

[Irving Freiler Stein Sr. \(1887–1976\)](#) ^[1]

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Irving Freiler Stein Sr. was a physician who studied women's reproductive health during the twentieth century in the United States. In partnership with his colleague, Michael Leventhal, Stein identified a women's reproductive disorder related to elevated male [sex hormones](#) ^[3], or [androgens](#) ^[4]. The syndrome was originally called Stein-Leventhal syndrome and later known as polycystic ovarian syndrome. While studying the syndrome, Stein also helped establish a treatment for the condition, through the surgical removal of ovarian tissues. Stein identified the symptoms related to the condition polycystic ovarian syndrome, a hormonal imbalance estimated to be the most common female reproductive disorder as of 2017.

Stein was born on 19 September 1887 to Emma Freiler and Adolf Stein in Chicago, Illinois. Stein was the seventh of ten children. In 1910, Stein graduated from the [University of Michigan](#) ^[5] in Ann Arbor, Michigan, with a bachelor of science degree. Two years later, in 1912, Stein graduated from [Rush Medical College](#) ^[6] in Chicago, Illinois, with his medical degree.

Following his graduation from medical school, Stein completed a two-year internship at Michael Reese Hospital in Chicago, Illinois. After his internship in 1914, he joined the Michael Reese Hospital's Department of Obstetrics and Gynecology as an assistant in surgery to physicians Carl Beck and Daniel N. Eisendrath. There, Stein focused on reproductive health in women, maternal care, and prenatal and perinatal infant health. By 1915, Stein became an attending physician in obstetrics and gynecology, able to see and treat his own patients. A few years later, in 1921, Stein married Lucile Oberfelder and together they had two children, Eleanor H. Rusnak and Irving F. Stein Jr. In addition to his surgical career at Michael Reese Hospital, Stein taught at [Northwestern University](#) ^[7] in Chicago, Illinois, in the Department of Obstetrics and Gynecology. During his time in Chicago, he held a number of different positions which was not uncommon in medicine at the time. Stein also had his own freelance consulting position with Highland Park Hospital in Highland Park, Illinois.

In 1926, Stein met physician Michael Leventhal, when Leventhal joined the staff at Michael Reese Hospital. Stein and Leventhal began to conduct research together on causes of sterility in women. At that time, Stein had also begun to document several cases of bacterial infections of the [vagina](#) ^[8]. In his examinations of women, Stein identified a type of bacteria found in the [vagina](#) ^[8] that was associated with itching, burning, and chafing, symptoms that directly followed the menstrual cycle. His findings were recorded in his first published paper in 1926, and very little research had been done on that topic before.

Also in 1926, Stein and fellow researcher Robert A. Arens published a study on ovarian abnormalities. A woman had presented with a fist-sized growth in her [uterus](#) ^[9]. To study the cause of the growth, Stein wanted to assess the anatomy of the entire reproductive system first. He developed a method to inject a gas, carbon dioxide, followed by a type of iodized oil into the [fallopian tubes](#) ^[10] to gain a clearer view of the structures via an early form of [x-ray](#) ^[11] and to determine if there were any abnormalities in her anatomy. Though he did not note any changes in the woman's [fallopian tubes](#) ^[10], Stein concluded that the patient had abnormally large ovaries. Following that paper, Stein increasingly focused his research on causes of sterility in women.

In the 1920s, researchers knew that obese women tended to have irregular or absent menstrual cycles. Researchers had also noted that women with excess facial and body hair tended to be infertile. Stein and Leventhal used those observations and sought to determine if there were any anatomical differences causing the conditions. A normal [ovary](#) ^[12] is light pink and about an inch in width and two inches in length. Stein and Leventhal found that many of the women they studied had ovaries two to four times the normal size. The women's ovaries were also filled with tiny, fluid-filled sacs, which were later identified as cystic ovaries. The ovaries were also gray and flat. In his 1935 paper, Stein called them [oyster](#) ^[13] ovaries. The early exploratory surgeries by Stein and Leventhal established that women showing symptoms of [infertility](#) ^[14], excess body hair, and irregular [menstruation](#) ^[15] also had irregular ovaries.

In 1935, Stein and Leventhal published a study where they observed that many of their patients shared similar symptoms including cystic ovaries. That led the researchers to examine the ovaries in those women further. The ovaries were considered cystic because they were filled with small, fluid-filled sacs that contained the immature eggs of the women. In the healthy ovaries of fertile women, eggs develop in the ovaries and begin as a follicle. When cysts form in the ovaries, it is typically an immature follicle getting stuck in the [ovary](#) ^[12] and never being released as an [egg](#) ^[16]. Because the eggs were not maturing in the woman, that also meant the cysts would affect her fertility by not allowing her to fully ovulate. To view the ovarian tissues, Stein removed small wedges of ovarian tissue from the women to observe under a [microscope](#) ^[17], a surgical procedure later known as a bilateral wedge resection. Stein observed the tissue to look for any potential abnormal findings in the structure of ovarian tissues. However, Stein and Leventhal found in addition that some of the women involved in the study began menstruating following the removal of the ovarian tissue, and some also became pregnant as a result of the [menstruation](#) ^[15] changes restoring fertility. Stein concluded that the biopsies were therapeutic, meaning they treated the symptoms of the women. Stein

continued his research into cystic ovaries and their effect on sterility in the 1930s.

In 1939, Stein published a paper documenting the history of contraceptives. He began his paper with the claim that Egyptians in 1850 BC used a mixture of crocodile dung, ant paste, and honey as a contraceptive. He also included the history of Chinese, Japanese, Indian, and Arabic methods of [birth control](#)^[18]. He continued his research in sterility, publishing another article in 1945 in which he distinguished between bilateral polycystic ovaries and sterility. In the paper he claimed that there was truly an underlying syndrome that tied those two symptoms together, and that many patients who exhibited both symptoms simultaneously also had other similar symptoms in common. In 1949, Stein published his use of wedge resection as a form of therapy for women with amenorrhea. Many of his patients' menstrual cycles and ovulatory patterns returned upon the removal of a small amount of tissue from their ovaries. Throughout the 1950s, researchers began using the term Stein-Leventhal syndrome to describe the range of the symptoms Stein was studying. Stein also remarried in 1954 to a woman named Ruth Steit after his first wife had died.

In 1958, Stein documented a group of women he had studied that exhibited the symptoms associated with Stein-Leventhal Syndrome, including excess body hair, irregularity and absence of menstrual cycles, and sterility. He concluded that [x-ray](#)^[11] techniques common at the time could be used to diagnose Stein-Leventhal syndrome, and if a woman presented with bilateral cystic ovaries common to the syndrome, physicians should surgically treat the condition. Stein indicated that the bilateral ovarian wedge resection, the same surgery he had conducted in 1935 that had surprisingly resulted in the return of [menstruation](#)^[15] for many women in that study, was the only reliable means of treatment for patients with Stein-Leventhal syndrome. Stein's later research concluded that the return of fertility is permanent in women with Stein-Leventhal syndrome who receive a successful wedge resection. He reported those results in one of his final publications in 1965.

Historian Greta Beighton cites Stein as a warm and caring clinician and an excellent teacher. Melvin Cohen, one of Stein's colleagues, also noted that Stein was a dignified and respected teacher, often found with a large group of fellow doctors and nurses following him while he did his rounds. In addition, Cohen stated that Stein was meticulous in everything he did, including patient care, surgery, and even his appearance, as Stein often wore a boutonniere to the hospital. Stein received many awards and was a member of many surgical societies throughout his career. Stein was also the president of the Chicago Gynecological Society in Chicago, Illinois, and the president of the American Society for the Study of Sterility in Chicago, Illinois. On 11 October 1976, Stein died in Glencoe, Illinois.

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Topic

[People](#)^[32]

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- [1] <https://embryo.asu.edu/pages/irving-freiler-stein-sr-1887-1976>
- [2] <https://embryo.asu.edu/keywords/reproductive-medicine>
- [3] <https://embryo.asu.edu/search?text=sex%20hormones>
- [4] <https://embryo.asu.edu/search?text=androgens>
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- [7] <https://embryo.asu.edu/search?text=Northwestern%20University>
- [8] <https://embryo.asu.edu/search?text=vagina>
- [9] <https://embryo.asu.edu/search?text=uterus>
- [10] <https://embryo.asu.edu/search?text=fallopian%20tubes>
- [11] <https://embryo.asu.edu/search?text=x-ray>
- [12] <https://embryo.asu.edu/search?text=ovary>
- [13] <https://embryo.asu.edu/search?text=oyster>
- [14] <https://embryo.asu.edu/search?text=infertility>
- [15] <https://embryo.asu.edu/search?text=menstruation>
- [16] <https://embryo.asu.edu/search?text=egg>
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- [33] <https://embryo.asu.edu/formats/articles>