From Small Wonder to Big Salvation:

How the Mass Production of Penicillin Became Possible in the Early 1940s

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Historical Paper

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In this historical project, I wanted to choose a topic during World War II (WWII) and the post-war era when the world witnessed the U.S.'s thriving medical sciences. In my research process, I found the history of penicillin truly intriguing because it demonstrates an almost unthinkable journey in which an accidental scientific discovery by Alexander Fleming in 1928 transitioned from a British laboratory into a momentous turning point in American history with penicillin in American mass production lines in the early 1940s. After it arrived in the U.S., penicillin's mass production was made possible in only a span of three years between 1941 and 1944, and it eventually saved millions of lives worldwide both during and after the war.

In my research, I collected three categories of resources. First, I researched the discovery of penicillin and subsequent scientific research in Europe in the 1930s and early 1940s. Both primary sources (e.g., Fleming and other scientists' medical publications) and secondary sources (e.g., periodicals depicting the early history of penicillin) helped me understand the development of penicillin in the scientific realm.

Second, a critical turning point in the history of penicillin was when Howard W. Florey and his research team at Oxford University turned to America for help with penicillin production in 1941. Most primary sources briefly mentioned the successful collaboration between American and British scientists in penicillin's clinical tests. However, why American scientists happened to be ready to meet the needs of the Oxford team remained largely unknown to the public. I decided to fill this gap. I wrote about how several generations of American scientists, supported by federal funding offered by the U.S. Department of Agriculture (USDA), had devoted themselves to developing mold fermentation methods since 1916, without which the production of penicillin in large quantities was impossible.

Finally, another vital piece in the historical puzzle of penicillin was how penicillin was put on the production lines of American pharmaceutical manufacturers (e.g., Merck & Co., Pfizer & Co., etc.) and effectively distributed for treatment. I found that the U.S.'s entry into WWII in December 1941 was a crucial moment when American pharmaceutical companies were motivated to mass-produce penicillin. My research showed that the USDA, the Office of Scientific Research and Development (OSRD), and the War Production Board (WPB) played diverse roles, all critical in connecting scientists, research labs, corporations, production facilities, and distribution agencies.

My paper is organized into three main sections to show the three essential processes mentioned above. Progressing chronologically, my paper analyzes the roles of key agents in academia, government agencies, and corporations in each stage. With more focus on the various roles played by several U.S. governmental agencies, I explained the necessary conditions and contexts for the mass production of penicillin to become a reality in the early 1940s. In conclusion, I emphasized the indispensability of the U.S. government, which was less visible and underappreciated in the history of penicillin, in supporting research and promoting researchindustry partnerships.

With abundant antibiotics available today, it is hard to imagine the dangers of infections in a world without them. In 1900, the average life expectancy was only 46.3 years for men and 48.3 years for women in the U.S.¹ Infectious diseases such as smallpox, cholera, diphtheria, pneumonia, and typhoid fever accounted for the high morbidity and mortality.² In the history of medicine, antibiotic substances were noted in theory as early as in Ancient Egypt, around 1000 B.C.³ Still, the naturally occurring antibiotics could not be verified until the 20th century. The amazing, accidental discovery of penicillin in a British laboratory in 1928 would eventually revolutionize how people fought infection. However, with no methods to mass produce the treatment, it initially offered little significant medical value. During World War II (WWII), American pharmaceutical companies overcame this hurdle by developing methods to scale up the production and distribution of penicillin. American scientists' mold fermentation research, funded by the U.S. Department of Agriculture (USDA) about 25 years prior, paved the way for this effective collaboration between American and British scientists in producing penicillin in large quantities. The U.S. government's indispensable role in building the research-industry network was vital in accelerating the mass production of penicillin in the early 1940s.

The Discovery of Penicillin in Great Britain

In 1877, Louis Pasteur and Jules François Joubert, two French scientists, made the first observations of naturally occurring antibacterial substances.⁴ However, the true significance of

¹ Elizabeth Arias and Jiaquan Xu, "United States Life Tables, 2018," *National Vital Statistics Reports* 69, no. 12 (November 2020): 36, https://www.cdc.gov/nchs/data/nvsr/nvsr69/nvsr69-12-508.pdf.

² W.A. Adedeji, "The Treasure Called Antibiotics," *Annals of Ibadan Postgraduate Medicine* 14, no. 2 (December 2016): 56-57, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5354621/.

³ H.W. Florey, "Penicillin: A Survey," *British Medical Journal*, no. 2 (4361) (August 1944): 169-171, https://pubmed.ncbi.nlm.nih.gov/20785574/.

⁴ Ibid.

this discovery was not recognized until about half a century later. In 1928, Alexander Fleming, a Scottish bacteriologist who worked at St. Mary's Hospital in London, noticed by chance that the bacteria he seeded in staphylococcus cultures began to break down when it came into contact with a greenish mold, later identified as *penicillium notatum*.⁵ As outlined in his first publication on this discovery, Fleming was initially intrigued by penicillin's ability to break down cells.⁶ Although his primary attention was not on penicillin's antibiotic effect, Fleming's accidental discovery of penicillin opened a new door for medical scientists to study antibiotic substances.

Throughout the 1930s, the practical value of penicillin was still in doubt, mainly due to the lack of feasible methods to isolate and mass-produce penicillin as a therapeutic compound for clinical use. In 1936, Australian scientist Howard W. Florey and his research team at Oxford University were devoted to solving this problem. On May 25, 1939, Florey's research team at Oxford conducted their first successful clinical penicillin test on mice, signifying a breakthrough in penicillin-related research. They produced small quantities of the first stable products containing penicillin from surface cultures and established penicillin's chemotherapeutic properties. In 1940, Florey's research team was ready to move forward to conducting clinical tests on patients.

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⁵ Gwyn Macfarlane, *Alexander Fleming: The Man and the Myth* (Cambridge, MA: Harvard University Press, 1984).

⁶ Alexander Fleming, "On the Antibacterial Action of Cultures of a Penicillium with Special Reference to Their Use in the Isolation of B. influenzae," *British Journal of Experimental Pathology* 10, no. 3 (June 1929): 226-23, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2048009/.

⁷ Robert Gaynes, "The Discovery of Penicillin – New Insights After More Than 75 Years of Clinical Use," *Emerging Infectious Diseases* 23, no. 5 (May 2017): 849-853, https://wwwnc.cdc.gov/eid/article/23/5/16-1556 article.

⁸ Peter Neushul, "Science, Government, and the Mass Production of Penicillin," *The Journal of the History of Medicine and Allied Sciences* 48, no. 4 (October 1993): 371-395, https://academic.oup.com/jhmas/article-abstract/48/4/371/777929.

⁹ Diane Bernard, "How a Miracle Drug Changed the Fight against Infection during World War II," *The Washington Post*, July 11, 2020, https://www.washingtonpost.com/history/2020/07/11/penicillin-coronavirus-florey-wwii-infection/.

Unfortunately, they encountered a formidable hurdle. With WWII in full swing across Europe, the British pharmaceutical companies could not produce penicillin on a large scale due to the war-related constraints on materials and workforce. The Oxford team was also worried that their penicillin samples would fall into the hands of the Nazi government, which then relied on sulfanilamide drugs produced by German companies. ¹⁰ They decided to turn to the U.S., which remained officially neutral in the war until December 1941, for help. The journey of penicillin from the British laboratory to the U.S. production line had begun.

The Collaboration between American and British Scientists

When Florey's research team at Oxford succeeded in penicillin's clinical tests in 1939, it did not catch much attention in the American public media. The first penicillin coverage in *The New York Times* appeared as late as October 20, 1940. This first report contained six pieces of news on science, and one of them was on penicillin. Penicillin was compared to sulfanilamide, the then germ-killer produced by German companies. Waldemar Kaempffert, the *Times* science news writer, sounded quite doubtful about this discovery and wrote, "It looks as if penicillin contains something as powerful as sulfanilamide. What is it? Nobody knows as yet."

In February 1941, the Oxford team published another milestone work with their successful clinical tests on patients. ¹³ They agreed that penicillin should leave the war-ravaged

¹⁰ Bernard, "How a Miracle Drug Changed the Fight against Infection during World War II."

¹¹ Waldemar Kaempffert, "Science the News: A New 'Sulfanilamide'," *The New York Times*, October 20, 1940, https://www.nytimes.com/1940/10/20/archives/science-in-the-news-electrically-warmed-divers.html?searchResultPosition=1.

¹² Ibid.

¹³ E.P. Abraham, E. Chain, C.M. Fletcher, A.D. Gardner, N.G. Heatley, and M.A. Jennings, "Further Observations on Penicillin," *Lancet* 238, no. 6155 (August 1941): 177–88, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(00)72122-2/fulltext.

Europe and enter a safer market. In June 1941, to avoid their penicillin samples falling into the Nazi's hands, Florey and Heatley rubbed their lab coats with the mold, knowing that the chemical would live for a long time on the fabric, and flew to the U.S.¹⁴

These two scientists were eager to share the magic of penicillin with their American fellows. They first visited Florey's old friend John Fulton, a physiology professor at Yale University. With Fulton's help, Florey and Heatley met with Charles Thom, the USDA's principal mycologist, Robert Coghill, the director of the USDA's Fermentation Division, and Andrew Jackson Moyer, the director of the USDA's Northern Regional Research Laboratory (NRRL) in Peoria, Illinois. Florey and Healey also went to Washington, D.C., where they met with Ross G. Harrison, Chairman of the National Research Council (NRC), and Percy Wells, head of the Eastern Regional Research Laboratory (ERRL).

The British scientists described their production problems at these meetings. It became clear that the NRRL in Illinois, where an elite group of fermentation specialists had been developing large-scale mold fermentation, would be an excellent place to work with Florey's team. One month later, the British and American scientists began their collaborative work in Peoria, Illinois. By adopting the American scientists' fermentation method, they figured out how to utilize a new fungal source from a moldy cantaloupe in a Peoria market as a new medium, making producing larger amounts of penicillin possible.¹⁸

 $^{^{14}}$ Bernard, "How a Miracle Drug Changed the Fight against Infection during World War II."

¹⁵ Robert A. Kyle, David P Steensma, and Marc A. Shampo, "Howard Walter Florey – Production of Penicillin," *Stamp Vignette on Medical Science* 90, no. 6 (June 2015): e63-e64, https://www.mayoclinicproceedings.org/article/S0025-6196(15)00304-3/pdf.

¹⁶ Ibid.

¹⁷ Peter Neushul, "Science, Government, and the Mass Production of Penicillin," *The Journal of the History of Medicine and Allied Sciences* 48, no. 4 (October 1993): 371-395, https://academic.oup.com/jhmas/article-abstract/48/4/371/777929.
https://academic.oup.com/jhmas/article-abstract/48/4/371/777929.
https://academic.oup.com/jhmas/article-abstract/48/4/371/777929.
https://academic.oup.com/jhmas/article-abstract/48/4/371/777929.

Florey and his Oxford team remained unrecognized for their contributions to the successful penicillin production until December 1943, when the American Pharmaceutical Manufacturers Association offered them an award for their experimental work in treating disease. Two years later, Fleming, together with Florey and Ernst Chain (one of Florey's team members), won the 1945 Nobel Prize for Physiology and Medicine (see Appendix A). It was not until then that the public started to understand the significance of the discovery of penicillin.

However, even less acknowledged and underappreciated in the history of penicillin were the heroes behind the scenes at the USDA, who collaborated enthusiastically with British scientists and offered their long-developed mold fermentation methods to make the mass production of penicillin a reality. The American scientists at the USDA began to study fermentation as early as 1916.²⁰ The first generation of chemists led by Charles Thom collected numerous Aspergilli and penicillium molds and closely examined these fungi's oxalic acid production capability. Their research helped develop mold fermentation methods for mass-producing gluconic acid. In the 1920s, the USDA started working with Pfizer & Co., Inc. — which would become the world's largest penicillin producer after 1941 — to develop mold fermentation methods.

In the 1930s, a group of scientists in Arlington, Virginia, made breakthrough progress in fermentation. In 1935, they patented a "submerged" fermentation method by which a mold was grown throughout the medium.²¹ This method was eventually used for mass-producing penicillin in 1941. In 1937, Andrew Moyer, who would collaborate with British scientists in July 1941 in

¹⁹ "Wins Scientific Award," *The New York Times*, December 12, 1943, <u>WINS SCIENTIFIC AWARD</u>; <u>Dr. Alexander Fleming</u>, <u>Discoverer of Penicillin</u>, <u>Honored - The New York Times (nytimes.com)</u>.

²⁰ Neushul, "Science, Government, and the Mass Production of Penicillin," 371-395.

²¹ Ibid.

Illinois, made a significant discovery of using corn steep liquor as a component in growth medium. Moyer's method led to a thirty-fold increase in penicillin production (see Appendix B).²²

Reasonably, the often-told story of the penicillin miracle is mainly about Fleming's accidental discovery of penicillium and the Oxford team's successful clinical tests. Whereas the fruitful cooperation between the American and British scientists was also praised, it is worth emphasizing that nearly 25 years of research on mold fermentation funded by the USDA and conducted by generations of American scientists was the essential foundation for the mass production of penicillin. If the American scientists had not been prepared so well with their mature fermentation methods, Florey and Healey might have had to return to Europe emptyhanded.

Penicillin in Mass Production and Its Big Salvation

Finding the key to solving the production problems of penicillin was only one side of the card. Convincing American pharmaceutical firms to invest in mass production lines was another hurdle. On October 8, 1941, Alfred N. Richards, Chairman of the Office of Scientific Research and Development (OSRD) 's Committee on Medical Research (CMR) and an old friend of Florey, took the initiative to organize the first penicillin meeting. This meeting invited research directors from a few large pharmaceutical manufacturers (e.g., Merck & Co., Pfizer & Co., etc.). Thom from the USDA reported the successful collaboration between the American and British scientists. The OSRD members showed their desire to fund additional equipment and personnel

²² Ibid.

to expedite penicillin production, but the pharmaceutical companies made no promises.²³ Richards hosted the CMR's second meeting on November 17, but no substantive progress was made.

A turning point ultimately arrived in December 1941. On December 8, the day after the Japanese attacked Pearl Harbor, the U.S. declared war on Japan. Several days later, Germany and Italy declared war on the U.S. On December 17, the CMR held its third penicillin meeting. Many chief executive officers (CEOs) of large pharmaceutical manufacturers showed up and expressed their willingness to cooperate with the OSRD and researchers. George W. Merck, President of Merck, was a leading voice for supporting large-scale penicillin production, although he had been pessimistic about it before. He said, "If these results could be confirmed in their laboratories, it was possible to produce the kilo of material for Florey, and industry would do it!"

In this meeting, the OSRD urged building government-research-industry partnerships and networks between American companies. Heatley joined Merck's research team right after this meeting. Pharmaceutical companies initiated a wide range of collaborative teams. In the following years, they would work together to solve different technical problems of penicillin production, such as fermentation, recovery, purification, and packaging.²⁵

Today, it is impossible to say for sure if the pharmaceutical manufacturers' drastic change in attitude toward mass-producing penicillin was due to the fantastic research results from American and British scientists, the OSRD's promised support to mitigate the risk, the

²³ Ibid.

²⁴ "Discovery and Development of Penicillin," American Chemical Society International Historic Chemical Landmarks. https://www.acs.org/education/whatischemistry/landmarks/flemingpenicillin.html#pharmaceutical-production.

²⁵ Ibid.

U.S.'s entry into WWII, or perhaps a combination of any of these factors. However, it is safe to argue that December 1941 was one decisive moment for the destiny of penicillin.

On January 7, 1942, President Franklin D. Roosevelt established the War Production Board (WPB) to supervise the production and allocation of defense supplies, materials, and services. The WPB kickstarted the production of penicillin. It played a predominant role in providing participating pharmaceutical manufacturers with the tremendous funds and materials necessary for large-scale production and expediting the distribution of penicillin.

The first American patient, Anne Miller, was diagnosed with septicemia (commonly known as blood poisoning) and treated with penicillin on March 14, 1942. Miller's doctor received the WPB's special approval to offer Miller a tablespoon of penicillin, which was half of the entire store of the antibiotic produced by Merck in the nation.²⁷ Miller was cured. At the end of 1942, the U.S. had only enough penicillin to treat fewer than 100 patients.

In 1943, thanks to the WPB's tremendous support, the American pharmaceutical industry accelerated its penicillin production (see Appendix C). By August 1943, "many millions of units (of penicillin) are now being made available." An increasing number of companies nationwide were devoted to manufacturing penicillin. The antibiotic drug was under strict allocation of the WPB and exclusively reserved for armed forces (see Appendix D). By September 1943, the U.S.

²⁶ "Records of the War Production Board," https://www.archives.gov/research/guide-fed-records/groups/179.html.

²⁷ Lily Rothman, "This Is What Happened to the First American Treated with Penicillin," *Times*, March 14, 2016, https://time.com/4250235/penicillin-1942-history/.

²⁸ William Laurence, "More Penicillin; America Speeds Production of This Bacteria Killer," *The New York Times*, August 1, 1943, https://timesmachine.nytimes.com/timesmachine/1943/08/01/85113917.html?pageNumber=80.
https://timesmachine.nytimes.com/timesmachine/1943/08/01/85113917.html?pageNumber=80.
https://timesmachine.nytimes.com/timesmachine/1943/08/01/85113917.html?pageNumber=80.
https://timesmachine.nytimes.com/timesmachine/1943/08/01/85113917.html?pageNumber=80.
https://timesmachine.nytimes.com/timesmachine/1943/08/01/85113917.html?pageNumber=80.

stock of penicillin was sufficient to satisfy the demands of the Allied Armed Forces. On March 15, 1945, penicillin was made available over the counter in U.S. pharmacies.³⁰

Without any doubt, penicillin saved many lives both during and after the war. During World War I (WWI), 12-15 percent of the wounded soldiers treated in front-line hospitals died from infections. This number dropped to three percent during WWII.³¹ Giving penicillin at an early stage prevented severe sepsis from developing and thus decreased casualties.³² Penicillin also helped lower the death rate of Allied soldiers because it was proven to be a hundred times more fatal to bacteria than sulfa drugs, which the Germans relied heavily on.³³ In the post-war era, as penicillin was increasingly used to treat diseases such as staphylococcal septicemia, syphilis, and gonorrhea, millions of civilians benefited from the newly developed antibiotics industry.

Conclusion

The history of penicillin is full of miracles. Most public reports focused on Fleming's accidental discovery of penicillium and the Oxford scientists' breakthrough clinical tests. Historical accounts of the antibiotics industry praised the contributions of American chemical corporations. Beyond any doubt, all of these factors accounted enormously for penicillin's success. However, what is also remarkable but underappreciated by the public was the U.S.

³⁰ Tom Calver, "75 Years of Penicillin in People," *Oxford News Blog*, February 12, 2016, https://www.ox.ac.uk/news/science-blog/75-years-penicillin-people.

³¹ John F. Fulton, "Penicillin, Plasma Fractionation, and the Physician," *The Atlantic*, September 1945, https://www.theatlantic.com/magazine/archive/1945/09/penicillin-plasma-fractionation-and-the-physician/655109/. Florey, "Penicillin: A Survey," 169-171.

³³ Richard Conniff, "Penicillin: Wonder Drug of WWII," *Military History* 30, no. 2 (July 2013): 40-43, https://www.historynet.com/military-history-july-2013-table-of-contents/.

government's "invisible hand" upholding basic research and promoting research-industry partnerships.³⁴ Thanks to the USDA's decades of funding and several generations of American scientists' advanced mold fermentation methods, Florey's team had access to the means of mass-producing penicillin. The OSRD's efforts to build the government-research-industry network set the mass production of penicillin in motion. The WPB's involvement eventually sped up penicillin production, allocation, and distribution in only three years.

In July 1945, Vannevar Bush, the director of the OSRD during WWII, wrote about how the U.S. government could continue supporting scientific research in peacetime in his report entitled "Science: The Endless Frontier," which would be delivered to President Truman and later serve as a critical foundation for the establishment of the National Science Foundation in 1950. Unsurprisingly, Bush used penicillin as his best example of the government's crucial role in advancing scientific progress. He wrote,

Penicillin reached our troops in time to save countless lives because the Government coordinated and supported the program of research and development on the drug. The development moved from the early laboratory stage to large scale production and use in a fraction of the time it would have taken without such leadership.³⁵

However, even Bush's enthusiastic account did not fully credit the U.S. government for its various roles in the transition of penicillin from the laboratory to mass production. He was correct about the leadership of the OSRD and the WPB in accelerating the mass production and

³⁴ Fred Block and Matthew Keller, *State of Innovation: The U.S. Government's Role in Technology Development* (Boulder: Paradigm, 2011), 7.

³⁵ Vannevar Bush, *Science: The Endless Frontier* (Washington, D.C.: United States Government Printing Office, 2021 [1945]), 68.

distribution of this miracle drug during WWII. However, Bush missed the USDA as the unsung hero who supported American scientists' mold fermentation research for decades.

The marvelous encounter between penicillin and fermentation methods was a critical turning point in the history of medicine, without which the success of penicillin would not be possible. Fleming, Florey, and his Oxford team are the engrossing superstars in the history of penicillin. But we should not forget that the USDA and numerous American scientists (e.g., Moyer, Thom, and their colleagues) powered the engine of penicillin production. One miracle led to another. The research-government-industry partnerships initiated and cultivated by the OSRD and the WPB eventually launched the often-admired penicillin marvel. Unpuzzling the penicillin story is incomplete until we identify both visible and invisible pieces. The U.S. government's persistent and patient support for research is less visible but indispensable, exemplified distinctly by the history of penicillin.

Appendix A

WINNERS OF THE NOBEL PRIZE FOR MEDICINE







Dr. Ernst B. Chain The New York Times Studio, 1945



Sir Howard W. Florey

Fleming received the 1945 Nobel Award for the discovery of penicillin, and Chain and Florey shared the prize for their contributions.

"Winners of the Nobel Prize for Medicine." *The New York Times*, October 26, 1945. https://www.nytimes.com/1945/10/26/archives/winners-of-the-nobel-prize-for-medicine-fleming-and-two-coworkers.html.

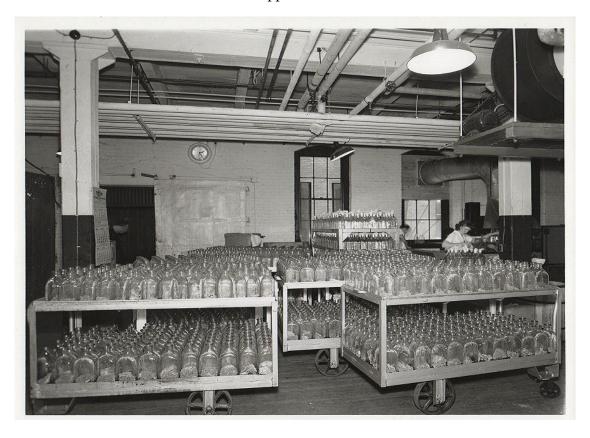
Appendix B



Researcher Andrew Moyer in the lab of the U.S. Department of Agriculture's Northern Regional Research Laboratory in Peoria, Illinois, in 1943.

 $\underline{https://www.hhhistory.com/2016/08/andrew-j-moyer-penicillin-pioneer.html}$

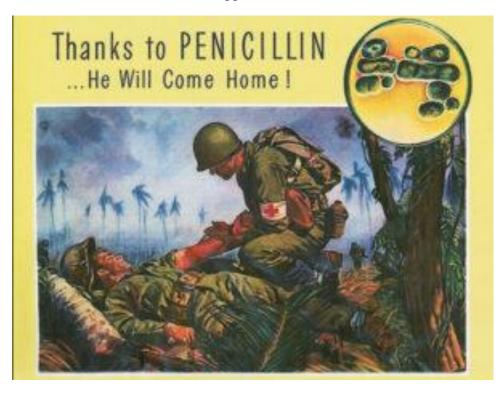
Appendix C



The Upjohn Company produced penicillin during World War II.

 $\underline{https://www.upjohn.net/other/warwork/penicillin/penicillin.htm}$

Appendix D



Advertisement for penicillin in Life Magazine by an unknown artist, August 14, 1944.

Penicillin was reserved for the Allied Armed Forces until 1945.

(Photo from the National World War II Museum)

 $\frac{https://update.lib.berkeley.edu/2021/08/09/i-keep-saying-it-was-a-miracle-experience-the-wonder-of-penicillin-through-oral-history/.$

Annotated Bibliography

Primary Sources

Books

Bush, Vannevar. *Science: The Endless Frontier*. Washington, D.C.: United States Government Printing Office, 2021 [1945].

This book is a report written by Vannevar Bush, who directed the OSRD during WWII and delivered to President Truman in July 1945. It became a classic piece that influenced the U.S. science policy in the post-war era. For the purpose of my paper, I used Bush's reflection on the government's efforts to successfully promote the medical industry during wartime to support my argument about the government's important role in the mass production of penicillin.

Government Documents and Archives

"Records of the War Production Board." https://www.archives.gov/research/guide-fed-records/groups/179.html.

The WPB was established in 1941 to develop and execute policies for producing defense materials during wartime. For my paper, I used government documents and reports restored from the archives to find out the specific policies related to the production and distribution of penicillin.

Periodicals

Abraham, E.P., Chain, E., Fletcher, C.M., Gardner, A.D., Heatley, N.G., and Jennings, M.A. "Further Observations on Penicillin." *Lancet* 238, no. 6155 (August 1941): 177–88. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(00)72122-2/fulltext.

This article published in the *Lancet* represents a critical milestone work conducted by the Oxford team. This publication reported the research team's successful clinical results on patients. I used this article to explain why the Oxford team was ready to move on to further tests on a larger scale in 1941.

Chain E., Florey, H.W., Adelaide, M.B., Gardner, A.D., Heatley, N.G., Jennings, M.A. and Orr-Ewing, J. "Penicillin as a Chemotherapeutic Agent." *Lancet* 236, no. 6104 (August 1940): 226-228.

PENICILLIN AS A CHEMOTHERAPEUTIC AGENT - The Lancet.

This article reports the results of the Oxford team's first successful clinical tests of penicillin on mice. I used this article to show how Florey's research team at Oxford pioneered penicillin-related research in 1939 and 1940.

Fleming, Alexander. "On the Antibacterial Action of Cultures of a Penicillium with Special Reference to Their Use in the Isolation of B. influenzae." *British Journal of Experimental Pathology* 10, no. 3 (June 1929): 226-23.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2048009/.

Fleming published his findings about penicillin's ability to break down cells and its antibiotic effect based on his accidental discovery of penicillin in 1928 and further research. I used this article to introduce the history of penicillin, which started in 1929. The Oxford team conducted their clinical tests in 1939 based on what was found by Fleming.

Florey, H.W. "Penicillin: A Survey." *British Medical Journal*, no. 2 (4361) (August 1944): 169-171.

https://pubmed.ncbi.nlm.nih.gov/20785574/.

Florey published this article in 1944 to show the different stages of the history of penicillin research. I found this article helpful for understanding the prior research on antibiotic phenomena before Fleming's discovery of penicillin. This article also helped me gain information about the development of penicillin during WWII.

Fulton, John F. "Penicillin, Plasma Fractionation, and the Physician." *The Atlantic*, September 1945.

 $\underline{https://www.theatlantic.com/magazine/archive/1945/09/penicillin-plasma-fractionation-and-the-physician/655109/.}$

This article reports some data to show how improving medicine, surgery, and medical care reduced the death rate during WWII compared to WWI. I found the data helpful in making a case about the contributions of penicillin to saving lives during WWII.

Kaempffert, Waldemar. "Science the News: A New 'Sulfanilamide'." *The New York Times*. October 20, 1940.

https://www.nytimes.com/1940/10/20/archives/science-in-the-news-electrically-warmed-divers.html?searchResultPosition=1.

I searched "penicillin" in the archives of *The New York Times*. This article was the first report about "penicillin" in this newspaper. The skeptical tone of the reporter showed that penicillin had not caught much attention in America. I used this article to set up the context for the collaboration between American and British scientists one year later.

Laurence, William. "More Penicillin; America Speeds Production of This Bacteria Killer." *The New York Times*. August 1, 1943.

 $\underline{https://timesmachine.nytimes.com/timesmachine/1943/08/01/85113917.html?pageNumber=80.}$

This article reports that many American chemical and pharmaceutical companies accelerated penicillin production in 1943. By September 1943, the U.S. stock of penicillin was sufficient to satisfy the demands of the Allied Armed Forces. I used some data reported in the article to show the WPB's and corporations' fast move in the mass production of penicillin.

"Wins Scientific Award." The New York Times. December 12, 1943.

WINS SCIENTIFIC AWARD; Dr. Alexander Fleming, Discoverer of Penicillin, Honored - The New York Times (nytimes.com).

Florey and his Oxford team remained unrecognized for their significant contributions to the ultimately successful production of penicillin until December 1943. The American Pharmaceutical Manufacturers Association offered them an award for their experimental work with penicillin in treating diseases. I used this article to show when the Oxford team started gaining public recognition.

Appendix Graphics

Photo: Researcher Andrew Moyer in the USDA's NRRL in Peoria, Illinois, in 1943. https://www.hhhistory.com/2016/08/andrew-j-moyer-penicillin-pioneer.html

I found this image on the above website. It could show how Andrew Moyer conducted his research and support the story in my paper.

The Upjohn Company produced penicillin during World War II. https://www.upjohn.net/other/warwork/penicillin/penicillin.htm

I found this image on the above website. I felt it could display the mass production of penicillin in the early 1940s and support the story in my paper.

Unknown artist, An advertisement photo for penicillin, *Life Magazine*, August 14, 1944. https://update.lib.berkeley.edu/2021/08/09/i-keep-saying-it-was-a-miracle-experience-the-wonder-of-penicillin-through-oral-history/.

This advertisement image, stored in the National World War II Museum, showed how much penicillin was highly praised in 1944. I found this image on the website of the

University of California, Berkeley's Library. I wanted to use it to depict that penicillin was mainly reserved for the Armed Forces during WWII.

"Winners of the Nobel Prize for Medicine." *The New York Times*, October 26, 1945.

https://www.nytimes.com/1945/10/26/archives/winners-of-the-nobel-prize-for-medicine-fleming-and-two-coworkers.html.

Fleming, Florey, and Chain received the 1945 Nobel Award for Physiology and Medicine. I found the image in this report and included it in my paper to show Florey and his research team were not recognized for their contributions to penicillin research until 1945.

Secondary Sources

Books

Block, Fred and Keller, Matthew. *State of Innovation: The U.S. Government's Role in Technology Development*. Boulder: Paradigm, 2011.

The book employs historical examples to show that the U.S. government's scientific and technological capacity was expanded by creating a network of federal laboratories and research institutes during WWII. The book helped me establish my core argument about the importance of the U.S. government in the mass production of penicillin.

Macfarlane, Gwyn. *Alexander Fleming: The Man and the Myth*. Cambridge, MA: Harvard University, 1984.

The book details Alexander Fleming's biography and explains how Fleming started his scientific career, paving the way for his marvelous discovery of penicillin. This book helped me write the first section of my paper, which tells how Fleming discovered penicillin by chance in 1929.

American Chemical Society (ACS) and Industrial Archives

"Discovery and Development of Penicillin." International Historic Chemical Landmarks.

https://www.acs.org/education/whatischemistry/landmarks/flemingpenicillin.html#pharmaceutical-production.

The American chemical corporations played an important role in the mass production of penicillin in the 1940s. For my paper, I used the documents found on the ACS website to explain why the American pharmaceutical companies decided to take part in the production of penicillin in 1941 and how they did so in the following years.

Periodicals

Adedeji, W.A. "The Treasure Called Antibiotics." *Annals of Ibadan Postgraduate Medicine* 14, no. 2 (December 2016): 56-57.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5354621/.

This article has detailed information about infectious diseases and how they were treated before and after the discovery of penicillin. I wanted to use some examples of infectious diseases mentioned in the article to show how people suffered from such diseases before the discovery of penicillin.

Arias, Elizabeth and Xu, Jiaquan. "United States Life Tables, 2018." *National Vital Statistics Reports* 69, no. 12 (November 2020): 36.

https://www.cdc.gov/nchs/data/nvsr/nvsr69/nvsr69-12-508.pdf.

I wanted to use some examples to show how much penicillin and other antibiotic drugs have changed the world throughout the 20th century and thus emphasize the significant implications of my project. I found the data about the U.S. population's average life expectancy at birth in 1900 in this article, which were used to show what was like before the invention of penicillin.

Bernard, Diane. "How a Miracle Drug Changed the Fight against Infection during World War II." *The Washington Post*, July 11, 2020.

https://www.washingtonpost.com/history/2020/07/11/penicillin-coronavirus-florey-wwii-infection/.

This article contains some small stories about how Florey's research team at Oxford started their penicillin-related research and how they travelled to the U.S. in 1941 to seek help with penicillin production. I added some details obtained from this article to my paper to make the story of penicillin's transition from Europe to the U.S. more complete.

Calver, Tom. "75 Years of Penicillin in People." *Oxford News Blog*, February 12, 2016. https://www.ox.ac.uk/news/science-blog/75-years-penicillin-people.

This article outlines the history of penicillin, focusing on the research conducted at Oxford University. I used the sources in the article to cross-check the main steps in developing penicillin in my paper.

Conniff, Richard. "Penicillin: Wonder Drug of WWII." *Military History* 30, no. 2 (July 2013): 40-43

https://www.historynet.com/military-history-july-2013-table-of-contents/.

This article reports some data to show how the different death rates of German soldiers and Allied soldiers resulted from using different antibiotic drugs. It shows that penicillin

lowered the death rate of Allied soldiers. I used the data to show how penicillin helped save lives during WWII.

Kyle, Robert A., Steensma, David P., and Shampo, Marc A. "Howard Walter Florey – Production of Penicillin." *Stamp Vignette on Medical Science* 90, no. 6 (June 2015): e63-e64.

https://www.mayoclinicproceedings.org/article/S0025-6196(15)00304-3/pdf.

This article tells the story of how Florey and Heatley started to collaborate with American scientists in 1941, who also helped the Oxford team set up meetings with different government agencies (e.g., the USDA and ERRL). I needed such details to explain why the collaboration between American and British scientists was possible only one month after Florey and Heatley arrived in the U.S.

Neushul, Peter. "Science, Government, and the Mass Production of Penicillin." *The Journal of the History of Medicine and Allied Sciences* 48, no. 4 (October 1993): 371-395. https://academic.oup.com/jhmas/article-abstract/48/4/371/777929.

This article shows how USDA-funded American scientists developed mold fermentation methods in the 1910s. I used this article to explain why American scientists were able to help the Oxford team and quickly solve the problem of mass-producing penicillin.

Rothman, Lily. "This Is What Happened to the First American Treated with Penicillin." *Times*, March 14, 2016.

https://time.com/4250235/penicillin-1942-history/.

This article tells the story of Anne Miller, the first American patient treated with penicillin in March 1942. Back then, penicillin was in extreme shortage and under strict allocation of the WPB. One year later, the U.S. stock of penicillin was sufficient to satisfy the demands of the Allied Armed Forces. I used Miller's story to show how fast the mass production of penicillin was made possible from 1942 to 1943.