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Emerging and other communicable diseases: antimicrobial resistance

Report by the Director-General

The wide and increasing use of antimicrobial agents in humans and animals, and in agriculture, has exerted intense pressure for microorganisms to develop resistance which is rapidly becoming a leading cause of concern for public health. In particular:

- resistant pathogens are emerging and spreading more rapidly than in previous decades;
- resistance is a world problem, affecting developed and developing countries, and rapidly spreading through international travel;
- treatment of infections caused by resistant microbes is increasingly hampered either by the prohibitive cost of existing "new generation" agents or by a total lack of effective antimicrobial agents;
- resistance should be viewed in the larger public health context.

The Health Assembly is invited to consider the resolution recommended by the Executive Board.

BACKGROUND

1. In the medical setting a resistant organism is one which is not inhibited or killed by concentrations of an antimicrobial agent in normal doses. Resistance has been detected in all types of microorganisms - bacteria, fungi, parasites, viruses. The main focus of this document and the resolution recommended by the Executive Board is resistant bacteria.

DETECTION OF RESISTANCE

2. Resistance in bacteria is most commonly evaluated as part of the standard laboratory investigation to establish the cause of infection and the choice of treatment. After the collection of specimens from the patient, and the isolation and identification of the infecting microbe, susceptibility testing may detect resistance. All these stages require trained personnel and facilities, incur costs and may be subject to cost-benefit analysis. There is no overall standard method for performing the tests nor for interpreting the results; recommended methods differ between and within countries, with significant implications for international comparison of data. Moreover, for the vast majority of patients, especially those not in hospital, empirical or "blind" treatment is prescribed.

FACTORS THAT FAVOUR THE EMERGENCE OF RESISTANCE

3. Antimicrobials used for any condition, real or feared, in any dosage and over any period of time add to the selective pressure on microorganisms to adapt or die, and they are not reserved for human medicine alone: more than half of the total production is used in animal and fish farming and in other aspects of agriculture, increasing further the likelihood of emergence of antimicrobial resistance.

4. Faith in the healing power of antimicrobials is often unjustified. Physicians under pressure from patients' expectations prescribe antimicrobials even in the absence of appropriate indications. Patients often fail to comply properly with the prescriptions and forget their treatment or interrupt it prematurely, creating an ideal environment for resistant microbes to emerge.

5. In some countries, low-quality antibiotics (poorly formulated or manufactured, or whose date for use has expired) are still sold and used for self-medication. In many economies the cost of newer antimicrobials (developed to replace drugs which have become powerless through resistance) cannot be borne, which leaves national health services with a poor choice of agents.

FACTORS THAT FAVOUR THE SPREAD OF RESISTANCE

6. Bacteria are extremely efficient at increasing resistance, not only by rapid multiplication of a single resistant strain but also by dissemination of resistance genes among strains of the same or different species. Resistant pathogens are transmitted from person to person as easily as susceptible strains. The intensive use of antimicrobials for prophylaxis and treatment makes hospitals a prime site for the emergence and spread of resistant pathogens. Data are lacking from most developing countries, but it has been estimated that in some developed countries up to 60% of all hospital infections are caused by resistant bacteria. In addition, the exposure of health care workers to resistant pathogens is a growing concern.

7. The enormous increase in international travel means that individuals exposed in one country to infections caused by resistant pathogens (e.g. those causing acute respiratory infections, cholera and other diarrhoeal diseases, gonorrhoea, malaria, typhoid fever) may introduce these into other countries where resistance can then spread.

CONSEQUENCES OF RESISTANCE

8. An untreated or poorly-treated infection increases the risk that the subject will die. Treatment failures lead to longer periods of infectivity, which increases the pool of infected people moving in the community, augmenting opportunities for spread of resistance and exposing the general population to the risk of infection with resistant strains. Failure to respond to the first-line therapy also prolongs illness, incurs increased direct costs (for additional laboratory tests, treatment, hospitalization, etc.) and indirect costs (loss of income or time away from the family). When infections are caused by bacteria resistant to antimicrobials given by mouth, treatment has to be changed to intravenous or intramuscular administration of second-line antimicrobials which are almost always more costly, having added indirect costs (needles, syringes, intravenous lines, specially trained nurses), and often associated with a higher risk of toxic side-effects. Where these second-line agents are unavailable, infections become effectively untreatable.

9. Antimicrobial resistance is adding to the already growing cost of health care because of the need to detect, isolate and treat patients infected with resistant organisms. As bacteria become resistant to the older and relatively inexpensive antibiotics, physicians prescribe newer, more expensive drugs or combinations of drugs. Moreover, prescribers tend to choose new drugs even in the absence of laboratory results, because of the real or perceived risk of resistance.

THE COMPLEX PROBLEM OF ANTIMICROBIAL RESISTANCE CALLS FOR MULTIPLE SOLUTIONS

10. The solutions required are set out below.

(1) Surveillance to define the extent of resistance in different pathogens and in different populations, to adjust treatment strategies and national drug policies, and to measure the success of intervention strategies

WHO's antimicrobial resistance monitoring programme works with developing countries to establish laboratory-based surveillance networks through provision of training, an external quality assurance scheme, laboratory reagents and computer software (WHONET). It also supports the gathering of data to evaluate the impact on human health of the use of antimicrobials in food animal production. Specialized networks exist for monitoring drug resistance in *Mycobacterium tuberculosis* and for leprosy. WHO also has a gonococcal antibiotic susceptibility programme in the Region of the Americas and the Western Pacific Region (now being extended to the South-East Asia Region) and a pilot study in southern Africa.

(2) Education of policy-makers, prescribers, health care professionals, and the general public, in order to reduce overuse and misuse of antimicrobial agents

WHO sponsors national policy workshops which aim to improve collaboration between decision-makers in health policy and planning in development of strategies for monitoring resistance and improving the rational use of antimicrobials. The global "network of networks" gathers and shares information electronically from national and regional resistance surveillance networks. Recommendations on use of antimicrobials form part of WHO disease control guidelines; advice is given to the general public, and simplified treatment schemes have been introduced to educate patients in the correct use of treatment for tuberculosis and leprosy.

(3) Regulation to achieve maximum availability and quality of antimicrobial agents in all the world's markets; instigation of, and adherence to, patent laws; control of unethical promotion of antimicrobial agents

WHO has developed guidelines on many aspects of regulation and encourages the wide dissemination and implementation of its *Ethical criteria for medicinal drug promotion*.[1]

(4) Research to develop new agents with new mechanisms of action, to study the cost implications of resistance and the cost-effectiveness of its detection, and to link laboratory data on resistance to treatment outcome

WHO encourages research on various aspects of antimicrobial use, including correlation between laboratory studies and clinical outcome, rapid and simple tests to detect resistance, and development of new agents appropriate for the world's needs.

MATTERS FOR THE PARTICULAR ATTENTION OF THE HEALTH ASSEMBLY

11. The Health Assembly is invited to consider the resolution recommended by the Executive Board in resolution EB101.R26.

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[1] *Ethical criteria for medicinal drug promotion*. Geneva, World Health Organization, 1988.