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Review article

THE ASCENSION OF WOMEN IN THE BIOMEDICAL SCIENCES DURING THE TWENTIETH CENTURY

USPON ŽENA U BIOMEDICINSKIM ZNANOSTIMA TIJEKOM DVADESETOG STOLJEĆA

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Summary

While scientists were always cognizant of the fact that they must be objective about the questions they ask of nature, there was a time when they were less willing to consider the diverse views that could be contributed by female participation. Undervalued in terms of their intellect, ambition, and curiosity, women found it difficult to compete for and/or retain a research post, particularly when they married. As a result, many women undaunted by existing convention had to work without remuneration or were financially supported by colleagues and/or relatives. But eventually, the time became right for a change in culture-bound attitudes. The present work revisits the inestimable accomplishments of five unique women in creating a positive environment for those scientists who have succeeded them.

Key words: *Women Biologists; Gerty Cori; Gertrude Elion; Marthe Vogt; Mary Pickford; Elinor Zaimis.*

Prologue

Scientists, like everyone else, harbor a set of beliefs and values which influence their work. Because research scientists and physicians contributed significantly to patriarchal ideology and placed constraints on women in the

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workplace during the first half of the twentieth century, women in science had to struggle against a patriarchal society that subjected them to a subordinate position and rejection to achieve their respective goals. Discouragement was also enhanced by the advent of the National Socialists in Germany who promulgated a view of science that was antithetical to objectivity. It was during this era that any woman who wished to pursue a career in research was faced with formidable obstacles. Fortunately, a few extraordinary women produced cracks in what had been a male club of research scientists by virtue of their extraordinary talents as research scientists.

Gerty Cori (1896-1957)

The first biographical sketch portrays the remarkable career of Gerty Cori (nee Radnitz), who became the first American woman to win the Nobel Prize in Physiology or Medicine despite several formidable obstacles encountered during her career.[1] Born in Prague in 1896 to an upper class Jewish family, Gerty received her early education at home. When her father was stricken with diabetes, he urged his daughter to become a physician in order to find a cure for the disease. However, it was her uncle, a Professor of Pediatrics at the University of Prague, who encouraged her to attend medical school, a place where she identified only a few other female students. World War I interrupted her education in 1916, while Gerty spent two years as an assistant at the medical school doing routine work. She eventually graduated from the medical school of the German University at Prague in 1920.

Gerty Cori (1896-1957)

[1] A portion of this biographical sketch is based on details of Gerty Cori's life and career in: Larner J. Gerty Theresa Cori; Biogr. Mem Natl. Acad. Sci. 1992; 61: 111-135. See also Cohn, M. Gerty Theresa Cori" A Comprehensive Historical Encyclopedia; Jewish Women's Archive; 1 March 2009. Whonamedit? Gerty Theresa Radnitz Cori. http://www.whonamedit.com/doctor.cfm/2189.html. (retrieved October 22, 2014).

Gerty, a woman of vitality and intelligence, became a constant companion of a fellow student, Carl Cori, during her first year of medical school in 1914. Gerty and Carl enjoyed outdoor activities and both had a strong interest in laboratory research. Gerty married Carl following graduation and then converted to Catholicism to assuage her husband's family, who feared that her Jewish background would jeopardize Carl's medical career. They subsequently accepted positions in Vienna and decided to pursue careers in medical research, rather than in clinical practice. They began a life-long research collaboration, publishing their first joint paper as students in 1920, which was an immunological study of serum complement.[2] This period encompassed troubled times in parts of Europe, including Austria, where economic depression and anti-Semitism were rampant. During 1921, Gerty worked as a member of the Pediatrics Department at Children's Hospital in Vienna where she carried out research involving temperature regulation in myxedema and developed as a research scientist. Meanwhile, Carl moved to the University of Graz, Austria, where he fulfilled his clinical responsibilities by carrying out laboratory analysis in the mornings and conducting research in the afternoons. It was while working in the clinic that Carl, observing the anti-Semitic behavior of his superior, plus the uncompromising prejudice against woman scientists, concluded that the existing environment was not a suitable one for Gerty. However, because of food shortages that existed in Austria, Gerty developed Vitamin A deficiency which forced her to return home to Prague.[3]

The political and economic upheaval that followed the defeat of the Austrians in World War I, as well as the lack of research funds, made career opportunities even more difficult. These factors prompted the Coris to seek opportunities outside of Europe. The Coris applied for positions overseas and even corresponded with the Dutch government to serve as doctors in Java (now Indonesia). Although Gerty was repeatedly warned that her continued collaboration with Carl might jeopardize his career, they were resolute in their desire to work together. In fact, Carl was offered faculty positions at

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2 Cori, K. und Radnitz G. Uber den gehalt des menschlichen an complement und normal amboceptor fur hammel blutkorperchen. Zeitschrift fur immunitatsforschung und Experimentelle Therapie. 1920: 29: 445.

3 American Chemical Society; National Chemical Landmarks. Carl and Gerty Cori and Carbohydrate Metabolism; 2004; pp. 1-16. Morrison, J. Mary Pickford: Pioneer of Endocrinology. In The Guardian; 27 August 2002. Silver, A. "Pickford (Lillian) Mary (1902-2002)". Oxford Dictionary of National Biography; Oxford University Press. (Jan. 2006). http://www.acs,org/content/acs/en/education/whatischemistry/landmarks/carbohydrate- metabolism,html (retrieved April 25, 2015).

several prestigious universities, but those institutions refused to hire Gerty. Fortunately, an opportunity arose that was the stepping stone for their remarkable careers. In 1921, Dr. Harvey Gaylord, who was Director of the New York State Institute for the Study of Malignant Diseases (now Roswell Park Cancer Institute) in Buffalo, New York, was touring Europe to recruit a scientist. This trip was prompted by Gaylord's astute realization that it was of prime importance to study cancer from a biochemical perspective. Furthermore, Gaylord was keenly aware that the best place to search for a top-notch biochemist was in Europe.[4]

Gaylord received excellent recommendations from European scientists about the young German-speaking Czech husband and wife team. As a result, in 1922 the Cori's received an offer to move to Buffalo, where Carl assumed a position as biochemist at Roswell Park Cancer Institute (RPCI). Fortunately, Gaylord also saw fit to offer Gerty a position as an Assistant Pathologist, and she emigrated six months later. At first, Gerty was responsible for microscopic diagnostic service, while Carl's duties focused on routine laboratory work for the hospital. The remainder of their time was spent on conducting research. Gerty and Carl readily adapted to their new environment and became naturalized citizens in 1928. Although they served on the staff of the first medical facility for dedicated cancer research and treatment in the United States, the Coris' major interest was not in cancer but in developing an understanding of how cells derive energy from carbohydrates. They combined these interests in 1928 with their groundbreaking report on carbohydrate metabolism in tumor cells, which influenced future research on the regulation of normal and abnormal cells.[5] Gerty continued to work in her husband's laboratory despite warnings to confine her duties to those in the pathology laboratory. She temporarily circumvented this problem by using only a single microscope to study the effect of thyroxin on the multiplication rate of *paramecium*. However, a year after their arrival, objections to their collaboration waned and by 1928 Gerty had permanently settled in Carl's laboratory as assistant biological chemist.

In the 1920's it was known that altered sugar metabolism could lead to diabetes and that insulin was able to counteract many effects of the disease. Since the underlying biochemical mechanisms involved with sugar

4 Mirand, E. Legacy and History of Roswell Park Cancer Institute (1898-1998); 2004; The Donning Company Publishers; Virginia Beach, Virginia. pp. 175-177. Mirand, E. Better Together. Nobel Laureates Drs. Carl and Gerty Cori were partners in life and research. Roswell Park Alumni News; Alumni Spotlight. 2011; pp. 4-5.

5 Mirand, E. Legacy and History of Roswell Park Cancer Institute (1898-1998). 2004; p. 175

regulation in the body were completely unknown, the Coris began their seminal investigations on carbohydrate metabolism. Their first joint report appeared in 1923, and during the next 12 years they produced more than 50 publications, most of them coauthored with primary authorship going to which one of them had done the bulk of the work. However, Gerty Cori also published eleven articles as sole author. Much more significant than the number of publications is that the work uncovered fundamental biochemical knowledge that is still relevant to this day and which all first year medical students learn.

The research accomplished by the Coris while at RPCI encompassed three major areas of research: (1) how glucose is stored in the liver as glycogen and metabolized when energy demands are high; (2) how this process is regulated by insulin and epinephrine; and (3) the identification and isolation of the enzymes involved in these processes. In 1929, the Coris proposed the theory that bears their names and later earned them a Nobel Prize. The discovery of the "Cori Cycle", which explains the utilization of energy by muscle and liver, stemmed from their work addressing the question as to what regulates blood glucose concentrations. The Cori cycle not only offered insight into how energy is utilized, but it also explained how hormones such as epinephrine influence the bioenergetics of this process by increasing the rate of conversion of glycogen to glucose, an effect reversed by insulin.[6]

Because RPCI was primarily an institution that focused on cancer research, the Coris considered moving to an institution where the scope of their research could be expanded. Another factor in their decision may have been the relative lack of research funds available. Several institutions offered Carl a position, but were unwilling to recruit Gerty. In 1931, a package deal was eventually provided that enabled the Coris to become equal partners in the laboratory. Carl was offered a research position at Washington University in St. Louis, which gratuitously included Gerty. Her salary was 10% of that offered to Carl. The gross disparity in salary existed even though, according to their son, Gerty was responsible for many of the original ideas. Nevertheless, the couple moved to St. Louis, where Carl became Chair of the Department of Pharmacology. University rules prohibited faculty appointments of two members of the same family, so Gerty was hired as a research fellow in Pharmacology. She worked for twelve years in this modest position

6 The details of the research carried out by the Coris can also be found in their Nobel Lecture of December 11, 1946, entitled "Polysaccharide Phosphorylase"; Elsevier Publishing Company, Amsterdam 1964. See also Reference 3.

until her husband was appointed Chair of the Biochemistry Department in the early 1940's. Gerty was then appointed Associate Professor of Research Biological Chemistry and Pharmacology in 1943, and was promoted to the rank of Professor of Biological Chemistry in 1947.[7]

It was at Washington University where each area of research initiated in Buffalo reached fruition. The investigations were broadly based in that they encompassed experiments *in vivo*, *in vitro* and later on isolated enzymes. In 1936, the Coris identified a key new phosphorylated intermediate in carbohydrate metabolism, glucose-1-phosphate. Gerty discovered that when energy is required, glycogen is converted to glucose-1-phosphate in muscle by a reaction catalyzed by the enzyme phosphorylase. Because the reaction was shown to be reversible, glycogen synthesis was successfully carried out *in vitro,* representing the first demonstration of the biosynthesis of a macromolecule in a test tube.[8] The success of these studies was a direct result of the development of precise analytical methods for the determination of glucose, glycogen, lactic acid, and inorganic and organic phosphates. Not only did this discovery provide further insight into how the carbohydrate cycle utilizes energy, it became extremely useful for understanding and treating diabetes mellitus. In addition, Gerty had long been interested in glycogen storage diseases. Now she was able to define the nature of glycogen storage diseases in children; one involving excessive amounts of glycogen, the other abnormally branched glycogen.[9] In 1947, the Coris were awarded the Nobel Prize "for their discovery of the course of the catalytic conversion of glycogen". Gerty Cori was not only the first American woman to be awarded the Nobel Prize in Physiology or Medicine, but the third woman world-wide; the previous recipients being Marie Curie and Irene Joliot-Curie.

Gerty Cori was the recipient of many other honors including: the Garvan Medal (1948), the St. Louis Award (1948), the Borden Award (1951) and an honorary Doctor of Science degree from Boston University (1948), Smith College (1949), Yale (1951), Columbia (1954) and Rochester (1955). In 1952, President Harry Truman named her to the National Science Board of the National Science Foundation. Gerty Cori was also honored by the release of a postage stamp in her name in 2008, which regrettably contained a printing error in the chemical formula of glucose-1-phosphate. In 2004, the American

7 Gerty T. Cori Papers. Bernard Becker Memorial Library Archives. Washington University School of Medicine. http://beckerarchives.wustl.edu/=collections/findingaid&id=8535&q=&rootcontenid=41.

8 Kornberg, A. Remembering Our Teachers. 2001 J. Biol. Chem. 276: 1-8.

9 Cori, G.T. 1953. Glycogen structure and enzyme deficiencies. Harvey Lectures 48: 145-171.

Chemical Society designated the research of Gerty and Carl Cori as a National Historic Chemical Landmark.[10] Her achievements are even more remarkable when it is realized that for many years she was marginalized in a non-tenure track research position at token salaries. Despite gender discrimination and nepotism rules, she never stopped pursuing her life-long interest in research and published nearly 150 articles.[11]

In addition to their accomplishments in research, Gerty and Carl Cori built a stimulating and vibrant working environment, which was considered one of the world's most prestigious centers for biochemical research.[12] The Coris' prodigious skills in elucidating mechanisms involved in carbohydrate metabolism attracted the most distinguished biochemists to St. Louis, including six Nobel Laureates: Severo Ochoa, Earl Sutherland, Arthur Kornberg, Christian DeDuve, Edwin Krebs, and Luis Leloir. Kornberg, in particular, used Coris' basic principles to discover the enzymatic mechanism of DNA synthesis. Later, he was integral in making discoveries which paved the way for gene cloning and much of molecular biology.

In 1947, while mountain climbing in Colorado, Gerty began to exhibit symptoms of a rare blood disease of the bone marrow called myelofibrosis.[13] However, despite severe pain, fatigue and multiple transfusions, she refused to curtail her laboratory activities and her work on the glycogen storage diseases continued for another ten years. Her courage and determination enabled Gerty to demonstrate that the diverse forms of the disease were characterized by a singular genetic error.[14] Gerty Cori's work in this area spawned a large number of studies on diseases of enzyme deficiency. But, this was to be her final contribution to science. On October 26, 1957, at the age of 61 she finally succumbed to renal failure.

Gerty Cori was characterized as a person with a sharp mind and a passion for science. She always expressed a strong work ethic, optimism, and a broad perspective in the pursuit of scientific knowledge. Her commitment to her

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10 National Chemical Historical Landmark; Carl and Gerty Cori and Carbohydrate Metabolism. 2004. American Chemical Society. http://www,acs,org/content/acs/en/education/whatischemistry/landmarks/carbohydratemetabolism'html.(accessed October 18, 2014).

11 Gerty Theresa Cori. Women in Medicine at Washington University School of Medicine; Becker Memorial Library. (http://beckerexhibits.wustl.edu/women/cori.htm (accessed October 28, 2014).

12 See Reference 8.

13 National Chemical Historical Landmark, 2004. p. 7.

14 Cori, G.T., Biochemical Aspects of Glycogen Deposition Disease. 1958. Bibliotheca Paediatrica 14: 344-358.

career can best be illustrated by the pronouncement that "the love for and the dedication to one's work seem to me to be the basis for happiness".[15] In her view, her scientific contributions were the result of her European education and the freedom and opportunities provided in the United States. As Arthur Kornberg noted in his tribute to the Coris, perhaps one could argue favorably that their monumental achievements deserve to be honored as much as the paladins of their era in politics, the military, and the arts.[16]

Gertrude Elion (1905-1998)

Gertrude Elion (1905-1998)

The next biographical sketch portrays the remarkable career of Gertrude Elion, another Nobel Laureate who was willing to endure repeated disappointments to ultimately achieve her life-long career goals to conduct biochemical research. Because her entry into research was preceded by unchallenging and non-paying jobs, the climb was steep; however, they did not deter Elion from accomplishing her ultimate objectives. The discrimination and disappointment that she endured in her quest to become a successful scientist set an example for anyone who aspires to a more challenging career.

Gertrude Elion was born in New York City; her father was a dentist and her mother a teacher.[17] A precocious student, Elion at 15 decided to major in chemistry after her grandfather died of cancer. She took advantage of the free education provided by Hunter College in New York City at the time to obtain an A.B. degree in Chemistry. After graduating from college in 1937, Elion was unable to continue her education because of financial difficulties created by the Great Depression. But, Elion was determined to progress in her education and within a year she generated sufficient funds to obtain a

15 Glories of the Human Mind by Gerty Cori. In Her Words. Women in the Health Sciences. Bernard Becker Medical Collection; Washington University School of Medicine. http:-becker exhibits.wustl.edu/mowihsp/words/Cori/Essay.htm (retrieved May 1, 2015).

16 See Reference 8.

17 Elion's early personal life is described in: Autobiography of Gertrude B. Elion. The Oncologist 2006: 11: 966-968; and in Avery, M.E. Gertrude B. Elion; A Biographical Memoir. National Academy of Sciences 2000: 78: pp. 17-29.

Master's Degree from New York University. Meanwhile, she also continued her quest to seek a more meaningful occupation. As a Chemistry major and a woman, she found it very difficult to find a job in science and so she took several positions, including serving as a receptionist and teaching high school students and nurses. Elion was also hired to test food products for the A&P grocery store chain, which she found repetitive and unstimulating.

Prior to the golden age of pharmacology that existed in the United Kingdom during the 1930's, pharmacology was considered a second tier biomedical science. The development of new drugs was a consequence of arduous trial-and-error and the element of chance, rather than rational design. The discovery of the sulfonamides as chemotherapeutic antimicrobial agents by Gerhard Domagk in 1935 was a direct consequence of screening a large number of diverse substances before sulfonamide containing dyes were synthesized by chemists at I.G. Farben in Germany. *Prontosil* was ultimately found to be the most effective of these dyes in protecting mice from a lethal dose of *H. streptococci*.[18] Domagk's development of sulfa drugs led Hitchings to believe that other substances that interfered with microbial metabolism could be employed as therapeutic agents.

In 1940, a biochemist named Donald Woods presented data favoring the possibility that sulfa drugs could arrest bacterial growth by acting as an anti-metabolite. The hypothesis that other anti-bacterial agents acted in a similar manner was subsequently proposed by a colleague, Paul Fildes. Elion and Hitchings decided to incorporate the Woods-Fildes theory into a template facilitating the transition of anti-metabolites from the laboratory to the clinic.[19] But, this would prove to be a prodigious task since only meagre biochemical evidence was available to aid in interpreting any experimental results. Nevertheless, Hitchings made the critical insightful decision to target nucleic acids (DNA and RNA) and seek differences in the acid metabolism among normal, cancer, bacterial and viral cells. Extending research into this previously unexplored area appeared to be a rational way to develop drugs that could differentially block the growth of cancer cells and microorganisms. This rationale would form the basis for developing new drugs against a variety of diseases and revolutionize the field of drug development.

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18 Rubin, R.P. 2007: A Brief History of Great Discoveries in Pharmacology. Pharmacol. Rev. 59: 315-318.

19 Lesch, J.E. The First Miracle Drugs. How the Sulfa Drugs Transformed Medicine; 2007; Oxford University Press, U.K., pp. 256-266.

Viewing drug discovery from a rational perspective, rather than by trial-and-error, Elion and Hitchings postulated that because normal cells rely upon the diet to replenish the body's supply, folic acid synthesis might be preferentially inhibited to advantage in neoplastic and bacterial cells.[20] The concept of differentially interfering with DNA biosynthesis would form the basis of understanding antimetabolites as antineoplastic and immunosuppressive agents. However, at the time, little was known about nucleic acid biosynthesis or the enzymes involved in this process. Although Elion was unfamiliar with purines or pyrimidines, she was given the task of investigating the purines, including adenine and guanine, which are two of DNA's building blocks. After spending time in the library to uncover what was known about purine metabolism, Elion began testing whether any compounds were biologically active. She employed an assay system that Hitchings and Elvira Falco had developed. This assay employed *Lactobacillus casei*, which could grow in a mixture of thymine and purine, as well as synthesize purines, if provided with folic acid. In 1948, Elion discovered that bacterial cells required certain purines in order to make DNA.[21] This finding led to the seminal hypothesis that if the incorporation of purines into bacterial cells could be interrupted by drugs, then the inhibition of nucleic acid synthesis and the suppression of bacterial growth might be expected as a consequence. This groundbreaking approach, if successful, would encourage new lines of experimentation and thereby develop new and more effective medications.

Elion then began to utilize her talents as a chemist by developing structural analogues to block DNA production and thus interfere with cell growth. Using the *L. casei* assay system, Elion established that 2,6-diaminopurine inhibited bacterial growth which was specifically reversed by adenine. Although 2,6-diaminopurine proved pharmacologically active, it produced severe side effects which precluded its use in therapy. Undaunted by this setback, Elion went on to discover that the substitution of oxygen by sulfur at the 6-position of guanine and hypoxanthine produced effective inhibitors of purine metabolism. Two of these compounds, 6-*mercaptopurine (6-MP)* and

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20 Chemical Heritage Foundation. George Hitchings and Gertrude Elion. http://www.chemheritage.org/discover/online-resources/chemistry-in-history/themes/pharmaceuticals/restoring-and-regulating-the-bodys-biochemistry/hitchings--elion.aspx. Hall L.C. A life-saving team: Gertrude Elion and Dr. George Hitchings; North Carolina Museum of History; Office of Archives and History. 2007.

21 Koenig, R. The Legacy of Great Science: The Work of Nobel Laureate Gertrude Elion Lives On. The Oncologist (Milestones in Oncology) 2006: 961-965.

6-thioguanine, displayed significant activity against a wide variety of tumors and leukemias when tested at the Sloan-Kettering Institute.[22]

Gertrude Elion was only 32 years old when she synthesized 6-MP and 6-thioguanine, two drugs that revolutionized the treatment of leukemia. As a consequence of her efforts, children stricken with this disease showed a remission in their symptoms when 6-MP was used in combination with other drugs. The importance of this discovery is underscored by the fact that the Food and Drug Administration approved its use 10 months after the clinical trials began and before all of the data defining its effectiveness became available.[23]

Although Elion began taking courses as a doctoral student, she would be required to spend one full year as a student at Brooklyn Polytechnical Institute. However, recognizing her innate talents as a researcher, Hitchings argued that Elion would not need an advanced degree to carry out her investigations and advised her against continuing the matriculation. So, Gertrude Elion became one of the few Nobel Laureates who never obtained a doctoral degree.[24] Even without an advanced degree, Elion was recognized for her accomplishments. She was elected to the prestigious National Academy of Sciences and awarded honorary degrees from several prestigious universities, including an honorary doctor of science degree from Harvard University. Because Elion achieved at the highest level, and her status as a first-rate scientist was never in question, she never expressed any misgivings about not obtaining a Ph.D. degree.

In early 1970, a decision was made by Burroughs Wellcome to move to Research Triangle Park in North Carolina. Here research output did not diminish, but turned to the development of antiviral agents.[25] Although, at the time, vaccination was the only approach to treating viral diseases, pioneering research projects involving antivirals were avoided because of the sup-

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22 "Physiology or Medicine 1988- Press Release" *Nobelprize.org.* Nobel Media AB 2013. Web. 23 May 2014. http//www.nobelprize.org/nobel_prizes/medicine/laureates/1988/press.htm]; See also Koenig, R. The Legacy of Great Science: The Work of Nobel Laureate Gertrude Elion Lives on The Oncologist (Milestones in Oncology) 2006: 11: 961-965.

23 Turney, J. National drug design: Gertrude Elion and George Hitchings. Wellcome Trust. http://welcome.ac.uk/About-us/75th-anniversary/WTVM051718.htm (retrieved May 25, 2015). Moran, L. Sandwalk: Strolling with a skeptical biochemist; pp. 1-12. http://sandwalk.blogspot.com/2008/11/nobel-laureates-george-hichings-html (retrieved April 28, 2015).

24 Autobiography of Gertrude G. Elion. The Nobel Prize in Physiology or Medicine. The Oncologist. 2006: 11: pg. 961-965. Avery, M.E. Biograph. Mem. 2000: 78: p. 21.

25 Elion, G.B. The purine path to chemotherapy. Science 1989: 244: 41-48.

position that any compound capable of suppressing viral infections would be extremely toxic. Nevertheless, a*cyclovir*, a drug synthesized by Howard Schaefer, was thoroughly investigated by Elion. She showed that this drug was not virucidal, but interfered with viral replication. Acyclovir is still the treatment of choice in several types of *Herpes simplex* and V*aricella zoster* infections.

In 1965, Elion attempted to improve the properties of 6-MP by using sulfur-substituted compounds.[26] Her discovery of *azathioprine, which* replaced 6-MP as an inhibitor of the immune response, enabled kidney transplantation to become a reality. Elion was also responsible for the introduction of *allopurinol* into the pharmacological armamentarium. Originally screened as a possible antineoplastic drug, *allopurinol* elicited an increase in the effectiveness of 6-MP by inhibiting its oxidative metabolism. Unfortunately, this drug produced a proportional increase i*n* the toxicity of 6-MP. But, since xanthine oxidase catalyzes the conversion of hypoxanthine and xanthine to uric acid, as well as the oxidation of 6-MP, *allopurinol* proved to be an effective agent in the treatment of hyperuricemia (gout).[26]

Elion's overwhelming success facilitated her gradual rise through the ranks until she became Head of the Department of Experimental Therapy in 1967. At the time, Elion was probably the only woman to hold a top-

ranking position in a major pharmaceutical firm. Despite the fact that the Nobel Prize Committee rarely honors scientists who develop new drugs, in 1988 Gertrude Elion and George Hitchings were awarded the Nobel Prize for designing new and effective therapeutic agents.[27] The simple moral of the story of Gertrude Elion is that sufficient determination and commitment help greatly to clear the path to success.

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26 Elion, G.B. The purine path to chemotherapy. Science 1989.

27 Moran L A. 1988. Nobel Laureates: George Hitchings and Gertrude Elion. The Nobel Prize in Physiology or Medicine, In: Sandwalk: Strolling with a skeptical biochemist; pp. 1-12. http://sandwalk.blogspot.com/2008/11/nobel-laureates-george-hichings-html (retrieved April 28, 2015).

Marthe Vogt (1903-2003)

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From the beginning of her life, Marthe Vogt was greatly influenced by a strong scientific environment. Born in Berlin, Vogt's parents were well-known neuroanatomists who associated with noted intellectuals of the time and welcomed educational endeavors and debate of issues. Early on, Vogt displayed a predilection for educational pursuits, becoming multilingual and ultimately graduating from Berlin University with both a medical degree and a doctorate in Chemistry. These accomplishments were an extreme rarity for women at the time. She subsequently worked without pay at the Institute of Pharmacology in Berlin in the laboratory of Paul Trendelenburg, where she met another researcher who would achieve international fame, Edith Bulbring. Vogt's prodigious talents did not go unnoticed. By the early 1930's, she became an established pharmacologist and by 1935 became head of the Chemical Division of the Kaiser Wilhelm Institute in Berlin.[28]

During the Nazi purge of the 1930's, a wide range of attitudes towards the National Socialist government were expressed by non-Jewish scientists, ranging from fanatical following, blind obedience, muted indifference, and expressed opposition. Although not of Jewish heritage, Vogt was one of the few who was outspoken in her disdain for the Nazis. After reading Hitler's biography *Mein Kampf*, she realized that scientific progress in her country would be suppressed by dogma, politics, and intolerance, and so she took a strong stand against her government. But it eventually became obvious to Vogt that she would have to leave Germany to continue her work.[29]

Respect for higher education had traditionally played a major role in German culture, and during the late 19th and early 20th centuries, the Germans had been the clear leaders of the scientific world. It was not until

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28 Greenfield, S. Marthe Louise Vogt FRS (1903-2003); In: Bindman, L. Brading A., and Tansey, T. Women Physiologists; London, Portland Press; 1993, p. 49-50.

29 Cuthbert, A.W. Marthe Louise Vogt. 8 September 1903-9 September 2003. Elected FRS 1952. Biogr. Mem. Fell. R. Soc. 2003: 51: 412-413.

the 1930's with the advent of Adolf Hitler and the National Socialists that the United States and United Kingdom took its place when theoretical science became inexorably displaced by political issues. Jews were not alone in leaving Germany. Many Aryan scientists departed because of political reasons or because they wished to pursue science unhindered by governmental influence. Marthe Vogt was one such individual.[30] In 1935, she left Germany with a Rockefeller Travelling Fellowship that enabled her to work at the National Institute for Medical Research in London under the eminent Sir Henry Dale.

Like many expatriots, Vogt made her most important contributions in the UK in the area of neuropharmacology. Her work focused on the topography of the brain and the role of catecholamines in animal behavior. Initially, she collaborated with Henry Dale, publishing a classical paper on the release of acetylcholine at the neuromuscular junction.[31] The team of which Vogt was a key member proved conclusively that nerves arising from the spinal cord released acetylcholine causing skeletal muscles to contract. This groundbreaking work literally defined the physiological basis of movement.

Vogt had the courage and tenacity to also undertake studies of the brain even though the techniques and instrumentation required were very rudimentary. Together with Wilhelm Feldberg, Vogt provided presumptive evidence that acetylcholine was a central neurotransmitter by measuring small amounts of choline acetyltransferase, the enzyme that catalyzes the synthesis of the neurotransmitter.[32] By helping to establish a role for acetylcholine in the central nervous system, Vogt's work not only cemented her reputation as a leading pharmacologist, but also set the stage for the rational design of drugs to combat diseases such as Parkinson's disease, schizophrenia, and depression.

Not satisfied with her accomplishments in defining a central role for acetylcholine, in a paper published in 1949, Vogt collaborated with John Gaddum to devise a series of tests to distinguish various sympathomimetic amines (particularly norepinephrine and epinephrine) in blood. [33] Her commitment to detail was exemplified in this study by establishing a set of eight bioassays which could be distinguished from one another by parallel

30 Cuthbert A.W. Biogr. Mem. Fell. R. Soc. 2003.

31 Dale, H.H., Feldberg, W. and Vogt, M. Release of acetylcholine at voluntary nerve endings. J. Physiol. 1936; 86: 353-380.

32 Feldberg, W. & Vogt, M. Acetylcholine synthesis in different regions of the central nervous system. J. Physiol. 1948: 107: 379-381.

33 Gaddum, J.H., Peart, W.S., & Vogt, M. The estimation of adrenaline and allied substances in blood. 1949: 108: 467-481.

quantitative assays. Vogt eventually transferred to Cambridge University to work with another esteemed physiologist, E.B. Verney, and then with J.H. Gaddum in London. In 1947, she moved to Edinburgh as a lecturer and 5 years later was elected a Fellow of the Royal Society, only the eighth women to be awarded that distinction.[34]

While in Edinburgh, Vogt also published a paper on the concentration of sympathin (adrenaline and noradrenaline) in the central nervous system.[35] Using fluorometric methods as well as bioassays, she found that the distribution of noradrenaline was not simply due to the presence of sympathetic vasomotor nerves, but was unevenly distributed. Moreover the catecholamine content could be modified by drugs, thus reaffirming a functional role for sympathetic amines in the brain that was distinct from actions on vasomotor nerves. In being one of the first to demonstrate the release of multiple neurotransmitters by the brain *in vivo*, Vogt also demonstrated their sensitivity to electrical stimulation and mode of anesthesia. This seminal work, which identified another neurotransmitter in the central nervous system, would spawn future studies and establish an international reputation for Vogt.

When World War II began, Vogt was still identified as an Enemy Alien Category A, even though she had begun the process of naturalization in 1933. She was therefore vulnerable to immediate incarceration and was summoned to appear in court. The judge ruled against her and she was taken to a police station for eventual imprisonment. But, on the way to the station a kindly policeman advised her to appeal. She was then given a brief period in which to find legal representation and garner support from prominent individuals who would speak on her behalf. When Verney and Feldberg learned of Vogt's plight, they notified Henry Dale who went to the Home Secretary and had the matter resolved. Consistent with her *persona*, Vogt reportedly reprimanded those who had supported her for bothering the British government at a time of war.[36]

In 1947, Vogt moved to Edinburgh where she first became Lecturer and then Reader in the Department of Pharmacology. Five years after her arrival there, Marthe Vogt was elected to the Royal Society, a distinction that up to that time had been previously awarded to only eight other women.

34 [34] Wright P. 2003. Marthe Louise Vogt. The Lancet. 362: (9397) 1769-1770.

35 Vogt, M. 1954. The concentration of sympathin in different parts of the central nervous system under normal conditions and after the administration of drugs. J. Physiol. 123: 451-481.

36 Marthe Vogt. In: The Telegraph. http://www.telegraph.co.uk/news/obituaries/1443084/Marthe-Vogt.html

In 1960, Marthe Vogt returned to Cambridge as Head of the Pharmacology Unit, Agricultural Research Council Unit of Animal Physiology; there she continued to maintain her scientific output. Recognizing that stress was a fundamental concept, Vogt studied multiple, rather than a single, neurotransmitter.[37] Vogt's research interests included investigations not only on cholinergic systems, but also on central dopaminergic and serotonergic systems.[38] Characterized as outspoken, principled, but compassionate, she was rigorous and precise in the pursuit of science and displayed an inordinate dedication to her work. Her research activity was characterized by cogent and creative ideas, detailed experimental analysis, and results that were always interpreted in a cautious manner.

By the time Marthe Vogt retired in 1968, she had received innumerable international honors for her work in neuropharmacology, including honorary membership in the American Academy of Sciences, British Pharmacological Society, Honorary D.Sc. and Honorary Member of the Physiological Society. In her personal life she found time to help refugees from Spain during the Spanish Civil War, assist displaced German Jews, and serve as a member of an anti-nuclear organization. In 1988, Vogt moved to La Jolla California to live with her sister, Marguerite, who was a noted cancer biologist. Marthe Vogt passed away in 2003, one day after her 100th birthday. She was not only a brilliant scientist, but a woman of indomitable spirit and vivacity. Her commitment to the basic principles of science was unequaled.

37 Cuthbert, A.W. Biogr. Mems. Fell. R. Soc. 2005; pp. 415-420.

38 Banister, R.J., Portig, P.J. Sharman, D.F. and Vogt, M. Release by tubocurarine of dopamine and homovanillic acid from the superfused caudate nucleus. J. Physiol. 1968; 194: 565-572. Holman, R.B. and Vogt, M. Release of 5-hyroxytryptamine from caudate nucleus and septum. J. Physiol. 1972; 223; 234-254.

Eleanor Zaimis (1915-1982)

Eleanor Zaimis (1915-1982)

The scientific exploits of the three women just chronicled should rank alongside those contributed by the paladins of the golden age of physiology/pharmacology that graced the United Kingdom and the United States well into the 20th century. However, there are also other women who should be cited because of their important contributions to our knowledge of physiology/pharmacology. One of these scientists includes Eleanor (Nora) Zaimis, who in collaboration with William D. Paton, provided the first clear distinction between the nicotinic receptors at the neuromuscular junction of skeletal muscle and those on postganglionic autonomic nerves, thus setting the stage for the development of drugs for treating hypertension.

Born Eleanor Christides into a wealthy Greek family, Zaimis spent most of her childhood in Rumania.[39] After graduating from Athens University in 1938, she was initially employed there in the pharmacology department where she taught medical students and conducted research on local anesthetics. She retained this position until 1947, and during this period that encompassed World War II she earned her medical degree with a thesis entitled *Antagonism between local anesthetics and quinine.*

Zaimis's extracurricular activities defined her as a flamboyant and defiant individual. As a member of the Greek national team for pistol shooting, she hid her pistols during World War II when the invading Nazis confiscated all weapons. During the war years, she was appointed Head of the youth centers in Athens. This experience made her cognizant of the health problems associated with poor sanitation and hygiene and prompted her to write a book on hygiene. From 1945-1947 she also served on a government committee to evaluate penicillin and streptomycin. In addition, realizing that knowledge about the chemical structure of pharmacological agents would

[39] A synopsis of Eleanor Zaimis's early life and career can be found in: Dolphin, A. C. Eleanor Zaimis (1915-1982). 1993: In: Bindman, L, Brading, A. and Tansey T. Women Physiologists; pp. 129-133.

be valuable for studies related to drug receptors, she obtained a B.Sc. degree in Chemistry in 1947.

Although married once in 1938, Zaimis married a second time in 1943 to John Zaimis, a naval officer and diplomat, and moved to England in 1947 as a British Council Scholar. Although she kept her married name and adopted British Nationality in 1954, Zaimis eventually separated from her husband several years later. After a brief period working as a research assistant at the University of Bristol in the Department of Pharmacology, Zaimis moved to the National Institute for Medical Research at Hampstead, where she served as lecturer and reader. It was in the Department of Chemistry and Physiology at The National Institute for Medical Research where Zaimis would earn acclaim by her collaboration with (Sir) William Paton, who was to become one of the most renowned pharmacologists of his time.[40]

Colleagues in the National Institute had been investigating the arrow poison and muscle relaxant *curare* prior to her arrival. But Paton and Zaimis decided to undertake a related study of the entire series of methonium compounds with carbon chain lengths from C2 to C12. With her expertise in chemistry, Zaimis synthesized the remaining members of the chemical group to identify peak activity in C6 and C10. Their comprehensive studies demonstrated that the longer chain methonium compounds (dexamethonium) produced neuromuscular blockade, while the shorter chain compounds (hexamethonium-C6) elicited blockade of autonomic ganglia. This work provided the first clear distinction between the nicotinic receptors of the neuromuscular junction of skeletal muscle and those on autonomic ganglia.[41]

At first, Paton and Zaimis mainly regarded the methonium compounds as research tools. However, in a letter to *Nature,* they briefly suggested that "C6 (hexamethonium) offers the possibilities of clinical usefulness in such fields as hypertension and vascular disease".[42] They later explored the potential clinical usefulness of the methonium compounds by heroically testing the effects of one or another of these compounds on themselves! They also participated in a clinical study of the effects of hexamethonium and

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40 A synopsis of this work can be found in: Paton, W.D.M. and Zaimis, E.J. 1952. Pharmacol. Rev. The methonium compounds. 4: 219-253.

41 Paton, W.D.M. Zaimis, E.J. & Colquhoun D. (Commentary) (1997). The pharmacological actions of polymethylene bistrimethylammonium salts. Brit. J. Pharmacol. 120: 57-59.

42 Paton, W.D.M. and Zaimis, E.J. 1948. Clinical potentialities of certain bisquaternary salts causing neuromuscular and ganglionic blockade. Nature 162: 810.

pentamethonium on the blood pressure of humans.[43] Prior to the 1950's, the inadequate treatment for hypertension had been rest, sedation, and venesection. As a result of the work of Zaimis and Paton, hypertension became a treatable disease when hexamethonium became available. However because of its non-selective actions, ganglionic blocking agents such as hexamethonium were soon preempted by more selective and less toxic anti-hypertensives.

After Zaimis moved to the School of Pharmacy at the University of London in 1948, she continued to work on ganglionic and neuromuscular blockade and explored various lines of research related to hypertension and migraine. In addition to the many papers Zaimis wrote, she and Paton co-authored a monograph entitled *Paralysis of Autonomic Ganglia by Methonium Salts* in addition to the review published in Pharmacological Reviews.[44]

Eleanor Zaimis possessed a broad range of scientific interests regarding the sympathetic nervous system as exemplified by her serving as Editor of a volume on *Nerve Growth Factor (NGF)*.[45] Her interest in NGF stemmed from the fact that the adrenergic neuron in sympathetic ganglia was dependent upon the growth factor for normal development. Although it was discovered in the early 1950's, the importance of NGF was viewed with significant skepticism until its role in the development of the nervous system was elucidated. The volume edited by Eleanor Zaimis played a significant role in enhancing interest regarding the importance of NGF, which eventually earned the Nobel Prize for Rita Levi-Montalcini in 1986.

In 1954, Zaimis was named Head of the Department of Pharmacology at the Royal Free Hospital School of Medicine, a medical school for women. For the next 25 years her research focused on analyzing drug interactions in the human body. Zaimis also continued her investigations of the sympathetic nervous system and introduced the technique of immunosympathectomy, which Sir Henry Dale proclaimed "an important new chapter in developmental physiology".[46] Because of her invaluable advice to pharmaceutical companies, Zaimis's collaborations with industry also proved to be very

43 Timmermann, C. 2008. In: Gaudilliere, J.P. Hexamethonium and the Treatment of High Blood Pressure, 1940's-1950's. 2008, The University of Manchester Library; pgs. 154-164. Hexamethonium and the Treatment of High Blood Pressure, 1940s-1950s. In: Therapeutic Agents between Plants, Shops, and Consulting Rooms. J.P. Gaudilliere and V. Hess (eds). 2008, Max Planck Institute for the History of Science, Berlin; pp. 153-163.

44 Paton, W.D.M. & Zaimis. E.J. 1952. Pharmacol. Rev.4: 219-253. Paton, W.D.M. and Zaimis E.J. 1951. Paralysis of autonomic ganglia by methonium salts. Brit. J. Pharmacol. 6: 1-168.

45 Zaimis, E. (Editor). 1972. Nerve Growth Factor and its Antiserum; Athlone, London, 273 pages.

46 Paton, W.D.M. (1982) Obituary of Eleanor Zaimis. Brit. Med. J. 285: 1280.

successful. Her studies on the chronic effects of low doses of drugs prompted her to warn clinicians that the deleterious side effects of drugs could nullify their beneficial actions.[47]

Recognition of her contributions was made when she became a member of the Royal College of Physicians in 1968 and a Fellow in 1974. In addition to these honors, Eleanor Zaimis also shared the Cameron Prize in 1956 and the Gairdner Foundation International Award in 1958 with Sir William Paton. Other accolades included becoming an honorary member of Rome Academy of Medicine, and being awarded the Cross of Commander of the Greek Order of Benevolence in 1962 and the Krakow Pharmacology Medal of the USSR Academy of Medical Sciences.[48]

Despite a heavy administrative load, Zaimis remained an active researcher and teacher until she neared retirement. However, she never forgot her roots and throughout her career she served as an advisor to the Greek government on university and pharmacological issues. In her later years she suffered from ill health and depression and retired to Athens in 1980. She passed away only two years after returning to her homeland. Although possessing a dominating personality, Zaimis was described as a generous person who contributed to the culture of both her native and adopted countries. But, perhaps even more importantly, Eleanor Zaimis played a major role in promoting the development of new drugs that would possess a more favorable balance of actions in terms of selectivity and freedom of toxic side effects.

47 Zaimis, E.J. In: Cardiomyopathies. Drug induced myopathies. Ciba Foundation Symposium. 2009. pp. 213-223.

48 Dolphin, A.C. In: Women Physiologists, 1993 pp. 131-133.

Lillian Mary Pickford (1902-2002)

Lillian Mary Pickford
(1902-2002)

Mary Pickford was a pioneer in the emerging field of neuroendocrinology by being a major participant in the development of the concept of neuroendocrine function in the neurohypophysis (posterior pituitary) and the hypothalamus. Born in India, where her father was a successful business man, Pickford returned to England in 1907 to be raised by her aunt and uncle. In 1925 she graduated from Bedford College having studied physiology, chemistry, and zoology. Encouraged by a family friend, Pickford decided on a career in medicine at an early age. Although the encouragement did not extend to the research laboratory, Pickford still decided to pursue a research career. However, because of the prejudicial attitudes harbored against women in science at the time, there existed a scarcity of jobs.[49]

Undaunted, Pickford found part-time work teaching the History of Science at University College, London, prior to becoming a research assistant there. Moreover, her long term aspiration to study Medicine was supported by her godmother who left Pickford a small inheritance in her will. This inheritance, plus income from part-time teaching, enabled Pickford to continue her clinical studies at University College Hospital.[50] She completed the program in 1933 and then took a position at Stafford General Infirmary as house physician. The position provided her with a variety of clinical experiences, which included mending broken bones, treating victims of mining accidents, and delivering newborns.

Pickford began to become ambivalent about returning to laboratory research.[51] However, her career took a crucial turn in 1936 when she was in-

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49 Silver, A. "Pickford (Lillian) Mary (1902-2002)). Oxford Dictionary of National Biography; Oxford University Press. (Jan. 2006). Retrieved 29 May 2015 (http://www.oxforddnb.com/view/article/77182).

50 Silver, A. "Pickford (Lillian) Mary (1902-2002)". Oxford Dictionary of National Biography; Oxford University Press. (Jan. 2006).

51 It was ironic that Pickford was encouraged by T.R. Elliott, Professor of Medicine at University College Hospital, to return to laboratory research, since many years earlier Elliott had abandoned research to pursue clinical work after he had carried out

troduced to the eminent physiologist Ernest Starling by a family friend. She harassed Starling until he somewhat begrudgingly found her a part-time position with E.B. Verney, who had been appointed Chair of Pharmacology at University College London. Verney had previously collaborated with Starling to develop the heart-lung preparation and had demonstrated the importance of the pituitary gland in regulating urine flow. Pickford spent three productive years (1936-1939) with Verney, who fostered her life-long interest in the mechanisms involved in antidiuretic hormone (ADH)-induced regulation of water balance by the pituitary gland. Her initial work on the synthesis and release of ADH and the control of urine flow would lead to experiments examining the effects of oxytocin on the reproductive system and vascular smooth muscle. She also explored the uterine and extra-uterine effects of estrogen, progesterone and a variety of vasoactive substances.[52]

In 1939, Pickford was offered a lectureship in Physiology at Edinburgh and because World War II had drastically reduced the number of academic staff, she was able to combine research with a heavy teaching load. During World War II, while on vacation leave in London, she helped overworked physicians with their varied duties by patrolling air-raid shelters and providing medical assistance.[53]

After war ended, Pickford undertook her most significant work. Although the role of acetylcholine as a peripheral neurotransmitter had been established by Otto Loewi and Sir Henry Dale and colleagues in the 1920's and 30's, Pickford examined the possibility that acetylcholine could regulate urine flow by a central action. While acetylcholine was being accepted by the scientific community as a neurotransmitter in peripheral nerves, the idea that it could also play a similar role in the central nervous system seemed much less compelling to many of her colleagues. Pickford demonstrated by intravenous administration that acetylcholine elicited an anti-diuretic effect by inducing the release of ADH. Secretion of ADH was also observed by the injection of acetylcholine into the supra-optic nucleus of the brain of an anesthetized animal.[54] Until the early 1950's it was not known whether ADH

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experiments which elucidated the fundamental concept of neurochemical synaptic transmission (Elliott, T.R. 1905; J. Physiol. 32: 401-467).

52 Phillips, M. Mary Pickford F.R.S. (1902-2002) In: Bindman, L, Brading, A. and Tansey T. Women Physiologists; 1993; pp. 41-42.

53 Professor Mary Pickford. The Telegraph. http:www.telegraph.co.ok/news/obituaries/1405118/Professor-Mary-Pickford.html. (Retrieved 8 May, 2015).

54 Pickford, M. and Watt, J.A. (1951). A comparison of the effect of intravenous and intracarotid injections of acetylcholine in the dog. J. Physiol. 1951; 114: 333-335.

and oxytocin, the hormone that stimulates uterine contraction during labor, were independent hormones. The results of her work with V.C. Abrahams provided evidence that ADH and oxytocin were separate substances.[55]

The experiments performed by Pickford were technically very difficult, but her exquisite technique provided convincing experimental data. While not offering conclusive proof that acetylcholine was acting as a central neurotransmitter, her findings provided strong support for the concept that acetylcholine serves as a central as well as a peripheral neurotransmitter substance. In carrying out her experiments, Pickford always took exquisite care that the experimental dogs suffered minimal pain and stress. But she felt that the experiments conducted on live animals produced more meaningful results as they relate to physiology.[56]

Pickford was at the forefront in the development of the concept of neuroendocrine function in the posterior pituitary gland and the hypothalamus. One of her key contributions to physiology was that ADH was a key factor in regulating urine flow. However the broad scope of her views was exemplified by her article in *Pharmacological Reviews*, in which she considered factors other than ADH that affect water regulation in the body.[57] These factors included hepatic disease and adrenal disorders that alter steroid balance. In addition, she noted that water excretion may also be diminished when blood pressure is reduced in the kidney or when renal vessels undergo vasoconstriction. Finally, she was aware that such vascular changes could also be produced by alterations in the activity of the renal nerves.

Because Pickford was a dedicated teacher, she was subsequently promoted from Lecturer to Reader in 1952 and in 1966 became the first woman to be appointed to a medical Chair at Edinburgh University. This was the same year that she was elected Fellow of the Royal Society. Among her other distinctions, she was an honorary member of the Physiological Society and in 1935 became first female member of the Pharmacological Society, *preceding* Edith Bulbring and Marthe Vogt. Her accomplishments as a pioneer of

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55 Abrahams, V.C. and Pickford, M. 1954. Simultaneous observations on the rate of urine flow and spontaneous uterine movements in the dog, and their relationship to posterior lobe activity. J. Physiol. 126: 329-346. Pickford, M. Stimuli that release hormones of the pars nervosa. In: Pioneers in Neuro-endocrinology (Meites, J. Donovan, B.T. & McCann, S.M. eds.) pp. 205-216; Plenum Press, New York.

56 Pickford, M. The action of acetylcholine in the supraoptic nucleus of the chloralosed dog. 1947. J. Physiol. 106: 264-270. Phillips, M. Mary Pickford F.R.S. (1902-2002) In: Bindman, L, Brading, A. and Tansey T. Women Physiologists; 1993; pgs. 43-44.

57 Pickford, Mary. Antidiuretic Substances. Pharmacol. Rev. 1952: 4: 254-283.

women in science clearly provide her with honored status in the pantheon of physiologists/pharmacologists of the 20th century.

Pickford remained at Edinburgh until she retired in 1972. However she continued to work 3 days a week as Special Professor of Endocrinology at the University of Nottingham, and in 1977 she spent 6 months as a Visiting Professor in Australia at the University of Brisbane. Mary Pickford authored over 60 papers and 13 book chapters and published a popular paperback *The Central Role of Hormones in 1969*.[58] Pickford greatly enjoyed being mistaken for her namesake in the United States, who was a celebrated silent movie star. However, there is no doubt that Pickford ranked among the group of scientists who made their indelible mark during the 20th century. The career of Mary Pickford a research scientist endured from the time she struggled to find a suitable job to her appointment as Professor of Physiology at Edinburgh University. Thus it was not surprising that she would often express hostility regarding the attitude shown to women scientists during this period. But above all, her determination to overcome all obstacles enabled Pickford to achieve great success in her chosen career. Her legacy endures because of her unique contributions to our understanding of basic physiological principles and to medical education. She died on the morning of her 100th birthday (August 14: 2002).[59]

58 Pickford, M. D.Sc. F.R.S. The Central Role of Hormones. 1969. pp. 112; Oliver & Boyd; Edinburgh.

59 Morrison, J. Mary Pickford: Pioneer of Endocrinology. In The Guardian; 27 August 2002. http://www.theguardian.com/news/2002/aug/27/guardianobituaries.obituaries (retrieved May 30 2015).

Epilogue

This narrative, which is encapsulated in the biographies of five prominent women scientists, hopefully provides perspective relative to the pursuit of science during an earlier time. There were many other women that I could have selected such as Rosalyn Yalow, Rita-Levi Montalcini, and Rosalind Franklin for example. But for the sake of brevity, I focused on certain women who helped to raise the discipline of Pharmacology, my own field of interest, to a level comparable to other basic biomedical sciences. Edith Bulbring, an elite member of this group, was also not included because so much has been written about her by a former colleague Alison Brading that anything I might add would just be superfluous.

The long and fruitful years in research enjoyed by the women portrayed in this work helped to set the tone for the marked change in the culture of scientific research as we know it today. Although the early success of women in science may be attributed to determination, thoroughness, an open mind, and sheer intellect, success was also achieved by those who had the foresight or tenacity to overlook or circumvent difficulty when encountered. Other potential factors which led to the development of an elite population of women scientists include: genetics, family values, and serendipity. In addition, the assistance of scientific stalwarts such as Sir Henry Dale, John Gaddum, E.B. Verney, and J.H. Burn as mentors helped to mitigate some of the challenges that these women endured. Their successes were also of major significance because of the encouragement they gave to other women engaged in scientific endeavors. Finally, it is my sincere hope that this historical account will serve to reaffirm and celebrate the traditions of excellence that the careers of these redoubtable scientists surely convey.

Acknowledgment:

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Sažetak

Dok su znanstvenici oduvijek bili upoznati s činjenicom da moraju biti objektivni vezano uz pitanja koja postavljaju o prirodi, u neka su vremena manje uzimali u obzir različite poglede žena. Podcjenjivanima u smislu svoje inteligencije, ambicije i radoznalosti, ženama je bilo teško natjecati se za radno mjesto istraživačice i/ili ga zadržati, posebice nakon udaje. Kao rezultat mnoge su žene, ne obazirući se na postojeće običaje, radile bez naknade ili su ih financijski pomagali kolege i/ili rodbina. Konačno, došlo je vrijeme za promjene u kulturološkim stavovima. Ovaj rad preispituje neprocjenjiva dostignuća petero jedinstvenih žena u stvaranju pozitivnog okruženja za znanstvenice nakon njih.

Ključne riječi: *biologinje; Gerty Cori; Gertrude Elion; Marthe Vogt; Mary Pickford; Elinor Zaimis.*