The Causes Behind the Global Crisis of Increasing Antibiotic Resistance and Strategies to stop this

Maja Szul

Introduction

Antibiotics are seen as a go-to solution by countless people, agricultural businesses and doctors across the world due to their ability to kill bacteria. So then, how are antibiotics transforming from wonders of modern medicine to increasingly inefficient?

In 1928, one of the first antibiotics, penicillin, was discovered, leading to its life-saving use in World War Two. From a world where a simple splinter could cause death by blood poisoning, penicillin had enabled the survival of bullet wounds and devastating injuries. It allowed people to survive different infections and more invasive treatments improving healthcare as a whole. During the war, it is estimated that it saved the lives of every one in seven wounded UK soldiers. [1]

This happened less than 100 years ago, therefore, antibiotics are a fairly new development, and yet resistance to them is growing at an alarming rate.

So, how exactly does antibiotic resistance develop and why is it happening so quickly?

The scientific answer is that over-exposure of bacteria to antibiotics provides opportunities for resistant bacteria to outcompete other bacteria strains, survive and multiply.

Firstly, random DNA mutations within the bacteria create a resistant strain possessing a new advantageous allele that allows it to survive when facing the antibiotic, while the unmutated, non-resistant strains are killed by the antibiotic which acts as a selection pressure. Over time, the resistant allele frequency within the population increases and they can no longer be treated by that antibiotic. [2]

As of today, in high income countries the development of resistant strains is created by over-prescription, use of left-over drugs, not completing a course of antibiotics and its over-use in agriculture. In low-income countries, the prior still apply along with the added risk of self-prescription through OTC (over the counter) drugs. These factors are underpinned by a lack of education and policies which will be discussed along with their preventions below.

Lack of Public Awareness

In a 2015 survey conducted across 12 countries (Barbados, China, Egypt, India, Indonesia, Mexico, Nigeria, Russian Federation, Serbia, South Africa, Sudan and Viet Nam), 64% of 10,000 responders believed that antibiotics can be used to treat colds and flu despite the conditions being caused by viruses on which antibiotics have no effect. [3] In a survey amongst European countries this percentage was still quite high at 57%. [4] This lack of awareness leads to wrongful use of antibiotics which accelerates antibiotic resistance. It is also shown that most participants across studies believed that antibiotic resistance was caused by changes in the human body. [5] These results indicate that many uninformed people cannot contribute to minimising antibiotic resistance and that they themselves may be unknowingly misusing antibiotics.

In regard to leftover antibiotics as an example, a 2017 article states that 33% of those who had left-over antibiotics intended to keep them for future use. [6] This use of old antibiotics without professional monitoring leads to many risks like development of resistant strains in cases where the antibiotics are not taken for the recommended course length or where taken when unneeded. This means that the period of time over which bacteria multiply while facing the antibiotic is longer increasing the chance of selection of more mutated strains which form. In addition to this, there is also risk of adverse reactions if taking other drugs.

The survey also showed that the less knowledgeable participants were those aged between 15-24, 65+ and black, Asian and ethnic minority groups. To increase public awareness, it's stated that information should be provided during primary (non-specialised) and secondary (specialised) care, as, despite public health campaigns, harmful assumptions are still prominent in public knowledge surrounding antibiotics. [6] Primary care (like seeing a GP) allows personalised explanations and the possibility of answering questions face to face as well as ensuring a wide reach to much of the population.

Access to OTC drugs

Despite the fact that antibiotics as over the counter drugs are widely banned from sale in many countries including the UK, some topical antibiotics (specific to localised areas) and eye drops do not require prescription [4]. These could potentially increase antibiotic resistance although monitoring and limited availability of licensed OTC drugs restricts the spread of resistance. In other lower income countries however, like India, OTC drugs are less regulated and so access is increased. [7] This may lead to more of the population acquiring and using antibiotics while unaware of when and how long to use them for. As a result of this over-use, the opportunities for resistant strains to develop and outcompete the non-resistant strains increases so the resulting risk of antibiotic resistance is higher. [7]

Over-Utilisation in Agriculture

Antibiotics are often used for livestock production and upkeep as a preventative measure instead of a treatment resulting in rapid selection of mutated microbes. For example, in the 1950s, tetracycline antibiotics were used which just three years later resulted in the resistance of *Shigella dysenteriae* [8] thus accelerating formation of resistant strains that could also impact humans. Common strategies suggested to reduce this are governmental policies banning use of some antibiotics and uses of molecular methods to target resistant bacteria (detailed in the conclusion). [8]

Lack of Medical Training/Education

Interestingly, research suggests that medical professionals may be adding to the problem of antibiotic resistance even in countries of higher income and more reputable education.

One factor due to which healthcare professionals may over-prescribe is due to trying to upkeep a good relationship with the patient. According to a study conducted in South Wales, doctors were aware of the low efficacy of prescribing antibiotics, yet they did so to maintain a good patient-doctor relationship. [10] A survey to support this found that 55% of GPs felt under pressure to prescribe antibiotics with 44% admitting to prescribing them in order for patients to leave the surgery. [11] A strategy to reduce this amongst doctors is to highlight the individual risk to the patient in taking antibiotics. To reduce patients wanting unnecessary antibiotics it is important to also inform them of the risks and stress the benefits of non-antibiotic treatments. [10]

A general lack of confidence and knowledge amongst healthcare staff may also cause over-prescription as a 2016 survey with 140 junior doctors across five London hospitals showed that only 5-13% thought their education on the use of antibiotics was good enough. [12]

Covid 19

The recent pandemic has also boosted concerns over antibiotic resistance as the behaviour of physicians had changed due to worries over co-infection in patients with Covid-19. This resulted in a higher rate of antibiotic use, despite, in many cases, there not being a secondary infection. [13] One study showing evidence for the over-use of antibiotics during the pandemic stated that 1.2% of Covid-19 patients had a documented co-infection however 60.1% of all Covid-19 patients in the study received antibiotics upon presentation of symptoms. [14] This clearly presents the over-prescription due to the pandemic and the need to clearly diagnose and test whether the patient requires antibiotics.

Conclusion

To summarise, in spite of the growth of medical research and medical technology there is still a constant increase in antibiotic resistance, and, as a result, deaths due to untreatable illnesses. In 2019, this was 1.27 million deaths globally and the trend is still increasing. [15]

However, this problem is due to rather simple factors: a lack of education and policies. The most agreed-upon strategies suggested throughout articles and studies to mitigate this problem are therefore education through schools, health campaigns and discussions between patients and doctors; stronger regulations regarding pharmaceutical promotion and OTC drugs as well as strengthening data and surveillance to maintain direct, efficient policies.

One scientific method included molecular therapies. An example of this is phage therapy consisting of viruses that exclusively target bacteria. The bacteria *Acinetobacter baumannii* (a common nosocomial pathogen) which has evolved resistance to many antimicrobial drugs has been shown to be lysed (broken into smaller parts) effectively by a newly formed phage cocktail. [9]

[9] Other strategies include restricting use of left-over medication through giving the exact number of tablets needed and the introduction of take-back programmes (where left-over antibiotics are returned). [5]

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