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# Antimicrobial Resistance: An Overview of Epidemiology, Transmission, Drivers of Resistance, Advanced Intervention and Preventive Measurements

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## ABSTRACT

Antimicrobial resistance (AMR) is a mechanism of resistance that interconnects with environment, pollution and water influencing a global threat to human health with predicted high mortality rate which will be far higher than other ongoing challenging diseases. AMR led the drugs to lose it effectiveness on microbes through resistance mechanism and made the disease more worsen to recover. This article on AMR aims to provide an overview by compiling current knowledge on this ongoing life threaten global concern and to improve our understanding by focusing on the drivers of resistance, transmission, one health perspective on AMR, its prevention and advanced interventional strategies.

**Keywords:** Antimicrobial resistance, transmission, epidemiology, one health prospective, advanced strategies and preventive measurements

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## Introduction

Antimicrobial resistance is one of the most influential global threats of 21 century to human health that has now become a political concern and discussed at social gatherings and G7 meetings as well. AMR is predicted to increase the mortality rate to about 10 million annually by 2050 if it remains untreatable. Antimicrobial resistance is triggered by bacteria, fungi and parasites when they withstand antimicrobial treatment, rendering cure ineffective and continue to cause infection [1]. Many studies considered that AMR is new due to its broad media attention but hoary showed resistance gene early in glacial bacteria over 2000 years ago and bacteria from permafrost over 30,000 years ago has antimicrobial resistance. It indicates that antimicrobial resistance came before this world discovered any antimicrobial drugs [2].

## Epidemiology

The WHO declared AMR as the global life threat. In 2019 AMR led to 4.9 million deaths in low-income countries. Without the implementation of any controlled measure, the death rate will dramatically climb to predicted mortality rate which is more higher than the death rate caused by tuberculosis with a number of 1.5 million, malaria with a rate of 643,000, and even higher than death number with 864,000 caused by HIV/AIDS [3].

## Mechanism of resistance

Microorganisms trigger resistance against antimicrobial agents through intrinsic and extrinsic pathways. Intrinsic resistance is acquired naturally by many microorganisms that don't require any preexisting interaction with drugs. Extrinsic resistance is acquired through external factors including horizontal gene transfer and chromosomal mutation that requires prior exposure [4].

## Transmission

Antimicrobial resistance spread through a massive network of transmission including human gut, environment and pollution. Human microbes contain 3.3 million genes which include 150 more genes than human genome itself. Due to close contact of microbes in gut, many events of HGT recorded that becoming the major cause of resistance in organisms [5]. Soil and water are considered as the most primitive residence of resistant genes which spread through contact between humans and food. Resistant genes are also discovered in most unforeseen areas with no population that show the ancient behavior of resistance in microbes [6]. Aquatic systems including hospital, wastewater and pharmaceutical waste act as major reservoir of resistance that promotes horizontal gene transfer and boosts the diversity of resistant genes in environment [7]. Air polluted by pharmaceutical discharge that contains high level of ARGs, antibiotics, biocides and metal provide resistance across environment and bacteria [8].

## One health Perspective Framework

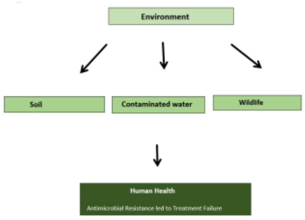


**Fig.1: One health perspective [9]**

## Drivers of AMR

### Antibiotic Misuse

Initially, antibiotics were used as miracle cure against infections that enhance life expectancy. Sir Alexander Fleming initiated this global era by decreasing the mortality rate. Later, due to overuse and misuse of antibiotic drugs in human environment it lost its effectiveness and contribute to the global challenge of antimicrobial resistance [10].

### Extracellular vesicles

Microbes (Bacteria, Fungi and parasite) release tiny bubble-like structure called extra cellular vesicles that help microbes to share resistance trait to survive against drugs. EVs share resistance traits through outer membrane vesicles(OMV), explosive outer membrane vesicle(EOMV) and cytoplasmic membrane vesicles(CMV) [11].

### Horizontal Gene transfer

Horizontal gene transfer is a major factor that leads to resistance from one bacterium to entire bacterial community through the process of conjugation, transduction and natural transformation. Process of Conjugation requires interaction of two bacteria for gene sharing. Transduction mechanism involves accidental gene transfer to cell during bacteriophage interaction. In natural transformation, bacteria use their natural competence ability to acquire resistance [12].

## Challenges

Data gap in low middle income countries due to poor infrastructure of laboratories, low health surveillance, poor diagnosis makes it challenging for researchers to understand the prevalence of resistance [13]. Reliable forecasting is difficult due to versatile nature of microbe's resistance which is making future prediction for control intervention complicated [14].

## Advanced Intervention

### Nano Antibodies

Nano antibodies are about 10-100 nm small silver or gold based antibiotic link nanoparticles. Nano particles provide protection against microbes by attacking their membrane and their biofilm that blocks the communication of microbes and enhances drug effectiveness [15].

### CRISPR-Cs9

CRISPR based tools are used to detect the AMR gene in clinical samples for fast diagnosis and to protect against infections. In case of AMR this technique is used to cut the plasmid that carry many resistant genes and prevent the horizontal gene transfer into many bacteria. This breaks the cycle of Resistance [16].

### Antimicrobial peptide

Antimicrobial peptide are small molecule that are part of our innate immunity which are stimulated by white blood cell and epithelial cells. AMPs act as antibodies against microbe by disturbing their membrane and biofilms and regulate the mechanism of chemotaxis and boost our immunity[17].

### Vaccines

Vaccination is a procedure of controlling infection that lead to unnecessary antibiotic consumption. High consumption of antibiotic enhance the chance of microbes resistance. These vaccination can lower the resistance by reducing antibiotic intake. The vaccination campaign program by WGS for awareness against typhoid covered almost millions of children and prevent the resistance by vaccination that lower the chance of antibiotics [18].

## Prevention

The WHO builds a five-objective plan for the prevention of AMR along 178 countries but only 25% of countries are adopting the objectives that include:

- Awareness strategies
- Extending surveillance
- Dropping the infection rate
- Controlling antibiotic use
- Discovering new medicine

For low Middle-Income Countries by working on only WASH (Water, Sanitation and Hygiene) and vaccine strategies can reduced 337,000 deaths annually [19].

**Conclusion**

AMR is not a threat only it is recognized as the current global crisis that needs urgent global action to control its prevalence. By focusing on advanced tools, one health perspective along WHO 5 objective strategic plans, we can halt the resistance. The future treatment plan on AMR needs a global commitment into action to enhance its effectiveness.

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