

Nikolae Paulescu - an unrecognized fighter in the treatment of diabetes

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Summary: Taking into account the number of people suffering from diabetes all over the world, it is understandable that there is a great interest in discovering the disease and its cause, as well as in finding an adequate therapy. Although the first data on diabetes date back to around 500 BC, it was first scientifically confirmed and described only at the end of the 19th century. In 1923, the Nobel Prize for the discovery of insulin was awarded to McLeod and Bunting, but the name of another doctor should be closely associated with this important discovery. It is prof. Nicolae Paulescu, a famous Romanian doctor, scientist and reformer of the educational system in this country. He devoted his entire career to research in medicine and adequate education of young people. Prof. Paulescu made the greatest contribution in the field of endocrinology when in 1921 he presented his studies on the effect of pancreatic extract on animals suffering from diabetes, which was equivalent to the discovery of insulin. However, the reward for this achievement was received by other scientists discrediting his contribution, and they found cover for it in his political views.

Key words: Nicolae Paulescu, diabetes, insulin.

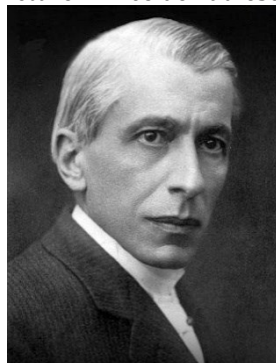
The history of discovering and trying to treat diabetes goes back thousands of years. The disease was first recorded in Ancient Egypt on a papyrus discovered in 1862, and diabetes was described as a disease characterized by strong thirst and excessive urination. Sanskrit writings (around 500 BC) describe the urine of the patient as "honey" [1].

Although it has been known for a long time, the disease was experimentally studied and described only at the end of the 19th century, when it was proven that the pancreas plays a central role in the development of this disease. The role of the pancreas in glucose metabolism, as well as the discovery of insulin, were not clarified until 1921, when Sir Frederick

Bunting and Charles Best proved that in dogs without a pancreas, diabetes could be prevented by giving an extract from the islets of Langerhans of the pancreas of healthy dogs. They managed to isolate insulin from the pancreas of beef at the University of Toronto, to purify it for clinical use, which made it possible to use it in the therapy of diabetes. Two years later, in 1923, the Nobel Committee for Medicine awarded the prize for the discovery of insulin to laboratory director McLeod and Bunting [2].

That history knows how to sometimes play rough with people, who have dedicated their lives to science and research, is shown by the case of prof. Dr. Nicolai Paulescu, a man who is not recognized for his discovery of insulin.

Picture 1-Nicolae Paulescu



The famous Romanian scientist, doctor and professor Nicolae Paulescu was born on October 30, 1869 in Bucharest. His family was well known in their community and benefited from aristocratic status. His father, Constantin Paulescu, a prominent merchant in Bucharest, represented the merchant class in the Romanian Parliament. His two daughters, Elena and Constanta, were alumni of the Bucharest Conservatory of Music, while the eldest, Nicolae Paulescu, is better known for his medical career [3].

His mother, Marija Dancovici, was a well-educated woman who came from another well-known merchant family [4].

During his childhood, Nicolai Paulescu was characterized by his teachers and family as "obedient and with a special capacity for memory, analysis and synthesis." He finished elementary school with a first prize with a laurel "for diligence in music and good governance" [3,4].

During his high school education, he acquired an impressive general culture by learning French, ancient Greek and Latin. This later enabled him to read works of classical philosophy in the original. His biology teacher, Dumitru Ananescu, instilled in him a love of the medical sciences with his superb mix of theoretical and practical demonstrations. Over the years, Paulescu constantly referred to his teacher's contributions to his education [5].

After finishing high school in 1888, he was admitted to the renowned medical faculty of the University of Paris. Here he had the opportunity to be taught by the most famous medical professors of the time: anatomy with

Louis Farabeuf (1841-1910), organic chemistry with Armand Gautier (1825-1894) and histology with Mastias Duval (1844-1907). However, the one who exerted the greatest influence on the further work of Nicolai Paulescu was prof. Dr. Etienne Lansereau (1829-1910), his professor of anatomy and pathology [3,4].

After graduating from the Medical University of Paris in 1891, he became an intern at the Hotel Dieu hospital where he continued to work with his mentor, prof. Etienne Lansereau. In gratitude for his entire work, prof. Lansereau took the necessary steps to hire him as chief of medicine at the Hospital Notre Dame de Perpetuel Secours. In 1897, Paulescu earned the title of doctor of medicine and surgery by defending the thesis "Investigation of the structure of the spleen" in which he describes the vascularization of the spleen and creates the first classification of epithelial glands. The next few years were very fruitful for the young Paulescu. He first obtained the title of Doctor of Natural Sciences at the Faculty of Natural Sciences in Paris (in 1899) with the theses "Experimental research on respiratory and heart rhythm under the influence of different body positions" and "Causes and mechanism of sudden death with a change in body position from horizontal to vertical". This thesis represents one of the first investigations into the phenomenon of sudden death. In 1901, he obtained the title of doctor of medicine at the Sorbonne University in Paris with the thesis "Comparative study of the effect of alkaline chlorides on living matter", providing valuable data on the behavior of living matter [5].

Picture 2-Nicolae Paulescu in Paris in 1897



In 1900, motivated by his patriotic, religious principles and homesickness, he returned to Romania where he assumed an active leadership role in the national reform of the educational, medical and research system. He left a deep mark on French medicine. He became a member of the French Academy and was awarded the Order of Academic Palms. Even more impressive is the fact that Notre Dame de Perpetuel Secours Hospital once a year offered two internship positions to Romanian students directly recommended by Nicolae Paulescu. This tradition continued even after his death. Unfortunately, it ended in 1940 after the outbreak of World War II [3,4].

When he returned to his homeland, Paulescu focused all his efforts on establishing the first physiology department at the "Carol Davila" University of Medicine and Pharmacy in Bucharest. He left Romania only for very short periods. It is worth noting that while he was working on this project, he was offered a professorship at the Faculty of Medicine in Fribourg, Switzerland and in Paris after his mentor's retirement. Each time he refused the offer and plunged deeper into his project of establishing a department of physiology [3,4].

Another field of interest is the reform and reorganization of the Romanian medical

education system. After the unification of Romania on December 1, 1918., the country had only 3 university centers: Bucharest, Iasi and Cluj-Napoca. Paulescu continued to fight for a better quality of life and work of students and to prioritize the practical part of medicine over the theoretical part [4,5].

As a scientist, he is the author of 46 experimental and clinical studies published in renowned international journals of the time. However, three of his experimental studies are still of undeniable importance today. It is the discovery of the role of the pituitary gland (proving that its absence leads to death), the transparietal approach to ablation of the pituitary gland, which later inspired the American neurosurgeon Harvey Cushing [6].

The third field of interest was the study of diabetes. His work in the field of endocrinology culminated in the discovery of insulin. He took his first steps in this field in 1899 when he started his work with prof. Dartreoma on the isolation and study of pancreatic products. However, these investigations were not completed or officially recorded due to Paulescu's return to Romania [3,4].

Picture 3 - Nicolai Paulescu's original office preserved in the Nicolai Paulescu Museum at the "Carol Davila" University of Medicine and Pharmacy in Bucharest



The next step was marked by the isolation of the "aqueous extract of the pancreas" in 1916, or as he called it pancrein. By injecting the extract into

the jugular vein of dogs with pancreatectomy-induced diabetes, he observed that the pathological blood glucose level temporarily

returned to normal. However, the insufficient purity of pancrein extract made it unusable for human consumption. Shortly after the end of these experiments, Paulescu was mobilized into the Romanian army, due to the upcoming Hungarian-Romanian war (1918-1919). After the war, starting in July 1921, he published four articles in which he described his research, the last of which, the most detailed, appeared at the end of August 1921 [3,7].

Between April 24 and June 23, 1921, Paulescu presented his 4 experimental studies at the Congress of the Paris Biological Society:

- Effect of pancreatic extract injected into the blood of diabetic animals [8]

- Effect of time elapsed since intravenous injection of pancreatic extract on diabetic animal [9]

- The influence of the amount of pancreas used in the preparation of the extract injected into the blood of a diabetic animal [10]

- Action of pancreatic extract injected into the blood of a non-diseased animal [11]

Also, on June 22, 1921, he sends the article "Investigation of the role of the pancreas in the digestion of nutrients" to the International Archives of Physiology in Liège, Belgium, which will be published on August 31, 1921. In this article, he first presented the effect of pancreatic extract on glycemia, glycosuria and acetonuria [12]. In other words, this article confirmed the discovery of insulin (pancrein).

Picture 3-Statue of Nicolai Paulescu in front of the Faculty of Medicine in Bucharest



However, all these findings were not recognized as revolutionary by the medical luminaries of the time. The news that the Nobel Prize was awarded to the Canadian team further radicalized his socio-political views in the context of his time (emergence of National Socialism), publishing some far-right articles and books [5]. This radicalization proved useful to his rivals in terms of discrediting Paulescu's

scientific contributions. He died in full academic maturity and creative activity at the age of 62, on July 27, 1931. He was buried in the White Cemetery in Bucharest. Posthumously, in 1990, he was elected a member of the Romanian Academy.

Conflict of interest: The authors declare that they have no conflict of interest.

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