

## Resisting the Challenge of Antimicrobial Resistance

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Antimicrobial Resistance (AMR) is a serious threat to global health that requires urgent action. This growing problem threatens the ability to effectively prevent and treat an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi.

How does antimicrobial resistance (AMR) occur? It develops when microorganisms and parasites evolve to withstand the effects of antimicrobial therapeutics that would have previously killed them or prevented their growth. For example, when bacteria develop characteristics that allow them to survive exposure to antibiotics, this essentially makes the antibiotics ineffective. AMR can result from physical or chemical characteristics of the environment impacting the microorganism or be inherently contained in the microorganism.

Reducing the prevalence of AMR is a World Health Organization (WHO) priority. Data mining of published studies, hospital data, diagnostic laboratories, national surveillance systems, research institutes and clinical trials from 204 countries and territories completed by the Global Research on Antimicrobial Resistance (GRAM) defined 23 bacterial pathogens and 88 drug-pathogen combinations. These pathogens and drug-pathogen combinations accounted for 1.27 million global deaths in 2019 that were directly attributable to a drug resistant infection. Using artificial intelligence (AI) models allowed estimation of the deaths (73%) that were caused primarily by six pathogens: *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. Only ischemic heart disease and stroke had more deaths.

The GRAM report found the burden of AMR mortality was highest in low and middle income countries, with Saharan Africa and South Asia having the highest attributable death rates from resistant pathogens. Approximately 1 in 5 of deaths linked to resistance were in children under 5! In the USA, the CDC (Centers for Disease Control and Prevention), estimates antibiotic resistance contributes to at least 2.8 million antibiotic resistant infections and 35,000 deaths each year with no foreseen reduction in upcoming years. Only increased prevalence is anticipated.

Another type of AMR, multi-drug resistant infections is currently estimated to cause 153,000 global deaths annually. As an example, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Streptococcus pneumoniae* are considered the leading causes of bacterial skin infections and community-acquired pneumonia. In the USA during 2017, the antibiotic resistance of *Clostridium difficile* allowed 12,800 people to die of the 223,900 people admitted for hospital care of this infection.

Why is AMR a global public health concern? It is brought about by antibiotic misuse (overuse, misuse or interrupted treatment). Who is responsible for increasing the spread of resistance? Food industries and physicians/patients who do not adhere to good antibiotic practice are the primary sources of encouraging this resistance to spread and accelerate globally.

Addressing this problem will require widespread change. These changes must include a shift in agricultural practices to reduce unnecessary use of antimicrobials in agriculture and their subsequent passage into the environment, improved antibiotic use and prescribing

by health practitioners (antibiotic stewardship), and the implementation of appropriate global surveillance systems at a local and national level which increases awareness of AMR. Primary targets for this increase in awareness must be among professional and occupational groups who use or prescribe antibiotics and ensuring public awareness and education in patients who are prescribed antibiotics or can purchase them...amazingly...in countries where no prescription is required!

Meeting the challenge to reduce unnecessary use of antibiotics for adult and child patients (including prenatal treatment and infants) who require antimicrobials to fight infections will require a multi-faceted approach.

Firstly, pharmacies, pharmacist/chemists, physician offices, physicians and medication insurance payment companies must ensure appropriate levels of use. This may require regulatory guidelines be established by enforcement agencies to prevent over prescribing and prescription refilling (similar to the new guidelines for opioid use in the USA).

Secondly, the use of antibiotics by veterinarians in animal treatment may need be controlled more extensively. Use of antibiotics in animals raised for subsequent consumption by humans and also, many crops grown by farmers must be controlled and use justified.

These antibiotic uses are also widespread in raw material production for common foods. As an example, the antibiotic chloramphenicol is injected into beehives to increase natural honey production for unrestricted human consumption use in foods and dietary supplements. Select countries (Canada for example) require many raw materials (such as honey) to be tested for the presence of chloramphenicol. The honey is often included as an active ingredient or flavoring agent in OTC (over-the counter) products including dietary supplements and weight loss products. The honey cannot be imported into Canada for use in human consumption products until tests show no presence of the antibiotic.

In summary, the extent to which antibiotics are present and possible for introduction into human life is extensive and expansive globally. Resisting the challenge to conquer antimicrobial resistance is not an option.

This challenge must be embraced...not resisted... to begin controlling the existing worldwide epidemic for AMR.

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