A History of Penicillin: The Miracle of Medicine

By John Paul Rogers

Abstract: The discovery of penicillin in 1928 was a breakthrough in the world of medicine. Bacterial diseases could now be treated rapidly and easily without the long, complex regimens prescribed by doctors before this time. Surprisingly, many in the public and medical communities accepted this new medicine quickly with (seemingly) very few skeptics about the application of this newfound medicine. This paper seeks to explain why that happened. Examining not only the discovery of penicillin and its contribution to modern medicine, but also analyzing how doctors treated bacterial diseases before the discovery such as diphtheria will accomplish this goal. These methods serve as a means of hypothesizing why the acceptance of penicillin was so rapid. The analysis will be accomplished using newspaper articles and medical journals from mainly the 19th and 20th centuries, using secondary sources only to supplement what cannot be found in the available sources.

Introduction

Imagine if you will, you wake up one day to find that you have some flu-like symptoms (a fever, sore throat, chills, a headache). You think nothing of it until the symptoms get progressively worse, now including trouble breathing and smelly discharge. You decide you need to go to the doctor. Lo and behold: the doctor diagnoses you with diphtheria![1] Not to worry, however, for he prescribes you some antibiotics and you go on your way knowing that in a few days you will be better. This easy method of treating a disease was not always available. If one had been living in the 19th Century, the doctor probably would have treated a patient with a long list of substances from ammonia to lithium or even sulphur.[2] It was not until Alexander Fleming, a Scottish bacteriologist, discovered the properties of the mold (which later became known as penicillin) in 1928 that man first harnessed the use of antibiotics. Beginning as far back as Ancient Egypt, some notion of antibiotic substances existed, however, the knowledge of the nature of the substance cannot be verified.[3] Penicillin gained almost universal praise for revolutionizing medicine and bringing it into the modern era by providing a safer alternative to the toxic and deadly treatments of the past. This discovery also provided doctors with a simple, stable way to treat infectious diseases that might otherwise cause serious injury or death. Fleming, along with Howard Florey and Ernst Chain (English and German scientists who helped synthesize penicillin for production), were awarded the Nobel Prize in Physiology or Medicine in

[1] Mayo Clinic Staff, "Diphtheria," *Mayo Clinic*, December 08, 2016, Accessed March 14, 2017, http://www.mayoclinic.org/diseases-conditions/diphtheria/symptoms-causes/dxc-20300514.

[2] Alfred Carpenter, "Diphtheria: Its Etiology And Treatment," *The British Medical Journal* 1, no. 1209 (March 1, 1884): 403-04, Accessed February 24, 2017.

[3] "Discovery and Development of Penicillin," American Chemical Society, Accessed March 14, 2017. https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/flemingpenicillin.html.

1945, less than twenty years after Fleming's discovery.[4] The work that penicillin did during World War II may have also fueled its praise as it cut the mortality rate on the battlefield.[5]

The following history moves beyond a simple, structural history of medicine to demonstrate how both the medical and public communities reacted to this newfound substance. Unlike with many new treatments introduced over the years (such as the treatments for and prevention of the waterborne disease called cholera), the praise for penicillin was almost universal, bringing these two communities together in a rare agreement.[6] The dangerous methods of treating many of the same diseases as penicillin may have contributed to penicillin's rapid acceptance. Penicillin was perhaps seen as a cure-all for bacterial infections and a way to avoid these dangerous methods of treatments from before its discovery. While virtually all scholars agree that the discovery of Penicillin constitutes a miracle of modern medicine, there is little-to-no work framing the social history of the medicine. [7] This lack of scholarship leaves open the opportunity to shed new light on the subject. Today the story of penicillin is also important, as medicine is possibly entering the post-antibiotic age that Fleming worried about where society has used so many antibiotics that diseases are becoming immune to the effects.[8] This new resistance may, in the next several decades, open opportunities for the formation of new diseases similar to the ones described or bring back diseases that were once treatable.

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[4] Eric Sidebottom, "The Discovery of Penicillin," in *Nobel Prizes that Changed Medicine*, ed. Gilbert Thompson, (London: Imperial College Press, 2012), 45.

[5] Lucille Wright, "Miracle Medicine Writing History at Army Hospital," *The Ogden Standard-Examiner*, July 5, 1943, Accessed March 8, 2017. https://www.newspapers.com/image/27174060.

[6] See *The Cholera Years* by Charles Rosenberg for more information about the debate over the treatment and prevention of cholera.

[7] "Discovery and Development of Penicillin," American Chemical Society.; B. Lee Ligon, "Penicillin: its discovery and early development," *Seminars in Pediatric Infectious Diseases* 15, no. 1 (January 2004): 52-57, Accessed February 24, 2017.

[8] C. Lee Ventola, "The Antibiotic Resistance Crisis: Part 1: Causes and Threats," *Pharmacy & Therapeutics* 40, no. 4 (2015): 277, Accessed March 14, 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/; Marie-Paule Kieny, "WHO's new priority list of antibiotic-resistant bacteria looks beyond the scourge of tuberculosis," *Statnews.com*, March 13, 2017, accessed April 6, 2017. https://www.statnews.com/2017/03/13/tuberculosis-who-bacteria-antibiotics/.

Chemicals, Tonics, and Scrapings, Oh My!

Many different methods for the treatment of various bacterial diseases existed before the discovery of penicillin. Many of the treatments described may seem outlandish by modern medical standards, such as using sulphur to treat a bad case of diphtheria (more on the reasoning behind this to come). Such practices, however, were commonplace in pre-penicillin medicine. Without the machines of modern medicine, doctors before the Twentieth Century did not truly know what caused diseases. Their inability to look at a disease on the microscopic level meant they could only diagnose and treat what they could physically examine. This lack of understanding meant that the doctors had to experiment to see what treated different symptoms. Most of these treatments were advertised in 19th century newspapers from across the United States and medical journal articles from Britain (due to the lack of American medical journals available as resources at the time of writing). Some of the ingredients in these treatments are now known to be dangerous with prolonged exposure, which is why they are highlighted here: showing that not all medical prescriptions of the past were safe.

Therapeutic practices form the central focus of this study. Understanding the specific symptoms of some diseases provides a better understanding as to why doctors did what they did. As stated in the story at the beginning of the paper, diphtheria is an infection that provides flu-like symptoms at first but progressively gets worse. According to the Mayo Clinic, the disease begins as an infection of the mucous membranes in the throat, however it can spread to other organs, possibly lead to serious injury or death.[9] Another bacterial infection prevalent throughout history (particularly the Nineteenth Century) is gonorrhea. Gonorrhea (also known as the clap) is

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[9] Mayo Clinic Staff, "Diphtheria."; The Mayo Clinic was chosen for these definitions because it is widely regarded as one of the top research hospitals in the world.

an infection that mainly targets the genitals, rectum, and throat.[10] This infection causes swelling, pus-like discharge and painful passing of substances through the affected area.[11] Pneumonia, an infection of the lungs occasionally caused by bacteria, is another disease which penicillin treats. The disease causes difficulty breathing, pus, and a fever.[12]

Figure 1: A Picture of a case of diphtheria. Note the lining on the esophagus.[13]

Many different chemicals were used to combat the symptoms of the diseases mentioned above as well as symptoms caused by related infections. Many doctors believed using these chemicals would produce results. One Dr. Alfred Carpenter, a physician in London in the late 1800s, provided a whole regimen to treat different infections like diphtheria. In his paper, he suggested using ammonia, "so as to reduce the acidity of the blood," along with a combination of another alkaline to help treat the infection itself.[14] The lower acidity of the blood allowed the

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[10] Mayo Clinic Staff, "Gonorrhea," *Mayo Clinic*, October 25, 2016, accessed March 21, 2017. http://www.mayoclinic.org/diseases-conditions/gonorrhea/home/ovc-20258677.
[11] "Gonorrhea - CDC Fact Sheet." CDC.gov. May 19, 2016. Accessed May 05, 2017. https://www.cdc.gov/std/gonorrhea/stdfact-gonorrhea.htm.
[12] Mayo Clinic Staff, "Pneumonia," *Mayo Clinic*, June 21, 2016, accessed March 21, 2017. http://www.mayoclinic.org/diseases-conditions/pneumonia/home/ovc-20204676.
[13] Digital image, Wikimedia Commons, accessed August 29, 2017. https://commons.wikimedia.org/wiki/Diphtheria#/media/File:Dirty_white_pseudomembrane_classically_seen_in_diphtheria_2013-07-06_11-07.jpg
[14] Alfred Carpenter, "Diphtheria," 404.

body to continue fighting the disease. To reduce the patient's fever, Dr. Carpenter also suggested the patient be given a "sulphocarbolate of soda" because of its "antiparasitic" properties. The doctor believed, it seemed, that an infection and/or the accompanying fever were the result of a parasite or perhaps another, unknown macro-organism (i.e. visible to the naked eye). In order to fight the infection locally in the throat, where symptoms like the thick, smelly mucous membrane were located (see above image), he suggested using powdered sulphur, combined with glycerin or honey. One alternative to the sulphur powder that he suggested was "sulphurous acid in solution" applied directly to the throat to stop the disease from spreading even further.[15] The reasoning behind this was that these harsh chemicals would reduce the visible symptoms within the throat, thereby getting rid of the disease.

Looking through various American newspapers, many interesting ways of treating patients with the similar symptoms as Dr. Carpenter's patients appeared. An article from 1861 in the *St. Cloud Democrat*, out of Minnesota, suggested treating the patient in a manner, "1st. To evoke and sustain all of the natural vital forces of the patient."[16] This could be attained, according to the article, by feeding the afflicted person nutritious foods. The most effective food was strong beef tea, which the article said that in the event of an inability to swallow can be administered rectally, followed by brandy and iron-rich foods such as red meat.[17] For both the first and second goals of treatments, the article also suggested using sesquioxides (e.g. aluminum oxide and other such materials) to keep the patient's strength and help clear the bad membrane from the throat.[18] This reasoning suggested that diseases like diphtheria were thought of as a weakness of the body caused by the lining that formed in the throat of the patient, hence why

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[15] Ibid.
[16] "Diptheria:- Its Origin and Cure," *St. Cloud Democrat*, January 24, 1861, accessed February 24, 2017.
[17] Ibid.
[18] Ibid.

they needed to keep their strength up and using the sesquioxides. This treatment would clear out the remaining weakness. Harsh chemicals were not the only substances used in the treatment of diphtheria, as many non-chemical treatments began formulating.

In the late 1800s, a doctor in Eugene, Oregon began to use an "anti-toxine" made from the blood of horses who had been subjected to diphtheria that was then injected into the patient.[19] This treatment was, according to the article, considered the forefront of medical technology at the turn of the century.[20] Using the blood of a horse exposed to and having survived an infection like diphtheria was thought to work in a similar manner to a vaccine. This injection was effective because it gave the patient blood, which had already fought off the disease they were afflicted with.[21] This treatment was similar to how vaccines inject a person with a virus to boost their immunity.[22] The article does not provide the success rate for this "anti-toxine", but does say that one girl was treated with this method.[23]

Dr. Conway Edwards had a three-stage treatment of infections of the genital region, such as gonorrhea. The first stage consists of calomel (mercury chloride) mixed with: sulphate of magnesia, jalap (a root), scammony (also a root), potassio-tartrate of antimony, and water.[24] This mixture was to be administered orally to the patient every four hours and the genitals soaked in water.[25] Dr. Edwards explained this combination of chemicals would reduce the patient's fever while bringing on the next stage of the infection, purposefully drawing out the infection for easier treatment. When the next stage occurred, the first mixture was discarded and replaced by:

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[19] "The New Diphtheria Treatment," *The Eugene Guard*, December 27, 1895, accessed February 24, 2017.
[20] Ibid.
[21] Ibid.
[22] For more on how vaccines work, see the CDC website:
https://www.cdc.gov/vaccines/hcp/conversations/downloads/vacsafe-understand-color-office.pdf
[23] "The New Diphtheria Treatment," *The Eugene Guard.*
[24] Conway T. Edwards, "On the Rapid Cure of Gonorrhœa," *The British Medical Journal* 6, no. 147 (July 22, 1843): 325, accessed February 24, 2017.
[25] Ibid.

liquor potassæ, oil of cubebs (a pepper), balsam of copaiba (an oil), hydriodate of potash, and hydrochlorate of morphia, again to be taken every four hours.[26] Instead of soaking the genitals in water, however, he instructed to begin the application of a lead lotion on a bandage to the affected area. These chemicals then drew the infection out even further, so that the last stage of treatment could dispose of the infection. The final step was to inject a mixture of acetate of lead and water into the urethra every two to three hours for the final two days.[27] The mixture, much like the use of sulphur on the affected area of the throat above, was the final step in destroying the disease. Mercury was also used to draw out and destroy the disease in a similar fashion to lead.[28]

In his book of treatments for various diseases from 1833, Daniel Whitney wrote about a regimen for the treatment of infections similar to gonorrhea. The long list of steps began with bloodletting, salt, a poultice made from bread and milk, and a cream of tartar.[29] Bloodletting, doctors believed, let whatever caused the disease to leave the body. He then suggested soaking the affected area in a mixture of warm milk and water, as well as injecting a mixture of water, lead sugar and gum arabic into the urethra several times per day.[30] After this, he stated that the genitals should be soaked in lead water; similar to what Dr. Edwards said a decade later.[31] Whitney also stated in the book that if inflammation was bad, the patient should rub a mercury ointment on the area.[32] Much like the treatment suggested by Dr. Carpenter, many medical professionals believed these harsh chemicals killed the visible symptoms of the infection.

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[26] Ibid. 326.
[27] Ibid.
[28] Ananya Mandal, MD, "Gonorrhea History," *News-Medical.net*, November 28, 2012, accessed March 21, 2017. http://www.news-medical.net/health/Gonorrhea-History.aspx.
[29] Daniel H. Whitney, "Gonorrhœa, or Clap," in *The Family Physician, and Guide to Health* (Penn Yan, NY: H. Gilbert, 1833), 128.
[30] Ibid.
[31] Ibid. 129; Edwards, "On the Rapid Cure of Gonorrhœa."
[32] Whitney, "Gonorrhœa, or Clap," 128.

Dr. John Popham suggested using an alkaline substance to fight off an infection like pneumonia. The alkaline substance that he described in his article is a salt produced from bicarbonate of potash.[33] The doctor then said to administer it orally by mixing it with a type of vegetable syrup called a mucilaginous liquid.[34] He also wrote about his findings on using this substance with patients, reporting that a majority of patients improved after several days of the medicine being administered. Other patients showed no improvements.[35] All of the patients, however, experienced gastrointestinal distress while taking the medicine, which subsided after several doses.[36] Like the other alkaline treatment above, doctors believed the body would absorb these substances and use them to fight off the infection they could not see.

These harsh, sometimes dangerous, chemicals were not the only substances used to treat infections like diphtheria and gonorrhea. Many doctors sold tonics they concocted for either a variety of diseases or as a "cure-all". However, these doctors often did not list the ingredients, so it is difficult to gauge why they believed these specific combinations constituted a cure. Two advertisements that appeared several months apart and in different areas of Pennsylvania were titled "How to Favor Your Friends" and "It's the Only Diphtheria Cure".[37] Both advertisements promoted Thompson's Diphtheria Cure, which cure done of the diphtheritic throat infection. These two advertisements did not state what the ingredients of the Cure were, but they cited different testimonials about how wonderful the drug is, and that it was sold for fifty cents (about $15 in 2017 dollars) at local drug stores.[38]

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[33] John Popham, "The Alkaline Treatment of Pneumonia," *The British Medical Journal* 2, no. 365 (1867): 586, accessed February 24, 2017.
[34] Ibid.
[35] Ibid.
[36] Ibid.
[37] "How to Favor Your Friends," *Evening Herald* (Shenandoah), October 10, 1896, accessed February 24, 2017.; "It's the Only Diphtheria Cure," *The Scranton Republican*, August 11, 1896, accessed February 24, 2017.
[38] Ibid.

Similar to the elixirs for the throat infections, there were many “cures” sold in drug stores for infections of other areas in the body, including the genitalia. In Washington, D.C., an advertisement appeared in a local paper for “Dr. Southey’s Great London Remedies” which advertised cures for a number of maladies including gonorrhea and impotency.[39] The advertisement claimed to have cures for these maladies that worked in three to six days. The advertisement stated to only buy it from Dr. Shuman himself otherwise it was not genuine.[40] Again, no ingredients are listed for this remedy, so it cannot be known why the doctor believed his remedy cured these afflictions. In another newspaper in Charleston, South Carolina, a man from Allentown, Pennsylvania wrote a testimonial about a cure for gonorrhea from a Dr. Helmbold.[41] The man, named as C. M. Swanson, described his symptoms, stating that the doctor’s elixir of “extract of buchu and rose wash” cured him of his ailment while adding that he was now the doctor’s “obedient servant” for curing him.[42] These ingredients were likely used to treat the inflammation and flush the disease from the body again.

Treatments that did not involve tonics or harsh chemicals were used as an attempt to produce the same results. One of these, used primarily for throat infections like diphtheria, was scraping. The same article in the *St. Cloud Democrat* as above suggested, with caution due to its dangerous nature, to use a hook or forceps to pull out the bad membrane in the throat manually, though this may lead to deadly hemorrhages.[43] Instead, the best method according to this article was to keep the patient in a hot, humid environment so that they could cough up the membrane.

[39] "Doctor Southey's Great London Remedies," *National Republican* (Washington, D.C.), February 13, 1861, accessed February 24, 2017.
[40] Ibid.
[41] C. M. Swanson, "A Stubborn Case of Gonorrhea Cured," *The Charleston Daily News*, May 13, 1871, accessed February 24, 2017.
[42] Ibid.
[43] "Diptheria:- Its Origin and Cure," *St. Cloud Democrat*.

Dr. Lewis Sayer of St. Cloud was the one to suggest this method.[44] The reasoning behind this was, much like applying sulphur to the area, to remove what they believed was the cause of the infection. In this case, that was the "bad membrane" of the throat caused by the diphtheria infection. Not all of the potential cures involved active treatment of the ailment.

Though less drastic, the Kansas State Board of Health did not issue a treatment, but rather a way to prevent the spread of the disease. This prevention called for secluding the afflicted person in a sunny, ventilated room without textiles, pets, or anything else on which the infection could stay and be transmitted.[45] If the infected person were to die, the article lists disinfectants to use for different sections of the room that the person was in.[46]

Today, most people would see many of the treatments for these diseases as careless or dangerous. Coating someone's throat with sulphur? Rubbing mercury and lead-based creams on their skin? Taking a drug concocted by a doctor that is advertised without the ingredients? Why would they do something like this? It is because doctors did not have a choice. They did not know how to create something that would naturally fight off the infection without long, sometimes dangerous, regimens. Doctors had to rely on what they could outwardly examine. This lack of a better means meant that doctors mainly relied on the visible symptoms of the diseases. The harsh chemicals and treatments visibly treated the symptoms, but the doctors could not see that they may have been poisoning their patients. Other notable infections and diseases treated in similar methods due to their bacterial natures were: streptococcus, staphylococcus, gangrene, etc.

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[44] Ibid.
[45] "Diptheria. Its Preventions and Restrictions--- Issued by the State Board of Health," *The Lebo Enterprise*, April 5, 1894, accessed February 24, 2017.
[46] Ibid.

Eureka! An Accident with Mold

September 3, 1928, the day that would change medicine forever. This was the day that a scientist walked into his lab to find a mold growing in a culture of staphylococcus bacteria he had prepared. The scientist observed that the mold appeared to reverse the growth of the bacteria.[47] At first, he named his new discovery "mould juice" and later penicillin, after the scientific name of the mold he found, *Penicillium notatum* (now known as *Penicillium chrysogenum*).[48] The scientist believed that this was a potential breakthrough in treating diseases that were similar to the staphylococcus and spent the next several years studying its properties and experimenting with it before public distribution began.[49]

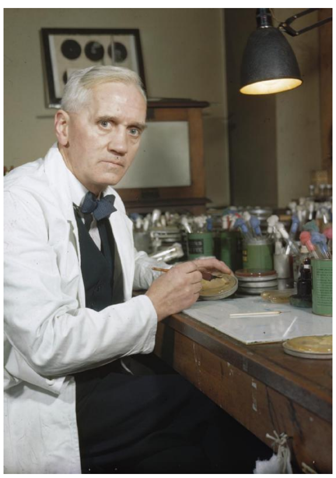

Figure 2: A picture of Fleming in his lab at St. Mary's
Source: Wikipedia

The scientist's name was Alexander Fleming. He became immortal on that fateful day in 1928. Even today, many (especially in the medical community) know his name. Who was the man behind the legend? Alexander Fleming was born in Darvel, Scotland (about 25 miles south of Glasgow) on August 6, 1881 to a farming family.[50] He was the seventh of eight children and his father died when he was seven years old.[51] When he was fourteen, he moved to London to live with one of his older brothers while attending Regent Street Polytechnic.[52] While going to school he worked as a clerk for a shipping company in London, eventually saving up enough money and earned enough scholarships to attend the St. Mary's Hospital School.[53]

[47] Kevin Brown and Kara Rogers, "Sir Alexander Fleming," *Britannica Academic,* February 12, 2009, accessed February 24, 2017.
[48] Ibid.
[49] Ibid.
[50] "Sir Alexander Fleming, M.D., D.Sc. F.R.C.P., F.R.C.S., F.R.S," *The British Medical Journal* 1, no. 4915 (March 19, 1955): 732, accessed February 24, 2017.; Brown and Rogers, "Sir Alexander Fleming."
[51] Ibid.
[52] "Sir Alexander Fleming, M.D., D.Sc. F.R.C.P., F.R.C.S., F.R.S," 732.
[53] Ibid.

While attending St. Mary's, Fleming realized that he wanted to enter the new field of bacteriology.[54] After his graduation, Fleming was hired by St. Mary's to temporarily work in the Inoculation Department, which sparked his interest in remaining as a researcher at the college.[55] Fleming eventually became a lecturer (and later professor) of bacteriology there.[56] During the First World War, he served as a bacteriologist in Boulogne, France where he researched the effects of different antiseptics.[57] He strayed from the common practice of using strong antiseptics (such as pure alcohol), which would damage the healthy tissue around the wound. Instead, he pioneered the use of saline on infected wounds. This method is still used to this day, making the discovery of penicillin not his only claim to fame.[58] From here, he returned to St. Mary's, where he would make his incredible discovery.

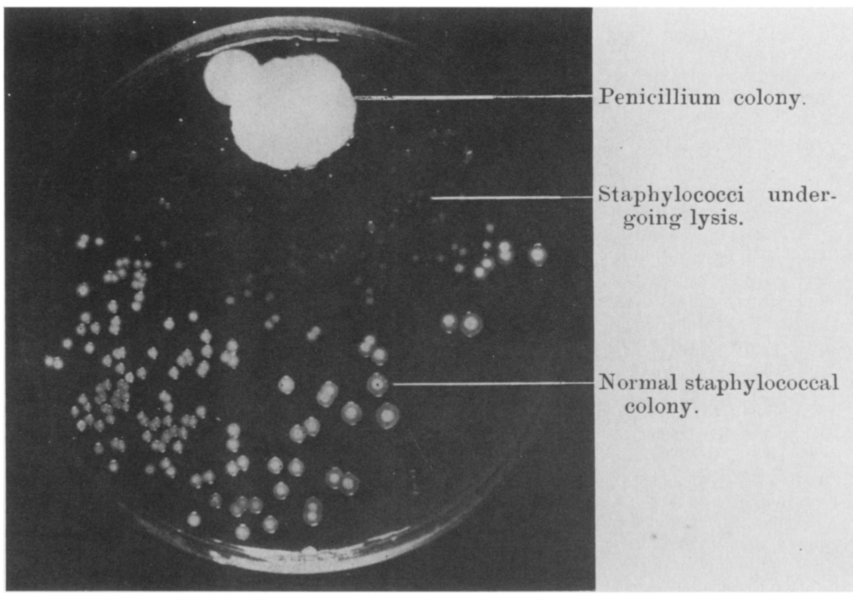

Figure 3: A picture of Fleming's original discovery[59]

[54] Brown and Rogers, "Sir Alexander Fleming."
[55] Ibid.
[56] "Sir Alexander Fleming, M.D., D.Sc. F.R.C.P., F.R.C.S., F.R.S," 733.
[57] Brown and Rogers, "Sir Alexander Fleming."
[58] Ibid.
[59] Alexander Fleming, "On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to Their Use in the Isolation of B. influenzae," *Reviews of Infectious Diseases* 2, no. 1 (Jan. & feb. 1980): 130, accessed February 24, 2017.

After he isolated the *penicillium* mold, Fleming let the mold grow for several days and then ran laboratory trials to see if his theory proved true in relation to other microbes. He noted this mold inhibited the growth of several kinds of bacteria, while other molds tested did not inhibit this growth.[60] From here, Fleming then took the fluid produced by the *penicillium* mold and tested it against several common, disease-causing bacteria: *B. typhosus,* staphylococcus, streptococcus, gonococcus, *B. diphtheriæ*, *B. anthracis*, and *B. influenzæ*.[61] The penicillin liquid inhibited the growth of all of these bacteria except for *B. typhosus* and *B. influenzæ*. Fleming continued these experiments by testing the sensitivity of twenty-three disease-causing bacteria, of which he found twelve to be sensitive to the fluid.[62] This variety of experiments also showed penicillin inhibited the growth of some bacteria even after strong dilution of the mold in a liquid.[63]

In 1929, a year after his discovery, Fleming published his findings and presented them to the Medical Research Club, where the response was not strong from other scientists.[64] In the publication, Fleming presented the properties he discovered in his new drug. Fleming found rapid heating, filtration, and dilution did not affect the antibacterial properties of the mold much. Fleming discovered, however, leaving the penicillin at room temperature for more than a week did diminish the power of the substance.[65] Fleming also discovered penicillin became much more

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60 B. Lee Ligon, "Penicillin: its discovery and early development," *Seminars in Pediatric Infectious Diseases* 15, no. 1 (January 2004): 52, accessed February 24, 2017.; Alexander Fleming, "Penicillin" (Lecture, Nobel Banquet, Stockholm, December 11, 1945), accessed March 8, 2017. https://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-lecture.pdf.

61 Fleming, "Penicillin," 1945.

62 Ibid.

63 Ibid.

64 Ligon, "Penicillin: its discovery and early development"; "Discovery and Development of Penicillin," American Chemical Society, accessed March 14, 2017. https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/flemingpenicillin.html.

65 Fleming, "On the Antibacterial Action of Cultures of a Penicillium,"131.

stable if it was made slightly more acidic, bringing the pH from nine down to about seven.[66] These were the only properties that Fleming was able to discover in those early experiments, for he did not even know why it inhibited the growth of the certain bacteria he tested.

Not many more tests were conducted on penicillin, though Fleming reportedly used it in 1932 to cure a colleague of pneumococcal conjunctivitis. This lack of tests lasted until 1939, the beginning of World War II.[67] A group of researchers at Oxford University, led by Howard Florey and Ernst Chain, began to work on a filtrate of the penicillin mold with the goal of beginning clinical trials.[68] The team soon made a breakthrough when they cured mice they infected with a deadly strain of streptococcus.[69] Florey called the results "promising", while Chain called them a "miracle".[70] Following this round of tests, the team began the first test of the drug on a human. This test was performed on a policeman who was infected by staphylococcus and streptococcus when scratched on the face by a rose thorn.[71] The experiment initially worked, but since penicillin was hard to produce in wartime (due to general supply shortages) the doctors did not have enough of the drug to continue treatments and the policeman died a month later.[72] An article published in the *Lancet*, prompted Fleming to visit the team at Oxford so that he may observe their work.[73] When Chain was told Fleming was there to meet them, Chain seemed surprised because he thought Fleming had died.[74]

[66] Ibid., 132.
[67] James Howie, "Penicillin: 1929-40," *British Medical Journal (Clinical Research Edition)* 293, no. 6540 (July 19, 1986): 158, accessed February 24, 2017; "Discovery and Development of Penicillin," American Chemical Society.
[68] "Discovery and Development of Penicillin," American Chemical Society.
[69] Ibid.
[70] Ligon, "Penicillin: its discovery and early development."
[71] "Discovery and Development of Penicillin," American Chemical Society; Sidebottom, "The Discovery of Penicillin," 60.
[72] "Discovery and Development of Penicillin," American Chemical Society; Sidebottom, "The Discovery of Penicillin," 60-61.
[73] Ligon, "Penicillin: its discovery and early development."
[74] Sidebottom, "The Discovery of Penicillin," 59.

Penicillin Aids Against Hitler

Scientists from the United States soon became involved with the penicillin experiments when a doctor from New York named Henry Dawson successfully purified some penicillin and administered it to a patient.[75] Dawson did not administer high enough doses of the drug and his patient died soon after the experiment began.[76] Florey visited the United States to advocate the use of penicillin.[77] While in the United States, he reconnected with an old colleague who became the chair of the Medical Research Committee in the United States. This meeting promised government funding for the mass production of penicillin.[78] The reason Florey went to the United States to start the production of penicillin is because British pharmaceutical companies refused to begin production on the costly experimental drug due to the constraints on materials and manpower that stemmed from the war.[79]

Production of the drug was time-consuming and relatively expensive as well due to the amount of materials and manpower required. This further complicated the process during the war. Because it took so long, many companies and universities, including Berkeley in California, began the development of the traditional form of penicillin Florey and Chain produced while simultaneously attempting to form a synthetic version of the drug, which would speed up production.[80] Synthetic penicillin, however, was not realized until over a decade later. This meant distribution had to wait on the long process that was currently in use. Penicillin cost fifty

[75] Ligon, "Penicillin: its discovery and early development."
[76] Ibid.
[77] Sidebottom, “The Discovery of Penicillin,” 60.
[78] Ibid.
[79] "Discovery and Development of Penicillin," American Chemical Society.
[80] "HUNDREDS OF EXPERTS WORK ON PENICILLIN: Florey Tells of Efforts to Get More for War Casualties," *The New York Times*, June 8, 1944, accessed February 24, 2017.; Fleming, "Penicillin"; Earle Ennis "Growing Germs to Fight Germs: Berkeley Takes Leading Role in Penicillin Drama," *Oakland Tribune*, September 19, 1943, accessed March 8, 2017.; "Until Synthetic Method Is Devised, Production Of Penicillin Will Remain Slow and Costly," *Shiner Gazette*, April 13, 1944, accessed April 5, 2017.

thousand dollars to make one kilogram and took a complete day to produce.[81] The United States War Production Board saw the results of drug trials, and ordered large-scale production in 1943. The Board hoped to have a large supply of penicillin for Operation Overlord, the invasion of Normandy.[82] The pressing needs of the war effort and slow development time forced many companies to prioritize the distribution of penicillin to the military rather than civilian hospitals on the home front.[83] By the end of the war in 1945, almost seven trillion units of penicillin were made in the United States and Great Britain every year. This overshadowed the original production capacity of twenty-one billion units.[84]

Figure 4: Women working in a Penicillin factory during World War II [85]

[81] "HUNDREDS OF EXPERTS WORK ON PENICILLIN," *The New York Times.*
[82] "Discovery and Development of Penicillin," American Chemical Society.
[83] Ibid.
[84] Ibid.
[85] Rupert Shepherd, *A Penicillin Factory, Girls filling bottles*, 1945, in *Wikimedia*. Accessed August 29, 2017.

Florey and another colleague by the name of Hugh Cairns traveled to North Africa to test the drug on people wounded in the war.[86] The drug was shown to work on soldiers serving on the frontline, greatly reducing the number of casualties from infections during the latter years of the war.[87] During the war, the British government hailed Fleming as a hero in an effort to boost the morale not only among soldiers fighting overseas but also to citizens who remained at home.[88] This worked for the most part, eliminating the fear from past wars and conflicts. This fear was that soldiers were not sure if they would die from a bullet wound or an infection caused by the bullet wound. Now, most soldiers did not have to fear a slow death from an infection caused by a non-life-threatening gunshot wound.

As of 1943, many scientists were still not sure why penicillin worked, but most did not care because it did.[89] In the same year, Fleming remarked that during his early experiments he did not believe that penicillin was, "the most powerful therapeutic substance yet used to defeat bacterial infections in the human body." Nevertheless he felt compelled to start a colony of the mold.[90] This same colony of mold was the one used in the development of penicillin until at least 1943.[91] By 1950, however, scientists discovered penicillin affects respiration and production of glutamic acid (which produces the cell walls in bacteria) in the infectious bacteria, allowing penicillin and/or the immune system to kill the bacteria without harming the host (though for some unknown reason, penicillin is toxic to guinea pigs).[92]

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[86] Sidebottom, "The Discovery of Penicillin," 61.
[87] "Penicillin," *The New York Times*, September 3, 1943, accessed February 24, 2017.; Lucille Wright, "Miracle Medicine Writing History at Army Hospital," *The Ogden Standard-Examiner*, July 5, 1943, accessed March 8, 2017.
[88] Sidebottom, "The Discovery of Penicillin," 63.
[89] "Penicillin," *The New York Times*.
[90] "DISCOVERER TELLS PENICILLIN STORY: Dr. Alexander Fleming Speaks From London in Broadcast to Accept Award Here," *The New York Times*, December 14, 1943, accessed February 24, 2017.
[91] Ibid.
[92] Karl H. Beyer, *Pharmacological Basis of Penicillin Theory* (Springfield, IL: Charles C. Thomas Publisher, 1950), 64, accessed February 24, 2017.

Three Cheers for Penicillin!

When the effects of penicillin became known to the public during World War II, the drug gained almost instant praise. Both the scientific and public communities gave the drug and the doctors behind the discovery (mainly Fleming) legendary status for discovering this new drug. Unlike other medical discoveries or debates of the past, there were very few who refuted the power of this drug made from a simple mold.

Though it was initially used to treat wounds on the front lines during World War II, penicillin was discovered by the public to treat many other diseases. Scientists had already known about these treatments, however. One disease that penicillin proved to be effective against was diphtheria. When penicillin became more widely available to doctors and the public after the war, a doctor named A. J. Levy in Illinois noted that a weeklong treatment of penicillin in either a spray applied directly to the affected area or a lozenge taken orally was very effective at destroying diphtheria. After this weeklong treatment, Dr. Levy noted the patient still did not show signs of diphtheria even a year after the treatment ended.[93] The newspaper praises the use of penicillin in the treatment of diphtheria due to its rapidity and effectiveness.

An article appearing in *The Daily Capital News* in Jefferson City, Missouri one year after the end of World War II noted that penicillin had a high success rate in curing gonorrhea, but some doctors differed on the method of delivering the drug.[94] Both the treatments discussed in the newspaper involved mixing the penicillin with another substance, but the success rates for the treatments did not differ substantially.[95] A similar article that appeared in *The Sandusky Register* in Ohio noted that penicillin was used to treat a kidney infection caused by

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[93] "Penicillin Lozenges May Provide Cure for Diphtheria Carriers," *Freeport Journal-Standard*, April 2, 1948, accessed February 24, 2017.
[94] William A. O'Brien, "Penicillin Destroys Gonorrhea Germs," *The Daily Capital News* (Jefferson City), October 11, 1946, accessed February 24, 2017.
[95] Ibid.

staphylococcus.[96] All three of these articles confirm that Fleming's initial tests were no fluke, but rather the birth of a highly effective medicine.

Being able to treat diseases like gonorrhea and staphylococcus quickly brought much praise to penicillin. Howard Blakeslee, a writer for the Associated Press wrote articles for newspapers across the country praising the drug, calling it a "New Era in Medicine" and stating that sulfas, one of the previous methods for the treatment of bacterial diseases, "pales" in comparison to penicillin.[97] Another newspaper author called the drug "magic" and declared "king and commoner alike" wanted to use the drug because of its wide array of applications.[98] This author states that while this is great, penicillin was not the greatest or the penultimate discovery in medicine. Rather, the author called the discovery a step towards a greater goal in medicine that the technology the time just could not achieve (this is the closest thing that was found to criticism about the new drug).[99]

Many other newspapers provided similar praise, calling the drug a miracle of modern science or even one of the greatest discoveries of all time. One newspaper even wondered how many accidental discoveries were discarded because a scientist with the curiosity of Fleming was not there to investigate them.[100] All this praise accentuated the fact that penicillin had no ill side effects. Much praise also came from the fact that many scientist believed that there were no toxic doses.[101] We now know that penicillin does have a toxic dosage, albeit a very high one.

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[96] Herman N. Bundesen, "Your Health," *The Sandusky Register*, February 17, 1948, accessed February 24, 2017.
[97] Howard W. Blakeslee, "Penicillin Pales Glory of Sulfas; No Bad Reactions," *Eau Claire Leader*, August 3, 1943, accessed March 8, 2017.; Howard W. Blakeslee, "Penicillin is New Era in Medicine," *The Bee* (Danville), August 2, 1943, accessed March 8, 2017.
[98] Al Jedlicka, "Penicillin, Latest Triumph of Medical Research, Marks Another Long Step Towards Distant Goal," *Shiner Gazette*, April 13, 1944, accessed February 24, 2017.
[99] Ibid.
[100] "Penicillin," *The New York Times*, September 3, 1943, accessed February 24, 2017.
[101] "Mould Kills Bacteria," *The Science News-Letters* 17, no. 475 (May 17, 1930): 314, accessed February 24, 2017.

Looking back at the methods of treating various diseases before penicillin, it is no wonder that many people praised the drug so quickly. Compared to the long, drawn-out, and sometimes dangerous treatment regimens of yesteryear, this new treatment was rapid and held virtually no risk. In the case of diphtheria, a patient could now avoid sulphur treatments and the hazardous throat scrapings. After penicillin patients could be treated with a simple drug that was either administered orally, intravenously or directly to the affected site for about a week, and the patient did not even have to worry about the disease recurring for a whole year!

The risk of using the potentially hazardous procedures went down, bringing the total death rate down. A soldier shot on the battlefield no longer had to worry about dying from an infection that he received from the wound. The closest event in terms magnitude prior to penicillin was the invention of the vaccination process, preventing people from getting sick from a disease before they even had it. In the eyes of the people who saw the introduction of penicillin, this was a revolution of medicine. What vaccines did for viruses, penicillin did of bacterial infections. This high praise catapulted Fleming into legendary status, ensuring that his name would be remembered throughout history as the man who accidentally discovered a cure-all of some of the most deadly diseases of the Nineteenth and Twentieth Centuries.

Conclusion

Bacterial infections like diphtheria, gonorrhea, pneumonia, and staphylococcus were once the scourge of mankind. Not only were these diseases dangerous, but prior to the discovery of penicillin treatments for these diseases were sometimes hazardous. Harsh chemicals, tonics with unknown ingredients, and potentially dangerous procedures contributed to the deadliness of these diseases. Doctors, however, did not know any other way to treat these illnesses. Doctors only knew how to treat visible symptoms of these diseases.

The accidental discovery of the properties of a mold called *Penicillium* by Alexander Fleming in 1928 changed all of this. Fleming discovered that this mold inhibited the growth of many bacteria that caused dangerous diseases. Though many dismissed him when he first published his findings, experiments by Howard Florey and Ernst Chain at the beginning of World War II showed the world that Fleming's discovery had merit. Though the drug was difficult to produce due to material and time constraints, many companies and universities began production immediately because they recognized the drug's potential during.

Though the drug did not reach the hands of the public until after the World War II, reaction was swift and overwhelmingly positive. This positive reaction by the scientific and public communities was due to the drug's safety and relatively short treatment time compared to the old treatment regimens. This propelled Alexander Fleming into stardom, making the mention of his name relevant to this day.

Fleming received fellowships from all over the United Kingdom, Europe, and North America.[102] He received eighteen honorary doctorates from numerous universities, and was named Commander of the Legion of Honor in France. Many medical societies named him as a senior member, and the King of Britain knighted him.[103] His grandest honor came in 1945 when he, along with the two men who found a way to produce penicillin for mass production and use (Howard Florey and Ernst Chain), were awarded the Nobel Prize in Physiology or Medicine for the discovery of penicillin.[104]

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[102] "Sir Alexander Fleming, M.D., D.Sc. F.R.C.P., F.R.C.S., F.R.S," 733-734.
[103] Ibid.
[104] Sidebottom, "The Discovery of Penicillin," 45.

Four years later in 1949, his wife, Sarah McElroy, died leaving behind Dr. Fleming and one son, Robert.[105] In 1953, two years before his death, Fleming married a Greek bacteriologist by the name of Amalia Coutsouris, who aided the allies during World War II.[106] On March 11, 1955, Alexander Fleming died suddenly in his home of a heart attack.[107] He was seventy-three years old. He will forever be etched in the annals of history because he discovered the bacteria-killing properties of a mold.

Though he knew his discovery was a gift to the world, Fleming left us with a few wise words, "I would like to sound one note of warning. Penicillin is to all intents and purposes non-poisonous so there is no need to worry about giving an overdose and poisoning the patient."[108] He continued, "It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body… Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant." He left us with one final warning, "Moral: If you use penicillin, use enough."[109]

Today, we know not only is the under usage of penicillin dangerous, but the over prescription of it (especially for diseases it does not treat such as viruses) is as well. Both the over- and under-prescription opens the door for diseases to grow immune. In 2015, the World Health Organization launched a campaign to fight antibiotic resistant diseases such as tuberculosis and new resistant staphylococci.[110] The need for new antibiotics and new measures in prescribing them is increasing, possibly leading the world into a post-antibiotic age. Fleming's

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105 "Sir Alexander Fleming, M.D., D.Sc. F.R.C.P., F.R.C.S., F.R.S," 734.
106 Ibid.
107 Ibid. 732.
108 Alexander Fleming, "Penicillin," 1945.
109 Ibid.
110 Marie-Paule Kieny, "WHO's new priority list of antibiotic-resistant bacteria looks beyond the scourge of tuberculosis," *Statnews.com*, March 13, 2017, accessed April 6, 2017. https://www.statnews.com/2017/03/13/tuberculosis-who-bacteria-antibiotics/.

discovery turned out to be a double-edged sword in this modern era. Many have taken these medicines for-granted. Most people today really worry about contracting diphtheria, and many have never even heard of it. Neither does one have to worry about the long-term consequences of the more common infections either, such as strep and gonorrhea. Many have become complacent in penicillin's usage, aiding these diseases to become more resistant. There are already diseases that have evolved to become resistant to antibiotics, such as Methicillin-Resistant Staphylococcus Aureus (commonly known as MRSA). Let us hope this new increase in resistance to penicillin and its counterparts can be stopped and does not produce more of these deadly diseases.

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