

## GYNECOLOGY

## Stein and Leventhal: 80 years on

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Eighty years ago a publication in this Journal proved seminal and transformative.<sup>1</sup> The report by Irving Stein and Michael Leventhal titled, "Amenorrhea associated with polycystic ovaries," has proven to be a remarkably lasting and influential publication, with the term Stein and Leventhal appearing in almost 10,000 and the terms polycystic ovary or polycystic ovarian in more than 28,000 publications since 1950, when citation data began to be compiled. Furthermore, the growth in related literature has been increasing exponentially: the 50 years between 1950 and 2000 saw a little more than 8000 publications on the topic, whereas the 15 year period between 2001 and 2015 (so far) has seen more than 20,000 related publications, a greater than 8-fold increase in publication rate after 2000.

Why has this publication proven to have such a lasting effect?

The short answer, of course, is that the report alluded to a disorder that today we know is highly prevalent (affecting 5-15% of women, depending on diagnostic criteria), morbid (the single most common cause of infertility and associated with a 5- to 7-fold increased risk of type 2 diabetes, an increased risk for endometrial cancer, and as probably increased risks for cerebrovascular and cardiovascular disease) and detrimentally affecting the quality of life.<sup>2</sup>

However, as we celebrate 80 years since its publication, it is pertinent to ask why this report? And was it truly seminal? The answers to these questions will not only help illuminate the founding of an important field of research but also help provide strong lessons for other investigators, new or established, who are working to develop their own impact in clinical science.

**In the beginning ...**

Irving Freiler Stein was born in 1887 in Chicago, the seventh of 10 children to Adolf Stein and Emma Freiler Stein. His father, born in Bohemia, Austria, and like his father-in-law, owned a brewery and a tavern. His mother had been born in New York, although of immigrant parents. Stein's grandparents had all immigrated to the United States in the mid- to late 1800s from the Czech Republic, with the exception of his

maternal grandmother, who was born in Darmstadt, Germany.<sup>3</sup>

Stein attended the University of Michigan and then Rush Medical College, graduating in 1912<sup>3-10</sup> (Figure 1A). We should recall that this was a tumultuous and changing period of time for medical education in the United States. Chicago was awash with proprietary medical schools, some no more than diploma mills, such that the 1910 Abraham Flexner report on medical education in the United States labeled Chicago, in terms of the quality of its medical schools, "the plague spot of the country."<sup>11</sup>

To its fortune, Rush Medical College had an affiliation with the University of Chicago, which had begun in 1898 and lasted until 1942, when the University of Chicago established its own medical school. Flexner himself noted that "... efficient and intelligent administration of the law would thus reduce in short order the medical schools of Chicago to three, Rush, Northwestern, and the College of Physicians and Surgeons. In the matter of entrance requirements, Rush alone is secure."<sup>11</sup>

Thereafter, Dr Stein served a 2 year internship at the Michael Reese Hospital after which he served 1 year as an Assistant in Surgery to Drs Carl Beck and D. K. Eisendrath, 2 well-known and well-published surgeons.<sup>6</sup> In 1915 he was appointed associate in obstetrics on the staff of the Michael Reese Hospital, an affiliation that was to continue until his death.<sup>6,12</sup> He also served as clinical staff at Highland Park Hospital and as faculty at the Northwestern University School of Medicine in the Department of Obstetrics and Gynecology, becoming an Emeritus Associate Professor in 1953.<sup>6</sup>

Shortly after graduating medical school, Dr Stein married Lucile Oberfelder (Figure 2), with whom he had 2 children, Eleanor Stein Rusnak and Irving F. Stein Jr, the latter a physician and long-term faculty member of the Department of Surgery at Northwestern University School of Medicine. Following Lucile's death in 1940 at the young age of 51 years, Dr Stein did not rewed until 1954, when he married Rosalind Ruth Weinberger Steif, a widow herself, to whom he remained married until his death at age 89 years in 1976.<sup>4-6</sup>

Professionally, Dr Stein was a well-recognized figure around Michael Reese Hospital (Figure 1, B-D) as he rounded on his patients with his retinue of students and junior staff, elegantly dressed, boutonniere in place. He was a warm and caring physician and an excellent teacher.<sup>5</sup> Like most teaching physicians of his day, he also maintained an active private practice.

His younger collaborator, Michael Leo Leventhal (born in 1901) attended the University of Chicago and subsequently graduated from Rush Medical College in 1924<sup>13</sup> (Figure 3A). Dr Leventhal met Stein while completing his internship at Michael Reese Hospital, whose staff he joined the following

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**FIGURE 1**  
**Dr Stein in 1912**



Dr Irving F. Stein as he appeared in his medical school graduation photo of 1912 (A), circa 1940 (B), circa 1955 (C), and in 1975, with George D. Wilbanks, MD, at the 40th anniversary celebration of the Stein and Leventhal report (D).

Figure 1, A and D, reprinted with permission of the Rush University Medical Center Archives; Figure 1B reprinted, with permission, from Gardner<sup>6</sup>; and Figure 1C reprinted with permission from Gordon.<sup>9</sup> Azziz. *Stein and Leventhal 80 years later. Am J Obstet Gynecol* 2016.

year (in 1925). Drs Stein and Leventhal together began to perform clinical research mostly related to the topic of sterility, a focus on scientific inquiry that was an important basis for their subsequent studies on the ovaries of amenorrheic women.

To this effect, Dr Leventhal records that between 1926 and 1935, this last the year they published their initial observations on the polycystic ovary, he served as assistant to Dr Stein. He also served as clinical assistant, then instructor, at the Northwestern University Medical School. Dr Leventhal,

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