

## Milestones

# George Papanicolaou and the cervicovaginal smear

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There have been few public health measures in the history of medicine that have transformed human life as we know it. A number of these have been in the form of immunizations and therapies. The only screening test which has been universally accepted and has stood the test of time is the Pap smear test for the early detection of cervical cancer. The test has been a part of standard public health service in Western countries and there has been a dramatic reduction in the incidence of cervical cancer. Success stories abound and even amongst the earliest reported community series, the results are startling. In British Columbia, there was a reduction of cervical cancer incidence from 28.4 per 100,000 in 1955 to 7.7 per 100,000 in 1977 when the cytological screening program was completely implemented<sup>1</sup>. The history of the Pap smear test and exfoliative cytology is relatively recent. Though exfoliative cytology had been described by Beale et al for diagnosing pharyngeal cancer as far back as 1827, the cervicovaginal smear was discovered by George Papanicolaou.

Papanicolaou was born on May 13, 1883 in the small town of Kymi on the island of Euboea, Greece. He was the third child of Nikolas and Maria Papanicolaou. Papanicolaou attended the University of Athens, where he studied literature, philosophy, languages and music. At the urging of his physician-father, Papanicolaou pursued a career in medicine, earning his medical degree in 1904. After military service, Papanicolaou continued his education at the Zoological Institute in Munich. He returned to Greece to pursue an academic career in biologic research. On the ferry home, he met Andromache (Mary) Mavroyeni whom he later married.

She played an important role in his career as his assistant when the couple moved to the United States later in life. Papanicolaou served as an army physician during the Balkan War, where he met several American volunteers who told him about the many career opportunities in the United States. The Papanicolaous arrived in New York City in 1913. Because they had limited funds, the couple took positions at Gimbel's department store. Papanicolaou's retail career was short, however, and within a few weeks, he found a laboratory position at New York Hospital. By 1914, he was working at Cornell Medical College under Charles Stockard (Figure 1).

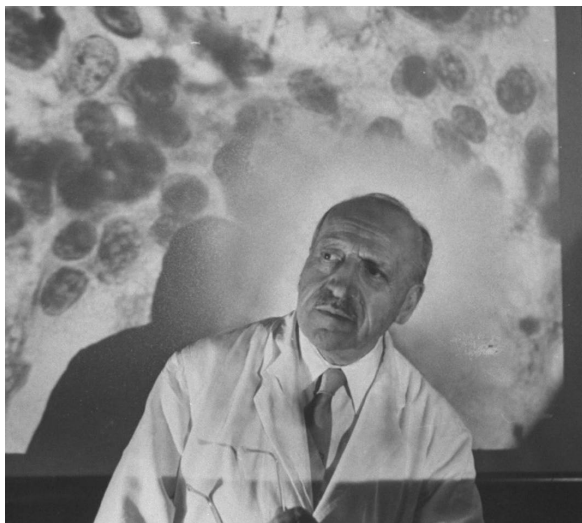


**Figure 1.** George Papanicolaou in the laboratory.

Papanicolaou was studying guinea pig oocytes and he needed to harvest the eggs just before ovulation. The only way to collect the eggs was to sacrifice the animals,

killing many animals whose eggs were not at the right point. He awoke one morning with the realization that guinea pigs have a menstrual cycle; it just had not been charted before. He knew that females of all higher animals have a periodic vaginal discharge. In the case of guinea pigs, it was probably too scanty to be visualized. Papanicolaou used a nasal speculum to collect samples, and examined the smears under his microscope. What he saw was exciting: diverse cell forms and a sequence of distinctive cytologic patterns. Papanicolaou was able to chart the cyclic ovarian and uterine changes each day, allowing him to predict ovarian status. He could then harvest the oocytes at the appropriate time. He published his research on the cytologic patterns in guinea pigs in the *American Journal of Anatomy* in 1917<sup>2</sup>.

Eventually, he began taking similar scrapings from women, and he soon noticed malignant cells in smears taken from women with cancer. By 1928, he had gathered enough data on cervical carcinoma cells and their detection to make a presentation on the topic at the Race Betterment Conference in Battle Creek, Michigan (Figure 2). He expected a warm reception; instead, he



**Figure 2.** George Papanicolaou lectures on exfoliative cytology.

was greeted with skepticism. At the time, most physicians and scientists thought the idea of examining scraped dead cells for cancer was ridiculous. The prevailing theory was that a biopsy and tissue exam was the only way to detect the disease. Despite the initial rejection of his idea, Papanicolaou persevered. In 1939, he collaborated on a clinical study with Herbert F. Traut, MD, a gynecologic pathologist at Cornell, to validate the diagnostic potential of the vaginal smear. They enrolled all women admitted to the gynecologic service of the New York Hospital. Each woman underwent a smear that Papanicolaou interpreted. Papanicolaou detected many asymptomatic cancer cases. Some were in such an early stage that they were undetectable on biopsy. Papanicolaou and Traut published their findings in a seminal monograph titled, "Diagnosis of uterine cancer by the vaginal smear<sup>3</sup>."

Although he retired from Cornell, Papanicolaou's career was not finished. In 1961, Papanicolaou realized a long-time dream: the establishment of a cytologic research institute. He was named Director of the Cancer Research Institute of Miami in 1962. Papanicolaou died of a heart attack in 1962. His research institute was later renamed in his honor. In 1960, he was nominated for the Nobel Prize in Physiology and Medicine, and was awarded the United Nations Prize in 1962<sup>4</sup>.

#### References

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