Antibiotic Resistance: The Silent Killer & It’s Possible Remedies

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Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria change in response to the use of these medicines. Bacteria, not humans or animals, become antibiotic-resistant. These bacteria may infect humans and animals, and the infections they cause are harder to treat than those caused by non-resistant bacteria. Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality. The world urgently needs to change the way it prescribes and uses antibiotics. Even if new medicines are developed, without behavior change, antibiotic resistance will remain a major threat. Behavior changes must also include actions to reduce the spread of infections through vaccination, hand washing, practicing safer sex, and good food hygiene. Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective. Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-used by the public. Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

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INTRODUCTION:
Serological milestones:\cite{1,2}
Adverse drug event: Harms resulting from the use of medication and include allergic reactions, side effects, overmedication, and medication errors.
Amplification: An increase in the number of resistant germs in a person, animal, or the environment.
Animal husbandry: The practice of breeding and caring for farm animals.
Antibiotic stewardship: Improving the way antibiotics are prescribed and used.
Antibiotic susceptibility testing: A way to describe how sensitive germs are to particular antibiotics. An antibiotic can stop the growth of or kill a susceptible germ.
Antibiotic resistance: When germs develop the ability to defeat the drugs designed to kill them. That means the germs are not killed and continue to grow.
Antibodies: Naturally occurring proteins produced by the body in response to invading germs.
Antimicrobials: Drugs that treat infections by killing or slowing the growth of germs causing infection.
\begin{itemize}
    \item Antibiotics: Drugs that treat infections caused by bacteria (e.g., strep throat, foodborne illness).
    \item Antifungals: Drugs that treat infections caused by fungi (e.g., athlete’s foot, yeast infections).
\end{itemize}
Beta-lactam antibiotics: A class of antibiotics that have been critically important to modern medicine. They kill bacteria by binding to proteins and thereby stop the germ from creating or properly forming a cell wall.
Biosecurity: Practices intended to reduce the risk of diseases being carried onto the farm, spread to the animals across the farm, and transmitted off the farm. This includes the property the animals are housed on and in, the people who interact with the animals, and the equipment and vehicles that come onto the property.
Carbapenems: A class of beta-lactam antibiotics active against many Gram-positive and Gram-negative organisms, usually reserved for treatment of the most resistant infections.
Carbapenemase: An enzyme produced by certain bacteria, including some Enterobacteriaceae, that makes carbapenems, cephalosporins and penicillins ineffective.
Cephalosporins: Antibiotics that kill bacteria by preventing the cell wall from properly forming.
Colonization: The presence of germs on or in the body without symptoms of an infection.
First-line antibiotics: Antibiotics recommended as the first treatment for infections because they maximize the chance of curing the infection while minimizing the chance of experiencing harms from antibiotics, including antibiotic resistance and side effects.
Germ: Very small living organisms including bacteria, fungi, parasites, and viruses. In this report, CDC uses “germ” to describe bacteria and fungi, including pathogens.
Gram-negative bacteria: A group of germs, characterized by having relatively thin cell walls, that are increasingly resistant to many available antibiotics. They often find new ways to develop resistance and can sometimes share these abilities with other bacteria, increasing the spread of resistance. Examples of Gram-negative bacteria include Acinetobacter species, P. aeruginosa, and E. coli.
Gram-positive bacteria: A group of germs, characterized by having thick cell walls, that are increasingly resistant to many available antibiotics. They often find new ways to develop resistance and can sometimes share these abilities with other bacteria, increasing the spread of resistance. Examples of Gram-positive bacteria include Streptococci, Staphylococci, and Enterococci.
Healthcare-associated germ: A germ patients can get while receiving medical treatment in hospitals, outpatient clinics, nursing homes, and other facilities where people receive care.
Infection control: Preventing or stopping the spread of infections.
Isolate: Pure samples of a germ.
Medically important antibiotics: Antibiotics that are commonly needed to treat infections in people.
**Microbiome:** The community of naturally-occurring microbes that live in or on the body (for example, stomach, intestines, skin).

**Mobile genetic elements:** Genetic material that can move from germ to germ and share resistance traits. This means that some germs can share their DNA and make other germs become resistant.

**Multidrug-resistant germs:** Germs that are resistant to multiple antibiotics available for treatment.

**Non-susceptible infections:** Infections that cannot be treated effectively with certain antibiotics.

**One Health:** A collaborative, multisectoral, and trans-disciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

**Pan-resistant infections:** Infections that are caused by germs resistant to all antibiotics available for treatment.

**Pathogen:** Harmful germs that can cause infection.

**Penicillin:** Antibiotics that kill bacteria by binding to proteins and thereby stop the germ from creating or properly forming a cell wall.

**Phages (bacteriophages):** Viruses that infect and replicate within bacteria. In some cases, phages can kill bacteria.

**Resistance mechanisms:** Defence strategies that germs develop to help them survive and avoid the effects of antibiotics.

**Susceptible infections:** Infections that can be treated effectively with antibiotics.

**Toxicity:** Poisonous or harmful.

**Virulence factors:** Characteristics that help a germ cause disease.[3]

Antibiotic is a substance isolated from bacteria which is active against the bacteria but not the host. An antibiotic is a type of antimicrobial substance active against bacteria. It is the most important type of antibacterial agent for fighting bacterial infections, and antibiotic medications are widely used in the treatment and prevention of such infections. They may either kill or inhibit the growth of bacteria. A limited number of antibiotics also possess antiprotozoal activity. Antibiotics are not effective against viruses such as the common cold or influenza; drugs which inhibit viruses are termed antiviral drugs or antivirals rather than antibiotics. Sometimes, the term antibiotic—literally "opposing life", from the Greek roots ἀντί anti, "against" and βίος bios, "life"—is broadly used to refer to any substance used against microbes, but in the usual medical usage, antibiotics (such as penicillin) are those produced naturally (by one microorganism fighting another), whereas nonantibiotic antibacterials (such as sulfonamides and antiseptics) are fully synthetic. However, both classes have the same goal of killing or preventing the growth of microorganisms, and both are included in antimicrobial chemotherapy. "Antibacterials" include antiseptic drugs, antibacterial soaps, and chemical disinfectants, whereas antibiotics are an important class of antibacterials used more specifically in medicine and sometimes in livestock feed.
Antimicrobial resistance (AMR or AR) is the ability of a pathogenic microbe to develop a resistance to the effects of an antimicrobial medication. The term antibiotic resistance (AR or ABR) is a subset of AMR, as it applies to bacteria that become resistant to antibiotics. Resistant microbes are more difficult to treat, requiring higher doses, or alternative medications which may prove more toxic. These approaches may also be more expensive. Microbes resistant to multiple antimicrobials are called multidrug resistant (MDR). Antibiotic resistance has become a global threat, and with Antibiotic Awareness Week, it is important to understand the series of events that have led the world to this predicament. World Antimicrobial Awareness Week [18-24 November 2020; Antibiotics: handle with care] (WAAW) aims to increase awareness of global antimicrobial resistance (AMR) and to encourage best practices among the general public, health workers and policy makers to avoid the further emergence and spread of drug-resistant infections. Originally touted as a miracle discovery, we are seeing that there can be too much of a good thing. The use of antibiotics has saved millions of lives, but its pervasive use to treat any infection, whether serious, minor, or even viral has led to the increase in antibiotic resistance. Antibiotics strictly target bacteria, but it is sometimes difficult to differentiate between viral and bacterial infections without costly tests. It is often less time-consuming and more cost effective to proactively prescribe antibiotics, rather than take precautions and prescribe only the correct treatment. Another issue with antibiotics is the inability to monitor patient intake. Antibiotic dosages are designed to eradicate entire populations of the pathogens.\(^4\)

When antibiotics are not taken for the entire prescribed course, pathogenic bacteria can adapt to the presence of low dose antibiotics, and eventually form a population that is completely resistant to the antibiotic regardless of the dosage. Antibiotic usage is also not exclusive to humans. Every day, antibiotics are used to treat livestock and fish to prevent infections. Similar to overuse in humans, uncontrolled use of antibiotics creates a reservoir of bacteria that could become resistant, thus rendering the antibiotic useless. As a result of cities becoming more densely populated, people are exposed to more pathogens all the time. Hospitals and clinics are seeing more and more patients with infections, and it is not always possible to curb the spread of a pathogen in a population. Identification, isolation or treatment of all infectious diseases are not often feasible, resulting in the addition of more pathogens to the local community. Coupled with lack of hygiene and poor sanitation, urban centers become and ideal breeding ground for bacteria.\(^5\)
Terms: On CDC’s website, antibiotic resistance is also referred to as antimicrobial resistance or drug resistance. Antibiotic resistance has the potential to affect people at any stage of life, as well as the healthcare. Each year in the U.S., at least 2.8 million people are infected with antibiotic-resistant bacteria or fungi, and more than 35,000 people die as a result. No one can completely avoid the risk of resistant infections, but some people are at greater risk than others (for example, people with chronic illnesses). If antibiotics lose their effectiveness, then we lose the ability to treat infections and control public health threats. Many medical advances are dependent on the ability to fight infections using antibiotics, including joint replacements, organ transplants, cancer therapy, and treatment of chronic diseases like diabetes, asthma, and rheumatoid arthritis.[6]

Brief History of Resistance and Antibiotics: CDC is leading efforts to combat antibiotic resistance through the Antibiotic Resistance Solutions Initiative. Penicillin, the first commercialized antibiotic, was discovered in 1928 by Alexander Fleming. Ever since, there has been discovery and acknowledgement of resistance alongside the discovery of new antibiotics. In fact, germs will always look for ways to survive and resist new drugs. More and more, germs are sharing their resistance with one another, making it harder for us to keep up.[7]

Select Germs Showing Resistance Over Time

<table>
<thead>
<tr>
<th>Antibiotic Approved or Released</th>
<th>Year Released</th>
<th>Resistant Germ Identified Year Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>1941</td>
<td>Penicillin-resistant Staphylococcus aureus 1942</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Penicillin-resistant S. pneumoniae 1967</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Penicillinase-producing Neisseria gonorrhoeae 1976</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1958</td>
<td>Plasmid-mediated vancomycin resistant Enterococcus faecium 1988</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin-resistant Staphylococcus aureus 2002</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>1959</td>
<td>Amphotericin B-resistant Candida auris 2016</td>
</tr>
<tr>
<td>Methicillin</td>
<td>1960</td>
<td>Methicillin-resistant Staphylococcus aureus 1960</td>
</tr>
<tr>
<td>Extended-spectrum cephalosporins</td>
<td>1980</td>
<td>Extended-spectrum beta-lactamase-producing Escherichia coli 1983</td>
</tr>
<tr>
<td>(Cefotaxime)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>1980</td>
<td>Azithromycin-resistant Neisseria gonorrhoeae 2011</td>
</tr>
<tr>
<td>Imipenem</td>
<td>1985</td>
<td>Klebsiella pneumoniae carbapenemase (KPC)-producing Klebsiella pneumoniae 1996</td>
</tr>
</tbody>
</table>
What is antibiotic resistance: Antibiotic resistance happens when the germs no longer respond to the antibiotics designed to kill them. That means the germs are not killed and continue to grow. It does not mean our body is resistant to antibiotics. Bacteria and fungi are constantly finding new ways to avoid the effects of the antibiotics used to treat the infections they cause. Infections caused by antibiotic-resistant germs are difficult, and sometimes impossible, to treat. In many cases, antibiotic-resistant infections require extended hospital stays, additional follow-up doctor visits, and costly and toxic alternatives.[8]

Why should we care about antibiotic resistance? Antibiotic resistance can affect any person, at any stage of life. People receiving health care or those with weakened immune systems are often at higher risk for getting an infection. Antibiotic resistance jeopardizes advancements in modern health care that we have come to rely on, such as joint replacements, organ transplants, and cancer therapy. These procedures have a significant risk of infection, and patients won’t be able to receive them if effective antibiotics are not available. Aside from healthcare, antibiotic resistance also impacts veterinary and agriculture industries.

How to Use Antibiotics:
Steps you can take to use antibiotics appropriately. Anytime antibiotics are used, they can contribute to antibiotic resistance. This is because increases in antibiotic resistance are driven by a combination of germs exposed to antibiotics, and the spread of those germs and their mechanisms of resistance. When antibiotics are needed, the benefits usually outweigh the risks of antibiotic resistance. When antibiotics are needed, the benefits usually outweigh the risks of antibiotic resistance. However, too many antibiotics are being used unnecessarily and misused, which threatens the usefulness of these important drugs.[9]

For example, too many antibiotics are being prescribed unnecessarily to humans in the United States. CDC estimates about 47 million antibiotic courses are prescribed for infections that don’t need
antibiotics, like for colds and the flu, in U.S. doctors’ offices and emergency departments each year. That’s about 30% of all antibiotics prescribed in these settings. Everyone has a role to play in improving antibiotic use. Appropriate antibiotic use helps fight antibiotic resistance and ensures these lifesaving drugs will be available for future generations.[10]

**Prevention and control:** Antibiotic resistance is accelerated by the misuse and overuse of antibiotics, as well as poor infection prevention and control. Steps can be taken at all levels of society to reduce the impact and limit the spread of resistance.[11]

**Individuals**
To prevent and control the spread of antibiotic resistance, individuals can:
- Only use antibiotics when prescribed by a certified health professional.
- Never demand antibiotics if your health worker says you don’t need them.
- Always follow your health worker’s advice when using antibiotics.
- Never share or use leftover antibiotics.
- Prevent infections by regularly washing hands, preparing food hygienically, avoiding close contact with sick people, practising safer sex, and keeping vaccinations up to date.
- Prepare food hygienically, following the WHO Five Keys to Safer Food (keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials) and choose foods that have been produced without the use of antibiotics for growth promotion or disease prevention in healthy animals.[12]

![Flowchart of antibiotic resistance](Image)

**Policy makers**
To prevent and control the spread of antibiotic resistance, policy makers can:
- Ensure a robust national action plan to tackle antibiotic resistance is in place.
• Improve surveillance of antibiotic-resistant infections.
• Strengthen policies, programmes, and implementation of infection prevention and control measures.
• Regulate and promote the appropriate use and disposal of quality medicines.
• Make information available on the impact of antibiotic resistance.\[13\]

Health professionals
To prevent and control the spread of antibiotic resistance, health professionals can:
• Prevent infections by ensuring your hands, instruments, and environment are clean.
• Only prescribe and dispense antibiotics when they are needed, according to current guidelines.
• Report antibiotic-resistant infections to surveillance teams.
• Talk to your patients about how to take antibiotics correctly, antibiotic resistance and the dangers of misuse.
• Talk to your patients about preventing infections (for example, vaccination, hand washing, safer sex, and covering nose and mouth when sneezing).\[14\]

Healthcare industry
To prevent and control the spread of antibiotic resistance, the healthcare industry can:
• Invest in research and development of new antibiotics, vaccines, diagnostics and other tools.

Agriculture sector
To prevent and control the spread of antibiotic resistance, the agriculture sector can:
• Only give antibiotics to animals under veterinary supervision.
• Not use antibiotics for growth promotion or to prevent diseases in healthy animals.
• Vaccinate animals to reduce the need for antibiotics and use alternatives to antibiotics when available.
• Promote and apply good practices at all steps of production and processing of foods from animal and plant sources.
• Improve biosecurity on farms and prevent infections through improved hygiene and animal welfare.

Recent developments: While there are some new antibiotics in development, none of them are expected to be effective against the most dangerous forms of antibiotic-resistant bacteria. Given the ease and frequency with which people now travel, antibiotic resistance is a global problem, requiring efforts from all nations and many sectors.\[15\]

Impact: When infections can no longer be treated by first-line antibiotics, more expensive medicines must be used. A longer duration of illness and treatment, often in hospitals, increases health care costs as well as the economic burden on families and societies. Antibiotic resistance is putting the achievements of modern medicine at risk. Organ transplantations, chemotherapy and surgeries such as caesarean sections become much more dangerous without effective antibiotics for the prevention and treatment of infections.\[16\]

WHO response: Tackling antibiotic resistance is a high priority for WHO. A global action plan on antimicrobial resistance, including antibiotic resistance, was endorsed at the World Health Assembly in May 2015. The global action plan aims to ensure prevention and treatment of infectious diseases with safe and effective medicines.

The “Global action plan on antimicrobial resistance” has 5 strategic objectives:
• To improve awareness and understanding of antimicrobial resistance.
• To strengthen surveillance and research.
• To reduce the incidence of infection.
• To optimize the use of antimicrobial medicines.
• To ensure sustainable investment in countering antimicrobial resistance.

A political declaration endorsed by Heads of State at the United Nations General Assembly in New York in September 2016 signalled the world’s commitment to taking a broad, coordinated approach to address the root causes of antimicrobial resistance across multiple sectors, especially human health, animal health and agriculture. WHO is supporting Member States to develop national action plans on antimicrobial resistance, based on the global action plan. WHO has been leading multiple initiatives to address antimicrobial resistance:
World Antimicrobial Awareness Week: Held annually since 2015, WAAW is a global campaign that aims to increase awareness of antimicrobial resistance worldwide and to encourage best practices among the general public, health workers and policy makers to avoid the further emergence and spread of drug-resistant infections. Antimicrobials are critical tools in helping to fight diseases in humans, animals and plants. They include antibiotics, antivirals, antifungals and antiprotozoa. WAAW takes place every year from 18 to 24 November. The slogan has previously been, “Antibiotics: Handle with Care” but changed to “Antimicrobials: Handle with Care” in 2020 to reflect the broadening scope of drug resistant infections.[17]

The Global Antimicrobial Resistance Surveillance System (GLASS): The WHO-supported system supports a standardized approach to the collection, analysis and sharing of data related to antimicrobial resistance at a global level to inform decision-making, drive local, national and regional action.[18]

Global Antibiotic Research and Development Partnership (GARDP): A joint initiative of WHO and Drugs for Neglected Diseases initiative (DNDi), GARDP encourages research and development through public-private partnerships. By 2023, the partnership aims to develop and deliver up to four new treatments, through improvement of existing antibiotics and acceleration of the entry of new antibiotic drugs.[19]

Interagency Coordination Group on Antimicrobial Resistance (IACG): The United Nations Secretary-General has established IACG to improve coordination between international organizations and to ensure effective global action against this threat to health security. The IACG is co-chaired by the UN Deputy Secretary-General and the Director General of WHO and comprises high level representatives of relevant UN agencies, other international organizations, and individual experts across different sectors.[20]

**DRUG-RESISTANT: CAMPYLOBACTER**


**ESBL (Extended spectrum beta-lactamases)-PRODUCING: ENTEROBACTERIACEAE** [Gram negative bacteria.]


DRUG-RESISTANT: NONTYPHOIDAL SALMONELLA [Gram negative bacteria. Species: S. typhi]


METHICILLIN-RESISTANT: STAPHYLOCOCCUS AUREUS [Gram positive bacteria. Species: S. aureus]

DRUG-RESISTANT: STREPTOCOCCUS PNEUMONIAE [Gram positive bacteria. Species: S.

**DRUG-RESISTANT: TUBERCULOSIS** [Gram positive bacteria. Species: *Mycobacterium tuberculosis*]

**Figure-6: Bacteria and antibiotic resistance**

**Conclusion:** Bacteria, not humans or animals, become antibiotic-resistant. These bacteria may infect humans and animals, and the infections they cause are harder to treat than those caused by non-resistant bacteria. Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality. Antibiotic resistance is when germs (bacteria, fungi) develop the ability to defeat the antibiotics designed to kill them. It does not mean your body is resistant to antibiotics. Increases in antibiotic resistance are driven by a combination of germs exposed to antibiotics, and the spread of those germs and their mechanisms of resistance. This naturally occurring process is accelerated when antibiotics are constantly present in the environment or in the germs’ hosts (e.g., patients). This is why antibiotics for medical care, animal health, and agriculture should be used only when necessary and only for appropriate durations. Patients should always be promptly treated with antibiotics when the drugs are needed for infections and to prevent sepsis.

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