

## **Briefing Note**

### **Antimicrobial Resistance: An Emerging Water, Sanitation and Hygiene Issue**

**WASH FOR  
HEALTH**

**© World Health Organization 2014**

All rights reserved. Publications of the World Health Organization are available on the WHO website ([www.who.int](http://www.who.int)) or can be purchased from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; email: [bookorders@who.int](mailto:bookorders@who.int)).

Requests for permission to reproduce or translate WHO publications – whether for sale or for non-commercial distribution – should be addressed to WHO Press through the WHO website ([www.who.int/about/licensing/copyright\\_form/en/index.html](http://www.who.int/about/licensing/copyright_form/en/index.html)).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

This publication contains the collective views of an international group of experts and does not necessarily represent the decisions or the policies of the World Health Organization.

Printed by the WHO Document Production Services, Geneva, Switzerland

## Contents

|   |      |
|---|------|
| List of contributors .....  | iii  |
| 1 Antimicrobial agents in the environment and antimicrobial resistance: an overview of the problem .....                | iv   |
| 2 Environmental presence and exposure source hotspots .....   | vi   |
| 3 Implications of environmental antimicrobial-resistant bacteria and AMR genes for human health .....                   | vii  |
| 4 Environmental antimicrobial agents, antimicrobial resistance and risk–based guidelines for water and sanitation ..... | viii |
| 5 Proposed directions for risk assessment, management, policies and research .....                                      | ix   |
| 5.1 Risk assessment .....   | ix   |
| 5.2 Risk management .....   | x    |
| 5.3 Policy / global level actions .....   | xi   |
| 5.4 Research needs .....  | xii  |
| 6 References .....  | xiii |

## List of contributors

### Lead authors

Mark D. Sobsey

*Department of Environmental Sciences and Engineering, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, United States of America*

Lydia Abebe

*Department of Environmental Sciences and Engineering, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, United States of America*

### Co-authors

Antoine Andreumont

*Laboratoire de bactériologie, Hôpital Bichat-Claude Bernard, Paris, France*

Nicholas J. Ashbolt

*Alberta Innovates Translational Research Chair in Water, School of Public Health, University of Alberta, Edmonton, Alberta, Canada*

Ana Maria de Roda Husman

*Laboratory for Zoonoses and Environmental Microbiology, National Institute for Public Health and the Environment (RIVM) – Centre for Infectious Disease Control, Bilthoven, the Netherlands*

Karina Yew-Hoong Gin

*Department of Civil and Environmental Engineering, Faculty of Engineering, National University of Singapore, Singapore*

Paul R. Hunter

*The Norwich School of Medicine, University of East Anglia, Norwich, England, United Kingdom*

John Scott Meschke

*Department of Environmental & Occupational Health Sciences, School of Public Health, University of Washington, Seattle, WA, United States of America*

Samuel Vilchez

*Department of Microbiology and Parasitology, Faculty of Medical Sciences, National Autonomous University of Nicaragua, León, Nicaragua*

## 1 Antimicrobial agents in the environment and antimicrobial resistance: an overview of the problem

The considerable overuse, careless use, inappropriate use and unregulated use of many antibiotics and other antimicrobial agents<sup>1</sup> in both human and veterinary medicine are well documented, as is the extensive and largely unregulated use of these agents in animal agriculture and aquaculture, including for growth promotion. Uncontrolled release and disposal of these agents to sanitary sewers and landfills and in effluent discharges from pharmaceutical production facilities are also known to occur.

These imprudent uses and abuses of antibiotics and other antimicrobial agents contribute to the extensive presence of their residues, their metabolites, multiple antimicrobial-resistant bacteria and their functional genes in human and animal wastes, in landfills and their leachates, in water, soil and sediments and in water-dependent food crops, such as seafood and produce. They persist for extended periods of time in many environmental compartments, even when antimicrobial use has ceased.

This briefing note is limited to consideration of antibacterial agents, antibacterial resistance and antibacterial resistance genes. Although it is recognized that antiparasitic, antiviral and antimycotic agents and resistance to them may also pose health risks, few studies have addressed the environmental health aspects of resistance to these agents.<sup>2</sup> With the recent trends in development and use of other antimicrobial agents, there may be an increase in parasitic, fungal and viral resistance, in which the aquatic environment is likely to play a role.

As a result of decades of use and abuse, antibiotics and other antimicrobial agents, their functional metabolites, antimicrobial-resistant bacteria and their antimicrobial resistance (AMR) genes are common and widespread contaminants in water and other environmental media, including wastewater and human excreta used for agricultural or aquacultural purposes or discharged to the environment, where they can persist for long periods of time. Although antibiotics and antibiotic resistance genes are considered natural components of the microbial communities that exist throughout the world's habitable environment, human impacts, including the introduction of synthetic antimicrobial agents, have radically changed their ecology.

Consequently, we now have further emergence and selection of new AMR traits in bacteria, including pathogenic bacteria of human health concern (Martinez, 2009a, 2009b; Wright, 2010), with well documented loss of antimicrobial treatment options for humans. The (aquatic) environment may play different roles in the emergence and spread of AMR, by (1) acting as a collecting vessel of resistant bacteria from animals and humans treated with antibiotics (i.e. anthropogenic resistance); (2) offering

---

<sup>1</sup> The term “antibiotic” is used here to represent any chemical substance produced by a microorganism or semi-synthetically that has the capacity to inhibit the growth of or to kill other microorganisms and is used to treat infections. The term “antimicrobial agent”, often abbreviated to “antimicrobial”, is used here to represent any chemical agent, including synthetic chemicals, that kills microorganisms or suppresses their multiplication or growth to prevent their pathogenic action and is used to treat infections.

<sup>2</sup> Low levels of the antiviral agent oseltamivir were detected in the aquatic environment by Söderström et al. (2009). They concluded that certain duck species may be exposed to the anti-influenza virus drug in water, which could promote the evolution of viral resistance. Azole resistance of the fungus *Aspergillus fumigatus* is an emerging problem for which there is evidence that its newly identified resistance mechanism probably develops in the environment (Verweij et al., 2012). This is because azoles are frequently used for crop protection and material preservation, and it is likely that breathing in the resistant spores of these *Aspergillus* strains from the environment leads to clinical infection.

direct and indirect exposure routes to humans and animals; (3) facilitating the spread of antimicrobial-resistant bacteria and resistance markers to other places (through surface water, groundwater, air, dust, wildlife); (4) acting as a reservoir for natural resistance markers; and (5) enabling the exchange of resistance markers between bacterial species.

Many enteric bacterial pathogens and associated faecal indicator bacteria, such as *Escherichia coli* and enterococci, are now multiple antimicrobial resistant, with some so resistant that infections cannot be effectively treated. A study has linked clinical isolates of multidrug-resistant enteric bacteria to the same bacteria found in environmental waters that were implicated in a possible waterborne community salmonellosis outbreak (Akinyemi et al., 2011), and there are other cases of increased human mortality and morbidity caused by antimicrobial-resistant bacteria (Barza & Travers, 2002; Travers & Barza, 2002; Helms et al., 2005; de Kraker, Davey & Grundmann, 2011). Therefore, there is a greater disease burden, measured as disability-adjusted life years (DALYs), from exposures to these bacteria via environmental media (water, wastewater, irrigated produce, etc.) and related pathways (e.g. faecally contaminated vectors such as flies, contact surfaces and contaminated hands). New strains or variants of highly resistant enteric bacteria of human health concern continue to emerge, are detectable in environmental media such as water and soil and are spreading globally, thus posing increased human health risks.

Among the Gram-negative enteric bacteria widely present in the environment and mammalian hosts, the development of extended spectrum beta-lactamase (ESBL) resistance in pathogens that cause considerable morbidity and mortality is recognized as a global public health concern (Ghafourian et al., 2014). An example of the continued emergence and spread of common enteric bacteria, such as *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter baumannii*, is the appearance of the blaNDM-1 gene to produce the New Delhi metallo- $\beta$ -lactamase NDM-1, which is a carbapenemase beta-lactamase enzyme that hydrolyses and inactivates the therapeutically important carbapenem antimicrobial agents (Bushnell, Mitrani-Gold & Mundy, 2013). Various sources document evidence for the increased presence of these NDM-1 bacteria in human and animal populations and the environment. Their profound resistance prevents effective antimicrobial therapy of infected and ill people, as there are currently no new antibiotics available to combat bacteria resistant to carbapenems.

## 2 Environmental presence and exposure source hotspots

Human excreta and wastewater are recognized and documented as major sources of antimicrobial agents, their metabolites, antimicrobial-resistant bacteria and their AMR genes because of the widespread and extensive use of antimicrobial agents by human populations. In many countries, facilities to treat municipal, community and household wastes that may harbour antimicrobial agents, antimicrobial-resistant bacteria and AMR genes are absent or inadequate, including ageing infrastructure such as leaking sewers that are often co-located with municipal water distribution pipes.

As a result, these contaminants are released directly into the environment where human exposures are likely and where antimicrobial-resistant bacteria and AMR genes are capable of persisting and spreading. Furthermore, human wastewater and excreta are used extensively in agriculture as sources of water and plant nutrients, and such use is encouraged by management practices such as ecological sanitation, municipal wastewater (re)use and water reclamation.

The potential for human exposure to such wastes is great. It is estimated that up to 90% of all wastewater is discharged untreated directly into rivers, lakes or the oceans (Corcoran et al., 2010). Therefore, the collection, prevailing management and purposeful or unplanned use of such wastes often result in increased prevalence and environmental release of antimicrobial contaminants, including antibiotics and other antimicrobial agents, their metabolites, antimicrobial-resistant bacteria and AMR genes (Schwartz et al., 2003; Lupo, Coyne & Berendonk, 2012). Municipal wastewaters in particular are major environmental reservoirs for antimicrobial agents, antimicrobial-resistant bacteria and AMR genes, and they also provide an environment that is conducive to the transfer of resistance genes to other bacteria before or after being discharged into the environment (Rizzo, Fiorentino & Anselmo, 2013; Rizzo et al., 2013).

There is increasing evidence that wastewater treatment plants are hotspots that sustain and further promote the propagation and selection of antimicrobial-resistant bacteria and AMR genes within their systems as well as function as major point sources that release them into the environment, where they disperse (Jury et al., 2011; Bouki, Venieri & Diamadopoulos, 2013). Although wastewater treatment processes can reduce concentrations of pathogens in wastewater, wastewater treatment plant effluents do not show appreciable removal of antimicrobial-resistant bacteria and AMR genes in general (Okoh & Igbinosa, 2010; Leclercq et al., 2013). Although wastewater treatment was shown to reduce the discharge to surface waters, wastewater effluents and other sources are likely co-contributors to ESBL loads in recreational waters, representing a possible exposure route (Blaak et al., 2014).

It has been suggested that other specific hotspots for antimicrobial-resistant bacteria and AMR genes are the waste discharges of pharmaceutical production facilities, hospitals and other health-care facilities. People in hospitals are constantly and extensively being treated with antibiotics and other antimicrobial agents, and their solid, faecal and liquid wastes have been documented as important sources contributing to the release and subsequent spread of antibiotics and other antimicrobial agents, antimicrobial-resistant bacteria and AMR genes in the environment (Mach & Grimes, 1982; Korzeniewska, Korzeniewska & Harnisz, 2013; Leclercq et al., 2013; Varela et al., 2013; Zhang et al., 2013; Amaya et al., 2012).

### 3 Implications of environmental antimicrobial-resistant bacteria and AMR genes for human health

There is growing public health concern that antimicrobial-resistant bacteria and AMR genes in human waste could potentially enter water sources via untreated or treated wastewater effluent and result in the exposure of human populations that use such water as drinking-water sources, for bathing, washing and other domestic sources, for primary contact recreation and as irrigation water. The use of human excreta solids (such as latrine wastes, septage and biosolids) containing antimicrobial-resistant bacterial pathogens for food and other crops is also a health concern. Although human exposures to antimicrobial-resistant bacterial pathogens from various environmental sources and by various exposure pathways could cause infections resulting in illnesses and deaths, the extent to which human health risks are increased from such exposures is inadequately characterized, poorly documented and therefore of uncertain magnitude (Ashbolt et al., 2013). However, as noted above, a study has linked multidrug-resistant enteric bacteria to the same bacteria that were implicated in a possible waterborne community outbreak of an enteric disease (Akinyemi et al., 2011). Furthermore, it is well documented that infection with antimicrobial-resistant pathogens carries an increased risk of mortality, longer treatment and longer stays in hospital, and the use of more expensive and more toxic second-line therapies. The potential risks from antimicrobial-resistant organisms in the water environment include (1) infection by antimicrobial-resistant pathogens present in the water (e.g. resistant *Campylobacter* spp., *Shigella* spp., *Salmonella typhi* and other *Salmonella* spp.); (2) colonization and subsequent infection with opportunistic pathogens, such as *E. coli* and enterococci; and (3) transient colonization with antimicrobial-resistant organisms that can then be a source of AMR genes for the normal flora through horizontal gene transfer; should an endogenous infection occur, it may be with an antimicrobial-resistant strain. Overall, there is a lack of reliable, well documented and validated human health risk assessments for antimicrobial-resistant bacteria and AMR genes from such environmental exposures, and currently there is inadequate information based on quantitative microbial risk assessment to inform the development and implementation of appropriate risk management systems.

The direct use of antibiotics and other antimicrobial agents and wastewater and excreta laden with them in various food production systems, such as animal agriculture and aquaculture, is also a concern in terms of the widespread presence and spread of antibiotics and other antimicrobial agents, their metabolites, antimicrobial-resistant bacteria and AMR genes in aquatic environments and in human food supplies. For example, an estimated 10% of the world's population is thought to consume wastewater-irrigated foods, and 20 million hectares of land in 50 countries are irrigated with raw or

预览已结束，完整报告链接和二维码如下：

[https://www.yunbaogao.cn/report/index/report?reportId=5\\_23973](https://www.yunbaogao.cn/report/index/report?reportId=5_23973)

