table 6.1 Indications for Hand Hygiene Actions

A. Wash hands with soap and water when hands are visibly dirty or visibly soiled with blood or other body fluids (**IB**) or after using the toilet (**II**).

B. If exposure to potential spore-forming pathogens is strongly suspected or proven, including outbreaks of *Clostridium difficile*, hand washing with soap and water is the preferred means (**IB**).

C. Use an alcohol-based handrub as the preferred means for routine hand antisepsis in all other clinical situations described below, if hands are not visibly soiled (**IA**). If alcohol-based handrub is not available, wash hands with soap and water (**IB**).

D. Perform hand hygiene:

1. **Before** touching a patient.
2. **Before** aseptic/clean procedure.
3. **After** body fluid exposure risk.
4. **After** touching a patient.
5. **After** touching patient surroundings (without touching the patient during the same care sequence).

Footnote to Table 6.1

The system for categorizing recommendations is adapted from the CDC/HICPAC system as follows:

Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

Category IB. Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale.

Category IC. Required for implementation, as mandated by federal and/or state regulation or standard.

Category II. Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

- Among indications for hand hygiene (*see Table 6.1*), it is worth noting that unless hands are visibly soiled, the use of an alcohol-based handrub agent is recommended for routine hand hygiene in all clinical situations (**IA**). Availability of an alcohol-based handrub at the point of care is recommended to improve compliance.
- Wearing of gloves should not be considered as an alternative to hand hygiene. Hand hygiene is required regardless of whether gloves are used or changed. Recommendations for glove use are: **1**) to wear gloves when contact with blood or other potentially infectious materials, mucous membranes, and non-intact skin can be reasonably anticipated; **2**) to remove gloves after caring for a patient; **3**) to not wear the same gloves for the care of more than one patient; **4**) to not wash gloves between patients; and **5**) to change gloves during patient care if moving from a contaminated body site to a clean body site.

Summary

Hand hygiene is the cornerstone of infection prevention. However, HCW compliance remains low unless subjected to successful promotion strategies. Improving hand hygiene practices constitutes one of the major challenges of infection control;

it is, however, associated with decreased cross-transmission and reduced infection rates and antimicrobial resistance transfer. Factors adversely affecting HCW compliance with recommended practices include poor access to sinks and hand hygiene materials, time required to perform conventional handwashing with soap and water, time constraint associated with a high intensity of patient care, and a high number of opportunities for hand hygiene per hour of care on a single patient in critical care.

Availability of an alcohol-based handrub at the point of care is recommended to improve compliance. Alcohol-based handrubbing is currently recommended as the primary tool for hand hygiene action and promotion because it reduces bacterial counts on hands more effectively than plain or antimicrobial soaps, can be made more accessible than sinks and other handwashing facilities, requires less time to use, and causes less skin irritation and dryness than washing hands with soap and water. Rubbing the hands together until the agent has dried is the essential part of the technique. Both easy access to hand hygiene facilities and the availability of skin care lotion appear to be necessary prerequisites for appropriate hand hygiene behavior. The promotion of alcohol-based handrubs at the point of care contributed significantly to an increase in compliance both in several clinical studies and in nationwide hand hygiene promotion campaigns. The availability of a handrub alone however, is insufficient to obtain sustained improvement in hand hygiene practices. Multimodal strategies are indicated and include: 1) system change, including alcohol-based handrub at the point of care; 2) education and training; 3) observation and performance feedback; 4) reminders in the workplace; and 5) patient safety climate. This approach involves a system change to make hand hygiene a priority, with alcohol-based hand rub as standard of care.

References

Pittet D, Mourouga P, Perneger TV, and Members of the Infection Control Program. Compliance with hand washing in a teaching hospital. *Ann Intern Med*. 1999. 130:126–130.

Pittet D, Boyce JM. Hand hygiene and patient care: Pursuing the Semmelweis legacy. *Lancet Infect Dis*. 2001. April:9–20.

Boyce JM, Pittet D. Guideline for hand hygiene in healthcare settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *MMWR*. 2002. 51[RR16]:1–44.

Pittet D, Hugonnet S, Harbarth S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *Lancet*. 2000. 356:1307–1312.

Sax H, Allegranzi B, Uckay I, Larson E, Boyce J, Pittet D. My five moments for hand hygiene: A user-centred design approach to understand, train, monitor and report hand hygiene. *J Hosp Infect*. 2007. 67:9–21.

World Health Organization. WHO Guidelines on Hand Hygiene in Healthcare. World Health Organization Press. Geneva. 2009.

Longtin Y, Sax H, Leape LL, Sheridan SE, Donaldson L, Pittet D. Patient participation: Current knowledge and applicability to patient safety. *Mayo Clin Proc*. 2010. 85:53–62.

Stewardson AJ, Allegranzi B, Perneger TV, Attar H, Pittet D. Testing the WHO Hand Hygiene Self-Assessment Framework for Usability and Reliability. *J Hosp Infect*. 2013. 83:30–35.

Allegranzi B, Gayet-Ageron A, Damani N, et al. Global implementation of WHO's multimodal strategy for improvement of hand hygiene: A quasi-experimental study. *Lancet Infect Dis*. 2013. 13:843–851.

CHAPTER 7

Isolation of Communicable Diseases

Bart Gordts, MD, MBA

Key Issue

The combination of standard precautions and isolation procedures represents an effective strategy in the fight against health care associated transmission of infectious agents. Current CDC-HICPAC proposed guidelines[1] describing the updated methods and indications for these precautions are straightforward, but effective barriers at the bedside are sometimes still lacking today. Key factors in achieving effective interruption of health care associated transmission in all hospitals are the availability of the necessary financial and logistic resources as well as the increase in compliance of healthcare professionals (HCPs) with the guidelines. Preventing transmission of infections by means of isolation procedures in a scientific and cost-effective manner represents a challenge to every healthcare institution. In 2007, the indications and methods for isolation as described in 1996[2] were updated taking into account the changing patterns in healthcare delivery, emerging pathogens and most importantly, additions to the recommendations for standard precautions. Moreover, the increasing prevalence of multi-drug resistant health care associated pathogens necessitated specific strategic approaches,[3] which cannot be considered separately from other isolation policies.

Known Facts

Isolation and barrier precautions aim to reduce or eliminate direct or indirect patient to patient transmission of health care associated infections that can occur through 3 mechanisms:

1. via contact, which involves skin (or mucosa) to skin contact and the direct physical transfer of microorganisms from one patient to another or via hands of a HCP. Transmission can be direct (skin to skin) or indirect (via a contaminated surface).

2. via respiratory droplets larger than 5 μm that are not suspended for long in the air and usually travel a short distance of less than 1 meter.
3. airborne transmission: particles less than 5 μm that remain suspended in the air longer and therefore can travel long distances and infect susceptible hosts several meters away from the source.

Besides patient to patient transmission, health care associated infections can be endogenous (patient is the source of pathogen causing his infection) or acquired from environmental sources like contaminated water supplies, medical equipment, IV solutions, etc. These infections are not prevented by isolation precautions.

The most cost-effective, simple and feasible way to prevent transmission of pathogens consists in a two-tier approach as described in the CDC-HICPAC guidelines[1]:

1. Standard precautions must be taken while caring for all patients. They represent a basic list of hygiene precautions designed to reduce the risk of transmission of bloodborne pathogens and those from contact with moist body substances.
2. In addition to standard precautions, extra barrier or isolation precautions are necessary during the care of patients with highly transmissible or epidemiologically important pathogens. These practices are designed to interrupt airborne-, droplet- and direct or indirect contact transmission.

Isolation and barrier precautions have also proven successful in limiting the epidemic spread of multiply resistant gram negative bacilli, methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococci[4] (VRE). Isolation precautions can also be assumed effective in the fight against health care associated epidemics caused by vancomycin intermediate or resistant *Staphylococcus aureus*[5] (VISA, VRSA), extended spectrum beta-lactamase (ESBL) producing enterobacteriaceae (like *Enterobacter* spp.), quinolone- or carbapenem resistant *Pseudomonas aeruginosa* and enterobacteriaceae, and multiresistant *Stenotrophomonas maltophilia* and *Acinetobacter spp.*[6]

Suggested Practice

All patients receiving care in hospitals or doctor offices, irrespective of their diagnoses, must be treated in such a manner as to minimize the risk of transmission of any kind of microorganisms from patient to HCP, from HCP to patient, and from patient to HCP to patient.

Standard Precautions

Standard precautions apply whenever there is contact with ruptured skin or mucous membranes, blood, all body fluids, secretions or excretions except sweat. They are designed to reduce the risk of transmission from both recognized and unrecognized sources of infection. Among these 'standard' precautions, hand hygiene among HCPs constitutes the single most important prevention of nosocomially transmitted infections. Standard Precautions combine the major features of universal precautions[7] and body substance isolation[8] and are based on the principle that all blood, body fluids, secretions, excretions except sweat, nonintact skin, and mucous membranes may contain transmissible infectious agents. HCP's should wash hands when soiled and disinfect hands when possibly contaminated, irrespective of whether gloves were worn. Hand hygiene should take place immediately after gloves are removed, before and between patient contacts, and any time one handles blood, body fluids, secretions or excretions, or potentially contaminated items or equipment.

Gloves should be worn if touching blood, body fluids, secretions, excretions, mucous membranes, broken skin or contaminated objects. Gloves must be changed between patients and before touching clean sites on the same patient.

A mask and eye protection as well as a gown should be worn to protect mucous membranes, skin and clothing during procedures that are likely to result in splashing of blood, body fluids, secretions, or excretions.

Patients, HCPs or visitors must not be exposed to contaminated materials or equipment. Reusable equipment should be cleaned and sterilized before reuse. Soiled linen should be transported in a (double) bag.

HCPs must protect themselves against bloodborne contamination by carefully handling sharp instruments like needles. Needles should not be recapped. All used sharps instruments must be placed in designated puncture-resistant containers.

No special precautions are needed for eating utensils and plates since hot water and detergents in hospitals are sufficient to decontaminate these articles. Rooms, cubicles, and bedside equipment should be appropriately cleaned.

In addition to these standard precautions, 'transmission-based precautions' must be used for patients known or suspected to be infected with highly transmissible or epidemiologically important pathogens which can spread by airborne or droplet transmission or by contact with dry skin or contaminated surfaces.

Examples of conditions necessitating isolation precautions and a summary of measures to be taken are shown in *Table 7.1* and *Table 7.2*.

Table 7.1 Indications for Standard and Isolation Precautions

Precaution category	*Condition*
Standard	All patients
Contact	Hemorrhagic fever such as Ebola, Lassa, and Marburg, (risk for) colonization or infection with multiresistant bacteria, *C. difficile* infection, acute diarrhea in incontinent patient, RSV infection, croup or bronchiolitis in young infants, skin infections like impetigo, major abcess, cellulitis or decubiti, staphylococcal furonculosis, pediculosis, scabies or cutaneous infections with *C. diphtheriae*, Herpes simplex virus, zoster.
Droplet	Meningitis, (suspected) invasive infection with *H. influenzae* type B or *N. meningitidis*, diphtheria, *M. pneumoniae*, pertussis, influenza, adenovirus, mumps, Parvovirus B19, rubella, streptococcal pharyngitis, pneumonia, scarlet fever in young children.
Airborne	Pulmonary or laryngeal (suspected) tuberculosis, measles, varicella; disseminated zoster.

Contact Precautions

Contact precautions must be taken when transmission can occur by skin to skin contact and the direct physical transfer of microorganisms as shown in *Table 7.1*.

Provide a private room, if possible. When not available, cohort patients infected with the same microorganism but with no other infection. Nonsterile gloves should be worn before entering the room. Apply hand washing and hand antisepsis as

in standard precautions. Be sure not to touch potentially contaminated surfaces or equipment. Wear a clean, nonsterile gown when entering and remove it before leaving the room. Limit patient transport to the unavoidable situation and maintain isolation precautions during transport. When possible, limit the use of patient-care equipment to a single patient.

Droplet Precautions

Apply droplet precautions for patients infected with pathogens that spread by respiratory droplets larger than 5 μm produced during coughing, sneezing, talking, or during invasive procedures such as bronchoscopy (*see Conditions in Table 7.1)*.

Private room as in contact precautions. If unachievable, maintain spatial separation of at least 1 m between the infected patient and other patients and visitors. Special ventilation is unnecessary and the door may remain open. Masks are worn if within less than 1 meter of the patient. Limit patient transport to the unavoidable and maintain isolation precautions during transport. When possible, limit the use of patient-care equipment to a single patient.

Airborne Precautions

Apply airborne precautions for patients infected with pathogens spread by respiratory droplets smaller than 5 μm produced during coughing, sneezing, talking, or during invasive procedures such as bronchoscopy (*see Conditions in Table 7.1)*.

As for the other infections requiring airborne precautions, patients suspected or known to be infected by M. tuberculosis should be nursed in a private room where the air flows in the direction from the hall into the room (negative air pressure), with 6 (minimum) to 12 (optimal) changes per hour and appropriate discharge of air outdoors. Negative air pressure can be created by placing a fan in the window and exhausting the air to the outside. High-efficiency filtration is necessary if the air is circulated in other areas of the hospital. Keep the door closed. Cohorting can be done in rare circumstances for patients infected with strains presenting with an identical antimicrobial susceptibility.

Respiratory protection should be worn both by HCPs and visitors when entering the room. The technical requirements for respiratory protection devices remain controversial: CDC guidelines[9] advocate masks with face-seal leakage of ≤10% and filter 1μm particles for > 95% efficiency (N95). However, a

molded surgical mask may be as effective in dealing with health care associated outbreaks and better complied with because of cost. Avoid transporting patients through other areas of the facility. If transport is unavoidable, the patient should wear a surgical mask that covers mouth and nose.

It is mandatory to maintain isolation until the diagnosis of tuberculosis is ruled out or, when confirmed, the patient is on effective therapy, improving clinically and has three consecutive negative sputum smears excluding the presence of acid fast bacilli. Patients infected with multidrug resistant M. tuberculosis should stay in airborne isolation throughout the hospitalization.

Table 7.2 Summary of Transmission-based Precautions

Precaution	*Contact*	*Droplet*	*Airborne*
Patient room	Private	Private	Private with specific ventilation requirements
Gloves	Before entering room	As in standard	
Hand hygiene	——— As in standard, with hand antisepsis ———		
Gown	If direct contact with patient or environment	——— As in standard ———	
Masks	Standard	Within 1 meter of patient	Before entering room special requirements
Other	——— Limit patient transport ———		

Protective Environment

A set of prevention measures termed 'Protective Environment' has been described in the CDC-HICPAC guidelines comprising engineering and design interventions that decrease the risk of exposure to environmental fungi for severely immunocompromised allogeneic hematopoietic stem cell transplant patients during their highest risk phase.[10] Specific air quality requirements include HEPA filtration of incoming air, directed room air flow, positive room air pressure, well-sealed rooms, ventilation to provide >12 air changes per hour, strategies to minimize dust, routinely cleaning crevices and sprinkler heads, and prohibiting dried and fresh

flowers and potted plants in the rooms. Protective environment does not include the use of barrier precautions beyond those indicated for standard and transmission-based precautions.

Implementation of Isolation Precautions

Hospitals are encouraged to review the recommendations and to modify them according to what is feasible and achievable. The success of transmission prevention in each institution relies on three keystones:

1. Availability to all HCPs an unambiguous written document describing the indications and procedures for isolation;
2. Successful implementation of the procedures through clear objectives and education off all HCPs;
3. Monitoring of the compliance with isolation procedures in a continuous improvement program.

Since clear indications and advised practices for isolation procedures are available to date, the further success of transmission prevention further relies upon:

- Accurate and early identification of patients at risk requiring isolation by:
  - availability of unambiguous written criteria for starting and discontinuing isolation;
  - initiation of isolation procedure as soon as the infectious disease is suspected;
  - active surveillance of risk factors among patients upon admission to the hospital or ward;
  - early laboratory diagnosis.
- Effective discharge planning for patients in isolation to be transferred to other healthcare facilities and effective admission planning for patients at risk of carrying infectious agents from other hospitals or nursing homes.
- Increased compliance of patients with the precautions through supportive efforts to facilitate adherence and through education about the mechanism of transmission and the reason for being placed in isolation.
- Instruction and information of visitors about infection prevention measures.
- Clear endorsement by hospital management and department heads.

References

[1]Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Available at: http://www.cdc.gov/niosh/docket/archive/pdfs/NIOSH-219/0219-010107-siegel.pdf

[2]Garner JS. Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol*. 1996. 17(1):53–80.(s).

[3]Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. Management of Multidrug-Resistant Organisms in Healthcare Settings. 2006. Available at: http://www.cdc.gov/hicpac/pdf/MDRO/MDROGuideline2006.pdf

[4]Hospital Infection Control Practices Advisory Committee. Recommendations for Preventing the Spread of Vancomycin Resistance. *Infect Control Hosp Epidemiol*. 1995. 16:105 13.

[5]Edmond MB, Wenzel RP, Pasculle AW. Vancomycin-resistant *Staphylococcus aureus*: Perspectives on Measures Needed for Control. *Ann Intern Med*. 1996. 124:329–34.

[6]Flaherty JP, Weinstein RA. Nosocomial Infection Caused by Antibiotic-resistant Organisms in the Intensive Care Unit. *Infect Control Hosp Epidemiol*. 1996. 17:236–248.

[7]CDC. Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. *MMWR*. 1988. 37(24):377–82, 87–8.

[8]Lynch P, Cummings MJ, Roberts PL, Herriott MJ, Yates B, Stamm WE. Implementing and evaluating a system of generic infection precautions: Body substance isolation. *Am J Infect Control*. 1990. 18(1):1–12.

[9]CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR Recomm Rep*. 2005. 54(17):1–141.

[10]CDC. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. Recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. *MMWR*. 2000. 49(RR-10):1–125.

CHAPTER 8

Patient Areas, Disinfection and Environmental Cleaning

Constance Wendt, MD

Key Issue

- The patient environment harbors a number of potential reservoirs for pathogens.

Known Facts

- Patients need a clean environment for their uncomplicated recovery.

Controversial Issues

- The extent to which environmental reservoirs contribute to health care associated infections remains unclear.
- The extent to which germicidal solutions should be used on environmental surfaces as opposed to non-germicidal cleaning methods remains unclear.

Suggested Practice:

- Patient areas should be cleaned periodically and after contamination.
- Patient areas should be protected from heavy dust.

Since the writings of Florence Nightingale in the 19th century the need for a clean patient care environment is unquestioned. However, uncertainty remains about the extent to which environmental reservoirs contribute to health care associated infections.

Environment reservoirs have been linked with outbreaks of health care associated infections, e. g. air filters, insulation materials, or surfaces. Other objects and surfaces known to harbor bacteria, such as flowers, toilets, and medical waste may also pose a risk for health care associated infections.

Housekeeping Surfaces

Housekeeping surfaces (floors, walls tabletops) have been associated with outbreaks of vancomycin-resistant Enterococci and methicillin resistant *Staphylococcus aureus* (MRSA) and more recently with *Clostridium difficile* and Noroviruses. The increasing incidence of resistant organisms has prompted further discussion on the need for routine surface disinfection. However, these special problems do not justify routine disinfection of all hospital floors and furnishings. It has been demonstrated that the rate of health care associated infections are not significantly different between units cleaned with disinfectants and those units cleaned with detergents.

Routine cleaning of housekeeping surfaces with detergents is sufficient in most circumstances. In case of outbreaks, especially when due to resistant microorganisms known to be harbored in the environment, additional cleaning with a disinfection solution may be indicated. A common reason given for environmental contamination with microorganisms may be the lack of adherence to facility procedures for cleaning and disinfection. Monitoring for adherence to recommended environmental cleaning practices is an important component for success in controlling cross-transmission by fomites. However, surface disinfection is not a substitute for standard infection control measures.

Spills of blood and body substances should be promptly cleaned and decontaminated.

Carpeting and Cloth Furnishings

Carpeting and cloth furnishings may be a source of dust containing microorganisms. These types of surfaces should be avoided were spills are likely, in patient rooms and in areas housing immunosuppressed patients. Routine cleaning of carpeting and cloth furnishings should be performed with well-maintained equipment designed to minimize dust dispersion. Wet cleaning should be performed using a method that minimizes the production of aerosols and leaves little or no residues. Carpeting that remains wet for more than 72 hours should be replaced.

Hospital Toilets

Cultures of hospital toilets have demonstrated that frequency and level of contamination is usually low, making the toilets an uncommon source of hospital infections. However, on units for mentally impaired adults, young children, or neurologically impaired patients heavy soiling with feces may occur resulting in cross-infections between patients.

Hospital toilets should be cleaned with a disinfecting solution. The bowl should be cleaned with a scouring powder and a brush, but disinfectants should not be poured in the bowl.

Flowers and Plants

The water containing cut flowers may yield high numbers of microorganisms including *Acinetobacter*, *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas* spp., *Serratia marcescens*, and *Flavobacterium*. Although it has not been demonstrated that microorganisms from cut flowers or potted plants were linked with health care associated infections, cut flowers and potted plants should be avoided in rooms of immunocompromised and intensive care unit patients. On other units flowers should be handled by support staff with no patient contact or gloves should be worn for flower handling. Antibacterial agents, e. g. 0.01%–0.02% chlorhexidine or 10ml of 1% hypochlorite can be added to the vase water.

Contaminated Laundry

Patients should have clean, freshly laundered bed linens. As it has been demonstrated that the handling of used bed linen may increase the concentration of airborne microorganisms, the disinfection of blankets has been suggested. However, there are no data to justify the additional cost and workload needed to disinfect blankets.

Soiled linen should be handled as little as possible and with minimum agitation. Soiled linens should not be sorted or prerinsed in patient care areas. Linens soiled with blood or body fluids should be deposited and transported in bags that prevent leakage.

Construction Projects

Construction projects have been linked to health care associated fungal infections. As a result, careful control measures should be implemented during hospital construction projects. These measures should include erection of physical barriers and temporary shut down of ventilation systems. If possible, air flow of ventilation systems should re-routed to protect sensitive areas. Traffic flow patterns for construction personal should be defined and separated from those of patients and health care workers.

Infective Solid Waste

Infective solid waste may come from patients under isolation precautions, laboratories and from the pathology. Sharp items and blood and blood products should also be considered infective.

Personnel handling infectious waste should be informed of the potential health and safety hazard. If necessary, the waste should be transported in sealed impervious containers and stored in areas accessible only to personnel involved in the disposal process.

Other Reservoirs

Other possible reservoirs of health care associated pathogens are summarized in *Table 8.1*.

Table 8.1 Possible Reservoirs of Infectious Agents in the Environment and Modes of Control

Reservoir	Associated Pathogen	Control
Patient Rooms		
• Air Filters	*Aspergillus*	Replace soiled filters periodically
• False Ceilings	*Rhizopus*	Barrier protection during reconstruction
• Fireproof Material	*Aspergillus*	Add fungicide to moist material
• Air-Fluidized Beds	-	Follow manufacturer's recommendation
• Mattresses	*Pseudomonas, Acinetobacter*	Use intact plastic cover; disinfect between patients

Table 8.1 Possible Reservoirs of Infectious Agents in the Environment and Modes of Control (continued)

Reservoir	Associated Pathogen	Control
Bathroom		
• Faucet Aerators	*Pseudomonas*	Clean regularly
• Sinks	*Pseudomonas*	Use separate sinks for handwashing and disposal of contaminated fluids
• Tub Immersion	*Pseudomonas*	Add germicide to water, drain and disinfect after each use
• Urine-Measuring Device	*Serratia*	Disinfect between patients, good handwashing
Routinely Used Medical Equipment		
• ECG Electrodes	*S. aureus*, Gram-negative rods	Disinfect after use or use disposable leads
• Stethoscopes	Staphylococci	Prudent to clean periodically with alcohol
• Electronic thermometers	*C. difficile*	Probe cover, disinfect each day and when visibly contaminated
• Thermometers (glass)	*Salmonella*	Disinfect between use
• Plaster	*Pseudomonas*, *Bacillus*, Clostridia, *Cunninghamella*	Use judiciously in immunocompromised patients or over nonintact skin
• Elasticized Bandages	*Zygomycetes*	Avoid in immunocompromised patients or over nonintact skin
Other Possible Sources		
• Chutes	*Pseudomonas*, Staphylococci	Proper design and placement
• Contaminated Germicides	*Pseudomonas*	Avoid extrinsic contamination and seek manufacturer's microbicidal efficiency verification of claims
• Ice Baths	*Staphylococcus*, *Ewingella*	Avoid direct contact with ice to cool IV solutions/syringes; use closed system for thermodilution

Table 8.1 Possible Reservoirs of Infectious Agents in the Environment and Modes of Control (continued)

Reservoir	Associated Pathogen	Control
Other Possible Sources		
• Water Baths	*Pseudomonas, Acinetobacter*	Add germicide to water bath or use plastic overwrap
• Pigeon Droppings	*Aspergillus*	Filter all hospital air; maintain filter efficiency
• Pets	*Salmonella*	Prudent to avoid in hospital setting (except seeing-eye dogs)

Adapted from Weber, DJ, and Rutala WA: Environmental issues and nosocomial infection. *in* Wenzel RP (Ed): Prevention and control of nosocomial infections; 3rd edition. Baltimore, MD: Williams and Wilkins; 1997. 491–514.

References

Weber, DJ, Rutala WA. Environmental issues and hospital acquired infections *in* Prevention and Control of Hospital Acquired Infection (3rd Edition), Wenzel, RP (Ed). Baltimore: Williams and Wilkins, 1997. Pgs. 491–514.

Streifel AJ. *in* Hospital Epidemiology and Infection Control (4th Edition), Mayhall, CG (Ed). Baltimore: Williams and Wilkins, 2012. Pgs. 1051–1058.

Centers for Disease Control and Prevention: Guidelines for environmental infection control in health care facilities: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR*. 2003. 52 (No. RR-10):1–42.

Siegel, JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee: Management of Multidrug-Resistant Organisms In Healthcare Settings, 2006. Available at: http://www.cdc.gov/hicpac/pdf/MDRO/MDROGuideline2006.pdf (Accessed 14 October 2013).

Siegel, JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings, June 2007. Available at: http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html (Accessed 14 October 2013).

CHAPTER 9

Reuse of Disposable Devices

Samuel R. Ponce de León, MD, MSc

It seems to me that reusing disposable devices has an element of poetic justice ingrained, if one can become poetic about economics.
—V.W. Greene

Key Issue

Reutilization of disposable devices is a common practice in most hospitals but there are no well-founded standard guidelines to assure the quality and the safety of this practice.

Known Facts

- Most disposable devices can be reused.
- Economic benefits can be obtained by reusing disposables.
- Sterilization is a well known and common practice in hospitals.
- Infections and malfunction are higher risks if the device is damaged in the re-sterilization process.
- There are diverse studies showing the security of reprocessing a variety of cardiac and urinary catheters, balloon-tipped catheters, guide-wires, implants, needles, surgical instruments, hemodialysers, laparoscopic instruments and pacemakers.
- There is evidence against the reuse of specific items with particular methods, such as Transducer Domes and Esophageal Stethoscopes with ethylene oxide sterilization.
- Risks associated with the reuse of disposable catheters include: infection, pyrogenic reaction, toxicity, particulate contamination, breakage-catheter integrity, catheter biocompatibility, risk for personnel, and risk for the environment.
- Patients should know that a reused item is is going to be utilized.

Controversial Issues

- The selection of the patients to utilize a re-sterilized-device implies an ethical issue that should be resolved in every facility.
- There is a relationship between complexity of disposables and difficulties of sterilization.
  - A clear limit should be established regarding the number of times an item can be reused.
  - The burden of complications due to reutilization is not known.
  - FDA consider those hospitals reusing disposable devices as manufacturers. The device should comply just as though it was a new one.
- Reuse of disposables increases the risk of exposure of HCW to body fluids and chemicals used for sterilization.
- It is impossible for every single facility to evaluate each item to be reused. In most cases decisions will be made based in published experience.
- Specialized sterilization companies maybe an option.
- Ethical, regulatory and legal implications should be considered.
- The reuse of disposable masks (N95 respirators) during epidemics or pandemics should be clearly regulated; the American Institute of Medicine does not recommend its reuse, but in the case of a pandemic there will a short supply.
- There are many questions and few answers (to many disposables and very few studies), and funding for this research is scarce.

Suggested Practice

Reuse of disposables should not be an ad hoc practice or treated casually. A facility committed to the reuse of single-use devices should have an institution-specific policy and work with clear guidelines to ensure the safety of patients.

The American Society for Hospital Service Personnel has published the following guidelines:

1. Review the package labeling and the manufacturer's guidelines for use and reprocessing the device.

2. If the manufacturer has not determined reprocessing parameters, obtain information about the material properties (steel, rubber, latex, PVC, etc). Ask the manufacturers if the product can be reprocessed; and if so, ask for recommendations.
3. Establish a list of form and function criteria which the reprocessed device will be expected to meet.
   These include:
   A.– Physical appearance (color, shape, size, etc.), and
   B.– Function (moving parts, tensile strength, flexibility, etc.).
4. Determine if you have the capability to demonstrate that the device can be adequately cleaned according to the material properties and cleaning methods available.
5. Determine if you have the capability to demonstrate that the device can be adequately sterilized according to material properties and sterilizing methods available.
6. Determine if reprocessing of this device is cost justified.
7. For each device, establish a testing protocol that identifies:
   - The quantity of items which must be tested to get an adequate study sample.
   - The number of times the device can be reprocessed and still meet the form and function criteria.
   - Employee safety considerations.
   - The procedures, chemicals, and equipment to be used in reprocessing.
   - Process controls, quality assurance monitoring, and documentation.
   - Testing of the reprocessed item in simulated use situations
   - The necessity of destructive auditing to identify unacceptable changes to the material properties or the presence of residual toxicity.
   - Documentation of testing results.
   - A method for labeling the reprocessed device and marking for successive reprocessing episodes.
8. Review testing protocols/results with appropriate review groups (administration, infections-control, ethics committee) and the manufacturer.

9. Determine the need for policies for pricing, informed patient consent, and documentation of the use of reprocessed devices.
10. Periodically review the use and methods.

Other specific recommendations are:

1. Have a procedure to ensure the destruction of pyrogens.
2. Start the cleaning and sterilization process as soon as possible.
3. For angioplasty catheters it is essential to inspect the balloon inflated and deflated before using it.

References

American Society of Anesthesiologists Committee on occupational health of operating room personnel. http://sprojects.mmi.mcgill.ca/hearth/cath-005.htlm.

National Academy of Sciences. Institute of Medicine. News April 27, 2006. (www.nationalacademies.org).

Green WW. Reuse of Disposable Medical Devices: Historical and Current Aspects. *Infect Control*. 1986. 7:508–513.

Crow S. The Slings and Arrows of Outrageous Fortune. *Infect Control*. 1986. 7:561–563.

Canadian Hospital Association. The Reuse of Single-Use Medical Devices. October 3, 2003.

Rutala WA. Disinfection, Sterilization, and Waste Disposal *in* Prevention and Control of Nosocomial Infections (3rd Edition), Wenzel RP (Ed). Baltimore: Williams and Wilkins, 1997. Pgs. 491–514.

McGregor M. The Reuse of Cardiac Pacemakers. *Can J Cardiol* 1992; 8:697–701.

Collier R. The ethics of reusing single-use devices. *CMAJ*. 2011. 183:1245.

Centers for Disease Control and Prevention. Reuse of single use medical devices. Accessed from: http://www.cdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf

CHAPTER 10

DISINFECTION

Summer Donovan, DO and
Gonzalo M.L. Bearman, MD, MPH

Key Issue

Proper sterilization and/or disinfection of medical devices, surgical devices, and contaminated surfaces is crucial to the prevention of pathogen transmission. The level of sterilization or disinfection depends on the planned use of the device.

Known Facts

- ***Definitions:***

  Cleaning is the removal of visible foreign material on objects or surfaces, and is normally performed manually or mechanically.

  Disinfection is the thermal or chemical destruction of pathogenic and other types of microorganisms. Disinfection does not kill all microbial forms, such as bacterial spores.

  Sterilization destroys or eliminates all microbial forms, including bacterial spores.
- Instruments that enter into normally sterile tissue or the bloodstream require sterilization. Medical devices that contact mucous membranes, such as flexible endoscopes and endotracheal tubes, normally require disinfection.
- About 51 million inpatient surgical procedures are performed each year in the United States.
- About 53 million ambulatory procedures are carried out each year in the United States.

Suggested Practice

EH Spaulding Approach to Disinfection and Sterilization

In 1968, Spaulding formulated an approach to disinfection of medical devices that is still used today. He classified items as critical, semicritical, or noncritical based on their risk of transmitting infection.

- Critical items confer a high risk of infection if contaminated with organisms.
  - Examples: surgical instruments, urinary catheters, biopsy forceps.
  - The level of cleaning required is sterilization.
- Semicritical items come into contact with mucous membranes or intact skin.
  - Examples: endoscopes, laryngoscope blades, vaginal speculum.
  - This category requires at least high-level disinfection.
- Noncritical items come into contact with intact skin, but not mucous membranes.
  - Examples: examination table top, baby weight scales, blood-pressure cuffs.
  - Low-level disinfection should be used to prevent secondary transmission of pathogens to patients.

Methods for Disinfection and Sterilization

- Sterilization destroys all microorganisms, including bacterial spores. Methods for sterilization include:
  - High temperature: steam and dry heat.
  - Low temperature: ethylene oxide (ETO) gas and hydrogen peroxide.
  - Liquid immersion: chemical sterilants.
- High-level disinfection kills all organisms except for high numbers of bacterial spores. Methods include:
  - Heat automated: pasteurization.
  - Liquid immersion: chemical sterilants or high-level disinfectants.
- Intermediate-level disinfection kills Mycobacteria, most viruses, and bacteria. This method does not kill bacterial spores.
  - Liquid contact: EPA-registered hospital disinfectants with tuberculocidal activity (e.g. chlorine-based products and phenolics).

- Low-level disinfection kills some viruses and bacteria. This method does not kill bacterial spores.
  - Liquid contact: EPA-registered hospital disinfectants with no tuberculocidal activity (e.g. chlorine-based products, phenolics, quaternary ammonium compounds, or 70%–90% alcohol).

Selection and Use of Method

The level of sterilization or disinfection depends upon the desired microbicidal activity of the method (s*ee Table 10.1*).

Recommended Procedures for Disinfection of Medical Devices

- Prior to disinfection or sterilization:
  - Clean all medical devices with water and detergent.
  - Ensure that the devise is free of any irregularities that could impair disinfection or sterilization (e.g. cracks in the surface). Discard items that cannot be cleaned properly or no longer function properly.
- Sterilize all critical items.
- Employ high-level disinfection for all semicritical items.
- Use low-level disinfection for all noncritical items.

Recommended Procedures for Disinfection of Environmental Surfaces

- Clean any surface in a patient care area when visibly soiled.
- Clean floors, tabletops, and other surfaces regularly (daily or three times per week), when spills occur, and when the surface is visibly soiled.
- Replace disinfectant solutions regularly (e.g. mopping solution every three patient rooms, and/or every hour).
- Use a high-level disinfectant for disinfection of critical surfaces.
- Use a hospital disinfectant for noncritical surfaces.
- If disinfectants are used to clean infant bassinets in between patients, the surface must be thoroughly rinsed and dried prior to reuse.

Table 10.1 Sterilization and Disinfection—Spectrum of Activity Against Pathogens.

Method	Example(s) of Method	Spectrum of Activity Against Pathogens				
		Bacterial Spores	Mycobacteria	Vegetative Bacteria	Fungi	Viruses
Sterilization						
High Temperature	Steam	+	+	+	+	+
Low Temperature	ETO gas, hydrogen peroxide, peracetic acid	+	+	+	+	+
Liquid Immersion		+	+	+	+	+
High-level Disinfection						
Heat Automated		–	+	+	+	+
Liquid Immersion	Glutaraldehyde, phenolics, hydrogen peroxide, peracetic acid	–	+	+	+	+
Intermediate-level Disinfection						
Liquid Contact	Chlorine compounds, phenolics	–	+	+	±	±
Low-level Disinfection						
Liquid Contact	Chlorine compounds, phenolics, quaternary ammonium compound, 70–90% alcohol	–	–	+	±	±

Modified from Rutala WA and Weber DJ. Disinfection and Sterilization in Health Care Facilities: What Clinicians Need to Know. Clinical Infectious Diseases 2004; 39:702–9

- In the case of a blood spill, use protective gloves prior to discarding any sharps and cleaning visible blood with absorbent material. Following cleaning, disinfect the area with an EPA-registered agent, specifically a germicide that is labeled for use with human immunodeficiency virus (HIV) or hepatitis B virus (HBV), or freshly diluted sodium hypochlorite solution.
- Several potential strategies exist for monitoring compliance and assessing environmental hygiene.
  - Adenosine triphosphate (ATP) bioluminescence is a fast and sensitive way to monitor effectiveness of cleaning and/or to implement a modified cleaning regimen. Less than 500 relative light units (RLU) suggest that a surface is clean. Some studies advocate that a more stringent cutoff of 250 RLU should be used.
  - Fluorescent markers (UV light) are a useful means of assessing and providing feedback about the frequency that high-touch surfaces are wiped by housekeeping. Complete or partial removal of fluorescent markers during terminal cleaning is correlated with less surface contamination.
- Hard surface disinfection techniques include, but are not limited to:
  - Copper and copper alloy cladding, silver, and triclosan products incorporated into hard surfaces. Copper technology has potent antimicrobial activity and has shown promise in the reduction of health care associated infections. Silver is known to have intrinsic antimicrobial activity. No evidence of benefit from silver-based products has yet been published. Triclosan has limited spectrum of antimicrobial activity and induces resistance over the long term, making this product of limited use in the clinical setting.
  - Quaternary ammonium salt surfactant coating. This may be another promising technology, but its utility has yet to be proven.
- Several approaches to whole-room disinfection exist.
  - UV light reduces bioburden of a wide spectrum of organisms, including C. difficile spores. An issue with this approach is that it only provides "line-of-site" killing and does not penetrate fabrics well.

– Hydrogen peroxide vapor achieves rapid bactericidal activity via the production of oxygen free radicals and is extremely effective when used following bleach disinfection. This approach has been shown to be less effective at reducing MRSA infection rates, but may be more effective overall than UV light in eliminating aerobic bacteria from surfaces.
– Titanium dioxide spray can be used on hard surfaces, soft surfaces, and fabrics to provide a long-lasting biocidal coating.

Special Circumstances

- Creutzfeldt-Jakob disease (CJD) is a neurodegenerative disorder caused by transmissible prions. It is incurable, universally fatal, and is resistant to most conventional disinfection and sterilization methods. Therefore, it is necessary to have in place special procedures for decontaminating items that possess a high risk of transmitting the disease. These include critical items and semicritical items contaminated with brain, spinal cord or eye tissue from patients known or suspected to have infection with CJD. The current recommended procedure is cleaning of the device and sterilization using a combination of sodium hydroxide and autoclaving.
  – Immerse the device in 1N NaOH for 1 hour, remove and rinse with water, then transfer to an open pan for autoclaving (for 18 minutes at 134ºC in a prevacuum sterilizer or for 1 hour at 132ºC in a gravity displacement sterilizer).
- In units with high rates of *Clostridium difficile* infection, use 5.25%–6.15% sodium hypochlorite solution for routine environmental disinfection.

Controversial Issues

- It is unclear whether certain critical items (e.g. laparoscopes and arthroscopes) require sterilization or high-level disinfection. Heat stable scopes should be steam sterilized. However, for items that cannot tolerate steam, sterilization with ETO can be too time-consuming to be practical. There is no good evidence that sterilizing all scopes improves patient outcome.

- Surfaces can become contaminated with organisms, leading to transmission between patients, either directly or via an intermediate health care worker. However, routine disinfection of surfaces is controversial because they are considered noncritical items (they touch only intact skin), and therefore carry a very low risk of infection. Although data show that the use of disinfectants lowers the microbial load on surfaces, evidence that this practice reduces rates of health care associated infections is lacking.
- Reuse of single use medical devices continues to be an evolving area. Although it may be safe to reuse certain single use items, concern remains about the possible risk of infection with such practices. Currently, the Food and Drug Administration (FDA), issue regulations for proper handling of these items.

Summary

Medical and surgical devices and environmental surfaces can be categorized according to their ability to transmit infection into critical, semicritical, and noncritical items. Use of this categorization scheme helps determine the level of sterilization or disinfection needed. In order to make an informed decision, it is important to understand the pros and cons of each method. Patient safety, cost, and effectiveness should all be taken into account. Each institution should have protocols for cleaning, sterilization and disinfection that are devised in conjunction with the infection control practitioner, medical staff, nursing, and housekeeping staff.

References

Cullen KA, Hall MJ, Golosinskiy A, Division of Healthcare Statistics. Ambulatory Surgery in the United States, 2006. *National Health Statistics Reports*. 2009. 11.

Rutala WA, Weber DJ, and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008. http://www.cdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf (Accessed 7 October 2013).

Rutala WA and Weber DJ. Disinfection and Sterilization in Health Care Facilities: What Clinicians Need to Know. *Clin Infect Dis*. 2004. 39:702–9.

Rutala WA and Weber DJ. Disinfection, Sterilization, and Control of Hospital Waste. Mandell: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (7th Edition), Philadelphia: Churchill Livingstone Elsevier, 2009. Pgs. 3677–3695.

Sherlock O, O'Connell N, Creamer E, Humphreys H. Is it really clean? An evaluation of the efficacy of four methods for determining hospital cleanliness. *J Hosp Infect*. 2009. 72:140e146.

Moore G, Smyth D, Singleton J, Wilson P. The use of adenosine triphosphate bioluminescence to assess the efficacy of a modified cleaning program implemented within an intensive care setting. *Am J Infect Control*. 2010. 38:617–22.

Boyce JM, Havill NL, Dumigan DG, Golebiewski M, Balogun O, Rizvani R. Monitoring the Effectiveness of Hospital Cleaning Practices by Use of an Adenosine Triphosphate Bioluminescence Assay. *Infect Control Hosp Epidemiol*. 2009. 30:7.

Currie B. Revisiting environmental hygiene and hospital-acquired infections. *Infectious Disease Special Edition*. September 2013, Volume 1.

Boyce JM, Havill NL, Havill HL, et al. Comparison of Fluorescent Marker Systems with 2 Quantitative Methods of Assessing Terminal Cleaning Practices. *Infect Control Hosp Epidemiol*. 2011. 32:12.

Havill NL, Moore BA, Boyce JM. Comparison of the microbiological efficacy of hydrogen peroxide vapor and ultraviolet light processes for room decontamination. *Infect Control Hosp Epidemiol*. 2012. 33:507–512.

CHAPTER 11

The Healthcare Worker as a Source of Transmission

Margreet C. Vos, MD, PhD

Key Issue

Within the hospital, healthcare workers (HCWs) are often exposed to infections. Any transmissible disease can occur in the hospital setting and may affect HCWs. HCWs are not only at risk of acquiring infections but also of being a source of infection to patients. Therefore, both the patient and the HCW need to be protected from contracting or transmitting health care associated infections by using recommended infection control measures.

Known Facts

- The infection control objectives of a hospital should be planned by the infection control committee and occupational health services. The focus of the committee and services must be personal hygiene, monitoring of carriage of specific micro-organisms, monitoring of infectious disease outbreaks and exposures and, after identifying infection risks, institution of preventive measures.
- Prevention of infectious diseases in HCWs serves three purposes: the health of the healthcare worker, the prevention of work restrictions, and the reduction of health care associated infections. The latter is discussed in this chapter.
- Education is an important factor for improving compliance with guidelines and prevention measures. All HCWs need to know about the risk of infection and the route of transmission of pathogens. Hand hygiene and standard precautions are the foundation for preventing transmission of infectious diseases to patients.

- Immunization should be used to protect HCWs from specific infectious agents. Preventing infections in HCWs will also prevent transmission of infections from HCWs to patients. Prompt evaluation of and institution of appropriate control measures for patients with signs and symptoms of transmissible infectious diseases will reduce the risk of health care associated diseases.
- In deciding the type of infection control procedures needed, one must consider the HCW's job, risk of exposure, and the suspected infectious pathogen.

A short overview of some of the most important infectious diseases transmitted by HCWs is presented below.

General

In a recent review, 152 health care associated infection outbreaks with a HCW as a source were identified. These outbreaks were mainly associated with surgery, neonatology, and gynecology departments. The most frequently encountered pathogens were Hepatitis B virus, S. aureus and S. pyogenes.

In general, the most important infection prevention measure is adequate hand hygiene. Hand disinfection as defined by the WHO guidelines specify 5 moments of hand hygiene. In short this comprises;

1. **Before** touching a patient.
2. **Before** aseptic/clean procedure.
3. **After** body fluid exposure risk.
4. **After** touching a patient.
5. **After** touching patient surroundings (without touching the patient during the same care sequence).

Skin Infections

Scabies. Scabies is transmitted by direct contact. In case of Norwegian (crusted) scabies, transmission is also through fomites, such as bed linens, floors, walls, furniture, clothes and the air. Symptoms of intense pruritius can develop 2 to 6 weeks after initial infestation. To prevent infection and to prevent a hospital outbreak, a HCW with skin exposure should receive prophylactic therapy, and to prevent re-infestation, the household contacts

should be treated too. In case of scabies crustosa, contact persons should be identified and should receive prophylactic treatment. Contact patients are those who shared the room or were otherwise direct or indirect exposed to skin scales. Contact health care workers are those having cared for the patient without taking precautions measures. Immunocompromised patients have a high chance of developing scabies crustosa, which is harder to recognize compared to "local" scabies and more infectious.

Staphylococcus aureus. About one-third of the population are persistent nasal carriers of *S. aureus* (SA), one-third are intermittent carriers, and one-third are unaffected. Other sites of colonization are the throat, perineum, skin, axilla, or hair. People with dermal lesions, such as eczema, are more likely to be carriers. Carriers may spread SA to patients, especially patients with wounds, intravascular catheters and other indwelling catheters. Dissemination of SA is by direct or indirect contact or, less commonly, by skin scales. Healthcare workers with active lesions caused by SA such as boils (even on an occult body area) or other skin lesions are more likely to transmit infection to others than nasal carriers. HCW's who are carriers of methicillin resistant *Staphylococcus aureus* (MRSA) are a high risk to patients, by transmitting MRSA from their skin, hands or nose to wounds or mucosal surfaces. MRSA seems to spread more easily than MSSA, probably due to selection during antibiotic use and probably not due to the presence of other virulence mechanisms in mecA positive micro-organisms.

During periods of high incidence of staphylococcal disease or epidemics of MRSA, identifying carriers by culturing patients and HCWs is useful. Carriers can be treated with 2% mupirocin ointment and disinfective soap washing. The optimal strategy for identifying and decolonizing HCWs who carry MRSA is unknown.

Group A *Streptococcus.* Group A *Streptococcus* (GAS) is a well-known pathogen of the skin and pharynx. Other reservoirs include the rectum and the female genital tract. Major modes of transmission are direct contact and large droplets. An increased incidence of wound infections by GAS should be investigated. Particular focus should be placed on carriage by HCWs.

Healthcare workers with overt infection due to GAS should be restricted from work until 24 hours after adequate therapy has been given or until cultures are proven to be negative. Overall, the risk of transmission of GAS from HCW to patients is considered low.

Herpes simplex. Herpes simplex type I can be transmitted from HCWs to patients through primary or recurrent lesions. Most infections are orofacial and transmitted by direct contact. Saliva also can be infectious. Because the main route of transmission is by contaminated hands after direct contact with the lesion, hand washing and disinfection before and after patient contact are the most important methods for preventing transmission to patients. Herpes simplex lesions of the fingers (herpetic whitlow) are an occupational disease of HCWs due to direct exposure to contaminated fluid such as vaginal secretions or skin lesions. Healthcare workers with herpetic whitlow must use gloves to prevent the spread of the herpes virus to patients. When caring for patients at risk of severe infection, such as preterm neonates, patients with severe malnutrition, severely burned, or immunocompromised patients, restriction of work of HCWs with herpes infections should be considered.

Enteric Diseases

Accute Diarrhea. Transmission of most microorganisms causing diarrhea in HCWs is by direct or indirect contact. Careful hand washing hygiene, especially after visiting the bathroom, is the most important measure for preventing transmission of these pathogens. Until symptoms are resolved, healthcare workers with acute infectious diarrhea should not care for patients. Even after resolution of the acute disease, HCWs may still carry enteric pathogens.

HCWs can be asymptomatic carriers of *Salmonella* spp or *Campylobacter* spp during the convalescent period or a protracted period thereafter. Testing for carriage may be unreliable and is therefore usually limited to food handlers, who are more likely to transmit disease to others. Careful hand washing after using the bathroom and before patient contact will prevent the transmission of enteric pathogens from most carriers. Antibiotic treatment is rarely indicated.

In case of norovirus, HCWs can be an important link in hospital outbreaks: infected HCWs may be asymptomatic upon arrival at work, get ill suddenly and consequently spread the virus by vomiting. On the other hand, they can be infected by patients. Patients should be isolated, HCWs should be sent home in the event that they manifest active disease. The advent of PCR testing makes the diagnosis of norovirus more feasible. During an outbreak of norovirus, hand hygiene with soap and water is preferable to alcohol based hand sanitizers.

Hepatitis A. Hepatitis A occurs rather infrequently as a health care associated infection. Prevention of transmission is through maintaining personal hygiene, especially through hand washing.

Respiratory Diseases

Common Cold. The common cold in adults is caused by the parainfluenza virus, adenovirus, rhinovirus, or respiratory syncytial virus. Healthcare workers are important sources of these viruses to patients. In general, to prevent health care associated transmission from HCWs to patients, infected HCWs should wash or disinfect their hands carefully before patient contact. The use of masks is optional but may be helpful in preventing transmission due to large droplets upon close contact. Routine use of gloves has no additional benefit; even if gloves are used, hands should be disinfected or washed after gloves are removed. In most people, viral upper respiratory infections are self-limiting. However, in immunocompromised patients, such as recipients of bone marrow transplants, these infections may progress to severe lower respiratory tract diseases with very high mortality rates. Infection control strategies include identifying, cohorting, and isolating of infected patients and limiting contact of symptomatic HCWs and visitors with high risk patients. Work restrictions for symptomatic HCWs may be considered, especially when working with immunocompromised patients. HCWs with upper respiratory infections and fever should generally consider staying home from work.

Influenza. Influenza epidemics are well known in hospitals. Transmission occurs from HCWs to other HCWs and patients,

and from patients to HCWs and other patients. Hospital infection control committees should implement an influenza vaccination program each year, several weeks before the influenza season. There is evidence that vaccination is associated with decreases in mortality, the number of febrile respiratory illness days and HCW absenteeism. During periods of influenza activity, personnel with acute febrile respiratory infections should not provide care to high-risk patients. The incubation period is 1 day before onset of symptoms and the period of communicability is from 1 day before until 7 day after onset of symptoms. Additionally, prophylactic antiviral agents may be used. Hospitals should have written guidelines for avian and pandemic influenza.

Pertussis. Vaccination of adults with whole-cell *B. pertussis* vaccine is not recommended because of local and systemic reactions. The acellular vaccine has been used for attempted control of hospital pertussis outbreaks but clinical effectiveness has not been proven. Active disease in HCWs should trigger a search for potentially exposed patients. Infection prevention measures should be taken. These include giving prophylactic antibiotic treatment to exposed neonates with low or negative IgG levels as these patients are at high risk for developing severe pertussis.

Varicella Zoster. Varicella zoster virus causes varicella or chickenpox in childhood. After years, due to reactivation, the virus can manifest as skin lesions (zoster or shingles), which may be widely disseminated in immunocompromised patients. Those lesions can be infectious to others through direct contact and cause varicella in susceptible persons.

Varicella is one of the most common health care associated diseases among HCWs. It is a highly contagious disease, and exposure to the virus is common in the healthcare setting. Most persons with a clear history of chickenpox in childhood are probably immune. Persons with a negative history can be immune but should be tested. Susceptible HCWs may acquire infection after exposure to infectious patients. Non-immune HCWs exposed to varicella should be excluded from work from day 8 to 21 after contact, to ensure that infection has not occurred. If the HCW develops disease, he/she should be excluded from work until all lesions are dry and crusty. Since such a policy

regarding work restriction is very expensive, vaccination of all susceptible workers should be done. A live-attenuated varicella vaccine was licensed for use in several, but not in all countries. Vaccination provides approximately 70% protection against infection and 95% protection against severe disease for 7 to 10 years after vaccination. Vaccination of HCW's is proven to be cost-effective.

Measles. Measles is transmitted by the airborne route. The same strategy as has been recommended for varicella-susceptible HCWs can be followed for susceptible HCWs exposed to measles. Prompt identification of HCWs and patients with rash and fever will help prevent further spread of this virus.

Tuberculosis. The infection Control Committee should indicate high-risk wards, were HCW's are routinely screened on tuberculosis. After conversion of the Mantoux test, or positive other newly developed screening tests (IGRA),prophylactic treatment is indicated to prevent open tuberculosis which is contagious for patients. Furthermore, all HCWs reporting symptoms suggestive of tuberculosis should have a medical examination and a chest radiograph. Suggestive symptoms are cough for more than 3 weeks, persistent fever, and weight loss. After identifying an HCW suffering from open tuberculosis, a prompt evaluation of all contacts must be instituted. Stringent measures regarding work restrictions are necessary. Healthcare workers should be receiving effective treatment and have negative sputum smears before returning to work. Bacille Calmette-Guérin (BCG) vaccination should be considered for all tuberculin skin test negative HCWs, unless previously vaccinated, in countries where tuberculosis is endemic or in hospitals where exposure to infectious TB cases is likely.

Bloodborne Pathogens

The management of HCWs infected with bloodborne pathogens has been reviewed by the AIDS/TB committee of the Society for Healthcare Epidemiology of America (SHEA). Recently, an updated CDC recommendation for the management of hepatitis B virus-infected Health-care providers and students was published. In general, prevention of infection is based on appropriate

infection control procedures to avoid blood contact from patient to HCW and from HCW to patient. The major emphasis is on applying blood precautions, practicing hand washing, minimizing contact with blood or blood-contaminated excretions, and handling all blood as potentially infectious. Education concerning bloodborne pathogens for all healthcare workers is recommended, not just those who are already infected.

Hepatitis B. Immunization with the hepatitis B virus (HBV) vaccine is the most important measure to prevent infection of the HCW by HBV. Each hospital must develop an immunization strategy. Healthcare workers with active HBV or those who are carriers of HBV are at risk for transmitting HBV to others. The risk of transmission of HBV is higher than that of the hepatitis C virus or human immunodeficiency virus, as is reflected in 38 outbreaks of HBV by HCW-to-patient transmission in the past 22 years.

Vaginal hysterectomy, major pelvic surgery, and cardiac surgery are associated with HBV transmission despite the use of proper infection control measures. With these surgeries, the chances of needle-stick injuries are presumably greater. Before increased use of infection control interventions, the risk of HBV transmission was also associated with dental procedures. The presence of high numbers of HBV-DNA copies in source HCW is almost always the case. Another route of transmission can be by hepatitis B positive HCWs with exudative dermatitis on body areas that may come in contact with patients.

Restricting HCWs from practice of gynecologic or (cardiac) surgery or performing dental procedures should be not be judged by the presence of a HBV infection only.The risk of transmission should be carefully established and monitored.The risk of transmission to patients, despite appropriate use of infection control measures, depends on the procedures performed and the levels of HBV-DNA. Treatment of the HBV infection can possibly decrease the number of copies of HBV-DNA below critical levels. Defined critical levels of the HBV-DNA varies between countries. For HBV positive HCWs who perform exposure-prone procedures, an expert panel should provide oversight of the HCWs practice and risk of transmission.

Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV). The risk of transmission of HIV is probably 100 times lower than hepatitis B, with that of HCV being somewhere between HIV and HBV. Healthcare workers known to be infected with HIV or HCV are strongly recommended to follow universal precautions as recommended in their hospital to minimize the risk of infection to others. Using double gloves for procedures is recommended. HIV- and HCV-infected HCWs should not be prohibited from patient care activities solely on the basis of their infection. Healthcare workers need not be screened routinely for HIV or HCV infection, except in cases of significant exposure of a patient to the blood or body fluid of an HCW.

AIDS. Healthcare workers infected with HIV can be infected with HIV-associated pathogens. In turn, these pathogens can be transmissible to patients. Examples are *Mycobacterium tuberculosis*, varicella zoster, and measles by aerogenic spread and *Salmonella* spp, *Cryptosporidium* spp, and all other enteric pathogens via fecal-oral exposure. For prevention of transmission, see the relevant part of this chapter.

Vaccine-Preventable Diseases

Healthcare workers may be exposed to vaccine-preventable diseases and then, after contracting the disease, be infectious to patients. It is recommended that HCWs be vaccinated or have demonstrated immunity to certain vaccine-preventable diseases. The infection control committee of each hospital has to develop policies requiring proof of immunity or, if needed, offer vaccination. Herd immunity of the hospital community is not reliable and unvaccinated HCWs are a potential risk to patients. For HCW's, the following diseases are vaccine-preventable and can be transmitted to patients during healthcare work; varicella, measles, pertussis, influenza A, hepatitis B, hepatitis A and to some extent tuberculosis.

Table 11.1 Work Restrictions for Healthcare Workers with Transmissible Infections

	Immunization Available	*Work or Patient Contact Restriction =*
Scabies	–	Until cleared by medical evaluation
S. aureus	–	Actively draining lesion Proven transmission With search-and-destroy strategies, MRSA carrier should be restricted until successfully treated
Group A *Streptococcus*	–	Until 24 hours adequate therapy, or proven negative cultures
Herpes simplex	–	In case of whitlow and caring for immunocompromised patients including neonates
Hepatitis A	+	Until 7 days after onset of jaundice
Common cold viruses (*see text*)	–	Consider contact restriction with high-risk patients (e.g., bone marrow transplants)
Influenza	+	Consider contact restriction with high-risk patients (e.g., bone marrow transplants)
Varicella	+	In case of active disease, postexposure in susceptible persons: day 8–21
Pertussis	+	In case of active disease
Measles	+	In case of active diseases, postexposure in susceptible persons: day 5–21
Tuberculosis	+	In case of active disease
HBV	+	Refer to local regulations: restriction from high-risk procedures.
HCV	–	–
HIV	–	Refer to local regulations

References

Bell D, Shapiro CN, Chamberland ME, Ciesielski CA. Preventing Bloodborne Pathogen Transmission from Healthcare Workers to Patients: The CDC Perspective. *Surg Clin North Am*. 1995. 75:1189–1203.

Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchmann SD, et al. Guideline for Infection Control in Healthcare Personnel, 1998. *Infect Control Hosp Epidemiol*. 1998. 189:407–463.

Centers for Disease Control and Prevention. Immunization of Healthcare Workers: Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infections Control Practices Advisory Committee (HICPAC). *MMWR*. 1997. 46(RR-18):1–42.

Chandler RE, Lee LE, Townes JM, Taplitz RA.Transmission of Group A Streptococcus Limited to Healthcare Workers with Exposure in the Operating Room. *Infect Control Hosp Epidemiol*. November 2006. 27(11):1159–63.

Danzmann L, Gastmeier P, Schwab F, Vonberg R-P. Health care workers causing large nosocomial outbreaks: A systematic review. *BMC Infectious Diseases*. 2013. 13:98.

Kuehnert MJ, Cardo DM, Infections Associated with Healthcare Personnel: Vaccine-Preventable Diseases and Bloodborne Pathogens. *Curr Infect Dis Rep*. December 2000. 2(6):475–483.

Ofner-Agostini M, Gravel D, McDonald LC, et al. A Cluster of Cases of Severe Acute Respiratory Syndrome Among Toronto Healthcare Workers After Implementation of Infection Control Precautions: A Case Series. *Infect Control Hosp Epidemiol*. May 2006. 27(5):473–8.

Shefer L, Dales L, Nelson M, et al. Use and Safety of Acellular Pertussis Vaccine Among Adult Hospital Staff During an Outbreak of Pertussis. *J Inf Dis*. 1995. 171:1053–1056.

WHO Guidelines on Hand Hygiene in Health Care. http://whqlibdoc.who.int/publications/2009/9789241597906_eng.pdf

Updated CDC Recommendations for the Management of Hepatitis B Virus–Infected Health-Care Providers and Students. *MMWR Recomm Rep*. July 2012. 61(3).

CHAPTER 12

Managing Antibiotic Resistance: What Works in the Hospital

Amy L. Pakyz, PharmD, MS and
Denise K. Lowe, PharmD, BCPS

Key Issue

Over the past several decades the incidence of antibiotic resistance by microorganisms has increased and transmission of these resistant microorganisms between hospitalized patients has been reported. Antibiotic resistance in the hospital impacts patient outcomes as well as healthcare-related costs.

Known Facts

- Antibiotic resistance is more common in hospitalized settings, primarily in intensive care units, although use of antibiotics in the community setting is often the origin of hospital antibiotic resistance.
- Nearly all microorganisms have displayed clinically important resistance to antibiotics. Mechanisms for resistance include genetic transmission (conjugation, transformation, and transduction) and biological modalities (destruction, transformation, active efflux, and receptor modification).
- Resistance to antibiotics can be classified as intrinsic or acquired, and can be transmitted vertically or horizontally, with horizontal transmission being the most significant means for emergence and spread.
- Indiscriminate use of antibiotics is a major factor in promoting antimicrobial resistance. Other factors that contribute to the entry of resistant pathogens into hospitals include: the transfer of patients with resistant pathogens from other healthcare facilities; patient-to-patient transmission of pathogens via the hands of healthcare workers; transfer of resistant genes among organisms.

- In 2013, the Centers for Disease Control and Prevention (CDC) categorized microorganisms that pose the greatest antimicrobial resistance threats to public health into three threat groups:
  - Urgent: *Clostridium difficile*, Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae*.
  - Serious: Drug-resistant *Acinetobacter*, Drug-resistant *Campylobacter*, Fluconazole-resistant *Candida*, Extended-spectrum, cephalosporin-resistant Enterobacteriaceae, Vancomycin resistant *Enterococcus* (VRE), Drug-resistant *Pseudomonas aeruginosa*, Drug-resistant nontyphoidal-*Salmonella*, Drug-resistant *Salmonella typhi*, Drug-resistant *Shigella*, Methicillin resistant *Staphylococcus aureus* (MRSA), Drug-resistant *Streptococcus pneumoniae*, Drug-resistant tuberculosis (multiple drug resistant and extensively drug resistant).
  - Concerning: Vancomycin-resistant *Staphylococcus aureus* (VRSA), Erythromycin-resistant *Streptococcus* Group A, Clindamycin-resistant *Streptococcus* Group B.
- Worldwide, there are problems with methicillin resistant *Staphylococcus aureus*—both health care associated MRSA and Community-associated MRSA (CA-MRSA).
- The explosion of infections with vancomycin-resistant *Enterococcus faecium* in US hospitals has been remarkable. Much lower rates have been reported from Europe.
- Resistance of gram-negative rods to quinolones and third generation cephalosporins continues to increase.
- Micorbial strains resistant to Ceftriaxone are called ESBLs because they carry extended spectrum βeta Lactamases enabling the bacteria to resist most βeta Lactam antibiotics. These bacteria are usually susceptible to carbapenems such as imipenem and meropenem.
- With the increased use of carbapenems has been the emergence of bacteria harboring carbapenemases, βeta lactamases that inactivate imipenem and meropenem. These strains are susceptible only to colistin.
- The emergence of *S.aureus* with intermediate levels of resistance to vancomycin (VISA) has been reported in several

countries. These strains have MICs of 8μg/mL. In 2002, two strains of *S.aureus* with high levels of resistance to vancomycin (VRSA) were reported in the U.S. These strains have MICs ≥32 μg/mL. As of October 2013, 13 patients in the U.S. have been identified with infections due to VRSA.

- The burden of antimicrobial resistance includes increased patient-related morbidity and mortality and higher healthcare costs.
- Adoption of new strategies designed to delay or prevent resistance is crucial since the introduction of new antimicrobial drugs into the market has substantially declined.
- Antimicrobial stewardship and infection prevention and control programs are the two key initiatives employed in combating the emergence and transmission of antibiotic resistance.

Controversial Issues

- The causes of antibiotic resistance in the hospital setting are not clearly known. The unnecessary use of antibiotics is important. Such high antibiotic use leads to the selection of resistant organisms. Once patients are colonized or infected with a resistant organism, the risk of cross transmission to other patients exists. The initiating problem is the selection of a resistant isolate under the "pressure" of antibiotic usage.
- More research is needed to best define specific infection prevention practices and strategies to limit or halt the transmission of multidrug-resistant organisms.
- The optimal duration of contact precautions for patients infected or colonized with multidrug-resistant organisms has not been established.
- The optimal circumstances and populations for the employment of active surveillance cultures as an infection prevention strategy are unknown.
- The adoption of a "bare below the elbows" (BBE) policy has occurred in many hospitals in the UK and North America. Although these strategies are based on common sense, it remains unknown if this practice reduces the transmission of resistant microorganism.

- Formulary restrictions and pre-authorizations are methods often applied to broad-spectrum antibiotics and those antibiotics associated with rapid resistance.
  - Results of clinical trials have not demonstrated a reduction in the overall emergence of antibiotic resistance among bacteria when restrictions or pre-authorizations have been utilized. Rather, the introduction of new or different antibiotic-resistant bacterial strains within the hospital setting has been reported.
  - Use of restrictions and pre-authorizations has been successful in specific outbreaks of infection with antibiotic-resistant bacteria, particularly in conjunction with infection control practice and educational activities.

Suggested Practice

Judicious Use of Antimicrobials

The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America developed a guideline document entitled: Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship.

Hospitals are encouraged to implement a multidisciplinary antimicrobial stewardship team that includes among its core members an infectious diseases physician and clinical pharmacist with infectious diseases training. Other important members of this team include a hospital epidemiologist, a clinical microbiologist, an information system specialist, and infection control professional.

Key Strategies: Antimicrobial Selection and Utilization

The following are recommended core strategies:

- Prospective audit with intervention and feedback
  - Prospective evaluation of antimicrobial use with direct feedback to the prescriber.
- Antimicrobial formulary restriction/preauthorization
  - Evaluate antimicrobials for inclusion on hospital formulary and restrict their use through formulary limitation or required preauthorization/justification.

The following are recommended elements of an antimicrobial stewardship program depending on an institution's resources, local antimicrobial use, and antimicrobial resistance problems:

- Education
- Guidelines and clinical pathways
- Antimicrobial order forms
- Streamlining or de-escalation of therapy
- Dose optimization
- Parenteral to oral conversion

Infection Prevention and Control Program:

The transmission and endurance of a problem pathogen in a healthcare institution depends on the patient base, selective pressure from antimicrobial use, and the number of patients colonized or infected with the problem pathogen.

A combination of interventions may need to be employed to prevent and control the spread of problem pathogens. Types of interventions used by institutions may vary depending on the types and significance of problem pathogens, the population of the institution, and available resources.

The Healthcare Infection Control Practices Advisory Committee (HICPAC) developed a guideline document concerning the management of multi-drug resistant organisms in healthcare settings.

In addition to following Standard Precautions for all patient encounters, the following are some recommended strategies:

- Improvements in hand hygiene,
- Use of Contact Precautions in patients with a multidrug-resistant organism until patients are culture-negative,
- Active surveillance cultures,
- Education,
- Enhanced environmental cleaning,
- Cohorting of patients,
- Decolonization, and
- Improvements in communication regarding patients with multidrug-resistant organisms between healthcare institutions.

Key components of every antimicrobial stewardship and infection prevention and control programs include:

- Administrative support
  - Seek and acquire the support of hospital administration and medical staff leadership for fiscal and human resources.
- Ongoing surveillance on a regular interval
  - Measure antimicrobial use and track use,
  - Monitor and track antimicrobial resistance trends (antibiograms) and newly emerging problem pathogens,
  - Measure the effectiveness of interventions.
- Education/Feedback
  - Provide educational interventions and training to medical care providers,
  - Disseminate information about program outcomes.

Additional Preventive Practices:

Guidelines for preventive practices are also included in the Center for Disease Prevention and Control's Campaign to Reduce Antimicrobial Resistance in Healthcare Settings.

This evidence-based 12-step initiative focuses on four overall strategies to guide clinicians in an effort to prevent the emergence of drug resistance in hospitals:

- Prevent infection
  - vaccinate (protect)
  - remove indwelling lines
- Diagnose and treat infection effectively
  - target the pathogen
  - consult with the experts
- Use antimicrobials wisely
  - practice antimicrobial control
  - use local data
  - treat infection not colonization
  - treat infection not contamination
  - know when to say "no" to vancomycin
  - stop treatment when infection is cured or unlikely
- Prevent transmission
  - isolate the pathogen
  - break the chain of contagion

The 12 steps can be tailored to specific hospital populations, e.g., dialysis, surgery, and emergency, critical and long-term care.

Promoting and practicing antibiotics stewardship can also involve the use of biomarkers for infection to reduce unnecessary use of antibiotics, and selection of the optimal type, dose and duration of therapy. Procalcitonin has been used successfully as a diagnostic and prognostic tool in various patient populations.Intravenous to oral switch reduces risk of catheter-associated infections and facilitates patient discharge. Inappropriate and unnecessary antibiotics use increases mortality whereas shorter-term treatment may limit the occurrence of negative patient outcomes.

Traditional techniques for the detection of pathogenic microorganisms that involve selective culturing and plating methods are both time-consuming and labor-intensive. Newer techniques provide rapid, selective and sensitive diagnostic tools, which can also be employed to identify uncultivable pathogens. The polymerase chain reaction (PCR) method is used for the selective and quantitative detection of single microbes, or simultaneous detection of multiple strains. Optical and electrochemical biosensory methods also provide enhanced detection of pathogens, and current techniques are being developed for on-site analysis. Other analytical detection methods include metabolic footprinting—the analysis of a microorganism's extracellular metabolites, which discriminates between mutated strains based on distinct metabolic phenotypes.

Other targeted interventions to minimize preventable infections include use of chlorhexidine-containing products for catheter insertions, mechanical ventilation (MV) and (pre-surgical) decolonization. These strategies have shown to significantly reduce the risk for infections with non-resistant and resistant pathogens.

Summary

Antibiotic resistance is increasing worldwide, and is associated with severe morbidity, mortality, and increased healthcare-related costs. A collaborative practice approach between clinicians, public health practitioners, and administrators needs to be implemented to help manage this serious infectious disease issue.

References

U.S. Department of Health and Human Services, Center for Disease Control and Prevention: Antibiotic Resistance Threats in the United States, 2013. http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf (Accessed 3 October 2013).

Maki DG, Safdar N, et al. Antimicrobial resistance: Waking up to the challenge supplement: prevalence, consequences, and solutions. *Pharmacotherapy*. 2007. 27:121S–125S.

Wenzel RP, Edmond MB. Managing antibiotic resistance. *N Engl J Med*. 2000. 343:1961–3.

Rybak MJ. Antimicrobial Resistance: Waking up to the challenge supplement: antimicrobial stewardship. *Pharmacotherapy*. 2007. 27:131S–135S.

Dellit TH, Owens RC, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007. 44(2):159–177.

Siegel, JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee: Management of Multidrug-Resistant Organisms in Healthcare Settings. 2006. http://www.cdc.gov/hicpac/mdro/mdro_0.html (Accessed 13 October 2013).

Spellberg B, Powers JH, et al. Trends in antimicrobial drug development: Implications for the future. *Clin Infect Dis*. 2004. 38(9):1279–1286.

Stelfox HT, Bates DW, et al. Safety of patients isolated for infection control. *JAMA*. 2002. 290:1899–1905.

Burger A, Wijewardena C, Clayson S, et al. Bare below the elbows: Does this policy affect handwashing efficacy and reduce bacterial colonization? *Ann R. Coll Surg Engl*. 2011. 93(1):13–16.

Centers for Diseases Control and Prevention. Get Smart for Healthcare. http://www.cdc.gov/drugresistance/healthcare/ha/12steps_HA.htm (Accessed 11 October 2013).

Schuetz P, Muller B, et al. Procalcitonin to guide initiation and duration of antibiotic treatment in acute respiratory infections: an individual patient data meta-Analysis. *Clin Infect Dis*. 2012. 55(5):651–62.

Magrini L, Travaglino F, et al. Procalcitonin variations after emergency department admission are highly predictive of hospital mortality in patients with acute infectious diseases. *Eur Rev Med Pharmacol Sci*. 2013. (Suppl 1):133–42.

Hohn A, Schroeder S, et al. Procalcitonin-guided algorithm to reduce length of antibiotic therapy in patients with severe sepsis and septic shock. *BMC Infect Dis*. 2013. 13:158–67.

Arnold HM, Micek ST, et al. Antibiotic stewardship in the intensive care unit. *Semin Respir Crit Care Med*. 2011. 32(2):215–27.

Chastre J, Wolff M, et al. Comparison of 8 days versus 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: A randomized trial. *JAMA*. 2003. 290(19):2588–98.

Sandberg T, Skoog G, et al. Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis: A randomized, open-label and double-blind,placebo-controlled, non-inferiority trial. *Lancet*. 2012. 380(9840):484–90.
Peltola H, Pääkkönen M, et al. Short- versus long-term antimicrobial treatment for acute hematogenous osteomyelitis of childhood: Prospective, randomized trial on 131 culture-positive cases. *Pediatr Infect Dis J*. 2010. 29(12):1123–8.
el Moussaoui R, de Borgie CA, et al. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: Randomized, double blind study. *BMJ*. 2006. 332(7554):1355.
Rodríguez-Lázaro D, D'Agostino M, et al. Real-time PCR-based methods for detection of Mycobacterium avium subsp. paratuberculosis in water and milk. *Int J Food Microbiol*. 2005. 101(1):93–104.
Caliendo AM. Multiplex PCR and emerging technologies for the detection of respiratory pathogens. *Clin Infect Dis*. 2011. 52(Suppl 4):S326–30.
Lazcka O, Del Campo FJ, et al. Pathogen detection: A perspective of traditional methods and biosensors. *Biosens Bioelectron*. 2007. 22(7):1205–1217.
Skottrup PD, Nicolaisen M, et al. Towards on-site pathogen detection using antibody-based sensors. *Biosens Bioelectron*. 2008. 24(3):339–348.
Mapelli V, Olsson L, et al. Metabolic footprinting in microbiology: Methods and applications in functional genomics and biotechnology. *Trends Biotechnol*. 2008. 26(9):490–497.
Szeto SS, Reinke SN, et al. Mutations in the Saccharomyces cerevisiae succinate dehydrogenase result in distinct metabolic phenotypes revealed through(1)H NMR-based metabolic footprinting. *J Proteome Res*. 2010. 9(12):6729–6739.
Baran R, Bowen BP, et al. Metabolic footprinting of mutant libraries to map metabolite utilization to genotype. *ACS Chem Biol*. 2013. 8(1):189–199.
U.S. Department of Health and Human Services. National Action Plan to Prevent Healthcare-Associated Infections: Roadmap to Elimination. http://www.hhs.gov/ash/initiatives/hai/exec_summary.html (Accessed 13 October 2013).
Climo MW, Yokoe DS, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med*. 2013. 368(6):533–542.
Zhang TT, Tang SS, et al. The effectiveness of different concentrations of chlorhexidine for prevention of ventilator-associated pneumonia: a meta-analysis. *J Clin Nurs*. 2013.
Afonso E, Llaurado M, et al. The value of chlorhexidinegluconate wipes and prepacked washcloths to prevent the spread of pathogens—a systematic review. *Aust Crit Care*. 2013.

CHAPTER 13

Organizing and Recording Problems Including Epidemics

Samuel Ponce de León, MD, MSc and
Alejandro E. Macias, MD, MSc

Key Issue

Surveillance is the foundation for organizing and maintaining an infection control program.

Known Facts

- Reviewing patient records, interviewing nurses and physicians, and reviewing microbiology results give the infection control team an accurate view of the frequency and type of infections associated with health care. At the same time, these activities give the infection control team or nurse a highly visible profile to all services and personnel, which helps to promote continuous improvement. Recently, surveillance monitors also the compliance with components of prevention bundles, such as hand hygiene, proper insertion and opportune withdrawal of devices, proper antisepsis, or bed inclination.
- Surveillance is the central activity from which all other related actions are sustained. Passive surveillance is not an accurate or effective method of infection control; surveillance must be active and continuous, in some cases focused on the highest risk areas. The extent (focal or hospital-wide surveillance) of this activity depends on hospital needs and resources.
- There being no other way to detect an epidemic in the earliest stage, frequently visiting the clinical units and the clinical laboratory allows for the early detection of outbreaks and provides information necessary to maintain the functioning of the overall program. The system ideally should detect two or three associated cases as soon as they appear and not after several cases or deaths have occurred.

- Reporting surveillance results is an essential element for an effective infection control program. Reports to clinical services must be regular, periodic, and presented in a non-antagonistic way to encourage change. For infection control activities to succeed, the program must include personnel dedicated exclusively to surveillance.
- For benchmarking against systems such as the National Healthcare Safety Network (NHSN) or other networks, the numerators of the rates focus usually on major device-associated infections (central line-associated blood stream infection, ventilator-associated pneumonia, and catheter-associated urinary tract infection) and those associated with procedures (wound infection and postoperative pneumonia). Denominators constituted by the numbers of discharged patients are inadequate to compare between institutions. Proper denominators are one thousand days of device use or one hundred procedures. Other surveillance reports can be the rate of hand hygiene compliance, the bacterial resistance, or the *Clostridium difficile*-associated diarrhea.
- The frequency of health care associated epidemics in developing countries is higher than those reported in the United States. This problem can be particularly severe in intensive care units because:
  1. The functioning of these units includes multiple invasive devices used without organized procedures and policies to prevent infectious complications;
  2. The improper re-use of disposable devices such as catheters, hemodialysis filters, and even needles, a practice attributed to financial limitations; and
  3. The lack of personnel with specific training in critical care.
- In developing countries, neonatal intensive care units have the highest risk for epidemics, most commonly caused by blood stream infections due to contamination of intravascular lines or infusates. These risks occur due to poor standards of care that should be avoided, such as inappropriate handling and storage of multiple vials for small doses of medications, use of glucose infusions that remain open in use during hours, and lack of hand hygiene in an overcrowded

and badly designed unit with a shortage of personnel. A common practice when confronting an epidemic is to close the unit and fumigate the area instead of following infection control recommendations. This approach is costly and inefficient.

- Hospitals without microbiology laboratory must make every effort to have one to perform, at least, critical cultures such as blood cultures.
- When confronting an outbreak of health care associated infection, reports in the literature are a valuable resource for preparing investigation and control.
- The organization of an infection control program in a hospital with very limited resources requires determination and good relations with the clinical staff.
- Because cutting costs is a constant goal for most hospitals, explaining the benefits of infection control procedures will help gain support for the program. It is worthwhile to calculate the savings and the implicit improvements in quality of care derived from the program.
- Maintain good channels of communication. The authorities must feel and know that the program is solving problems instead of creating them. The attitude of the infection control group should be optimistic and creative; there is always the possibility of improvement, even if the level that you reach is not the same as the one reported by others.

Controversial Issues

- Definitions of health care associated infections may be controversial. Definitions must be understood as tools for surveillance and will not always concur with the clinician's view. For example, a patient with fever for a few hours and positive blood and catheter tip cultures for *Staphylococcus epidermidis* should be recorded as an infection associated with health care even if the clinician does not prescribe specific treatment and the fever disappears by withdrawing the line. On the other hand, clinicians tend to diagnose pneumonia more liberally than infection control personnel.
- Definitions must be simple and meet hospital purposes. Hospitals without microbiology support can develop definitions

based exclusively on clinical data. The Pan-American Health Organization (PAHO) has published a booklet with clinical definitions. The definitions proposed by Wenzel may be useful for hospitals with limited resources.

General Recommendations for Surveillance

- Surveillance must be based on practical definitions.
- Surveillance must be continuous on wards and the microbiology laboratory.
- For every instance of suspected health care associated infection forms should be filled out recording diagnosis, age, ward, dates of admission and discharge, outcome, type of infection, and etiologic agent.
- Monthly results of surveillance should be reported to the clinical services in a simple format and the results presented at the infection control meeting. Decisions to improve infection control need to be discussed and implemented. For benchmarking, denominators must be constituted by one thousand days of device use or one hundred procedures.

General Recommendations in Epidemics

- An epidemic is an infection control emergency; measures should be taken as soon as an epidemic is suspected.
- The first step in controlling an epidemic is to reinforce and monitor general recommendations of infection control in the ward where the cases are occurring. A case definition is made (e.g., *Enterobacter cloacae* bacteremia in neonates in the neonatal intensive care unit) and then current case rates are compared against previous rates (pre-epidemic period).
- After reviewing cases, additional recommendations should be given to the staff in order to prevent new cases. From evidence, sound hypothesis must be established to avoid wrong conclusions and unnecessary closure of medical wards. *Table 13.1* shows some examples of these hypotheses.
- Maintain frequent communication with the clinical staff in the unit or ward involved and give them all relevant information from your analysis.

Table 13.1 Evidence-based Working Hypothesis to Study and Control Common Hospital Outbreaks

Outbreak	Working hypothesis
Gram-negative bacteremia in neonates	Contaminated intravenous lines or infusates
Candidemia	Contaminated parenteral nutrition solutions
Ventilator-associated pneumonia	Contaminated respiratory equipment
Streptococcal surgical site infection	Healthcare worker carrier of Group A streptoccoccus
Tuberculosis	Exposure to TB patient without effective respiratory protection
Diarrhea in children	Exposure to rotavirus (or other viruses) without effective contact precautions
Diarrhea in adults	Prolonged use of antibiotics and absence of adequate source control
Multidrug-resistant Gram-negative infection	Antibiotics used without supervision

Summary

Hospital-wide surveillance is needed to start a program of infection control and to identify the highest-risk areas. There is a trend to focus surveillance in high-risk areas, specifically intensive care units, because of the efficiency for detecting the most severe health care associated infections and outbreaks, as compared against hospital-wide surveillance. However, for hospitals beginning surveillance, it may be better to institute a hospital-wide system in order to know the particular characteristics of the institution. This will also facilitate the collection of endemic rates in every ward. With time, surveillance activities may be limited to high-risk areas. Institutional reports of infections must be made periodically to promote the elimination of health care associated infections.

Control of epidemics requires a reinforcement of general measures of infection control. The infection control team should talk to the personnel on the wards, emphasizing and monitoring hand washing, isolation practices, and stringent adherence to procedural recommendations and to the components of preventive bundles. Depending on the characteristics of the outbreak, specific recommendations must be given (*see Table 13.1*).

References

Chitnis AS, Edwards JR, Ricks PM, Sievert DM, Fridkin SK, Gould CV. Device-associated infection rates, device utilization, and antimicrobial resistance in long-term acute care hospitals reporting to the National Healthcare Safety Network, 2010. *Infect Control Hosp Epidemiol*. 2012. 33:993–1000.

Gastmeier P, Stamm-Balderjahn S, Hansen S, Nitzschke-Tiemann F, Zuschneid I, Groeneberg K, Rüden H. How Outbreaks Can Contribute to Prevention of Nosocomial Infection: Analysis of 1,022 Outbreaks. *Infect Control Hosp Epidemiol*. 2005. 26:357–61.

Hong KB, Oh HS, Song JS, Lim JH, Kang DK, Son IS, Park JD, Kim EC, Lee HJ, Choi EH. Investigation and control of an outbreak of imipenem-resistant *Acinetobacter baumannii* Infection in a Pediatric Intensive Care Unit. *Pediatr Infect Dis J*. 2012. 31:685–90.

Kaier K, Wilson C, Hulscher M, Wollersheim H, Huis A, Borg M, Scicluna E, Lambert ML, Palomar M, Tacconelli E, De Angelis G, Schumacher M, Wolkewitz M, Kleissle EM, Frank U. Implementing strategic bundles for infection prevention and management. *Infection*. 2012. 40:225–8.

Macias AE, Muñoz JM, Galvan A, Gonzalez JA, Medina H, Alpuche C, Cortes G, Ponce de León RS. Nosocomial Bacteremia in Neonates Related to Poor Standards of Care. *Ped Infect Dis J*. 2005. 24:713–16.

Ponce de León RS. Nosocomial Infections in Latin America: We Have to Start Now. *Infect Control*. 1984. 5:511–12.

Ostrosky Zeichner L, Báez Martínez R, Rangel-Frausto MS, Ponce de León RS. Epidemiology of Nosocomial Outbreaks: Fourteen-Year Experience at a Tertiary Care Center. *Infect Control Hosp Epidemiol*. 2000. 21:527–8.

Ponce de León RS, Macias AE. Global Perspectives of Infection Control *in* Prevention and Control of Nosocomial Infections (4th Edition), Wenzel RP (Ed). Baltimore: Lippincott Williams & Wilkins, 2003. Pgs. 14–32.

Wenzel RP. Management Principles and the Infection Control Committee *in* Prevention and Control of Nosocomial Infections (2nd Edition), Wenzel RP (Ed). Baltimore: Williams & Wilkins, 1993. Pgs. 207–13.

Wenzel RP, Thompson RL, Landry SM, Rusell BS, Miller PJ, Ponce de León RS. Hospital Acquired Infections in Intensive Care Patients: An Overview with Emphasis on Epidemics. *Infect Control*. 1983. 4:371–5.

Zaidi M, Sifuentes J, Bobadilla M, Moncada D, Ponce de León RS. Epidemic of *Serratia marcescens* Bacteremia and Meningitis in a Neonatal Unit in Mexico City. *Infect Control Hosp Epidemiol*. 1989. 10:14–20.

CHAPTER 14

Horizontal vs Vertical Infection Control Strategies

Richard P. Wenzel, MD, MSc

Key Issues

There is an increasing literature supporting the idea that horizontal infection control programs [targeting all organisms at one or more anatomic sites] has been more effective than vertical programs [targeting a single organism e.g. methicillin resistant *Staphylococcus aureus* (MRSA)].

Known Facts

- Hand washing performed assiduously before and after seeing patients has clearly impacted total infection rates, is easy to perform, and is inexpensive.
- Team based approaches to the insertion and management of central vascular catheters (CVC) has been shown to reduce CVC—associated bloodstream infections by almost 70%.
- In separate studies the use of chlorhexidine baths have been linked to the reduction of MDR acinetobacter bloodstream infections and the colonization and bloodstream infections due to vancomycin resistant enterococci (VRE) and MRSA.
- A single switch from iodophor surgical prep to a chlorhexidine-alcohol prep reduced surgical site infections by 40%.
- A cluster randomized study of ICU patients given routine nasal decolonization and chlorhexidine baths was shown to be superior to options of 1) screening for MRSA and then providing "positives" decolonization and baths or 2) screening and isolation alone.

Controversial Issues

- There are still those who maintain the value of some vertical programs with a spectrum of approaches from total hospital patient culturing and isolation vs screening of high risk surgical patients (those undergoing cardiac surgery and both orthopedic and neurosurgical patients receiving implants).

Suggested Practice

- The platform of a good infection control program should be based on horizontal approaches. The question to be asked is: *What incremental value would an additional vertical program add and at what cost and adverse consequences?*

Summary

Horizontal infection control interventions have a marked effect on total infection rates relative to vertical interventions and usually are much less costly.

References

Wenzel RP, Bearman G, Edmond MB. Screening for MRSA: A Flawed Infection Control Intervention. *Infect Control Hosp Epidemiol*. 2008. 29:1021–8.

Wenzel RP, Edmond MB. Infection Control: The Case for Horizontal Rather than Vertical Infection Interventional Programs. *Internat J Infect Dis*. 2010. (Suppl 4):S 3–5.

Wenzel RP. Minimizing Surgical Site Infections. *N Engl J Med*. 2010. 362:75–7.

Huang SS, Septimus E, Kleinman K, et al. Targeted Versus Universal Decolonization to Prevent ICU Infections. *N Eng J Med* 2013. 8:2255–65.

Edmond MB, Wenzel RP. Screening Inpatients for MRSA—Case Closed. *N Engl J Med*. 2013. 368:2314–5.

CHAPTER 15

Positive Deviance in Infection Prevention

Alexandre Marra, MD

Keywords
Positive deviance; solutions, innovation, initiative, compliance, leadership.

Key Issue

Positive Deviance (PD) is based on the observation that in every community there are certain individuals or groups, whose uncommon practices enable them to find better solutions to problems than their neighbors or colleagues despite having access to the same resources. These individuals are known as positive deviants.

Known Facts

- The PD approach is totally different form from the traditional approach for stimulating performance improvement in any area.
- In PD the healthcare workers (HCWs) decide how the work should be done and they promote discovery among their peers.
- The leadership and managers support frontline workers in implementing new ideas into their routine.
- A core principle of PD is the belief that solutions to seemingly intractable problems already exist. Another important concept is that problems are discovered by members of the community, and the positive deviants with a spirit of creativity and innovation will share experiences, discuss these problems, and remove the barriers to find the solutions.
- There are many descriptions of successful stories of PD in different sectors from public health to education to business.
- PD has also been used to control methicillin resistant *S. aureus* (MRSA) in the healthcare setting.

- Using PD can improve hand hygiene compliance. Nurse managers need to facilitate discussion among frontline workers and give positive deviants opportunities to express their feelings about best practices for hand hygiene and to discuss what needs to be changed, what needs to be improved, what is wrong and what is right.
- One of the strategies from the PD project for improving hand hygiene compliance is to show the number of alcohol gel aliquots dispensed per unit and to compare data and HCW impressions.
- All hospital personnel (doctors, nurses, physical therapists, speech pathologists, nutritionists and pharmacists) need to act as infection preventionists. Moreover, all hospital quality indicators need to be discussed at group meetings. Priorities need to be analyzed and strategies need to be defined. Everyone should understand some specific processes, such as central venous catheter insertion and hand hygiene compliance, and bring valuable information that could be addressed during PD meetings or case discussions.
- Many solutions were suggested by the positive deviants in hospital settings. Some examples include: changing the position of the alcohol rub dispensers to allow easier access and use; putting alcohol gel dispensers on mobile x-ray machines; changing the procedure for monitoring the consumption of alcohol handrub product, which was initially performed by one single staff member each 48 hours and gradually evolved to become the responsibility of every professional involved with patient care at the end of their shifts.

Controversial Issues

- Infection control personnel know that improvement processes have a tremendous impact on the quality of care, but the question remains as to how to initiate and sustain these improvements.
- The first step is to decrease the distance between infection control unit personnel and healthcare workers.
- PD promotes ownership of problems by frontline workers, and empowers the positive deviants to implement infection control prevention processes.

- The next step is to accept and support ideas that arise during the team observations in their daily practice.
- At first glance the strategies employed by the deviants may not seem to be very unusual or innovative.
- The PD challenge is to disseminate these strategies to others.
- The leaders need to believe that PD can advance engagement of front line staff in prevention efforts and implementation of all interventions.
- Participants discuss ways to stimulate a discussion with noncompliant individuals in a positive manner.

Suggested Practice

- Positive deviance tries to improve processes every single day, by analyzing work flow, questioning possible errors, and promoting the view that all tasks are significant as they are important for the final result. And the improvement is continuous as staff, learns together, shares tasks, knowledge and ideas, and continues analyzing all tasks and actions.
- The goal is for the team to be responsible for identifying opportunities for improvement, and to propose solutions and to follow the proceedings.
- The structure and the PD process offer a space for discussion of experiences, ideas and plans that emerge from team participation.
- The exercise to practice thinking can lead to high-impact actions. An example was the idea to place alcohol gel on portable X-rays machines that traverse the hospital, so that radiologic technicians have the ability to use alcohol gel at any time during their activities.
- Most important is that all the changes that have occurred or are occurring are developed by people performing the tasks. The socialization of thought and attitude become the main role of PD.

Summary

Positive deviance (PD) may have an important role for infection prevention and patient safety in the hospital. PD has been applied in the healthcare setting to improve hand hygiene compliance, reduce methicillin resistant *S. aureus* (MRSA), and

reduce bloodstream infections in an outpatient hemodialyis center. PD promotes dialogue among leaders, managers and healthcare workers (HCWs), which is a key factor in estabilishing a safety culture. It also enables cultural changes aimed at empowering frontline workers (the positive deviants) to innovate and improve compliance with infection prevention measures.

References

Buscell P. More we than me: How the fight against MRSA led to a new way of collaborating at Albert Einstein Medical Center. 2008. http://c.ymcdn.com/sites/www.plexusinstitute.org/resource/resmgr/docs/more-we-than-me-mrsa-vol1no5.pdf

Gawande A. Better—A surgeon's notes on performance (1st Edition). New York: Metropolitan Books, 2007.

Jain R, Kralovic SM, Evans ME, Ambrose M, Simbartl LA, Obrosky DS, Render ML, Freyberg RW, Jernigan JA, Muder RR, Miller LJ, Roselle GA. Veterans Affairs initiative to prevent methicillin-resistant *Staphylococcus aureus* infections. *N Engl J Med*. 2011. 364:1419–30.

Lindberg C, Downham G, Buscell P, Jones E, Peterson P, Krebs V. Embracing collaboration: A novel strategy for reducing bloodstream infections in outpatient hemodialysis centers. In press: *Am J Infect Control*. 2013. 41:513–9.

Marra AR, Guastelli LR, Araújo CMP, et al. Positive deviance: a new strategy for improving hand hygiene compliance. *Infect Control Hosp Epidemiol*. 2010. 31:12–20.

Marra AR, Guastelli LR, Araújo CMP, et al. Positive deviance: A program for sustained improvement in hand hygiene compliance. *Am J Infect Control*. 2011. 39:1–5.

Marra AR, dos Santos OFP, Cendoroglo Neto M, Edmond MB. Positive Deviance: A new tool for Infection Prevention and Patient Safety. *Curr Infect Dis Rep*. 2013 Sep 28. Epub ahead of print.

Marsh DR, Schroeder DG, Dearden KA Sternin J, Sternin M. The power of positive deviance. *BMJ*. 2004. 329:1177–79.

Pascale R, Sternin J, Sternin M. The power of positive deviance: How unlikely innovators solve the world's toughest problems. Boston: Harvard Business Press, 2010.

Positive Deviance Initiative. http://www.positivedeviance.org

Singhal A, Buscell P, Lindberg C. Inviting Everyone: Healing Healthcare through Positive Deviance. Bordentown: Plexus Press, 2010.

Ribeiro de Macedo RD, Oliveira Jacob EM, Pio da Silva V, et al. Positive deviance: Using a nurse call system to evaluate hand hygiene practices. *Am J Infection Control*. 2012. 40:946–50.

CHAPTER 16

Bundles in Infection Prevention and Safety

Rebekah W. Moehring, M.D., M.P.H.

Key Issue

Delivery of evidence-based infection prevention interventions is highly dependent on an individual provider's knowledge, motivation, and skills, which can result in poor or inconsistent implementation of best practices. Care "bundles" are small, straightforward, sets of evidence-based practices that,when implemented collectively, improve the reliability of their delivery and improve patient outcomes.[1]

Known Facts

- Elements of a care bundle are individual interventions with high evidence-basis (Level 1, randomized controlled trial evidence) of improving patient outcomes.
- A small number of elements, between four and six, are contained within a bundle for simplicity and ease of delivery.
- Every element of the bundle must be implemented with complete consistency to achieve the optimal effect of the collective bundle. Providers must follow every bundle element for every patient, every time. The goal of grouping the elements is to promote positive habit-forming behavior among providers and thus reliable care processes.
- Bundle elements must occur at the same time or same care setting in order to ensure they are performed together. As an example, the central venous catheter insertion bundle is completed once upon inserting a new catheter, followed by daily reassessments while the catheter is in place.
- Elements of a bundle are measured in an "all or nothing" manner to simplify assessment of compliance for feedback to providers and to emphasize the completion of every component.[2]

- Three well-known and widely practiced care bundles promoted by the Institute for Healthcare Improvement (IHI)[3] include the following:
  1. Central Line Bundle for prevention of catheter related bloodstream infections[4,5]
     a. Hand hygiene
     b. Maximal barrier precautions upon insertion
     c. Chlorhexidine skin antisepsis
     d. Optimal catheter site selection, with avoidance of the femoral vein for central venous access in adult patients
     e. Daily review of line necessity with prompt removal of unnecessary lines
  2. Ventilator Bundle[6,7]
     a. Elevation of the head of the bed
     b. Sedation vacations and assessment of readiness to extubate
     c. Peptic ulcer disease prophylaxis
     d. Deep vein thrombosis prophylaxis
     e. Daily oral care with chlorhexidine
  3. Severe Sepsis 3-Hour Resuscitation Bundle for management of patients with severe infections[8]
     a. Measure lactate level
     b. Obtain blood cultures prior to administration of antibiotics
     c. Administer broad spectrum antibiotics
     d. Administer 30mL/kg crystalloid for hypotension or lactate ≥4mmol/L
- The central line bundle is credited with the impressive decline in incidence of central line associated infections over the past decade.[9]
- Bundled interventions are effective way to implement change and improve the "culture" of patient safety by promoting teamwork, and providing feedback and accountability to improve care.[3,10]

Controversial Issues

- Additional bundle elements (e.g. greater than 6) will jeopardize simplicity and may negatively impact the bundle's effectiveness or consistency of delivery.
- Bundle elements must not be static, but must adapt to changing evidence and best practices.
- When bundled interventions produce evidence of improved patient outcomes, it is difficult to separate the relative impact of any single element contained within the bundle. Thus, when looking to update or improve the bundle, it is difficult to remove any one element for another.
- Individuals focused on performance improvement may confuse a "bundle" with a "checklist."[1] In general, checklists may include elements that have good evidence or theoretical basis for best practices, but not the high-level evidence that make up the key elements of a bundle. Checklists may include extra, optional tasks or reminders; in contrast, every element of a bundle is critical and must be completed every time for every patient.
- Given the recent popularity and success of the central line and ventilator bundles, individuals may be tempted to label any multifaceted intervention as a "bundle." However, a true bundle must contain scientifically proven, simple interventions, with the goal of adding consistency for optimal patient outcomes.
- Care bundles may include elements that do not directly relate to infection prevention (e.g. deep venous thrombosis prophylaxis in the ventilator bundle).

Suggested Practice[2]

- Identify areas where evidence-based infection prevention practices are inconsistently followed to target for a bundled intervention. Existing bundles promoted by the IHI are a good place to begin (*see above*).[3]
- Identify a set of 4 to 6 evidence-based interventions that apply to a group of patients with a common disease ina common practice setting, and that can be delivered as part of a single process of care.

- Recruit and motivate providers to deliver the interventions every time for every patient with an indication.
- Measure compliance as "all or nothing;" feed back compliance data to providers.
- Adjust the delivery system and address logistical concerns to make it easy to deliver the bundle as part of the system of care and workflow.
- Measure relevant patient outcomes to determine the effect of the bundle.

Summary

The concept of care bundles grew out of the quality movement, largely driven by the Institute for Healthcare Improvement's 100,000 lives campaign launched in 2006.[11] Well-known and successful, nationwide quality initiatives resulted in widely implemented standards for processes of careto improve the delivery of evidence-based infection prevention practices.

Care bundles are made up of four to six elements that each has a high level of evidence basis for incorporation into routine practice. Consistent delivery of each element is achieved by grouping these elements together as a single process, encouraging and motivating providers to deliver them for every patient every time, measuring compliance with the bundle as a whole, and then feeding these data back to further motivate and establish accountability.

The most well-known model of a successful infection prevention care bundle is the central line bundle. This intervention includes elements at the time of insertion and for daily reassessments while the catheter remains in place. Implementation of the central line bundle is supported by a high level of evidence demonstrating reduction in rates of central-line associated bloodstream infections.[5] Similarly, this bundle of interventions has been credited with the nationwide decline in incidence of central line associated infections over the last decade.[9] These standard, bundled practices are now routine for many providers caring for patients with central lines. Executing all components of the central line bundle and reporting compliance data for the bundle processes are now considered a standard for accredited hospitals.[4]

Due to prior success of bundled interventions, it is tempting to create new management and prevention bundles for many different disease processes. In fact, the word "bundle" has taken on a magical quality in the infection prevention literature. However, there is one significant problem with grouping multifaceted interventions together when testing them in research or quality improvement settings: the effect of each element of the bundle cannot be distinguished from the other concurrently implemented elements. Thus, it is difficult to determine which part of a bundle may be responsible for the positive effect on patient outcomes if each element is not tested individually. When the time comes to update or adjust a bundle to incorporate new evidence-based practice, it is challenging to define which elements are essential and which can be retired. Further, the addition of additional steps in the process may cause the bundle to lose its simplicity, which is the essential quality that makes a care bundle easy to implement and effective in real-world practice.

Care bundles serve to improve healthcare worker practice, and as with any intervention, the implementation of the bundle must be carefully planned and supported. Simply using the term "bundle" and declaring it to be the standard will not achieve success without ongoing motivation and data feedback.[12] For programs wishing to capitalize on the implementation success of bundling, a key step to ensure reliable use is measurement and feedback of bundle compliance. Auditing of bundle compliance should be as an "all or nothing" measurement; in other words, if one element is not followed then there is no partial credit for bundle compliance. This ensures that every element is followed every time, instead of inconsistent or partially compliant practice.

Given the prior successes, we can expect to see development of more bundled interventions for infection prevention, patient safety, and healthcare quality initiatives of the future. Indeed, the use of care bundles can systematically improve the consistent delivery of high-quality care and evidence-based practice.

References:

[1]Haraden C. Institute for Healthcare Improvement Website: What is a bundle? http://www.ihi.org/knowledge/Pages/ImprovementStories/WhatIsaBundle.aspx (Accessed 14 October 2013).

[2]Marwick C, Davey P. Care bundles: The holy grail of infectious risk management in hospital? *Current opinion in infectious diseases*. August 2009. 22(4):364–369.

[3]Institute for Healthcare Improvement Website: Evidence-Based Care Bundles. http://www.ihi.org/knowledge/Pages/Changes/default.aspx (Accessed 14 October 2013).

[4]O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis*. May 2011. 52(9):e162–193.

[5]Pronovost P, Needham D, Berenholtz S, et al. An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. *N Engl J Med*. December 28, 2006. 355(26):2725–2732.

[6]Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Joint Commission journal on quality and patient safety/Joint Commission Resources*. May 2005. 31(5):243–248.

[7]Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care-associated pneumonia, 2003: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR*. March 26, 2004. 53(RR-3):1–36.

[8]Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Critical Care Medicine*. February 2013. 41(2):580–637.

[9]Vital signs: Central line-associated blood stream infections—United States, 2001, 2008, and 2009. *MMWR*. March 4, 2011. 60(8):243–248.

[10]Jain M, Miller L, Belt D, King D, Berwick DM. Decline in ICU adverse events, nosocomial infections and cost through a quality improvement initiative focusing on teamwork and culture change. *Quality and Safety in Health Care*. August 2006. 15(4):235–239.

[11]Berwick DM, Calkins DR, McCannon CJ, Hackbarth AD. The 100,000 lives campaign: Setting a goal and a deadline for improving health care quality. *JAMA*. January 18, 2006. 295(3):324–327.

[12]Furuya EY, Dick A, Perencevich EN, Pogorzelska M, Goldmann D, Stone PW. Central line bundle implementation in US intensive care units and impact on bloodstream infections. *PLoS One*. 2011. 6(1):e15452.

CHAPTER 17

The Hospital Environment

William A. Rutala, PhD, MPH and
David J. Weber, MD, MPH

In the last thirty years, evidence has accumulated that the hospital environment represents an important source of health care associated pathogens for hospitalized patients. Potential environmental sources of pathogens include air (e.g., *Aspergillus*), water (e.g., *Legionella*), environmental surfaces (e.g., *Clostridium difficile*), medical devices e.g., endoscopes), and many other items in the patient's environment.

Key Issues

Pathogens may spread from an inanimate environmental reservoir to the patient by one or more routes including airborne, common-vehicle, contact or vector-borne. Airborne transmission describes organisms that have a true airborne phase as part of their pattern of dissemination, such as tuberculosis and varicella. In common-vehicle spread, a contaminated inanimate vehicle serves as the mechanism of transmission of the infectious agent to several people. Common vehicles may include ingested food or water; blood and blood products; and infused products such as medications or intravenously administered fluids. In contact spread, the patient has contact with the source and that contact is either direct, indirect, or droplet. Direct contact occurs when actual physical contact occurs between the source and the patient. Indirect contact refers to transmission from the source to the patient through an intermediate object, which is usually inanimate (e.g., endoscopes). Finally, droplet spread refers to the brief passage of an infectious agent through the air when the source and patient are within several feet of each other. Arthropod-borne health care associated infections have not been reported in the United States.

Known Facts

In this section, we will briefly review environmental reservoirs and the pathogens that have been linked with infection in patients admitted to the hospital (*Table 17.1*). We attempt to indicate the strength by which the linkage to health care associated infections has been investigated and the control measures.

Controversial Issues

Few of the aforementioned recommendations (*Table 17.1*) regarding methods to prevent transmission of pathogens from the environment to patients are based on controlled trials. Rather, the recommendations are based on the success of interventions used to control outbreaks.

There are many unresolved issues associated with the environment that are related either to the degree to which some specific environmental items poses a hazard (e.g., computer keyboards) or to the appropriate control to a known environmental hazard (e.g., routine microbiologic sampling of water for *Legionella*). Among the unresolved issues in the area of environmental hazards or their control are:

- the risks and benefits of animals used for animal-assisted therapy;
- the hazard posed by contaminated personal devices such as stethoscopes, hand-held computers, pagers;
- the hazards associated with bioinformatic devices such as computer keyboards and touch-screen devices;
- the benefit of new surface decontamination technologies such as UV light, hydrogen peroxide vapor;
- the need for protective isolation (including limitation of fresh fruits/vegetables, flowers, potted plants);
- the role of potable water as a source of fungal infections in immunocompromised patients;
- the need to routinely culture potable water for *Legionella*;
- Role of attire (e.g., long sleeves, coats).

Table 17.1 Reservoirs of Infectious Agents in the Environment[a,b]

Reservoir Reservoir	Associated Pathogens	Transmission	Significance[a]	Prevention and Control
Air Filters	*Aspergillus*		Moderate	Replace soiled filters periodically
Laundry chutes	*Pseudomonas, Staphylococcus*	Airborne	Low	Proper design and placement, chute doors
False ceilings	*Rhizopus*	Airborne	Moderate	Barrier protection during reconstruction
Fireproof materials	*Aspergillus*	Airborne	Low	Add fungicide to moist material
Humidifiers/nebulizers	*Acinetobacter, Legionella, Pseudomonas*	Airborne, Droplet	High	Avoid when possible; use sterile water; disinfect between uses
Outside construction/ Inadequate ventilation	*Rhizopus, Aspergillus*	Airborne	High	Use at least 95% efficiency filters in hospital; filter all hospital air
Pigeon droppings	*Aspergillus*	Airborne	Low	Maintain filter efficiency; filter all hospital air
Inhaled medications	*Pseudomonas, Klebsiella, Serratia*	Inhalation	Moderate	Sterile preparation by pharmacy
Showers	*Legionella, Group A Streptococcus*	Inhalation	Low	Prohibit with immunocompromised patients
Ventilators	*Pseudomonas*	Inhalation	Moderate	Follow current CDC guidelines
Bronchoscopes	*Pseudomonas, Mycobacteria*	Contact	High	Pseudoepidemics common; follow disinfection guidelines
Contaminated germicides	*Pseudomonas, Bacillus*	Contact	High	Avoid extrinsic contamination and seek verification of manufacturer's microbicidal efficacy claims
Dialysis water	GNR	Contact	Moderate	Follow guidelines: dialysate >2000 organisms/ml; water >200 organisms/ml
ECG electrodes	*S. aureus*, GNR	Contact	None	Disinfect after use or use disposable leads

Table 17.1 Reservoirs of Infectious Agents in the Environment[a,b] (continued)

Reservoir Reservoir	Associated Pathogens	Transmission	Significance[a]	Prevention and Control
Elasticized bandages	*Zygomycetes*	Contact	Moderate	Avoid in immunocompromised patients or over nonintact skin
Electronic thermometers	*C. difficile*	Contact	Low	New probe cover for each patient, disinfect each day and when visibly contaminated
Endoscopes	*Salmonella, Pseudomonas*	Contact	High	Follow proper disinfection procedures
Faucet aerators	*Pseudomonas, Stenotrophomonas*	Contact, Droplet	Low	No precautions necessary
Ice baths	*Staphylococcus, Ewingella*	Contact	Moderate	Avoid direct contact with ice to cool IV solution/syringes; use closed system for thermodilution
Intraaortic balloon pump	*Pseudomonas*	Contact	Low	Add germicide to water reservoir
Mattresses	*Pseudomonas, Acinetobacter*	Contact	Moderate	Use intact plastic cover, disinfect cover between patients
Plaster	*Pseudomonas, Bacillus*	Contact	Moderate	Use judiciously in immunocompromised patients or over nonintact skin
Potable water	*Pseudomonas, Serratia,* non-tuberculous *Mycobacteria, Acinetobacter, Legionella*	Contact, Droplet, Ingestion	High	Follow CDC and public health guidelines
Water Walls, Decorative Fountains	*Legionella*	Droplet	Moderate	Prudent to avoid in immunocompromised patient care areas
Pressure transducers	*Pseudomonas, Enterobacter, Serratia*	Contact	Moderate	Disinfect transducer between patients and replace disposable dome/transducer; use aseptic technique
Sinks	*Pseudomonas*	Contact, Droplet	Low	Use separate sinks for hand washing and disposal of contaminated fluids

Table 17.1 Reservoirs of Infectious Agents in the Environment[a,b] (continued)

Reservoir Reservoir	Associated Pathogens	Transmission	Significance[a]	Prevention and Control
Suction apparatus	*Klebsiella, Salmonella, Pseudomonas, Proteus*	Contact, Droplet	Low	Avoid backflow and aerosolization; disinfect between patient use
Thermometers (glass)	*Salmonella*	Contact	Moderate (rectal)	Disinfect between use
Tubs for immersion	*Pseudomonas*	Contact	Moderate	Add germicide to water; drain and disinfect after each use
Urine-measuring devices	*Serratia*	Contact	Moderate	Disinfect between patients, good hand washing
Water baths	*Pseudomonas, Acinetobacter*	Contact	Moderate	Add germicide to water bath or use plastic overwrap
Electric breast pumps	*Pseudomonas, Klebsiella, Serratia*	Ingestion	Moderate	Follow guidelines
Enteral feeds	GNR	Ingestion	Low	Use sterile commercial feeds or aseptically prepared feeds; refrigerate; minimize manipulation; use closed administration set
Food[a]	*Salmonella, S. aureus, Clostridium, Vibrios,* hepatitis A, Norovirus	Ingestion	High	Follow local public health guidelines
Ice/Ice machines	*Legionella, Enterobacter, Pseudomonas, Salmonella, Cryptosporidia*	Ingestion, Contact	Moderate	Periodic cleaning; use automatic dispenser
Medications (extrinsic)	*Staphylococcus, Streptococcus,* GNR	Injection, Inhalation	High	Use aseptic technique
Compounding pharmacies	Fungi	Injection	High	Ideally, conform with federal manufacturing standards on on sterile/aseptic preparation

Table 17.1 Reservoirs of Infectious Agents in the Environment[a,b] (continued)

Reservoir Reservoir	Associated Pathogens	Transmission	Significance[a]	Prevention and Control
Air-fluidized beds	Enterococcus	Contact	Low	Follow manufacturer's recommendations
Carpets	—	—	None	Prudent to avoid in areas of heavy soiling
Privacy curtains	MRSA, VRE	Contact	None	Prudent to minimize risk (e.g, disinfect, laundry after Contact Precaution patients)
Flowers	GNR	—	None	Prudent to avoid in the ICU and immunocompromised patients' rooms
Fresh vegetables	Aerobic GNRs, *Listeria*	—	None	Prudent to avoid in immunocompromised patients
Pets	*Malassezia, S. aureus*	Contact	Low	Prudent to avoid in hospital setting (except service animals or animal-assisted therapy)
Stethoscopes	*Staphylococcus*	—	None	Prudent to clean periodically with alcohol
Toilets	GNR	Droplet	Low	Utilize good hand washing
Medical waste (not sharps)	—	—	None	Follow state and federal regulations
Eyewash stations	*Pseudomonas, Legionella*	Contact	Low	Have potable water available for eye flush
Toys	*Pseudomonas, Rotavirus*	Contact	Low	Disinfect toys between patients, avoid water-retaining bath toys
Computer keyboards	*S. aureus, Acinetobacter*	Contact	Low	Disinfect periodically, hand wash after use
Surfaces	VRE, MRSA, *C. difficile*	Contact	Moderate	Hand wash with soap and water/alcohol after contact with patient environment; disinfect surfaces periodically and terminally

[a] High, multiple well-described outbreaks due to this reservoir; moderate, occasional well-described outbreaks; low, rare well-described outbreaks; none, actual infection not demonstrated; GNR, gram-negative rods; VRE, vancomycin-resistant *Enterococcus*; MRSA, methicillin resistant *Staphylococcus aureus*.

[b] Modified from 1, 2.

Suggested Practice

Fortunately in the past ten years, a number of authoritative guidelines have been published that provide scientifically-based recommendations to prevent transmission of health care associated pathogens to the patient from environmental reservoirs.

- Hand hygiene before and after patient contact is crucial to prevent transmission of pathogens from the patient's environment to other patients.[3]
- All hospital construction and renovation must utilize recent guidelines to prevent acquisition of airborne fungi (such as *Aspergillus*) to immunocompromised patients.[4]
- Proper cleaning, disinfection/sterilization of reusable medical devices.[1,2,5–7]
- Aseptic manipulation of all medications.[1]
- Proper surveillance for *Legionella* and institution of control measures in the event of *Legionella* cases.[4]
- Surface disinfection of the environment to prevent transmission of methicillin resistant *S. aureus*, vancomycin-resistant *Enterococcus*, and *C. difficile*.[1]

Summary

The environment continues to serve as a source of health care associated infections. Key measures to reduce environment associated nosocomial infections include ongoing surveillance; appropriate evaluation of excess cases (epidemics); proper cleaning, disinfection, and sterilization of patient devices and the surface environment; and adherence to recommendations for protecting patients during building renovations and construction. New issues (e.g., computer keyboards, reprocessing prion contaminated medical devices, emerging pathogens such as multidrug-resistant organisms, SARS) will continue to challenge the infection control clinician for the foreseeable future.

References

[1]Weber DJ, Rutala WA. The Environment as a Source of Nosocomial Infections *in* Prevention and Control of Nosocomial Infections (4th Edition), Wenzel RP (Ed). Baltimore: Lippincott Williams & Wilkins, 2003. Pgs. 575–595.

[2]Rutala WA, Weber DJ. Environmental Issues and Nosocomial Infections *in* Infection Control in Intensive Care. Farber BF (Ed). Churchill Livingstone, 1987. Pgs. 131–171.

[3]Boyce JM, Pittet D. Healthcare Infection Control Practices Advisory Committee, HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Guideline for Hand Hygiene in Healthcare Settings. *Infect Control Hosp Epidemiol*. 2002. 23:S3–S40.

[4]Centers for Disease Control. Guidelines for Environmental Infection Control in Healthcare Facilities, 2003. *MMWR*. 2003. 52(No. RR-10):1–44.

[5]Rutala WA, Weber DJ. Healthcare Infection Control Practices Advisory Committee, 2008. CDC Guideline for Disinfection and Sterilization in Healthcare Facilities. http://www.cdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf

[6]Rutala WA, Weber DJ. Selection and use of disinfectants in healthcare *in* Hospital Epidemiology and Infection Control, Mayhall CG (Ed). New York: Lippincott Williams & Wilkins, 2012. Pgs. 1180–1212.

[7]Petersen B, Chennat J, Cohen J, Cotton PB, Greenwald DA, Kowalski TE, Krinsky ML, Park WG, Pike IM, Romagnuolo J, Rutala WA. Multisociety guideline on reprocessing flexible GI endoscopes: 2011. *Infect Control Hosp Epidemiol*. 2011. 21:527–537.

CHAPTER 18

Food: Considerations for Hospital Infection Control

Susan Assanasen, MD, and
Gonzalo M.L. Bearman, MD, MPH

Key Issues

- The responsibility of a hospital food service is to provide nutritious and safe food to patients and employees.
- Although food safety has dramatically improved in the last decades, outbreaks of health care associated gastroenteritis continue to occur worldwide.[1,2]
- A growing number of hospitalized patients are susceptible to infectious diseases. These include the elderly and immunocompromised hosts.
- Additionally, complex and large-scale production of food and water is a potential target for bioterrorism.
- The outbreaks may result from breakdown in only one-step of food safety control measures.

Known Facts

- Foodborne illnesses can be caused by bacteria, virus, parasites, prions, toxins, or chemical contaminants.
- The clinical presentations are broad and can be quick in onset, such as in toxin mediated outbreaks. Others have long incubation periods, such as hepatitis A, and prion associated diseases.
- Due to highly susceptible and frail populations, such as the elderly, outbreaks of health care associated gastroenteritis have a higher crude mortality than their community acquired equivalents.[2,3]
- Outbreaks of highly contagious organisms such as norovirus (attack rates>50%) may also affect staff and visitors. This has resulted in ward closure in up to 44% of reported outbreaks.[4]

- Common foodborne pathogens that are easily transmitted through food and can cause severe illness are norovirus, *Salmonella*, *Clostridium perfringens*, *Shigella*, Enterohemorrhagic or Shigatoxin producing *E. coli*, *Campylobacter*, *Listeria monocytogenes*, *Vibrio*, *Yersinia enterocolitica, Staphylococcus aureus*, Hepatitis A virus, *Giardia*, and *Cryptosporidium*.[5] Incidence varies according to geographic area, season, and availability of laboratory diagnosis, and change over time.[1,2]
- Fresh vegetables or fruits have been implicated as vehicles for foodborne pathogens as these products are typically sold to the consumer in ready-to-eat form, do not generally contain preservatives, and rarely undergo any heat processing prior to consumption.
- Noroviruses (formerly called Norwalk-like viruses) are considered the most common cause of sporadic gastroenteritis in developed countries. These are particularly prevalent in nursing homes and hospitals.[6]
- Health care associated outbreaks caused by noroviruses are difficult to prevent and control due to:[6,7]
  1. Low infectious dose (10–100 viral particles).
  2. Very short incubation period (12–48 h).
  3. Resistance to inactivation by freezing, heating to 60°C, routine chlorine of water, low pH levels, and treatment with ethanol, or detergent-based cleaners.
  4. Multiple routes of transmission, including faecal-oral route and probable respiratory spread via aerosols of vomitus.
  5. Genetic variability and short-term immunity.
  6. Prolonged viral shedding after recovery (several weeks).
- Eggs are major vehicles for *Salmonella* infection in humans. Egg-associated salmonellosis is linked to external contamination of the shell during passage through the hen cloaca, and internal contamination by penetration of the bacteria through the eggshell, via microscopic cracks.[8]

- Currently, there are increasing reports of multidrug-resistant zoonotic foodborne infections. Emerging resistance of *Salmonella* and *Campylobacter* species contribute to excess mortality and morbidity in both outbreaks and sporadic cases of illnesses.[9]
- *Listeria monocytogenes* is a ubiquitous pathogen and has been recovered in plants, soil, silage, sewage, slaughterhouse waste, human feces (1–10%), animal feces, processing environments, and catering facilities. Although Listeriosis is uncommon, the fatality rate in high-risk individuals (such as pregnant women, older people, and immunocompromised hosts) is as high as 20–50%. The organism can proliferate at –18 to 10°C.[10] Consequently, Listeria may be transmitted in foods that have been kept properly refrigerated. Thorough cooking to 75°C can destroy the *Listeria*. In developed countries, the contamination in ready-to-eat (RTE) meats is primarily due to post-cooking contamination.
- *Cryptosporidium*, and *Giardia* are resistant to routine chlorination of water. In 1993, *Cryptosporidium* caused the largest documented outbreak of gastrointestinal disease in a developed country (estimated 403,000 cases) due to contaminated drinking water supply.[11]
- Although *Clostridium difficile,* a common cause of health care associated diarrhea, is transmitted via contaminated hands and environment, community-acquired *C.difficile* may be acquired by exposure to spores from soil, contaminated foods, and exposure to household contacts with *C.difficile* diarrhea.[12]
- Hazard Analysis Critical Control Point (HACCP) is a systematic approach for the identification, evaluation, and control of potential hazards at every stage of food operation. This system emphasizes the role of continuous problem solving and prevention rather than solely relying on spot-checks of manufacturing processes and random samples of finished food products.[13]
- HACCP involves major seven principles:
  1. Analyzing hazards;
  2. Identifying critical control points (CCPs);

3. Establishing preventive measures with critical limits for each control point;
4. Establishing procedures to monitor the critical control points;
5. Establishing corrective actions to be taken when monitoring shows that a critical limit has not been met;
6. Establishing procedures to verify that the system is working properly; and
7. Establishing effective recordkeeping to document the HACCP system.

- Currently, HACCP is recognized as an effective food safety assurance system. The success of a HACCP system depends on training and constant supervision of employees in the importance of their role in producing safe foods.
- Although implementation of HACCP system on hospital food service is still voluntary in most countries, several hospitals have adopted these principles to ensure that hospital food is safe for consumption by high-risk patients.
- To provide safe food in hospitals, adherence to HACCP is critical. In a study by the Food and Drug Administration (FDA), important foodborne illness risk factors in US hospitals were:[14]
  1. Improper holding, time and temperature of the food;
  2. Contaminated equipment and inadequate protection from contamination; and
  3. Poor personal hygiene and lack of adequate toileting and hand washing facilities.
- Food-borne bacteria can multiply if food is not maintained at an appropriate temperature (below 5˚C or 41˚F for refrigeration and above 57˚C or 135˚F for hot holding), and if there are delays between food preparation and distribution. Enteric viruses are particularly problematic pathogens as they are more resistant to heat, disinfection, and pH changes than enteric bacteria. In addition, viral contamination does not alter the appearance, smell or taste of food. Lastly, viruses can survive for days or weeks on hospital environment.
- Hand washing can effectively reduce the transmission of bacteria and viruses.

- Hand washing with soap and water followed by hand drying with paper towels (not hot air dryers) is the standard procedure for hand decontamination in food safety practices.[15] Alcohol-based hand rubs are inferior as these products neither inactivate viral pathogens such as norovirus, nor can destroy the spores of *C.difficile*.

Controversial Issues

- Most health care associated foodborne pathogens are spread by the faecal-oral route. The primary source of outbreaks may be contaminated food/water, and infected/colonized patient, visitor, staff, or food handler. Contact with infected/colonized animals may also cause enteric diseases, especially in immunocompromised hosts.[16]
- Most enteric outbreaks are caused by a single agent, but coinfections may occur, especially if the source is sewage contaminated food or water.
- DNA fingerprinting of foodborne bacteria by PFGE is available for *E coli* O157:H7, *Salmonella*, *Listeria monocytogenes*, *Shigella*, and *Campylobacter* isolates.
- The CDC estimates that approximately 18–20% of foodborne outbreaks are associated with an infected food worker.[17] Transmission of foodborne pathogens can occur from pre-symptomatic, symptomatic and post-symptomatic food handlers. Transmission of infections is dependent upon the amount of infectious agent excreted, the degree of contamination, the compliance and effectiveness of personal hygiene, the stability of pathogens in food and environment, the virulence of organisms, the food type/amount consumed, cooking process, food preservation techniques, and immune status of patients.
- Outbreak investigations of health care associated gastroenteritis are complicated and only few illnesses are definitively linked to food.
  1. In some situations, it is not clear whether workers are the cause or the victims of enteric outbreaks. This is because some healthcare workers may deny infection or illness for a variety of reasons.

2. Transmission of organisms during outbreaks frequently occurs by multiple sources, including person-to-person contact, contaminated environments (fomites), consumption of contaminated food or water, and airborne inhalation.

Suggested Practice

- For the control of foodborne infections in the hospital, it is necessary to:
  1. Optimize and standardize methods for the detection of foodborne pathogens;
  2. Develop rapid surveillance networks to detect and report outbreaks at an early stage;[18]
  3. Emphasize the importance of food safety quality control and management systems; and
  4. Heighten awareness about the presence and spread of these organisms by foodhandlers and promote the good hygienic practices.
- The hospital food service must develop a food safety management system, such as HACCP, that meets food standard requirements. This should be fully reviewed by certified food safety professionals or local, external inspections. All food should be obtained from approved sources in compliance with Federal, State, and local laws and regulations.
- Foods containing raw or partially cooked eggs, fish, and meat should not be served.
- Food containing unpasteurized milk and fruit juices should not be served.
- Pests and flies should be controlled to reduce the risk of food contamination in hospitals.
- Powdered infant formula (PIF) is not a sterile product. To reduce the risk of infection, the reconstitution of powdered formula should be undertaken by caregivers using good hygienic measures and in accordance with the product manufacturer's food safety guidelines.[19]
- All food handlers must be aware that high standards of personal hygiene are important. In the hospital setting, food handlers also include nurses or domestic staff who distribute or serve meals. Therefore, these personnel should be educated about food hygiene and HACCP.

- Bare hand contact of ready-to-eat foods should be eliminated through the use of gloves, bakery papers and food handling utensils.
- The "touchless or hands free" faucets and paper towel dispensers are preferred to reduce the risk of cross-contamination.
- All food handlers should wash their hands and exposed portions of their arms:[20]
  1. Before engaging in food preparation, including working with exposed food, clean equipment and utensils, and unwrapped single service and single-use articles;
  2. After touching bare human body parts other than clean hands and clean, exposed portions of arms;
  3. After using the toilet room;
  4. After caring for or handling service or aquatic animals
  5. After coughing, sneezing, using a handkerchief or disposable tissue, using tobacco, eating, or drinking;
  6. After handling soiled equipment or utensils;
  7. During food preparation, as often as necessary to remove soil and contamination and to prevent cross contamination when changing tasks;
  8. When switching between working with raw food and working with ready-to-eat food;
  9. Before donning gloves for working with food; and
  10. After engaging in other activities that contaminate the hands.
- All food handlers shall keep their fingernails trimmed, filed, and maintained so the edges and surfaces are cleanable and not rough.
- Food handlers who have direct contact to unwrapped food, clean equipment, utensils, and linens should wear clean outer clothing and wear hair restraints such as hats, hair coverings or nets, beard restraints, and clothing that effectively covers body hair.
- All food handlers with vomiting, diarrhea, jaundice, sore-throat with fever, and infected or draining skin lesions must stop working immediately and report to their manager and to the hospital's Occupational Health Department.[20]

- Any cuts, wounds, or open sores on the hands and exposed portions of their arms must be completely covered by impermeable bandage. The lesions on other parts of the body must be covered by a dry, durable, tight-fitting bandage.
- Criteria for the return to work of an infected or colonized food handler with a foodborne pathogen are varied. The details are available at http://www.cfsan.fda.gov/~acrobat/fc05-2.pdf.
- Early case identification of foodborne illnesses can prevent further transmissions. Through early detection, the identification and removal of contaminated products from the commercial market can be expedited.
- Physicians should promptly report hospitalized cases of enteric infections to the infection control team and to the appropriate public health authorities. In addition, physicians and other healthcare professionals can help prevent and control foodborne diseases by educating their patients about the risks of foodborne illness, and providing sound advice on safe food-handling and consumption practices.
- Once an outbreak of health care associated gastroenteritis is suspected, infection control measures should be instituted immediately, prior to the results of confirmatory tests. The three most important actions during an outbreak are:
  1. Effective hand hygiene with soap and drying with hand towels;
  2. Isolation of affected patients, restriction of movement of staff, patients and visitors and exclusion of affected staff;
  3. Enhanced cleaning of the environment and equipment with appropriate disinfectants, such as sodium hypochlorite at 1000 ppm for suspected norovirus outbreaks, and at 5000 ppm (1:10 dilution of household bleach) for *C.difficile* outbreaks.[21,22]
- The IC team should be invited to help in the evaluation of the catering contract, set up quality measures such as HACCP, and participate in the inspection of hospital food handling areas.

- In high prevalence areas of Hepatitis A virus (HAV) infections, vaccination should be considered for all food handlers not immune to HAV. Due to the low incidence of HAV infection and high cost of vaccine, mass immunization for all food service workers in the US is not cost effective, except during epidemics.
- A low microbial diet is recommended for hematopoietic stem cell transplant (HSCT) recipients for at least 3 months after transplantation and until all immunosuppressive drugs are discontinued.[23] Besides general food safety practices, HSCT recipients should not eat any raw or undercooked meat, seafood, and eggs or foods that might contain them (e.g., certain preparations of hollandaise sauce, Caesar and other salad dressings, homemade mayonnaise, and homemade eggnog). HSCT recipients should avoid contact with animal feces to reduce the risk for toxoplasmosis, cryptosporidiosis, salmonellosis, and campylobacteriosis.
- Strain-specific recombinant norovirus-like particles (VLPs) are being evaluated as a potential vaccine for prevention of norovirus infection or illness.

Summary

- Health care associated enteric outbreaks, although rare, have been reported.
- Incorporation of HACCP principles at every stage of food handling is crucial for ensuring food safety.
- Food processors, manufacturers, wholesalers, retail outlets, and restaurants play a key role in maintaining the safety of food products and food ingredients.
- Strict implementation of temperature control and hygienic measures is the most important preventive measure in the hospital setting.
- Effective hand washing with soap and water before and after the handling of all foodstuffs is critical for infection control.
- To reduce the fecal oral transmission of gastrointestinal pathogens from the contaminated hospital environment, patients and their families should be educated on proper personal hygiene and sanitation.

References

[1]Lynch M, Painter J, Woodruff R, Braden C, Centers for Disease Control and Prevention. Surveillance for Foodborne-Disease Outbreaks—United States, 1998–2002. *MMWR Surveill Summ*. November 10, 2006. 55(10):1–42.

[2]Meakins SM, Adak GK, Lopman BA, O'Brien SJ. General Outbreaks of Infectious Intestinal Disease (IID) in Hospitals, England and Wales, 1992–2000. *J Hosp Infect*. January 2003. 53(1):1–5.

[3]Kendall PA, Hillers VV, Medeiros LC. Food Safety Guidance for Older Adults. *Clin Infect Dis*. May 1, 2006. 42(9):1298–304.

[4]Hansen S, Stamm-Balderjahn S, Zuschneid I, Behnke M, Ruden H, Vonberg RP, et al. Closure of Medical Departments During Nosocomial Outbreaks: Data From a Systematic Analysis of the Literature. *J Hosp Infect*. April 2007. 65(4):348–53.

[5]American Medical Association; American Nurses Association-American Nurses Foundation; Centers for Disease Control and Prevention; Center for Food Safety and Applied Nutrition, Food and Drug Administration; Food Safety and Inspection Service, US Department of Agriculture. Diagnosis and Management of Foodborne Illnesses: A Primer for Physicians and Other Healthcare Professionals. *MMWR Recomm Rep*. April 16, 2004. 53(RR-4):1–33.

[6]Centers for Disease Control and Prevention (CDC). Norovirus Activity—United States, 2006–2007. *MMWR* August 24, 2007. 56(33):842–6.

[7]Estes MK, Prasad BV, Atmar RL. Noroviruses Everywhere: Has Something Changed? *Curr Opin Infect Dis*. October 19, 2006. (5):467–74.

[8]Braden CR. *Salmonella enterica* Serotype Enteritidis and Eggs: A National Epidemic in the United States. *Clin Infect Dis*. August 15, 2006. 43(4):512–7.

[9]Molbak K. Human Health Consequences of Antimicrobial Drug-Resistant *Salmonella* and Other Foodborne Pathogens. *Clin Infect Dis*. December 1, 2005. 41(11):1613–20.

[10]Ramaswamy V, Cresence VM, Rejitha JS, Lekshmi MU, Dharsana KS, Prasad SP, et al. *Listeria*—Review of Epidemiology and Pathogenesis. *J Microbiol Immunol Infect*. February 2007. 40(1):4–13.

[11]Dawson D. Foodborne Protozoan Parasites. *Int J Food Microbiol*. August 25, 2005. 103(2):207–27.

[12]McFarland LV, Beneda HW, Clarridge JE, Raugi GJ. Implications of the Changing Face of *Clostridium difficile* Disease for Healthcare Practitioners. *Am J Infect Control*. May 2007. 35(4):237–53.

[13]Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration (FDA). Hazard Analysis Critical Control Point (HACCP). April 17, 2006. Available at: http://www.fda.gov/Food/GuidanceRegulation/HACCP/ucm2006811.htm (Accessed 24 October 2007).

[14]FDA National Retail Food Team, U.S. FDA Report on the Occurrence of Foodborne Illness Risk Factors in Selected Institutional Foodservice, Restaurant, and Retail Food Store Facility Types. September 14, 2004. Available at: http://www.fda.gov/Food/GuidanceRegulation/RetailFoodProtection/FoodborneIllnessRiskFactorReduction/ucm089696.htm (Accessed 24 October 2007).
[15]Michaels B, Keller C, Blevins M, Paoli G, Ruthman T, Todd E, et al. Prevention of Food Worker Transmission of Foodborne Pathogens: Risk Assessment and Evaluation of Effective Hygiene Intervention Strategies. *Food Service Technology*. March 2004. 4(1):31–49.
[16]Steinmuller N, Demma L, Bender JB, Eidson M, Angulo FJ. Outbreaks of Enteric Disease Associated with Animal Contact: Not Just a Foodborne Problem Anymore. *Clin Infect Dis*. December 15, 2006. 43(12):1596–602.
[17]Todd E., Greig J. Outbreaks Where Food Workers Have Been Implicated in the Spread of Foodborne Disease. September 28, 2006. Available at: http://www.fsis.usda.gov/PDF/Slides_092806_ETodd2.pdf (Accessed 24 October 2007).
[18]Scallan E. Activities, Achievements, and Lessons Learned During the First 10 years of the Foodborne Diseases Active Surveillance Network: 1996–2005. *Clin Infect Dis*. March 1, 2007. 44(5):718–25.
[19]Drudy D, Mullane NR, Quinn T, Wall PG, Fanning S. *Enterobacter sakazakii*: An Emerging Pathogen in Powdered Infant Formula. *Clin Infect Dis*. April 1, 2006. 42(7):996–1002.
[20]U.S. Department of Health and Human Services Public Health Service. U.S. The 2005 FDA Food Code. October 5, 2007. Available at: http://www.fda.gov/food/guidanceregulation/retailfoodprotection/foodcode/ucm2016793.htm (Accessed 24 October 2007).
[21]Chadwick PR, Beards G, Brown D, Caul EO, Cheesbrough J, Clarke I, et al. Management of Hospital Outbreaks of Gastroenteritis Due to Small Round Structured Viruses. *J Hosp Infect*. May 2000. 45(1):1–10.
[22]Blossom DB, McDonald LC. The Challenges Posed by Reemerging *Clostridium difficile* Infection. *Clin Infect Dis*. July 15, 2007. 45(2):222–7.
[23]Centers for Disease Control and Prevention; Infectious Disease Society of America; American Society of Blood and Marrow Transplantation. Guidelines for Preventing Opportunistic Infections Among Hematopoietic Stem Cell Transplant Recipients. *MMWR Recomm Rep*. October 2000. 49(RR-10):1–125.

CHAPTER 19

Hospital Water

M. Sigfrido Rangel-Frausto, MD, MSc, MQ

Key Issue

Hospital water is frequently an overlooked, important and controllable source of health care associated infections. Numerous outbreaks have been linked to contaminated water. Potable water is still an unmet need in many developing countries. CDC and WHO had published guidelines for water quality in health care facilities.

Known Facts

- Hospital potable water must have <1 coliform bacterium/100 mL. High levels of bacteria in hospital water, dialysate water, sinks, faucets, shower heads has been associated with outbreaks or hand colonization.
- The buildup of biofilms and the corrosion of distribution lines and tank surfaces resulting from poor design or aging of distribution systems and water stagnation are the primary cause of diminished water quality.
- Colonization in more than 30% of hospital water has been associated with cases of Legionnaires' disease. Hospital water colonization by *Legionella* spp. could be long lasting and associated periodically with outbreaks.
- Risk of illness may be influenced by several factors beside water contamination.
- In developing countries, high levels of water contamination correlating with low levels of chlorination have been linked to bloodstream infections outbreaks by enterobacterias, including *Klebsiella* spp, *Enterobacter* spp.
- Patient exposure to waterborne organisms occurs while showering, bathing, drinking, or with the contact of medical equipment (tube feed bags, endoscopes, respiratory equipment) rinsed with tap water.

- The development of a safety program for water intended for human consume must be implemented in every health-care facility.

Controversial Issues

- Use of sterile water for all patients.
- Maintaining high concentration of chlorine to reduce *Legionella* colonization.
- Routine point-of-use water filtration.
- Copper may decrease water and environment colonization.

Suggested Practice

- A high level of suspicion for cases of water borne infections should be maintained, especially if clusters of infections occur.
- Hospital water should not routinely cultured.
- Water used for dialysis should be sampled monthly, and bacteria must be <200 bacteria/mL.
- Dialysate should be also cultured and similar levels of bacteria must be maintained.
- Use sterile water for rinsing nebulization devices and other semicritical respiratory-care equipment.
- Chloride levels in hospital water should be tested periodically. Chlorination should be tested not only in the incoming tap water, but across the hospital, especially in high-risk areas like intensive care units or where immune-compromised patients exist.
- Hospital tap water should be not given to immunosuppressed patients. Use sterile water instead. If not possible filters or boiling could be a safe alternative.
- Cooling towers should be, if possible, directed away from hospital's air-intake system, and the design the cooling towers should be such that volume of aerosol drift is minimized. Install drift eliminators and regularly use a effective biocide, according manufacturers recommendations.
- In case of a single confirmed case of health care associated Legionnaires' disease, or two possible cases in less than 6 months, begin an epidemiological and environmental

investigation. Alert hospital personnel so a high level of suspicion for the detection of new cases is maintained. This prospective surveillance should be maintained at least 2 months after the last case. If there is evidence of continuous transmission, hospital water should be sampled, and potential areas for aerosolized water should be looked. If hospital water is contaminated with *Legionella* spp., start decontamination procedures:

1. Superheating: flushing outlet for at least 5 minutes with water =65°C, (post warning signs at each outlet being flushed to prevent scald injury) or
2. Hyperchlorination: >10 mg/L of free residual chlorine.

- Follow up cultures should be done at 2 weeks intervals for three months to evaluate actions taken. If no further positive cultures are found. Then cultures should be obtained monthly for another 3 months. If positive cultures are found reassess the implemented control measures, modify them accordingly, re-implement decontamination and considerer combinations.

Summary

Many bacteria can survive in water and have been linked to health care associated infections including: *Pseudomonas aeruginosa, Burkholderia cepacia, Serratia marcescens, Citrobacter freundii, Clostridium difficile, Acinetobacter baumani, Flavobacterium meningosepticum, Aeromonas hydrophila, atypical Mycobacteria*, *Legionella* spp, parasites and virus among others. Furthermore *Salmonella*, Vibrio, Rotavirus, *Cryptosporidium* and other enteric organisms have been reported in developing countries. In *Table 19.1* some examples of hospital water linked outbreaks are shown.

Routine cleaning, disinfection and policies for use and changing of water from potential reservoirs should be implemented and periodically reviewed. In high-risk units the routine use of point-of-use filters may be a cost effective intervention to decrease colonization and health-care associated infection rates.

Table 19.1 Examples of Hospital Water-linked Outbreaks

Microorganism	Reservoir	Infection
P. paucimobilis	water bottles for rising tracheal suction	Pneumonia
S. marcescens	water of humidifiers	Pneumonia
M. xenopi	hot water taps	Pneumonia
M. chelonae	contaminated equipment	Otitis
M. chelonae	contaminated water tank	Nasal Septum Cellulitis
L. pneumophila	hospital water, cooling towers	Pneumonia
Acinetobacter spp.	water bath used to thaw fresh plasma	Bacteremia
P. aeruginosa	water bath used to thaw cryoprecipitate, hospital water	Bacteremia, Pneumonia
P. aeruginosa	tub water contamination	Folliculitis, Skin Infections
C. difficile	bath	Diarrhea
S. maltophilia	hospital water	Bacteremia
Cryptosporidium	hospital water	Diarrhea

References

Weber, DJ, Rutala WA. Environmental Issues and Nosocomial Infections *in* Prevention and Control of Nosocomial Infections (3rd Edition), Wenzel RP (Ed). Baltimore: Williams & Wilkins, 1997. Pgs. 491–514.

Centers for Disease Control and Prevention. Guideline for Prevention of Nosocomial Pneumonia: Part 1. Issues on Prevention of Nosocomial Pneumonia. *Resp Care*. 1994. 39:1191–1236.

Centers for Disease Control and Prevention. Guideline for Hand Washing and Hospital Environmental Control. *MMWR*. 1985. 37(24).

Rangel-Frausto MS, Rhomber P, Hollis RJ, et al. Persistence of Legionella Pneumophila in a Hospital's Water System: A 13-year Survey. *Infect Control Hosp Epidemiol*. 1999. 20:793–797.

Anaissie EJ, Penzak SR, Dignani M. The Hospital Water Supply as a Source of Nosocomial Infections. *Arch Intern Med*. 2002. 162:1483–92.

Ortolano GA, McAlister MB, Angelbeck JA, Schaffer J, et al. Hospital Water Point-Use-Filtration: A Complementary Strategy to Reduce the Risk of Nosocomial Infection. *Am J Infect Control*. 2005. 33:S1–19.

Dyck A, Exner M, Kramer A. Experimental based experiences with the introduction of a water safety plan for a multi-located university clinic and its efficacy according to WHO recommendations. *BMC Public Health*. 2007. 7:34.

Macias AE, Muñoz JM, Herrera LE, Medina H, Hernandez I, Alcantar D, Ponce de León RS. Nosocomial Pediatric bacteriemia: The role of intravenous set contamination in developing countries. *Infect Control Hosp Epidemiol*. 2004. 25:226–30.

Zhou ZY, Hu BJ, Lin YE, Watanabe H, Zhou Q, Gao XD. Removal of waterborne pathogens from liver transplant unit water taps in prevention of healthcare-associated infections: a proposal for a cost-effective, proactive infection control strategy. *Clin Microbiol Infect*. 2014. 20:310–14.

World Health Organization. Guidelines for drinking water quality. Geneva Switzerland. *WHO*. 2004.

Centers for Disease Control and Prevention. Guidelines for environmental infection control in health care facilities: Recommendations of CDC and the healthcare infection control practices advisory committee (HICPAC) *MMWR*. 2003. 52:1–48.

CHAPTER 20

Laboratory Areas

Betty A. Forbes, Ph.D.

Key Issue

Laboratory workers are exposed to a variety of potential occupational health risks that include infectious materials and cultures. Laboratory-acquired infections (LAIs) are defined as all infections acquired through laboratory activities, regardless of their clinical or subclinical manifestations. Biosafety guidelines have evolved from the efforts of the microbiological and biomedical communities to reduce LAIs. The actual risk of a laboratory-acquired infection is difficult to measure because there is no systematic reporting to appropriate government agencies or at a professional society level to monitor the number of laboratory workers that acquire infections associated with the workplace. More recent surveys have revealed a shift in the pattern of LAIs from the early collective studies published by Sulkin and Pike who reported on over 4000 laboratory-associated infections between 1949 and 1974, with a mortality of 4.1%. For example, in a 2002–2004 survey of clinical laboratory directors, approximately one-third of laboratories reported the occurrence of at least 1 laboratory-acquired infection with shigellosis, brucellosis, and salmonellosis being the 3 most common LAIs followed by *Staphylococcus aureus, Neisseria meningitis, E. coli* 0157:H7, *Coccidiodes immitis, Clostridium difficile* and *Bacillus anthracis*. To minimize the risk of LAIs, a program that encompasses a combination of engineering controls (including laboratory design), safe laboratory practices, employee education, personal protective equipment (PPE), and medical measures that include surveillance, risk assessment, vaccination, and postexposure prophylaxis is required. Of significance, the development of such programs to minimize risks associated with the handling and disposal of infectious agents is based on an understanding of the pathogenicity of the agent, host

susceptibility, source of infection, and the method of transmission of the infectious agent. Most risks from biological hazards can be reduced through the use of appropriate microbiological procedures and techniques, containment devices and facilities, and protective barriers.

Known Facts

- More recent surveys in the US from 1978 through 1982, and in 1986, reported an annual incidence of 3 to 3.5 infections per 1,000 laboratory employees per year Wilson and Reller estimated that the annual rate of LAIs in the US is approximately 1 to 5 infections per 1000 employees.
- Harding and Byers indicated that clinical diagnostic laboratories accounted for 45% of all laboratory-acquired infections. Laboratory workers, especially those in microbiology, are at greater risk of becoming infected than is the general population.
- The causative incident or source for most laboratory-acquired infections is unknown.
- There is a dearth of evidence-based research and publications focused on biosafety. In 2008, the Centers for Disease Control and Prevention (CDC) convened a Blue Ribbon Panel of laboratory representatives from a variety of agencies, laboratory organizations, and facilities to review laboratory biosafety in diagnostic laboratories. These guidelines were intended to improve safety specifically for diagnostic laboratories that handle specimens from humans and animals. Finally, the Clinical and Laboratory Standards Institute also has published guidelines for the protection of laboratory workers from occupationally acquired infections (M29-A3); an updated version of these guidelines is expected to be published in early 2014.

Principal Routes of Laboratory Transmission

Inhalation—aerosols are a serious hazard because they are common in laboratory procedures.

- Pipetting, blenders, pouring, non-self contained centrifuges, sonicators, vortex mixers, flaming a loop that may generate respirable-size particles (<0.05 mm in diameter) that remain airborne for protracted periods.

- Other materials that can act as droplet nuclei include lyophilized cultures, dried materials on laboratory benches and stoppers and bacterial and fungal spores.
- Procedures and equipment that generate respirable size particles also generate larger size droplets (>0.1 mm in diameter) that can contain multiple copies of an infectious agent. These larger size droplets settle out of the air rapidly, contaminating gloved hands, work surfaces and possibly mucous membranes of the persons performing the procedure.
- Technique can significantly impact aerosol output and dose—experiments show that aerosol burden with maximal aeration is about 200 times greater than aerosol burden with minimal aeration.

Inoculation

- Parenteral inoculation of infectious materials with syringe needles or other contaminated sharps such as blades and broken glassware.
- One of the leading causes of laboratory-associated infections.

Contamination of skin and mucous membranes

- Spills, sprays and splashes into eyes, mouth or nose and hand-to-face actions.
- Spills, sprays and splashes on intact or non-intact skin.
- Contaminated surfaces and equipment.

Ingestion

- Occurs through mouth pipetting, transfer of organisms to the mouth from contaminated items such as pencils or fingers.
- Consumption of food or drink in the laboratory.
- Accidental splashes that fall into the mouth.

Levels of Containment

In general, the strategy for minimizing the occupational exposure of laboratory workers to infectious agents is based on microorganism containment which includes physical factors such as facility design and safety equipment, standard microbiological practices, and administrative controls. Microorganisms encountered and the procedures performed are stratified by risk. The primary risk criteria used to define the four ascending levels of containment, biosafety levels (BSL) 1 through 4 are

infectivity, severity of disease, transmissibility and the nature of the work being conducted. Each increasing BSL number implies increased occupational risk from exposure to a microorganism or performance of a procedure and thus, is associated with more stringent control and containment practices:

- Primary containment: provides physical separation of the infectious agent from the laboratory worker.
- Primary barriers: strict adherence to microbiological practices and techniques and use of biological safety cabinets (BSCs; *Table 20.1*), safety centrifuge containers, and PPE (for example, gloves, masks, face shields, coats, gowns, respirators), sharps protection.

Table 20.1 Classes and types of BSCs

BSC CLASS	Type of Protection	Miscellaneous Comments
I	Personnel and environmental[a,b]	Partial containment cabinets
II A1, A2, B1, and B2	Personnel, environmental and product[c]	All have HEPA-filtered, vertical laminar airflow. Cabinet types vary by minimum air velocity, exhaust, type of ducting, agents allowed for use (eg. biological,volatile radionucleotides, toxic chemicals)
III	Personnel, environmental and product Provides a physical barrier between the user and the agents for maximum protection	Totally enclosed with gas-tight construction

[a] Personnel protection: protects personnel from harmful agents used inside the cabinet
[b] Environmental protection: protects the environment from harmful agents/contaminants generated or used in the cabinet
[c] Product protection: protects products/experiment from contaminants in the room environment and from cross contamination inside the cabinet

- Secondary containment: includes facility design and serves as a secondary barrier to protect all works within the facility and protect the outside environment.

A brief overview of practices and techniques, safety equipment and facilities for recommended BSLs is shown in *Table 20.2*. In addition, the more common agents that cause laboratory-acquired infections with their corresponding routes of transmission and primary practices, containment and facilities in the laboratory are summarized in *Table 20.3*. In light of significant national and international events, biosecurity measures have been implemented and subsequently expanded to protect microbial agents from loss, theft, diversion or intentional misuse. In the US, Select Agent regulations have led laboratory managers, scientists, scientific and institutional leaders and others to implement and improve the security of biological agents and toxins within their facilities; advisory recommendations for biosecurity programs are detailed in the CDC *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*, 5th edition. Agents that could pose as severe threats to animal or plant health (i.e. select agents) are identified in *Table 20.3*. Detailed information regarding biosafety levels that are recommended for specific bacteria, fungus, parasites and viruses can be found in textbooks and a variety of websites such as those listed below:

http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm
http://whqlibdoc.who.int/publications/2004/9241546506.pdf
http://www.phac-aspc.gc.ca/ols-bsl/lbg-ldmbl/index.html
http://www.cdc.gov/mmwr/preview/mmwrhtml/su6101a1.htm

Risk Assessment

The assignment of an infectious agent to a biosafety level must be based on a risk assessment. Occupational risk assessment criteria are influenced by the type of manipulations or activities performed with the agent, the experience of the laboratory worker, and the infectious agent. Thus, each task, procedure, or activity performed in the laboratory must be analyzed for its potential risk to the employee who performs the task. The international community has developed a common risk classification scheme in which infectious agents are categorized into 4 risk groups based on their relative risk to cause laboratory-associated infections.

Table 20.2 Summary of Essential Components of BSLs for Activities Involving Infectious Agents
(Adapted from CDC-NIH guidelines, 2007).

BSL	Practices	Primary Barriers and Safety Equipment	Facilities (2° Barriers)
1	Standard microbiological practices: eg. hand hygiene; no mouth pipetting, eating, drinking, smoking, applying cosmetics or storing food; policies for safe handling of sharps; decontaminate work surfaces after completion of work or any spill; universal biohazard symbol signage; pest management program; appropriate training.	– Wear PPE (laboratory coats, gloves and/ or protective eyewear or face protection when indicated)	– Bench tops impervious to water, resistant to heat, organic solvents. – Laboratory chairs covered with non-porous material. – Sink for handwashing
2	BSL-1 practice plus: biohazard signs, limited access, 'sharps' precautions, biosafety manual defining waste decontamination and medical surveillance, demonstrated proficiency in standard and special microbiology practices before working with BSL-2 agents.	– Class I or II BSCs and other physical containment devices used for all manipulations of agents that result in splashes or aerosols – PPEs (laboratory coats, gloves, face protection) as needed	BSL-1 plus autoclave available
3	BSL-2 plus controlled access, decontamination of all waste, protective clothing and baseline serum of laboratory personnel for certain agents (eg. hepatitis B virus).	– Class I or II BSCs and other physical containment devices used for all open manipulations of agents – PPEs as for BSL-2 plus respiratory protection as needed	– BSL-2 plus controlled access, self-closing, double door access, air exhaust to outside, negative airflow into laboratory
4	BSL-3 plus clothing change before entering and showering on exit, all material decontaminated on exit from facility	– **All** procedures conducted in class III BSCs or Class I or II BSCs in combination with full body, air-supplied, positive-pressure personnel suit	– BSL-3 plus separate building or or isolated zone, dedicate supply and exhaust, vacuum, and decontamination systems

Table 20.3 The More Common Causes of Hospital Clinical Laboratory-Acquired Infections
(Adapted from WHO, 2004 and CDC, 2007 publications)

Agent	Laboratory-Acquired Infections: Sources and Routes of Transmission	Primary Practices, Containment and Facilities	SELECT AGENT
Bacillus anthracis	Primarily cutaneous anthrax by either direct and indirect contact of broken skin with culture and contaminated surfaces or accidental parenteral exposure.	BSL-2	Yes
Brucella species	Most frequently reported laboratory infection by airborne and mucocutaneous routes. Cases have occurred by sniffing cultures or working on open bench tops aerosols, mouth pipetting, accidental parenteral inoculation, sprays into eyes, nose and mouth.	BSL-2	Yes
Burkholderia mallei and *Burkholderia pseudomallei*	Aerosol and cutaneous exposures usually while handling bacterial cultures.	BSL-2 when handling clinical specimens; BSL-3 whenever infectious aerosols or droplets are generated. Gloves should be worn particularly when working with infectious material.	Yes
E. coli—Shiga toxin producing	Unknown route of transmission but suggested that prolonged survival on stainless steel surfaces and low infectious dose may contribute to laboratory transmission by accidental ingestion.	BSL-2. Gloves should be worn when hands may come in contact with potentially infectious materials.	No

Table 20.3 The More Common Causes of Hospital Clinical Laboratory-Acquired Infections (continued)
(Adapted from WHO, 2004 and CDC, 2007 publications)

Agent	Laboratory-Acquired Infections: Sources and Routes of Transmission	Primary Practices, Containment and Facilities	SELECT AGENT
Franciscella tularensis	Tularemia commonly reported laboratory-associated infection by direct contact of skin and mucous membranes with infectious material.	BSL-2 when handling clinical specimens. Laboratory personnel should be informed of the possibility of tularemia when specimens are submitted for diagnostic testing. BSL-3 for all other manipulations or suspect cultures.	Yes
Leptospira species	Ingestion, parenteral inoculation, direct and indirect contact of skin or mucous membranes with cultures or infected tissues or body fluids.	BSL-2. Gloves should be worn when handling cultures.	No
Mycobacterium tuberculosis complex	Primary acquisition by exposure to laboratory-generated aerosols; tubercle bacilli may survive on heat-fixed smears.	BSL-2 for non-aerosol-producing manipulations of clinical specimens. BSL-3 for laboratory activities associated with the propagation and manipulations of cultures.	No
Neisseria gonorrhoeae	Rare. Accidental parenteral inoculation and direct or indirect of mucous membranes with contact infectious or contaminated solutions.	BSL-2. Gloves should be worn when hands may come in contact with potentially infectious materials.	No

Table 20.3 The More Common Causes of Hospital Clinical Laboratory-Acquired Infections (continued)
(Adapted from WHO, 2004 and CDC, 2007 publications)

Agent	Laboratory-Acquired Infections: Sources and Routes of Transmission	Primary Practices, Containment and Facilities	SELECT AGENT
Neisseria meningitidis	Parenteral inoculation, droplet exposure of mucous membranes, infectious aerosol and ingestion.	BSL-2 for specimens and cultures. All sterile-site isolates should be manipulated in a BSC.	No
Salmonella and *Shigella* species	Risk primarily from the ingestion of the organism or infectious material (numerous cases of laboratory-acquired infections have resulted from handling proficiency testing strains); less common, parenteral injection.	BSL-2	No
Treponema pallidum	Parenteral inoculation, contact with mucous membranes or broken skin with infectious clinical materials.	BSL-2	No
Yersinia pestis	Direct contact with cultures and infectious materials, inhalation of infectious aerosols or droplets during manipulation.	BSL-2; BSL-3 for laboratory activities associated with high potential for droplet or aerosol production.	Yes
Blastomyces dermatitidis	Inoculation and presumably by inhalation of conidia.	BSL-2; BSL-3 for propagating and manipulating sporulating cultures.	No

Table 20.3 The More Common Causes of Hospital Clinical Laboratory-Acquired Infections (continued)
(Adapted from WHO, 2004 and CDC, 2007 publications)

Agent	Laboratory-Acquired Infections: Sources and Routes of Transmission	Primary Practices, Containment and Facilities	SELECT AGENT
Coccidioides immitis	Inhalation of arthrospores and accidental percutaneous inoculation.	BSL-2 for clinical specimens; BSL-3 for propagating and manipulating sporulating cultures.	No
Histoplasma capsulatum	Inhalation of conidia, accidental cutaneous inoculation.	BSL-2 for clinical specimens; BSL-3 for propagating and manipulating sporulating cultures.	No
Blood and tissue protozoal parasites	Majority of laboratory-acquired infections involved need-stick or other cutaneous exposure to infectious stages through abraded skin.	BSL-2	No
Intestinal protozoal parasites	Primarily by ingestion	BSL-2	No
Trematodes	Primarily through accidental needlesticks and by contamination of mucosal membrane and skin abrasions	BSL-2	No
Nematodes	Ingestion of infective eggs or skin penetration by infective larvae	BSL-2	No

Table 20.3 The More Common Causes of Hospital Clinical Laboratory-Acquired Infections (continued)
(Adapted from WHO, 2004 and CDC, 2007 publications)

Agent	Laboratory-Acquired Infections: Sources and Routes of Transmission	Primary Practices, Containment and Facilities	SELECT AGENT
Rickettsial agents—*Coxiella burnettii* and *Rickettsia prowazekii*	Exposure to infectious aerosols and parenteral inoculation	BSL-2 for non-propagative laboratory procedures	Yes
Common blood-borne viruses—hepatitis viruses (A, B, C, and D) and HIV	Parenteral inoculation, droplet exposure of mucous membranes, and contact exposure of broken skin	BSL-2; BSL-3 may be indicated for activities with potential for droplet or aerosol production, other activities involving concentrations of infectious materials. Gloves should be worn when working particularly with infectious material.	No
Parvovirus B19	Exposure to infectious aerosols	BSL-2	No
Arboviruses and related zoonotic viruses: 597 viruses listed in CDC document.	Exposure to infectious aerosols, inoculation, and/or contact with skin or mucous membranes	BSL-2 through 4 based on risk assessment derived from information provided by a variety of sources, viral mode of transmission, frequency and severity of laboratory- acquired infections, and the availability of a vaccine	Many are classified as select agents

These groups are categorized based on particular characteristics of the infectious agent such as their pathogenicity, infectious dose, mode of transmission, host range, and availability of effective preventive measures and effective treatment. These risk groups were developed to help laboratories determine the best laboratory practices and environmental requirements for containment. Other factors associated with laboratory operations including specimen volume, potential for aerosol generation, quantity and concentration of infectious agents, agent stability in the environment, and type of work proposed should also be taken into consideration.

Administrative Elements of a Safe Clinical Laboratory

- Biosafety, exposure control, and chemical hygiene plans including accidental spills of infectious organisms or release of infectious microorganisms into the laboratory or facility environment.
- Comprehensive plan for management and disposal of infectious waste including blood and blood products.
- Respiratory protection program.
- Personal protective equipment program and procedures.
- Provision of medical surveillance for infections that may result from exposure to agents encountered in the performance of routine duties or when early diagnosis reduces the risk of serious consequences of the infection (eg. rickettsial infections).
- Safety manual that is understood by employees and includes the occupational risks and consequences of infection.
- Promotion of safety awareness through training programs and required adherence to safety procedures.
- Consistent observance by all workers of proven safety and microbiological practices.
- Documentation and reporting of all occupational injuries, illnesses and incidents of potential exposure.

References

Baron EJ, Miller M. Bacterial and fungal infections among diagnostic laboratory workers: Evaluating the risks. *Diagn Microbiol Infect Dis*. 2008. 60:241–246.

Centers for Disease Control and Prevention. Biosafety in Microbiological and Biomedical Laboratories (BMBL), (5th edition) U.S. Department of Health and Human Services and the Institutes of Health, US Government Printing Office, Washington. 2007.

Centers for Disease Control and Prevention. Guidelines for safe work practices in human and animal medical diagnostic laboratories: Recommendations of a CDC-convened, Biosafety Blue Ribbon Panel. *MMWR*. 2012. 61:1–105.

Clinical Laboratory Standards Institute. Protection of laboratory workers from occupationally acquired infections: Approved guideline (3rd edition). CLSI document A49-A3 2005.

Collins CH, Kennedy DA. Laboratory Acquired Infections (4th edition). Butterworth-Heineman, Oxford, England, 1999.

Harding AL, Byers, KB. Epidemiology of laboratory-associated infections *in* Biological Safety: Principles and Practices (3rd edition), Fleming, DO, Hunt, DL, (Eds). Washington, DC: ASM Press, 2000. Pgs. 35–54.

Health Canada. Laboratory Biosafety Guidelines (3rd edition). Ottawa, Canada, 2004.

Pike RM. Laboratory-associated infections. *Health Lab Sci*. 1976. 13:105–114.

Pike RM. Laboratory-associated infections: Incidence, fatalities, causes and prevention. *Annu Rev Microbiol*. 1979. 33:41–66.

Sewell DDL. Laboratory-associated infections and biosafety. *Clin Microbiol Rev*. 1994. 8:389–405.

Singh K. Laboratory-associated infections. *Clin Infect Dis*. 2009. 142–147.

Sulkin SE, Pike RM. Viral infections contracted in the laboratory. *N Engl J Med*. 1949. 241:205–213.

Wilson ML, Reller LB. Clinical laboratory-acquired infections *in* Hospital Infections, Bennett JV, Brachman PS (Eds). Pgs. 343–355.

World Health Organization Laboratory Biosafety Manual (3rd edition). World Health Organization, Geneva, Switzerland, 2004.

CHAPTER 21

The Pharmacy

Patricia Pecora Fulco, PharmD.

Key Issue

The pharmacy plays a pivotal role in infection prevention and safety in the hospital.

Known Facts

- Infections occur when pharmacological formulations are contaminated with microbes. This may occur during manufacture, or when medications are improperly prepared, handled, stored, or become outdated.
- Contamination may occur within the pharmacy or in other areas of the hospital when healthcare workers finalize the preparation of medications and administer them.
- Contamination of medications and solutions occurs through 3 routes:
  1. Direct contact;
  2. Use of contaminated ingredients; and
  3. Air-borne contamination.
- Contamination of intravenous fluids is particularly problematic because of the potential to cause serious illness.
- Inappropriate prescribing of antimicrobials is an important cause of drug-resistance. Pharmacists should participate in an antimicrobial stewardship program (ASP) (in coordination with an infectious diseases physician and microbiologist) to optimize antimicrobial usage in the healthcare setting. The goal of an ASP is to decrease antimicrobial resistance, secondary infections (e.g., *Clostridium difficile*) and to prevent toxicities. ASPs are cost effective and have demonstrated a decrease in suboptimal antimicrobial use.
- Optimizing antimicrobial dosing for patient-individualized characteristics (organism, pharmacokinetic/pharmacodynamic parameters and renal/hepatic alterations) is an additional role fulfilled by the clinical pharmacist.

- Many pharmacies now monitor antimicrobial concentrations (e.g., vancomycin) to ensure optimal pharmacotherapy for the correct infectious diseases indication and adjust dosing according to established algorithms.
- Pharmacists often dispense discharge medications to patients. Patient education may ensure that antimicrobials are used properly after discharge.

Controversial Issues

Although national regulatory agencies and hospital committees have set standards for aseptic practices within the pharmacy, the extent to which asepsis needs to be confirmed is controversial. Should all products that are compounded in the pharmacy be tested by culturing samples? Should products obtained from an outside vendor be tested? Due to the emergence of large companies that supply intravenous solutions to multiple hospitals, infections caused by low-level contamination may be scattered over a large number of hospitals. An individual hospital may see only one infusate or injection medication related infection, which would not normally trigger an investigation within the hospital. Although controversial, a national surveillance system could be developed to monitor bloodstream isolates and, potentially, serve as a means to trace the source of such scattered infections.

Rational use of antimicrobials has been shown to reduce the emergence of resistance pathogens. The pharmacy, working as a member of an ASP committee, should play a key role in developing institution guidelines for the rational use of antimicrobials to prevent drug resistance, minimize adverse drug events, enhance patient outcomes and prevent hospital acquired infections. Controversy exists over how much autonomy should be given to the individual provider. In some cases, a short course of therapy is allowed until laboratory results return. In other cases, medications have been made available only for highly selected indications. Controversy usually arises when policies are perceived to impair a prescriber's ability to treat a patient effectively, or when restrictions are perceived as being driven by finances rather than health concerns.

Suggested Practice

- The pharmacy should implement and follow procedures from the United States Pharmacopeia, Chapter 797, to prevent

compounded sterile products (CSPs) from the following:

1. Microbial contamination;
2. Exposure to excessive bacterial endotoxins;
3. Variability in the intended strength of correct ingredients;
4. Unintended chemical and physical contaminants; and
5. Ingredients of inappropriate quality.

- Employees should be trained in aseptic technique before making preparations or administering medications.
- Limit the activities of staff members who exhibit symptoms of infection.
- Single-dose vials should be used within one and six hours, respectively, if compounded outside or inside a laminar airflow workbench (ISO Class 5 environment). Multiple-dose vials may be discarded after 28 days from initial use. All vials should be labeled with beyond use dates.
- For products that are reconstituted, only sterile diluents should be used. Utmost care should be taken not to introduce contaminants from the outside of containers into the interior. If liquid is to be injected through a vial membrane, the membrane should be disinfected before being pierced.
- Syringes that are used to inject medications or liquids into the container should be sterile and preferably single-use disposable ones.
- Recommend proper labeling, dating, and storage of sterile products.
- Establish ASP strategies for minimizing the development of resistant strains of microorganisms as well as for optimizing therapeutic outcomes in individual patients. Individual physicians or departments should be involved in the development and implementation of policies that affect them.
- A tracking system should be devised in case of a product recall. The tracking system should allow identification of patients who received potentially contaminated medications.
- Pharmacy areas should be kept clean. Food should not be consumed in areas where CSPs are handled. Clean rooms, where CSPs are prepared, should be free of visible dust, and access should be limited. Detailed policies should be maintained for the activities allowed in the clean room.

- Personnel preparing sterile medications should wear clean clothing covers and gloves along with completing annual competencies to ensure proper aseptic technique. Hands should be washed before and after CSPs are prepared. Employees should not prepare sterile products if they have rashes, sunburn, weeping sores, broken skin, conjunctivitis or respiratory infections. When preparing sterile or potentially toxic solutions such as chemotherapies, laminar airflow workbenches (ISO Class 5 environment) are strongly recommended.
- The pharmacy should ensure that medications are appropriately handled and stored throughout the institution. Medications should be stored according to manufacturers' instructions. All CSPs should have an appropriate beyond-use-date (expiration) printed on the outside of the container. Environmental conditions should be checked periodically, including the daily temperature log of refrigerators and the competency of laminar airflow workbenches.
- The pharmacy should educate providers to help minimize medication side effects.
- The infection control committee should include representation from the pharmacy.
- An ASP pharmacist should have specialty training in infectious diseases.

Summary

The pharmacy plays various roles in infection prevention and safety. The pharmacy should ensure that medications and solutions are not contaminated. Policies should address training and annual performance evaluation of employees, and they should be reviewed annually to ensure they reflect current best practices. Employees with acute respiratory, gastrointestinal, and skin infections should not be permitted to handle medications. To promote rational use of antimicrobials, pharmacists should work closely with hospital committees and physicians, encourage multi-disciplinary collaboration within the health system and evaluate compliance with policies. Importantly, pharmacists often have an opportunity to counsel patients about medication adherence, proper storage and handling of medications/devices, and medical waste disposal. In all of these areas, the pharmacy may have a major impact on the success of an infection control program.

References:

American Society of Health-System Pharmacists. ASHP Statement on the Pharmacist's Role in Infection Control. *Am J Health-Syst Pharm*. 1998. 55:1724–6.

American Society of Health-System Pharmacists. ASHP Statement on the Pharmacist's Role in Antimicrobial Stewardship and Infection Prevention and Control. *Am J Health-Syst Pharm*. 2010. 67:575–7.

Chiller TM, Roy M, Nguyen D, Guh A, Malani AN, Latham R, et al. Clinical findings for fungal infections caused by methylprednisolone injections. *N Engl J Med*. 2013. 369:1610–9.

Climo MW, Israel DS, Wong ES, Williams D, Coudron P, Markowitz SM. Hospital-wide restriction of clindamycin: Effect on the incidence of *Clostridium difficile*-associated diarrhea and cost. *Ann Int Med*. 1998. 128:989–95.

Dellit TH, Owens RC, McGowan JE, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society of Healthcare Epidemiology of America Guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007. 44:159–77.

Kastango ES. American Society of Health-System Pharmacists (ASHP). Blueprint for Implementing USP Chapter 797 for Compounding Sterile Preparations. *Am J Health-Syst Pharm*. 2005. 62:1271–88.

Mattner F, Gastmeier P. Bacterial contamination of multiple-dose vials: A prevalence study. *Am J Infect Control*. 2004. 32:12–6.

Pedersen CA, Schneider PJ, Scheckelhoff DJ. ASHP National Survey of Pharmacy Practice in Hospital Settings: Monitoring and Patient Education—2006. *Am J Health-Syst Pharm*. 2007. 64:507–20.

Rybak M, Lomaestro B, Rotschafer JC, Moellering R, Craig W, Billeter M, et al. Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. *Am J Health-Syst Pharm*. 2009. 66:82–98.

Schwartzberg E, Rubinovich S, Hassin D, Haspel J, Ben-Moshe A, Oren M, et al. Developing and Implementing a Model for Changing Physicians' Prescribing Habits—The Role of Clinical Pharmacy in Leading the Change. *J Clin Pharm Ther*. 2006. 31:179–85.

Smith RM, Schaefer MK, Kainer MA, Wise M, Finks J, Duwve J, et al. Fungal infections associated with contaminated methylprednisolone infections. *N Engl J Med*. 2013. 369:1598–609.

United States Pharmacopeia. Pharmaceutical Compounding—Sterile Preparations. 2012. Chapter 797, Pgs. 1–38.

CHAPTER 22

The Operating Room

Marie-Claude Roy, MD, MSc

Key Issues

Two to five percent of patients undergoing surgical procedures suffer from surgical site infections (SSIs). These infections continue to burden patients with important morbidity, mortality and immense costs, the latter mainly explained by a doubling of the hospital length of stay. Because SSIs are primarily acquired during the surgical procedure while the wound is opened, a number of infection control practices merit scrutiny in the OR. The measures presented herein address environmental and surgical issues as well as some patient-related risk factors which are controlled once the patient is in the OR.

Known Facts

Most SSIs arise from the patient's endogenous flora which contaminate the wound by direct contact. Therefore, preparing patients for surgery should aim at decreasing the microbiologic burden of the patient's bowels, skin, respiratory tract, genital tract, etc…, depending on the procedure being performed. Examples of measures which decrease the microbiologic burden include: showering the patient with chlorhexidine before surgery, giving antimicrobial prophylaxis immediately before skin incision and applying mupirocin to the nares. Accordingly, the extent of endogenous bacterial contamination at surgery depends on the type of procedure being performed: clean, clean-contaminated, contaminated or dirty. The risk of SSI increases from <2% for the former to as high as 40% for the latter. The traditional wound classification is only a moderate predictor of the risk of SSI because other factors, host and surgical factors, also influence this risk.

Exogenous contamination of wounds is also important in the pathophysiology of SSIs, particularly for clean surgical

procedures. Airborne particles contaminated with live bacteria can enter sterile surgical fields during operation, particularly when implants are being placed (e.g., total hip prostheses).

The main source of airborne bacteria in the OR originate primarily from the skin of individuals in the room. The number of persons present in the OR as well as their level of activity, the type of surgery, the quality of air provided, the rate of air exchange, the quality of staff clothing, the quality of cleaning process and the level of compliance with infection control practices all influence airborne contamination. Although these may seem trivial issues for contaminated or dirty procedures, they are very important to consider in clean and clean-contaminated surgery.

Suggested Practices

Environmental Issues

The surgical suite should be divided into three designated areas: unrestricted, semi-restricted and restricted. Personnel can wear street clothes and there is no traffic limitation in the unrestricted area. A semi-restricted area is limited to authorized personnel only and patients. Surgical attire is recommended as well as headgear in this area. In the restricted area (i.e. ORs, clean core, scrub sink areas), surgical attire and head covering but also masks are required where open sterile supplies or scrubbed persons are present.

Modern operating rooms which meet current air standards in the United States should be virtually free of particles larger than 0.5μm when no people are in the room. To achieve this, ORs should be equipped with positive-pressure systems to ensure that air travels from ORs to adjacent areas, thus minimizing inflow of air to the room. This positive pressure system is challenged every time a door is opened.

Ventilation of ORs should filter air at a minimum of 15 changes/hour of which at least three changes should be with fresh air. In developed countries, this air should be high-efficiency filtered (HEPA). The temperature of ORs should be kept between 18°C and 24°C, with humidity of 30% to 60%.

For hospitals with limited resources where the aforementioned recommendations could not be attained, less expensive strategies to keep air as clean as possible are listed here:

- keep personnel to minimum in the OR during a procedure;

- limit idle conversations as this creates dispersion of bacteria;
- keep doors closed; and
- keep entries into the OR to a minimum during a procedure.

Cleaning and disinfection of the operating theatre should follow a precise schedule: all horizontal surfaces should be cleaned every morning before any intervention, horizontal surfaces and all surgical items (e.g., tables, buckets) should be cleaned between procedures. At the end of the working day, a complete cleaning of the operating theatre should be performed. Once a week, a complete cleaning of the operating room area, including all annexes such as dressing rooms, technical rooms, cupboards is advisable.

On the other hand, routinely culturing the OR environment is unnecessary because inanimate objects and surfaces are seldom the cause of SSI.

Preparation of the Surgical Team

All members of the surgical team who will work on the operating field should scrub arms and hands with chlorhexidine, iodophors or hexachlorophene for at least 5 minutes before the first procedure of the day, and for 2 to 5 minutes between subsequent procedures. The first scrub of the day should include a thorough cleaning underneath fingernails. The use of an alcoholic chlorhexidine solution has a greater residual antimicrobial activity, which could give a theoretic advantage during a long surgical procedure. Hand rubbing with aqueous alcoholic solution may be as effective as traditional hand scrubbing and also better tolerated by the surgical team.

All jewelry should be removed, and artificial nails must not be worn as these are associated with enhanced hand colonization with bacteria and fungi.

After performing the surgical scrub, members of the surgical team should keep hands up and away from the body so that the water runs from the tips of the fingers toward the elbows.

Sterile gloves should be of good quality, as approximately 10% of gloves are inadvertently punctured during surgery. Wearing two pairs of gloves is advisable in orthopedic surgery where as many as 50% of gloves are punctured. Because 30% of glove perforations are invisible, some experts recommend routinely changing gloves in long procedures. Gloves should

be changed immediately after any accidental puncture. Some experts also recommend routine changing of the outer gloves after draping, as this procedure is likely to contaminate gloves.

The operative site should be scrubbed with a detergent and an antiseptic soap should be applied, working from the proposed operative site outward. Antiseptics recommended for this practice include chlorhexidine, iodophors, and iodine. The best reduction in bacteria at the surgical site has been achieved with chlorhexidine-alcohol when compared with povidone-iodine in a surgical population undergoing clean-contaminated surgery. In this report, a greater than 40% decrease in total SSI rates was achieved in the chlorhexidine-alcohol group.

Sterile drapes must be placed on the patient and on any equipment included in the sterile field. Once a sterile drape is in position, it must not be moved.

Members of the surgical team entering the OR when an operation is about to begin or already underway should wear a mask and headgear which fully covers hair, sideburns and neckline. Experimental studies using tracer particles have shown that bacteria can be shed from hair, exposed skin, and mucous membranes of both OR personnel and the patient's skin. This is why we use barriers (masks, gowns, hoods and drapes) in the OR. Although no clinical studies have proved that the use of these barriers have led to a decrease in SSI rates, they are recommended not only for the purpose of reducing shedding of microorganisms in the OR but also as part of standard precautions.

Shoe covers can be replaced by ordinary shoes dedicated exclusively to the operating theater, because no significant difference was found in floor contamination whether personnel wear shoe covers or ordinary shoes. These latter shoes must be easy to wash.

Scrub suits should cover most bare skin to decrease shedding of microorganims from uncovered skin, because individuals shed up to 10^9 epithelial cells per day, many of which carry bacteria. This practice should be followed by all personnel working in the OR, not just those working in or near the operating field.

Strike-through in operating gowns is also a potential source for contamination, particularly at the sleeve or abdominal area. For procedures at high risk of blood contamination, a waterproof apron or more resistant gowns should be worn.

Meticulous operative techniques reduce the risk of SSI: surgeons should obliterate dead spaces, where possible, they should handle tissues gently, limit use of electrocautery and remove all devitalized tissue before closure. Good surgical technique may be reflected in shorter durations of procedures which are clearly associated with a lower risk of SSI.

Scheduling dirty cases at the end of the day is a practice which should be abandoned.

Antibiotic-coated sutures should not be used for the purpose of decreasing SSI rates.

Any member of the surgical team who suffers from a skin lesion such as a boil should refrain from working in the OR for such an individual may be dispersing tremendous amounts of bacteria, namely *Staphylococcus aureus,* in the air of the OR. Dermatitis of the hands sometimes caused by glove allergy should also be taken seriously for the same reason.

Patients Issues

Antibiotic prophylaxis is a very important preoperative practice and excellent guidelines have recently been published. The choice of antibiotic according to the procedure, the dose according to the patient's weight and the timing of administration are all important issues to consider and are part of the process measures of the Surgical Care Improvement Project (SCIP) launched in the US in 2002. Proper antimicrobial prophylaxis involves administering the first dose within 60 minutes before incision to obtain adequate tissue levels of antibiotic. Thus, the antibiotic should be administered in the OR by a designated person who should also make sure that it is repeated if the intervention is prolonged (for example, cefazolin should be repeated every 3–4 hours if the procedure lasts longer than 4 hours). Using a checklist for preoperative briefing ensures that the antibiotic is correctly administered in the OR.

Any perioperative event that causes vasoconstriction, for example hypothermia or subtle hypovolemia, alters the oxygenation of normal soft tissues, which in turn may result in higher infection rates. The effect of hypothermia on the development of SSI has been studied particularly well in patients undergoing colorectal surgery, but also in breast, varicose vein, and hernia surgeries.

Avoiding hypothermia reduces SSI rates and has led to the mandate from the Joint Commission of the Surgical Care Improvement project (SCIP) in the US to warm patients to 36° C in the OR and within 15 minutes of their arrival in the post-anesthesia care unit. Recent draft guidelines recommend maintaining normothermia for all types of procedures but the best approach to do this is not yet determined.

Hyperglycemia is a risk factor for SSI independent from diabetes. It has been associated with an increase in SSI after colorectal, spinal surgery, pancreatic, vascular, cardiac surgery and mastectomy. A more stringent glucose control should be followed intra-operatively as well as post-operatively. Experts recommend less than 200 mg/dL for a maximum glucose target for all operations and for diabetic patients as well as non-diabetics.

Another process measure included in SCIP is hair removal. As hair removal with a razor is clearly associated with increased risk of SSI, hair removal before surgery should be done with a clipper immediately before the intervention if necessary, or no hair removal.

Controversial Issues

ORs equipped with laminar airflow system provide almost sterile air, yet a very few studies show a significant decrease in SSI rates for surgical procedures performed in this type of OR. Some of these experiments did not control for the antimicrobial regimen received as surgical prophylaxis, thus precluding any conclusion on the exact role of the laminar flow system. Furthermore, a recent review evaluating SSIs following orthopedic prostheses, concludes it would be a waste of resources to establish new ORs with laminar airflow and even questionable as to whether laminar flow systems in existing ORs should be replaced by conventional ventilation systems. The CDC offers no recommendation for performing orthopedic implant operations in rooms supplied with laminar airflow.

The association between wearing nail polish by surgical team members and the risk of SSI has not been studied adequately.

The design and composition of surgical attire should minimize bacterial shedding into the environment. Cotton does not reduce airborne contamination because the pore size between

threads largely exceeds the size of skin scales. Furthermore, wet cotton fabric allows easy passage of bacteria to the outside of a gown as a result of the surgeon's sweating or from fluids such as blood. A number of other fabrics (close-woven polyester, disposable non-woven, plastic-membrane) have been tested against strike-through and examined for transfer of bacteria from skin scales from underneath the clothe. It is not known which type of fabric reduces airborne contaminants while also providing comfort.

Likewise, there are also conflicting data regarding the difference in SSI rates when adhesive plastic drapes are used instead of conventional one (cotton). It appears that theses adhesive drapes impregnated or not with antibiotic, are not necessary for the purpose of decreasing SSI rates.

Not all studies show a benefit of supplemental oxygen to the wound during surgery. Those who are in favor recommend starting supplemental oxygen at induction and suggest it should be given for at least 2 hours after closure. Although the optimal concentration of oxygen to prevent SSI is unknown, experts recommend its use for ventilated patients during general anesthesia and for all types of surgical procedures.

No well-controlled studies evaluate whether restricting the use of surgical scrubs to the OR suite or allowing them outside the OR will make a difference on SSI rates. Some hospitals require covering gowns when surgeons/nurses leave the OR still wearing surgical scrubs. It would make sense to change grossly soiled scrubs, scrubs worn while changing dressings on wards between surgical procedures, and probably changing scrubs after wearing them for 8 hours or more. No recommendation can be made on how and where to launder scrub suits.

Some surgeons irrigate the open wound with an antiseptic or antibiotic solution before closure. No recommendation can be made because of insuffisant data to support this measure.

Summary

Preparation of the surgical team and maintaining a clean operating environment are important because a number of intraoperative risk factors contribute to the development of SSIs. Very little has changed over the years concerning the surgical

rituals of scrubbing, gowning and gloving perhaps because of a lack of scientific data or for ethical reasons. Many of these rituals still hold today not only for the prevention of SSIs but also for the protection of the surgical team. In clean surgical procedures, particularly when an implant is inserted, these rituals merit attention because airborne contamination by members of the surgical team from their skin contribute to SSIs. Wearing proper surgical attire, keeping OR doors closed and traffic to a minimum are simple measures that decrease airborne contamination. Applying basic principles of antisepsis in the OR should be a priority for every member of the surgical team. Newer approach to prevention of SSIs (eg, glucose control, normothermia, increased oxygen) may decrease SSI rates, thereby decreasing morbidity and healthcare costs.

References

Mangram AJ, Horan TC, Pearson ML, et al. Guideline for Prevention of Surgical Site Infection. *Am J Infect Control*. 1999. 27:97–134.

World Health Organization. Prevention of Hospital-Acquired Infections: A Practical Guide. Ducel G, Fabry J, Nicolle L, (Eds). World Health Organization, 2002.

Roy M-C. Modern Approaches to Preventing Surgical Site Infections. *in* Prevention and Control of Nosocomial Infections (4th Edition), Wenzel RP (Ed). Baltimore: Lippincott Williams & Wilkins, 2003. Pgs. 369–384.

Lafreniere R. Infection Control in the Operating Room: Current Practices or Sacred Cows? *J Am Coll Surg*. 2001. 193:407–416.

American Institute of Architects. Guidelines for Design and Construction of Healthcare Facilities. 2006.

Boyce JM, Pittet D. Guidelines for Hand Hygiene in Healthcare Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *Infect Control Hosp Epidemiol*. 2002. 23:S3–S40.

Wong ES. Surgical Site Infections *in* Infection Control and Hospital Epidemiology, Mayhall CG (Ed). Baltimore: Lippincott Williams & Wilkins, 2004.

Gastmeier P, Breier A-C, Brandt C. Influence of laminar airflow on prosthetic joint infections: A systematic review. *J Hosp Infect*. 2012. 81:73–78.

Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm*. 2013. 70:195–283.

Alexander JW, Solomkin JS, Edwards MJ. Updated recommendations for control of surgical site infections. *Ann Surg*. 2011. 253:1082–1093.

Darouiche RO, Wall MJ, Itani KMF, et al. Chloehexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *New Engl J Med*. 2010. 362:18–26.

Bratzler DL. Update on the draft CDC/HICPAC guidelines for prevention of SSIs. Symposium presented during Infectious Diasease Week, San Francisco, October 2013.

CHAPTER 23

Keeping the Environment Safe in Infection Prevention and Control: Focus on Countries with Limited Resources

Adriano G Duse, MT, MBBCh, DTM&H, MScMed, MMed (Microbiology), FCPath (SA)

Key Issues

Ever-increasing budgetary constraints and contracting out cleaning services have resulted in an overall deterioration in hospital hygiene practices in healthcare facilities (HCFs) of many developing countries.

The increasing numbers of health care associated infections (HAIs) and, disturbingly, the emergence of multiple- and extensively-drug resistant HAI pathogens over the last decade are of major concern. Microorganisms such as methicillin resistant *S. aureus* (MRSA), glycopeptide-resistant enterococci (GRE), *C. difficile*, and *Acinetobacter* species, can survive on environmental surfaces for weeks to months.

Although the extent to which environmental cleanliness contributes to HAIs remains hotly debated and controversial, an increasing body of recent evidence has shown that removal of these microorganisms by cleaning with or without disinfection can reduce HAI pathogen transmission. However, environmental cleaning, particularly of hand-touch surfaces, is performed inadequately in many HCFs.

Currently available automated area decontamination technologies using UV light or hydrogen peroxide vapor or mists could be a useful adjunct to routine manual cleaning and disinfection in some hospital settings.

In addition to reducing environmental reservoirs for microorganisms, environmental cleaning has an important aesthetic purpose and is crucial for patient confidence.

Environmental aspects covered in this chapter include air, water, hand-touch surfaces, curtains, carpets, specialized patient care areas, linen, flowers and waste disposal.

Known Facts

- ***Air.*** The role of air in the transmission of microorganisms is best discussed on an organism-specific basis. Airborne transmission of *Mycobacterium tuberculosis,* Varicella-zoster, measles and influenza viruses is clearly established, and guidelines to reduce risks of transmission are available (CDC). Shedding or dispersal into the air of Gram-positive organisms such as *Staphylococcus aureus* and *Streptococcus pyogenes* in operating theatres or newborn nurseries has been documented. *Legionella pneumophila* outbreaks have been associated with contaminated cooling towers and hot water systems with subsequent dispersal into the air. *Aspergillus* and other fungal spores are easily dispersed through the air during building constructions/renovations/maintenance and are of major concern in wards with neutropaenic patients.
- ***Water.*** There are numerous reports in the literature detailing the association of health care associated infections with medical devices (e.g., respiratory therapy equipment, fibre-optic endoscopes etc.) that have been exposed to contaminated hospital water reservoirs (e.g., potable tap water, sinks, faucet aerators, etc.) Furthermore, environmental water reservoirs have been convincingly associated with infection involving aerosolization from these sources: faucet aerators associated with *Pseudomonas* infections and showerheads associated with *Legionella*. Ice machines have been implicated in the transmission of various pathogens including *Cryptosporidium parvum*.

  Several reports have linked hydrotherapy pools and tanks with the infection. The combination of organic debris from infected patients and elevated temperatures in these reservoirs favours growth of microorganisms.
- ***Carpets.*** The evidence that floors are directly associated with infection risks is scant. However, microbes are present in greater numbers on carpeting and if carpets are installed

they should be washable, have waterproof backing and sealed joints, and not be damaged by application of commonly used disinfectants. Noroviruses can remain viable for up to 10 days in carpets and it is therefore essential to clean them thoroughly. Steam cleaning is recommended for carpets and soft furnishings. To prevent fungal growth, wet carpets should be thoroughly dried. It is prudent to avoid carpets in isolation wards, high-traffic zones, and areas with frequent or large volume blood and other body fluid spillage such as surgical and obstetric wards.

- ***Specialized Patient Care Areas.*** The role of the operating room environment in causing surgical site infections is dealt with elsewhere in this handbook.

  The use of ultraclean rooms for certain patient categories in a general hospital remains controversial. These facilities are expensive and do not seem to provide clear benefit.
- ***Linen.*** Bed linen can become rapidly contaminated with colonized skin scales. Frequent changing is therefore of limited value. Linen should be changed on discharge of the patient or if it becomes soiled, wrinkled, stained or contaminated with potentially infective material. Privacy curtains have been shown to harbour organisms such as MRSA, GRE, *Acinetobacter* and *C difficile* and should be washed if visibly soiled and in certain outbreak situations. Although there is no clear guidance on how frequently privacy curtains must be routinely changed it seems prudent that, particularly during non-outbreak situations, they are removed and washed on a regular (e.g. monthly) basis.
- ***Plants/Flowers.*** Potted plants and flowers (particularly vase water) are well-established reservoirs of opportunistic pathogens. Since the mechanism for transmission requires that plant or vase water is handled, hands become contaminated and patient care is subsequently provided, hand washing after handling these items should eliminate the risk of hand contamination.
- ***Waste Disposal.*** There is no evidence to suggest that most clinical (potentially infectious) waste (with the exceptions of microbiological waste and contaminated syringe needles) constitutes a significant public hazard. Household waste

contains a least 100 times as many potential human pathogens as clinical waste. Segregation of clinical and domestic wastes in healthcare settings is important to contain costs, and avoid accidents and litigation. In areas where municipal waste disposal is not provided, e.g., in some developing countries and rural areas, burial of waste is common.

Controversial Issues

- The extent to which environmental reservoirs contribute to health care associated infections remains controversial. It is clear that the importance of cleaning needs to be backed up by robust scientific evidence. Although there is a lot of emerging literature highlighting the importance of a clean environment in infection prevention and control more studies, backed by established methods of assessment, need to be conducted.
- Use of detergents versus disinfectants for environmental (surfaces, noncritical) cleaning.
- Impact of disinfectant use on the emergence of antimicrobial resistance and need for biocide rotation.
- Routine use of automated area decontamination (AAD) technologies (e.g. using hydrogen peroxide, peracetic acid or UV irradiation).
- Microbial sampling of the environment.

Suggested Practice

General

- Meticulous hand washing is extremely important in preventing the transmission of microorganisms from the environment to patients, since most pathogens that may survive for prolonged periods of time in the environment are most likely to be transmitted by hand transfer. The use of non-aqueous, alcohol-based hand antiseptics is ideally suited to all healthcare facilities including those where hand washing facilities are scant and water is scarce.
- The environment should not be conducive to the multiplication of microorganisms and should be kept dry, clean, well-ventilated and ideally exposed to sunlight. Maintaining surfaces and equipment dry is important, as wet surfaces and equipment promote microbial growth and possible spread of pathogens.

- Cleaning procedures should be defined, applied consistently, and compliance to these validated. Cleaning personnel should be properly trained and responsibility for implementation of cleaning practices needs to be assigned.
- Contaminated near-patient hand-touch sites (e.g. drip stands, overbed tables, monitors, etc.) are likely to provide the greatest risk to patients as healthcare personnel frequently touch them. As ward cleaners infrequently clean hand-touch sites, nursing personnel should assume responsibility to ensure that they are regularly decontaminated.
- Products used for cleaning and decontamination of the environment should be used according to the hospital policy, manufacturer's instructions, and available scientific information.
- Infrequently touched ("non-hand-contact") environmental surfaces should be cleaned with a detergent when visibly soiled and as required to maintain an aesthetically pleasing environment.
- Dedicated noncritical equipment should be used on patients infected with multiply antibiotic resistant organisms. If this is not possible, shared noncritical items must be cleaned and disinfected between patient use.

Specific Interventions

- ***Air.*** Good air management is difficult to achieve in many healthcare facilities. An air maintenance programme should be in place and filters should be replaced periodically. Air-related outbreaks of legionellosis or aspergillosis, particularly in facilities where there are immunocompromised patients, prompt immediate investigation and consultation with a competent engineer. Potential sites of contamination need to be determined and appropriate corrective action must be taken.

  Patients with an airborne communicable disease (e.g. TB) should be isolated in a single room, if possible, or cohorted. Rooms with good airflow (open windows in many rural hospitals, use of extractor fans to the outside environment, or high volume ventilation greater than six air changes per hour including a good fresh air mix) lead to a reduced risk of TB transmission. Use of ultraviolet germicidal irradiation (UVGI)

may be considered in designated enclosed areas or booths for sputum induction. In rural healthcare facilities, where engineering controls are lacking, collection of sputum in sunny, open-air environments (outside the building) is advocated.

- ***Water.*** Legionellosis is an important disease for which an environmental reservoir (hot water in buildings) has been identified and for which specific preventive measures (e.g. water system management, superheating and/or use of biocides such as chlorine) are well described and advocated.

  Hydrotherapy pool water should be adequately filtered and chlorinated, hydrotherapy tanks should be cleaned thoroughly between each treatment and sharing of facilities by patients with open skin lesions should be avoided.

  Haemodialysis water has been clearly demonstrated to cause pyrogenic reactions (from endotoxins from Gram negative bacteria) and/or bacteraemia. Several types of bacteria are capable of surviving and multiplying in distilled, deionised, reverse osmosis and softened water, all of which may be used in haemodialysis. Water used to prepare dialysis fluid and the dialysate should be sampled monthly. The microbiologic limits for haemodialysis fluids vary in different countries according to the standard used. It should however be noted that the more stringent standards become the more difficult and impractical they become to implement in developing countries.

  Healthcare facilities should develop a routine maintenance programme for water filtration equipment to prevent bacterial overgrowth in filters and replace faulty ones. Water used for hand washing in oncology wards, diluting disinfectants, haemodialysis units, and rinsing semicritical items, may be heavily contaminated with organisms such as *Pseudomonas* and may pose a risk.

  Facilities should be prepared for situations where water is inaccessible (e.g. disaster situations, disruptions in water supply): ready-to-use disinfecting products that do not require rinsing must be available.

  Water in under-resourced areas can be made safer by solar disinfection using solar box cookers that reach pasteurisation temperatures, boiling (10 minutes), chemical disinfection, and filtration.

Environmental Surfaces:

- Walls and ceilings are unlikely to pose a significant infection hazard and should be periodically cleaned and not routinely disinfected in non-outbreak situations unless known contamination (e.g. blood splashes) has occurred. Cleaning of floors without the use of a disinfectant suffices in most instances. Levels of bacterial contamination on floors can be restored to their original values within 2 hours of cleaning, regardless of whether disinfectants are used or not.
- ***Linen.*** Although infectious risks associated with linen are low, it should be handled with care both in the ward and in the laundry. Persons handling soiled linen should do so with minimum agitation and must wear gloves. Linen should be transported to the laundry in a sealed bag. Linen from particularly hazardous and transmissible infections (e.g. viral hemorrhagic fevers) should be autoclaved before washing. Linen can be disinfected by heat (70°C for 3 minutes or 80°C for 1 minute) or with an appropriately diluted chlorine solution.
- ***Pest Control.*** A pest-control strategy in areas like kitchens cafeterias, laundries, central sterile supply services, operating rooms, and other areas prone to infestation is particularly important in healthcare facilities in developing countries. Screens on windows that open to the outside may be of particular Importance in regions where insect vector-borne infections are endemic.
- ***Waste Disposal.*** Disposal of waste must comply strictly with legislation. Clinical waste must be contained to prevent leakage, and sharps must be discarded into puncture-resistant containers. Disposal strategies include incineration, autoclaving followed by disposal with regular waste, mechanical/chemical disinfection, microwave decontamination and compacting. Waste such as blood, suctioned fluids, excretions and secretions can be poured down a sanitary sewer.

  Alternatives for disposal of medical waste commonly seen in countries with limited resources include: incineration of small amounts of waste in a metal drum, landfills or burial in refuse pits that are securely fenced off to prevent access to human and animal scavengers. Alternating layers of waste and ash help to reduce the smell.

Dealing with the Controversies

Detergent or disinfectant?

- Cleaning with detergent and water is usually adequate for surfaces and items remote from the patient or in contact with healthy, intact skin ("noncritical" items). Thorough cleaning renders most items free of infection risk and safe to handle. Disinfectants should only be used on environmental surfaces where potential risks are identified (e.g. decontamination of potentially infectious spills or of isolation rooms). Wet cleaning and damp dusting procedures are required to ensure that microorganisms are not made airborne from the surfaces that are being cleaned. All cleaning solutions should be changed regularly and cleaning utensils should be thoroughly washed, cleaned and dried before reuse.
- Terminal cleaning (when patient is discharged from the room or when isolation is discontinued) should be done as an opportunity to clean areas not routinely accessible.
- Currently accepted guidelines should be used for the disinfection and sterilization of semicritical and critical items.

Biocide rotation and antimicrobial resistance:

- Although there is laboratory evidence that low-level biocide resistance can be associated with cross-resistance to other biocides and some antibiotics, the significance of these phenomena in the clinical setting remains controversial.
- Rotation of biocides is probably unnecessary. No evidence is currently available that appropriately and correctly selected biocides have resulted in failures (arising from the selection or development of, non-susceptible microorganisms) in the clinical setting. Greater attention directed to environmental cleanliness, hand washing and personal hygiene is much more important.

Environmental cultures:

- Routine culturing of environment air is not advocated; it should only be performed when there is an epidemiological indication and for educational or research purposes. Because environmental sampling is costly, overused and misused, it should be conducted only with the approval and under the guidance of a competent infection control practitioner.

Use of automated area decontamination (AAD) technologies:

- The contribution of the environment in health care associated infections has been increasingly recognized in recent years. Manual cleaning and disinfection is carried out inadequately in many settings making the introduction of AAD technologies, *as an adjunct and not a replacement to routine cleaning,* a persuasive option. It will however be important to determine the clinical impact of the introduction of an AAD system in lowering health care associated infection rates rather than only measuring the impact of this technology on lowering environmental bioburden.

Summary

Inappropriate use of disinfectants, excessive microbiological sampling of the hospital environment and excessive and complex cleaning policies are neither cost-effective nor conducive to compliance in countries with limited resources. Healthcare facilities in developing countries will find it increasingly more difficult to comply with stringent protocols from developed countries. Adaptation of these protocols to realistically take into account the constraints of local situations and available resources is crucial to the success of environmental infection control programs. Rational, simple protocols based on sound principles of infection control, hand washing, and common sense will go far in minimizing environmental risks of infection.

References

Babb J. Decontamination of the Environment, Equipment and the Skin *in* Control of Hospital Infection (4th Edition), Ayliffe GAJ, Fraise AP, Geddes AM, Mitchell K, (Eds). London: Arnold, 2000. Pgs. 92–129.

Boyce JM. Environmental contamination makes an important contribution to hospital infection. *J Hosp Infect*. 2007. 65(Suppl 2):50–54.

Dancer SJ. Mopping up hospital infection. *J Hosp Infect*. 1999. 43:85–100.

Dancer SJ. The role of environmental cleaning in the control of hospital acquired infection. *J Hosp Infect*. 2009. 73:378–385.

Daschner F. The Hospital and Pollution: Role of the Hospital Epidemiologist in Protecting the Environment *in* Prevention and Control of Nosocomial Infections (2nd Edition), Wenzel RP (Ed). Baltimore: Williams and Wilkins, 1993. Pgs. 993–1000.

Department of Health, United Kingdom. Standard principles for preventing hospital acquired infections. *J Hosp Infect*. 2001. 47(Suppl):S21–S37.

Dharan S, Mouroga P, Copin P, Bessmer G, Tschanz B, Pittet D. Routine disinfection of patient's environmental surfaces. Myth or reality? *J Hosp Infect*. 1999. 42:113–117.

Global consensus conference on infection control issues related to antimicrobial resistance. Global consensus conference: Final recommendations. *Am J Infect Control*. 1999. 27:503–513.

Lederer W. Infection control in a small rural hospital in Uganda. *J Hosp Infect*. 1997. 35:91–95.

Lynch P, Jackson M, Preston GA, Soule BM. Infection Prevention with Limited Resources. Chicago: Etna Communications, 1997. Pgs. 71–74.

Guidelines for Environmental Infection Control in Healthcare Facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR*. June 6, 2003. Vol. 52, No. RR-10.

Murtough SM, Hiom SJ, Palmer M, Russell AD. Biocide rotation in the healthcare setting: Is there a case for policy implementation? *J Hosp Infect*. 2001. 48:1–6.

Phillips G. Microbiological aspects of clinical waste. *J Hosp Infect*. 1999. 41:1–6.

Rhame FS. The Inanimate Environment *in* Hospital Infections (4th Edition), Bennett JV, Brachman PS (Eds). Philadelphia: Lippincott-Raven, 1998. Pgs. 299–324.

Rutala WA, Weber DJ. Surface disinfection: Should we do it? *J Hosp Infect*. 2001. 48(Suppl A):S64–S68.

Talon D. The role of the hospital environment in the epidemiology of multi-resistant bacteria. *J Hosp Infect*. 1999. 43:13–17.

Vesley D, Streifel AJ. Environmental Services *in* Hospital Epidemiology and Infection Control (2nd Edition), Mayhall CG (Ed). Philadelphia: Lippincott Williams and Wilkins, 1999. Pgs. 1047–1053.

Weber DJ, Rutala WA. Environmental Issues and Nosocomial Infections *in* Prevention and Control of Nosocomial Infections (2nd Edition), Wenzel RP (Ed). Baltimore: Williams and Wilkins, 1993. Pgs. 420–449.

CHAPTER 24

The Emergency Department and Receiving Areas

Pawan Suri, MD, and
Ravindra Gopaul, MD,

Key Issue

Healthcare workers in the emergency department and receiving areas need to be aware of the risks posed by blood and air-borne infections, and take measures to limit exposure through early identification and isolation of high risk patients.

It is mandatory to identify and isolate patients with highly contagious infections (e.g. tuberculosis) or when exposure to a bioterror agent is known or suspected.

Known Facts

Universal precautions are promoted by the Centers for Disease Control and Prevention because when patients initially present seeking medical care, it is often not known if their blood may contain the hepatitis B or C viruses, human immunodeficiency virus (HIV), or other pathogens. All blood should be considered potentially contaminated, and efforts should be made to avoid direct contact, mucous membrane exposure, and sharp injuries.

In addition, respiratory protection is prudent when caring for patients with suspected or confirmed tuberculosis or other highly contagious air-borne infections (e.g., SARS).

Controversial Issues

- With respect to isolation, there is limited data comparing the cost and efficacy of different methods (provider face masks, negative pressure rooms etc.).The type of isolation used is based on the mode of disease transmission. Overall, the costs associated with initiating basic isolation precautions are usually low and the benefits far outweigh the expense.

- The benefit of ventilation measures in the hospital on tuberculin conversion in healthcare providers is still under investigation. Higher tuberculin conversion rates have been reported among personnel who work in nonisolation patient rooms or rooms with fewer than 2 air exchanges per hour. Guidelines for the prevention of health care associated transmission of tuberculosis recommend minimum air change rates of 2 to 15 per hour.
- There is scarce data on the ability of healthcare workers to identify patients at risk for transmitting infections. Patients with active pulmonary tuberculosis are often missed at emergency triage. In retrospect, some of these patients may have presented with typical symptoms and risk factors that are easily overlooked in a busy triage environment. Each emergency department should evaluate its process to see if opportunities for earlier diagnosis of tuberculosis exist.

Suggested Practice

- Provide patient educational material about hand and respiratory hygiene/cough etiquette in emergency receiving and waiting areas.
- Mandatory careful hand hygiene, preferably with alcohol based hand sanitizer, before and after each patient encounter.
- Gloves and isolation gowns should be worn when contact with blood and body fluids is likely.
- Goggles or face masks should be worn when splashing of blood or body fluids is anticipated.
- Appropriately sized face masks should be worn in cases of suspected air-borne infection (e.g. tuberculosis, SARS).
- Triage personnel should be trained to identify high risk patients with potential communicable infections.
- Patients who appear unusually ill, especially with cough, should be isolated (>3 feet distance) or provided a mask to limit risk to healthcare personnel and other patients.
- Patients who may have had a chemical exposure from a bioterror attack should be isolated and decontaminated as soon as possible.
- Efforts should be made to minimize staff flow between isolated and non-isolated patients.

Summary

The adoption of reasonable healthcare safety precautions, as listed above, can minimize transmission of most contact-related infections in the emergency department. All personnel handling blood, body fluids or sharps should be vaccinated against hepatitis B. Providing and using sharp containers reduces the risk of blood borne infections.

Risk of airborne infections can be minimized through use of rooms with exhaust fans or adequate ventilation.

Occupational exposure to blood or droplets should be reported. Post-exposure counselling and therapy, if necessary, should be offered to all clinical personnel.

References

Centers for Disease Control and Prevention. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. *MMWR*. 2001. 50 (RR-l1):l–54.

Centers for Disease Control and Prevention. Guidelines for Environmental Infection Control in Healthcare Facilities. *MMWR*. 2003. 52(RR-10):1–42.

Menzies D, Fanning A, Yuan L, et al. Hospital Ventilation and Risk for Tuberculous Infection in Canadian Healthcare Workers. *Ann Intern Med*. 2000. 133:779–789.

Sokolove PE, Rossman L, Cohen SH. The Emergency Department Presentation of Patients with Active Pulmonary Tuberculosis. *Acad Emerg Med*. 2000. 7:1056–1060.

Siegel, JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee: 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings, June 2007. Available at: http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html.

CHAPTER 25

HIV Infection and AIDS in Low- and Middle-Income Countries

Philippe Van de Perre, MD, PhD

Key Issues

Thirty years after it was first recognized in Africa, HIV infection is one of the leading cause of adult deaths in many cities in low- and middle-income countries, and it has significantly increased childhood mortality. Despite considerable efforts to control the epidemic, HIV continues to spread at a rapid pace in developing countries. Of an estimated 34 million people infected by HIV world-wide(as of December 2010), 3.4 million were children less than 15. For the sole year 2010, new HIV infections were 2.7 million in adults and 390,000 in children. Although the yearly number of newly acquired infections continues to decline, most people newly infected with HIV live in sub-Saharan Africa.[1] An estimated 1.8 million people died of HIV infection during 2010.

In the last decades, the development of new antiretroviral (ARV) drugs (*Table 25.1 and 25.2*) and the extended access to Antiretroviral Therapy (ART) for HIV-infected patients have been accompanied by a dramatic reduction in HIV-associated mortality. Today, for those who have access to ARV drugs, HIV infection should be considered as a manageable chronic illness. In 2010, the World Health Organization estimated that 6.65 million people from low- and middle-income countries received ART, including 456,000 children.[1] The coverage of antiretroviral drugs for preventing Mother-to-Child Transmission (MTCT) of HIV has also steadily increased over the last years and was estimated to be 48% in 2010.[1] The global challenge remains to scale up access to ARV drugs for all HIV-infected individuals who need it together with preventing the acquisition of new infections.[2]

Table 25.1 Antiretroviral Drugs Used in the Treatment of HIV Infection
As of February 8, 2013

Multi-class Combination Products

Brand Name	Generic Name	Manufacturer Name*
Atripla	efavirenz, emtricitabine and tenofovir disoproxil fumarate	Bristol-Myers Squibb and Gilead Sciences
Complera	emtricitabine, rilpivirine, and tenofovir disoproxil fumarate	Gilead Sciences
Stribild	elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate	Gilead Sciences

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Brand Name	Generic Name	Manufacturer Name
Combivir	lamivudine and zidovudine	GlaxoSmithKline
Emtriva	emtricitabine, FTC	Gilead Sciences
Epivir	lamivudine, 3TC	GlaxoSmithKline
Epzicom	abacavir and lamivudine	GlaxoSmithKline
Hivid	zalcitabine, dideoxycytidine, ddC (no longer marketed)	Hoffmann-La Roche
Retrovir	zidovudine, azidothymidine, AZT, ZDV	GlaxoSmithKline
Trizivir	abacavir, zidovudine, and lamivudine	GlaxoSmithKline
Truvada	tenofovir disoproxil fumarate and emtricitabine	Gilead Sciences, Inc.
Videx EC	enteric coated didanosine, ddI EC	Bristol Myers-Squibb
Videx	didanosine, dideoxyinosine, ddI	Bristol Myers-Squibb
Viread	tenofovir disoproxil fumarate, TDF	Gilead
Zerit	stavudine, d4T	Bristol Myers-Squibb
Ziagen	abacavir sulfate, ABC	GlaxoSmithKline

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Brand Name	Generic Name	Manufacturer Name*
Edurant	rilpivirine	Tibotec Therapeutics
Intelence	etravirine	Tibotec Therapeutics
Rescriptor	delavirdine, DLV	Pfizer

continued

Table 25.1 Antiretroviral Drugs Used in the Treatment of HIV Infection
As of February 8, 2013 (continued)

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Brand Name	Generic Name	Manufacturer Name
Sustiva	efavirenz, EFV	Bristol Myers-Squibb
Viramune (Immediate Release)	nevirapine, NVP	Boehringer Ingelheim
Viramune XR (Extended Release)	nevirapine, NVP	Boehringer Ingelheim

Protease Inhibitors (PIs)

Brand Name	Generic Name	Manufacturer Name*
Agenerase	amprenavir, APV (no longer marketed)	GlaxoSmithKline
Aptivus	tipranavir, TPV	Boehringer Ingelheim
Crixivan	indinavir, IDV,	Merck
Fortovase	saquinavir (no longer marketed)	Hoffmann-La Roche
Invirase	saquinavir mesylate, SQV	Hoffmann-La Roche
Kaletra	lopinavir and ritonavir, LPV/RTV	Abbott Laboratories
Lexiva	fosamprenavir calcium, FOS-APV	GlaxoSmithKline
Norvir	ritonavir, RTV	Abbott Laboratories
Prezista	darunavir	Tibotec, Inc.
Reyataz	atazanavir sulfate, ATV	Bristol-Myers Squibb
Viracept	nelfinavir mesylate, NFV	Agouron Pharmaceuticals

Fusion Inhibitors

Brand Name	Generic Name	Manufacturer Name*
Fuzeon	enfuvirtide, T-20	Hoffmann-La Roche & Trimeris

Entry Inhibitors – CCR5 Co-Receptor Antagonist

Brand Name	Generic Name	Manufacturer Name*
Selzentry	maraviroc	Pfizer

HIV Integrase Strand Transfer Inhibitors

Brand Name	Generic Name	Manufacturer Name*
Isentress	raltegravir	Merck & Co., Inc.

Source: FDA http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm118915.htm

Table 25.2 FDA approved generic formulations of antiretroviral drugs used in the treatment of HIV infection
As of February 8, 2013

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Generic Name	Manufacturer Name
abacavir tablets USP, 300 mg	Mylan Pharmaceuticals, Inc.
nevirapine tablets USP, 200 mg	Prinston Pharmaceutical, Inc.
nevirapine tablets USP, 200 mg	Apotex Corporation
nevirapine tablets USP, 200 mg	Matrix Laboratories Limited
nevirapine tablets USP, 200 mg	ScieGen Pharmaceuticals, Inc
nevirapine tablets USP, 200 mg	Mylan Pharmaceuticals, Inc.
nevirapine tablets USP, 200 mg	Hetero Labs Limited, Unit-III
nevirapine tablets USP, 200 mg	Micro Labs Limited
nevirapine tablets USP, 200 mg	Strides, Inc.
nevirapine tablets USP, 200 mg	Cipla Limited
nevirapine tablets USP, 200 mg	Aurobindo Pharma Limited
nevirapine oral suspension USP, 50 mg/5 mL	Aurobindo Pharma Limited
lamivudine and zidovudine tablets, 150 mg/300 mg	Aurobindo Pharma Limited
lamivudine and zidovudine tablets, 150 mg/300 mg	Lupin Limited
lamivudine and zidovudine tablets, 150 mg/300 mg	TEVA Pharmaceuticals USA
zidovudine Injection USP, 10 mg/mL, packaged in 200 mg/20 mL Single-use Vials	PharmaForce Inc.
didanosine (ddI) delayed release capsules, 125 mg, 200 mg, 250 mg, and 400 mg	Matrix Laboratories Limited
zidovudine 60 mg tablets for pediatric dosing	Aurobindo Pharma Limited
stavudine for oral solution, 1 mg/mL	Aurobindo Pharma Limited
stavudine capsules (15 mg, 20 mg, 30 mg, and 40 mg)	Aurobindo Pharma Limited
stavudine capsules (15 mg, 20 mg, 30 mg, and 40 mg)	Hetero Drugs Limited

continued

Table 25.2 FDA approved generic formulations of antiretroviral drugs used in the treatment of HIV infection
As of February 8, 2013 (continued)

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	
Generic Name	**Manufacturer Name**
didanosine (ddI) delayed release capsules, 125 mg, 200 mg, 250 mg, and 400 mg	Aurobindo Pharma Limited
zidovudine oral solution USP, 50 mg/5 mL, oral solution—zidovudine, AZT, azidothymidine, ZDV (Pediatric formulation—50 mg/ 5 mL)	Cipla Limited
zidovudine, AZT, azidothymidine, ZDV (300 mg tablet)	Matrix Laboratories, Inc.
zidovudine, AZT, azidothymidine, ZDV (100 mg capsule)	Cipla Limited
didanosine (ddI) for oral solution (pediatric powder), 10 mg/mL	Aurobindo Pharma Limited
zidovudine, AZT, azidothymidine, ZDV (100 mg capsule)	Aurobindo Pharma Limited
zidovudine, AZT, azidothymidine, ZDV (300 mg tablet)	Aurobindo Pharma Limited
zidovudine oral solution USP, 50 mg/5 mL, oral solution—zidovudine, AZT, azidothymidine, ZDV (Pediatric formulation—50 mg/ 5 mL)	Aurobindo Pharma Limited Ranbaxy Laboratories Limited
zidovudine, AZT, azidothymidine, ZDV (300 mg tablet)	
zidovudine, AZT, azidothymidine, ZDV (300 mg tablet)	Roxane Laboratories
didanosine (ddI) delayed release capsules	Barr Laboratories, Inc.

Source: FDA http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm118944.htm

Known Facts

- Both HIV type 1 (HIV-1) and HIV type 2 (HIV-2) are circulating in low- and middle-income countries. HIV-2, which is mostly spread in West Africa where it co-exists with HIV-1, is less transmissible and less pathogenic than HIV-1. HIV-2 as HIV-1 group O are naturally resistant to non nucleosidic reverse transcriptase inhibitors.

- All groups of HIV-1 (group M, N and O) as well as all genotypic subtypes of HIV-1 group M (subtypes A to K) and Recombinant Circulating Forms (CRFs) are co-circulating in low- and middle-income countries but regional distribution of groups, subtypes and CRFs varies considerably.
- Transfusion of HIV contaminated blood is still responsible for about 10% of overall transmission events.
- Blood banking organization, selection of blood donors and HIV testing of blood donations are effective in preventing transfusion-associated infections.
- Sexual transmission remains by far the most frequent route of transmission in adults. Sexually Transmitted Infections (STI) are facilitating HIV transmission by sexual intercourse.
- Control of STI at the community level is a cost-effective strategy to prevent sexual transmission of HIV.
- MTCT of HIV involves almost exclusively HIV-1 and can occur *in utero,* during labor and delivery and postnatally by breastfeeding. MTCT rate is estimated 20–30% in breastfeeding populations in the absence of prophylaxis.
- Prevention of MTCT by treating HIV-infected pregnant women and their neonates with antiretrovirals is highly efficacious.[3] Postnatal HIV transmission through breastfeeding poses a difficult public health problem that can be prevented by administering antiretroviral prophylaxis to lactating mothers or, as a pre exposure prophylaxis (PreP) to their breastfed babies.[3,4]
- Susceptibility to acquisition of HIV and clinical course of HIV disease are highly variable and may be determined at the individual level by the existence of genetic factors such as deletions on the genes coding for cellular cofactors for viral entry (such as CCR5) or their promotors. New strategies to prevent sexual transmission are in development, the efficacy of some of them, such as vaginal microbicides[5] and PreP,[6] having been demonstrated.
- More than 85% of fatal overwhelming infections associated with HIV as well as the first five causes of mortality in HIV-infected African patients (*Table 25.3*) are potentially amenable to a simple, effective and frequently affordable

anti-infectious treatment or prophylaxis, such as the use of cotrimoxazole.[7] The most devastating public health impact of HIV-1 infection on other endemic diseases is on tuberculosis. In sub-Saharan Africa, the annual incidence of tuberculosis is more than 15-fold greater in HIV-infected individuals than in HIV-uninfected individuals. In patients eligible for ART with active TB, antiretroviral therapy should be initiated shortly (2 weeks) after the initation of TB treatment.[8]

Table 25.3 Principal causes of death in HIV-infected African patients
(autopsy study, n = 247; Abidjan, Côte d'Ivoire, 1991)

Rank order	*Causes of death*	*Prime cause of death**
1	Tuberculosis	32 %
2	Bacteremia	11 %
3	Cerebral toxoplasmosis	10 %
4	Pyogenic pneumonia	8 %
5	Pyogenic meningitis	5 %

* Proportion of deaths considered as primarily caused by the given condition.

- Clinical management of HIV-infected patients is based on access of healthcare quality services: diagnosis and treatment of tuberculosis and of other infectious diseases (pneumococcal disease, bacteraemia,). As a priority, lifelong ART should be administered in a patient with HIV associated signs or symptoms (WHO clinical stage 3 or 4) and/or with less than 350 CD4+ T cells per µl. ART should be initiated in all adult individuals with HIV with CD4 count > 350 cells per µland < 500 cells per µl regardless of WHO clinical stage.[2] In infants and children with HIV infection, ART should be initiated as soon as the HIV diagnosis is confirmed, if possible during the first year of life.
- HIV is highly sensitive to physic and chemical environment and to widely used disinfectants. Reinforced hospital hygiene measures are of practical importance to minimize the risk of exposure to HIV-containing blood and body fluids in the healthcare settings. Postexposure prophylaxis by means of a combination of ARV [generally three drugs given

as soon as possible after exposure, for one month] is highly efficacious in preventing acquisition of HIV-1 infection after accidental exposure to the virus in the healthcare setting.[9] An adjustment of regimen according to the index patient profile of antiretroviral resistance may be necessary.

Controversial Issues

- Scaling up access to ART in low- and middle-income countries, and monitoring it in terms of adherence, efficacy, tolerance and sustainability remain major challenges. Adherence is critical for treatment success and the best ways for optimizing adherence are under scrutiny. The most optimal way to follow up the biological efficacy of ART in low- and middle-income countriesremainsdebatable. Several schemes have been proposed: clinical follow up only, clinical follow up and CD4 counts, or same with viral load measurements to detect viral escape.
- In HIV infected individuals,co-infections with hepatitis C (HCV) or B (HBV) viruses are frequent. Although considerable progress have been accomplished in treating these co-infections jointly with HIV, the access to anti-HCV and some anti-HBV drugs remains problematic in many low- and middle-income countries.
- Access to second and third lines of ART remains extremely problematic in many low- and middle-income countries. The best combinations to propose in second and third lines are under evaluation.
- The interactions between HIV infection and other tropical diseases, such as malaria, other parasitosis, or malnutrition, remain largely undetermined. Also, the complex interactions between HIV disease progression and reactivations of chronic infections, such as infections with herpesviruses, and immune activation remain to be clarified.
- The recent WHO guidelines on prevention of MTCT of HIV have the ambition to eliminate the MTCT of HIV and recommend, in particular in generalized epidemics,that all pregnant and breastfeeding women infected with HIV should initiate ART which should be maintained at least for the duration of MTCT risk. Particularly in generalized epidemics, all pregnant or breastfeeding women with HIV

infection should initiate lifelong ART, regardless of clinical or immunological stage.[2] The individual benefit of this strategy, in particular for asymptomatic women with high CD4 count, the long term maternal adherence and even the efficacy in preventing postnatal HIV transmission and MTCT in subsequent pregnancies are all unknown, since these guidelines have been based mostly on expert advice and less on scientific evidence.[10] Several studies on prolonged maternal and/or infant ARV prophylaxis during breastfeeding are ongoing in order to determine if it can achieve elimination of breastfeeding transmission of HIV-1.

- Treatment as Prevention (TasP) strategy, consisting as administering ART to all HIV infected individuals regardless of their CD4 T cell count or HIV viral load with the aim of both interrupting transmission and universalizing ARV treatment for the individual's own benefit, is attractive. The long term individual and societal benefits and the cost-effectiveness of this strategy remain, however, controversial and are the subjects of ongoing large-scale trials.
- Although some encouraging results have been obtained in recent years, a preventive HIV vaccine has remained elusive. Various existing preventive strategies combined in comprehensive packages are presently under investigation.

Suggested Practices

- Prevention and clinical and psychosocial management and a continual struggle against discrimination/stigmatisation are all integral parts of HIV/AIDS control programmes. Each of these components is not sufficient in itself but all are synergistic.
- Voluntary counselling and testing for HIV is the entry point of HIV prevention and care and has to be made available widely.
- In terms of prevention the following strategies should be implemented:
  - STI diagnosis and treatment at the community level (based on well validated treatment algorithms) as well as large access to male and female condoms and, in some circumstances, vaginal microbicides and PreP;

- Blood bank organization, blood donors' selection and HIV testing of blood donations;
- Increased accessibility of mother and child to high quality healthcare services (antenatal clinics, basic obstetrical needs, nutritional education) including a thoughtful package of antenatal care. Provision of ART to breastfeeding or pregnant women as per 2013 WHO recommendations;[2]
- Reinforcement of available health programmes (TB control, malaria control, expanded programme on immunization, maternal and child care, family planning, et cetera);
- Access of all health professionals to post exposure prophylaxis in case of accidental exposure to blood or body fluids potentially containing HIV and hepatitis viruses.

• In terms of psychosocial and clinical management the following strategies should be implemented:
  - Skilled, acceptable, accessible and sustainable voluntary HIV counselling and testing services;
  - Simple clinical algorithms for clinical management of HIV disease and treatment of infectious episodes by means of available essential drugs and including nutritional support;
  - Decentralised management and community support;
  - Improved integrated strategies to diagnose and treat TB;
  - As a priority, initiation of a combination of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI), preferentially as a fixed-dose combination, in all individuals with HIV related signs and symptoms and/or of a CD4+ T cell count of less than 350 per μl together with a meaningful encouragement for adherence and careful clinical and biological monitoring (biochemistry in search for drug toxicity, CD4 count and HIV viral load for monitoring of treatment efficacy). ART should also be initiated in all individuals with HIV and a CD4 count > 350 cells per μl and < 500 cells per μl regardless of WHO clinical stage;
  - In patients not eligible for ART, prophylaxis of opportunistic infections by antibiotics (such as daily cotrimoxazole), together with a careful monitoring of HIV clinical course is to be implemented.

References

[1]WHO/UNAIDS/UNICEF Global HIV/AIDS response—Epidemic update and health sector progress toward Universal Access—Progres Report 2011 http://www.who.int/hiv/pub/progress_report2011/summary_en.pdf

[2]World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing hiv infection—Recommandations for a public health approach. June 2013. http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_eng.pdf

[3]The Kesho Bora Study Group. Triple-antiretroviral prophylaxis during pregnancy and breastfeeding compared to AZT/sdNVP prophylaxis to prevent mother-to-child transmission of HIV-1: The Kesho Bora randomized controlled clinical trial. *Lancet Infect Dis*. 2011. 11:171–80.

[4]Coovadia HM, Brown ER, Fowler MG, Chipato T, Moodley D, Manji K, Musoke P, Stranix-Chibanda L, Chetty V, Fawzi W, Nakabiito C, Msweli L, Kisenge R, Guay L, Mwatha A, Lynn DJ, Eshleman SH, Richardson P, George K, Andrew P, Mofenson LM, Zwerski S, Maldonado Y; HPTN 046 protocol team. Efficacy and safety of an extended nevirapine regimen in infant children of breastfeeding mothers with HIV-1 infection for prevention of postnatal HIV-1 transmission (HPTN046): A randomized, double-blind, placebo-controlled trial. *Lancet*. 2012. 379:221–228.

[5]Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, Kharsany AB, Sibeko S, Mlisana KP, Omar Z, Gengiah TN, Maarschalk S, Arulappan N, Mlotshwa M, Morris L, Taylor D; CAPRISA 004 Trial Group. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010. 329:1168–1174.

[6]Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, Tappero JW, Bukusi EA, Cohen CR, Katabira E, Ronald A, Tumwesigye E, Were E, Fife KH, Kiarie J, Farquhar C, John-Stewart G, Kakia A, Odoyo J, Mucunguzi A, Nakku-Joloba E, Twesigye R, Ngure K, Apaka C, Tamooh H, Gabona F, Mujugira A, Panteleeff D, Thomas KK, Kidoguchi L, Krows M, Revall J, Morrison S, Haugen H, Emmanuel-Ogier M, Ondrejcek L, Coombs RW, Frenkel L, Hendrix C, Bumpus NN, Bangsberg D, Haberer JE, Stevens WS, Lingappa JR, Celum C; PartnersPrEPStudy Team. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012. 367:399–410.

[7]Anglaret X, Chene G, Attia A, Toure S, Lafont S, Combe P, Manlan K, N'Dri-Yoman T, Salamon R. Early Chemoprophylaxis With Trimethoprim-Sulphamethoxazole for HIV-1-Infected Adults in Abidjan, Cote d'Ivoire: A Randomized Trial. Cotrimo-CI Study Group. *Lancet*. 1999. 353:1463–1468.

[8]Blanc FX, Sok T, Laureillard D, Borand L, Rekacewicz C, Nerrienet E, Madec Y, Marcy O, Chan S, Prak N, Kim C, Lak KK, Hak C, Dim B, Sin CI, Sun S, Guillard B, Sar B, Vong S, Fernandez M, Fox L, Delfraissy JF, Goldfeld AE; CAMELIA (ANRS 1295–CIPRA KH001) Study Team. Earlier versus later start of antiretroviral therapy in HIV-infected adults with tuberculosis. *N Engl J Med*. 2011. 365:1471–81.

[9]Kuhar DT, Henderson DK, Struble KA, et al. Updated US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis. *Infect Control Hosp Epidemiol*. 2013. 34:875–92.

[10]Van de Perre P, Tylleskar T, Delfraissy JF and Nagot N. Evidence-based public health policies: The case of the prevention of mother-to-child HIV transmission. *Brit Med J*. 2013. 346:f3763.

CHAPTER 26

Tuberculosis

Paul R. Allyn, MD, and Timothy F. Brewer, MD, MPH

Key Issue

Tuberculosis (TB) remains one of the leading causes of preventable deaths in adults worldwide. The vast majority of TB cases and deaths occur in low resource areas. Health care associated transmission of TB to healthcare workers and patients occurs in both high and low-income countries. Effective infection control practices can reduce the risk of TB transmission in healthcare settings.

Known Facts

- Transmission of TB primarily occurs via inhalation of infectious airborne droplet nuclei.
- Transmission of TB to healthcare workers and health care associated outbreaks of TB among patients, including multidrug-resistant TB (MDR-TB), have been well documented in industrialized and low resource countries.
- Healthcare workers are at increased risk for both latent TB infection (LTBI) and active TB disease compared to the general population.
- Human immunodeficiency virus (HIV) infected healthcare workers with latent TB infection have a high risk of progressing to active TB disease.
- Patient factors associated with TB transmission include coughing, smear-positivity, disease of the larynx or lungs, cavitary disease on chest radiography, and inappropriate anti-TB therapy.
- Procedures that result in the aerosolization of *Mycobacterium tuberculosis* such as bronchoscopy, sputum induction, endotracheal intubation, respiratory suction, and autopsies have resulted in TB transmission to healthcare workers.

- Many TB patients, including those with MDR-TB, may be effectively treated in community-based settings avoiding hospitalization and reducing the risk of health care associated transmission.
- Treatment of LTBI reduces the risk of active TB disease.
- Effective infection control practices lower the risk of new TB infections in healthcare workers and patients.

Controversial Issues

- The benefit of environmental controls such as ultraviolet germicidal irradiation (UVGI) or increasing the number of air changes per hour (ACH) to > 12 in reducing health care associated transmission of TB is unknown.
- Universal screening of healthcare workers in TB endemic countries for HIV infection.
- Screening and treatment of healthcare workers in TB endemic countries for LTBI.
- Use of surgical masks worn by suspected or confirmed TB patients to prevent health care associated transmission.
- Efficacy of N95 masks in reducing health care associated transmission of TB when other controls are in place.

Suggested Practice

Preventing TB transmission in healthcare facilities requires early identification, isolation, and treatment of patients with active TB disease. Recommended infection control strategies to reduce TB transmission depend on the prevalence of active TB in the patient population and the resources available to implement control programs. Unfortunately, the areas with the greatest need for TB infection control policies often have the fewest resources for creating and maintaining effective control programs. Many inexpensive interventions can significantly reduce the risk of TB transmission in healthcare settings.

Administrative Controls

Administrative controls are the first and most-important level of TB control in healthcare settings. The following measures should be taken:

- Assign responsibility to an infection control officer, nurse, or other employee for implementation, enforcement, and evaluation of TB infection control policies.

- Conduct a TB risk assessment at the facility to include identifying the number of TB patients seen at the facility, the amount of time TB patients spend in different areas such as emergency rooms (ER), waiting rooms, or wards, the prevalence of HIV among healthcare workers and patients, the specific role of the healthcare workers and their potential exposures to infectious droplets.
- Develop and implement a TB infection control policy to ensure prompt detection, isolation, and treatment of persons with suspected or confirmed TB disease. Once policies have been established and put into place, ongoing enforcement and education for healthcare workers are crucial as studies have shown that adherence to TB control measures falls over time without continuous education and monitoring. Repeat risk assessments at least yearly to determine if control measures are sufficient and effective.
- Evaluate the use of current facilities and the need for renovation or development of new spaces to provide adequate implementation of controls.
- Ensure timely availability of laboratory testing, processing, and reporting, specifically by providing and optimizing the turnaround time for sputum testing and culture.
- Ensure proper cleaning and disinfection of potentially contaminated equipment (e.g. endoscopes).
- Perform active surveillance of healthcare workers for active TB disease. Consider screening healthcare workers for LTBI and treating them if present.
- Develop an educational program for all healthcare workers. This should provide information on TB transmission, recognizing the signs and symptoms of active TB, understanding the interaction between TB and HIV, and the control policies in place to prevent TB transmission to healthcare workers and patients.
- Provide HIV screening to healthcare workers. HIV-positive healthcare workers should limit time spent in high-risk TB transmission areas (e.g. emergency rooms, TB wards, sputum collection areas, and bronchoscopy suites), undergo routine screening for active TB, and have access to both antiretroviral therapy and isoniazid preventive therapy.

- Promptly identify patients with TB symptoms and separate them from other patients, including those with active TB, until they can undergo sputum testing, preferably with a World Health Organization (WHO) recommended rapid diagnostic test. Specific symptom criteria for triage will depend on the setting and patient population, but should include cough greater than 2 weeks, hemoptysis, fever, weight loss, and night sweats.
- Isolate patients diagnosed with active TB from other patients, especially from those patients with known or suspected HIV. Specific criteria for isolation (e.g. smear positivity, culture status) will depend on local settings and patient population. MDR-TB and extremely drug-resistant TB (XDR-TB) patients should also be separated from other patients, including those with drug sensitive TB, as transmission may occur between groups. If individual isolation rooms are not available, a cohort system may be used.
- Continue airborne isolation of patients with active TB until they are no longer infectious.
- Educate patients with suspected or confirmed TB about respiratory hygiene and cough etiquette at the time of triage. They should be provided with surgical masks, tissues, or cloths and instructed to turn their heads and cover their mouths when coughing or sneezing.
- Promptly initiate anti-TB therapy in patients diagnosed with active TB according to treatment guidelines developed by the WHO, United States Centers for Disease Control (CDC), or similar expert group.
- Minimize time spent in healthcare settings. Routine hospitalization to commence TB treatment is not necessary and should be reserved for those patients who otherwise require inpatient care. Pursue outpatient evaluation and treatment where appropriate.
- Use appropriate signage to indicate isolation areas and to promote cough etiquette.

Environmental Controls

Environmental controls consist of those measures that prevent the spread and reduce the concentration of infectious droplet nuclei in ambient air.

- Adequate ventilation in healthcare settings is essential for preventing the transmission of TB and other airborne infections. Particular attention should be paid to high-risk transmission areas such as emergency rooms, waiting rooms, sputum collection areas, TB wards, procedure areas, and TB isolation rooms.
- Natural, mixed-mode, and mechanical ventilation systems may be used. The choice of ventilation system depends on an assessment of the facility and should be informed by local programmatic, climatic, and socioeconomic conditions. Any ventilation system requires ongoing monitoring and maintenance on a regular schedule.
- Regardless of the type of ventilation system used, design should seek to achieve airflow from the source of potential contamination to air exhaust points or to areas away from other patients that allow for sufficient air dilution.
- In high-income nations, TB patients and those undergoing evaluation for TB should be isolated in airborne infection isolation (AII) rooms. These rooms are designed with negative pressure so that air flows from the corridor into the room and not from the room into the corridor. Such rooms should be mechanically ventilated to a minimum of 12 air changes per hour (ACH).
- Natural ventilation systems may be used where resources preclude the construction or maintenance of AII rooms. In fact, studies have shown that natural ventilation may provide better ventilation than rooms with mechanical ventilation with up to 28–40 ACH. Factors associated with improved ventilation include opening windows and doors, larger window and door openings, cross-ventilation, and wind speed. As noted above, careful attention should be paid to direction of airflow to avoid contamination of surrounding areas. Consider placing high-risk isolation areas on upper floors of buildings, higher elevations, or downwind of non-TB and HIV wards.
- Well-designed, maintained, and operated fans can improve ventilation and air mixing. Such mixed-mode ventilation systems may be used if natural ventilation alone does not provide adequate ventilation. A window fan exhausting air outside is also a relatively inexpensive way of creating a negative pressure room, though the efficacy of this approach

in preventing health care associated TB transmission is unknown.

- Other low-cost strategies to reduce transmission in TB-endemic, low-resource settings include separate open-air shelters or waiting rooms for patients with suspected TB awaiting or undergoing evaluation, installation of large windows, skylights, high-level windows or vents installed just under the ceiling, or opening vents or windows on doors to help improve cross-ventilation. Consider designing buildings with up-sloping ceilings or roofs with open gaps or windows at the high points to allow for stack ventilation. This also creates natural airflow as hot air rises. Simple wind-driven turbines placed on the roof may also help extract air from the building and improve ventilation.
- Conduct periodic air exchange measurements and airflow evaluation.
- For closed mechanical ventilation systems where resources allow, air from TB isolation rooms should be exhausted outside away from intake fans or waiting areas and passed through high-efficiency particulate (HEPA) filters before being re-circulated. Though the effectiveness of HEPA filters in preventing health care associated transmission of TB is not well established, they remove 99.7% of particles ≥ 0.3 μm in size. *M. tuberculosis* droplet nuclei are between 1 μm and 5 μm in size and should be removed by filtration.
- Consider the use of ultraviolet germicidal irradiation (UVGI) where resources and expertise allow. The goal of UVGI is to inactivate airborne droplet nuclei. The two most common forms of UVGI are upper room irradiation and duct irradiation. In upper room air irradiation, UV lights are shielded and directed towards the ceiling away from patients to reduce the risk of skin and eye toxicity while providing germicidal benefit. Well-designed UVGI upper room systems can disinfect *Mycobacteria* or surrogate organisms in a test room equivalent to 10–20 ACH. Duct irradiation is used to disinfect air exhausted from TB isolation rooms. UVGI should not be used in place of optimized ventilation systems or HEPA filters. These systems are potentially hazardous if not installed correctly, so need to be designed and installed by well-qualified engineers and technicians.

Personal Protection

- All healthcare workers should wear N95 particulate respirators when caring for patients with infectious TB, especially during high-risk procedures such as sputum induction, intubation, or bronchoscopy, and when caring for patients with drug-resistant TB. N95 masks filter ≥ 95% of particles 1 μm in size when used properly with a tight facial seal. Surgical masks are useful for TB patients to reduce the number of infectious particles in the air, but have only 50% filter efficiency and lack a tight facial seal, so should not be used by healthcare workers in place of N95 masks.

Summary

TB remains one of the leading causes of preventable morbidity and mortality worldwide with approximately 8.7 million new cases and 1.4 million deaths every year. 98% of cases and deaths occur in low resource countries. About one-third of the world's population is estimated to be infected with *M. tuberculosis* and therefore at risk for developing active TB. Individuals co-infected with HIV and TB, including healthcare workers, have a very high risk of developing active TB and should be treated with isoniazid preventive therapy if they have no contraindications. Institutional transmission of TB has occurred throughout the world and healthcare workers are at high risk for acquiring TB infection and active disease. Many administrative steps for TB control, such as improving the evaluation and separation of suspected TB cases, cough etiquette, prompt initiation of anti-TB treatment, and avoiding unnecessary hospitalization may be possible without a large financial investment. Some environmental controls such as AII rooms, HEPA filters, and UVGI may be cost prohibitive in many settings in TB endemic countries, but opening windows and doors, adding fans to improve airflow and create negative pressure, or installing skylights will improve ventilation and may reduce the risk of TB transmission for relatively low cost. Personal protection of healthcare workers and visitors with N95 particulate respirators is also recommended whenever caring for infectious TB or suspected TB patients. Even in low resource settings, healthcare workers should be provided with N95 particulate respirators,

especially in high-risk transmission settings such as aerosolization procedures or when in contact with MDR-TB or XDR-TB infected patients. Ongoing assessment, proper implementation, and continuous reinforcement of TB infection control practices should reduce or eliminate the spread of TB in healthcare settings.

References

Centers for Disease Control and Prevention, Jensen P, Lambert L, Iademarco M, Ridzon R. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in healthcare settings. *MMWR*. 2005. 54:1–141.

Shenoi SV, Escombe AR, Friedland G. Transmission of drug-susceptible and drug-resistant tuberculosis and the critical importance of airborne infection control in the era of HIV infection and highly active antiretroviral therapy rollouts. *Clin Infect Dis*. 2010. 50(Suppl 3):S231–7.

World Health Organization. Implementing the WHO policy on TB infection control in health-care facilities, congregate settings and households. World Health Organization, Geneva, 2010.

World Health Organization. Policy on TB infection control in healthcare facilities, congregate settings and households. World Health Organization, Geneva, 2009.

CHAPTER 27

Diarrhea

Made Sutjita MD, PhD, and Herbert L. DuPont, MD

Key Issues

A diarrheal disease outbreak in a healthcare facility may affect patients, healthcare workers, and visitors. Surveillance, and initiation of prompt infection control management practices will reduce the morbidity and mortality rate.

Known Facts

- Definitions of diarrhea vary but generally include the passage of liquid or watery stools, three or more times per day. Microorganisms that invade or inflame the intestinal mucosa often elicit a febrile response in addition to causing diarrhea. Diarrhea in a patient with unexpected fever should be considered as infectious gastroenteritis regardless of culture results. If diarrhea occurs in a febrile patient whose fever has other likely causes, the identification of pathogenic microorganisms is necessary to establish the diagnosis.
- The known incubation period of an infectious agent is important in determining whether a given infection is health care associated. The interval between the time of admission and the onset of clinical symptom must be longer than the known minimum incubation period of the infectious agent. Alternatively, health care associated gastroenteritis can be determined if a stool culture obtained shortly before or just after admission is negative for a given pathogenic agent and the agent is subsequently cultured from the patient's stool.
- Microorganisms that cause diarrhea outbreaks in the community are also able to cause health care associated outbreaks. Some forms of diarrheal disease, such as food poisoning caused by enterotoxin-producing strains of *Bacillus cereus*, *Clostridium perfringens* and *Staphylococcus aureus* have not been demonstrated to be directly transmissible from person

to person in the hospital. Common bacteria reported to cause health care associated gastroenteritis include various strains of diarrheagenic *Escherichia coli, Salmonella spp., Yersinia enterocolitica, V. cholerae,* and most importantly *Clostridium difficile*.

- The most important viral agents include rotaviruses in non-immunized infants and young children and noroviruses in all age groups. In an epidemiologic investigation in England during the period 2002–03, noroviruses were found in 63% of health care associated gastroenteritis outbreaks. Other viruses such as adenoviruses type 40 and 41 have also been implicated in health care associated outbreaks. In a child-care setting, the low inoculum enteric pathogens are most important: rotaviruses, noroviruses, *Shigella* strains and *Giardia* strains.
- It is important to distinguish between non-infectious diarrhea and infectious gastroenteritis in the hospital setting. Health care associated diarrhea or diarrhea of non-infectious origin, such as that caused by cathartics, tube feeding, inflammatory bowel disease, surgical resection, and anastomoses should be differentiated from diarrhea of infectious origin.
- The rate of health care associated gastroenteritis varies among hospitals and services. The NNIS (National Nosocomial Infections Surveillance) in the USA reported a health care associated gastroenteritis infection rate of 2.27 per 1000 discharges, for the period of January 1990 through December 1994. *C. difficile* is the most commonly identified cause of health care associated diarrhea. Since 1996, rates of *C. difficile* associated diarrhea (CDAD) have tripled. Infection rates and causes of health care associated gastroenteritis in developing countries have not been well studied. Nonetheless, outbreaks are reported with increasing frequency. *Salmonella spp* are the most common cause of health care associated gastroenteritis in India, Pakistan, and Tunisia.
- Risk factors for health care associated gastroenteritis can be classified by intrinsic and extrinsic factors. Intrinsic factors include an abnormality in the mucosal defense, such as achlorhydria, impairment of intestinal motility, and alteration of

normal enteric flora. Neonates with undeveloped immunity or patients with an immune deficiency state, such as those on immuno-suppressive drugs or with HIV infection and AIDS, are at increased risk to develop health care associated gastroenteritis. Extrinsic factors include nasogastric tube feeding while receiving cimetidine or proton pump inhibitors, which allow intestinal colonization of bacteria. Such a setting is normally found in an intensive care unit.

- Modes of transmission of infectious agents causing gastroenteritis are typically through the fecal-oral route. The transmission occurs either by contact spread from patient to patient, patient to healthcare worker (HCW), or HCW to patient (either direct or indirect), or through common vehicle spread. Contaminated vehicles such as food, water, medications, or devices and equipment can play a significant role in the transmission of the agents.

Controversial Issues

- *Salmonella spp* were reported as the most common cause of health care associated gastroenteritis in some developing countries but the infection rate of other enteric pathogens is not well known. Without the established mechanism for routinely reporting health care associated outbreaks, the 'true' infection rate of given pathogens is underestimated.
- The availability of "over-the-counter" antibiotics without a physician's prescription in many developing regions has led to the development of resistant microorganisms in many regions. This often complicates the management of a diarrheal disease outbreak.
- Antibiotics given to poultry for growth promotion leads to the development of resistant microorganisms which can be potentially harmful and cause disease in humans.

Suggested Practice

- Diarrheal diseases can be prevented by following simple rules of personal food hygiene.
- Effective hand washing is among the most important measures to reduce the risks of transmitting microorganisms

from one person to another or from one site to another in the same patient. HCWs should wash their hands with a non-antimicrobial soap and water or an alcohol-based waterless antiseptic agent. An anti-microbial soap and water should be used when hands are visibly dirty or contaminated with feces.

- *C. difficile* is the most important cause of health care associated diarrhea in industrialized countries. If an outbreak of CDAD is suspected or identified soap and water should be used for hand hygiene when caring for diarrhea patients since alcohol-based hand rubs are not effective against these spore-forming bacteria.
- Gloves play an important role in reducing the risk of microorganism transmission, and preventing contamination of the hands when touching patients and fomites. Attempts should be made to reduce the likelihood of the hands of the HCW being contaminated with microorganisms from a patient or a fomite and of infecting another patient. In this case, gloves must be changed between patient contacts and hands must be washed after gloves are removed.
- Gowns and other protective apparel provide barrier protection and reduce the likelihood of transmission of microorganisms. Gowns, boots, or shoe covers provide protection against splashes or exposure to infective material. When a gown is worn during the care of a patient infected with an epidemiologically important microorganism, it should be removed before leaving the patient's environment.
- A private room is important to prevent direct or indirect contact transmission of the microorganism. Whenever possible, a patient with infectious diarrhea is placed in a private room with hand washing and toilet facilities. A sign of "contact isolation" should be placed in front of the door to warn visitors or other HCWs. Patients infected by the same microorganism may share a room (cohorting), provided they are not infected with another potentially transmissible microorganism.
- Limiting the transport of a hospitalized patient with infectious diarrhea may also reduce the opportunities for transmission of the microorganism in the hospital.

- The patient's room, bed and bedside equipment should be cleaned thoroughly. In a patient with stool positive for VRE (vancomycin resistant enterococci), adequate disinfection of environmental surfaces, i.e., bed rails, tables, carts, commodes, doorknobs, or faucet handles, is indicated. Enterococci are not causing diarrhea, but may cause blood stream infection in susceptible patients. Enterococci are known to survive in the inanimate environment for prolonged periods of time.
- Urine, feces, and soiled linen should be considered potentially infectious and handled or disposed appropriately as discussed elsewhere. Personnel handling these materials should wear gloves and other protective apparel as described above.
- For rooms housing a patient with CDAD household bleach (1000 ppm sodium hypochlorite or 5 tablespoons of 6% bleach to 1 gallon water) should be used for disinfecting hard surfaces routinely or after cleaning a soiled area. If possible allow the surfaces to remain wet for 10 minutes then air dry.
- Education of hospital personnel through initial orientation and annual in service education should include food handling sanitation, hand washing and hand hygiene techniques, personal hygiene and employee health.
- Unprocessed vegetables and fruits should be thoroughly washed under running water before preparation or use.
- Foods should be prepared and served with clean utensils to avoid direct contact.
- Food grinders, choppers, mixers and other kitchenware should be cleaned, sanitized, dried, and reassembled after each use.
- Prepared foods should be transported to other areas in closed food carts or covered containers.
- Food must be stored sufficiently above floor level and away from walls. Perishable foods should be stored at or below 40° F and frozen food at 0° F or lower. Stored food should be rotated and used first before newly prepared food.

- Please review Chapter 18 Food: Considerations for Hospital Infection Control, for more detailed information.

Summary

It is important to establish a hospital surveillance program in which clinical patterns of infection are monitored on a regular basis. A "low-budget" surveillance program probably can be carried out by daily review and tabulation of bacteriologic reports from the hospital microbiology laboratory. Both cooperation and effective communication between hospital epidemiology and the microbiology laboratory personnel are essential.

In addition to the patient population, surveillance must include hospital personnel, particularly food handlers, nurses and other medical staff. An employee health service or an employee clinic ideally should be easily accessible to each employee. Food handlers, nurses, and ancillary staff having direct contact with patients should report to the employee health service when they experience an episode of diarrhea. In this case, stool cultures should be performed and the ill employee temporarily removed from work until the clinical course of the disease and culture result can be evaluated. Workers should not return to work until their diarrhea is resolved and two stool cultures obtained at least 24 hours apart show negative results.

A health care associated infectious gastroenteritis outbreak may occur due to the transmission from carriers of a specific pathogenic microorganism. Carriers can be patients or hospital personnel. Surveillance carried out on a regular basis should detect any episodes of gastroenteritis among patients and hospital personnel. Temporal clustering of cases should alert infection control personnel to the possibility of an outbreak. Occasionally, an outbreak may occur due to contaminated vehicles such as food, equipment, or oral medication. If such a vehicle is identified, its removal or disinfection may help to terminate the outbreak.

Patients with infectious gastroenteritis should be discharged from the hospital as soon as their condition allows them to be managed on an outpatient basis.

References

Books

Crookson ST, Hughes JM, and Jarvis WR. Nosocomial Gastrointestinal Infections *in* Prevention and Control of Nosocomial Infections (3rd Edition), Wenzel RP (Ed). Baltimore: Williams & Wilkins, 1997. Pgs. 925–75.

DuPont HL, Ribner BS. Infectious Gastroenteritis *in* Hospital Infections (4th Edition), Bennet JV, Brachman PS (Eds). Philadelphia: Lippincott-Raven, 1998. Pgs. 537–50.

Slutsker L, Villarino ME, Jarvis WR, Goulding J. *in* Hospital Infections (4th Edition), Bennet JV, Brachman PS (Eds). Philadelphia: Lippincott-Raven, 1998. Pgs. 333–41.

Weinstein JW, Hierholzer W Jr, Garner JS. Isolation Precautions in Hospitals *in* Hospital Infections (4th Edition), Bennet JV, Brachman PS (Eds). Philadelphia: Lippincott-Raven, 1998. Pgs. 189–98.

Guideline for Hand Hygiene in Healthcare Settings. *MMWR*. 2002. 51:1–56.

Blaser MJ, Smith PD, Ravdin JI, Greenberg HB, Guerrant RL (Eds). Infections of the Gastrointestinal Tract (2nd Edition). Philadelphia: Lippincott Williams & Wilkins, 2002.

Manuscripts

Lopman BA, Reacher MH, and Vipond IB, et al. Epidemiology and Cost of Nosocomial Gastroenteritis, Avon, England, 2002–2003, *Emerging Inf Dis*. 2004. 10:1827–34.

Gerding DN, Johnson S, Peterson LR, Mulligan ME, Silva J Jr. *Clostridium difficile*-associated diarrhea and colitis. *Infect Control Hosp Epidemiol*. 1995. 459–77.

On Line Resources

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6034a7.htm (Accessed 10 July 2013).

http://www.cdc.gov/mmwr/pdf/ss/ss6202.pdf (Accessed 10 July 2013).

CHAPTER 28

Skin and Soft Tissue Infections

Antoni Trilla, MD, MSc

Key Issue

Skin and soft tissue (SST) infections are not uncommon in the hospital setting. SST infections attended most frequently in hospitalized patients are mainly cellulitis/erysipelis, the majority being community acquired. Methicillin resistant *S. aureus* (MRSA) infections are mainly health care related, but increasingly community-acquired MRSA strains are being recognized.

In addition to localized complications, skin and soft tissue infections may cause life-threatening bacteremia or a sepsis syndrome. Currently, linezolid seems to be more effective than vancomycin for treating people with SST infections, including SST infections caused by MRSA.

Known Facts

The most common agent is *Staphylococcus aureus*, followed by *Streptococcus pyogenes* and anaerobic gram-negative bacilli. Amongst special populations (diabetic patients, patients with burn wounds), aerobic gram-negative bacilli, including *Pseudomonas aeruginosa*, should be considered. *Staphylococcus aureus* is found in the normal skin, as a transient colonizing organism, often linked to nasal carriage (anterior nares). Pre-existing conditions, such as tissue injury (surgical wounds, trauma, pressure sores) or skin inflammation (dermatitis), as well as other diseases (insulin-dependent diabetes, cancer, chronic renal failure on hemodialysis, intravenous drug abuse, and HIV infection) are risk factors for skin colonization and/or secondary infection by *Staphylococcus aureus*.

Staphylococcal Skin Infections

Key Issue: Impetigo is the most common skin infection. It is a superficial primary skin infection, often caused by *Streptococcus pyogenes* (90%) or *Staphylococcus aureus* (10%) infection.

Impetigo may appear as a complication of other skin disorders, like eczema, varicella, or scabies.

Known Facts: Often seen in children, impetigo is readily transmitted in households and hospitals. The increasing frequency of skin disorders in HIV-infected patients should also be noted and the diagnosis of impetigo considered.

Controversial Issues: The use of several antibiotics (mupirocin, fusidic acid, erythromycin, tetracycline) as topical treatment for impetigo has been shown to have a ~90% efficacy in clinical trials. The use of topical antibiotics decreases bacterial colonization and infection, and promotes faster wound healing. Oral antibiotic treatment (erythromycin, an antistaphylococcal penicillin, amoxicillin + clavulanic acid) has been used with a similar success rate. The emergence of multidrug-resistant *S.aureus* strains, including MRSA mupirocin-resistant strains, is a matter of concern. The introduction of these strains (from the community setting) should be monitored in hospitals, also if topical treatments with agents like mupirocin are widely used for long periods of time.

Suggested Practice: Standard hygienic measures and contact isolation procedures should be used in patients with impetigo. This practice must be encouraged, especially in neonatal and pediatric intensive care units, as well as for patients with HIV infection and a rash.

Staphylococcal Scalded-Skin Syndrome (SSSS)

Key Issue: SSSS is a severe *Staphylococcus aureus* infection with extensive bullae and exfoliation.

Known Facts: It occurs in children, but rarely in adults. Several epidemics have been reported in nurseries and neonatal intensive care units (NICU). Its clinical picture is related to the production of a powerful exotoxin by the *S. aureus* strains. Most cases develop acute fever and a scarlatiniform skin rash. Large bullae soon appear, followed by exfoliation. Also known as *toxic epidermal necrolysis*, this disease can be due to other infections or drug reactions.

Controversial Issue: The use of corticosteroids alone is not recommended for SSSS.

Suggested Practice: The use of an antistaphylococcal penicillin is the antibiotic treatment of choice. Topical treatment includes cool saline compresses.

Skin and Soft Tissue Infections in Patients with Diabetes

Key Issue: Diabetic patients are at higher risk for developing skin and soft tissue (SST) *Staphylococcus aureus* infections.

Known Facts: Hyperglycemic states are linked with a higher nasal and skin carriage rate of *S.aureus*. The impaired cell-mediated immunity of these patients is an important factor.

Controversial Issues: Diabetic patients may develop SST infections with organisms different from those in non-diabetics. The most severe condition is the *acute dermal gangrene syndrome*. This syndrome, related to a deep tissue infection and dermal necrosis, is often associated with prior trauma or surgery. It includes two different conditions:

1. *Necrotizing fasciitis*, affecting the fascia and producing the complete necrosis of subcutaneous tissue. It is often associated with high fever, sepsis and septic shock. The mortality rate is very high (30%).
2. *Progressive bacterial gangrene*, a more slowly progressive infection, related to surgical wounds, ileostomy sites, and exit site of drains (intra-abdominal or thoracic), which affects the hypodermis. The patient has a low grade fever or no fever at all. Local signs of infection are prominent.

Other syndromes include *Meleney's gangrene*, where the clinical picture is slowly progressive and without deep fascial involvement; *Fournier's gangrene*, if the perineal zone is involved; *streptococcal gangrene*, if *Streptococcus pyogenes* is the causative agent, or *nonclostridial anaerobic synergistic myonecrosis* if the muscles are also involved. These SST disorders are nearly always due to polymicrobial infections, with *Streptococcus pyogenes* and *Staphylococcus aureus* being the most commonly isolated microorganisms.

Autologous platelet-rich plasma (PRP) is a treatment that contains fibrin and high concentrations of growth factors and has the potential to aid wound healing. There is currently no evidence to suggest that autologous PRP is of value for treating chronic wounds.

Suggested Practice: Systemic antimicrobial treatment based on the most likely pathogens (including penicillin, antistaphylococcal penicillin, amoxicillin+clavulanic acid, a first or second generation cephalosporin), together with extensive and repeated surgical *débridement* are needed and must be started early.

Diabetic foot complications are responsible for more than 1 million of leg amputations every year. Diabeticd foot infection (DFI) can dramatically increase the risk of amputation. Many ulcer classification systems have been proposed to stratify the severity of the infectious process, but the definition of a specific therapeutic approach still remains an unsolved problem. The microbiology of these infections is often complex and can be polymicrobial. Treatment of these infections depends on the severity and extent of infection. Treatment should involve a multi-disciplinary team approach involving surgeons and infectious disease specialists. No single agent or combination of agents has been shown to be superior to others. Empiric antibiotics for DFIs vary based on the severity of the infection, but must include anti-staphylococcal coverage.

Burn Wound Infections

Key Issue: Burn wound patients and burn wound units are potential portals of entry for health care associated outbreaks due to MRSA and *Pseudomonas aeruginosa* infections. *Staphylococcus aureus* is responsible for 25% of all burn wound infections, followed by *P. aeruginosa*.

Known Facts: The most likely reservoirs for these infections are the hands and nares of healthcare workers (*S. aureus*, MRSA), the burn wound itself and the GI tract of burn patients (*S. aureus, P. aeruginosa*), and the inanimate environment of the burn unit, including the surfaces and/or the equipment (*S. aureus*, MRSA, *P. aeruginosa*).

Suggested Practice: Common standard isolation precautions, together with contact isolation precautions are important to prevent health care associated infections in burn units. Topical treatment using mafenide acetate, silver sulfadiazine, bacitracin/ neomycin/polymyxin, 2% mupirocin, together with systemic, antistaphylococcal and anti-*Pseudomonas* antibiotics should be reserved for documented or clinical infections.

Pressure Sores (Decubitus Ulcers)

Key Issue: Pressure sores appear in 6% of patients admitted to healthcare institutions (range 3 to 17%), and are the leading cause of infection in long-term care facilities.

Known Facts: The prevention of pressure sores includes the control of local factors such as unrelieved pressure, friction, moisture, or systemic factors such as low serum albumin, fecal incontinence, and poor hygienic measures. The infection is polymicrobial, and includes gram-negative bacilli, *Staphylococcus aureus*, *Enterococcus* spp and anaerobes. The average number of isolates in infected pressure sores is four, including three aerobic and one anaerobic bacteria. Pressure sores are sometimes associated with severe systemic complications, including bacteremia, septic thrombophlebitis, cellulitis, deep tissue and fascial necrosis, and osteomyelitis. The development of clinical tetanus is unlikely, although still possible. In patients with bacteremia and pressure sores, the sores were considered to be the source of the bacteremia in half the cases. Overall mortality was 55%, with approximately 25% of deaths attributable to the infection. Therefore, pressure sores must be considered a potential source for nosocomial bacteremia.

Controversial Issues: A Cochrane review conclude that honey dressings do not increase rates of healing significantly in venous leg ulcers when used as an adjuvant to compression. Honey might be superior to some conventional dressing materials, but there is considerable uncertainty about the replicability and applicability of this evidence. There is insufficient evidence to guide clinical practice in other types of wounds.

Iodine is often used in the treatment of wounds. A systematic review concludes that Iodine did not lead to a reduction or prolongation of wound-healing time compared with other (antiseptic) wound dressings or agents. In individual trials, iodine was significantly superior to other antiseptic agents (such as silver sulfadiazine cream). Based on the available evidence from clinical trials, iodine is an effective antiseptic agent and does not impair wound healing.

Suggested Practice: Antibiotic treatment, together with surgical care and débridement of the sores, is needed. Taking into

account the most likely microorganisms, a second-generation cephalosporin is one of the drugs of choice. The combination of a beta-lactam antibiotic with an aminoglycoside, or clindamycin plus an aminoglycoside, or a cephalosporin plus metronidazole are other therapeutic options, but one must be especially cautious in using aminoglycosides in diabetic patients.

Nosocomial Bacteremia Due to SST Infection

Key Issue: Nosocomial bacteremia secondary to SST infections has a low frequency rate. According to National Nosocomial Infections Surveillance (NNIS) data, only 5 to 8% of all bacteremic episodes were secondary to SST infections.

Known Facts: Patients with poorly controlled diabetes and cancer are a high-risk group for developing this infection. In one large series from the US National Cancer Institute, 12% of all bacteremic episodes in cancer patients were secondary to SST infection. However, only 6% of those cases were associated with severe neutropenia. In neutropenic patients, *ecthyma gangrenosum* due to *Pseudomonas aeruginosa* SST infection must be considered. Intravenous drug abuse (IVDA) is a worldwide problem. SST infections are common among IVDA, *S. aureus* is the most common microorganism (30% of cases). The common clinical presentations are subcutaneous abscesses, cellulitis, and lymphangitis, most often (60%) located in upper extremities. Bacteremia is one of the most severe and common complications among IVDA, with 40% of all episodes due to *S. aureus*.

Suggested Practice: If bacteremia develops in an IVDA, septic thrombophlebitis or endocarditis should be considered, and antibiotic treatment started as soon as possible.

References

Braunstein I, Wanat KA, Abuabara K, McGowan KL, Yan AC, Treat JR. Antibiotic Sensitivity and Resistance Patterns in Pediatric Staphylococcal Scalded Skin Syndrome. *Pediatr Dermatol*. 2013 Aug 23. doi: 10.1111/pde.12195.

Caravaggi C, Sganzaroli A, Galenda P, Bassetti M, Ferraresi R, Gabrielli L. The management of the infected diabetic foot. *Curr Diabetes Rev*. January 1, 2013. 9(1):7–24.

Jull AB, Walker N, Deshpande S. Honey as a topical treatment for wounds. *Cochrane Database Syst Rev*. February 28, 2013. 2:CD005083. doi:10.1002/14651858.CD005083.pub3.

Martinez-Zapata MJ, Martí-Carvajal AJ, Solà I, Expósito JA, Bolíbar I, Rodríguez L, Garcia J. Autologous platelet-rich plasma for treating chronic wounds. *Cochrane Database Syst Rev*. October 17, 2012. 10:CD006899. doi:10.1002/14651858.CD006899.pub2.

May AK. Skin and soft tissue infections: the new surgical infection society guidelines. *Surg Infect (Larchmt)*. June 2011. 12(3):179–84. doi:10.1089/sur.2011.034.

Park H, Copeland C, Henry S, Barbul A. Complex wounds and their management. *Surg Clin North Am*. December 2010. 90(6):1181–94. doi:10.1016/j.suc.2010.08.001.

Raya-Cruz M, Ferullo I, Arrizabalaga-Asenjo M, Nadal-Nadal A, Díaz-Antolín MP, Garau-Colom M, Payeras-Cifre A. Skin and soft-tissue infections in hospitalized patients: Epidemiology, microbiological, clinical and prognostic factors. *Enferm Infecc Microbiol Clin*. May 15, 2013. pii:S0213-005X(13)00077-3. doi:10.1016/j.eimc.2013.03.004.

Roberts AD, Simon GL. Diabetic foot infections: the role of microbiology and antibiotic treatment. *Semin Vasc Surg*. June 2012. 25(2):75–81. doi:10.1053/j.semvascsurg.2012.04.010.

Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan EL, Montoya JG, Wade JC; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. *Clin Infect Dis*. November 15, 2005. 41(10):1373–406.

Yue J, Dong BR, Yang M, Chen X, Wu T, Liu GJ. Linezolid versus vancomycin for skin and soft tissue infections. *Cochrane Database Syst Rev*. July 12, 2013. 7:CD008056. doi:10.1002/14651858.CD008056.pub2.

Vermeulen H, Westerbos SJ, Ubbink DT. Benefit and harm of iodine in wound care: A systematic review. *J Hosp Infect*. November 2010. 76(3):191–9. doi:10.1016/j.jhin.2010.04.026.

CHAPTER 29

Bloodstream Infections

Melanie Brown MD, Gonzalo Bearman MD, MPH

Definition

Blood stream infections(BSIs) are defined as one or more positive blood cultures associated with systemic signs of infection such as fevers, chills, and/or hypotension. BSIs can be divided into primary BSIs vs. secondary BSIs. Primary BSIs occur without another known nidus of infection. Secondary BSIs develop from another detectable area of infection thought to be the source of the bacteremia. An example of a secondary BSI includes a patient with a urinary tract infection and subsequent bacteremia.

Key Points

- BSI are often are iatrogenic owing to invasive procedures or devices such as placement of central catheter lines.
- Catheter-related BSIs are the most common cause of health care associated bacteremia.
- In contrast, peripheral venous catheters rarely cause BSI.
- Prevention of catheter-related BSIs is a high priority infection control initiative.

Known Facts

- An estimated 250,000 cases of BSIs occur annually in the USA.
- 80,000 of these are catheter-related BSIs that occur in ICUs.
- BSIs greatly increase hospital cost and length of stay.
- The estimated BSI attributable mortality rate is between 12–25%.
- Catheter-related bloodstream infections account for 11% of health care associated infections.
- Most frequently isolated BSI organisms include coagulase-negative staphylococci (31%), *S. aureus* (20%), enterococci (9%), *Escherichia coli* (6%), *Klebsiella* species (5%), and *Candida* species (9%).

- Implementation of proven infection reduction techniques is associated with 60% decrease in catheter related BSI rates in US intensive care units.

Suggested Practices to Prevent BSI:

- Education and training of healthcare workers.
- Hospital infection control policy with surveillance for intravascular device-related infection.
- The use of central line bundles comprised of five key components:
  1. Appropriate hand hygiene involving the use of alcohol-based waterless hand cleaner or antibacterial soap and water with adequate rinsing.
  2. The use of maximal barrier precautions meaning strict adherence to hand hygiene, the wearing of surgical cap, mask, sterile gown and sterile gloves, and use of sterile drapes.
  3. Skin preparation with 2% chlorhexidine in 70% isopropyl alcohol.
  4. Using the optimal catheter site such as the subclavian and avoidance of femoral site.
  5. Ongoing daily reviews of central line necessity and removal as soon as possible.
- Disinfection of injection ports prior to use and stopcocks should be capped when not in use.
- Use Teflon or polyurethane catheters instead of polyvinyl chloride or polyethylene catheters.
- Sterile gauze dressing changes should occur every 2 days. Transparent dressing changes should occur every 7 days.
- Chlorhexidine-impregnated sponge (Biopatch) placed at catheter site is associated with significant reduction in BSI rates.
- Daily skin cleansing with 2% chlorhexidine wash reduces BSI rates.
- Use of antimicrobial-coated catheters should be considered if duration of device use is longer than 5 days.
- Replace tubing used for blood products, lipid emulsions and propofol infusions.

- Use sutureless securement devices to reduce intravascular catheter infection risk.
- Use peripheral catheters as opposed to central venous catheters whenever possible.
- Tunneled central venous catheters should be preferentially employed for long term use(>7days of catheterization).

Practices Currently Not Recommended

- Do not use topical antibiotics at insertions sites except when using dialysis catheters.
- Do not use in-line filters for infection prevention.
- Do not use prophylactic systemic or intranasal antibiotics prior to central line insertion to prevent catheter colonization or BSI.
- Do not use antibiotic lock solutions routinely. Antibiotic locks should only be used under special circumstances such as patients with history of multiple catheter related bloodstream infections despite adequate precautions.
- Do not use guidewire catheter exchanges to prevent infection or to change out suspected infected catheters.
- Do not routinely use anticoagulant therapy to reduce catheter-related infection risk.

Summary

The most common cause of health care associated bacteremia is catheter-related bloodstream infection. These infections increase morbidity, mortality, length of stay and hospital costs. Implementing the above practices has been shown to decrease these rates and improve quality of care for our patients.

References

O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad I, Randolph A, Rupp ME, Saint S, and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the Prevention of Intravascular Catheter-Related Infections. *CDC*. 2011.

O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, Masur H, McCormick RD, Mermel LA, Pearson ML, Raad I, Randolph A, Weinstein RA. *MMWR*. August 9, 2002. 51(RR-10).

Abad CL, Safdar N. Catheter-related Bloodstream Infections. *Infectious Disease Special Edition*. September 2011. 14.

Fagan RP, Edwards JR, Park BJ, Fridkin SK, Magill SS, Incidence Trends in Pathogen-Specific Central Line–Associated Bloodstream Infections in US Intensive Care Units, 1990–2010. *Infect Control Hosp Epidemiol*. September 2013. 34(9):893–899.

Mermel LA, Farr BM, Sherertz RJ, Raad I, O'Grady NP, Harris JS, Craven DE. Guidelines for the Management of Intravascular Catheter-Related Infections. *Infect Control Hosp Epidemiol*. April 2001. 22(4):222–242.

Timsit J-F, Schwebel C, Bouadma L, Geffroy A, Orgeas MG, Pease S, Herault M-C, Haouache H, Calvino-Gunther S, Gestin B, Armand-Lefevre L, Leflon V, Chaplain C, Benali A, Francais A, Adrie C, Zahar J-R, Thuong M, Arrault X, Croize J, Lucet J-C, Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: A randomized controlled trial. *JAMA*. March 25, 2009. 301(12):1231–1241.

Pronovost P, Needham D, Berenholtz S, et al. An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. *N Engl J Med*. 2006. 355:2725–2732.

CHAPTER 30

Managing Vascular Catheters

Andreas F. Widmer, MD, MS

Key Issues

- Intravascular (IV) catheters are frequent sources of bloodstream infections. Surveillance belongs to the basic requirements of any infection control program.
- Reports should be given in number of infections per 1000 catheter days rather than per 100 patients.
- Catheter-associated bloodstream infection (CA-BSI) is the most commonly used for surveillance and is defined as a central line that was in use during the 48-hour period before development of the bloodstream infection (BSI) and no other obvious source was identified (subset of primary bacteremia).
- Catheter-related BSI (CR-BSI) is defined as CA-BSI with the addition of a positive catheter tip culture or positive differential time to positivity.
- Current scientific evidence allows to decrease the incidence to below one per 1000 catheter days.

Known Facts

- IV-catheters are a frequent source for bloodstream infections.
- The incidence of infection depends on the catheter type, type of hospital setting (intensive care unit vs ward), the catheter care, underlying diseases of the patient, and the type and resources for the prevention program.
- Polyurethane or silicon catheters have a lower risk of complications than others. Triple-lumen catheters have similar risks for infection as have single-lumen catheters, but more lumens are associated with more manipulations.
- A common portal of bacterial entry is the insertion site during the first 2 weeks after catheter placement.

- After 2 weeks, the hub (the connection between the catheter and the infusing tube) becomes the predominant source of bacterial entry.
- Most CA-BSIs are observed in intensive care units or burn units.
- Each catheter day adds to the overall risk of CR-BSI: Remove catheters as soon it is clinically possible is a key component for prevention of CA-BSI.
- Healthcare education, training and monitoring or insertion, maintenance are paramount to prevent CR-BSIs.
- Full barrier precautions with gloves, gown, cap and large drapes prevent early infections.
- Hand hygiene, specifically the alcoholic hand rub, must be enforced before placing any catheter.
- Infusion time for lipids should not exceed 24 hours, for blood 4 hours.
- Routine replacement of intravascular catheters does not prevent CA-BSIs.
- Clinical signs and symptoms have a poor sensitivity and specificity for CA-BSIs.

Suggested Practice

Catheters in general

- Perform surveillance for device-use and CA-BSIs in intensive care units, burn units and hematology-oncology units.
- Daily check indication for intravascular line, use automatic removal orders, if necessary.

General recommendation for the choice of intravenous access

- < 5 days: Peripheral catheter.
- 5–10 days: CVC: jugular site preferred: higher rate of infection compared to the subclavian access, but lower non-infectious risk (bleeding, pneumothorax).
- 5–28 days: CVC: Subclavian access site.
- Alternative: Percutaneous peripherally inserted CVC (PICC-lines) for outpatient therapy.
- 28 days: tunneled (eg. Hickmann) or totally implanted catheters (e.g., port-a-cath).
- Avoid the femoral access site.

- Replace catheters that are placed under emergency conditions under poor aseptic conditions, once the hemodynamic condition of the patient has stabilized, but at least within 48 hours.
- Check proper fixation of the catheter, discourage idle catheters.
- Do not routinely culture IV catheters.

Antisepsis, dressings and tubing

- Use sterile alcohol to disinfect the insertion site. In resource-limited areas, the WHO hand hygiene alcohol may be used.
- Chlorhexidine is state-of-the art disinfectant for catheter care. Convenient, but more expensive are chlorhexidine containing dressings.
- Infusate tubing: replace not more frequently than ≥3 days.
- Use clean or sterilized gauze as dressing immediately after insertion. After 1 day, use gauze after routine disinfection with alcohol with chlorhexidine, and change every other day. More expensive, chlorhexidine-containing transparent dressings are highly effective to prevent CA-BSIs, any may be left in place for 5–7 days.
- Gauze dressings should be replaced every two days or transparent dressing every 7 days, or if they do not adhere anymore.
- Minimize numbers of stopcocks attached to the catheter.
- Do not routinely use in-line filters.

Peripheral intravenous catheters

- CR-BSIs by peripheral catheters are always preventable, the incidence of phlebitis (a physicochemical problem) should not exceed 20%.
- Do not routinely replace peripheral catheters, but daily check the need for the catheter and the insertion site.

Central venous catheters

- Use maximal barrier precautions including gown, sterile or at least new gloves, and large sterile drapes when placing a central-venous line.

- Use guide wire exchange for malfunctioning catheters and in febrile episodes, where the source of infection is unlikely the catheter. A new puncture for a catheter is recommended if the insertion site has evidence of infection (e.g., redness, pus, pain).
- Consider a coated catheter (minocycline-rifampin or chlorhexidine/sulfodiazine), if the patient is at high risk of CA-BSI and the incidence of CA-BSI exceeds 5/1000 catheter days. However, full adherence to simple training in IV insertion, full barrier precautions and chlorhexidine for catheter care can cut CA-BSIs close to zero.
- Use chlorhexidine as disinfectant for the regular care of the insertion site. Octenidine is an alternative in Europe, if no commercial chlorhexidine-containing dressing is used.

Long-term catheters

- Never replace long-term catheters for diagnostic purposes only. Negative blood cultures taken through the catheter have a very high negative predictive value to rule out CR-BSI in patients with fever of unknown origin. For suspected episodes of CR-BSI, take simultaneously blood cultures through the catheter and by venipuncture if an automated BC system is available (time to positivity: 2 hours difference meets the case definition of CR-BSI).
- Do not administer prophylactic antibiotics before insertion.
- CR-BSIs due to coagulase-negative staphylococci can be successfully treated by the antibiotic lock technique (Vancomycin or EDTA-Minocycline). The ethanol lock is a promising alternative.

Arterial catheters

- Replace peripheral arterial catheters routinely not more frequently than every 5 days.
- Routinely replace disposable or reusable transducers, tubing, continues-flush device and flush solution at 96-hour intervals.
- Minimize manipulations of the pressure monitoring system and use a closed-flush system.
- Disinfect the diaphragm before accessing the system or use a stopcock.
- Use disposable transducers.

Controversial Issues

- Needleless devices reduce the risk for sharp injuries to healthcare workers, but are associated with higher risk for CRIs.
- Maximum hang time of other parenteral fluids.
- Routine replacement of CVC after episodes of secondary bloodstream infections from another body site.
- Use of impregnated catheters and chlorhexidine sponges in small children.
- Treatment of febrile patients with a positive microbiologic for coagulase-negative staphylococci from a removed catheter and negative blood cultures. Treatment is recommended if *S.aureus* is isolated, even if blood cultures are negative.

Summary

Two principal pathways are involved in the pathogenesis of catheter-related infections: First, bacteria can colonize the outer surface of the catheter, migrate from the catheter-skin interface over the external surface of the catheter to the catheter tip. Second, bacteria can colonize the hub, the connection between the infusion set and the catheter followed by migration down the internal surface of the catheter. Clinical signs and symptoms are commonly lacking even in established CA-BSIs. A bundle of prevention strategies (education, hand hygiene and full barrier precautions prior insertion, use of chlorhexidine for catheter insertion care, and appropriate selection of catheter and insertion site) has been shown to almost eliminate CA-BSIs (zero-risk), or at least < 1/1000 catheter days. Coated catheters should only be considered for high-risk patients and/or if other strategies have failed to reduce the rate of CR-BSIs <3/1000 catheter days.

References

Widmer AF. Intravenous-Related Infections *in* Prevention and Control of Nosocomial Infections (3rd Edition), Wenzel RP (Ed). Baltimore: William & Wilkins, 1997. Pgs. 771–806.

Pronovost P, Needham D, Berenholtz S, et al. An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. *N Engl J Med*. 2006. 355:2725–2732.

Bouza E, Alvarado N, Alcala L, Perez MJ, Rincon C, Munoz P. A Randomized and Prospective Study of Three Procedures for the Diagnosis of Catheter-Related Bloodstream Infection Without Catheter Withdrawal. *Clin Infect Dis*. 2007. 44:820–6.

O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad II, Randolph AG, Rupp ME, Saint S. Healthcare Infection Control Practices Advisory Committee (HICPAC) Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis*. 2011. 52(9):e162–93.

Rosenthal VD, Maki DG, Salomao R, Moreno CA, Mehta Y, Higuera F, Cuellar LE, Arikan OA, Abouqal R, Leblebicioglu H. International Nosocomial Infection Control Consortium. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. *Ann Intern Med*. October 17, 2006. 145(8):582–91.

CHAPTER 31

Hospital Acquired Urinary Tract Infection

Emanuele Nicastri MD, PhD and
Sebastiano Leone MD

Key Issues

"The decision to use the urinary catheter should be made with the knowledge that it involves risk of producing a serious disease." Even through this statement was formulated by Paul Beeson about fifty years ago, it still maintains relevant for both patients and healthcare workers (HCWs). Urinary catheters represent the major risk factor related to the acquisition of hospital acquired urinary tract infection (HUTIs). Catheter-associated urinary tract infection (CA-UTI) is the most common type of hospital acquired infection, accounting for approximately 40% of such infections and for most of the 900,000 patients with health care associated bacteriuria in the U.S. each year. Each year approximately 96 million urethral catheters are sold world-wide, nearly a quarter of which are sold in the United States. Approximately 30% of initial urinary catheterizations are unjustified, and one-third to one-half of days of continued catheterization are unjustified. Many of these catheters are inserted in the emergency room without a documented order, and providers are not aware that the catheter is in place in 21–8% of cases. The reduction of inappropriate use of indwelling urinary catheters, the use of a closed drainage system, and the early removal "as soon as possible" of the catheter already in place, are the main tools to reduce HUTIs.

Known Facts

In the United States, between 16% and 25% of hospitalized patients have an indwelling urinary catheter in place. The daily rate of acquiring bacteriuria among hospitalized patients with urinary catheters is approximately 3% to 10%, and between 10

to 25% of patients with bacteriuria will develop symptoms of UTI. Of patients with a symptomatic CA-UTI, 1–4 % develop bacteraemia and, of these, 13–30 % die.

The costs of CA-UTI are modest compared with other device-associated infections but the large number of patients with indwelling urinary catheters results in a substantial burden. Each CA-UTI adds approximately $675 to the costs of hospitalization and when bacteraemia develops, this additional cost increases to at least $2800.

Micro-organisms causing endemic HUTIs derive from the patient's own flora or from the hands of HCWs during catheter insertion or manipulation of the collection system. Bacteria can enter the urinary tract in catheterized patients in three ways: introduction of organisms into the bladder at the time of catheter insertion or periurethal route or intraluminal route.

The most frequent pathogens associated with CA-UTI in hospitals reporting to National Healthcare Safety Network between 2009–2010 were *Escherichia coli* (26.8%) and *Pseudomonas aeruginosa* (11.3%), followed by *Klebsiella* spp. (11.2%), *Candida albicans* (8.9%), *Enterococcus faecalis* (7.2%%), *Proteus* spp. (4.8%), other *Enterococcus* spp. (4.8%), *Enterobacter* spp. (4.2%), other *Candida* spp (3.8%) and *Enterococcus faecium* (3.1%). A smaller proportion was caused by *Staphylococcus aureus* (2.1%), coagulase-negative staphylococci (2.2%), *Serratia* spp. (1.0%), *Acinetobacter baumannii* (0.9%), and other pathogens (7.7%). Urinary tract pathogens such as *Serratia marcescens* and *Pseudomonas cepacia* have special epidemiological significance. Since these micro-organisms do not commonly reside in the gastrointestinal tract, their isolation from catheterized patients suggests acquisition from an exogenous source, likely through the hands of personnel. HUTIs comprise perhaps the largest institutional reservoir of health care associated antibiotic-resistant pathogens, the most important of which are vancomycin-resistant enterococci and extended-spectrum β-lactamase–producing *Enterobacteriaceae*.

A continuously closed urinary drainage system is pivotal to the prevention of CA-UTI. For short-term catheterization, this measure alone can reduce the rate of infection from an inevitable 100% when open drainage is employed to less than 25%.

Breaches in the closed system, such as unnecessary emptying of the urinary drainage bag or taking a urine sample, will increase the risk of catheter-related infection and should be avoided. Before manipulating the closed system, hands must be washed with an antiseptic agent and gloves worn.

Noninfectious complications secondary to indwelling urinary catheters are common, and in case of long-term catheterization are 4 times higher than CA-UTI. Although the most frequent complications are minor (for example, leakage around the catheter), serious complications, such as urethral strictures and gross hematuria, occur in a substantial proportion of patients. Moreover, long-term catheterization and catheter use in patients with spinal cord injury result in even greater illness, with more than 30% of patients having several complications.

Studies comparing meatal cleansing with a variety of antiseptic/antimicrobial agents or soap and water demonstrated no reduction in bacteriuria when using any of these preparations for meatal care compared with routine bathing or showering. Meatal cleansing is not necessary and may increase the risk of infection. Daily routine bathing or showering is all that is needed to maintain meatal hygiene. The most important, potentially modifiable risk factor, identified in every study, is prolonged catheterization beyond 6 days (RR 5.1-6.8); by the 30th day of catheterization, infection is near-universal. Thus, every operative strategy should be aimed to reduce the duration of the urinary catheter at *minimum*.

Controversial Issues

Systemic antimicrobial prophylaxis is likely to reduce the risk of HUTIs for short-term catheterizations in critical care areas. In a recent Cochrane review of antibiotic prophylaxis for short-term catheter bladder drainage in adults, the authors concluded that there are limited evidence that antibiotic prophylaxis reduce the rate of bacteriuria and other signs of infection, such as pyuria, febrile morbidity and Gram-negative isolates in surgical patients who undergo bladder drainage for at least 24 hours postoperatively, and there was also limited evidence that prophylactic antibiotics reduced bacteriuria in non-surgical patients. Moreover, there are concerns about selection of antibiotic-resistant bacteria and yeasts.

Another proposed approach to prevent CA-UTI is to coat catheters with antibacterial materials. Randomized clinical trials suggest the use of medicated urinary catheters to reduce urinary catheter-related bacteriuria. Small studies have demonstrated a significant reduction in bacterial HUTIs with the use of catheters impregnated with anti-infective solutions such as nitrofurazone and minocycline combined to rifampin. Catheters coated with minocycline and rifampin had significantly lower rates of Gram-positive bacteriuria (7.1% vs. 38.2%; $p<0.001$). Nevertheless similar rates of Gram-negative bacteriuria and candiduria have been reported, and the risk of developing antimicrobial resistance needs to be further investigated. A similar concern on the selective antibiotic drug pressure has been raised with regard to an indwelling urethral catheter coated with gentamicin sulphate on the inner and outer surface. A multicentre study including 177 patients was conducted to determine the CA-UTIs inhibition effect by nitrofurazone-coated catheters. In this study, the incidence rate of CA-UTI was lower in the nitrofurazone-coated catheter group compared with the control group. When the catheters were maintained for >5 days but <7 days, the incidence rate of catheter-related infection was statistically significantly lower in the experimental group compared with that in the control group. Finally, Johnson conducted a meta-analysis of randomized or quasi-randomized clinical trials of antimicrobial urinary catheters to assess the efficacy of these for preventing CA-UTIs. The author observed that, compared with control catheters, antimicrobial urinary catheters can prevent or delay the onset of catheter-associated bacteriuria in selected hospitalized patients. However, it is necessary to confirm further the effectiveness of antibiotic-coated catheters over long-term periods.

An alternative option to the use of antibiotic impregnated catheters, coating the catheter surface with an antiseptic, such as a silver compound, could reduce the presence of the biofilm on the surface of the catheter. Early studies with a silver oxide-coated catheter reported no benefit for preventing bacteriuria, but silver alloy catheters were subsequently reported to decrease acquisition of bacteriuria, although symptomatic infection was not adequately evaluated. In a meta-analysis, Crnech

and Drinka found that commercially available silver-coated silicone urinary catheters only offer modestly greater benefits than uncoated catheters made of silicone and that silicone catheters simply have better properties than latex catheters and they are only minimally improved by silver coating. More recently, in a multicentre randomized controlled trial, Pickard et al. observed that silver alloy-coated catheters were not effective for reduction of incidence of symptomatic CA-UTI. In conclusion, current evidence does not support a clinical benefit for use of silver alloy-coated indwelling catheters, and routine use of these catheters is not recommended.

A novel silicone urinary catheter with a trefoil cross-section was found to result in decreased rates of bacteriuria, urethroscopic damage and histopathological inflammation compared to a standard indwelling urinary catheter in a rabbit model. More innovation is required with respect to catheter design and the trefoil silicone catheter should be evaluated in human clinical trials, but based on the preliminary animal model data it appears promising for short-term catheterization.

Suggested Practices

- Educate HCWs about the appropriate indications for indwelling urinary catheters:
  - patients with anatomic or physiologic outlet obstruction,
  - patients undergoing surgical repair of the genitourinary tract,
  - critically ill patients who need to measure the daily urinary output.
- Educate HCWs about alternative strategies for the management of urinary incontinence (for example, condom or intermittent catheters and special undergarments).
- Provide patients with information about the need, insertion, maintenance and removal of their catheter.
- Educate HCWs about the infectious complications and adverse events associated with urinary catheterization.
- Educate HCWs about the optimum selection of the smallest gauge catheter for free urinary outflow.
- Educate HCWs about the correct techniques for catheter insertion and care.

- Educate HCWs to adopt and maintain the sterile continuously closed system of urinary drainage.
- Educate HCWs about avoiding catheter irrigation unless needed to prevent or relieve obstruction.
- Educate HCWs about maintaining unobstructed urine flow.
- Maintain adequate urine flow at all times. Ideally, sufficient fluid to maintain urine output of greater than 100 ml/h should be given if it is not contraindicated by the patient's clinical condition.
- Gravity drainage should be maintained.
- Educate HCWs about minimizing the duration of the urinary catheter.
- Do not change catheters unnecessarily or as part of routine practice.
- Consider the use of catheters with anti-infective surface at least for those patients at high risk of serious complications of catheter-associated bacteriuria.
- Consider automatic "stop orders" for indwelling urinary catheters; these orders should require that the catheter either be removed or reordered after a specified period of catheterization.
- Use quality-control patient audits to design programs to decrease inappropriate use of indwelling urinary catheters.
- Develop and implement a periodic surveillance system of HUTI.
- Document all procedures involving the catheter or drainage system in the patient's records.

Bundle Strategy

The implementation of bundle programs against CA-UTI should be part of the minimum requirements to develop a patient-based infection control program. Recently in the West Georgia Medical Center a significant reduction from 5.2 to 1.5 per 1000 catheters ($p=0.03$) was obtained using a bundle policy based on four evidence-based interventions (IB recommendations from the Guideline for the Prevention of CA-UTI HICPAC 2009): (i) the

exclusive use of silver alloy catheters, (ii) the use of securing devices to prevent movements of the catheter, (iii) repositioning of the catheter if it was found on the floor and (iv) stop order for most surgical patients. Similar policy based on the Keystone Bladder Bundle Initiative was introduced in the Michigan Hospitals in 2009 with a 25% reduction in CA-UTI rates.

Strategies to limit barriers to a bundle implementation program could include: incorporating urinary management as part of patient safety program, such as a fall reduction program, explicitly discussing the risks of indwelling urinary catheters with patients and families, and engaging with emergency department nurses and physicians.

Summary

The development of a nursing, physician, and laboratory team to review and revise protocols and procedures for better catheter management can promote the proper indications for urinary catheter placement and management. A continuously closed system of urinary drainage is the cornerstone of infection control and clear criteria for the removal of urinary catheters without a physician's order are part of bundled strategies for the reduction of CA-UTI. Novel urinary catheters impregnated with antibiotic drugs or coated with anti-infective material exhibit antimicrobial activity that significantly reduces the risk of HUTI for short-term catheterizations. These represent the first major advance for preventing HUTIs since the wide-scale adoption of closed drainage systems. It remains unclear whether medicated urinary catheters will also lead to decreases in the clinically important outcomes of catheter-related bacteraemia and mortality. Each medicated catheter exceeds the cost of a standard, non-coated non-impregnated urinary catheter tray. In the future, a major biotechnology effort to reduce the prevalence rate of HUTIs and indeed of all hospital-related infections is likely to be represented by vaccines against important multi-drug resistant micro-organisms such as enteric Gram-negative bacilli and staphylococci.

References

Agency for Healthcare Research and Quality. Evidence Report/Technology Assessment No. 43, Making Healthcare Safer: A Critical Analysis of Patient Safety Practices, AHRQ Publication No. 01-E058. Available at: http://archive.ahrq.gov/clinic/ptsafety/pdf/ptsafety.pdf (Last access 15 January 2003).

Beeson PB. The Case against the catheter. *Am J Med*. 1958. 24:1–3.

Clarke K, Tong D, Pan Y, et al. Reduction in catheter-associated urinary tract infections by bundling interventions. *Int J Qual Health Care*. 2013. 25:43–9.

Crnich CJ, Drinka PJ. Does the composition of urinary catheters influence clinical outcomes and the results of research studies? *Infect Control Hosp Epidemiol*. 2007. 28:102–3.

Darouiche RO, Smith JA Jr, Hanna H, et al. Efficacy of antimicrobial-impregnated bladder catheters in reducing catheter-associated bacteriuria: A prospective, randomized, multicenter clinical trial. *Urology*. 1999. 54:976–81.

Ha US, Cho YH. Catheter-associated urinary tract infections: New aspects of novel urinary catheters. *Int J Antimicrob Agents*. 2005. 28:485–90.

Hollingsworth JM, Rogers MA, Krein SL, et al. Determining the Noninfectious Complications of Indwelling Urethral Catheters: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2013. 159:401–10.

Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis*. 2010. 50:625–63.

Johnson JR, Kuskowski MA, Wilt TJ. Systematic Review: Antimicrobial urinary catheters to prevent catheter-associated urinary tract infection in hospitalized patients. *Ann Intern Med*. 2006. 144:116–26.

Krein SL, Kowalski CP, Harrod M, et al. Barriers to reducing urinary catheter use: A qualitative assessment of a statewide initiative. *JAMA Intern Med*. 2013. 173:881–6.

Lee SJ, Kim SW, Cho YH, et al. A comparative multicentre study on the incidence of catheter-associated urinary tract infection between nitrofurazone-coated and silicone catheters. *Int J Antimicrob Agents*. 2004. 24(Suppl 1):S65–9.

Lusardi G, Lipp A, Shaw C. Antibiotic prophylaxis for short-term catheter bladder drainage in adults. *Cochrane Database Syst Rev*. 2013. 7:CD005428.

Nicolle LE. Urinary catheter-associated infections. *Infect Dis Clin North Am*. 2012. 26:13–27.
Pickard R, Lam T, MacLennan G, et al. Antimicrobial catheters for reduction of symptomatic urinary tract infection in adults requiring short-term catheterisation in hospital: A multicentre randomized controlled trial. *Lancet*. 2012. 380:1927–35.
Saint S, Greene MT, Kowalski CP, et al. Preventing catheter-associated urinary tract infection in the United States: A national comparative study. *JAMA Intern Med*. 2013. 173:874–9.
Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: Summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. *Infect Control Hosp Epidemiol*. 2013. 34:1–14.
Sun Y, Zeng Q, Zhang Z, et al. Decreased urethral mucosal damage and delayed bacterial colonization during short-term urethral catheterization using a novel trefoil urethral catheter profile in rabbits. *J Urol*. 2011. 186:1497–01.
Tambyah PA, Knasinski V, Maki DG. The direct costs of nosocomial catheter-associated urinary tract infection in the era of managed care. *Infect Control Hosp Epidemiol*. 2002. 23:27–31.
Trautner BW, Hull RA, Darouiche RO. Prevention of catheter-associated urinary tract infection. *Curr Opin Infect Dis*. 2005. 18:37–41.

CHAPTER 32

Pneumonia

Javier Ena, MD, MPH

Key Issues

Implementation of guidelines for preventing, diagnosing and treating pneumonia can reduce the mortality and morbidity associated with this condition.

The implementation of various measures at a time (Prevention bundles) have proven in clinical trials to be more effective than isolated single measures to reduce the risk of acquisition of health care associated pneumonia (Objective zero pneumonia).

Known Facts

Hospital acquired (or nosocomial) pneumonia, ventilator associated pneumonia, and health care associated pneumonia are leading causes of morbidity and mortality in hospitalized patients.

According the criteria defined by the American Thoracic Society/Infectious Disease Society of America there are three types of pneumonia related with healthcare:

- Hospital aquired (or nosocomial) pneumonia is pneumonia that occurs 48 hours or more after admission and did not appear to be incubating at the time of admission.
- Ventilator associated pneumonia is a type of hospital-acquired pneumonia that occurs more than 48 to 72 hours after endotracheal intubation.
- Health care associated pneumonia is defined as pneumonia that occurs in non-hospitalized patients that have had extensive healthcare contact, as defined by one or more of the following: intravenous therapy, wound care, intravenous chemotherapy within the prior 30 days, or residence in a nursing home or other long term facility, or hospitalization in an acute care hospital for two or more days within the previous 30 days, or attendance at a hospital or hemodialysis clinic within the prior 30 days. The last category

identifies patients at risk of being infected by multidrug resistant microorganisms and clearly differentiates from those patients with community-acquired pneumonia.

Controversial Issues

Most studies have relied on clinical criteria to diagnose pneumonia, which is known to be unreliable. Therefore outcomes evaluated in clinical trials are prone to bias.

The use of selective decontamination of the digestive tract has been evaluated in several randomized clinical trials and meta-analysis showing controversial results. In addition, there is concern about promoting the growth of resistant bacteria.

Monitoring of gastric residual volume at regular intervals prior to starting or increasing enteral feedings did not prove to reduce the rate of ventilator associated pneumonia.

The use of silver-coated endotracheal tubes has produced controversial results regarding the risk of ventilator associated pneumonia and mortality.

Subglottic drainage: the use of specially designed endotracheal tubes that allow continuous or intermittent aspiration of subglottic secretions has shown to reduce the risk of ventilator associated pneumonia in a meta-analysis of 13 studies (RR 0.55, 95% CI 0.46–0.66). However, these tubes cost more than standard endotracheal tubes and are not widely available. Intermittent suction and continuous suction showed similar benefit with no impact on mortality. Studies analyzing the potential cost-benefit of using tubes with subglottic secretion drainage showed unclear results.

Hydrocortisone (200 mg per day for five days followed by 100 mg per day on day six and 50 mg per day on day seven) showed in a modified intention-to-treat analysis to reduce the risk of health care associated pneumonia in patients with severe trauma compared with placebo. However, in other populations such as patients with traumatic brain injury glucocorticoids have shown to increase mortality.

Suggested Practice

The Society of Healthcare Epidemiology of America and the Infectious Diseases Society of America published in 2008 a series of recommendations to reduce the risk of ventilator associated pneumonia [SHEA, IDSA]. However, the method that

has been gaining ground in the last decade is the "care bundle." The idea is that recommendations used in combination, all of the time, have a greater effect on the positive outcome of patients than single measures. The elements of the care bundle based on the highest level of evidence, i.e. systematic review of randomized trials and single randomized clinical trials are:

1. Oral care: the incidence of ventilator associated pneumonia is significantly reduced by oral antiseptics such as chlorhexidine (relative risk [RR] 0.56, 95% CI 0.39–0.81). The suggested regimen is chlorhexidine 0.12% oral solution (15 mL twice daily until 24 hours after extubation).
2. Patient positioning: supine positioning appears to predispose patients to aspiration and the development of health care associated pneumonia. A recent meta-analysis of 5 clinical trials showed that semirecumbent position was associated with a reduction of ventilator associated pneumonia compared to supine position (RR=0.57, 95% CI 0.39–0.83).
3. Daily assessment of readiness to extubate: daily sedation interruption decrease the time patients are connected to ventilator. Patients therefore can assist extubation and control their secretions. Despite concerns on self extubation, pain, anxiety and, poor synchronization with ventilator, literature shows patients undergoing daily interruptions experienced complications at 2.8% vs. 6.2% compared to those subjected to conventional techniques. For every 7 patients treated with the intervention, 1 life was saved (number needed to treat was 7.4, 95% CI 4.2 to 35.5).
4. Hand hygiene, glove and gown recommendations adherence: multi-modal programs incorporating education, performance feedback, and hand hygiene devices resulted in reduction in ventilator-acquired pneumonia. Provider hand contamination during patient care in the ICU is a modifiable risk factor for reducing ventilator associated pneumonias. A study carried out in a single ICU showed that ventilator-associated pneumonia (rate per 1000 ventilator-days) were significantly reduced after introduction of the program [3.7 vs. 6.9] $P < .01$.
5. Stress ulcer prevention: the role of gastric pH in the pathogenesis of health care associated pneumonia is still controversial.

Bacterial colonization of the stomach is enhanced by drugs that lower the gastric acidity (i.e. histamine H2 agonists, antacids, proton pump inhibitors). The administration of sucralfate prevented stress ulcers without modifying the gastric pH.

6. Deep venous thrombosis prevention**:** for acutely ill hospitalized medical patients at increased risk of thrombosis, the American College of Chest Physicians recommend anticoagulant thromboprophylaxis with low-molecular-weight heparin, low-dose unfractionated heparin bid, or fondaparinux (Grade 1B). In acutely ill hospitalized medical patients who receive an initial course of thromboprophylaxis, guidelines suggest against extending the duration of thromboprophylaxis beyond the period of patient immobilization or acute hospital stay. For critically ill patients who are bleeding, or are at high risk for major bleeding, the recommendation is to use mechanical thromboprophylaxis with graduated compression stockings (Grade 2C) or intermittent pneumatic compression (Grade 2C) until the bleeding risk decreases, rather than no mechanical thromboprophylaxis.

The latter 6 measures were grouped together by the Joint Commission on Accreditation of Healthcare Organization (JCAHO) to form the ventilator-care bundle. All of the measures, except measure 3, can be applied to prevent any type of health care associated pneumonia.

Summary

Nosocomial pneumonia is currently classified as hospital acquired pneumonia, ventilator associated pneumonia, and health care associated pneumonia. It constitutes the second most common cause of health care associated infection overall. The primary mechanism for acquisition of health care associated pneumonia is the presence of microaspiration or macroaspiration of upper respiratory secretions into the lungs. Preventive measures are directed to reduce the risk of overt or subclinical aspiration of bacteria colonizing the upper respiratory tract. A series of 6 measures grouped together to form the ventilator-care bundle have proven to be more effective than single measures to improve patients' outcomes.

References

Blanquer J, Aspa J, Anzueto A, Ferrer M, Gallego M, Rajas O, Rello J, Rodríguez de Castro F, Torres A; Sociedad Española de Neumología y Cirugía Torácica. SEPAR Guidelines for Nosocomial Pneumonia. Arch Bronconeumol. October 2011. 47(10):510–20.

Koff MD, Corwin HL, Beach ML, Surgenor SD, Loftus RW. Reduction in ventilator associated pneumonia in a mixed intensive care unit after initiation of a novel hand hygiene program. *J Crit Care*. October 2011. 26(5):489–95.

Labeau SO, Van de Vyver K, Brusselaers N, Vogelaers D, Blot SI. Prevention of ventilator-associated pneumonia with oral antiseptics: A systematic review and meta-analysis. *Lancet Infect Dis*. November 2011. 11(11):845–54.

Leng YX, Song YH, Yao ZY, Zhu X. Effect of 45 degree angle semirecumbent position on ventilator-associated pneumonia in mechanical ventilated patients: A meta-analysis. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue*. October 2012. 24(10):587–91.

Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT, Taichman DB, Dunn JG, Pohlman AS, Kinniry PA, Jackson JC, Canonico AE, Light RW, Shintani AK, Thompson JL, Gordon SM, Hall JB, Dittus RS, Bernard GR, Ely EW. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): A randomized controlled trial. *Lancet*. January 2008. 12;371(9607):126–34.

CHAPTER 33

Mechanical Ventilation

Caroline Landelle, PharmD, PhD, and
Didier Pittet, MD, MS

Key Issue

Tracheal intubation and mechanical ventilation (MV) are the most important risk factors for health care associated pneumonia in critically ill patients (3- to 21-fold increase in the risk).

Known Facts

- Ventilator-associated pneumonia (VAP) is a common and highly morbid condition in critically ill patients. Incidence varies between 5% and 67%, depending on case mix and diagnostic criteria. The overall attributable mortality of VAP is 13%. In surviving patients, it causes substantial morbidity, resource utilization, and extends hospital length of stay by at least 4 days.
- Early-onset VAP accounts for at least one-third of pneumonia cases in the critical care setting. This entity should be distinguished from late-onset episodes because of the different microbiologic spectrum, risk factors, and outcome. As pathogens causing aspiration pneumonia reflect the oropharyngeal microbial flora at time of aspiration, those causing early-onset VAP more likely reflect normal oral flora or pathogens responsible for community-acquired pneumonia (*Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*). Nevertheless, multidrug resistant (MDR) pathogens may also be involved in early-onset pneumonia, especially in settings with a high prevalence of antibiotic overuse.
- Pathogens colonizing the respiratory tract and causing VAP are derived from either endogenous or exogenous sources. Those colonizing the upper respiratory tract (oropharynx, sinus cavities, the nares, and dental plaque) may be aspirated. Potential exogenous sources are a contaminated environment (sinks, faucets, etc.), contaminated equipment

(MV devices, ventilator circuits, etc.), contaminated enteral feeding, contaminated aerosols, and other colonized patients in the intensive care unit (ICU). Ventilator associated pneumonia can result when the inoculum is large, the microbes virulent, and host defenses impaired. The stomach is an uncommon source of microorganisms for pneumonia in ventilated patients. Hematogenous spread from infected intravascular or bacterial translocation of the gastrointestinal tract lumen occurs much less frequently.

- Emergent intubation, prolonged MV through an endotracheal tube, repeated intubation and contaminated ventilator circuits increase the risk of VAP.
- Unnecessary intubation should be avoided at all times. Non-invasive positive-pressure ventilation (NIPPV) could be used as an alternative ventilation mode in ICU patients.
- Adequate initial antimicrobial treatment decreases the clinical impact of VAP.

Controversial Issues

- The United States Centers for Disease Control and Prevention (CDC) definitions of health care associated pneumonia have been widely used for infection control surveillance and rely predominantly on clinical and radiographic criteria (sensitivity and specificity range between 45–100% and 7–76% for clinical variables, and 8–88% and 27–96% for radiographic features, respectively), although the results of additional diagnostic tests may also be used. However, the greatest challenge is the absence of a simple and reliable gold standard to verify the value of diagnostic procedures. Histologic and bacteriologic examination of lung tissue remains the optimal standard to establish the diagnosis of pneumonia, but these techniques require an open-lung biopsy or autopsy.
- A working group driven by the CDC to improve VAP surveillance recently proposed new definitions of ventilator-associated events, i.e., ventilator-associated conditions (VAC), infection-related ventilator-associated complications (IVAC), and possible and probable pneumonia. VAC are defined as at least 2 calendar days of stable or decreasing daily minimum positive end-expiratory pressure (PEEP), or a daily minimum fraction of inspired oxygen (FiO_2)

followed by an increase in daily minimum PEEP by at least 3cmH_2O sustained for at least 2 calendar days, or an increase in daily minimum FiO_2 by at least 20 points sustained for at least 2 calendar days. VAC includes pulmonary oedema, atelectasis, acute respiratory distress syndrome, and VAP. In patients with VAC, IVAP is defined by concurrent inflammatory signs and at least 4 days of new antibiotics. Possible and probable pneumonia are defined by concurrent pulmonary Gram stains and cultures. Chest radiography is no longer required. The impact of these new definitions on strategies for VAP surveillance and prevention is unknown. Obviously, their practicality and usability in low-resource settings deserves further attention.

- Numerous studies have evaluated the performance of bronchoscopic and non-bronchoscopic procedures for the diagnosis of VAP. Invasive techniques include protected bronchoalveolar lavage (BAL), non-bronchoscopic ("blind") BAL, and "blind" protected specimen brush. The use of any of these techniques should be encouraged in patients at high-risk for MDR or other difficult-to-treat pathogens. Diagnosis by invasive methods requires a considerable commitment of resources, but can potentially reduce cost of care and may lower the use of broad-spectrum antibiotics and the subsequent development of antimicrobial resistance. However, the clinical impact of BAL remains a subject of debate and controversy persists about the optimal diagnostic strategy for VAP. The interpretation of the sensitivity and specificity of any given sampling technique may be severely hampered by the distorting effect of previous antibiotic exposure on the yield of bacterial cultures. In patients pre-treated with antibiotics, sampling should be performed before introducing a new antibiotic regimen.
- A number of adjunctive or alternative methods for VAP diagnosis have been proposed, such as sputum or endotracheal aspirates' culture, identification of intracellular microorganisms (ICOs) by Giemsa stain of BAL specimens and measurements of cytokines (e.g. soluble triggering receptor expressed on myeloid cells-1 [sTREM-1]), or inflammatory mediators (e.g. procalcitonin). But studies show contradictory results and their values are unclear.

- Selective oropharyngeal decontamination (SOD) and selective digestive decontamination (SDD) have been studied for many years. These involve the use of topical oral antibiotics for SOD, and topical oral and intestinal antibiotics, often with a systemic antibiotic added during the first few days of the regimen for SDD, with the goal being the elimination of potential pathogens from the oropharynx and/or gastrointestinal tract. With the eradication of endogenous bacterial sources, infection may be avoided. SOD and SDD are effective in reducing the incidence of VAP in the ICU. The use of topical antibiotics seems to be effective also in preventing all ICU-acquired infections, while the effectiveness on mortality needs to be investigated in further research. Importantly, the main concern associated with the use of SOD or SDD remains the development and spread of antimicrobial resistance. Overall, the currently available evidence does not support the use of SOD or SDD as a preventive strategy on a large scale, particularly in settings with endemic cross-transmission of multidrug resistant microorganisms.
- It was uncertain whether a 45° bed head elevation was effective or harmful with regard to the occurrence of clinically suspected VAP, microbiologically confirmed VAP, and decubitus and mortality. Furthermore, it was unknown whether 45° elevation for 24 hours a day increased the risk for thromboembolism or hemodynamic instability. Experts recommend elevating the head of the bed of mechanically ventilated patients to a 20° to 45° position and preferably to a ≥30° position, as long as it does not pose any risks or conflicts with other nursing tasks, medical interventions, or patients' wishes.
- Since the early 2000s, several multimodal strategies to prevent VAP have been applied in before-after studies. Most have been associated with VAP reduction. "Bundle" strategies are now applied in the ICU, but it remains difficult to assess the significance and effect of each individual measure on VAP prevention. A great deal of attention must be given to factors that might improve adherence with preventive measures.

Suggested Practice

1. Numerous preventive measures have been recommended in 2005 by the American Thoracic Society with a high- or

moderate-level of evidence. Since then, some studies and meta-analyses have confirmed their efficacy:

  - Effective infection control measures: education and training of healthcare workers, high compliance with alcohol-based handrubbing as the main measure for hand hygiene, and isolation to reduce cross-infection with MDR pathogens should be used routinely.

- Surveillance of high-risk patients to determine trends and detect outbreaks of VAP within the ICU. Infection rates should be presented to intensive care physicians and nurses on a regular basis (feedback).
  - Low or reduced staffing levels have a negative impact on patient safety and health care associated infections in critically ill patients and are associated with lapses in infection control practices, thus facilitating cross-transmission of pathogens. A substantial proportion of VAP could be avoided if nurse staffing could be maintained at a higher level.
  - Keeping the teeth and mouth clean, preventing the build-up of dental plaque on teeth or secretions in the mouth may help to reduce the risk of developing VAP. Effective oral hygiene care (OHC) is important for ventilated patients. OHC that includes either chlorhexidine mouthwash or gel is associated with a 40% reduction in the odds of developing VAP in critically ill adults. There is no evidence that OHC including both chlorhexidine and tooth brushing is different from OHC with chlorhexidine alone. There is only weak evidence to suggest that povidone iodine mouth rinse is more effective than saline in reducing VAP.
  - Limiting the use of continuous sedation and paralytic agents that depress cough coupled with sedation vacations and weaning protocols that facilitate removal of the endotracheal tube are strongly recommended to reduce days of mechanical ventilation (MV) and lower VAP rates.
  - Unnecessary intubation and repeated intubation should be avoided. Non-invasive positive-pressure ventilation (NIPPV) should be used whenever possible.
  - Orotracheal intubation and orogastric tubes should be preferred over nasotracheal intubation and nasogastric tubes to prevent health care associated sinusitis and to reduce the risk of VAP.

- The endotracheal tube cuff pressure (Pcuff) should be maintained at approximately 20–30 cm H_2O to prevent leakage of contaminated oropharyngeal secretions and gastric content around the cuff into the lower respiratory tract. Pcuff continuous regulation using an automatic device that continuously displays the levels of Pcuff in real time has been evaluated with contradictory results.
- The main cause of VAP is due to the aspiration of secretions containing bacterial pathogens into the lower respiratory tract. Aspiration of subglottic secretions requires the use of specially designed endotracheal tubes containing a separate dorsal lumen that opens into the subglottic region. The use of endotracheal tubes with subglottic secretion drainage has shown to be effective for the prevention of VAP, but the cost-effectiveness of the strategy deserves further investigation.
- Contaminated condensate should be carefully emptied from ventilator circuits and condensate should be prevented from entering either the endotracheal tube or inline medication nebulizers.
- Enteral nutrition is preferred over parenteral nutrition to reduce the risk of complications related to central intravenous catheters and to prevent reflux villous atrophy of the intestinal mucosa that may increase the risk of bacterial translocation.
- A restricted transfusion trigger policy for transfusion of red blood cell and other allogeneic blood products is recommanded; leukocyte-depleted red blood cell transfusions can help to reduce VAP in selected patient populations.

2. The following measures are recommended in the absence of a strong level of evidence: avoid unnecessary aspirations; saline instillation before tracheal suctioning; cleaning, disinfection, and sterilization of reusable components and appropriate maintenance of equipment; use of sterile water for rinsing reusable equipment; not implementing ventilator circuit changes unless specifically indicated; change of filters in the breathing circuit every 7 days; use of gloves when handling respiratory secretions; use of heat and moisture exchangers; and stress bleeding prophylaxis.

3. The following measures are suggested without definitive scientific evidence of their benefit: silver-coated endotracheal tube; use of probiotics; closed-suction systems; use of SOD or SDD; kinetic bed therapy, PEEP; physiotherapy; inclined position; intensive insulin therapy; and mucus shaver.
4. The following measures have not demonstrated their efficacy: early tracheotomy; prone position; and iseganan.

Summary

VAP is the most frequent ICU-acquired infection in mechanically ventilated patients and is associated with considerable morbidity and costs, significant antibiotic use, and high mortality rates. Microaspiration of oropharyngeal secretions contaminated by endogenous flora around the endotracheal tube cuff is the major route for microbial invasion. Diagnosis can be difficult and considerable controversy remains regarding the optimal approach. A large number of preventive measures and strategies have been proposed with variable degrees of effectiveness. Consequently, physicians should first consider preventive measures with a demonstrated impact on patient outcomes, such as optimal infection control practices (particularly, hand hygiene), NIPPV, sedation and weaning protocols, oral hygiene care, and endotracheal tube with drainage of subglottic secretions. Clearly, there is no single preventive mechanism that will completely avert this complication, and patients at risk of VAP must be approached with a package or bundle of preventive measures. The use of a "ventilator bundle" appears attractive in many ways, although the choice of practices incorporated in this bundle needs critical evaluation. Successful VAP prevention relies on multimodal, multidisciplinary strategies.

References

Girou E, Schortgen F, Delclaux C, Brun-Buisson C, Blot F, Lefort Y, Lemaire F, Brochard L. Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. *JAMA*. 2000. 284:2361–67.

Klompas M. Does this patient have ventilator-associated pneumonia? *JAMA*. 2007. 297:1583–93.

Klompas M. Ventilator-associated events surveillance: A patient safety opportunity. *Curr Opin Crit Care*. 2013. 19:424–31.

Berton DC, Kalil AC, Teixeira PJ. Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients

with ventilator-associated pneumonia. *Cochrane Database Syst Rev.* 2012. 1.
Pileggi C, Bianco A, Flotta D, Nobile CG, Pavia M. Prevention of ventilator-associated pneumonia, mortality and all intensive care unit acquired infections by topically applied antimicrobial or antiseptic agents: A meta-analysis of randomized controlled trials in intensive care units. *Crit Care*. 2011. 15:R155.
Niël-Weise BS, Gastmeier P, Kola A, Vonberg RP, Wille JC, van den Broek PJ; Bed Head Elevation Study Group. An evidence-based recommendation on bed head elevation for mechanically ventilated patients. *Crit Care*. 2011. 15:R111.
Klompas M.Ventilator-associated pneumonia: Is zero possible? *Clin Infect Dis*. 2010. 51:1123–6.
American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005. 171:388–416.
Hugonnet S, Chevrolet JC, Pittet D. The Effect of Workload on Infection Risk in Critically Ill Patients. *Crit Care Med*. 2007. 35:76–81.
Shi Z, Xie H, Wang P, Zhang Q, Wu Y, Chen E, Ng L, Worthington HV, Needleman I, Furness S. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev*. 2013. 8.
Burns KE, Adhikari NK, Keenan SP, Meade MO. Noninvasive positive pressure ventilation as a weaning strategy for intubated adults with respiratory failure. *Cochrane Database Syst Rev*. 2010. (8).
Muscedere J, Rewa O, McKechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: A systematic review and meta-analysis. *Crit Care Med*. 2011. 39:1985–91.
Subirana M, Solà I, Benito S. Closed tracheal suction systems versus open tracheal suction systems for mechanically ventilated adult patients. *Cochrane Database Syst Rev*. 2007. (4).
Delaney A, Gray H, Laupland KB, Zuege DJ. Kinetic bed therapy to prevent nosocomial pneumonia in mechanically ventilated patients: A systematic review and meta-analysis. *Crit Care*. 2006. 10:R70.
Wang F, Wu Y, Bo L, Lou J, Zhu J, Chen F, Li J, Deng X. The timing of tracheotomy in critically ill patients undergoing mechanical ventilation: A systematic review and meta-analysis of randomized controlled trials. *Chest*. 2011. 140:1456–65.
Abroug F, Ouanes-Besbes L, Elatrous S, Brochard L.The effect of prone positioning in acute respiratory distress syndrome or acute lung injury: A meta-analysis. Areas of uncertainty and recommendations for research. *Intensive Care Med*. 2008. 34:1002–11.

CHAPTER 34

Diphtheria, Tetanus, Pertussis

Jack Levy, MD

Key Issues

Active immunization of the general population is effective to control the transmission of these infections in the community, as well as an eventual risk of infection in the hospital setting.

Known Facts

- Diphtheria and pertussis are transmissible from person to person, whereas tetanus is not. Transmission of diphtheria occurs mainly from close contact with secretions from the nose, throat, eye or skin of a patient, according to the site of infection, or with a carrier. Transmission of pertussis occurs by close contact via aerosolized droplets from patients with disease. Infants <4 months are at highest risk of severe disease. Transmission of tetanus occurs by introduction of tetanus spores into the organism through a contaminated wound. Tetanus spores can be introduced via the umbilical cord during delivery, causing *tetanus neonatorum*, an important health problem in developing countries.
- Diphtheria, tetanus and pertussis are mainly community acquired infections. The high immunization coverage obtained by local programs in industrialized countries and by the WHO EPI has considerably reduced the global burden of diphtheria, tetanus and pertussis.
- Universal vaccination in infancy against these 3 illnesses is done using a combination vaccine.
- Diphtheria and tetanus vaccines consist of single purified antigens: diphtheria and tetanus toxoids. Diphtheria vaccines used for children until the age of 6 years contain 6.7 to 30 floculation units (Lf) of toxoid, whereas a vaccine with a reduced amount of antigen (not more than 2 Lf) should be used for individuals older than 6 years.

- There are 2 types of pertussis vaccines: whole cell vaccine (Pwc) and acellular vaccines (Pa). The oldest and globally most widely used is thePwc vaccine. This vaccine is highly protective, although there are differences between preparations. However, Pwc vaccines are usually not administered after the age of 7 years. Pa vaccines consist of 2 or 3 purified antigens. They are less reactogenic than Pwc vaccines and have demonstrated their protective efficacy in clinical trials. However the duration of protection is probably shorter than that afforded by Pwc preparations. Combination of Pa vaccines with other vaccines recommended for infant immunization (Diphtheria, tetanus, IPV, Hib and HBV) exist. Pa-based vaccines remain significantly more expensive than whole cell preparations.
- Long term protection against diphtheria, tetanus and pertussis by vaccination requires primary immunization followed by the administration of booster doses of these vaccines. Pa vaccines suitable for use in adolescents and adults have now been developed. As older children and adults with mild or atypical disease remain a source of contamination for young infants who are at highest risk for severe manifestation, administration of these vaccines to adolescents or young adults is now widely recommended in industrialized countries in an attempt to obtain longer term protection and to provide indirect protection to infants. Different strategies have been proposed to achieve the latter objective (the so-called cocoon vaccination, vaccination during pregnancy).
- Transmission of diphtheria, tetanus and pertussis in the hospital setting, although very rare, can occur. An infected patient can be the source of diphtheria or pertussis transmission whereas contaminated surgical material has been reported as a possible cause of tetanus.

Controversial Issues

- Rare severe neurological events leading to permanent brain damage occurring in infancy have been attributed to immunization with Pwc vaccine in the 1970s, leading to the interruption of pertussis vaccination programs in some industrialized countries. This has been followed by a recrudescence of pertussis in these countries, thereby demonstrating

the role of vaccination in controlling the disease. Whether these neurological events were only temporally related or caused by vaccination has been a source of controversy. One large case control study performed in England has not established a causal relationship between such neurological events and pertussis vaccination.

- Pa vaccines have been demonstrated to be effective in large clinical trials. However, in recent years, a recrudescence in the number of cases of pertussis has been reported in a number of countries where the Pa vaccines have replaced Pw vaccines in the immunization programs, warranting the use of booster doses in adolescence and adulthood.
- Pwc vaccines remain widely used in countries with limited resources. In a number of industrialized countries, Pwc vaccines are still preferred on the basis of cost benefit evaluations and/or because they have demonstrated their effectiveness over the long term.

Suggested Practice

- All interventions that allow reaching high vaccine coverage should be promoted (*Table 34.1*). Vaccination schedules vary according to local practice; guidelines are proposed by WHO Extended Program of Immunizations (EPI).
- Measures to prevent hospital transmission should be implemented. For diphtheria and pertussis, they aim at protecting other patients and hospital personnel. For tetanus, which is not transmissible from person to person, they aim at avoiding the rare case of infection from contaminated hospital material and maintaining adequate standard of care for wound management and obstetrical practice (*Table 34.2*).

Table 34.1 Interventions to Reach High Vaccine Coverage Against Diphtheria, Tetanus and Pertussis

– Universal childhood vaccination against diphtheria, tetanus and pertussis consisting of 3 to 4 doses of combination vaccine starting not later than 3 months of age.
– Administration of a booster dose of diphtheria-tetanus vaccine at the age of 4 to 6 years, combined with acellular pertussis if affordable and of a booster dose of diphtheria-tetanus every 10 years thereafter.

continued

Table 34.1 Interventions to Reach High Vaccine Coverage Against Diphtheria, Tetanus and Pertussis (continued)

– In countries using Pa vaccines in their childhood immunization programs, the booster used at adolescence should be a diphtheria- tetanus-Pa formulation suitable for use in adults. Strategies of adult vaccination should be implemented for indirectly protecting very young infants).

– When managing a wound, review of the history of tetanus immunization and administration of a booster dose of diphtheria-tetanus and human tetanus immune globulins according to previous vaccination and to the severity of the wound.

– In countries where a significant proportion of women of childbearing age are not immunized against tetanus, implementation of vaccination programs of pregnant women according to WHO EPI guidelines.

Table 34.2 Measures to Prevent Hospital Transmission of Diphtheria, Tetanus and Pertussis

Diphtheria

– Patient isolation: standard + droplets / and contact if cutaneous.

– Identification of exposed individuals and implementation of the following measures:
  – Throat culture for *C. diphtheriae*, as pharyngeal carriage is possible despite antitoxic immunity,
  – Review of prior history of vaccination, completion of primary program if pending or administration of a booster dose of vaccine appropriate for age if last dose not given within the preceding 5 years,
  – Surveillance for 7 days for evidence of disease, and
  – Antimicrobial prophylaxis with erythromycin for 7 days to previously unimmunized or insufficiently immunized individuals, and to carriers; to be prolonged if carriage not eradicated.

Tetanus

– Appropriate wound management: includes cleaning and debridment of the wound if necessary and administration of tetanus (and diphtheria) vaccination and human tetanus immune globulin according to the characteristics of the wound and of the history of previous vaccination.

– Appropriate sterilization of hospital supplies (surgical, injections and sutures material).

– Appropriate obstetrical practices, including sterile umbilical cord cutting.

continued

Table 34.2 Measures to Prevent Hospital Transmission of Diphtheria, Tetanus and Pertussis (continued)

Pertussis

- Patient isolation: standard + droplets.
- Identification of exposed individuals and implementation of the following measures:
  - Review of prior history of vaccination, completion of primary program if pending or administration of a booster dose of vaccine if last dose of vaccine has been given > 3 years,
  - Surveillance for 21 days for evidence of disease, and
  - Antibiotic prophylaxis with erythromycin for 14 days to close contacts regardless of immunization status advocated by most authorities on the basis that vaccine induced protection is not absolute and wanes with time (no booster given after the age of 7 years).

References

Plotkin SA, Orenstein WA, Offit PA (Eds). Vaccines. WB Saunders Company, 2008.

Red Book, Report of the Committee on Infectious Diseases. American Academy of Pediatrics, 2012.

Last JM, Wallace RB (Eds). Public Health and Preventive Medicine. Appleton and Lange, 2007.

ACIP recommended immunization schedules for persons aged 0 through 18 years and adults aged 19 years and older—United States 2013. *MMWR*. 2013. 62.

Pertussis vaccines: WHO position paper. *WHO Weekly Epidemiological Record*. 2010. (85)40:385–400.

CHAPTER 35

Measles

Patrick De Mol, MD, PhD, and Philippe Lepage, MD, PhD

Key Issue

Measles is caused by rubeola virus, one of the most contagious pathogenic agents known. Despite progress in global immunization, measles remains a major infectious cause of mortality in developing countries and is responsible for more than 100,000 deaths in children each year. The importance of health care associated transmission of measles varies substantially from one region to another according to local measles epidemiology and to vaccine coverage. Whatever the local incidence of measles, the hospital represents a critical site for cross-infection. Characteristics of hospital care settings present numerous risk factors for measles transmission.

Known Facts

Measles virions remain viable for a few hours when suspended in air. Therefore, cough of infected patients can be an important source of virus for susceptible individuals exposed in confined rooms. Infection has been described without face-to-face contact with an infected subject. Transmission may occur when the contagious individual has left the room up to 2 hours before the arrival of susceptible subjects.

Patients with measles are contagious from 3 to 5 days before the onset of rash and 1 to 2 days before the onset of fever. This highly contagious prodromal phase significantly facilitates the spread of measles in the hospital and complicates control measures. Patients with measles remain contagious until 4 days after the onset of rash.

Even in populations with good vaccine coverage, medical facilities can be the place for transmission of measles to patients and to healthcare workers. Indeed, the hospitals combine the factors of infected children, susceptible persons (e.g., those too young for immunization, debilitated patients), and crowding.

In industrialized countries, most cases of health care associated measles are transmitted patient-to-patient. However, non-immune healthcare workers are also often involved. Healthcare staff in developed countries who acquire measles most frequently are those in direct contact with patients (physicians, nurses). In contrast, most healthcare workers in developing countries have been definitively immunized by wild viruses during childhood and do not contribute significantly to health care associated transmission.

Healthcare infected children with measles have higher case-fatality and complication rates and recover more slowly than community-infected patients. The increased complication rate in children with healthcare associated measles is likely due to young age (infants) and the presence of underlying disease. In African countries, HIV infection is frequent in hospitalized children and is associated with prolonged measles infection and increased mortality.

Immunization is generally performed in children 9 months of age or older in developing countries and in children 12 months of age or older in industrialized nations. Young non-immune infants are therefore highly susceptible to health care associated measles. Young children are also at increased risk of health care associated infection because of frequent contacts with healthcare facilities such as maternal and child healthcare clinics. In addition, young age is an important risk factor for severe illness.

Several studies have suggested that hospital transmission is important in developed nations and that attendance at hospital facilities is a significant risk factor for acquiring measles. All types of healthcare settings have been implicated; direct or indirect exposure to measles virus in waiting rooms and in emergency departments has been shown to be a significant risk factor during community outbreaks in the US. Low relative humidity and lack of fresh-air circulation in waiting rooms may facilitate measles transmission.

During outbreaks in developing countries, hospital transmission appears to contribute to measles incidence in urban communities. In rural populations, however, no significant level of transmission appears to be linked to hospital contact, especially if vaccination coverage remains moderate.

Controversial Issues

Safe and effective measles vaccines that can be administered before 6 to 9 months or age are needed to reduce the number of susceptible individuals and the burden of disease.

Fears contribute to poor vaccination rates in some parts of the population, particularly in industrialized countries. Links between measles vaccination and autism or inflammatory bowel diseases have been proposed. There is now strong scientific evidence against the hypothesis that measles vaccination may be implicated as a causative agent in these two diseases.

Suggested Practice

- High rates of measles vaccination coverage must be maintained in the community for herd immunity. This intervention will minimize the number of susceptible individuals. In industrialized nations, 2 doses of measles vaccine are required to obtain prolonged protection.
- A high level of awareness of the dangers of measles must be maintained among medical staff. Healthcare personnel should be informed about the risk of hospital transmission of measles to non-immune subjects.
- Patients with fever and rash must be placed in respiratory precautions. These subjects should not enter the common waiting areas of healthcare facilities. Where possible, these patients should be taken to a room reserved for respiratory isolation. It is also important that waiting and treatment rooms be adequately ventilated.
- For developing countries, WHO recommends that children between 6 months and 9 years of age should be vaccinated against measles upon admission to hospital, even if there is evidence of previous measles immunization. The protection rate of measles vaccination is about 80 to 90% in developing countries. In industrialized countries, only unvaccinated patients need to be vaccinated upon admission.
- Various studies have shown that measles vaccination is effective in preventing measles in exposed subjects if vaccination is given within 72 hours of exposure. The vaccine efficacy varied between 68 and 100%.

- Gamma globulins should only be used for patients with congenital immune function disorders or during immunosuppressive therapy.
- Staff members should be immune to measles. Most adults in developing countries have natural measles immunity.
- In industrialized countries, healthcare personnel without adequate measles antibody titers or documented vaccination should be vaccinated. Strong recommendations and high vaccination coverage against measles in health-care workers could contribute to eliminate measles in the general population.

Summary

Measles is a serious and very contagious disease. Health care associated transmission of measles remains a threat and may prove to be an important obstacle to the elimination of measles. Maintaining a high coverage of measles vaccination in the community is the most important preventive strategy against the disease. Other helpful interventions to limit health care associated transmission include: postexposure vaccination, immunization of hospitalized patients, increasing awareness of the clinical presentation of measles in healthcare facilities, and respiratory isolation of suspected or proven cases. Newer, safe vaccines that are more immunogenic in the first year of life and more stable in tropical countries are needed.

References

Biellik RJ, Clements CJ. Strategies for Minimizing Nosocomial Measles Transmission. *WHO Bull*. 1997. 75:367–375.

Botelho-Nevers E, Gautret P, Biellik R, Brouqui P. Nosocomial Transmission of Measles: An Updated Review. *Vaccine*. June 8 2012. 30:3996–4001.

Botelho-Nevers E, Cassir N, Minodier P, et al. Measles among Healthcare Workers: A Potential for Nosocomial Outbreaks. *Euro Surveill*. January 13, 2011. 16(2). doi:pii:19764.

CDC. Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013. Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports*. 2013. 62:1–64.

Chen RT, Goldbaum GM, Wassilak SG, Markowitz LE, Orenstein WA. An Explosive Point-Source Measles Outbreak in a Highly Vaccinated Population. *J Epidemiol*. 1989. 129:173–182.

Choi WS, Sniadack DH, Jee Y, et al. Outbreak of Measles in the Republic of Korea, 2007: Importance of Nosocomial Transmission. *J Infect Dis*. July 2011. 204(Suppl 1):S483–490.
Davis RM, et al. Transmission of Measles in Medical Settings: 1980 to 1984. *JAMA*. 1986. 255:1295–1298.
Groth C, Bottiger B, Plesner A, Christiansen A, Glismann S, Hogh B. Nosocomial Measles Cluster in Denmark Following an Imported Case, December 2008–January 2009. *Euro Surveill*. February 26, 2009. 14(8).
Liu L, Johnson HL, Cousens S, et al. Global, Regional, and National Causes of Child Mortality: An Updated Systematic Analysis for 2010 with Time Trends since 2000. *Lancet*. 2012. 379:2151–2161.
Madsen KM, Hviid A, Vestergaard M, et al. A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism. *N Engl J Med*. 2002. 347:1477–1482.
Marshall TM, Hlatswayo D, Schoub B. Nosocomial Outbreaks—A Potential Threat to the Elimination of Measles? *J Infect Dis*. 2003. 187(Suppl 1):S97–101.
Ruuskanen O, Salmi TT, Halonen P. Measles Vaccination After Exposure to Natural Measles. *J Pediatr*. 1978. 93:43–45.

CHAPTER 36

Herpes Zoster Vaccine

Richard P. Wenzel, MD, MSc

Key Issues

An effective vaccine is available to minimize the risk of zoster infection and its related morbidity.

Known Facts

There is a 30% lifetime risk of zoster among people who have had chicken pox. Zoster can cause severe pain at times and can be complicated by post-herpetic neuralgia, central nervous system issues including encephalitis, and peripheral nerve palsies.

The currently available zoster vaccine now recommended for people aged 50 or over will reduce the attack rate by 50% and will reduce post-herpetic neuralgia by 67%. It is a live attenuated vaccine.

The vaccine is administered subcutaneously—given at a 45° angle. It is stored frozen but can be kept in a refrigerator for up to 72 hours before reconstitution and then administered to the patient. The diluent for reconstitution should be stored separately at room temperature (68°–77°F) or in a refrigerator.

The vaccine contains 19,400 pfu/dose—higher than the 1,350 pfu/dose of the monovalent varicella vaccine.

Contraindications include failure to administer the vaccine within 30 minutes of reconstitution; pregnancy; immune suppression; active or untreated tuberculosis; and a history of anaphylactoid reactions to gelatin, neomycin or the vaccine.

Controversies

It is not clear if the vaccine should be used routinely in people who have already experienced shingles. However, retrospective analyses show no harm, and thus prior shingles is not a contraindication.

Suggested Practice

If available, this vaccine should be administered to people aged 50 or older who have no contraindications.

References

Oxman MN, Levin JM, Johnson GR, et al. Shingles Prevention Study Group. A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults. *New Engl J Med*. 2005. 352:2271–84.

Yawn B, Saddier P, Wollan PC, et al. A Population—Based Study of the Incidence and Complication Rates of Herpes Zoster before Zoster vaccine introduction. *Mayo Clin Prog*. 2007. 82L 1341–9.

Kimberlin DW and Whitley RJ. Varicella Zoster Vaccine for the Prevention of Herpes Zoster. *N Engl J Med*. 2007. 356:1338–43.

Schmader KE, Levin MJ, Gnann JW, Jr., et al. Efficacy, Safety and Tolerability of Herpes Zoster Vaccine in Persons Aged 50–59 years. *Clin Infect Dis*. 2012. 54:922–8.

CHAPTER 37

Human Papillomavirus

Joshua White, MD

Key Issue

HPV transmission by fomites has been hypothesized leading to concern for health care associated transmission from patient to patient via transvaginal ultrasound probes, biopsy forceps and cryotip probes used for gynecologic procedures. Concern also exists for respiratory transmission of HPV to the health-care practitioner through inhalation from the smoke plume produced by laser treatment of HPV lesions, including cutaneous and anogenital warts as well as respiratory papillomas. Finally, health care associated transmission of HPV has been postulated to occur through the shedding of fomites from warts onto environmental surfaces, given its ability to survive for up to 7 days in both wet and dry environments.

Known Facts

- HPV is a circular, double stranded, non-enveloped DNA virus of the Papillomaviridae family and Papillomavirus genus of which there are more than 100 different types.
- Most HPV infections are subclinical and transient, generally involving the male and female genital tract.
- Risk factors for HPV acquisition include early age of first intercourse, an increased number of sexual partners, smoking tobacco, HIV infection (even in the absence of AIDS) and immunosuppression.
- Transmission is primarily through sexual intercourse, including through oral and anal sex, as well as perinatally from mother to child.
- A well-established link exists between HPV and cervical cancer, with approximately 70% of cases due to HPV types 16 and 18. Other common HPV types that can cause cervical cancer include 31, 33 and 45.

- HPV has been linked to other cancers including vulvar, vaginal, penile and anal squamous cell carcinoma as well as oropharyngeal squamous cell carcinoma.
- HPV causes anogenital condylomata ("genital warts"), primarily HPV types 6 and 11. HPV is the most common STI worldwide, with an estimated prevalence of 25% in sexually active young women.
- HPV has been linked to a disease process know as recurrent respiratory papillomatosis, which presents as wart-like lesions on the vocal folds but may also involve the supraglottic or subglottic regions and the respiratory tract. Children often present with hoarseness and an abnormal cry, or even respiratory distress, while adults are more often asymptomatic. Pathogenesis is unclear in adults but is thought to be due to the spread of HPV types 6 and 11 from anogenital lesions through oral contact. Children are thought to acquire the virus through contact with an infected birth canal. The incubation period ranges from one to several months.

Controversial Issues

- Fomites represent a less established mode of HPV transmission, either from dehydrated squames shed from the epidermal surface of warts or in secretions from the genital tract. This presents concern for health care associated spread on medical instruments, surfaces, and even clothing, as HPV has been shown to persist in both wet and dry environments for a number of days.
- Concern exists for potential person to person transmission of HPV via fomites from genital secretions through contamination of transvaginal ultrasound and other endocavitary probes. However, there are no case reports that prove this form of transmission.
- A number of cases of genital HPV infection have been reported in presumed virgins, suggesting but not proving that environmental fomites shed from genital secretions were the causative vector rather than through sexual contact.
- Similarly, genital HPV has been reported in children unlikely to have been sexually abused, suggesting the possibility of infection through acquisition of environmental fomites.

- The development of respiratory papillomatosis has been linked to inhalation of HPV types 6 and 11 from the smoke plume generated during laser ablation of genital warts.

Suggested Practice

- All transvaginal ultrasound probes should be cleansed with a high-level disinfectant after every patient exam, even if they were covered by a condom/ probe cover given their proven breakage/ failure rate. All other ultrasound exams that involve contact with tissue other than intact skin (eg. mucous membranes) should undergo the same type of disinfection.
- Vaginal/gynecologic instruments including, but not limited to cryotip probes and biopsy forceps should undergo high-level disinfection procedures as listed in the CDC's "Guideline for Disinfection and Sterilization in Healthcare Facilities" (2008).
- All disinfecting agents must be virucidal, as many commonly used agents (such as 70% ethanol) may be highly bactericidal but not adequately virucidal for eradicating HPV.
- Ultraviolet C is a promising method of sterilization for the eradication of HPV from instruments but current evidence does not clearly support its use.
- Condoms or probe sheaths should be securely fastened to the ultrasound probe by an elastic band or similar device to prevent gross contamination of the probe with blood or cervico-vaginal secretions.
- Practitioners performing transvaginal ultrasound exams or other gynecologic procedures should wear gloves, masks and goggles/ eyewear to protect against fluid splashes into mucous membranes including the mouth and eyes, with consideration of gowns as well depending on the specific procedure.
- Practitioners performing laser ablation of cutaneous or vaginal warts, as well as respiratory papillomas, should hold the vacuum tip of the smoke evacuator on the laser apparatus within 1cm of the treatment field, as up to 50% of particulate matter has been demonstrated to escape into the air if held greater than 2cm away. This places the practitioner at risk of inhaling HPV particles.

- Practitioners performing laser ablation of cutaneous or vaginal warts, as well as respiratory papillomas, should wear basic PPE including but not limited to gloves and surgical masks.

Summary

HPV transmission from patient to patient through the use of endovaginal ultrasound for diagnostic and therapeutic procedures has been hypothesized but never clearly demonstrated. Endovaginal ultrasound is used commonly by both obstetrician/gynecologists and emergency room physicians as a diagnostic tool during the work-up of pelvic pain and vaginal bleeding. The ultrasound probe is an ideal vector for cross-transmission of HPV if not sterilized correctly, as it makes close contact with the cervix and vaginal wall during examination. The CDC's "Guideline for Disinfection and Sterilization in Healthcare Facilities" defines endovaginal ultrasound as a semicritical device given its direct contact with mucous membranes. The guideline states that the use of a condom or probe cover does not change this definition given their proven failure rate. Although ultrasound manufacturers generally provide ultrasound sheaths for coverage of the probe, many hospitals utilize latex condoms as a more affordable alternative. A single comparative study supports the use of condoms over probe sheaths, citing significantly less perforations in condoms at 1.7% (3 of 180) versus 8.3% (15 of 180) of probe covers during routine use for endovaginal ultrasound over a 10 month period.

Contamination of transvaginal ultrasound probes with blood or vaginal fluids despite the use of a latex condom has been demonstrated during the course of routine patient care. A study at an academic medical center in Houston, Texas explored this issue with a sample size of 173 patients seen over 9 months in their emergency department. Visual contamination of the probe was noted in 2% of patients (3 of 173), while contamination by means of positive hydrogen peroxide testing was recorded in 5% (8 of 173), indicating that many cases of probe contamination were not visible**.** Notably, the duration of the ultrasound exam was not correlated with a positive test. Two cases of visible contamination occurred at the rim of the condom, leading the authors to suggest securing the rim for each exam (eg. with an elastic band). This report suggests that the lack of visible blood or body fluids does

not rule out contamination of the probe and therefore disinfection must occur between each and every patient examination.

HPV DNA has been detected on the surface of properly covered transvaginal probes after standard disinfection following routine patient care. In one prospective study, 3.5% (7 of 198) of endovaginal ultrasound probes were HPV DNA positive over a 5 month period in a gynecology department of a university hospital in Lyon, France. Probe samples were obtained within 15 minutes of removal of the disposable probe cover. This was followed by standard disinfection of the probe with a low level disinfection wipe. The majority of the HPV strains isolated (6 of 7) represented high risk types. No breakage in probe covers or blood/ body fluids were observed by visual inspection.

HPV transmission from patients to healthcare workers theoretically may occur through the inhalation of smoke during the laser ablation of cutaneous and anogenital warts as well as laryngeal papillomas. The concern for cross-transmission of HPV is related to the laser's mechanism of action. When the laser interacts with tissue, a "smoke plume" forms and consists of vaporized material, steam, particulate matter and potentially intact HPV virions or viral DNA. A primary theoretical concern is the development of laryngeal papillomatosis through inhalation of the smoke plume, esp. from genital warts containing HPV types 6 and 11. A smoke evacuator, which functions as a vacuum system with a filter attached to the laser, is considered the most effective precaution in preventing inhalation of the smoke plume. Use of a standard surgical mask, surgical gloves and gowns are also recommended for HPV risk reduction during laser ablation of HPV lesions.

A single case of healthcare acquired laryngeal papillomatosis is reported in the literature, postulated to have occurred through inhalation of genital or colorectal HPV in a smoke plume. The healthcare worker reported the use of appropriate PPE as well as a built-in suction device in the endoscope itself for removal of the laser plume, but notably the operating room did not possess a stand-alone smoke evacuator system.

The authors of one small series of patients measured the amount of HPV DNA present in the smoke plume created from the laser ablation of laryngeal papillomas. No HPV DNA was detected; the authors' argued that their results were due to the

fact that laryngeal papillomas contain much lower copy numbers of HPV DNA (1 to 50 copies per cell) as compared to several hundred per cell present in plantar warts.

A number of studies have detected HPV DNA in the smoke plume produced by CO2 lasers during the ablation of anogenital condylomata. The authors of one study found that 30% (3/10) of smoke plumes contained HPV DNA, all of which were HPV type 6 and matched the HPV type of the corresponding patients. HPV DNA has also been detected from the smoke plume produced from the ablation of plantar and mosaic warts. One series collected vapor from the laser plume using a bubble filled chamber filled with PBS solution and found that 29% (2 of 7) were HPV positive. A similar study collected the laser plume vapor with a vacuum device with filter from 8 plantar warts and found a higher rate of HPV positivity at 62.5% (5 of 8) of samples.

The ability of HPV to survive on environmental surfaces in the form of fomites is supported by several scientific reports. Bovine papillomavirus type 1 obtained from cattle warts and pseudotype HPV 16 virions (which have the same capsid proteins as wild type HPV16 virions) are often used as surrogates for wild-type HPV, given the difficulty of producing large amounts of HPV from human warts or lesions. Supportive findings include the ability of pseudotype HPV 16 virions to resist desiccation for one week; the ability of BPV1 and HPV16 to resist the effects of 10mM EDTA; and the ability of small amounts of BPV1 to survive after treatment with 70% ethanol. All BPV1 and pseudovirus HPV16 notably were inactivated by autoclave treatment at 121C for 30 minutes.

HPV DNA has been detected on surgical gloves, biopsy forceps and cryoprobe tips before and after disinfection (with 30% Savlon and 90% ethanol solution) after use on patients with external anogenital condylomata acuminate, cervical condylomata and cervical intraepithelial neoplasia. Fifty percent of gloves (8 of 16) tested positive for HPV DNA after they were used to examine patients with anogenital condylomata acuminate; 1.6 % (1 of 62) of biopsy forceps after disinfection were HPV positive, and finally 4.5% (1 of 22) of the cryoprobe tips were HPV positive.

Genital type HPV DNA strains have been detected on environmental surfaces in a genitourinary clinic where cryotherapy treatment for genital warts was routinely performed. HPV DNA

was detected on the surface of cryotherapy guns, on patient equipment throughout the clinic, and even in male and female patient bathrooms in the medical office. Notably, a total of 19 HPV types were detected, all of which were associated with genital infection.

References

Abramson AL, DiLorenzo TP, Steinberg BM. Is Papillomavirus detectable in the plume of laser-treated laryngeal papilloma? *Arch Otolaryngol Head Neck Surg*. 1990. 116:604–607.

Casalegno J-S, et al. High risk HPV contamination of endocavitary vaginal ultrasound probes: An underestimated route of nosocomial infection? *PLOS one*. 2012. 7:10.

CDC. Guideline for Disinfection and Sterilization in Healthcare Facilities. 2008.

Ferenczy A, Bergeron C, Richart RM. Human papillomavirus DNA in fomites on objects used for the management of patients with genital human papillomavirus infections. *Obstetrics and Gynecology*. 1989. 74:6.

Garden JM, et al. Papillomavirus in the vapor of carbon dioxide laser-treated verrucae. *JAMA*. 1988. 259:1199–1202.

Gloster HM, Roenigk R. Risk of acquiring human papillomavirus from the plume produced by the carbon dioxide laser in the treatment of warts. *J Am Acad Dermatol*. 1995. 32:436–41.

Hallmo P, Naess O. Laryngeal papillomatosis with human papillomavirus DNA contracted by a laser surgeon. *Eur Arch Otorhinolaryngol*. 1991. 248:425–427.

Lewin JM, Brauer JA, Ostad A. Surgical smoke and the dermatologist. *J Am Acad Dermatol*. 2011. 65:636–41.

Roden RBS, Lowy DR, Schiller JT. Papillomavirus is resistant to desiccation. *JID*. 1997. 176:1076–9.

Rooks VJ, et al. Comparison of probe sheaths for endovaginal sonography. *Obstet Gynecol*. 1996. 87 (1):27–9.

Sawchuck WS, et al. Infectious papillomavirus in the vapor of warts treated with carbon dioxide laser or electrocoagulation: Detection and protection. *J Am Acad Dermatol*. 1989. 21:41–9.

Storment JM, Monga M, Blanco JD. Ineffectiveness of latex condoms in preventing contamination of the transvaginal ultrasound transducer head. *Southern Medical Journal*. 1997. 90:2.

Strauss S, et al. Contamination of environmental surfaces by genital human papillomaviruses. *Sex Transm Infect*. 2002. 78:135–138.

Weyandt GH, et al. Low risk of contamination with human papilloma virus during treatment of condylomata acuminata with multilayer argon plasma coagulation and CO2 laser ablation. *Arch Dermatol Res*. 2011. 303:141–144.

CHAPTER 38

TRANSFUSIONS

Kimberly Williams Sanford, MD

Key Issues

In the United States, approximately 30 million units of blood components are transfused annually and though steps are taken to ensure the blood supply is safe, there are infectious and non-infectious transfusion related adverse events. In 2011, the Food and Drug Administration reported 58 documented transfusion related mortalities. Due to the risks and the high costs associated with transfusion and treatment of adverse events, hemovigilance programs and blood utilization/management programs have been the subject of national organizations and transfusion services to improve patient safety.

Known Facts

- Most patients are concerned about the transmission of blood borne pathogens from transfusion; however, the greatest risk to patients is the non-infectious complications of transfusion.
- Three of the most common causes for transfusion related mortality are transfusion related acute lung injury (TRALI), transfusion associated sepsis and hemolytic transfusion reactions. Most hemolytic events are related to human errors.
- Bacterial screening is still a major concern primarily in platelets because they are stored at room temperature and without a preservative. It is estimated that between 1:1000 and 1:4000 units are contaminated, but the incidence of septic transfusion reaction is much lower: 1:25,000 platelet transfusions and 1:250,000 red cell transfusions.
- Approximately 41,000 blood donations are needed daily in the United States to support patients requiring transfusion.
- Nucleic acid testing to screen for blood-borne pathogens and excluding donors with high-risk backgrounds or behaviors have decreased the risk of transfusion related disease transmission considerably.

- To reduce the cost of donor testing, all DNA testing of donors is performed in mini-pools where 8 to 16 donor sera are pooled together and the nucleic acid testing is performed on the pool. If the mini-pool nucleic acid test (MP-NAT) is positive then each donor in the pool is individually tested.
- Currently, the risk of transfusion transmitted infections in the United States is low and therefore pathogen reduction technology, although theoretically attractive, does not provide additional benefit. At this time there is no pathogen reduction technology used in the United States although some of these technologies are utilized in other countries.
- Leukocyte reduction of blood products reduces the transmission of CMV and reduces the risk of HLA alloimmunization to prevent platelet transfusion refractoriness.

Controversial Issues

- Directed donations increase the risk of post transfusion hepatitis since most donors feel obligated to donate and may not answer questions regarding high risk behavior honestly.
- Autologous donations are not recommended because it induces a presurgical anemia in the patients, patients still experience transfusion reactions from storage issues, and the risk of mistransfusion with the wrong unit of blood still exists.
- Leukocyte reduction theoretically decreases the incidence of febrile non-hemolytic transfusion reactions (FNHTR) caused by cytokines released from leukocytes in stored cellular blood components; however, universal leukocyte reduction has not decreased the incidence of FNHTR. This suggests there are other causative agents for FNHTR.
- Transfusion related immunomodulation (TRIM) related to non-leukocyte reduced blood components is associated with suppression of the recipient's immune defenses and related with increased infections and risk of malignancy. Therefore, universal leukocyte reduction was believed to reduce the clinical sequelae caused by TRIM but these results have been contradictory.

Suggested Practices

- Consider alternatives before transfusion and optimize the patient's pre-surgical hemoglobin.
- Hemoglobin levels alone should not be an indication for transfusion. Patients should be assessed for signs and symptoms of anemia.
- Blood collections facilities must follow a standardized protocol for screening and interviewing potential donors (*Table 38.2*).
- The FDA requires routine screening for syphilis (non-treponemal test), Hepatitis B virus, Hepatitis C virus, Human Immunodeficiency Virus (HIV1-2), Human T-leukemia Virus (HTLV-I/II), Trypanosoma cruzi and West Nile Virus.
- Blood transfusion and the use of derivatives should follow a careful protocol with registration of donor, serological studies, recipient, reasons to be transfused, and amount transfused.
- Platelets should be subject to strict protocols to make sure bacterial contamination has not occurred, including 24–48 hours cultures.
- Discontinue all transfusions immediately when a patient is experiencing adverse symptoms, check that the unit is labelled with the correct patient and medical record number and report it to the blood bank.
- Patients experiencing dramatic elevations in temperature (>2C) during transfusion or fevers associated with chills and hypotension should have cultures of the blood component bag and the recipient's blood performed to exclude transfusion associated microbial infections.

Table 38.1 Infectious Disease Agents Associated with Transfusion-Associated Infections

Infectious Disease Agents	Risk of Transfusion Transmission
Hepatitis B virus	Low (1 in 1/220,000–357,000 units when anti-HBc is performed)
Hepatitis C virus	Very low (1 in 1.1 million units when MP-NAT used)
Human immunodeficiency virus 1–2	Very low (1 in 1.5 million when MP-NAT used)
Hepatitis A, D, E viruses	Low to very low
Hepatitis G virus	Absent
Cytomegalovirus	Risk of transmission in susceptible patients transfused with seronegative cellular components is 1–2%, risk of transmission with leukoreduced cellular components is 2–3%
vCJD, Dengue virus, Babesia spp,	Agents with significant scientific evidence of risk to blood safety
Chikungunya virus, St Louis encephalitis virus, Leishmania spp, Plasmodium spp, Trypanosoma cruzi	Agents with scientific evidence of risk to blood safety
Chronic wasting disease, Hepatitis A, HHV-8, HIV variants, Human parvovirus B19, Influenza A (H5N1), Spumavirus, Borrelia burgodorferi	Agents with absent to low scientific evidence of risk to blood safety
Viruses: Colorado Tick fever virus, Crimean-Congo hemorrhagic fever virus, Eastern equine encephalitis, Epstein-Barr virus, Hepatitis G virus, Hepatitis B virus variants, Hepatitis E virus, Herpes viruses (excluding CMV & HHV-8), HTLV variants, Influenza A & B, Japanese encephalitis virus, La Crosse virus, Lassa virus, Lymphocytic choriomeningitis, Marburg virus, Monkeypox virus, Mumps, Papillomaviruses, Polyomavirus, Porcine endogenous retrovirus,Porcine parvovius, Rhabdovirus, SARS coronavirus, Tick-borne encephalitis, Torque teno virus, Vaccinia virus, Variola virus, Western equine encephalitis virus	Agents evaluated but no prioritization for risk to blood safety

Table 38.1 Infectious Disease Agents Associated with Transfusion-Associated Infections (continued)

Infectious Disease Agents	Risk of Transfusion Transmission
Rickettsial Agents: Anaplasma phagocytophilium, Erlichia chaffeensis, Orientia tsutsugamushi, Rickettsia prowazekii, Rickettsia rickettsii	Agents evaluated but no prioritization for risk to blood safety
Bacterial Agents: Coxiella burnetti, Borrelia spp, Brucella spp, Yersinia enterocolitica, Yersinia pestis	Agents evaluated but no prioritization for risk to blood safety
Protozoan & Nemotode Agents: Filariae, Toxoplasma gondii, Trypanosoma brucei	Agents evaluated but no prioritization for risk to blood safety

Table 38.2 Physical Examination Requirements of Donors

General Appearance	Must Appear in Good Health
Skin	Venipuncture site must be free of lesions and free of stigmata of IV drug abuse
Temperature	≤37.5 C, measured orally
Pulse	Regular and between 50–100 beats per minute, <50 bpm may be accepted if an athelete
Blood pressure	Not > 180 systolic and 100 diastolic
Hemoglobin and Hematocrit	≥12.5 g/dL or 38%, respectively

Table 38.3 Criteria for Protection of Recipients of Donor Blood

Reason for Deferral	Length of Deferral Period
• Viral hepatitis after 11th birthday	Indefinite
• Family history of CJD	Indefinite
• Travelers who have spent more than 3 months in the United Kingdom or 5 years total in Europe due to risk of vCJD areas	Indefinite
• Received a blood transfusion in the United Kingdom or France	Indefinite

Table 38.3 Criteria for Protection of Recipients of Donor Blood (continued)

Reason for Deferral	Length of Deferral Period
• Received bovine insulin manufactured in UK	Indefinite
• Receipt of dura mater or pituitary growth hormone of human origin	Indefinite
• Confirmed positive test for HbsAg or repeatedly reactive test for anti-HBc	Indefinite
• Laboratory evidence of HCV infection	Indefinite
• Laboratory evidence of HTLV-1 infection	
• Have donated the only unit of blood to a patient who developed HIV or HTLV and had no other probable cause of infection	Indefinite
• Use of bovine insulin manufactured in UK	Indefinite
• Use of Etretinate (Tegison)	Indefinite
• History of babesiosis or Chagas disease	Indefinite
• Obvious stigmata of parenteral drug use or use of a needle to administer non-prescription drugs	Indefinite
• Receiving money or drugs for sex	Indefinite
• Acitretin (Soriatane)	3 years after last dose
• Malarial infection	3 years after resolution of symptoms
• Lived for more than 5 years in • malaria-endemic areas	3 years after departure if asymptomatic
• Paying for sex	12 months
• History of syphilis or gonorrhea, treatment for syphilis or gonorrhea, or positive syphilis screening test	12 months after completing treatment
• Receipt of blood products, human tissue, or • plasma-derived clotting factors	12 months
• Hepatitis B immune globulin administration	12 months
• Any other unlisted vaccine	12 months

Table 38.3 Criteria for Protection of Recipients of Donor Blood (continued)

Reason for Deferral	Length of Deferral Period
• Tattoo	12 months
• Mucous membrane exposure to blood	12 months
• Nonsterile skin penetration, including tattoos or permanent makeup, unless applied by a state-regulated entity with sterile needles and ink that has not been re-used	12 months
• Residing with or having sexual contact with an individual with viral hepatitis	12 months
• Sexual contact with an individual with HIV or high risk for HIV	12 months
• Incarceration >72 consecutive hours	12 months
• Travelers to malaria-endemic areas	12 months after departure regardless if asymptomatic or prophylaxis
• Dutasteride (Avodart)	6 months after last dose
• Recent blood donation	8 weeks for whole blood donation, 16 weeks for 2 unit RBC apheresis; 48 hours for plasma-, platelet- or leukopheresis
• Pregnancy	Defer until 6 weeks post-partum/ post-termination. Exceptions are for transfusion to the infant w/ physician approval
• Live attenuated vaccines: German measles (rubella) and Chicken pox (varicella zoster) vaccines	4 weeks
• Finasteride (Proscar, Propecia)	1 month after last dose
• Isotretinoin (Accutane)	1 month after last dose
• Clopidogrel (Plavix) and Ticlopidine (Ticlid)	14 days (donor excluded from platelet donation)

Table 38.3 Criteria for Protection of Recipients of Donor Blood (continued)

Reason for Deferral	Length of Deferral Period
• Live attenuated vaccines: Measles (rubeola), polio (Sabin oral), mumps, typhoid (oral), and yellow fever vaccines	2 weeks
• Smallpox vaccine	21 days or until scab falls off in a donor without complications from vaccine. In donors with severe complications from the vaccine, 14 days after resolution of symptoms. Asymptomatic contacts of vaccine recipient doesn't require deferral
• West Nile virus	14 days after resolved or 28 days after onset, whichever is longer. Positive WNV ab test without symptoms, no deferral.
• Warfarin (Coumadin)	7 days (excluded from platelet donation)
• Aspirin and piroxicam (Feldene)	48 hours (excluded from platelet donation)
• Toxoids, synthetic or killed vaccines: Anthrax, Cholera, Diphtheria, Hepatitis A, Hepatitis B, Influenza, Lyme, Paratyphoid, Pertussis, Plague, Pneumococcal polysaccharide, Polio (Salk injection), Rabies, Rocky Mountain spotted fever, Tetanus, Typhoid (injection), Recombinant HPV vaccine	None (if donor is afebrile and symptom-free)
• Stigmata of alcohol intoxication or habituation	Exclude donor, no specific period of time stated
• Other travel	Refer to www.cdc.gov/travel
• Antibiotics	As defined by medical director

Transfusion transmitted blood borne infections have decreased considerably after implementation of more rigorous donor screening and routine testing for the most common transfusion-associated pathogens. The FDA requires donor testing for HBsAg and anti-HBc which reduces the risk of transfusion transmission to 1/220,000-357,000 units. The HBV DNA testing does not further reduce this risk because during the infectious period, HBV DNA levels are low and are below the threshold of detection for mini-pool nucleic acid testing (MP-NAT). This method works well for HCV, HIV and WNV DNA testing but is not effective for HBV. Hepatitis C was one of the most common causes of post-transfusional hepatitis, but with the use of serologic assays to detect HCV antibodies combined with HCV MP-NAT the risk of transfusion transmitted HCV is now 1 in 1.1 million units. The window period from time of infection to time of detection of HCV virus with MP-NAT is only 7.4 days. Due to the high incidence of HIV transfusion transmitted infections in the mid to late 1980's, more rigorous donor screening to exclude donors engaged in high risk behavior, such as intravenous drug use, high risk heterosexual behavior and all males who have ever had sex with other males. This rigorous screening combined with serologic testing to detect antibodies to HIV-1, HIV-2, and MP-NAT reduced the window period to 9 days and dramatically reduced the risk of transmission to 1 in 1.5 million.

Bacterial contamination of blood products has become a growing concern and is one of the top 3 causes for transfusion related fatalities. The source of the contamination is the donor's skin during the phlebotomy or the donor has asymptomatic bacteremia at the time of collection. The amount of bacteria initially contaminating the unit is small, but the bacteria proliferate during storage. This is a higher risk for platelets because they are incubated at room temperature whereas red blood cells are refrigerated during storage. The different storage temperatures also select for different bacteria. Gram positive skin contaminants proliferate best in platelets and psychrophilic enteric organisms are the most common contaminating bacteria in refrigerated red blood cells. To reduce the risk of bacterial contamination, in 2008 the AABB required all donor centers to use collection bags that divert

the first 10–40 ml of blood to minimize the risk of skin bacteria contaminating the collected product. Also in 2004, the AABB required all blood collection centers to implement a process to limit the bacterial contamination of all platelets. Most blood centers store the platelets for 24 hours before sampling the units for culture and then incubate the cultures 12–24 hours before releasing the units to transfusion services.

References

AABB Association Bulletin #04-07. Actions Following an Initial Positive Test for Possible Bacterial Contamination of a Platelet Unit. October 14, 2004.

AABB Association Bulletin #12-04. Recommendations to Address Residual Risk of Bacterial Contamination of Platelets. October 14, 2012.

American Red Cross Blood Facts and Statistics. Available at http://www.redcrossblood.org/learn-about-blood/blood-facts-and-statistics. (Accessed 22 January 2014).

Busch MP, Glynn SA, Stramer SL, et al. A new strategy for estimating risks of transfusion-transmitted viral infections based on rates of detection of recently infected donors. *Transfusion*. 2005. 45:254–64.

Food and Drug Administration. Fatalities reported to FDA following blood collection and transfusion: Annual summary for fiscal year 2011. Rockville, MD: CBER Office of Communication, Outreach, and Development, 2011. Available at http://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/UCM300764.pdf. (Accessed 22 January 2014).

Herbert PC, Fergusson D, Blajchman MA, et al. Clinical outcomes following institution of the Canadian universal leukoreduction program for red blood cell transfusions. *JAMA*. 2003. 89:1941–9.

Klein HG, Anderson D, Bernardi MJ, et al. Pathogen Inactivation: Making decisions about new technologies. Report of a consensus conference. *Transfusion*. 2007. 47:2338–47.

Standards for Blood Banks and Transfusion Services (28th edition). Bethesda, MD: AABB.

Stramer SL, Hollinger FB, Katz LM, et al. Emerging infectious disease agents and their potential threat to transfusion safety. *Transfusion*. 2009. 49:2S; 1S–235S.

Zou S, Stramer SL, Notari EP, et al. Current incidence and residual risk of hepatitis B infection among blood donors in the United States. *Transfusion*. 2009. 49:1609–20.

CHAPTER 39

Preparing the Patient for Surgery

Helen Giamarellou, MD, PhD

Key Issue

Appropriate skin preparation plus antimicrobial prophylaxis decrease the incidence of both superficial and deep wound infections (surgical site infection) after certain operations.

Known Facts

A preoperative shower, preparation of the skin with antiseptics in the operating room, and a single preoperative dose of a first- or second-generation cephalosporin are extremely important to significantly decrease wound infection rates. Regrettably, several postoperative doses of prophylaxis are generally administered in several medical centers leading to excess cost and the emergence of multiresistant bacteria.

Controversial Issues

- Hair removal from the operative site is still disputed.
- Assessment of risk factors in clean operations requires more studies.
- Weight-based dosing for antimicrobial prophylaxis in obese patients should be clarified.
- Duration of prophylaxis for cardiothoracic procedures should be determined.
- The safety and efficacy of topical antimicrobials in non-opthalmic procedures have not been clearly established.

Definitions

Wound infection has been defined as purulent discharge from an incision, regardless of whether organisms are cultured. In 1992, the CDC redefined the term as "surgical site infections," and divided them into superficial and deep infections. The superficial infections involve only the skin and subcutaneous tissues while deep infections involve at least muscle and fascial layers. Incisions may be contaminated by the patient's own normal

flora or by flora from the environment, including the operative team. Correct surveillance of wound infection extends to 30 days following surgery. In the case of implants, surveillance is extended for up to 1 year.

The traditional surgical wound classification system was established based on the exposure of the incision to bacterial contamination (*Table 39.1*). Infection was reported in 3.3% of clean wounds, in 10.8% of clean-contaminated, in 16.3% of contaminated, and in 28.6% of dirty wounds. In the Study of the Efficacy of Nosocomial Infection Control (SENIC), a new classification based on patients' risk assessment rather than wounds was developed. Risk factors included abdominal operations, operations exceeding 2 hours, and having three or more associated discharge diagnoses. Patients with no risk factors were at low risk for infection (1%), those with one factor at moderate risk (3.6%), and those with two or more factors at high risk (8.9% to 27%). The National Nosocomial Infection Surveillance (NNIS) system, in 1991, attempted to redefine risk factors. The following risk factors provided a greater discrimination for the patient at risk of wound infection: (1) a contaminated or dirty wound class; (2) high preoperative risk as defined by an American Society of Anesthesiologists (ASA) preoperative assessment score of three or more; and (3) a duration of operation exceeding the 75th percentile for a given procedure since long operations generally include greater blood loss, increased complexity and violations of asepsis. Malnutrition, advanced age, obesity, diabetes mellitus, renal insufficiency, cirrhosis, coexisting remote body-site infections, recent surgical procedure, length of preoperative hospitalization, known colonization with MRSA or VRE, extremes of age, placement of foreign bodies, malignancy, and the use of steroids or immunosuppressive drugs represent additional risk factors for wound infection.

Patient Preparation for Surgery

Preparation of patients for surgery aimed at preventing postoperative wound infection is based on appropriate skin care and antimicrobial prophylaxis. Nevertheless, appropriate treatment of remote infections before elective operations and adequate control of blood glycose levels perioperatively are also recommended. Decolonization of nasal carriage of *S. aureus* before placement of foreign material with intranasal mupirocin is indicated.

Table 39.1 Classification of Surgical Wounds

Clean
Elective, not emergency
No entry into the gastrointestinal, respiratory, genital or uninfected urinary tracts
No signs of acute inflammation or infection
Nontraumatic
No violations of aseptic technique
Non penetrating trauma
Wounds primarily closed and drained (if necessary) with closed drainage
Clean-Contaminated
Urgent or emergency case that is otherwise clean
Entry into the gastrointestinal, respiratory, genital or urinary tract under controlled conditions and without significant contamination
Biliary tract, oropharynx, vagina and appendix included if no evidence of infection is present
No major break in aseptic technique is encountered
Contaminated
Nonpurulent inflammation;
Major contamination following entry into the gastrointestinal or respiratory tracts
Entrance of genitourinary or biliary tracts in the presence of acute infection
Fresh traumatic wounds(<4 hours old)
Chronic open wounds to be grafted or covered
Major break in aseptic technique
Dirty
Penetrating trauma > 4 hours old
Acute bacterial inflammation or pus encountered
Perforated viscus encountered
Traumatic wound with retained devitalized tissue, foreign material, fecal contamination, and/or delayed treatment

Decontamination of the skin preoperatively is very important to prevent wound infection, particularly in clean procedures. A preoperative shower with an antiseptic soap seems to reduce the

incidence of postoperative infections. Chlorhexidine gluconate was significantly superior when compared to povidone-iodine and triclocarban medicated soap showers. Hair removal at the operative site by shaving, particularly the night before surgery, should be abandoned since shaving produces significant injury. Subsequently, the injured skin sites are colonized and serve as a niche of bacterial contamination of surgical wounds. The risk of wound infections from clippers or a depilatory cream have been found to be lower than that from shaving and if necessary it should be done immediately before operation. Interestingly, patients with no hair removal may have even lower rates of wound infection. Skin preparation in the operating room should be performed by trained personnel. The preparation starts with a careful cleansing of the operative site with a detergent (with or without a degreasing agent). The antiseptic is applied in concentric circles starting at the proposed operative incision site. An alcoholic (70%) plus chlorhexidine gluconate or an iodophor scrub are usually used.

Suggested Practice in Antimicrobial Prophylaxis

- A single, full therapeutic dose of an antibiotic should be given intravenously within 60 minutes before surgical incision (15–60 minutes) to ensure effective tissue concentrations throughout the operative period. An exception to this rule is cardiac surgery where two doses of the selected antibiotic seem to be necessary. However, prophylaxis should not be extended beyond 24 hours following surgery. Antibiotics are effective when given before inoculation of bacteria at the surgical site, whereas they are ineffective if given three to four hours after the surgical incision. Continuing prophylaxis until all indwelling drains and intravascular catheters are removed is strongly discouraged. As long as adequate serum and tissue drug level against probable pathogens are maintained during the operation, a single dose is as effective as multiple doses.
- The selection of the appropriate drug should be based on the most likely bacteria to cause infection in each situation, its safety profile as well as the local resistance surveillance patterns. A single drug should be used, whenever possible. Cephalosporins, in particular, cefazolin, is ideal for prophylaxis because of its broad spectrum of activity,

the moderately long serum half-life, low toxicity, ease of administration, and low cost. In clean-contaminated cases and in clean operations involving the surgical placement of foreign material (e.g., heart valves, vascular grafts, orthopedic hardware, etc) or whenever risk factors coexist, cefazolin alone should be administered. In clean contaminated operations with entry into the gastrointestinal tract as well as in penetrating abdominal trauma or primary appendectomy, cefazolin plus an agent active against anaerobes like metronidazole as well as cefotetan or cefoxitin as single agents, should be used. However, administration in contaminated and dirty operations is considered therapy and not prophylaxis. Third-generation cephalosporins are more costly and promote the emergence of resistant strains. In general, they should not be used for routine prophylaxis.

- In colorectal surgery and in institutions where there is increasing resistance to first and second generation cephalosporins among gram-negative isolates from SSIs, ceftriaxone plus metroniadazole should be preferred over ertapenem. For patients with beta-lactam allergies, metronidazole or clindamycin plus an aminoglycoside or a fluoroquinolone or aztreonam could replace as above the suggested regimens.
- In the case of massive hemorrhage (>1,5 Lt), or whenever the duration of operation exceeds two half-lives of the preadministered antibiotic(s), intraoperative redosing should be given. The redosing interval should be measured from the time of administration of the preoperative dose, not from the beginning of the procedure.
- Since staphylococci are the major threat in infected prostheses, vancomycin instead of cefazolin should be used in institutions with a high predominance of methicillin resistant strains as well as in ß-lactam allergic patients. Because of prolonged infusion time required for vancomycin (1h) it should be administered within 120 min before surgical incision.
- In cardiac and orthopaedic procedures mupirocin should be given intrnasally to all patients known to be colonized with *S. aureus*.
- In colorectal procedures mechanical bowel preparation combined with oral neomycin sulfate plus erythromycin base or

metronidazole should be given in addition to IV prophylaxis.

- In laparoscopic biliary tract procedures where some risk factors can not be determined before the procedure, it may be reasonable to give a single dose of antimicrobial prophylaxis to all patients.
- With the exception of ophthalmic procedures, topical administration of antibiotics as prophylaxis, based on their lack of efficacy and the possibility of adverse reactions, is not recommended.

Conclusions

There is no doubt that appropriate antibiotic prophylaxis reduces morbidity and costs by preventing surgical site infections. However, it should be emphasized that antibiotic overuse and misuse for surgical prophylaxis accounts for as many as half of all antibiotics costs prescribed in USA hospitals and contributes to the emergence of multidrug-resistant microorganisms particularly whenever the one single preoperative dose is exceeded. Based on the importance of the application of correct perioperative antibiotic prophylaxis as well as the appropriate preparation of patients for surgery, it has been recently suggested that hospitals should establish a multidisciplinary team including surgeons, anaesthesiologists, nurses, pharmacists, infection control specialists and clinical microbiologists, who should develop and implement a relevant protocol.

References

Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm*. 2013. 70:195–283.

Classen DC, Evans RS, Restomic SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical wound infection. *N Engl J Med*. 1992. 326:281–6.

De Lalla F. Surgical prophylaxis in practice. *J Hosp Infect*. 2002. 50(Suppl A):9–12.

European Center for Disease Prevention and Control Technical Report: Systemic review and evidence-based guidance on perioperative antibiotic prophylaxis. Stockholm: ECDC, 2013 Catalogue number TQ-01-13-279-EN-C.

Mangram AC, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. *Infect Control Hosp Epidemiol*. 1999. 20(4):250–78.

CHAPTER 40

Infection Control in Obstetrics

J.A.J.W. Kluytmans, MD, PhD, J. Veenemans, MD, PhD

Key Issue

Neonatal sepsis and postpartum endometritis (PPE) are mostly caused by organisms in the mothers' vaginal flora. The risk of these infections can be substantially reduced by simple infection control measures. However, in developing countries they still cause substantial morbidity and mortality, in both hospital and community settings.

Known Facts

- The most important microorganisms causing neonatal sepsis are group B streptococci (GBS) and *Escherichia coli*.
- Neonatal GBS sepsis can be prevented by administering intravenous antibiotics to the mother during labour. The decision to provide such prophylaxis is guided by the presence of risk factors for neonatal GBS sepsis (*see below*), or by the presence of vaginal GBS colonization.
- Caesarean section is the most important risk factor for post-partum maternal infection and is associated with a 5 to 20-fold increased risk of infection compared to vaginal delivery.
- Single dose antibiotic prophylaxis reduces the risk of infections after caesarean section (wound infection, endometritis and urinary tract infection) in all patients (both emergency and elective procedures).
- Outbreaks of classical childbed fever caused by group A hemolytic streptococci still occur albeit sporadically. They warrant prompt investigations into the source, including a search for carriers among HCW.
- During labour there is frequent and often uncontrolled contact with blood and other body fluids. Transmission rates of blood borne pathogens are high when preventive measures are neglected.

In developing countries, vaginal deliveries often take place in settings with limited resources and under unhygienic circumstances. Cheap and accessible interventions to reduce the risk of both neonatal and maternal infections are necessary. Examples of such measures include cleaning of the birth canal with an antiseptic and washing of the cord stump with chlorhexidine.

Controversial Issues

- There is debate about whether antibiotic prophylaxis in caesarean sections should be given before skin incision or after cord clamping. Current evidence suggests that the administration of prophylaxis before skin incision is superior to prophylaxis after cord clamping in reducing the risk of infection, with no evidence of increased risk of neonatal complications.[1,2]

Suggested Practice

- Standard infection control measures should be taken before, during and after labour. During labour, gloves should be worn at all times and it is advisable to wear a gown, a mask and eye protection during all procedures.
- Antibiotic prophylaxis should be administered during vaginal delivery at 4 hour intervals to high risk patients (*see below*) to prevent GBS sepsis in the neonate.
- In case of a caesarean section, a single dose antibiotic prophylaxis (cefazolin) should be administered intravenously to all patients, preferably 30 min before incision.
- In limited resource settings, cleaning of the birth canal with a disinfectant during vaginal examinations and other (instrumental) procedures can be used to reduce the risk of both neonatal sepsis and maternal infections.
- Vaginal exams should be kept to a minimum to limit the risk of infection.
- Anti-tetanus prophylaxis should be provided in case of delivery outside the hospital and of unsafe abortion.
- In settings with high infection risk, post-delivery care of the cord stump should be performed with chlorhexidine washings.

Summary

The importance of infection control in obstetrics was established when Semmelweis made his historical observations during the second half of the nineteenth century. Standard hygienic precautions by health care professionals are the best way to avoid health care associated spread of pathogens In addition, simple measures can largely prevent infections that are caused by micro-organisms of the mother's endogenous flora. In developed countries most infectious complications of delivery are now relatively rare, but in developing countries the burden of neonatal and maternal postpartum morbidity and mortality due to bacterial infections remains high.

Neonatal Sepsis

The most important pathogens causing neonatal sepsis are group B streptococci (GBS) and *Escherichia coli*. The newborn becomes colonized with these micro-organisms during the passage of the birth canal. Prevention of infections with GBS can be achieved by providing intravenous high dose antibiotics every 4 hours until delivery to women who are colonised with GBS and/or to women with risk factors for neonatal GBS sepsis (delivery at <37 weeks gestation, membrane rupture for > 18 hours, intra-partum temperature > 100.4 F). The feasibility and cost-effectiveness of screening for GBS colonisation during pregnancy depend on the setting. GBS prophylaxis should always be given to women who had GBS bacteriuria earlier in the course of pregnancy, and to those who previously had a child with GBS sepsis. High dose intravenous penicillin or ampicillin are the drugs of first choice. In patients who are allergic to penicillin, clindamycin is administered.

In poor resource settings, implementation of sterile procedures during cord clamping, and proper care of the cord area are of major importance. Infection of the cord stump (omphalitis) is an important cause of neonatal morbidity and mortality in community and primary care settings in developing countries, and recent review of the evidence shows that a substantial reduction in neonatal mortality can be achieved when using antiseptics to care for the cord stump instead of dry cord care (as recommended by the World Health Organisation) (RR all-cause mortality 0.77, 0.63 to 0.94).[4]

Post-partum Endometritis

Post-partum endometritis (PPE) is a serious complication of delivery. Infections are often polymicrobial, caused by the mother's endogenous flora, and outbreaks are rare. The incidence of PPE is much higher following caesarean sections than following vaginal deliveries. As for the prevention of any surgical infection, general principles to prevent PPE include sound surgical technique, skin antisepsis and timely antimicrobial prophylaxis. Although emergency Caesarean sections are associated with a higher infection rate then elective procedures, antibiotic prophylaxis is effective in both high-risk patients (in labour after membrane rupture) and low risk patients (intact membranes, not in labour).[3] In addition, single dose prophylaxis (cefazolin plus metronidazole) is recommended by WHO following operative vaginal delivery, manual removal of the placenta, curettage of the uterus, or in case of fourth degree tears.[7] Despite adequate antimicrobial prophylaxis, the rate of PPE after caesarean section remains high (10–20%), and further prevention depends largely on the elimination of risk factors, such as reducing the number of vaginal examinations during labour. Manual removal of the placenta after a caesarean section is associated with a higher incidence of endometritis than spontaneous extraction of the placenta, which is preferred when possible.

In poor resource settings, when antibiotic prophylaxis is not available, cleaning of the birth canal with an antiseptic (chlorhexidine 0.25–0.50%) at every vaginal examination during active labour can prevent both maternal and neonatal infections. Data from non-randomised studies have suggested a reduction in infection risk as well as in colonisation rate,[4] but evidence from subsequent randomised trials is inconclusive.[5,6] The efficacy of this intervention may strongly depend on the background infection risk, and because it is a safe and inexpensive measure to reduce the risk of infection, it should certainly be used when other alternatives are not available.

Although classical childbed fever caused by group A beta-hemolytic streptococci is rare, outbreaks do occur. If so, immediate control measures, including screening for carriers among healthcare workers and other patients, are mandatory.

Blood Borne Pathogens During Delivery

Blood borne pathogens are a threat to mother, child and health-care worker during delivery. Scalp electrodes are contraindicated if the mother is infected with hepatitis B, C or HIV, and in mothers with hepatitis B the newborn should be immunized after delivery. In mothers infected with HIV, antiretroviral therapy during pregnancy and in the newborn reduces the risk of vertical transmission.[9]

Blood exposure occurs frequently during labourlabour. Gloves are frequently punctured. Needle stick injuries and splashes occur frequently. Therefore, gloves should be worn at all times, and it is advisable to wear gowns, masks and eye protection.[7]

Herpes Simplex Virus (HSV)

Mothers with active genital HSV infections should be handled with barrier precautions. HCW and the mother should wear gloves when touching the infected area or materials (gauzes etc.).

References

[1]Sun J, et al. Prophylactic administration of cefazolin prior to skin incision versus antibiotics at cord clamping in preventing postcaesarean infectious morbidity: A systematic review and meta-analysis of randomized controlled trials. *Gynecol Obstet Invest*. 2013. 75:175–178.

[2]Sullivan SA, Smith T, Chang E, et al. Administration of cefazolin prior to skin incision is superior to cefazolin at cord clamping in preventing postcaesarean infectious morbidity: A randomized, controlled trial. *Am J Obstet Gynecol*. 2007. 196:455.e1-e5.

[3]Smaill FM, Gyte GML. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. *Cochrane Database of Systematic Reviews*. 2010. Issue 1. Art. No.: CD007482. DOI: 10.1002/14651858.CD007482.pub2.

[4]Imdad A, Bautista RMM, Senen KAA, et al. Umbilical cord antiseptics for preventing sepsis and death among newborns. *Cochrane Database of Systematic Reviews*. May 31, 2013. (5):CD008635.

[5]Stade BC, Shah VS, Ohlsson A. Vaginal chlorhexidine during labour to prevent early-onset neonatal group B streptococcal infection. *Cochrane Database of Systematic Reviews*. 2004. Issue 3. Art. No.: CD003520. DOI: 10.1002/14651858.CD003520.pub2.

[6]Lumbiganon P, Thinkhamrop J, Thinkhamrop B, Tolosa JE. Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV). *Cochrane Database of Systematic Reviews*. 2004. Issue 4. Art. No.: CD004070. DOI: 10.1002/14651858.CD004070.pub2.

[7]World Health Organization 2000. Managing complications in pregnancy and childbirth: A guide for midwives and doctors. http://whqlibdoc.who.int/publications/2007/9241545879_eng.pdf

[8]Mead PB, Hess SM, Page SD. Prevention and Control of Nosocomial Infections in Obstetrics and Gynecology in Prevention and Control of Nosocomial Infections (3rd Edition), Wenzel RP (Ed). Philadelphia: Williams and Wilkins, 1997. 995–1016.

[9]Siegfried N, van der Merwe L, Brocklehurst P, Sint TT. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. *Cochrane Database of Systematic Reviews*. 2011. Issue 7. Art. No.: CD003510. DOI: 10.1002/14651858.CD003510.pub3.

CHAPTER 41

The Infection Hazards of Human Cadavers

P.N.Hoffman, T.D.Healing, and S.E.J.Young

Key Issue

Cadavers may pose hazards to those handling them. The recently dead may have been infected by a wide range of pathogens, those presenting particular risks include tuberculosis, streptococcal infection, gastro-intestinal organisms, the agents causing transmissible spongiform encephalopathies (e.g. Creutzfeld-Jacob disease), hepatitis B and C, HIV infection, severe acute respiratory syndrome (SARS), hemorrhagic fever viruses, and possibly meningitis and septicaemia (especially meningococcal). None of the organisms that caused mass death in the past (e.g. plague, cholera, typhoid, tuberculosis, smallpox) is likely to survive long in burials.

Known Facts

- Most of the micro-organisms that cause death do not survive for long after the host dies or are not readily transmissible in that context.
- Soft tissues remaining on a cadaver could present an infection risk.
- Long buried bodies reduced to skeletons are not a hazard.
- A possible hazard in old burials is anthrax, which can form resistant spores but this is unlikely.

Controversial Issues

There is a theoretical concern that smallpox may survive in buried bodies, but the risk from minimal residual virus in dry scabs is not considered to present a valid infectious threat. People should not be vaccinated specifically to deal with this hazard as the risk of smallpox vaccination greatly outweighs the infection risk.

Suggested Practice

Whether dealing with the recently dead or with old burials, and regardless of which infectious agents may be present, the risk of acquiring infection can be greatly reduced by:

- covering cuts or lesions with waterproof dressings;
- careful cleansing of any injuries sustained during procedures;
- good personal hygiene; and
- the use of appropriate protective clothing (*see Table 41.1*).

Text

Most people have little to do with the dead, although they may at some time in their lives need to deal with the cadavers of relatives or friends during burial rituals. Some have jobs that regularly bring them into contact with cadavers, exposing them to the risk of acquiring infections. These include doctors (especially pathologists), nurses, mortuary attendants, members of the emergency services, forensic scientists, embalmers, funeral directors, religious officials or others who routinely prepare bodies for the funeral or who perform final rites, and members of the emergency services.

In most circumstances the diseased living are a much greater hazard than are the dead, even those who have died of infectious disease. Whilst a person is alive, invading pathogens can multiply and are readily transmitted. The patient is a continuing source of infection. Once the host is dead, most micro-organisms stop multiplying and die rapidly as a result of microbial competition as the body decomposes.

The Recently Dead

The diseases and organisms which may pose particular risks vary in different parts of the world but include tuberculosis, streptococcal infection, gastro-intestinal organisms, Creutzfeld-Jacob disease, viral hepatitis and HIV infection, a number of viral infections (particularly viral hemorrhagic fevers such as Lassa, Marburg or Ebola), SARS-like viruses, and possibly meningitis and septicaemia (especially meningococcal) (*see Table 41.2*). In general, the use of appropriate protective clothing will greatly reduce the risk of acquiring infection but some additional precautions may be advisable for particular infections.

Table 41.1 Use of Protective Clothing

Hands

Examination gloves (latex or nitrile). For handling hazardous material. Wear whenever handling bodies. Should be worn once only and then discarded. Always wash hands after use. Latex gloves provide short-term (10-minute) protection against formaldehyde; nitrile gloves give longer-term protection.

Respiratory Protection

Filter masks. Filter mask to EN 149 FFP2 (or equivalent, e.g. N95) for specific hazards (e.g. lead dust, fungal spores and other aerosols)

Specifically-manufactured surgical masks. These may provide protection against splashes, particularly if water-repellent, but cannot be as effective as filter masks as their fit to the wearer's face allows particles to bypass any filtration the mask fabric may offer

Cloth surgical masks. These provide little protection and may give a false sense of security but are better than nothing.

Splash Protection

Face: Visor. Protection against hazardous splashes to eyes, nose and mouth (also mechanical protection).
Respiratory protective masks and cloth or paper surgical masks normally provide splash protection to mouth and nose only. Some surgical masks incorporate a transparent eye-protecting visor.

Body: Apron. Where splashing to body may occur (hygienic preparation, embalming, collection of traumatised bodies, post-mortem examinations). Best worn under gowns or coats if splashing is likely to be profuse.

Feet: Rubber boots. In wet situations (mortuaries, embalming rooms, collecting severe multiple trauma cases).

Whole Body Protection

Gowns/Coats. To protect clothing against splashing.

Coverall with hood. To protect clothes and hair from impregnation with dusts, spores etc. Other protective clothing (safety helmets, boots, safety glasses, work gloves) should be worn as required to protect against mechanical injury.

Tuberculosis

Opening cadavers of individuals infected with tuberculosis is dangerous and workers in morbid anatomy, pathologists, mortuary technicians and medical students have a comparatively high rate of tuberculin conversion. BCG vaccination and an annual chest X-ray is advised for such individuals.

Table 41.2 Infections Where Bagging is Essential and Viewing, Embalming Cosmetic Enhancement and Hygienic Preparation Should Not Be Done

INFECTION
Anthrax
Plague
Rabies
Smallpox
Viral hemorrhagic fevers
Yellow fever
Transmissible spongiform encephalopathies (e.g. Creutzfeldt-Jakob Disease)
Streptococcal disease (group A)
Viral hepatitis (B, C, non-A non-B)

Bagging = placing the body in a leak-proof plastic body bag.
Viewing = allowing the bereaved to see, touch and spend time with the body prior to disposal.
Embalming = injecting chemical preservatives into the body to slow the process of decay. Cosmetic enhancement of the appearance of the body may be undertaken to improve the appearance for viewing.
Hygienic preparation = cleaning and tidying the body so it presents a suitable appearance for viewing (an alternative to embalming).

Meningitis and Septicaemia

- Meningitis can be caused by a wide range of organisms but only tuberculosis (*see above*) and meningococci are likely to present a risk.
- Septicaemia is a common terminal event and can be caused by many different organisms (often the patient's own flora) most of which present no hazard. Only cases of meningococcal septicaemia or of infection with group A streptococci pose a risk. Life threatening infections with the latter can result from quite trivial contact and injuries.

Gastrointestinal Organisms

Faecal leakage from bodies is very common. All those handling cadavers should:

- Wear single-use gloves and impervious single-use aprons;
- Take care not to contaminate their instruments or their working environment; and

- Wash their hands carefully after procedures and before eating, drinking or smoking.

The bodies of those who have died of diseases such as cholera or typhoid should not be buried in places where they could contaminate water sources.

Transmissible Spongiform Encephalopathies (TSEs)

These are rare conditions typically presenting as Creutzfeldt-Jakob and variant Creutzfeldt-Jakob disease. The causative agents of these diseases are highly resistant to most disinfectants and to heat. They are not inactivated reliably by chemical disinfection or conventional heat sterilisation. Only fully trained staff should undertake post mortem examinations in patients thought to be at risk of, or who are known or suspected as having, TSEs. If examination of the brain only is required, the skull should only be opened inside a large plastic bag fitted over the head and neck of the cadaver. In addition full single-use PPE (including coverall, apron, double gloves, full face visor or surgical mask with visor) should be used. If a full post mortem is required, including the removal of viscera and spinal cord, the body should be examined in a high risk autopsy suite.

Hepatitis

- Hepatitis A is transmitted by the faecal-oral route and presents the same hazard as other gastro-intestinal pathogens. A highly effective vaccine is available.
- Hepatitis B is extremely infectious and the incidence of this infection continues to increase in many countries. A highly effective vaccine is available and staff working in hospital mortuaries, and embalmers, should routinely receive immunisation against this infection. The bodies of those who have died of, or were known to be infected with, this virus should be handled only by those wearing full protective clothing.
- Hepatitis C is also highly infectious although probably less so than hepatitis B. It is transmitted by the same routes as hepatitis B, there is no vaccine, and similar precautions to those for hepatitis B should be taken.

HIV

The routes of transmission of hepatitis B and of HIV are similar and the precautions required to prevent the transmission of the former should be adequate to prevent transmission of the latter. HIV is less infectious than hepatitis B and the risk to those handling infected cadavers is therefore proportionately less. HIV can survive for many days post-mortem in tissues preserved under laboratory conditions. Care should be taken when handling unfixed, HIV-infected material from cadavers, or when undertaking post-mortem examinations on those infected with HIV. Embalming the bodies of those known or suspected of being infected is not recommended.

Those infected with HIV are often infected with other organisms (such as mycobacteria) which may be more infectious (albeit less dangerous) than the HIV infection itself.

Viral Hemorrhagic Fevers

Viruses such as Ebola and Marburg are highly infectious and are readily transmitted by contact with infected blood, secretions and organs. Most of the known outbreaks have been health care associated. Great care should be exercised when dealing with those who have died of such infections. Staff should wear gloves, protective gowns, masks and eye protection. Post mortem examinations should not be carried out. Bodies should be bagged as soon as possible and should be buried with appropriate precautions (*see below*) or cremated.

Reduction of Risk

Post-mortem Rooms

- Post-mortem rooms should be structured such that the risks to those working in them are minimised. Provision of proper ventilation, lighting, running water and good drainage is essential.
- Workers must use single-use gloves for each procedure and, after removal, wash their hands immediately.
- The environment should be cleaned with a broad spectrum disinfectant daily.
- Instruments should be washed in a washer-disinfector, autoclaved or immersed in a broad-range, non-corrosive

disinfectant after initial cleaning. The reasons for the use of a disinfectant other than hypochlorite are:

i) Hypochlorite is corrosive and may damage surfaces or instruments, and

ii) Formaldehyde is likely to be present in postmortem rooms (and embalmers' premises) and the reaction between hypochlorite and formaldehyde can produce a potent carcinogen (bis-chloromethyl ether).

Some hospital post-mortem departments bag all bodies for transfer to funeral directors. This can be counter-productive in terms of safety as bagging a body may be the main means by which the hospital can communicate to the funeral director that the body may present special risks. In countries where confidentiality precludes reference to specific infections, the type of risk involved can be identified by attaching labels advising generic precaution types (e.g. enteric, blood borne) to the bag.

Preparation of the Dead for Funerals

- Often only a simple "hygienic preparation" may be carried out, frequently by relatives or religious officials. This usually involves washing the body, dressing the cadaver, tidying the hair and possibly trimming the nails and shaving. Such rapid procedures are frequently followed in many countries, particularly the hotter ones, where burial or other disposal of the cadaver follows death within 24 hours (either for practical or religious reasons). Under these circumstances many pathogens may still be viable but, provided there is considered to be only a low level of risk, then the use of gloves and simple protective clothing and/or good personal hygiene by anyone handling the bodies is an acceptable and effective safety measure.
- In some instances, for example where the person has died of a highly infectious disease such as Ebola or hepatitis B, even hygienic preparation is not safe. A list of such infections is given in *Table 41.2*.
- Embalming may be undertaken as a means of temporary preservation by reducing microbial activity and slowing decomposition and is usually a straightforward process, but

the embalming of cadavers which have been in accidents or which have been the subjects of post-mortem examination is more difficult. They may be badly damaged and present particular hazards because of damaged bones, bone splinters, and (occasionally) due to sharp items, such as intravenous cannulae, left in the body. Cosmetic work on cadavers may also present hazards if the body has been damaged. There can sometimes be considerable contamination of the body with blood, faeces and other body fluids if it is bagged, presenting an extra risk to embalmers and others involved in preparation of the body. This is another reason to avoid universal bagging of bodies by hospitals. Embalming practices such as the open drainage of the vascular system lead to excessive environmental contamination and should be avoided.

- All instruments used for embalming or for preparing bodies for the funeral should be cleaned in hot water and detergent and can be sterilised in an autoclave, heat disinfected or soaked in a disinfectant after careful cleaning. Disinfectants should be used to clean up any spills of blood or body fluid, single-use gloves being used to protect the hands from contact with the spill. Hands should always be washed after finishing a session.

Emergency Service Personnel

- The major hazard facing emergency service personnel is spilt blood and any risk can be greatly reduced by preventing contact with blood (use of gloves, face and eye protection, and protective clothing where necessary).
- Bodies that have been decaying for some time, including those that have been in water for extended periods of time, present little risk. The organisms likely to be present are their own body flora and water or environmental organisms. The use of proper protective clothing and good personal hygiene will protect personnel handling such material.
- Bodies should always be transported to mortuary facilities in waterproof body bags or cleanable, fluid retentive (e.g. fibreglass) temporary coffins.

Disposal of the Dead

Each society has its own methods of disposal of the deceased. These must be respected as far as possible although in a few instances (such as deaths due to highly infectious agents such as Ebola) cremation or deep burial with the cadaver in a leak-proof plastic body bag may be the only safe procedures.

Immediately following disasters where there has been substantial loss of life, there seems to be a tradition to bury or cremate the dead as quickly as possible "to prevent the spread of disease". In reality however, the dead bodies of disaster victims pose a minimal infectious risk to the survivors. The spectrum of disease amongst the deceased in a rapid onset natural disaster (such as a tsunami) will be the same as that amongst the survivors. Of those deceased that had an infectious disease at the time of their death, the risk that they will disseminate it will be lower than it was during their life and those that did not have an infectious disease offer a negligible risk. The imperative of immediate disposal of the dead diverts resources from searching for and caring for the survivors at a critical time in any rescue operation. It also hampers or prevents the identification of the dead, removing part of the grieving process from their relatives as well as prolonging their uncertainty as to the possible survival of the victims. The legal consequences of lack of identification (e.g. uncertainty of spouses about death of partners, inheritance or welfare benefit problems) can cause long-term hardship for the deceased relatives.

If bodies cannot immediately be identified and sufficient temporary mortuary space with refrigeration is not available they should be buried in marked graves with at least one metre of earth over the cadavers (to prevent access by scavengers and pests) to allow subsequent exhumation. Careful and detailed records of such interments must be kept. Once identified, they should be dealt with following the normal religious and social practices of the affected areas as far as possible. Burial sites must be chosen so as to avoid the risks that water sources may be contaminated.

Those handling the bodies should take basic infection control precautions: Impervious gloves, single-use or disinfected

after use), impervious apron or coverall, impervious footwear, face protection if splashing is likely. Respiratory-protective masks are not necessary. The use of chloride of lime to prevent the spread of infection in these circumstances is to be avoided. It has little effect and is dangerous to those applying it. This applies equally to emergency and non-emergency situations, such as exhumations of graves and crypts.

References

Advisory Committee on Dangerous Pathogens. Management of Hazard Advisory Committee on Dangerous Pathogens. Management of Hazard Group 4 viral haemorrhagic fevers and similar human infectious diseases of high consequence. 2012. Available at: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947382005

Ball J, Desselberger U, Whitwell H. Long-lasting viability of HIV after patient's death. *Lancet*. 1991. 338:63.

Department of Health England. Guidance on prevention of CJD and vCJD by Advisory Committee on Dangerous Pathogens' Transmissible Spongiform Encephalopathy (ACDP TSE) Risk Management Subgroup. Annex H: After death. 2012. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/209766/Annex_H_-_After_death.pdf

Gamble MR. Hazard: Formaldehyde and Hypochlorites. *Laboratory Animals*. 1977. 11:61.

Hawkey PM, Pedler SJ, Southall PJ. *Streptococcus pyogenes*: A forgotten occupational hazard in the mortuary. *BMJ*. 1980. 281:1058.

Health and Safety Executive. Health Services Advisory Committee. Safe working and the prevention of infection in the mortuary and the post-mortem room (2nd Edition). 2003. Available at: http://www.hse.gov.uk/pubns/priced/mortuary-infection.pdf

Health and Safety Executive. Controlling the risks of infection at work from human remains: A guide for those involved in funeral services (including embalmers) and for those involved in exhumation. Health and Safety Executive. 2005. Available at: http://www.hse.gov.uk/pubns/web01.pdf

Morris SI. Tuberculosis as an occupational hazard during medical training. *Am Rev Tuberculosis*. 1946. 54:140–58.

Morgan O. Infectious disease risks from dead bodies following natural disasters. *Rev Panam Salud Publica*. 2004. 15(5):307–12.

Newsom SWB, Rowlands C, Matthews J, Elliott CJ. Aerosols in the mortuary. *J Clin Pathol*. 1983. 36:127–32.

Smith GS. Tuberculosis as a necropsy room hazard. *J Clin Pathol*. 1953. 6:132–4.

de Ville de Goyet C. Stop propagating disaster myths. *Lancet*. 2000. 356:762–764.
West DJ. The risk of hepatitis B infection among health professionals in the United States: A review. *Am J Med Sci*. 1984. 287:26–33.
Wolff HL, Croon JAB. The survival of smallpox virus (Variola Minor) in natural circumstances. *Bull World Health Organ*. 1968. 38 492–3.
World Health Organization/Pan American Health Organization. Management of dead bodies in disaster situations. Washington, DC: WHO/PAHO, 2004. Available at: http://www.paho.org/

CHAPTER 42

Streptococcus pyogenes (Group A Streptococcal Infections)

Belinda Ostrowsky, MD, MPH

Keywords
Streptococcus pyogenes, Group A streptococcus, standard precautions, postpartum infections, post surgical infections, long term care facilities, evaluation of clusters, typing.

Key Issues

- Handwashing is one of the most important infection control practices for the prevention of spread of infection with *Streptococcus pyogenes* [Group A streptococcus (GAS)].
- One health care associated postpartum or postsurgical invasive GAS infection should prompt enhanced surveillance and streptococcal isolate storage; two or greater cases caused by the same strain of GAS should prompt an epidemiological investigation that includes the culture of specimens from epidemiologically linked health care workers (HCWs).
- There are relatively new guidelines and specific actions to address potential clusters/outbreaks of GAS infections in long term facilities.
- In a larger context GAS remains a challenge in terms of best prevention strategies for developing countries.

Known Facts

- Group A streptococci frequently colonize the throats of asymptomatic persons and may also colonize the skin, rectum and vagina.
- Streptococcal disease is ordinarily spread by direct person-to person contact. In cases of pharyngitis and respiratory infections, droplet nuclei of saliva or nasal secretions are the mode of spread. Crowding such as occurs in schools or military barracks favors interpersonal spread of the organism in community outbreaks. Fomites can also be a source of streptococcal transmission.

- A variety of clinical presentations may occur, including pharyngitis, otitis media, quinsy, skin and soft tissue infections (pyoderma, impetigo, erysipelas, and scarlet fever), pneumonia and puerperal fever.
- Most GAS infections are relatively mild illnesses. More recently invasive and serious GAS infections have become concerning.
- Invasive Group A streptococcal infection is defined as isolation of GAS from a normally sterile site (e.g., blood) or by the isolation of GAS from a nonsterile site in the presence of the streptococcal toxic shock syndrome or necrotizing fasciitis.
- Postinfectious complications of GAS infections include Rheumatic Fever with secondary aortic and mitral valve injury and glomerular nephritis. Pharyngeal strains of GAS can result in either syndrome. Infections of the skin are only associated with the acute glomerular nephritis.
- Streptococcal infections should be treated to limit secondary complications.
- Outbreaks of pharyngitis and impetigo in school-age children or in group settings are common.
- Clusters/outbreaks are less common, but have been described mainly in two healthcare settings, postpartum and postsurgical populations. There has also been recent interest in health care associated clusters in long term care facilities.

Controversial Issues

- No controlled trials have evaluated the effectiveness of chemoprophylaxis in preventing invasive GAS disease among household contacts of persons with invasive GAS infections. Given the infrequency of these infections and the lack of a clearly effective chemoprophylaxis regimen, the available data do not support a recommendation for routine testing for GAS colonization or for routine administration of chemoprophylaxis to all household contacts of persons with invasive GAS at this time.
- The global strategies for prevention of GAS on larger scale remain complex.

Suggested Practice

- Standard precautions, including handwashing are the most important infection control practices for the prevention of spread of infection with GAS such as minor/limited skin infections, wounds and burns and endometritis (puerperal sepsis).
- HCWs should wear gloves and gowns for contact with the skin of patients with major lesions, wounds and purulent discharge. Place the patient in a private room. When a private room is not available, place the patient in a room with a patient(s) who also has infection with the *S. pyogenes* (cohorting). Discard the gloves after use and wash hands thoroughly between patient contacts. Contact isolation may be discontinued after 24 hours of directed antistreptococcal therapy.
- For GAS infections that involve the pharynx and respiratory tract, such as pneumonia and Scarlet Fever in infants and children, HCWs should use standard and droplet precautions, including use of a surgical mask when working within 3 feet of the patient. Logistically, some hospitals may want to implement the wearing of a mask to enter the room of affected patients. Place the patient in a private room. When a private room is not available, cohorting should be used. When a private room is not available and cohorting is not achievable, maintain spatial separation of at least 3 feet between the infected patient and other patients and visitors. Special air handling and ventilation are not necessary, and the door may remain open.
- HCWs who are known or suspected to have infection or colonization of their respiratory tract with *S. pyogenes* should wear a mask to reduce respiratory spread of their organism.
- Attempt to eradicate colonization in those HCWs who are proven sources of outbreaks (description evaluation of cluster/outbreak in healthcare setting below).
- Newer typing modalities, including whole-genome sequencing (compared to traditional pulsed field gel electrophoresis) may be needed to elucidate the epidemiology in some clusters.

Summary

Streptococcus pyogenes (Group A β-hemolytic streptococcus) is a gram-positive, catalase-negative cocci. It can be carried in the pharynx, skin, vagina and rectum asymptomatically. There are a wide variety of clinically presentations of GAS. Although the most common GAS infections are mild (i.e. pharyngitis, skin infections) if left untreated there can be serious secondary sequelae, including Rheumatic Fever and glomerular nephritis.

More concerning in recent years are invasive GAS infections. Invasive GAS infection is defined as isolation of GAS from a normally sterile site (e.g., blood) or by the isolation of GAS from a nonsterile site in the presence of the streptococcal toxic shock syndrome or necrotizing fasciitis.

Worldwide, rates of invasive disease increased from the mid-1980s to early 1990s. Rates of invasive disease have been stable over the last several years in the United States. However, there have been increases in the severity of disease, including those associated with M-1 and M-3 serotypes (*emm* gene types 1 and 3). Resistance to erythromycin has increased worldwide.

By estimates from Centers for Disease Control and Prevention (CDC), using the Active Bacterial Core Surveillance (ABCs) Report in the year 2012 there were approximately 10,700 cases of invasive GAS and 1150 deaths due to GAS infection in the United States.

Direct contact with patients or carriers and large respiratory droplets are the primary means of acquisition. Disease caused by *S. pyogenes* is most common in late winter and early spring. In the community setting, outbreaks of pharyngitis in school children and other congregate settings are common in these months. Contaminated hands of HCWs are an important means of transmission, particularly outside of the setting of the operating room. Appropriate gloving and good handwashing techniques are important to emphasize in efforts to control an outbreak. The addition of contact precautions for wound, skin and soft tissue and droplet precautions for pharyngeal and respiratory infections in infants and children are appropriate infection control practices. Prompt identification and investigation of an outbreak of healthcare associated *S. pyogenes* infection will assist in its control.

In health care settings outbreaks have been described mainly in two populations; postpartum and postsurgical patients. GAS infections are also reported in burn patients (wound), bacteremias in the setting of intravascular catheters devices and pneumonias.

There are two recent guidelines (since 2002) that are excellent resources for addressing infection control related to GAS infections and particularly in these high risk settings, one related to an expert panel meeting by CDC in the United States and the second by Public Health Agency of Canada. Highlighted from these comprehensive guidelines are distilled below.

In 2000, CDC hosted a workshop to formulate recommendations for household contacts of those with invasive GAS infections and for responding to healthcare associated clusters, including postpartum and postsurgical invasive GAS infections. The recommendations from this panel were published in 2002.

In this CDC expert panel review, a household contact is defined as a person who spent at least 24 hours in the same household as the index patient during the seven days before the onset of the case patient's symptoms. Review by the committee of two prospective studies that were designed to identify subsequent cases among household contacts (who were observed for a total of 66.5 million person-years) identified only five confirmed cases of subsequent invasive disease. There are no controlled trials that have evaluated the effectiveness of chemoprophylaxis in preventing invasive GAS disease among household contacts of persons with invasive GAS infections. In addition, antimicrobial therapy can have undesirable side effects, including adverse reactions and selection for resistant organisms.

Thus, the committee did not recommend routine screening for and chemoprophylaxis to household contacts. However, they suggested that providers and public health officials may choose to offer chemoprophylaxis to household contacts who are at an increased risk of sporadic disease [HIV infection, diabetes mellitus, varicella zoster (Chicken pox) patients <10 years of age, cancer, heart disease, injection drug use, steroid use, ≥65 years of age] or mortality due to GAS (≥65 years of age). HCWs should routinely inform all household contacts of persons with

invasive GAS disease about the clinical manifestations of pharyngitis and invasive GAS infection (e.g. fever, sore throat, and localized muscle pain and emphasize the importance of seeking medical attention if contacts develop such symptoms).

Given the potential for prevention of additional cases, the CDC panel recommended that even one case of postpartum or postsurgical GAS infection should prompt an epidemiological investigation by the hospital's infection control personnel, which should include enhanced surveillance and storage of GAS isolates from the index patients and any other cases for at least six months. Enhanced surveillance should include one or both of the following: 1) review of microbiological records and autopsy reports from the previous six months and/or 2) review of operative, labor and delivery, and medical records from within the hospital.

If two or greater cases are identified within a 6-month period, they may have a common source of GAS transmission. Isolates should be compared by an appropriate typing method (i.e., PFGE, serotyping, other molecular methods). Isolates that differ probably are community acquired, but enhanced surveillance should be initiated.

If two cases are found to be caused by the same strain within a 6-month period, screening of HCWs is strongly recommended to prevent further cases of serious infection. If infection-control personnel choose to screen healthcare workers, screening should be considered for HCWs who were present at delivery and for those who perform vaginal examinations before delivery (for postpartum cases) and for all HCWs present in the operating room during surgery and those who change dressings on open wounds (for postsurgical cases). If screening of HCWs is undertaken, sites from which specimens should be obtained and cultured include throat, anus, vagina, and any skin lesions. Screened HCWs may return to work pending culture results. However, HCWs identified as colonized should be suspended from patient care duties until they have received chemoprophylaxis for 24 hours and their streptococcus strains should be compared with patient strains using the same typing methods.

If a HCW is epidemiologically linked to the case patient and the strain the HCW is carrying is the same as the strains isolated

from patients, the committee suggests follow-up cultures should be done for the HCW (CDC suggestions 7–10 days after the completion of therapy). If no colonized HCW is identified or if HCWs are colonized with strains unrelated to the outbreak strain, the search for colonized HCWs could be broadened to include those HCWs without immediate epidemiological links to all case patients. This might include, for example, HCWs who had direct contact with most but not all case patients.

The Public Health Agency of Canada published their Guidelines for the Prevention and Control of Invasive Group A Streptococcal Disease in October, 2006. This 26 page resource adds to the previously described US review in that it offers simple and clear definitions, an extensive glossary, review of the literature and references by topic area, and particular sections on GAS infection control and investigation in the childcare and long term care facilities settings. Two areas of difference from the US guideline relevant for the infection control community are summarized below.

The Canadian workgroup's consensus on chemoprophylaxis for contacts was slightly more inclusive than the U.S. guideline above, in that it does suggest prophylaxis for the closest contacts of confirmed severe cases of GAS infections, including streptococcal toxic shock syndrome, soft tissue necrosis, meningitis, pneumonia, other life-threatening conditions or a confirmed case resulting in death (and did not identify the underlying conditions of the contacts as a factor as strongly as the U.S. guideline).

For the long term care setting, in addition to strict enforcement of standard infection control precautions, this guideline lays out what may constitute a cluster/outbreak and steps to investigate for and address a potential clusters/outbreaks. It suggests that in this setting 1) an incidence rate of culture-confirmed invasive GAS infections of > 1 per 100 residents per month or 2) at least two cases of culture confirmed invasive GAS infection in one month in a facility with fewer than 200 residents or 3) an incidence rate of suggested invasive or non-invasive GAS infection of > 4 per 100 residents per month should be an impetus for action.

This guideline suggests when a confirmed case of GAS infection in a long term care facility is identified that the following additional steps should be taken: 1) retrospective chart review of facility's residents over the four–six weeks prior to the case for other culture confirmed or any suggestive cases of invasive or non-invasive GAS infection and 2) assess the potential sources of infection from outside the facility. If an excess of these infections is identified, then the next steps would be: 1) screen patient care staff for GAS, 2) based on size of the facility screen some or all facility residents for GAS (using a cut off of 100 beds, < 100 beds screen all residents, > 100 beds screen residents within the same care unit as the case), 3) offer prophylaxis for all those identified with colonization with GAS, 4) question non-patient care staff about recent GAS infection and screen those with positive history 5) obtain genotyping of GAS isolates and "test of care" those with outbreak related strains, 6) rescreening of GAS positive residents and staff identified and 7) active surveillance for GAS infections for one to two months. If no excess if identified, especially if there is evidence of outside source for the index case, then active surveillance alone for two–four weeks to establish absence of additional cases is warranted.

In summary, handwashing is the corner stone of infection control for GAS infections. Additional precautions including contact and droplet precautions are appropriate for use by HCWs for specific other presentations of GAS infection. For certain high-risk household contacts of GAS infection, prophylaxis maybe appropriate. For healthcare associated GAS infections enhanced surveillance, saving isolates and screening/prophylaxis of epidemiologically-linked HCW in certain setting may aid in prevention of further infections. Some additional surveillance and investigation in the long term care setting may also be appropriate when there is suspicion of clusters/breaks in this setting. CDC also has web-based tools to aid in investigations of clusters of GAS (Available at CDC website: http://www2.cdc.gov/ncidod/dbmd/abcs/calc/calc_new/index.htm).

Several clusters have been described in the U.S. and international literature that have suggested that traditional typing protocols, such as pulse-field gel electrophoresis, may not be

sensitive enough to allow fine epidemiological discrimination of GAS isolates. Whole-genome sequencing presents a valid alternative that allows accurate fine scale epidemiological investigation of clusters of GAS. Examples include a postpartum GAS cluster in Australia in 2010 that using this technic to prove relatedness of strain type *emm* 28 isolated from puerperal sepsis cases from the same hospital from isolates from other hospitals (supporting suspected patient to patient transmission or common sources). CDC and several other referral laboratories are available with expertise and resources to help with typing of suspected clusters (CDC strep labs: http://www.cdc.gov/ncidod/biotech/strep/strepindex.htm).

In 2005, WHO published A Review of the Technical Basis for the Control of Conditions Associated with Group A Streptococcal Infections looking more from an international, global-public health perspective. Although not completely related to healthcare associated transmission, it lays out a broader plan for GAS control. It sites that the most successful GAS control activities have combined multiple strategies including primary prophylaxis, treatment of skin infections, health promotion, secondary prophylaxis and RHD registers. Although effective, these comprehensive programs require a substantial commitment from individuals and organizations (including Ministries of Health). It also suggests that in light of the current lack of a clear strategy for primary prevention of GAS infections, there is definitely a place for a safe, effective, affordable and practical GAS vaccine. It appears likely that the vaccine most advanced in development—a multivalent, type-specific vaccine—will not provide sufficient and long-lasting protection in less developed countries, although this should be assessed. This document underscores that GAS remains a challenge throughout the world in the community and in healthcare settings.

References

CDC. The Prevention of invasive Group A Streptococcal infections workshop participants. Prevention of invasive Group A Streptococcal disease among household contacts of case patients and among postpartum and postsurgical patients: Recommendations from the Centers for Disease Control and Prevention. *Clin Infect Dis*. 2002. 35:950–959.

Public Health Agency of Canada. Guidelines for the Prevention and Control of Invasive Group A Streptococcal Disease. *CCDR* 2006. 32S2:1–26.

CDC. National Center for Immunization and Respiratory Diseases: Division of Bacterial Diseases Group A Streptococcal (GAS) Disease. Frequently asked questions. CDC website, revised 4/3/08, Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/groupastreptococcal_g.htm

CDC. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Group A Streptococcus, 2012. Available at: http://www.cdc.gov/abcs/reports-findings/survreports/gas12.html

Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. June 2007. Available at: http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html

Ben Zakour NL, Venturini C, Beatson SA, Walker MJ. Analysis of a *Streptococcus pyogenes* puerperal sepsis cluster by use of whole-genome sequencing. *J Clin Microbiol*. July 2012. 50(7):2224–2228.

CDC. The CDC *Streptococcus* Laboratory, revised 8/30/12. Available at: http://www.cdc.gov/ncidod/biotech/strep/strepindex.htm

WHO. A Review of the Technical Basis for the Control of Conditions Associated with Group A Streptococcal Infections. 2005. Available at: http://whqlibdoc.who.int/hq/2005/WHO_FCH_CAH_05.08.pdf

CHAPTER 43

Staphylococcus aureus

Michael P. Stevens, MD, MPH and
Michael B. Edmond, MD, MPH, MPA

Key Issue

Staphylococcus aureus is a major human pathogen that commonly causes healthcare associated and community-acquired infections. It is a highly virulent organism that is exhibiting increasing antibiotic resistance.

Known Facts

- Colonization with *S. aureus* is common. A national, population-based study of non-hospitalized persons in the U.S. found 32% of persons to be colonized with methicillin susceptible *S. aureus* (MSSA) and 1% colonized with methicillin resistant *S. aureus* (MRSA).
- *S. aureus* is a major cause of healthcare associated infections (HAIs), accounting for 15% of all HAIs in the United States.
- Regarding antimicrobial resistance, *S. aureus* is typically characterized by its susceptibility patterns to penicillinase-resistant penicillins (e.g., methicillin) and vancomycin.
- The *mecA* gene encodes for penicillin binding protein 2a(PBP2a) which confers resistance to all ß-lactam antibiotics.
- Over half of all *S. aureus* strains acquired in U.S. healthcare facilities are resistant to methicillin.
- Historically, MSSA strains were mostly acquired in the community, whereas MRSA strains were typically acquired in healthcare facilities. However, community-associated MRSA (CA-MRSA) is now the predominant cause of purulent skin and soft tissue infections in the outpatient setting.
- CA-MRSA tends to differ from health care associated MRSA in that community-associated strains are more likely to be susceptible to TMP/SMX and tetracyclines.

- CA-MRSA often manifests as skin and soft tissue infections and may be misdiagnosed as a "spider bite." CA-MRSA is responsible for the majority of purulent skin and soft tissue infections presenting to U.S. emergency rooms.
- Virtually all of the community-associated strains contain the Panton-Valentine Leukocidin (PVL) gene which is associated with lysis of white blood cells and tissue necrosis. These strains characteristically cause skin and soft tissue infections, often in healthy children and young adults, as well as a severe, multilobar, necrotizing pneumonia that often occurs with or following influenza.
- Classification of MRSA strains into community-associated and hospital-associated based on exposure to the healthcare setting is no longer reliable.
- Risk factors for staphylococcal colonization and infection include disruptions of the skin (insulin injections, hemodialysis, allergy therapy, IV drug use, eczema, burns), underlying diseases (respiratory infections, HIV infection), prolonged hospitalization, and exposure to other infected or colonized individuals. However, in many patients with CA-MRSA infections, these risk factors are not present.
- >80% of cases of *S. aureus* bacteremia are caused by endogenous strains (i.e., a strain colonizing the patient is responsible for invasive infection).
- The most common sources of *S. aureus* bloodstream infection are catheters (46%), skin/soft tissue/bone (27%), lower respiratory tract (11%), and urinary tract (10%).
- Vancomycin intermediate *Staphylococcus aureus* (VISA), vancomycin resistant *Staphylococcus aureus* (VRSA), and heteroresistant *Staphylococcus aureus* (hetero-VRSA) have all been reported.
- The Clinical and Laboratory Standards Institute defines staphylococcal vancomycin minimum inhibitory concentrations (MICs) of ≤2 μg/mL as susceptible, 4–8 μg/mL as intermediate, and ≥16 μg/mL as resistant. Practically speaking, vancomycin should be avoided for severe infections where the staphylococcal isolate has an MIC of ≥2 μg/mL due to a high likelihood of treatment failure.

- Hetero-VRSA are defined as strains of *S. aureus* that contain subpopulations of vancomycin-resistant daughter cells but for which the MICs of the parent strain are only 1–4 μg/mL. These subpopulations typically have MICs 2–8 fold higher than the original clinical isolate. When grown in the absence of vancomycin, the subpopulation of cells reverts back to the lower MIC of the parent strain.
- Patients who develop infection with VISA and VRSA often have serious comorbid disease states such as renal failure and diabetes, a previous history of infections with MRSA, recent vancomycin use, the presence of foreign material (including intravenous catheters and prosthetic devices) and recent hospitalizations.
- Major route of transmission for *S. aureus* is direct or indirect contact; airborne transmission is uncommon.
- Colonized healthcare workers may be the source of outbreaks in the hospital setting.

Controversial Issues

- The effectiveness of routine surveillance cultures to detect MRSA colonized patients followed by isolation of the patient in order to reduce MRSA infection and colonization in high prevalence settings is probably not effective.
- The role of decolonizing agents in the non-outbreak clinical setting remains undefined. In particular, use of mupirocin for all patients in the ICU setting (universal decolonization), raises concerns for the development of high rates of resistance.

Suggested Practice

MSSA

- Use standard precautions.

MRSA/VISA

- Use contact precautions (gloves and gowns). Enforce hand washing with antiseptic agents (chlorhexidine gluconate or alcohol-based products) for staff, visitors, and infected or colonized patients.
- Consider private room or cohorting the infected or colonized patient with other MRSA patients.

- Offer decolonization with intranasal mupirocin for patients with recurring infections and for colonized personnel.
- If the MRSA patient is transferred, notify receiving healthcare facility.
- No special precautions for home discharge are required; emphasize good hand washing.

VRSA

- Contact precautions, including a private room, are recommended.
- Minimize the number of people in contact with or caring for the patient.
- Educate all healthcare personnel about the epidemiology of VRSA and the appropriate infection control precautions.
- Initiate epidemiologic and laboratory investigations with the assistance of the public health department.
- Consult with the public health department before transferring or discharging the patient.

Summary

In the community, *S. aureus* is best known as the cause of furuncles and soft tissue infections. In the hospital environment, *S. aureus* may cause life-threatening infections, such as pneumonia, bloodstream or surgical site infections, and is considered one of the most important health care associated pathogens.

The nares are the usual reservoir for *S. aureus*, but other locations such as moist or hairy body areas, skin defects, wounds, and burns also can become colonized. Methicillin resistant *S. aureus* carriage may be eradicated with application of topical mupirocin to the anterior nares, although recolonization often occurs. This therapy should be limited to patients with recurring MRSA infections or colonized hospital personnel to prevent the development of resistance.

The most common mode of *S. aureus* transmission is direct contact of body surface to body surface. Sexual transmission of MRSA has been described and manifests as folliculitis or abscesses of the pubic, vaginal or perineal areas. The airborne route is less efficient but may occur in patients with *S. aureus* pneumonia or large burn wounds. It has been shown that

colonized individuals with viral upper respiratory tract infections may shed *S. aureus* into the air. Transmission via indirect contact with inanimate objects such as instruments can occur, and *S. aureus* can be detected on many surfaces in hospitals, including stethoscopes and laboratory coats.

Strategies for the management of *S. aureus* and especially MRSA colonization or infection must focus on the type of spread. Epidemic outbreaks are successfully handled with prompt application of infection control measures. Application of precautions such as patient isolation, hand washing with antiseptic agents, and glove usage can interrupt the chain of transmission and control the outbreak. Institutions with repeated introduction of MRSA from the community or other facilities are unlikely to be able to eradicate this pathogen.

Vancomycin remains the mainstay of therapy for systemic MRSA infections. For MRSA-associated necrotizing pneumonia some experts recommend the addition of an antibiotic active at the ribosomal level (e.g., rifampin or clindamycin) to terminate toxin production. For relatively minor skin infections, the use of doxycycline or trimethoprim/sulfamethoxazole (TMP/SMX) is typically recommended in addition to incision and drainage of abscesses.

Fortunately, infections due to VISA and VRSA have remained uncommon. In the United States, there have been thirteen cases ascribed to VRSA. Importantly, strict compliance with infection control guidelines is necessary to minimize cross transmission within healthcare facilities. When identified, public health departments should be involved in the management of these cases.

Treatment options for VISA and VRSA are few, and clinical experience is limited. Quinupristin-dalfopristin and linezolid are bacteriostatic for VISA/VRSA. Newer potential therapies include daptomycin, ceftaroline, ceftobiprole, telavancin and tigecycline. Susceptibility of VISA/VRSA has also been reported to chloramphenicol, minocycline, tetracycline, doxycycline and trimethoprim/sulfamethoxazole (TMP/SMX). Expert consultation with an infectious diseases specialist should be sought for the management of VISA and VRSA cases.

References

Chang S, Sievert DM, Hageman JC, et al. Infection With Vancomycin-Resistant *Staphylococcus aureus* Containing the vanA Resistance Gene. *N Engl J Med*. 2003. 348:1342–7.

Drew RH. Emerging Options for Treatment of Invasive, Multidrug-Resistant *Staphylococcus aureus* Infections. *Pharmacotherapy*. 2007. 27:227–49.

Graham PL 3rd, Lin SX, Larson EL. A U.S. Population-Based Survey of *Staphylococcus aureus* Colonization. *Ann Intern Med*. 2006. 144:318–25.

Liu C, Bayer A, Cosgrove SE, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children: Executive Summary. *Clin Infect Dis*. 2011. 52:285–92.

Talan DA, Krishnadasan A, Gorwitz RJ, et al. Comparison of *Staphylococcus aureus* from Skin and Soft-Tissue Infections in US Emergency Department Patients, 2004 and 2008. *Clin Infect Dis*. 2011. 53:144–9.

von Eiff C, Becker K, Machka K, Stammer H, Peters G. Nasal Carriage as a Source of *Staphylococcus aureus* Bacteremia. *N Engl J Med*. 2001. 344:11–6.

Wenzel RP, Edmond MB. Vancomycin-Resistant *Staphylococcus aureus*: Infection Control Considerations. *Clin Infect Dis*. 1998. 27:245–9.

Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study. *Clin Infect Dis*. 2004. 39:309–17.

Hidron AI, Edwards JR, Patel J, et al. NHSN Annual Update: Antimicrobial-Resistant Pathogens Associated with Healthcare-Associated Infections: Annual Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infect Control Hosp Epidemiol*. 2008. 29:996–1011.

Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2013. Available online at: www.cdc.gov/drugresistance/threat-report-2013. (Accessed 1 October 2013).

Huang SS, Septimus E, Kleinman K, et al. Targeted Versus Universal Decolonization to Prevent ICU Infection. *N Engl J Med*. 2013. 368:2255–65.

CHAPTER 44

Enterococcal Species

Michael P. Stevens, MD, MPH, and
Michael B. Edmond, MD, MPH, MPA

Key Issue

Enterococci are important health care associated pathogens because: 1) they are normal flora in the human gastrointestinal tract, 2) antimicrobial resistance allows for their survival in an environment with heavy antimicrobial usage, 3) they contaminate the hospital environment and survive for prolonged periods of time, and 4) contamination of the hands of healthcare workers coupled with poor hand washing compliance provides the potential for spread in the hospital.

Known Facts

- Enterococci are common health care associated pathogens, accounting for 12% of all healthcare associated infections.
- The organism is of relatively low virulence but may be difficult to treat in the compromised host, particularly when multidrug resistant.
- Resistance to nearly every known antibiotic has been described for various strains of enterococci.
- The vanA gene, which confers high-level vancomycin resistance in enterococci, has been detected in *Staphylococcus aureus* strains in a small number of patients in the United States.
- Vancomycin resistance due to vanC is intrinsic and found in *E. casseliflavus* and *E. gallinarum*. vanC organisms do not appear to be epidemiologically important, and isolation of patients harboring these organisms is not necessary.
- Currently 30% of all enterococcal isolates in the United States involved in HAIs are resistant to vancomycin. However, the two most common species display marked variability in vancomycin susceptibility, with 77% of *E. faecium* and 9% of *E. faecalis* isolates resistant to vancomycin.

- Risk factors for acquisition of vancomycin resistant enterococci (VRE) include prior use of antimicrobial agents (vancomycin, third generation cephalosporins, antianaerobic drugs), length of hospital stay, enteral feedings, intraabdominal surgery, presence of a decubitus ulcer, high colonization pressure, and severity of illness.
- Patient populations at highest risk for VRE colonization and infection include dialysis patients, organ transplant patients, patients with hematologic malignancies, and bone marrow transplant patients. Studies have found that approximately 30% of patients following liver transplantation are colonized with VRE, of whom over 25% develop infection. Up to 40% of allogeneic hematopoietic stem cell transplant patients are colonized, of whom over 33% develop VRE bloodstream infections in the early period post-transplant.
- Treatment with antianaerobic drugs has been shown to promote high density colonization.
- Colonization of the GI tract with VRE is typically of long duration, in some cases persisting for years.
- Rectal swab cultures for VRE have suboptimal sensitivity.
- Colonization of healthy healthcare workers in the United States is unusual.
- Risk factors for VRE bacteremia include neutropenia, gastrointestinal colonization, and hematologic malignancy.
- VRE colonization is highly prevalent in some long-term care facilities, which serve as reservoirs of resistant organisms for importation into acute care facilities. However, morbidity due to VRE in the nursing home population is low.

Controversial Issues

- Treatment of VRE infections is problematic. Therapy should include drainage of localized infections, when possible. Daptomycin, a cyclic lipopeptide, is bactericidal against VRE. Quinupristin/dalfopristin may be clinically useful for the treatment of infections due to *E. faecium* but is inactive against *E. faecalis*. Linezolid has good activity against VRE and an advantage is its 100% oral bioavailability, allowing for oral therapy. Quinupristin/dalfopristin, linezolid, and tigecycline are bacteriostatic against enterococci. Resistance has been detected for all three of these agents.

- A few reports have described attempts to decolonize the gastrointestinal tract of VRE but results have been suboptimal. Ramoplanin has been shown to suppress carriage of VRE, but following discontinuation of the drug, the organism can again be detected in the stool.
- Infection control controversies include the effectiveness of active surveillance cultures and subsequent isolation of colonized patients to control health care associated transmission, whether drugs that suppress GI colonization result in decreased health care associated transmission and whether vancomycin restriction leads to decreased rates of VRE infection and colonization.

Suggested Practice

- Prudent use of antimicrobial drugs
- For patients with VRE infection or colonization:
  - Place in private room or cohort with other VRE infected/colonized patients. Gloves and gowns should be worn on entering the patient's room.
  - Strict compliance with hand washing is critical—a medicated hand washing agent (e.g., chlorhexidine or alcohol-based hand rub) should be used.
  - Noncritical items (e.g., stethoscopes, thermometers, etc.) should be left in the patient's room.
  - Isolation can be discontinued when three stool cultures, each one week apart, are all negative.
  - Phenolic and quaternary ammonium disinfectants are effective against VRE; however, adequate contact time is essential.

Summary

Enterococci are ubiquitous gram-positive cocci that are part of the normal flora of humans and other animals. Infections caused by enterococci include urinary tract infections, abdominal-pelvic infections, wound (especially decubitus ulcers and diabetic foot) infections, and endocarditis.

Strains of enterococci have acquired resistance to virtually all available antimicrobial agents. In general, antimicrobial resistance has been more problematic for *E. faecium* than *E. faecalis*.

The prevalence of vancomycin resistance among the enterococci has reached high levels. In 1989, less than 0.5% of enterococcal isolates from ICU and non-ICU settings were vancomycin resistant. Currently, 30% of all enterococcal isolates involved in HAIs in the United States are vancomycin resistant. However, when stratified by species, *E. faecium* isolates demonstrate a markedly higher proportion of vancomycin resistance than *E. faecalis* isolates.

Numerous case-control studies have evaluated risk factors for the development of colonization and/or infection with VRE. A variety of antimicrobial agents have been implicated and include vancomycin, ceftazidime, aminoglycosides, ciprofloxacin, aztreonam, and antianaerobic drugs. Other risk factors have included severity of illness, length of hospital stay, hematologic malignancy or bone marrow transplantation, and mucositis. Colonization of the GI tract has been shown to be a risk factor for the development of VRE bacteremia. Environmental contamination with VRE is common, especially when the patient has diarrhea.

To control VRE in the hospital setting, we recommend placing colonized/infected patients in a private room. Gloves and gowns should be worn on entering the patient's room, and strict attention paid to hand hygiene. In addition, there should be no sharing of noncritical items (i.e., BP cuffs, stethoscopes, etc., should remain in the patient's room). Housekeeping staff should wipe down all horizontal surfaces in VRE patient rooms daily.

In addition to infection control measures, controlling VRE requires prudent use of antibiotics. Vancomycin should be avoided for routine surgical prophylaxis unless high rates of MRSA exist. Vancomycin should also be avoided for the treatment of a single positive blood culture growing coagulase-negative staphylococci if contamination is likely. Vancomycin should not be used for selective gut decontamination or for routine prophylaxis of low-birth weight infants, continuous ambulatory peritoneal dialysis patients, or intravascular catheters.

References

de Bruin MA, Riley LW. Does Vancomycin Prescribing Intervention Affect Vancomycin-Resistant Enterococcus Infection and Colonization in Hospitals? A Systematic Review. *BMC Infect Dis*. 2007. 7:24.

DeLisle S, Perl TM. Vancomycin-Resistant Enterococci: A Road Map on How to Prevent the Emergence and Transmission of Antimicrobial Resistance. *Chest*. 2003. 123:504S–518S.

Hayden MK. Insights into the Epidemiology and Control of Infection with Vancomycin-Resistant Enterococci. *Clin Infect Dis*. 2000. 31:1058–1065.

McNeil SA, Malani PN, Chenoweth CE, et al. Vancomycin-Resistant Enterococcal Colonization and Infection in Liver Transplant Candidates and Recipients: A Prospective Surveillance Study. *Clin Infect Dis*. 2006. 42:195–203.

Rice LB. Emergence of Vancomycin-Resistant Enterococci. *Emerg Infect Dis*. 2001. 7:183–187.

Weinstock DM, Conlon M, Iovino C, et al. Colonization, Bloodstream Infection, and Mortality Caused by Vancomycin-Resistant Enterococcus Early After Allogeneic Hematopoietic Stem Cell Transplant. *Biol Blood Marrow Transplant*. 2007. 13:615–621.

Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study. *Clin Infect Dis*. 2004. 39:309–317.

Hidron AI, Edwards JR, Patel J, et al. NHSN Annual Update: Antimicrobial-Resistant Pathogens Associated with Healthcare-Associated Infections: Annual Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infect Control Hosp Epidemiol*. 2008. 29:996–1011.

Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2013. Available online at: http://www.cdc.gov/drugresistance/threat-report-2013/ (Accessed 1 October 2013).

CHAPTER 45

PNEUMOCOCCUS

Roman Pallares, MD, and Imma Grau, MD

Key Issues

Streptococcus pneumoniae (*pneumococcus*) remains a major pathogen worldwide, mainly in young children (<5 years), adults with immunosuppressive or chronic diseases as well as smokers and alcohol abusers, and older adults (>=65 years). Pneumococcal disease is more common in developing countries, and occurs more often during winter and early spring. In recent years, important changes in the epidemiology of pneumococcal infections have been observed:

1. The emergence and spread of multiple antibiotic-resistant pneumococci which make pneumococcal infections (e.g., meningitis) difficult to treat;
2. The increasing prevalence of pneumococcal disease in the elderly and in young adults with serious underlying diseases (e.g., HIV, malignancies);
3. The increasing recognition of pneumococcal infections in patients admitted to healthcare institutions and nursing homes, childcare centers, and other closed institutions (e.g., jails, military camps). Several of these infections appeared as outbreaks due to antibiotic-resistant pneumococci; and
4. In the last decade (2000s), there was a reduction in the incidence of pneumococcal infections after the introduction of 7-valent pneumococcal conjugate vaccine (PCV7) in children.

Infection control measures for preventing pneumococcal infections in hospital and healthcare settings, and nursing home facilities have not been widely considered in the literature.

Known Facts

Streptococcus pneumoniae is the leading cause of community-acquired pneumonia, otitis media, sinusitis, exacerbation of

chronic bronchitis and adult meningitis. Patients with severe pneumonia or meningitis may have a mortality rate of about 20–30%.

Pneumococcus is transmitted from person-to-person by close contact and can colonize the nasopharynx of healthy people. The prevalence of nasopharyngeal colonization varies widely with age as well as environmental and seasonal conditions. Thus, the nasopharyngeal carrier rates in children are approximately 30–50%, and over 95% of them were initially colonized before the age of 2. The pneumococcal serotypes that colonize the nasopharynx in children show a high rate of antibiotic resistance. In adults, the rates of nasopharyngeal pneumococcal colonization decrease to approximately 5–10%.

Several studies have shown a link between age and susceptibility to pneumococcal infection, with an incidence peak in children aged less than 2 and another one in elderly people. Pneumococcal disease in young adults occurs mainly in patients with underlying conditions (e.g., chronic and immunosuppressive diseases, smoking, high alcohol intake).

Failure to produce antibodies is a determining factor for the susceptibility to pneumococcal infection, and it occurs mainly in patients with multiple myeloma, chronic lymphocytic leukemia and lymphoma, as well as in HIV-infected patients. Patients with splenectomy, diabetes mellitus, malnutrition, chronic renal failure, chronic liver disease, heart failure, chronic obstructive pulmonary disease (COPD), asthma, smoking and high alcohol intake are also at risk of pneumococcal infection.

A previous viral infection, mainly due to influenza virus, is a major predisposing condition of pneumococcal pneumonia. Viral infections modify the local defense mechanisms of the respiratory tract, contributing to nasopharyngeal colonization and facilitating the entrance of microorganisms into the pulmonary alveolus. Other processes that modify the local defense mechanisms of the respiratory tract such as chronic bronchitis, allergic conditions, and smoke or toxic inhalation may also predispose to pneumococcal pneumonia.

The pneumococcus can be transmitted among persons in closed institutions. For example, children attending day care centres have an increased risk of pneumococcal nasopharyngeal

colonization and pneumococcal infections; this increased risk also occurs in adults who live with these young children. The spread of *Streptococcus pneumoniae* leading to colonization or infection has been documented in hospitalized patients, in nursing home residents as well as in persons admitted to military camps and prisons and other closed communities, being likely to cause epidemic outbreaks.

The emergence of antibiotic resistance in pneumococci has become a problem worldwide. Resistance to penicillins, cephalosporins as well as to macrolide and fluoroquinolones has been increasingly reported. Prior antibiotic use and health care associated acquisition of the infection are important risk factors for antibiotic-resistant pneumococcal infection.

Controversial Issues

Little is known about the prevalence of nasopharyngeal carriage and the modes of transmission of *Streptococcus pneumoniae* among hospitalized patients or nursing home residents. Moreover, there is little information regarding pneumococcal infections occurring in the hospital setting. It is often difficult to differentiate between endemic health care associated pneumococcal infections and small outbreaks in hospitals. Studies on serotypes and clones may help to identify the pneumococcal strains causing outbreaks in the hospital.

While it is well known that health-care workers (HCWs) can transmit infections to patients, the extent to which this occurs for *Streptococcus pneumoniae* is less appreciated. We can hypothesize the following modes of transmission:

1. From HCWs to patients by exhaling or coughing the pneumococcus. This may occur when the HCW is a nasopharyngeal carrier and has close contact with the patient using inadequate precautions;
2. From patient to patient by means of contaminated respiratory secretions (sputum or saliva). In this case, HCWs can disseminate the pneumococcus through contact with contaminated material when using inappropriate barrier precautions (e.g., gloves, gowns, masks); and
3. From patient to patient by exhaling or coughing the pneumococcus in overcrowded hospitals and long-term care institutions where space and ventilation are inappropriate.

Once colonized, hospitalized patients are at risk for pneumococcal infections when:

1. They suffer from serious underlying diseases with impaired immunity, chronic pulmonary conditions, and other debilitating diseases;
2. They receive antibiotics which may select resistant pneumococci; and
3. They undergo instrumentations (e.g., endotracheal or nasopharyngeal tubes) or surgical procedures (e.g., surgery of abdominal cavity, lungs, and head and neck).

Recent studies of health care associated pneumonia have found that *Streptococcus pneumoniae*, among other gram-positive cocci, is increasingly recognised as an important agent.

Health care associated pneumococcal pneumonia can be classified into two categories:

1. Early pneumonia (<5 days) occurs mainly in patients who require emergent tracheal intubation (e.g., head trauma with low level of consciousness). This infection is usually caused by the own patient's flora (previous pneumococcal carriers), and the intubation process spreads the pneumococcus into the lower respiratory tract.
2. Late pneumonia (>= 5 days) may occur more often in patients undergoing surgery, who are immunosuppressed or debilitated, as well as in intubated patients in ICUs. This is more often caused by drug-resistant strains. Other health care associated pneumococcal infections may include: health care associated sinusitis in patients with nasogastric tube; meningitis after otic surgery or neurosurgery; and post-surgical intra-abdominal infection.

Few data are available regarding the global burden of pneumococci in health care associated pathogens. In our institution (Hospital Bellvitge, University of Barcelona) among all episodes of pneumococcal bacteremia, about 10–15% are health care associated. In addition, *Streptococcus pneumoniae* accounted for 1–2% of all health care associated bacteremias, and for 10–15% of all health care associated bacteremic pneumonias.

Suggested Practices

The hospital epidemiologist and infection control practitioners should know the target population at high risk for pneumococcal

infections (see *Controversial Issues*), and identify possible outbreaks caused by multiple antibiotic resistant strains in the hospital setting. It is fundamental for the microbiology laboratory to conduct a surveillance of all pneumococcal isolates and their antibiotic susceptibility and to study, when necessary, serotypes and clones.

Infection control measures for health care associated pneumococcal infections have not been widely established. In order to properly implement these measures, we should consider the following:

1. Compliance with barrier precautions;
2. Prudent use of antibiotics; and
3. Use of pneumococcal vaccination.

Although it is thought that transmission of pneumococci in the hospital is uncommon, the application of isolation measures and barrier precautions could be necessary, particularly when an outbreak caused by multiple antibiotic-resistant strains is detected. During an outbreak, these patients should be isolated in a single room, and HCWs should ensure the following infection control measures: appropriate hand washing and correct utilization of gloves, gowns and masks when in contact with respiratory secretions. In addition, disinfection of respiratory equipment should be strengthened.

During an outbreak caused by a multi-resistant pneumococcal strain in a closed institution, the screening of nasopharyngeal carriers could be appropriate. However, the administration of antibiotics to persons in contact with infected patients to eradicate the carriers is a controversial issue.

Prudent use of antibiotics is essential to prevent the emergence of resistant pneumococci. Prolonged use of beta-lactams, particularly at low doses, is associated with carriage of penicillin resistant pneumococci in children. Thus, antibiotics may produce a selective pressure of pneumococci harbouring in the nasopharynx, eliminating the susceptible strains and emerging the resistant ones, mostly concentrated in a few serotypes and clones. The appropriate use of antibiotics is particularly important in the hospital setting, nursing homes and other closed institutions where the emergence and spread of resistant pneumococcal clones is easier.

Prevention of pneumococcal infection by means of vaccination programs is essential. The use of PPV-23 may prevent the development of pneumococcal bacteremia in adults, but it is not immunogenic in children. Recently, the use of conjugate pneumococcal vaccines (PCV7, PCV9, and PCV13)) in children has been associated with a decreased incidence of pneumococcal disease. However, it is not well elucidated if these vaccines produce a permanent reduction of carriers or if there would be a replacement with serotypes not included in the vaccine. Future vaccine developments including the pneumococcal surface proteins, which are non-serotype dependent, may substantially improve the current options.

Summary

Streptococcus pneumoniae is increasingly reported as a pathogen causing infections in hospitals, healthcare settings and nursing homes. These infections are often due to multiple antibiotic resistant pneumococcal serotypes and are likely to appear as small outbreaks. Therefore, it is mandatory for the microbiology laboratory to survey all invasive pneumococcal isolates together with their antibiotic susceptibility and study of serotypes and clones whenever necessary.

Currently, there is scarce information about the prevalence of pneumococcal carriers and the transmission mechanisms of *Streptococcus pneumoniae* in hospitals and nursing homes. Besides, infection control measures to prevent endemic and epidemic health care associated pneumococcal infections have not been properly undertaken. However, compliance with barrier precautions, prudent use of antibiotics in the hospital setting and the administration of pneumococcal vaccine should be strengthened when an outbreak is suspected.

Since the introduction of pneumococcal conjugate vaccines in children, there has been a decline in the incidence of invasive pneumococcal disease. However, there are some preliminary data suggesting that emergence of virulent clones of non-vaccine serotypes may be a problem in the near future. Epidemiological surveillance is essential to evaluate the best vaccination strategy in different patient populations.

References

Nuorti JP, Butler JC, Crutcher JM, et al. An outbreak of multidrug-resistant pneumococcal pneumonia and bacteremia among unvaccinated nursing home residents. *N Engl J Med*. 1998. 338(26):1861–1868.

Cimolai N, Cogswell A, Hunter R. Nosocomial transmission of penicillin-resistant *Streptococcus pneumoniae*. *Pediatr Pulmonol*. 1999. 27(6):432–434.

Bresnitz E, Grant C, Ostrawski S, et al. Outbreak of pneumococcal pneumonia among unvaccinated residents of a nursing home—New Jersey. *JAMA*. April 2001. 286(13):1570–1571.

Weiss K, Restieri C, Gauthier R, et al. A nosocomial outbreak of fluoroquinolone-resistant *Streptococcus pneumoniae*. *Clin Infect Dis*. 2001. 33(4):517–522.

Melamed R, Greenberg D, Landau D, et al. Neonatal nosocomial pneumococcal infections acquired by patient-to-patient transmission. *J Infect Dis*. 2002. 34(5):385–386.

Tan CG, Ostrawski S, Bresnitz EA. A preventable outbreak of pneumococcal pneumonia among unvaccinated nursing home residents in New Jersey during 2001. *Infect Control Hosp Epidemiol*. 2003. 24(11):848–852.

Subramanian D, Sandoe JAT, Keer V, et al. Rapid spread of penicillin-resistant *Streptococcus pneumoniae* among high-risk hospital inpatients and the role of molecular typing in outbreak confirmation. *J Hosp Infect*. 2003. 54(2):99–103.

Bouza E, Pintado V, Rivera S, et al. Nosocomial bloodstream infections caused by *Streptococcus pneumoniae*. *Clin Microb Infect*. 2005. 11(11):919–924.

Whitney CG, Pilishvili T, Farley MM, et al. Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: A matched case-control study. *Lancet*. 2006. 368(9546):1495–1502.

Lyytikainen O, Klemets P, Ruutu P, et al. Defining the population-based burden of nosocomial pneumococcal bacteremia. *Arch Intern Med*. 2007. 167(15):1635–1640.

Pallares R, Liñares J, Vadillo M, et al. Resistance to penicillin and cephalosporin and mortality from severe pneumococcal pneumonia in Barcelona, Spain. *N Engl J Med*. 1995. 333(8):474–80.

Guillet M, Zahar JR, Timsit MO, et al. Horizontal transmission of *Streptococcus pneumoniae* in the surgical ward: A rare source of nosocomial wound infection. *Am J Infect Control*. 2012. 40(1):71–72.

CHAPTER 46

LEGIONELLA

Marc Struelens, MD, PhD

Key Issue

Health care associated legionellosis (also called Legionnaires' disease) is a serious pneumonia caused by inhalation of *Legionella* in aerosols from a contaminated hospital water system. Prevention should be based on a risk management plan including targeted surveillance for cases, adequate design and maintenance of water distribution system and adherence to appropriate respiratory care practices.

Known Facts

- *Legionella* cause up to 10% of health care associated pneumonias; depending on the country, surveillance data indicate that 2 to 15% of cases of legionellosis are health care associated. Cases may occur sporadically or as epidemics.
- The majority of cases are caused by *Legionella pneumophila*, with over 80% caused by *L. pneumophila* serogroup 1.
- The mortality is 10–15% and is increased by a delay in diagnosis and starting specific antimicrobial treatment.
- *Legionella* sp are part of the normal flora of fresh water bodies and proliferate to high concentrations as biofilms in man-made hot water systems with a temperature of 25–42˚C. Hospitals with contaminated water systems are at increased risk of health care associated legionellosis.
- Transmission to hospitalized patients occurs most frequently by inhalation of aerosols generated by using outlets (faucets, shower) of a heavily contaminated domestic water system and less commonly by direct bronchial instillation during respiratory care using tap water.
- Risk factors for transmission include the concentration of *Legionella* in water, the virulence of the strain, the extent of aerosol exposure and patient immune status.

- Patients at increased risk are those under immunosuppresion, particularly organ transplant recipients, treated with corticosteroids, male, elderly, smokers and those with chronic lung diseases.
- Diagnosis requires the use of special methods, including culture of respiratory secretions on special media, detection of urinary antigen (*L. pneumophila* serogoup 1 mainly), serology and PCR.
- Most outbreaks were reported in hospitals with extensive contamination (>30% positive outlets) and high concentration ($>10^3$/L) of *Legionella* in water.
- Health care associated outbreaks can be controlled effectively once the source is identified and adequate water disinfection is carried out (shock treatment followed by long-term suppressive measures).

Controversial Issues

- The true incidence of health care associated legionellosis is unknown due to under-diagnosis and under-reporting.
- The predictive value of monitoring the concentration of *Legionella* in hospital water systems is undefined, due to non-standardization of sampling, wide temporal variation in bacterial concentration over time and variation in patients' exposure and susceptibility in different institutions. Public authorities in different countries have issued various norms of maximal *Legionella* concentration for hospital water systems (ranging from 10^1 to 10^4 /L).
- The optimal methods of water disinfection including thermal disinfection (>60°C), hyper-chlorination, ultra-violet light, copper-silver ionization, monochloramine and chlorine dioxide treatment have not been defined.

Suggested Practice

- Each hospital should develop and implement a *Legionella* Risk Management Plan, with the assistance of Management, Technical Plant, Microbiology and Infection Control departments.
- This plan is composed of the following parts: (1) plan & technical description of the water systems, and identification

of weak points (eg, temperature below 55°C, stagnation, corrosion); (2) bacteriological survey of *Legionella* contamination of the system; (3) analysis of patients population at risk and surveillance for cases of pneumonia; (4) risk control measures and maintenance of the systems to prevent cases or control transmission after a cluster of cases, if any.

- Surveillance for cases of *Legionella* pneumonia should use the combination of at least two diagnostic methods such as culture and urinary antigen tests.
- Prevention and control measures should aim at reducing the proliferation of *Legionella* and avoiding the generation of aerosols. Codes of good engineering practice exist in most countries and should be consulted. The main rules are to ensure water temperature <20°C or >50°C, regular water circulation and cleanliness of the system.
- The selection and operation of a water treatment program including *Legionella* disinfection should be made by competent technical services. Microbiological water monitoring is useful to assess the efficacy of the program.
- Respiratory care and flushing of naso-gastric tubing should be done with sterile water.
- The detection of sporadic or cluster of cases of health care associated legionellosis should prompt an immediate investigation to identify the source of contamination. Genotyping *Legionella* isolates from cases and the suspected environmental source is useful to confirm the source. Shut down the suspected source and disinfect it or remove the aerosol producing equipment. Consider general shock treatment of water system if it is extensively contaminated.

References

Exner M, Kramer A, Lajoie L, Gebel J, Engelhart S, Hartemann P. Prevention and Control of Healthcare-Associated Waterborne Infections in Healthcare Facilities. *Am J Infect Control*. 2005. 33(Suppl 5):S26–40.

O'Neill E, Humphreys H. Surveillance of Hospital Water and Primary Prevention of Nosocomial Legionellosis: What is the Evidence? *J Hosp Infect*. 2005. 59:273–9.

Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. CDC: Healthcare Infection Control Practices Advisory Committee, Guidelines for Preventing Healthcare-Associated Pneumonia. 2003; Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR*. 2004. 53(RR-3):1–36.

Kim BR, Anderson JE, Mueller SA, et al. Literature Review—Efficacy of Various Disinfectants Against *Legionella* in Water Systems. *Water Res*. 2002. 36:4433–44.

Health and Safety Commission 2000. Legionnaires' Disease. The Control of *Legionella* Bacteria in Water Systems. Approved Code of Practice and Guidance L8. Sudbury, UK: HSE Books. ISBN 0-7176-1772-6.

CDC. Legionellosis—United States, 2000–2009. *MMWR*. 2011. 60:1083–6.

Irons JF, Dunn MJ, Kefala K, et al. The Effect of a large Legionnaires' Disease Outbreak in Southwest Edinburgh on Acute and Critical Care Services. *QMJ*. 2013. 106:1087–94.

CHAPTER 47

Carbapenem-resistant *Enterobacteriaceae*

Eva-Brigitta Kruse, MD and Hilmar Wisplinghoff, MD

Key Issues

Carbapenem-resistant *Enterobacteriaceae* (CRE), especially carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae*, are increasingly prevalent pathogens in hospitalized patients and can cause a variety of infections such as urinary tract infections, wound infections and respiratory tract infections. Their importance derives from the fact that they can spread rapidly in the hospital setting, and that they are commonly multi-drug resistant, leaving few therapy options.

Known Facts

Enterobacteriaceae like *E. coli*, *Klebsiella spp*., *Enterobacter spp*., *Citrobacter spp*. or *Proteus spp*. are gram-negative rods that can be part of the normal enteric flora. Previous antibiotic therapy, underlying systemic illness, and prolonged hospital stays have been identified as risk factors for colonization of patients with carbapenem resistant strains. The use of catheters and mechanical ventilation (MV) is also associated with an increased risk of CRE colonization. In addition, CRE can be transmitted through direct contact with contaminated surfaces, colonized or infected patients, or more frequently by the hands of health care workers and other hospital personnel. Some species, such as *Klebsiella* spp., have demonstrated a propensity to cause large health care associated outbreaks. Since most *Enterobacteriaceae* are part of the normal intestinal flora, asymptomatic colonization with CRE is common, however, as with other resistant organisms, CRE colonization increases the risk of CRE infection. This is of special importance in neonates, ICU patients and immunocompromised patients.

The prevalence of CRE varies widely between different species and different geographical regions. In the US, carbapenem-resistance rates are quoted as 0.1% and 5.3% for *E. coli* and *K. pneumoniae,* respectively, while in Europe, most countries report resistance rates below 1% for both pathogens. However, local and regional differences can be enormous: All over the world, several regions have been identified where CRE are endemic, e.g. in Greece, parts of South-east Asia or the north-eastern region of the USA. Even in settings where resistance rates are still low, a steady rise over the past decade has been observed.

Depending on the virulence of the particular pathogen, the site of colonization, and a variety of host-related factors, CRE can cause nearly all kinds of infections, most commonly urinary tract infections, pneumonia (usually ventilator-associated (VAP)), wound infections or bloodstream infections. As CRE are commonly multi-drug resistant, comprehensive antimicrobial susceptibility testing is mandatory and treatment should be adapted accordingly.

In most countries, scientific societies and/or public health agencies have published guidelines and recommendations on how to handle CRE colonization and infection, and how to prevent transmission and limit spread. These can be used as a basis and should be adapted to local circumstances to implement an effective programme in the hospital or other health care facilities.

Controversial Issues

Generally, there are currently only limited data available on a number of important issues regarding detection, management and treatment of CRE. There is currently no generally agreed recommendation for the laboratory detection of carbapenem resistance. Currently available methods include screening via routine antibiotic susceptibility testing using ertapenem, meropenem or faropenem and/or the cultivation of bacteria on different CRE-selective media. For confirmation, several methods including the modified Hodge test, inhibitor-based assays, molecular methods or mass spectrometry (MALDI-TOF) may be used. Molecular methods, while having a high specificity and sensitivity, are currently not widely used in the routine detection due to various practical and financial issues.

The impact of routine surveillance cultures throughout the hospital stay is currently not supported by strong evidence and therefore not generally recommended. They may, however, be useful during outbreak situations and in high-risk patients with prolonged hospital stays.

While cohorting patients and staff in an outbreak setting seems to be beneficial, it is uncertain if the spread of CRE in non-outbreak situations can be successfully limited by these practices as well.

There is currently no decolonization strategy with proven efficacy, even though attempts have been made to eradicate CRE from the gastrointestinal tract through selective digestive decontamination. The long-term effectiveness and adverse effects of this approach, especially in an endemic setting, are unclear so that it is not a generally recommended measure. Similarly, daily chlorhexidine bathing has been performed to contain outbreaks, but its value in eradicating CRE and limiting spread is still under investigation.

Suggested Practice

- Identify high-risk patients on admission to the hospital and/or on admission to high-risk areas such as intensive care units. High-risk patients should include those from regions, countries or institutions where CREs are endemic, patients with a recent history of CRE colonization, and those who have had a recent contact with a known CRE carrier (e.g. shared a hospital room).
- Screen high-risk patients on admission to the hospital. Pre-emptive single-room isolation should be performed until a negative screening result is confirmed.
- Work together with a laboratory that uses fast and accurate methods for CRE detection and is able to provide rapid notification of the results. Early identification is vital both for effective therapy and infection control measures.
- Notify the hospital infection control team if transmission on the ward is suspected and suggest appropriate control measures, including potentially additional screening on the ward affected.

- Observe hand hygiene as suggested by the WHO at all times, with all patients, and with all procedures. Of special importance are hand disinfection before and after contact with a patient and his or her surroundings, and the correct use of gloves.
- Use full contact precautions for CRE patients, including the wearing of gowns and gloves and single-room isolation. If care in a single room is not possible, at least provide a separate toilet for the patient and perform barrier precautions at the bedside.
- Perform daily decontamination of the patient environment, using effective disinfectants. Single-use equipment should be preferred where possible. All other equipment must be properly decontaminated before use on another patient.
- Restrict the use of devices (venous catheters, urinary catheters etc.) as far as possible and review their need on a daily basis.
- Implement an antimicrobial stewardship programme in the hospital to improve antimicrobial therapy and decrease the development of resistance and therefore colonization pressure.
- Make sure all staff are aware of the standard hygiene measures and additional barrier precautions and know when and how to perform them. Regular training is important; monitoring of compliance with infection control measures is recommended. CRE measures should be part of a comprehensive institutional infection control program.
- Be aware of national guidelines and notification systems as appropriate. If CRE patients are transferred to other hospitals or care facilities, ensure CRE status is communicated before transfer.

Summary

Carbapenem resistance has increased in all regions of the world over the past decade. Colonization and infection rates are rising and have reached endemic levels in some regions. Although there is little specific evidence for many infection control measures, there is agreement on the general components of an adequate control programme. These include surveillance and rapid identification of CRE carriers, barrier precautions for all CRE patients (single-room care, wearing protective equipment), adherence to hand hygiene and standard hygiene regimes, safe and effective

disinfection measures, education, and continuous training of all staff, organizational awareness of the problem of multi-drug resistant organisms and the implementation of appropriate infection control and antimicrobial stewardship programmes.

References

CDC. CDC National Center for Emerging and Zoonotic Infectious Diseases, Division of Healthcare Quality Promotion. Guidance for Control of Carbapenem-Resistant Enterobacteriaceae (CRE). 2012 CRE Toolkit. http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html (Accessed 19 August 2013).

Swaminathan M, Sharma S, Poliansky Blash S, et al. Prevalence and Risk Factors for Acquisition of Carbapenem-Resistant Enterobacteriaceae in the Setting of Endemicity. *Infect Control Hosp Epidemiol*. 2013. 34(8):809–17.

CDC. Vital Signs: Carbapenem-Resistant Enterobacteriaceae. *MMWR*. 2013. 62(9):165–70.

Glasner C, Albiger B, Buist G, et al. for the European Survey on Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) working group. Carbapenemase-producing Enterobacteriaceae in Europe: A survey among national experts from 39 countries. *Eurosurveillance*. February 2013. 18(28):pii=20525.

Hara G, Gould I, Endimiani A, Pardo P, Daikos G, Hsueh P, et al. Detection, treatment, and prevention of carbapenemase-producing Enterobacteriaceae: Recommendations from an International working group. *J Chemother*. 2013. 25:129–40

Mattner F, Bange FC, Meyer E, Seifert H, Wichelhaus TA, Chaberny IF. Preventing the spread of multidrug-resistant gram-negative pathogens: Recommendations of an expert panel of the German Society for Hygiene and Microbiology. *Dtsch Arztebl Int*. 2012. 109(3):39–45.

Robert-Koch-Institut, Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO). Hygienemaßnahmen bei Infektionen oder Besiedlung mit multiresistenten gramnegativen Stäbchen. http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Kommission/Downloads/Gramneg_Erreger.pdf;jsessionid=C958194A6A51315CB103A63FCCCF05F7.2_cid372?__blob=publicationFile. (Accessed 19 August 2013).

WHO. WHO Guidelines on Hand Hygiene in Health Care. http://whqlibdoc.who.int/hq/2009/who_ier_psp_2009.07_eng.pdf. (Accessed 19 August 2013).

Kruse EB, Aurbach U, Wisplinghoff H. Carbapenem-Resistant Enterobacteriaceae: Laboratory Detection and Infection Control Practices. *Curr Infect Dis Rep*. October 12, 2013.

CHAPTER 48

Bacterial Enteric Pathogens: *Clostridium difficile*, *Salmonella*, *Campylobacter*, *Shigella*, *Escherichia coli* and others

Olivier Vandenberg, MD, PhD, Michèle Gerard, MD
and Awa Aidara Kane, PhD,

Key Issue

Clostridium difficile, *Salmonella*, *Campylobacter*, *Shigella*, *Escherichia coli*, *Yersinia enterocolitica*, *Vibrio cholerae*, and *Vibrio parahaemolyticus* are among the various agents which may cause acute gastrointestinal infections in long-term care facility residents and health care workers.

Known Facts

- *Clostridium difficile*-associated diarrhea (CDAD) a very common health care associated infection, is associated with substantial morbidity and mortality and imposes an important financial burden on healthcare institutions. Three steps are necessary for the development of CDAD: distortion of the normal faecal flora (usually by antibiotics), acquisition of the pathogen (i.e., *Clostridium difficile)*, and toxin production by the *Clostridium difficile* strain. Risk is modified by host susceptibility factors including older age, manipulation of the gastrointestinal tract (enemas, surgery), chemotherapy, laxative use, antiperistaltic drugs, length of hospital stay, and rate of endemic disease in the hospital. *Clostridium difficile* persistently contaminates the hospital environment through the formation of spores that persist for prolonged periods. The hands of hospital workers have been documented to be contaminated frequently by *Clostridium difficile* following contact with patients who are asymptomatically colonized or who have CDAD, or by contact with the environment of these patients. *Clostridium difficile* has

been transmitted by commodes, bathing tubs for neonates and rectal thermometers.

- Salmonellosis is the most commonly reported foodborne disease resulting from improperly handled animal and poultry products. Ninety-two percent of all cases are due to raw or partially cooked eggs but undercooked poultry, beef, and pork also are significant sources. Contamination may occur either during food processing by contact with animal products/faeces, or during food preparation from food handlers. Chronic carriers of *Salmonella* pose a particular risk for transmitting this infection.
- In developing countries, nontyphoid *Salmonella* spp are increasingly important health care associated pathogens, causing septicemia in children. Most of these *Salmonella* spp are resistant to multiple antibiotics. The dissemination of these resistant strains occurs from person-to-person. The majority of outbreaks have occurred in neonatal and paediatric wards, but community outbreaks in villages have also been reported.
- *Campylobacter* is one of most commonly recognised causes of bacterial gastroenteritis in man. Raw or inadequately heat-treated milk and inadequately treated water have been incriminated as sources of massive outbreaks of infection. Direct transmission is mainly occupational (farmers, butchers, abattoir workers, poultry processors), but domestic animals can bring infection into ordinary homes. Inter-human transmission has been described infrequently in young children. Health care associated spread within neonatal units has been observed on rare occasions. The putative causes of these outbreaks were an inadequately disinfected communal baby bath and an incubator that was not disinfected between babies.
- Shigellosis is one of the most common causes of gastroenteritis. Transmission is due to improper handwashing and inadequate toilet facilities and occurs via food items such as soups, salads, and sandwiches; however, person-to person spread and transmission by flies may also occur, since few organisms are necessary to cause disease. After ingestion of a very low inoculum (< 100 of shigella organisms), patients typically present with dysentery and fever. Patients are infectious during the acute infection and until the organism is no longer present in the faeces.

- Enterohemorrhagic *Escherichia coli* (EHEC), particularly *E.coli* serotype O 157:H7, is the leading cause of hemorrhagic colitis and hemolytic uremic syndrome (HUS). EHEC infections have been associated with the ingestion of contaminated hamburgers, milk, water, fruit, and vegetables. However person-to person transmission is possible.
- Transmission of enterotoxigenic *E.coli* (ETEC) occurs mainly by food and water. It rarely occurs from person—to person.
- Enteropathogenic *Escherichia coli* (EPEC) is an infrequent cause of outbreaks of diarrhoea in hospitalised infants.
- Enteroaggregative *Escherichia coli* is an emergent enteropathogen which has been associated with both health care associated and community outbreaks worldwide.
- *Vibrio cholerae* is transmitted primarily via contaminated water and by the ingestion of contaminated shellfish. Person-to-person spread is uncommon. Hospital workers rarely contract the disease.
- *Vibrio parahaemolyticus* is a common pathogen in countries where raw and undercooked seafood is consumed. Symptoms can vary but patients usually present with nausea, vomiting, and cramps. Fever and chills sometimes can occur.
- *Yersinia enterocolitica* is a common cause of enterocolitis in children in developed countries. It is characterized by either watery or bloody diarrhoea with abdominal pain and fever. Improperly cooked pork and milk are the main sources of transmission. Health care associated transmission occurs very rarely.

Controversial Issues

- Gastroenteritis caused by bacterial pathogens often may be confused with enteric infections caused by parasitic, fungal, or viral agents.
- The decision whether or not to use antibiotics or antimotility drugs is difficult in the absence of specific laboratory diagnosis of the bacterial pathogens.
- Indiscriminate treatment with antibiotic agents or antimotility drugs may create serious problems by encouraging the development of multi-drug resistant bacteria or chronic carriers.

- The incidence of acute gastroenteritis caused by enteric pathogens is greatly underestimated in many locations because of limited surveillance, limited laboratory facilities to diagnose the common bacterial agents, or both.

Suggested Practice

- Most bacterial enteric pathogens are transmitted by direct contact. Effective handwashing practice is the most important measure to prevent transmission. Additional interventions include:
  1. Glove use when handling faecally contaminated items. Hand hygiene after glove use is essential and often forgotten;
  2. Improvements in hygiene and socio-economic conditions;
  3. Safe water supply and sanitary disposal of faecally contaminated materials;
  4. Environmental interventions including proper disinfection of rectal thermometers between use by different patients, proper disinfection of endoscopes, proper terminal disinfection of rooms and surface disinfection with hypochlorite;
  5. Thorough cooking of food; and
  6. Isolation of ill persons with personal sanitary or commode.
- Food service personnel must be very careful about personal hygiene, working habits, and their health. All health care and food service personnel with an acute diarrhoeal illness should stop working until diarrhoea has resolved.
- Antibiotics should not be routinely used to prevent transmission. When antibiotics are used to treat patients, appropriate doses and duration of therapy should be used.
- Adequate laboratory facilities are mandatory allowing all enteric bacteria isolated from health care associated infections to be well characterized. Establishing a provisional microbiology laboratory is also a valuable tool to investigate and control outbreaks even in remote areas.

Summary

A wide variety of organisms may cause outbreaks in long-term facilities (*Clostridium difficile, Salmonella, Campylobacter, Shigella, Escherichia coli* O157:H7, and others). Gastroenteritis caused by these different groups of bacteria is a leading cause of morbidity and mortality in developing countries. However, difficulty in identifying certain enteric pathogens in many laboratories leads to marked under-reporting.

The majority of the gastrointestinal pathogens are transmitted through the faecal-oral route. These pathogens can survive in soil, water, and food. Outbreaks are frequently related to ingestion of contaminated food or water and occur more frequently in developing countries. Improvements in hygiene and socio-economic conditions can dramatically reduce the transmission of these organisms.

Many studies from the developing world have emphasized the emerging importance of multidrug-resistant *Salmonella* spp as health care associated pathogens in children. The clinical microbiologist should be responsible for the identification of all isolates of health care associated infections and work effectively with all other members of the infection control committee to identify and control outbreaks.

References

Knight CL, Surawicz CM. Clostridium difficile Infection. *Med Clin North Am*. 2013. 97:523–36.

Wadula J, von Gottberg A, Kilner D, de Jong G, Cohen C, Khoosal M, Keddy K, Crewe-Brown H. Nosocomial outbreak of extended–spectrum beta-lactamase-producing Samonella isangi in pediatric wards. *Pediatr Infect Dis J*. 2006. 9:843–844.

Vandenberg O, Skirrow MB, Butzler JP. *Campylobacter* and *Arcobacter in* Topley and Wilson's Microbiology and Microbiolial Infections (10th Edition), Boriello SP, Murray PR, Funke G (Eds). London: Hodder Arnold, ASMA Press, 2005. Pgs. 1541–1590.

Villaseca JM, Hernández U, Sainz-Espuñes TR, Rosario C, Eslava C. *Enteroaggregative Escherichia coli* an emergent pathogen with different virulence properties. *Rev Latinoam Microbiolo*. 2005. 47:140–159.

Murni I, Duke T, Triasih R, Kinney S, Daley AJ, Soenarto Y. Prevention of nosocomial infections in developing countries, a systematic review. *Paediatr Int Child Health*. 2013. 33:61–78.

CHAPTER 49

Other Enterobacteriaceae

Heike von Baum, MD, Constance Wendt, MD

Key Issue

Enterobacteriaceae (other than enteropathogenic *Salmonella*, *Shigella*, and *E. coli*) are important health care associated pathogens. Hundreds of different types of beta-lactamases including extended spectrum beta-lactamases (ESBL) have been characterized in multiresistant Enterobacteriaceae. A new challenge is the worldwide spread of carbapenemase-producing and thus panresistant Enterobacteriaceae (CRE). Most prominent are carbapenemase-producing *Klebsiella pneumoniae* (KPC) as well as New Delhi metallo-ß-lactamase (NDM) or OXA-48 carbapenemase positive strains. Multiresistant Enterobacteriaceae have emerged as significant health care associated pathogens and are frequently isolated from urine, respiratory secretions and wounds.

Known Facts

- In an endemic situation, colonization or infection among hospitalised patients results primarily from the patients' preexisting indigenous flora.
- Hospital transmission of Enterobacteriaceae frequently involves the hands of healthcare workers or contaminated inanimate surfaces.
- Outbreaks of multiresistant Enterobacteriaceae have been linked to understaffing, overcrowding and poor hygiene practices in the hospital.
- Colonization with Enterobacteriaceae predisposes the hospitalized patient for health care associated infections.
- Risk factors for acquiring (multiresistant) Enterobacteriaceae are severity of illness, mechanical ventilation (MV) and presence of indwelling devices.
- CRE acquisition outside of healthcare institutions has been linked to food products, travel to high risk areas and medical tourism.

- Patients with CRE bacteremia have high mortality rates (up to 50%) due to limited treatment options.
- Alcohol-based hand rubs are the most efficacious agents for reducing the number of Enterobacteriaceae on the hands of healthcare providers.

Controversial Issues

- The impact of antibiotic restriction on the emergence and spread of multiresistant Enterobacteriaceae in the hospital is under investigation. Several studies examined the effect of restricted use of antibiotics particularly third-generation cephalosporins and carbapenems on the prevalence of resistant Enterobacteriaceae offering conflicting results.
- Many patients are colonized with (multiresistant) Enterobacteriaceae at the time of admission to ICUs. Thus it remains controversial whether policies confined to ICUs or selected departments have an impact on the overall prevalence of Enterobacteriaceae. Several studies have shown a low rate of hospital transmission of ESBL producing Enterobacteriaceae (susceptible to carbapenems) except for specific high risk areas e.g. NICUs.
- Detection of ESBL producing Enterobacteriaceae remains a challenge for the microbiology laboratory. Routine methods may fail to identify all ESBL producing strains. Laboratory detection and reporting have to be improved according to approved standards e.g. the NCCLS guidelines.
- Detection of CRE has been facilitated by removing the requirement for carbapenemase testing through a change in the definition of susceptibility breakpoints.

Suggested Practice

Prevention of Transmission

- Strict hand hygiene.
- Identification and elimination of environmental sources.

Multiresistant Strains

- Isolation of patients colonized or infected with CRE.
- Consider isolation of colonized or infected patients with ESBL producing strains (susceptible to carbapenems) in specific high risk areas.

– Contact precautions: gowns, gloves, and single-use or dedicated equipment.
– Education of staff and evaluation of nursing care practices.
– Increase nurse-to-patient ratio, if feasible.
– Screen high-risk patients for CRE at admission.
– Screen epidemiologically linked cases to CRE patients.

Outbreak Situation

– Cohort patients and healthcare providers.
– Consider chlorhexidine bathing of CRE patients.
– Identify further colonized and/or infected patients.
– Intensify communication with microbiology laboratory.
– Review the antibiotic policy of the affected wards.
– Contact the Health department and discuss public health support.

Prevention of the Evolution of Colonization with Enterobacteriaceae to Infection:

- Discontinue the use of indwelling devices as soon as possible.
- Promote antibiotic stewardship.

For specific recommendations concerning enteropathogenic Enterobacteriaceae, bladder catheterisation, ventilators, and preoperative patient care, see the appropriate chapter.

Summary

The predominant genera of Enterobacteriaceae are *Escherichia, Klebsiella, Enterobacter*, *Citrobacter, Proteus, Serratia, Salmonella* and *Shigella*. Enteric pathogens are not discussed in this chapter.

Colonization of the gastrointestinal tract and less frequently the respiratory tract is common in non-hospitalized patients. Colonized patients in the hospital have a significantly increased risk to develop an infection. Hospital transmission occurs via the hands of healthcare workers or via contaminated equipment and supplies.

Since 1983, the prevalence of Gram-negative rods producing extended-spectrum-ß-lactamases (ESBL) has steadily increased. A recent threat is the worldwide spread of carbapenemase producing, panresistant strains (CRE). Outbreaks have been described most frequently with ESBL-producing

Klebsiella or multiresistant *Enterobacter* strains. Identification of ESBL-producing Enterobacteriaceae and CRE remains difficult due to the limited sensitivity of diagnostic standard procedures in the microbiology laboratory.

References

Centers for Disease Control and Prevention: Guideline for Hand Hygiene in Health—Care Settings. *MMWR*. 2002. 51(RR-16):1–47.

Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. Twenty Second Informational Supplement (January 2012), CLSI document M 100-S22. Wayne, Pennsylvania, 2012.

Harbarth S, Sudre P, Dharan S, et al. Outbreak of *Enterobacter cloacae* Related to Understaffing, Overcrowding, and Poor Hygiene Practices. *Infect Control Hosp Epidemiol*. 1999. 20:598–603.

Centers for Disease Control and Prevention: Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE) 2012 CRE Toolkit http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html.

Ben-David D, Maor Y, Keller N, et al. Potential role of active surveillance in the control of a hospital-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* infection. *Infect Control Hosp Epidemiol*. 2010. 31:620–626.

Gupta N, Limhago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: Epidemiology and Prevention. *Clin Infect Dis*. 2011. 53:60–67.

Marchaim D, Chopra T, Bhargava A, et al. Recent exposure to antimicrobials and carbapenem-resistant Enterobacteriaceae: The role of antimicrobial stewardship. *Infect Control Hosp Epidemiol*. 2012. 33:817–830.

Tschudin-Sutter S, Frei R, Dangel M, et al. rate of transmission of extended-spectrum beta-lactamase-producing Enterobacteriaceae without contact isolation. *Clin Infect Dis*. 2012. 55:1505–1511.

CHAPTER 50

PSEUDOMONAS AERUGINOSA

H. Wisplinghoff, MD, and Harald Seifert, MD

Key Issue

Pseudomonas aeruginosa is an important health care associated pathogen that causes serious health care associated infections and contributes significantly to morbidity and mortality.

Known Facts

P. aeruginosa is an aerobic Gram-negative rod that can be isolated from soil, water, plants, animals and humans, where it is uncommonly encountered as part of the normal transient flora. Human colonization occurs mostly at moist sites such as perineum, axilla and the ear. High concentrations of *P. aeruginosa*, among other pathogens, may also be found in the subungual areas of the hands.

Even though colonization in healthy individuals outside the hospital is rare, colonization rates may exceed 50% in patients with severe burns (skin), on mechanical ventilation (MV) (lower respiratory tract), receiving chemotherapy (GI-tract) or antimicrobial agents (any site).

Minimal nutritional requirements, the ability to grow in distilled water, and tolerance against a wide range of physical conditions contribute to the success of this opportunistic pathogen. Hospital reservoirs are predominantly moisture-associated and include sinks, showers, respiratory equipment, IV fluids, disinfectants, food mixers and vegetables. Outbreaks have been traced to a variety of sources including respiratory therapy equipment, endoscopes, contaminated mattresses, disinfectants, contaminated water supplies, iv solutions and environmental sources such pools used for physical therapy or hydrotherapy.

P. aeruginosa is the overall fifth most common health care associated pathogen, with a crude mortality ranging from 28% (ward) to 48% (ICU) in patients with health care associated bloodstream infection. Clinical manifestations include mostly

nosocomial or healthcare associated infections such as pneumonia (second most common cause of health care associated pneumonia), urinary tract infections (UTI, fourth), wound infections (surgical, fourth), bone and joint infections, and bloodstream infection (BSI, seventh), but also infections that are usually community-acquired such as gastrointestinal infections, skin and soft tissue infections, bacterial keratitis or ("malignant") otitis externa. A different clinical entity is lower respiratory tract infection in CF patients. Increasing resistance of *P. aeruginosa* to many commonly used antimicrobial agents leading to multi-drug resistant (MDR) strains often leaves few therapeutic options. Repeated susceptibility testing is warranted, due to the potentially rapid development of resistance to certain antimicrobial agents.

This organism is also a major cause of infection in highly compromised patients especially patients with cystic fibrosis (CF), neutropenia (and other immunosuppressive conditions) or severe burns.

Controversial Issues

Data on the impact of common environmental sources or patient-to-patient transmission on morbidity due to *P. aeruginosa* are still limited. The original source of the organism and the mode of transmission are often difficult to assess in an outbreak situation.

Suggested Practice

Adherence to standard infection control guidelines should limit the spread of *P. aeruginosa*. However, special attention is warranted in high-risk patients and hospital environments with endemic *P. aeruginosa*. Measures include:

- Hand disinfection between patient contacts using antiseptic agents (e.g., chlorhexidine or alcohol-based disinfectants).
- Wearing gloves when attending a patient, especially in ventilated patients, patients with severe burns and patients known to be colonized with *P. aeruginosa*.
- Mechanical cleaning of all medical equipment before sterilization, especially equipment used for mechanical ventilation (MV) and endoscopes.
- Proper sterilization of all respiratory therapy equipment including nebulizers and resuscitation bags.

- Using sterile fluids for nebulizers and preventing contamination of medication nebulizers and humidifiers.
- Using sterile water instead of tap water to rinse tracheal suction catheters.
- Avoiding the use of stock solutions for preparation of IV fluids.
- Avoiding the re-usage of a previously opened vial of water or sodium chloride solution for injection.
- Appropriate handling and storage of medical solutions.
- Surveillance, i.e. monitoring the prevalence of *P. aeruginosa*, especially of MDR strains.
- Detecting and eliminating potential reservoirs of cross-transmission.

If a cluster of infections due to *P. aeruginosa* is detected, potential reservoirs including all medical solutions such as IV fluids and sterile water should be screened in order to quickly detect and eliminate a potential reservoir. High-risk patients such burn-patients and immunocompromised patients should be monitored closely so that appropriate infection control measures can be implemented early.

Summary

P. aeruginosa is a major cause of health care associated infections that affects all patient populations and contributes significantly to morbidity and mortality. Colonization usually precedes manifest clinical infection. *P. aeruginosa* has been found to be an independent predictor of mortality in some studies of health care associated bloodstream infection.

Outbreaks have been traced to contaminated solutions (tracheal irrigate, mouthwash, iv-fluids), water, disinfectants and inadequately disinfected or sterilized endoscopes, ventilators or contaminated mesh grafts in burn patients but have also been linked to direct transmission via the hands of hospital personnel. Important measures of prevention include the detection and elimination of potential reservoirs, especially moist areas, the appropriate storage and handling of medical solutions, the monitoring of high-risk patients such as ICU- or burn-patients and the immediate investigation of detected clusters of infections due to *P. aeruginosa*.

References

Wisplinghoff H, et al. Nosocomial Bloodstream Infections in United States Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study. *Clin Infect Dis*. 2004. 39:309–17.

Kang, C-I, et al. Clinical Features and Outcome of Patients with Community-Acquired *Pseudomonas aeruginosa* Bacteraemia. *Clin Microbiol Infect*. 2006. 11:415–418.

Wisplinghoff H, Seifert H. *Pseudomonas aeruginosa, Acinetobacter baumannii* and other non-fermenting gram-negative bacilli *in* Cohen, Powderly & Opal: Infectious Diseases. 2010.

Jefferies JM, et al. *Pseudomonas aeruginosa* outbreaks in the neonatal intensive care unit—A systematic review of risk factors and environmental sources. *J Med Microbiol*. 2012. 61:1052–61.

Otter JA, et al. The role played by contaminated surfaces in the transmission of nosocomial pathogens. *Infect Control Hosp Epidemiol*. 2011. 32:687–99.

Kerr KG, Snelling AM. *Pseudomonas aeruginosa*: A formidable and ever-present adversary. *J Hosp Infect*. 2009. 73:338–44.

Tamma PD, et al. Combination therapy for treatment of infections with gram-negative bacteria. *Clin Microbiol Rev*. 2012. 25:450–70.

Fujitani S, et al. Pneumonia due to *Pseudomonas aeruginosa*: Part I: Epidemiology, clinical diagnosis, and source. *Chest*. 2011. 139:909–19.

CHAPTER 51

Helicobacter pylori

Veronique Y. Miendje Deyi, PharmD, PhD,
and Anne Dediste, MD

Key Issue

Helicobacter pylori (*H. pylori*) is the most prevalent chronic bacterial infection in humans, colonizing the stomach of approximately 50% of the world's population. Appropriate cleaning and disinfection (called reprocessing procedures) of endoscopes is mandatory to avoid health care associated transmission.

Known Facts

- *H. pylori* infection is associated with peptic ulcer disease, dyspepsia, idiopathic thrombocytopenic purpura, iron deficiency anemia, low-grade gastric Mucosa-Associated Lymphoid Tissue (MALT) lymphoma and non-cardiac gastric cancer.
- Most persons infected with *H. pylori* are asymptomatic.
- *H. pylori* is commonly acquired in childhood, and in developing countries the prevalence of *H. pylori* infection is as high as 50% by the age of 5 years.
- The rate of acquisition is higher in developing countries. In industrialized countries, *H. pylori* transmission has decreased over the last years, but lower socioeconomic status and household hygiene practices are key factors leading to a higher prevalence of colonization.
- Treatment is strongly recommended in peptic ulcer disease and low-grade MALT lymphoma when *H. pylori* is present.
- Iatrogenic transmission of *H. pylori* by upper gastrointestinal endoscopy has been documented but is nowadays limited in developed countries due to the use of single-use biopsy forceps and traceability of reprocessing of the endoscopes.

- *H. pylori* is susceptible to most commonly used high level disinfectants and, therefore, iatrogenic inoculation of the bacterium by endoscopy is unlikely if appropriate reprocessing procedures are strictly adopted.

Controversial Issues

- Humans are the natural reservoir of *H. pylori*. The pathogen is spread mainly through person-to-person transmission, either by fecal-oral or oral-oral routes. However, at least three other possible vectors have been suggested as possible routes of transmission: water, food and animals.
- Risk factors for infection include overcrowded households, institutionalization, low education of the parents, poor sanitation and poor water supply but both positive and negative studies have been published around these issues.
- There is no evidence to suggest that asymptomatic patients should be treated. It is reported that *H. pylori* colonization may confer protection against several disorders including esophageal diseases, asthma and allergic disorders.
- In developing countries, presumptive treatment seems to be followed by recurrence in many cases. Reinfection is also not infrequent in developed countries.
- There is increasing evidence to suggest that *H. pylori* plays a role in modulating systemic disease processes.
- A recent meta-analysis including 15 studies demonstrated an increased risk of *H. pylori* infection among gastroenterology personnel.
- Active or passive immunization is important for future prevention efforts; unfortunately, research in vaccine development is still unsuccessful.

Suggested Practice

- Wear personal protective equipment (gloves, gowns, mask and protective eyewear) during potentially contaminating procedures such as endoscopy, exposure to patient's secretions (feces, vomitus, gastric aspirates) and when possibly contaminated objects (syringes, biopsy forceps, pH electrodes) are handled.

- Strictly observe reprocessing procedures of gastrointestinal endoscopes and biopsy forceps as well as endotherapy devices (if not single-use) between patients.
- Wash instruments before disinfecting them.
- Use an appropriate disinfectant.
- Leave endoscopes in the disinfectant as long as recommended.
- If single-use biopsy forceps are not available, wash them before sterilization as well as devices breaching the gastric mucosa, because they are regarded as critical items.

Summary

Overwhelming evidence now confirms that *H. pylori* is a worldwide infection and plays a major etiologic role in the development of chronic superficial gastritis and peptic ulcer disease. *H. pylori* infection is also strongly associated with distal gastric adenocarcinoma and MALT lymphoma. The bacterium colonizes 25 to 50% of the general population in developed countries while in most developing countries colonization rates can be as high as 80 to 90%, especially in poor socioeconomic and sanitary conditions. Most infected persons tend to be asymptomatic, with only a minority (3–15%) developing peptic ulceration and even fewer gastric cancers (<3%).

How exactly *H. pylori* is transmitted and spreads in the community remains unclear. The human stomach is the only substantial reservoir of *H. pylori* that has been identified thus far, and the bacterium is believed to spread through person-to-person transmission. Both fecal-oral and oral-oral routes of transmission have been substantiated in different studies. On the one hand, the fecal-oral route is supported by both the presence of *H. pylori* in feces, although rarely detected and epidemiological evidence gathered in developing countries. On the other hand, the presence of the bacterium in gastric juice, dental plaque and saliva supports the assumption of an oral-oral transmission route. Indeed, African mothers feeding their infants with pre-masticated food have been identified as a risk factor for *H. pylori* infection in young children and several studies showed an increasing risk of infection within gastroenterology personnel.

Nevertheless both routes of transmission may co-exist, and besides, new potential reservoirs of *H. pylori* have now been identified, such as nonhuman primates, cats, flies, and environmental sources such as water.

The third and least common route of *H. pylori* transmission is iatrogenic inoculation of strains from one patient to another through a contaminated endoscope. Fiberoptic endoscopic examination of the gastrointestinal tract is known to result in iatrogenic transmission of infectious agents, such as *Salmonella* spp, *Pseudomonas* spp, *Acinetobacter* spp and viruses. Since the proportion of individuals positive for *H. pylori* is about half the world's population, the potential for endoscopic contamination with *H. pylori* and further iatrogenic transmission is high. Several studies have shown that endoscopes and biopsy forceps readily get contaminated after endoscopic examination of *H.* pylori-positive patients. Iatrogenic transmission of the bacterium has been estimated to occur in 4/1000 endoscopies when the infection rate in the population is about 50% but reprocessing (disinfection) and traceability has been improved. *H. pylori* has been found in vitro to be sensitive to common chemical disinfectants within 15 to 30 seconds, but a strict minimum of 10 min immersion is recommended. It is important to note that cleaning with soap and water and rinsing with alcohol have proved to be insufficient to decontaminate endoscopes and biopsy forceps. Cleaning followed by the use of 2% glutaraldehyde (or automated peracetic acid or chlorine dioxide 30 ppm) has been shown to effectively prevent *H. pylori* transmission.

A number of guidelines for cleaning endoscopes have been published. Endoscopes are classified by Spaulding as semicritical items, and should at least undergo high-level disinfection. Accessories such as biopsy forceps (if not single use) that breach the mucosa, are regarded as critical devices and therefore must be mechanically cleaned and then sterilized after each use.

How medical equipment should be disinfected is detailed elsewhere in this guide, and only a few points related to upper gastrointestinal endoscopy will be described here:

- As the status of the patient is often not known, all patients should be considered as potentially contaminated and, hence, the material used to treat them should be subjected to the same procedure.

- Every endoscopic procedure should be performed with a clean, disinfected endoscope.
- Endoscopic units must have written guidelines for decontamination and traceability.
- Manual brushing of the endoscope surface, valves, all internal channels (they should be thoroughly flushed with water and detergent), and endoscopic accessories (biopsy forceps, pH electrodes) must be done immediately after each patient to prevent secretions from drying. This step is mandatory before the disinfection process (even if an automated washer is used). Water, mechanical action, and suitable detergents or enzymatic products are used.
- Disinfection: the endoscope should be immersed in 2% glutaraldehyde or other equivalent chemical disinfectant. All channels must be filled with the disinfectant. A 20-minute exposure time is recommended to achieve high-level disinfection. However, if this is impracticable due to turnover pressure and when *Mycobacterium tuberculosis* is not suspected, an immersion of 10 to 20 minutes is usually considered acceptable.
- It is then necessary to rinse the instruments with preferably sterile water, internally and externally to remove all traces of disinfectant, as glutaraldehyde and most chemical disinfectants can have serious side effects. If tap water is used, rinsing the external surface as well as all channels with 70% alcohol and thoroughly drying them with compressed air are recommended.
- Alternatively, automatic wash machine endoscope can be used after manual brushing to wash, disinfect and rinse the endoscopes.
- In all cases, drying the channels with compressed air will prevent bacteria from growing in a moist environment.
- The equipment should be stored with care and it is best to hang the endoscopes to drain any excess water in channels (especially in areas where forced air drying is not possible).

In conclusion, although much more understanding of the exact ways of transmission of *Helicobacter pylori* in the community is needed to develop specific guidelines to limit the spread of

the infection in the general population, it is clear already that thorough cleaning and disinfection schedules can prevent iatrogenic transmission of common bacterial (including *H. pylori)* and viral infections from one patient to the next one through contaminated endoscopes.

References

Akamatsu T, Tabata K, Hironga M, et al. Transmission of *Helicobacter pylori* Infection via Flexible Fiberoptic Endoscopy. *Am J Infect Control*. 1996. 24:396–401.

Azevedo NF, Guimarães N, Figueiredo C, Keevil CW, Vieira MJ. A New Model for the Transmission of *Helicobacter pylori*: Role of Environmental Reservoirs as Gene Pools to Increase Strain Diversity. *Crit Rev Microbiol*. 2007. 33:157–169.

Cover TL, Blaser MJ. *Helicobacter pylori* in health and disease. *Gastroenterology*. May 2009. 136:1863–73.

Ford AC, Axon ATR. Epidemiology of *Helicobacter pylori* infection and public health implications. *Helicobacter*. 2010. 15(Suppl 1):1–6.

Koletzko S, Jones NL, Goodman KJ, Gold B, Rowland M, Cadranel S, Chong S, Colletti RB, Casswall T, Elitsur Y, Guarner J, Kalach N, Madrazo A, Megraud F, Oderda G; *H pylori* Working Groups of ESPGHAN and NASPGHAN. Evidence-based guidelines from ESPGHAN and NASPGHAN for *Helicobacter pylori* infection in children. *J Pediatr Gastroenterol Nutr*. August 2011. 53(2):230–43.

Malfertheiner P, Megraud F, O'Morain C, et al. Management of *Helicobacter pylori* infection: *The Maastricht IV/Florence Consensus Report*. Gut 2012. 61:646–664.

Mandeville KL, Krabshuis J, Ladep NG, Mulder CJ, Quigley EM, Khan SA. Gastroenterology in developing countries: Issues and advances. *World J Gastroenterol*. June 21, 2009. 15(23):2839–54.

Nelson DB, Muscarella LF. Current Issues in Endoscope Reprocessing and Infection Control During Gastrointestinal Endoscopy. *World J Gastroenterol*. 2006. 12(25):3953–3964.

Peters C, Schablon A, Harling M, et al. The occupational risk of *Helicobacter pylori* infection among gastroenterologists and their assistants. *BMC Infectious Diseases*. 2011. 11:154 doi:10.1186/1471-2334-11-154.

Rutala WA, Weber DJ. Sterilization, high-level disinfection, and environmental cleaning. *Infect Dis Clin North Am*. 2011. 45–76.

Suerbaum S, Michetti P. *Helicobacter pylori* Infection. *N Engl J Med*. 2002. 347(15):1175–1186.

CHAPTER 52

Fungi

Sergio B. Wey, MD

Key Issue

The incidence of health care associated fungal infections has increased in recent years, and antibiotic resistance is an issue in some hospitals.

Known Facts

- The incidence of candidemia is higher in critical-care units than in other parts of the hospital. In developed countries, it is the 4th leading cause of bloodstream infections.
- The overall incidence of nosocomial fungemia has increased, with most cases involving *Candida* species, and many such infections are related to the use of intravascular catheters.
- Most cases of nosocomial fungemia found in intensive care unit patients are not associated with recognized immune defense defects.
- Fungemia is associated with a high short-term mortality rate.
- It is already well documented that *Candida* infections, even candidemia, can be transmitted on the hands of colonized healthcare personnel.
- The evidence for cross infection by *Candida,* particularly in ICUs, has increased in the literature.
- The incidence of *Candida* non-albicans infections is increasing, and they tend to be more resistant to azoles than *C. albicans* strains.
- There is a strong relationship between *Candida parapsilosis* fungemia or systemic infection and hyperalimentation using intravascular devices.

C. glabrata has emerged as an important cause of candidemia, especially among neutropenic patients who have received fluconazole prophylaxis.

- Invasive candidiasis is usually caused by dissemination of endogenous *Candida* species that have colonized a patient's gastrointestinal tract.
- Up to 25% of episodes in the ICU of catheter-related UTI are caused by different species of *Candida*. Candiduria is especially common in patients receiving prolonged urinary catheterization and broad-spectrum systemic antimicrobial agents.
- In breakthrough candidemia, the same risk factors seen in de novo candidemia are encountered, although more frequently.

C. glabrata and *C. krusei* are the leading causes of breakthrough candidemia in patients with cancer.

- Hospital construction and renovation have been associated with an increased risk for health care associated fungal infection, particularly Aspergillosis, among severely immunocompromised patients.

Controversial Issues

- The role of susceptibility testing as a guide to selecting appropriate therapy for all of these infections is still incompletely defined.
- The ideal population of ICU patients who would benefit from antifungal prophylaxis. In part, the existing endemic rate of candidemia is important in decision-making.
- The efficacy of antibiotic prophylaxis for patients who demonstrate colonization with *Candida* is undocumented.
- No antimicrobial regimen has been reported to be clearly effective in preventing aspergillosis. Further studies are needed to determine the optimal strategy for aspergillosis prevention.
- Whether the hospital water-distribution system could be a reservoir for airborne molds that leads to secondary aerosolization of these molds in patient shower facilities.

Suggested Practice

- Proper use of antibiotics and strict protocols for invasive procedures.
- Define therapy based on yeast identification.

- The most important infection control measures for the prevention of fungal colonization of indwelling intravascularcatheters are quite similar to those recommended for bacterial infections. Standard practice in the treatment of candidiasis is to remove existing intravascular catheters for patients with candidemia or acute hematogenously disseminated candidiasis, especially in nonneutropenic patients.
- Antifungal therapy is necessary in all cases of vascular catheter-related candidemia.
- Tunneled CVCs or implantable devices should be removed in the presence of documented catheter-related fungemia.
- The removal of all central venous catheters from all patients with candidemia is considered to be standard care.
- Bone marrow allogeneic recipients should be administered antifungal prophylaxis to prevent invasive disease with *Candida* species during neutropenia. The choice of drug will depend on the level of fluconazole resistance and the risk of *Aspergillus*.
- Hospital construction or renovation areas should have negative air pressure relative to that in adjacent patient care areas, if no contraindications exist for such pressure differential.
- Patients with fungal infections of their catheters should be monitored for dissemination.

Summary

The past three decades have witnessed major changes in hospital populations and in the technology used in healthcare. As a result, there has been an improvement in patient survival; some of these patients are highly susceptible to infection. These patients often have diseases and complications that require the use of invasive techniques for both monitoring and treatment.

Candida and *Aspergillus* are responsible for the vast majority of health care associated fungal infections. However, severalother species can cause infection in debilitated hospitalizedpatients such as: *Trichosporum*, *Fusarium*, etc.

Fungemia is associated with a high short-term mortality rate. The crude mortality is 40%. The attributable mortality due to health care associated candidemia has been estimated to be half or more of the crude mortality.

Several studies have identified risk factors for the development of health care associated fungemia. Among the clinical characteristics that most consistently increase this risk are neutropenia, use of wide-spectrum antibiotics, bone marrow or solid organ transplant, diabetes, severe burns, premature birth, hyperalimentation, antecedent surgery (especially abdominal surgery), and indwelling catheters.

Candidemia generally occurs in patients who are debilitated; other risk factors are renal impairment, and multisite candidal colonization, all of which are common in ICU patients.

It has been well documented that transmission of *Candida* can occur via the hands of colonized healthcare personnel.

There have been several candidemia outbreaks in different patient populations. Many of these were associated with cross transmission by the hands of hospital personnel.

There is a strong relationship between *Candida parapsilosis* fungemia, or systemic infection, and hyperalimentation using intravascular devices. In fact, the adherence of *C. parapsilosis* to plastic materials exceeds that of *C. albicans*.

There in increased variation in the proportion of cases due to *C. albicans* relative to those caused by non-albicans species.

As is the case with antibacterial agents, the increased use of antifungal agents has led to the development of antifungal resistance.

The impact of fluconazole use in the ICUs has resulted in selective pressure favoring the appearance of more resistant species such as *C. glabrata* and *C. krusei*.

The incidence of *Fusarium* spp. infection is increasing, particularly in immunocompromised patients.

Disseminated fusariosis is an uncommon disease, and the reasons for the increasing incidence are multiple.

Some reports suggest a strong correlation between *Malassezia furfur* sepsis and the use of intravascular catheters.

Despite significant advances in the management of immunosuppressed patients, invasive aspergillosis remains an important life-threatening complication.

In the past two decades, the incidence of invasive aspergillosis in this population has continued to increase. Factors that predispose patients to invasive aspergillosis include prolonged

granulocytopenia, the development of graft-versus-host disease, immunosuppressive therapy, the use of adrenal corticosteroids, and the prolonged impairment of host defenses associated with diseases such as chronic granulomatous disease.

Environmental factors also play a key part in the pathogenesis of invasive aspergillosis, therefore, infection control measures play a critical role in reducing exposure of hospitalized patients to *Aspergillus*.

References

Blumberg HM, Jarvis WR, Soucie M, Edwards JE, Patterson JE, Pfaller MA, Rangel-Frausto MS, Rinaldi MG, Saiman L, Wiblin RT, Wenzel RP and the NEMIS Study Group. Risk Factors for Candidal Bloodstream Infections in Surgical Intensive Care Unit Patients: The NEMIS Prospective Multicenter Study. *Clin Infect Dis*. 2001. 33:177–86.

Garbino J. Secular Trends of Candidemia Over 12 Years in Adult Patients at a Tertiary Care Hospital. *Medicine (Baltimore)*. 2002. 81(6):425–33.

Pfaller MA, Diekema DJ. Epidemiology of Invasive Candidiasis: A Persistent Public Health Problem. *Clin Microbial Rev*. 2007. 20:133–63.

Wenzel RP, Gennings C. Bloodstream Infections Due to Candida Species in the Intensive Care Unit: Identifying Especially High-Risk Patients to Determine Prevention Strategies. *Clin Infect Dis*. 2005. 41(Suppl S)389–393.

Herbrecht R, Denning DW, Patterson TF, et al. Voriconazole versus Amphotericin B for Primary Therapy of Invasive Asperigillosis. *N Engl J Med*. 2002. 347:408–415.

Maschmeyer G, Haas A, Comely OA. Invasive Aspergillosis: Epidemiology, Diagnosis and Management in Immunucompromised patients. *Drugs*. 2007. 67:1567–1601.

Gutiérrez SM, Heredia M, Gómez E, Gómez JI, Tamayo E. Candidemia in ICU patients with sepsis. *Crit Care Med*. November 2013. 41(11):e 385.

Ben-Ami R, Halaburda K, Klyasova G, Metan G, Torosian T, Akova M. A multidisciplinary team approach to the management of patients with suspected or diagnosed invasive fungal disease. *J Antimicrob Chemother*. November 2013. 68(Suppl 3):iii 25–33.

CHAPTER 53

VIRUSES

M.W.H. Wulf, MD, C.M.A. Swanink, MD, PhD,
and Andreas Voss, MD, PhD

Key Issue

Viral infections are common in the community and can cause a variety of symptoms.

Known Facts

- The diagnosis is based on antigen detection, antibody response, electron microscopy, virus isolation, or polymerase chain reaction, which may be laborious and/or time-consuming. Based on the route of transmission, viral infections can be classified into four categories:
  1. Gastrointestinal Infection;
  2. Respiratory Tract Infection;
  3. Exanthematous Disease (skin lesions, vesicles); and
  4. Bloodborne Infection.

Gastrointestinal Infection. Gastrointestinal infections are caused by several viruses that can be found in feces, such as: enteroviruses (polioviruses, coxsackieviruses A and B, echoviruses), adenoviruses, rotaviruses, astroviruses, caliciviruses (e.g., norovirus, sapovirus), coronaviruses, hepatitis A virus and hepatitis E virus. Some of these are also found in respiratory secretions (enteroviruses, adenoviruses, coronaviruses, norovirus) and may cause symptoms of an upper respiratory tract infection. Outbreaks were reported in daycarecenters, sport facilities, hospitals and nursing homes.

- The route of transmission is predominantly fecal-oral, often via contaminated hands. Transmission of norovirus by aerosol during vomiting appears common. Thus, infection control strategies should focus on contact with fecally contaminated items and include gowns, gloves, and hand hygiene (*see Table 53.1*). In general, masks are not advised

but should be worn during close contacts or high-risk procedures (e.g., bronchial toilet) and when taking care of vomiting patients with norovirus infections.
- Most infections are mild, self-limiting, and do not require any specific therapy.

Respiratory Tract Infection. Symptoms of respiratory tract infections may vary from common cold to life-threatening pneumonia or pneumonitis.The severity of the clinical symptoms is largely dependent on host defenses. Cytomegalovirus, for example, can cause severe pneumonitis in the immunocompromised host whereas most infections are subclinical in the immunocompetent host. Viruses that cause respiratory tract infections include influenza viruses, parainfluenza viruses, respiratory syncytial virus, adenoviruses, enteroviruses, rhinoviruses, human metapneumovirus and coronaviruses (SARS, MERS CoV). Many other viruses can be found in respiratory secretions, such as cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus (HSV), human herpes virus type 6 (HHV-6), measles, mumps, human parvovirus B19, rabies virus, rubella virus, poxviruses, and varicella-zoster virus (VZV).
- Route of transmission is via airborne spread or via contaminated hands. Infection control measures should be aimed at aerosol transmission and direct contact and may include isolation, masks, gowns, gloves, and hand hygiene.
- Influenza virus vaccination should be considered for high-risk patients (for detailed information see the WHO website) and healthcare workers. In case of an outbreak, especially when the strain is not controlled by the vaccine, prophylaxis with amantadine (only influenza A, within 48 hours of exposure) or oseltamivir (influenza A & B) may be useful for both patients and healthcare workers.

Avian Influenza A: Although the risk of health care associated transmission is low, due to the high mortality of influenza A H5N1 infections, precautions should be taken. Standard droplet and contact precautions are recommended. During aerosol generating procedures, eye protection and a respirator as protective as N95 /FFP2 is recommended. Suspected cases should be reported to local health authorities. Post-exposure prophylaxis with oseltamivir can be considered for HCW at

high risk for infection (http://www.who.int/influenza/resources/documents/pharmacological_management_h5n1_05_2006/en/#Riskcategories) but resistance has been described. Up-to-date information is available on http://www.who.int/csr/disease/avian_influenza/en/index.html.

- In case of exposure to rabies virus, injection of human rabies immune globulin (HRIG) in the exposure site within 24 hours is recommended, followed by vaccination.

Exanthematous Disease. Many viral infections can cause exanthema, vesicles, or other skin lesions. The most common viruses are enteroviruses, herpes simplex virus (HSV), human herpes virus type 6 (HHV-6), varicella-zoster virus (VZV), measles, human parvovirus B19, and rubella virus.

- The routes of transmission are via respiratory secretions (all), feces (enteroviruses), urine (congenital rubella) and skin lesions (HSV, VZV, coxsackievirus A). Infection control measures are listed in *Table 53.1*.
- A combined vaccine for mumps, measles, and rubella (MMR) should be given to children at the age of 12 to 18 months or 6 and 9 months and to susceptible adults when vaccination is not contraindicated.
- Vaccines for mumps, measles, varicella and rubella are live attenuated vaccines and should not be given to severely immunocompromised patients.
- Antiviral therapy is available for HSV and VZV.
- Neonates and susceptible immunocompromised adults and pregnant women who had contact with chickenpox or shingles should be given a dose of varicella-zoster immune globulin (VZIG) within 3 days after exposure. Varicella-zoster immune globulin may not prevent infection but it may reduce the severity of infection.
- Susceptible HCW that have been exposed to VZV should be excluded from work with patients at risk during the incubation period (21 days). Susceptible contacts from patients with chicken pox should be isolated during the incubation period. VZIG lengthens the incubation period! HCW who have received vaccination, may continue their work unless they develop clinical signs of VZV infection.

Table 53.1 Infection Control Measures for Selected Viral Pathogens

Virus/Infection	*Infective Material*	*Isolation/ Precautions*	*Gown*	*Gloves*	*Mask*	*Single Room*	*Prevention/ Postexposure Prophylaxis*
Adenovirus	resp. secretions, feces	contact	(+)	+	(+)	–	
AIDS/HIV	blood, body fluids	universal	–	+	–	–	(+) eye protection, + triple therapy
Avian influenza	resp. secretions, feces	contact, droplet	+	+	+	+	eye protection & FFP2/N95 mask in aerosol generating procedures Post-exposure prophylaxis
Astrovirus	feces	enteric	(+)	+	–	–	
Calicivirus	feces	enteric	(+)	+	–	–	
Coronavirus	resp. secretions, feces	contact	(+)	+	(+)	–	
Coxsackie A virus (hand-foot-mouth disease, herpangina)	resp. secretions, feces, lesions, secretions	contact	(+)	+	(+)	–	
Cytomegalovirus	resp. secretions, urine, breast milk	body fluids	–	+	(–)	–	+ avoid contact during pregnancy (+) gancidovir (anti-CMV-immuneglobulin)
Dengue virus	blood	universal	–	+	–	–	+ avoid mosquito exposure, repellents
Enterovirus	resp. secretions, feces	contact	(+)	+	(–)	–	
Hantavirus (e.g., Puumala)	rodent excreta	none	–	–	–	–	
Hemorrhagic fever (Ebola, Marburg, Lassa)	blood, body fluids	strict	+	+	+	+	(+) eye protection, + ribavirin may be useful for Lassa fever
Hepatitis A and E viruses	feces	enteric	(+)	+	–	–	+ vaccination and immune globulin for HAV

Table 53.1 Infection Control Measures for Selected Viral Pathogens (continued)

Virus/Infection	*Infective Material*	*Isolation/ Precautions*	*Gown*	*Gloves*	*Mask*	*Single Room*	*Prevention/ Postexposure Prophylaxis*
Hepatitis B and D viruses	blood, body fluids	universal	–	+	–	–	(+) eye protection, + vaccination and HBIG
Hepatitis C, F, G viruses	blood, body fluids (?)	universal	–	+	–	–	(+) eye protection, (–) interferon
Herpes simplex virus (localized)	lesions, secretions	drainage, lesions, secretions	–	+	–	–	(+) acyclovir
Herpes simplex virus (disseminated)	lesions, secretions, resp. secretions	contact	+	+	(–)	+	(+) acyclovir
Herpes zoster virus (localized)	lesions, secretions	drainage, lesions, secretions	–	+	–	(–)	(+) VZIG
Herpes zoster virus (disseminated, varicella)	lesions, secretions, resp. secretions	strict	+	+	+	+	(+) vaccination, VZIG
HIV/HTLV	blood, body fluids	universal	–	+	–	–	(+) eye protection, + triple therapy
Influenza virus	resp. secretions	respiratory	–	(+)	(+)	+	(+) vaccination, amantadine, oseltamivir, zanamivir
Measles	resp. secretions	respiratory	–	(–)	(+)	(–)	+ vaccination (MMR)
Metapneumovirus (human)	resp. secretions	respiratory	+	+	(–)	+	+ single room only in children

Table 53.1 Infection Control Measures for Selected Viral Pathogens (continued)

Virus/Infection	*Isolation/ Infective Material*	*Precautions*	*Gown*	*Gloves*	*Mask*	*Prevention/ Single Room*	*Postexposure Prophylaxis*
MERS CoV	resp. secretions	strict	+	+	+	+	+ negative pressure room, N-95/FFP-3 or FFP 2 mask,
Mumps	resp. secretions	respiratory	–	(–)	(+)	(–)	+ vaccination (MMR)
Norovirus	resp. secretions, feces, vomit	enteric	(+)	+	(+) when vomiting	–	+ hand disinfection (!)
Parainfluenza virus	resp. secretions	contact	–	(+)	(+)	–	
Parvovirus B19	resp. secretions,	blood contact	–	+	(+)	–	+ avoid contact during pregnancy
Poliovirus	resp. secretions,	feces enteric	(+)	+	(–)	–	+ vaccination
Rabies virus	resp. secretions	respiratory	(+)	+	(+)	–	+ HRIG at exposure site, vaccination
RSV bronchiolitis	resp. secretions	contact	+	+	(–)	+	+ single room only in children
Rotavirus feces,	resp. secretions	contact	+	+	(+)	–	+ hand disinfection (!)
Rubella virus	resp. secretions	contact	+	+	+	+	+ avoid contact during pregnancy, vaccination (MMR)
SARS: *see Chapter 50*	resp. secretions, feces	strict	+	+	+	+	+ negative pressure room, N-95/FFP-3 or FFP 2 mask, + eye protection (goggles or face shield)
Varicella	resp. secretions, lesions	strict	+	+	+	+	(+) vaccination, VZIG
Yellow fever	blood	–	–	+	–	–	+ avoid mosquito exposure, vaccination

+ = advised; (+) = only during high-risk procedures (e.g., bronchial toilet, soiling), high-risk patients, or close contact;
(–) = questionable, probably not necessary; – = not necessary

- Less frequently occurring viruses that can cause health care associated infections include those causing hemorrhagic fevers such as arenaviruses (Lassa, Machupo, Junin), and Filoviruses (Marburg and Ebola). These viruses require strict isolation because they are transmitted by blood and body fluids (*see Bloodborne Infection, below*).

  Several arboviruses, such as dengue and yellow fever, and rickettsiae may cause hemorrhagic skin lesions but they are vectorborne, and person-to-person transmission does not occur.
- Hantaviruses may cause hemorrhagic fever with renal syndrome but may also cause a pulmonary syndrome with rapid respiratory failure and cardiogenic shock. Hantaviruses are transmitted via infected rodent excreta. Person-to-person transmission does not occur; therefore, no preventive measures are required.

Bloodborne Infection. Hepatitis B virus (HBV), hepatitis C virus (HCV), human T-cell leukemia/lymphoma virus (HTLV), human immunodeficiency virus (HIV), and viral hemorrhagic fevers (VHF) (e.g., Lassa, Marburg, Ebola) are examples of bloodborne infections. Other viral infections that can be transmitted by blood are CMV, EBV and HHV-6 because these viruses persist in leukocytes. Transfusion-related transmission of West-Nile virus has been described.

- Routes of transmission are blood and body fluids, including breast milk. The risk of infection after a needlestick is 5 to 40% for HBV, 1 to 10% for HCV, and <0.5% for HIV. For VHF, exact data on transmission after needlestick accidents are missing, but it is known that high concentration of viruses are found in blood during the febrile period.
- Universal precautions should be taken when handling blood in all patients and attention given to save disposal of needles and sharps.
- Effective postexposure prophylaxis for HBV consists of passive immunization with hepatitis B immune globulin (HBIG) followed by active immunization with recombinant hepatitis B vaccine.

- Interferon prophylaxis after exposure to HCV is questionable.
- Triple therapy with a combination of a protease inhibitor and two nucleoside reverse transcriptase inhibitors is probably useful as HIV postexposure prophylaxis.
- Ribavirin is an effective treatment for Lassa fever and may be useful as prophylaxis for Lassa fever.

Vaccination

- Vaccination is available for polioviruses, hepatitis A, hepatitis B, varicella, influenza, measles, mumps, rubella, and rabies.
- Vaccines for mumps, measles, varicella and rubella are normally live attenuated vaccines and should not be given to severely immunocompromised patients.

References

Control of Communicable Diseases Manual (17th Edition), J Chin, (Ed). Washington: American Public Health Association, 2000.

Fields Virology (4th Edition), DN Fields, DM Knipe, PM Howley, (Eds). Philadelphia: Lippincott-Raven Publishers, 2001.

Hu DJ, Kane MA, Heymann DL. Transmission of HIV, Hepatitis B Virus, and Other Bloodborne Pathogens in Healthcare Settings: A Review of Risk Factors and Guidelines for Prevention. World Health Organization. *Bull World Health Organ*. 1991. 69:623–630.

Bridges CB, Harper SA, Fukuda K, Uyeki TM, Cox NJ, Shingleton JA. Prevention and Control of Influenza. *MMWR*. 2003. 52(RR08):1–36

Bridges CB, Harper SA, Fukuda K, Uyeki TM, Cox NJ, Shingleton JA. Detection of West Nile Virus in Blood Donations. *MMWR*. 2003. 52(38):916–919.

Avian Influenza, Including Influenza A (H5N1) in Humans. WHO Interim Infection Control Guideline for Healthcare Facilities. May 10, 2007.

Interim Infection Prevention and Control Recommendations for Hospitalized Patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV) http://www.cdc.gov/coronavirus/mers/infection-prevention-control.html

CHAPTER 54

MERS and Lessons from SARS

Richard P. Wenzel, MD, MSc

Key Issue

Previously Severe Acute Respiratory Syndrome (SARS) was one of the latest epidemics to challenge infection control experts in the early years of the 21st century. The etiology is a novel coronavirus especially capable of being transmitted in hospitals. Only assiduous infection control practices were effective for control. More recently a new coronavirus emerged in Saudi Arabia and has spread to other portions of the Middle East and to Europe: Middle East Respiratory Syndrome—MERS. The important lessons from SARS for infection control are summarized herein. These lessons could be employed in the early management of any new epidemic of respiratory infections when the etiology is initially unknown.

Known Facts

- SARS emerged in the Southern Chinese Province of Guangdong in November 2002, but was not recognized until February 2003. Subsequently, a global epidemic occurred with a crude mortality worldwide of almost 10% but with considerably higher rates in some locales among patients older than 65 years. In a small hospital outbreak of MERS, the mortality was 65%.
- The etiology of SARS was found to be a novel coronavirus that very likely has a natural reservoir in one or more animals indigenous to Southern China, possibly the Himalayan or masked palm civit.
- The incubation period for SARS is 2–10 days, for MERS is 5 days.
- Half of the victims were healthcare workers.

- The SARS virus spreads primarily via large droplets, thus transmission usually requires close contact. It is possible that occasionally droplet nuclei transmission (airborne) can occur. Furthermore, because the virus is found in the bloodstream early, transfusion-related or sharps injury-associated infection remains a theoretic possibility. Lastly, because the virus is shed in the stool for approximately 30 days and can survive in the environment for 1–4 days, it is likely that the environment plays an important role in some cases of transmission.
- Although steroids and ribavirin have been used empirically for therapy, no efficacy data from controlled studies exist to prove that either drug affects outcome favorably.
- Healthcare workers who failed to use masks properly while managing SARS patients were more likely to become infected than those who used the masks properly.
- MERS is an emerging new coronavirus, possibly with a higher mortality than SARS and with possibly less transmissibility. Infection control (~30% currently) will be critical in containing this latest coronavirus.

Controversial Issues

- Recognition of the SARs epidemic was important and much credit goes to the late Carlos Urbani, MD, who alerted the world from his hospital in Hanoi. Of interest, the web-based international surveillance system for emerging pathogens—*ProMED-mail*—had reports of SARS weeks before the World Health Organization (WHO) reported the epidemic.
- There is critical need for all countries to report new epidemics immediately.
- Quarantine, if used, must be employed with care and compassion.
- The WHO showed great leadership by coordinating much of the global response to SARS.
- Because of the fears of healthcare workers, more attention to be paid to psychological support when epidemics affect them and threaten their health and lives.

Suggested Practice

Some of the key points in the management of SARS cases—which may help with MERS—are shown in *Table 54.1*. The wearing of tight-fitting masks, preferably N-95 with high filtering ability, is the most essential part of infection control protection of healthcare workers. Hand washing is also very important for infection control. Double gloving is thought to be important. Even if one has used gloves, a healthcare worker should wash hands after removing the gloves. Gowns and eye protection should be used and hair covers and shoe covers used if available. If available, place the patient in a room with negative air pressure.

Table 54.1 Management of Suspected MERS

Isolate the patient

- Place the patient in a private room with negative pressure, if possible.
- Wear two pairs of gloves, a gown, masks (N-95 if available), and eye protection (with face shield, if available, rather than goggles).
- Just before leaving the room, remove the gown and top set of gloves in the room.
- After leaving the room, wash gloved hands with alcohol, remove face shield and mask, placing both in disposable trash.
- Remove and discard the second set of gloves.
- Wash hands carefully after removing gloves.
- Limit the number of healthcare workers caring for patient.
- Limit the number of visitors.

Perform diagnostic studies if possible

- To rule out known causes of community-acquired pneumonia and to rule in SARS.

Maintain a clean environment

- Use chlorine solutions on bedside counters and on medical equipment that can tolerate the disinfectant, such as IV poles, at least daily.
- Supplemental oxygen for hypoxemia.
- Antibacterial agents for community-acquired pneumonia.
- Consider a neuraminidase inhibitor for treatment of influenza, if available.

Whenever healthcare workers exposed to initially non-isolated patients, it was ideal if they could be furloughed to their homes alone for 10 days before returning to work in the hospital. This may be very important for limiting transmission of MERS within the hospital. Ideally, family members would move to a relative's home during the 10 day furlough.

Summary

MERS is a new and formidable epidemic that is challenging infection control. Like SARS, the primary reservoir may be in bats. Unlike SARS, the secondary reservoir is likely in camels. Although close contact was necessary for transmission most of the time, the possibility exists for coincident transmission via airborne route and fomites. To contain this novel coronavirus, there is no room for error or relaxation of the highest standards of all features of infection control. The lessons from SARS may help to control MERS while we learn more about its epidemiology.

References

Abdullah A, McGreer A, Perl TM, et al. Hospital Outbreak of Middle East Respiratory Syndrome Coronavirus. *N Engl J Med*. 2013. 369:407–16.

Perlman S, McCray PB. Person-to-Person Spread MERS Coronavirus—An Evolving Picture. *N Engl J Med*. 2013. 369:466–7.

Wenzel RP, Bearman G, Edmond MB. Lessons from SARS: Implications for Infection Control. *Arch Med Res*. Nov–Dec 2005. 36:610–6.

Wenzel RP, Edmond MB. Managing SARS Amidst Uncertainty *N Engl J Med*. 2003. 348:1947–1948.

Holmes KV. SARS—Associated Coronavirus *N Engl J Med*. 2003. 348:1948–1951.

Seto WH, Tsang D, Ching TY, et al. Effectiveness of Precautions Against Droplets and Contact in Prevention of Nosocomial Transmission of Severe Acute Respiratory Syndrome (SARS). *Lancet*. 2003;. 361:1519–1520.

Wenzel RP, Edmond MB. Listening to SARS: Lessons for Infection Control. *Ann Intern Med*. October 2003. 139(7):592–593.

CHAPTER 55

Parasites

Claudia Jarrin MD, and Gonzalo Bearman, MD, MPH

Introduction

There are three categories of health care associated parasitic infections: ectoparasites, enteric parasites, tissue and blood parasites. Children, post-transplant patients and patients infected with HIV are especially at risk for severe infection.

Health care associated parasitic infections are infrequently reported in developed countries which can result in underdiagnosis and unwanted delay of installment of proper preventive measures. A study in 2009 including 1,265 intensive care units in 75 countries showed that the overall incidence of parasitic health care associated infections was 0.48%. Ectoparasitic infections such as scabies and pediculosis can cause large hospital outbreaks.

Enteric parasites are usually endemic in an important part of the population living in developing countries. In this group, parasitic health care associated outbreaks probably are more common, but detection is hampered due to the high prevalence of parasitic infections and the limited financial resources.

Ectoparasites

Potential health care associated infections caused by ectoparasites include the pediculoses, scabies, mites and myiasis.

- Infestation with the itch mite *Sarcoptes scabei* is an important cause of health care associated infections. Scabies is transmitted directly from person-to-person via skin-to-skin or sexual contact. Infected fomites may contribute to transmission within households and institutions. About half percent of cases occur in individuals with poor hygiene. However, about 30% of scabies cases affect people who are very concerned with their hygiene. In the latter group, diagnosis can be missed or delayed. There were 23 health care associated outbreaks reported between 1985 and 2012.

Clinical manifestations are intense pruritus and burrows over the distal extremities, waist and axilla. Particularly important, Norwegian or crusted scabies is associated with cell-mediated immunodeficiencies such as HIV/AIDS.

The incubation period may be up to four or six weeks before itching and scratching begin. This long period often delays outbreak recognition with further transmission of mites by asymptomatic contacts. Larger outbreaks correlate with diagnostic delay and high mite density, such as the case of Norwegian scabies. Patients with crusted scabies can have thousands of mites on their skin as opposed to the average five to 15 harbored by the usual symptomatic person with common scabies. The presence of animals inside hospitals can be source of mites which are unusual for humans.

- Head lice infestation by *Pediculis humanus capitis* is transmitted person-to-person by direct, even if only brief, head-to-head contact. Health care associated transmission is low apart from close patient-to-patient contact in i.e. pediatric ward playrooms or institutions. *P. humanus corporis*, agent of body lice, is transmitted via direct contact or with exchange of infested clothing or bedding. It is of negligible risk in hospital settings in developed countries. This risk is also true for transmission of the pubic louse, *Phthirus pubis*, which are transmitted via direct venereal skin-to-skin transfer.
- The pigeon mite, *Dermanyssus gallinae,* has been involved in health care associated outbreaks. Infection with this mite causes pruritic papular rash which can be misdiagnosed as scabies. Usual source of the mite are pigeon roosts found on or near ventilatory ducts or outside air-conditioners.
- Health care associated infestation of body tissues by larvae of various fly species, myiasis, is not uncommon. Myiasis results from deposition of eggs of gravid flies in open wounds, which can develop towards motile larvae within a few days. Treatment involves mechanical removal of larvae and wound debridement if needed. Myiasis most commonly occurs in hospitals in the tropics and subtropics with open air access to the patient, but is also reported in temperate areas during warmer months.

Enteric Parasites

- Intestinal parasites can cause diarrhea in 12–17% of health care associated epidemics and 1% of endemic outbreaks, especially on surgical wards. Immunosuppressed patients and those with prolonged antibiotic courses are at higher risk.
- Enteric protozoans are the most common agents involved in health care associated outbreaks. These include: *Cryptosporidium parvum*, *Giardia lamblia, Entamoeba histolytica/dispar, Blastocystis sp., Balantidium coli, Cyclospora cayetanensis* and *Isospora belli*.
- Fecal material of infected patients may contain helminthic eggs or larvae, or protozoan cysts, oocysts, or trophozoites. All protozoan cysts or oocysts are immediately infective when passed in stool. Trophozoites may only survive briefly in the environment and are killed by gastric acid; therefore, contributing less to transmission.
- *Giardia* is the most common enteric protozoan infection in the United States. Contaminated water is the most common way of transmission. Person-to-person transmission occurs occasionally and foodborne transmission is seldom.
- *Cryptosporidium* can cause diarrhea in both immunocompromised and immunocompetent hosts. In the latter, diarrhea is usually self-limited. This is an important agent causing diarrhea in the HIV population.

  Suboptimal hand washing or fomite contamination of environmental surfaces can be involved in transmission. Furthermore, the cysts are very resistant to environmental conditions and most of the disinfectants commonly used have low or none antiparasitic activity. Perinatal health care associated transmission from mother to newborn is possible. Suspected airborne transmission from animal to human has been reported.
- Helminths can cause isolated outbreaks in solid organ transplant recipients. Infections are usually associated with water or food contamination. Enteric helminth parasites transmitted from person-to-person are *Enterobius vermicularis, Strongyloides stercoralis* and *Hymenolepis nana*. This is possible because an intermediate host is not required

and eggs *(E. vermicularis, H. nana)* or larvae (S. *stercoralis)* are directly mature (infective) in stool. These features are also responsible for autoinfection. When conditions allow fecal contamination of the healthcare environment (i.e. in recreational areas) and helminth eggs are enabled to mature, other roundworms, such as hookworm, trichuris and toxocara species, can also be the source of outbreaks. Patients shedding proglottids of *Taenia solium* in the hospital environment are a potential important source of infection. Eggs liberated from the proglottides are immediately infectious and can, when swallowed by humans, cause severe pathology of i.e. the central nervous system (cysticercosis). *Strongyloides stercoralis* can cause hyperinfection in patients on chronic immunosuppression with steroids and in those infected with HIV and HTLV-1.

- Other less frequent water-associated outbreaks include *Entamoeba histolytica/dispar, Balantidium coli, Cyclospora cayetanensis, Microsporidium* species, the tissue parasite *Toxoplasma gondii* and the free living *Acanthamoeba* species. Due to the small size and robust nature of the transmission stages of parasites, i.e. cyst, oocyst and spores, removal by water treatment is difficult.
- Free-living amoebae in water networks and oxygen humidifier reservoirs of hospitals have been shown to be an important reservoir of pathogens as *Legionella pneumophila*. In addition, these amoebas serve as reservoir for different mycobacterial species and Alphaproteobacteria, such as *Rhodoplanes* and *Methylobacterium*. The ability to multiply in free-living amoeba offers these bacteria protection from biocides and enhances their virulence in humans. Human infection occurs via inhalation of aerosols containing free bacteria or, alternatively, infected amoebae itself could be the infectious particles that bring the pathogens to the longs.

Tissue and Blood Parasites

Organ transplant and blood transfusion recipients are at higher risk.

- The most common protozoan infection related to blood and blood products transfusion is *Plasmodium falciparum* followed by *P. vivax*. This is an important problem in endemic

areas. Furthermore, all species of *Plasmodium* can remain potentially invasive for 7 days in preserved blood and up to 2 years in frozen blood. In most cases, post-transfusion malaria results in death.

Plasmodium species can also be transmitted between hospitalized patients when physical barriers such as windscreens and bed nets are not in use. In non-endemic countries health care associated malaria is infrequently observed. However, especially in patients hospitalized with high parasitaemia of P. *falciparum,* small amounts of blood can result easily in health care associated transmission to other patients and/or staff. Other means of transmission are through organ transplant, needle stick injuries, improper catheter use and administration of intravenous drugs –especially in developing countries, and contact with a rogue mosquito that escaped from a mosquito colony in the laboratory setting.

- *Babesia microti,* cause of babesiosis and normally transmitted to humans via the tick *Ixodes scapularis,* can cause health care associated infections via blood transfusions. This problem is especially recognized in North America. Advanced age, immunosuppression and asplenia are risk factors for severe disease.
- African trypanosomiasis, normally transmitted by tse-tse flies, can also be transmitted by blood transfusion. Donors can remain asymptomatic for up to 6 months.
- American trypanosomiasis, caused by *T. cruzi* is predominantly transmitted via the bite of an infected triatomid bug in endemic areas and can be transmitted by blood transfusion. It is the second most common means of acquiring this infection. Transmission by needle stick injury and kidney transplantation has also been reported. For persons who have had accidental exposures, administration of a two-week course of presumptive therapy should be considered while awaiting results.
- *Leishmania spp*. causing visceral leishmaniasis can be transmitted by blood transfusion. In blood the parasites are observed in leukocytes. In endemic areas differentiation between visceral leishmaniasis due to arthropod vector and blood transfusion infection is difficult.

- Health care associated transmission of toxoplasmosis is most often after heart or kidney transplantation and infrequently due to white blood cell transfusions. Laboratory-acquired toxoplasmosis in research personal is not uncommon due to contact with infectious (often cultured) material by skin punctures, eye splashes or open wounds.
- Microfilariae of the blood helminths *Mansonella ozzardi, Loa loa, Diptetolonema perstans* and *Wuchereria bancrofti* have been observed in blood of asymptomatic donors. No illness or mild disease was recorded in recipients of such blood.

Controversial Issues

- For different reasons, report of parasitic health care associated infections is suboptimal in both developing and developed countries which presents a challenge to Infection Control since this underestimation can result in delay of diagnoses and installment of proper preventive measures.
- Expertise in laboratory diagnoses of specific parasitic infections is often limited.
- Even with high standards of treatment, including physical and chemical disinfection methods, contamination with enteric parasites occurs.
- Screening for parasitic infections which potentially can be transmitted by blood transfusion i.e. malaria and Chagas disease, requires locally adapted strategies to take into account both care for the recipient as well as unnecessary waste of blood donations.

Prevention

- Effective hand washing and routine glove use are the most important preventive measures since many immunocompetent patients may be asymptomatic carriers. Sanitary control is also important in preventing the presence of insects such as mosquitos and flies that propagate parasitic infections.

  Time of shedding of *Cyclospora* and *Isospora* oocysts in stools can be shortened by treatment with cotrimoxazole and *Giardia* by metronidazol or tinidazol.

There is no established therapy for *Cryptosporidium*. HAART is the only proven treatment in patients with advanced HIV and *C. parvum*. Oocysts can be removed from drinking water by either boiling for one minute or by filtering water. Full details are provided by the CDC Preventions Website. *Cryptosporidium* can be inactivated on surfaces or instruments by i.e. 10% formal saline, 5% ammonia for 18 hours or full-strength (12%) commercial bleach for 10–15 min.

- The corner stone to prevent blood-transfusion-associated protozoal infections, i.e. malaria, trypanosomiasis (African and South American), babesiosis and leishmaniasis, is donor selection using questionnaires and use of screening tests. After a visit to a malaria endemic area blood donors are deferred from blood donation for periods varying from 4–6 months, 3 years or even permanently, depending on the origin of the donor (born and lived in endemic area, European visitor), having experienced febrile episodes in the period after the visit and country of blood donation. In the USA and Canada a deferral time of 12 months after return from an endemic area is applied for blood donors. Use of serological tests for malaria in the tropics is, given the high prevalence of malaria in most countries, of little use and deferring on basis of positive antibody tests too drastically can reduce the local donor pool. Antigen tests and microscopy can be used instead, but sensitivity is suboptimal. Routine screening for babesiosis in not in common practice.
- To prevent American trypanosomiasis (Chagas disease) in endemic areas, questionnaires, serological tests for *T.cruzi* and treatment of blood with gentian violet are used; the latter being an effective strategy to prevent health care associated blood transfusion. In non-endemic countries use of questionnaires for Chagas disease are often targeted to special donor groups, i.e. visitors or immigrants of South America. Performing serological screening is not done routinely in non-endemic countries but is considered in the USA when a FDA licensed test should be available.
- To prevent transfusion-acquired leishmaniasis in some countries (USA, Ireland) donors are deferred for 12 months when they visited endemic countries, especially Iraq. Also donors

with multiple scars and fresh cutaneous leishmaniasis are deferred. In other countries use of specific questionnaires or antibody testing is not routinely performed.

- Serological testing for *T. gondii* of both donor and recipient in advance should, in case of mismatch, alert the clinician of potentially life threatening complications. Prophylaxis with pyrimethamine can be provided to the recipient. Alternatively anti toxoplasmosis treatment can be started when seroconversion and clinical manifestations occur, although clinical symptoms often are non-specific.
- To prevent myiasis patients should be advised to keep wounds and draining orifices clean and covered. Efforts should be made to reduce flies in the health-care environment.
- Prompt recognition of scabies followed by immediate implementation of preventive measures is the mainstay for the containment of health care associated outbreaks. Simultaneous mass prophylaxis is the most efficient strategy for terminating ward outbreaks and may prevent ward closure. In case of crusted scabies, contact precautions should be strictly implemented including use of disposable gloves, gowns and shoe covers. Local treatment with 5% permethrin cream, applied overnight on two occasions one week apart, is highly effective. Lindane lotion 1% is an effective, cheap alternative but is potentially more toxic. In addition to local treatment in crusted scabies oral treatment with ivermectine at a dose of 200 ug/kg, at one to three doses, is beneficial.

Summary

Health care associated parasitic infections can be caused by enteric, blood, tissue and ectoparasites. Frequency of infection is low in developed countries where infections are mostly driven by ectoparasites. From developing countries only few data are available. Proper detection of outbreaks requires adequate diagnosis which, in both settings, often has restrictions. In developing counties outbreaks are difficult to detect due to high background prevalence. Enteric protozoan parasites, malaria, American trypanosomiasis, toxoplasmosis, scabies (classic or crusted) and myasis are among the most frequent reported health care associated infections. Patients with AIDS, children and transplant recipients are particularly at risk.

References

Aygun G, Yilmaz M, Yasar H, Aslan M, Polat E, Midilli K, et al. Parasites in nosocomial diarrhea: Are they underestimated? *J Hosp Infect*. 2005. 60:283–285.

Betancourt WQ, Rose JB. Drinking Water Treatment Processes for Removal of *Cryptosporidium* and *Giardia*. *Veterinary Parasitology*. 2004. 126:219–234.

Góralska K, Kurnatowski P. Parasites as etiological factors of nosocomial infections. *Annals of Parasitology*. 2013. 59(1):3–11.

Herwaldt B. Laboratory-Acquired Parasitic Infections from Accidental Exposures. *Clinical Microbiology Reviews*. 2001. 659–688.

Jain SK, Persaud D, Perl TM, Pass MA, Murphy KM, Pisciotta JM, Scholl PF, Casella JF, Sullivan DJ. Nosocomial Malaria and Saline Flush. *Emerging Inf Dis*. 2005. 11:1097–1099.

Khan A, O'Grady S, Muller M. Rapid control of a scabies outbreak at a tertiary care hospital without ward closure. *American Journal of Infection Control*. 2012. 40:451–455.

Karanis P, Kourenti C, Smith H. Waterbome Transmission of Protozoan Parasites: A Worldwide Review of Outbreaks and Lessons Learnt. *Journal of Water and Health*. 2007. 5:1–38.

Lettau LA. Nosocomial Tranmission and Infection Control Aspects of Parasitic and Ectoparasitic Diseases: Part I. Introduction Enteric Parasites. *Infect Control Hosp Epidemiol*. 1991. 12:59–65.

Lettau, LA. Nosocomial Transmission Infection Control Aspects of Parasitic and Ectoparasitic Diseases Part II. Blood and Tissue Parasites. *Infect Control Hosp Epidemiol*. 1991. 12:111–121.

Sherman RA, Roselle G, Bills C, Danko LH, Eldridge N. Healthcare-Associated Myiasis: Prevention and Intervention. *Infect Control Hosp Epidemiol*. 2005. 26:828–832.

Thomas V, Herrera-Rimann K, Blanc DS, Greub G. Biodiversity of Amoebae and Amoeba-Resisting Bacteria in a Hospital Water Network. *Applied and Environmental Microbiology*. 2006. 72:2428–2438.

Vorou R, Remoudaki HD, Maltezou HC. Nosocomial Scabies. *J Hosp Infect*. 2007. 65:9–14.

Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA*. 2009. 302:2323–2329.

CHAPTER 56

New Technologies in Infection Prevention

Surbhi Leekha, MBBS, MPH

Key Issue

- New technologies for the prevention of health care associated infections (HAI) are developing at a rapid pace. This chapter provides a broad overview of emerging technologies in the following categories: environmental cleaning and disinfection (including antimicrobial impregnated clothing), automated hand hygiene monitoring, and HAI surveillance.
- While a handful of these technologies have been associated with reduction in either cross-transmission of micro-organisms or prevention HAIs, many are in their nascent stage and require further evaluation particularly with regards to clinical efficacy.
- The utilization of technology in infection prevention practice is exciting because many of these tools (e.g., self-disinfecting surfaces) are "passive" interventions that do not rely on human behavior for implementation.

Known Facts

- There has been a renewed interest in the role of the hospital environment as a reservoir for pathogens. Various pathogens have been shown to survive for prolonged periods on inanimate surfaces, and may be transmitted to patients either through direct contact, or via the hands of healthcare workers.
- Patients admitted to hospital rooms that previously housed patients colonized or infected with methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus* (VRE), multidrug resistant *Acinetobacter baumannii*, multidrug resistant *Pseudomonas aeruginosa*, or *Clostridium difficile*, are more likely to acquire the same pathogen during their hospital stay.

- The inadequacy of routine hospital cleaning is well described, and improved environmental cleaning has been associated with reduction in HAI incidence. This has led to the search for novel methodologies to reduce the risk of acquiring a pathogen from the healthcare environment.

Technologies for monitoring the quality of environmental cleaning:

- Traditionally, little attention has been paid to tools used to monitor the cleaning of the hospital environment, with visual inspection being used most frequently, and culturing of surfaces limited to research or outbreak settings. More recently, the use of objective tools for monitoring the quality of cleaning has been promoted.
- Two types of monitoring systems have been evaluated in research studies, and adopted for routine use by many hospitals. The first uses an invisible gel that dries on surfaces following application, and resists abrasion unless that surface is thoroughly cleaned. This mark can be discovered using a fluorescent marker if effective cleaning has not been performed, and thereby help evaluate the efficacy of cleaning practice.
- The second tool uses adenosine triphosphate (ATP) bioluminescence to measure organic ATP on surfaces using a luciferase assay and a luminometer. This technology assesses the cleanliness of a surface rather than the cleaning practice.
- Both these systems have been shown to be effective in improving the cleaning practice, but there is little evidence to show that their use reduces the transmission of pathogens.
- Evaluation of cleaning using these monitoring systems has spurred the development and assessment of new technologies for cleaning and disinfection described below.

Disinfection technologies: Whole room disinfection

- Known antimicrobial agents have recently been explored for whole room surface decontamination utilizing novel "no-touch" technologies. Two agents that have been studied the most, and are available commercially, include hydrogen peroxide (H_2O_2) and ultraviolet (UV) radiation.
- Hydrogen peroxide based systems use either pressure-generated H_2O_2 aerosols or heat-generated H_2O_2 vapor delivered in a high velocity air stream.

- The use of H_2O_2-based systems has been associated with reduction in environmental contamination, control of health care associated outbreaks, decrease in acquisition of pathogens such as MRSA and VRE, and decrease in the incidence of *Clostridium difficile* infection (CDI). It has also been recently shown to be useful in reducing the microbial contamination of unused medical supplies, with potential cost savings associated with retaining supplies that would otherwise be discarded.
- UV light based disinfection systems have been associated with reduction in microbial contamination. Reduction in the incidence of CDI using a portable pulsed xenon UV light system was observed in one single center non-randomized study.
- Both H_2O_2 and UV radiation are toxic, necessitating that staff and patients leave the rooms while these technologies are being employed. This limits their use to terminal or discharge cleaning, and potentially to clean unused supplies or shared equipment.
- The use of H_2O_2 vapor or aerosols also requires surfaces to be free of debris that can only be accomplished through manual cleaning.
- The turnaround time for H_2O_2 vapor based cleaning in published studies ranges from 2–8 hours which may be prohibitive for room turnover in many hospitals, although newer delivery platforms that require less time are being developed.
- While UV light disinfection promises shorter process times (~ 10 minutes), because radiation can only travel in straight lines, it can only disinfect objects in its direct path–"line-of-sight" disinfection.
- Both technologies require significant upfront expenditure and may be cost-prohibitive for many hospitals.

Disinfection Technologies: Antimicrobial treated surfaces

- Compounds with antimicrobial properties developed with the intent of coating or impregnating surfaces include silver, copper, triclosan, and quaternary ammonium.
- While all these compounds have been shown to kill microorganisms on contact *in vitro*, only copper containing surfaces have been studied in the healthcare setting to any significant degree.

- In a recent randomized controlled trial in a single institution, patients cared for in ICU rooms with copper alloy surfaces had a significantly lower rate of incident HAI and colonization with MRSA or VRE than patients cared for in standard hospital rooms.
- Two other technologies that are currently under evaluation include surfaces with altered topography, and surfaces containing light-activated germicides. The former utilizes the science of microtopography to alter surfaces such its configuration inhibits formation of biofilm and associated microbial colonization. The latter technology is based on the incorporating compounds that exhibit antimicrobial activity when irradiated by visible light, into hospital surfaces—titanium dioxide is the most developed product in this category. Both these technologies require further evaluation in healthcare settings.

Disinfection technologies: Antimicrobial treated textiles

- Similar to hard surfaces, several candidate compounds have been explored for treatment of textiles for use in healthcare settings.
- In a double-blind, randomized controlled trial of a complex element compound antimicrobial privacy curtains in ICUs, a significant delay in time to microbial contamination of the antimicrobial curtains was noted. However, when sampled at time points beyond day 10, there was no difference in the contaminated proportion between standard and antimicrobial curtains.
- Results from studies evaluating healthcare worker uniforms impregnated with antimicrobial compounds have been conflicting: while one crossover study showed a decrease in MRSA (but not VRE or gram negative) burden with quaternary ammonium impregnated scrubs, another randomized controlled study failed to show a decrease in the overall microbial burden with use of antimicrobial scrubs.

Automated Technology for Hand Hygiene Monitoring

- Healthcare worker compliance with hand hygiene remains suboptimal. Monitoring compliance with hand hygiene is essential but resource-intensive for infection prevention departments, and could be overcome through the use of automated hand hygiene monitoring systems.

- Automated HH monitoring systems monitor the entrance and exit of HCWs from patient rooms using motion sensing technology, and link the movement to electronic monitoring of alcohol-based hand rub dispensers.
- Advantages of such systems include little ongoing resource consumption (following initial installation), reducing bias from Hawthorne effect of known observers on the unit, and the ability to record large numbers of observations leading to more robust rates, including rates individualized for each HCW. Some of these systems also have the capability of providing real time monitoring and feedback to individuals.
- Studies have shown that these systems are associated with increase in hand hygiene compliance, and potentially with improvement in rates of HAI.
- The initial cost to set up such a system is likely to be significant, the opportunities most easily monitored (room entry and exit) might not be most relevant to patient care, and there is a possibility of losing the opportunities for detailed observation, direct interaction and feedback from observers including the infection preventionists.
- There is some concern that radiofrequency and Wi-Fi based devices may interfere with existing electronic medical devices.
- These systems are still being studied, and their accuracy, functionality, and acceptability remain to be validated further.

Information Technology for Infection Surveillance

- The focus of infection prevention programs has increasingly shifted from being surveillance-centric to actively implementing infection prevention practices. This could be greatly facilitated by the use of automated surveillance systems that can potentially save hours used in manually reviewing test results or tracking information on presence of devices etc.
- Hospitals have been using both indigenously developed and commercially available software for infection surveillance.
- In one study, hospitals that had adopted automated surveillance technology were more likely than those that manually track infections to have fully implemented evidence-based practices to reduce HAI.
- The ultimate impact of automated surveillance technology on HAI prevention is unknown at this time.

- Any automated surveillance technology will be highly dependent on the quality of the clinical and laboratory data captured by an existing hospital electronic medical record.

Controversial Issues

While it is recommended that an objective technology be utilized for monitoring environmental cleaning, it is unclear whether a fluorescent gel based cleaning practice monitoring system or an ATP based cleanliness monitoring system represents the better method.

- Although studies have shown reduction in the microbial burden of the healthcare environment through the use of new disinfection technologies, their role in reducing HAIs is not well established.
- The durability of effect of antimicrobial compounds intended for long-term use (e.g., in HCW uniforms or hospital surfaces) is unknown.
- Antimicrobial resistance to compounds used to coat or to impregnate surfaces and clothing has not been evaluated.
- The cost of acquisition of these technologies is likely to be significant, and only a handful of studies have evaluated potential cost savings with these technologies.

Suggested Practice

- New technological advances may be used to supplement, not substitute, basic evidence-based infection prevention and control practices such as hand hygiene.
- Ensure implementation of and adherence to proven basic infection prevention practices prior to adopting new technology e.g., in the case of environmental cleaning, this includes ensuring thorough cleaning using traditional disinfectants.
- There is some evidence to support the use of objective technology to monitor the quality of environmental cleaning.
- Evidence to support routine use of new technologies for environmental disinfection is lacking but may be useful in the setting of an outbreak as a supplemental measure.
- The following are some important considerations prior to proceeding with routine use of a new product or technology for infection prevention:

- Evidence of efficacy from clinical studies; evidence of antimicrobial activity from *in vitro* studies should not be the sole basis for introducing new technology for routine use.
- Available alternatives.
- Cost: weigh the cost of new technology against the cost of attempting to improve human behavior and practice, and potential impact on HAI incidence.
- Impact of any new chemicals on the environment, medical equipment, and on the safety of healthcare workers and patients.
- Effect on the day-to-day operation of the hospital.

Summary

New technologies are being developed, commercialized, and offered to hospitals at a rapid pace; however, robust research to support the use of most of these products is lacking. Ultimately, technology hold great promise in eliminating many of the manual steps in infection prevention but these technologies need to be tested in well-designed clinical studies, and evaluated using criteria such as those described above before adopting for routine use.

References

Otter, JA, Yezli S, French GL. The role played by contaminated surfaces in the transmission of nosocomial pathogens. *Infect Control Hosp Epidemiol*. 2011. 32(7):687–99.

Carling, PC, Parry MF, Von Beheren SM. Identifying opportunities to enhance environmental cleaning in 23 acute care hospitals. *Infect Control Hosp Epidemiol*. 2008. 29(1):1–7.

Dancer, SJ, et al. Measuring the effect of enhanced cleaning in a UK hospital: A prospective cross-over study. *BMC Med*. 2009. 7:28.

Carling, PC, Bartley JM. Evaluating hygienic cleaning in health care settings: What you do not know can harm your patients. *Am J Infect Control*. 2010. 38(Suppl 5):S41–50.

Carling, PC, et al. Improving cleaning of the environment surrounding patients in 36 acute care hospitals. *Infect Control Hosp Epidemiol*. 2008. 29(11):1035–41.

Boyce, JM, et al. Monitoring the effectiveness of hospital cleaning practices by use of an adenosine triphosphate bioluminescence assay. *Infect Control Hosp Epidemiol*. 2009. 30(7):678–84.

Otter, JA, et al., The role of 'no-touch' automated room disinfection systems in infection prevention and control. *J Hosp Infect*. 2013. 83(1):1–13.
Falagas, ME, et al. Airborne hydrogen peroxide for disinfection of the hospital environment and infection control: A systematic review. *J Hosp Infect*. 2011. 78(3):171–7.
Otter, JA, et al. Saving costs through the decontamination of the packaging of unused medical supplies using hydrogen peroxide vapor. *Infect Control Hosp Epidemiol*. 2013. 34(5):472–8.
Levin, J, et al. The effect of portable pulsed xenon ultraviolet light after terminal cleaning on hospital-associated *Clostridium difficile* infection in a community hospital. *Am J Infect Control*. 2013. 41(8):746–8.
Weber, DJ, Rutala WA. Self-disinfecting surfaces: Review of current methodologies and future prospects. *Am J Infect Control*. 2013. 41(Suppl 5):S31–5.
Salgado, CD, et al. Copper surfaces reduce the rate of healthcare-acquired infections in the intensive care unit. *Infect Control Hosp Epidemiol*. 2013. 34(5):479–86.
Bearman, GM, et al. A crossover trial of antimicrobial scrubs to reduce methicillin-resistant Staphylococcus aureus burden on healthcare worker apparel. *Infect Control Hosp Epidemiol*. 2012. 33(3):268–75.
Burden, M, et al. Bacterial contamination of healthcare workers' uniforms: A randomized controlled trial of antimicrobial scrubs. *J Hosp Med*. 2013. 8(7):380–5.
Boyce, JM. Measuring healthcare worker hand hygiene activity: Current practices and emerging technologies. *Infect Control Hosp Epidemiol*. 2011. 32(10):1016–28.
Carling, PC. The need for clinically relevant studies of non-touch disinfecting systems. *J Hosp Infect*. 2013. 84(4):340.
Halpin, H, et al. Hospital adoption of automated surveillance technology and the implementation of infection prevention and control programs. *Am J Infect Control*. 2011. 39(4):270–6.

CHAPTER 57

Left Ventricular Assist Device—Related Infections

Richard P. Wenzel, MD, MSc.

Key Issue

With many of the world's population developing congestive heart failure, yet the known limited supply of hearts available for transplantations, and improved medical technology, left ventricular assist devices (LVADs) are increasingly being used as both destination therapy and as bridges to transplantation. In late stage congestive heart failure, patients with LVADs been shown to have a 48% reduction in death vs those medically managed as shown in the REMATCH study. Because LVAD related infections are common and serious, a brief discussion is essential.

Known Facts

Infections after LVAD receipt occur in 18–59% of patients and are usually caused by antibiotic resistant bacteria such as MRSA, VRE, Candida species and highly resistant MDR gram-negative rods

Infections after LVAD placement may be *device specific* (the drive line, the pocket or the pump itself); *device related* (endocarditis, blood stream infection, mediastinitis or the surgical site); *or non-device related* (pneumonia, urinary tract infection or *C.difficile* infection).

LVAD endocarditis may present with few or no symptoms, including only fever or progressive cachexia; sometimes the patients may present with a device associated mechanical issue only such as inlet obstruction, outflow rupture or bleeding within the device.

Controversial Issues

Optimal perioperative antibiotics given to prevent infections after LVAD placement are unclear. Many centers in the U.S. employ a combination of Vancomycin, a Fluoroquinolone, Fluconazole and a βeta-lactam antibiotic.

Optimal therapy has not been clarified by clinical trials and is usually empirical with broad coverage until the antibiograms of isolated organisms are reported.

Suggested Practice

In the workup of LVAD patients with likely infection, the following may be useful:

- Peripheral blood WBC
- Exit site culture of pus
- Cardiac ECHO
- Blood cultures

If a pocket infection is of concern:

- Ultrasound, CT or nuclear scan
- Image guided aspiration

If the LVAD is removed, obtain the following cultures:

- Anterior and posterior LVAD surface
- Outflow and inflow cannula
- Tissue cultures
- Drive line cultures

As for prophylaxis, a hospital performing LVAD placement should consider being informed by those organisms recovered and the associated antibiograms.

Summary

With only 4000 hearts each year available for transplantation globally, there are increasing numbers of CHF patients receiving LVADs. Such patients have high risk of developing as infection, usually with MDR bacteria or yeast. Optimal perioperative antibiotics have not been established.

References

Hannan MM, Husain S, Mattner F, et al. Working Formulation for the Hannan MM, Husain S, Mattner F, et al. Working Formulation for the Standardization of Definitions of Infections in Patients Using Ventricular Assist Devices. *J Heart Lung Transplant*. 2011. 30:375–84.

Miller LW, Pagani FD, Russell SD, et al. Flow Device Patients Awaiting Heart Transplantation. *N Engl J Med*. 2007. 357:885–96.

Topkara VK, Kondareddy S, Malik F, et al. Infectious Complications in Patients with Left Ventricular Assist Device: Etiology and Outcomes in the Continuous—Flow Era. *Ann Thorac Surg*. 2010. 90:1270–7.

Aslam S, Hernandez M, Thornby J, et al. Risk Factors and Outcomes of Fungal Ventricular Assist Device Infections. *Clin Infect Dis*. 2010. 30:644–71.

CHAPTER 58

Hand Hygiene Monitoring

Rekha Murthy, MD and Jonathan Grein, MD

Key Issues

Hand hygiene (HH) compliance by healthcare workers (HCW) is an important quality measure in reducing healthcare associated infections, and monitoring compliance to provide feedback is critical to improving performance.

Known Facts

- HH remains the cornerstone of infection prevention, and improvements in compliance have been associated with reduction of health care associated infections and pathogen transmission.
- Healthcare facilities should take a comprehensive, systematic approach to assessing HH performance and provide regular feedback to improve compliance based on established goals.
- The ideal approach to monitoring HH compliance should be free of bias, not interfere with HCW activities or behavior, assess the quality of each HH episode, and reliably capture each HH opportunity even during complex care activities. It should not require excessive staffing time or other resources, and be able to provide real-time and specific feedback to improve performance.
- Bias plays a critical role in assessing compliance, and efforts should be taken to minimize its impact. The major types of bias are:
  - Observation bias: The behavior of those being observed is changed by the knowledge that they are being observed. Otherwise referred to as the "Hawthorne" effect.
  - Observer bias: The systematic error introduced by variations in the observation method. This bias can be minimized through the use of experienced observers that conduct observations with a consistent, validated approach.

  - Selection bias: The systematic error introduced through the selection of time and setting for which the observation occurs. This can be minimized by randomly choosing locations, time of day, and type of HCW to be observed.
- The CDC and WHO both provide a variety of educational material and tools to conduct HH surveillance. Additionally, free applications for smartphones and tablets are available (i.e., iScrub Lite).
- A standardized approach to conducting HH surveillance has not been widely adopted across healthcare institutions, making inter-facility comparisons of compliance rates difficult. The WHO provides a standardized HH observation method, based on the "My five moments for HH" model. This tool provides a consistent approach for trained observers.
- A multidimensional approach utilizing HH compliance monitoring with feedback has been shown to result in sustained improvement in HH compliance, including in resource-limited settings.
- Feedback of HH compliance is critical to improve performance, and should optimally include accurate real-time feedback specific to individual HCW.

Direct Observation

This is the most common approach, and typically involves trained (and often covert) observers utilizing a standardized and validated observation tool. This is considered the gold standard for assessing HH compliance, and is the only approach that can assess all HH opportunities. This method can assess HH technique, provide immediate feedback, and can identify other infection control opportunities. It may also allow observers to troubleshoot and provide local solutions for barriers to compliance. Importantly, this approach suffers from many limitations. It is a time-consuming and labor-intensive process that only captures a small proportion (<1–3%) of all HH opportunities. It frequently excludes nighttime and weekend shifts, can be limited by visibility or patient privacy issues, can suffer from poor inter-user reliability, and is subject to several types of bias (most notably observation bias).

Self-reporting or peer-reporting of HH compliance will over-estimate compliance and is considered unreliable. Utilizing patients as observers may be useful in settings where visibility or patient privacy limit observation from trained observers (such as ambulatory clinics). Experience with this approach is limited, and it has suffered from poor response rates and inconsistency. Concerns regarding negative impacts on patient-provider relationships have not been demonstrated in studies. Though only a limited amount of information regarding HH compliance may be provided, it may be a useful strategy in some settings, and may help to further engage patients in their care. This approach may not be easily scalable or appropriate for inpatient settings.

Indirect Assessment of Product Consumption

Monitoring product usage, such as soap, paper towels, or quantity of alcohol-based hand rub (ABHR), has been used as a surrogate for HH compliance. This approach can assess trends in a large number of HH events, incorporates day and night shifts, requires less manpower than direct observation, and minimizes bias. Benchmarks have become available for ABHR usage (in liters per 1,000 patient days), stratified by unit type, that allow for trending and monitoring progress towards established goals. This method does not assess the number of HH opportunities, and can therefore only provide an estimation of compliance. Patient acuity and other factors will impact usage and must be accounted for when estimating compliance. Studies correlating observed compliance with increased product utilization have been mixed, though a correlation between increased ABHR usage and reduced MRSA rates has been described. Other limitations include the lack of HCW specific information, inability to assess HH technique or provide immediate feedback, and inability to account for usage by patients or visitors.

Electronic counting devices have been developed to offset some of the above limitations. These devices allow for collection of time and date-specific information, and can provide dispenser-specific information helpful in assessing optimal dispenser type and placement. Usage data can be wirelessly downloaded to reduce manual data collection. Limiting factors include significant technology support, cost of device installation, as well as maintenance and routine battery replacement.

Electronic HH Compliance Systems

A wide variety of electronic devices has become available to assess HH compliance. These systems use a variety of sensors to detect HCW entry into a room or patient "zone," and can prompt HCW if HH product is not dispensed within a certain time after entry or exit. Some systems can detect the presence of alcohol on HCW hands, and can allow HCW-specific tracking with special badges. Additionally, certain systems utilize wireless technology (including WiFi, RFID, or ultrasound) to track HCW location in real-time, which may offer other advantages such as tracking inventory or assessing workflow patterns. These systems capture a large number of HH opportunities, can provide specific real-time feedback, and have been shown to significantly improve HH compliance, though published data has been limited to small settings over short periods of time.

Although advances in this technology appear promising, certain limitations remain. These approaches may be costly, require sensor installation and maintenance, and require significant technology support that may be limited by existing technology infrastructure. No electronic system is able to assess all HH opportunities, such as HH prior to aseptic procedures, following exposure to bodily fluids, or when patients are outside the hospital room. Although accuracy has been generally high when compared to direct observation, even small inaccuracies are significant if used to hold individual HCW accountable for non-compliance. These systems have variable ability to assess HH compliance during high frequency or complex care events. Ensuring HCW acceptance of these methods requires organizational planning and advanced preparation.

Video monitoring to assess HH has been shown to improve HH compliance. This approach requires careful camera placement to limit patient privacy concerns, requires installation and hard-wiring, and utilizes external auditors to evaluate compliance.

Controversial Issues

- The ideal approach to monitoring HH compliance is not clear; each has numerous advantages and limitations. Although direct observation is considered the gold standard, it suffers from many important limitations that limit its generalizability. The accuracy and reliability of each approach is not well understood.

- There is variability in the assessment of "compliance." Institution-specific approaches vary regarding their approach to measuring compliance, training observers, and in the volume or frequency of observations performed. This variability makes comparison of compliance rates between institutions difficult. Although tools are available to provide a consistent approach, they are not yet widely adopted.
- Although general improvements in HH have been associated with reduced healthcare associated infections, the optimal "threshold" for HH compliance to improve clinical outcomes is not understood.
- Outpatient and ambulatory care areas provide unique challenges to monitoring HH compliance, are less studied, and optimal approaches in these areas are not well understood.
- Public reporting of HH compliance is controversial. Inconsistent HH monitoring approaches between institutions, resource constraints, and concerns that public reporting may drive artificial increases without improving performance are common arguments against public reporting.
- Optimal approaches to improving and sustaining HH compliance are not understood. Models utilizing HCW-specific accountability and consequences for non-compliance may be effective but remain poorly studied.
- There are limited data on the long-term impact of various approaches to sustaining HH compliance, including cost-effectiveness, HCW acceptance, or impact on health care associated infections.

Suggested Practice

The optimal approach to monitoring HH compliance is variable, and depends on organizational goals and available resources. A high degree of institutional leadership support and visibility, coupled with allocation of resources for ongoing HH monitoring and feedback, is critical to any successful HH campaign. Healthcare institutions should develop a sustainable, credible, and reliable process to monitor HH that is accurate and attempts to minimize bias. Most often, direct observation by trained observers utilizing a consistent approach with validated tools is the primary method of choice, though this may be done in

conjunction with other methods. Efforts to improve performance should utilize pre-existing quality-improvement structures, and should emphasize a process for direct and timely feedback. If the performance improvement process relies on HCW-specific accountability and consequences for non-compliance, then a high degree of accuracy for each observation is essential, along with strong leadership support.

Summary

The growing recognition of the importance of HH monitoring as a component of infection prevention programs in healthcare facilities has led to advances in direct and indirect measurement approaches. Though limitations apply to all of these methods, tools are available to aid implementation of HH measurement and feedback to support these efforts in a variety of settings.

References

Boyce JM. Measuring healthcare worker hand hygiene activity: Current practices and emerging technologies. *Infect Control Hosp Epidemiol*. 2011. 32:1016–28.

WHO guidelines on hand hygiene in health care. First global patient safety challenge. Clean care is safer care, 2009. http://whqlibdoc.who.int/publications/2009/9789241597906_eng.pdf (Accessed 1 November 2013).

Boyce JM, Pittet D. Guidelines for hand hygiene in health-care settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA hand hygiene task force. *Infect Control Hosp Epidemiol*. 2002. 23:S3–S40.

Measuring hand hygiene adherence: Overcoming the challenges. The Joint Commission, 2009. http://www.jointcommission.org/Measuring_Hand_Hygiene_Adherence_Overcoming_the_Challenges_/ (Accessed 4 November 2013).

Gould DJ, Drey NS, Creedon S. Routine hand hygiene audit by direct observation: Has nemesis arrived? *J Hosp Infect*. 2011. 77:290–3.

Muller MP, Detsky AS. Public reporting of hospital hand hygiene compliance-helpful or harmful? *JAMA*. 2010. 304:1116–7.

Sax H, Allegranzi B, Chraiti MN, Boyce J, Larson E, Pittet D. The World Health Organization hand hygiene observation method. *Am J Infect Control*. 2009. 37:827–34.

Larson E. Monitoring hand hygiene: Meaningless, harmful, or helpful? *Am J Infect Control*. 2013. 41:S42–5.

Marra AR, Moura DF, Paes AT, dos Santos OF, Edmond MB. Measuring rates of hand hygiene adherence in the intensive care setting: A comparative study of direct observation, product usage, and electronic counting devices. *Infect Control Hosp Epidemiol*. 2010. 31:796–801.

Sroka S, Gastmeier P, Meyer E. Impact of alcohol hand-rub use on methicillin-resistant *Staphylococcus aureus*: An analysis of the literature. *J Hosp Infect*. 2010. 74:204–11.

Rosenthal VD, Pawar M, Leblebicioglu H, Navoa-Ng JA, Villamil-Gomez W, Armas-Ruiz A, et al. Impact of the International Consortium (INICC) multidimensional hand hygiene approach over 13 years in 51 cities of 19 limited-resource countries from Latin America, Asia, the Middle East, and Europe. *Infect Control Hosp Epidemiol*. 2013. 34:415–23.

CHAPTER 59

Healthcare Personnel Attire in Non-Operating Room Settings

Tara Palmore MD, FACP and
Gonzalo Bearman MD, MPH, FACP

Key Issues

The role of healthcare personnel (HCP) attire in cross-transmission of pathogens remains unclear. Guidance on HCP attire in non-operating room settings should attempt to balance professional appearance, comfort, and practicality with the potential risk that attire will contribute to the spread of health care associated microbes. Institutions considering these optional measures should introduce them with a well-organized communication and education effort directed at both HCP and patients.

Known Facts

- There is a growing awareness of the potential role of fomites in the transmission of health care associated microorganisms.
- Studies have demonstrated contamination of HCP apparel (scrubs, white coats, ties) with potential pathogens, although the role of clothing in transmission of these microorganisms to patients has not been established.
- Most studies on patient attitudes toward HCP attire indicate that patients favor formal attire, including a white coat.
- Patients generally do not perceive white coats, formal attire, or neckties as posing infection risks; however, when informed of potential risks associated with certain types of attire, patients are willing to change their preferences for physician attire.
- No clinical studies have demonstrated cross-transmission of health care associated pathogens from a HCP to a patient via apparel. A number of small prospective trials have documented contamination of HCP apparel with a variety of pathogens. These findings raise a hypothetical concern for pathogen cross-transmission to patients.

- Name tags have been identified consistently by patients as an important component of HCP attire.

Controversial Issues

- The United Kingdom (UK) has adopted a "bare below the elbows" (BBE) approach (wearing of short sleeves and no wristwatch, jewelry, or ties during clinical practice), based on the theory that the strategy will limit patient contact with contaminated HCP apparel and promote better hand and wrist hygiene.
- The impact of BBE on HCP bacterial counts remains poorly defined. One randomized trial comparing bacterial contamination of white coats against BBE found no difference in total bacterial or MRSA counts (on either the apparel itself or the volar surface of the wrist) at the end of an eight-hour workday.
- Uptake of BBE in healthcare settings has been variable.
- To date there is no definitive evidence that a BBE approach to inpatient care results in improved HAI outcomes.
- The optimal frequency for laundering apparel is not clear based on the current literature. Apparel worn at the bedside that comes in contact with the patient or patient environment should ideally be laundered after daily use.
- Whether HCP attire for non-surgical settings should be laundered at home or professionally remains uncertain. A combination of washing at higher temperatures and tumble drying or ironing has been associated with elimination of both pathogenic Gram-positive and Gram-negative bacteria from HCP clothing.

Suggested Practice

- Although the choice of HCP attire may affect infection rates, evidence-based measures to prevent HAIs (e.g. hand hygiene, appropriate device insertion and care, isolation of patients with communicable diseases, environmental disinfection) should take priority.
- Facilities may consider adoption of a BBE approach to inpatient care as an infection prevention adjunct. There are no data to guide the optimal choice of alternate attire, such as scrub uniforms or other short-sleeved personal attire. This approach is supported by biological plausibility and is unlikely to cause harm.

- In facilities where white coats are used for professional appearance, commonsense measures should be considered. HCPs engaged in direct patient care should possess two or more white coats and have access to a convenient and economical means to launder white coats. Also, institutions should provide coat hooks that would allow HCP to remove their white coat (or other long-sleeved outerwear) prior to contact with patients or patients' immediate environment.
- Neckties should be secured to prevent them from coming into direct contact with patients or patients' immediate environment.
- Any apparel worn at the bedside that comes in contact with patients or patients' environment should be laundered after daily use.
- If laundered at home, apparel should be washed in a hot water wash cycle followed by a cycle in the dryer.
- All HCP footwear should have closed toes, low heels, and non-skid soles.

Summary

The role of HCP attire in cross-transmission of health care associated pathogens has not been established. HCP attire frequently becomes contaminated with bacteria during the course of clinical care. This includes scrubs, neckties, and white coats, with pathogens such as *S. aureus*, MRSA, VRE, and Gram-negative bacilli. The impact of apparel microbial burden on occurrence of HAI is undefined. Although patients frequently express preferences for certain types of HCP attire, including white coats, they were willing to change their preferences when informed of potential risks associated with HCP attire. Patient comfort, satisfaction, trust, and confidence in their physicians is unlikely to be affected by practitioners' attire choice, with the exception of name tags, which they viewed as essential.

A BBE approach is in effect in the U.K. for inpatient care; this strategy may enhance hand hygiene to the level of the wrist, but its impact on HAI rates remains unknown. Facilities may consider adoption of a BBE approach to inpatient care as an adjunctive infection prevention measure. The optimal choice of alternate attire, such as scrub uniforms, remains unknown. This strategy is supported by biological plausibility and is

unlikely to cause harm. In facilities where white coats are used for professional appearance, HCP engaged in direct patient care should possess two or more white coats and have access to a convenient means of laundering the white coats. The benefit of institutional laundering of HCP scrubs versus home laundering for non-OR use remains unproven. Institutions should provide coat hooks that would allow HCP to remove their white coat (or other long-sleeved outerwear) prior to contact with patients or the patient's immediate environment.

Ties should be fastened so as to not come into direct contact with the patient or immediate patient care environment. Shoes should have closed toes, low heels, and non-skid soles. Name tags should be used and easily visible.

Reference

Ardolino A, Williams LA, Crook TB, Taylor HP. Bare below the elbows: What do patients think? *J Hosp Infect*. 2009. 71:291–293.

Baevsky RH, Fisher AL, Smithline HA, Salzberg MR. The influence of physician attire on patient satisfaction. *Acad Emerg Med*. 1998. 5:82–84.

Bond L, Clamp PJ, Gray K, Van D, V. Patients' perceptions of doctors' clothing: Should we really be 'bare below the elbow'? *J Laryngol Otol*. 2010. 124:963–966.

Fischer RL, Hansen CE, Hunter RL, Veloski JJ. Does physician attire influence patient satisfaction in an outpatient obstetrics and gynecology setting? *Am J Obstet Gynecol*. 2007. 196:186–5.

Gallagher J, Waldron LF, Stack J, Barragry J. Dress and address: Patient preferences regarding doctor's style of dress and patient interaction. *Ir Med J*. 2008. 101:211–213.

Gherardi G, Cameron J, West A, Crossley M. Are we dressed to impress? A descriptive survey assessing patients' preference of doctors' attire in the hospital setting. *Clin Med*. 2009. 9:519–524.

Hueston WJ, Carek SM. Patients' preference for physician attire: A survey of patients in family medicine training practices. *Fam Med*. 2011. 43:643–647.

Ikusaka M, Kamegai M, Sunaga T, et al. Patients' attitude toward consultations by a physician without a white coat in Japan. *Intern Med*. 1999. 38:533–536.

Li SF, Haber M. Patient attitudes toward emergency physician attire. *J Emerg Med*. 2005. 29:1–3.

Major K, Hayase Y, Balderrama D, Lefor AT. Attitudes regarding surgeons' attire. *Am J Surg*. 2005. 190:103–106.

Matsui D, Cho M, Rieder MJ. Physicians' attire as perceived by young children and their parents: The myth of the white coat syndrome. *Pediatr Emerg Care*. 1998. 14:198–201.
McKinstry B, Wang JX. Putting on the style: What patients think of the way their doctor dresses. *Br J Gen Pract*. 1991. 41:270, 275–278.
Nair BR, Attia JR, Mears SR, Hitchcock KI. Evidence-based physicians' dressing: A crossover trial. *Med J Aust*. 2002. 177:681–682.
Palazzo S, Hocken DB. Patients' perspectives on how doctors dress. *J Hosp Infect*. 2010. 74:30–34.
Rehman SU, Nietert PJ, Cope DW, Kilpatrick AO. What to wear today? Effect of doctor's attire on the trust and confidence of patients. *Am J Med*. 2005. 118:1279–1286.
Shelton CL, Raistrick C, Warburton K, Siddiqui KH. Can changes in clinical attire reduce likelihood of cross-infection without jeopardising the doctor-patient relationship? *J Hosp Infect*. 2010. 74:22–29.
Baxter JA, Dale O, Morritt A, Pollock JC. Bare Below the Elbows: Professionalism vs Infection Risk. *Bulletin of The Royal College of Surgeons of England*. 2010. 92:248–251.
Toquero L, Abournarzouk O, Owers C, Chiang R, Thiagarajah S, Amin S. Bare below the elbows—the patient's perspective. *Quality and Patient Safety 2*. 2011.
Munoz-Price LS, Arheart KL, Lubarsky DA, Birnbach DJ. Differential laundering practices of white coats and scrubs among health care professionals. *Am J Infect Control*. 2013. 41:565–567.
Burden M, Cervantes L, Weed D, Keniston A, Price CS, Albert RK. Newly cleaned physician uniforms and infrequently washed white coats have similar rates of bacterial contamination after an 8-hour workday: A randomized controlled trial. *J Hosp Med*. 2011. 6:177–182.
Gaspard P, Eschbach E, Gunther D, Gayet S, Bertrand X, Talon D. Methicillin-resistant *Staphylococcus aureus* contamination of healthcare workers' uniforms in long-term care facilities. *J Hosp Infect*. 2009. 71:170–175.
Loh W, Ng VV, Holton J. Bacterial flora on the white coats of medical students. *J Hosp Infect*. 2000. 45:65–68.
Lopez PJ, Ron O, Parthasarathy P, Soothill J, Spitz L. Bacterial counts from hospital doctors' ties are higher than those from shirts. *Am J Infect Control*. 2009. 37:79–80.
Treakle AM, Thom KA, Furuno JP, Strauss SM, Harris AD, Perencevich EN. Bacterial contamination of health care workers' white coats. *Am J Infect Control*. 2009. 37:101–105.
Wiener-Well Y, Galuty M, Rudensky B, Schlesinger Y, Attias D, Yinnon AM. Nursing and physician attire as possible source of nosocomial infections. *Am J Infect Control*. 2011. 39:555–559.

Munoz-Price LS, Arheart KL, Mills JP, et al. Associations between bacterial contamination of health care workers' hands and contamination of white coats and scrubs. *Am J Infect Control*. 2012. 40:e245–e248.
Burger A, Wijewardena C, Clayson S, Greatorex RA. Bare below elbows: Does this policy affect handwashing efficacy and reduce bacterial colonisation? *Ann R Coll Surg Engl*. 2011. 93:13–16.
Willis-Owen CA, Subramanian P, Kumari P, Houlihan-Burne D. Effects of 'bare below the elbows' policy on hand contamination of 92 hospital doctors in a district general hospital. *J Hosp Infect*. 2010. 75:116–119.
Farrington RM, Rabindran J, Crocker G, Ali R, Pollard N, Dalton HR. 'Bare below the elbows' and quality of hand washing: A randomized comparison study. *J Hosp Infect*. 2010. 74:86–88.
Jacob G. Uniforms and workwear: An evidence base for developing local policy. *NHS Department of Health Policy* [serial online]. 2007.
Patel SN, Murray-Leonard J, Wilson AP. Laundering of hospital staff uniforms at home. *J Hosp Infect*. 2006. 62:89–93.
Lakdawala N, Pham J, Shah M, Holton J. Effectiveness of low-temperature domestic laundry on the decontamination of healthcare workers' uniforms. *Infect Control Hosp Epidemiol*. 2011. 32:1103–1108.
Chiu MC, Wang MJ. Professional footwear evaluation for clinical nurses. *Appl Ergon*. 2007. 38:133–141.
Wilson JA, Loveday HP, Hoffman PN, Pratt RJ. Uniform: An evidence review of the microbiological significance of uniforms and uniform policy in the prevention and control of healthcare-associated infections. Report to the Department of Health (England). *J Hosp Infect*. 2007. 6:301–307.

CHAPTER 60

Ebola Virus Disease

J. Daniel Markley, DO, Gonzalo Bearman MD, MPH, and Richard P. Wenzel, MD, MSc

Key Issue:
The 2014 Ebola epidemic is the largest in history, with widespread transmission in multiple countries in West Africa. Several countries in Europe and the United States have received patients with Ebola, most of whom are healthcare workers transported home for care.

Known Facts

- Ebola virus disease, previously known as Ebola hemorrhagic fever, is a rare and deadly disease caused by infection with one of the Ebola virus species (Zaire, Sudan, Bundibugyo, or Tai Forest virus).
- Ebola viruses are found in several African countries. The first Ebola virus was discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo. A second outbreak in Sudan occurred simultaneously. Since then, over 20 outbreaks have appeared sporadically in Africa.
- Ebola virus is spread through direct contact with the blood or body fluids (including but not limited to feces, saliva, sweat, urine, vomit, and semen) of a person who is sick with Ebola. The virus in blood and body fluids can enter another person's body through broken skin or unprotected mucous membranes in, for example, the eyes, nose, or mouth.
- After the onset of symptoms, as the disease progresses high grade viremia occurs.
- Ebola virus is not thought to be spread through air or by water.
- People with Ebola symptoms become more infectious with progressive symptoms. As a result, exposure to the virus is more likely when someone is bleeding or vomiting.

- The incubation period for the disease, from exposure to when signs or symptoms appear, is 2 to 21 days, but the average is 8 to 10 days.
- Signs of Ebola include fever and symptoms such as severe headache, fatigue, muscle pain, vomiting, diarrhea, abdominal (stomach) pain, or unexplained hemorrhage (bleeding or bruising).
- Ebola poses minimal risk to travelers or the general public who have not cared for or been in close contact (within 3 feet or 1 meter) with someone sick with Ebola for a prolonged period.

Controversial Issues

- While transmission through indirect contact with Ebola virus via fomites has been documented, current evidence suggests this is a rare occurrence.
- The risk of infection after skin contamination with Ebola is unknown, therefore until further research provides additional data, contamination of even intact skin must be completely avoided.
- Ebola virus has been detected in semen after patients have recovered, however it is not known if the virus can be transmitted through sex (including oral sex). Consequently, it is recommended that men who have recovered from Ebola abstain from sex (including oral sex) for three months.
- Ebola virus has been detected in breast milk, however it is not known if the virus can spread from mothers to their infants through breastfeeding.
- Because healthcare workers have accounted for up to 25% of Ebola cases in prior outbreaks, personal protective equipment (PPE) must be redesigned to be more comfortable and easy to don.
- Ideal PPE for healthcare workers must 1) be impervious to fluid, 2) cover all skin and all underclothing, 3) be easy to don, 4) be easy to remove while minimizing the risk for self contamination, 5) provide maximal comfort for healthcare workers, and 6) be easy to dispose of while minimizing contamination of healthcare workers.

Suggested Practice for the Management of Ebola Virus Disease in Healthcare Settings

General Principles

- Identify and isolate the Ebola patient in a single patient room with a closed door and a private bathroom as soon as possible.
- Limit the number of healthcare workers who come into contact with the Ebola patient (e.g., avoid short shifts), and restrict non-essential personnel and visitors from the patient care area.
- Monitor the patient care area at all times, and log, at a minimum, entry and exit of all healthcare workers who enter the room of an Ebola patient.
- Ensure that a trained observer watches closely each donning and each doffing procedure, and provides supervisory assurance that donning and doffing protocols are followed.
- Ensure that healthcare workers have sufficient time to don and doff PPE correctly without disturbances.
- Ensure that practical precautions are taken during patient care, such as keeping hands away from the face, limiting touch of surfaces and body fluids, preventing needlestick and sharps injuries, and performing frequent disinfection of gloved hands using an alcohol-based hand rub (ABHR), particularly after handling body fluids.
- Dedicated medical equipment (preferably disposable) should be used to provide patient care.
- All non-dedicated, non-disposable medical equipment used for patient care should be cleaned and disinfected according to the manufacturer's instructions.

Personal Protective Equipment for Healthcare Worker:

- **Powered Air Purifying Respirator (PAPR):** A PAPR with a full face shield, helmet, or headpiece. Any reusable helmet or headpiece must be covered with a single-use (disposable) hood that extends to the shoulders and fully covers the neck and is compatible with the selected PAPR. The facility should follow manufacturer's instructions for decontamination of all reusable components.

  - A PAPR with a self-contained filter and blower unit integrated inside the helmet is preferred.
  - A PAPR with external belt-mounted blower unit requires adjustment of the sequence for donning and doffing, as described below.
- **N95 Respirator:** Single-use (disposable) N95 respirator in combination with single-use (disposable) surgical hood extending to shoulders and single-use (disposable) full face shield.
- Single-use (disposable) fluid-resistant or impermeable gown that extends to at least mid-calf or coverall without integrated hood.
- Single-use (disposable) nitrile examination gloves with extended cuffs. Two pairs of gloves should be worn. At a minimum, outer gloves should have extended cuffs.
- Single-use (disposable), fluid-resistant or impermeable boot covers that extend to at least mid-calf or single-use (disposable) shoe covers. Boot and shoe covers should allow for ease of movement and not present a slip hazard to the worker.
- Single-use (disposable), fluid-resistant or impermeable apron that covers the torso to the level of the mid-calf should be used if Ebola patients have vomiting or diarrhea. An apron provides additional protection against exposure of the front of the body to body fluids or excrement.

Personal Protective Equipment for Trained Observer

A trained observer should not enter the room of a patient with Ebola, but will be in the PPE removal area to observe and assist with removal of specific components of PPE, as outlined below. The observer should not participate in any Ebola patient care activities while conducting observations.

- Single-use (disposable) fluid-resistant or impermeable gown that extends to at least mid-calf or coverall without integrated hood.
- Single-use (disposable) full face shield.
- Single-use (disposable) nitrile examination gloves with extended cuffs. Two pairs of gloves should be worn. At a minimum, outer gloves should have extended cuffs.

- Single-use (disposable) fluid-resistant or impermeable shoe covers. Shoe covers should allow for ease of movement and not present a slip hazard to the worker.

Donning and Doffing:

Please refer to the CDC website:
http://www.cdc.gov/vhf/ebola/hcp/procedures-for-ppe.html

- Facilities should ensure that space and layout allow for clear separation between clean and potentially contaminated areas. It is critical that a one-way flow of care moving from clean areas (e.g., area where PPE is donned and unused equipment is stored) to the patient room and to the PPE removal area.
- There should be an area outside the Ebola patient room (e.g., a nearby vacant patient room, a marked area in the hallway outside the patient room) where clean PPE is stored and where healthcare workers can don PPE before entering the patient's room.

Disinfection

- Disinfect immediately any visibly contaminated PPE surfaces, equipment, or patient care area surfaces using a registered disinfectant wipe.
- Perform regular cleaning and disinfection of patient care area surfaces, even absent visible contamination.
  - This should be performed only by nurses or physicians as part of patient care activities in order to limit the number of additional healthcare workers who enter the room.

Summary:

Ebola virus disease is a rare infection with high mortality and no effective antiviral treatment. Ebola virus is spread through direct contact with the blood or body fluids (including but not limited to feces, saliva, sweat, urine, vomit, and semen) of a person who is sick with Ebola. The cornerstone of infection prevention for Ebola is prompt recognition of the disease, isolation patients and meticulous use of personal protective equipment. The donning and doffing of personal protective equipment should be done by trained personnel and should be overseen by a trained

observer. The ideal PPE for healthcare workers must be impervious to fluid, cover all skin and all underclothing be easy to don and doff while minimizing the risk for self-contamination, provide maximal comfort for healthcare workers and be easy to dispose of while minimizing contamination of healthcare workers. Facilities should ensure that space and layout allow for clear separation between clean and potentially contaminated areas. It is critical that a one-way flow of care moving from clean areas to the patient room and to the PPE removal area. Visibly contaminated PPE surfaces, equipment, or patient care area surfaces should be promptly disinfected using a registered disinfectant. Disinfection should be performed by nurses or physicians as part of patient care activities in order to limit the number of additional healthcare workers who enter the room.

References:

Edmond MB, Diekema DJ, Perencevich EN. Ebola Virus Disease and the Need for New Personal Protective Equipment. *JAMA*. 2014. October 28.

Del Rio C, Mehta AK, Lyon GM, et al. Ebola Hemorrhagic Fever in 2014: The Tale of an Evolving Epidemic. *Ann Intern Med*. 2014. November 18. 161(10):746-748.

CDC: Key Messages—Ebola Virus Disease, West Africa (updated 11/19/2014). http://www.cdc.gov/vhf/ebola/.

Index

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W

X

Y

Z

International Society for Infectious Diseases
9 Babcock Street, Unit 3
Brookline, MA 02446 • USA
Phone: (617) 277-0551
Fax: (617) 278-9113
E-mail: info@isid.org
Web site: http://www.isid.org

ISBN 0-9749031-0-8