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George Papanicolaou (1883–1962): Discoverer of the Pap smear

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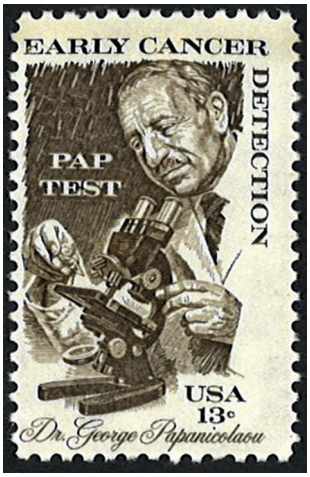
George Nicholas Papanicolaou was a pioneer in elucidating the physiology and cytologic characteristics of the female reproductive system. He is best known for creating the Papanicolaou test, commonly known as the Pap smear, which revolutionised the early detection of cervical cancer.

EARLY CAREER Born on May 13, 1883, in the town of Kimi on the island of Euboea, Greece, Papanicolaou was one of four children. He attended the University of Athens, majoring not in biology, but music and the humanities. However, his physician father influenced his eventual decision to pursue a career in medicine. In 1904, he graduated from medical school with top honours.

After graduation, Papanicolaou worked in the military as an assistant surgeon for a short time, then returned to his hometown, Kimi. For the next two years, he cared for leprosy patients on the outskirts of his hometown. These outcasts were socially isolated, and Papanicolaou gave them both medical and personal care with compassion and grace. However, his desire to work in science soon took hold and he travelled to the University of Munich in Germany, receiving a PhD in zoology in 1910. At this leading research institution, he worked with Professor Ernst Haeckel, one of the first great supporters of Darwinism.



FROM GREECE TO AMERICA Shortly thereafter, Papanicolaou married Andromache Mavroyeni (Mary), who was from a famous military family. The young couple returned to Greece following the death of his mother. When the First Balkan War broke out in 1912, Papanicolaou returned to military service as a lieutenant in Greece's medical corps. However, he became interested in career opportunities in the United States (US) and decided to emigrate, arriving in New York on October 19, 1913. This was a bold and momentous choice, given that neither husband nor wife spoke English and "*the couple had, in cash, only slightly more than USD 250.00, the amount required to enter the US*".

Arriving with little money and no arrangements for employment, both Papanicolaou and his wife were forced to take any job that they could get. Mary worked at a department store as a seamstress and Papanicolaou was a rug salesman at the same store, but he lasted only one day. He subsequently took other jobs: violin player in a restaurant and clerk at a Greek newspaper. In 1914, he finally obtained a position at New York University's Pathology Department and Cornell University Medical College's Anatomy Department, where his wife joined him as a technician.

PAP TEST While Papanicolaou's research would eventually be on human physiology, he began his studies with guinea pigs. In 1916, while studying sex chromosomes, he deduced that reproductive cycles in the experimental animals could be timed by examining smears of their vaginal secretions. From 1920, he began to focus on the cytopathology of the human reproductive system. He was thrilled when he was able to discern differences between the cytology of normal and malignant cervical cells upon a simple viewing of swabs smeared on microscopic slides. Although his initial publication of the finding in 1928 went largely unnoticed, that year was filled with other happy events for Papanicolaou. He became a US citizen and received a promotion to Assistant Professor at Cornell. As part of his research at the New York Hospital, he collaborated with Dr Herbert Traut, a gynaecological pathologist, eventually publishing their landmark book in 1943, *Diagnosis of Uterine Cancer by the Vaginal Smear.* It described physiological changes of the menstrual cycle and the influence of hormones and malignancy on vaginal cytology. Importantly, it showed that normal and abnormal smears taken from the vagina and cervix could be viewed under the microscope and be correctly classified. The simple procedure, now famously known as the Pap smear or test, quickly became the gold standard in screening for cervical cancer. As it cost little, was easy to perform and could be interpreted accurately, the Pap smear found widespread use and resulted in a significant decline in the incidence of cervical cancer.

Papanicolaou was not the first to show that cancerous cells could be identified under the microscope. That honour goes to British physician Walter Hayle Walshe, who referred to this phenomenon in a book on lung diseases one century before. Nor was Papanicolaou the first to study cervical cytopathology in women. In 1927, a Romanian physician by the name of Aurel Babeş used a platinum loop to collect cells from a woman's cervix to detect the presence of cancer. However, medical history has sided with Papanicolaou as the originator of the Pap test, as the two methods were viewed to be substantially different. Still, in

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honour of Babeş, Romania refers to the test as Methode Babeş-Papanicolaou.

In 1951, Papanicolaou became Emeritus Professor at what was then Cornell University Medical College, where two laboratories now bear his name. Shortly thereafter, in 1954, he published *Atlas of Exfoliative Cytology*, a treatise containing comprehensive information on the cytology of both healthy and diseased tissue, not just in the female reproductive system but also in other organ systems. In total, Papanicolaou authored four books and over one hundred articles. He was the recipient of numerous awards, including honorary degrees from universities in the US, Italy and Greece. The scientific world recognised him with the Borden Award of the Association of American Medical Colleges (1940), the Amory Prize from the American Academy of Arts and Sciences (1947), the prestigious Albert Lasker Award for Clinical Medical Research from the American Public Health Association (1950) and the Medal of Honor from the American Cancer Society (1952). Additionally, he was conferred honorary membership in the Obstetrical and Gynecological Society of Athens and the New York Academy of Sciences. His image was featured on the Greek 10,000-drachma currency note prior to its replacement by the euro and on various Greek stamps. In 1978, the US Postal Service honoured him with a commemorative 13-cent postage stamp.

PERSONAL LIFE Papanicolaou was a dedicated scientist, as modest as he was hardworking. He did not take vacations, worked seven days a week and relished immersing himself in the wonders of his research. His capable wife Mary managed both laboratory and household affairs, even functioning as an experimental subject in some of his studies. After nearly 50 years at Cornell, Papanicolaou finally decided in 1961 to leave New York to develop and head the Cancer Institute of Miami. Mary was both thrilled and relieved, as she was increasingly concerned over his recent distracted behaviour and fascination with dream analysis and parapsychology. Unfortunately, Papanicolaou died within three months of his arrival in Miami, suffering a fatal myocardial infarction on February 19, 1962. He was 78 years old. In his honour, the Miami Cancer Institute was renamed the Papanicolaou Cancer Research Institute. In a 1998 article, an admiring author accurately summed up this great pioneer's discovery: "*His monumental contribution proved that cancer can be beaten… the Papanicolaou screening test will remain one of the most powerful weapons against this disease. Those of us who looked upon him as a guiding star will always owe him our gratitude, and those women who were helped by his test owe him their lives.*"

BIBLIOGRAPHY

- Carmichael DE. The Pap Smear: Life of George N. Papanicolaou. Springfield, IL: Charles C Thomas Pub Ltd, 1973.
- Papanicolaou Society of Cytopathology. Dr. George Nicholaus Papanicolaou [online]. Available at: http://www.papsociety.org/gpbio.html. Accessed February 19, 2008.
- Georgios Papanikolaou. Available at: https://en.wikipedia.org/wiki/Georgios_Papanikolaou. Accessed September 6, 2015.
- George Nicholas Papanicolaou. In: Whonamedit? A dictionary of medical eponyms [online]. Available at: http://www.whonamedit.com/doctor.cfm/2402.html. Accessed February 19, 2008.
- Michalas SP. The Pap test: George N. Papanicolaou (1883-1962). A screening test for the prevention of cancer of uterine cervix. Eur J Obstet Gynecol Reprod Biol 2000; 90:135-8.
- George Papanicolaou Biography (1883-1962). Available at: http://www.faqs.org/health/bios/80/George-Papanicolaou.html. Accessed February 24, 2008.
- Papanicolaou GN, Traut HF. The diagnostic value of vaginal smears in carcinoma of the uterus. 1941. Arch Pathol Lab Med 1997; 121:211-24.
- Vilos GA. The history of the Papanicolaou smear and the odyssey of George and Andromache Papanicolaou. Obstet Gynecol 1998; 91:479-83.