Georgios Papanikolaou

]Name:Youssef Abanoub

group:19ls3a

Georgios Papanikolaou

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Life

Born in Kymi, Greece, Papanikolaou attended the University of Athens, where he studied literature, philosophy, languages and music. Urged by his father, he pursued a medical degree, which he received in 1904. Afterwards, he was conscripted into military service. When his obligation ended in 1906, he returned to Kymi to practice medicine with his father. In 1907, he began studying under Ernst Haeckel at the University of Jena for one semester before moving to University of Freiburg, where he was supervised by August Weismann. Again he left after one semester, this time to join University of Munich, from which he graduated with a doctoral degree in zoology in 1910.[1][2] Afterwards, Papanikolaou returned to Athens and married Andromachi Mavrogeni, who later became his laboratory assistant and research subject.[3][4][5] He then departed for Monaco, where he worked for the Oceanographic Institute of Monaco, participating in the Oceanographic Exploration Team of Prince Albert I of Monaco (1911).[6]

In 1913, he emigrated to the United States in order to work in the department of Pathology of New York Hospital and the Department of Anatomy at the Cornell Medical College of Cornell University.

He first reported that uterine cancer could be diagnosed by means of a vaginal smear in 1928, but the importance of his work was not recognized until the publication, together with Herbert Frederick Traut [de] (1894–1963), of *Diagnosis of Uterine Cancer by the Vaginal Smear* in 1943. The book discusses the preparation of vaginal and cervical smears, physiologic cytologic changes during the menstrual cycle, the effects of various pathological conditions, and the changes seen in the presence of cancer of the cervix and of the endometrium of the uterus. He thus became known for his invention of the Papanicolaou test, commonly known as the Pap smear or Pap test, which is used worldwide for the detection and prevention of cervical cancer and other cytologic diseases of the female reproductive system.

Papanicolaou was the recipient of the Albert Lasker Award for Clinical Medical Research in 1950.[7]

In 1961, he moved ~~to Miami, Florida, to develop the~~ Papanicolaou Cancer Research Institute[8][9][10] at the University of Miami, but died there on 19 February 1962[11][12] prior to its opening. His wife Andromachi "Mary" Papanikolaou continued his work at the Papanicolaou Cancer Research Institute

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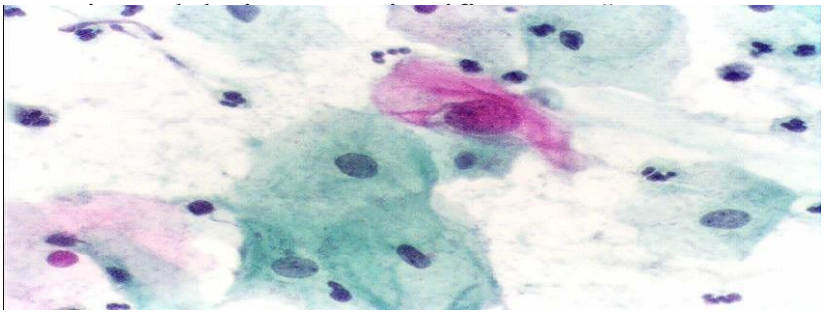
after his death, and died in Miami in October 1982

Discoveries

The fact that malignant cells could be seen under the microscope was first pointed out in a book on diseases of the lung, by Walter Hayle Walshe (1812–92), professor and physician to University College Hospital, London, in 1843. This fact was recounted by Papanikolaou.

In 1928, Papanikolaou told an incredulous audience of physicians about the noninvasive technique of gathering cellular debris from the lining of the vaginal tract and smearing it on a glass slide for microscopic examination as a way to identify cervical cancer. That year, he had undertaken a study of vaginal fluid in women, in hopes of observing cellular changes over the course of a menstrual cycle. In female guinea pigs, Papanicolaou had already noticed cell transformation and wanted to corroborate the phenomenon in human females. It happened that one of Papanicolaou's human subjects was suffering from uterine cancer.

Upon examination of a slide made from a smear of the patient's vaginal fluid, Papanicolaou discovered that abnormal cancer cells could be plainly observed under a microscope. "The first observation of cancer cells in the smear of the uterine cervix," he later wrote, "gave me one of the greatest thrills I ever



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The Romanian physician Aurel Babeș made similar discoveries in the cytologic diagnosis of cervical cancer.[13] He discovered that if a platinum loop was used to collect cells from a woman's cervix, and the cells were then dried on a slide and stained, it could be determined if cancer cells were present. This was the first screening test to diagnose cervical and uterine cancer. Babeș presented his findings to the Romanian Society of Gynaecology in Bucharest on 23 January 1927. His method of cancer diagnosis was published in a French medical journal, La Presse Médicale, on 11 April 1928,[14] but it is unlikely that Papanicolaou was aware of it. Moreover, the two techniques are different in their design. Therefore, although Babeș's publication preceded Papanicolaou's, the design of the Pap test belongs to Papanicolaou since he had already tried it in 1925 in "Women's Hospital". Recent papers have proven that Babeș's method was different from Papanicolaou's and that the paternity of the Pap test belongs solely to Papanicolaou.[15] Despite this, it must be said that O'Dowd and Philipp[13] believe that Babeș was the true pioneer in the cytologic diagnosis of cervical cancer,[13] and in a spirit of recognition and fairness, in Romania, cervical testing is referred to as the *Méthode Babeș-Papanicolaou* in honor of Babeș.[16]

At a 1928 medical conference in Battle Creek, Michigan, Papanicolaou introduced his low-cost, easily performed screening test for early detection of cancerous and precancerous cells. However, this potential medical breakthrough was initially met with skepticism and resistance from the medical community. Papanicolaou's next communication on the subject did not appear until 1941 when, with gynecologist Herbert Traut, he published a paper on the diagnostic value of vaginal smears in carcinoma of the uterus.[17] This was followed two years later by an illustrated monograph based on a study of over 3,000 cases. In 1954, he published another memorable work, the *Atlas of Exfoliative Cytology*, thus creating the foundation of the modern medical specialty of cytopathology.

Commemorations

In 1978, Papanikolaou's work was honored by the U.S. Postal Service with a 13-cent stamp for early cancer detection.

Between 1995 and 2001, his portrait appeared on the obverse of the Greek 10,000-drachma banknote, until its replacement by the euro.[18]

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On 13 May 2019, the 136th anniversary of his birth, a Google Doodle featuring Papanikolaou was shown in North America, parts of South America, and parts of Europe and Israel.

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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*."

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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.

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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 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

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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.

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.

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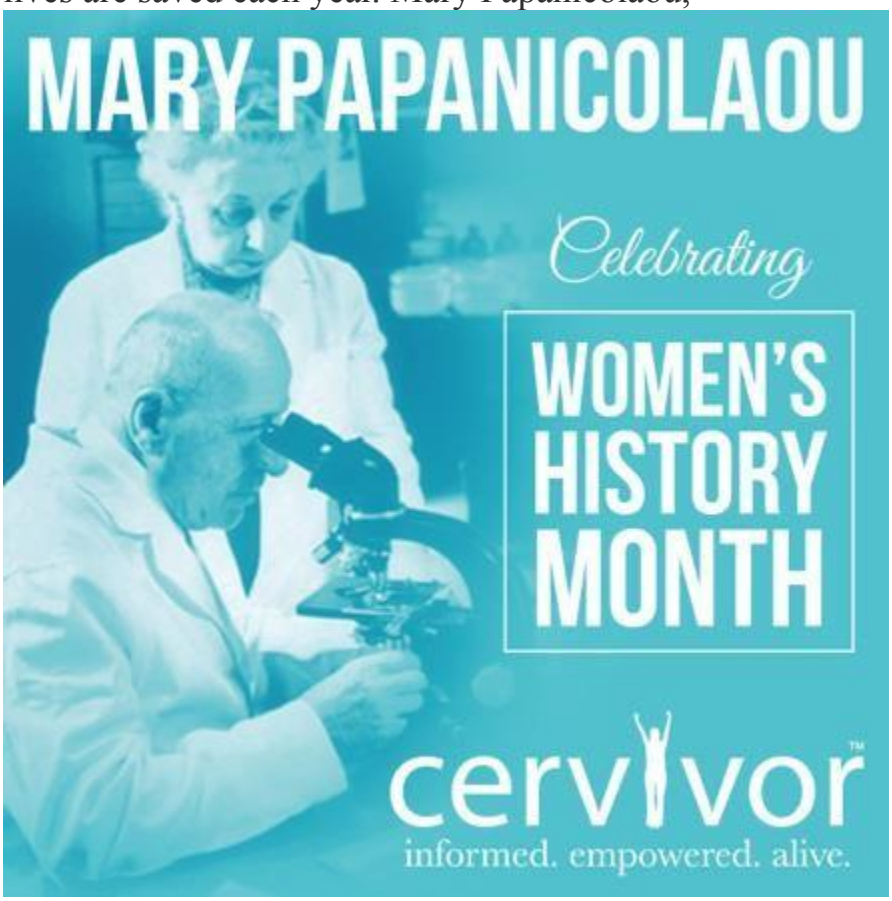
In the mid-1910s, Dr. Papanicolaou was conducting research at Cornell, but because he himself was not a clinician, he lacked access to human patients – except one: his wife. For years, Mary volunteered as an experimental subject for her husband, climbing up on to his examination couch nearly daily so that he could sample her vaginal fluids and cervical cells, which he would smear on a glass slide and examine them under a microscope. It is reported that Mary held gatherings for female friends who agreed to have their cervixes sampled, providing additional subjects for her husband's research.

After one of these women was later diagnosed with cervical cancer, Dr. Papanicolaou was able to determine that cancerous and precancerous cells were visible on the samples. In 1928, he presented these findings at a medical conference, kickstarting the research and refinement that ultimately led to the Pap smear test. With Mary's willingness to have her cervix sampled daily (for years!) she lay the foundation for the invention of the Pap test and ultimately, for the HPV test and HPV vaccine. Thanks to Mary and her husband, cervical cancer can be detected early, cervical cancer mortality rates have plummeted and thousands of lives are saved each year. Mary Papanicolaou,



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