Edgar Allen (1892–1943)

Edgar Allen identified and outlined the role of female sex hormones and discovered estrogen in the early 1900s in the US. In 1923, Allen, through his research with mice, isolated the primary ovarian hormone, later renamed estrogen, from ovarian follicles and tested its effect through injections in the uterine tissues of mice. Allen's work on estrogen, enabled researchers to further study hormones and the endocrine system.

Allen was born in Canyon City, Colorado, on 2 May 1892, to Edith Day and Asa Allen. Allen's father was a physician. When the family relocated to Providence, Rhode Island, Allen attended public school at Pawtucket and Cranston High, in Pawtucket and Cranston, Rhode Island, respectively. While living in Rhode Island, Allen spent his free time sailing off the coast of Rhode Island, where he learned to navigate the currents of Narragansett Bay and Long Island Sound. The death of Allen's father in 1921 left the family in financial trouble, forcing his mother to work as a librarian and the children to work while going to school.

Allen attended Brown University, in Providence, Rhode Island. In 1915, Allen completed his undergraduate degree in biology at the age of 23. Allen earned his master's degree in biology from Brown a year later. In 1917, Allen volunteered to serve in World War I. During his time in the war, he served with the Brown Ambulance Unit in the Medical Corps and on a mobile unit of the US Sanitary Corps operating in France.

While serving in the war, Allen returned to the US in 1918 and married Marian Pfieffer, one of his classmates from Brown University. The Allens had two daughters together, Frances Isabelle Allen and Majorie Eleanor Allen. In 1919, Allen received an honorable discharge from the army and returned to graduate studies at Brown University, working toward a PhD in biology. Before finishing his PhD, Allen took a research position as instructor at Washington University in St. Louis, Missouri.

At Washington University, Allen focused on oogenesis, the process of egg (ova) production and development in females. To study oogenesis, Allen dissected female mice during the different stages of their reproductive estrous cycles. The estrous cycle, unlike the menstrual cycle in humans, involves the absorbance of the uterine tissue (endometrium) by the uterus, not the loss of tissue through the vagina. After dissecting the mice, Allen looked for developmental changes in the egg cells located on the ovaries. His research showed that oogenesis occurs throughout the reproductive cycle of sexually mature female mice, settling debate in the early twentieth century about whether or not all eggs are fully formed and mature at birth.

During his research with oogenesis, Allen noticed a connection between ovarian follicle development in female mice, during which cells containing immature eggs develop and later release during the estrous cycle, and the thickening of the tissue lining the uteruses in those female mice. As a result of that work, Allen hypothesized that the ovarian follicle housed the primary female sex hormone and, when released, contributed and controlled the changes in the uterine lining. That idea provided the framework for Allen's attempt at locating and identifying the primary ovarian hormone that later would receive the name estrogen.

Allen completed his graduate work two years later in 1921, earning his PhD in biology from Brown University with his doctoral dissertation on the estrous cycle in mice. Allen's doctoral dissertation became his first published scientific piece in 1922. His dissertation and research documented the tissue changes that occur in the sex organs of female mice during their reproductive estrous cycles. Estrous, which takes place in some female mammals, is a cycle that uses hormones to ready the

lining of the uterus for an egg to implant upon it.

After completing his doctoral dissertation, Allen again studied egg production. He tested his hypothesis that the changes observed in the uterine lining during the estrous cycle were caused by the production of the primary ovarian hormone during ovarian follicle development. In 1923, Allen published his findings with co-author Edward Adelbert Doisy, a biochemist at Washington University who had previously researched sex hormones and who would later win the Nobel Prize for Physiology or Medicine in 1943 for his work with vitamin K. Doisy and Allen isolated estrogen from hog ovarian follicles using alcohol. The alcohol separated the desired hormone (estrogen) from unwanted proteins, lipids, and amino acids. Allen and Doisy performed four tests and thus provided a method to isolate estrogen and reasons to think that ovarian follicles produced it.

The first test involved injecting the purified estrogen extract into sterilized mice to prove that estrogen and not another substance had been isolated. The results showed that in the absence of ovaries in mice, a normal estrous could take place with the addition of estrogen. Therefore, they concluded the extract was in fact estrogen.

Allen and Doisy showed in their second test that if they injected sterile female mice with their extract, the mice behaved so as to court mates, indicating that the extract caused the mice to go into heat and begin their estrous cycle. They showed in the third test that injections of the extract in three-week-old mice caused the mice to become sexually mature in two to four days. Because the mice became sexually mature approximately thirty days earlier than usual, Allen and Doisy concluded that the isolated hormone led to the sexual maturation of sex organs and the development of secondary sexual characteristics, such as the enlargement of breasts.

The final experiment compared Allen and Doisy's isolated hormone liquid from the ovarian follicles with extracts of corpora lutea, which are specific sites on the ovaries. After eggs are released, the corpora lutea signal for the nourishment of the uterine lining. The corpora lutea extract did not contain estrogen, just as Allen and Doisy predicted, which disproved the theory that the corpora lutea contained and produced the primary ovarian hormone, estrogen. Allen and Doisy concluded from the four tests that the extracted follicular compound contained the primary ovarian hormone, as when administered alone it caused natural endocrine processes and functions that mimicked the naturally occurring cycle. Their results enabled researchers to develop hormone therapies involving estrogen, as the hormone could now be isolated and given to women with lower levels of estrogen.

After publishing his work on estrogen, Allen moved to the University of Missouri in Columbia, Missouri, in 1923, where he chaired the department of anatomy. In 1930, Allen became the dean of the School of Medicine and director of the University Hospitals at the University of Missouri. While in those positions, Allen continued his research. In 1928, he collaborated with Jean Paul Pratt, a physician at Henry Ford Hospital in Detroit, Michigan. Allen, Pratt, and a group of researchers devised one of the first plans to safely remove living human eggs (ova) from the uterine tubes of women. Together, Allen and Pratt correlated the conditions of the recovered eggs with the menstrual cycles of the patients, concluding from their five recovered eggs that ovulation occurred somewhere in the middle of a female's reproductive cycle around the fifteenth day.

Allen and Pratt also conducted one of the first therapeutic clinical experiments using estrogen injections in women who had abnormal menstrual cycles. Allen and Pratt found that if they injected those women with estrogen, their menstrual flows increased and returned to normal. Allen contributed to the early study of estrogen hormone therapy in women by conducting research that alleviated minor complications that stemmed from the menstrual cycle.

In 1933, Allen became a professor of anatomy and a chairman of the department of anatomy at Yale University School of Medicine in New Haven, Connecticut. At Yale, Allen studied cancer and its relation to reproductive hormones. In 1941, Allen conducted an experiment testing the effects of long-continued use of estrogen injections on the cervixes of mice. When treated with weekly doses of estrogen, the mice showed a 62 percent occurrence of cancer-like lesions on their cervixes, causing some to die. Allen concluded that the high rate of cancer found in those groups of mice emphasized estrogen's importance in cervical cancer development. Allen's work on cancer development contributed to theories of estrogen and the problems it can cause in both animals and in humans when produced in higher than normal levels.

Allen received many awards. The French government in Paris, France, elected him to the Legion of Honor in 1937, and the Royal College of Physicians in London, England, awarded him the Baly Medal in 1941. Allen never won a Nobel Prize, but he received four separate nominations for the award in 1934, 1936, 1938, and 1940. Allen's work with the follicular hormone and oogenesis in mammals led to his first nomination in 1934. In 1936 and 1938, his work with the estrous cycle in mice led to his second and third nominations. Allen received his fourth and final nomination in 1940 for his research on sex hormones.

Allen died on 3 February 1943 of a heart attack off of the coast of Rhode Island, while volunteering with the Coast Guard during World War II. Allen was fifty years old.

Sources

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