

## The WHO policy package to combat antimicrobial resistance

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### Introduction

To bring international attention to a growing public health threat, the World Health Organization (WHO) selected antimicrobial resistance as the theme for World Health Day 2011. Antimicrobial resistance is a threat to all branches of medical and public health practice. It challenges the control of infectious diseases, jeopardizes progress on health outcomes by increasing morbidity and mortality and imposes huge costs on societies. In the European Union, about 25 000 patients die each year from infections caused by selected multidrug-resistant bacteria and the associated costs are estimated at about 1.5 billion euros per year.<sup>1</sup> In the United States of America, infections with pathogens resistant to antimicrobials cost the health-care system in excess of 20 billion United States dollars (US\$) annually and generate more than 8 million additional hospital days. The annual societal costs exceed US\$ 35 billion.<sup>2</sup>

Antimicrobial resistance is not a new problem. In 1998, the World Health Assembly adopted a resolution urging Member States to take action against it. In 2001 WHO published the *WHO global strategy on containment of antimicrobial resistance* along with a series of recommendations aimed at enabling countries to define and implement national policies in response to antimicrobial resistance.<sup>3</sup> In 2005 another World Health Assembly resolution on antimicrobial resistance cautioned about the slow progress and called for the rational use of antimicrobial agents by providers and consumers. Thus, the essential strategic interventions to control antimicrobial resistance have been known for some time. So far, however, national and global responses have been inadequate. In fact, few of the recommended policy changes have been pursued.

### Lack of commitment and data

Though actions to combat antimicrobial resistance are taken forward by individual programmes and institutions, the effort is often fragmented and not comprehensive. Attention focuses on sensational individual events, such as the reports in 2010 about the new type of carbapenem resistance linked to the description of a new  $\beta$ -lactamase enzyme, NDM-1,<sup>4</sup> in different parts of the world, but little emphasis is given to the wider threat of antimicrobial resistance and the need for sustained containment efforts. The issue has not been prioritized by national governments. A paucity of surveillance data on antimicrobial resistance contributes to a poor understanding of the scale of the problem and hampers an effective response to it. It also makes it difficult to regularly update diagnostic and treatment guidelines based on strong scientific evidence and to implement effective measures to prevent and control infections.

### Unassured drug quality and irrational use

Fragmented health services and lack of access to quality-assured medicines at an affordable price often lead patients to take incomplete courses of treatment or to resort to sub-standard medicines, which create ideal conditions for the selection of resistant organisms. While poor provider knowledge and a lack of standard treatment guidelines are key contributors to improper antimicrobial prescription practices, the problem stems from a complex interplay of factors. Insufficient training and supervision of health personnel, lack of access to rapid diagnostic facilities to support treatment decisions, perverse economic incentives such as profits from both prescribing and dispensing, and inappropriate marketing of pharmaceuticals can all lead to improper prescribing.<sup>5</sup> The absence of legislation regulating the

quality and use of antimicrobials and poor enforcement efforts foster the unauthorized dispensing of antimicrobials by poorly trained persons and contribute to indiscriminate use.<sup>6</sup>

### Poor prevention and control of infections

Weak infection prevention and control practices lead to the increased transmission of resistant microorganisms.<sup>7</sup> This is particularly challenging in resource-limited settings with poor health infrastructures and a shortage of health-care staff. Inadequate laboratory capacity limits the ability to rapidly detect resistant microorganisms for prompt treatment and control measures.

### Research languishing

While antimicrobial resistance is rapidly spreading, research and development for new antimicrobial agents, diagnostics and vaccines are languishing. Very few pharmaceutical companies are still developing antibiotics. By 2008, eight of the 15 major pharmaceutical companies that at one time had antibiotic discovery programmes had abandoned them and two others had reduced them.<sup>8</sup> A study in 2004 showed that of 506 drugs in development by 15 large pharmaceutical companies and seven major biotechnology companies, only six were antibiotics. Approval of new antibacterial agents by the United States Food and Drug Administration decreased by 56% between 1998 and 2002.<sup>9</sup> In 2008, a study of antibiotic development involving small firms as well as large pharmaceutical companies revealed that only 15 of 167 antibiotics under development had a new mechanism of action.<sup>10</sup> If the current trend continues, before long there may not be effective antimicrobials with which to treat patients with serious infections.

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**Box 1. The World Health Organization's policy package to combat antimicrobial resistance**

- Commit to a comprehensive, financed national plan with accountability and civil society engagement
- Strengthen surveillance and laboratory capacity
- Ensure uninterrupted access to essential medicines of assured quality
- Regulate and promote rational use of medicines, including in animal husbandry, and ensure proper patient care
- Enhance infection prevention and control
- Foster innovations and research and development for new tools

**WHO's policy package**

Increasing numbers of bacteria are becoming resistant to antimicrobials and there is a need to take urgent action. On World Health Day, WHO introduced a policy package to combat antimicrobial resistance (Box 1). This package reframes the critical actions to be taken by governments to stimulate change by all stakeholders.

The first overarching component is for governments to commit to a comprehensive national plan against antimicrobial resistance that brings together all the required recommended measures. A national inter-sectoral steering committee should be established to guide actions by several stakeholders under the overall stewardship of the government. Adequate resources should be earmarked and an accountability framework should be set up, with measurable indicators to be reported annually. A well informed public is a catalyst to health actions; thus, building strong public awareness is vital. Civil society representatives should be involved in the development of antimicrobial resistance policies, their implementation and the monitoring activities.

A second component is strengthening surveillance and laboratory capacity. The surveillance of antimicrobial resistant organisms and the tracking of the use of antimicrobials are both essential. There is also an urgent need to build laboratory capacity to ensure reliable and rapid test results on which to base prescribing decisions and measures for the prevention and control of infections. Standard protocols are needed to assess antimicrobial resistance trends consistently over time and across geographical areas. Surveillance data should be regularly reported and shared at the regional and global levels. Antimicrobial resistance surveillance systems must be expanded to veterinary services and supported by food safety

authorities to help assess the impact on human health of the use of antimicrobials in animals for human consumption.

Third, governments must guarantee uninterrupted access to essential medicines of assured quality. An effective national body is necessary to develop the essential medicines list based on standard treatment guidelines. Sufficient public financing for essential medicines, including recommended antimicrobials, should be provided. Efficient systems for managing drug procurement and distribution should be put in place to avoid interruptions in supply or wastage. Issues with drug quality need to be tackled through comprehensive drug regulations. A national drug regulatory authority that is responsible and accountable for all aspects of drug regulation should be structured as an independent coordinating body in the ministry of health, separate from drug supply and management. Regulatory tools should be developed and personnel appropriately trained to ensure consistency and transparency in regulatory functions.

Fourth, the rational use of antimicrobials is essential for containing antimicrobial resistance. The promotion of national standard treatment guidelines calls for proper training and supervision of health personnel and for mechanisms to make diagnostic support available.<sup>11</sup> To reduce their irrational use, antimicrobials should only be sold with a prescription and this should be strictly enforced in all pharmacies. Local incentive structures must be examined to identify factors influencing prescription practices. Methods of payment and reimbursement should be in line with standard treatment guidelines to discourage irrational use. Independent and unbiased information on antimicrobial use should be provided to health personnel and consumers. Promotional activities by pharmaceutical companies should be

regulated and monitored to prevent industry from misinforming patients and from offering financial incentives to providers. The overuse and misuse of antimicrobials in animals for human consumption must be addressed through surveillance of antimicrobial use in animals destined for food, training of veterinarians and farmers and, most critically, through legislative and regulatory measures.<sup>12</sup>

Fifth, policies and practices for the prevention and control of infections are indispensable in fighting antimicrobial resistance. A proper organizational structure for developing and managing such policies and practices, combined with environmental designs for their application, need to be adopted in health facilities. These practices are also necessary in congregate settings and communities.

Finally, operational research and research and development to make new tools available are crucial in combating antimicrobial resistance. This includes improving current diagnostic tests and antimicrobials and designing incentives to engage industry in the development of new tools. Regulatory bottle-necks need to be eliminated and resources must be mobilized for rapid access to new tools.

The drivers of antimicrobial resistance are interlinked, and so are the solutions. Single, isolated interventions have little impact. Strong leadership and political will are required to bring about bold changes in policies, organize health systems and legislative structures as required, and translate knowledge and recommendations into practice. With new multidrug-resistant microorganisms being disseminated in tandem with well known older pathogens, the window of opportunity is rapidly closing: no action today, no cure tomorrow. ■

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Corrigendum

In volume 89, Number 4, April 2011, p. 280, the legend for Fig. 1 should have been “South Africa 2001” for the solid green line and “South Africa 2006” for the dotted green line.

Fig. 1. Death rates in South Africa relative to global rates of death from selected causes, 1996–2006

