

Miracle Cure: The Creation of Antibiotics and the Birth of Modern Medicine

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William Rosen never had the opportunity to have a signing for his new book that was just released this past May 2017. He never got to do a book tour for Viking, take questions at the end of a talk about source material, or see it for sale on Amazon. Sadly, Rosen, a former editor turned non-fiction author, passed away at his home in Princeton, New Jersey on 28 April 2016 of a rare form of cancer.(1) I never had the pleasure of discussing his career or even the research that went into writing this important and highly-readable contribution to the disciplines of medical history and the history of chemistry; but I wish I had.

In 2013, Rosen the patient was in the fight of his life when he visited Rutgers University. It was there that he viewed a letter written to Professor Selman Waksman from the editor of *Biological Abstracts*. The editor was asking one of the titans of bacteriology (the 'Man of the Soil' as he was dubbed by *Time* in 1949) for an appropriate name for a new class of drugs. Waksman was in the midst of commanding a war against bacteria by analyzing literally hundreds of thousands of soil samples for unique forms of the enemy from the around the globe. Presciently he replied that they should be called 'antibiotics.' That historical encounter with the past emboldened Rosen the author to explore the sources of modern pharmacology in his posthumously released book entitled *Miracle Cure: The Creation of Antibiotics and the Birth of Modern Medicine*. Ironically, were it not for a specific drug that was synthesized a decade earlier he would have passed sooner, and we would never had the pleasure of enjoying such a good story.

Rosen begins his examination of antibiotics history with its origins in the medical history of the 19th century. Newly-built chemistry labs in the universities of Europe during the end of the Napoleonic Era were examining diseases from a more scientific perspective. Nations struggled for hegemony, and their chemical endeavors were a reflection of what kind of place their leadership envisioned. Despite the discoveries of Louis Pasteur, by the 1870s France had ceded not only territory to the Second Reich but also its grip on industrial chemistry. Fueled by coal, a united Germany became the premier location for a new industry, dye making, which led to prescription drug production. Led by chemists Robert Koch, Paul Ehrlich, Emil Behring, and powerfully-backed companies the discipline moved at a meteoric pace. As Rosen so aptly describes, new subfields, such as histology, the study of tissues, and new technologies, such as powerful microscopes, allowed regimented Prussian-style laboratories to take a blob of paint and learn how it reacted

to different compounds. In these challenging and complex formula descriptions, Rosen truly excels as a historian of science. He provides complexity, while at the same time not overwhelming the reader with too much jargon.

Thus, it is in dye companies such as Bayer that we begin to see the origins of the pharmaceutical industry of today. Out of these German streamlined laboratories came the most widely prescribed drug in the world (although this author would argue it was aspirin in 1910), Salvarsan. Described as a both a 'magic bullet' that could cure a whole panel of maladies, it was also a chemotherapeutic agent. However, most important of all it was the first example of germ theory in practice. The new drug attacked several strains of pneumonia, and interestingly enough, is still used today as a diagnostic tool for identifying the presence of strep throat. Rosen makes it clear though that what the Germans perfected before 1914 were not necessarily breakthrough drugs that were magic bullets or vaccines for prevention, but rather the infrastructure and mechanisms to continue to fund ongoing lab research. This was absolutely essential, especially during the inter-war years, as industrial laboratories expanded into the production of antibiotics. Rosen does an adequate job emphasizing the role that the First World War had on chemical developments in Germany. He personalizes this section of the book by describing the impact the destruction had on Gerhard Domagk, a soldier assigned to the medical corps in the Ukraine. Afterwards, Domagk became a researcher and clinician at the University of Munster. It was there that he developed the seeds of a major breakthrough when he utilized white blood cells coupled with a staph pathogen in his examination of the vertebrate immune system. Once the staph cell was weakened with antiseptics (another development Rosen outlines by examining the career of Joseph Lister) it was much easier for the white blood cells to destroy the invader. By the late 1920s the seeds for discovering how to unlock the secrets of diseases were ready for planting.

Rosen examines the most crucial phase of antibiotic research, as he looks into the experimental phase of these companies and laboratories. Due to the lack of governmental intervention, these labs were given broad brushes in which to conduct their research. This was a true golden age of investigation that spanned only ten years, and it was one that was built through a global community of chemists, laboratory technicians, university professors, and administrators both male and female. Rosen does an excellent job of explaining how tuberculosis and pneumonia were the leading causes of death in the United States, with a particular highlight being his review of the hagiography associated with Alexander Fleming. Possibly what is most fascinating about the discovery of penicillin is that it did not solely occur in a Petri dish in Fleming's lab. While he did, by happy accident, grow some spores while on vacation, the attribution was assigned to him by an over-zealous colleague at St. Mary's Hospital in London. The press ran with the quote, and the rest became history.

The real story of the development of penicillin right before the advent of the Second World War comes from the work of Howard Florey and his team at the Dunn Laboratories. Dunn was a hodgepodge of brilliant yet eccentric chemical researchers headed by Florey. He attempted to keep in check, once Fleming brought a sample of spores to him, the ideas of a German émigré of Jewish-decent named Ernst Chain. Chain was a waterfall of ambition, and they were at constant odds over credit, funding, and direction of the project. With the help of an able-bodied chemist named Norman Heatley, who had a penchant for equipment construction, and a future Nobel-winning crystallogist/x-ray specialist named Dorothy Crowfoot Hodgkin, Dunn produced a small batch of penicillin in its purest form.

With the Nazis on the loose throughout Europe, and Britain with its back up against the Atlantic, Florey turned to American industry to assist with production on a mass scale. Rosen is at his best when describing the trip to the United States. Florey literally and figuratively found the proper soil. In New York City at the Rockefeller Foundation, in Illinois at the Northern Lab, and with the support of a host of chemical companies including Squibb, Merck, Pfizer, Parke-Davis, and many others, Florey's new team helped bring modern medicine to a new level. Rosen offers wonderfully-rich descriptions of important players like the bacteriologist Mary Hunt. She discovered one of the most important mold samples for growing penicillin by happening upon a Peoria, Illinois fruit stand and discovering an infested cantaloupe. He also relates the story of Anne Miller, who lay in a hospital bed afflicted with blood poisoning after a miscarriage in New Haven,

Connecticut. Rosen found her chart in the Smithsonian's National Museum of American History Archive. Her attending physician knew a friend of Florey's was being treated in that very hospital. Through persuasion and persistence he was able to secure the first five grams of penicillin to be used on a patient. The dosage was enough to save Ms. Miller's life.

Perhaps the highlight of Rosen's research on the rise of antibiotics examines the Florey-Chain-esque relationship of Selman Waksman, the mentor and lead scientist at Rutgers and his student, Albert Schatz. It was Schatz, sequestered in a basement laboratory, who began to test soil samples from as many places as he could muster. With Waksman's connections to Britain, and Schatz's ambition for a Nobel, the two formed a dynamic duo. What they uncovered were loads of bacterial examples. Through test after test, they finally secured, with the help of entities such as the Mayo Clinic in Minnesota, the next step in antibiotic evolution-streptomycin. This new incarnation solved the puzzle of tuberculosis and a host of other bacterial diseases, but where Rosen excels is what comes after the discovery. As he outlines, once Merck & Co. saw the profits begin to roll in from this new drug, they only saw money. Unlike the Germans before them, who were antipatent, and valued patience, skill, and luck above all else, once the capital reared its head, it turned Jekyll into Hyde. Such was the case with Schatz who was snookered by Waksman into signing over his share of the credit for \$1.00, and had to sue in Federal Court in order to restore his claim. Such was the future, as Big Pharm had arrived.

Rosen then moves on to explain the present role of pharmaceuticals and drug companies, as *Miracle Cure* turns its focus in its final chapters to the selling and the 'detail men' that hawked what the lab produced. Here Rosen uncovers sordid tales of advantage and astronomical claims left and right, though with the professionalization of medical care in the West there were victories as for instance, statistics and laboratory results become an integral part of research and development before drugs were released onto the market. However, the competition between the drug companies reached a fevered pitch as the diversity of antibiotics slowly tapered. Bacteria are sticky foes because they are constantly changing and adapting. Chemists must do so as well and advertising agencies cannot make grist for the mill out of thin air, however much they might try. Here Rosen introduces us to the famous art dealer Arthur Sackler, who was a brazen huckster in the ad business. Sackler single-handedly created the idea that drug sales could increase through carefully constructed media advertisements placed in respected trade journals like the *Journal of the American Medical Association*. Cloaked within these ads were enticements for doctors to order the latest miracles for their patients. The race was underway to raise the most profits.

As Rosen delineates, all of this rampant commercialization came under scrutiny when Parke-Davis, a major pharmaceutical player, developed a new runaway antibiotic called Chloromycetin, which took on the insectborne bacteria known as typhus. All seemed well, data supported claims, and summarily the new drug spread like wildfire. That was until Dr. Albe Watkins, a doctor in Southern California, suddenly lost his own 9-yearold son after he was given a dosage of Chloromycetin. Watkins was convinced he smelt a rat, and started a movement that would rival some of the stuff that goes viral on social media today, in order to get the attention of the Director of the FDA's Division of Antibiotics, Henry Welch. This set in motion a decadelong debate about the role of government officials in influencing policy. Welch became the kickback poster boy for Big Pharma as it was uncovered that he took money from Pfizer to feather his own nest. Rosen does a solid job of pointing out that although Welch is a dastardly character to be sure, he was also one of the first to pick up on Paul Ehrlich's idea that when drugs are combined they can be better. Proponents of what have become known as 'fixed-dose combination drugs' form the backbone of physician prescriptions even to this day, and it can be said have greatly influenced events such as the current burgeoning opioid epidemic.

Particularly in the United States, this runaway train was slowed, as Rosen helps us to understand by examining Congressional oversight during the Kennedy administration. Through the work of Senator Estes Kefauver and other bureaucrats, but more importantly the endeavors of Dr. Frances O. Kelsey of the FDA's drug review council, they spurred the United States government to action. It was Kelsey though who provided the impetus to get involved when she refused to rubber stamp the newly released antibiotic for expectant mothers called thalidomide. Her skepticism and then her research sensibilities led her to

investigate the bogus claims that were being made about the drug's effectiveness to curtail morning sickness. (2) Her actions saved countless lives as the drug was pulled from the shelves. The thalidomide scandal led to the total reclassification of drugs in America, Kelsey's appointment as the first czar of investigative steps to FDA approval, and spawned numerous movements worldwide. Thus, as Rosen tells us, the machine of pharmaceutical innovation would never have existed were it not for the antibiotic revolution.

Overall, William Rosen has provided us with a huge amount of food for thought in this important monograph and placed the chemistry lab at the center of the development of antibiotics. Over the past 20 years historiographical contributions to both the history of medicine and chemistry have grown exponentially with popular works like Siddhartha Mukherjee's *Emperor of the Maladies: A Biography of Cancer* (3) comes to mind. Chemistry is still a 'new science', with the historiographical record continuing to evolve. Unlike other sciences, many 19th century cornerstones in the field have been utterly discarded. With such rapid growth, the 'adaptability of chemists', as Rosen eloquently quotes, could be ascribed as a theme of the profession. Coupled with the story of the rise of major pharmaceutical companies and the professionalization of healthcare is the main question that Rosen asks us to grapple with: What is the best way to know what actually cures disease? The answer is not so easy, and it leads to other questions of what was the intent upon production, and who's to blame when drugs go awry? Maybe we will never really know what medical inventions actually work?

During the 1930s and 1940s, the lack of government oversight allowed for antibiotic research to flourish. Restrictions were so loose they led to over 100 deaths by poisoning in the Massengill Company disaster and the tardy passage of the Pure Food, Drug, and Cosmetic Act in the same year, 1938. In the end, though, collaboration occurred organically among the community of chemists, professors, doctors, and other professionals. However, the products were left to boards of directors, avaricious companies, advertising firms, some well-meaning and not-so doctors, and of course, the general public. The results have been mixed at best. However, as Rosen reminds us, doctors at one time could only set a bone, deliver a baby, or speculate on the arch of an illness—so this book really does describe a revolution in medicine. One unintended effect was produced; with the over-prescription of antibiotics, the bacteria have adapted to fight another day.

Rosen's background in editing and publishing is evident in this book. He writes succinctly, and uses just the right amount of metaphorical turns of phrase. I do not think I ever would have thought to compare I. G. Farben and the New York Yankees, although they both existed during the same time period (p. 95), but it works. Where the monograph falls short at times is in contextualizing his story within the greater historical movements of the time period in which he is examining. For instance, when he sets the stage for the First World War (p. 59-60) he states that the Europeans were 'applauding the start of hostilities'. This is highly debatable in light of the work of Niall Ferguson and other historians who make the argument that Germany and/or Britain did not want warfare to commence in 1914 or after.

Another area where Rosen falls a bit short is in his discussion of the conspicuous consumption of the early 20th century and the subsequent rising standards of cleanliness and health reforms of the 1920s. Of course, this was spawned not just by the Great War, but also the great influenza that followed. Rosen makes no mention of the impact of this series of events on the chemistry laboratory, which I believe would provide the reader with the proper backdrop. And, one could argue that with aspirin's inability to fight these types of global pandemics the door was ajar for new, more effective, medications.

I also believe that he should have drawn on a more diverse group of sources, especially concerning secondary material. I could not imagine a work such as this without citing the scholarship of David Courtwright, Jeremy Greene, Elizabeth Watkins, Joseph Gabriel or Seth Rasmussen's finely edited series entitled, *Briefs in the History of Chemistry*.(4) Also, I think we would have benefitted from more visuals of advertisements from 1950s and 1960s than just the one example (p. 229). I realize these rights are expensive and challenging to obtain, but they do enliven the subject matter from a material culture point of view.(5)

These criticisms aside, I was deeply impressed not only with William Rosen's personal drive and determination to pursue this subject, but also his storytelling. The narrative approach and style he employs works so well that this is book you will want to read as a scholar or for general interest. As students of history we are always thinking about the past and what we will produce in a writing project. Yet, on a more personal level Rosen's work also probed my thinking about my own mortality. What will we leave behind that future generations of scholars and writers will remember us by? To alter the quote used at the end of *Miracle Cure*: How about an expression of faith in the adaptability of the historian? Thank you for your bravery Mr. Rosen, you showed us the strength to adapt. Rest in peace.

Notes

- 1. William Rosen's obituary can be found at: http://obits.nj.com/obituaries/starledger/obituary.aspx?pid=179843766 [2]Back to (1)
- 2. Thalidomide was featured as a major theme during multiple seasons on the incredibly popular BBC Series, *Call the Midwife*.Back to (2)
- 3. Siddhartha Mukherjee, *Emperor of the Maladies: A Biography of Cancer* (New York, NY, 2010). Back to (3)
- David Courtwright, Forces of Habit: Drugs and the Making of the Modern World (Cambridge, 2001), Jeremy Greene, Generic: The Unbranding of Modern Medicine (Baltimore, MD, 2014) and Greene and Elizabeth S. Watkins, eds. Prescribed: Writing, Filling, Using, and Abusing the Prescription in Modern America (Baltimore, MD, 2012), Joseph Gabriel, Medical Monopoly (Chicago, IL, 2014), and Springer Briefs in the History of Chemistry, ed. Seth Rasmussen (Heidelberg, 2013-Present).<u>Back to</u> (4)
- 5. Steven M. Rooney and J. N. Campbell, *How Aspirin Entered Our Medicine Cabinet* (Heidelberg, 2017). In our own work we went so far as to obtain from Ebay examples of aspirin bottles from the major advertisers in the 1950s and 1960s.<u>Back to (5)</u>

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