Antimicrobial Resistance: Coming to a World Near You

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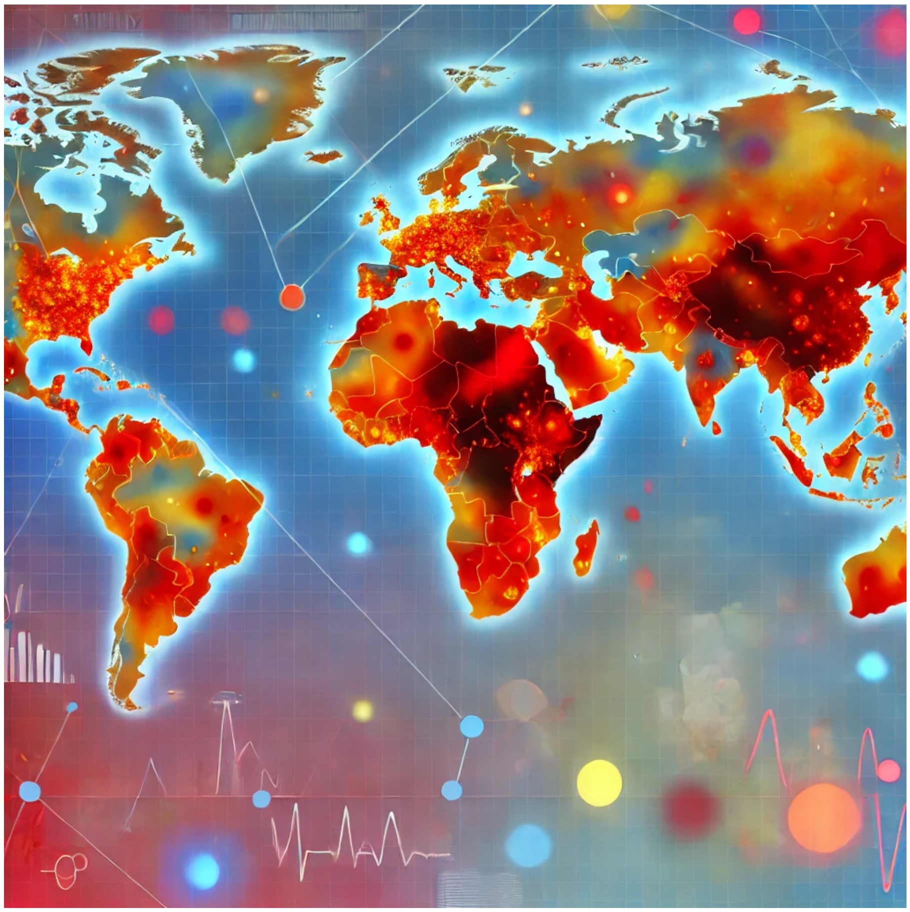

What is Antimicrobial Resistance?

Antimicrobial and or antibiotic resistance (AMR/ABR) is described as the phenomenon in which bacterial infections are not eliminated by the standard protocol of antibiotic drug use. According to the Centers for Disease Control and Prevention (CDC), at least 2 million individuals are diagnosed annually with resistant bacterial infections in the United States and of those, at least 23,000 people die because of the untreatable infection (Dadgostar, 2019). The burden of disease is estimated at approximately 1.7 million deaths globally making AMR one of the leading causes of death – surpassing tuberculosis and HIV – and on pace to reach 10 million deaths per year globally in 2050 (Murray et. al, 2019).

Resistance can occur in a multitude of ways. A bacterium can acquire resistance through genetic mutation or horizontal gene transfer, adapt to environmental signals causing transient resistance, or have resistance based on the qualities and makeup of the bacteria. While the development of resistance is a natural phenomenon, overuse and misuse of antibiotics drives AMR (Christaki et. al, 2019).

Factors that Lead to Antimicrobial Resistance

As antibiotic resistance threatens to reverse decades of advancements in medicine, it is pertinent to assess the multitude of factors that are driving this phenomenon and how human interaction with the environment propels the cycle, as shown in Figure 1.

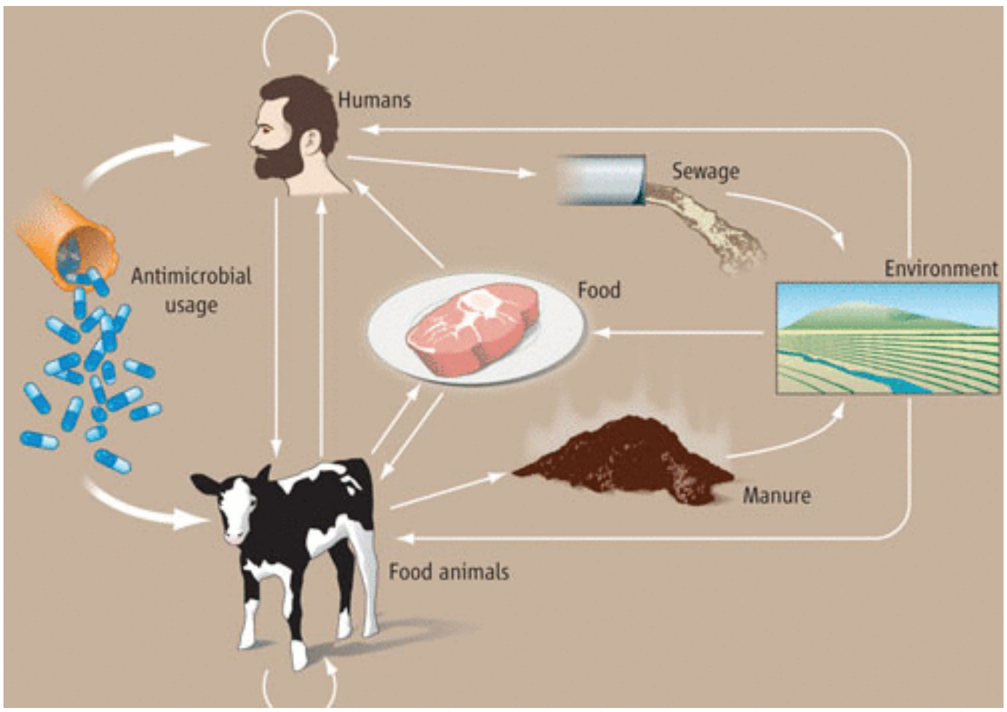

Figure 1: Environmental factors contributing to antibiotic resistance.

Misguided Use of Antibiotics

In a study conducted by Washington University and The Pew Charitable Trust analyzing insurance claims found that unnecessary use of antibiotics prescribed to children resulted in $74 million in excess health care costs in 2017 alone, increasing the risk of individual adverse drug events among patients receiving antibiotics inappropriately (The Pew Charitable Trusts, 2023). A 2023 study published in the Journal of Medicine examined 51 million patient encounters over the course of 15 years to find that antibiotics were over prescribed in nearly half of all cases of upper respiratory infections. This misuse increased the risk of adverse health events such as candidiasis, clostridium difficile, and more frequent OR visits by approximately 30% (Carmicheal et. al, 2022).

Antibiotic use in the Meat/Poultry Industry

Veterinary antibiotics which were initially intended to treat infections and offset the poor living conditions of the animal have been inappropriately utilized as prophylactic agents, feed adjuvants, and growth promoters for our animal food products. This remains prevalent globally with approximately 80% of annual consumption of antibiotics occurring in food animals with major countries being required to meet the growing demand for the population and maintain animal health, as shown in Figure 2 – with China (23%) and the U.S. (13%) making up just over ½ of global antibiotic usage. While antibiotic dose protocols generally last for more than two weeks, in the case of certain animals such as chickens, administration of the drug often lasts during the entire production period.

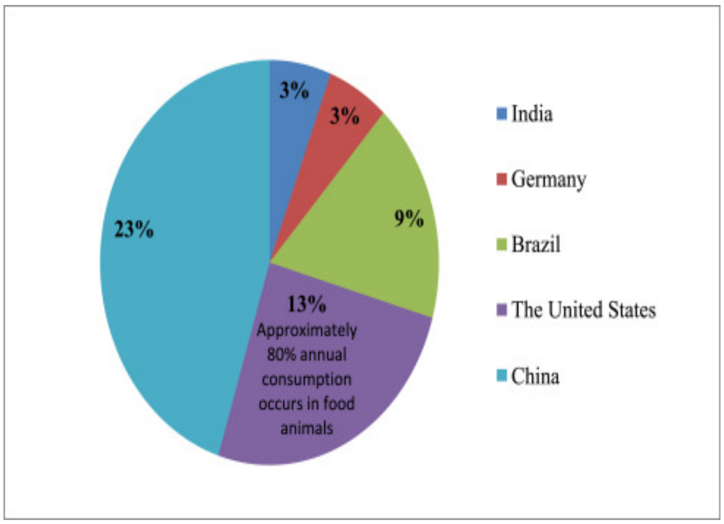

Figure 2: The top five countries based on antibiotic use during food-animal production.

This prolonged and off-schedule use of antibiotics has led to leftover traces of antibiotics being present in various food animal products including but not limited to dairy, chicken, eggs, and beef. It is estimated that between 30%-90% of these animals' antibiotic consumption are released through their urine and manure (Samreen et. al, 2021). These antibiotic reservoirs remain present on farms leading to contamination and run off into the surrounding environment.

Agricultural and Industrial Runoff

Overuse of antibiotics isn't the only factor contributing to growing resistance. Agricultural and Industrial runoff waste from both healthcare and food industries also contribute to the spread of genetic elements prone to resistance (Figure 3). Heavy metal pollution brought on by urbanization and industrialization pose a risk not only to the surrounding environment but to antibiotic resistance due to their ability to work synergistically with bacteria to promote growth in antibiotic resistant genes (Edet et. al, 2023). A study published in 2022 which took samples from the Jiangling river in China found an estimated 218 antibiotic resistance genes which were associated with eight different antibiotic classes (Lu et. al, 2022).

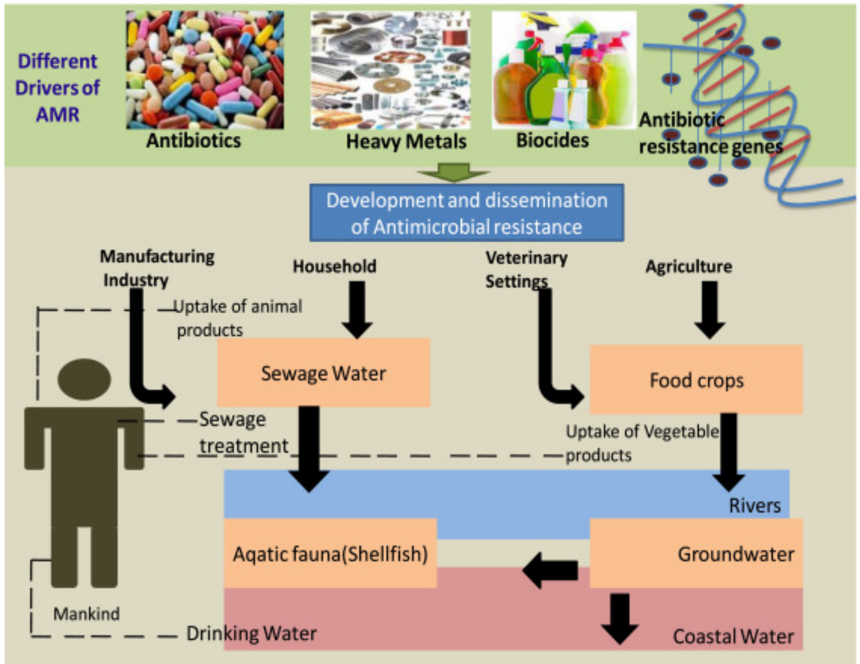

Figure 3: Drivers of antimicrobial resistance within the environment.

In addition to heavy metals, biocides such as formaldehyde and chlorhexidine have been shown to facilitate mutations within bacteria. Low-income countries are at greater risk due to less frequent surveillance and lack of sanitation in both the environment and healthcare industries (Samreen et. al, 2021).

Climate Change

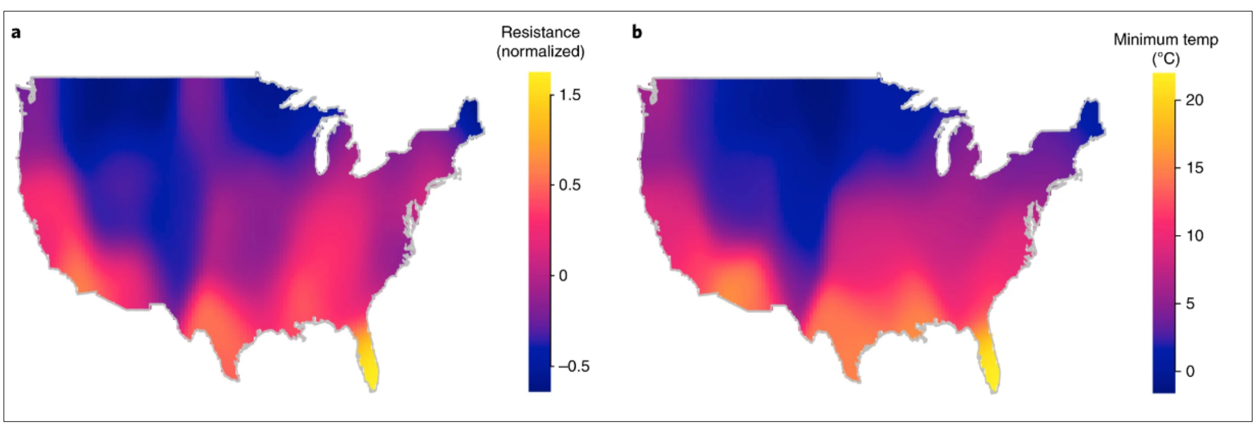

Figure 4: A. Mean antibiotic resistance for E. coli. B. The 30-year average minimum temperatures.

Rising temperatures due to climate change are found to be indirectly linked with antimicrobial resistance. For instance, Figure 4 shows the close overlap between antibiotic resistance for E. coli and the 30-year average minimum temperatures across the U.S. Increasing temperatures and rising sea levels are linked to a greater occurrence of flooding and precipitation, which in turn lead to more ideal conditions for bacteria such as cholera and campylobacter to thrive resulting in more frequent infections (Burnham, 2021). Frequent extreme weather events are also capable of wreaking havoc on our wastewater infrastructure leading to more emerging pollutants in both soil and water breeding more resistant bacterial reservoirs (Magano et. al, 2023). More frequent infections could necessitate increased use of antibiotics.

The Economic Dilemma behind the Lack of New Antibiotics

Antimicrobial resistance costs the U.S. healthcare system as much as $20 billion dollars annually, according to the CDC. Research conducted by the World Bank determined that AMR would further propel the rate of poverty, specifically in low-income countries, as ARM leads to longer hospital stays, greater use of antibiotics, and the overall loss of productivity (Prestinaci et. al, 2015).

In the most recent summary conducted on antibacterial agents in clinical and preclinical development by the World Health Organization in 2023, there are approximately 57 antibiotics in pipeline and of these 32 were developed to address the updated 2024 WHO's bacterial priority pathogen list. However, only four were found to be effective against the pathogens rated the most critical pathogens for their accelerated resistance tendencies (World Health Organization, 2023). In comparison to a non-communicable disease such as diabetes with over 100 different drugs in development, antibiotics are regarded by pharmaceutical companies as poor investment (Billingsley & Doskicz, 2022).

The estimated rate of failure in creating antibiotics is approximately 95%. As a result of antimicrobial resistance any new antibiotics developed and approved are likely to be used in hospitals and healthcare settings as a last resort which yielded low sales and marginal profit (Årdal et al., 2019). These aspects limit economic incentives for research and development and point to antibiotic alternatives.

Antibiograms – the Missing Weapon in the Fight Against AMR

To assess both the current and future risk associated with antimicrobial resistance, multiple outlets of data need to be referenced to elicit a comprehensive platform. Antibiograms, produced at a regional or hospital level, characterize cases of bacterial infections, whether they have developed resistance, and to which antibiotic in order to guide a healthcare provider in prescribing the correct medication (Klinker et. al, 2021). Having access to antibiograms in addition to diagnostic and lab data is necessary to define current risk of resistance. However, due to the extensive laboratory testing and skilled personnel required to maintain and develop an antibiogram, even areas and health systems with significant resources often lack a current or a robust program to produce an antibiogram.

Antibiograms can come in several formats and styles, with a sample appearing in Figure 5.

Pathogen (*n*)	FEP	TZP	MEM	C/T	I/R
E. coli (6095)	87	95	99	98	99
Klebsiella spp. (4097)	91	89	98	95	99
P. aeruginosa (3649)	78	78	77	95	93

Figure 5: Traditional antibiogram listing the antibiotics used to treat pathogen and its (isolates).

HSR.*health*'s Approach to AMR

HSR.*health* develops GeoAI-based solutions to predict health risks and their causative factors. Mapping the current state of AMR involves tracking the number of infections, hospitalizations, mortality, and morbidity due to antibiotic resistant bacterial pathogen within a region and for a given time period. In addition, environmental data on heat levels, livestock antibiotic use, and sanitation infrastructure are important in assessing risk level by area.

Our GeoMD Platform can display this information as well as create trends to predict the growth of antimicrobial resistance over time by pathogen and by area. Data and risk levels will be displayed in both a tabular antibiogram, as well as a map visualization providing an easy to read, graphical representation of resistance. This solution will aid medication prescribing, strategic planning, and preventative actions to mitigate the overall burden associated with antimicrobial resistance.

Are we Entering a Post-Antibiotic World?

As antibiotic resistance infections become more common, it is crucial to come up with solutions that tackle the various environmental and human made factors contributing to resistance. With HSR.*health*'s GeoAI-based solutions, we can support health systems, the public health community, and the pharmaceutical industry fully recognize the extent of the problem as well as promote efforts to lessen the global burden of disease from antimicrobial resistance. The alternative represents the loss of the tremendous public health gains made due to the discovery of antibiotics in the early 1900s just a little over a century later.

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