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HISTORY OF DIABETES MELLITUS IN ROMANIA

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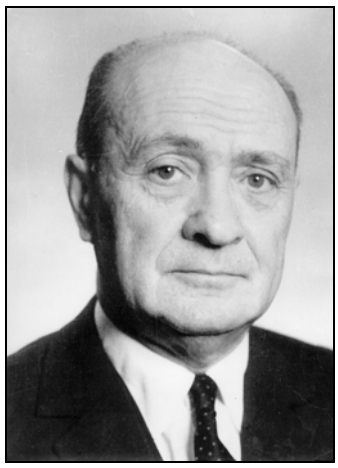
ASSISTANCE OF DIABETES IN ROMANIA

Diabetology is a recent specialty, which has become a necessity when diabetes has become such an important issue that it consumes between 7–15% of the health budgets of different countries. The growing number of patients, as well as the increase in their survival, have led to the establishment of special services for diabetic patients, because, due to the chronic nature of the disease, the need for precise nutritional care, sometimes sophisticated treatment (special syringes, pens or insulin pumps) and a mandatory periodic assessment, the personnel involved in these activities must be properly trained.

Traditionally, in Europe, diabetes care has been provided by either internal medicine or endocrinology or "endocrine-metabolic" services. Within these specialties, it soon became apparent that those caring for diabetic patients no longer have the time to care for other categories of people. Whether the basic specialty was internal medicine or endocrinology, physicians who assisted diabetic patients self-specialized in the field of "diabetology", becoming de facto diabetologists.

In Romania, since the middle of the last century, Professor Ion Pavel (1897–1992) intuited the social dimension of diabetes and created one of the first specialized services for this category of patients in Europe. As the main activity of following these patients is outpatient, the first organizational nuclei were called Antidiabetic Centres. For the more difficult cases (insulin-dependent diabetes) or for the complicated ones, specialized Clinics have appeared and, in time, a postgraduate and university education of profile.

During the formation of the specialty of "diabetes", the justification of its existence was difficult, speaking of a specialty for "a single disease". It was agreed, therefore, that the specialty be named Diabetes, Nutrition and Metabolic Diseases. The dimensions and problems related to this name proved, however, to be too wide to be well mastered by a single specialist. In many countries, nutrition, for example, is an independent specialty, and metabolic diseases include many widespread conditions: obesity, dyslipidemia, hypoglycemia, malnutrition, and many genetically determined metabolic diseases. The latter are found especially in paediatric services. Although in theory the specialty of Diabetes, Nutrition and Metabolic Diseases provides for the coverage of these broad territories, in practice the specialists bearing this title are, in fact, "diabetologists". Over 98% of their activity is dedicated to diabetes.



Ion Pavel

Organizing diabetes into a "national network" system (including a Diabetes Centre for each county) was a good solution for the period 1950–1980. After this date, it became increasingly clear that the number of patients per specialist was between 2,000 and 5,000. Increasing the number of places to reside was beneficial, but proved insufficient to cover the problem. The fact that in 2004 there was 3 more counties without a Diabetes Centre (in the absence of the diabetologist) may lead to the dangerous conclusion that "it is possible even so". It is possible, of course, at the cost of

high mortality and severe, costly and humanly disastrous chronic complications.

This is the situation at the beginning of 2004, when the Institute of Diabetes, Nutrition and Metabolic Diseases "N. C. Paulescu" drew up a project to optimize healthcare in this specialty, using an additional number of specialists, leading to a diabetes / patient ratio of no more than 1: 1,000. Taking into account only registered patients, to which is probably added an equal number of unregistered), the number of specialists in the country should be at least 450. Currently it is well below half.

In parallel with this action, we are considering a project to decentralize the care of diabetic patients, setting up Diabetes Centres in each city with a population of more than 20,000 inhabitants. There will be a "county network" of diabetes in each county. In smaller centres, specialist care for diabetic patients will need to be provided by resident or general practitioners, adequately trained for this purpose. An evaluation of the effects of this initiative could be made at the next edition of this Treaty.

THE BEGINNING OF ROMANIAN SCIENTIFIC MEDICINE: CAROL DAVILA (1828–1884)

In 1852, the young French doctor Carol Davila, a graduate of the Faculty of Medicine in Paris, was sent to Wallachia by the French government, at the request of Prince Barbu Stirbei, with a precise mission: to organize the local health sector. He remained permanently in Romania, obtaining Romanian citizenship in 1866, following a decision of the Parliament. Until this date, he had carried out a vast activity of organizing the military sanitary sector and protecting public health. In 1855 he founded the "School of Small Surgery", so that in 1857 together with Nicolae Kretzulescu he founded the "National School of Medicine and Pharmacy", whose graduation diploma will be recognized by similar educational institutions in France and Italy. In its current form, the Faculty of Medicine in Bucharest was founded in 1859. After 145 years of uninterrupted activity, the University of Medicine and Pharmacy in Bucharest is "the oldest, largest and best medical school in Romania"[19].

In parallel, Carol Davila is the promoter of the medical scientific movement, founding in 1857 the "Scientific Medical Society" (whose first secretary he was), as well as the first medical publications: The Romanian Doctor (1859), the Medical Monitor (1862), the Medical Gazette (1865). He founded, in 1876, the "Red Cross Society" and the "Society of Natural Sciences". He wrote the first Romanian Pharmacopoeia[1, 5, 13, 21, 22].

Carol Davila

In 1860 he was appointed general of the Romanian Army, in which year he became involved in the organization of the "Botanical Garden of Bucharest", designed as an educational base for students and a recreational base for the population of Bucharest[17].

In 1866 he participated in the accession to the throne of Carol I, in front of whom, like a prophet, he unfolded the map of Romania comprising Transylvania, Bucovina and Basarabia, telling him: "Here is the Land of Your Majesty".

In the War of Independence (1877–1878) he led the army's sanitary service, caring for the wounded in both belligerent camps. He was one of the close advisers of King Carol I, the maker of modern Romania.

He published important medical works: Syphilis Prophylaxis (1853), Atmospheric Air (1871).

Until his death, on August 26, 1884, at the age of 56, he established numerous medical services, as well as the "Elena Doamna" Asylum[17].

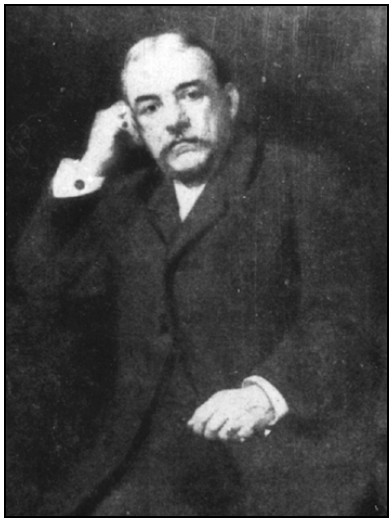
Although he had some adversities during his life, his merits were nevertheless recognized. Napoleon III (who had granted, at the insistence of Carol Davila, Romanian students' special privileges since 1857) awarded him the "Legion of Honour", being decorated by the President of the French Republic, the Emperor of Russia, the King of Italy and finally by the Romanian Senate (the moment of advancing to the rank of Major General). Post-mortem, the University of Medicine and Pharmacy from Bucharest, a hospital and a

street in Bucharest bear his name. A bust made by Brâncuşi in 1903 is in the Army Military Museum.

PEOPLE AND IMPORTANT EVENTS IN THE HISTORY OF ROMANIAN DIABETOLOGY

A brief history of Romanian diabetology can be found in the work Diabetes in Romania, published in 2001[9]. On the pages 718–727 can be found the titles of works in the field of diabetes, signed by great internists, neurologists or endocrinologists of the time, but also by some doctors whose biography we know less. In this regard, diabetology historiography has to recover many delays.

1870 – N. Kalinderu (1835–1902) obtains his doctorate in Paris, where he studied medicine (between 1858–1863). He worked as a doctor at the Colentina (1874–1878) and Brâncoveanu (1878–1902) hospitals. In 1893 he published Nervous Disorders in Diabetes (Medical Romania 1: 185–192).



Nicolae Kalinderu

1883 – Christea Buicliu (1857–1916) defends at the Faculty of Medicine in Paris the Doctoral thesis "Notes sur quelques points de la simptomatologie du diabete". This may be the first scientific paper on diabetes, written by a Romanian. In 1903, he published in the journal Hospital: The Pancreatic Diabetes with an introduction to Glycosuria (vol. 23, no. 9, p. 337–347). After his return from Paris, he will work as a professor at the Brâncovenesc Hospital, being among the first doctors with concerns for diabetes[9].

Christea Buicliu

1892 – Alexandru N. Vitzu (1852–1902), supported by palaeontologist Grigore Cobălcescu (1831–1892), studied physiology at the Sorbonne (1877–1882), in the laboratory of Paul Bert. In 1892, he founded in Bucharest the "Institute of Experimental Physiology" attached to the Department of Zoology and Animal Physiology at the Faculty of Sciences, of which he was the first professor. He studied endocrine function of the pancreas and kidney, as well as neurophysiology studies. In 1894 he published "A New Function of the Pancreas. Pancreatic diabetes. The role of internal secretions in nutrition." In 1895 he published the Doctrine of Internal Secretions in terms of their role in the body (representing the first small Treaty on diabetes). In 1901 he published "Recherches expérimentales sur la sécrétion interne des reins »[9].

Alexandru N. Vitzu

1893 – E. Sterian publishes "Reflections on spinal cord disease in diabetes" (Medical Romania 1: 459–462).

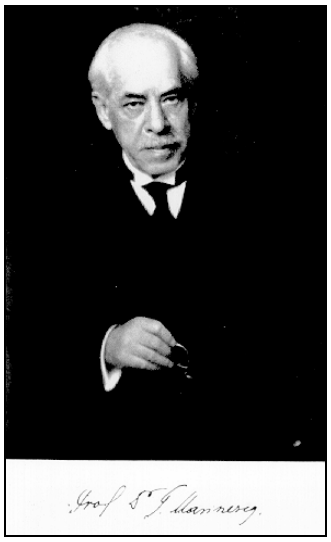
1901 – N. C. Paulescu, after defending the 3 doctorates in Paris, establishes at the Faculty of

Medicine from Bucharest, the Department of Physiology, which he will lead uninterruptedly until 1931, the year of his death[9, 10].

Faculty of Medicine from Bucharest

1901 – Gheorghe Marinescu (1863–1938), founder of the Romanian School of Neurology, repeatedly addressed issues related to the nerve complications of diabetes. He issued the theory of "reflex trophicity", which has a wide application in the pathology of the "diabetic foot". In 1901, he published "Alterations in the peripheral nerves and secondarily in the cells of the anterior horns of the marrow in case of diabetes. Pseudostepsis" (Hospital 21:12, 321). In 1909, he published in Paris the work "La cellule nerveuse", prefaced by Ramon y Cajal, one of the exceptional works of European medical literature at the beginning of the last century. In 1924, he addresses histochemically the problem of oxidizing enzymes involved in life phenomena. He approaches, in his studies, the problem of alcoholism (1930), the role of vitamins (1934), as well as a series of philosophical-medical problems, in the works "Matter, life and cell" (1914) or "Determinism and causality in the field of biology" (1937). In 1925, he published a monograph on the life and work of Charcot (1925), dedicated to the great French neurologist he met in Paris and whose name is linked to the complication of diabetes known as the "Charcot's foot". In 1934, Gh. Marinescu and I. Nicolescu published "À propos des relations du noyau tuberien Peri-Ventriculaire avec le diabète sucrée" (C. R. Soc. Biol. 116: 21, 557).

1907 – Appears in Paris N. C. Paulescu's "L'Hypophyse du cerveau", Ed. Vigot. It is one of the most important works of the early twentieth century. The technique of transtemporal hypophysectomy (the original method imagined by Paulescu and described for the first time in this Treaty) was considered, at that time by the famous American endocrinologist H. W. Cushing, as the most important achievement in the field. Paulescu's contribution in this chapter of endocrinology (to which he contributed with many original experiments) risks being overshadowed by his prodigious research activity carried out between 1911 and 1928[9, 10].



Gheorghe Marinescu

1907 – The work of C. I. Parhon (1874–1969) and M. Goldstein (1872–1955) "Les sécretions internes" is published in Paris. Pathology and Physiology, Masson. In 1930, Parhon published his doctoral dissertation "Research on the vascular action of insulin" 32 pages[10].

1911 – N. Paulescu publishes in "Annales de Biologie de Paris" (vol. I, p. 228) the first of a series of his works dedicated to the origin of hepatic glycogen, continued until 1920. These studies focused, in essence, on the pathogenesis of diabetes[9, 10].

1913 – At the "Bethlehem" Hospital in Bucharest (St. Vincent de Paul), on the current territory of the Institute of Endocrinology, N. Paulescu opens a medical consultation service, especially for diabetic patients. In the opening lesson held on May 12, 1913, Paulescu says: "Medicine studies man and, alone among the sciences, has man as the only object of his study"[10].

1915 – Th. Mironescu publishes "A serious case of pancreatic diabetes" (Bul. Soc. Med. si Nat., Iaşi, 10-12, 109–114).

1920 – Volume II of N. Paulescu's "Traité de Physiologie Médicale" appears, published in French and distributed by Ed. Vigot in Paris. In this paper appear in extenso the first experimental data aimed at isolating and characterizing the

pancreatic endocrine secretion. We are tempted to believe that such a work, published in Paris, could not be missing from Canadian libraries, especially at the University of Toronto, where the head of the physiology discipline was J. J. R. MacLeod, a personality recognized as an authority on carbohydrate metabolism. In fact, in 1926 MacLeod published an important work, Carbohydrate Metabolism and Insulin, where Paulescu's works are mentioned correctly [9, 10].

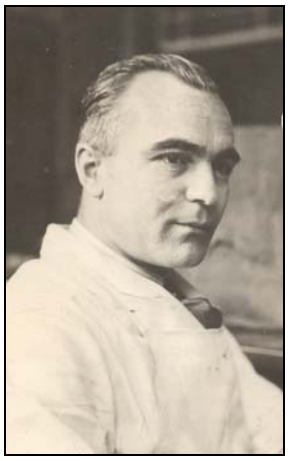
1921 – On July 23, in "Comptes Rendus de la Société de Biologie" in Paris, N. Paulescu's appears the four short papers on the systematic investigation of the physiological and pharmacodynamic characteristics of pancreatic endocrine secretion : (1) "The action of the extract pancreatic injected into the blood of a diabetic animal"; (2) "The action of the pancreatic extract injected into the blood of a normal animal" (3) "The influence of the amount of pancreas used to prepare the extract injected into the blood of a diabetic animal"; (4) "The influence of the time elapsed since the injection i.v. of the pancreatic extract in a diabetic animal". All four appeares in the same issue of the journal and were known to Canadian authors, who cite them in their paper published in February 1922[9, 10, 11].

1921 – On August 31, appears in "Archives Internationales de Physiologie" (vol. 17, pp. 85–109) the fundamental work that sums up all the systematic investigations of N. Paulescu regarding the pancreatic endocrine secretion. The paper is entitled "Recherces sur le role du pancreas dans l'assimilation nutritive". It is the birth certificate of insulin[9, 10, 14, 15].

1930 – N. Paulescu mentions the glycosylation of plasma albumin, in volume IV of the Lancereaux-Paulescu Medical Treaty, in the following paragraph on page 5: "In fact, when glucose is injected into the blood, it passes quickly into the urine. Moreover, physiological chemistry shows that glucose is, in the blood, in a state of more or less stable combinations with albumin – of which only a part can be dissolved – either by alcohol (apparently called sugar) or by mixing with acids (so-called protein sugar) – and which can then be highlighted by the cupro-potassium reagent."[9, 10].

1930 – Gh. Litarczec (1888–1954) publishes "Contribution aux relations qui existe entre l'obésité le diabète à l'aide des épreuves fonctionnelles de l'appareil insulaire" (Bull. Mem. Soc. Méd. Des Hopitaux). In 1943, he published "The Problem of Diabetes" (Hospital 63: 3–4, 57–69). In 1948 he published an important monograph, "Elements of General Pathophysiology of Nutrition", in which the biochemical issue of diabetes, analysed in depth, recalls the internship of Rockefeller (1925) and the collaboration with Professors Folin and Benedict, who remained in the history of diabetes through their methods for determining blood glucose (see Chapter 1, History of Diabetes). From 1949 to 1954 he led the Medical Clinic of the Cantacuzino Hospital as a Professor, thus approaching the Nutrition Clinic of Prof. I. Pavel, located in the same building, one floor above. It should be mentioned that at "Elements of General Pathophysiology of Nutrition", contributed the future Professor Radu Păun, who discreetly promoted the biochemical current of diseases in the five-volume Treaty of Medicine (1953–1958) and the 13-volume Treaty on Medicine. (1976–2001) [8].

Gheorghe Litarczec



Grigore T. Popa

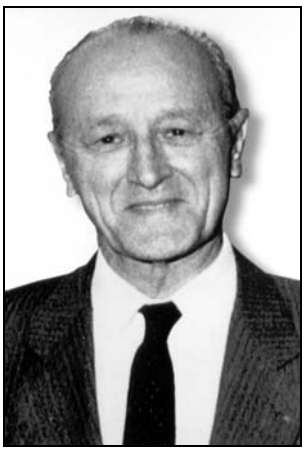
1931 – Together with Una Fielding, Grigore T. Popa, professor of anatomy at the Faculty of Medicine in Iasi, described the pituitary portsystem, a discovery that highlighted the relationships between the endocrine and diencephalon apparatus. As a result of this discovery, there was a major interest in identifying such circulatory systems in other organs as well. N. Simionescu *et al.* have described such a system in the pancreatic islets[20].

An exceptional personality of the Romanian medical thought, with ample philosophical implications, Gr. T. Popa is the author of a recently published work, entitled "Reforma spiritului" (Ed. Viața Medicală Românească, Bucharest, 2002). It represents the full text of the 3 lectures presented in the Hall of the Romanian Academy (the scientist was elected as member of the

Romanian Academy in 1936; he was expelled from it in 1948, the year in which he died, at the age of 56; he was recently reinstated in the academic rights).

He was an assistant to Professor Fr. Rainer (1920); professor of anatomy and anthropology (1923); fellow of the Rockefeller Foundation (1925); training at the University of London (1927), collaborates with Nobel laureates A. V. Hill and H. Dale (1928); invited to lecture at Cambridge and Oxford (1940); Dean of the Faculty of Medicine from Iaşi (1938); then transferred to Bucharest, as a professor at the chair of Francisc Rainer and Dean of the Faculty of Medicine in Bucharest (1942).

1934 – In the internal medicine service at Colţea Hospital, led by Ion Nanu Muscel (1862–1938), the young Ion Pavel (1897–1991) creates a small diabetes department. This concern is attested by Jean Vague, who, during this period visited the service of Ion Nanu Muscel from the Colţea Hospital from Bucharest. Jean Vague is the first to distinguish between abdominal and peripheral adipose tissue[20].



Jean Vague

1939 – Ion Pavel makes at the Colţea Hospital from Bucharest a first inventory of a group of diabetic patients hospitalized (notebooks containing the medical data of diabetic patients)[18].

1942 – Ion Pavel establishes (in the middle of the World War II) a Diabetes Register containing 25 sections, written in a large notebook, on the 2 pages of the open register. In the same year, Ion Pavel published in the Bulletin of the Romanian Academy of Medicine the work "Une statistique des diabétiques à Bucarest et les enseignements qui en découlent". The first record of diabetes dates back to 1943, which will undergo several changes over time[18].

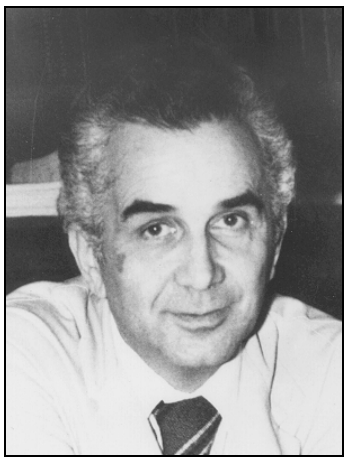
1944 – Ion Pavel publishes the first edition of "Le diabète" (with subsequent editions in 1955, 1965, 1974). The work received the Paris Academy of Sciences Award. It is the first work in the world in which the social dimension of diabetes is strongly emphasized[18, 20].

1949 – Ion Pavel establishes the "Clinic of Nutrition and Dietetics" (which he led until 1967) and the "Antidiabetic Centre in Bucharest", staffed with 6 social workers. The first antidiabetic centre in Bucharest was housed in the "Boyar Stables", where the "horse ambulance" of the "Cantacuzino" Hospital was once parked. This situation emphasizes once again that great ideas do not need too favourable conditions to be realized. Conditions come naturally as a complement and are imposed by necessity[18, 20].

1953 – The first "Anti-Diabetical Centres" are born, founded by Ion Pavel's students: Gh. Băcanu in Timişoara, V. Sfârleaza in Craiova, V. Gligore in Cluj [6] and Gh. Crețeanu in Iaşi[9].

1956 – Nicolae Simionescu (1926–1995) publishes important data on island angioarchitecture that creates a porto-arterial system, through which insulin and glucagon come into contact with neighboring acinar tissue (St. Cercet. Endocrinol. 7: 495–506, 1956). In 1957, N. Simionescu published significant data on insular neogenesis in the pancreatic ducts, a process stimulated by vagotomy

1957 – N. Chişiu establishes in the service of Prof. Ion Pavel an experimental Medicine laboratory (also called "Animaleria"). Several immunological techniques with wide practical applicability have been developed in this laboratory. The laboratory was disbanded in 1977, after N. Chişiu died in the March 4 earthquake of the same year.



Nicolae Simionescu


Viorel Gligore


Gheorghe Crețeanu


Gheorghe Băcanu


Iulian Mincu

1963 – After receiving the Prize of the French Academy of Medicine for his monograph "Le diabète", I. Pavel is elected a corresponding member of the Romanian Academy (full member in 1990)[20].

1963 – Within the Society of Internal Medicine (component of the former USSM: Union of Medical Sciences Societies), the Nutrition Diseases Section is established, headed by Ion Pavel until 1974. In 1975, on the occasion of the organization of the First National Diabetes Congress, Nutrition and Metabolic Diseases (annual event), the presidency of the Society is taken by I. Mincu and kept (in the spirit of the time) until 1999. The next presidents were N. Hâncu (1999–2001), C. Ionescu-Tîrgovişte (2001–2003), D. Cheța (2003–2005).

1966 – I. Pavel and R. Piepte publishes "Etude sur le diabète héréditaire au cours de 3,4 générations successives" (Diabetologia 2: 281–285, 1966). The legacy of diabetes will remain one of the major concerns of I. Pavel, a chapter in which he had original internationally recognized contributions.

1967 – The specialty of Diabetes, Nutrition and Metabolic Diseases is born and the Chair of the same name led by Prof. I. Mincu, which initially functioned only in post-graduate education, and since 1990 in university education; since 1997, the Chair is led by Prof. C. Ionescu Tîrgovişte.

1970 – At the VII Congress of the IDF in Buenos Aires (Argentina), I. Pavel supports Paulescu's priority in the discovery of insulin (on the occasion of the upcoming half-century of the great discovery).

1972 – I. Mincu and S. Câmpeanu publish the work Diabetic Angiopathy, in Medical Publishing House, Bucharest, which will be translated and published in 1976, in De Gruyter Publishing House, under the title "Macro and Microangiopathy".

1973 – Introduction of 3-year secondary education in Diabetes, Nutrition and Metabolic Diseases. The first series of 7 specialists was formed in 1976. Subsequently, the trained specialists set up Diabetes Centres in the counties without this service.

1974 – Since 1974 the generation of diabetologists who contributed to the expansion and consolidation of the diabetes network in Romania is affirmed: V. Gligore (1920–2001) in Cluj-Napoca, Gh. Crețeanu (1922–1991) in Iaşi, Gh. Băcanu (b. 1926) in Timişoara and I. Mincu (b. 1927) in Bucharest.


George Emil Palade

1974 – George Emil Palade receives the Nobel Prize in Medicine, following the discovery of ribosomes, the site of protein secretion in the cell. Although he did not work directly in the field of diabetes, he can be considered one of the founders of cell biology. The study of the endothelial cell paved the way for understanding chronic vascular complications in diabetes[3, 7].

1975 – The first National Congress of "Diabetes, Nutrition and Metabolic Diseases" was organized, initially under the name of "Romanian Diabetology Days". The event was then organized annually, the last (2003) being organized in Craiova (Maria Moţa), and the next (30th Congress) will take place in May 2004, in Eforie Nord. The summaries of the Congresses were published in the annual volume Acta Diabetologica Romana. The titles of the annual communications between 1975 and 2001 were published in the paper Diabetes in Romania (edited by C. Ionescu-Tîrgovişte).

1977 – I. Mincu publishes the Treaty on Diabetes Sugar, Medical Publishing House, Bucharest.

1982 – It is organized in Bucharest, with the participation of J. Ph. Assal (Switzerland) and M. Berger, "The Second Eastern European Diabetes Education Seminar". These are two prominent personalities of diabetology, who have constantly supported Romanian diabetes[9].

Jean Philippe Assal

1983 – T. Trandaburu publishes in Ed. Academiei the work "Comparative histophysiology of the endocrine pancreas", containing interesting original research, insufficiently appreciated at the time of their publication.

1984–1987 – The Bucharest-Düsseldorf Study is carried out in Bucharest, in which a 5-day structured education program for type 1 diabetes was transferred with excellent results from Düsseldorf to Bucharest. On this occasion, for the first time, glycemic self-control and determination of glycosylated hemoglobin were introduced in Romania. From the large team of specialists involved in this study (I. Mincu, D. Cheţa, C. Ionescu-Tîrgovişte, C. Dumitrescu), the greatest effort was made by Ioana Bruckner. The moral author of this study remains the late Prof. Michael Berger and his wife, Ingrid Mulhausser, of Dusseldorf, Germany[9].

Michael Berger and Ingrid Mulhausser

1985 – The Electrophysiology Laboratory is established, headed by Eng. S. Prună, incorporated since 1998 in the Romanian Telemedicine Department[9].

1986 – The Treaty on Nutrition and Metabolism Diseases, Medical Publishing House, Bucharest (volume coordinator I. Mincu) appears under the editorship of R. Păun

1987 – D. Cheţa publishes the monograph Immunometabolic Interrelations, Academy Publishing House, Bucharest.

1988–1998 – Institute of Diabetes, Nutrition and Metabolic Diseases participates (coordinator C. Ionescu-Tîrgovişte) in the multicentre study EURODIAB-ACE (epidemiology of type 1 diabetes in the age group 0–14 years) and EURODIAB-PCS (study of chronic complications of type 1 diabetes). The two submissions, coordinated at European level by Anders Green (Denmark) and John Fuller (UK), were completed by the publication of over 40 important papers in those fields[9]].

1988–1998 – Institute of Diabetes, Nutrition and Metabolic Diseases participate (coordinator C. Ionescu-Tîrgovişte) to the international study DIAMOND, as well as to the studies GETREM (study of remission in type 1 diabetes) and IDA (branch of the epidemiological study EURODIAB extended to the age group 15–29 years)[9].

1989 – C. Ionescu-Tîrgovişte signs on behalf of Romania, in the mountain resort in northern Italy, the famous Declaration of St. Vincent, in the direction of which appreciable results in the reduction of chronic diabetic complications have been obtained in time. The 15th anniversary of this event will take place during the Diabetes Congress in Eforie Sud during the session dedicated to the "BlackSeaDiab Medical Union"[9].

1990 – The monograph Hypoglycemias appears (I. Mincu and C. Ionescu-Tîrgovişte), Medical Publishing House, Bucharest (Romanian Academy Award).

1990 – Introduction of university education in Diabetes, Nutrition and Metabolic Diseases in the form of a 7-day module[9].

1992 – N. Horeț publishes The Endocrine Pancreas, Medical Publishing House, Bucharest.

1993 – The Institute of Diabetes, Nutrition and Metabolic Diseases is established, named after the illustrious physiologist N. C. Paulescu (under the ministerial legislature of I. Mincu).

1993 – Re-establishment, within the Institute "N. C. Paulescu", of the Experimental Diabetology service (coordinator D. Cheța).

1995 – The "BlackSeaDiab Medical Union" is established in Stockholm, at the initiative of Romania (C. Ionescu-Tîrgovişte), including a network of Diabetes Centres from the 12 countries bordering the Black Sea basin (see the map from the end). Within it were organized 7 workshops and the research project funded by the European Union BlackSea TeleDiab, in which Eng. S. Prună invested a lot of time and energy[9].

1995–1999 – Carrying out an extensive study of genetic epidemiology on the population with type 1 diabetes in Romania, within a bilateral cooperation Oxford-Cambridge (John Todd) – Institute "N. C. Paulescu "(C. Ionescu-Tîrgovişte, C. Guja).

1995 – V. Şerban establishes in Buziaş the Cristian Şerban Foundation, dedicated to the care of children with diabetes. Establishes, within the paediatric network, the organization ONROCAD. Since 1996, ONROCAD organizes an annual Diabetology Meeting on diabetes in children and adolescents, with valuable international support[4].

The building of Foundation „Cristian Şerban"

1996 – V. Şerban and S. Brink publish the monograph "Diabetes Mellitus of the Child and the Adolescent".

1997 – C. Ionescu-Tîrgovişte publishes the small Treaty entitled "Modern Diabetology", Technical Publishing House, Bucharest (560 p.).

1998 – Radu Dorel, immunologist at the Institute I. Cantacuzino develops an experimental model of double transgenic mouse, starting from the transgenic mouse TCR-HA (valuable experimental model in the study of type 1 diabetes). In this model, mice with transgenes encoding a receptor on T lymphocytes for a peptide in the structure of murine influenza virus hemagglutinin (TCR-HA) and mice with transgenes encoding the same peptide on the surface of pancreatic β-cells (Ins-HA) are used.

1999 – The biannual organization of the Scientific Sessions of the Institute "N. C. Paulescu".

Maya Simionescu

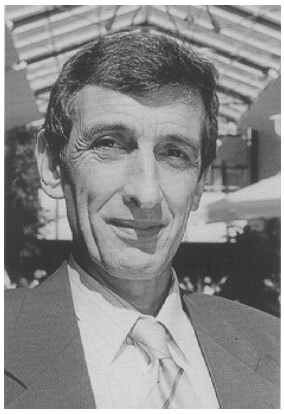
1999 – D. Cheța publishes in Ed. Wiley the monograph Preventing diabetes mellitus.

1999 – N. Hâncu initiates the "EPIDIAB" Program, which aims to inventory new cases of diabetes in 12 counties of the country, as well as to evaluate chronic diabetic complications at the onset of the disease.

1999 – R. Lichiardopol publishes the work Insulin secretion and insulin resistance in the etiopathogenesis of type 2 diabetes, Scaiul Publishing House, Bucharest.

2000 – Ioana Micle (the first paediatric diabetologist) publishes a comprehensive paper on the issue of diabetic children, entitled "Paediatric Diabetology. Theory and practice", Ed. Marineasa, Timişoara.

Nicolae C. Paulescu



Sir George Alberti

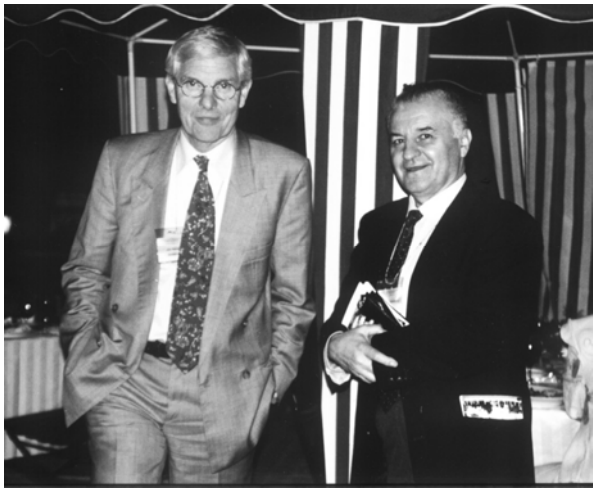
Ion Iliescu

Nicolae Cajal

2001 – The Romanian Federation of Diabetes, Nutrition and Metabolic Diseases is established, at the initiative of N. Hâncu (Cluj-Napoca). Within it were organized two "postgraduate courses Nicolae Paulescu", under the auspices of EASD, and two annual Congresses (2002 in Cluj-Napoca and 2003 in Satu Mare).

2001 – On August 31, the bronze statue of N. C. Paulescu was unveiled in front of the Faculty of Medicine in Bucharest, with the participation of the incumbent IDF President, Sir George Alberti (Great Britain), the President of Romania (Ion Iliescu) and Prof. N. Cajal (President of the Medical Department of the Romanian Academy).

2002 – Institute "N. C. Paulescu" from Bucharest participates at the "International Genetics Consortium" (C. Guja, C. Ionescu-Tîrgovişte), within the European branch coordinated by J. Nerup and F. Pociot (Denmark).



Constantin Ionescu-Tîrgovişte with Jorn Nerup
la ultimul Congres de Diabet, Craiova, 2003.

2003 – On the occasion of the 10th Scientific Session of the Institute "N.C. Paulescu " was unveiled the Lancereaux-Paulescu Anniversary Plaque (100 years since the publication of the first volume of the Lancereaux-Paulescu Medical Treaty), as well as the busts of the two scientists.

The unveiling of a copy of the same anniversary plaque, which was to take place at the Hôtel-Dieu Hospital in Paris, has been postponed.

Anniversary plaque Lancereaux-Paulescu.

2003 – N. Hâncu publishes in Ed. Springer the collective monograph Cardiovascular risk in type 2 diabetes mellitus.

2003 – At the initiative of the Institute „N. C. Paulescu", the "College of Nutrition" (director C. Ionescu-Tîrgovişte) is established within the University of Medicine and Pharmacy of Bucharest.

2003 – C. Ionescu-Tîrgovişte is elected corresponding member of the Romanian Academy.

2004 – The 11-th Scientific Session of the Institute "N. C. Paulescu", with the topic "Immunogenetics and diabetes".

2004 – I. A. Vereşiu, N. Hâncu and G. Roman publish the work Insulin and insulin treatment, Echinox Publishing House, Cluj-Napoca.

NICOLAE C. PAULESCU – LIFE AND ACTIVITY[9, 10]

Bust N. Paulescu

1869 – October 30 – Nicolae C. Paulescu is born in Bucharest.

1880 – Certificate of graduation of primary classes and student at Mihai Bravul Gymnasium.

1887 – Baccalaureate Diploma in Letters and Sciences.

1888 – He leaves for Paris, where he enrols in the Faculty of Medicine.

1892 – External through competition of the Hospitals of Paris.

1894 – Intern at the Hôtel-Dieu Hospital, in the Prof. E. Lancereaux Clinic.

1897 – Doctor of Medicine, Paris.

1897 – Certificate of Higher Education – Biological Chemistry, Faculty of Sciences, Sorbonne, Paris.

1897 – Deputy Physician of Notre Dame du Perpétuel Secours Hospital, under the leadership of Prof. E. Lancereaux.

1897 – Editorial Secretary of the periodical Journal of Internal Medicine.

1898 – Certificate of Higher Education – General Physiology, Faculty of Sciences, Sorbonne, Paris.

1899 – Doctor of Natural Sciences, Paris.

1899 – The first works, together with the physiologist Dastre from the Sorbonne, in order to isolate the active product of the internal secretion of the pancreas.

1900 – Aggregate at the Department of Physiology, Faculty of Medicine, Bucharest.

1901 – Doctor of the University of Paris.

1902 – Academy Officer, "Academic Palms" order, France.

1903 – The first volume of the Lancereaux-Paulesco Medical Treaty appears.

1904 – Permanent Professor of Physiology, Faculty of Medicine, Bucharest.

1906 – The second volume of the Lancereaux-Paulescu Treaty on Medicine appears.

1907 – The first world-famous work, L'Hypophyse du Cerveau, describing the personal method of temporal extirpation adopted by Harvey Cushing in human neurosurgery.

1912 – The third volume of the Lancereaux-Paulescu Medical Treaty appears.

1919 – The first volume of the Treaty on Medical Physiology appears.

1920 – The second volume of the Treaty on Medical Physiology appears, written in French and published by Vigot Publishing House, Paris. Inserted for the first time in this volume are the antidiabetic effects of aqueous pancreatic extract in experimental diabetes. He announces the discovery of the treatment of human diabetes.

1921 – April 24 – June 23. The second work with worldwide resonance. Four papers to the Society of Biology on the discovery of pancreas (insulin):

1. "The action of pancreatic extract injected into the blood of a diabetic animal";

2."The action of the pancreatic extract injected into the blood of a normal animal";

3. "Influence of the amount of pancreas used to prepare the extract injected into the blood of a diabetic animal";

4. "The influence of the time elapsed since the intravenous injection of the pancreatic extract on a diabetic animal".

1921 – 31 August. The article "Research on the role of the pancreas in nutritional assimilation" - an exhaustive memoir of the discovery of insulin (pancreas), appears in the International Archives of Physiology.

1921 – The third volume of the Treaty on Medical Physiology appears.

1922 – April 10. Patent: "Pancreas and the process of its manufacture", Ministry of Industry and Commerce.

1923 – May 31. Publication in the International Archives de Physiologie of the second memoir on pancreas: "Some chemical and physical reactions

applied to the aqueous extract of the pancreas to get rid of excess protein substances."

1923 – August 10. Publication in the Archives Internationales de Physiologie of the third memoir on pancreas: "Various procedures for introducing the pancreatic extract into the body of a diabetic animal."

1924 – Article Traitement du diabète in Presse Médicale.

1924 – March. The third world-famous work: Ambard's laws and his constant urea-secretion are erroneous. The first memoir published in the Journal of Urology.

1926 – June. "Ambard's laws and his constant urea-secretion are wrong." Second memoir published in the Journal d'Urologie.

1928 – The fourth volume of the Lancereaux-Paulescu Medical Treaty appears. The first chapter is devoted to the issue of the priority of insulin discovery.

1931 – The work Localization of social instincts on the cortex of the frontal lobes of the brain appears in the Archives Internationales de Physiologie.

1931 – July 19. Professor Nicolae C. Paulescu dies.

1969 – Ian Murray, Scottish diabetologist, founding member of IDF, publishes Insulin: Credit for its Isolation on his own initiative (Br. Med. J., Sept. 13, p. 651). It is the first work in a series in which, for the first time, Paulescu's priority in discovering insulin is demonstrated on the basis of documents. The problem is repeated in two monographs published by I. Pavel in 1976 and 1982, as well as in other 2 monographs published by C. Ionescu-Tîrgovişte in 1996; one of them (The Re-Discovery of Insulin), published in English, was launched on the occasion of the 75th anniversary of the discovery of insulin.

2001 – 31 August. The statue of the great scientist is unveiled in front of the Faculty of Medicine in Bucharest.

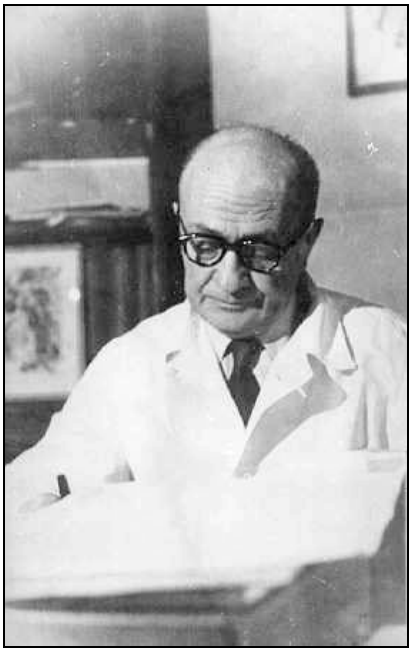
ION PAVEL – LIFE AND ACTIVITY[18]

1897 – March 14. Ion Pavel is born in Bucharest.

1907–1914 – He attended high school at St. Sava College, Bucharest.

1914–1916 – Years I and II of the Faculty of Medicine, Bucharest.

1919–1921 – External of the Civil Hospitals from Bucharest.



1922 – He defends his doctoral thesis in medicine and surgery Schick's reaction and immunity in diphtheria in our country.

1922–1930 – Assistant at Colţea Medical Clinic, led by Prof. I. Nanu-Muscel.

1924–1926 – Medical specialization studies in Paris, first with Prof. M. Chiray.

1927 – He publishes, in collaboration with M. Chiray, "La vésicule biliaire et ses voies d'excrétion", which receives the Montyon Prize of the Academy of Sciences in Paris, a book that consecrates him internationally, followed by a new edition in 1936. He receives the title of University Lecturer.

1930 – Honorary associate professor, then final (1939) at Colţea Medical Clinic.

1939 – Primary care physician of internal medicine, initially at the Institute of Surgery, then from 1941 at Colţea and Cantacuzino Hospitals, where he worked until 1967 and established the Antidiabetic Centre, an institution whose organization was later taken over by almost all centres for combating diabetes in Europe

1943 – Receives the Oroveanu Grand Prize of the Romanian Academy for the book Les Icteres; for this work he will also receive the Dagnan-Bouveret Prize from the Institute of France.

1944 – The book Le Diabète is published, for which he later receives the Dragowitch Prize awarded by the Paris Academy of Sciences.

1949–1967 – Leads the Clinic of Nutrition and Dietetics at Cantacuzino Hospital, as an associate professor and professor (since 1954).

1963 – Corresponding member of the Romanian Academy; member of the Academy of Medical Sciences.

1970 – Participates in the IDF International Congress, where he supports the report on his lifelong research on the prevention of pre-diabetic diabetes, leads the Symposium on Genetics in Diabetes and supports its priority N. Paulescu in the discovery of insulin.

1976 – Corresponding member of the Academy of Medicine in Paris; the first book in English on N. Paulescu's Priority in Insulin Discovery appears, followed in 1986 by a volume of correspondence about the true discoverer of insulin.

1985 – The study of Prof. Morsiani *et al.* "Pavel's dynamic screening for type 2 diabetes. 14-year results in a region of northern Italy."

1990 – Member of the Romanian Academy.

1991 – March 6. Professor Ion Pavel dies.

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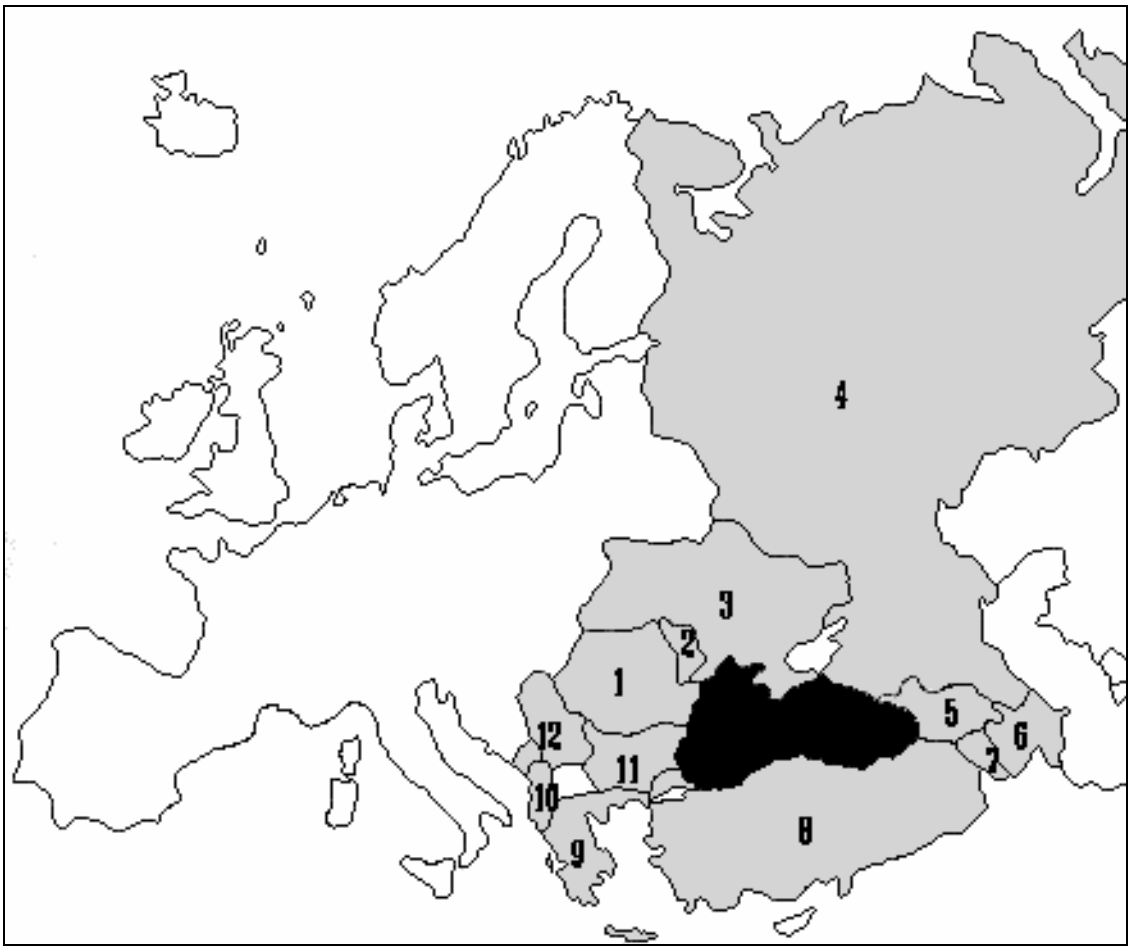

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1. România
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