

Antibiotic resistance: Protecting antibiotics - the declaration of the world alliance against antibiotic resistance

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Introduction

Antibiotic resistance (ABR) is a very serious public health issue. Antibiotics have been “miracle” drugs during many years, but their activity has been reduced sharply by many mechanisms of resistance. New mechanisms make the strains of Gram-negative bacteria resistant to the 3rd generation cephalosporins, and carbapenems. It is very urgent to act to slow down this phenomenon by global and international programs. We must, in particular, use far fewer antibiotics, which must be actively protected like a precious treasure.

The increase in antibiotic resistant bacteria poses a major healthcare threat. In the face of an almost complete absence of new antimicrobial drugs in development,^[1] ABR has become one of the main public health problems of our time. Margret Chan, general director of the World Health Organization, warned recently: “Post antibiotic era is almost upon us.” David Cameron, the UK prime minister, recently called for a “global action to tackle the growing threat of resistance to antibiotics.” Antibiotics are a unique class of medications because of their potential societal impact; use of an antibiotic in a single patient can select for ABR that can spread to other people, animals, and the environment, making an antibacterial used in one patient ineffective for many others. Bacterial resistance can evolve rapidly. As bacteria acquire resistance mechanisms, the altered bacterial genetic material coding for resistance mechanisms can be transmitted at times readily between bacteria, broadening the reach and extent of resistance. Treatment failures because of multidrug resistant (MDR) bacteria, once rare, notable, and limited to hospitals, now occur

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very commonly in hospitals, in particular in the Intensive Care Unit, and increasingly in the community as well. Methicillin-resistant *Staphylococcus aureus* (MRSA) infections, in particular due to community-acquired MRSA,^[2] are extremely prevalent in many countries, including some European ones (European Center for Diseases Control and Prevention. EARSS-Net database. <http://www.ecdc.europa.eu>),^[3] the USA, South America and Asia. Prevalence of MRSA infections decreased in the last few years in many European countries, and this can be considered as a very positive and promising result. Vancomycin-resistant enterococci (VRE) are also very frequent, with large differences between countries. In the European point prevalence study organized by ECDC,^[4] VRE prevalence was going from 1% to >50%. The prevalence of *Escherichia coli* and *Klebsiella pneumoniae* harboring extended-spectrum beta lactamases is increasing regularly worldwide^[5] reaching 50-70% for *E. coli* in some European or Asian countries.^[3,5] In the European point prevalence study, prevalence of *K. pneumoniae* with carbapenemases was going from 1% to >50%.^[4,6] Some infections are nowadays due to bacteria resistant to all antibiotics (Pan resistance). Those infections require very complex associations of high doses of old and new antibiotics, and mortality is very high. It is estimated that at a minimum 25,000 patients in Europe and 23,000 in the USA die each year from

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infections caused by resistant bacteria (CDC, ECDC). The cost of ABR is tremendous, whether measured as the personal and societal burden of illness, death rates, or healthcare costs.

Although it is a never-ending phenomenon, ABR is directly related to the volume of antibiotics used. We are using increasing amounts of antibiotics in health care and agriculture, and discharging these active drugs into the environment.^[7] The impact of widespread antibiotic use is enormous, promoting the development and dissemination of antimicrobial resistance.

We must change how antibiotics are used and adopt proactive strategies, similar to those used to save endangered species.^[8] Preservation of the efficacy of antibiotics and to the stabilization of antibiotic-susceptible bacterial ecosystems should be global goals.

Safeguarding antibiotics will require a concerted effort by patients and prescribers. The primary goal of world alliance against antibiotic resistance (WAAAR) is to raise awareness about the urgency and magnitude of the threat and to promote an international dialogue to assist in effective responses. WAAAR is a group of 700 individuals from 55 different countries representing all the key stakeholders (physicians, veterinarians, microbiologists, surgeons, pharmacists, nurses, evolutionary biologists, ecologists, environmentalists, patient advocacy groups). The Alliance receives support from >140 learned societies or professional groups throughout the world. WAAAR is a nonprofit organization open to professionals and consumers worldwide. WAAAR receives no funding from the pharmaceutical industry.

The Alliance, in particular through this declaration, is dedicated to lobbying actively for an antibiotic preservation and to raising awareness among antibiotic prescribers, politicians and policy-makers, patient safety and advocacy groups, the pharmaceutical industry, international health organizations and the general population. Individual actions, no matter how well intended, are doomed to failure unless there is an international dialogue, a common sense of purpose, and broad consensus on how best to proceed.^[9]

World Alliance Against Antibiotic Resistance Advocates for the Following 10 Actions in a Solemn Declaration (June 23rd):

1. Promotion of awareness of all the stakeholders-including the general public-of the threat represented by ABR. Strong cooperation among international political and/or economic organizations etc., all together must take the lead of this action against ABR
2. Organization, in each country, ideally by Ministries of Health or regulatory bodies, of a financed national plan for the containment of ABR, with the participation of all stakeholders, including patient advocacy groups
3. Continuous access to antibiotics of assured quality, especially in middle and low-income countries
4. Integrated Surveillance of ABR and antibiotic use
 - Standardized monitoring of antibiotic use and resistance at institution, regional, and country (comprehensive national data instead) level (through a Centers for Diseases Control and Prevention model) to allow comparative statistics (benchmarking), to be updated preferably in real-time and at least every 12 months. This will require adequate laboratory capacity using international standardized methods that may be facilitated by a centralized technologic coordinating infrastructure and information technology
5. Use of diagnostic tests
 - Appropriate use of existing diagnostic tests and development and implementation of new rapid, cost-effective and accurate diagnostic tests, adapted to the local context, to aid in distinguishing bacterial and nonbacterial etiologies. Rapid diagnostics may help clinicians avoid unnecessary treatments, rapidly select appropriate targeted therapies and inform the duration of treatment
6. Antibiotic stewardship (prudent, controlled and monitored approaches to the use of antibiotics)
 - In humans (hospitals, long term care facilities and primary care)
 - In animals (animal husbandry, agriculture, aquaculture and animal health/veterinary setting), in a "one health" philosophy
 - Progressive elimination of the "over the counter" (i.e. available without a prescription) access to antibiotics (systemic and topicals) for humans or animals
 - Ban of the use of antibiotics as growth promotion in food animals and exceptional use in prophylaxis.
 - Rational use of metaphylaxis (prophylaxis when some animals in the livestock are sick, or at high risk to be sick), and of animal treatment
 - Limitation of the use of critically important antibiotics in humans and animals (e.g. carbapenems)
7. Educational efforts for change
 - Educational programs directed at children/

- teenagers on antibiotics, bacterial resistance, and infection control (e-Bug model)
- Development of large coordinated, effective information and awareness campaigns directed at the public on expectations about the rational/appropriate use of antibiotics
 - Continuous education and training programs in the curriculum for all health care professionals in all settings (veterinarians, medical, dental, nursing, pharmacy and allied health care schools) and continuing professional education programs, on the rational use of antibiotics, including indications, dosing and duration of therapy. Education of farmers
8. Containment of bacterial transmission and prevention of infection
 - Promotion of universal hand hygiene and all infection control interventions that have been proven to reduce rates of resistance
 - Relentless efforts to prevent transmission of MDR organisms in healthcare, food production and animal husbandry
 - Programs to limit the contamination of drinking water with MDR bacteria, as well as contamination of the environment
 - Promotion of the use of available vaccines, in humans and animals
 9. Basic and applied research and development of new antibiotics
 - Increased support for basic and applied research is aiming at curbing bacterial resistance in human and veterinary medicine
 - Use of the principles of orphan drugs for new antibiotics
 - Incentives to stimulate research of new drugs (antibiotics and novel compounds) and vaccines via regulatory pathways that allow for fast track development
 - New economic business models to support the cost of innovation while safeguarding public health interests
 10. Request for UNESCO to include the antibiotic concept in the list of the intangible cultural heritage
 - We urge all of you to participate in this crusade, in your field of interest. The medical miracle of antibiotic therapy must be protected.^[10] This is a global priority and our duty. Please, help us to act NOW, by supporting this declaration, to promote wiser use of antibiotics in animal and human health, and the necessary accompanying political actions to support better education, integrated surveillance for public health action, and research.

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