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Introduction

There is a prominent source of danger rising in number from year to year. Even though it is invisible to the naked eye, it presents a future where humanity's miracle medicine becomes worthless and HIV, common flu, or food poisonings pose lethal outcomes to patients.

Antimicrobial resistance kills 4.9 million people every year and this trend has been dramatically increasing every year. "AMR affects countries in all regions and at all income levels. Its drivers and consequences are exacerbated by poverty and inequality, and low- and middle-income countries are most affected."



Map of the density of a particular type of bacteria resistant to antibiotics

Even though there is high awareness of the issue's seriousness it has been shown that the knowledge of the threat does not produce behavior to stop or mitigate the crisis of AMR. The main source of AMR is poorly dosed antibiotics and other antimicrobials both in human health care and agriculture especially in livestock where new resistant microbes develop. Every couple of years a type of antibiotic and other antimicrobial medicine loses its effect due to AMR. It affects not just in-patients, but everyone.

This issue lacks the attention it deserves as it is still a common practice to utilize antibiotics both in medicine and agriculture without prescriptions in many countries of the world. By focusing on this pressing matter not only would the annual deaths connected to AMR drop but the era of global crisis with insufficient medication for common diseases would also be postponed if not avoided.

Definition of Key Terms

- AMR Anti-microbial resistance occurs when bacteria, viruses, fungi, and parasites change over time and no longer respond to medicines.
- Antimicrobial Medicine that kills microorganisms that cause infections in humans, animals, and plants.
- Antibiotic A specific type of antimicrobial that is effective against bacteria
- Superbug A microorganism (usually bacteria) no longer responds to antimicrobials designed to kill them.
- LDLIC Low Development and Low-Income Countries are countries whose (national) income is low and have few human assets.
- E. coli Escherichia coli is a type of bacteria that is commonly found in the gut of warm-blooded animals. They are harmful to their host, thus E. coli being resistant is a huge threat.
- Last resort antibiotics Extremely strong antibiotics are used only when all other antibiotics have failed.
- Stewardship The job of supervising or taking care of something, such as an organization or property.
- Multidrug resistance When a certain microbial is resistant to not just one but two or more types of antimicrobials.

General Overview

The threat posed by AMR is rising every year, however as the result of scientific effort its major causes were mapped out. It has been found that the most prominent source of the rising resistance levels is the misuse of antimicrobials in agriculture and live feeding. The second most influential source is the misuse and overdose of antimicrobials in human healthcare. In LDLIC the lack of access to clean water and sanitization is an extra factor.



https://www.news-medical.net/news/20190430/United-Nations-sounds-alarm-bell-on-drug-resistantinfections.aspx

Growth enhancers for chicken, pig, and other animals are often mixed with low-dose antimicrobials that in the short term result in faster development and a higher percentage of meat or fat. However, this low-dose antimicrobial environment quickly produces microbes by natural selection that will be resistant to that particular antimicrobial. Then these microbes reproduce and pollute the livestock and the environment where they are raised, infecting both the next generation of the animals and the people consuming them. This is a fast process meaning it usually takes 1-5 years to create AMR and make any kind of antimicrobials ineffective.

The other prominent cause is overdose and unnecessarily prescribed antimicrobials in human health care. There is a trend especially in America that patients demand their general practitioners and doctors to prescribe antimicrobials (usually antibiotics), and they comply for patient satisfaction. Another case is when the doctors are not sure what the cause of the illness is of their patient, but antimicrobials might cure them. The problem with this is the same with agriculture but the natural selection of mutated bacteria happens directly in humans and their close environment.



Natural selection of resistant bacteria

Microbes mutate naturally, so it frequently happens that they develop resistant genes, but in an optimal environment, these genes do not give them benefits over non-resistant microbes. However, when there is some kind of antimicrobial substance present, by natural selection only resistant microbes will survive and multiply. With the transmission of these through air, water, human interactions, crops, and livestock all parts of the globe will be dominated by AMR. What makes the issue more serious and harder to tackle is that one microbiota can be resistant to multiple types of antimicrobials. Furthermore, once a microbial gains resistance they can transmit it to other non-resistant ones by direct contact or the release of DNA snippets in the form of plasmids. This makes regulating resistance even more challenging.

Major Parties Involved

UK: The United Kingdom takes a steadfast stance on AMR, acknowledging its significant impact on global health. In response to this pressing issue, the UK has devised a comprehensive strategy aimed at tackling AMR from various angles. The government's 20-Year Vision and 5-Year National Action Plan on AMR serve as foundational documents outlining the country's commitment to combating the rise of antibiotic resistance.

- **USA:** In the United States, combating AMR is a priority, evident in the National Action Plan for Combating Antibiotic-Resistant Bacteria. The U.S. strategy emphasizes surveillance, research, and development of new antibiotics. Regulatory agencies like the FDA work to ensure the responsible use of antibiotics in healthcare and agriculture. International collaborations and partnerships are also integral to the U.S. approach, aligning with the global nature of the antimicrobial resistance challenge.
- India: India recognizes AMR as a serious health concern and has taken steps to address it. The National Action Plan on Antimicrobial Resistance has been established, focusing on promoting responsible use of antibiotics, strengthening surveillance, and enhancing research. Collaborative efforts with international organizations and neighboring countries underscore India's commitment to a global approach in tackling AMR.
- **China:** China has implemented a comprehensive strategy to combat antimicrobial resistance (AMR), recognizing the detrimental impact of misuse and overuse of antimicrobials. Notably, China's health authorities have taken steps to reduce antimicrobial usage among hospital inpatients, achieving a significant decline from 59.4% in 2011 to 36% in 2019. Despite these efforts, challenges persist, as evidenced by the alarming statistics of 73,000 people developing multi-drug-resistant tuberculosis in 2017.
- **Russia:** Russia is committed to addressing AMR through a multifaceted approach, including raising awareness via advocacy efforts, capacity-building activities in AMR surveillance, and collaborative research studies on drug-resistant microorganisms. Russia actively supports Eastern Europe and Central Asia in combating AMR by promoting good agricultural practices and prudent antimicrobial use. Russia conducts national laboratory assessments, maintains a laboratory reagents bank, and contributes expertise on AMR regulation. The focus is on effective monitoring, analysis, and research to develop alternatives to antimicrobials.

Timeline of Events

1940 - Scientists working on penicillin have found E. coli bacteria-producing chemicals that make them resistant towards penicillin.

1948 - Antibiotics could legally be used on animals and crops to promote growth and prevent diseases.

1990 - AMR levels had not been decreasing, and many new drugs were proven to be ineffective. Bacteria resistant to multiple drugs are no longer the exception but the rule.

2015 - WHO declares global AMR emergency, initiating an action plan to solve the issue. This includes raising awareness, better surveillance, and financially motivate pharma companies to research new antimicrobials.

2019 - Over six million people have died in 2019 associated or directly linked to AMR.

Previous Attempts to Solve the Issue

DEVELOPING MORE ANTIMICROBIALS

A first-sight straightforward approach to solving AMR is just to develop more antimicrobials. The problem with this is that development is slow and expensive, so it is not usually profitable for big pharma companies. This makes it impossible to consistently develop newer and newer antimicrobials.

A solution to this would be to somehow motivate pharmaceutical companies to invest in antimicrobial research. Furthermore, it has been shown that microbes, especially bacteria can and are resistant to multiple types of antimicrobials, thus adding in more of them just worsens the lifespan of freshly developed antimicrobials.



POLICY GUIDANCE

As mentioned earlier, the main cause of AMR in human healthcare is the unnecessary prescription of antimicrobials (especially antibiotics) when a patient does not have a bacterial disease. However, there is no viable method or technology to find out the exact cause of the

illness, so doctors prescribe antimicrobials anyway because they expect the worst case. Another problem is prescribing them for too long or for too short a period, which again promotes developing resistance.

To aid doctors, many sources were written with detailed descriptions of the most frequent bacterial diseases with recommended treatment. Nonetheless, these documents are not yet widely known or translated.

Possible Solutions and Approaches

PHAGE THERAPY



Bacteria are the most dangerous of microbials. Fortunately, there is a deadly weapon against them: phages. Phages act like viruses to bacteria, and they reproduce by killing them. Moreover, they can be highly engineered, therefore unlike antibiotics which target various microorganisms including human cells, phages target one specific bacteria. This "outsmarts" the resistance coming from natural selection happening at antibiotics. However, this technology was lost for a long time after the rise of antibiotics, hence most countries have not legalized phage therapy. The only exceptions are Georgia, Russia, and Poland but the latter two had put some restrictions on its use. Also, India is actively pursuing legalization.

ONE HEALTH

AMR is a complex problem that requires sector-specific actions in the human health, food production, animal, and environmental sectors, and a coordinated approach across these sectors. One Health refers to an integrated, unifying approach that aims to achieve optimal and sustainable health outcomes for people, animals, and ecosystems. It recognizes that the health of humans, domestic and wild animals, and plants are closely linked and interdependent. The One Health approach to preventing and controlling AMR brings together stakeholders from relevant sectors to communicate and work together in the design, implementation, and monitoring of programs, policies, legislation, and research to mitigate AMR and attain better health and economic outcomes.

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E. coli WHO fact sheet

https://www.who.int/news-room/fact-sheets/detail/ecoli#:~:text=Escherichia%20coli%20(E.%20coli),can%20cause%20severe%20foodborne%20dis ease.

Very Helpful Timeline

https://www.sciencelearn.org.nz/interactive_timeline/15-antibiotics-and-antimicrobialresistance-a-timeline

Excellent Video on The Whole Topic https://youtu.be/P6htK_5ZFpU?si=902CsgAmKib18Sk_

Demonstration of the Quick Pace Resistance Develops https://youtu.be/bDa4-nSc7J8?si=sN25_gKYEMLbddkX

Scientific Paper in depth Timeline

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6928725/

Policy Guides

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