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### EDITOR'S NOTE

With the appearance of this first issue in 2000 the Bulletin for the History of Chemistry enters a new era of publication. Issues will now be designated as volumes rather than numbers, beginning with this Volume 25. Pagination within a calendar year will be continuous, and a collective table of contents will appear in the last number of each year. Whereas the literature citation for this journal formerly indicated a number (i.e., 1, 21, etc.), the italic symbol henceforth will designate the volume.

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“INSTRUCTIONS FOR AUTHORS” see page 72

## MERCK IN AMERICA: THE FIRST 70 YEARS FROM FINE CHEMICALS TO PHARMACEUTICAL GIANT\*

*Leon Gortler, Brooklyn College of the City University of New York*

In 1668 Friedrich Merck purchased an apothecary, the Engel-Apotheke (the Angel Pharmacy) in Darmstadt, Germany. One hundred and fifty years later, Heinrich E. Merck, a friend and collaborator of Justus Liebig, took over the family business and began its conversion to a manufacturer of pharmaceuticals and fine chemicals. The company, E. Merck, became a major producer of alkaloids, including morphine, codeine, and cocaine (1).

Throughout the 19<sup>th</sup> century, E. Merck exported products to the US, but it did not have a sales or distribution office in this country. Late in the century, Lehn & Fink, E. Merck's US distributor, used E. Merck labels on inferior non-Merck products. In an effort to protect its American interests and its good name, E. Merck opened its own sales office in New York in 1887. Theodore Weicker, who had been with the firm in Darmstadt for 10 years, was placed in charge of the New York office.

In 1891 the firm decided it was time for a member of the Merck family to begin tending the company's business in the US, and the company sent George Merck (Fig.1), Heinrich Merck's grandson, to New York. George, who was only 23 at the time, had already spent seven years being trained in the family business. When he arrived in the US, he founded Merck & Co. in partnership with Theodore Weicker. In the beginning the company concentrated on the importation of drugs and chemicals, primarily those of the parent company, E. Merck. The intent, however, must have been eventually to establish a manufacturing presence in the US. In 1903 Theodore Weicker sold his share of the business to George Merck and, with another partner, purchased E. R. Squibb & Sons (1, 2).



**Figure 1.** George Merck holding his two-year-old son, George W. Merck in Darmstadt, Germany, 1896.

Merck & Co. had to endure a major US depression (1892-1895); but by 1896 the company occupied its own new building at University Place and 8th Street in New

York City, and in 1897 it opened a very stylish pharmacy on the north side of the new building (Fig. 2). Merck's best customers, the German druggists in New York and vicinity, were irate at this encroachment by their supplier. After two years, George Merck bowed to the demands of his customers and closed his elegant apothecary (3).



*Figure 2.* Merck & Co. pharmacy in New York city, 1897.

By 1897 Merck & Co. had annual sales of over \$1 million. George Merck purchased 120 acres of wooded countryside near Rahway, NJ in February, 1900; in 1903, shortly after he became a US citizen in 1902, the company began manufacturing some of its own chemicals in a plant built on the Rahway property. Merck & Co. also began manufacturing in St. Louis in 1903, in a plant that was first leased and later (1905) purchased from Herf and Frerichs. This plant had already been producing iodides and other staples of the pharmaceutical industry. Manufacturing in St. Louis was abandoned in 1908, but the site continued to serve as the St. Louis branch of Merck & Co. and was used as a distribution center for the Midwest and western US.

Merck & Co. was no longer merely a branch of the German company. It incorporated in New York in 1908 and gradually expanded its product line of American-made narcotics — including morphine and cocaine. By 1910 sales had exceeded \$3 million, and in 1911, Merck set up its own subsidiary in Canada; but there were still very strong ties to Germany. Most of the production was carried out according to German manufacturing processes; German immigrants were often used in the plants, and E. Merck was still the majority stockholder in the American company.

In 1917, when the US entered World War I, George Merck was forced to break formal ties with the German branch of the family and with E. Merck. He voluntarily turned over almost 80% of Merck stock, E. Merck's share of the company, to the Alien Property Custodian. In

1919, the Property Custodian decided to sell the Merck stock at public auction, much to the dismay of George Merck. Merck called upon and received the support of two investment banking companies, Goldman Sachs and Lehmann Brothers. There were five bidders at the auction. Monsanto started the bidding at 2.4 million dollars, but 25 minutes later George Merck once again had complete control of the company at a cost

of 3.75 million dollars (4).

Merck continued to grow in the early 1920s and by 1925, when George Merck, warned of poor health, passed on the presidency to his 31-year-old son, George Wilhelm, Merck & Co., Inc. was one of the "Big Three" fine chemical producers in the US with sales of \$6.1 million (5, 6). The senior Merck died a year later, on October 21, 1926 at the age of 59.

Despite the profitability, George Merck had heavily mortgaged the company when he purchased the shares from the Alien Property Custodian. He had financed the purchase with the sale of preferred stock (7); and, according to Adolph Rosengarten, Jr., a former director (1932-1942, 1946-1974) and the largest Merck stockholder, by 1925 or 1926, Merck was in arrears on the preferred stock (8). As luck would have it, the four Rosengarten brothers, Adolph, Frederick, George, and Joseph, the owners of Powers-Weightman-Rosengarten (PWR), a large fine chemical company based in Philadelphia, "...wanted to retire and enjoy life." In the words of Adolph Rosengarten, Jr., (8):

Father (Adolph senior) liked to shoot grouse in Scotland in the summer, Uncle Fritz liked to fish anywhere he could, Uncle George liked to fish for tarpon off the Florida Keys, and Uncle Joe was satisfied to stay home and play golf because he was stone deaf.

PWR wanted to merge with another chemical company and leave the day-to-day operations to the new partner.

They wanted to merge with Pfizer, but the Attorney General determined this merger would violate anti-trust laws. Merck was an ideal candidate because, as Adolph, Jr. put it, “We were solvent and they weren’t.” With the merger in 1927, a new company, Merck and Co., Inc., was formed. The Merck Corporation, the new name adopted by the original firm, and PWR transferred all property to the new company, which now had combined assets of about \$9 million, and PWR lent \$5 to 6 million to the new company. As part of the merger, Frederick Rosengarten became chairman of the board, and Adolph and George became members of the board. George W. Merck became president of the new company (9). This was the first of two major mergers that determined the future of Merck. In each instance the merger significantly influenced the continued growth and development of the company.

PWR was, like Merck, a long-line chemical firm, selling over a thousand products. The offerings of the two companies were sufficiently different that they complemented one another. As a result of the merger the combined company had a “large enough inventory to carry it through three years of the Depression without having to make anything (10).”

The new company, with sales in 1928 of over \$13 million, could afford to make a heavy investment in research and development. After the merger George Merck brought in his brother-in-law, George W. Perkins, the son of a famous banker, as chief operating officer. Perkins was influential in establishing the new research unit. Merck and Perkins, with the advice and guidance of Alfred Newton Richards, a noted clinical pharmacologist at the University of Pennsylvania, went searching for someone to run the new research operation (11). They first went to Princeton—Perkins’ alma mater—where they found a young organic chemist, Randolph Major, who was to lead Merck research for the next 26 years.

A research unit had actually begun in 1916, probably an acknowledgment that chemicals would no longer be available from Germany. William Engels had become director of the research laboratories in 1918. Until 1930 the “research labs” were spread throughout the manufacturing facility in Rahway, probably because the primary function of “research” was to service the manufacturing end of the company. In a 1932 memo, Major listed four main functions of “research” prior to 1930 (12):

- Transformation of laboratory processes into processes suitable for the factory.
- General improvement of processes.
- Study of methods for keeping and preserving materials after they are made.
- Investigation of complaints by customers which could not be handled by others.

In 1930 Major set up the Laboratory for Pure or Fundamental Research with six chemists and made plans for a new research laboratory to house this unit. Engels headed up the Laboratory for Applied Research with an additional ten chemists. At the end of his 1932 memo, Major made a point of mentioning papers that had been published in the previous two years and his intention of publishing most of the “results of scientific value” from the “laboratory of pure research.” This set the tone for Merck research. George W. Merck had a vision of a research laboratory the equal of any academic department, and publications from the new research unit were a step in that direction.

Major had a knack for choosing productive programs and productive people.



**Figure 3.** Randolph T. Major (*left*) Director of Research and Development, William H. Engels (*second from left*), Associate Director, examining an intermediate in the synthesis of pantothenic acid with team of chemists who synthesized it in 1940: (*left to right*) Karl Folkers, Assistant Director of Research, J. Finkelstein, J. C. Keresztesy, and E. T. Stiller.

His most successful early program was to isolate, determine the structures of, and synthesize as many vitamins as possible. The origin of this program is not clear. He may have observed considerable activity in vitamin research in Europe and little in the US, and/or he may have foreseen the possibility of enriching foods with vitamins or using pills to treat people with vitamin deficiencies. It is difficult to believe that he had any idea of just how profitable this program would become.

In 1934, Merck hired Karl Folkers who had earned a Ph.D. with Homer Adkins at Wisconsin and then served as a postdoctoral fellow with Treat B. Johnson at Yale. Johnson instilled in Folkers an interest in compounds with biological activity. Folkers made a life's work—some say an obsession—of isolating and synthesizing biologically active molecules. He was the perfect fit for Merck's vitamin program. Folkers' description of Major's approach to directing his researchers is revealing (13):

He was not a man who directed you. He said, "Here's a problem. Good luck." Then he left you on your own.

After a few years of Major's leadership, Merck, collaborating with R.R. Williams at Bell Labs, had done significant work on thiamine, vitamin B<sub>1</sub> (14). Synthesized in 1936, it soon accounted for over 10% of Merck's sales. In 1938-39 Folkers and his group isolated and synthesized vitamin B<sub>6</sub>, and in 1940 they reported the synthesis of pantothenic acid, another of the B vitamins (Fig. 3).

It was one thing to search for biologically active molecules, determine their structures and synthesize them. This was the work of organic chemists. It was quite another matter to determine whether molecules were, in fact, biologically active, and once isolated, whether they would prove useful and safe for the prevention or healing of disease. For this there was a need for pharmacologists and biologists. It was difficult to hire first rate pharmacologists in this country because of the stigma attached to working in industry. Pharmacologists working in industry were not permitted membership in the American Society of Pharmacology and Experimental Therapeutics; and a member who went to work in industry was forced to resign from the Society. Alfred Newton Richards, one of the founders of the Society, had to resign his membership when he began consulting for Merck. The restriction was eventually withdrawn and Richards' membership in the Society was reinstated.

With the help of Richards, Merck hired Dr. Hans Molitor of Austria in 1932 to head the new Merck Institute of Therapeutic Research. Molitor expected to return to Vienna within a few years but, in the end, remained as head of the Institute until 1956. The Institute, housed in Rahway and funded by Merck, was an independent facility because a New Jersey law prevented industrial companies from conducting animal research. Cooperation between the Institute and the Laboratory for Pure and Fundamental Research was essential for isolating and developing new pharmaceutical products. In 1933 the three research arms of Merck, the Laboratory for Pure and Fundamental Research, the Laboratory for Applied Research, and the Merck Institute of Therapeutic Research, moved into a new building at the Rahway facility.

In 1937, Major hired Max Tishler, another eventual key participant, for his research team. Tishler (Fig. 4) had graduated from Tufts and had taken his Ph.D. under Elmer Kohler at Harvard (15). After obtaining his doctorate, he stayed on at Harvard for another three years, teaching, doing research, and revising James Conant's textbook (16) (Conant was, by then, president of Harvard). Tishler, because he was Jewish, had difficulty finding an academic or industrial position. Kohler recommended Tishler to Major; Conant recommended him to George Merck, and Max was hired. Carl Addinall, a Merck employee and a former Harvard graduate student who had been Max' instructor in Chem 5, also rec-



Figure 4. Max Tishler, circa 1963

ommended Max to his supervisor at Merck (17). Randolph Major, Karl Folkers, and Max Tishler, were to lead Merck's research and development programs for almost 40 years.

Tishler's first job at Merck was to find ways to synthesize riboflavin, vitamin B<sub>2</sub>, to bypass the German process patents. Within two years Merck was manufacturing and marketing riboflavin. Folkers was driven to find new vitamins and exploit their use. Tishler was motivated not only to find new products, but also to follow them all the way to the customer. In a 1983 interview, he said (18):

One of the greatest thrills I had in riboflavin was when the plant was producing the first kilogram of stuff. I was there! It was a great thrill.

He had followed riboflavin from the bench through the pilot plant and the factory, getting involved in every step of the process.

Tishler was the ultimate process chemist. He loved to take new compounds from the research bench and develop efficient processes for producing the compounds on a large scale and interacting with the chemical engineers in building a production plant. He was also endowed with enormous energy. Lew Sarett, in a 1990 interview, said (19):

Max was born with an energy level that was like an avalanche and a brain that was incandescent. It was scintillating—the combination of energy and ability was extraordinary. I've never known a guy like that.

Next came World War II and Merck became involved in two projects that had an enormous impact on the future development of the company. The first project was one involving the adrenal corticosteroids. The isolation and synthesis of these steroids were a major government priority, and the project was organized as an international consortium. At the time Merck signed up to participate in the program, there was no steroid chemist on the staff. However, Professor Everett Wallis of Princeton, a Merck consultant, recommended that Merck hire one of his graduate students, Lewis Sarett (Fig. 5). Sarett had only been attending graduate school for 2 1/2 years, but under the circumstances Princeton approved his leaving with a doctorate. In January of 1942 Sarett was sent to the Mayo Clinic in Rochester, Minnesota to work with E. C. Kendall, one of the world's experts on these hormones (20). His mission was to find out how



Figure 5. Lewis Sarett (left) with Edward C. Kendall and George W. Merck (seated) in Sarett's Rahway laboratory.

Merck could be of help. By 1944, Sarett had prepared 18 mg of the first synthetic cortisone (21, 22). Sarett would go on to lead Merck's fundamental research efforts and eventually succeed Tishler as president of Merck Sharp & Dohme Research Laboratories (MSDRL).

The development group, under Tishler's direction, supplied Sarett with large batches of intermediates as he worked toward the final synthesis. They were gearing up to produce large amounts of cortisone in case it proved to be useful. It turned out not to have any war time use, but Merck process chemists eventually produced about a kilo of cortisone for testing. This was fortunate for Merck, the medical community, and the public, because, in 1948, Philip Hench at the Mayo Clinic, using Merck produced material, discovered that cortisone was an effective anti-inflammatory agent that could be used to alleviate the severe symptoms of rheumatoid arthritis. Tishler reported that Hench did not discover the value of cortisone until he had used about 100 g of Merck product (23). If Merck had made only 25 g of material, the Golden Age of Steroid Chemistry, the late 1940s and the 1950s, might have been set back several years. Hench and Kendall, along with Tadeus Reichstein, shared the 1950 Nobel Prize in Physiology or Medicine for their work on cortisone. One of the many beneficiaries of cortisone was the painter Raoul Dufy whose arthritic condition had essentially ended his

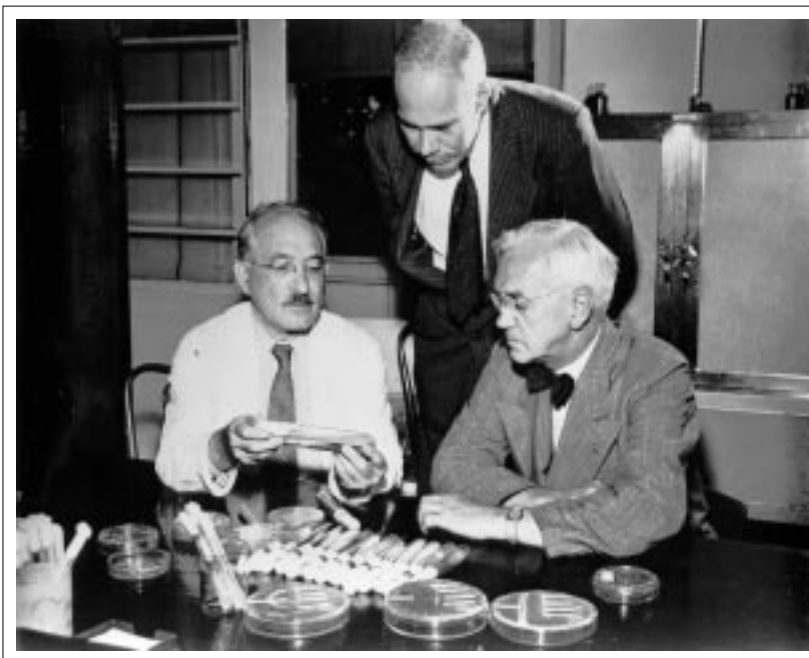
career. Cortisone restored his ability to paint, and as a gesture of gratitude he gave Merck the reproduction rights to five of his paintings. Merck was then in a position to begin manufacturing cortisone. Under Tishler's leadership the development group, starting from desoxycholic acid, reduced the number of synthetic steps from over 40 down to 26; and they improved the yields sufficiently to make synthetic cortisone economically viable (24). The Merck process was so efficient that it continued to be economically competitive even after Upjohn discovered the biological oxidation of C-11 that significantly reduced the complexity of the cortisone synthesis (25).

The other major wartime project was penicillin. Merck again volunteered to become involved in the government program even though the company had little experience in fermentation. Merck scientists initially thought they could synthesize penicillin, as opposed to isolating it from a fermentation broth, but as one Merck chemist put it, "this was not the right horse to bet on." When early attempts at the preparation of penicillin by fermentation went badly, Merck again turned to an outside consultant, Selman Waksman from Rutgers (Fig. 6). Waksman sent one of his graduate students, Boyd Woodruff, to Merck to observe and help solve the fermentation problems. The difficulties were eventually solved and Merck became a contributor of penicillin during the war. Compared to Pfizer and Squibb, Merck was not a big producer of penicillin immediately after the war, but eventually the company became one of the largest manufacturers of penicillin. Fermentation became very important for Merck and has been used for the production of a number of major Merck products, among them streptomycin, cefoxitin, ivermectin, and lovastatin.

After World War II Merck planned to build a plant at its Stonewall facility in Elkton, Virginia for the production of streptothricin, an antibiotic discovered by Waksman and Woodruff, which was effective against bacteria where penicillin failed. However, before construction began, they found that streptothricin was highly toxic. Fortunately, within a few months Waksman and his students discovered streptomycin, which exhibited the same antibacterial spectrum as streptothricin but was not toxic. Streptomycin turned out to be effective against tuberculosis; and Merck, at the request of Waksman, turned its exclusive patent rights to streptomycin over to a Rutgers foundation for licensing to all the pharmaceutical houses. This magnanimous act was partly in the interests of public health and partly in the long-term interests of Merck in maintaining productive relationships with foundation and academic research (26, 27).

In the early 1940s Karl Folkers and his group began searching for the anti-pernicious anemia factor present in liver extracts (28). The Merck group was not alone; Glaxo and Lederle were also working on the problem. The relatively small number of patients suffering from this debilitating disease could only survive by consuming large amounts of liver on a daily basis. Obviously there was something in the liver that was important, but isolating the factor seemed nearly impossible.

Although one could obtain liver extracts and divide them into fractions, the only assay available required a patient who was suffering from the disease. To find a patient and follow the effect of feeding a specific liver fraction was a slow, frustrating process. With luck and a prepared mind, Folkers located a researcher at the University of Maryland, Mary Shorb, who had discovered a simple biological



**Figure 6.** Selman W. Waksman (left), Randolph T. Major, and Alexander Fleming, the discoverer of penicillin, circa 1948. Fleming shared the 1945 Nobel Prize in Medicine with Chain and Florey for their work on penicillin. Waksman won the 1952 Nobel Prize for his work on antibiotics.



assay that responded to liver extracts. Merck microbiologists soon found Shorb's assay was specific for the anti-pernicious anemia factor, vitamin B<sub>12</sub>. At about the same time Merck researchers discovered that the streptomycin broth, the waste from the production of streptomycin, contained vitamin B<sub>12</sub>. Using this new source of B<sub>12</sub> and the new assay, B<sub>12</sub> was isolated in a short period of time, just ahead of the isolation by Glaxo and Lederle. Vitamin B<sub>12</sub> turned out to be a red compound, but the color is only discernible at high concentration. Once it is sufficiently concentrated, the color can be used as a guide in its isolation. Just months before B<sub>12</sub> was isolated, the company had decided to drop the project because too much time and too many resources had been expended in this search for the cure for a relatively minor disease. But Major and Folkers, realizing how close they were to success, quietly carried on the quest (29).

After all this effort Merck had isolated the anti-pernicious anemia factor: a scientific achievement, but hardly one to provide much income for the company. Then they discovered that B<sub>12</sub> was, in the words of Karl Folkers (30):

**the** growth factor for animals, and that meant that Merck would have a profit deluxe in contrast to a vitamin for a rare disease.

After World War II Merck rapidly expanded into a number of foreign markets, taking up some of the void left by the decimation of the European chemical and pharmaceutical houses. By the early 1950s exports constituted about 20% of Merck's sales, which had soared from \$24 million in 1940 to \$171 million in 1951 (5); but Merck was still selling chemicals in traditional industry style. It produced chemicals and pharmaceuticals and sold them in bulk to others for packaging, distribution, and sales to the consumer. Some of Merck's biggest customers, the pharmaceutical houses, were now producing their own products. If Merck were to retain a significant market share, its newest products, penicillin, streptomycin, and cortisone seemed to call for a different approach, one where a sales force would contact physicians directly (31).

Merck could not effect this change easily on its own, but a merger with Sharp and Dohme seemed to be an ideal solution for both companies. Sharp and Dohme was a Philadelphia firm with research, pharmaceutical manufacturing, packaging, and marketing skills. With no chemical manufacturing facilities of its own, however, it had, in fact, been a major Merck customer. Merck brought a world class research unit and an extensive chemical and pharmaceutical manufacturing organiza-

tion to the merger. Combining the two companies—particularly the research units—caused some pain, but resulted in a far stronger company. The merger was eased somewhat by the fact that the president of Sharp & Dohme, William Dempsey, and the chairman of its board, John Zinnser, had previously worked for Merck.

Two scientists helped enormously in the success of the merger, as far as Merck Sharp & Dohme Research Laboratories (MSDRL) was concerned. One was Max Tishler, who was appointed president of MSDRL in 1956, a post he was to hold until 1969. The other was Karl Beyer, who was employed at Sharp & Dohme in the West Point laboratories outside Philadelphia. An MD whose specialty was medical physiology and pharmacology, Beyer felt his major goal in life was to find and produce therapeutic substances. As a "biological Max Tishler" he fit beautifully into the new system. Had it not been for the merger, Beyer would have resigned from Sharp and Dohme because it had no development chemistry or chemical manufacturing facilities (32).

Within a few years of the merger, Beyer and James Sprague, a former Wisconsin student of Homer Adkins who had followed Karl Folkers to Yale and Treat Johnson's Laboratory and who was the head of Medicinal Chemistry at West Point, produced chlorothiazide (Diuril). As the first major diuretic, its sales exceeded all expectations. This was Merck's entry into the area of hypertension, and it was done with enormous success (33, 34).

In 1950, a few years before the 1953 merger, George W. Merck, who had been president of Merck from 1925, gave over the presidency to James Kerrigan. George W. Merck remained as Chairman of the Board until his death in November 1957. Kerrigan, who had worked for the senior George Merck as a teenager, eventually served George W. Merck as vice president for sales and later commercial vice president before he was appointed president. His tenure as president, from 1950 to 1955, included the merger with Sharp & Dohme and the expansion of global operations; but Kerrigan was not the person to guide Merck through all the problems of the merger. So, in 1955, John (Jack) Connor, who had been general counsel and secretary of Merck, was appointed President and CEO, positions he held until 1965 when he became Secretary of Commerce under Lyndon Johnson. Connor led Merck through the consolidation with Sharp & Dohme, the enormous expansion of international operations (MSDI) and through some serious attacks by the Federal Trade Commission and Senator Kefauver (35).

These are some of the highlights of the first 70 years of Merck in America. This was a period in which Merck & Co., enhanced by major mergers in 1927 and 1953, grew from a distributor of German chemicals, to a manufacturer of fine chemicals, to a manufacturer of pharmaceuticals with an outstanding research organization, and, finally, to a full fledged pharmaceutical company with worldwide manufacturing, research, and distribution.

### ACKNOWLEDGMENT

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- B, E, and F. Compound E turned out to be cortisone.
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### ABOUT THE AUTHOR

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## A BRIEF HISTORY OF PFIZER CENTRAL RESEARCH\*

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*Joseph G. Lombardino*

Pfizer Inc. celebrated its 150th anniversary in 1999. I will attempt to present a thumbnail sketch of the history of this company and of how it became the global pharmaceutical giant it is today. My special emphasis will be on the Central Research Division and the key role it played in the history of Pfizer Inc.

Two cousins, Charles Erhart, a confectioner, and Charles Pfizer, a chemist, were both in their mid-twenties when they came to the United States from Germany in 1849. They were the first of the innovative entrepreneurs that later came to be the standard for employees of Pfizer Inc. With \$2,500 of their own money and a \$1,000 mortgage, they set up shop in a two-story brick building on Bartlett Street in Brooklyn, New York. Initially, they sold high quality chemicals like santonin, a major treatment for intestinal worms that was a prevalent human disease in those days. Pfizer, the chemist, prepared this high-quality chemical and Erhart, the confectioner, flavored it to make it more palatable. Through their combined efforts it became a very successful product for the little company. This represented the first team effort at Pfizer—a technique that would be utilized extensively

in the coming years. Within ten years the cousins were importing chemicals like mercurials, camphor, boric acid, tartaric acid, and citric acid extracted from lemons. They provided cream of tartar, iodine, and morphine during the Civil War, and their business grew rapidly. By 1865 they achieved \$1.4 million in sales and employed 150 workers.



Charles Erhart

Through the late 1800s and early 1900s Pfizer Inc. expanded steadily but with no big spurts in growth. From 1917 to 1929 James Currie, Pfizer's first research chemist, developed a process for producing citric acid by fermentation of sugar. Currie came from the Department of Agriculture, where he was trying to produce an American brand of Roquefort cheese by fermentation. He was not successful. He then tried to ferment sugar to produce oxalic acid but again failed. However, he noticed an interesting byproduct in this fermentation: citric acid. Currie contacted Pfizer, related his finding, was hired, and, with his assistant Jasper Kane, eventually developed a large-scale fermentation process for citric acid. This process, called SUCIAC (sugar to citric

ric acid conversion), was developed in response to the short supply of citric acid because of the high cost and variable supply of lemons from abroad. The fermentation process for citric acid was never patented, but it was kept a company secret.

In 1923 Jasper Kane made a major breakthrough in the citric acid fermentation process. He found a way to use molasses as a substrate, instead of the more expensive refined sugar. By 1929, through Pfizer's use of the new process, lemons were no longer needed for making citric acid; and citric acid production at Pfizer, all via fermentation, totaled 10 million pounds, with the product taking over almost the whole market at that time.

In addition to citric acid, another major fermentation success for Pfizer involved the production of penicillin on a commercial scale. The story of Alexander Fleming and his accidental discovery of penicillin in 1927 is a familiar one. Fleming's discovery might have remained a laboratory curiosity if a practical, large-scale production method had not been found. World War II increased the urgency for producing penicillin in quantity, but large-scale penicillin production could not be developed in war ravaged England. So Pfizer, in 1941, was asked by the US and British governments to accomplish large-scale penicillin production by means of deep tank fermentation. Merck, Lederle, and Squibb were also asked to join in this effort, with all the companies required to share their findings.

Initially, Pfizer used shallow trays for the fermentation process, producing just 24 milligrams (40,000 Oxford Units) of penicillin in 1943. Then Pfizer made a risky decision to commit \$ 3 million for a deep-tank fermentation plant, which opened in a converted ice plant in March, 1944. By switching to a new penicillin mold (derived from cantaloupes) and using corn steep liquor in the broth, Pfizer scientists increased yields of penicillin from the deep-tank process dramatically.

By 1944 Pfizer was a world leader in producing penicillin by fermentation, actually supplying 90% of the penicillin to US troops who landed on D-Day, June 6, in France. For this effort Pfizer earned the "E" award for excellence in war production. By December, 1944 Pfizer was producing 125 billion Oxford Units of penicillin, with all of Pfizer's technology being shared with the other companies in the penicillin effort. Consequently, so much penicillin was produced that prices fell from 20 dollars to 20 cents per 100,000 Units. Penicillin, which saved so many lives in World War II, was not sold under a Pfizer label. Later, Pfizer produced strep-



Charles Pfizer

tomyacin from fermentation with cultures supplied by Selmen Waksman. The scaled-up process eventually produced 3200 kilograms per month of this important antibiotic.

At about this time, a soil sample screening program was established at Pfizer to search for even more potent antibiotics. This led to the discovery of a new class of antibiotics, the tetracyclines, in the Lederle laboratories in 1948. By 1950, the structures of the tetracyclines were elucidated by a Pfizer research team working with R. B. Woodward of Harvard. Meanwhile, Pfizer research uncovered PA-76, (Pfizer antibiotic, 76th sample), later named Terramycin, from soil samples. This agent was effective against 100 infectious organisms. Pfizer Inc. had total sales of \$60 million in 1950, the year this fermentation product was approved by the FDA in less than six months. Then a key decision was made. Pfizer President, John Smith, told his successor, John McKeen, (who had joined Pfizer in 1926 and later rose to become the company's Chief Executive Officer), "Let's sell Terramycin ourselves; go into the pharmaceutical business if we have to." That was a critical decision and a big risk, since Pfizer would be venturing into unknown territory and would also anger the major wholesaler customers who were previously sellers of all Pfizer products. The decision, however, was a financial success. Sales of Terramycin, the first pharmaceutical with Pfizer's name on the bottle, rose to \$45 million in just two years and accounted for 42% of company revenues. At that time, 55 Pfizer salesmen were selling the new antibiotic.

Together with Wilber Lazier, Karl Brunnings hired the 1950s group of Pfizer scientists who were the next generation of innovators for the company. A new group of chemists joined Pfizer's research team in the early 1950s, some of whom later went on to hold key positions in the company. They began their careers, as did the present author, in 1957, working in a small laboratory in Brooklyn, New York. Among these chemists was Gerald Laubach, a chemist who came from M.I.T. and headed the synthetic medicinal section of Pfizer's research. Later he was to become president of Pfizer Inc. William McLamore was a chemist from Harvard University who later became the inventor of several Pfizer drugs, including Diabinese. Robert Feeney, from Yale University, played a critical role in establishing a licensing department for obtaining products like Procardia XL from external sources. Lloyd Conover came to Pfizer from the University of Rochester. He played a critical role in the synthesis of Tetracycline and later headed up the Sandwich, U.K. research site and then Pfizer's animal health research. Rex Pinson, also from the University of Rochester, rose to become head of Medicinal Research. Barry Bloom, a chemist from M.I.T., was named President of Pfizer Central Research when it became a separate global division in 1971. Eventually he was Pfizer's Corporate Vice-President for R & D.

By 1953 the Pfizer sales force had grown to 1300, and company sales in that year had risen to \$127 million dollars. Lloyd Conover succeeded in the chemical modification of chlortetracycline to produce the antibiotic Tetracycline, which was marketed in 1954. Now, with two major antibiotics to sell, McKean opted to expand Pfizer's operations and sales into Europe, a risky decision for a small US-based company. But John McKean had the vision to see the importance of markets outside the US. In 1957 the company opened a research laboratory in Sandwich, England with 6 scientists on staff. This small laboratory has grown today to fill a very large research site in Sandwich and contributed some of Pfizer's major modern pharmaceuticals, such as Norvasc and Viagra.

In 1958 Pfizer launched Diabinese for treating diabetes; this drug was the first non-antibiotic, small molecule pharmaceutical from Pfizer. The long plasma half-life and convenient dosing regimen made this sulfonylurea a commercial success. In 1960, research operations in the US were consolidated in Groton, Connecticut. On 19 acres of land already owned by the company across the street from the fermentation manufacturing

plant, a new research facility was built in order to consolidate the various R&D departments. Having all the key scientific disciplines on one site was correctly viewed as vital to facilitating communications and thus making drug R&D more efficient.

There were other important changes occurring. At that time the synthetic organic chemistry camp was vying with the microbiologist fermentation chemists to gain control of the future direction for research. Would the Pfizer Company remain a fermentation-based company or not? Would synthetic organic chemistry produce the Pfizer drugs of the future? The outcome of these questions would not be settled for several years.

In 1960 John McKean set the seemingly impossible goal of \$500 million in sales by 1965 ("5X5"). As an employee, I remember how wildly impossible this goal seemed, but it was achieved. That same year, Pfizer headquarters moved from Brooklyn to a new skyscraper in midtown Manhattan at 42nd Street and 2nd Avenue.

Under the leadership of Gerald Laubach, Vice-President for Medicinal Products, a revamped research organization became more productive through systematic, well-planned, and scientifically managed R&D procedures. The organization adopted a philosophy of mission oriented research. Laubach required specific goals for the science being done, and he emphasized the rationally designed organic chemical as a source for future medicines. This move also coincided with the beginning of the first move to utilize informal multidisciplinary teams assigned to specific projects. Over time, synthesis of small organic chemicals as potential drugs became the accepted philosophy for research, and fermentation-based research decreased significantly.

In the decade of the 1960s, the Kefauver-Harris Amendments dramatically increased the cost, time, and difficulty of developing new pharmaceuticals. Pfizer Inc., concerned about its future as a pharmaceutical company, responded by diversifying into almost 30 nonpharmaceutical businesses. These included buying Barbasol shave cream, Desitin ointment for diaper rash, Pacquin hand cream and Coty cosmetics. Pharmaceutical research was continuing at Pfizer, however, with some successes during that period. Products developed during the 1960s and 1970s included Renese, a diuretic, the Sabin polio oral vaccine, which Pfizer produced on a commercial scale, Vibramycin, an antibiotic, Navane, an antipsychotic, and Sinequan, for depression.

In 1971 Central Research was formed as a separate, worldwide organization with centralized management out of Groton, Connecticut. This reorganization further improved the efficiency of Pfizer's R&D, although the R&D budget was still quite small compared to that of competitors, only about 5% of corporate sales. Groton was a small site with only a few chemists, biologists, metabolism chemists, and clinicians among the few hundred employees, a laboratory for bulk chemical materials, and a library. Barry Bloom was chosen to head the centralized management of Pfizer Research worldwide, while Sandwich was reorganized under the leadership of Lloyd Conover. New research management in Groton set focused goals, coordinated all projects, and held regular reviews of the growing R&D portfolio by a single group of research managers. The company experienced significant growth in sales in the 1970s from under \$1 billion to almost \$3 billion, but with almost flat R&D budgets and staffing. There was still concern among some Pfizer Corporate leaders about the wisdom of becoming mainly a pharmaceutical company and about investing too heavily in R&D. There were also some disappointments within R&D, such as failure of potential major products at late stages of development. These included Tolamolol, an antihypertensive, and Tibric Acid, a cholesterol-lowering agent. A successful antihypertensive agent, Minipress (Prazosin), was launched in 1976, however. Despite these relatively lean years of research productivity, Jack Powers, Chief Executive Officer from 1965 to 1972, strongly supported investing in R&D, even when corporate funds were limited. He recognized that Pfizer needed to support research as an investment for the future. Powers retired in 1972, appointing Gerald Laubach as President and Edward Pratt as Chief Executive Officer and Chairman of Pfizer Inc.

Pfizer's major product in the 1980s was Feldene, a drug for arthritis. The company's entry into arthritis research began in the 1960s with a team of two individuals, Ted Wiseman and the present author. Before success was achieved, a five-year research project was needed to identify an appropriate drug candidate, and then more than a decade to do extensive clinical trials and to select the best of the newly discovered oxicams and to secure its approval. The length of this project derived mainly from our determination not to follow the existing structural leads, then mainly carboxylic acids. Our goals raised the hurdles for the project, but in the end afforded a superior product from a medical and commercial point of view. The Feldene project was started

in 1962 and concluded in 1982 with the US launch of the product—a 20-year period, about half the span of my career. It is not unusual for a project to require this length of time. For example, the project to produce Diflucan, a major antifungal agent from Pfizer, also took 20 years from the start in 1970 to the launch in 1990. Feldene became Pfizer's largest selling drug product at the time, with peak annual sales of up to \$700 million by the late 1980s. This contributed significantly to corporate sales which more than doubled from \$2.5 to \$5.7 billion. The success of Feldene apparently convinced Pfizer's leaders that pharmaceutical research had a future and could lead to very successful commercial products.

Ed Pratt, Chief Executive Officer from 1972 to 1992, was a strong supporter of R&D during this period. He recognized the need to raise the R&D budget from the \$50-million level (5% of sales) when he became CEO in 1972 to the 15-20% of sales needed to make the research organization a strong force and to build for the future. This daring investment in the 1970s transformed Central Research and laid the groundwork for Pfizer to become a productive research organization in the 1980s and 1990s. Feldene's clinical studies, the Zithromax project, and the Norvasc and Diflucan projects had their origins in the 1970s. Increasing R&D investment was a risky decision at a time when the pharmaceutical industry was under great pressure from the regulators. Eventually, Pratt spent a total of \$6 billion on Pfizer's R&D during his tenure. As company annual revenues grew from over \$1 billion in the 1970s to \$7 billion in the 1990s, R&D funding increased from \$8 million in 1971 to \$179 million in 1981 and then to \$757 million in 1991.

The growth of Central Research at all its worldwide sites created its own set of challenges, since increasing size brought increasing managerial problems. How does one manage such a large complex worldwide organization? Communications became more challenging; keeping the larger organization focused on the major goals became a problem. One solution involved formation of a senior management committee, the brain child of Walter Moreland and John Niblack, with the support of Barry Bloom. In this system both discovery and development are highly focused, goal-oriented, and managed by teams of scientists who report to a small group of senior managers. In the discovery phase, each research project has an operating plan with clearly defined goals, timelines, and milestones. The plan for the project is endorsed by management and reviewed regu-

larly. The latest technology is employed in order to make discovery efforts as efficient as possible. In the drug development phase, a similar group of senior managers from key departments regularly reviews the status, plans, and problems of each of the development projects. This management group hears the recommendations of the project teams and then makes the decisions on large expenditures, project terminations, and prioritization of projects.

In 1986 the present author helped to organize a project management group in Central Research and to establish the matrix team system. This was not an easy change in Pfizer's culture, but eventually the team environment for developing drugs gained acceptance. The Early Candidate Management Teams (ECMTs), led by scientists, manage a drug development project up to the start of Phase 3 clinical trials. The teams are made up of about 8 members from the key technical disciplines involved in the development project. These teams generate the pre-IND data and carry out Phases 1 and 2 in the clinic. Later, cross-divisional Global Development Teams (GDTs) plan and govern Phase 3 trials needed for NDA filing.

The productivity of Pfizer's own research and its licensing efforts increased dramatically in the 1980s and 1990s. Modern products launched by Pfizer in this period include: Feldene, an antiarthritic; Procardia XL, an antihypertensive; Unasyn, an injectable antibiotic; Zoloft, an antidepressant; Zithromax, an antibiotic; Zyrtec, for treating allergies; Norvasc, an antihyperten-

sive; Diflucan, an antifungal agent; Lipitor, a cholesterol-lowering agent; Aricept, a drug for Alzheimer's Disease; Trovan, an antibiotic; Viagra, for erectile dysfunction; and Celebrex for arthritis. During this same period two major potential agents failed in the development stage: Sorbinil was lost in Phase 3 because of a rash problem, and tenidap was withdrawn after filing because of a perceived effect on bone density. Such is the risky nature of pharmaceutical research. Tens of thousands of compounds are synthesized, and millions of tests are run annually, ultimately to bring 12 to 18 compounds into development, from which one product per year is likely to reach the marketplace.

Today the current leaders of Pfizer's R&D are George Milne as Central Research President and John Niblack as Vice-Chairman, Pfizer Inc. They are setting a new direction for Pfizer in the modern age of pharmaceutical research that will carry the firm into the 21st century. Major expansions are underway at Pfizer research sites worldwide. A total of more than one million square feet of R&D laboratory space is being added to these global research sites. Under the current Chief Executive Officer, William Steere, R&D annual investment has grown to over \$2 billion.

The corporation has sold the divisions that no longer fit into the core health care businesses: for example, the minerals operation, the Coty cosmetics business, and the Food Science group.

So the corporation has expanded dramatically in almost five decades. As the R&D budget has grown to over \$2 billion, the R&D staff has increased to over 6,000 people worldwide. The acceleration in growth of the staff and in funding for R&D during the 1980s was made



Pfizer's 42nd Street, NYC, World Headquarters Building



possible by Feldene sales. Later, sales of other successful products permitted even faster growth in R&D in the 1990s. As a result of past R&D successes, Pfizer currently has strong corporate sales from major, important pharmaceuticals that will be under patent until beyond 2004-2006. In addition, a strong pipeline of future new products at various stages of development and significant growth in R&D, both in facilities and people, combine to make Pfizer Central Research a major force and a critical factor in the future success of the company. The innovative, entrepreneurial spirit initiated by the team of two cousins in 1849 has led to a giant organization with almost 50,000 individuals working in teams on five continents, a company where innovation and entrepreneurship are the lifeblood for the future.

The author's view of all this, from over 40 years of observing the growth of Pfizer Central Research and the parent company, Pfizer Inc., is that the success is due to the efforts of thousands of dedicated employees led by a relatively few visionary leaders. Their combined efforts brought us to where we are today and will lead us into a bright future.

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## ABOUT THE AUTHOR

Joseph G. Lombardino, 13 Laurel Hill Drive, Niantic, CT 06357/USA, is a graduate of Brooklyn College and earned the Ph.D. in organic chemistry from the Polytechnic University of New York. In 1957 he joined Pfizer as a medicinal chemist; for 29 years he conducted laboratory research, leading to 64 publications and 56 US patents. Later, he formed and headed the Department of Development Planning at Pfizer Central Research. He retired in 1999, after 41 years of service.

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## THE METAMORPHOSIS OF SMITH-KLINE & FRENCH LABORATORIES TO SMITH KLINE BEECHAM: 1925-1998\*

*Glenn E. Ulllyot, Barbara Hodsdon Ulllyot, and Leo B. Slater*

The history of SmithKline Beecham is a wonderful example of the American success story: humble beginnings; hard work; a good reputation; growth; mergers; modest success; disappointments; breakthroughs; and ultimately, great success! But its previous successes have not made this company complacent, for today it is also an excellent model of an evolving, global pharmaceutical company.

This paper will cover many aspects of SmithKline, but the focus will be on the development of four products: “Benzedrine,” “Thorazine” (chlorpromazine), “Dyazide” (a combination of triamterene and hydrochlorothiazide), and “Tagamet” (cimetidine). These successes demonstrate the importance of research, as well as of marketing, but they also underline the importance of good people who are dedicated to their work and to the betterment of society. This story of a business is fundamentally a human story.

### In the Beginning

Although the Research Division was established in 1925, we must begin our story in 1830, when John K. Smith

founded a small apothecary shop on North Second Street in Philadelphia. His brother, George, joined him in 1841, and they formed John K. Smith & Co. The business grew and soon had a reputation for fine, pure products and became a leading drug wholesaler. Four years later, when John Smith died, George continued to build the company’s reputation. He was known for catering to the exact requirements of physicians, and for using methods that were quite advanced for his time. George took orders from as far away as central Pennsylvania and New Jersey. It was not unusual for other dealers to make semi-annual visits to his store to

place orders that would last for six months. By 1855, George Smith had not only expanded his store but had opened a second shop at 149 North Third Street.



Employees at the Cherry Street laboratory of Smith, Kline & Company in Philadelphia. Although the company was founded as a wholesale-retail business, in the 1880s it founded a small manufacturing laboratory to produce a few staple products. *Photo courtesy SmithKline Beecham.*

In 1865, Mahlon N. Kline, an ambitious young bookkeeper, joined the business. Together they continued to emphasize the purity of their manufactured products, with guaranteed quality. Kline soon sought a greater challenge and moved into sales, where he gained many new accounts. He also began to attend the Philadelphia College of Pharmacy, so that he would understand more of the business. A decade later he became a partner, and the company was renamed Smith, Kline & Company.

French Richards & Co., another well-established Philadelphia wholesaler, was absorbed by Smith, Kline & Co. in 1891, and the new company was named Smith, Kline and French. In due course, SK&F became Philadelphia's leading drug house, with hundreds of products—from tonics to medicines and liniments to perfumes. Furthermore, SK&F had established a pharmaceutical laboratory, where "Eskay's Neurophosphates" were developed, products which helped to facilitate the company's rapid growth. In 1893, SK&F instituted even stricter standards of quality and purity for its growing group of products, emphasizing its concern for providing exceptional quality to its customers. By the end of the nineteenth century, SK&F had expanded not only to a six-story building on Arch Street, but also into two adjoining buildings.

### A Focus on R&D

An important turning point came in 1925, when the Research Division of SK&F was established with the hiring of Dr. Fred P. Nabenhauer, an organic chemist. (He was the second person hired to conduct research, ultimately retiring in 1955. The first chemist, Dr. William L. Long, left the company to attend medical school, but later returned to serve for many years as Director of the Research and Development Division. He was one of the guiding lights in the advancement of research at SK&F.) Thus began the company's focus on research and development. In 1926 the first product from organic chemical research was "Oxo-ate B" (calcium *o*-iodoxybenzoate), designed to relieve swelling and muscle spasms in arthritis and rheumatism. This was followed in 1929 by "Benzedrine," an amphetamine designed to alleviate the symptoms of nasal congestion, hay fever, colds, and other upper respiratory conditions.

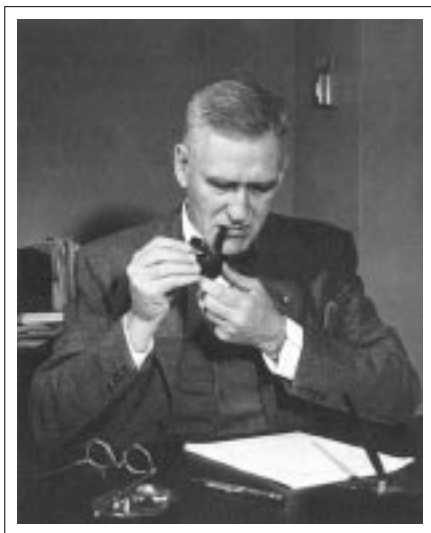
SK&F, led by Dr. Nabenhauer and later joined by Dr. George Connit, was conducting research on amphetamines at the same time as a California chemist, Dr. Gordon A. Alles. Dr. Alles believed that amphetamines

would make a good synthetic substitute for ephedrine, which had previously been used to treat asthma and nasal congestion. Based on his own experiments, Dr. Nabenhauer independently recommended amphetamines for the relief of nasal congestion. When SK&F became aware of Dr. Alles' research, they proposed a cooperative alliance for its development. By 1932, "Benzedrine" had become SK&F's first really big product. Much of the money made from "Benzedrine" was returned directly into research, and the company began to expand. Shortly thereafter, in 1934, Dr. Rudolph H. Blythe, a pharmacist, arrived on the scene to organize the Pharmaceutical Research Section, which he directed until his retirement in 1966.

Glenn E. Ullyot was the third chemist to be hired, in 1937, joining some 225 fellow employees at an ill-equipped building (formerly an abattoir during the Civil War) at Delaware Avenue and Poplar Streets. Two very significant additions to the scientific team in the late 1930s were Dr. Edward J. Fellows, a pharmacologist, and Dr. Arthur E. Heming, a biochemist. They, together with Dr. Ullyot, were named Associate Directors of R&D in 1957. (When Ullyot retired in 1975, there were almost 13,000 employees.) In 1943 organic chemistry became one of a number of scientific sections in the rapidly mushrooming laboratory groups under the direction of Dr. Walter Kerr, a biochemist. By 1950, the organic staff, under the direction of Dr. Ullyot, numbered eighteen persons, including the following Ph.D.s: Paul N. Craig, James F. Kerwin, James W. Wilson III, and Charles L. Zirkle. These chemists, subsequently joined by Andrew Anderson, and Drs. Bryce Douglas, Bernard Loev, Irwin Pachter, Robert F. Raffauf, Blaine Sutton, and Joseph Weinstock, formed the nucleus of an ever-expanding research team.

While SK&F was conducting its research on amphetamines, it was discovered that they exert a significant effect on the central nervous system. In 1939, SK&F began to investigate potential modifications of amphetamines and found one that was twice as effective as "Benzedrine." Researchers started to explore possible medical applications; the result was "Dexedrine," brought out in 1944 and marketed as a mood lifter and appetite suppressor. It soon found other applications, however, including use as a treatment for narcolepsy and for the reduction of post-surgical effects of anesthesia.

After World War II, SK&F continued to grow, and the company recognized the need for better facilities. In 1948 construction began on a big, yellow brick build-



Francis Boyer. As Executive Vice-President of the company, in the early 1950s he helped to negotiate the deal with Rhône-Poulenc that enabled SK&F to license chlorpromazine. *Photo courtesy SmithKline Beecham.*

ing at 1530 Spring Garden Street. This was the former site of the Baldwin Locomotive Works and, before that, of Bush Hill, said to have been the home of Alexander Hamilton. (Today this building is used primarily as a manufacturing facility.)

The development of Spansules was the next big success in the parade of products at SK&F. Beginning in 1945, Dr. Harold A. Clymer began looking for a time-release mechanism. In 1949 the group leader, Dr. Donald R. MacDonnell, while shopping in a supermarket, happened to note a container of nonpareils, little chocolate discs covered with a pebbling of white granules. Why not fill capsules with granules coated with medication that would dissolve at different intervals? This device enabled the medication to release the required initial dose rapidly, and then to release gradually very small doses to maintain a therapeutic level for ten to twelve hours. The "Spansule" sustained release capsule, the result of seven years of research and over 35,000 man-hours, was first used for "Dexedrine" in 1952. It became most famous eight years later, however, as the "tiny time pills" in " Contac," the first all-day cold remedy and the company's best-selling cold medicine.

### The First Major Breakthrough

As a result of focused research on a substance with infinite possibilities, a new and exciting chapter in SK&F

history opened. The success demonstrated the skills and foresight of Francis Boyer, then Executive Vice-President of the company, who was bilingual in the French language, and Dr. Wesler Scull. Boyer and Scull went to France to investigate the licensing of a new drug known as chlorpromazine. It was a mysterious compound, with many properties. The French thought of it as a "potentiator," a substance which prolonged the action of other drugs. Although two other American drug companies had turned down this compound, SK&F researchers, led by Dr. J. Kapp Clark, later Director of Research and Development, wanted to study it. They confirmed the laboratory pharmacology reported by the French and in SK&F clinical tests it was shown that the drug was indeed effective. So, Boyer continued talks (in French!) with Rhône-Poulenc; in 1952, SK&F was offered the opportunity to license chlorpromazine. Although chlorpromazine was found to possess several possible medical applications, Dr. Scull, then Director of Development Research, felt that the most important application was its astonishing calming effect on violent mental patients. The drug actually rescued patients from their psychotic states and restored them to lucidity. Boyer and SK&F agreed to pursue the use of chlorpromazine in mental illness, and in 1954 "Thorazine" was approved by the FDA for use in nausea and vomiting, and in neuropsychiatry. Though Freudian psychiatrists initially resisted the idea of using chemical treatment, "Thorazine" and its sister drugs "Compazine," acquired from the same French company, and "Stelazine," were quickly developed as useful drugs and were widely adopted in mental hospitals. The last mentioned drug was prepared in a classical extension of developing on a "lead" compound in Dr. Ulliyot's Medicinal Chemistry Section, notably by Dr. Craig.

From the historical standpoint, chlorpromazine and the alkaloid reserpine are the two substances which encouraged a chemotherapeutic approach to mental illness. Dr. Ulliyot and Dr. Maxwell Gordon noted in their 1968 article in the *Kirk-Othmer Encyclopedia of Chemical Technology* (1):

...electroshock, insulin shock, prefrontal lobotomy, etc, were thought to be the answer when they were first introduced. But the relative undesirability of these treatments can be judged by the fact that in some hospitals today they are virtually no longer employed as routine measures in psychotherapy... In modern institutions today there is a marked absence of the restraining devices, cold packs, noise, agitation, and confusion that have always characterized the mental disease wards.

Thus, treating mental illness with drugs proved to be a far more humane method than electroshock therapy or prefrontal lobotomy. The result was a dramatic, widespread release of mental patients from state institutions. In the US the resident mental patient population dropped 4.8% between 1965 and 1966, and 19% between 1955 and 1966 (1).

### The Next Big Development

The next big development was in the field of diuretics, one which SmithKline entered in 1955. The goal was a safe, effective, orally active diuretic. After years of testing many compounds for diuretic activity by a team including Dr. Joseph Weinstock and led by Dr. Ulylyot, the FDA approved "Dyrenium" in 1964, almost three years after the government evaluation began. Soon after SK&F's entrance into the field of diuretics, Dr. David Wheatley noticed an article in the *British Medical Journal* which indicated that the same substance that gave color to butterfly wings also caused hyperplasia, enlargement of the kidney (2). Dr. Virgil Wiebelhaus, who joined the diuretic group in 1956, began to investigate this substance, a pteridine compound. For almost a decade, SK&F scientists tested various pteridine compounds. None was completely successful, however, until triamterene. The diuretic team had endured several years of research and two clinical failures, but its members were confident they were on the right course with pteridines. In 1958, preliminary tests on triamterene indicated that it had good diuretic properties, and by 1960, clinical trials had been initiated. Dyrenium was compounded with hydrochlorothiazide (HCTZ) to make "Dyazide." HCTZ, a member of the group known as thiazides, was then in use as a diuretic, but it had the potentially harmful property of depleting potassium from the human body. The new dual compound, however, overcame this problem.

Although SK&F's marketing staff was less than enthusiastic, "Dyazide" did extremely well; along with "Contac" it carried the company through some lean times in the late 1960s and the early 1970s, when the "Thorazine" patent expired and the price fell. In fact, during this period there were no new breakthrough drugs in the development stage, and the company was forced reluctantly to discharge 200 employees in 1969. There had been a discouraging venture into the unfamiliar field of cosmetics, aimed at the teen market under the brand name of "Love," and suntan products, "Sea & Ski."

### The Tagamet Story

Of the four primary products discussed in this paper, "Tagamet" became by far the most profitable. However, it has been said that, without the income from "Dyazide," there would have been no funds to support the research that led to "Tagamet." Developed in the mid-1970s by a team of British scientists including Dr. James Black, Dr. William A. M. Duncan, Dr. C. J. Durant, Dr. C. Robin Ganellin, and Dr. E. M. Parsons, all working at SK&F's laboratory at Welwyn Garden City, England, "Tagamet," also known as cimetidine, is a histamine blocker, an H<sub>2</sub>-receptor antagonist, which was designed to treat peptic ulcers and other gastrointestinal disorders. When he joined SK&F in 1969, Dr. Black already held a theory concerning histamines. He knew that they encouraged gastric acid production in stomach cells and believed that, through application of his previous work on beta-blockers, it would be possible to inhibit this production. His predictions proved correct; by pursuing this avenue of research, Dr. Black and his team were able to develop a receptor-specific antagonist for histamines. The histamine research was slow: in the first four years of work, Dr. Black's team synthesized over 200 compounds, with no success. In the meantime, SK&F was discharging employees. The directors in Philadelphia were considering shutting down the program but ultimately decided to give the British researchers a little more time. The British team did not disappoint Philadelphia! It soon identified a possible active compound. Although the first few efforts resulted in antagonists which were either too weak or too toxic, the third attempt was a success, and "Tagamet," the world's first H<sub>2</sub>-receptor antagonist, came into being (3). Introduced in Great Britain in 1976, it was released in the United States less than a year later. Almost immediately "Tagamet" became an extremely popular method of treating ulcers, not because it was more effective than other traditional antacids, but because when it was taken daily, it helped to prevent the recurrence of ulcers. Sir James Black received the Nobel Prize in Medicine in 1988 for his work on beta-blockers and H<sub>2</sub> blockers.

It should be noted that on November 24, 1997 in Harlow, UK and again on February 27, 1998 in King of Prussia, Pennsylvania, the discovery of histamine H<sub>2</sub>-receptor antagonists was designated as an International Historic Chemical Landmark, conferred jointly by The Royal Society of Chemistry and the American Chemical Society.

## The Continued Growth of SK&F

In 1973, the firm's name was changed to SmithKline Corporation and SmithKline & French Laboratories—carrying on the name so familiar for 82 years—was retained for the pharmaceutical division. The company was well positioned for expansion and growth. By 1982 a



Anti-infectives facility in Upper Merion, Pennsylvania.  
Photo courtesy SmithKline Beecham.

new \$48 million headquarters had been built in Philadelphia's Franklin Plaza and later, a large, modern research facility in King of Prussia, Upper Merion, a suburb of Philadelphia. The firm had also acquired Allergan, an eye and skin care business, and Beckman Instruments, a California-based company which specialized in diagnostic and measurement instruments. As a result, the company became known as SmithKline Beckman, a name it retained for almost a decade. Allergan and Beckman Instruments were spun off in 1989 when SmithKline Beckman merged with Britain's Beecham Group, forming today's SmithKline Beecham. This merger resulted in a company that is one of the world's largest research and development organizations, with annual sales of over 12 billion dollars. Today, SmithKline Beecham is recognized for its cutting-edge scientific research and its many successful product developments. Much of this success has been due to good management and excellent marketing. However, it is fundamentally the talented and hardworking individuals, the scientists dedicated to basic research, who have enabled SmithKline Beecham to become the company which today is known and respected around the world.

## ACKNOWLEDGMENT

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## ABOUT THE AUTHORS

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### FUTURE ACS MEETINGS

Spring 2000 — San Francisco, CA

Fall 2000 — Washington, DC

Spring 2001 — San Diego, CA

Fall 2001 — Chicago, IL

Spring, 2002—Orlando, FL

Fall, 2002—Boston, MA

Spring, 2003—New Orleans, LA

Fall, 2003—New York, NY

Spring, 2004—Anaheim, CA

Fall, 2004—Philadelphia, Pa

Spring, 2005—San Diego, CA

Fall, 2005—Washington, DC

Spring, 2006—Atlanta, GA

Fall, 2006—San Francisco, CA

Spring, 2007—Chicago, IL

Fall, 2007—Boston, MA

Spring, 2008—San Antonio, TX

Fall, 2008—Philadelphia, PA

Spring, 2009—Salt Lake City, UT

Fall, 2009—Washington, DC

Spring, 2010—San Francisco, CA

Fall, 2010—New York, NY

## THE LIFE CYCLE OF STERLING DRUG, INC.\*

*Joseph C. Collins and John R. Gwilt*

The foundations of Sterling Drug were laid by William E. Weiss and Albert H. Diebold, boyhood friends in Canton, Ohio. Weiss graduated from the Philadelphia College of Pharmacy in 1896 and went to work in a drug store in Sistersville, West Virginia. Diebold raised funding from his father's company, Diebold Safe and Lock, and in 1901 the friends set up business together in Wheeling, WV. In fact, Sterling operated a plant in that town until 1962.

The history of the Corporation can conveniently be divided into five periods:

- 1901-1917 The Neuralgyline Period
- 1917-1928 Sterling Products I
- 1928-1933 Drug Inc.
- 1933-1942 Sterling Products II
- 1942-1988 Sterling Drug, Inc.

### The Neuralgyline Period

On May 4, 1901, Weiss and Diebold, with three local business men as partners, established the Neuralgyline Company with the sole purpose of manufacturing and selling a pain-relieving preparation which they called "Neuralgine." There is now no company record of its composition, but it seems to have been a mixture of acetanilide, caffeine, and sodium salicylate. Total sales in 1901 were \$10,000. During 1902 that entire amount was invested in advertising, partly in the Pittsburgh newspapers and partly on signs nailed to trees and posts. This generated sales of \$60,000 in 1902 and set a pattern for the future. Over the next few years, the other

partners were bought out. Weiss and Diebold realized that expansion required more product lines and that these would best be obtained by acquisition. This policy continued throughout the life of the organization, at least 130 companies being acquired, directly or indirectly,



*Figure 1.* Where it all began: in 1901 the Neuralgyline Company occupied two upstairs rooms in this house in Wheeling, WV.

from 1902 through 1986. Ironically, the eventual fate of Sterling Drug was its acquisition by Eastman Kodak in 1988.

Purchase of the Knowlton Danderine Company in 1906 brought the first major brand. The name "Sterling" came with the acquisition of the Sterling Remedy



Company of Attica, Indiana. It had been founded by H. L. Kramer to market “No-To-Bac,” a product designed to help people stop smoking. The formula, however, was strongly constipating, so Kramer developed a product containing cascara, which he named “Cascarets;” this was much the more successful product. Another laxative product, but based on senna, came with the California Fig Syrup Company in 1912. The corporation also diversified into advertising via Thompson-Koch (still Sterling’s in-house agency through 1985) and other agencies. In 1913, Weiss and Diebold, recognizing the need for improved financial organization, set up Synthetic Patents. This division held intangible assets (trademarks, etc.) and tangible assets (offices and plants) separately from the trading activities. Then in 1914, with World War I looming, they set up Proprietary Agencies as an overseas trading company.

### Sterling Products I

By 1917, Neuralgine was no longer a major product, and the company name—Neuralgyline—was difficult to say and remember. Weiss and Diebold reviewed the trading names available and switched to Sterling Products. Because supplies of drugs from Germany had been cut off by the Allied blockade, they set up the Winthrop Company to manufacture the active ingredients. After the entry of the US into World War I on April 6, 1917, the Custodian of Enemy Property began seizing the assets of German companies. Those of Bayer were taken over on January 10, 1918; and on December 12, 1918 they were offered for auction at the Bayer plant in Rensselaer, NY. Weiss, the successful bidder, acquired Bayer for \$5.3 million. He sold the dyestuffs division of the business to Grasselli for \$1.5 million; this passed successively to GAF (General Aniline and Film) and then in 1984 to BASF.

### Sterling’s Long-term Relationship with Bayer

The Bayer Company had been established in Germany in 1863 by Friedrich Bayer, a dyestuffs merchant, and

Johann Weskott, a cotton dyer. Carl Duisberg was hired as a research chemist in 1884 and sought a use for surplus *p*-nitrophenol. This led to the introduction of acetophenetidine under the trade name Phenacetin. All Bayer’s requirements in the US were imported from Germany, but US customs duties were so onerous that competitors smuggled in supplies from other sources through Canada and Mexico and thus dominated the market.



Figure 2. The first product: Neuralgine.

Acetylsalicylic acid was first marketed in 1899 in Germany under the trademark Aspirin. Prompted by its loss of sole rights to phenacetin, Bayer attempted to patent aspirin and to protect the trademark wherever possible. It had been a policy of German industry to protect its monopolies by not manufacturing outside Germany. However a new US tariff law made it necessary to manufacture dyestuffs and pharmaceuticals within the country, so in 1903 Duisberg visited the US to review manufacturing opportunities. As far back as 1881, Bayer had purchased 25% of the Hudson River Aniline and Color works at Riverside Avenue, Rensselaer, New York. Duisberg decided to acquire the outstanding equity and to remodel this plant. He also bought the American Color and Chemical facility on Rensselaer Island and moved its equipment to Riverside Avenue. In the US, Bayer continued to defend its monopoly of aspirin by threatening lawsuits against anyone, especially pharmacies, selling material from other sources. When the patent expired in February 1917, the trademark was reduced to generic status by the concerted efforts of other suppliers, notably Lehn & Fink (which, paradoxically, was acquired by Sterling in 1966) and by United Drug (which associated with Sterling in 1928 to form Drug Inc.).

Bayer had promoted aspirin as an ethical medicine, sold only through pharmacies. Sterling now positioned it with their patent medicines and increased sales dramatically in the US (and in Canada where “Bayer Aspirin” attained trademark status) over the next six decades. By contrast, Bayer Aspirin was sold by Sterling as an ethical medicine in the UK, Australia, and some other markets; sales dwindled and the product had generally disappeared from those markets by the 1960s. Bayer attempted to recover its name and the Bayer Cross trademark in various markets over the years. In 1970, Ster-

ling surrendered them in territories other than the US, Canada, Jamaica, and Trinidad for a consideration of \$2.8 million. In 1986, with the agreement of Sterling, the Rhinechem Corporation (a US holding company) was renamed Bayer USA Inc. Finally, when Sterling was broken up in 1994, Bayer USA was able to buy back the Bayer Aspirin business.

Sterling continued with pharmaceutical acquisitions, such as Phillips Milk of Magnesia in 1923. The first entry into a specialized dental business came in 1927 with acquisition of Cook Laboratories, manufacturers of dental syringes, and this was complemented in 1928 by the Antidolor Company, which produced dental anesthetics and other adjuncts. Sterling Products now took a surprising change of direction.

### Drug Inc.

In 1900, Louis Kroh Liggett established a medicines distribution business in Boston, Mass., and found that many drug stores were compounding their own proprietary

nonmedicinal products, e.g., stationery (Marcus Ward), rubber goods (seamless rubber), dressings (absorbent cotton). Because promotional costs were low, Rexall products were priced very competitively and by 1930 there were about 10,000 Rexall agencies in North America. On the death or retirement of the owners, Liggett purchased outlets and operated them under his own name. He also acquired the Owl Drug chain in the western US and the May chain of Pittsburgh. By 1930 he controlled 706 stores in North America. His only overseas venture had been to acquire the Boots Pure Drug Company in the UK in 1920. Boots then had some 860 retail stores and they too made their own-brand products that sold at a low mark up. Later they also manufactured products for Sterling Drug and for Upjohn and for Vick; this had become necessary because of high UK import duties on finished medicines.

Two ideas men—George M. Gales of United Drug and Al Diebold of Sterling Products—were good friends and seem to have been responsible for the concept of an association of the two companies. Each company was



*Figure 3.* The Bayer plant at Rensselaer, NY, purchased by Weiss in 1918.

preparations. He persuaded forty of them to subscribe \$4,000 each to set up a central manufacturing facility in the Back Bay area. The original druggists formed a loose association as the “Rexall” agents (“Rexall” meaning “king of all”). With expansion of the business a more formal structure was required, and the United Drug Company was established in 1916. Other manufacturing companies were acquired, mostly to supply

making about \$7 million annual profit. Sterling spent heavily on advertising and marketing; United Drug controlled about 20% of the estimated 60,000 drugstores in North America. Sterling’s products would of course not become exclusive to United Drug outlets, but the Liggett stores and the Rexall agents would receive special terms; in return, they would give better displays and run promotions. United Drug and Sterling Products were there-

fore consolidated on March 2, 1928 into a new holding company, Drug Incorporated. It was a colossal outfit for its time, with about 37,000 employees. In 1930, not a year noted for prosperity, the sales of Drug Inc. were over \$160 million; and its net income was about \$21 million (at 1999 values, these figures would be \$1.5 billion and \$196 million, respectively). But the strength of the new organization lay in the fact that the original components continued to act independently. Indeed Sterling continued to acquire companies, such as Life Savers, Bristol-Myers, and Vick.

There was no regulatory or other legal opposition to the formation of Drug Inc., nor any legal pressures to break it up. The difficult issue was the question as to how the profits should be shared. United Drug had assumed a heavy debt burden, particularly with the acquisition of the Owl Drug chain where Liggett was buying sales volume rather than earnings. In 1932, Sterling's profitability was about 30% of sales, as compared to United's 5%. Eventually there was agreement on a Plan of Reorganization, dated August 7, 1933. For every ten shares in Drug Inc., a stockholder received five in Sterling Products, four in United Drug, two in Vick, two in Bristol-Myers, and one in Life Savers; and the business was partitioned along those lines. Drug Inc. existed for just five years and five months. It traded while the economy sank into the depths of the depression. Yet its sales and profits continued to grow and it broke up smoothly with little impact upon individuals.

## Sterling Products II

The pace of acquisitions increased. The dental business was strengthened by the addition of R.L. Watkins (Dr. Lyons' Tooth Powder) and Delatone. The American Ferment Company brought a range of products based on papain. Creamalin antacid came with the Cleveland Chemical Company. Other major acquisitions included the Ironised Yeast range, and the pHisoDerm products (Fairchild Brothers and Foster) which later led to pHisoHex, a major surgical scrub.

Up to this time, overseas business had not been a major preoccupation. The Proprietary Agencies division exported packed stock. Phillips Milk of Magnesia was manufactured by Boots in the UK, and California Syrup of Figs was made by Parke-Davis in the UK, South Africa, and Australia; but these arrangements were made to avoid excessive import duties on packed stock. The first big move towards foreign business came with the acquisition in 1938 of the Sydney Ross Company of

Newark, New Jersey, which had several plants in Latin America. This put Sterling in a strong position to fill the void left by the interruption of supplies from Europe (and especially from IG Farbenindustrie) to those markets during and following World War II. Marketing was supported by the formation of International Advertising Services in 1941.

During the period 1920 through 1926 Sterling had entered into a series of agreements with IG Farbenindustrie of Germany, with the general awareness of the authorities in Washington. However, under the trading conditions arising from the outbreak of World War II in Europe, these agreements were declared to be in breach of the anti-trust laws, and in December 1941 Weiss and Diebold had to resign. Weiss, returning to Wheeling, WV, died in an automobile accident in September 1942. Diebold retired to Palm Beach, FL, and died in 1964; his official obituary refers to him as the founder of American Home Products and of the Neuralgyline Company; there is no reference to Sterling.

## Sterling Drug, Inc.

Edward S. Hills, a semi-retired lawyer whose firm had represented Sterling in trade mark negotiations, was named the new chairman of Sterling; but the effective operating officer was the former treasurer, James Hill, Jr., who kept Sterling on course. Because of possible confusion with other companies' names, Sterling Products could not be licensed to carry on business in certain states and so on October 15, 1942 the company name was changed to Sterling Drug, Inc. A major acquisition in 1942 was the Salvo Chemical Corporation. It had been founded in 1930 to convert lignin from lumber wastes into vanillin. Sterling already sold this compound for flavorings through its General Drug division; but because the big tonnages were used in rubber for tires, Sterling was now in the critical war materials business. Effluent treatment was a problem until Salvo found that the organic content was destroyed by aeration in water at high temperatures and pressures, leading to the Zimpro process used, for example, for the treatment of sewage sludge in major cities such as Chicago. Fortuitously, the reaction is exothermic and so actually generates energy. The Frederick Stearns Company, founded in 1855 also by a pharmacist, was bought by Sterling in 1944. It owned the Nyal trademark, having acquired the New York and London Medicine Company in 1904, but this product range was better known in Australia. The medical director of Stearns, Mark Hiebert, MD, became presi-

dent of Sterling in 1955 and succeeded Hill as chairman in 1962 on the latter's untimely death. (Hiebert in turn was succeeded in 1972 by Clarke Wescoe, MD, a former Chancellor of the University of Kansas; when he retired in 1984, Jack Pietruski became chairman). In 1945 the Hilton-Davis Company was acquired, partly to complement the existing chemicals operations at Rensselaer but more particularly as a captive source of salicylic acid (the increasing demand for acetylation by the Bayer Aspirin process led to the purchase also of the McKay Davis Chemical Company in 1947).

Sterling's first move into vaccines and sera came in 1954 when the Bayer Biological Institute was set up in former racing stables near Newmarket, England. Superannuated racehorses were used to produce antibodies for veterinary preparations. This and the rest of the UK veterinary business were sold to Pfizer in 1962. Meanwhile in the US, various poultry vaccine businesses (Dorn & Mitchell, Delaware Poultry Laboratories) were acquired in 1958 and sold in 1985. Other ventures into biologicals included a short-lived human influenza vaccine unit at Rensselaer in 1965 and a range of fluorescent antibodies for the rapid identification of microorganisms, made and sold in the UK from 1966 through 1969.

The next big leap in growth came in 1958. Until that time, most foreign activity was in Latin America (through the Sydney Ross Company) and through uncoordinated units in Australasia, the Philippines, South Africa, and the UK. Canada operated virtually as part of the US, but business in most other countries was carried on through agents. The reorganisation outside the US was based more on personalities than on logic. However, it did lead to the setting up of Sterling companies in many more countries: in virtually all those in western Europe, in the major countries in Africa and the Middle East, in India and Pakistan, and elsewhere. This expansion was accompanied by the building of a number of new manufacturing plants. Changes in local regulations and in trade agreements meant that there was a shifting pattern of agency and manufacturing arrangements over the years; but, during its last two decades of existence, Sterling generally operated about seventy plants located in about forty countries and had direct or agency marketing in over 130 countries.

Despite all this activity, the policy of acquisition continued, but the emphasis moved towards household and similar consumer goods. Perhaps the most important acquisition was that of Lehn & Fink in 1966.

Founded in New York in 1874, the business had been one of the major players in breaking Bayer's stranglehold on aspirin in the US in 1917. It brought with it subsidiaries, notably Schulke & Mayr (disinfectants in West Germany), Hinds (cosmetic creams), and Beacon Wax. A further disinfectant manufacturer, Phagogène in France, was added in 1971. In 1973, Sterling acquired the Izal business in the UK, a move that largely complemented the Lehn & Fink operations. Izal was founded in 1880 to sell household disinfectants and now included furniture polishes (Ronuk), floor treatments and other cleaning systems, and barrier creams. The Ronuk division went on to develop various do-it-yourself wood treatment products. Sterling then acquired a similar US firm Minwax in 1977, and Thompson and Formby (waterproofing of brickwork and other exterior surfaces) in 1986. There was a return to pharmaceutical acquisitions in 1985 and 1986—notably Maggioni of Italy—and then Sterling came to the end of the road.

### The Fate of Sterling

On January 4, 1988, Hofmann-La Roche made a hostile bid to take over the entire assets of Sterling Drug, Inc. Sterling in turn sought a "white knight" and on February 22, 1988, Sterling became a division of Eastman Kodak for the sum of \$5.1 billion. Eastman Kodak saw Sterling—especially its ethical pharmaceuticals and its diagnostic imaging—as complementary to its own health sciences business. In particular the facilities in Sterling's major research centers in Rensselaer (NY), Alnwick (UK), and Dijon (France) would be of great help in screening and evaluating compounds available to Eastman Kodak. It was decided to centralize all US research in magnificent new facilities in Upper Providence Township, PA. The building was only partly occupied, however, when Eastman Kodak decided in 1994 to dispose of its health-related businesses. The Sterling segment was broken up as follows:

In 1991 Sanofi and Sterling had formed a strategic alliance, so in 1994 Sanofi bought Sterling's worldwide ethicals business for \$1.675 billion and immediately sold the diagnostic imaging portion to Nycomed of Norway for \$425 million.

SmithKline Beecham purchased the worldwide over-the-counter pharmaceuticals business for \$2.9 billion and promptly sold the US portion to Bayer for \$1 billion. So, after 75 years, Bayer Aspirin in the US returned to its original owner.



**Figure 4.** The Rensselaer research complex and (behind it) the East Greenbush manufacturing plant at the time of Sterling's acquisition by Eastman Kodak in 1988.

Reckitt and Colman of the UK bought the Lehn & Fink business for \$1.5 billion; this was partly funded by the sale of the Colman mustard business.

### What Did Sterling Achieve?

In the first four decades under Weiss and Diebold the annual sales grew from \$10,000 to \$50 million. Over the next four and a half decades, four successive chief operating officers continued to drive up the sales, achieving \$2.3 billion in 1987, the last full year. There were four major factors contributing to this growth:

- an aggressive acquisition policy over the years.
- innovative marketing, especially in the UK in the 1960s.
- an imaginative research program for discovering and evaluating novel new chemical entities.
- expansion into nondrug areas, especially household and other consumer products, but also into bulk specialty chemicals.

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### ABOUT THE AUTHORS

Joseph C. Collins received his Ph.D. degree from the University of Wisconsin and joined Sterling Winthrop Research Institute in 1958 as a research chemist. In 1962 he accepted an appointment as Chairman of the Chemistry Department at Illinois Wesleyan University. In 1967 he returned to Sterling as Director and then Vice President for Chemistry. He retired from Sterling as Vice President for Technical Affairs in 1987. His address is 178 West Shore Drive, Valatie, New York 12184. John R. Gwilt earned his Ph.D. at the University of London. He joined Sterling Drug, Inc. in 1947 in the UK. He transferred to Sterling's headquarters in New York in 1967 and retired as a Corporate Vice-President shortly after Sterling was acquired by Eastman Kodak in 1988. He resides at Wellstone House, Hartwell Road, Road, Northampton NN7 2NT, England

## THE EARLY HISTORY OF PARKE-DAVIS AND COMPANY\*

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*Milton L. Hoefle, Warner Lambert-Parke Davis*

### Introduction

By the end of the Civil War Detroit was a prosperous and bustling city. The completion of the locks and canal at Sault Ste. Marie in 1855 had opened the way for transporting the iron ore and copper from Michigan's Upper Peninsula to the markets in the east. By 1860 Michigan was the largest producer of iron ore and copper in North America (1). Both of these products were critical in the North's victory in the Civil War, and the mining and transport of these materials was highly profitable. In Detroit gracious homes lined the tree-shaded streets which led into Woodward Avenue, and the most prosperous citizens were building mansions on estates along the river off of East Jefferson Boulevard.

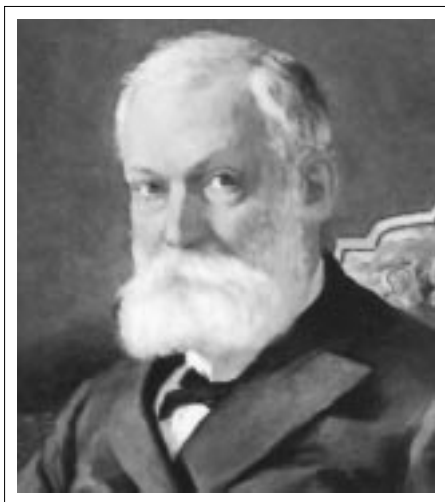
Times had not proven to be that prosperous, however, for Dr. Samuel Duffield, who owned a small drug store at the corner of Gratiot and Woodward Avenues. The experience of the Civil War and the large number of people moving west had demonstrated the need for a greater supply of medicinal preparations (2). So in 1862 Dr. Duffield had begun to make a number of items in larger amounts than required for his own use and to sell them to other pharmacists and doctors. Dr. Duffield's store was strictly a one-man operation, and most nights found him working late in the crowded laboratory in the back of his store. Here he had a still that could produce two barrels of alcohol a day and presses for making extracts. In the Detroit City Directory he advertised "ether, sweet spirits of nitre, liquid ammonium, Hoffman's anodyne, mercurial ointment, etc." But the

shipping service to Detroit was poor and potential customers in the major population centers in the east were skeptical of any company located in what they considered to be a backwoods town. Consequently, it was difficult to find anyone to extend credit or to invest in such a business (3).

Then in 1866 Dr. Duffield met Hervey C. Parke who was interested in starting a new business. Hervey Parke was 38 years old. He had managed a copper mine and then owned a successful hardware store in Michigan's Upper Peninsula. In 1865 he sold his store and moved his wife and two children back to Detroit because of the better business opportunities there. On October 26, 1866, the partnership of Duffield and Parke was formed, and this event is recognized as the beginning of Parke-Davis and Company.

### Part I – 1866-1900

Soon the increased competition of the eastern drug firms made the new partners realize the necessity of finding someone who could promote and sell their products. So in 1867 a young, ambitious, wholesale drug salesman was brought into the firm as the third partner. This was George S. Davis, the son of a prominent Detroit resident. After high school he chose going into business rather than attending college. He was only 22 when he joined the partnership, but he had already established himself as an outstanding salesman. Although sales continued to expand, new troubles kept appearing. Dr. Duffield's health began to fail and he needed to spend



Hervey C. Parke

more time with his wife who had become seriously ill. In time, Dr. Duffield became disheartened and withdrew from the business in order to go into private practice as a physician. So in 1871 Parke and Davis became the owners of the company that was to bear their name for the next century.

Hervey Parke and George Davis had very different personalities. Where the former was quiet, gray bearded, and dignified, the latter was young, flamboyant, and full of ideas for increasing their business. Under their direction the company entered an era of unprecedented growth. Both men were committed to the belief that the high quality of their products was a major selling point, and the motto "Medicamenta Vera" or "truth in medicine," first adopted by Dr. Duffield, continued to be one of their major concerns.

In order to gain both publicity and new products, Davis began sending expeditions to far-off corners of the world to collect various plants used by the native peoples. Starting in 1871 expeditions were sent into the wilds of Central and South America, Mexico, the Pacific Northwest, the West Indies, and the Fiji Islands. Over a twenty-year period, Parke-Davis introduced 50 new drugs, and most of these proved to be of sufficient value to be recognized in the *United States Pharmacopoeia*. Probably the most familiar product, Cascara Sagrada, introduced in 1876, is still used today (4).

The best-documented expedition financed by Parke-Davis was that of Henry H. Rusby, who recorded his adventures in a book called *Jungle Memories* (5). Rusby had just received his medical degree from New York University, and he was hired by Parke-Davis as a "botanist and pharmacologist." Late in the fall of 1884

George Davis asked him how soon he could leave for Bolivia because he wanted to obtain a large supply of coca leaves so that this drug could be investigated. Rusby quickly gathered up all the equipment that he might need and by January was on a boat headed to South America. He was just 22 years old and setting out alone on a trip that would take two years. He would cross the Isthmus of Panama and travel down the rough western coast of South America to Bolivia. From here he would cross the Andes and then travel the length of the Amazon River from its western tributaries to the Atlantic Ocean. While in the Bolivian jungles Rusby kept hearing reports about the bark of a mystery tree called "cocillana" which was reported to possess a remarkable range of therapeutic uses. Finally a native identified this mysterious tree and Rusby immediately had it cut down and its bark removed and dried. In order to test the properties he administered a small amount to one of his native companions and it produced an increase of mucus in the mouth and throat. A double dose was then given to two other natives with similar results. Thus encouraged, Rusby again doubled the dose and took it himself. The result was "nausea, pallor, and an abundance of thin watery mucus from the nose." Based on these findings and what information he could gather, Rusby considered that this drug had properties similar to those of ipecac and that it had commercial possibili-



George S. Davis

ties. So he hired natives to gather 600 pounds of this bark which was then packed, carried over the mountains, and shipped back to Detroit.

In the late 1800s Parke-Davis supplied a group of leading physicians with samples of new products and little pamphlets called "Working Bulletins." These pub-

lications provided all the known information about the preparations and their physiological effects. In turn the physicians were invited to report their experience with the drug, which would then appear in later issues. It is interesting to note that Cocillana bark was listed in the 1888 catalog just two years after Rusby sent back the first sample. Cocillana never replaced ipecac but eventually was utilized in cough preparations, and Rusby received a royalty of 10 cents per pound of bark.

The first manufacturing plant was located in downtown Detroit, but by 1873 the rapidly increasing demand for Parke-Davis products made it necessary to build new manufacturing facilities at Joseph Campeau Street and the Detroit River. This location would be the home of Parke-Davis for the next century. There were two major manufacturing operations; extracting plant materials and rolling pills. By 1874 the Parke-Davis catalog listed 254 types of fluid extracts, 300 types of sugar coated pills, 74 solid extracts, 53 concentrations, 46 medicinal elixirs, 23 medicinal syrups, 15 medicinal wines, 8 alkaloids, and chloroform (6).

Because additional money was needed to finance the expansion, Davis had the job of trying to encourage Detroit businesses to invest in the company. But money was tight following the recession of 1873 and so it was not until January 14, 1875 that Parke-Davis and Company became a corporation under Michigan law. Parke was the president while Davis was the general manager, and there were three other stockholders who had paid in capital totaling about \$82,000. By 1876, exactly 10 years after Duffield and Parke had joined forces, the company reported its first profit of \$5,264.65 and Parke-Davis had become Detroit's largest industry next to manufacturing stoves. During this period George Davis was the real driving force. In addition to selling, he managed the production and laboratory facilities; if salesmen were needed, he trained them. Most importantly, his restless genius was responsible for a number of brilliant and farsighted decisions that would result in Parke-Davis becoming one of the most respected pharmaceutical companies in the world by the turn of the century.

One of the major problems encountered by the pharmacists and physicians at that time was the variation in the strengths of the prepared medicinal extracts on the market. These could range from being worthlessly weak to death-threateningly strong. Obviously, the drug manufacturers wanted to avoid the possibility of their products killing anyone, so they tended to err on the weak side. Consequently, most doctors felt more secure in either compounding the drugs themselves or dealing with a pharmacist they knew and trusted. Davis was keenly aware of this situation and hired a chemist to work on the problem. In 1879 a process for standardization by chemical assay was developed, and the first standardized medicinal drug in history was placed on the market. This led to a systematic investigation of standardizing other liquid formulations and in 1883 Parke-Davis announced a list of twenty such "normal liquids (7)."



First factory

By the early 1890s medical research scientists began to realize the potential usefulness of animal glands as a source of new medicinals. Parke-Davis was quick to begin research in this new field and in 1893 introduced desiccated thyroid gland as a treatment for glandular disorders. Because the

new biological materials did not lend themselves to chemical standardization, in 1897 Parke-Davis introduced the idea of physiological standardization in which the effect of the drug in test animals was quantified. Two decades later over 1,100 Parke-Davis products would be standardized by these methods.

Other pharmaceutical companies recognized the significance of standardization and developed methods of their own so that over a relatively short period of time this principle was adopted by the whole industry. However, Parke-Davis' leadership and diligence were widely recognized and appreciated. In order to maintain standards it was also necessary to establish quality control. Thus, in 1886 Parke-Davis initiated the practice of using lot numbers on the labels of all their products. Since that time every item produced has carried



its own control number. This number is the key to the complete history of the product and each ingredient used in its manufacturing including the source and testing. It was not until 1962 that the FDA required all drug manufacturers to do this.

By 1890 Parke-Davis was a successful and prosperous company. It had finally succeeded in breaking into the competitive eastern market, and a full-scale manufacturing operation was built in Walkerville, Ontario, to take care of that business. In the same year a Parke-Davis branch was established in London, England, in order to enable the company to extend its sales to Europe. New buildings were also going up on the waterfront property, and the number of employees was steadily increasing. A big bicycle shed was built on Jos. Campeau to shelter all of the bicycles which were the favorite form of transportation. Parke-Davis employed a large number of women, especially in the Capsule and Finishing Departments. The women wore long ankle-length skirts fashionable in that era, protected by starched aprons brought from home. Work started at 7:00 a.m. and ended at 5:30 p.m.; and on Saturday everyone worked from 7:00 a.m. to 1:00 p.m. All of the capsules were handmade and the rate of pay for hand trimming and joining capsules was 8¢ per thousand. A top operator could earn up to 80¢ a day.

It was at this time that George Davis met a young Japanese chemist, Jokichi Takamine, who had come to the United States to try and interest the distilling industry in a potent starch-splitting enzyme that he had developed. Davis was impressed and immediately hired him as a consultant. Taka-Diastase was marketed in 1895 as a digestive aid and became very popular. Once again Davis' intuitive ability to recognize talent was evident, because in 1900 Takamine isolated adrenaline and was part of the team working in the Parke-Davis laboratory that identified the chemical structure. Later, after returning to Japan, Takamine became the first president of Sankyo. Because of this common bond a close relationship has existed between the two companies since that time.

In 1894 the German scientist, Emil Behring, and the French scientist, Emile Roux, announced the discovery of an antitoxin for the treatment of diphtheria. George Davis immediately realized that it would bring tremendous prestige to his company if such an antitoxin could be produced commercially because at that time diphtheria was one of the most deadly of the common diseases. Moving quickly, he recruited two scientists

from the University of Michigan to set up the first commercial biological laboratory in this country. On March 19, 1895, a Detroit physician administered a shot of Parke-Davis diphtheria antitoxin to an ailing company employee. This marks the first time that a commercially produced serum was given to anyone in the United States. Two years later Antistreptococcic and Antitetanic serums were marketed. In fact, the serums and vaccines that were developed in this biological laboratory were to provide the bulk of the sales for the next twenty-five years.

It is ironic that just at the time that Parke-Davis was doing so well and George Davis was making decisions and initiating actions that would shortly make it the most successful pharmaceutical company in the world, the personal life of Davis became chaotic and tragic. As the business prospered the lives of the two partners grew apart. Hervey Parke still quietly took care of the finances. Around Detroit he was known as a successful, conservative man and a philanthropist. On the other hand, George Davis remained a bachelor although he was said to be an ardent admirer of beautiful women. He owned a big mansion on East Jefferson and a 500 acre farm on the lakefront where he kept his racehorses. He had a luxurious yacht for sailing on Lake St. Clair, and he was a well-known and popular figure around Detroit where he entertained lavishly. A great admirer of Napoleon Bonaparte, Davis had an extensive collection of relics of Napoleon. He also liked to collect rare "first editions" and by 1886 he owned a library of more than 5,000 books. He became intrigued by the prospects of California real estate and invested large sums of money, and this proved to be his undoing.

In 1893 business was booming and then suddenly the bottom dropped out of the market. The failure of British banks had caused British investors to unload American securities for cash, the result being a drain of gold reserves. This caused Americans to become apprehensive and to start withdrawing their savings from the banks. In turn hundreds of banks failed, thousands of businesses closed, and hundred of thousands of people were thrown out of work all across the country. The great panic of 1893 was on. In the resulting depression Parke-Davis suffered only a minor setback, but George Davis' heavy investment in California land proved to be a catastrophe. He lost vast sums of money, and in order to cover some of his losses, he drew on Parke-Davis for more money than he was due. Naturally, the stockholders objected. Although Hervey Parke, the president, stood by his partner through the resulting

storm, eventually it was necessary to ask Davis to resign. After almost 30 years of service, his stock was turned in as partial payment of his indebtedness and he was given a "leave of absence." In order to pay off his debts Davis sold his mansion, his farm, his beloved Napoleon collection, his yacht, and even his racehorses. From the time that he had started with a salary of \$60 a month until his resignation in November, 1896, this unusual man had allowed over a million dollars to slip through his fingers. Suddenly after 30 years of hard work and brilliant leadership, everything was gone. In 1903 he was forced to declare bankruptcy, and at that time the Board of Directors voted him a special pension in recognition of his many contributions. He lived quietly in various rooming houses and seemed to have no regrets. He seldom mentioned Parke-Davis but often talked about the beautiful racehorses he had owned. He died in 1930 at the age of 85 and only a few people attended the short burial service in Elmwood Cemetery.

After George Davis was forced to leave the firm, Hervey Parke continued as president, but was less and less active in the actual management because of poor health. The prominent Detroiters who had bought Davis' stock were named to the Board of Directors, and other names appeared more and more frequently in the company records. Then on February 8, 1899, Hervey Parke died. At his funeral in Detroit's St. John's Episcopal Church the large sanctuary was so crowded that special seating had to be reserved because all the leaders of Detroit's business and social life were present.

So, we come to the end of an era. Over the period of slightly more than 30 years the efforts of two men working in concert had directed the development of a pharmaceutical company from obscurity to a position of international prominence. Indeed, by the spring of 1904 Parke-Davis proudly proclaimed itself to be "The World's Largest Pharmaceutical Manufacturing Concern."

The middle of the 19<sup>th</sup> century was the time for pharmaceutical pioneers. Familiar names like Merrill, Lilly, Squibb, and Warner all date back to this period. It also marked the beginning of systematic research in the field of medicine. Thus, in 1864 Louis Pasteur proved that airborne microbes caused fermentation and putrefaction. In turn this work stimulated Lister to experiment with antiseptic agents, and this ushered in the modern age of surgery. But the amazing success of Parke-Davis and Co. must be attributed to Davis' ability to recognize the importance of the new discoveries

and to find a way to capitalize on the new possibilities. At the same time Hervey Parke managed to balance the enthusiasm of his young partner with a sense of reality and to keep the company financially solvent during some very turbulent times. The single most important contribution to their success, however, was the development of standards of purity and strict adherence to maintaining the quality of their products. The favorable publicity that resulted was the basis of Parke-Davis' international reputation, and as this reputation grew so did sales.

## Part II – 1900-1974

The beginning of the 20<sup>th</sup> century marked the start of a new era for Parke-Davis and for the United States. The automobile had arrived. In Detroit the police posted speed limits of 8 miles per hour in order to halt reckless driving. The popular Theodore Roosevelt as President was busy reforming the government of the United States. The leading sentiment of the time was "There's nothing wrong with society that the government can't fix." Under Roosevelt America was becoming a world power and there was recognition that human rights were as important as the rights of property (8). Americans had a new sense of pride in themselves and their country. Most of all, everyone was enjoying prosperity.

The founders of Parke-Davis were replaced by new leaders, but everything else remained the same. Since the company was so successful there was no need to risk being a pioneer and to blaze new trails. With sales continuing to grow the name Parke-Davis was recognized throughout the world as being associated with the highest quality products available. In no way did the new managers want to lose this reputation. So from 1900-1930 subsequent managers were able to maintain Parke-Davis' preeminent position by expanding upon that which the two partners had started. Thus, the first commercial biological laboratory that George Davis had established in 1894 was a major contributor to this success. In the lab that started with three horses and a few guinea pigs, the number of horses rapidly increased to several hundred. The company leased two large stables adjoining their river front property from the Detroit United Railway System, but soon these were overcrowded. The city of Detroit was also expanding so that the Parke-Davis property was gradually surrounded by residential areas. So it was a very popular decision in 1907 when the company purchased a large farm near Rochester, Michigan, and started moving all of the animals out there. The animals at Parkedale were prob-

ably the best fed and cared for in the world. Horses were required for the production of serums used against diphtheria, tetanus, and gangrene. During World War I there was a tremendous demand for Antitetanic Serum and ultimately over 600 horses were kept on the farm.

The period leading up to World War I was a happy time for the more than 3,000 employees of Parke-Davis. There were company picnics and boat excursions. There were social clubs and dances, bowling leagues and company sponsored athletic teams. The company pioneered a profit sharing and old age pension plan. There was a general feeling of being a member of a big, happy family; and a strong mutual sense of loyalty developed between the company and its employees that would last for almost fifty years. In 1927 F. O. Taylor, who was Chief Chemist at the time, wrote, "Long years of service by those in both high and humble positions gives to Parke-Davis and Company an *esprit de corps* of immeasurable value and assurance that replacement in the ranks shall fully carry on, and indeed improve, the traditions of the past (9)." This company spirit was certainly helpful in the difficult times resulting from the depression that followed the stock market crash of 1929. All of the employees agreed to a cut in pay so that no one was laid off. Profits were down but the company's record of never missing a dividend since the first one in 1878 was maintained (10). But because of the focus on traditions the company began to fall slowly behind its competitors in sales.

This trend continued until 1946 when a soil sample collected from a field in Venezuela yielded an unusually active antibiotic, Chloromycetin. This unique substance showed outstanding activity against typhus and typhoid fever. The structure was quickly identified, and the small group of organic chemists was successful in synthesizing the compound. The development of this drug was accomplished in a remarkably short period of time. By 1949 Chloromycetin was released to the medical profession, and within three years the sales of this product alone totaled \$120 million. The company had regained its premier position in the US.

By 1952 there was an increasing number of reports of hypoplastic anemias following the administration of Chloromycetin. At this time over eight million people had been treated successfully with this drug, and there had been remarkably little sign of any toxicity. But concern about this problem resulted in the council on Pharmacy and Chemistry of the American Medical Association issuing a report to the Committee on Research and

appointing a subcommittee on blood dyscrasias in June, 1952 (11). This was followed up by a report of the Council on Pharmacy and Chemistry in 1954 (12), which advised the restriction of the use of chloramphenicol to the treatment of typhoid fever and other infectious diseases caused by organisms resistant to other antibiotics. The sales that initially plummeted in 1952 gradually increased so that by 1960 Parke-Davis once again led all US pharmaceutical companies in sales. As the onslaught of bad publicity continued, the sales of Chloromycetin in the US gradually dwindled to almost nothing.

By 1961 Parke-Davis was in a downward spiral. The expansion brought about by the success of Chloromycetin had resulted in higher fixed costs, and there were no new products available to ease the pressure. Finally, a hostile takeover bid by Revlon forced the Board of Directors to consider alternative buyers of the company. They settled on the New Jersey conglomerate, Warner-Lambert, which purchased Parke-Davis in 1970. The merger was finalized in 1974.

Today the old Parke-Davis plant at Joseph Campeau and the Detroit River has been converted into a big riverfront complex of apartment buildings, shopping center, hotels, and upscale office buildings. The name "Parke-Davis" now identifies the ethical pharmaceutical division of the Warner Lambert corporate family. This division includes the former Parke-Davis research facility in Ann Arbor and the manufacturing plant at Holland, Michigan.

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"Parke-Davis 1866-1966, A Backward Glance", *Parke-Davis Review*, P. Walker, Ed., Parke-Davis and Co., 1966, 23, No. 1-9.

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## ABOUT THE AUTHOR

Milton L. Hoefle, Ph.D., University of Minnesota with W. M. Lauer, began working for Parke, Davis and Co. in 1953 in Detroit. In 1959 he moved to the new research laboratories in Ann Arbor and remained there until retiring in 1986 as director of Cardiovascular Chemistry.

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## THE HUNGARIAN PHENOMENON IN ISRAELI SCIENCE

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*Gábor Palló, Hungarian Academy of Science*

### The Hungarian Phenomenon in the History of 20th-Century Science

Around the turn of the century, an exceptionally gifted intellectual generation was born in Hungary. It was a result of an unprecedentedly peaceful period of the otherwise stormy history of the country, which came about after the establishment of the dual Austro-Hungarian Monarchy in 1867. This generation produced the musicians Béla Bartók and Zoltán Kodály, the psychologists Sándor Ferenczy and Imre Hermann, the philosophers György Lukács and Károly Mannheim, the economists Károly Polányi and Miklós Kádor, the movie maker Alexander Korda, and the writers Mihály Babits and Frigyes Karinthy.

In this extremely fertile soil a whole galaxy of scientific geniuses was also formed. The names of George von Békésy and George von Hevesy, Eugene Wigner and John von Neumann, Leo Szilárd and Edward Teller, Michael Polányi and Theodore von Kármán, Albert Szent-Györgyi, and Dennis Gábor became well known all over the world, particularly, since many of them won the Nobel Prize and played crucial roles in developing the atomic bomb. These scientists formed a more or less closed circle and constituted what I call the Hungarian phenomenon in 20th century science. I define the latter this way. 1) Although the sciences in Hungary did not exceed an average level at that time, Hungarian culture produced a highest-level group of scientists. 2) Compared to the size of the population, the number of

these highest-level scientists was exceptionally large. 3) These scientists, after a Hungarian middle class education, left the country and achieved their success outside the country, mostly in the United States. 4) The scientists under discussion formed a group, or at least a network; that is, they established contacts (a) to each other, (b) to the other Hungarian emigrants, and (c) kept their contacts with the Hungarian scientific community. 5) The group had some characteristic features that distinguished it from other scientific groups, and these features can, in principle, be described.

This paper raises the question as to whether the Hungarian phenomenon existed in several countries or only in the United States, and, particularly, whether or not it existed in Israel. What kind of roles in general did the Hungarian natural scientists play in Israel? Since many of the above mentioned scientists were of Jewish origin, the question is more than justified.

### Early Science in Palestine

In answering these questions, it should be taken into consideration that most of the Hungarian-phenomenon scientists left Hungary around 1920, when the right-wing and antisemitic Horthy government took over. They moved to America or Great Britain from Germany when the Nazis won the 1933 election. Though the international Zionist movement, headed by Theodor Herzl (a graduate of the Budapest "fasori gimnázium," the same high school as Neumann and Wigner's), was officially established in 1897, it was only in 1917 that the Balfour

declaration promised the establishment of a Jewish national state in Palestine, a distant part of the Ottoman empire. During the 1920s, under British administration, Jewish immigration into Palestine began to grow and, because of the Holocaust, by the 1940s the country became a target of the large Jewish exodus from various countries.

For the first wave of the migrating Hungarian scientists, including Szilárd, Neumann, Wigner, and Teller, around 1920, Israel could not compete with Germany, with its lively scientific life, its modern laboratories, and great personalities. The primary goal of these scientists was to study and to become not just good but brilliant experts. Israel at that time could not offer very much to these ambitious young people.

Though the idea of establishing a Jewish university preceded even the first Zionist Congress, and Herzl also supported the idea, the Hebrew University's twelve foundation stones, symbolizing the twelve tribes of Israel, were laid "on the barren crest of Mount Scopus" in Jerusalem only in 1918 (1). It was opened in 1925, one year later than the Technion, the institute of engineering, which also was a result of an old desire to create



Albert Szent-Gyorgyi, *courtesy Oesper Collection*

a school for training Jewish immigrants who would establish the industry in the country. This idea came up as early as 1901, and in 1912 the Sultan gave permission to erect three buildings for the purpose on Mount Carmel, in Haifa. The institute was finally opened for 18 students in 1924 (2).



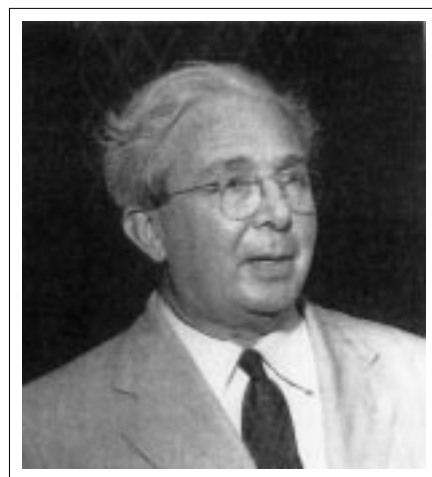
George von Hevesy, *courtesy Oesper Collection*

These institutions were new then, and for the young geniuses they could not offer a promising scientific atmosphere built on a long tradition and with well-equipped laboratories; neither could the Daniel Sieff Research Institute, the predecessor of the Weizmann Institute. It began its work in 1934, but, as a visitor described, "It was a small, isolated research outpost, situated practically in the desert. Visitors were lodged in a small clubhouse attached to the Institute, and during the night they could hear the jackals howling in the nearby orange groves (3)." This institute grew into a really large and significant scientific center only after 1949, upon the foundation of the Weizmann Institute.

All the other higher education institutions and scientific centers are much younger. Bar-Ilan University was inaugurated in 1955, Tel Aviv University in 1956. Teaching began in 1963 at Ben Gurion University, in Beer Sheva, Negev; but it was ceremonially opened only in 1969. These could only give research and teaching opportunities for the postwar immigrants.

### The Hungarian-phenomenon Scientists in Israel

Israeli conditions before the second World War could compete neither with Germany's lively scientific life nor with the unlimited possibilities in the United States. Still, some eminent Hungarian scientists had very significant relations with Israel.



Leo Szilard, *courtesy Oesper Collection*

Leo Szilárd had been introduced to Weizmann, an excellent chemist before rising to become the head of

the international Zionist movement and then the first President of the State of Israel. Michael Polányi, the physical chemist, later philosopher, suggested that Weizmann consider Szilárd as a possible faculty member, when Weizmann was working hard on organizing a physics institute at the Hebrew University. Polányi, directing one of the departments of the Kaiser Wilhelm Institut für Physikalische Chemie in Berlin/Dahlem, formed an informal group around him consisting of well known young Hungarians. The director of the institute was Fritz Haber, the Nobel laureate discoverer of the ammonia synthesis and for many reasons the leading personality of the German chemistry community, who greatly appreciated the whole group. Haber, with another classic figure of chemistry Richard Willstätter, also tried to mediate between Szilárd and Weizmann; but, for unknown reasons, the effort did not succeed (4).

Eugene Wigner, on the other hand, invited to visit Jerusalem in 1935, was offered the professorship of physics at the Hebrew University. Unlike Szilárd, Wigner was inclined to accept the position but finally refused, because he felt he would lessen the chances of his close friend and colleague, Ladislaus Farkas, when he, Wigner, already had a post in the United States, and Farkas had no other suitable opportunity. Wigner paid many visits to Israel later, gave important talks, and participated in meetings, by which he contributed to the nuclear physics of the country, including the work of the Dimona reactor in Negev (5).

Edward Teller's involvement began in the 1960s and has continued up until the present. His closest friend and colleague, the nuclear physicist Yuval Ne'eman, cooperated with him in many important matters concerning the application of nuclear power to various engineering goals, such as digging a canal through the desert. Ne'eman characterized Teller's Israeli role this way (6):

Edward has met and talked at length with every Israeli Prime Minister or Minister of Defence since 1966.

As a committee member, he advised the experts on the defense technologies, nuclear reactor technologies, and other related matters. Teller was also of help to the larger Israeli scientific community. He gave courses at Tel Aviv University and initiated the establishment of the Faculty of Engineering there, the first dean of which became Yuval Ne'eman. For his contributions the Technion awarded Teller its Harvey Prize. "Edward Teller," wrote Ne'eman, "has taken up his share in Israel's worries—and has also brought Israel closer to

Western values and closer to the USA (6)." Besides Wigner and Teller, other Hungarian-phenomenon scientists also visited Israel several times. Kármán described stories about his visits in his biography. Denis Gábor, Nobel laureate physicist, and Nicholas Kürti, professor of physics in Oxford and fellow of the Royal Society, maintained their relations with, among others, Ferenc Körösy, professor of chemistry at Ben Gurion University (7).

### The First Hungarian Immigrant Scientists to Palestine

Despite the unfavorable conditions in the early years, some very significant Hungarian scientists moved to Jerusalem to be part of Hebrew University. Among the earliest professors was Mihály (Moshe) Fekete (1886-1957), one of the exceptionally creative mathematicians of his time, who, with his masters, Lipót Fejér and Manó Beke, greatly contributed to the formation of the Hungarian phenomenon. His works on the theory of numbers, theory of functions, and numeric sets made him a well known scientist while still quite young. Besides Budapest, Fekete studied in Göttingen, the center of mathematics at that time. After returning to Budapest in 1914, he completed his Habilitation at Budapest University and gained an assistant position there, which he soon lost for political reasons. In 1919 and 1920 totalitarian regimes of various colors followed each other, and many great Hungarian scientists or their families suffered as a result. As a gifted teacher, Fekete was advised to accept as a private student an especially talented high school boy, because the level of this boy far exceeded everything expected in a high school. His name was John von Neumann. In this way, Fekete be-



Edward Teller, courtesy Oesper Collection.

came to Palestine in 1935, he was offered the professorship of physics at the Hebrew University. Unlike Szilárd, Wigner was inclined to accept the position but finally refused, because he felt he would lessen the chances of his close friend and colleague, Ladislaus Farkas, when he, Wigner, already had a post in the United States, and Farkas had no other suitable opportunity. Wigner paid many visits to Israel later, gave important talks, and participated in meetings, by which he contributed to the nuclear physics of the country, including the work of the Dimona reactor in Negev (5).

came Neumann's first instructor in higher-level mathematics.

Realizing the lack of opportunity to find a university position in Budapest, Fekete decided to move to Jerusalem in 1928. He soon adjusted to the new surroundings there and became a most important personality in the university. He imported to Israel the special Hungarian style of mathematics. With his scientific and teaching abilities, he soon became a professor in the Einstein Institute of Mathematics and contributed to the establishment of the faculty of science and to increasing opportunities for research in the field of natural sciences in general. It was quite an accomplishment if one considers that in the university founders' goal there was only "the glorious spiritual past traditions of Judaism, and the burning, irresistible desire to revive them (8)." Fekete and his fellow scientists established an alliance with the head of the Academic Council of the University, Chaim Weizmann. For a while, Weizmann's successor in the Academic Council could be of help; he was Albert Einstein. To be more effective, Fekete worked as Dean of the Faculty of Science several times and became the Hebrew University's rector between 1945 and 1948. Before his death in 1957, he was awarded the Israel Prize, the highest distinction of the country (9).

### The Chemistry Clan: First Generation

The Hungarian phenomenon in Israel was more evident in chemistry than in mathematics. Indeed, a news item stated that Andor Fodor "...was the university's first teacher, and that he had been invited by Dr. Chaim Weizmann to organize its Chemistry Institute, which became the cornerstone on which the future Faculty of Science was based (10)."

Fodor was born in Budapest in 1884, graduated from high school in Graz, and conducted his chemistry studies at the Budapest Technical University and ETH in Zurich. He began his scientific career as an organic



John vonNeumann, *courtesy Oesper Collection.*

chemist there, then continued in Stockholm and Berlin. Fodor became *Privatdozent* in physiological chemistry in Halle in 1919, then "...reached the conclusion that the situation of the Jews was such that they would be forced to seek a secure refuge for themselves (11)." He became a Zionist and moved to Jerusalem in 1923, where he accomplished the pioneering work of establishing modern chemistry, including a building, at the opening of the Hebrew University. The very first classes in chemistry and many significant scientific results came from Fodor's institute. His memorable scientific activity embraced various fields of organic chemistry, biochemistry, and colloid chemistry, for which he produced a book in 1925 (12). However important Fodor's activity was, he has been severely criticized for being overly ambitious. He gained the reputation of exploiting his junior associates as slaves, which poisoned the atmosphere of the institute. Weizmann definitely had to take some action. In a letter Weizmann wrote, "The setting up of a natural science faculty should begin immediately. This would, first of all, break the rule of the so-called biological clique, Klinger [a biologist professor]—Fodor *et tutti quanti* (13)."

This was a difficult period in the history of the university because the leaders had to decide about the model they wanted to apply. Einstein favored the German, Judah Leon Magnes, the University Chancellor, the American model. Einstein became disappointed in this controversy and refused the professorship in the physics institute. Weizmann had to seek other scientists to occupy the positions in the physics department (which proved very difficult) and in the chemistry institute, to balance Fodor's influence. Wanting to employ a physical chemist, he chose another Hungarian, L á s z l ó (L a d i s l a u s) Farkas. "Personally I don't know him at all. But I think," wrote Weizmann, "he is one of the best young physico-chemists, if not the best of them. I know that Fritz Haber has this



Michael Polanyi



opinion and so, I may say, had Rutherford (13).” In fact, they had already corresponded one year earlier, when Farkas, on Szilárd’s suggestion, described his ideas about producing purified water. At the end of his long letter, Farkas wrote to Weizmann (14):

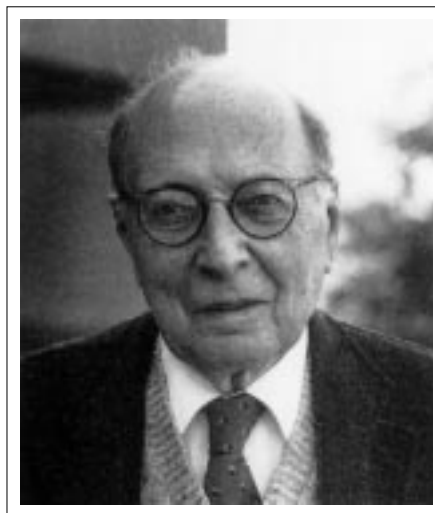
Ich versichere Sie, falls mir Gelegenheit gegeben wird, in Palästina zu arbeiten, dass ich meine ganze Kraft daran setzen werde sowohl in wissenschaftlicher Hinsicht wie auch in der Bearbeitung technischer Probleme, die das Land betreffen, mein Bestes zu leisten (14).

Ladislaus Farkas was born in Dunaszerdahely in 1904 and was two years older than his brother Adalbert, whose life and career run parallel (15). They graduated from high school in Hungary but became chemical engineers in the Viennese Technische Hochschule; and then both began to work in the Kaiser-Wilhelm Institut für Physikalische Chemie. In 1928 the director of the institute, Fritz Haber, accepted Ladislaus as his personal assistant. By that time the Farkas brothers had done beautiful work on *ortho* and *para* hydrogen and on deuterium, and they soon became well known experts on hydrogen. In the Berlin institute they became part of the group of the Hungarian-phenomenon scientists around Michael Polányi; and, because Wigner was Polányi’s graduate student, Ladislaus developed a lifelong friendship with him also (16).

The Farkas brothers’ exceptionally promising career was interrupted by the Nazis in 1933. All the important people around them, Haber, Polányi, Wigner, and Szilárd had to leave Germany. Both Farkases found only temporary positions in Rutherford’s laboratory, then in the Institute of Colloid Chemistry in Cambridge; and, although Szilárd and Polányi tried to help them, they were probably not happy with the positions finally opened to them in English industry or at Bristol University (17). Thus, Weizmann’s invitation to Ladislaus to become a professor in Jerusalem could not have arrived at a better time. Zionism played no role in his immigration to Palestine (18). Adalbert followed a year later in 1936 and remained until 1941, when, in spite of the major efforts by many scientists, including Albert Einstein, he could not receive more funds in the country (19). With his American wife, Adalbert settled in the United States, where he has continued to live.

In the 1930s the brothers could continue their fruitful scientific investigations and participate in the life of the international scientific community. The institute worked well; it was rather well equipped and had a growing number of graduate students. Ladislaus proceeded

with his hydrogen studies and extended his interests to the hydrocarbons. As they wanted to contribute to Israel’s industry, they expanded their research subjects toward practical problems. Adalbert, for instance, invented a new type of wrapping paper to



Eugene Wigner, courtesy Oesper Collection.

preserve oranges during transportation. Ladislaus was appointed head of the Central Committee for the Development of the Chemical Industry in Palestine in 1939. This proved particularly important during the war, when the institute produced glassware and chemicals needed by the army and did research on the utilization of the country’s raw materials, etc. Farkas’ ingenious activity reminds one of his Hungarian colleagues’ activities in the United States that were vital in developing the atomic bomb. He became the scientific secretary of the Scientific Advisory Committee to the Palestine War Supply Board, just as Kármán, Szilárd, and Neumann participated in similar committees in America (20). After the war, Ladislaus Farkas made tremendous efforts to develop his institute by replacing old instruments and redirecting research toward pure science. He died in an airplane crash in 1948, en route to purchase scientific instruments in the United States.

Farkas introduced modern physical chemistry to Israel, and he imported the Hungarian-phenomenon mentality of working in the most competitive front line of science and of applying the latest theoretical approaches. He was part of this group. One of his Hebrew University graduates, Michael Schwartz, moved to Manchester to work with Polányi (21). Polányi contributed to the Farkas Memorial Volume edited by Adalbert and Wigner (22).

### The Chemistry Clan: Second Generation

The later developments of the physical chemistry department and of chemistry in Israel showed Farkas’ great impact. After his accident, the leaders of the university

approached Adalbert to occupy his brother's vacated chair. This seemed an obvious solution, and Adalbert considered it seriously, but finally decided against it, saying that he had built up a new existence and home in the US (23).

The new permanent head, and real successor, was also a Hungarian and former student of Farkas: Gabriel Stein, born in Budapest in 1920. After graduating from a Budapest "Realgymnasium," he immigrated to Palestine in 1938 and received his masters degree as Ladislaus Farkas' student. He earned his Ph.D. under another former Haber student, Joseph Weiss, in Durham, England, where Stein remained until 1951 (24). Then he returned to Jerusalem and joined the department of physical chemistry, where he soon became head. Gabriel Stein led the department back to the direction set by Farkas and elevated the scientific level to its former height. It is also Stein's achievement that two of his students, Joshua Jortner and Raphael B. Levine, became two of the most prominent physical chemists of the country (25).

In the early 1970s, the Hebrew University chemistry departments were reorganized, and as a result a major institute was set up. This time another Hungarian was appointed the head of the institute: Saul Patai, editor of the book series *The Chemistry of Functional Groups*, comprising 100 volumes. The Patai family immigrated to Palestine in 1938, as traditional Zionists. Raphael Patai, Saul's brother, who died recently, was a famous cultural anthropologist and linguist. One of his last works was the book, *The Jewish Alchemists*. Their father, President of the Pro Palestine Association, had visited Palestine many times before the family settled there. Saul, born in Budapest in 1918, attended the university in Budapest for two years and then became a student of Andor Fodor; but he received his masters degree under Ladislaus Farkas in 1941. In his main research fields—the mechanism of organic reactions, the reactions of olefins, and the chemical reactions in solid state—he achieved important scientific results. Patai, like many other prominent Hungarians, contributed to defense-related research; after the Yom Kippur War, he organized a research group devoted to such subjects (26). He died in 1998.

### The Chemistry Clan: Third Generation

The third generation of Hungarian chemists arrived in Israel after the 1956 Hungarian revolution. Its two outstanding personalities are Ferenc Körösy and Ruben

Pauncz, both foreign members of the Hungarian Academy of Sciences, and neither of them associated with Hebrew University. Both began to work at the Technion, but Körösy, contrary to his own wishes, soon moved to Beer-Sheva. They were not the first Hungarians at the Technion. In addition to several engineers (P.W. Ernst, A. Gileadi, B. Kinori, M. Vajda) and the famous mathematician Paul Erdos, who never lived permanently anywhere, but regularly taught at the Technion as a visiting professor (27), they also met at the university Shlomo Bien, a former graduate student of Géza Zemplén's famous organic chemistry school at Budapest Technical University (28).

Ferenc Körösy, born in Budapest in 1906, also belonged to the group of the Hungarian-phenomenon scientists and was in contact with many of them. Teller, his old friend, was his classmate at the university in Karlsruhe. While Teller changed to physics, Körösy continued as a chemist and returned to Budapest to occupy a position in the laboratory of the Tungsram factory, probably the only high tech plant in Hungary in the period between the wars. As a result, he was involved in the research and development of the krypton bulb, the greatest innovation of the factory. This laboratory employed many of the best scientists of the time, including Michael Polányi, who was living permanently in Manchester, and for a shorter period even Denis Gábor and Edward Teller.

The Körösy family had a long Zionist tradition, the reason why Ferenc Körösy decided to move to Israel. By 1957, however, when he could realize his plan, he was over fifty; and it was not easy to begin a new career. Nevertheless, he worked on very important projects in Israel, mostly in inorganic chemistry, and found satisfaction with his new life (29).

Ruben Pauncz, born in 1920, achieved immediate success upon his arrival in Israel. In Hungary, working at Szeged University, he was the first scientist engaged in quantum chemistry in that country. In Israel, as the Technion chemistry faculty was modernizing the curriculum in the middle 1950s, Pauncz was instrumental in introducing quantum chemistry. As a result, right after his arrival in 1957, he was able to begin teaching and could continue his productive research work on, among other things, the application of the quantum chemistry methods to alternate hydrocarbons, in cooperation with his colleagues in Uppsala and Florida. He published four books in English on quantum chemistry. In this way, Pauncz fits into the long series of Hungarian sci-

entists who contributed to the knowledge transfer into Israel. Although he never belonged to a specific scientific school, since he was self taught in the new discipline, Pauncz brought his knowledge with him from Szeged. This is how he also became the first quantum chemist in Israel, his second home. Endowed with exceptional teaching abilities and recognized as a most popular professor of the university, Pauncz trained generations of gifted quantum chemists, who by now have established a lively professional community at the Technion (30).

### Conclusions

Without surveying the entire, long list of Hungarian scientists, one can conclude that, in fact, there existed a Hungarian phenomenon in Israel. It would also be worth investigating the history of Hungarian social scientists, including Joshua Blau, a Hebrew and Arabic linguist and the only Hungarian member of the exclusive Israeli Academy of Science, or Joseph Ben-David, an excellent sociologist, formerly a chemist, who exerted a great impact on the sociology of science not only in Israel but throughout the world. However, on the basis of the analysis of only the most significant cases of natural scientists, some important features of the Israeli Hungarian phenomenon have been identified. 1) Quite a few Hungarian scientists settled in Israel, and many were in close contact with the most famous ones. They can be considered a part of the Hungarian-phenomenon group, or perhaps an Israeli extension of it. Even some of the greatest Hungarian scientists had direct or indirect involvement in Israeli science. 2) Unlike in the US, where the physicists had the most eminent roles, in Israel the chemists became the most successful. 3) Zionism often played a part in their migration to Israel, but this Zionism was positive in the sense that it was a stance for Israel and not against Hungary. 4) Some characteristic features of the Hungarian scientists became evident: their modern theoretical approach and a frequent combination of this theoretical inclination with a practical orientation. These features, in an atmosphere of special political awareness, resulted in success in the military-related fields. 5) The Hungarians contributed to the knowledge transfer into Israel in two ways. First, they represented the most advanced level of their scientific field; and, second, they brought with them the fertile Hungarian culture and middle-class life style.

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## THE CONTRIBUTIONS OF E. H. S. BAILEY TO THE DEVELOPMENT OF PURE FOOD AND WATER LAWS IN KANSAS

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*Carolyn Bailey Berneking*

During his 50-year tenure at the University of Kansas, E. H. S. Bailey trained thousands of chemists and helped establish a strong, dynamic Chemistry Department. He dedicated his life to educating Kansans about the need for clean water, proper labeling, and unadulterated foods. His many publications, analyses of industrial products, desire to educate, and leadership in the Kansas State Board of Health brought national recognition to the University of Kansas Chemistry Department (1).

Scientific developments in the nineteenth century began to revolutionize chemistry. Advances in bacteriology and the invention of the achromatic microscope in the 1830s brought about the first serious laboratory testing and analysis of water, milk, and foods. The number of laboratories in medical schools, universities, health departments, and hospitals increased. Many new scientific publications began to appear. In January 1879 in an address to the Medical Society of New York, Edward

Robinson Squibb, a pharmacologist and pioneer in anesthesia, proposed a national statute to regulate food and drugs. He convinced Senator Warner Miller of New York State to introduce such a bill on December 20, 1881, to the Forty-seventh Congress of the United States, but it was defeated by a group of prosperous manufacturers of patent medicines who lobbied against the bill. Squibb died before he could see his dream come to fruition. Twenty-five years later, such a law was passed by the United States Congress as the Federal Pure Food and Drugs Act of 1906 (2).



The young Bailey

During these times of important advances in science and technology, Edgar Henry Summerfield Bailey was born on September 17, 1848, in the manufacturing village of Baileyville, near Middlefield, Connecticut. He was the only son of Russell E. and Hannah Miller Bailey. Russell owned a machine shop that made wooden coffee mill handles for a hardware factory, later turning out

clothes wringers for a washing machine company and spools and spindles for textile mills. The son grew up in this environment, building machinery, mill dams, and water wheels. After he completed education at the district school, he attended the Wesleyan Academy in Wilbraham, Massachusetts, where he became especially interested in chemistry, physics, and geology (3). After

and drinking waters often were polluted. During the next fifty years of teaching and research, he helped bring healthy food and safe drinking water to the people of Kansas.

Bailey's meager laboratory was in the basement of Fraser Hall, one of only two buildings on the campus.



University of Kansas Chemistry Laboratory

Wesleyan he attended the Sheffield Scientific School at Yale University from which he received a bachelor's degree in 1873. He spent another year at Yale doing graduate study and teaching before assuming his first full-time teaching position at Lehigh University in Bethlehem, Pennsylvania, at an annual salary of \$1,000. Along with his teaching, Bailey performed commercial work, analyzing iron, zinc, and manganese ores, coal, limestone, furnace gas, and other industrial products. He remained at Lehigh for nine years, gaining experience in performing commercial chemical analyses and preparing himself to teach mineralogy, metallurgy, and assaying (4).

Following the American pattern at the time, Bailey studied in Europe at the Kaiser Wilhelm University at Straßburg under Dr. Rudolph Fittig (5). In 1883 he received the degree of Doctor of Philosophy from Illinois Wesleyan University (6) and became head of the University of Kansas Chemistry Department. He arrived in Lawrence when it was a town of board walkways, mud roads, and community drinking cups. Disease was widespread; contaminated food was common,

The entire chemistry library consisted of 22 of his own books. As the only teacher in his department he had no assistance other than what the more advanced students were able to give. He taught a remarkable spread of subjects, including general chemistry, qualitative chemistry, quantitative chemistry, organic chemistry, assaying, mineralogy, metallurgy, blowpipe analysis, toxicology, physiological chemistry, and *materia medica*. In 1885, perhaps out of sheer enthusiasm, he added a course in domestic and sanitary chemistry. The University of Kansas thus became one of the first universities to offer a course in the practical applications of chemical principles to everyday life. This led to the establishment of the Department of Home Economics and to Bailey's writing one of the first textbooks in the field in 1914: *The Source, Chemistry and Use of Food Products* (7).

After the Federal Pure Food and Drug Act was passed in 1906, Bailey began to press for such an act in the state of Kansas. He sent the first food analysis to the State Board of Health in January 1906 (8), in which he reported that two-thirds of the food analyzed contained preservatives and adulterants. The report was copied

widely by the press and caused a sensation throughout the state. It was also met with opposition, especially from the owners of the packinghouses. For example, when sausages were examined and reported to be artificially colored and to contain a preservative, the attorney for the packinghouse complained to Governor Edward W. Hoch that the packing house was being ruined since people quit buying its sausages. Politicians and lawyers tried to bribe the Board of Health staff to look the other way when inspecting their meat products. In spite of the pressures, the governor supported the State Board of Health and, on the basis of previous work at the Chemistry Department, the Kansas Pure Food and Drug Act was passed on February 14, 1907 (9).

Enforcement of this law was placed in the hands of the State Board of Health which delegated the examination of foods and drugs to Julius T. Willard at the Kansas State Agricultural College in Manhattan and to Bailey at the University of Kansas Chemical Laboratory. The latter facility became known as the State Food Laboratory (10). Under the auspices of the state board, sectional meetings were held throughout the state for the purpose of educating everyone whose business related to the Kansas Pure Food and Drug Act. The committee chairing these meetings consisted of Bailey, Lucius E. Sayre of the Pharmacy Department at the University of Kansas, Willard, and Samuel J. Crumbine, the state health officer. During one of these meetings, Bailey listed the following examples of the most commonly adulterated foods in Kansas (11):

Flour bleached by an electrical process; sugar whitened with bluing; butter mixed with too much water; pickles hardened with alum; pure cider vinegar made of a malt substance and colored with burnt sugar; lemon extract made of diluted alcohol passed through the shadow of a lemon and colored with coal tar yellow; vanilla extract made of artificial substances, colored with burnt sugar and flavored with prune juice; spices from which the essential oils have been removed; meat that has been artificially preserved with sulphites and brightened in appearance; and tomato catsup artificially colored and preserved.

Keeping food safe was not an easy task, since manufacturers were trying to cut costs, often by slipping cheap substitutions into foods. To do its work, the State Food Laboratory purchased products to analyze. These products, their manufacturers, and the chemist's findings were listed in the newspapers. A report on the Primrose Extract of banana was typical (12):

Primrose Flavoring Extract of Banana, Manufacturing Department of Parkhurst-Davis Mercantile Com-

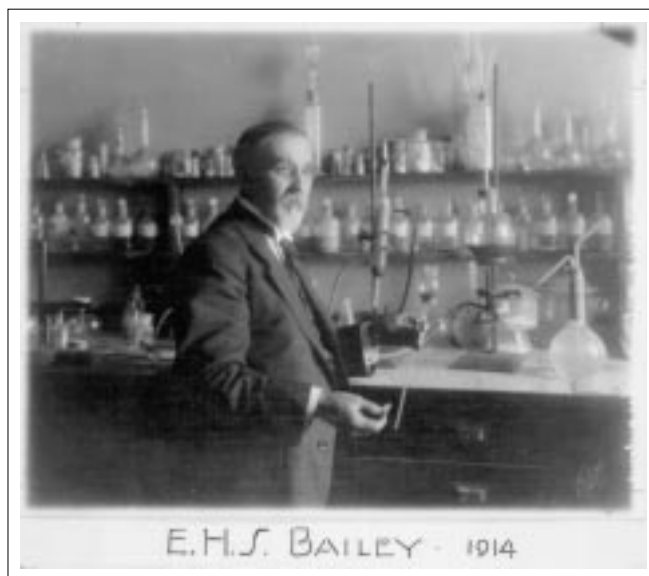
pany, Topeka, Kan. Amount contained in bottle, 50 grams, or 1.8 fluid ounces. This contained 28.6 per cent of alcohol, by weight; artificial flavoring, 16.5 per cent, by volume; coloring material, a coal-tar dye. As it is not practical to make a concentrated extract of banana, there seems to be no objection to the sale of an artificial preparation like this. It should not be labeled Extract of Banana, however, but Artificial Banana Flavoring. Compound ethers are very often used in making these so-called "pure-fruit flavors." The materials should be sold upon their merits and not under an assumed name, for there is usually no fruit used in their preparation.

Bailey's findings revealed many forms of adulteration. He found that copper had been added to canned vegetables to produce a natural-looking green color. A commercial sausage had a large amount of starch added to allow the use of more fat or water. Jams and jellies, made from treated cider mill refuse, proclaimed Bailey (13):

..had their compositions so exposed that if they had not been already as red as aniline colors could make them, they would have blushed to acknowledge that no fruit whatever had been used in their manufacture.

Lead chromate was put into lemon drops; burnt sienna, a mineral substance, was used to imitate chocolate; butter and cheese were colored to appear golden. Bailey hoped this practice of coloring food to make it attractive would be eliminated, saying, "A dyed food like a made-up complexion will cease to be admired (14)."

The State Food Laboratory also examined the purity of grains. Because the bleaching of flour could cover up many imperfections, Bailey suggested the public could avoid eating unwholesome or musty flour by us-



ing unbleached flour. The public's preference for white bread over dark bread dated back to the time when a cheaper bread was made from rye flour or badly milled wheat flour that was only bought by the poor. Because the bleached flour was white, it was thought to be pure. Instead of purifying the flour by bleaching with nitrogen dioxide, however, this process rendered the flour so antiseptic that it resisted the digestive juices and thus was unhealthy. The consumer now wants (15):

...nice, white bread to set before her guests. It doesn't matter that this flour is usually bleached by chemicals, just as much as your straw hat is bleached by sulfur fumes, and your sheeting is bleached by chloride of lime in the bleachery.

To make the public aware of these adulterations Bailey began publishing pamphlets and writing articles for the newspapers. One such pamphlet, "Some Simple Kitchen Tests to Detect the Adulteration of Foods," was distributed throughout the state. Anyone could perform these simple tests, and the pamphlet was popular with housewives who kept it handy in the kitchen drawer. He wrote articles in the *Topeka Daily Capital* under a column called "Sanitary Suggestions" with such titles as "What Water Shall We Drink?" and "The Art of Coloring Food (16)."

The size of cans and containers for foods was a concern handled by the State Food Laboratory. When a weights and measures law was passed in 1911, its enforcement was delegated to the State Board of Health. Bailey tried to teach people to be aware of both the content and weight of the food they bought (17):

Pound packages originally contained sixteen ounces, and quart cans held two pints; but the commercial conscience slept, and while it slept the thrifty manufacturer, in order to further increase his profits, trimmed off an ounce here, and half a gill there.

Food in state institutions was also under the jurisdiction of the State Board of Health, and often it was found to be of poor quality and lacking nutritional value. Since Bailey was chemist for the State Board of Health he tried to improve the situation by making dietary studies of such institutions as the Kansas State Penitentiary in Lansing, the State Industrial Reformatory in Hutchinson, the Osawatimie State Hospital, and the Girls' Industrial School in Beloit. He was also called upon from time to time to testify in court trials concerning poisons and drugs. At one such trial the defendant had supposedly disposed of his wife with poisoned chocolates. When Bailey declared the chocolates untainted, the judge asked where they were. Bailey replied that he had eaten them (18).

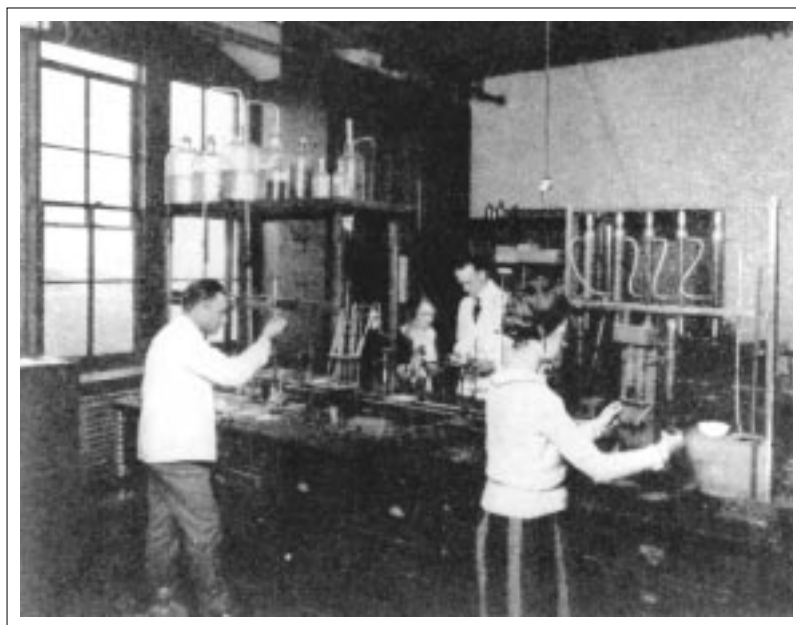
In addition to Bailey's work to protect the public from fraud and impure food, he was concerned about the state's water. When in 1889 the Kansas Legislature authorized The University of Kansas to undertake "a complete geological survey of such portions of the state of Kansas as have any natural products of economic importance," Bailey was an obvious leader for the resulting Kansas Geological Survey, in partnership with Erasmus Haworth (physical geology and mineralogy) and Samuel Williston (paleontology) (19). Between 1898 and 1908 this trio of scientists wrote *The University Geological Survey of Kansas*. This nine-volume work included their explorations on Kansas' paleontological sites, coal, gypsum, mineral waters, oil, gas, lead, and zinc. Bailey's primary contribution to this survey was an analysis of the state's mineral waters, which includes descriptions of and notes about the resorts, bath houses, and hotels built around the mineral springs. He described the Great Spirit Spring in Mitchell County that the Indians had always regarded as sacred. It was unusual in that it did not flow like a spring but rose from a mound of stone, seldom overflowing, and seeped back into the surrounding porous rock. He commented on the large bathhouse and hotel built in Geuda Springs where the Geuda Springs Town and Water Company bottled water for sale, along with lemon sour, ginger ale, and other carbonated beverages. He noted that the flow from one of the largest springs in the state at Sun Springs in Brown County was estimated to be 5,000 gallons an hour. He also mentioned the sanitarium at Bonner Springs, Wyandotte County built around the springs for the treatment of mental and nervous disorders (20). As the cities became more populated, the danger of infection from the wells by surface drainage increased. In a town on the Smoky Hill River it was suspected that a cesspool was polluting a well about 150 feet away. To determine whether this was correct, a solution of iron sulfate was put into the cesspool, and in about 48 hours the residents tasted the bitter iron. Chemical analysis of the well water proved that the users were drinking their neighbor's diluted sewage. Another example of this type of pollution occurred at the beet sugar plant in Garden City where the used pulp was thrown out on the ground and allowed to ferment and decompose. These instances prompted a warning from Bailey and Bartow (21):

Shallow wells or springs in densely populated areas or in loose, porous soil, or near a known source of pollution, should always be tested. To conclude that just because water is bright, clear and sparkling makes it safe to drink is dangerous because the very gases of decomposition may make the water look sparkly.



The mining industry was another cause of river pollution. An analysis of the run off waters showed large quantities of iron sulfate and sulfuric acid, which prevented the survival of fish (22).

The best source of drinking water, said Bailey, was a city water and sewage plant, where the whole quantity could be supervised carefully and analyzed frequently. The first such plant was built in Lawrence in 1886, with the Kansas (Kaw) River as its supply. Rainwaters falling off the roofs into cisterns or reservoirs were



Food Laboratory

recommended in the rural areas as safe if they were obtained from a well-painted shingle roof where the first run-off had been discarded so as to wash the roof thoroughly. But boiling water was the safest way to free it of contamination (23).

Southeastern Kansas and southwestern Missouri were of great economic importance because of their lead and zinc mines, which yielded in 1909 about 9% of the total lead output and almost 50% of the total zinc output of the United States. Bailey's chemistry department was an important location for the training of analysts and mineralogists for the coal and metal ore mining industries, as well as for the oil and gas industries. He carried out the first analysis of Kansas oil and natural gas, the forerunner of the helium industry (24). Hamilton Cady, who succeeded Bailey as head of the Chemistry Department, cited an example of his wide influence as a technologist in an address (25):

A shipment came [to the laboratories] from Utah of a peculiar mineral, alunite. This mineral, after being heated, would partly dissolve in water, and from the solution alum could be crystallized. Some years later, I saw an unusual mine operation in south-eastern Utah, and upon inquiring I found they were alunite mines, being worked by the same process Bailey had suggested. A Bailey industry way out there in Utah.

During the fifty years of Bailey's tenure at the University of Kansas (1883-1933), his students made important contributions to the development of the industrial resources of the state. Some went into the zinc and lead mining industries in the south-eastern part of the state. Others were employed by the gas, oil, and glass industries, as well as in the short-lived sorghum industry at Medicine Lodge, Topeka, Ottawa, and Fort Scott. The smelters, oil refineries, soap factories, and packing plants at Kansas City, St. Joseph, and Omaha hired many Kansas chemists. In this manner, chemists played an important role in improving the lives of Kansans. Bailey never wavered in his crusade to safeguard the public against impure and injurious foods and to protect them from the frauds of mislabeling and misbranding. He believed that the public's good health could be maintained through knowledge gained from the chemist's experiments, and he devoted his life to sharing this knowledge with the people of Kansas (26).

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6. Bailey's thesis was entitled "On Manganese, Including a Discussion of the Methods for its Graviometric and Volumetric Estimation." [Copies of the thesis are available from the author.] In 1874 Illinois Wesleyan University, Bloomington, IL, was the first school in the US to offer degrees of Bachelor of Arts, Bachelor of Philosophy, Master of Arts, and Doctor of Philosophy, in absentia. The program was patterned after the ones already in effect in several British Universities, Oxford, Cambridge, and University of London. The purpose was to fill an urgent and legitimate need on the part of many mature individuals throughout the United States who desired to further their education but were unable to leave their current employment. In 1882 when Professor Bailey received his doctoral degree, Prof. C. M. Moss was Dean of the College of Liberal Arts and also director of the nonresident work. Branches of this department were established in both Canada and England. A total of 750 students finished their degrees in this program between 1881 and 1890, reaching a high point in 1900/1901 when 478 were enrolled. Nonresident work was discontinued with the end of the school year in June 1910. E. H. Cates, "The History of Non-resident Courses at Illinois Wesleyan," *The Home Study Review*, Winter 1965, 16-20.
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## ABOUT THE AUTHOR

Carolyn Bailey Berneking, a native of Kansas City, MO, earned her master's degree in library science at Emporia State University, Emporia, KS. She researches topics in local history and is involved in local preservation activities. Since her retirement she has served as a volunteer in the University Archives, Kenneth Spencer Research Library, University of Kansas, Lawrence, KS. She is the granddaughter of E. H. S. Bailey.

## 1999 DEXTER AWARD

The Dexter Prize Committee of HIST has selected **Dr. Mary Jo Nye**, the Thomas Hart and Mary Jones Horning Professor of the Humanities and Professor of History at Oregon State University, as recipient of the **1999 Dexter Award for Outstanding Achievement in the History of Chemistry**. Professor Nye is the author of four books and more than three dozen articles on the history of chemistry and its interactions with physics. For 25 years she participated actively in the formation of leading undergraduate and graduate programs in history of science at the University of Oklahoma, and she served for three years as President of the History of Science Society. The award will be presented at a luncheon at the conclusion of the Dexter Award Symposium at the 219<sup>th</sup> National American Chemical Society meeting in the spring, 2000, in San Francisco.

## ***DIE EDELGEBORNE JUNGFER ALCHYMIA: THE FINAL STAGE OF EUROPEAN ALCHEMY***

*Vladimír Karpenko, Charles University, Czech Republic*

### **Introduction**

The term “alchemy” encompasses a broad spectrum of activities that appeared in the Hellenistic world in the first centuries of our era and then, through Arabic mediation, reached Latin Europe by the mid 12<sup>th</sup> century. Out of numerous attempts to define this science, that proposed by Sheppard (1) appears the most suitable because it includes the two main goals of alchemy: the enhancement of matter and the improvement of human existence. Concerning the former, it should be achieved by the transmutation of base metals into precious ones, while the second main direction strove for improvement of humans by extending their life, the further stage of which was seen as attaining a higher spiritual level. Sheppard’s definition marks off both extreme limits, encompassing everything that can be included in alchemy; in reality, the spectrum of various alchemical activities was a continuum, situated between both extremes.

Alchemists continued their efforts surprisingly long in Europe, in spite of the failure of alchemy to fulfill its promises. The ultimate decline is observed here as late as the 18<sup>th</sup> century, but scholarly works defending this science appeared even in the beginning of the following century (2). A statistical approach (3) to alchemical literature is revealing: at least two, if not three, marked flourishes of alchemy occurred between the introduction of book printing and 1800. One is apparent in the second half of the 16<sup>th</sup> century, the second one in the beginning of the 17<sup>th</sup> century and, eventually a third one

followed the Thirty Years War. German titles represent one third out of all alchemical books that appeared over the whole studied period (4). This is a witness of the live interest paid to alchemy in Central Europe; the majority of these books are still awaiting scholarly research.

Alchemical literature underwent gradual change, being at the beginning often theoretical explanations of the composition of matter and recipes for the preparation of philosopher’s stone, elixirs, etc. Yet none of these miracles was effected; no true transmutation of metals succeeded. An example of the fate of alchemical claims to cure all illnesses was their failure during epidemics of plague that broke out in Europe by the mid 14<sup>th</sup> century. As a result of this continuous series of failures, defenses of alchemy began to appear. Well-known are short testimonies of such recognized personalities as Helvetius or van Helmont (5), but even entire books were written with the same intent: to testify that transmutation is a real and feasible process. This kind of alchemical work, particularly common in the 17<sup>th</sup> and 18<sup>th</sup> centuries, can be roughly divided into two main groups. In the first, the author compiled important ideas from older sources, as did Kelley in his treatise (6), to mention a typical example. In the second, the author collected stories about successful transmutations to prove the truth of his claims, while also including a thorough and penetrating analysis of alchemy. The book *Die Edelgeborene Jungfer Alchymia* discussed in the present paper belongs to the second group. Familiar with arguments in opposition to alchemy, its author led a polemic against them;

thus, this book is not only a passive description of alleged successes, but an active explanation of alchemy as a science; hence, *Die Edelgeborne Jungfer Alchymia* is an extraordinary work in late European alchemy.

This book appeared in 1730, too late to exert significant influence on science in general and alchemy in particular. By then new chemical discoveries, including the first known chemical elements (cobalt, 1737/8; nickel, 1751), had changed the scene (7). Moreover, the relatively high number of alchemical books still in print at that time produced an informational noise in which *Die Edelgeborne Jungfer Alchymia* was lost (8). Yet this book of limited influence on the 18<sup>th</sup> century scientists is of interest to present scholars for the following reasons. It is an illustration of the state of late alchemy, written by a practicing, erudite alchemist. Some of his descriptions of experiments reflect doubts as to the possibility of transmutation, which had developed even among believers like himself. In defense of alchemy, key arguments of its opponents are summarized, and the attempts of the author to disprove them reflect the alchemical way of thinking. It is one of a large collection of alchemical stories. In the present work, important details of this book will be discussed within the broader framework of alchemy in general and its late European stage in particular.

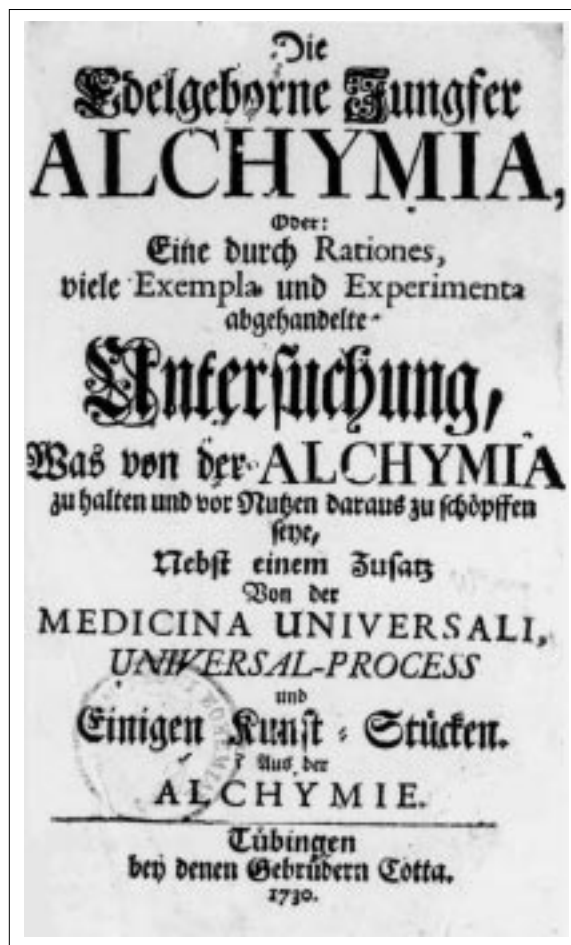
### The Book and the Author

The history of this book is quite extraordinary, and its origin is still not explained completely. Originally, there appeared an anonymous, 424-page book entitled *Die Edelgeborne Jungfer Alchymia* (9) [referred to hereafter as *Die Edelgeborne*], dated 1730. In this same year, the identical German text was published by Samuel

Roth-Scholz under a different title, *Ehren-Rettung der Alchemie* (10). Ferguson (11), analyzing the origin of this book, found yet a third, identical version from the same year, entitled *V.F.S.P. Edelgeborne Jungfer Alchymia* (12). Further searching led him to conclude that the author was J. C. Creiling (13), and that the manuscript which appeared simultaneously under three different titles was completed as early as 1717. The title page and list of contents were included in Roth-Scholz's *Bibliotheca Chemica*. In Ferguson's opinion, the title *Ehren-Rettung der Alchemie* must have been withdrawn or canceled almost immediately, because copies bearing this title are extremely rare. Creiling's authorship was confirmed by Frick (14), who rediscovered the manuscript mentioned by Roth-Scholz in the archives of Bochum, Germany. This manuscript had been presented to Carl Arnold Kortum (1745 - 1824) by Creiling's daughter-in-law in 1784. Kortum confirmed that it was that one which appeared as *Ehren-Rettung der Alchemie*. No explanation has been found as to why this book appeared under the name *Die Edelgeborne*, not

to mention its third title. According to Ferguson, all three books are identical.

Johann Konrad Creiling (born July 9, 1673, Löchgau, Württemberg; died September 13, 1752, Tübingen) was a talented son of a parish priest. He studied theology, history, anatomy, botany, and mathematics at the Tübingsche Seminarium, where he obtained the degree "eines Magisters der Weltweisheit" in 1692. He then pursued mathematics, studying in Basel with Bernoulli, in Paris with l'Hôpital and de la Hire, and with other scientists. Creiling then spent 44 years as a professor of natural science [Naturlehre] and geometry [Meßkunst] at the University of Tübingen. According to Kortum, Creiling was an extraordinarily learned man with a deep interest in "der Höheren Chemie," alchemy. He employed several assistants in his private laboratory,



Title page

and kept a detailed diary between 1737 and 1751, a resource Frick did not find in the Bochum archive. Ferguson also cites Creiling's further works on mathematics (15) and alchemy (16).

Creiling explains his reason for writing this book in the preface. As a young scholar studying nature, he came across processes concerning changes in metals. In his search for experts in this field he found some, but they turned out to be swindlers. Later he met "a doctor," almost 80 years old, said to be a "master," who accepted Creiling as his "filius artis;" but after fifteen years it became evident that he also was a fraudulent alchemist. Disappointed by this experience, Creiling decided to search independently for cases of successful transmutation and to study original alchemical literature. This narration is a classical alchemical story involving an anonymous master, who, having donated the philosopher's stone and presided over successful transmutations, disappeared, leaving no traces (17). Later, when the fortunate adept had used up his precious gift, he was at a loss because he did not know the recipe. An exceptional example is the attempt by the alchemist von Richthausen to solve this problem when he had depleted his supply of the tincture, allegedly received from a stranger. An announcement was officially published seeking the unknown master. Should the producer of this miraculous substance appear before the court of Austrian Emperor Ferdinand III (1608 - 1657), he was promised a reward of 100,000 thalers (18). Creiling's version of his study of alchemy is a typical account in which both mysterious teachers and impostors appear.

As is apparent from the second mentioned title of Creiling's book [*Die Ehren-Rettung*], it was written in defense of a science that "was given to people, as a gift from God and a celestial wisdom under the disdainful name alchemy." The intention to purge alchemy of its bad image apparently led the author to symbolize it as an innocent virgin. This symbol was widely used in alchemy: the assumption and coronation of the Virgin were understood as the glorification of matter (19); and, as pointed out by Gebelein (20), St. Mary was identified sometimes with Sophia, the personification of wisdom. Distillation, a process so crucial in alchemy, was given the sign of the Virgin (21). It may be significant that the word "alchemy," die Alchemie, is feminine in the German language.

## The Contents of the Book

*Die Edelgeborne* is divided into five chapters:

*I. Ob die Verwandlung der Metallen möglich seye?* (Whether a change of metals is possible?); pp 1 - 19). This chapter is devoted to the most common objections against alchemy. Their rejection by the author illustrates the typical argumentation of alchemists.

*II. Ob die Verwandlung der Metallen irgendwo würcklich geschehen?* (Whether a change of metals has really happened anywhere?); pp 20 - 306. Among the characteristic arguments alchemists used to defend their science were stories of alleged successful transmutations. Testimonials by renowned scholars were popular (5); but also various artifacts of precious metals, allegedly produced by transmutation, kept in cabinets of curiosities, were common in European castles since the Renaissance (22). The major part of *Die Edelgeborne* deals with stories of this kind. From the most widely known episodes are those about Helvetius [Johann Friedrich Schweitzer], Johann Böttger, Alexander Seton, Paracelsus, Nicolas Flamel, Arnald from Villanova, Albertus Magnus, Johann Kunckel, Basil Valentin, Robert Boyle, the Saxonian Elector Augustus and his wife Anna, and David Beuthers. Particular attention is paid to the Emperor Rudolf II and two outstanding figures of his time, Edward Kelley and John Dee; but even the impostor Domenico Manuel Caetano is included in this chapter. Baron von Chaos, Wenzel Seyler, Ramon Lully, and General Paykull are involved in accounts of coins or medals being struck from the alleged alchemical metal. Cited from Reyher (23) are cases of coinage from the cities of Erfurt, Mainz, and Gotha.

*III. Ob man einige experimenta habe, aus welchen die Möglichkeit der Verwandlung der Metallen kan abgenommen werden?* (Whether there are any experiments from which a possibility of change of metals can be deduced?); pp 307 - 349. Creiling, a practicing alchemist himself, cites some experiments from other sources; but more valuable are the comments based on his own observations. In expounding on his own view of the composition of matter, Creiling describes the state of alchemy in its final stage.

*IV. Was von der Medicina Universali, dem Auro potabili, u.d.g. zu halten seye?* (What should be thought of Medicina Universalis, Auro potabili, and the like?); pp 350 - 384). Creiling's discussion of the medicinal properties and the use of the "universal medicine," as he denoted the potable gold, is not quite clear; his inter-

est was primarily focused on the transmutation of metals.

V. *Ob die Alchymia jemanden, und besonders grossen Herren zu rathen seye?* (Whether Alchymia should be recommended to anybody, particularly to lords?); pp 385 - 396). For centuries, alchemy had been the domain of the aristocracy; only later did wealthy burghers participate. Here Creiling poses the general question of the position of alchemy in his time. This science, considered as *donum dei*, was supposed to be accessible solely to those chosen by God. At the end of the book two short descriptions of alchemical processes are given (24), followed by the list (25) enumerating allegedly successful acts performed through the art of alchemy.

### Creiling's Defense of Alchemy

It was a difficult task to defend alchemy in the first half of the 18<sup>th</sup> century, for strong arguments posed by its opponents had gradually prevailed by that time. Creiling chose to respond to five of the most common objections by opponents of this science that appeared with increasing frequency in the previous few centuries. Each of Creiling's arguments will be dealt with separately below.

The first objection against alchemy entertained by Creiling was the claim that different species created by God cannot be mutually changed. For example, the opponents say that an apple tree cannot be transformed into a cherry tree (26). Creiling's argument on this point is crucial, because it touches on the very basic tenet of alchemy: whether transmutation is indeed possible at all. In an effort to provide a convincing positive answer, alchemists had collected arguments for support of transmutation over centuries.

In the Hellenistic world (27, 28), it was believed that the Aristotelian elements, the supposed constituents of matter, could be mutually transformed by the change of one quality. Jabir (who will be considered the author of Jabirian corpus in this paper) defended a similar approach in his detailed explanation of the "inner" and "outer" qualities of metals (29). Theoretically, transmutation was thus considered a quite possible process, but this led to a second question: could everything indeed be mutually transformed, or are there certain limits? Along with this theoretical support alchemists needed practical proof that transmutation can be *achieved by humans*. Alchemical literature abounds in discussions

of transmutations effected by some external intervention, usually by a miraculous substance such as the philosopher's stone, elixir, etc. These examples pertained almost exclusively to metals. As stated by Al-Iraqi (active in the 13<sup>th</sup> cent. AD) (30):

We say and maintain that two species of natural things which differ radically and essentially cannot be changed and converted into the other by the Art, as, for example, man and the horse. But these six bodies can be mutually converted: thus lead may be converted into silver,..." [as the six bodies gold, silver, copper, iron, lead, and tin are enumerated in the preceding paragraph of the text].

While there was no doubt that the mutual change of metals occurred with an external agent, other chemical reactions which could be performed without any such agent were mistakenly understood as transmutations. The striking example of the reduction of metallic copper on the surface of iron from cupric solutions misled even as highly skilled a craftsman as Lazarus Ercker (1528/30 - 1594) (31). Another process that could have supported belief in transmutation was cupellation (32), because it could be misinterpreted as the change of a part of lead into silver. In Renaissance Europe, cupellation was already a very sensitive method to detect even small impurities in precious metals declared by some alchemists to be the purest preparation [for the methods of the alleged transmutation see Karpenko (33)]. Even more intriguing is the fact that alchemy attained one of its greatest efflorescences by that time: it is enough to remember the Rudolfian era in Bohemia (34). A seemingly unlimited possibility for the transmutation of metals was thus confirmed.

Later, however, doubts about transmutation arose from the realm of chemical reactions. For example, Alexander von Suchten (? 1520 - ? 1590) (35) excluded the possibility of transmutation of copper to gold, and lead to tin (36), but without explaining why. The erroneous explanation of valid observations led Robert Boyle (1627 - 1691) to the conclusion that there exist chemical reactions, such as the alloying of metals, in which the components forming a given substance remain unchanged, as, for example, when various metals are alloyed. On the other hand, he explained the synthesis of lead acetate as a transmutation, because it did not decompose into the original constituents in subsequent distillation (37). This approach to argumentation in favor of alchemy, based on gaps in contemporary chemical knowledge, persisted until the 19<sup>th</sup> century. An excellent example is given by Schmieder (38), who claimed that alchemists must not be misled by the argument their

opponents usually use: *Species in speciem non mutatur*. According to him the opponents say that it is unlikely that oxygen could be changed into carbon, and therefore, the same should be valid for the probability that lead or silver could become gold. In Schmieder's opinion, the fact that pure metals [regulinische Metalle] are not divisible [he means into their supposed elementary constituents] is nothing more than an assumption based solely on experience; but it is far from the truth (39):

The inability to decompose them [metals] does not mean the impossibility.

He further gives the argument that bodies belonging to one class have something in common. Acids, for example, extracted from plants all contain oxygen, carbon, and hydrogen. The proportion of these elements, and of possible additional elements, determine the resulting type of acid. Likewise, nobody doubts the chemical similarity in the family of metals, and thus there must be something common contained in them as well. It is, according to Schmieder (40), "Mercurius, or however we want to call it."

While the intervention of an external agent seemed to prevail in the transmutation of metals, quite a different kind of process could be invoked by nature. Even in ancient times, a belief existed that flies are born from fouling flesh, and this phenomenon entered alchemical literature as an example of transmutation. Latin Geber (41) writes that a strangled calf changes into bees and a dead dog into worms. Later, less extreme and thus more convincing examples were brought in as arguments, the most spectacular being van Helmont's (1577 - 1644) experiment with a willow tree, seemingly proof that water can be transmuted into wood (42). Boyle, who repeated the same experiment, but with a shorter duration, arrived at a somewhat less optimistic conclusion (43). Quite another kind of example of a change induced by nature appears in the treatise of Fabre (1588-1658) (44, 45). The author observes that for millennia people accepted as a matter of fact that all food and drinks taken into their bodies are transformed either into red human flesh or to blood of the same color. This, according to Fabre, supports the idea that a stone exists which is able to produce a red or white color in metals.

These second kinds of processes, induced by nature, were modeled from the observation of living matter, when no apparent external intervention of a mysterious substance was involved, unlike the transmutation of metals with the aid of the philosopher's stone. Yet the natural processes were less readily accepted, as ex-

emplified in Schmieder's words (46); he found it more surprising when apricots are found growing on a grafted plum tree than when metals are made more precious. In using natural phenomena to argue against transmutation, Nicolas Guibert (? 1547 - ? 1620) stated that various members, even of the same species, cannot be changed, either by nature or by art (47). He compared the disappearance of members of the animal and mineral kingdom, using as representative examples, respectively, a horse and the metal lead. The horse disappears through death, an irreversible process; conversely, the death of lead is its calcination, which is reversible because the metal can be recovered from its oxide.

From the above examples it can be seen that alchemists could defend their ideas by citing natural or externally induced transformations; and this is what Creiling actually did when he defended alchemy. In his comments (48), he stressed that the words "species" and "genus" are "school-words" [Schulwörter] that should be understood as technical terms only, not as symbols of limits of possible changes. When an animal, say a cow, feeds on grass, some amount of this grass is transformed into the flesh of this animal. There occurs thus a certain kind of transmutation. Because the differences between metals are much smaller than those between living things, the transmutation of metals should be easier, and therefore, quite a plausible process. The analogy with a cow is due to Fabre (45), although Creiling does not mention this author. Either he did not know Fabre's book, or else this kind of argument was so widely accepted among the contemporary alchemical community that he felt no need to cite a source.

Over the whole span of alchemy, divine influence was considered as playing an important, sometimes even crucial, role in this activity. Surprisingly, Creiling, as late as the first half of the 18<sup>th</sup> century, emphasizes strongly the religious aspects in the three remaining arguments in defense of alchemy.

The second objection addressed by Creiling is the observation that the alchemical literature contains many contradictory assertions concerning the possibility of transmutation. This literature indeed abounds with contradictions: the philosopher's stone is described by some as a solid substance, by others as a liquid; information about the duration of transmutation varied widely (from days to months); and statements on the technical details of the "Great Work" itself were often conflicting. While Creiling acknowledges the existence of discrepancies, he argues that there are discrepancies even in the words



of God in Scriptures and yet nobody doubts their truth. According to him the same is true with alchemy; in this science the discrepancies are only illusory, and there is one truth hidden behind them. Discrepancies and illegible segments in alchemical texts, dating from early times, is usually explained as an intentional device to limit use of the treatises to initiated readers, and purposely to make the texts inaccessible to outsiders. The Chinese Taoist scholar Ko Hung (approx. 280 - 340 AD) expressed this attitude quite clearly many centuries ago (49):

I therefore compose this book solely to inform connoisseurs.

Creiling does not comment on discrepancies as an intentional corruption of information but rather takes recourse in a unique religious argument, which seems outdated at the dawn of the European Enlightenment. According to him even the most sacred text is an example of confusion; but he pursues the idea no further. Shortly before Creiling, in his comments on the later edition (1725) of Fabre's book, Horlacher used the classical alchemical explanation (50):

...one has not to look at and to take notice of the recipe (or process), but of the secret meaning of the philosophical sentences of this teaching...

This was a typical approach used since Ko Hung's time; the potential adept has to search behind the letters of the text.

It was not an easy task to reject the third objection to alchemy: centuries of failures. According to nonbelievers, "this science has been nothing but a sweet dream." To counter this argument, Creiling repeats traditional claims of the alchemists but includes two conditions. First, none can learn alchemy alone but must be initiated by a Master of the Art, who can decipher the secret language. Here Creiling, who describes himself as a true alchemist, seemingly contradicts his claims from the introductory part of his book: namely, that, having revealed his teacher as a deceiver, he continued to study alone. This apparent contradiction is explained by the second condition: good fortune with the teacher alone does not guarantee eventual success, because alchemy is a gift of God. Thus, only God selects the people who will succeed in the Great Art. This motif of alchemy as *donum dei*, which appeared in the Hellenistic world, played an important role during the whole alchemical era (51). According to his own claims, Creiling ranked himself among those who had been selected by God, for he was able to succeed solely by studying books (52).

The fourth objection to alchemy is a religious one. Is it not a sin to perform alchemy? If indeed, according to Old Testament doctrine, *everything* created by God was good (53), any attempt to improve it could be looked upon as claiming oneself to be higher than God, or in other words, that God's work was not perfect. If, however, alchemy is seen as *donum dei*, to what extent are mortals allowed to use this divine gift, if at all? Intense religious alchemical views are given in Siebmacher's treatise. This author rejects the idea that alchemy could have been a sort of black art exercised by the powers of hell (54). He nevertheless warns that Satan, "that grim pseudo-alchemist" lies in wait; that only true faith in God leads to success. It is an obvious attempt to distance alchemy from everything that smacked of sorcery and black magic, at the time of the last wave of witch hunts in central Europe (55). Siebmacher even went so far as to identify the philosopher's stone with Jesus Christ (56):

We shall thus understand that the earthly philosophical Stone is the true image of the real, spiritual, and heavenly Stone Jesus Christ.

Creiling responds to this religious objection with a practical example (57). Would it be a sin if gold were made from iron, which, like other metals, is in itself already perfect because it serves people? His negative answer is justified by the creation of a yet more noble metal. He chooses two other examples which he describes as transmutations: the formation of beautiful red cinnabar from mercury and sulfur and creation of a deep blue color from black cobalt. Such processes are not sinful, according to Creiling, because nobody objects to them. He still regarded as transmutations the very same chemical processes that many of his contemporaries already explained as changes different from transmutation. In fact, it was the synthesis of cinnabar and production of other salts that eventually led researchers to the idea of a chemical compound. Yet Creiling rejects as transmutation attempts where alloys are made only to resemble gold, calling them "a common practice." The "true" alchemy is thus the real transmutation, the change of the substance.

The last point is not an objection against alchemy because it is based upon the *a priori* principle of the transmutation of metals. Rather it raises the question of the efficiency of alchemists over nature. While nature needs millennia to bring metals to full perfection, the alchemist claims to simulate in a laboratory the same metallic processes within a substantially shorter time, the length of a human life. The ancient conception of

ripening of metals in the bowels of earth (58) was reflected in the writings of as skilled an expert as Vannoccio Birunguccio (1480 - 1539), who, in his *Pirotechnia*, comments on the formation of antimony (59):

.....it might be a material that is about to reach metallic perfection, but is hindered from doing so by being mined too soon.

Georgius Agricola (1494 - 1555) writes in *De Re Metallica* in a similar way about the generation of metals by nature (60).

Creiling's comment on this point (61) is not quite convincing. While he stresses the necessity of artificial intervention, in this case by an alchemist, he carefully avoids the very basis of this objection: the acceleration of the human over the natural processes. He compares the intervention of an alchemist to that of a gardener, both striving to bring conditions to perfection faster than nature does. Creiling's rather reserved response may have reflected opposing opinions (62) which appeared in the 18<sup>th</sup> century. Common metals do form within the earth, but nature then leaves them in a form unchanged until the end ("until the end of the world") and "does not work them further into gold."

### Creiling's View of the Composition of Metals and of Transmutation

The composition of metals, indeed of matter in general, was a key question for alchemists, because they constructed their theories of transmutation on its answer. Three main theories were gradually proposed and worked out: the Aristotelian theory of four elements, the sulfur-mercury theory attributed to Arabic alchemists, and, eventually, the Paracelsian tria prima: mercury, sulfur, and salt [for details see Leicester (63)]. Over time, intertwined and more or less confused views developed in which the important role was attributed to mercury, as a rule in its vaguely characterized "philosophical" form and later, in the 17<sup>th</sup> century, also to antimony (64). Although significant progress in the chemical treatment of metals, especially in the production of their salts, developed from the 16<sup>th</sup> century onward, yet the absence of a consistent theory of the composition of metals led inevitably to two opposing explanations of these transformations. Either they were alchemical transmutations or some process other than transmutation. It was during this transitional period that Creiling wrote his book, and in his discussion he had to deal with the fundamental question of metallic composition. Perhaps

it is surprising that Creiling, an experienced and dedicated alchemist, does not propose any theory of his own but instead chooses among those already existing. He was attracted to authors who proposed the existence of a larger number of basic principles than the classical three or four in order to solve the misunderstanding of the nature of chemical reactions. Creiling writes in the introductory part of his Chapter III (65) that many alchemists are "blind" and do not understand anything about the real composition of metals. He recommends the work of Andrea de Solea (66) as a correct explanation. According to Solea the body of metals [Metallische Corpus] consisted of seven constituents: 1 earth [eine Erde], 2 stone [Stein], 3 earth-ashes [Erd-Asche], 4 earth-liquids [Erden-Flüsse], 5 glass of earth refuse [Glas des Erden Müll], 6 color of earth [die Erden-Farb], 7 soot of earth (der Erden-Ruß). After enumerating these constituents, Creiling continues (65):

...And when this Corpus, that is composed from these seven pieces, is brought by the smelter's hand from fragile state to the ductile of metal, it [metal] comes back to the hand of the alchemist, who decomposes it again in its Cinereum, Calicem, Laterem, Vitrum, Colorem, Fulginem, Subterraneas.

This sentence illustrates the status of late alchemists, who actually studied the reactivity of metals. They considered salts and oxides produced in these reactions to be the constituents present originally in metals. Creiling judged that the author who explained this "anatomia metallorum" in an excellent way was F. Clinge (67); therefore, he reproduces in full the passage on copper anatomy from that work, a set of chemical reactions that are difficult to characterize now because of the obscure language of the alchemists. These reactions led to eight alleged constituents of copper; the additional one to Solea's classification being the caput mortuum. Clinge, however, supposed that the true basic constituents of metals were solely the three Paracelsian principles. His classification of "anatomia veneris" was as follows: 1 soul [Anima], 2 terra benedicta of the soul, or the soul of Mercurius [der Anima Terra benedicta, nemlich die Anima oder Mercurius], 3 sulfur, or the other principle, 4 its earth-color that shows which dress sulfur carries concealed under its blue color [seine Erd=farbe, die da anzeigt, was vor Kleidung der Schwefel unter seiner blauen Farbe verborgen trage], 5 the earthglass-flux [das Erdglas-Flux], 6 soot of metals [den Metallen Ruß], 7 salt, or the third principle, 8 caput mortuum, or terra damnata. According to Clinge, there were three principles that actually comprise a metal, while the rest of the enumerated components were "excrementa." Their

number varied among different metals: gold was pure; it consisted solely of the three principles, while silver contained a bit of earth, and iron much more coarse earth.

In their attempts to save their science, alchemists could not ignore the similar works done by chemists, and Creiling was no exception. That he was also acquainted with contemporary trends in chemistry is shown in his comment (68):

At our time Becher has devised his Terras, and famous Mr Stahl explained them better than Becher could do, but the obscurity of principles (Principiorum) and confusion of names persist like before: some used to call Arsenic what others call Mercurium, the third [ones] Sulfur, the fourth [ones] Alumen Fumosum, or some call it even Sal Metallicum,... What, after all, depends on a name?

Creiling took Becher's terra pinguis to be only one further species among many "earths" that confused alchemists and chemists and thus did not warrant much attention. After Creiling describes at length this view of the composition of metals, the question remains as to what he actually understands metallic transmutation to be. In his words, he, as a true philosopher, does not care about the wrangle over words [Wort=gezänck] when alchemists try to describe transmutation because most of them know nothing about it. He gives this definition (69):

I understand under transmutation of metals nothing else, than an extraordinary gift from God, or the Art, through which one gets another [metal] instead of the [original] one, should it happen through the immediate change, or not, be this metal present before hidden in the other [metal], or be it through composition, or another transposition of particles [particulen], or coarctation and a change of Pororum, or [through] a violent action of a common substance, or a substance that penetrates metallic spirit, which [substance] can separate the heterogeneity and collect homogeneous [being], or even through the almighty miraculous hand of God, or in any known or unknown way.

In his polemic against opponents of alchemy, called here "philosophi," Creiling recommends (70):

Should these Herren Philosophi also creep once into those ore mines and try to pay a little attention to the way metals are growing, they would find with all [ores] a fatty mercurialish-metallic, I would say a goldish nature,....

He was convinced that the ability to ripen into gold was hidden in all metals as an *a priori* attribute of inherent "goldish nature." Transmutation was hence simply a process that served to enhance this ability.

Creiling's comment on the possibility of mutual changes of metals (Chapter III) is based on gilding by amalgam (71). Yet, as he notes, gilding is only a mechanical action that does not touch the interior of a metal. When, however, a metal is attenuated [attenuirt] through the action of Mercurium Physice (no detailed explanation of this process is given), then even a minute amount of the tincture can penetrate its pores [Poros]. According to Creiling, this tincture is nothing other than a purified and liquefied gold, attenuated through the action of mercury. This substance should then penetrate the "minimas atomos" of liquid metals like wax or oil and turn these metals into gold.

These comments of Creiling deserve particular attention because they are a reflection of corpuscular views that had already appeared in the works of the Latin Geber (72). The idea that some substance, by entering the pores of another substance, changes the latter into something new was to Creiling a process that could be compared with the coloring of white wine with a dark juice from red grapes. As Creiling points out, however, it could be objected that in this case the substance being changed was wine from the very beginning, unlike mercury, lead, tin, copper, or silver, which are not types of gold. Creiling counters this objection by the argument that all the enumerated substances are metals, just as wine is always wine, whether red or white. Thus, according to Creiling, the transmutation of metals is possible just as the conversion of white to red wine. At the same time, Creiling nevertheless rejects Becher's speculation that gilded silver wire when extended can be transmuted into gold. He explains that in this case it is only a mechanical action during which nothing enters the pores of silver and, therefore, no transmutation can occur.

### Creiling between Alchemy and Chemistry

From his writing Creiling appeared to vacillate between defending and doubting alchemy, a reflection of the state of matters in the 18<sup>th</sup> century, a period in which alchemy was still sufficiently strong to afford some convincing arguments in favor of transmutation. At the same time there was a growing number of observations that forced even such devoted alchemists as Creiling to "alter" or "adjust" their opinions. Several examples from Chapter III of *Die Edelgeborne* will be presented in more detail in order to shed light on Creiling's tenuous position between alchemy and chemistry.

Creiling (73) repeats the story noted by Morhof (74), according to which "through the action of a com-

mon sulfur, gold is extracted from copper, or it even ripens within copper." This story tells of an artisan who melted down one *zentner* [old unit; in Creiling's time usually 51 - 58 kg] of copper and added sulfur repeatedly to the molten metal in order to bring it to "ripeness." When he returned sometime later, he found ten ounces of the purest gold. Creiling accepts this story as proof of transmutation, but the account is actually second-, if not third-hand, perhaps being originally a real and reasonable method, namely the separation of metals with sulfur. As early as the 12<sup>th</sup> century Theophilus, in his treatise *On Divers Arts* (75), described a method to separate gold from silver by use of sulfur, which was to be added to the molten mixture of both metals "for the sulfur does not consume any of the gold, but only the silver..." Here, there is a metallurgical technique which could have been misinterpreted and eventually transformed into the account described by Creiling. Extraction of gold from silver with sulfur and a small amount of copper, described, for example, by Biringuccio (76), could well be the basis for another purported transmutation.

The second account in Chapter III illustrates Creiling's exact approach to experiments; it is based on his attempt to verify a supposed transmutation process he found elsewhere, the heating of cinnabar [HgS] with fine silver filings, as described in 1684 by Freiherr (Baron) Wilhelm von Schröder, who stood in high esteem in the German alchemical community (77). In spite of the obscure style, a reader can surmise that during the heating, a material sublimes and a black substance appears. The blackish substance, supposed to be cinnabar by Schröder, was apparently black Ag<sub>2</sub>S. As a certain amount of cinnabar decomposed, mercury sublimed. Von Schröder found the products of this reaction to be "peculiar," but nevertheless, he considered the process to be the transmutation of cinnabar into silver. The recipe gains importance by virtue of Creiling's commentary as a result of his own experimentation. Creiling, the firm believer in transmutation of metals, was sure that, contrary to von Schröder's opinion, no transmutation occurred in this particular case. He writes (78):

...some 20 years ago being curious I performed this last experiment and found that no transmutation of cinnabar is happening here (as is usually supposed, and Herr Schröder seems to cling to this opinion), but solely silver precipitates in the shape of cinnabar particles, and of the whole silver as much goes off as the little particles weigh, I will not keep it from an interested reader, but will faithfully remind so that nobody here can be deceived by it...

Creiling's experiment bore a feature of modern chemistry, a quantitative approach, less than half a century after Schröder's recipe. Creiling had happened upon a quantitative approach as is obvious from his statement "... as the little particles weigh..." and was convinced it was not transmutation, not the change of the essence of silver, as is expressed from his words that "*silver precipitates in the shape of cinnabar.*" In other words, no silver was lost. Creiling might have applied the same quantitative approach to other reactions as well and arrived at the general conclusion against transmutation. The time was not yet ripe for such discovery, however, and Creiling did not view this one exception sufficient to shatter his conviction. Creiling tried to explain the reaction of cinnabar by comparing it to that between iron and copper (II) sulfate, one of the pillars of alchemy, seemingly an unshakable proof of transmutation (79). Surprisingly, Creiling the fervent alchemist did not consider this crucial reaction to be transmutation, although he does not explain how he arrived at such a revolutionary conclusion. The first attempts to prove that this reaction is not transmutation appeared in the beginning of the 17<sup>th</sup> century, but they remained unnoticed (80). Even later, Boyle's explanation (81) of this process did not shatter the belief of loyal alchemists so that, for example, Horlacher (82) held firmly to the position that iron can be transmuted into copper. Nearly 70 years later, a treatise appeared dealing exclusively with vitriol; here, in the sixteenth experiment, this reaction is characterized correctly as the precipitation of copper on the surface of iron (83). Yet at about the same time Baron Tschoudy, in his *Alchemical Catechism* (84), wrote that "Mars can be easily converted into Venus" but "not Venus into Mars."

Further on in Chapter III (85) Creiling cites "an easy experiment" from Laurentius Meisner (86), which should convince any skeptic of the validity of alchemy. A mixture of galmei [ZnCO<sub>3</sub>], vitriol [CuSO<sub>4</sub>], and sulfur should be distilled and the "water" prepared in this way should be poured to "solutio Lunae." A black powder precipitated from this solution should produce gold when melted with borras [borax ?]. In this typical alchemical recipe, quite difficult to decipher, one can only speculate that the black powder is the highly insoluble Ag<sub>2</sub>S. Yet, the recipe continues: "Pour common water under the other water and throw a sheet of copper into it, whereupon a beautiful deposit of silver calx falls to the bottom; pour the water out, so thou hast thine silver again..." This text apparently describes the reduction of silver from its solution by metallic copper, as expected from the electrochemical potentials of the two metals.

Creiling writes that the deposited metal is silver, thus the “water” used for this second experiment was a part of “solutio Lunae.” The last sentence of this paragraph explains the aim of these experiments “.....quod Alchymia & Metallorum transmutatio sit ars verissima.” In contrast to Creiling’s conclusion that this is a transmutation, N. Guibert (47) carried out a similar experiment with the intention of disproving transmutation.

In another experiment (87) described by Creiling in Chapter III, he presents himself as a devout alchemist. When a mixture of Luna cornea [AgCl] and half its weight of sal ammoniac [NH<sub>4</sub>Cl] is sublimed, there is produced a light-yellow “flores,” a sublimate ascending to the top of the vessel and deposited there. When tapped at the top, these “flowers” fall into the melted luna cornea which turns immediately to “the most beautiful goldish color.” This is nothing more than the melting of silver chloride whose fused form, as “luna cornea” or “horn silver,” turns from a yellow substance into a transparent, viscous orange-yellow liquid (88). At most the addition of ammonium chloride to the dry substance might make the color less intense because of its own white color. According to Creiling, pure gold can be extracted from this luna cornea after its reduction, although he gives no details of this process and offers no quantitative data. Perhaps this experienced chemist considered the process to be transmutation because he isolated minute amounts of gold, present as impurity in his sample of luna cornea. He closes this paragraph with the telling words, “Yet, one has not to expect any profit of it, but only the exploration of truth and a stimulus to further philosophical observations.”

In Chapter IV of his book, Creiling discusses “medicina universalis (89).” He is willing to accept a substance as a “universal medicine” provided it removes everything harmful from the body and blood. He thinks, however, that there is not just one, but there may be many such medicines; and that such a medicine, contrary to the claim of Arnald from Villanova (90), can not cure all illnesses simultaneously. In Creiling’s opinion, significant differences between “universal medicines” exist; there is only one that cures and purifies metals from their imperfect state to the “health of gold” (Gesundheit des Goldes), but he doubts whether one medicine could exist which would act similarly on the human body, the reason being that, contrary to metals, scientists do not know the actual cause of human life or understand what keeps humans alive.

This last point shows Creiling to be a man who stood at the threshold between alchemy and chemistry and

apparently interested in iatrochemistry. Rather careful concerning the possibilities of universal medicine, he was of the opinion that, contrary to metals, the composition and function of the human body are not sufficiently understood. He could not suspect that the same was true for metals as well in his time.

## Conclusions

*Die Edelgeborne Jungfer Alchymia* belongs to those works that allow deeper insight into the final stage of European alchemy. In the closing chapter of his book, Creiling, a believer in alchemy, did not search for causes of its failures within alchemy itself. In his opinion, the cause was not in this science, but in the supposed results of alchemical activities, in promised material riches, and longevity. No wonder that anybody who knew the Art was not willing to reveal its secret to those not familiar with alchemy. Therefore, the only way was to study on one’s own and try to understand the secret of the Great Art; but whom will God enlighten that he will understand? A motif of alchemy as *donum dei* appears here once again and completes the circle. Can it be expected that anybody so enlightened, selected by God, would readily disclose this highest secret? Creiling’s answer is at once negative but contradictory, because he indeed discloses the secrets.

A further point to be stressed here is the question of experimental results and the disposition of products from the recipes he describes. Warning that no riches can be expected, only a deeper understanding of natural phenomena, he opines (91):

.....a journey to America has already helped many 100 people to great fortunes,... (while)...one should expect much less from one or other lucky effects, which he gets through alchemy...one lucky among 100,000 unlucky laborants [alchemists] can be counted.

This is a marked retreat from the position alchemy had occupied in the late European Renaissance, when alchemists were cautious in their promises and sought support from rich aristocracy. There is no longer danger in 1730, as there was three centuries before, when a Czech alchemist wrote (92):

.....beware thee of lords and of high [standing] people, lest thou shouldst not do anything [together] with them nor to rely upon their promises, because they upon seeing the immense work, nobody will do justice to thee, because who has a power, that has a law....

In Creiling's time, as he complains, not many wealthy people were willing to support alchemical studies, exceptions being those of Becher and Stahl. Creiling considered Becher's theory to be a partial work ["particular-Arbeit"] only, which did not explain the essence of the problem. The lack of rich supporters was for Creiling only one of the obstacles; the other was the lack of honest laborants [alchemists]. Although Creiling did not express it openly, he implies that alchemy has come around again to its beginning and that it was necessary to purge this science and return it to its former glory.

Not understanding fully all the changes in European science of his time, Creiling repeated several experiments from older sources but clung tenaciously to the alchemical idea of transmutation, even though he sometimes observed conflicting results. He never advanced to the idea of a chemical compound. Contradictory statements in his book are a reflection of doubts he felt. *Die Edelgeborne Jungfer Alchymia* documents how the deep roots of alchemy still persisted in Europe in the first half of the 18<sup>th</sup> century.



Medal struck by the Austrian Emperor Ferdinand III in 1648 from gold produced allegedly by the alchemist Richthausen (see Ref. 22)

## REFERENCES AND NOTES

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- In the present paper alchemical activities of the last 150 years will not be considered.
- <http://www.levity.com/alchemy/referlib.html>; here data about printed alchemical works are summarized.
- According to Ref. 3, out of the total 4,675 books listed there were 1,703 Latin (36%), and 1,667 German (36%) texts.
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- M. E. Weeks and H. M. Leicester, *Discovery of the Elements*, J. Chem. Educ., Easton PA, 7<sup>th</sup> ed., 1968, 148ff.
- According to the chart mentioned in Ref. 3, approximately 15 new titles appeared annually between 1725 and 1750.

9. *Die Edelgeborne Jungfer Alchymia*, oder: Eine durch Rationes, viele Exempla und Experimenta abgehandelte Untersuchung, Was von der Alchymia zu halten und vor Nutzen daraus zu schöpfen seye, Nebst einem Zusatz von der Medicina Universali, Universal-Process und einigen Kunst=Stücken aus der Alchymie. Tübingen bey denen Gebrüder Cotta. 1730.
10. *Ehren-Rettung der Alchymie*, oder Vernünftige Untersuchung, was von der herrlichen Gabe, welche die himmlische Weisheit denen Menschen geschencket, und insgemein mit dem verächtlichen Namen der Alchymie belegt wird, zu halten seye. Durch rationes, auch viele curiosa Exempla und Experimenta abgehandelt. Wobey noch von der Medicina Universali Meldung geschieht. Sammt einem Anhang des Universal-Processes zweyer alten wahrhafften Philosophorum, und kurtzer Consignation etlicher Kunst-Stücke aus der Alchymie. Nicht nur denen Liebhabern dieser edlen Wissenschaften, sondern auch allen andern, was Standes seyn mögen, nützlich und vergnüglich zu lesen. Ehedessen geschrieben von einem bekannten Philosopho. Nun aber auf vieler verlangen an Tag gegeben von einem Liebhaber der Chymie. Herrenstadt, bey Samuel Rothscoltzen, MDCCXXX.
11. J. Ferguson, *Bibliotheca Chemica*, J. Maclehose & Sons, Glasgow, 1906, Vol. I, 182-184.
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24. The first process (pp 396 - 406), written in French, is from the work [title not cited] of D. Zecaire (Zachaire) dated 1567, the second one (pp 407 - 416) in German is a process ascribed to Trevisanus.
25. This list begins: "The old philosophi wrote that it is not their work to make gold and silver, but to perform greater miracles..." These miracles are then described in 59 numbered sentences; the last one is as follows: "Minera perpetua, or to have a gold and silver mine on the oven, from which can be taken at any time *as required*, unceasingly, and without END." The last word END (ENDE) is in capital letters and denotes simultaneously the end of the whole book.
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31. *Beschreibung Allerfürnemsten Mineralischen Erzt unnd Berckwerksarten / wie dieselbigen / und eine jede in sonderheit / irer natur und eigenschafft nach / auff alle Metaln Probirt / und im kleinem feuer sollen versucht werden / mit erklerung etlicher fürnehmen nützlichen Schmelzwercken im grossen feuer / auch Schaidung Goldt / silber / und ander Metalln / sampt einem bericht des Kupffer saigens / Messing brennens / unnd Salpeter siedens / auch aller saltzigen Minerischen proben / und was denen allen anhengig in fünf Bücher verfast / Dergleichen zuvor niemals in Druck kommen. Allen liebhabern der Feuerkünst / jungen probirern und Berckleuten zu nutz / mit schönen Figuren oft abriß der Instrument / trewlich und fleissig an Tag geben. Durch Lazarus Ercker. Gedruckt zu Prag inn der Alten Stadt /*

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  36. Alexandri von Suchten/ Eines wahren Philosophi und der Arzneyen Doctoris Chymische Schrifften/ all/ so viel deren vorhanden/ Zum erstenmahl zusammen gedruckt/ mit sonderbahren Fleiß von vielen Druckfehlern gesäubert/ vermehret/ und in zwey Theile/ als die Teutschen und Lateinischen/ verfasst. Franckfurt am Mayn/ In Verlegung Georg Wolffs/ Buch. in Hamburg/ Druckts Johann Görlin. Anno MDCLXXX, p 281.
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  42. E. J. Holmyard, *Makers of Chemistry*, Oxford University Press, Oxford, 1953, 120.
  43. R. Boyle, *The Sceptical Chymist*, J.M.Dent & Sons, London, 1967, 65, 188; later Boyle found that van Helmont had done the same experiment earlier (p 67).
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  53. Genesis 1:31: "And God saw every thing that he had made, and, behold, it was very good."
  54. Wasserstein der Weysen, das ist, ein Chymisch Tractätlein, darin der weg gezeigt, die Materia genennet, vnd der Process beschrieben wird, zu dem hohen geheymnuss der Vniversal Tinctur zukommen, vor diesem niemalen gesehen. Darbey auch zwey sehr nützliche andere Büchlein der gleichformigkeit vnd Concordanz wegen angehenckt, Nemlich: I. Iohan von Mesung; II. Via veritatis der einigen warheit. Zum verschub in offenen truck gefertigt. Francofurti. Bey Lucas Jennis zu finden. Anno 1619. This book is also mentioned by Schmieder (Ref. 38, p 352). According to Ferguson (Ref. 11, p 383 ff) most historians agree that the author of this book was Johann Ambrosius Siebmacher (or Johann Antonio). He lived in Nürnberg and Augsburg around the beginning of the 17<sup>th</sup> century. His popular book appeared in further editions 1661, 1670, 1703, 1704, 1709, 1710, 1743, and 1760. Ferguson (p 385) mentions that Kopp quoted the 1736 edition under the letters J. S. N., perhaps meaning Johann Siebmacher Nürnbergensis. In the present paper Part IV, p. 12 of the text is cited from the internet translation: <http://www.levity.com./alchemy/hydrolit.html>.
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  59. *The Pirotechnia of Vannoccio Biringuccio*, transl. by C. S. Smith and M. T. Gnudi, Dover Publications, New York, 1990, 91.
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  61. Ref. 9, p16.



62. Der Hermetische Philosophus oder Haupt=Schlüssel Derer Zu der Chymie gehörigen Materien/ Ursprung/ und Herkommen aller Metallen und Mineralien, Johann Gabriel Grahl Buchhandlung, Frankfurt und Leipzig, 1709, 24.
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66. Although Creiling does not give the title of this work, it is obviously *Philosophische Grund-Sätze von Verbesserung der Metallen* which appeared, according to Ferguson (Ref. 11), as Part II of *Drey curieuse bishergantz geheim gehaltene nun aber denen Liebhabern der Kunst zum besten an das Tages-Licht gegebene Chymische Schrifften*, J. S. Strauss, Leipzig, 1723, Franckfurt am Mayn, 1733. Almost nothing is known about the author except that he published under the name Basil Valentin. Ferguson wrote his name Solea (Nicolaus), while in Christian Gottlieb Jöcher's *Allgemeines Gelehrten=Lexicon*, Leipzig, 1751, Theil IV, p 662, the name is Solea Andreas.
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76. Ref. 59, p 202.
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83. Anonymous, *Der Triumph=Wagen des Vitriol* oder Natur und kunstmäßige Beschreibung von der Generation, und Wundern dieses großen Subjects der Alchymie einem jeden eifrigen Forscher und Sucher dieser edlen Kunst zum Nutzen aufgeführt von E.L.D.K., bey Johann Georg Fleischer, Frankfurt und Leipzig, 1770, 45.
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85. Ref. 9, p 346.
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87. Ref. 9, p 344.
88. J. W. Mellor, *A Comprehensive Treatise on Inorganic and Theoretical Chemistry*, Longman, London, 1923, Vol. III, 391.
89. Ref. 9, p 357ff.
90. Ref. 21, p 123.
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## THE FIRST OIL WELL IN THE WORLD

*Fathi Habashi, Laval University*

In the recent article (1) entitled “The Art of Distillation and the Dawn of the Hydrocarbon Society” published in the *Bulletin for History of Chemistry*, the author states that Edwin L. Drake (1819-1880) drilled at Titusville, Pennsylvania a well that produced crude oil on August 27, 1859. “Thus the oil industry began as we know it today.” In this connection, the present writer would like to point out that the oil industry actually began one year earlier in 1858 when the Canadian entrepreneur James Miller Williams (1818-1890) (Fig. 1) drilled and successfully produced oil in the township of Enniskillen between Lake Erie and Lake Huron near the town later named Oil Springs in what is now Southwest Ontario. In 1857 Williams had begun looking for oil on the banks of the Thames River, at Bothwell. Unsuccessful, he moved to the gum beds of Enniskillen, Lambton County. On Black Creek, a tributary of the Sydenham River, he extracted oil, yielding 5 to 100 barrels of oil a day. When drilling was made 100 feet below the rock, the well produced 60 barrels a day. Williams built a simple refinery on the banks of Black Creek, and his operation, the J. M. Williams Company, was actually North America’s



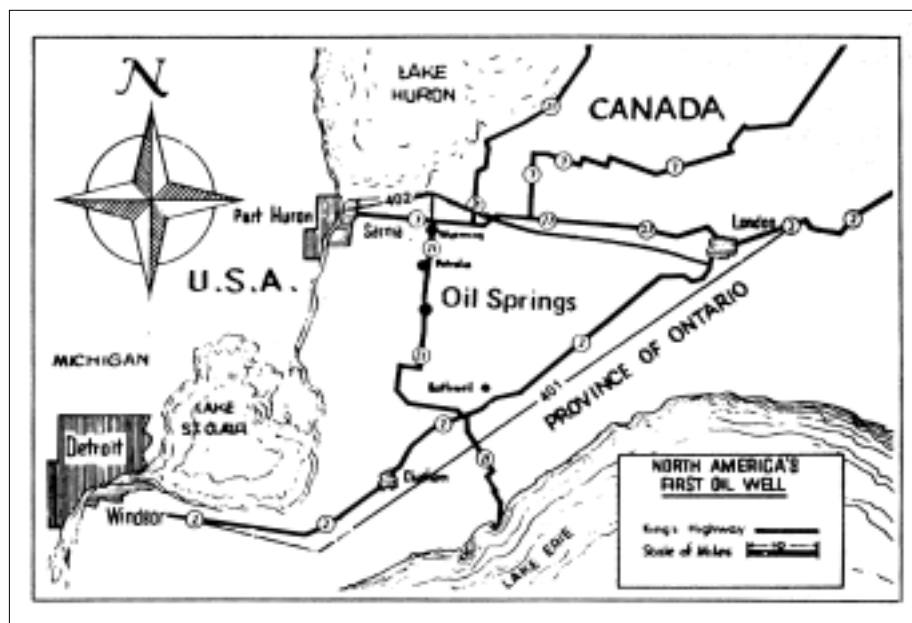
**Figure 1.** James Miller Williams (1818-1890) courtesy Oil Museum of Canada, Oil Springs, Ontario.

first oil company. In 1860 his company became known as the Canadian Oil Company. Nearly a hundred wells were drilled in the area, and production averaged 20 barrels a day. In 1860 James Williams moved his refinery to Hamilton where he carried on business until he died in 1890 (2).

Although Canada had launched North America’s first oil boom, developments in the United States were taking place that would eventually overshadow Canadian efforts. When Drake drilled a hole at Titusville and found oil at about 21 meters, he quickly took credit as being the “father” of the oil industry in North America. By 1860, the US was producing over thirty times the Canadian oil production.

### The “Gum Beds”

Even before Williams dug his well, the sticky crude oil called “gum beds” of the area caused by oil seepage near the creek had been refined into asphalt, paints, and resins by native peoples and had been reported by early French explorers. In fact, the world’s first oil company, the International Mining and Manufacturing Company, had received its charter



*Figure 2.* Location of North America's first oil well in Oil Springs, Ontario (near Sarnia). *Courtesy Oil Museum of Canada.*

from the Canadian Parliament in 1854 to produce asphalt, varnishes, burning fluids, and caulking materials for ships. Lack of transport for their products forced the owners to sell out to Williams, who took commercial development a step further by digging a well which produced 50 barrels of oil per day in 1858.

### Petrolia

A few kilometers north of Oil Springs is the small town of Petrolia, which in its heyday was the richest little town in Canada. Store shelves were stocked with exotic imports. Wealthy oilmen, builders, and merchants erected their fine mansions, an opera house, and a racing track. Oil field fires destroyed many early frame buildings. As a result fire stations were as important to the community as the oil derricks. The arrival of the Great Western Railway in 1858 and the commercial oil find at Oil Springs that same year led to dramatic growth of Sarnia. Refineries were built and oil arrived first by train and in 1865 by wagon. Refined and crude oil was shipped as far as London and Liverpool in England.

In 1862, at the height of the oil boom, Southwestern Ontario was called Canada West. A plank road was built linking the "Oil Capital of the World," Oil Springs, with Sarnia. Regular stage coach lines covered the 25 miles route four times a day. It was a toll road that al-

lowed crude oil to be transported to Sarnia and to refining centers beyond. Paved sections of the historic thoroughfare have become a principal route between Sarnia and central Lambton County.

The Oil Well Supply Company was founded in 1866 in Petrolia by Hector McKenzie, a machinist who later joined forces with a blacksmith James Joyce, to manufacture drill rings, special tools for the oil industry, as well as pumps and valves. Petrolia was also the seat of "Nitro" plants. Nitroglycerine was used to "shoot" oil wells to make them more productive. The detonation caused by the explosive would crack the oil-bearing formation and free more oil for production. The manufacture and transport of the liquid explosive constituted a dangerous business. All the "Nitro" plants eventually blew up.

Oil wells were pumped dry; demand changed from time to time, and outside competition hurt the domestic market. In addition, the economic depression in the 1870s greatly slowed down the regional petroleum industry. However, the slowdown in Canada was a boon to other countries. In 1874 the first contingent of Petrolia drillers left for Java, and others followed to Persia, Romania, Venezuela, Borneo, and Austria. They took with them their tools, blueprints, their expertise, and determination.

## Sarnia

New oil and gas deposits are being discovered each year throughout southwestern Ontario and out in the Great Lakes. At Sarnia, Canada's "Chemical Valley," are the most modern oil refineries, processing hundreds of thousands of barrels of oil daily and the many satellite plants processing its byproducts for thousands of uses. The Bushnell refinery, the first along the river, built in 1871, was later bought by Standard Oil and eventually became the site of Imperial Oil's modern refinery. Other heavy industry, including foundries and manufacturing plants, was located nearby. However, it was World War II that stimulated growth within the construction of petrochemical industries. The Japanese had cut off supplies of natural rubber from the Far East and the Allies needed a substitute. Polymer Corporation (now Polysa) was set up next door to Imperial Oil to produce synthetic rubber from Imperial's feedstock.

The oil drilling technology developed in these fields was exported worldwide by local drillers. Many of the original oil and refining companies are still located in nearby Sarnia. Approximately 400 wells still produce oil from the fields where the boom began over a hundred years ago. In the past 100 years, local wells have produced over 10 million barrels of oil. Experts believe that only a portion of the oil reserves has been tapped and that the potential for additional production exists.

## Biographical Note

Williams was born September 14, 1818 in Camden, New Jersey of Welsh parentage. He left school early and was apprenticed to a Camden carriage maker. In 1840 his family moved to London, upper Canada, when he was 22. In 1842 he married and began a carriage manufacturing business. In 1846 he moved to Hamilton and joined the Hamilton Coach Factory. When Williams sold his carriage interests in 1852, he served as a city alderman. In 1856 he again sold his business and bought the International Mining and Manufacturing Company. This operation, on property called Victoria and later known as Oil Springs, lasted for three or four years, but his interests were diverted when he began his quest for oil in 1857.

At the London Exhibition in 1862 Williams received two medals: one for being the first to produce crude oil and the second as the first to refine oils. In 1865-66, with a capital of \$50,000, the company increased its

employees and production. An advertisement listed the firm as manufacturing illuminating and machinery oil; and as wholesale dealers in benzine and coal oil lamps. Their celebrated product was "Victoria Oil." In 1867, he became Hamilton's first provincial representative at the Ontario Legislature, on a Liberal ticket. In 1870, the directory showed his office at 27 King Street West and a refinery on the eastern limits, with his son and James Cummings as partners. A year later, he appeared as president of the Canadian Carbon Oil Company and was elected to parliament.

On retirement from parliament in 1879 Williams was appointed Registrar for Wentworth, a post he held until his death. It appears that in 1880 he sold his oil interests in Hamilton and went into the metal stamping industry, one of the first to make stamped tin ware. He died on November 25, 1890, at age 72. He was buried in the Hamilton Cemetery, Lot 6, E3.

## REFERENCES AND NOTES

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## ABOUT THE AUTHOR

Fathi Habashi is Professor of Extractive Metallurgy, Department of Mining & Metallurgy, Laval University, Cité Universitaire, Québec, Canada G1K 7P4. Among his many publications are *A History of Metallurgy*, 1994; *Principles of Extractive Metallurgy*, 4 volumes, 1969-1998; and *Handbook of Extractive Metallurgy*, 4 volumes, 1997. He can be reached by e-mail: Fathi.Habashi@gmn.ulaval.ca

[See Saltzman's response, p 67.]

**AUTHOR SALTZMAN RESPONDS:**

December 6, 1999

I am grateful to Fathi Habashi for pointing out that the first oil well was not the one drilled by Edward Drake on Oil Creek near Titusville, Pennsylvania in 1859, as is the common perception. In writing this paper my major concern was with the role that chemistry played in the realization of this venture. Benjamin Silliman Jr., who provided the analyses of the oil seeps, showed that by fractional distillation a product equivalent to the kerosene then being made by destructive distillation of coal could be obtained. It must be remembered that by 1858 the kerosene for lighting was being produced in large quantities by the processes developed by the Canadian Abraham Gesner and the Scot James Young. The Canadian well produced so little crude oil that it gained modest significance as a source of kerosene. It is the vast amount of crude oil that was found in Pennsylvania that led to the decline of the coal oil industry and the rise of the extraction of oil as a major industry in the United States initially and very soon thereafter in other parts of the world. *Martin D. Saltzman, Professor of Natural Science, Providence College, Providence, RI 02918.*

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## BOOK REVIEWS

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*The Diffident Naturalist: Robert Boyle and the Experimental Philosophy.* Rose-Mary Sargent, University of Chicago Press, Chicago, IL, 1995. xi + 355 pp. Paper, \$26.

*Robert Boyle and the Limits of Reason.* Jan W. Wojcik, Cambridge University Press, Cambridge, 1997. xvi + 243 pp. Hardcover, \$59.95.

Recent years have seen a great revival in historical writing on Robert Boyle, the 17th-century Anglo-Irish nobleman's son best known for "Boyle's Law." He has been celebrated not only for his positive contributions to the early development of hydrostatics and chemistry, but for his advocacy of the experimental method. In his own day, learned men and women throughout Europe knew his name as one of the most thoughtful English proponents of the "new and experimental philosophy," making a visit to his laboratory an almost mandatory stop on their tours of England. Poor Boyle frequently had to entertain visitors, keeping him from the work to which he otherwise devoted every day but Sunday. He and his assistants accomplished enough, however, to make his name well known still; his *Sceptical Chymist* has been in print almost constantly since it was first published in 1661. Boyle has recently recaptured the interest of historians as a representative of the kind of science pursued by the so-called virtuosi. A virtual industry has come into being devoted to writing about the scientific world of Boyle's time as seen through the prism of his life and work, while at the same time Michael Hunter and others have been busy scrutinizing, cataloguing, and publishing his voluminous manuscript papers.

The works of Sargent and Wojcik were published before their authors were able to take advantage of the new information emerging from Boyle's papers, although they had glimpses of that new work, so their books rely mainly on his published works for evidence of his views. It is well known, and acknowledged by both authors, that Boyle took great care to present his polished pieces in a form that would give as little offense as possible, so his first thoughts and more risky hypothesizing seldom show up in his books. Moreover, his potentially explosive opinions about the medical establishment of his time remain mostly hidden from his readers, while he is virtually silent on anything closer to the centers of power. Both authors are well aware that Boyle's thoughts and his published words may not be identical. Nevertheless, as accounts of Boyle's public expressions, both books give us very balanced treatments, especially Sargent's.

Sargent attempts an overview of Boyle's intellectual world and the place of his thoughts within it, and as a result gives us the best general account of his ideas we have had in a generation or two. She divides her analysis into three parts. In the first, the background scene in philosophy, law, and experimentalism is painted in broad strokes but with enough color to make it interesting. Boyle's religious outlook—he famously took up his work as a "Christian virtuoso"—is given in more detail in the second part. The third section takes up his experimental endeavors. This last section will interest historians of science especially for Sargent's tempered but well-considered criticisms of other recent accounts of Boyle's scientific practices; such comments are enough so that readers who want simply to get a view of Boyle's outlook will likely not be distracted (although this re-

viewer found her several negative pronouncements about “contextualist” history irritating). All three sections find Sargent interpreting the words of Boyle and his predecessors with confidence and ease. She, like so many others, finds the center of his concerns to be in uncovering God’s creation so as to appreciate Him better through his works. Religiously and temperamentally, he always remained “diffident,” refraining from bold claims or generalizations announced to be certain. He was a humble experimental scientist, seeking the causes of things but remaining always prepared to reconsider hypotheses in the face of new evidence, which had to be gathered through persistent and patient investigation. Sargent’s final and most detailed examples—from Boyle’s investigations into the causes and consequences of cold temperatures—illustrate very well the way in which he struggled by experiment to stabilize and to make sense of the stunning variety of nature’s phenomena. Sargent has produced an impressive synthesis from Boyle’s best known published books and a few of his lesser known treatises, although whether it well represents his more private work and thoughts is yet to be seen.

The theme of Boyle as a person whose experimental science emerged from his theological concerns is developed further in Wojcik’s book. To the author, Boyle is best assessed as a lay theologian, whose early religious education and eclectic reading turned him away from full confidence in reason. Some parties, most notably the Socinians, argued that nothing in scripture contradicted human reason; others, such as Hobbes and Spinoza, developed rational systems that seemed to leave no place for God, at least once the world was created. The development of such doctrines led away from religious conflict, but also away from Christian trinitarianism and other basic tenets of faith. Boyle left a place in his heart and mind for mysteries beyond human comprehension—in this Wojcik agrees entirely with Sargent that he is well described as diffident. But Wojcik

goes farther. A seldom examined treatise of Boyle’s, *Things Above Reason* (1681), is the main text, supplemented with some of his other theological treatises. From such works, Wojcik finds Boyle to be one who had doubts about the ability of reason to appreciate fully the wonders of God and his works. Because of this, Boyle considered evidence about the world gathered through our senses and tested by considered experiments to be the only way that one could come close to truth about creation and its creator. In other words, the best path toward comprehensive religious knowledge lay through the senses rather than reason, coupled with an acknowledgment that what we learn of the material world depends on a spiritual power that can be only inferred. In limiting the powers of reason in this way, Boyle had to depend on probabilistic conclusions rather than ones that had complete certainty. His science was not that of a mathematical proof but of a close and exacting description of phenomena suggesting as many questions as answers.

Exactly what turned the young Boyle from moral philosophy and theology toward experimental science in the mid 1640s is something we may never fully understand from the extant record. Whether some line of thought or inner experience might have been enough to alter the focus of his work is open to question, as must be the issue of how much his science depended on his religious outlook. That he saw no contradiction between his experimentalism and his faith is quite clear, unless one wants to take the position that he protested too much. Both Sargent and Wojcik take him at his word, and that is probably best, at least until we know more from the manuscript sources. As clear and learned interpretations of Boyle’s public professions in favor of a virtuous experimental science, both books can be highly recommended. *Harold J. Cook, Departments of the History of Medicine and History of Science, University of Wisconsin, Madison, WI 53706-1510*

*Natural Dyestuffs and Industrial Culture in Europe, 1750-1880.* R. Fox and A. Niete-Galan, Ed., Science History Publications/USA, Canton, MA, 1999. xxix + 358 pp. \$49.95

It is a common misconception that there is little of interest to chemist historians concerning natural dyestuffs. To rectify this false perception, a workshop on natural dyestuffs history was held at Oriel College, Oxford, January 4-6, 1996, organized by Robert Fox, Professor of History of Science at Oxford University. Under the sponsorship of the European Science Foundation, a distinguished group gathered to discuss various aspects of natural dyestuffs. This volume contains eleven papers from the workshop and presents to the reader a comprehensive discussion of natural dyestuffs and the industry that developed around them.

These papers deal with the subjects from the perspectives of the history of science, the history of technology, economic history, and the history of art to produce an integrated study at many levels. These eleven papers are divided into four main subject areas. The first deals with the question of whether there is really any chemistry than can be associated with the natural dyestuffs. The second and third discuss questions concerning the role of geography, the markets and the skills of the workers in Europe exploiting natural dyes, and the role natural dyestuffs played in the development of the factory system. The final section deals with the decline of natural dyestuffs and the transition to the science-based synthetic dyestuff industry. From the perspective of the chemist historian, the most satisfying parts of this volume are the first and last sections. The papers in these sections will form the basis of this review.

Bernadette Bensaude-Vincent and Augusti Niete-Galan open the volume with a paper, "Theories of dyeing: a view on a long-standing controversy through the works of Jean-Francois Persoz." Persoz (1805-1868) was involved in many theoretical controversies concerning the dyeing action of natural colorants. A particularly vitriolic controversy occurred with Walter Crum (1796-1867), a Scottish calico printer. Beginning in the eighteenth century French chemists such as Charles-Francois Dufery, Pierre-Joseph Macquer, and Claude Louis Berthollet contributed several treatises on dyeing. Whether the mechanism of dyeing was mechanical or chemical in nature was at the heart of the various controversies. Macquer and Berthollet were the first to

discuss dyeing in terms of the 'new chemistry' with oxygen as the agent of the changes in color and chlorine as a new bleaching agent. Chemical affinity between the fabric, the dye, and the solvent was implied to be the reason for varying degrees of fixation of the dyes.

In 1846 Jean-Baptise Dumas published his views on the theory of dyeing, in which he proposed that there could not be an exclusively physical or chemical explanation. In this same year Jean-Francois Persoz presented his own ideas in a four-volume work, *Traite theoretique et pratique d'impression des tissus*. Persoz, a recognized expert on dyes, served in several official positions associated with the dye industry. As a chemist he was very much concerned with theoretical problems, especially molecular explanations. He viewed chemical reactions as the result of the rearrangement of atoms in a molecule. This put him on a collision course with Walter Crum, who had studied chemistry with Thomas Thomson at Glasgow. Crum succeeded Thomson in the chair of chemistry at Glasgow in 1852. Crum advocated a purely mechanical view that the dye penetrated the fiber, while Persoz took the view that it was deposited on the surface and a reaction then occurred. Crum argued that, since cotton could be dyed without destruction of the fiber, the process had to be more mechanical than chemical. Persoz insisted it was a chemical attraction between metal oxides in the fiber and the organic dye that was responsible for the coloring. Neither Persoz nor Crum was able to convince the other, but the controversy is important in that it allowed the dyeing problem to be reformulated on a new physico-chemical basis. Some of the details of the investigations that followed are discussed in this paper.

The papers by Gerard Empotz and Girolamo Ramunni in French, and hence less accessible to the general reader, round out this first section. Ramunni presents a discussion of the controversy among French chemists associated with the true coloring matter of the red natural dyestuff madder or Turkey red. In 1868, Carl Graebe and Carl Liebermann synthesized alizarin, thus establishing it as the key component of natural madder. Rumanni chronicles disputes over the mechanism of the natural dyeing process through a discussion of papers that appeared in *Annales de chimie et de physique*. The end result of this research did not produce a comprehensive answer, but it stimulated significant work that would later be useful.

In his paper, "Chimie des colorants et qualité des couleurs face au changement technique dans les années



1860,” Gerald Empotz discusses the contributions of Persoz, Michael-Eugene Chevrene, and Paul Schutzberger in the era that preceded the change to synthetic dyestuffs. These investigators were more interested in the use of chemistry to establish quality control than in the potential of chemistry to create new dyes. They were fearful for the most part that synthetic dyestuffs would decimate an industry that was associated with so much artisan skill. A general conclusion is that there may have been an attempt to use chemistry to explain the dyeing process but that there was no systematic science of natural dyestuffs.

The last three papers of the collection are of special interest to the chemist historian. Richard L. Hills presents a fascinating study, “James Watt and Bleaching.” Hills has studied Watt’s papers, which have only recently become available, to highlight this little known facet of Watt’s career. This is concerned with the development of a process to make chlorine in sufficient quantities and at a suitable price so that it could be used commercially for bleaching. Watt maintained a lifelong interest in chemistry and especially in its application to commercial ventures. In a visit to Paris in 1786, Watt learned of the bleaching power of chlorine from its discoverer Berthollet. Watt immediately recognized the possibility of chlorine as a replacement for other methods then being used to bleach cotton. Watt’s father-in-law James McGregor, who was in the textile business in Glasgow, became his partner in the venture. Hill’s paper describes Watt’s improvement of the Berthollet process for preparing chlorine and the development of the equipment to produce chlorine on a commercial scale. Our lack of awareness of this aspect of Watt’s career, according to Hills, stems from the secrecy in which Watt shrouded his operations to prevent their being copied and stolen. Others soon developed competing processes to make chlorine; this venture never afforded the rewards that the steam engine did for Watt, to whom must be given the long overdue credit for developing a chemical apparatus which could produce chlorine safely and easily.

Anthony Travis presents a case study of the transition from natural to synthetic dyes through a discussion

of the career of Heinrich Caro (1834-1910). Caro was unique in that he was a chemically trained textile colorist, whose early career in Germany was centered on natural dyestuffs and the calico printing industry and who made the transition to the new synthetic dyestuffs. In 1859, Caro left Germany to work at Rober, Dale & Co. in Manchester, the center of the textile industry in England. Initially Caro worked in natural dyestuffs, but by 1862 he was completely involved in the new coal tar-based aniline dyes discovered by Perkin in 1856. Over the next five years Caro participated in the discovery of novel dyestuffs and finding more efficient processes for products already on the market. He also did technical service work for his employer. Returning to Germany in 1866, he worked with Bunsen at Heidelberg for two years until he joined BASF. There Caro was instrumental in the development of azo dyes and synthetic indigo. The many contributions made by chemists such as Caro in producing new synthetic dyes and understanding their chemistry led to the gradual collapse of the natural dyestuffs industry in many parts of Europe by the 1880s.

Christian Simon, in “The transition from natural dyestuffs to synthetic dyestuffs: the case of Basel 1850-1940,” shows that natural dyestuffs were not as quickly replaced by synthetic materials as is generally assumed. His paper is a case study of the firm J. R. Geigy, which, from 1860-1940, operated two adjoining plants, one for natural and the other for synthetic dyes. According to Simon, there is an abundance of archival material to assess how these two coexisting ventures fared. The author presents a comprehensive history of the development of the Geigy Company and shows that there was a linkage between the natural and synthetic dyes at times and that they complemented each other for almost eighty years. By the 1940s natural dyes had essentially disappeared because their cost rendered them noncompetitive.

All the papers in this volume include extensive notes which offer the reader further opportunities to explore the subjects in greater detail. *Martin D. Saltzman, Providence College, Providence, RI 02918.*

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Articles of 4-12 pages, typed, double-spaced (excluding references) should be submitted as hard copy (2 copies) and also on diskette, preferably formatted in Word or Wordperfect, to **Editor, Bulletin for the History of Chemistry**, at the University of Michigan. Chemical formulas, to be kept to a minimum, should be computer-generated and printed on separate sheets, with a clear indication of their location in the ms. Authors are encouraged to provide photographs (black and white glossy prints) and drawings (black ink) to enhance the publication. Include a legend for photos, drawings, graphs and credits if appropriate. Diskettes, photographs, and drawings will be returned at the authors' request.

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