
Antimicrobial drug resistance

Report by the Secretariat

1. Since the 1940s, antimicrobial medicines have substantially reduced mortality from infectious diseases and have provided protection against infectious complications for many modern medical practices including surgery, neonatal care and cancer treatment. However, the extensive use, misuse and overuse of antimicrobials in both human and animal health¹ have increasingly raised levels of antimicrobial resistance in a wide range of pathogens (bacteria, viruses, fungi and parasites) – in all countries and patients of all age groups. With increasing travel and trade in food, drug resistance can spread rapidly, as exemplified by the resistance-inducing enzyme metallo-beta-lactamase-1 (NDM-1), which confers resistance to carbapenems, an important group of antibiotics: it was first detected in one country in 2008 but has now been found on all continents.
2. New resistance mechanisms are emerging, which make it difficult or impossible to treat certain infections. Examples include hospital-acquired and community-acquired infections, such as those affecting children (such as pneumonia and meningitis) and sexually transmitted infections (such as gonorrhoea). The development of new antimicrobial agents and other interventions for preventing and treating infectious diseases, including diagnostics and vaccines, is not keeping pace with the loss of existing medicines.
3. Infections caused by drug-resistant pathogens increase mortality across all settings, and can lead to prolonged stays in hospital and increased risk of admission to intensive care units. Hospital-acquired infections with multiresistant bacteria already cause around 80 000 deaths annually in China, 30 000 in Thailand, at least 25 000 across the European Union and at least 23 000 in the United States of America.
4. Antimicrobial resistance threatens the long-term sustainability of the public health control of many communicable diseases, including tuberculosis, malaria and HIV/AIDS.
5. In 2011, there were an estimated 630 000 cases of multidrug-resistant tuberculosis among the world's 12 million prevalent cases of tuberculosis. Nearly 4% of new cases and about 20% of previously treated cases are multidrug-resistant. Only 50% of multidrug-resistant cases can be effectively treated. On average, the cost for treating one case of multidrug-resistant tuberculosis is equivalent to the cost of treating 100 susceptible tuberculosis cases. An even more severe form of resistance, extensively drug-resistant tuberculosis, has been identified in 84 countries.²

¹ The world medicines situation 2011. Geneva: World Health Organization; 2011.

² Global tuberculosis report 2012. Geneva: World Health Organization; 2012.

6. The prevalence of HIV drug resistance among people starting antiretroviral therapy in 12 low- and middle-income countries rose from nearly 5% in 2007 to nearly 7% in 2010.¹ Levels of HIV drug resistance can reach 10% to 17% in high-income countries.

7. In South-East Asia, artemisinin is the medicine of last resort for treatment of falciparum malaria and resistance to it is threatening malaria control.²

8. Beyond the immediate public health impact on morbidity and mortality from these diseases, antimicrobial resistance incurs substantial health-economic and economic costs. The annual cost due to antibiotic-resistant infections has been estimated to be €1500 million in the European Union and US\$ 2000 million in Thailand. In January 2013, the World Economic Forum warned that antimicrobial resistance is one of the major global health security risks that the world needs to tackle and called attention to the fact that losses of gross domestic product from antimicrobial resistance range from 0.4% to 1.6%.

THE CURRENT RESPONSE TO ANTIMICROBIAL RESISTANCE

9. Since WHO's publication of the global strategy for containment of antimicrobial resistance in 2001, the Health Assembly has adopted several resolutions on the subject (the latest being WHA60.16 concerning the rational use of medicine and WHA62.15 on prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis). Various initiatives have been launched, including in 2011 a call for action on World Health Day, with a policy package for stakeholders.³ Most recently, the Director-General convened the Strategic and Technical Advisory Group on Antimicrobial Resistance, which held its first meeting in Geneva on 19 and 20 September 2013.

10. Some Member States have developed national action plans or strategies to counter antimicrobial resistance. In a continuing survey, 29 of 92 (32%) Member States have reported having a comprehensive national action plan. The proportion varies from about 60% among high-income countries to less than 20% among low- and middle-income countries.

11. Across the African Region, some existing initiatives, such as the integrated disease surveillance and response, provide a platform from which to strengthen public health laboratories and monitoring of antimicrobial resistance.

12. In the Region of the Americas surveillance networks for monitoring resistance in common bacterial infections, malaria and multidrug-resistant tuberculosis are well established. Integrated surveillance of antimicrobial resistance has been conducted in several countries. Efforts to strengthen laboratory capacity and infection prevention and control continue, and 10 of 19 Latin American countries surveyed run national programmes on antimicrobial resistance. Strategies and actions are being implemented to improve the use and quality of medicines, and to harmonize medicines regulation in the Region. At the 51st Directing Council of the Pan American Health Organization, Member States requested the Pan American Sanitary Bureau to prepare a regional strategy and plan of

¹ WHO HIV drug resistance report. Geneva: World Health Organization; 2012.

² World malaria 2012 report. Geneva: World Health Organization, 2012.

³ World Health Day 2011: Policy briefs. <http://www.who.int/world-health-day/2011/policybriefs/en/> (accessed 1 November 2013).

action for the containment of antimicrobial resistance that would serve as a guide for national policies and operating plans.¹

13. In 2002 the Regional Committee for the Eastern Mediterranean adopted resolution EM/RC49/R.10, calling on Member States to take actions to tackle antimicrobial resistance. Several activities have subsequently been developed to promote the rational use of medicines and strengthen infection prevention and control.

14. In 2011, the Regional Committee for Europe adopted a regional strategic action plan on antimicrobial resistance (resolution EUR/RC61/R6), with a focus on antibiotic resistance and a separate action plan for extensively and multidrug-resistance tuberculosis. Most European Union countries have extensive and well-functioning networks for monitoring antibacterial resistance and amounts of antibacterial medicines used but this is not necessarily the case in Member States that are not members of the European Union. Partners are therefore focusing on supporting the latter countries to strengthen surveillance of and strategies on antimicrobial resistance. In addition to the Regional Committee's resolution, the European Commission has adopted resolutions and strategies encouraging and enabling its Member States to take action in all sectors of concern, including research and development.

15. In 2011, health ministers in the South-East Asia Region signed the Jaipur Declaration on Antimicrobial Resistance, agreeing to institute a comprehensive approach to combating antimicrobial resistance. Also, the Regional Committee adopted resolution SEA/RC63/R4 on prevention and containment of antimicrobial resistance and endorsed a regional strategy.²

16. The Regional Committee for the Western Pacific recently adopted resolution WPR/RC62.R3 on antimicrobial resistance. Member States in the Region have programmes in place to strengthen surveillance of resistance among patients with tuberculosis, malaria, HIV/AIDS and common bacterial infections. Most high- and upper-middle-income countries in the Region have established routine surveillance of antimicrobial resistance, at least in health care settings, and have some level of national oversight, quality assurance and national and local policy-making.

THE NEED FOR GLOBAL ACTION

17. Many gaps remain in the efforts to contain antimicrobial resistance, and members of the Strategic and Technical Advisory Group on Antimicrobial Resistance at its first meeting were unanimous in calling for urgent renewal and expansion of action to tackle this growing public health threat. Although many diverse bacterial, viral, fungal and parasitic pathogens show resistance, many of the most immediately urgent concerns relate to bacteria and antibiotic resistance. For some specific diseases there are programmes that already address resistance.

18. WHO's publication in 2001 of a global strategy for containment of antimicrobial resistance has not resulted in a widely accepted global action plan, and a lack of awareness of the impact of such resistance persists in all sectors. The Strategic and Technical Advisory Group on Antimicrobial

¹Document CD51/15, Rev.1, Add.I.

² WHO. Regional strategy on prevention and containment of antimicrobial resistance, 2010–2015. New Delhi: Regional Office for South-East Asia; 2010.

Resistance therefore specifically recommended that WHO should lead the development and coordination of a global action plan on antimicrobial resistance that highlights:

- integration of prevention of antimicrobial resistance into all health systems and practice (both human and animal health)
- reduction of antimicrobial use in all sectors, where appropriate
- emphasis on hygiene and infection prevention and control
- recognition that extending quality health care through universal health coverage and awareness are important enabling factors
- technical and service innovation across all aspects of a global action plan.

NEXT STEPS

19. **Intersectoral engagement.** Antimicrobial resistance is primarily a health issue, but also has significant animal health, economic, social and developmental aspects. Health ministries need to engage with other sectors, and WHO must work with other organizations in order that they are empowered and engaged in contributing to the development and implementation of a global action plan on antimicrobial resistance.

20. **National plans.** All countries urgently need to commit themselves to a comprehensive, financed national plan to combat antimicrobial resistance. The Secretariat will provide support and guidance to Member States in developing and implementing their national action plans and policies, and work with them to develop and put in place appropriate targets and outcome indicators.

21. **Knowledge and information.** The evidence on both the magnitude, epidemiology and economic impact of antimicrobial resistance and the effectiveness of control measures needs to be strengthened. For many countries this will entail strengthening surveillance and laboratory capacity, and the collection and reporting of data on antimicrobial resistance and of medicine use in human, animal and agriculture sectors. The Strategic and Technical Advisory Group on Antimicrobial Resistance has advised the Director-General to establish a baseline assessment of capacity at country and regional levels, and report on antimicrobial resistance surveillance data and use of antimicrobial medicines, in order to guide policies and action plans and to monitor their effectiveness. WHO should also develop global standards for data collection and reporting, and facilitate development of national and regional surveillance networks.

22. **Medicines regulation.** Better national and international regulatory mechanisms and practices are needed in order to optimize access to good-quality antimicrobial medicines and their use, to limit the spread of antimicrobial resistance through excessive or inappropriate use, and to eliminate substandard/spurious/falsely-labelled/falsified/counterfeit antimicrobial medicines. In addition, the Strategic and Technical Advisory Group on Antimicrobial Resistance recommended that the Organization work with regulatory and other networks to ensure optimal use of antimicrobials, and with FAO and OIE to limit antibiotic use, as well as to stop antibiotic use for non-therapeutic purposes in livestock and agriculture.

23. **Prevention of infection.** National plans need to take into account the importance of infection prevention and control. Prevention of infection both limits the need for antimicrobial medicines, and

reduces the spread of antimicrobial resistance. National and global action plans need to give priority to renewed advocacy, awareness and promotion of sanitation, hygiene and infection prevention and control practices, including the use of vaccines. The Secretariat will provide support to Member States with evidence-based guidance on appropriate interventions and their implementation and guidance on vaccines and immunization.

24. **Technology innovation.** There is currently insufficient investment in the development of new medicines, diagnostics and other tools to detect and control infections. At the same time, innovative business models are needed to support a long-term, sustainable approach to the development, production and conserved use of antimicrobial medicines. The Strategic and Technical Advisory Group on Antimicrobial Resistance recommended that WHO work with life-science industries and other sectors to facilitate the development, application and evaluation of (i) diagnostics and diagnostic tools and (ii) new treatment and prevention options, including new business models to encourage investment in and preservation of new products.

25. **Service innovation.** Member States should identify and promote best practices and strengthen collection of evidence in order to encourage innovation in service delivery and social mobilization. The Secretariat will work with Member States to identify and foster networks and centres of excellence that can provide technical and service leadership at national, regional and global levels. That cooperation will also focus on building capacity and developing continuous health promotion, education and communication programmes that can change culture, understanding and demand for antimicrobial medicines.

ACTION BY THE EXECUTIVE BOARD

26. The Board is invited to take note of this report.

= = =