How Bacteria Become Resistant to Antibiotics

Antibiotic resistance is an acquired defense mechanism by which bacteria are no longer susceptible to an antibiotic. When bacteria develop resistance to an antibiotic, the effectiveness of that antibiotic in preventing or curing disease decreases. The use of antibiotics in human medicine, as well as food animals, has increased the prevalence of antibiotic resistance among all bacteria, thus increasing the incidence of bacterial infections caused by resistant strains.

How do antibiotics kill bacteria?

To understand antibiotic resistance, it is important to know how antibiotics work. Antibiotics kill or inhibit the growth of bacteria through one of five different mechanisms (Figure 1).

1. **Disrupt bacterial cell-wall integrity.** Maintaining structure and integrity of bacterial cell walls is vital to their survival; some antibiotics can attack the cell wall and kill the bacteria [used by antibiotics such as the penicillins, their derivatives (for example, cephalosporins) and others].
2. **Alter the cell membrane.** The cell membrane acts as a barrier that maintains the environment inside the cell; some antibiotics cause membranes to leak, thereby destroying the cell (used by antibiotics such as ionophores and topical products such as polymixin B).
3. **Inhibit bacterial protein synthesis.** Some antibiotics, once inside the bacteria, interfere with the synthesis of essential cellular proteins, eventually killing off the bacteria (used by antibiotics such as tetracyclines and others).
4. **Inhibit bacterial DNA and RNA synthesis.** DNA and RNA provide the genetic code that results in protein synthesis by the bacteria. Without the DNA or RNA, bacterium cannot make proteins necessary to proliferate (used by antibiotics such as fluoroquinolones and others).
5. **Disrupt metabolic pathways.** Certain antibiotics enter the cell and obstruct key metabolic pathways needed by the bacteria to survive (used by antibiotics such as sulfonamides and others).

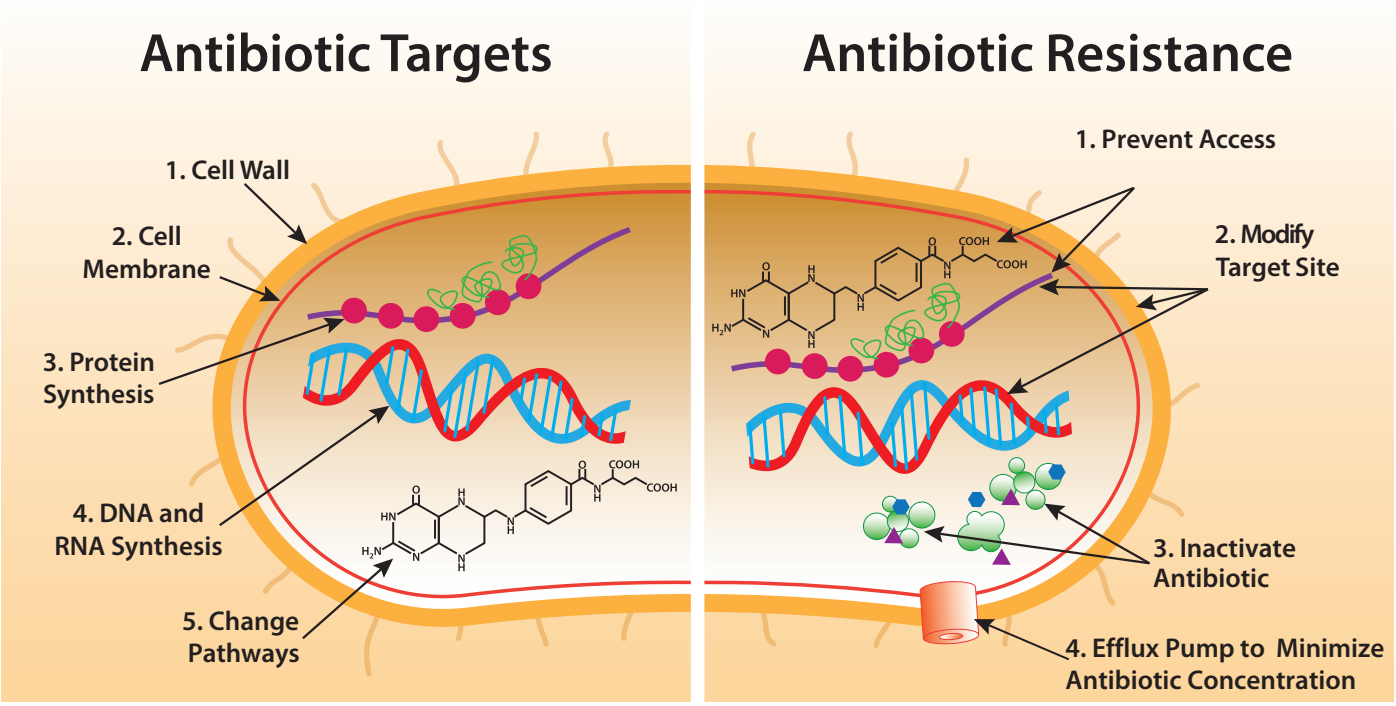

Figure 1. Antibiotic targets and mechanisms for acquiring antibiotic resistance.

How do bacteria survive and ultimately become resistant?

The four predominant mechanisms of acquired antibiotic resistance in bacteria (Figure 1):

1. **Prevent access.** Some bacteria develop resistance by altering their cell wall to prevent the antibiotic from entering the bacteria.
2. **Modify target site.** Some bacteria develop resistance to antibiotics by changing the shape or structure of the binding site for the antibiotic within the bacteria. Because the antibiotic is no longer able to bind with it, the antibiotic is rendered ineffective.
3. **Inactivate antibiotic.** This usually involves the production of an enzyme or compound by the bacteria that inactivates the antibiotic.
4. **Minimize antibiotic concentration.** Antibiotics must accumulate in bacteria cells at concentrations high enough to kill or inhibit the growth of the bacteria. Some bacteria are able to literally "pump" the antibiotic out of the cell, decreasing the concentration and effectiveness of the antibiotic.

If bacteria is not sensitive to an antibiotic, does that mean it has acquired resistance?

Not necessarily, because some bacteria have natural structural or other characteristics that may allow them to tolerate a particular antibiotic or class of antibiotics. This innate ability to resist a particular antimicrobial agent is called natural or intrinsic resistance. In the case of intrinsic resistance, the antibiotic was never effective on those bacteria as opposed to acquired resistance where the antibiotic previously killed or inhibited the bacteria, but no longer does. We do not have control over intrinsic resistance, but we can influence acquired resistance by how we use antibiotics.

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