

Review: History of Antibiotics

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1. Introduction

The word "antibiotics" describes naturally occurring compounds from a variety of microorganisms, including bacteria and fungus, that have the capacity to stop the growth of other microorganisms and kill their cells [1]. The word "antimicrobials," which refers to natural, semi-synthetic, and synthetic chemicals capable of preventing the proliferation of germs and causing them to undergo apoptosis, has supplanted the term "antibiotics" due to the manufacture of semi-synthetic derivatives in the modern period [2]. The man was nearly always at risk for infections prior to the development of medicines. Pneumonia, meningitis, and TB were among the illnesses that received little or no treatment. Major epidemics were a constant source of concern for humanity. High infection-related death rates were observed in specialties like hematology, pediatrics, and surgery [3]. Medicine has evolved since then and for many years. Doctors were allowed to expand and progress their studies without the anxiety of infection. Hematology and surgery were among the thriving specialties. Furthermore, diseases like tuberculosis have been successfully treated, and for many decades, people have been freed from the fear of serious pandemics (like the plague and syphilis) and illnesses. Antibiotics were gradually ingrained in the general public's mind as a lifesaver [4]. Numerous novel antimicrobial drugs with diverse modes of action have been identified over time, and it is commonly known that the existing arsenal offers total defense against practically all infections [5]. Antimicrobials are now commonly used medications in agriculture, animal and fish

production, as well as in medicine as growth-enhancing or growth-protective medicines [6, 7]. At this stage, it is crucial to note that chemotherapeutic medications that target bacteria and that those made from living things are known as antibiotics, whilst those made artificially in a lab are known as antimicrobials [8].

1.1 Aim

The current historical study offers details on the development and application of antibiotics over time, as well as their role in treating microbial infections and advancing medical research generally.

2. Review Methods

The study material included pertinent works and scientific papers on the topic, including those listed in the study's literature. Using the following keywords: antibiotics, history of antibiotics, penicillin, the methodology was based on a literature search of reviews and research studies taken from Medline, Pub Med, Iatrotek, a Greek database, and the Hellenic Academic Libraries Association (HEAL-Link). Articles written in languages other than Greek and English were excluded based on this criterion.

2.1 Antibiotics Over the Years

More than 2,500 years ago, the ancient Chinese used antibiotics for the first time. Chinese people have found that moldy soybeans have medicinal qualities and have used them to treat

diseases like carbuncles and furuncles (pimples). Alexander [9] Because molds and plants produce antibiotic compounds, many other ancient civilizations, such as the Egyptians and Greeks, have already employed them to cure illnesses. However, substances that provide antibiotic action were unknown at the time [1, 10]. Apart from the structure of small organisms and plants, microbes, and fungi, Robert Hooke was the first scientist to see under a rudimentary microscope in 1665, marking the beginning of microbial observation [11]. Hooke claimed that tiny "kits" known as cells were the tiniest units of life after noticing a thin cork sliced. He was able to observe individual cells using a two-lens, upgraded composite microscope. Cell theory, which holds that all living things are composed of cells, was first proposed with Hooke's discovery [8]. After building microscopes with zoom lenses ranging from X300 to X500, Anton van Leeuwenhoek started observing protozoa and big bacteria a few years later, in 1674. He built 400 microscopes, and he was the first to use some of them to view live microbes [2]. Based on his observations, he contended at the Royal Society of London in 1676 that the microorganisms he had seen through the huge lenses were living [12]. Van Leeuwenhoek created intricate drawings of these microscopic creatures that lived in the water, on faces, and in objects he removed from the mouth. The earliest bacteria and protozoa were shown in these drawings [13]. But since academics at the time were not allowed to use microscopes, microbiology didn't really start until two centuries later, when Luis Pasteur and Robert Koch were able to link bacteria to diseases. Pasteur established the fundamentals of microbiology in 1859, Koch demonstrated in 1876 that carbon bacilli are linked to carbon disease, and in 1882, tuberculosis was finally connected to tuberculosis mycobacteria [14]. The first antibiotic, pyocyanase, was discovered by two German researchers, Rudolph Emmerich and Oscar Löw, in the late 1890s. It was made from the cultivation of the microbe *Pseudomonas aeruginosa* and was used to treat cholera and typhus in patients, though its efficacy and safety were questioned [15]. Paul Ehrlich developed the arsenic-based medication Salvarsan in 1909, which worked against the bacterium *Treponema pallidum*, which causes syphilis. The groundwork for the future advancement of antibacterial drugs was established by this discovery [16]. However, Alexander Fleming's 1928 discovery of penicillin, which is still utilized in therapeutic treatments today, marked a turning point in the development of antimicrobial medications [17]. Ernest Duchesne first reported *Penicillium* sp.'s antibacterial qualities in France in 1897. But it wasn't until Alexander Fleming discovered penicillin that his work had an impact on the scientific world. The first sulphonamide, prothosyl, was identified by Bayer's research team in 1932, and Gerhard Domagk demonstrated its effectiveness against serious bacterial infections that same year [18]. Penicillin, a byproduct of the fungus *Penicillium*, was the first antibiotic that physicians could purchase in 1946. It can be regarded as "a child of the war" because the Second World War was the time of much observation and study prior to its creation [2]. Since penicillin was able to treat all infections brought on by streptococci and staphylococci, its discovery was considered a contemporary marvel. It is simple to comprehend the relief that followed this finding, considering that these two bacteria are responsible for the majority of known diseases [19]. The discovery of streptomycin and tetracycline at the end of the 1940s and the beginning of the 1950s led to the

widespread acceptance of antibiotic chemotherapy in clinical practice. These medicines worked well against *Bacillus tuberculosis* and other harmful bacteria [2]. For the first time, scientists began to pay attention to the existence of drugs and, more specifically, hormones in the environment in the 1970s [1]. The 1980s saw a decline in interest in the subject of hormones and a surge in studies on the prevalence of chemicals including heavy metals, polycyclic aromatic hydrocarbons, chlorinated dioxins, pesticides, and detergents in the environment. Additional compounds, including antibiotics, anti-rheumatic medications, and analgesics, have been included in study lists since the mid-1990s [2, 19].

2.2 The Contribution of Fleming

Scottish pharmacologist and biologist Sir Alexander Fleming conducted studies in immunology, bacteriology, and chemotherapy. Along with Florey and Chain, he was awarded the 1945 Nobel Prize in Physiology and Medicine for discovering the first antibiotic, penicillin, in 1928. The lysozyme enzyme was discovered in 1922, which is another significant finding [20]. Fleming was researching the characteristics of staphylococci in 1928. His prior research had already earned him a reputation as a clever researcher, but he was also a negligent lab technician, frequently forgetting the microbial crops he was working on and keeping his lab in a generally disorganized state [17]. Fleming threw the microbial cultures tablets into a detergent container after discovering, upon returning from vacation, that many of them were deformed, or contaminated with a fungus. He took some of the tablets that weren't immersed in the detergent, though, because he needed to demonstrate to a guest what he was searching for. Then he saw a bacterial-free area surrounding the mold. If the mold had created a bactericidal material, this should have occurred [21]. The novel compound was given the name penicillin because Fleming was able to isolate a mold specimen and properly recognized it as a penicillin fungus. Fleming looked on the bactericidal effects of penicillin on a variety of microbes. He discovered that it did not effect the bacteria that cause typhoid or paratyphoid fever, for which he was then looking for a cure, but it did impact staphylococci and almost all other Gram-positive pathogens. Even though gonorrhea is brought on by a Gram-negative bacterium, it was also impacted [12]. However, because the material was unstable and ineffective, attempts to treat human infections with it did not show promise. Oxford University researchers have just recently looked into the prospect of creating stable penicillin in large enough amounts to cure human illnesses. The medication was first used to treat severe infections in 1941. The patients who took penicillin recovered quickly and completely, which produced remarkable outcomes. The United Kingdom was unable to produce penicillin on a significant scale due to World War II. The United States has created techniques for the antibiotic's mass manufacture, analysis, and stabilization. An era known as the "golden age of chemotherapy" began with the development of penicillin [21]. Numerous growth-inhibiting chemicals, bacteria, and some fungi were found after 1948. Although Fleming's discovery was published in the *British Journal of Experimental Pathology* in 1929, it wasn't until ten years later that its significance became clear. Fleming persisted in his research, but he soon discovered that growing penicillin was challenging, and that separating the antibiotic compound from the mold was even more challenging. In

1932, Flemming himself stopped using penicillin. In his opinion, penicillin would not be significant in the fight against infections because of its sluggish effect and issue with mass manufacture [20].

Additionally, Fleming believed that penicillin would not last long enough in the human body to fully eradicate bacteria. However, Fleming gave up on his penicillin research just before Florey and Chain began their study and began large manufacture with funding from the US and UK governments. Following the bombardment of Pearl Harbor, mass production started. There was enough penicillin on hand to meet the demands of all the injured allied forces during the Normandy invasion [17].

3. Conclusion

There are very few instances in human history where a discovery fundamentally altered the path of events. Examples of such nodal discoveries include the fire, the wheel, the gunpowder, and nuclear energy. The discovery of antibiotics is unquestionably one of the most significant turning points in the history of human civilization [22]. Antibiotics gradually become recognized as a lifesaver. The advantage of modern therapy is the availability of potent and secure antibiotic compositions. But as seasons and times have changed, doctors and patients must now be retrained to use antibiotics appropriately due to the possibility of overusing them. Therefore, in order for antibiotics to remain the "guardian-angel" of all patients, it is imperative that both citizens and health scientists use them appropriately.

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