

Ending the AMR Cycle

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According to the World Health Organisation's (WHO) annual review of antibacterial agents in clinical and preclinical development, the R&D pipeline for new antibacterial medicines is insufficient to tackle the challenge of increasing emergence and spread of antibiotic resistance. Furthermore, the availability and access to new and existing antibiotics, including generics, is a challenge for countries of all income levels. The Global Leaders Group on AMR recently reiterated that the world faces a serious antibiotic pipeline and access crisis that requires innovative financing measures.



Antimicrobial resistance (AMR) among bacterial pathogens is a silent pandemic and an urgent global public health threat. These superbugs, which are able to resist multiple antibiotics, are on the rise and have claimed millions of lives worldwide as well as long-term disabilities, and high economic costs associated with the healthcare burden.

According to a study by the Global Research on Antimicrobial Resistance (GRAM) Project published in the Lancet, 33 common bacterial infections were either directly or indirectly responsible for 7.7 million deaths in 2019. MRSA, an infection that primarily occurs in people who've been in hospitals or other healthcare settings, alone caused more than 100,000 deaths in 2019. These bacterial pathogens are deadlier than most better monitored pathogens such as malaria, HIV or tuberculosis.

The overuse and misuse of antibiotics have led to the emergence of AMR, which is a complex problem that requires a multi-pronged approach to address. The annual AMR death toll is expected to double by 2050 without sufficient intervention.

Environmental sustainability

The constant presence of antimicrobials in our environment increases the spread of AMR driven by the environmental impacts of the manufacture, use and disposal of antimicrobials. In both livestock and humans between 40 and 90 per cent of an antibiotic dose administered is excreted in faeces or urine. In agriculture, these excretes frequently reach the environment and are contaminating soil, plants and water. Pharmaceutical effluent discharge from manufacturing sites have also shown contamination often greater than those of agriculture and humans.

Climate change is also increasingly becoming a problem by altering the distribution and transmission of many food-borne, water-borne and vector-borne diseases. In response more antibiotics are being dispensed and used to build resistance. And while there is no immunity to the effects of climate change, there are regions affected stronger than others. More frequent and extreme weather-related events, such as floods, storms and extended heat waves impact those with less the most and lead to further socioeconomic deprivation leading to a higher risk of disease spread.

Optimising the use of antimicrobials has the potential to not only greatly reduce risk of people getting hospitalised but also reduce greenhouse gas emission and effluent discharge. This prudent use of resources leads to environmental sustainability, a state where resources cause minimal harm to the environment without compromising population needs.

Direct approach

A direct 4D's treatment approach has been proposed, which includes the right drug, dose, duration, and de-escalation of therapy to curb AMR.

The 4D approach emphasises the importance of selecting an appropriate antimicrobial agent based on the susceptibility of the microorganism causing the infection, using an appropriate dose that achieves therapeutic levels in the body, administering the antimicrobial agent for an appropriate length of time, and modifying antimicrobial therapy based on microbiological results and clinical response. To identify the right drug the use of rapid diagnostics is necessary to accurately identify the cause of the infection and determine the appropriate antibiotic.

The right dose refers to using an appropriate amount of an antimicrobial agent that achieves therapeutic levels in the body. This requires consideration of factors such as patient age, weight, and renal function. Administering the right dose also has a direct impact on the amount of antibiotics excreted through faeces and urine.

The right duration refers to the appropriate length of time for which an antimicrobial agent should be administered to treat an infection. This requires consideration of factors such as the severity of the infection, the site of infection, and the patient's response to treatment.

Lastly, de-escalation of therapy refers to modifying antimicrobial therapy based on microbiological results and clinical response. This involves discontinuing or narrowing antimicrobial therapy once the causative organism has been identified and susceptibility testing has been performed.

The successful implementation of the 4D's approach requires a multidisciplinary approach that involves healthcare providers, policymakers, and patients. Especially the expanded use of rapid diagnostics, such as point-of-care tests (POCTs) is critical to its implementation. POCTs can quickly and accurately identify the cause of an infection and determine whether antibiotics are necessary. POCTs can be used directly at the site of patient care, allowing for quicker delivery of results that directly influence clinical decisions.

Despite its promising use, rapid diagnostics face many obstacles. The accurate identification of the bacterial pathogens requires blood and other samples. Collecting these samples is a long and laborious process. The identification of bacteria from blood cultures can be made even more challenging if an insufficient amount of blood is collected or if the patient has already taken an antibiotic. In addition, delays can occur with laboratory processing or transportation, especially if the facilities are outside the hospital or medical facility. Also contamination can be a frequent problem during blood culture collection. Many

bacteria can also be very finicky and difficult to culture in standard automated systems. And even with automated systems, highly trained and skilled human operators are needed to interpret results and identify the bacteria.

Practical solutions

There is the need to explore alternatives to the present way on how we tackle the spread of AMRs. The Centre for Sustainable Healthcare has proposed a sustainable healthcare guide in which it includes the principles of prevention, autonomy and lean service delivery.

For a more sustainable approach, there is the need to implement a prevention strategy focused on an effective way to reduce the unintentional exposure to antimicrobials, optimising antimicrobial use, and investing in innovation for supply and appropriate access to antimicrobials.

Better patient education enhances engagement and autonomy.

Pharmaceutical inappropriate disposal, e.g. through sewage is an issue that enhances the spread of AMRs. Increased public awareness could lead to individual change behaviours and ultimately lead to a more sustainable hospital waste management.

Just like the 4D approach, the sustainable approach requires the inclusion of non-invasive testing, such as POCTs, which lead to a more streamlined care delivery and service. POCTs remain an important instrument to identify the pathogens before commencing treatment, avoiding unnecessarily prolonged antimicrobial treatment and ultimately reducing resource used during the treatment regimen.

Bioavailability of intravenous (IV) medications is always higher than that of their oral counterpart leading to the patient getting relief earlier. .

While there will not be a single weapon to tackle AMR we need to explore ways to not only directly curb the infection but to stop the cycle of how antimicrobials are spread through a more sustainable approach.

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