Survival of the Fittest

Many common antibiotics are no longer effective against certain resistant bacteria. This problem is fast becoming a global crisis.

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Ten million people are in danger. By 2050, infections could kill this many people - every year - if antimicrobial resistance continues to spread.¹ The silent battle between bacteria and modern medicine is everywhere. Certain microbes have developed resistance to formerly effective medicines. They have become stronger than mankind’s attempts to destroy them. Nearly 2,000 people per day die from drug-resistant microbial infections. Margaret Chan, Director General of WHO fears a “post-antibiotic era in which common infections will once again kill.” [1]

For nearly a century, people thought they were winning the war. In the fight against disease-and-illness-causing bacteria, Alexander Fleming is celebrated as a hero. He observed in 1928 that fungus molds could kill bacteria. [2] By 1941, compounds from the penicillin fungus were used to treat bacterial infections. [3] Thanks to antibiotics, doctors could also treat bacterial infections that were once deadly. [4] But the victory didn’t last long. Within a few years, the first cases of penicillin resistance - carried by Staphylococcus aureus - appeared. Scientists then developed a new weapon, the antibiotic methicillin – a chemically-modified penicillin. [5] But bacteria soon developed resistance to methicillin as well. Michael Borek, Therapeutic Area Head Medical Office at Sandoz, is not surprised at bacteria’s resilience. “The more antibiotics in use, the higher the resistance,” he says.

Microbes versus Medicine

How could resistance grow so strong? Borek suggests the answer is found in the underlying evolutionary mechanism: “When the addition of an antibiotic to a population creates selection pressure, those strains that are resistant to it are favored.” People take penicillin, for example, but the bacteria in the body are not all killed. Some of the microbes adapt, and the next generation survives future attacks by the same drug. [6] The patient, or a healthcare worker, might unknowingly pass on the resistant bacteria to other people. And not just bacteria are adapting to medicine. Other microorganisms, including certain viruses and parasites, are also becoming resistant to antibacterial, antifungal, antiparasitic and antiviral therapy. Together, these drugs are referred to as antimicrobials, leading to the overall problem of antimicrobial resistance.

One prominent bacterium, methicillin-resistant Staphylococcus aureus (MRSA) is well known for its capability to withstand antibacterial drugs – and for causing infections in hospital patients. Such infections result in longer hospital stays, and are more often deadly than other types of infection, because they are so difficult to treat. [6] Unfortunately, the pathogen army has also recruited new troops, and these are proving particularly dangerous in hospitals.
Antibiotic Resistance

Main routes of transmission

Some bacterial infections are very difficult to treat because various antibiotic resistances exist. There are two important sources of resistant bacteria: veterinary and human medicine.

The situation is genuinely alarming

Borek explains that there are two groups of bacteria identifiable by a chemical method. When it is possible to stain the bacteria with a certain dye, these are called Gram positive. The other group is Gram negative. For the past three-quarters of a century, medicine primarily has fought Gram positive bacteria such as Staphylococcus aureus. However, Gram negative bacteria, including certain Enterobacteriaceae species and Pseudomonas aeruginosa, are causing serious infections and showing increasing resistance. [7]

Today, Gram-negative bacteria are increasingly responsible for hospital-acquired infections. [8] Especially in intensive care units, the density of such microbes is high, and the resulting infections are very difficult to treat. In 2014, the WHO found high levels of resistance worldwide in seven common pathogens – five of them Gram negative. [9] As Borek states, “The situation is genuinely alarming.”

Fighting Back

But microbes haven’t won yet. "Spreading knowledge and awareness to the public is an important step to slow down the rise of antimicrobial resistance," explains Borek. Education and antimicrobial stewardship - prescribing antimicrobials selectively and establishing procedures that reduce infections – can help. Borek states there is even more that can be done. “We want to provide the public with safe and effective antibacterial drugs. At Sandoz, we have a large portfolio that enables physicians to use a variety of antibiotics to treat bacterial infections.” This way, microbes do not develop resistance to drugs that they have been exposed to regularly.

With rapid diagnostics, physicians could reduce the use of broad-spectrum antibiotics, often a first-line therapy against the most probable pathogens. But this puts a high selection pressure on a variety of bacteria species. A highly specific therapy, on the other hand, minimizes the amount of affected microbes, and slows down their development of resistance, explains Borek. “A revolution would be the species-specific treatment of the causative bacteria of an infection. For this to occur, it would be necessary to identify the microbes immediately.” That way, physicians would not have to wait for the results of a laboratory analysis, which often takes a day or more. They could start a targeted therapy immediately.
Searching for alternatives

While the rate of resistance can be slowed, evolution never stops. Sooner or later, people will need new drugs. The battle plan has been slow in coming. Between 2002 and 2012, for example, the US Food and Drug Administration (FDA) approved just seven new antibiotics, four of which showed adverse effects or were later withdrawn from the market. [10] Reinforcements are on the way. Since 2013, six new antibiotics have been introduced, perhaps encouraged by an initiative from the Infectious Diseases Society of America (IDSA) to create 10 systemically-administered antibiotics by 2020. [11] “Antibiotics are life-saving drugs that are taken only a few times in a person’s life for perhaps two weeks. By contrast, development is time-consuming, expensive and associated with certain regulatory limitations,” says Borek. And developing new antibiotics is also a financial risk, leading some pharmaceutical companies to abandon this field.

Novel formulations of existing antibiotics could provide the next line of defense. [12] These drugs are more targeted, which makes therapy more effective, reduces side effects and increases the chance that the patient completes therapy. According to antibiotics expert Borek, novel active substances play a key role. “We collaborate closely with Novartis. And there’s an upward trend in the development of antibacterial substances. Novartis has a few in the general pipeline, some of them in the clinical phase II and III.”

New Strategies

Researchers continue to search for new treatment methods. Using antibodies that specifically target a pathogen is one new way to deal with resistant bacteria. [13] The protein complexes lead to inactivation of the bacterium or its toxins, for example. Other therapy options include probiotics and vaccines. Innovation could produce the secret weapon for antibacterial therapy in future, and scientists all over the world are joining the fight. Antibiotic expert Borek is seeing lots of new ideas and approaches. As a result, he remains optimistic, saying, “I’m not expecting a post-antibiotic apocalypse in the coming years.”

Links:
[9] #Prevention

Fullnoten:

Lead image: Gut bacterium Escherichia Coli surrounded by erythrocytes. Some strains invade the body and cause infection, for example, in the blood system. Some Gram-positive bacterium show antibiotic resistance. Credit: dpa picture alliance

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