Antibiotic Policies
Antibiotic Policies

Controlling Hospital Acquired Infection
Preface

Healthcare-associated infections (HAIs) are an increasing problem worldwide and need to be addressed urgently. In the European Union, about 7% of patients in acute care hospitals experience HAIs; recent analysis discloses an even higher prevalence in developing countries. The international contributors to this book, in drawing on their considerable experience in different settings, perform an important function by clarifying the main issues for tackling HAIs. Their assessment necessarily covers both the characteristics of the principal pathogens and the key organisational and operational factors implicated for hospitals and their staff. This detailed analysis is accompanied by discussion of best practice for preventing and managing the challenges presented by HAIs. I welcome the emerging perspective from this book that emphasises that the options for antibiotic policy must cover a broad range of activities. There are policy issues to face for surveillance, for prudent and responsible prescribing, for developing and implementing guidelines for infection control, and for raising awareness of the threat of HAIs throughout the medical profession and with patients.

The present volume is very valuable in communicating strong messages concerning the nature of the burden to individuals and to health systems, but also about the opportunities for change to improve patient safety. From my own experience with Academies of Science across Europe (who, as the European Academies Science Advisory Council, have also reported on some of these issues, www.easac.eu), I know that there is still much to be done to engage with decision-makers at all levels about these matters.

I am also convinced that there is an urgent requirement to increase collective commitment to biomedical research and innovation because otherwise the longer-term battle against HAIs and associated antibiotic resistance will be lost. We need this research—integrating epidemiology, social and biomedical sciences—so that we can better understand the behaviour of both microbial and human populations. Moreover, we need to become more adept in translating the research advances into faster development of novel, improved, diagnostics and therapeutics and their use in new and better ways.

To be effective, therefore, public health policy for the use of those antimicrobial agents presently available to us must be well coordinated with innovation policy.
In addition, strategy for human health must be aligned coherently with strategy for veterinary health. The common element in developing all of these policies is the reliance on robust, validated evidence. Taken together, the individual contributors in this book, assembled by insightful editors, play a vital role in collating that definitive evidence and assessing its implications, notwithstanding the inevitable uncertainties occasioned by the rapid pace of change in burden of infection and the varying experience in different countries. This book serves a twin purpose in helping to construct a more informed evidence base for coherent policy making while, at the same time, providing practical advice for health professionals in the prevention and control of HAIs.

Volker ter Meulen
Past president of European Academies Scientific Advisory Council (EASAC)
Past president of the Leopoldina
# Contents

**Healthcare Associated Infections—The Size of the Problem** ........................................... 1
Eimear Brannigan and Alison Holmes

**The Antibiotic Paradox** ........................................................................................................ 15
Ian M. Gould

**The Epidemiology of Pan/Extreme Drug Resistance** .................................................. 27
Yoshiro Hayashi and David L. Paterson

**Hospital Antibiotic Stewardship to Control Resistance—How Should It be Done?** .................................................................................................................. 39
Ian M. Gould

**Controlling *Clostridium difficile* Infection and the Role of Antibiotic Stewardship** .......................... 53
Ed J. Kuijper, S. Johnson, A. Goorhuis and M. H. Wilcox

**The Control of MRSA** .......................................................................................................... 63
Evelina Tacconelli and G. De Angelis

**The Role of Antibiotic Policies in Controlling VRE** .................................................. 81
Abhijit M. Bal

**The Control of ESBL-Producing Bacteria** ........................................................................... 91
Peter M. Hawkey

**Controlling Hospital-Acquired Infection due to Carbapenem-Resistant Enterobacteriaceae (CRE)** .................................................................................................................. 105
Mitchell J. Schwaber, Yehuda Carmeli and Stephan Harbarth

**Control of Multi-Drug Resistant *Acinetobacter* Infections** .................................. 117
Paschalis Vergidis and Matthew E. Falagas
The Control of Multidrug-Resistant *Pseudomonas*: Insights into
Epidemiology and Management ........................................... 127
Evangelos J. Giamarellos-Bourboulis

Multidrug-Resistant Infections in Low-Resource Health Care Settings ... 141
Cara Winters and Hellen Gelband

Germ Shed Management in the United States .......................... 163
Kevin Outterson and Olga Yevtukhova

Required Actions to Control Antimicrobial Resistant
Healthcare-Associated Infections ........................................... 183
Inge C. Gyssens and Jos W. M. van der Meer

Index ..................................................................................... 203
Contributors

G. De Angelis  Department of Infectious Diseases, Università Cattolica, Rome, Italy  
etacconelli@rm.unicatt.it

Abhijit M. Bal  Consultant Microbiologist and Honorary Clinical Senior Lecturer,  
Crosshouse Hospital, NHS Ayrshire and Arran, Lister Street, Kilmarnock KA2 0BE, Scotland, UK  
e-mail: abhijit.bal@nhs.net

Eimear Brannigan  Hammersmith Hospital, 2nd Floor Hammersmith House, Du Cane Road, W12 0HS London, UK  
e-mail: eimear.brannigan@imperial.nhs.uk

Yehuda Carmeli  National Center for Infection Control, Israel Ministry of Health,  
6 Weizmann Street, 64239 Tel Aviv, Israel  
Division of Epidemiology and Preventive Medicine, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel  
e-mail: mitchells@tasmc.health.gov.il

Matthew E. Falagas  Alfa Institute of Biomedical Sciences (AIBS), 9 Neapoleos Street, 15123 Marousi, Athens, Greece  
e-mail: falagas@tufts.edu, m.falagas@aibs.gr

Hellen Gelband  Center for Disease Dynamics, Economics and Policy, 1616 P Street, NW, Suite 600, Washington, DC 20036, USA  
e-mail: gelband@cddep.org

Evangelos J. Giamarellos-Bourboulis  4th Department of Internal Medicine,  
ATTIKON University Hospital, 1 Rimini Street, 124 62 Athens, Greece  
e-mail: egiamarel@med.uoa.gr

A. Goorhuis  Department of Medical Microbiology, Leiden University Medical Center (LUMC), Albinusdreef 2, 2333 ZA, Leiden, The Netherlands  
e-mail: E.J.Kuijper@lumc.nl

Ian M. Gould  Department of Medical Microbiology, Aberdeen Royal Infirmary,  
Foresterhill, AB25 2ZN Aberdeen, Scotland  
e-mail: i.m.gould@abdn.ac.uk
Stephan Harbarth  Infection Control Program, Geneva University Hospitals & Medical School, 1211 Geneva 14, Switzerland

Peter M. Hawkey  School of Immunology and Infection, University of Birmingham, Edgbaston, B15 2TT, Birmingham, UK
e-mail: peter.hawkey@heartofengland.nhs.uk

Yoshiro Hayashi  The University of Queensland, UQ Centre for Clinical Research, Herston, Brisbane, Australia
e-mail: y.hayashi@uq.edu.au
Royal Brisbane and Women’s Hospital, Department of Intensive Care Medicine, Herston, Brisbane, Australia

Alison Holmes  Hammersmith Hospital, 2nd Floor Hammersmith House, Du Cane Road, W12 0HS London, UK
e-mail: alison.holmes@imperial.ac.uk

S. Johnson  Departments of Research and Medicine, Hines Veterans Affairs Hospital and Loyola University Medical Center, Chicago, IL, USA

Ed J. Kuijper  Department of Medical Microbiology, Leiden University Medical Center (LUMC), Albinusdreef 2, 2333 ZA Leiden, The Netherlands
e-mail: E.J.Kuijper@lumc.nl

Kevin Outterson  Boston University School of Law, 765 Commonwealth Avenue, 1140, Boston, MA 02215, USA
e-mail: mko@bu.edu

David L. Paterson  The University of Queensland, UQ Centre for Clinical Research, Herston, Brisbane, Australia
e-mail: david.antibiotics@gmail.com

Mitchell J. Schwaber  National Center for Infection Control, Israel Ministry of Health, 6 Weizmann Street, 64239 Tel Aviv, Israel
e-mail: mitchells@tasmc.health.gov.il

Evelina Tacconelli  Department of Infectious Diseases, Università Cattolica, Rome, Italy
e-mail: etacconelli@rm.unicatt.it

Jos W. M. van der Meer  Department of Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
e-mail: J.vanderMeer@aig.umcn.nl

Paschalis Vergidis  Department of Medicine, Mayo Clinic College of Medicine, Rochester, MN, USA

M. H. Wilcox  Department of Microbiology, Old Medical School, Leeds General Infirmary, Leeds, UK

Cara Winters  3644 N. 52nd St, Phoenix, AZ 85018, USA

Olga Yevtukhova  Boston University School of Public Health, 715 Albany Street, Talbot Building, Boston, MA 02118, USA
Introduction

Hospitals, by their very nature, are dangerous places. Sick and infected patients are clustered together in one institution, often in close proximity to those who are immunosuppressed due to recent surgery, chemotherapy or transplantation. Contact between these various patient groups is easily achieved via the hands of healthcare workers (HCWs), use of shared equipment or the hospital’s air handling system. Thus, for many virulent pathogens, hospitals can effectively act as a giant PCR machine, rapidly multiplying the number of resistant isolates encountered, but with no need for Taq polymerase. Until recently, the key focus of many health bureaucracies has been primarily on the quantity of healthcare—namely patient throughput, hospital length of stay and size of patient waiting lists. It is only in recent years as hospital-associated infections have become increasingly common and more difficult to treat, that there has been a greater emphasis on healthcare quality—particularly in terms of limiting the emergence and spread of antimicrobial resistant pathogens.

Overall, progress in understanding and successfully controlling healthcare-associated infections (HAIs) has been painfully slow. Although many of the important issues associated with antimicrobial resistance were nicely summarised in the 2001 World Health Organization (WHO) report—“WHO—Global strategy for containment of antimicrobial resistance” [1], the public release of this important document was an unfortunate disaster, with its long-scheduled US public launch being only 30–60 min after the first terrorist attacks on the World Trade Center on 11th September 2001. Thus, this strategy received little public attention and in the months that followed with the subsequent, but unrelated, anthrax attacks, tens of thousands of Americans, instead of limiting their antibiotic use, were given prolonged courses of ciprofloxacin and other agents as post-exposure prophylaxis [2]. Nevertheless, many of the issues raised in this important WHO strategy remain highly relevant today. The problem, however, is that the severity of the antimicrobial resistance issue has increased dramatically during the past 10 years since 2001, such that what was previously a storm cloud on the horizon is now a cyclone/hurricane directly affecting patient care and outcomes.

In broad terms, there are two means by which patients can develop multi-resistant infections—they can either develop their own resistant pathogen, or they can acquire someone else’s strain.
Emergence of new resistant pathogens is directly related to antimicrobial selection pressure either via the mutation of new resistance genes or the alteration of bacterial ecology (e.g. in the gut) that facilitates the transfer of naturally occurring or emergent resistance genes from one bacterial class to another. The use and misuse of antibiotics is intimately involved in both these mechanisms—particularly if antibiotic dosing is inappropriately low such that Darwinian selection of resistant strains is facilitated. Of course, antibiotic use in food production can have the same effect as direct human antibiotic misuse, since it can select for both resistant pathogens (e.g. fluoroquinolone-resistant *Campylobacter* in chicken meat) or resistance genes such that food consumption results in either direct fecal colonisation or acquisition of resistance genes by routine gut flora [3, 4]. Antibiotic stewardship is therefore not simply a hospital issue.

Cross-transmission of resistant pathogens between patients is a relatively simple process in many hospitals and is therefore a key focus of hospital infection control initiatives. However, supposedly simple concepts such as improved hand hygiene and reliable cleaning of shared hospital equipment and the hospital environment have proven difficult to implement in practice, largely because they require a change in human behaviour [5–7]. Culture-change programs in healthcare are time-consuming, expensive, non-glamorous and require ongoing maintenance to be effective and result in sustained behavioural change. Nevertheless, programs such as the “WHO Patient Safety: Clean Care is Safer Care” is a good example of where effective culture-change in terms of improved hand hygiene compliance (with increased use of alcohol-based hand-rub) can have a major impact on rates of nosocomial infections [8].

Issues related to hospital design are also crucial to limiting transmission of resistant pathogens. The ideal hospital would probably consist entirely of single-bed rooms, each with an ensuite bathroom. Simple infection control axioms such as “one bum per toilet” seem obvious if one aims to limit disease transmission, but are rarely implemented in practice—generally because of perceived increased costs. Yet, the advantages of such a hospital design would be the ready physical separation of infected from non-infected patients and potential savings (both human and financial) in preventing hospital-associated infections [9, 10].

Within hospitals, appropriate antibiotic prescribing is paramount. However, successful antibiotic stewardship programs are not necessarily easy to implement and generally depend on the presence of senior Executive commitment to the program, clearly defined (preferably evidence-based) antibiotic prescribing guidelines and an effective system of monitoring and oversight [1, 11, 12].

It is in this broad context of rapidly emerging and widespread antimicrobial resistance that this text “Antibiotic policies: controlling hospital-acquired infection” is so relevant, since it concisely aims to summarize the current situation regarding antimicrobial resistance, both in terms of the general policies needed for control and the specific issues related to key multi-resistant pathogens.
References