



THE MEDICAL PRIORITIES OF NICOLAE C. PAULESCU

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The majority of the members of the medical community know that N.C. Paulescu is the discoverer of insulin (Pancreine). However, at an careful analysis his field of interest was related with many physiological aspects, even if the majority of them are related to endocrine glands and metabolic function of the liver and, of course, of the pancreas. Here we made a short review of his main priorities, which cover many domains of medical sciences.

1. 1897: Using the catheterization of the supra-hepatic vein in animals (the catheter inserted through the external jugular vein, right auriculum and inferior vena cava) he demonstrates (contrary to the current time opinion) that **the coagulation duration of the blood from the supra-hepatic vein is the same with that of the blood obtained from the portal vein or peripheral veins**. *Archives de Physiologie, no. 1, January 1897, p. 21*;
2. 1897: he performs **the head-to head anastomosis** of the mucosa of **veins, uretherus and choledocus** (together with Reynier). *Bulletines et Memoires de la Societe de Chirurgie de Paris*;
3. 1897: **classification of the vascular glands** in three distinct categories (1) **epithelial** (such as liver and pancreas), that exhibit both an **external secretion** (drained on specific pathways, bile and pancreatic juice) and an **internal secretion** (delivered directly into blood); (2) **epithelial** that have no excretory ducts and deliver their **secretory product directly into blood** (such as thyroid and adrenals); (3) **conjunctive-lymphatic** that have no excretory ducts (such as spleen, thymus and lymph nodes). *Doctoral thesis in medicine – Paris 1897*;
4. 1898: utilization of a subcutaneous sterile collagen injection (gelatin) as **treatment of aneurisms** specifically for the aortic aneurism. Prior to this, he demonstrates in dog experiments the **absorption of collagen from the peritoneum and the subcutaneous tissue**, infirming its “non-dialyzable” nature (together with Lancereaux). *Bulletin Academie de Medicine, 22 Juin 1897*;
5. 1898: studies regarding the **function of thyroid** and diseases associated with this as well as the effects of the **iodotirin treatment** (BAUMANN thyroid extract) not only in thyroid insufficiency (hypotiroidism), but also in chronic metabolic disorders (obesity, gout or other degenerative diseases), with favorable results. *Journal de Medicine Interne, 1 January 1899*;
6. 1898: researches regarding the **„cellular specificity in cancers”**, i.e. the development of cancer from the cells of the tissue where it appears. He confirms this by analyzing thyroid cancer that produces an excess of thyroid hormones, expressed through hyperthyroidism. He contradicts in this way the theory of the “cellular indifference” (i.e. the non-specific nature of cancer), this point of view being confirmed subsequently. *Journal de Medicine Interne, 15 November 1898*;
7. 1908: he publishes the monography **„L’Hypophyse du Cerveaux”**, in which he describes his original technique of **trans-temporal hypophysectomy** technique, commented by the illustrious American surgeon Harvey Cushing (1869–1939) as „by far, the most important contribution in the field”. Through this method, Paulescu demonstrates for the first time, **the vital nature of hypophysis** (stop of the development of the experiment animal); *L’Hypophyse du Cerveaux. I vol., 146 pag., Vigot Edit., Paris, 1908*;
8. 1911: The indirect discovery of **“incretinic effect”** of the intestinal mucosa, showing that the oral administration of glucose is followed by a powerful increase in the glycogen accumulation of the liver, in contrast with the intravenous administration of the same quantity of glucose, which has any effect on

- that liver function. Paulescu N.C., *Sur la formation du glycogène dans la foie, par suite d'injections de divers sucres, dans la veine porte. Annales de Biologie 1911, Vol. I, p. 228, Paris.*
9. 1911–1913: numerous experiments regarding the **glycogenic function of the liver**, demonstrating experimentally for the first time **the role of the internal secretion** of the pancreas on this function. He also demonstrates experimentally **the sources of liver glycogen**: *maximum after carbohydrate intake*, still important after *protein intake* but almost *null after lipid intake*. He demonstrates the quasi-generalized and *relatively uniform distribution of glycogen in the liver* [2], [3], [4], [5], [6], [7], [8], [9];
 10. 1912–1916: he conceptualizes diabetes as **a disorder in the utilization of biochemical fuels**, not only of carbohydrates, but also lipid and protein. This is a visionary concept that was really accepted only in the last 10 years;
 11. 1920: He describes magisterially the relationship between obesity and diabetes: „*Most often the obese become glycosuric, as if the two disorders, – obesity and fat diabetes – represent two phases of the same pathogenic process*”;
He magisterially demonstrates the **distribution of the adipose tissue**, mentioning for the first time the **different significance of the abdominal fat** (mesenteric and epiploic) *versus* subcutaneous fat
 12. 1920: he described in detail his original technique for **total pancreatectomy** in dogs, considered by him a *sine qua non* condition for the development of experimental diabetes;
 13. 1920: he establishes the blood glucose lowering effect after the administration of his pancreatic extract (called by him *Pancreine*), mentioning for the first time the therapeutically induced **hypoglycemia**;
 14. 1920: he establishes for the first time the **protein anti-catabolic effect** (by determining the values of urinary and blood urea before and after the administration of his pancreatic extract);
 15. 1920: he establishes the **dose-response relationship** of the pancreatic extract on blood glucose (the glucose lowering effect of pancreatic extracts being evidenced by several researchers since 1893 but Paulescu's data were much more relevant than the previous);
 16. 1920: the description of the physiological role of instincts witch influences the nutrition behavior leading to obesity, alcoholism and addiction for various substances. By extension, some individuals or collective instincts might explain some social conflicts;
 17. 1921: he establishes the **duration of action** for his pancreatic extract (its pharmacodynamics) after i.v. administration „*the effect starts immediately after injection, reaches a maximum after 2 h and exhausts after 12 h*” [12], [13];
 18. 1921: he establishes for the first time the **anti-ketogenic effect** of his pancreatic extract [12], [13];
 19. 1921: he establishes the **physiologic nature** of the antidiabetic pancreatic hormone (called by him *Pancreine*) that decreases blood glucose not only in diabetic animals but also in healthy animals [12], [13];
 20. 1922: obtains a **patent** for **”Pancreine and its production technique”** [14];
 21. 1923: attempts to localize the various instincts in the brain. *Traité de Médecine*, vol. III, p. 606–625.

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