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J.N. Campbell

How Aspirin Entered Our Medicine Cabinet



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Steven M. Rooney · J.N. Campbell

How Aspirin Entered Our Medicine Cabinet

Steven M. Rooney
Independent Scholar
Irving, TX
USA

J.N. Campbell
Independent Scholar
Spring, TX
USA

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*for Teri, who suggested it, and for Cory,
in memorium*

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About the Authors

Steven M. Rooney taught AP Chemistry at The Episcopal School of Dallas for thirteen years. After starting his career in research, he believed fervently in getting students interested in science by showing them how to think for themselves. Steven received an M.S. in chemistry from the University of Missouri–St. Louis. As an independent scholar, he lives in Dallas with his wife Teri, and their small parrot, Gypsy.

J.N. Campbell is an independent scholar whose interests include, twentieth century mass culture, and the vast swath that is, World History. He received his M.A. in History from the University of Kentucky, and an M.A. from the Parsons School of Design. A native Texan, he lives in Houston.

Abstract

This brief traces the story of one of our most common medicines—aspirin. On a journey involving diverse characters, shady business deals, innovative advertising, and good old-fashioned luck, Rooney and Campbell describe how aspirin was developed and marketed on a global scale. Starting at the beginning of the twentieth century, the authors explain the use of aspirin during the First World War, the development of competition drugs such as acetaminophen after the Second World War, and the application of aspirin to heart disease through the present. On a broader level, Rooney and Campbell show that the development of America's modern pharmaceuticals was a complex weaving of chemistry and mass culture. They argue that aspirin's story provides a way to understand the application of complex chemical formulas into medical results. This brief is of interest to historians of chemistry and medicine as well as the general educated reader.

Keywords Aspirin, history of • Bayer, history of • Medical history • Heart attacks/stroke • Headache • Drugs, history of • Great influenza • Advertising • Mass culture • Medicine

Chapter 1

Aspirin's Space

1.1 Introduction

Have you ever caught a glimpse behind the mirror of a medicine cabinet that was not your own? Decorum frowns on such actions; there is something inherently personal in there. In 2015, journalist Katy Schneider did what could be perceived as just another human-interest piece for *New York Magazine* when she somehow convinced five people to open one of their most private spaces—the medicine cabinet [1]. However, with great insight, she was sanctioned a behind-the-scenes-tour into the inner sanctum of a pharmacist, a dancer, a model, a former dental assistant, and a drag queen. Photographer Bobby Doherty provided an image of each interior, and the owners gave a brief synopsis, with some cogent analysis and humorous admissions, of the contents of this private space.

The pharmacist, right on cue, divided the space into two areas, one for daily maintenance, and the other for situations that might arise, like Band-Aids for cuts and scrapes. The dancer emphasized the effects of the harsh New York winter on the sinuses. The model touted the perks of constantly receiving swag from her profession, especially in the form of beauty products. The former dental assistant shared a private vignette concerning her battle with lupus, and the bevy of pharmaceuticals that were needed to win this war. Finally, the drag queen espoused the benefits of essential oils, and explained how to concoct special deodorants and mouthwashes that promote natural health. Each of these individuals, and their respective medicine cabinets, all had one major theme in common, they all possessed pharmaceuticals whose sole purpose was alleviating and preventing pain; what could be characterized as a personal one-stop shop for treating you. Interestingly enough, most of these cabinets contained some form of one the most important and longest-lasting medications to ever come from a chemistry laboratory—aspirin [1].

This is the story of how aspirin entered the medicine cabinet. After 1899, it became a permanent fixture inside this private space, but as the century wore on

other products could be found inside. Despite this rampant competition, aspirin remained. Despite being termed a “miracle drug” by generations of aspirin consumers, it is actually a tale of contradictions. Aspirin evolved through time. Questions abound. Invented or re-invented? What is the proper dosage for an average male or female? If it is really the same formula, how do successive generations market aspirin to the general public? From a global perspective, how did the violence that was exhibited over the course of the twentieth-century compare with the development of a medication that sought to relieve analgesic pain? Most importantly, how did aspirin, which began in the modern chemistry lab, finally get translated into medicine? Aspirin, the solution to the headache and the panacea for heart-related issues, serves to this day as an answer to pain. In other words, its history is much more than something common, but despite this assertion, it was not born from a miracle.

The historical scholarship of aspirin is diverse, but most research has focused on the drug's impact on society, how it was marketed, or the politics of the business deals behind the ownership of the patents [2, 3]. However, few works have synthesized the study and development of modern aspirin by placing it firmly in the realm of the organic chemistry lab. During the late nineteenth century in Europe and the United States, labs began to push the limits of chemistry. Rather than isolating natural species or compounding other known active reagents, the birth of aspirin signaled the beginning of a new synthetic class of pharmaceuticals.

This piece seeks to tell aspirin's story through the lens of three spaces, the chemistry lab, the medicine cabinet, and the doctor's office, where this drug evolved over the course of modern history. By examining each of these spaces, we can see how aspirin's role over the course of twentieth century and into the next, changed how the prescribing of medicine impacted the prosecution of pain, and reinvented the notion of prevention.

First, the late nineteenth century chemistry laboratory, which was an integral location to aspirin's birth, became the gateway for new pharmaceuticals, as a race ensued to find answers to the most perplexing questions across multiple fields. The lab, first housed at universities and then within major companies, became an intersection where education, industry, medicine, technology, government and economics all combined to try to solve issues that plagued nations.

Second, a relatively new space within the home, the bathroom, and its indispensable inner sanctum, the medicine cabinet, blossomed with a meteoric effect before the First World War. Competition for space in the room within the room bred opportunity for companies, their agents and attorneys, and of course, for the consumers. This is a tale that encompasses a complex assortment of characters and deals, patents and plots, which were motivated by the search for unmitigated profits. Print, radio, and eventually television, all vied for sales.

Lastly, during the post-War era, the doctor's office became a complex space where a new cadre of medical school trained physicians and evidence-based scientists interpreted the results from the research laboratory. Alongside this shift in professionalization, the development of a highly competitive pharmaceutical

industry intersected with the debate over heart health to push aspirin in new directions that were previously unfathomable.

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Chapter 2

Aspirin and the Chemistry Laboratory

2.1 A National Chemistry Defined

Western nations in Europe or in the Americas during the second half of the nineteenth century, whether rising or established, were what historian Benedict Anderson termed as “imagined communities.” Even though members of a nation will never meet one another, their beliefs, attitudes, and sentiments are similar. Paradoxes abound though. In a nation you are both inherently limited in your ability to unite giant swathes of people; at the same time your state and its borders are sovereign, and thus defined. Likewise, while everyone on the planet has a nationality, not all of them are the same; hence they are *sui generis*, unique in every way possible [1, p. 5].

To make a good nation that reflects who you are as a people you need several identifying factors, such as a foundation story, identifiable symbols, governmental structures, an army and or a navy, and a set of university systems, just to name a few. The nation became the catalyst for power and a means by which to expand [1, p. 7].¹ The development of chemistry as a discipline, especially within the

¹Nationalism spread after the political revolutions of the eighteenth century that began in America and France. After Napoleon’s defeat in 1815, fervor spread throughout Latin and South America, and influenced the European revolutions of 1848. With the unification of Germany, Italy, and Japan around 1870, nationalism influenced older empires such as China in 1911 and Turkey in 1920. Nationalism also influenced former colonial possessions from India to Kenya, and helped to dissolve the Eastern Bloc countries of the former Soviet Union. It was a truly a global set of events that to this day continue to divide and unite nations as they grapple with issues that range from the use of environmental resources, immigrant migration, usurpation of democracy, and even to who will host the Olympic Games. For a primer on this subject see: Marks [13].

university, became a byproduct of nation building. As science progressed over the course of the nineteenth century, countries began to promote its development with the purpose of strengthening national ties and furthering their own industrial capacity, expressing hegemony, and especially, securing the health of their people.

After the Napoleonic Wars, Europe remained in relative peace until 1914.² By 1850, Western nations were scrambling for the right to expand their own power both at home and abroad. With the advent of the Industrial Revolution, the new loom technology for weaving, a host of other means of mechanization, and the building of advanced factories that could produce low-cost cloth, they now began to develop colonial markets for these new ready-made wares. Synthetic dyes were essential to the powerful textile industries that spanned the globe.³ The engine that drove this massive increase in production was coal. The energy emitted from this source dwarfed the power of wood, and the result of its decomposition was tar [2]. Used in the making of roads to eventually the creation of pharmaceuticals, tar was the basis for a new set of products and industries that would transform the world.

In order to understand the chemical composition of tar and its uses, laboratories were built to study and process the new approach to this promising field. The chemistry built the laboratory, but the laboratory also built the modern discipline that we know today. Beginning in Britain, the Industrial Revolution migrated to the continent of Europe, thus inaugurating a stimulating age of study, both within universities and eventually in companies that were devoted to the making of products for public consumption.⁴

A transformative consumer good that would change the world was the German created aspirin. Before it could be born though, first, the architecture of the lab was integral to its development. Understanding the tools, and in many cases literally creating the equipment from scratch, would be necessary to solve the puzzle of aspirin's chemistry. However, who owned the expertise to this chemistry? Nations both collaborated and competed for the right to claim that their scientific endeavors were supreme. After German hegemony was established in this respect, it would

²Warfare did occur on the continent when it came to the formation of a modern Germany, and in the United States. Under Otto von Bismarck and Kaiser Wilhelm I, they fought a series of conflicts that were quite successful against Denmark, the Austro-Hungarian Empire, and France, which led to unification after 1870. The Crimean War of the 1850s was also one of the other major events that challenged the European Alliance system. The other major event in America concerned their Civil War, and there were flash conflicts around the world that pitted the colonial powers against one another.

³European nations, like Britain, France, Germany, and Russia, were part of a new generation that vied for colonial power after 1850. Britain, especially with its development of its colony in India, was a key example of using the population to develop new customers. The British restricted production of local cloth in order to subvert competition. Of course, the Gandhi-led movement of the 1930s and 40s successfully destroyed the notion of British rule by establishing a free and independent India in 1947. For a broad-sweeping study on this subject see: Bobbitt [14].

⁴Both Britain and Germany possessed huge deposits of coal in their respective backyards. This is what allowed Britain to sprint ahead in industrial production, however, by 1900 Germany was right on pace to pass them at the dawn of the new century. See: Stearns [15].

take a visionary company led by innovative thinkers such as Carl Duisberg, who understood both the complexities of the coal tar industry, the dye business, and the possibilities that lay in pharmaceutical production. It was the German, Friedrich Bayer, who created a new kind of company with a new kind of industrial chemist for the future. Finally, the results of these advancements from the laboratory became the basis for leading aspirin into the next century, thus inaugurating the first global medicine for a new age.

2.2 Lab Architecture: A Revolution in Equipment Ensues

In 1868, Kaiser Wilhelm's army decimated the forces of Denmark and then dispatched the Austro-Hungarian Empire on the battlefield. In order to do his part, Adolphe Wurtz, a French chemist, turned his pen into a sword against the Germans. He published the *Dictionary of Pure and Applied Chemistry*, which was a rousing portrayal of the future of organic chemistry. Yet, there was a vindictive statement in the compellation with the assertion that, "chemistry is a French science." With this salvo, a German counterpart named Hermann Kolbe offered a rebuttal in an article published in the *Journal for Practical Chemistry* where he counterattacked by espousing the history of German science and their innovations within the laboratory [3].⁵ Not long after, a Russian contingent joined the debate over who held the most dominant position in chemistry. Through several journal articles they chided the French for their overt arrogance, and the Germans for having responded in such a manner.

Taking what initially appeared as the high road, the Russians proposed, despite the Franco-Prussian War, that both sides should table their differences in the name of science and in the spirit of internationalism.⁶ Of course, Russia sought to develop its own chemical program (plus their government had a long-standing alliance with France to consider), and knew that German science was already beginning to dominate future development. While although it was true that chemistry was for everyone, there was evidence that national pride, investment, and the secrets of the laboratory were not. Warfare and science went hand-in-hand, and the discord that the alliance system tried to avert was only setting the table for the possibility of a much larger conflict. How did German advancements in organic chemistry become

⁵Hermann Kolbe (1818–1884) was the senior editor of a series of papers in the *Journal für Praktische Chemie*, which became some of the most important foundations for organic chemistry. His sharp wit and conservative interpretations fueled several feuds with colleagues that led to his professional demise.

⁶The Franco-Prussian War (1870) was a seminal event for the future of a united Germany—a second Reich. Otto von Bismarck used this opportunity to put military precision on display, and evaporate the chance of a two-front war with France's long-time ally, Russia. The German army decimated its opponent and obtained the territorial rights to Alsace-Lorraine; a year later they were unified as one country.

so prolific that the French, the Russians, and even the British would marvel at their contributions? The story begins at a German university with a vision of the potential for an organic chemistry laboratory.

The study of organic chemistry in Europe during the early nineteenth century was closely tied with the continuing evolution of early chemical laboratories. Even by 1850, the study of this new branch of science was still a relatively new phenomenon. With Darwin and Spencer's investigations into the natural world, and now that transportation was continuing to accelerate at such a rapid pace, ideas, data, and a thirst for understanding organic material was as furious as ever. Justus von Liebig was the first to publish his work on organic chemistry and its practical uses for both the fertilizer and agricultural markets [4].⁷ Universities, both in Europe, and on a much smaller scale at least initially in the United States, worked to keep up with these demands. As nations sponsored studies into branches of science they deemed suitable for investigation, competition and collaboration drove discovery. By 1824, while working as an assistant professor at the University of Giessen, Liebig began to emphasize the importance of the lab for increasing knowledge, and helped to take it from amateur tinkering to professional systematic research.

The new laboratory became an efficient means of conducting and advancing technology, because Liebig knew that organic chemists needed to focus their efforts on the analysis beyond the instruction of just technique and chemical preparations. He constructed the lab in the most unlikely of spaces—a small-unused guardhouse. Financing it on his own because the University did not agree with his intention to operate the space with the precision of a factory, Liebig's approach meant that a set of codes or standards would be adopted. Along with these measures, a hierarchy of power, which guided the production of chemical experiments, would become a cornerstone for implementing future developments [5, 6, p. 93].

As the principal, Liebig would write, lecture, and administrate about his own research to his more senior students, and in turn they would educate the newer pupils on the basics of research in the laboratory. If his experiments called for a new type of receptacle he would have a glassblower create an apparatus to accomplish his needed task. There were other major advancements besides turning out highly qualified organic chemists. The floor plan of the lab included the construction of fume cupboards housed over laboratory benches. Cabinets for storing laboratory apparatus and chemicals were spaced accordingly against walls for easy access. Reagent bottle racks for the storing of chemicals at the back of the benches made for extra storage space. [6, pp. 97–99].⁸

⁷Justus von Liebig (1803–1873) was the son of a pharmaceutical and chemical dealer. He was apprenticed to an apothecary, which before 1820 were inextricably linked to the study of chemistry. Dissatisfied under this tutelage he moved to Paris to study under the chemist, Joseph Gay-Lussac. With the help of Alexander von Humboldt he joined the faculty at the University of Giessen, where he remained until he received the chair in chemistry at the University of Munich in 1852.

⁸This fume cupboard was the precursor to today's fume hood for drawing out noxious fumes.

The laboratory at the University of Giessen itself was a small space by modern standards since it measured only about 580 square feet.⁹ The furnaces used for heating were located at the rear of the laboratory, so they could be safely serviced from the exterior. Later, in the corners there were new glass lined fume cupboards, which could be raised or lowered for better control of escaping chemical fumes; or just for separating oneself from the dangerous experiment taking place in the fume cupboard. These were near this heat source, so they could use the draught of the furnace to exhaust any noxious fumes from experiments. The lab benches along the walls and the bottle racks that contained chemicals at the backs of the benches were equipped with cabinets designed for an apparatus for distillation. Lower tables in the middle of the lab would eventually be used for other experiments. The front wall was equipped with a drying kiln, and had large windows for light and additional ventilation. Finally, a hatch at the back of the lab was present, so Liebig could instruct the researchers of the laboratory from his office [6, p. 96].¹⁰

Over the next several decades, the introduction of the Bunsen burner, central gas and water main lines, and electrical outlets would be incorporated into the laboratory in order to elevate it to modern specifications [7]. Once these innovations were in place, the small academic lab was scaled for large industrial applications of organic chemical synthesis. By the second half of the nineteenth century, other institutions of higher learning started to emulate the example that German universities (which at first were reticent about such foreign practices) were employing in their philosophy to establish the chemistry laboratory as a central location for advancing scientific study for educational purposes.

In the 1880s, the center of the scientific world in chemistry officially moved from France to Germany. This shift in academic supremacy can be traced to the rise of organic chemistry and the establishment of the German synthetic dye industry. The dye business owed much of its success to rich coal deposits that could be found in Prussia in northeast Germany, especially in Silesia and Westphalia. Since Germany was geographically blessed, the industry was looking for ways to remain as a leader in synthetic organic dyes. This gave Germany the ability to move into the manufacture of the new field of pharmaceuticals. The key for commercial development would be to align with German academic institutes for consultation on lab architectural construction. However, it would take a new kind of company to lead this enterprise that would change the future of organic chemistry and the pharmaceutical trade forever.

⁹It is not uncommon to find modern laboratories more than ten times the size of the Giessen laboratory.

¹⁰This “hatch” appears to have served rather like a butler’s pantry would have just off the dining room in a house of some means; a veritable portal in which Liebig could monitor the activities in his lab.

Fig. 2.1 Carl Duisberg, c. 1899 (Photo courtesy of Edgar Fahs Smith Collection, Kislak Center, University of Pennsylvania)



2.3 A New Kind of Company Breeds a New Kind of Chemist

Carl Duisberg had pluck, fortitude, a clear vision for what he wanted out of life, and probably most of all, good, old-fashioned, luck. If he had listened to his father he probably would have turned into one of the most competent ribbon manufacturers in all of Western Europe. Instead, his zeal for chemistry, and a sponge-like ability to understand complex arguments carried him along. He also was blessed with a mother, who wanted him to build a life of significance that had nothing to do with ribbon, and he had the opportunity to rise through a university system that was open to males that were industrious enough; Duisberg had this last trait in spades. By 1883, at a critical juncture in his life, he obtained a coveted research post at the University of Strasbourg, which happened to be sponsored by an up-and-coming synthetic dye company called Bayer [6, pp. 245–246] (Fig. 2.1).

Twenty years prior to Duisberg's arrival, Friedrich Bayer got his start as a dye salesman and partnered with Johann Friedrich Weskott, a master dyer, to form *Farbenfabriken Bayer*.¹¹ Companies that were able to produce the most distinctive dyes had a distinct advantage over their competition since demand was high for fashionable colors and the latest consumer goods [6]. After completing his doctorate at the University of Jena, Duisberg became a fulltime patent dye consultant for Bayer.¹² With a serious mind, and a background in both the chemical and legal

¹¹Friedrich Bayer (1825–1880) founded the aspirin company that bears his name by attracting energetic young men that were part of the new partnership between universities and industry.

¹²Carl Duisberg (1861–1935) grasped the mission that Friedrich Bayer envisioned. Like most Prussians, who took part in university training and in military service, Duisberg combined savvy business sense with chemistry to be the organizing force behind Bayer at the turn-of-the-century. After taking a trip to America, he was greatly influenced by the design of vertical integration



Fig. 2.2 The Wuppertal-Elberfeld, Germany, one of Bayer's new laboratories, 1891 (Photo courtesy of Corporate History & Archives, Bayer AG)

fields, he knew that holding the patent and or a trademark on new dyes would be lucrative for the company, as well as, essential for continued growth. The Bayer research laboratory in Wuppertal-Elberfeld was opened in 1891 (Fig. 2.2), and in the same year Duisberg was given a free hand to draw up new plans for an expanded factory facility in an area north of Cologne, known as; Leverkusen.

Here Bayer acquired the alizarin red factory of Leverkus and Sons, and they soon founded its first major outpost outside of Europe in Rensselaer, New York. Bayer, under Duisberg's influence (he joined their board by 1900), was now becoming a giant in the chemical industry through its ability to branch out into the research and development of new trade—pharmaceuticals [8, p. 14].¹³

The profitability of the synthetic dye industry that Duisberg sought to expand upon gave rise to industrial laboratories that were devoted to organic chemistry. In

(Footnote 12 continued)

(two or more stages of production under one company) when he toured Standard Oil. For over four decades he presided over Bayer until it was assumed into the conglomerate I.G. Farben in the 1930s. For a thorough treatment of Duisberg's career see the German article: Stock [16].

¹³Concerned that other German dye firms would begin to develop antipyretics, Duisberg had the idea of converting a waste product into a synthetic drug for pain relief called phenacetin in 1888. It became a staple in pharmacies for over 90 years until it was pulled from production due to long-term damage of the kidneys.

the 1850s, compounds isolated from coal tar led to the production of synthetic dyes. The German industrial chemical research laboratories were modeled on the academic institutions of the time, of which the new Bayer research laboratory was crafted [6, p. 248]. They were fitted with the standard laboratory benches, and chemical bottle racks that contained water, gas, and electrical works; along with new drains for evacuation. Still, the industrial research laboratory was meant for efficiency and its architecture resembled a production line. The benches were closer and the aisles were narrower, and though the details on the fittings were not as lavish as with university laboratories, the workspaces were more compartmentalized, which led to the workers being closely supervised. This was a very competitive time for the crafting of an organic synthesis and protecting trade secrets was a high priority. Yet, even more significant was the establishment of an industrial hierarchy. Like the Prussian army's system of rank, in order to maintain an efficient organization in the lab, individuals were classified by their dress, with managers distinguished by their suits, and mid-level chemists wearing jackets without ties. Meanwhile, wearing their brown aprons or coats, which were similar to what we would think of as a lab coat today, identified the lowest wage earners. Having a social hierarchy sent a clear message concerning the mission statement of the lab, and assisted in the successful carrying out of goals [6, p. 249].

Duisberg's pharmaceutical branch of Bayer was established in 1893 when a laboratory in the attic was constructed for that express purpose. Three years later, a new structure was built, that resembled the academic facilities of the day even more than the main dye center at Bayer. Standard laboratory benches, storage cabinets, and chemical bottle racks were in place, along with high ceilings and large windows. Gas, water, and electrical fixtures, as well as, plenty of fume cupboards were part of the new framework. Bayer's investment in research and development was a major reason why they were able to not only remain competitive, but were able to reach the pinnacle of the production of chemical synthetic products [6, 252].

2.4 Aspirin's Chemistry

With the development of the organic chemistry laboratory, first with the structural framework established by Justus von Liebig, and then carried out by companies such as Bayer, industrially produced pharmaceuticals would change the landscape of the market. This meant that by 1900, consumers could begin to count on more consistency with their products. Purity became the word most often-used. The most important example of these developments was aspirin.

The common name for an organic molecule that chemists call acetylsalicylic acid (ASA) (Fig. 2.3), the aspirin molecule is formed from only three different types of atoms; carbon, hydrogen, and oxygen. It has a molecular weight of 180.2 g per mole. Aspirin is a molecule, and hundreds of times smaller by mass than the enzymes in which it is known to inhibit. The reaction of these enzymes leads to

Fig. 2.3 The aspirin molecule

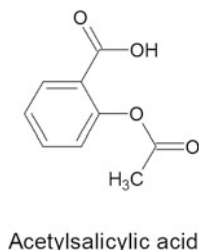
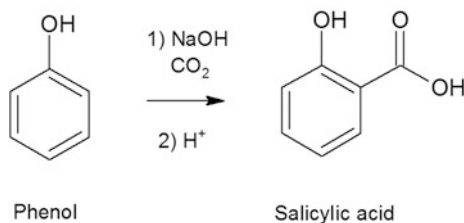


Fig. 2.4 Kolbe-Schmitt reaction



beneficial results and the harmful side effects, which by the late nineteenth century were hallmarks of what would become known as aspirin.¹⁴

When a compound isolated from a plant source is needed on a large industrial scale the main issue becomes cost. Besides discovering and isolating organic compounds the goal of a synthetic organic chemist, even to this day, is to find a way to increase the yield of an organic compound and lower expenditures. Hermann Kolbe, the defender of German science, was able to solve this issue by providing copious amounts of salicylic acid at a reasonable cost. In 1859, the Kolbe process for synthesizing salicylic acid from phenol was first published. Known as the Kolbe-Schmitt reaction for the purposes of commercial production of salicylic acid it is then used to produce aspirin. The method starts with the organic compound phenol and the strong base sodium hydroxide, which will deprotonate the phenol to produce sodium phenoxide (Fig. 2.4). This in turn reacts with carbon dioxide under high heat and pressure until the carbon dioxide adds to the sodium phenoxide to yield a carboxylate, known as sodium salicylate. It then reacts with strong acid to yield the desired product, salicylic acid [9, 10].

¹⁴Precursors of aspirin, such as willow bark, have been around for centuries, and the drug was mentioned in archives by the Egyptians, the Greeks, and referenced most notably in a paper written by clergyman Edward Stone (1702–1768) in 1763. Stone had discovered that by grinding up the bark of the white willow tree and giving it to people who were suffering from malaria, their aches and pains would subside and their fever would become reduced. The antipyretic (fever-reducer), analgesic (pain-reliever), and anti-inflammatory compound found in willow bark is salicin. The name comes from German chemists who isolated the active ingredient from the white willow bark tree, *Salix Alba* in 1828. For a more thorough treatment of aspirin's early developments see: Jack [17] and Stone [18].

Phenol was first isolated from coal tar in 1834, and within a decade, the name was given to the compound after being isolated in pure white crystalline form. Frenchman Charles Gerhardt was the first to synthesize acetylsalicylic acid by reacting sodium salicylate with acetyl chloride.¹⁵ At the time, it was not easy to isolate a pure sample of acetylsalicylic acid from this process. Nothing came from this impure and crude product of acetylsalicylic acid until forty years later when Felix Hoffmann devised a better way of synthesizing the substance we now know as aspirin [11].

By this point, salicylic acid synthesized from phenol (carbolic acid) and carbon dioxide was widely known to possess a powerful external germicide. Physicians in Europe were continuing to scour for an internal one because phenol was too corrosive to living tissue to be swallowed. Kolbe was convinced through a series of experiments that salicylic acid was an effective germicide and recommended it to physicians for use on patients suffering from a range of disorders. Initial results were surprising since patients who were given salicylic acid reported improvement; though most died from bacterial infections and disease. Soon the effects became clear to physicians that salicylic acid was curing only those patients who would have survived whether they had ingested the compound or not. His initial hypothesis was erroneous; salicylic acid is not broken down in the body to yield phenol, and is not an effective internal germ-killer.

Even though Kolbe was incorrect about the internal germicidal properties of salicylic acid, the compound was providing a host of benefits. From this it was discovered that patients that were prescribed salicylic acid had their pain and headaches relieved, fever reduced, and rheumatism cured. Though originating as a tar-based product it was not an internal germicide, but was an effective pain reliever that had one serious drawback. Side effects included irritation of the mucous membranes in the mouth, esophagus, and the stomach to the point that patients preferred their initial ailment rather than taking on another. Chance once again played a pivotal role at Bayer when Felix Hoffmann, a chemist on staff, whose father was one of the patients battling the side effects of salicylic acid, proffered a major breakthrough.¹⁶ Under Duisberg's leadership, Bayer was already interested in finding a better alternative for salicylic acid at the same time Hoffmann's father was suffering from its side effects. With the backing of Bayer's new industrial

¹⁵Charles Gerhardt (1816–1856) was one of the most influential French chemists of his generation, and probably would have taken issue with the assertions made by his countryman, Adolphe Wurtz. Especially, since he believed fervently in collaboration with colleagues both in England and on the continent.

¹⁶Felix Hoffman (1868–1946) worked for Bayer as the head of pharmaceutical sales until his retirement in 1928. The creation story behind Hoffmann's synthesis was disputed during the 1990s when evidence came to light that another researcher named Arthur Eichengrün (1867–1949), who worked at Bayer at the same time, was actually the one who synthesized aspirin. Due to his Jewish heritage, it was believed that the Nazis deleted him from the record. Bayer AG officially denied such allegations, and to this day continues to support Felix Hoffmann and his place in its history as the chemist that created modern aspirin. See: Sneader [19].

Fig. 2.5 Felix Hoffmann c. 1899 (Photo courtesy of Corporate History & Archives, Bayer AG)



laboratory capacity, Hoffmann set out to search for a more effective pain reliever with less side effects (Fig. 2.5).

Knowing that the hydroxy group ($-\text{OH}$) of the salicylic acid was most likely the cause of discomfort, Hoffmann understood that by removing the hydrogen he could replace it with a substitute and might produce a valuable compound. This result would provide the benefit of salicylic acid without the irritating side effects. In his research Hoffmann came across a derivative of salicylic acid where the hydrogen of the hydroxy group was replaced with an acetyl group (COCH_3). This particular byproduct was actually prepared about forty years earlier by Gerhardt, known as acetylsalicylic acid. Hoffmann's experiments improved upon it by increasing the product yield after using salicylic acid and acetic anhydride as reactants, instead of acetyl chloride and sodium salicylic used by Gerhardt. This refined method of producing acetylsalicylic acid enabled Bayer to produce, test, market, and trademark this compound under a new name. With Duisberg's guidance, Bayer chiseled into history a new synthetic pharmaceutical from several roots. The *a* comes from the world acetyl, while the *spir* from the plant *Spiraea ulmaria* from which salicylic acid was extracted. And, finally, the *in* was a common root name attached to medicine at the time. Hence, aspirin, became the freshly christened name for what would become this revolutionary drug (Fig. 2.6).¹⁷

As early tests showed, aspirin appeared to pass through the stomach's acidic environment without change, but it lost its acetyl group in the small intestine to yield salicylic acid that gets absorbed, and then carried through the bloodstream. As it turned out, Hoffmann's hunch about the acetyl group making the irritating effects of salicylic acid was accurate; he also devised a superior way of synthesizing aspirin. He was not the first chemist to concoct a means to make aspirin, however, in August of 1897, he wrote in his laboratory journal an improved means for the

¹⁷For a more thorough treatment of the word aspirin and its origins see: Weissmann [20].

Fig. 2.6 Example of one of Bayer's early German-made aspirin bottles, c. 1899 (Photo courtesy of Corporate History & Archives, Bayer AG)



synthesis that yielded a more complete conversion of salicylic acid to acetylsalicylic acid. This method, with slight modifications, is still used in industry and chemistry labs the world over today [12].

The organic chemistry laboratory was transformed from a space conceived in the universities of Europe. Once a fixture there, the lab became a place where, with factory-like precision, production could be streamlined for quality and quantity; later, the German influences revolutionized, first the dye-making companies of the West, and then through the control of patents and trademarks, greatly transformed the pharmaceutical industry in the future. These “factories” of formulas drove the building of the laboratory under those like Justus von Liebig, and vice-versa, it helped to construct the chemistry for drugs such as aspirin, under the auspices of a new kind of industrial chemist, like Carl Duisberg at Bayer [8, pp. 135–137]. Aspirin’s development was directly attributed to the equipment and university training that chemists now found standard in their field. Next, the medicine cabinet would be filled with the new products that were pumped from the industrial laboratory, and eventually, to the consumer.

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Chapter 3

Aspirin and the Medicine Cabinet, Part I

3.1 Aspirin Finds a Home

By the end of the nineteenth century, as the organic chemistry laboratory arrived as a staple in the academic and industrial centers of the West, a different kind of space, the bathroom, became a permanent “fixture” in the majority of homes. No longer detached from the house, this new space became an area where privacy and cleanliness intersected. New architectural forms that could be found in the rest of the house became commonplace in the bathroom, such as hexagonal tile, light fixtures, and especially, millwork. Along with technological developments like the toilet, a bathtub that could also double as a shower, special varnished wallpaper that was designed with a layer of protection against steam, and pipes that carried hot or cold water in and drains that flushed soiled water out, the bathroom came equipped with what became known as the medicine cabinet [1, 2].

This new repository became an inner sanctum unto itself.¹ Thus, privacy was redefined. Requiring storage for smaller personal items the cabinet provided the resident with a compartment for immeasurable secrets. Initially, millwork companies specialized in the use of matching woods to customize their designs to suit the needs of their clients. The design of cabinets was roughly two by three feet in size.

¹Medicine cabinets can be found in most homes today, but period examples exist in historic homes beginning around the 1900. Towns and cities through historic houses with non-profit affiliations have attempted to preserve the integrity of the early twentieth century bathroom and its environs.

With hinged doors and equipped with a hasp, or even later, a magnet to keep the door secured, once open, shelves were present to house a variety of items (Fig. 3.1).² Later, medicine cabinets became metal, and most were located over a sink with the customary mirror so that one could inspect oneself before going out into the world. The space allowed reflection on the inside and on the outside of the body.³

At the turn of the twentieth century, items for the medicine cabinet included a host of products that were becoming standards of hygiene. Rising industrialization, coupled with the increase in wage-earning potential, fueled consumption. Mass culture popularized these items to the point of creating a feeding frenzy over the pursuit of beauty. Now everyone could open their cabinet, reach in, and choose from a plethora of new and improved items that were crafted to aid a variety of different maladies. These included soap, toothpaste, hair tonic, petroleum jelly, Band-Aids, shaving equipment, and of course, aspirin.⁴

Of all the products found in the medicine cabinet, aspirin, in a short amount of time, became the first global medicine for a new age. Inexpensive to produce and marketed in a massive scale, this new drug democratized the relief of pain by allowing people of all walks of life to afford it. Three major events both promoted and challenged aspirin's hegemony of the medicine cabinet before 1950. The First World War, and the Great Influenza that followed, changed medicine forever as the globe grappled with the inability to cope with an enormous amount of death and disease. Next, the rise of advertising in the 1920s forced companies during the interwar years to define budgets for the sole purpose of swaying consumers to buy their product. Finally, the Second World War, the capstone of the whole period, redefined science and medicine by developing alternatives to aspirin, such as acetaminophen. These pharmaceutical developments would relegate aspirin to the status of common as the second half of the century arrived.

²The McFaddin-Ward House (1906) is a Beaux-Arts Style home, with a Carriage House and Servants' Quarters, constructed in Beaumont, Texas. A historic house museum since 1981, it has an excellent tour, along with its wonderful collection of period furnishings to 1950. The medicine cabinet, seen above (Fig. 3.1), is located in the third floor bathroom. The seagull wallpaper is a sanitary reproduction (varnished during the period for water-proofing from steam—another innovation from the dye stuff business) of the original design. Curatorial staff discovered it behind the medicine cabinet during their investigations.

³The Kenneth E. Bering Center at the Smithsonian National Museum of American History's website (americanhistory.si.edu) is a reliable place to begin when exploring the domestic life of this time period.

⁴Some well-known brands got their start during the early parts of the twentieth century include products made by Johnson & Johnson, Vaseline, and Colgate. See: Take Good Care of Yourself. <http://americanhistory.si.edu/object-project/household-hits/medicine-cabinet>, Kenneth E. Bering Center, Smithsonian National Museum of American History.

Fig. 3.1 Medicine cabinet, circa 1906 (Photo courtesy of the McFaddin-Ward House Museum, Beaumont, Texas)



3.2 The Modern World Arrives: Production Trumps Consumption

Industrialization changed the world with the unleashing of an unbound Prometheus [3]. In particular, German firms during the late nineteenth century were typically bureaucratic and against competition, much to the chagrin of their American counterparts who attempted to evade legislation, such as the Sherman Anti-Trust Act, which sought to weaken monopolies.⁵ The German model of business originated from the coal and tar business, which spawned the dye companies that formed the basis for the medical industry. Firms worked in concert with professors in the German university system to build advanced laboratories, and since the chemical

⁵The Sherman Anti-Trust Act was passed in 1890 to prohibit certain business practices that were anti-competitive, and would be used by the administration of Theodore Roosevelt to take on and break up the power of Big Business (i.e. the trusts such as oil and steel).

industry was so strong, they had an airtight hold on patents which were recognized around the world as a protection of their rights [4].

The global race for colonies and maintaining empires pressed science to keep up with the latest innovations in order to spur on nationalism and commerce. Civilizing products flowed in all directions, to Africa, South America, and Southeast Asia. These emerging markets provided Western nations with a bevy of potential customers, whether they wanted to partake in the purchase of products or not [5]. In Western nations ethnic diversity forced some states, like the Austro-Hungarian Empire, to constantly manage their approach to workers' rights through negotiation on one side to the outright use of violence on the other.

On the eve of the First World War, everyone, whatever their socio-economic status in the West, could access some form of what would become known as aspirin. Sold first in powder form and then in the popular tablet, aspirin was primarily the creation of *Farbenfabriken Bayer*, which had a major plant in Rensselaer, New York. Bayer came to dominate the global market by securing trademarks in places like the United States by 1900, but it arrived at this position in a way no other company did before. Before the Great War, as it came to be called, Bayer did little advertising that was directed toward the consumer; except for, beginning in 1904, marking its products with the Bayer cross which configured the company's name in horizontal and vertical lettering with the "y" becoming the common overlap [6, pp. 15, 33]. Most business such as this was seen as inappropriate, and the way to sell products was to cater to pharmacies and doctor's offices. Bayer was not a traditional drug maker with a background in medicine. Their competitiveness in industrial production led them to develop divisions that could focus on making aspirin, but they were not initially interested in Bayer being associated with the name aspirin [4].

Some of the reasons for conducting business in this manner included governments that sought to curb competition issues, and from the numerous suits in the courts that Bayer brought against renegade druggists who were peddling forms of aspirin. The smuggling of aspirin, since it became fairly easy to manufacture, was vastly truncated with the backing of the courts that upheld Bayer's right to patent protection. The rule of law ended the black market trade before 1914, and allowed Bayer to upgrade its output to the medical profession and the pharmaceutical market. However, with the strengthening of this new and powerful German industry a shift in thinking moved the medical profession to see the value of synthetic drugs. The only roadblock to Bayer's hegemony was a court ruling in Britain against them being able to patent the word "aspirin," as their own. As the court reasoned, aspirin was the "general" name in the trade; so therefore, any company could use the word. Despite this impediment, in the end corporate investment in the drug development process came to be viewed as a positive, despite the fact that prices now could be fundamentally manipulated by this emerging market. The tenuous alliance between pharmaceutical companies and the medical profession was born [6, p. 200, 7, 8, pp. 36–37].

3.3 The Crisis of Europe Spreads: German Bayer's Shell Game

Carnage, destruction, and a redrawing of the significant parts of the world are just some of the images conjured after 1914. It would be a massive understatement to say that the pharmaceutical industry was transformed by the events that touched all parts of the world. Before, patents and medicine did not go hand-in-hand. It was unseemly behavior to seek a patent for medicine since the contents were perceived by most to be too mysterious. However, with the changes due to patent law infringement, companies such as Bayer strengthened their hand, but like the modern day calls for tort reform, now the floodgates were open to utilize the international justice system to secure rights. Everyone from the American Medical Association (AMA) to the National Association of Retail Druggists in the United States had to respect the rule of law [7, pp. 116, 119].⁶

The First World War changed all of this in 1914, as Europe divided itself between Allies, Central Powers, and neutral states. As a global conflict, this was never going to be a war the Germans could ever have won. Essentially fought on four different fronts—in Belgium and northern France; second, from the Baltic through Galicia; a third near Austria and Italy; and finally, a front in and around the Balkans and the Black Sea. Certainly, other theaters existed, such as in the Middle East and in East Africa, but everything hinged on the Western Front. With Russia's exit from the war in 1917, Germany's infrastructure was left virtually untouched by the war's end, thus avoiding the destruction of the homeland [9, p. 201, 10].

At the beginning of 1914, Bayer sought to consolidate its international holdings since the outcome of the Great War was so negligible. Of course, the pundits, politicians, and everyday soldiers on both sides expected a speedy conclusion; a home by Christmas scenario or before the leaves changed color. Yet, once 1915 arrived and the Western Front slowly pitched back-and-forth with little alteration, people around the globe began to realize the seriousness of doing business in such a climate. Bayer was no different. With Britain now on the opposite side of the Kaiser, Bayer turned its attention to neutral North and South American markets where they held both the patent and the trademark on aspirin. With connections to Latin America secure for the time being, Bayer knew that the United States was the land where business-as-usual would remain free and open. Despite this, Bayer's motivating force in Germany, Carl Duisberg instructed his American counterpart

⁶The American Medical Association (AMA) was founded in 1847, and fully incorporated by the end of the century. Starting in 1906, the AMA's Council on Pharmacy and Chemistry began to issue regular reports covering remedies that they believed were acceptable to professional physicians; a year later this list was renamed the New and Nonofficial Remedies (NNR). See: Gabriel [7, pp. 197–198].

Emanuel von Salis, to explore means by which to hide their assets, so that if the United States joined the Allies, it would be difficult to ascertain who truly owned the company.⁷

The Williams and Crowell Color Company was a new dye firm in Providence, Rhode Island. Unsuspecting and hoping to cash in on the need for military uniforms, the company was low on transferable capital. Bayer filled this void, and talks began to secure investment rights [6]. The idea was a simple one; if war came, Williams and Crowell would serve as a front for Bayer. The dye firm would receive certain allowances, and Bayer would avert the eye of the Wilson Administration, and the ire of the American press, which gradually was looking for anything remotely German to criticize as Nativism rose during this time period.⁸

This plan could have worked were it not for the sudden enormously lucrative profits that were hit hard by the new income tax that became commonplace during the Progressive Era. The situation was further exacerbated by the appointment of the ubiquitous A. Mitchell Palmer, who became the head of the newly created Office of Alien Property.⁹ Palmer was the sort of man that only sought the making of his own name [11, pp. 42–43]. A toady of Wilson, he would rise to become attorney general and lead the famous Palmer Raids that rounded up and deported alien suspects of espionage. Finally, with America's entry into the war in 1917, Palmer's agency turned its attention to the some 950 million dollars in German investments and to Bayer, by then one of the most lucrative German companies in the entire world [8, p. 145]. Everyone identified the power of the Bayer cross and

⁷The Great Phenol Plot of 1915 in past scholarship was an oft-told story associated with Bayer and aspirin. Essentially, phenol could be used in Thomas Edison's production of disc records, used to make high explosives, and of course, aspirin. With trade lines severed due to the British blockade, Germany sought to find new sources of phenol to aid the war effort and keep up their lucrative aspirin production. With the help of a front company they began to buy massive amounts of phenol from Edison, and then reselling what was not used to make aspirin to non-war-related industries. The architect of this deal for the Germans was Hugo Schweitzer, a Bayer chemical adviser. After being tailed by the Secret Service he left a briefcase on a train, thus exposing the phenol deal. The documents were leaked to the *New York World* in order to espouse anti-German sentiment. In the end, Bayer's reputation was damaged by this story, and led many to perceive it as an agency full of spies. Calling it a "plot" could be a bit of a dramatization since it was more of a shady business deal than a case of international intrigue. For a thorough treatment of this topic see: Mann and Plummer [6, pp. 38–42].

⁸Racial profiling, eugenics—a scientific philosophy behind creating a master race, and conflict were all part of the cultures of the early twentieth century world. Patriotic fervor spilled over in America once they entered the First World War on the side of the Allies. Anything associated with Germans was vilified such as cabbage being renamed Liberty Cabbage; German-named streets, such as Berlin in New Orleans, were changed to names like General Pershing Avenue; and nativistic passion led to the harassment, deportation of German immigrants, and in the Prager Case in Illinois, the public lynching of a suspected German-spy who turned out to be just an ordinary mine worker. See: Tooze [24] and Kennedy [25].

⁹A. Mitchell Palmer (1872–1936) has mainly been treated as a villain in history due to his aggressive raids that were conducted at the end of the First World War. He is also credited with stirring up the threat of communist incursions in what became known as the first Red Scare. See: Reynolds [26].

knew of aspirin's association with the company. Systematically, all of Bayer's key members of upper management found themselves in the custody of Palmer's agents. Bayer's American holdings were now in the hands of the Wilson Administration, and were slated for auction in order to line the pockets of the federal government.

The one bright spot for Bayer during the dark days before the United States entered the First World War was Ernst Möller.¹⁰ Outspoken and assertive, despite his lower standing in the company at the time, he was sent by the firm from Germany to serve as its export manager [6, p. 145]. He was one of the first to think of selling the relief of analgesic pain from the perspective of the consumer. Möller knew aspirin could be something that everyone could carry in a gentleman's breast pocket or in a lady's handbag. His idea was to develop a pocket-sized aspirin can that measured roughly three inches long and could hold about a dozen tablets. Marked with the by-now famous Bayer cross, these small tins, with their handy snapping lid, could sell for less than ten cents.¹¹ An example of one of these advertisements that was common in newspapers can be found in the morning edition of the *Albuquerque Journal* from 9 May 1917 (Fig. 3.2). An advertisement, pictured in the upper right hand corner of page three is a rendering of the Bayer Cross with the words, "your guarantee of purity," written just above several sealed receptacles of Bayer aspirin. As Möller saw it, the way into everyday consumer's medicine cabinets was by tapping into their emotions by appealing to the notion of safety [12, p. 47, 13].

The Americas were ripe for taking, especially with the vibrant newspaper culture that made the era of yellow journalism possible. Billboards and advertisements in print were becoming commonplace, and it was the department store culture of the early twentieth century that enticed consumers to come to great temples for a shopping experience like no other [14]. This coupled with the expansion of the automobile industry, such as Henry Ford's Model T in fashionable black, gave people more mobility and exposure to consumer messages.¹² Aspirin fit directly into this specific product placement, along with the other usual suspects, that found their way into the medicine cabinets of all kinds of people from different socio-economic backgrounds.

On the eve of America's entry into the war, and with continental lines of trade unable to flourish from Germany, Möller became the czar for Bayer's trade to the

¹⁰Not much is known about Ernst Möller's background or origin in Germany (the Bayer AG Archives have no mention of Möller's existence). We know Carl Duisberg disagreed with his tactics concerning the promotion of aspirin in the United States. Once Möller sided with Sterling Products, and began to work for them after the acquisition of American Bayer, his former German countrymen shunned him. After the early 1920s Möller is dropped from the record.

¹¹A later version of the design of the Bayer's aspirin tin can be found in Fig. 4.1.

¹²In 1913 the Ford Model T dropped in price from \$950 to \$600, which was still more money than the average American family earned annually. But momentum was building. Historians estimate that despite the onset of the Depression as many as half of the thirty million households had access to a car by 1930. For a comprehensive study of Ford see, Brinkley [27].

Albuquerque Morning Journal, Wednesday, May 8, 1917. Three

SENATE APPLAUDS BALFOUR'S SPEECH ON STRUGGLE FOR WORLD FREEDOM

Head of British Mission Declares Full Strength of Allied Nations Must Be Used to Insure Success.

**SUBMARINE MENACE
WILL BE OVERCOME**

Declares Germany Undermines Power of England and United States to Resist Conquest.

Washington, May 8.—(Special Telegram.)—The House today passed the Balfour declaration of war, which declares that the full strength of the allied nations must be used to insure success in the struggle for world freedom.

The declaration is a strong statement of the determination of the allied nations to use their full strength to overcome the submarine menace.

The declaration is a strong statement of the determination of the allied nations to use their full strength to overcome the submarine menace.

SPIONAGE BILL STILL DEBATED BY U. S. SENATORS

La Follette's Amendment to Espionage Bill Likely to Go Through.

Washington, May 8.—(Special Telegram.)—The Senate today continued its debate on the Espionage Bill, which was introduced by Senator La Follette.

The bill is a strong statement of the determination of the allied nations to use their full strength to overcome the submarine menace.

AN EXECUTIVE ADVICE

The newly elected president will be the first to receive the executive advice of the cabinet. This is a duty of the president to the people, and it is a duty of the cabinet to the president.

SOUTHERN ROADS QUITE UNABLE TO MAKE ENDS MEET

At present, the Southern Railway is unable to make ends meet. The company is in a financial straits, and it is unable to pay its bills.

"The Bayer Cross—Your Guarantee of Purity"

Tablets in Pocket Boxes of 12—Bottles of 24 and 100. Capsules in Sealed Packages of 12 and 24.

Bayer-Tablets of Aspirin

FLIPS FROM THE FILLUMS

AT THE THEATRE TODAY.

"The Fillums" is a new play by the famous playwright, and it is a play that is sure to be a success.

Albuquerque Business Directory

SEE THESE ADVERTISERS

Albuquerque Music Store 100 North 1st Street Phone 178, 441 West Central	T. S. Mills Furniture Co. 100 North 1st Street Phone 178, 441 West Central	Knock, the Builder 100 North 1st Street Phone 178, 441 West Central
Farmer Washington The Washington 100 North 1st Street Phone 178, 441 West Central	Cleaning and Pressing 100 North 1st Street Phone 178, 441 West Central	PIONEER BAKERY 100 North 1st Street Phone 178, 441 West Central

Fig. 3.2 Bayer Aspirin advertisement, Albuquerque Journal, 9 May 1917 (Photos courtesy of Chronicling America: Historic American Newspapers Library of Congress)

Pacific [6]. With aspirin under his firm control, profits in the meantime soared with the backing of the patent. Before its expiration, advertising budgets were expanded, and just as wars tend to do, war profiteers made handsome sums. Ironically, the long protracted war in Europe, and the efforts of Palmer stymied Bayer's growth potential. With the sinking of the ocean liner *Lusitania*, which killed 128 Americans, and the plot by a German ambassador to entreat the Mexican government to enter the First World War against the United States, Wilson's desire for

peace was put on hold.¹³ Even the isolationists could hardly argue that America's entry into the war was a negative. After a year of American involvement on the Western Front, the German government had no influence globally to defend its foreign investments. Bayer in America was on its own, with only the likes of Palmer, who was bent on destroying their position.

Germany's inability to achieve victory at sea, battle low morale throughout ruthless industrialized warfare campaigns with massive casualties, and the failure to control their own financial markets were against them. Despite huge gains industrially Germany gambled away key resources by honoring a hollow alliance system that ended up dissolving the Austro-Hungarian Empire and cleaving German society in half [9, p. 48]. By the end of the First World War, German assets such as colonies, businesses, and connections were all the new property of the Allies. Great Britain, France, and the United States attempted to sort out the complicated notion of self-determination that Wilson so avidly prescribed. The crippling Treaty of Versailles provided the opportunity to humble Germany for its crimes against freedom and ingenuity, of course, it was also the chance to redraw the map of Europe, grab patents, restructure deals, and harness capitalism [15].¹⁴

3.4 A Global Influenza and Aspirin's to Blame?

By 1919, the world came to two major understandings. First, machines could be converted to serve modern warfare in the most hideous of manners. The meat grinder proved it at the Somme, Ypres, Marne, or any other field of death that carved men's flesh into bits, so much so, that for the first time in the history of warfare more deaths occurred due to bullets and shrapnel than to disease [16]. And ironically the second, that the Great War dilapidated societies to such an extent that they would be ripe for what would become known as the Great Influenza. Of course, it took time to understand the effects of what would eventually be dubbed the "Spanish Flu" due to an outbreak on the Iberian Peninsula, but in the end at least 40 million would succumb to this disease.¹⁵ The real issue at this time was the question of treatment. How should the flu be combated [17]?

¹³This event has come to be known as the Zimmerman Telegram.

¹⁴The Big Four—Great Britain, France, Italy, and the United States, crafted the Peace of Paris in 1919, and the subsequent Treaty of Versailles that crippled the German economy. With bad blood came heavy reparations that were impossible to pay back. American loans propped up the German government, which led to hyperinflation and an unstable economic climate. The map of the world was also redrawn with such changes as a new Yugoslavia, Czechoslovakia, and Poland. Also, a mandate system emerged out of the defunct Ottoman Empire in the Middle East with the creation of the pseudo-colony states of Iraq and Syria, as well as an independent Turkey. See: Fromkin [28] and MacMillan [15].

¹⁵For the purposes of this study the terms Great Influenza and Great Pandemic will be used since Spanish Flu gives the false impression of regionalism. The flu was a global event.

The initial explanation to this question begins with the oft-cited story of where the outbreak was believed to have commenced—Kansas. On an army base in the wheat belt some men became ill. That sickness rolled from this point. With the American military build-up and the Allied Expeditionary Force set to land in France under the auspices of General John J. Pershing, men arrived in two waves, first—84,000 in March 1918, and 118,000 by April of the same year. Spreading to both sides of the Western Front, and even jumping the English Channel and affecting everyone from King George V on down the social ladder, the flu was deadly in that the majority of them suffocated by a lethal accumulation of blood and other fluid in the lungs. Unlike other flu epidemics before or after, the influenza of 1918 killed young adults. One in every hundred American males between the ages of 25 and 34 succumbed to the flu. Some historians believe it was more lethal to the German army than the shells that rained down, and helped to end the First World War by November 1918 [9].

As far as an antidote to the Great Influenza, nothing seemed to provide assistance for alleviating its symptoms.¹⁶ The first signs of the flu that found their way into U.S. Army camps were not treated all that seriously. However, within months as the death toll increased, aspirin and a myriad of other drugs were prescribed in various dosages in order to combat the disease. The medical profession and the general public initially blamed aspirin for being the carrier of the disease in various U.S. cities, due to xenophobia, but gradually they turned back to the “miracle drug” which seemed to be the most effective means by which to treat the flu [11, 18]. As a fever reducer, aspirin was a major player in tackling it, and as one scholar purported, “people knew it had been tremendously helpful, one of the few medicines to make any difference.” The linchpin for this argument was that aspirin production and sales more than doubled from 1918 to 1920, so in other words, it made sense that the drug came out of the Great Pandemic ready to dominate the pharmaceutical market, thus inaugurating the “aspirin age” [19].¹⁷

The interpretation of aspirin’s role in combating the Great Influenza is problematic since it has not taken into account the latest medical research from the Twenty-First Century. First, it presupposes that aspirin must have reduced fevers, alleviated lung infections, and overall solved as many medical conditions as possible. And second, scholars bolster these claims by stating that because we do not know how many people actually took doses of aspirin, so that must mean that it did well for itself in battling the greatest pandemic in history [20]. However, two pieces of evidence, one from the period and a recent development in the field of infectious

¹⁶From an Indiana town that banned spitting on public streets to the New York City Health Commissioner who tried to slow transmission of the epidemic by organizing the opening and closing of businesses into shifts in order to avoid over-crowding on the subways, individuals and governments alike, tried all kinds of approaches to combating the flu virus. See: Aimone [29].

¹⁷The book, *The Aspirin Age, 1919–1941* (1st ed., 1949), in actuality just used the word aspirin in the title, and in point of fact did not include an article on the drug in its compellation of essays. But, the name has remained.

diseases, shed some important light on how aspirin actually hindered the recovery of those affected by the flu, thus proving this drug was not so much of a miracle.

To begin with, aspirin, whether produced by Bayer or some other entity, always instigated a debate concerning dosage. One end of the spectrum argued that it was harmless at any level of consumption, while others warned against its toxicity level. Bayer, through its advanced chemistry departments did its best to espouse the benefits of using only their aspirin by increasing its advertisement budgets in Europe, the Americas, and even as far as the Pacific Rim by 1917, much of this attributed to the efforts of Ernst Möller. Of course, imitators attempted to dupe the consumer with “fake” chalk-based aspirin, but salicylates were from a chemical standpoint, relatively understandable to concoct by a well-equipped chemistry laboratory. The era of the First World War crystallized the debate over dosage. The extreme violence that was found on the Western Front and the arrival of the Great Influenza by 1918 tested aspirin's ability to revive those that were injured on the battlefield or bedridden by the flu.

The homeopathic community severely critiqued the use of aspirin to treat the epidemic. Founded in the late eighteenth century as a form of medicine that placed emphasis on trial and error, the placebo effect, and focusing on a patient's history and personality, homeopathic treatments are seen even today as nothing short of quackery. Despite its dismissal, homeopathic treatments during the Great Influenza were especially popular in lieu of “allopathic” physicians' inability to treat infections. Despite being called absurd by critics and historians themselves, the homeopathic approach was just, if not more, accomplished in their success than synthetic medicine in 1918 [17]. In short, they have to be considered.

Just before the advent of the war against the flu, David B. Jewett M.D., the editor of the *Journal of the American Institute of Homeopathy*, assigned another physician, W.A. Dewey M.D., the task of compiling some fifty primary accounts of the effects of influenza during 1918 [21, pp. 353–354]. The record offers fascinating insight into the treatments, survival rates, and the role of aspirin. Most of these doctors did not believe the use of aspirin was a positive choice, were untrustworthy of its treatment of their patients, and spoke fervently of its over-prescription. Whether from Seattle, Chicago, or Washington D.C., homeopathic doctors reported from children's homes, army bases, and makeshift hospitals. They believed that tar products were harmful to the immune system, a common argument against aspirin during the period, and the high-level dosages were thought to be unsafe. Using herbal remedies such as Gelsemium, Rhys Fox, and Eupatorium, homeopaths combined these substances into what at the time was becoming non-traditional remedies for the flu. Homeopathic treatments have gone in and out of fashion since 1920. The point is not that the numbers that are provided are bogus as far as treatment successes. Taken only on this account, it of course yields a pause as to whether this approach was one hundred percent effective. Rather when we look at the current research of Dr. Karen M. Starko in 2009, and coupled with the concern over aspirin's ability to treat the Great Influenza do we have more cause to question its role as a miracle drug?

As an infectious disease specialist, Dr. Starko's unexplored approach presented a straightforward and fascinating hypothesis, which argues that salicylate therapy for influenza during 1918–1919 resulted in toxicity and pulmonary edema, bacterial infections, and overall mortality [22].¹⁸ Essentially, aspirin was as deadly as the crank homeopaths predicted.¹⁹ With Bayer's loss of its patent in 1917, and America's entry into the First World War at the same time, coupled with the Great Influenza, the United States military purchased large amounts of aspirin upon the recommendation of the Surgeon General, Rupert Blue.²⁰

Since the Federal Trade Commission (FTC) was in its infancy after 1914, aspirin packaging possessed few warnings and no dosage requirements [6, p. 9]. The clearinghouse for the latest advances in pharmacology, the *Journal of the American Medical Association*, at the time suggested a dose of 1000 milligrams every 3 h. This is roughly twice the daily allowance considered safe today. Doubling the dose given at six-hour intervals can cause, according to Dr. Starko, a 400% increase in the medicine that remains in the body [23].

Taken together, this research paired with the primary testimony by homeopathic doctors across the United States in 1918, speaks to the point that aspirin might be more of a cause of the Great Influenza than it was a solution. Lacking a professional medical community that was unable to address the volume of death that the flu brought on, addresses the notion that despite its popularity in the press, Bayer's inability to control production made aspirin overtly common. With no ability to neither inoculate nor adequately treat this disease with the latest drugs, doctors' over-prescription of aspirin led to possibly lethal effects.

More exploration into the amount of aspirin prescribed is certainly necessary, but just because it was thought to be such a popular consumer item by 1920 does not make it a panacea; nor does testimony of the homeopathic community rank in the realm of the absurd. What this period proves is that chemistry's war against an opponent such as a Great Pandemic is part science, but it is also about how the medical and pharmacological communities sold the medicine. Likewise, Bayer's solvency in the wake of 1919 would change the trajectory of aspirin's story on both sides of the Atlantic.

¹⁸Dr. Karen M. Starko is a graduate of the Temple University School of Medicine and is a former epidemiologist, along with her research at the Centers for Disease Control; she conducted clinical studies as a physician and consultant for several biotech companies in California. She is also a specialist on the topic of Reye syndrome, which especially effects young children, and is a debilitating brain and liver disease that can lead to death. The taking of aspirin can facilitate its rapid progression.

¹⁹Historian John M. Barry, the foremost authority on the Great Pandemic, also portrays the homeopaths reporting in this particular article as "absurd." Interestingly enough, a 2009 New York Times article covering Dr. Starko's hypothesis received a quote from Barry. His response to her research was patronizing, and wrote off her assertions due to the fact that "it was unknown how many people consumed aspiring during the outbreak." Homeopathic medicine continues to be a hotly-debated topic, see: Burnham [30] and more specifically Haller and Flannery [31].

²⁰Rupert Blue (1868–1948) served as the Surgeon General throughout the Wilson Administration.

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Chapter 4

Aspirin and the Medicine Cabinet, Part II

4.1 A Tale of Two Bayers

By the end of 1918, as the world reeled at the prospect of more death not at the end of a gun, but rather at the hands of the non-discriminating flu epidemic, Bayer's former hold on the aspirin market was in a free-fall. Now firmly in the clutches of the Alien Property Custodian (APC), the German-based firm faced the prospect of being carved up piecemeal [1, p. 49]. The international division in the United States was up for public auction, and back home foreign investors were seeking to claim mysteriously open shares that were available through the inner workings of the Versailles Peace Treaty. For the time being, Carl Duisberg's dream of a hegemonic empire of Bayer crosses was at an end.

On Thursday December 12, 1918, Sterling Products from Wheeling, West Virginia poisoned the well as far as some were concerned in the international pharmaceutical community. At the time the purchase price was exorbitant, but in the long run it was an incredible investment; Sterling had just bought Bayer Company, Inc. and suddenly they became part of the largest producer of aspirin on the face of the planet [2, pp. 146–147].¹ Sterling Products received all of the German company's U.S. connections, their formulas, and even their stationery and ink pens. Those assets would lead the two hucksters that started Sterling in the improvisational patent medicine business to conclude that they had hit the jackpot.

With a budget of one million dollars (which at the time was a handsome sum) slated for advertising, Sterling would transform the consumer drug market into what historians have dubbed the "aspirin wars" [1, p. 51]. The only issue that arose from

¹Sterling outbid Dupont and Paine Webber, with a final purchase price of \$5,310,000. Not bad for a patent medicine business that focused mostly on advertising and not chemistry. In 1988, Eastman Kodak acquired Sterling Products, known as Sterling Drug; then, in 1994, Bayer AG, the original company, finally reacquired the Bayer aspirin name that was lost during the First World War. Before this publication was due at press, Bayer AG announced they were in the process of acquiring the seed company, Monsanto, for \$66 Billion.

the sale was the fact that of the sixty-four products that Bayer made in America, pretty much all of them were such complex chemical formulas that the folks from Wheeling had no idea how to begin production. The clock was ticking considering the surplus stock that remained in Rensselaer, New York was dwindling rapidly [3, pp. 148–149]. Gone were the chemists and the plant managers; they were deported during the war or quit under the strain of anti-German sentiment. What occurred next was an intricate set of negotiations that were something out of a novel between Sterling and the mother company back in Germany.²

Carl Duisberg must have bristled at the prospect of Sterling acquiring a division of the company he worked so hard to build and preserve. When William Weiss, the President of Sterling, approached Bayer in Germany, it was a cry for assistance.³ Fortunately, Weiss had the brilliant Ernst Möller at his disposal, the stalwart member of his new staff who could translate and facilitate a contractual agreement. After some legal wrangling and probably much that was lost in translation, deals were struck. Of course, Sterling would have even more negotiating power had the courts not de-fanged his company with a similar ruling to the one that occurred earlier in Britain with the name aspirin being declared universal and not the province of Bayer [1, pp. 59–63].

By April 1923, two deals were struck that had a massive impact on the future of aspirin. The first contract allowed Sterling's Winthrop Chemical Company, which was frantically placing want-ads for chemists, contractors, floor sweepers, and the like, to make the products Weiss had purchased through the U.S. government fire sale. Leverkusen Plant, the home of Bayer in Germany, would consult by providing technical expertise in the laboratory, and in return Duisberg's company would receive half the profits. The second contract was essential to Sterling since their specialty was sales rather than manufacturing. The new markets included the U.S., Canada, Britain, South Africa, and a 75/25 split in favor of the German Bayer when it came to the profits from aspirin in Latin America.

In general, the Weiss-Duisberg agreement was never truly finished, nor was it amicable, but this fragile peace was the best that could come out of a difficult situation. If it were not for the German Democratic Weimar Republic's inability to control hyperinflation, Bayer would have spent more time in the courts fighting to preserve the losses it suffered after the First World War. Since the economy was in shambles after the Treaty of Versailles, it was futile for Duisberg to defend his company's position any further. He had more significant issues to concern himself with as his idea to create a cartel of industries under the new name, I.G. Farben,

²The German-owned Bayer also lost its holdings in the newly formed U.S.S.R., where Lenin's Communist Revolution made public all private businesses and their holdings.

³William Weiss (1877–1942) started Sterling Products, a patent medicine business, with his childhood friend, Arthur Diebold, whose father's company, Diebold Safe and Lock, is still in existence to this day. Both men were trained as pharmacists, and by 1912 they were worth over \$4 million dollars. The Bayer deal, as they saw it, was not about the dye business or even the aspirin formula, but rather what they were paying for were the trademarks.

came to fruition in 1925. Of course, within two decades the conglomerate would be decimated by the gamble of Hitler and his Nazi Reich [4].⁴

The story of Sterling's rise to become the most powerful drug company in the world was not without controversy. Having obtained a boost from the American seizure of property, they capitalized on aspirin's name by consulting the superior knowledge that emanated from the German chemistry laboratory. It was this expertise that helped Sterling survive the disintegration of Farbenfabriken Bayer and allowed it to flourish by manufacturing pharmaceuticals. However, since they lost the right to directly associate Bayer with the name aspirin, literally hundreds of "aspirin" products hit the market during the inter-war years. Suddenly, competition would take the original chemical formula that Bayer made in the late nineteenth century chemistry lab in a whole new direction.

4.2 The Amazing Race to Take Good Care of Yourself

By the 1920s, health reformers and the burgeoning advertising companies promoted like never before the shiny porcelain bathroom as the center for not only personal cleanliness, but also for good health. Of course, defining "good health" was a matter of perspective, since previous eras of medicine extolled the virtues of drugs, such as heroin and cocaine, as being non-habit forming for consumers. New print material such as newspapers, catalogs, and magazines hired new tastemakers, backed by scientists, to disseminate these ideas and to provide consultation on which products would be suitable for use and to decorate the home [6].⁵ What was the appropriate color for bathroom tile or for the kitchen walls? What were the best products to use on a daily basis before leaving for work? How affordable was it for the average consumer to stay hygienic on a daily basis?

A battle raged over not just whether products were new, but rather who would control the means by which they were portrayed in mass culture. Thus, turning the heads of the consumer mattered most, as a key to gain entrance in their pocket-books.⁶ The race was on to garner four modes that could be explored to understand

⁴Fascist regimes in Germany and Japan consolidated these state-sponsored businesses in order to control production. For example, aircraft parts could be combined with ball bearing manufacturing plants, which could be linked to engine production for the making of tanks, and so on. I.G. Farben was the umbrella organization for the chemical industry in Germany. Likewise in Japan, which had copied many of the German systems for government and industry after the Meiji Restoration of 1868, they had a similar set of cartels called zaibatsus. See: Weber [5]

⁵By the 1920s, magazines like *Good Housekeeping*, and tastemakers such as Emily Post and Helen Koues, instructed their readers to express their own personalities in order to reflect the highest order of hygiene and taste. By the way, white, for bathroom tile, would be a suitable answer, as it was easier to see dirt and grime; and green apple for kitchens, due to its calming influence. See: Foy [7]

⁶This particular point is outlined from a psychological and sociological point of view by, Sedivy and Carlson [8].

aspirin advertising and the role that chemistry played or did not in its creation before the Second World War. First, how the cultivation of brand identity was marketed using new technology—such as radio and eventually, television; next, looking at how convincing consumers to switch to an alternative trade name was so significant; then, how introducing a supposed new product could take shape in a saturated market; and finally, how to use one's company to lobby the channels of government to further positions against competition. Each of these principles of advertising can be found with relevant examples in the story of aspirin during the 1920s and 1930s [9].

For starters, brand identity was massively important when it came to the aspirin market. If you could “hook” a consumer early on with a specific product then you had a possibility of having them as a customer for the rest of their lives. By the 1920s, Bayer now had hundreds of competitors once the pain and death of war and disease became a memory. They came from all over, retail druggists, jobbers, tablet companies, chain stores, street vendors, and suppliers all claimed to have access to the latest and most pure form of aspirin for sale. They developed colorful packaging with a list of remedies, that were at times outlandish but in principle, healthy competition breeds better products. More choices can raise standards, while weeding out the goods that are not living up to the standards that consumers demand. In answer, Sterling Products ramped up its advertising budget with the objective of not only maintaining, but also wiping out its new competition. New forms of media emerged that would help sell aspirin as never before.

The 1920s marked what would become known as the golden age of radio. Pumping hundreds of thousands of dollars into radio spots became Sterling's primary frontier for reaching out to medicine cabinets in the Western Hemisphere. By 1934, Bayer had sponsored radio programming on the National Broadcasting Company (NBC) through 75 stations nation-wide, and they even secured a program of American music complete with regular announcements about the purity of their aspirin. The goal was to reach the masses of consumers who huddled around their radios after the Great Depression struck in 1929, because they knew Americans regularly listened to President Franklin D. Roosevelt's famed fire-side chats.⁷ Destitute families in the Dust Bowl, around the soup kitchen lines, and out West in the groves of America's orchards all clung to their radios and the ads that linked them to the outside world. One-fifth of all advertisements on the radio pertained to drugs and cosmetics, which meant that the market was saturated due to the massive profits that these products could garner [3, p. 152].

By becoming the nation's fourth largest radio advertiser, Sterling cemented its place among the most successful competing forces in the pharmaceuticals. By 1936, as I.G. Farben in Germany dealt with the death of Carl Duisberg, consolidated its business activities in the Third Reich, and braced for a tumultuous end to the decade, Sterling spent almost a half million dollars on radio commercials and an additional

⁷Roosevelt gave a series of 30 evening radio conversations between 1933 and 1944.

300,000 dollars on magazine spreads [4].⁸ Clearly, despite the Depression, the unemployment lines, and the inability of the Roosevelt Administration to grapple with the alleviation of the economic woes of the country, people were still buying Bayer and other aspirins as well. Creating brand identity, in the midst of a saturated market proved how much companies that produced analgesic pain medication needed their chemistry laboratories. Now science and marketing began to merge in ways like never before. As Sterling proved during the auction of American Bayer, without a viable staff of chemists there would be no chance to translate formulas into brand medicine.

Besides crafting a viable brand in the laboratory, companies took to the airwaves, and through the newsstands by sinking huge amounts of money in order to take on the Bayer cross. Swaying consumers was the objective of every company that sought profits. Sometimes getting a consumer to switch to another brand required sending specific messages that would force the most loyal customers to switch. What ensued was nothing short of a war—a war of words, ideas, and symbols.

At the end of the nineteenth century, and even after the rapid modernization of our world at the conclusion of the First World War, the person within the family unit who indirectly held the power to make choices was—the woman. Ever since the cult of domesticity was formalized during the middle of the nineteenth century, women commanded significant positions when it came to household management [9]. Child rearing, conforming to proper levels of hygiene, and in general, organizing the home was their province. Despite the creation of the “new” woman due to the achievement of universal suffrage, increased wages, and expansion of social boundaries outside the home, females were still viewed as the weaker and more emotional of the sexes. Advertising continued to portray them as hysterical, nervous, and, most importantly, they were seen as the vehicle to sell a myriad of products [10, p. 139].

Aspirin companies at the time viewed women through the prism of their husbands, and also as de facto heads of the household. Printed advertisements portrayed women as panicky and unable to relax like the men around them. The only suitable means by which to calm them was taking an aspirin. Doctors in white coats were shown in some depictions to implore them to “take two aspirin and call them in the morning,” if they were not better. These ads were not even selling the physical pain relieving qualities that aspirin possessed for headaches, but rather for the emotional relief that women supposedly needed.

In the end, chemistry and medicine in this respect were not at the forefront of convincing women that they needed to calm their emotional outbursts with aspirin. This was less about science than it was about relying on passé explanations for

⁸Interestingly enough it was I.G. Farben that constructed the largest advertising sign in the world by constructing a two-story lighted Bayer cross on the roof of one of its factories. Of course, by the early 1940s it had to be taken down due to the start of the war and due to blackouts. After the Second World War, Bayer AG rebuilt the giant lit tablet as an homage to its predecessor. See the image of the Bayer sign in Mann and Plummer [1, p. 87].

relieving the broad definition of pain, which had existed since the pre-modern era. Companies constructed complex ads that would appeal to what women were told they should be feeling by finding an affordable solution to their problems [10, p. 143]. Despite such an antiquated viewpoint of women's constitutions, aspirin firms did whatever they could to distinguish themselves from one another in order to gain new business.

Utilizing outmoded cultural tropes to sway consumers from competitors was just one means by which aspirin companies sold their products. They also spent much of their budgets on working with their chemistry laboratories to concoct new and innovative versions of aspirin to entice customers. This was a challenging prospect for new companies because of market saturation, and especially attempting to keep up with Bayer. Some companies like Alka-Seltzer provide a good example of how niche businesses employed chemistry coupled with creativity.

All organizations claim a creation story. At times, this narrative becomes integral to future dealings as they remake their own stories to suit new frontiers of business. Coca-Cola's association with World War II soldiers, Wal-mart's small town roots, and Apple's garage-born startup, all originated with a simple straightforward idea.⁹ Alka-Seltzer was born as a company with just such a creation story. According to myth its President, A.H. Beardsley, happened to be in a small town in Indiana during a flu outbreak in 1927 and noticed that the employees were healthy by drinking a daily dose of aspirin and bicarbonate of soda [1, pp. 143–144].

The staff chemist at his Miles Medical Company recreated the formulation, which promised "quick relief." The new product combined aspirin with sodium bicarbonate, but also secretly contained, citric acid and monocalcium phosphate in an effervescent tablet. First conceived of as a cold tablet that would relieve headaches, upset stomach, and fever that accompanied the flu. Through deceptive and ingenious advertising campaigns over the years, Alka-Seltzer became associated with the relief of a broad range of maladies. By expanding the field of symptoms that the drug treated, Alka-Seltzer redefined aspirin's chemistry and generated popular acclaim for generations. The round tablet that "fizzed" was a product that was both soluble and supposedly provided instant relief [2, p. 162]. Once again, aspirin companies proved they could find new means by which to sell the same product.

The final principle of advertising in this new age pertained to mediating the relationship with new agencies that concerned themselves with the regulation of competition. The worldwide Great Depression brought governmental intervention to a whole new level. For over two decades, after the first appearance of modern

⁹Coca-Cola was developed in Atlanta, Georgia in 1886 and interestingly enough was originally intended as a patent medicine. During World War II, it was transported around the world to the Allied soldiers who battled the Axis Powers. Wal-mart opened its first store in Rogers, Arkansas, and would change shopping both in large cities and small towns. With almost 90% of its stock from China, Wal-mart has transformed the one-stop consumer experience. Apple was founded by Steve Jobs, Steve Wozniak, and Ronald Wayne in 1976, and turned out its first personal computer in the garage of Jobs' parents in Los Altos, California. See: Cohen [11].

aspirin, neither doctors, chemists nor consumers still had any idea what the short or long-term effects were of taking this drug. Some companies, such as Alka-Seltzer, added ingredients, much to the chagrin of the AMA, which finally saw this practice as disingenuous to the spirit of the Pure Food and Drug Act of 1906.¹⁰ The real issue for them was the lack of governmental intervention, as painkillers now claimed that they cured everything from headaches to the common cold [3, p. 150]. At the time though, without the ability to sanction what products were safe and which were possibly harmful, it was not required to list the chemical compounds on the side of packaging.

In an attempt to stir those in power to action, so that the run-away train of aspirin advertising would come to a halt, were the muckraking journalists of the period. In the tradition of writers Lincoln Steffens and Ida Tarbell, a new wave of journalists, such as Arthur Kallet, sought to raise the alarm against consumers blindly taking products that were making claims well beyond what they could deliver [3, p. 155].¹¹ Once again, they pointed the spotlight on the misdeeds of companies that engaged in shady dealings.

By 1936, this campaign led the Consumers Union to publish the first of its *Reports* with an annual appraisal of goods and services taken as gospel.¹² Finally, after a variety of editorials that questioned what they perceived to be fatal poisons, the Roosevelt Administration and the Congress were forced to act by passing the Food, Drug, and Cosmetic Act of 1938. The threshold for reaction came when the Massengill Company of Bristol, Tennessee caused the deaths of over 100 men, women, and even children. The disaster occurred after a liquid version of sulfanilamide containing a highly toxic solvent was introduced to customers after a popular version was sold widely in Nazi Germany. Astoundingly, the only penalty before 1938 was a small fine for violating a label law [1, pp. 147–149].

Something had to change, and it did. Reactively, the new act created the Food and Drug Administration (FDA), whose purpose was to police the labels on drugs, force companies to come clean about the active ingredients in their products, and to also provide customers with accurate dosages. While, the FDA did not possess the right to scrutinize advertisements, this would be the province of the FTC; the machinery was now in place for future administrations to restrict the rights of

¹⁰The Pure Food and Drug Act of 1906 was part of Theodore Roosevelt's Progressive Era legislation to protect the American consumers against products both foreign and domestic that posed a threat to health; it created a Bureau of Chemistry that served as a watchdog to aid government prosecution.

¹¹Lincoln Steffens (1866–1936) was a journalist from New York that became the editor for McClure's Magazine, a leading publication that sought to expose some of the leading issues of the day. Ida Tarbell (1857–1944) was a writer who specialized in the inequalities associated with the business practices of the Standard Oil Company. Finally, Arthur Kallet was part of a new generation of consumer advocates that wrote on health and safety; during the 1950s the House Un-American Activities Committee accused him of being a communist. For a thorough treatment of the Progressive Era and its impact on 20th Century muckraking see: Painter [12].

¹²To this day, *Consumer Reports* is still a staple in appraising the viability of products in the United States.

patients to self-treatment by demarcating an over-the-counter drug from a prescription drug. Considering the history of patent medicine and the overall lack of concerted medical research into aspirin's effects, this was overall a major step in the proper direction.

Bayer, during this period, was able to dodge federal oversight simply because nothing was found, except aspirin in their product. What a difference a decade would make for a product that possibly caused so much death at the hands of the Great Influenza. Capitalizing on this momentum a company called Home Products was able to purchase the product line known as Anacin. Started by a pharmacist, who moonlighted as a dentist in Minnesota, Anacin contained aspirin, acetanilid, caffeine, and quinine sulfate, and was marketed as a headache treatment [3, p. 153]. Considered reasonably safe, aspirin's effectiveness led many in the medical community to express concern about its accessibility. However, with the homeopathic community in disarray after 1920, and the AMA with only limited influence as the only clearinghouse for medical knowledge, little was known nor decided concerning aspirin's effects on people of all ages. It would take a massive global conflict, the reformulation of chemistry as a science, and a virtual transformation in medical care that would lead aspirin into the next phase of its development for a new age.

4.3 The Ad Man Cometh: Bayer Gets a Run for Its Money

As the greatest global conflict the world ever saw raged from the surf on the island of Tarawa in the Pacific to the sands of El-Alamein in North Africa to the skies over the English Channel, Bayer continued to wage its own war against some staunch competition. Despite massive amounts of violence and the deaths of civilians and soldiers alike, aspirin did its utmost to provide some kind of relief for the Allies and the Axis Powers. Medics and field stations all dispensed it from their kits, along with bandages, morphine, and a host of new processes, including evacuation techniques that emerged for treating battlefield wounds.¹³

Between the wars, Bayer remained the gold standard for aspirin purity and quality. Sterling did such a complete job with their bloated advertising budget that Bayer completely dominated the Western Hemisphere. However, by the start of the Second World War, Bayer in the United States encountered some stiff competition. Anacin, and a new company called Bufferin (Fig. 4.1), challenged Bayer's pre-eminence by creating a three horse match race for aspirin customers' pocketbooks

¹³Throughout history, warfare and advances in technology have always followed parallel trajectories. For instance, during the Second World War the American military invented for use in the field what would become two everyday household products; one for keeping things lubricated, WD-40, and the other for its instantaneous adhesive ability, duct tape (made by a division of Johnson & Johnson called Revolite).

Fig. 4.1 Bayer, Anacin, and Bufferin Packaging, circa 1950 (Photo courtesy of Nicole Girouard)



[1, p. 160].¹⁴ Of course, with the war in full swing, aspirin maximized production to keep up with demand. This new level of competition would set the stage for the future of both chemistry and medicine after 1945.

When Home Products purchased Anacin, they did not sell the product as hard as they could. Once the Depression came, they changed their strategy by employing a new chairman, Alvin Brush, who brought on a parsimonious promoter-extraordinaire named William Laporte. As a hardscrabble New Yorker with a college degree, Brush worked his way through the companies of Albert Diebold, the initial partner of William Weiss of Sterling Products. With a strong sense of purpose he looked at Anacin, which after five years was mediocre at best, as a cash cow. Likewise, Laporte was the kind of man who could make something out of nothing. He had a penchant for cutting back business expenditures to the point of nixing everything from company cars to toilet paper in the women's restrooms. He cut the inessentials, as he said, and shared Brush's opinion that Anacin could sell like wildfire if it had the right tone attached [1, pp. 154–156].

Crafting a set of spots that played upon people's desire for good news, a sound decision in an uncertain time, and knowing they were swallowing a tested product, Laporte and his ad team hammered the airwaves with a straightforward message. Capitalizing on Anacin's multiple ingredients they sold it as a drug that was based on "the prescription principle," which meant that it could be trusted by the medical community. Of course, no one really knew what that meant necessarily since the medical community was still trying to come to an agreement about professionalization.¹⁵ Nonetheless, the radio spots deftly never mentioned the fact that Anacin

¹⁴Drug makers since the nineteenth century used colorful and distinctive packaging to catch consumer's eye and also sell their wares. The packaging of Bayer, Anacin, and Bufferin were no different (Fig. 4.1). Only recently in its history has Bayer moved from a brown and yellow to a green and yellow color scheme.

¹⁵As will be discussed in the next chapter the medical community, both for physicians and pharmacists, was undergoing a massive revolution in training, standards, and in the use of new technologies after 1945.

contained aspirin, which was a brilliant move to screen the product from being associated as a competitor to Bayer [3, p. 155].¹⁶

Like Anacin, a new aspirin-based product called Bufferin rolled onto the scene just after the conclusion of the Second World War. Founded initially by Diebold, and eventually spun off to a subsidiary called Bristol-Myers, it created a third option for consumers by utilizing a unique feature that Bayer and Anacin could not [2, p. 210]. Chemists for Bristol-Myers, which had been making drugs in bulk for doctors back in the patent medicine days, were experimenting with the interaction between antacids and aspirin. What they discovered through their trials was that antacids helped to rapidly absorb the aspirin into a person's bloodstream. Bristol-Myers new product stormed onto the over-the-counter market with a powerful message that it could combine two points of attack at once. Bufferin launched a vigorous "twice as fast" campaign by utilizing a creative means to translate advertisements—the television.

In 1947, as Europe tried to figure out the new divisions between East and West, and the Americans worked to dismantle the Japanese economy, and rebuild it in its own image, there were roughly 15,000 television sets in the United States. Within ten years there would be over 32 million TVs, as they became known [1, pp. 158–159]. The new frontier for aspirin exploded with individual commercials that could be purchased by smaller companies that were seeking their own place in the sun. A new breed of advertising men were born, who crafted a fresh philosophical approach to the biz. For the likes of Draper Daniels and Rosser Reeves, two rising stars from Madison Avenue, they saw the saturated field of television coming down to the offer of a Unique Selling Proposition (USP) [13, pp. 190–191].¹⁷ What this encompassed was the idea that customers were not simply impulse shoppers, but rather had only so much time during a commercial to take in one singular idea with them. Repetitive messages would have a lasting impact, as long as the product was seen as relevant to the era.

Reeves took the Anacin account. Knowing virtually nothing about chemistry or even how it worked did not matter. What would make the difference for this maestro was conjuring an annoying set of images of pain. In a boardroom during one of his famous pitches he pitched the famed "pounding hammers." He quickly sketched a head with three distinct areas; first, the hammer pounded away in a box; next, a spring coils and releases; and finally, a massive lightning bolt struck two terminals. Add an overzealous announcer and phrases such as, "stops headache,"

¹⁶Anacin did not publicly admit that it contained aspirin until the 1980s.

¹⁷Draper Daniels (1913–1983) was a Chicago-based ad man for the Leo Burnett firm. He is credited with the creation of the now-famous Marlboro Man campaign, among many others. Likewise Rosser Reeves (1910–1984) was equally influential as the managing director for the Ted Bates Agency. His Anacin ad made more in a 59s spot over the years than *Gone With the Wind*. Both men inspired Matthew Weiner's AMC Series *Mad Men* (2007–2015) that portrayed the raucous world of advertising in the 1950s and 1960s. See, <http://www.newyorker.com/culture/cultural-comment/the-original-resonant-existentially-brilliant-mad-men-finale> (Accessed May 21, 2016).

and “relieves pressure,” this became the recipe Reeves sold [1, p. 159]. By placing emphasis on speed and the infuriating sounds of pain, he created such a hated set of images that were played for years, over and over and over again. It was nothing short of a brilliant move simply because it was memorable.

Anacin sold like crazy, and with a production cost of \$8400.00, it was a bargain. By portraying Bayer as the famous “Brand X,” Anacin leveled the playing field, and Bufferin was right behind them selling its ability to relieve a new malady—the tension headache. Still placing emphasis on the emotional component of relieving analgesic pain, now all three aspirin titans took to television sets around the country to plead their cases of why their product was the fastest, most effective means to treat pain [13, 192–193]. Literally, millions of dollars were at stake, and the United States government was watching with much interest.

The commercial war between the aspirin companies eventually led to a standoff with the FTC. Each drug company claimed originality and a unique approach to treating pain. For the FTC, there was little chemical research mechanism in place to test these claims. Of course, Bayer, Anacin, and Bufferin all provided their own studies, but mostly they were manipulated to further their own cause rather than supplying accurate objective information. Finally, at the beginning of the 1960s the FTC ordered its own study of aspirin, which went horribly wrong after it was mistakenly published in a trade magazine. Sterling was the first to act, not surprisingly, by producing a commercial that exposed how they were the fastest acting of the three brands, even though the only real results from the study proved that none of the aspirin brands were any faster than the others. This drew the ire of the FTC even further, and that meant the attorneys took over [1, pp. 163–167]. Mired in litigation throughout the 1960s, the U.S. government, occupied at home and abroad with more pressing matters, could never collect enough evidence to prove that the aspirin companies said anything that was not accurate.

4.4 The Dawn of a New Chemistry

Despite the setbacks for the FTC against the major aspirin companies, it was a hollow stalemate in that Sterling, Home Products, and Bristol-Myers had larger problems to deal with at the end of the Second World War that did not include government intervention. Like all conflicts that incorporate such expansive swaths of territory and people, a modern war such as this one, like the American Civil War, the Russo-Japanese War, or the First World War before it, saw a huge acceleration in technology. Pharmaceuticals and medical breakthroughs were no different, and the products that became available for the everyday medicine cabinet would never be the same.

In 1933, the McNeil Laboratory was founded on the memory of its namesake Robert McNeil.¹⁸ As a family business, two of the grandsons of the founder happened to be graduates of Yale University, which during the Second World War served as a training ground for many of the eager young minds that would produce some of the most interesting and engaging ideas of the mid-century. Bob McNeil possessed a degree in physiological chemistry, while the other, Henry McNeil, studied applied economic science [2, pp. 212–213]. It was the perfect combination of chemistry and marketing.

By the mid-1950s the McNeil Labs introduced their first line of new products that incorporated acetaminophen, which until this time was only partially researched as an effective analgesic. They decided it should be called—Tylenol. Their timing was impeccable. The aspirin wars, coupled with a new set of doctors trained in the most-current medical school environments, believed aspirin was untested and in need of more careful study. Dr. James Roth of the University of Pennsylvania and others, found acetaminophen to be non-habit forming, without the side effects of gastrointestinal bleeding that aspirin could cause, and even safe for children [14].¹⁹ Tylenol's birth impacted the aspirin market, because it was initially sold directly to doctors and pharmacists, who at the time were undergoing their own revolution in both status and professionalization.

The medicine cabinet, like the chemistry laboratory before, was the space most impacted by aspirin's meteoric rise in production and use. Between the First and Second World Wars, the aspirin market was globalized, and claimed by marketing and ad men to be the panacea for everything from the common headache to the Great Influenza. People placed their hope in it to save their families, while others pointed to its poisonous effects when supplied in sizeable quantities. As the twentieth century marched on into the Cold War, a new space, the doctor's office, would take center stage, as aspirin's benefits were debated by a new generation forged in the violence and death that preceded 1945. Now more than ever, an

¹⁸Robert McNeil purchased a drugstore in Philadelphia, Pennsylvania in 1879. For the next three decades he built a local pharmacy that eventually expanded into pharmaceutical research and drug manufacturing. His son Lincoln McNeil took over the business in 1925, and it was his two sons, Bob and Henry, who were passed the torch of the business in the 1955.

¹⁹Tylenol was first introduced as an elixir for children, before expanding its line into a number of products that included caplets and gel tabs. In the late 1950s, Johnson & Johnson bought McNeil Laboratories, and it became a cornerstone for their massive empire of products. While, although it cannot be precisely pinned down, the development of pain relievers, like Tylenol, during this period officially relegated aspirin to the realm of being understood in the lexicon, at least in the West, as "common." Interestingly enough, other, more controversial pharmaceuticals produced by drug companies to this day, use aspirin's status as a common drug to influence the public's perception of their own products—thus making the illusion of safety. A case in point could be a medical professional named Edward Hallowell, a leading advocate for ADHD medications such as Adderall, who surmised on a regular basis during press junkets that brain altering drugs such as these were "as safe as aspirin." See: Schwarz [15].

emphasis on medical results would drive pharmaceutical companies to seek new profits over what was already an age-old question; what kind of impact did aspirin have on the heart?

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Chapter 5

Aspirin and the Doctor's Office

5.1 Dr. Bowen E. Taylor, a New Kind of Physician

Dr. Bowen Eacritt Taylor attended medical school at the University of Nebraska and took part in the most advanced era to date of modern medicine.¹ By the 1940s, gone were the hucksters that peddled patent medications that demeaned and vilified the doctor as a charlatan; now the AMA was an organization that had the power to lobby Washington and to protect its membership. It was a new time.

As a medical student, the future Dr. Taylor donned a white lab coat as he learned from textbooks and operated on cadavers. A turning point in his life came after medical school with a two-year stint in the U.S. Army during the Second World War. Afterwards, he took part in one of many aspirin-related trials that became part of the debate over the question of dosage and what it actually did to the human body over time. The results of those trials influenced his opinion about aspirin for the rest of his long career. As a specialist in internal medicine and cardiology, both personally and professionally, he believed, until his death in 2011, that aspirin should be taken each day of your life. He was convinced that aspirin's benefit to the heart, in an era of elevated cholesterol and blood pressure, was the best preventive medicine [1].

The scientific influences of the industrial chemistry lab coupled with a desire by the medical community to think differently about an age-old product, such as aspirin, drove this kind of thinking. By examining the roles played by three different classifications of medical professionals that assisted in unlocking the long-term potential of aspirin, we can better understand the impact of this important drug. Thus, the results from such aspirin research both propagated in the doctor's office and from the organic chemistry laboratories, would offer a new lease on life, and now a different status in the medicine cabinet.

¹Thanks to Terry Taylor, Katy, Texas, who related this family story about his grandfather, Dr. Bowen E. Taylor (1919–2011).

5.2 A Revolution in Chemistry and Medicine Begins

The first half of the twentieth century saw unprecedented strides in the fields of organic chemistry and medicine.² The acceleration of war and violence actually spurred the development of innovative notions of prevention. As discussed in previous chapters, aspirin rose to prominence first in the chemistry laboratory, and then became a staple in the medicine cabinet. There, it jockeyed for position with a myriad of other products. The Second World War changed everything from how pharmaceuticals were produced to how they were marketed. All of this would have a lasting impact on aspirin's resurrection.

By 1950, people across the globe were experiencing massive leaps in medical knowledge. Germ theory became accepted, X-rays were commonplace, and vaccines for everything from tuberculosis to scarlet fever were now incredibly successful. I.G. Farben led production of the forerunner to antibiotics, while electron microscopes could detect viruses that were before cloaked in mystery. By the 1930s, the medical profession in general underwent a variety of different forms of professionalization. Leading the charge was the AMA, which now had the educated, science-trained personnel on their burgeoning rosters that could enhance their credibility [2, p. 160].

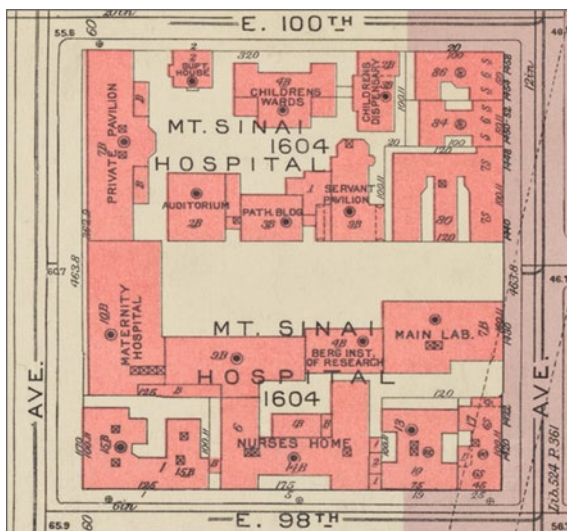
Now medical knowledge was far too complex for just the country doctor or the home patient, with its intricate formulas and powerful pharmaceuticals. Doctors, which began to include women, now trained at accredited universities, had to complete extensive intern and residency shifts, and had to pass stringent board examinations, all of which a generation ago was never part of the process. A license was not just a piece of paper, but required a set of comprehensive steps that had to be reviewed over the course of a career. Before this time period, specialization was frowned upon since it was seen as manipulative, and not helpful to the broad brush that was needed to be a general practitioner [3].

The shift also included a total revolution in the architecture of the hospital and the doctor's office.³ Before 1900, hospitals were associated with only death and not so much with recovery. It was probably safer to have a doctor come to your home to administer treatment, rather than visit a hospital. Sanatoriums, also called hospitals, were where the mentally challenged were placed and were seen as repositories for those that could not function effectively in society. The World Wars, along with the battle that was waged against the Great Pandemic, accelerated the solutions to these

²Some scholars have suggested that during the early twentieth century, medicine was the most open, and least criticized, the profession has ever been; while it might be suggested that the second half of the twentieth century, though marred by giant pharmaceutical conglomerates and medical malpractice suits, could be characterized as the era of collegiality. For the time being, globalization has eclipsed the notion of nationalism. See: Gabriel [2].

³Globally speaking, for instance, doctors in China remain some of the most maligned and disrespected professionals. Great contrast to the shift that has occurred in the West; that said, there are some real success stories where U.S. doctors went to China and turned around some troubled hospitals. Thanks to Dr. William C. Mayborn for this information.

Fig. 5.1 Mount Sinai Hospital Block, Plate 120-Part of Sects. 5&6, Manhattan Land Book, New York City, 1955 (Courtesy of the New York Public Library)



issues by controlling testing, bed rest, and quarantining. Hospitals became new temples of research and analysis that were built with emergency care units, disease control, and of course, surgical and obstetrics theaters. Professional nurses and doctors who were armed with new training methods staffed these new spaces. At larger urban hospitals, the latest advancements in surgical equipment facilitated for more complex procedures (Fig. 5.1).

Housed within these new hospitals, or in close proximity, were new and improved pharmacies. Like doctors, pharmacists underwent an educational revolution in training and licensing in the 1930s [2, p. 161].⁴ But, medical professionals disregarded them as their technical expertise improved and the growth of synthetic drugs became more prevalent. Pharmaceuticals were no longer solely created inside the pharmacy, thus, the physic or the chemist, as they were called in Europe, began to be seen less as a consultant, and not an extension of the scientific community. With the destruction of I.G. Farben after the demise of the Third Reich, and its subsequent revival in a much different form in West Germany after 1945, the American drug market blossomed both in its biological manufacturing and synthetic production lines. The industrial research laboratory became the focal point,

⁴The important role played by pharmacists, before 1950, can be seen in popular culture, especially in the scene from Frank Capra's *It's A Wonderful Life*, where the young George Bailey saves his employer Mr. Gower, the pharmacist, from killing a patient. Taking place in 1919, Mr. Gower was grief-stricken after learning that his son had just died from the Great Influenza, and proving the power of the compounding pharmacy, mixes poison into a customer's order. George stops him, but in the dream sequence with Clarence the Angel, He was not there to keep Mr. Gower from killing the patient, and from losing his business. Interestingly, the actor, H.B. Warner, who played Mr. Gower, went to medical school for a time before dropping out to become an actor. See: <http://www.tcm.com/tcmdb/person/202080%7C64520/H-B-Warner/> (Accessed on May 30, 2016).

instead of your local pharmacy, for the new and innovative ideas that sought to answer the most perplexing questions of this new medical age.

5.3 The General Practitioner: Dr. Lawrence L. Craven

The link between the clean white sanitized hospital and the efficient well-organized chemical and pharmaceutical factory became the third and final space that helped to solidify aspirin's place as one of the most important developments in drug production by 1945—the doctor's office. As this section will examine, the doctor's office became one of the most important points of dissemination for the prescription of the proper dosage of aspirin during the second half of the twentieth century. Translating the latest and most scientific results from the field of medicine and chemistry, this space, with its connection to the chemistry lab and the professionalized hospital, would transform aspirin's role even to this day.

With new hospitals being constructed first in cities, and then in larger towns, as regional centers for rural landscapes, doctors now began looking for spaces where their patients could come for consultations, tests, and to have thorough examinations by trained staffs. Equipped with their own nursing staffs, these offices could perform a myriad of procedures both in general practice, and later, for distinct specializations. This was the location where aspirin had its first connection with being beneficial to heart health, and a case in point was the work of Dr. Lawrence L. Craven.

Born in Iowa in 1883, and a graduate with a M.D. from the University of Minnesota College of Medicine and Surgery right before entering into service in the First World War, Dr. Craven was part of the migration out West during the Dust Bowl of the 1930s [4]. Landing a general practice in Los Angeles, California he built a reputation for offering personal attention, and he possessed an innate sense concerning the prevalence of heart attacks that he was witnessing in the post-1945 era. By the early 1950s, his powers of observation led him to notice that a number of his patients, who were recovering from post-operation surgery, were chewing large amounts of Aspergum, which was a product that contained small dosages of aspirin. The results were fascinating because bleeding occurred in many of them. Dr. Craven wondered if there was a connection between aspirin and the anti-clotting that continued in the patients that chewed the gum.

Publishing his results in a minor medical journal, the *Mississippi Valley Medical Journal* in 1953, he found that of the 1465 healthy male patients that took up to 650 mg of aspirin, as an anti-coagulant, most did not suffer any coronary issues for several years [5]. He also concluded that men suffered more heart attacks than women due to the fact that they were less likely to engage in the taking of medication. Interestingly, this turned the argument, from the earlier part of the century on its head that portrayed women as emotional and in need of something to calm their nerves. Dr. Craven pointed out that in general, men were not very conscientious when it came to their own health. After the publication of this paper, he

actually reported receiving numerous responses from general practice physicians from around the country who agreed with his assessment that aspirin could provide useful treatments to curb the onset of coronary thrombosis.

Dr. Craven's work proved that anti-platelet treatment could be studied just as effectively by a general practitioner as a large research hospital. Even though much of his work was discredited, he published his research not only in a local newspaper, but also in second-tier peer-reviewed medical journals [6]. He knew that the art of medicine included listening as a means by which to conduct research. The doctor's office thus proved that aspirin trials could begin in the unlikeliest of places. Next, it was time for larger research labs and hospitals to join the general practitioners of the world to prove why aspirin worked the way it did as an anti-coagulant, and how to settle the question of proper dosage.

5.4 The Evidence-Based Researcher: Dr. Harvey J. Weiss

Despite its long history, it seems odd to think of aspirin as an untested medication. However, by the 1960s, building on both the industrial capacity of chemistry labs, and the work of members of the medical community like Dr. Craven, new trials began to further the possibilities for aspirin to be thought of as a preventive medication. It became a question of credibility. In order to reach the medicine cabinet with a different approach it would require more than just television commercials and full-page ads. Sure, they were still relevant and brought in high profits, but something was changing in the space that aspirin was occupying. Now it was becoming clear in the laboratories and doctor's offices that aspirin was more than just a pain reliever. A new breed of research-oriented physicians were now focusing on ideas that drew upon past assertions, but it was the mechanisms they employed that brought fresh eyes to an old subject. These studies were personified by the work of Dr. Harvey J. Weiss.⁵

Dr. Weiss, an eminent doctor of bleeding disorders from Mount Sinai Hospital and Columbia University, began to use a new device called an aggregometer that measured the effect of coagulation on the platelets [7, p. 262].⁶ An ingenious, yet

⁵See Michael Lewis. *The Undoing Project: A Friendship That Changed Our Minds* (New York: W.W. Norton and Company, 2016). Lewis examines the work of two Israeli psychologists, Amos Tversky and Daniel Kahneman, who influenced the development of behavioral economics by arguing why we should not trust human intuition. Specifically, Lewis, in "Going Viral" outlines the ways in which evidence-based research in medicine influenced the decision-making process for diagnosing patients. This is particularly applicable to the studies that were carried out with aspirin to this day (Chap. 8) pages 212 – 237.

⁶Mount Sinai Hospital, where Harvey Weiss conducted most of his research, is an excellent example of a hospital that combined hospital services and doctor's offices. Founded in the nineteenth century, it was the second Jewish medical center in the country. After adding the Berg Research Laboratory after 1945 (Fig. 5.1), by the late 1960 s it opened a medical school that began

simple test tube equipped with a light and a photoelectric cell was developed by a couple of hematologists. The aggregometer helped to define the rate at which the platelets stick together. Dr. Weiss put this latest test to work by assigning low doses, about 300 mg of aspirin to ten healthy men (of which six were fellow physicians), in order to see if the anti-clotting time would reduce the risk of heart-related issues. What he observed was that aspirin served the dual purpose of halting platelet aggregation, while reducing the factors that caused heart attacks. In a more celebrated journal called the *Lancet*, Dr. Weiss argued that these breakthroughs would revolutionize the notion of what aspirin could do. He and another colleague, Dr. Louis M. Aledort, perceived that people who consumed the tablet would make a pinprick last three minutes longer than those that did not. In the end, "aspirin," they said, "may have anti-thrombotic properties" [8].

Why at this stage of the research of aspirin's capability as an anti-coagulant and a its role as a preventive medication, did Dr. Harvey Weiss have a much easier time "selling" his results than Dr. Lawrence Craven? Part of the reason rested in that Dr. Weiss was part of a new generation of what could be called the era of the evidence-based researcher. By the 1960s, doctors and chemists published their results in publications that were reviewed and read by their peers. Dr. Craven did so; yet, he was not taken seriously, even though he had his own lab, so to speak, in his doctor's office. But, new scholarly publications printed results that came from laboratory environments, which were specifically funded and geared to producing data, and were connected to the hospital architecture. The notion of a trial as part of the scientific method of investigation was not something new either in medicine, as Bayer had proved before the First World War. However, with the new industrial labs behind them, physicians that were trained in modern medical schools and had the ability to take part in post-doctoral programs that offered specific specializations could now concern themselves with constructing usable methodologies knowing that the resources would be behind them.

For the first time in the history of organic chemistry, as related to the production and testing of pharmaceuticals, scientists had the ability to influence each other's work in a more efficient manner. That is the process that Dr. Weiss and many others were partaking. Together with the findings of other groups, Dr. Weiss's discovery was a key step in understanding the piece of machinery that would allow low doses of aspirin to prevent coronary thrombosis [9]. But, he did not do it alone because he stood on the backs of others whose research was sound and important. Dr. Weiss's contribution was a major one, but what is more interesting is that with the equipment now in place to produce medical results, others could make new findings beyond whether aspirin affected platelets. Henry Collier, Priscilla Piper, and Sir John Vane all benefited from this collegiality and a sense they were all working on similar problems [7, p. 281]. Aspirin now had a variety of different specialists

(Footnote 6 continued)

to graduate some of the top students in the country. To this day, it is one of the leaders in medical research and care in the United States.

working towards a more complex understanding of the long-term effects on the human body.⁷ This modification in perspective would benefit the next generation of scientists and medical personnel, namely embodied in that respect by the work of biochemist Dr. Philip W. Majerus.

5.5 The Biochemist: Dr. Philip W. Majerus

On June 8, 2016, Dr. Philip W. Majerus passed away. The initial headline in the *New York Times* print version of the obituary read, that Dr. Majerus “recognized the benefits of aspirin’s heart benefits.” The same article’s title in the online version was changed from “recognized” to “discerned” [10]. The subtle alteration was significant because Dr. Majerus’s contributions to aspirin-related research were about more than recognition, and rather about a synonym of discern, that being, detection. This word implies a certain amount of perceptibility to carefully study a subject to the point of discovering something that is so nuanced that it could invariably be overlooked. Dr. Majerus was not the type to miss anything.

He was born into a family that owned a five and dime in Quincy, Illinois. After completing a B.S. degree at Notre Dame in 1958, he graduated from Washington University’s School of Medicine. Like many of his contemporaries, Dr. Majerus completed a postdoctoral program; for him it was at the National Institute of Health. Joining the United States Public Health Service after 1963, instead of serving as a doctor in Vietnam, Dr. Majerus’s career moved in the direction of evidence-based research [10]. Biochemistry helped to focus his attention on aspirin. After studying the work of Dr. Harvey Weiss, Dr. John Vane, and many others, he was influenced to focus his research on trying to explain the biochemical impact of aspirin on platelets.

Based in St. Louis, Missouri at Washington University as a professor of biochemistry, Dr. Majerus had the idea, along with his postdoctoral research fellow, Gerald Roth, to get his hands on some aspirin, a lot of aspirin. He rang up the local Rexall Drug Company, and spoke to the manager about securing 100 bottles of aspirin at 160 mg, along with the same amount of a placebo. By the next morning he supposedly had all the resources he needed to conduct the trials that he wanted. After six months, eighteen of the twenty-five patients who were taking the placebo developed dangerous blood clots. Of the nineteen who received a daily lower dose of aspirin, only six formed clots. Dr. Majerus and his team discovered that the drug modified an enzyme, which in turn helped the molecule to constrict the blood

⁷Sir John Vane (1927–2004) was a pharmacologist at the Royal College of Surgeons of England who worked with Priscilla Piper, a graduate student at the University of London. Henry Collier, a biochemist at Parke Davis, referred her to Vane, after hearing about his path-breaking research. Vane received the Noble Prize in Medicine in 1982 for his work with aspirin and prostaglandins, and was knighted by the queen. He did not do any of his research alone though, and could not have achieved such results without the help of Piper and many others.

vessels. By aggregating the platelets, he also proved that aspirin lengthened their durability [11].

Dr. Majerus, like Drs. Taylor, Craven, and others in the field before him, personally believed in the power of aspirin's ability to reduce the threat of cardio-vascular related events. He took aspirin every day, and even refused to take part in studies because he did not want to entertain the possibility of being given a placebo. Towards the end of his long career, he received the Bristol-Myers Squibb Award for distinguished work in cardio-vascular metabolic research in 1998, and even though he was lauded by contemporaries as responsible for conducting some of the most original work on aspirin, he was not alone [10, 12].⁸ Like, Dr. Weiss, he was part of a chain in the history that linked three generations of physicians and biochemists. Dr. Majerus helped to bring some of the assertions that were first posed by Dr. Lawrence Craven, and were expounded upon by Dr. Harvey Weiss and others. It was not that one physician was brighter or knew their subject more completely. They were all part of different periods in the arc of understanding aspirin's chemistry and its promotion as a drug of prevention.

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⁸This is the same Bristol-Myers that developed Bufferin, Bayer's rival beginning in the 1950s, and merged in 1989 with another nineteenth century pharmaceutical company called the Squibb Corporation.

Chapter 6

Aspirin Endures

6.1 The Future of Heart Health: Chemistry's Role

During the 1980s, after three decades of research, hundreds of different trials, and many successes and failures, aspirin as antidote to heart related issues was not statistically viable. In the eyes of the federal government, which had monitored the pharmaceutical market in some form or fashion since the Wilson Administration, there still was not enough evidence. All of this changed, when a relatively new technique called meta-analysis that was developed by a statistician, named Dr. Richard Peto, convinced the FDA and most of the cynics that the aspirin research was sound [1, pp. 318–320, 2, p. 272].¹ Now it was up to the FTC to try and curb the claims that were now being published in every newspaper, magazine, on the television, and eventually on the Internet. Finally, aspirin's role as a preventive medication, which was supported by the majority of the medical community, had arrived.

For centuries aspirin was used as a way to reduce fever, headaches, and on a host of other maladies. Today, there are over fifty drugs that are available over the counter in which aspirin appears as the active ingredient. Aspirin reduces the ability of platelets to clump together, and the anti-blood clotting is useful in patients with coronary diseases like atherosclerosis. The narrowing of the arteries causes an increase in blood pressure, and in turn can cause plaque to tear away from the arterial wall causing a clotting response. Platelets will then plug the damage in the artery restricting blood flow, which can result in a heart attack. Likewise, if the blood flow is blocked to an artery to the brain, a stroke can result. Aspirin prevents the clumping of platelets by inhibiting the function of enzymes called cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). These enzymes are responsible for the production of compounds known as prostaglandins [3].

¹Dr. Richard Peto (1943-Present) is also a leading expert on deaths associated with tobacco use.

Prostaglandins were first discovered in the 1930s by a Swedish researcher, Ulf von Euler.² He confirmed earlier reports that human seminal fluid stimulated the contractions of uterine muscle, and was able to isolate the compounds that caused this response and called them prostaglandins. We know now that prostaglandin production does not take place exclusively in the prostate gland, as they are synthesized in most tissue cells. Prostaglandins are similar to hormones because they trigger a particular response in specific target tissue. Unlike hormones that are made in a specific area of the body and are carried to target tissue by the bloodstream, prostaglandins are synthesized within the cell tissue where they are needed. They are synthesized in the body from a 20-carbon polyunsaturated fatty acid known as arachidonic acid, and are unsaturated carboxylic acids that contain a five-member ring as part of a 20-carbon skeleton. The name of the prostaglandin is designated by the type of substitutes on the ring and the number of double bonds on the side chain of the molecule. The molecule is first given the designation PG, which stands for prostaglandin, and then a letter designation is assigned to the different types of prostaglandins. There are nine types of prostaglandins, and each type is designated by a letter, A through I, with the number of carbon-carbon double bonds of the side chain being designated by a subscript number, 1, 2, or 3 [4].

Prostaglandins are a member of a larger class of compounds called eicosanoids. All eicosanoids contain 20-carbons and are derived from fatty acids. The eicosanoid family includes prostaglandins, leukotrienes, and thromboxanes. These are known to have a variety of physiological effects, especially when the tissue is damaged, they are known to activate the inflammatory response producing pain. Bacterial infections will cause a response in the hypothalamus to produce prostaglandins, which will result in fever. When blood vessels are damaged, a type of eicosanoid, known as thromboxane A₂, is released. This eicosanoid is a vasoconstrictor and will trigger constriction of injured blood vessels and platelet aggregation. In opposition, prostacyclin, an eicosanoid known as PGI₂, has the opposite effect of thromboxane A₂. PGI₂ inhibits platelet aggregation. Prostaglandins are also known to regulate menstruation, prevent contraception, and PGE₂ is known to induce labor by causing uterine contractions. Others are involved in inhibiting acid secretions in the stomach and stimulate mucus secretion that protects the stomach from digesting itself. It is clear that prostaglandins have enormous potential for treating a wide variety of ailments. Once these hormone-like compounds are fully understood, their benefit to mankind will be far reaching.

As this study has shown, for over a century the role of aspirin in reducing fever and relieving pain continues to be remarketed as new and improved. Other analgesics, like acetaminophen and ibuprofen, claimed to be more effective than aspirin and offer faster relief. However, the fact is the main ingredient of aspirin, acetylsalicylic acid, remains as effective as any drug to hit the market. Strong marketing and ad campaigns in the 1970s and 1980s have tried to reduce aspirin's market

²Ulf von Euler (1905–1983) was a physiologist and pharmacologist who is known for his work with neurotransmitters, for which he received the Nobel Prize for Medicine in 1970.

share and convince consumers other analgesics are superior. Now, more than ever, the conversation on television and in print revolves around the number of tablets or caplets a consumer has to take, along with the effectiveness of pain relief.³ However, aspirin has still found new life. The discovery of the benefits of aspirin in the area of heart health in the prevention of heart attacks and blood clots in the late twentieth century gave aspirin renewed resurgence.

New data now finds that aspirin may also be used in the prevention of certain types of cancers. Studies are starting to reveal that long term use of aspirin may be effective in the prevention of colorectal, prostate, mouth, esophageal, ovarian, lung and breast cancers. Researchers caution that more studies are needed and the possible mechanisms for the prevention of cancer via aspirin therapy are just now starting to be understood. One of the leading theories on the prevention of certain types of cancers involves the inhibition of the production of a particular prostaglandin that may be involved in the production of these cancers. It is quite possible that aspirin may one-day benefit humans in the area of cancer prevention, the way that aspirin now benefits humans in the area of heart health.

The future of aspirin and its many benefits does not stop with cancer research, as there are areas of health that may still benefit from aspirin. It has been suggested that aspirin could be beneficial to the immune system. This could open the possibility of aspirin being used as an anti-viral drug in the future. Another use would combine aspirin with an anti-cholesterol, and beta-blocking drug. Combining these three could further reduce the possibility of heart attack and stroke, while possibly cutting the cost for consumers of these drugs.

Dr. Kathryn Uhrich, a research professor at Rutgers University, has probed the uses of aspirin by manipulating its composition into a polymer. Known as PolyAspirin, part of the polymer is an anhydride, which will react when exposed to water found in the body to form the active ingredient found in aspirin, salicylic acid [2, p. 272]. It can be engineered to degrade in the body, so that the drug can be released at different rates. The polymer can release it slowly over longer periods of time, and could be designed to release over periods of days, weeks, or even months. Remarkably, this would give doctors more control over how much of a dose each patient received over time.

PolyAspirin is applicable for biodegradable sutures or coatings for implants that are placed in the body where inflammation and pain often occur due to the trauma that has taken place in the tissue of the affected area. The drug would not be ingested orally or injected intravenously, instead delivered right where it is needed most, bypassing areas like the stomach and intestine where irritation is most likely to occur. These developments are still in the research phase, and are pending FDA approval, while being used in clinical trials. Pain relieving polymers that can regulate and target the release of medication is an exciting idea with the potential to

³For instance, Aleve, a Johnson & Johnson product, emphasizes in its ad campaigns the, "all day long, all day strong" slogan, to promote the fact that you do not have to take so many of their product to receive pain relief. Aleve is a NSAID called Naproxen, and is billed as being an effective means by which to treat arthritis.

improve the lives of millions of patients; just another means in which aspirin continues to evolve as one of the most significant discoveries through an act of science.

6.2 Conclusion

Dr. William S. Fields had a unique patient under his care, who made his living with a particular skill set that few could master.⁴ His right arm could hurl a baseball at over 100 miles an hour from sixty feet, six inches. The only issue was he had collapsed on the floor of the Astrodome in Houston, Texas during the 1980 season after suffering a deadening in his arm; which meant a massive stroke [5].⁵ Dr. Fields had done his best since this event to give him a chance to return to the game that he was dominating. The patient's name was J.R. Richard, a pitcher for the Houston Astros, and what he experienced was a blood clot located in his neck that nearly killed him. Richard ended up surviving several operations, but never pitched again in the major leagues. For a short time he ended up homeless in Houston, living on the street, after being released by the Astros.⁶

As a neurologist for over 25 years, by the 1980s, Dr. Fields had seen his fair share of strokes; the devastation that afflicted families faced, and he had spent his career trying to figure out their causes. Prevention was an extremely challenging task since the early warning signs could be so innocuous. Yet, Dr. Fields had an advantage. Schooled in the post-War medical school era, Dr. Fields, like Dr. Majerus and Dr. Weiss, took part in the revolution that fueled a new era of chemistry and medicine. He also began at an early juncture looking into the effects of aspirin in low doses on the brain and nervous system [6, 1, pp. 312–315]. His initial conclusions brought about the thinking that there could be a strong connection between blood flow, the spinal column, and the brain. Like the heart health trials, Dr. Fields led a number of studies that helped him arrive at the conclusion that aspirin could make the difference against this neurological disorder [6, 2, pp. 263–264].

After a century of evolution, from a chemistry laboratory in Germany to the medicine cabinets of everyday folks across the globe, and finally, to the doctor's offices that have battled heart disease, the most destructive killer of human beings on the planet, aspirin remains. Touching almost every aspect of a person's life,

⁴Dr. William Fields (1914–2004), was one of Texas' first neurologists, and was a pioneer in the field, especially in his studies of aspirin and the prevention of strokes. He was one of the first faculty members in 1970 of the University of Texas, M.D. Anderson Cancer Research Center, and served as the first chairman of the neuro-oncology department from 1984–1988.

⁵Thanks to Jerry Michalsky, Baytown, Texas for relating the story of J.R. Richard and his brief Major League Baseball career.

⁶J.R. Richard (1950–Present) rebounded from his affliction and continues to live in Houston, Texas, where to this day he takes part in ministry work.

either through the application of home health care remedies, through a local pharmacy, in the most advanced research labs, or even by way of the billion dollar industry's advertisements on television or in print, aspirin continues to be the most prolific medication—even into this century. Its survival was due in part to people's search for antidotes to everything from the common headache to influenza to warding off heart attacks.

Over its lifetime, aspirin's chemistry altered very little, but how the physicians, scientists, advertising agents, and consumers interpreted its possibilities, did. The story of aspirin includes a complex weaving of industrial development, governmental control, consumer advocacy, the building of the professional development of chemists and medical personnel, and all of its development accelerated by global conflict. Aspirin, whether in powder form or through a tablet or caplet, found its way into our medicine cabinets through trust, and a promise that it had the ability to change our lives. In the end, because of the chemistry, that was not a miracle, only a means by which to realize how to prosecute pain and enhance the possibility of prevention. What will the medicine cabinet of the future look like? We can surmise, with relative certainty, that a glimpse behind the mirror would include the medicine for the next global age—aspirin.

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