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# The Antibiotic Revolution

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*Time Magazine* named Alexander Fleming as one of the 100 Most Important People of the 20th Century for his discovery of penicillin and stated; "It was a discovery that would change the course of history. The active ingredient in that mould, which Fleming named penicillin, turned out to be an infection-fighting agent of enormous potency" ("Sir Alexander Fleming | The Generalist). A revolutionary development in science is a change in the way scientists perceive a certain idea or belief. According to Thomas Kuhn, a revolution is a complete overturn to a new idea; there is newness where people have to turn away from what came before. At the same time, the idea is built on old ideas that have helped the new idea come about. The finding of Penicillin by Alexander Fleming in 1928 was a revolutionary development in the field of science. The discovery revolutionized the way infections were treated as well as impacted the scientific field, the medical field, the pharmaceutical industry, and all of humanity. Alexander Fleming's discovery of Penicillin sparked the development of antibiotics, which has continued to save people's lives since the revolution, making him a revolutionary figure. Despite the fact that Fleming was not solely responsible for the revolutionary development, it was his discovery of Penicillin that led to the development of antibiotics. Kuhn would qualify the discovery of Penicillin by Alexander Fleming as a revolution because it led to a paradigm shift. Prior to the discovery of Penicillin, patients died from trivial injuries and infections. Fleming's discovery of Penicillin is revolutionary because it changed the worldview of the way doctors treat patients with infectious diseases; and as a result of the antibiotic revolution, individuals are not vulnerable to death by bacterial diseases.

The discovery of Penicillin meets Kuhn's criteria for a paradigm-shift and its accompanying transition from normal science to a shattering of the worldview of the way diseases were cured. A paradigm is a dominant achievement that sets the rules for the time. Kuhn believes that "research under a paradigm must be a particularly effective way of inducing paradigm change" *(Structure 52).* Before the antibacterial properties of penicillin were discovered, scientists worked within the realm of normal science in the pre-antibiotic paradigm. According to Fleming, before he discovered Penicillin, "there was not a chemical antiseptic which by this simple in vitro test could be considered as an antiseptic of the first class for the restriction of growth of bacteria in human tissues" (Fleming *Penicillin* 386). Fleming was working in the normal science paradigm of antiseptics before he discovered Penicillin, which would later qualify as its own paradigm of antibiotics. Kuhn says "normal science…is a highly cumulative enterprise, eminently successful in its aim, the steady extension of the scope and precision of scientific knowledge *(*Kuhn *Structure 52).* In an existing science, which is called normal science, the progress that occurs only expands the paradigm and does not change it. In 1871, the English surgeon Joseph Lister was working within the normal science parameter and observed that the penicillin mold was able to halt the growth of germs. Two other researchers, John Tyndall in 1875 and D.A. Gratia in 1925, also noticed these properties of penicillin because they were operating within a paradigm (Horvitz 118). Therefore, paradigm bound research generates the prospect of paradigm change because within a paradigm a search for change does not exist therefore there is room for meaningful research. Kuhn says that when meaningful research does occur, as in the case of Fleming's predecessors, "new and unexpected phenomena are, however, repeatedly uncovered by scientific research and radical new theories have again and again been invented by scientists" *(*Kuhn *Structure 52).* However, meaningful research that uncovers new theories is not always enough to create a paradigm shift. Neither Tyndall nor Gratia were effective enough to create a paradigm shift because "…like Lister, they hadn't seemed to appreciate the significance of their observations, nor did they conduct the necessary experiments to find out exactly why the mold killed bacteria" (Horvitz 118). In one publishing in *The British Medical Journal*, Fleming acknowledges the discovery of Penicillin as his own when he states, "I can claim some merit in the discovery, as without a doubt the same mold has contaminated hundreds of thousands of culture plates and has merely regarded as a nuisance" (Fleming *Penicillin* 386). The first few discoveries of it only generated the prospect of paradigm change and it was not until Fleming's discovery that the anomaly could no longer be accompanied by the current paradigm.

According to Kuhn, accumulation within a paradigm allows the paradigm to expand but only until it becomes too broad and a new anomaly comes about. The new anomaly causes science to enter the crisis situation. Until Fleming rediscovered Penicillin and found it as an effective antibiotic, physicians had little ability to treat patients who had infections. The only thing they could do was wait and hope that patient's immune system would destroy the infection (Friedman 169). If this did not happen then the only thing the doctor could do was attempt to ease the patient's death. However, once the properties of penicillin were discovered, science could not turn back to a time when inhibiting bacteria growth was unknown. Once an anomaly comes about, science enters a crisis and there is a possibility for change because there is now something that is not considered the norm in the paradigm. Science entered the crisis situation when the anomaly of a mold inhibiting bacteria was discovered. When a paradigm is felt to be insecure, science enters the pre paradigm period, which "is regularly marked by frequent and deep debates over legitimate methods, problems, and standards of solution *(*Kuhn *Structure 47-48)*. Kuhn would call this time prior to the time when Penicillin was rediscovered by Fleming and continually researched and put into effect the pre-paradigm period. The pre paradigm period would still be considered normal science because not enough was discovered to completely shatter the current paradigm. However, the pre paradigm period ended in 1928 in the lab of Alexander Fleming in St. Mary's Hospital with the discovery of the anomaly properties of Penicillin resulting in the shattering of the existing paradigm.

If the new anomaly can no longer be accommodated by the existing scheme and there is enough support for the new anomaly, there is a paradigm shift, which is known as revolutionary science. According to Kuhn, revolutionary science "is a reconstruction that changes some of the field's most elementary theoretical generalizations as well as many of its paradigm methods and applications" (*Structure* 84-85). Fleming's discovery fits Kuhn's criteria for a paradigm shift. For Fleming, his revolutionary science began with a Eureka Moment not only for him, but also for the world of science and medicine. According to Kuhn, there are times in science known as a Eureka Moment, which is defined as the instant when a new anomaly is discovered and everything changes. For Kuhn Eureka Moments happen in normal science, which lead to a revolution and eventually displace an earlier time-honored paradigm for a more compelling one. Fleming's finding of penicillin was a Eureka Moment because it was an accidental discovery that would change the course of history.

The actions that Fleming took before his Eureka Moment were essential to his discovery of penicillin. In the summer of 1928, Fleming left London on Holiday. Before he left, he was experimenting with cultures of staphylococci, but forgot to place them in incubators to keep warm and accidently left them out in the open in his disorganized lab (Horvitz 116). When he returned in September, Fleming checked on his cultures in the petri dishes and observed many of his staphylococci culture plates were covered with fungus, a mold that he would name penicillin. What interested him even more was that "around the large colony of a contaminated mould the staphylococcus colonies became transparent and were obviously undergoing lysis (Fleming *On the Antibacterial Action of Cultures 129).* This mold seemed to be inhibiting the bacterial growth. A normal scientist may have throw thrown the petri dish away. However, Fleming wanted to further research the cause of the occurrence in the petri dish, making him a revolutionary scientist. In this Eureka Moment, Fleming had discovered Penicillin. Fleming once wrote "it was astonishing that for some considerable distance around the mould growth the staphylococcal colonies were undergoing lysis (the dissolution or destruction of cells)…what had formerly been a well-growing colony was now a faint shadow of its former self" (Horvitz 117-118). Fleming's purist of his discovery of the anomaly of the unexpected phenomenon of the antibacterial properties of the penicillin mold led to the paradigm shift. "This lysis, or destructive process, he realized, was what was responsible for discoloring his microbes. He correctly deducted that the mold must have released a substance that simultaneously destroyed existing bacteria and inhibited their further growth "(Horvitz 118). This anomaly opened up the transition from normal science to revolutionary science because it shattered the current worldview on the curtailment of bacteria growth.

Kuhn says that the circumstances of the discovery can determine if an anomaly is world shattering enough to create a paradigm shift. Occurrences in Fleming's lab were major attributes to his discovery of penicillin. Fleming usually left the window of his lab open since his lab was small and musty. In one of the labs on the floor below him, a young Irish mycologist named C.J. La Touche was working on a strain of penicillin mold. Not only was Fleming's window left open but the doors between the staircases were left open as well. Since La Touches' lab lacked a fume hood, the spores of mold were not kept isolated in the room and managed to drift into Fleming's Penicillin while he was away on Holiday (Horvitz 116). The weather was another circumstance, which helped the mold spores flourish onto Fleming's petri dishes. While Fleming was away, the temperatures dropped significantly lower than usual and then returned to warmer temperatures. The cold weather allowed the penicillin to take root and grow on the staphylococci. Then, the warmer temperatures allowed the staphylococci to flourish until they covered the entire petri dish, expect for the area directly exposed to the penicillin mold (Horvitz 117). However, Fleming's luck continued because it was the particular strain of the bacteria of staphylococci that allowed the mold growth (Friedman 172). Another circumstance that would have changed the discovery of Penicillin was if the mold landed on the petri dishes after it was covered with staphylococci, the mold would not have been able to grow (Friedman 172). Without the unplanned circumstances of Fleming's lab and the weather, the anomaly of the penicillin mold would never have been discovered.

According to Kuhn, one cannot plan for revolutionary science and must work within normal science until an anomaly occurs. Fleming once said, "Do not wait for fortune to smile on you; prepare yourselves with knowledge "(Horvitz 116). If Fleming were not working in the context of normal science, he would never have entered into revolutionary science. Fleming would then agree with Kuhn's belief that "normal research, which is cumulative, owes it success to the ability of scientists regularly to select problems that can be solved with conceptual and instrumental techniques close to those already in existence" (Kuhn *Structure* 96). It was Fleming's knowledge that he gained while following the fundamentals of normal science that allowed him to recognize the anomaly of penicillin. Kuhn believes that "the results gained in normal research are significant because they add to the scope and precision with which the paradigm can be applied" (Kuhn *Structure* 36). If he had not trained himself in normal science, he never would have been able to make a revolutionary discovery (Horvitz 118). Since Kuhn says that normal science problems do not "aim to produce major novelties" (Kuhn *Structure* 35), when a major novelty comes about there has to be a shift into revolutionary science. It was the fact that Fleming was a perspicacious scientist that he was able to recognize the mold as an anomaly. If Fleming had never prepared himself in normal science, he never would have been able to make the revolutionary discovery.

As a scientist, Kuhn diverged from the fundamentals of normal research and was interested in the anomaly he found. According to Kuhn, a revolutionary scientist does not follow the rules. Fleming felt inclined to look into his discovery because he saw it with a new perception, which makes him a revolutionary scientist. Fleming even acknowledged that it was his curiosity that enabled him to go against normal science and explore the anomaly when he stated, "my only merit is that I did not neglect the observation and that I pursued the subject as a bacteriologist…I was sufficiently interested to pursue the subject" (Horvitz 119). Since Fleming worked as an individual in the tradition of the nineteenth-century lone researcher, he was able to pursue his finding because he was not tied by the deadlines that come with research grants (Brown 7). Fleming was a scientist who followed normal science, however, was not so engrossed with the fundamentals, which afforded him the ability to enter into revolutionary science.

Once Fleming had discovered the anomaly of Penicillin, he began to investigate the mold and began to work within a new paradigm in revolutionary science. Fleming began investigating at what point the mold would stop killing off bacteria. He started to dilute the mold the broth was in and "continued to dilute it further and further, but even when he had diluted the broth to eight hundredths of its original strength, the mold still retained its lethal power against the bacteria" (Horvitz 120). Since nothing with this kind of lethal power had been discovered before, there had to be a complete overturn of the beliefs that came before. Kuhn says, "the transition from a paradigm in crisis to a new one from which a new transition of normal science can emerge is far from a cumulative process, one achieved by an articulation or extension of the old paradigm" (Kuhn *Structure* 84-85). Within this new paradigm, Fleming found that "the miraculous substance had an added advantage in that it was several times as potent as pure carbolic acid, which, while killing bacteria, also burns the tissues. Fleming and his colleagues repeated the procedure with pneumococci, the bacteria that cause pneumonia, and produced the same astonishing results" (Horvitz 120). These results lead to what Kuhn would consider a revolutionary development in science because it transformed the way we think about and view infections. Kuhn believes that "changes in the standards governing permissible problems, concepts, and explanations can transform a science...and even the world" (Kuhn *Structure* 106). Kuhn says "The proliferation of competing articulations, the willingness to try anything, the expression of explicit discontent, the recourse to philosophy and the debate over fundamentals, are all symptoms of a transition from normal to extraordinary research" (Kuhn *Structure* 91). The discovery of Penicillin follows Kuhn's symptoms of extraordinary research within a new paradigm.

Fleming's Eureka Moment turned into a paradigmatic shift because he tested and proved his new scientific fundamentals to be true. After the immediate discovery, Fleming then exposed a specimen of his salvia in an incubator, and because the salvia was full of bacteria, it grew. Once penicillin was added to the specimen, some colonies were killed while others survived. Penicillin seemed to be effective against some types of bacteria and not others (Horvitz

120-121). The reason for this lies in the way in which penicillin works. Penicillin inhibits the bacterial enzymes responsible for cell-wall synthesis and activates other enzymes to break down the organisms' protective walls. Therefore, penicillin is not effective against microorganisms that do not have call walls (Horvitz 122). However, this did not stop Fleming from continuing his pursuit of the advancement of Penicillin. "In 1929 Fleming made his work public, saying that he thought this may be an effective antiseptic for applying in the form of ointment, or for injecting into the blood of people infected with certain diseases" (Rowland 97). In one of Fleming's papers in 1931, he declared "it is suggested that it may be an effective antiseptic for application to, or injection into, areas infected with penicillin-sensitive microbes" (Fleming *Penicillin* 386). As more Penicillin was prepared, it was found to be a successful antibiotic drug that did indeed inhibit the growth of many different types of bacteria (Rowland 97-98). The Penicillin was prepared in a broth with which he continued to work; however Fleming never tried to separate out the specific microbe-destroying elements that made it resistant to bacteria (Horvitz 121). Before Penicillium broth could be used on humans, it had to be tested as being non-toxic. Fleming experimented with the broth on mice and rabbits by injecting it into their ears. Since the animals showed no ill effects, he was able to try the broth out on humans (Horvitz 121). Fleming "irrigated an infected eye, an inflamed maxillary sinus, and the infected surface of an amputated leg with a penicillin solution" (Friedman 174). In 1932, Fleming ended his investigation and development of Penicillin due to his lack of funding and chemical expertise of purifying the penicillin broth. However, he kept the string of Penicillin and continued to make samples of the mold available for other researchers. (Horvitz 121). Fleming's desire to challenge the existing paradigm and change the fundamentals was brought to a halt because of what the discipline considered acceptable problems and solutions at the time.

According to Kuhn, when a paradigmatic shift creates problems, it is not until a new solution has come about that the paradigm is completely replaced. When looking back, one may not be able to understand the context of the reasoning of people at that time. However, according to Kuhn, we must always remember to place ourselves in the time of the revolution. At the time, one reason Fleming stopped his study was because he could not comprehend the thought that a bacterial infection within the body could be helped by the injection or ingestion of penicillin (Friedman 174). Another reason is that Fleming never tested Penicillin in an infected animal because his superior, Sir Almroth Wright (along with his colleagues), believed that "antibacterial drugs are a delusion" (Friedman 174). It was impossible for scientists to see the great potential the antibiotic drug Penicillin could have since nothing like it had been discovered before. "It was not the first time, nor would it be the last, that recognition of a revolutionary medical discovery was delayed for many years because medical thinking was constrained by an obsolete paradigm of reasoning" (Friedman 174). Despite that fact that Fleming stopped his research of the anomaly, his discovery had already created a paradigm shift because scientists could no longer go back to the idea that human infections were incurable (Horvitz 121). According to Kuhn, when a new paradigmatic shift occurs, there is a new theory that replaces the old and therefore there is newness where people have to turn away from what came before. However, according to Kuhn, the new paradigm is only completely accepted and considered revolutionary when a community supports it. Fleming's halt in his research did not stop the revolution from happening; it only prolonged the inevitable.

For the paradigm of penicillin and antibiotics to continue, there needed to be a scientific community of support for the drug and researchers to pursue penicillin. The two scientists that supported and continued Fleming's work and the new paradigm were Howard Florey and Ernst

Chain. Fleming influenced Florey after he read one of his articles on penicillin in 1929, because Florey was interested in natural substance that could kill bacteria (Horvitz 122). In 1939, Florey convinced Chain to join his team at Oxford University in the School of Pathology. At Oxford, Chain managed to get a sample of Fleming's mold and start experimenting with the Penicillin. "They planned to generate…a body of fundamental research that might show how certain microorganisms produce, secrete, or otherwise elaborate antibacterial enzymes. This indeed was revolutionary thinking—searching for substances produced by one microorganism that might kill other microorganisms" (Friedman 179). Unlike Fleming, Florey and Chain were supported by the Rockefeller Foundation and were able to purify the penicilliums broth into a drug. (Horvitz 122-123). Once they had the financial support and began to purify the mold, Chain discovered that penicillin was a stable molecule that could be converted into a brown powder. Fleming credits the two researchers for "extracting an impure active agent and keeping it in the dry state" and for allowing to continue the paradigm that he started. (Fleming *Penicillin* 386). This powder "is many more times powerful than the most potent of the sulphonamide compounds" (Fleming *Penicillin* 386). When Chain and Florey tested the dried penicillin on mice, their urine turned brown which proved that the penicillin did not loose any potency though the body. Once they successfully tested penicillin on mice, they tried it out on the their first human patient, Albert Alexander, who was suffering from a dangerous bacterial infection (Horvitz 123). However, the paradigm was again constrained by another problem. Scientists could not continue duplicating their tests on humans because the penicillin could not be made on a large scale (Horvitz 123). Support was again needed in the antibiotic revolution, however this time the community was the pharmaceutical industry. In the early 1940s, Florey succeeded in getting several major pharmaceutical companies to produce penicillin so that that the Oxford researchers would have the cash and resources necessary to continue with their experiments on humans (Horvitz 123). Penicillin created the paradigm shift because the same people that were saved from Penicillin would have died if it had not been discovered.

According to Kuhn, luck and timing have a significant influence on scientific discovery, and Penicillin is no exception. Right when Florey and Chain were able to produce Penicillin into a form of a drug, World War II broke out. When the United States entered the war in December 1941, Florey managed to persuade American drug manufactures to mass-produce penicillin in order to reduce the battlefield deaths caused by infected wounds (Horvitz 124). The Penicillin revolution was able take off because it had a support system beyond the scientific community. This support came from the US government when they provided grants to drug companies to help pay for the expensive equipment needed to make penicillin (Horvitz 124). After the war, the paradigm shift was completed because antibiotics began to spread across the world. The antibiotic paradigm was so compelling that a world with the paradigm prior to the discovery of antibiotics was inconceivable.  As more penicillin was produced, its decrease in cost allowed impoverished and war-devastated countries to attain it (Horvitz 124). Florey stated "the introduction into clinical medicine of penicillin therapy and the antibiotic therapy stemming from it has…completely revolutionized the treatment of bacterial infection in both man and animals, and rendered the large majority of them, including the most severe ones, amendable to successful therapeutic control" (Florey *Penicillin*). Penicillin did not only alter the scientific and medical field but spread into the life of lay people.

Penicillin was a discovery that changed the world because it was the catalyst for the antibiotic revolution. The development of the antibiotic altered the scientific imagination in such as way as to how to cure bacteria infections. Since the paradigm shift transformed not only the thought-world of scientists but also the medical field, the pharmaceutical industry and the way people think of death, Penicillin is categorized as a macro revolution. Before the antibiotics revolution, doctors were unable to cure patients with a simple infection. With the discovery of the drug Penicillin, the cure for life threatening diseases became possible (Brown 195). The antibiotic was used to treat throat infections, pneumonia, spinal meningitis, gas gangrene, diphtheria, syphilis, and gonorrhea. Mothers no longer feared life-threatening infections during childbirth. Doctors could now perform Long and complex surgical procedures with much greater assurance that the patient would survive from a postoperative infection (Horvitz 124). The development of Penicillin changed the cultural perspective of the connection between bacterial diseases and death. Once antibiotics were discovered, humans were not as fragile as they were before. Humans became resilient to most bacteria infections and for a moment, could even consider themselves invincible. Brown, the author of *Penicillin Man: Alexander Fleming And The Antibiotic Revolution* stated, “the pre-antibiotic age now seemed like the dark ages of modern medicine compared to the golden sun of the antibiotic age” (Brown 195). Once the paradigm of antibiotics was supported, Kuhn would say that the old paradigm could never return because of the new knowledge that existed. Penicillin was the impetus to the revolution because it created a paradigm shift.

However, the paradigm is again in danger because antibiotics are not creating the great effect they once were. In 1945, Fleming along with Florey and Chain were awarded the Noble Peace Prize for their discovery. Fleming ended his speech with a warning:” The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant” (Sir Alexander Fleming - Banquet Speech an infection-fighting agent of enormous potency"). One of they key facts that came from the anomaly of Penicillin was that it only works when a certain amount is used. Fleming gave a hypothetical situation where "Mr. X. has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs. X gets pneumonia and is treated with penicillin. As the strep- rococo are now resistant to penicillin the treatment fails. Mrs. X dies. Who is primarily responsible for Mrs. X's death?" (Sir Alexander Fleming - Banquet Speech an infection-fighting agent of enormous potency"). Fleming was predicating the future situation that is now a reality. The ineffectiveness of antibiotics is a result of the individual's misuse of the medication rather than the physician who prescribes the antibiotic. According to Fleming, the person responsible for the death of Mrs. X was Mr. X because his "negligent use of penicillin [which changed] the nature of the microbe. *Moral:* If you use pen- cillin, use enough. (Sir Alexander Fleming - Banquet Speech an infection-fighting agent of enormous potency"). As mentioned by Fleming, antibiotics are only effective when they are used correctly. When they are misused, the infection is not eradicated and can continue to spread. If antibiotics are continuously overused, they become ineffective because a person's immune system may become resistant to Penicillin. If people are not more cognizant of this paradigm, they may end the paradigm of antibiotics without even knowing it. However, the problem with this is that Kuhn says an old paradigm cannot become rejected until a new paradigm can take its place. Kuhn states, "a scientific theory is declared invalid only if an alternative candidate is available to take its place" (Kuhn *Structure* 77). It is not only up to scientists to continue this paradigm of antibiotics but it is also the responsibility of the community of patients to use their antibiotics correctly and avoid the problem of drug resident antibacterial infection.

It took Alexander Fleming, Florey and Chain, the Oxford Group, the scientific community, World War II, the Pharmaceutical industry, and patients with bacterial infections to support Penicillin and embrace the paradigm shift. It was much more than the discovery of Penicillin, which led to the paradigmatic shift. When the new anomaly can no longer be accepted, science enters revolutionary science. According to Kuhn, a revolutionary development in science has the ability to transform the way we think about and view science because "Changes in the standards governing permissible problems, concepts, and explanations can transform a science...and even the world" (Kuhn *Structure* 106). The problem of how to cure patients with bacterial infections was solved with the development of Penicillin. This change transformed the science of how doctors treated patients with infectious diseases. According to Kuhn, if the new anomaly can no longer be accommodated by the existing scheme and there is enough support for the new anomaly, there is a paradigm shift. This scientific technique of a paradigm shift is exactly what happened when Fleming unexpectedly found penicillin one day in his laboratory. The revolutionary discovery of Penicillin by Fleming far exceeds a simple scientific paradigmatic shift. Who would have thought that Fleming's auspicious discovery would create a paradigmatic shift that saves the lives of millions of people?

To the best of my knowledge, the ideas and content of this paper are my own, unless otherwise indicated in a note.

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