

Editorial
NC Paulescu's "Traite de Physiologie Medicale"
Summary of Achievements During a Life Dedicated to Medical Science

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It was our intention that by the end of 2010, we would succeed in republishing the famous "Traité de Physiologie Médicale" (3 volumes, 2300 pages), 90 years after its original publication. This will be the first installment of a "Fundamental Works of Romanian Medicine" collection, which must also contain seminal works such as Gheorghe Marinescu's "La Cellule Nerveuse", Cornil and Babes's "The Treatise of Microbiology" and others.

Until now, for those working in the field of Diabetes, this treatise has been regarded only as his first announcement of the discovery of insulin ("pancrein", as the author originally named it). Indeed, at the end of the chapter presenting his most important experiments, he states the following: "This data shed a new light on the pathogenesis of this syndrome, and also give us the key to its treatment." The "new light" of the pathogenesis meant the confirmation of his vision on diabetes, as a disorder that involves all of the metabolic pathways of the body's main fuels (carbohydrates, lipids and proteins), and that this is due to the dysfunction in the secretion of the antidiabetic hormone discovered by him, demonstrating that its intravenous injection led to the correction of these disturbances. If his concept of the pathogenesis of diabetes, published in 1920, as a disturbance of the entire energy

metabolism had been understood in his time, the diabetological body of knowledge would have known a faster a shorter road to progress.

Aside from these widely known pieces of information, the republication of this treatise has brought to light several unexpected aspects: a) physicians from other fields have had the opportunity to find out that the roots of many of their respective fields of medicine can be traced back to the chapters of this comprehensive work; b) even more importantly, we managed to identify at least 20 medical firsts in various fields which greatly amplify the importance of Paulescu's contribution to medical progress, both nationally and internationally. It is a great honor for us to mention among these the following:

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, n 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. 1911-1913: 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];
 9. 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;

10. 1920: he magisterially demonstrates the **distribution of the adipose tissue**, mentioning for the first time the different significance of the abdominal fat (mesenteric and epiploic) and subcutaneous fat. 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*”;
11. 1920: he demonstrates in detail his original technique for **total pancreatectomy** in dogs, considered by him a *sine qua non* condition for the development of experimental diabetes;
12. 1920: he establishes the blood glucose lowering effect after the administration of his pancreatic extract, mentioning for the first time the therapeutically induced **hypoglycemia**;
13. 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);
14. 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);
15. 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;
16. 1920: attempts to localize the various instincts in the brain. *Traité de Médecine*, vol III, p. 606-625 ;
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].

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