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| k | **What Doesn't Kill us Only Makes us Stronger**  What happened to antibiotics? Once considered the universal answer to infectious disease, we now know their effective life span is limited. The problem, simply, is that we "got complacent," says Barry Kreiswirth of the Public Health Research Institute, who makes a living analyzing strains of tuberculosis that resist as many as nine antibiotics.  It's not just TB. "The global increase in resistance to antibiotics, including the emergence of bacterial strains that are resistant to all available antibacterial agents, has created a public health problem of potentially crisis proportions." That's the word from the American Medical Association (AMA), which studied the issue in 1995, and seldom fulminates in such alarmist terms. The very success of antibiotics accounts for part of the resistance problem, argues Julian Davies of the University of British Columbia. The life-saving drugs have "changed the way diseases have been treated." It's not only that they are sometimes used to treat viral infections, against which they are impotent. It's also that they are used as "props" when safer methods [think of sanitation or quarantine might be preferable. The experts are sounding the alarm about antibiotic resistance because of grim new evidence:  *Resistance happens quickly*, in parallel with the use of antibiotics. An 11-year study of cancer patients at a hospital in Switzerland (see the 4/28/94 New England Journal of Medicine) found that no strains of Escherichia coli (a common intestinal bacteria that can be pathogenic) resisted any of the fluoroquinolone antibiotics between 1983 and 1990. But between 1991 and 1993, 28 percent of the strains tested were resistant to all five of them. During the study period, the percentage of patients getting antibiotics rose from 1.4 percent to 45 percent.  *It's widespread*. In Atlanta, a 1994 study of infections caused by Streptococcus pneumonia found that 25 percent of 431 patients had a bug that resisted penicillin, and that 25 percent of all cases were resistant to several antibiotics.  *It spreads quickly*: thanks in part to jet planes. Resistant tuberculosis has spread from New York City to Denver, Florida, Nevada and Paris.  *Bacteria learn from our mistakes:* Once resistance develops, all offspring of that bacterium get it. "Once the resistant strain is made, everybody who is infected with it will have that resistance problem," says Kreiswirth. And because these organisms then pick up further resistance to other drugs, he says, "All it's going to do is get worse."  *They spawn in our hospitals:* About 2 million Americans are infected in hospitals each year and more than half of these infections resist at least one antibiotic, according to Dennis Maki, a University of Wisconsin-Madison expert in hospital infections. In 1992 alone, 13,300 hospital patients were killed by drug-resistant bacteria in the United States.  Resistance is an especially vexing problem for people with impaired immune systems such as AIDS, and cancer patients, and recipients of organ transplants. About 90 percent of AIDS patients who get multiple-drug resistant TB die. Even the last-ditch antibiotics are being overwhelmed. Of particular concern is Vancomycin resistance, which is becoming fairly common in certain strains of enterococcus, a common gut bacteria. While enteroccocci generally do not cause life-threatening disease, the gene for the resistance may spread to more deadly organisms like Staphylococcus aureus. That transfer has already taken place in a lab dish and could occur elsewhere.  Any time bacteria are exposed to an antibiotic, they are under "selective pressure" that allows only resistant forms to survive and reproduce. So the basic rule in slowing the evolution of resistance is reducing the unnecessary use of antibiotics. A key problem is the routine feeding of antibiotics to farm animals: Davies notes that, by weight, half of all antibiotics are given to livestock and fish in a prophylactic attempt to prevent disease. That argument gets support from a new report by the CDC Morbidity and Mortality Weekly Report, on Multidrug-Resistant Salmonella, serotype Typhimurium. A quote from this alarming document:  *"A drug-resistant Salmonella Typhimurium subtype, associated with severe human illness, has emerged in the United States... A new emerging subtype, known as S. Typhimurium Definitive Type 104 (DT 104), characterized by multiple antimicrobial resistance, has been present in the United Kingdom since 1984... Studies in the United Kingdom showed that S. Typhimurium is present in animals (farm, wild, and pets), and that it can be transmitted from farm animals and pets to humans. Those studies also showed that eating beef, pork, or poultry products have been associated with outbreaks of disease in people... S. Typhimurium DT 104 has been detected recently in the United States, and its incidence and distribution are being actively studied to assess and address the threat to public health."*  In at least half the world, antibiotics can be sold over-the-counter, Davies adds. That's something many experts suggest should be avoided. Yet even in places where antibiotics require a physician's prescription, there's a tendency to overuse them, Davies says. One danger zone, he says, is the prophylactic use of antibiotics during surgery. "Surgeons are not infectious disease people, and while they may rightly feel that their patients are at risk if they don't use antibiotics prophylactically, whether that's really good, I don't know." Again, such widespread use is likely to foster the evolution of resistant strains. Instead of relying on antibiotics, Davies suggests that surgeons "ought to be able to set up an operating theater so it is sterile, so there is no opportunity for infection. With modern technology," He says, "That should not be out of the question."  So how do bacteria "learn" to defeat antibiotics? That's a feverishly important question in an era of mounting resistance to life-saving drugs. Unfortunately, the answers are disturbing. "Molecular biology is telling us ... what the resistance mechanisms are, although we don't know all the details," says microbiologist Julian Davies of the University of British Columbia. Most people assume that bacteria rely on mutations to gain resistance to antibiotics.  Mutations do come into play when drug manufacturers modify an existing antibiotic to overcome resistant bugs. In that case, the bacteria already possess a gene to defeat the antibiotic, and it mutates to regain mastery over the modified antibiotic. There are, however, other mechanisms for resistance:  1. In spontaneous mutation, bacterial DNA may change spontaneously, as indicated by the starburst. Drug-resistant tuberculosis arises this way  2. In a form of microbial sex called transformation, one bacterium may take up DNA from another. Penicillin-resistant gonorrhea results from transformation.  3. Most frightening, however, is resistance acquired from a small circle of DNA called a plasmid. Plasmids can flit between bacteria of various types -- they generally must be touching -- and carry multiple resistance. In 1968, 12,500 Guatemalans died in an epidemic of Shigella diarrhea, caused by a microbe harboring a plasmid that conferred resistances to four antibiotics.  Images & Captions Courtesy FDA (www.fda.gov)  So far, we know three ways bacteria can become resistant to an antibiotic. But what if there are other ways we are unaware of? The bulk of research in this area is geared towards finding new alternatives to antibiotics in the event that they should become ineffective. This research seems to be taking us in the wrong direction. While alternatives are always welcome additions to the arsenal against pathogens, we should learn to use what we have now. To do this effectively, we need to know *all* ways that antibiotics can become ineffective. In this experiment, we will test one possibility for how this happens. We know bacteria can adapt (in several ways) once they have been exposed to the antibiotic, but is the same true if they face other bacteria? This possibility comes from the idea of a gym. People go to a gym to work out and to get stronger. If it were somehow possible to test two men against the same attacker, whom neither of them had seen before what would happen? The attacker would have equal success against both men. What would happen if one man, however, had been working out for six months before hand? He would have more success in defending himself, and in ultimately defeating the attacker. This is our idea. Our experiment is designed to determine if bacteria can become stronger against a previously unencountered enemy simply by "working out," in this case fighting other bacteria. | |
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