Antibiotic Resistance

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Microbiology
Antimicrobial resistance (AMR) is the ability of microorganisms that cause disease to withstand attack by antimicrobial medicines.

The ability of pathogens that works against the antibiotics, is termed **Antibiotic Resistance**.

Antimicrobials like antibiotics, antivirals, and others are losing their effectiveness because of antimicrobial resistance.

Up to half of antibiotic prescriptions is unnecessary or inappropriate.

If patients have a sore throat, the physician should take a throat culture test. If the test results indicate that a bacterial infection is present, then antibiotics should be prescribed to treat the infection. There is no sure way of knowing whether a cold or sickness is a bacterial infection without a test.
# Evolution of Antibiotic Resistance

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Year Deployed</th>
<th>Resistance Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulphonamides</td>
<td>1930s</td>
<td>1940s</td>
</tr>
<tr>
<td>Penicillin</td>
<td>1943</td>
<td>1946</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>1943</td>
<td>1959</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>1947</td>
<td>1959</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>1948</td>
<td>1953</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1952</td>
<td>1988</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1956</td>
<td>1988</td>
</tr>
<tr>
<td>Methicillin</td>
<td>1960</td>
<td>1961</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>1961</td>
<td>1973</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>1960s</td>
<td>Late 1960s</td>
</tr>
</tbody>
</table>
Common causes

1. Overuse

Physicians

Incorrect diagnosis and Prescribing Antibiotics for Viral (Seasonal Flu) infections, 2 or more antibiotics together, unnecessary long courses of antibiotics

Kills Resident Bacterias (Normal flora)

Some are survived

Antibiotic resistant genes

Passing of these genes to Pathogenic bacterias

Antibiotic resistance
Common causes

2. Misuse

Patients

Not finishing full course of antibiotics

Misuse

Leaving 1 or 2 doses

Some bacteria not killed

Resistance developed for future antibiotic treatment
Common causes

3 antibiotics

Antibiotics

Available as OTC medicines

Inappropriate use

Overuse or Misuse

Antibiotic resistance
Common causes

4. Healthcare Workers

Hospital

Healthcare Workers

Not following infection control protocols

Resistance transferred by bacteria swapping genes
Common causes

5. Hospitalized Patients

Hospital

Patients with compromised health

Exposed to Pathogenic organisms

Increased usage of different antibiotics

Rapid development of Resistance
6. Animal Feed

Animal feed

Mixed with antibiotics to prevent infections and to promote growth

Resistant organisms in animals

Spread to Human
Common causes

7. Antibiotics in food and water

Antibiotics found in beef cattle, pigs and poultry

Drainage with antibiotics contaminates groundwater

Same antibiotics mixed with municipal water systems

we get antibiotics in our food and drinking water

promote bacterial resistance.
Common causes

8. Antibiotic resistance in genetically modified crops

Antibiotic-resistance genes

Inserted into the plant in early stages of development to detect specific genes of interest e.g. herbicide-resistant genes or insecticidal toxin genes

They are not removed from the final product

Antibiotic-resistance genes could be acquired by microbes in the environment
Types of Resistance

1. Natural or inherent resistance
2. Mutational resistance
3. Acquired (Extra chromosomal) resistance

Natural or inherent resistance

Bacteria may be inherently resistant to an antibiotic.

Examples:
1. An organism lacks the target of the antibiotic molecule
   Amino glycosides are resistant in strict anaerobes due to the absence of an adequate transporter which leads to impermeability of drug
2. The cell wall of gram-negative bacteria, is covered with an outer membrane that inhibits the entry of the antibiotic.
   3. E.Coli contains AcrE as Multidrug efflux system and P.aeruginosa contains MexB.
   4. Klebsiella contains AmpC cephalosporinase for the inactivation of antibiotic.
Types of Resistance

Mutational resistance

1. Target site modification (Mutation in rDNA genes (rpsL) Streptomycin resistance) and change in PBPs (penicillin binding proteins) β-lactam resistance.

2. Reduced permeability or uptake

3. Metabolic by-pass (overproduction of DHF (dihydrofolate) reductase or thi- mutants in S. aureus trimethoprim resistance)

4. Derepression of multidrug efflux systems
Types of Resistance

Acquired (Extrachromosomal) resistance

1. Drug inactivation (Enzymes like β-lactamases, aminoglycoside-modifying enzymes and chloramphenicol acetyltransferase inactivate the antibiotics.)

2. Efflux system (Tetracycline is pumped out by efflux pumps)

3. Target site modification (Erm methylases, methylates the 23S component of the 50S ribosomal subunit which leads to resistance)

4. Metabolic by-pass (DHF reductase enzyme becomes resistant and causes trimethoprim resistance).
Mechanisms of Bacterial Resistance

1. Enzymatic degradation of the drug
2. Modification of the drug's target
3. Reduced permeability of the drug
4. Efflux pumping of Antibiotics
5. Modification of Target ribosomes
6. Alteration of Pathway
Mechanisms of Bacterial Resistance

Enzymatic degradation of the drug

Beta lactamase (Penicillinase)

Breaks Beta lactam ring of penicillins and cephalosporins

Inactivation of drugs

Resistance to Beta lactam antibiotics
Mechanisms of Bacterial Resistance

Modification of the drug's target

Bacteria (MRSA)

Induces mutation of gene coding for target proteins

Changing of the structure of target

Resistance

Methicillin Resistant Staphylococcus Aureus (MRSA) is a very dangerous pathogen and it develops the resistance by this mechanism. It is resistant to antibiotics like Beta lactams, Carbapenems, etc.
Mechanisms of Bacterial Resistance

**Reduced membrane permeability**

- **Bacteria**
- Reduces the production of Porin and other membrane channel protein
- Reduction of the permeability of membrane
- Drugs (Antibiotics) can’t pass through membrane to kill bacteria
- Resistance

Bacterias develop resistance against Chloramphenicol by reduced permeability of bacterial cell membrane.
Mechanisms of Bacterial Resistance

Efflux pumping of Antibiotics

Bacteria

Produces specialised membrane proteins which act as pumps

Pump out antibiotics

Reduction of antibiotic concentration

Resistance

Efflux pumps are active against the antibiotics like Tetracyclines (Greatest activity), Beta lactam antibiotics and Flouroquinolones.
Mechanisms of Bacterial Resistance

Modification of Target ribosomes

Bacteria

Modifies ribosomal RNA

Inhibition of therapeutic activity of antibiotic

Resistance

Bacteria develop resistance against Amino glycosides (Streptomycin) by the mutation of protein in 30S ribosomal subunit.
Mechanisms of Bacterial Resistance

Alteration of Pathway

Bacteria

Alternative metabolic pathway which can’t be inhibited by antibiotics

Inhibition of therapeutic activity of antibiotics

Resistance

Bacterias develop resistance against Sulfonamides (Trimethoprim) by this mechanism.
Consequences of Antibiotic Resistance

In a recent study, 25% of bacterial pneumonia cases were shown to be resistant to penicillin, and an additional 25% of cases were resistant to more than one antibiotic.

Drug-resistant bacteria is responsible for about 25,000 human deaths annually in Europe.

Increased costs associated with prolonged illnesses, including expenses for additional tests, treatments and hospitalization, and indirect costs, such as lost income.

Investment in antibiotic development is discouraged, due to…

1. The development of resistance
2. The pressure to reduce the use of antimicrobials
3. The weak market incentives
4. Increasing difficulty and cost to develop new effective antibiotics.
Possible Solutions for Antibiotic Resistance

Stop unnecessary antibiotic prescriptions. □
Finish antibiotic prescriptions. □
Use the right antibiotic in an infectious situation as determined by antibiotic sensitivity testing. □
Use antibiotics in rotation. □
Use combination of antibiotics if necessary. □
Promote Vaccine recommendations. □
Implement *infection control measures*, such as hand washing, isolation precautions, and immunization. □
Develop new effective antimicrobials or alternatives for treatment. □
Cooperate with international partners to contain the risks of AMR. □
Improve monitoring and surveillance of antibiotic use in humans and animals. □
Promote research and innovation. □
Improve communication, education and training. □
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