ANTIBIOTICS: RETROSPECTIVE AND PERSPECTIVE

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Abstract

The history of antibiotics is one of the major revolutions in medicine, transforming deadly infectious diseases into easily treatable ones. It has evolved from the ancient use of mold to the development of modern, precision-guided drugs. The discovery of antibiotics helped overcome plague, tuberculosis, pneumonia, syphilis, and sepsis. They also made complex surgeries, organ transplants, and chemotherapy possible, which carry a high risk of infection. Today, there are approximately 200 different antibiotics worldwide. They are divided into groups based on their mechanism of action (for example, penicillins, cephalosporins, and macrolides). However, the main problem in modern medicine has become antibiotic resistance - the ability of bacteria to mutate and develop resistance to drugs due to improper or excessive use.

Keywords: Revolutions in medicine, precision-guided drugs, antibiotic resistance.

Introduction

If a piece of bread develops an unsightly bluish-green growth somewhere on the crust, it's likely thrown away. And that's a reasonable thing to do. But if the same thing had happened in ancient Egypt, the bread would have been used to treat people with a nasty cut or infection. In fact, some scientists have discovered that ancient civilizations in Egypt, Greece, China, and Rome used rather strange substances, such as bread mold and certain muds, to treat wounds. The question is: why did they do this? And the most obvious answer is: it must have worked! The idea of using microbes against microbes, along with observations of microbial antagonism, dates back to Louis Pasteur. In particular, Pacier wrote that "in the process of fighting each other, microbes produce specific substances as weapons of defense and attack." And what else are antibiotics if not weapons of attack by one microbe against another? Modern antibiotics—penicillin, streptomycin, and others—are derived from the metabolic products of various organisms—bacteria, molds, and actinomycetes. These substances either kill or inhibit the growth and reproduction of pathogenic microbes.

Results

It wasn't until the late 1800s that more modern scientists began to understand why things like mold and dirt were so effective at treating infections. One of the most important clues was the discovery of a scientist named Paul Ehrlich. He discovered that when he added certain dyes to a dish of bacteria, only some of the bacteria were stained—meaning they absorbed the dye. This led him to believe that if he could create a chemical that acted like a dye but killed bacteria, it could be very useful for treating diseases. He began by modifying a drug already in use to treat several other illnesses.

In his lab, he tweaked the molecule in different ways and then tested how well the new molecule killed bacteria in rabbits. He tried 605 different chemical combinations before discovering that he could kill the germs that cause syphilis, a disease common at the time. This drug is considered an antibiotic because it kills or inhibits bacterial growth. Could it be that the bread pans and mud used by ancient civilizations also contained antibiotics?

The era of antibiotics, in the modern sense of the word, began with the remarkable discovery of penicillin by Alexander Fleming. In 1929, the English scientist Alexander Fleming published a paper that brought him worldwide fame: he reported a new substance isolated from mold colonies, which he named penicillin. This marked the beginning of the "biography" of antibiotics, which are rightfully considered the "drug of the century." The paper noted the high sensitivity of staphylococci, streptococci, and pneumococci to penicillin. The anthrax pathogen and diphtheria bacillus were less sensitive to penicillin, while the typhoid bacillus, cholera vibrio, and others were completely insensitive.

It may seem crazy at first, but an accidental contamination in another scientist's laboratory, that of Alexander Fleming, not only showed that these ancient doctors were onto something but also changed the way scientists and doctors treated disease.

Alexander Fleming was a Scottish biologist with a keen interest in bacteria that cause infections. He served in the army during World War I, where he saw many soldiers die from infections in their wounds rather than from the wounds themselves. After years of research, repeatedly trying to find a substance capable of killing harmful bacteria, he decided to take a leave of absence. However, before leaving, he accidentally left a Petri dish containing bacteria open on his lab bench. Upon returning from leave, he noticed a bluish-green mold (like mold on bread) growing in one of the Petri dishes. He also noticed that the bacteria in the Petri dish failed to grow near the mold. Upon noticing this, he remarked, "That's funny." He then took samples of the mold to determine why bacteria wouldn't grow near it. Fleming discovered that the mold belonged to the species Penicillium notatum and produced a substance that destroyed many types of harmful bacteria. This substance, which he named penicillin, was the first antibiotic produced in a living organism to be isolated and described by a scientist.

Alexander Fleming discovered an antibiotic that forever changed medicine. However, it took another decade before a pair of chemists was able to extract enough penicillin to treat infections. Fortunately, penicillin could be produced on a mass scale around the time the United States entered World War II, saving thousands of lives.

While penicillin is still used for some treatments today, it is not as effective against bacteria as it was in the mid-1900s. This is because many types of bacteria have developed resistance to penicillin. In fact, many types of bacteria have developed resistance to many different antibiotics, which is a huge problem for both patients and the doctors trying to treat them.

However, A. Fleming did not report the type of mold from which he isolated penicillin. This was clarified by the renowned mycologist Charles Westling. However, the penicillin discovered by Fleming had several drawbacks. In liquid form, it quickly lost its potency. Due to its low concentration, it had to be administered in large quantities, which was very painful.

Fleming's penicillin also contained many harmful and undesirable protein substances from the broth in which the penicillium mold was grown. As a result, the use of penicillin for treating patients was delayed for several years. Only in 1939 did doctors at Oxford University Medical School begin studying the possibility of using penicillin to treat infectious diseases. G. Florey, B. Hayne, B. Chain, and other specialists drew up a plan for a detailed clinical trial of penicillin. Recalling this period of work, Professor Florey wrote: "We all worked on penicillin from morning until night. We fell asleep thinking about penicillin, and our only desire was to unravel its mystery."

This intense work bore fruit. In the summer of 1940, the first white mice, experimentally infected with streptococci in Oxford University laboratories, were saved from death thanks to penicillin. The results helped clinicians test penicillin on humans. On February 12, 1941, E. Abrazam administered the new drug to terminally ill patients dying from blood poisoning. Sadly, after several days of improvement, the patients eventually died. However, the tragic outcome occurred not as a result of penicillin but due to its unavailability in sufficient quantities.

Beginning in the late 1930s, studies of the natural distribution of actinomycetes and subsequent research by G. Gause and other scientists on the antibacterial properties of soil microorganisms laid the foundation for antibiotic production. The domestic drug penicillin was developed in 1942, and during World War II, thousands of wounded and sick people were saved.

The triumphant advance of penicillin and its worldwide recognition ushered in a new era in medicine—the era of antibiotics. The discovery of penicillin stimulated the search for and isolation of new active antibiotics. Thus, gramicidin was discovered in 1942 (G.F. Gause et al.). In late 1944, S. Waksal and his team conducted experimental testing of streptomycin, which soon became a rival to penicillin. Streptomycin proved highly effective in the treatment of tuberculosis, explaining the rapid growth of the industry producing this antibiotic. S. Waksal first coined the term "antibiotic," referring to a chemical substance produced by microorganisms that can inhibit the growth or even destroy bacteria and other microorganisms. This definition was subsequently expanded.

In 1947, another penicillin antibiotic, chloromycetin, was discovered and demonstrated its effectiveness. It was successfully used to treat typhoid fever, pneumonia, and Q fever. Between 1948 and 1950, auromycin and terramycin were introduced, with clinical use beginning in 1952. They proved effective against many infections, including brucellosis and tularemia. In 1949, neomycin, an antibiotic with a broad spectrum of activity, was discovered. Erythromycin was discovered in 1952.

Thus, the arsenal of antibiotics expanded annually. Streptomycin, biomycin, albomycin, chloramphenicol, synthomycin, tetracycline, terramycin, erythromycin, colimycin, mycerin, imaninin, ecmolin, and several others were developed. Some of these have a targeted effect on specific microbes or groups of microbes, while others have a broader spectrum of antimicrobial activity across a variety of microorganisms.

Hundreds of thousands of microbial cultures are isolated, resulting in tens of thousands of drugs. However, all of these require careful study.

The history of antibiotic development is full of unexpected and even tragic events. Even the discovery of penicillin was accompanied by both success and disappointment. Penicillinase, a substance capable of neutralizing penicillin, was soon discovered. This explained why many bacteria are resistant to penicillin (for example, the colibacillus and typhoid fever bacteria contain penicillinase).

Following this, other observations shook the belief in penicillin's all-conquering power. It was established that certain microbes acquire resistance to penicillin over time. This accumulated evidence supported the idea that there are two types of antibiotic resistance: natural (structural) and acquired.

It also became known that several microbes can produce a similar protective substance against streptomycin - the enzyme streptomycinase. This would seem to have led to the conclusion that penicillin and streptomycin were becoming ineffective treatments and should not be used. As important as the findings were, and as threatening as they were for antibiotics, scientists did not jump to such hasty conclusions. Instead, they reached two important conclusions: first, to seek ways to suppress microbes' protective properties, and second, to study this self-defense mechanism more deeply.

In addition to enzymes, some microbes are protected by vitamins and amino acids.

A major drawback of long-term treatment with penicillin and other antibiotics was the disruption of the physiological balance between microorganisms and macroorganisms. Antibiotics do not discriminate but suppress or kill any organism within their range of action. As a result, microbes that facilitate digestion and protect mucous membranes are destroyed, and a person begins to suffer from microscopic fungi.

Great care is required when using antibiotics. Precise dosages must be observed. After testing, each antibiotic is submitted to the Antibiotic Committee, which decides on its suitability for practical use.

Antibiotics with prolonged action in the body continue to be developed and improved. Another direction in antibiotic improvement is the development of formulations that allow administration via injection rather than by syringe.

Phenoxymethylpenicillin tablets are formulated for oral administration. The new drug has successfully

passed experimental and clinical trials. It possesses several valuable properties, the most important of which is its resistance to gastric acid. This is precisely what ensures the success of its production and use. Once dissolved and absorbed into the bloodstream, it exerts its therapeutic effect.

The success of phenoxymethylpenicillin tablets has met scientists' expectations. The arsenal of tablet antibiotics has been expanded to include several others with broad-spectrum activity against various microbes. Tetracycline, terramycin, and biomycin are currently well-known. Chloramphenicol, synthomycin, and other antibiotics are administered orally.

Thus, the semisynthetic drug ampicillin was developed, inhibiting the growth of not only staphylococci but also the microbes that cause typhoid fever, paratyphoid fever, and dysentery.

All of this was a new and significant development in the study of antibiotics. Conventional penicillins are ineffective against the typhoid-paratyphoid-dysenteric group. New prospects are now opening up for the wider practical use of penicillin.

A major scientific development was the discovery of new streptomycin preparations—pasomycin and streptosaluside—for the treatment of tuberculosis. It turns out that this antibiotic can lose its effectiveness against tuberculosis bacteria that have become resistant to it.

The development of dibiomycin at the All-Union Research Institute of Antibiotics was an undoubted achievement. It has proven effective in the treatment of trachoma.

Science is moving forward, and the search for antibiotics against viral diseases remains one of the most pressing scientific challenges. In 1957, the English scientist Isaacs reported the discovery of a substance he called interferon. This substance is formed in the body's cells as a result of viral penetration. The therapeutic properties of interferon have been studied. Experiments have shown that the viruses that cause influenza, encephalitis, polio, and smallpox are most sensitive to its action. Moreover, it is completely harmless to the body.

Liquid antibiotics in suspension form have been created. Due to its potent therapeutic properties, pleasant aroma, and sweet taste, this liquid form of the antibiotic has found widespread use in pediatrics to treat various diseases. They are so convenient to use that they are even given to newborns as drops.

In the era of antibiotics, oncologists could not help but consider using them in cancer treatment. Could microbes produce anti-cancer antibiotics? This task is much more complex and challenging than discovering antimicrobial antibiotics, but it fascinates and excites scientists. Antibiotics produced by actinomycetes, fungi with ray-like properties, have generated great interest among oncologists.

Several antibiotics are being carefully studied in animal experiments, and some are being used to treat cancer in humans. Actinomycin, actinoxanthin, pluramycin, sarcomycin, and auratin are important components in the search for active yet safe drugs. Unfortunately, many of the anticancer antibiotics developed so far do not meet this requirement.

Hope for success lies ahead. We dream of defeating cancer. The dream of conquering space once seemed impossible, but it has come true. These dreams will also come true.

Thus, the most effective antibiotics have proven to be those produced by actinomycetes, molds, bacteria, and other microorganisms. The search for new antibiotic-producing microbes continues on a broad front worldwide.

As early as 1909, Professor Pavel Lashchenkov discovered the remarkable ability of fresh chicken egg whites to kill many microbes. During destruction, they dissolve (lyse). In 1922, the English scientist Alexander Fleming studied this interesting biological phenomenon in depth and named the microbe-dissolving substance lysozyme. The discovery of lysozyme sparked great interest among biologists, microbiologists, pharmacologists, and physicians of various specialties.

Experimenters were interested in the nature, chemical composition, and effects of lysozyme on microbes. Of particular importance was the question of which pathogenic microbes lysozyme was effective against and which infectious diseases it could treat.

Lysozyme has been found in varying concentrations in tears, saliva, sputum, spleen, kidneys, liver, skin, intestinal mucosa, and other organs of humans and animals. Furthermore, lysozyme has been found in various fruits and vegetables (horseradish, turnips, radishes, cabbage), and even flowers (primrose). Lysozyme has also been found in various microbes. Lysozyme is used to treat certain infectious diseases of the eyes, nose, and oral cavity, among others.

The widespread popularity of antibiotics has led to them often becoming a kind of “home remedy” and being used without a doctor’s prescription. Of course, such use is often dangerous and leads to adverse reactions and complications. Careless use of high doses of antibiotics can cause more severe reactions and complications. It's important to remember that antibiotics can damage microbial cells, introducing toxic microbial breakdown products into the body and causing poisoning. This often affects the cardiovascular and nervous systems and disrupts normal kidney and liver function.

Antibiotics have a potent effect on many microbes, but certainly not on all. There are no universally effective antibiotics yet. Scientists are striving to develop so-called broad-spectrum antibiotics. This means that such antibiotics should be effective against a wide range of microbes, and such antibiotics have been developed. These include streptomycin, tetracycline, chloramphenicol, and others. However, precisely because they kill a wide variety of microbes (though not all), the ones that remain become aggressive and can cause harm. At the same time, they have a bright future.

Antibiotics are now also used to treat animals and birds. Thanks to antibiotics, many infectious diseases in birds are no longer a scourge in poultry farming. In livestock and poultry farming, antibiotics have come to be used as growth promoters. When combined with certain vitamins added to the feed of chickens, turkeys, piglets, and other animals, antibiotics promote growth and weight gain.

Conclusion

Scientists have every reason to believe that, in addition to stimulating growth, antibiotics will also have a preventative effect on poultry diseases. Studies have shown that among birds, calves, and piglets, morbidity and mortality, for example, from intestinal infections (diarrhea), have been significantly reduced with the use of antibiotics.

Bacterial evolution occurs much faster than our drug development process. This means that bacteria resistant to a particular antibiotic develop soon after its development. This also means that the same type of antibiotic won't work next time. Doctors will need to develop a better plan to combat the new infection.

Thus, antibiotic resistance occurs when some bacteria acquire a gene that allows them to survive the antibiotics intended to kill them. New genes can arise in bacteria through mutation, or a gene can be transferred from one bacterium to another through horizontal gene transfer. When these bacteria multiply and spread, they create a major problem because many people become ill. When treating antibiotic-resistant infections, doctors must use other antibiotics. Sometimes, these other options may not work or cause serious side effects.

Let's hope that antibiotics will also defeat other diseases.

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