

Losing Our Battle with Bacteria, Viruses and Parasites

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Infections by bacteria, viruses and parasites are commonplace occurrence. Treatment to infections by bacteria is usually done with the help of antibiotics. However, increasingly, resistance to antibiotics has become a global problem with a significant economic and security impact. And this puts all of us and our loved ones in great danger. The microbial resistance to some of the common antibiotics (or anti-microbials) is a current growing challenge to healthcare professionals. Globally, this danger is widespread and growing at an alarming rate.

In Malaysia, antibiotic prescribing has been rates are high in both public and private primary care settings. Excessive and inappropriate antibiotic treatments, especially in private clinics, are leading to significant growth of resistance to many antibiotics. With the need for understanding the widespread of antimicrobial resistance and necessary measures to address and control it, National Surveillance of Antimicrobial resistance was initiated in 1998 with coordination of Institute of Medical Research. This was followed by the initiation of National Surveillance on antimicrobial utilization in 2001 coordinated by Pharmacy practice and Development Division, Ministry of Health, Malaysia. Subsequently, the National antibiotic and infection control programme in 2003 and National antimicrobial resistance

committee with 4 technical working groups were established to ensure prudent use of antibiotics and minimize the hospital acquired infection.

It's evident that antibiotics have become widely used for minor ailments, with both healthcare providers and patients contributing to increasing demand. Many patients expect antibiotics from their General Practitioners, and a significant number of doctors prescribe antibiotics upon patient request, even if they believe it's unnecessary. This pressure stems from concerns that patients may switch doctors if antibiotics aren't prescribed. Inappropriate antibiotic prescriptions are common for conditions like the common cold, cough, sore throat, and gastroenteritis, despite the knowledge that antibiotics are not effective against these illnesses.

AMR is expected to kill around 4.73 million people in Asia alone in 2050 and in Malaysia is at a worrying level due to their frequent and widespread use and abuse in the health sector. There are 45 hospital microbiological laboratories conducting antibiotics susceptibility testing of bacteria isolated from patients in the country where 43 belong to government hospitals

and 2 from university hospitals. The statistics show antibiotic resistance in Malaysia has increased when the National Antibiotic Resistance studies revealed an increased flow of Vancomycin resistance rate to the bacteria *Enterococcus faecium* went up to 14.1 percent in 2018 compared to 3.1 and 4 percent in 2021 and 2022 respectively.

According to the National Surveillance of Antibiotic Resistance (NSAR) report by Malaysian Ministry of Health in 2022, it is revealed that, for instance, an increased use of an antibiotic for intestinal infection, Vancomycin, has escalated the resistance rate to the bacteria *Enterococcus faecium*. Antibiotics such as ceftazidime, cefotaxime, cefuroxime as well as cefepime have increased resistance for *Escherichia coli*. Ciprofloxacin resistance for *Salmonella enterica* serotype Typhi has increased to 27.3 % in 2022. Fusidic acid used in the form of creams or ointments for these skin infections. It works by interfering with bacterial protein synthesis, thereby stopping the growth and spread of bacteria on the skin. Increased resistance was prominently noted fusidic acid in 2022. Resistance rate of penicillin G, ceftriaxone and ciprofloxacin for *Neisseria gonorrhoeae* is increased in 2022 as compared to 2021. Sadly,

this means somewhere, some Malaysians are facing the danger of their infections being unable to be treated.

Antimicrobial Resistance: A Looming Global Crisis and Ethical Dilemma

The term antimicrobial refers to the drug that selectively kills microorganisms (bactericidal) or prevents the growth of them (bacteriostatic) to save humans from infections caused by these microorganisms. Though much wider, in common parlance, we call it antibiotics. Antibiotics, often referred to broadly as antimicrobials, are crucial components of modern medicine as they are essential for treating numerous infectious diseases. The discovery of penicillin in 1928 by the Nobel Prize-winning Scottish scientist Alexander Fleming marked a milestone in healthcare. Since then, antibiotics have become indispensable in mainstream healthcare, effectively combating bacterial infections and saving countless lives worldwide.

Antimicrobial resistance (AMR) occurs when microorganisms like bacteria, viruses, and parasites develop the ability to resist the effects of medicines meant to kill or stop them growing, such as antibiotics, antivirals, and antimalarials. This resistance makes standard treatments less effective, allowing infections to persist and potentially spread to others. AMR is a global issue affecting humans, animals, and crops, leading to longer illnesses and increased deaths. Compounding the problem, there are too few new antimicrobial drugs being developed to replace older ones that are becoming less effective. Economically, AMR causes losses due to reduced productivity from illness and higher treatment costs.

The overuse and/or incorrect use of antibiotics have rendered some



strains of bacteria untreatable, allowing the growth of the so-called superbugs to mutate and multiply further in the system. Superbugs kills between 1.27 million and 4.95 million people because of bacterial antimicrobial resistance, more than HIV/AIDS or malaria. 65% of sepsis deaths globally were caused by bacterial infection. The remaining 35% were caused by other pathogens such as viruses, fungi, and parasites. AMR not only leads to loss of life and disability but also imposes substantial economic burdens. According to the World Bank, AMR could drive up healthcare expenses by an extra US\$ 1 trillion by 2050. Moreover, it could potentially cause annual gross domestic product (GDP) losses ranging from US\$ 1 trillion to US\$ 3.4 trillion by 2030.

Antibiotic resistance poses one of the most significant global health threats today, capable of impacting individuals of any age, in any part of the world. There is a rising trend where infections like pneumonia, tuberculosis, and gonorrhoea are increasingly becoming harder to treat effectively or are losing their effectiveness altogether.

As antibiotic effectiveness declines and superbugs proliferate, a profound ethical dilemma arises. Fairly distributing and responsibly using effective antibiotics becomes crucial as their scarcity worsens across generations. The looming prospect is a world where healthcare providers struggle to combat increasingly resistant superbugs, especially among younger populations. This raises urgent questions about the equitable allocation of this vital public resource. Is it ethical to risk leaving future generations without effective antibiotics, amidst the escalating threat of antimicrobial resistance?

How Bacteria Develop Resistance?

Certain bacteria are naturally resistant to specific antibiotics due to their structure. Others develop

resistance in two main ways: through genetic mutations or by acquiring resistance genes from other bacteria.

Mutations are rare changes in the genetic material of bacteria, occurring roughly in one out of a million to ten million cells. Some mutations enable bacteria to produce enzymes that render antibiotics ineffective. Mutations can also alter or eliminate the target within the bacterial cell that antibiotics normally attack. Bacteria can also develop resistance by blocking the transport of antibiotics into their cells or by acquiring resistance genes through a process called conjugation, where genetic material is exchanged during mating.

In some cases, bacteria pick up free DNA containing resistance genes from their environment, leading to the emergence of fully resistant bacterial strains. The overuse of broad-spectrum antibiotics, like second and third-generation cephalosporins, speeds up the development of resistance, including to methicillin, a drug related to penicillin

Another significant issue is the use of antibiotics as additives in animal feed to promote growth in poultry. When these antibiotics are given to animals, they can enter the food chain and contribute to antibiotic

resistance in humans. In the US, around 70% of antibiotics are used in livestock, and globally, more than half of all antibiotics produced are used in veterinary medicine.

UN Assembly on AMR

The United Nations (UN) plays a pivotal role in addressing antimicrobial resistance (AMR) through coordinated global policies and strategies, advocating for integrated approaches across human health, animal health, agriculture, and the environment.

UN agencies like the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) raise awareness through campaigns and reports, emphasizing the urgent need for action at national and international levels. The WHO provides technical guidance to countries, assisting in the development of national action plans that include surveillance of antimicrobial use and resistance, promoting appropriate antimicrobial practices, and strengthening healthcare systems.

The UN supports global monitoring and reporting on AMR trends, identifies hotspots, and evaluates intervention impacts. Through fostering international collaboration and partnerships among member states, NGOs, academia, and the private sector, the UN promotes research, development of new antimicrobials, and innovative approaches to combat AMR. Addressing AMR is integral to achieving Sustainable Development Goals like Goal 3 (Good Health and Well-being) and Goal 2 (Zero Hunger), reflecting the UN's broader efforts to advance global health and sustainable development.

The UN General Assembly high-level meeting in New York on AMR will be held on September 2024 to emphasize on a crucial chance for global leaders to collectively tackle the imminent danger that

AMR poses to global health, food security, and the attainment of the 2030 Sustainable Development Goals. At this meeting, 193 member states will strongly commit to curbing this global challenge for human health, food production, the environment, and ultimately growth and development.

Current Global Challenge

Antibiotics have been used not just to combat sickness, but to promote weight gain and faster growth in farm animals for several decades. The world economic forum has identified antibiotic resistance as a global risk beyond the capacity of any organization or nation to manage or mitigate alone. In developed economies, this includes higher health care cost and decreases in labor supply, productivity, household incomes, and national come and tax revenues.

New antibiotics were being discovered or invented at a rapid rate, so it was easy to move on to a better, stronger antibiotic if the first one didn't work. However from the early 1960's, the situation began to appear bleaker as bacteria were found to develop resistance through the several ways. At the same time, as the decades passed, the rate of discovery of new antibiotics began to slow. Since the early 1980's, pharmaceutical companies have focused more on profit taking drugs such as statins.

As such there is no major new class of antibiotics has been discovered since 1987 and too few antibacterial agents are in development to meet the challenge of drug resistance. As the prevalence of antibiotics are increasing day by day, the important surgical and medical treatments like organ transplants, intestinal surgery, caesareans, joint replacements and cancer chemotherapy would become highly dangerous to perform. Furthermore, life threatening infectious diseases such as pneumonia, TB, HIV and malaria will again become common.

Global Action Plan to Overcome AMR

Antimicrobial resistance is not a new problem but one that is becoming more dangerous; urgent and consolidated efforts are needed to avoid regressing to the pre-antibiotic era.

Leaders from different countries in UN assembly gathering have recognized the need for stronger systems to monitor drug-resistant infections and the volume of antimicrobials used in humans, animals and crops, as well as increased international cooperation and funding. They pledged to strengthen regulation of antimicrobials, improve knowledge and awareness, and promote best practices of antimicrobials usage — as well as to foster innovative approaches using alternatives to antimicrobials and new technologies for diagnosis and vaccines.

The World Bank research report in May 2016 concludes that AMR would increase poverty and affect poorest countries the most. Drug-resistant infections have the potential to cause a level of economic damage similar to—and likely worse than—that caused by the 2008 financial crisis. Up to 28 million people, mostly in developing countries, would be pushed into poverty by 2050. Health care costs in low-income countries would rise by 25% while livestock production in these countries would decline by as much as 11%.

Without effective containment of antimicrobial resistance (AMR), achieving the Sustainable Development Goals for 2030—including ending poverty, hunger, ensuring health, reducing inequality, and global development partnerships—becomes more challenging. AMR's impact on poverty is alarming: in a high AMR scenario, it could push an additional 24 million people into extreme poverty by 2030, mostly

affecting low-income countries. This exacerbates the difficulty in reaching the World Bank Group's goal of eradicating poverty by 2030.

Steps can be taken at all levels of society to reduce the impact and limit the spread of resistance. The general public can help by taking actions such as preventing infections to avoid the need for antibiotics, only using antibiotics when prescribed by a certified health professional, always taking the

WHO is coordinating a global campaign to raise awareness of antibiotic resistance and encourage best practices among the public, policymakers, health and agriculture professionals to avoid further emergence and spread of antibiotic resistance.

full prescription, never using left-over antibiotics and never sharing antibiotics with others. Prescribers also respond to people's expectations and demands, so increasing everyone's understanding of when antibiotics may be of benefit, and when not, should decrease the frequency that they are offered.

This year the world antibiotic awareness week has been held from 14-20 November 2016. The campaign aimed to improve awareness of global antibiotic resistance and to encourage the best practices among the general public, health workers, policy makers and agricultural sectors to avoid the further emergence and spread of antibiotic resistance.

The target aims of this awareness week will be to raising awareness

of antimicrobial resistance and promoting behavioural change through public communication programmes that target different audiences in human health, animal health and agricultural practice as well as consumers is critical to tackling this issue. Including the use of antimicrobial agents and resistance in school curricula will also promote a better understanding and awareness from an early age.

Making antimicrobial resistance a core component of professional education, training, certification, continuing education and development in the health and veterinary sectors and agricultural practice will help to ensure proper understanding and awareness among professionals.

The global community must also encourage sustainable investments in new medicines, diagnostic tools, vaccines, and alternative interventions. Research and development is needed to produce new treatments that can be deployed against multi-drug resistant infections. To stimulate the development and production of affordable, equitable access to new medicines, diagnostic tools, vaccines, and alternatives, these medications may need to be de-linked from price and sales volume.

Current Research on Antimicrobial Resistance: Global and Malaysian Perspectives

Research on antimicrobial resistance (AMR) is ongoing globally and in Malaysia, focusing on various aspects to address this critical public health issue. Here are some current areas of research:

Global Research:

New Antimicrobial Agents: There is a continuous search for new antimicrobial compounds, including antibiotics and alternatives such as bacteriophages and antimicrobial peptides, to combat resistant pathogens.

Antimicrobial Stewardship:

Research focuses on strategies to promote responsible use of antibiotics in healthcare settings, agriculture, and veterinary medicine to slow down the development and spread of resistance.

Diagnostic Tools: Developing rapid diagnostic tests that can quickly identify resistant pathogens and guide appropriate treatment decisions is a priority. This includes molecular diagnostics and point-of-care tests.

Surveillance and Epidemiology:

Monitoring the prevalence and trends of AMR globally through surveillance networks and databases to understand patterns of resistance and inform public health policies.

One Health Approach: Recognizing the interconnectedness of human health, animal health, and the environment in AMR, research explores integrated approaches to mitigate resistance across these sectors.

Research in Malaysia:

Surveillance and Epidemiology:

Malaysian researchers participate in global AMR surveillance efforts and conduct local studies to monitor resistance patterns in hospitals, communities, and food production systems.

Clinical Research: Investigating resistance mechanisms of common pathogens in Malaysian healthcare settings and evaluating treatment outcomes to optimize antibiotic therapy.

Antibiotic Use and Policy: Studying antibiotic prescribing practices in Malaysia to develop guidelines and policies that promote rational use and reduce unnecessary antibiotic consumption.

Public Awareness and Education: Researching effective strategies to raise awareness about AMR among

healthcare providers, patients, and the public to encourage responsible use of antibiotics.

Alternative Therapies: Exploring alternative treatments to antibiotics and evaluating their efficacy in Malaysian contexts, such as herbal remedies or probiotics.

Overall, both global and Malaysian research efforts on antimicrobial resistance are crucial for understanding, preventing, and managing this complex challenge to global health. Collaborative research initiatives and interdisciplinary approaches are essential to combatting AMR effectively.

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