A Primer for Media

Antimicrobial Resistance in the Western Pacific Region

World Health Organization
Western Pacific Region

ANTIMICROBIAL RESISTANCE

Contents

World Health Organization
Western Pacific Region

ANTIMICROBIAL RESISTANCE

1

INTRODUCTION

Antimicrobial resistance poses a profound threat to health and society. It is a global public health concern with economic, social and political implications that is global in scope and impacts human health, animal health, agriculture, food security and economic development at large.

In order to preserve the miracle of modern medicine, antimicrobials, before it is too late, it is important that containment of antimicrobial resistant is widely recognized as a development agenda issue beyond human health. Given the multi-sectoral nature of the public health concern, actions taken to prevent the emergence and spread of antimicrobial resistance will also directly support achieving the Sustainable Development Goals.

To facilitate a multi-sectoral approach to contain antimicrobial resistance, countries need to develop plans that commit resources to the containment of antimicrobial resistance with efforts by all stakeholders. This must be based on a “One Health” approach, encompassing both human and animal health, in recognition of the fact that human health, animal health and ecosystem health are inextricably linked. Surveillance of antimicrobial resistance and systematic monitoring of antimicrobial use are also key to containing the problem.

WHO is actively working with countries to develop country specific national strategies to combat AMR. At the same time, the scientific community worldwide is working hard to find solutions and, as we leave behind the “golden age” of antibiotics, offer new hope that the disaster of a world completely without antibiotics can be averted.

Antimicrobial resistance is a major public health threat

Antimicrobial resistance is driven by both appropriate and inappropriate use of anti-infective medicines to treat diseases in humans and the widespread use of antibiotics in animal husbandry. Antimicrobial resistance includes antibiotics to treat bacterial infections; antiviral drugs, including antiretroviral therapy to treat HIV, and influenza medications; antiparasitic drugs such as those used to treat malaria; and antifungal medications.

The result is that a growing number of diseases are becoming difficult or even impossible to treat, allowing a common infection to develop into a life-threatening condition. Diseases caused by resistant microbes become harder and more costly to treat. Not only do they require more expensive second- and third-line medications, but the delays in effective treatment ramp up the costs of medical care, increasing mortality as well as heightening the risk of complications and spread of infection.

Antimicrobial-resistant infections extract a high cost at the individual level, in terms of increased suffering and higher mortality, and at the societal level, through increased health-care costs and a less healthy population.

How antimicrobial resistance happens

NATURAL SELECTION

Microorganisms undergo a natural process of adaptation to the antimicrobial agents used to treat them. Through natural selection microorganisms exchange resistant traits, and resistant strains survive and aggregate.

OVERUSE AND MISUSE

The natural process of resistance due to adaptation already means that antibiotics have a limited lifespan, but this process has been accelerated by the overuse and misuse of antimicrobial medicines. Antibiotics are often overprescribed, or used to treat viral infections that they cannot combat. In countries lacking reliable supplies of affordable, quality medicines, antimicrobial resistance – such as resistance to antimalarial medications – is fuelled by supplies of spurious, falsely labelled, falsified or counterfeit medicines often containing too little of the active compound.

ANIMAL HUSBANDRY AND AQUACULTURE

Antibiotics used to treat human diseases are also given to livestock in subtherapeutic doses, not to treat infections, but to promote growth and prevent disease outbreaks among animals kept in factory farming conditions. Both antibiotics and the resistant bacteria make their way into the food chain via contaminated food products and through the water supply system.

ENVIRONMENTAL EXPOSURE

Poorly managed pharmaceutical manufacturing practices and poor water management in some countries lead to antibiotic contamination of water supplies.

The impact

Antimicrobial-resistant infections cause at least 50 000 deaths a year in Europe and the United States of America alone. Reliable data on the global burden are scarce, but a low estimate puts the figure at 700 000 deaths a year *(1)*. If left unchecked, it is estimated that by 2050 the figure will rise to 10 million deaths annually, or 350 million deaths in the coming 35 years *(1)*.

Asia and the Pacific are projected to account for 4.73 million antimicrobial-resistant-related deaths by 2050 *(1)*. There is a large economic cost attributed to drug-resistant infections. Studies commissioned by the Review of Antimicrobial Resistance estimate that at 10 million deaths a year, antimicrobial resistance could cost up to US$ 100 trillion and slice 2% to 3.5% off global gross domestic product *(1)*.

The impact of antimicrobial-resistant infections is expected to affect developing countries most severely. Progress in treating HIV, tuberculosis and malaria, all of which disproportionately affect the developing world, is being jeopardized by the growing threat of antimicrobial resistance. In China, for example, malaria has almost been eradicated, but such gains could be reversed by resistance to current first-line malaria treatments.

Four categories of antimicrobial resistance

ANTIBIOTIC RESISTANCE

Antibiotic resistance is the single biggest category of antimicrobial resistance and refers to antibiotic drugs used to treat bacterial infections. Antibiotic resistance has emerged to drugs that treat a wide range of bacterial diseases, including tuberculosis, gonorrhoea and infections affecting the digestive system, skin, urinary tract and respiratory tract.

The loss of effective antibiotics affects not only the treatment of common diseases, but also large areas of modern medicine: organ transplantation, cancer chemotherapy and major surgery all rely on the use of antibiotics. The antibiotic era, when new drug discoveries more than kept pace with emerging resistance, is over. With a thin pipeline of new drugs, and escalating resistance, these achievements of modern health care are at serious risk, potentially foreshadowing a post-antibiotic era.

In the Western Pacific Region, antibiotic resistance is being fuelled by widespread misuse and overuse, and the faster spread of resistant bacteria as people migrate and travel more. Poor hygiene and lax infection control in hospitals and other health-care settings are also key factors. Insufficient control of antibiotic distribution and sale for both human and animal use plays a part. In Viet Nam, for example, 88% of antibiotics used in urban areas and 91% of those used in rural areas are sold without a prescription *(2)*.

Lack of accountability at government, facility and individual levels is also responsible for the growth of antibiotic resistance.

ANTIPARASITIC RESISTANCE

For antiparasitic resistance, malaria is the main disease of concern, followed by helminthiasis (disease caused by intestinal worms).

Malaria is endemic in 10 countries in the Western Pacific Region: Cambodia, China, the Lao People's Democratic Republic, Malaysia, Papua New Guinea, the Philippines, the Republic of Korea, Solomon Islands, Vanuatu and Viet Nam. Both *Plasmodium falciparum* – one of the most common and most deadly forms of the disease – and *Plasmodium vivax* are prevalent in the Region. There are an estimated 717 million people in the Western Pacific at some risk for malaria, while 41 million people are at high risk, with ethnic minorities and migrant workers disproportionately affected *(3)*.

The first-line treatment is combination therapy containing artemisinin and its derivatives, a group of drugs that are isolated from *Artemisia annua*, or sweet wormwood plant. Although many countries in the Western Pacific Region have been very successful in reducing their malaria burden and several are on course to eliminate malaria, resistance to treatments is a growing threat, and new foci of artemisinin-resistant *P. falciparum* malaria are being detected *(4)*. Resistance to artemisinin has been detected in five countries of the Greater Mekong Subregion: Cambodia, the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam. In many areas along the Cambodia–Thailand border, *P. falciparum* has become resistant to most available antimalarial medicines.

Artemisinin resistance has emerged partly due to the natural evolution of the parasite but also because the disease is not always treated with the right drug combination in the right dosage, and because of the continued use of artemisinin monotherapy. Also partly to blame are fake and substandard malaria drugs, which fill the gap in the market created when health systems are not robust enough to offer reliable access to the right medications.

Helminthic infections of concern in the Western Pacific include lymphatic filariasis (in the Pacific islands) and intestinal schistosomiasis (notably in China, Cambodia, the Lao People's Democratic Republic and the Philippines).

ANTIVIRAL RESISTANCE

HIV

Resistance to antiretroviral medications to treat HIV is a potential threat to public health in the Western Pacific Region. Of the estimated 1.4 million people living with HIV in the Region, 520 000 people are receiving antiretroviral therapy *(5)*. Resistance to antiretroviral medications is expected to rise with more people placed on treatment as national HIV programmes push toward treating 90% of all people living with HIV by 2020, or over one million people in the Region. If resistance rises to such an extent that first- and second-line treatment regimens are no longer effective, it could unravel all the successes of national AIDS programmes in getting treatment to people living with HIV.

Globally, in 2010 resistance was estimated at approximately 5% in countries that had not yet begun to scale up treatment access, but since 2010 resistance has been as high as 22% in some areas *(6)*. Indication of antiretroviral resistance in the Region recently arose with Papua New Guinea reporting 16% resistance to antiretroviral drugs used in first line treatment regimens.

Influenza

Resistance to antiviral drugs to treat influenza has also become a concern, especially given the pandemic threats that have emerged in recent years. Resistance to frequently used drugs to prevent influenza – has been detected for virtually all influenza A viruses circulating in humans. As antiviral resistance remains a public health threat, the WHO Global Surveillance and Response System monitors the evolution of influenza viruses and provides recommendations for laboratory diagnostics, vaccines, antiviral susceptibility and risk assessment.

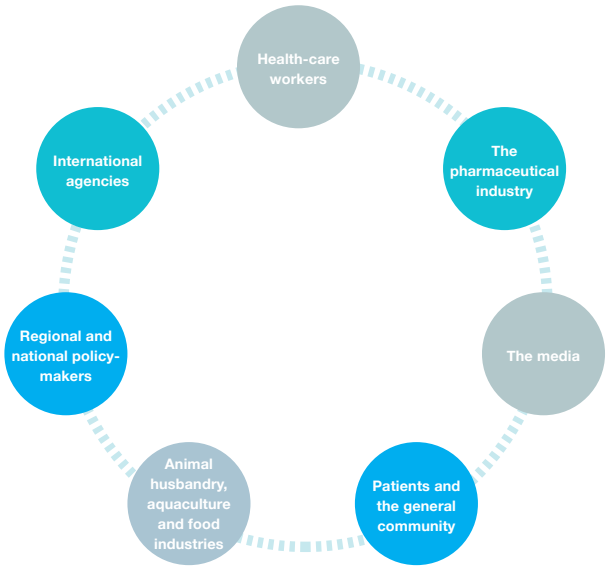
ANTIFUNGAL RESISTANCE

The fungus *Candida* is a common cause of health-care-associated bloodstream infections, and some types of *Candida* are becoming increasingly resistant to the current first-line and second-line antifungal medications, fluconazole and echinocandins *(7)*.

Containing antimicrobial resistance

TACKLING ANTIMICROBIAL RESISTANCE: INVOLVING ALL STAKEHOLDERS

Tackling the growing threat of antimicrobial resistance needs the active commitment of everyone and there are several key stakeholder groups that must take action:



When to act? NOW!

We can still change the course of antimicrobial resistance if we act now to preserve the effectiveness of our current antimicrobials for future generations.

WHO AND ANTIMICROBIAL RESISTANCE

WHO is playing a leading role in promoting action both globally and in the Western Pacific Region across all sectors. In 2001, WHO launched its Global Strategy for Containment of Antimicrobial Resistance, in which it presented 87 prioritized recommendations for health-care workers, industry, researchers, the media, patients' representatives and national authorities. It has since been actively supporting Member States to develop their own national strategies and plans.

In October 2014, WHO Member States in the Western Pacific Region endorsed the Action Agenda for Antimicrobial Resistance in the Western Pacific Region. The agenda spells out specific actions that countries can take to develop their national plans, raise awareness of antimicrobial resistance and strengthen their health systems to better contain and monitor antimicrobial resistance.

A Global Action Plan on Antimicrobial Resistance was adopted by the World Health Assembly in May 2015.

References

1. O'Neill J. Antimicrobial resistance: tackling a crisis for the health and wealth of nations. London: Review on Antimicrobial Resistance; 2014.
2. Ha Ngo Thi Bich. The National Action Plan on Antimicrobial Resistance in Vietnam: period from 2013 to 2020 [presentation]. Hanoi: Ministry of Health; 2015 (http://203.157.15.46/photo/ghsa/present_20150507/amr/ghsa06_c1110msngo-vietnamsnationalactionplanonamr20150427.pdf, accessed 23 October 2015).
3. World Malaria Report 2014. Geneva: World Health Organization; 2014 (http://www.who.int/malaria/publications/world_malaria_report_2014/wmr-2014-regional-profiles.pdf?ua=1, accessed 23 October 2015).
4. Malaria [website]. Manila: World Health Organization Regional Office for the Western Pacific; 2015 (http://www.wpro.who.int/topics/malaria/en/, accessed 25 October 2015).
5. HIV/AIDS data and statistics [website]. Manila: World Health Organization Regional Office for the Western Pacific; 2015 (http://www.wpro.who.int/hiv/data/en/, accessed 23 October 2015)
6. Antimicrobial resistance. Fact Sheet No. 194. Geneva: World Health Organization; 2015 (http://www.who.int/mediacentre/factsheets/fs194/en/, accessed 24 October 2015)
7. Antifungal resistance [website]. Atlanta: US Centers for Disease Control and Prevention; 2015 (http://www.cdc.gov/fungal/antifungal-resistance.html, accessed 24 October 2015).

WPR/2016/DHS/002

World Health Organization
Western Pacific Region

ANTIMICROBIAL RESISTANCE

2

ANTIBIOTIC RESISTANCE

Antibiotic resistance is the single biggest category of antimicrobial resistance and refers to antibiotic drugs used to treat bacterial infections. Antibiotic resistance is not a new phenomenon: resistance to penicillin, for example, was detected as early as 1945, just seven years after it was introduced.

Since then, antibiotic resistance has emerged in drugs to treat a wide range of bacterial diseases, including tuberculosis, gonorrhoea and infections affecting the digestive system, skin, urinary tract and respiratory tract.

In the Western Pacific Region, antibiotic resistance is being fuelled by widespread misuse and overuse, and the increased spread of resistant bacteria as people migrate and travel more. Poor hygiene and infection control in hospitals and other health-care settings are also key factors. Lack of control over antibiotic distribution and sale for both human and animal use is also responsible for the growth of antibiotic resistance. Table 1 presents information about the main classes of antibiotics and the year resistance was first observed.

Table 1. Antibiotic classes and year resistance first observed

ANTIBIOTIC CLASS	EXAMPLE	YEAR OF DISCOVERY	YEAR OF INTRODUCTION	YEAR RESISTANCE OBSERVED
Sulfadrugs	Prontosil	1932	1936	1942
β-lactams	Penicillin	1928	1938	1945
Aminoglycosides	Streptomycin	1943	1946	1946
Chloramphenicols	Chloramphenicol	1946	1948	1950
Macrolides	Erythromycin	1948	1951	1955
Tetracyclines	Chlortetracycline	1944	1952	1950
Rifamycins	Rifampicin	1957	1958	1962
Glycopeptides	Vancomycin	1953	1958	1960
Quinolones	Ciprofloxacin	1961	1968	1968
Streptogramins	Streptogramin B	1963	1998	1964
Oxazolidinones	Linezolid	1955	2000	2001
Lipopeptides	Daptomycin	1986	2003	1987
Macrocyclics	Fidaxomicina	1948	2011	1977
Diarylquinolines	Bedaquiline	1997	2012	2006

[a] Targeting *Clostridium difficile*.
Source: Adapted from Lewis *(1)*.

Table 2. Resistance and decreased susceptibility to antibiotics

BACTERIUM	YEAR OF INTRODUCTION	YEAR RESISTANCE OBSERVED
Enterococci	Infections anywhere in the body, but especially in the intestines, urinary tract and wounds	Many types, especially vancomycin
Escherichia coli	Gastroenteritis, urinary tract infections, neonatal meningitis	Third-generation cephalosporins, fluoroquinolones
Klebsiella pneumoniae	Pneumonia, infections of the lower biliary tract, surgical wound sites and urinary tract	Carbapenems
Mycobacterium tuberculosis	Multidrug-resistant tuberculosis	Isoniazid and rifampin
Mycobacterium tuberculosis	Extensively drug-resistant tuberculosis	Isoniazid and rifampin, plus fluoroquinolone and at least one of three injectable second-line drugs: amikacin, kanamycin, capreomycin
Neisseria gonorrhoeae	Gonorrhoea	third-generation cephalosporins
Nontyphoidal salmonella	Salmonella	Fluoroquinolones
Shigella species	Shigellosis	Fluoroquinolones
Staphylococcus aureus	Pneumonia, soft tissue infections, methicillin-resistant Staphylococcus aureus (MRSA)	Methicillin
Streptococcus pneumoniae	Meningitis, pneumonia, septicaemia	Penicillin

Source: Adapted from Lewis *(1)*.