*Journal of BUON* **12:** 139-144, 2007
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# Professor Miltiades Papamiltiades (1907-1987): 20 years since the death of an eminent Greek anatomopathologist and cytologist

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## Summary

*Professor Miltiades Papamiltiades was an outstanding Greek anatomopathologist and cytologist. By his researches on lymphatic vessels and the invention of new staining techniques in exfoliative cytology, continued the work of his predecessor George Papanicolaou against the cancer.*

**Key words:** anatomopathologist, cytologist, lymphatic vessels, Miltiades Papamiltiades, new staining techniques

## Introduction

The appearance and success of a new discipline in medicine is dependent on adequate methods and instruments, and on a favourable climate of opinion which can permit a new idea to flourish. Clinical cytology found both in the middle years of the 19th century, two centuries after the invention of the microscope and in a favourable intellectual climate.

From the first years of the 20th century the cellular theory had attracted a great number of scientists.

Unquestionnably, the cytology explosion in USA, due to the work of the Greek pioneer George Papanicolaou (1883-1962) [1], offered the way of an early cytological diagnosis of cancer, with culmination of the invention of "Pap Test" [2].

Among other disciples of George Papanicolaou [3] who continued his struggle against cancer, figures the Greek cytologist and anatomopathologist Miltiades Papamiltiades (1907-1987) whose name is closely associated with the study of the lymphatic vessels, contributing thus to better knowledge of the lymphatic pathways along which metastases are disseminated and with the invention of new staining techniques in exfoliative cytology [4].

Twenty years since the death of Professor Papamiltiades in 1987, we consider it useful to study the scientific contribution of this outstanding anatomopathologist and cytologist.

## His life

### *First years*

Miltiades Papamiltiades, the eldest son of a school teacher, was born on 9 August 1907 at the large village of Amfikleia, situated at the foot of Mount Parnassus in Greece, where Miltiades and his young brother Dimitrios passed their infancy. In Amfikleia, on 2004, the Greek authorities inaugurated a museum on his honor.

From his earliest childhood Papamiltiades experienced the Balkan War, the First World War amd the defeat of the Greeks in Asia Minor in 1922, followed by the uprooting of the Greek population of Ionia. He completed his secondary studies at the high school in Amfikleia. As the family resources were very meager after the death of his father, he was obliged to engage courageously in various outside activities to help his younger brother [5].

### *Medical studies, activities in Greece*

Papamiltiades studied medicine at the Faculty of Medicine, University of Athens, between 1925 and 1931, and obtained his diploma in 1931 (Photo 1). In 1937 he submitted his thesis *Researches on the structure of the lacrimal caruncle in man and certain mammals*, an anatomopathological study based on long and careful research. At the age of 21 he was fortunate enough to join the staff of the Department of Anatomy



**Photo 1.** In 1930, aged 23, in the room of dissection with another four medical students.



**Photo 2.** In 1940, during his military service as a medical officer.

under Professor George Sclavounos, with whom he held the post of departmental demonstrator from 1928 to 1931, from which time he began the teaching of anatomy which he pursued for nearly 40 years to the benefit of thousands of students. From 1931 to 1933 he held a post as assistant in the Laboratory of Histology and Pathological Anatomy of the Ophthalmological Clinic of the University of Athens. Subsequently, he became head of practical studies in Anatomy and Physiology in the Medical Faculty in Athens (1933-1945). He was also Professor of Anatomy and Histology at the Athens Military Academy between 1937 and 1940 and then at the National Academy of Physical Education in Athens from 1940-1945.

After completing his military service as a medical officer during the Second World War (Photo 2), he was to leave his country in 1945, at the age of 38 years, to spend a period in France.

*Career in France*

He spent 17 years of intensive and fruitful work in Paris. In 1957 he married Denyse (Photo 3), a young French woman who bore him two children Athina and Nicolas and proved an ideal wife.

At the start of his long stay in France he was awarded a grant by the French government from 1945 to 1948. Subsequently, he worked in the Anatomy Department of the Faculty of Medicine in Paris under the direction of such famous masters as Rouvière, Olivier, Delmas, and Vallois (Director of the *Institut de Paléontologie Humaine*), with whom he was closely associated and whose faithful pupil he remained.

He was a staff member of the Anatomy Department of the Paris Medical Faculty from 1945 to 1962



**Photo 3.** In 1984, with his wife Denyse.

(Photo 4), holding the following appointments:

- Research assistant at the *Centre National de la Recherche Scientifique* (CNRS)
- Visiting foreign assistant
- Director of the Cytology Laboratory at the Bacteriology Department (Prof. Huet) at the Nanterre Hospital in Paris from 1951 to 1953
- Director of Research Laboratory in the Anato-



**Photo 4.** In 1962, in the lab of anatomy of the University of Paris with Professors Delmas and Peyres.



**Photo 6.** In 1963, in Amsterdam, with the queen of the Netherlands Juliana, at the International Congress of the Anatomists.

my Department (Professor Cordier), and in 1959 he became Master of Medical Sciences (*maître de conférences*) of the University of Paris (Photo 5).

*Career in Athens and elsewhere*

He returned to Athens in 1962, where he succeeded George Apostolakes in the Chair of Anatomy of the Faculty of Medicine (Photo 6). He held this post for 9 years (1962-1968) and (1974-1977) (Photo 7). From 1970 to 1972 he was Visiting Professor at the Institute of Anatomy of the University of Geneva, and from 15 February to 15 November 1972 he held the post of consultant histopathologist for the World Health Organisation in Cyprus (Photo 8).

## Teaching

Papamiltiades was a renowned teacher who trained thousands of students. He possessed a sort of natural majesty. His great height, his grave expression, his peaceful gaze, a certain reserve, all contributed to give him a truly imposing presence, though he did not have the lively eloquence that rouses the enthusiasm of an audience. But a certain hesitation in speech helped to emphasise his phrases, gracefully supplemented by beatiful drawings.

As the "chief", he was the head of a spiritual family based on confidence and unity. He was benevolent with his pupils and kept an eye on their studies - monitoring, discussing and unhesitatingly accepting the conclusions he found precise.

After his retirement, he continued his scientific activity, advising all those who cared to consult him on subjects to do with anatomy and exfoliative cytology. Until his death he greeted every visitor, young or old, with courteous amiability and spontaneous welcome.

He was 80 years old when he was overtaken by a



**Photo 5.** In 1963, in his laboratory of Anatomy, University of Paris.



**Photo 7.** In 1966, in his laboratory of Anatomy, University of Athens.



**Photo 8.** In 1975, aged 68, at the Faculty of Medicine, Athens.

cerebral vascular accident in Athens in July 1987. His loss plunged into mourning both Greek anatomy and the foreign colleagues who had known and loved him. Such were the life and work of this man, who became one of the most renowned Greek anatomist of 20th century and one of the most renowned of contemporary anatomists (Photo 9).

## Scientific work

It is difficult to summarise his scientific work, which includes notes, communications, and a great number of articles and memoirs. It is considerable and varied and extends to every field of anatomy, histology and cytology. Study of the lymplatic system as well as the invention and application of new staining methods in exfoliative cytology were his chief interests.

### *Lymphatic system*

a) Respiratory system

*Lymphatics of the pulmonary artery* (1952) [6]. He was the first to describe the lymphatics of the pulmonary artery in man, together with their efferents and nodal connections.



**Photo 9.** In 1980, with the President of the Hellenic Republic Konstantin Karamanlis.

*Lymphatics of the bronchi and pulmonary segments* (1958) [7]. He was the first to give a detailed desrciption of the infrastructure of the lymphatic system of the lungs, thereby contributing to a better understanding of the paths of spread of carcinoma, something of particular value for both clinicians and surgeons.

*Influence of the first respiration on the form and function of the lymphatic plexuses of the lung in the newborn* (1971) [8]. He reported the existence of a large number of lymphatic vessels within the lung, as well as a large amount of lymph, and demonstrated the effect of the first respiratory excursion in the newborn on the vessels in question.

b) Female genital organs

*Some details of the anatomy of the lymphatics of the ovary* (1958) [9].

*Relations between the hormonal activity of the ovary in women and the mechanisms of neoformation of its lymphatic plexuses* (1961) [10].

*Special functions of the lymphatics of the ovary and their anatomic and functional relations with the tubes* (1963) [11].

*Investigations into the arrangement of the lymphatics of the body of the uterus* (1966) [12].

*Functional significance of the lymphatic connections of the ovary with the adjacent organs of the female genital tract* (1971) [13].

*Possible role of the lymphatics of the female genital system in sterility* (1972) [14] .

*Lymphatic connections of the ovary with the tubes and the uterus* (1972) [15].

*Functional significance of the lymphatic spaces of the tubes* (1972) [16].

*The utero-ovarian lymphatic-bearing system in*

*women and its function* (1972) [17].

His researches on the lymphatic system of the female genital organs enabled him to demonstrate modifications and proliferation of the lymphatic vessels in the ovaries, due to their role as vehicles of the hormones. His conclusions were adopted by, among others, Professor George Papanicolaou [18].

### *Other systems*

*Veins of the thymus* (1948) [19]. This study supplied new information as to the arrangement of the thymic venous circulation and was a reply to certain authors who claimed that, in this organ as in many others, the venous and arterial circulations were exactly superimposed.

*Communication between the anterior chamber of the eye and the lymphatic system* (1951) [20]. He was able to show the efferent lymphatics, which begin at the outer or inner angle of the eye, are injected together with the episcleral venules, and continue via the main efferent lymphatic trunk into the parotid nodes.

*Cavernous sinus* (1951) [21]. He described certain types of cavernous sinus whose structure did not correspond to the classical description. His observations were confirmed by the work of PE Duroux, A Bouchet, I Bossy and Fr Calas.

*Communication between the anterior chamber and the lymphatic plexus of the ocular conjunctiva in man* (1956) [22]. These studies confirmed the existence of a pathway for the seeping of aqueous fluid into the lymphatic network of the conjunctiva. Moreover, this work was a response to the criticism by Professor Amsler of Gerota's method for the study of the lymphatic connections of the anterior chamber of the eye.

*Lymphatics of the spinal ganglia* (1960) [23].

*Observations on the anatomical disposition of the lymphatic networks of the heart* (1964) [24].

*Lymphatic networks of the nasal mucosa* (1970) [25]. He gave a description of the topographic distribution of the lymphatic networks in the nasal mucosa, providing information explaining some of its functions.

### *Exfoliative cytology*

*Cytodiagnosis of the action of folliculin* (1953) [26]. He discussed 1) the cytology corresponding to the histologic structure of the vaginal epithelium; 2) the technique for vaginal smears (removal, fixation, staining); 3) hormonal influence on cytologic composition; 4) the interpretation of the cytologic composition of the slides; 5) the practical value of examination of vaginal smears in hormonal diagnosis.

*On the composition of two hematoxylins for cytologic staining* (1953) [27]. He succeeded in preparing two forms of hematoxylin which gave excellent results: Lugol's hematoxylin and hematoxylin with zinc sulfate. These have the advantage of being ready for immediate use without overstaining the cytoplasm. The Lugol variety favors the staining of eosinophils and the zinc sulfate preparation that of the basophils. They bring out the chromatin network of the nucleus and are resistant to the acidity of differential cellular and histologic stains. Lugol's hematoxylin favors differential staining. The zinc sulfate stain is used in the USA in histochemical staining for the demonstration of nucleoproteins and in Europe for normal and malignant cytodiagnosis.

*A critical study and some practical notes on the staining of vaginal smears* (1954) [28]. This study discusses the advantages and disadvantages of different cytologic stains.

*A simple and rapid method for staining of endocrine vaginal smears* (1954) [29]. This stain, specific for hormonal vaginal smears, contains zinc sulfate/hematoxylin, acidochrome, and basochrome. The acidochrome is an indicator which electively stains the eosinophils. The basochrome is a mixture without free acids whose chief stain is light green reinforced by methylene blue. The time for such staining and the number of manipulations are minimised, and dry or moist smears are stained with the same precision. It is very stable and perfectly differentiates eosinophils from basophils, preserves the transparency of the cytoplasm and brings out very well the structure of the nucleus. This method of staining is a currently employed in pathological laboratories in France and other countries.

*A method for rapid staining of the hypophysis with Lugol's hematoxylin* (1955) [30].

*The action of hematoxylin with zinc sulfate on nitric stains (naphthol yellow) and oxyquinones (alizarin) in cytologic staining* (1957) [31].

*Injection of lymphatics: 1) with colored cedar-oil and 2) with plastic substances* (1961) [32]. The advantage of this over other methods is the exact definition of the internal networks of the various organs.

## Conclusion

The contribution of Miltiades Paramiltiades in the field of anatomy and cytology was outstanding. Especially in the domain of exfoliative cytology, he in-

vented a new staining technique which was to bear his name, applied as the prime method of cytodiagnosis by cytologists in France, Spain, Switzerland and Latin America (Photo 6). He also invented a new method for investigation of the lymphatic vessels by injection of a new stain, contributing to better knowledge of the lymphatic pathways along which metastases are disseminated (Photo 7). This method has been adopted and employed by several university laboratories.

The studies of Miltiades Papamiltiades, which are now classics, have been adopted by very many of the leading personalities in medicine.

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