Penicillin: the Commodification of Medication, and World War II

By

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Strep throat, bronchitis, and gonorrhea are all relatively common infections, with distinct symptoms and causes. However, they have one distinct similarity that is unrelated to their symptoms, instead focusing on they are treated. Each of these infections can be treated with a member of the penicillin family, a widely used antibiotic originally obtained from the mold. Penicillin, its production, and its uses have changed over time, creating a vital commodity that treats previously fatal infections. Due to a combination of media attention and wartime necessity, penicillin went from an under-researched curiosity to a vital method of treating infections during World War II. In particular, researchers such as Howard Florey and the Oxford University team, and the team in Delft, the Netherlands, played a significant role in the shift from less effective treatments such as sulfanilamide to penicillin. This paper will cover methods used to treat infections prior to penicillin's discovery, the discovery of penicillin, research that was conducted throughout the 1930s and 1940s, the impact penicillin had on World War II casualties, and public perception of the drug. It will also briefly discuss the ways in which penicillin has been produced.

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the introduction of penicillin into medical regimens. In many cases, these numbers improved again with the addition of penicillin.

Alexander Fleming is the researcher most commonly credited with the discovery of the antibiotic properties of . Despite the lack of research Fleming conducted, he and his accidental discovery have become something of a legendary event. While he does deserve a portion of the credit, his discovery was, after all, an accident. In 1928, after taking a brief vacation, he returned to his lab to see the staphylococcus cultures he had been working with had been contaminated with "various micro-organisms," or mold.[14] Fleming noted that when the staphylococcus colonies came into contact with the mold, they began to break down, suggesting that the mold had a "bacteriolytic" property.[15]

Upon discovering this, Fleming did conduct a small amount of research and later published his findings in the in 1929. For example, he noted that heating it for one hour at a relatively high heat had no effect, boiling the liquid reduced its effectiveness, and "autoclaving [it] for 20 minutes at 115 degrees C. practically destroy[ed] it." He also found that penicillin dissolves in water and saline solutions and can be safely filtered with a Seitz filter to obtain a "sterile active mould broth."[16] He tested the toxicity of penicillin by injecting 20 cubic centimeters of the antibacterial broth into a rabbit and found it did not harm the rabbit. He also found eight hours after adding penicillin to a staphylococcus

appeared to doubt the true value of penicillin, as he heavily emphasized his research of penicillin's ability to break down cells rather than its antibacterial abilities.[18]

It was not until later researchers, such as the team in Delft, the Netherlands and Dr. Howard Florey and the team at Oxford University, that penicillin-related research became more intense. This research did not begin until after the outbreak of World War II. Florey, who was one of the first researchers to determine that penicillin had vast potential in clinical settings, was part of the Oxford team that included Ernst Chain, Edward Abraham, and Norman Heatley. In 1940, the team was able to conduct the first trials on living organisms—in the case of their tests, mice.[19] Eight mice were injected with a strain of Streptococcus, a bacterium that can cause strep throat, scarlet fever, and other infections.[20] Four of the mice were left as a control to determine what would occur if the mice were left untreated, while four were injected with purified penicillin extracted from mold. Within hours, the control mice had died, while mice that had been treated with penicillin had survived the night.[21] While the mice that had been treated eventually died, they survived three times as long as the control group.[22]

According to John Patrick Swann, the Oxford team "produced enough penicillin to treat six patients," though some died due to complications or the lack of medication.[23] The most well-known example of this is the case of Albert Alexander, a middle-aged man from Oxford, P.02 0 Tdrj0.26[(e)-34

England whose eye had been infected with streptococcal and staphylococcal bacteria. Norman Heatley claimed that upon beginning Alexander's treatment, he observed "dramatic improvement." At the time of his treatment, Alexander was given the largest single dose of penicillin received by any human: 200 milligrams. This was followed by several additional doses. However, there was not enough penicillin to see his treatment through, and he died one month after he stopped receiving medication.[24] When he was admitted to the hospital, Alexander was originally treated with a sulfa drug, which resulted in no improvement and "gave him a terrible rash."[25]

As World War II continued, research began in the Netherlands. Researchers had access to a variety of fungi through the Centraalbureau voor Schimmelcultures (CBS). The CBS's collection of fungi included . Upon their occupation of the Netherlands, Germany requested the CBS's sample of

several tests—rabbits and mice, for example, were treated with penicillin after being infected by a strain of staphylococcus and recovered with no notable toxic effects.[28]

Initially, it was unclear to the Delft team if the substance extracted from their mold was the same substance as the penicillin Fleming extracted from . As a result, they referred to it as Bacinol, though it was later discovered to be the same substance. However, this had the

infected burns and septic wounds."[37] Unlike other penicillin-based drugs, vivicillin could "be produced in large quantities at comparatively low cost."[38] The ability to produce large amounts of penicillin-derived drugs was vital; as a result of the difficulty producing large amounts of medication affordably, what little penicillin was produced was exclusive to military use. With the ability to produce more medication affordably came the ability to potentially open its use to civilians.

Reports from the Defense Casualty Analysis System (DCAS) further support the idea that penicillin played a significant role in the war.

generally accepted number is somewhere around five million.[40] When considering that the German military relied primarily on sulfa drugs and did not have access to penicillin, it becomes clear that this may have had some impact, regardless of how minimal.

One account in the written by two British military doctors claimed that they received over 700,000,000 doses of penicillin during the first half of 1944 alone from both American and British producers; however, their use of penicillin was limited to specific types of injuries and illnesses. Despite the limits on usage and the limited number of patients treated, the authors were confident that penicillin made a drastic difference in the number of deaths. According to the article, there were "many instances where the man's life was beyond question saved solely because this drug was available."[41] Furthermore, they discussed their observations of the success of wounds treated with penicillin versus sulfa drugs. In one case, 170 soft tissue wounds were treated using penicillin powder, with almost every wound healing fully. In another, 68 wounds were sutured and treated with sulfa drugs, while a second group of wounds were sutured and treated with penicillin. The wounds treated with sulfa drugs failed to heal properly or completely 23 percent of the time, while similar failures were noted in only 17 percent of the wounds treated with penicillin.[42] A similar trend was noted in the treatment of femur fractures—slightly over one percent of femur fracture patients died due to infection when treated with penicillin, while over eight percent died while treated using methods

[40] "World War II," Encyclopedia Britannica, Encyclopedia Britannica, Updated March 14, 2021, https://www.britannica.com/event/World-War-II.

[41] J. S. Jeffrey and Scott Thomson, "Penicillin In Battle Casualties," 2, 4346 (July 1944): 2, https://lib-proxy.radford.edu/login?url=https://www.jstor.org/stable/20345710.

[42] J. S. Jeffrey and Scott Thomson, "Penicillin In Battle Casualties," 2.

standard for the time. About eight percent of patients required amputation when treated using the standard methods, compared to only three percent when they were treated using penicillin.[43]

It is clear that penicillin played a significant role in reducing death and long-lasting injuries during World War II. The medication's benefits were obvious as early as Florey's tests

Heatley's lab used "cookie tins, pie tins, milk bottles, trays, plates, and bedpans," to ferment penicillin on the surface of cultures.[47] In the case of penicillin, fermentation refers to the growth of the mold. One of the commonly used methods was a ceramic bed pan, which Heatley designed. In worst case scenarios, vessels as obscure or unusual as a dog bath were used.[48] The nutrient liquid used for fermenting penicillin tended to be corn steep liquor; Andrew Moyer was the mind behind this discovery.[49] Corn steep liquor results from the creation of cornstarch, and "proved an excellent growth medium" that "boosted penicillin production."[50] The shift to corn steep liquor from the yeast extract that was previously used increased production by thirty times, drastically aiding mass production.[51]

The shift from surface fermentation to submerged fermentation was, by all accounts, a vital development. In this method of fermentation, the mold was grown in large drums that were constantly moved to provide the mold with oxygen. This method resulted in a drastic increase in the amount of penicillin one culture could produce, as was able to grow throughout the vat rather than growing only on the surface of a small, shallow container.[52] One of the first, if not the first attempt to discover a more efficient alternative to surface fermentation was the "rotating pressure fermenter" developed by Color Laboratory.[53] By 1944, a factory in New York owned by Pfizer contained 14 fermentation drums, each of which could hold thousands of gallons of the nutrient liquid.[54]

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[47] Heatley was a researcher and manufacturer of penicillin at Oxford. Coniff, "Penicillin: Wonder Drug of WW2," 41.
[48] S. N. Arseculeratne and G. Arseculeratne, "A re-appraisal," 345.
[49] Peter Neushul, "Science, Government, and the Mass Production of Penicillin," , 48 (1993): 376, SuperSearch.
[50] Coniff, "Penicillin: Wonder Drug of WWII," 41.
[51] Neushul, "Science, Government, and the Mass Production of Penicillin," 379.
[52] Swann, "The Search for Synthetic Penicillin," 156.
[53] Neushul, "Science, Government, and the Mass Production of Penicillin", 381.
[54] Coniff, "Penicillin: Wonder Drug of WW2," 43.

"100 times more powerful than … sulfa drugs," the article once again referred to penicillin as a "miracle" with "amazing properties."[62]

It is clear that many of the most well-known newspapers in the United States have prominently featured articles describing penicillin and its role in World War II. Unlike articles published by researchers, such as the Oxford team's article in and Fleming's original article, these are easily accessible to the public. Notably, Fleming's mentions of 's antibiotic properties went largely unnoticed until World War II, when various research teams began to look more closely at it. This could be partially attributed to the lack of media attention n

that he supported this decision.[64] It is likely such regulations caused concern and frustration in the general public, as media consistently discussed penicillin and cures associated with it, such as that of Anne Miller, a young woman who became seriously ill after a miscarriage.[65] Unlike in Britain, however, the United States aimed to produce enough penicillin for use during the war and for civilians if other treatments proved ineffective—this likely improved the opinion Americans had toward penicillin.[66] To support this need, production increased significantly during 1944, when the first commercial plant for mass production, owned and operated by Pfizer, began operating, resulting in other companies following their example.[67] Penicillin continued to be pushed as something of a miracle cure throughout the early to mid-1940s, especially in the United States, despite its rarity and restrictions. This potentially canceled out any negative perceptions associated with the lack of penicillin and any regulations resulting in its exclusive use for the war effort. For example, in the United States, comic books for children outlined penicillin's usefulness.[68] Notably, penicillin was not exempt from the overwhelming amount of propaganda designed to rally civilians, soldiers, and workers during World War II. Posters were hung in places such as fermentation plants, one of which contained a message for

"types" of penicillin produced and sold by different pharmaceutical companies, there are different forms of penicillin. During World War II, for example, penicillin was primarily produced in two forms: a powdered form, and a liquid form. According to one account, the powdered form was primarily used for soft tissue wounds. It was put on wounds, sometimes several times, to prevent infection before being sutured closed.[70] Powders were also used on fractures that broke the skin, head wounds, and face wounds.[71] Injections, on the other hand, were used for infections that had already taken hold, such as gangrene.[72] Penicillin was also injected following the closure of wounds with powder penicillin, either to prevent or cure infection.[73] As penicillin has a relatively short half-life, injections were done frequently—sometimes as often as every three hours, as was the case with Albert Alexander, the first person the Oxford team treated with penicillin.[74] However, due to the limited nature of penicillin, especially early on, patients' urine was collected to recover penicillin. The urine was purified, and the penicillin was rem (s)-11 th52 Tme

penicillin and media attention brought penicillin to the forefront of many people's minds upon the outbreak of World War II.

Bibliography

Primary Sources

"96.1% of 1,375,000 Wounded Yanks Saved in Army Hospitals in Europe, Chief Reports." May 28, 1945. https://search-proquest-com.lib-proxy.radford.edu/hnpwallstreetjournal/docview/107316600/DC956DE4169D4E9APQ/21?accountid=13401.

Bernstein, Adele. "Medical Group To Convene in D.C. Sept. 30." , September 20, 1943. https://lib-proxy.radford.edu/login?url=https://www-proquest-com.lib-proxy.radford.edu/historical-newspapers/medical-group-convene-d-c-sept-30/docview/151682982/se-2?accountid=13401.

Cable to

Florey, Howard W. “The Use Of Micro-Organisms For Therapeutic Purposes.”

Self, Sydney B. “Miracle Drugs Make This the ‘Safest’ War for Soldiers Ever Fought by Americans.” October 22, 1942. https://search-proquest-com.lib-proxy.radford.edu/docview/131418546/5276F42571864E1EPQ/7?accountid=13401.

Washington Bureau of Chicago Sun. “More Penicillin To Be Available.” , September 26, 1943. https://lib-proxy.radford.edu/login?url=https://www-proquest-com.lib-proxy.radford.edu/historical-newspapers/more-penicillin-be-

51 (2002): 185-200. https://doi.org/10.1016/s0065-2164(02)51006-6.

Centers

Quinn, Roswell. “Rethinking Antibiotic Research and Development.”

103, no. 3 (March 2013): 426-434. SuperSearch.

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