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How do antibiotics kill bacterial cells but not human cells?

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In order to be useful in treating human infections, antibiotics must selectively target bacteria for eradication and not the cells of its human host. Indeed, modern antibiotics act either on processes that are unique to bacteria--such as the synthesis of cell walls or folic acid--or on bacterium-specific targets within processes that are common to both bacterium and human cells, including protein or DNA replication. Following are some examples.

Most bacteria produce a cell wall that is composed partly of a macromolecule called peptidoglycan, itself made up of amino sugars and short peptides. Human cells do not make or need peptidoglycan. **Penicillin**, one of the first antibiotics to be used widely, prevents the final cross-linking step, or transpeptidation, in assembly of this macromolecule. The result is a very fragile cell wall that bursts, killing the bacterium. No harm comes to the human host because penicillin does not inhibit any biochemical process that goes on within us.

Bacteria can also be selectively eradicated by targeting their metabolic pathways. **Sulfonamides**, such as sulfamethoxazole, are similar in structure to para-aminobenzoic acid, a compound critical for synthesis of folic acid. All cells require folic acid and it can diffuse easily into human cells. But the vitamin cannot enter bacterial cells and thus bacteria must make their own. The sulfa drugs such as sulfonamides inhibit a critical enzyme--dihydropteroate synthase--in this process. Once the process is stopped, the bacteria can no longer grow.

Another kind of antibiotic--**tetracycline**--also inhibits bacterial growth by stopping protein synthesis. Both bacteria and humans carry out protein synthesis on structures called ribosomes. Tetracycline can cross the membranes of bacteria and accumulate in high concentrations in the cytoplasm. Tetracycline then binds to a single site on the ribosome--the 30S (smaller) ribosomal subunit--and blocks a key RNA interaction, which shuts off the lengthening protein chain. In human cells, however, tetracycline does not accumulate in sufficient concentrations to stop protein synthesis.

Similarly, DNA replication must occur in both bacteria and human cells. The process is sufficiently different in each that antibiotics such as **ciprofloxacin**--a fluoroquinolone notable for its activity against the anthrax bacillus--can specifically target an enzyme called DNA gyrase in bacteria. This enzyme relaxes tightly wound chromosomal DNA,

thereby allowing DNA replication to proceed. But this antibiotic does not affect the DNA gyrases of humans and thus, again, bacteria die while the host remains unharmed.

Many other compounds can kill both bacterial and human cells. It is the selective action of antibiotics against bacteria that make them useful in the treatment of infections while at the same time allowing the host to live another day.