

## HISTORY OF THE HUNGARIAN SOCIETY OF LABORATORY MEDICINE

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The Hungarian Society of Laboratory Medicine (HSLM) was established in Budapest in 1946, right after the end of World War II. Its professional program was developed by several professors and associate professors of the Medical School of Péter Pázmány University, and pathologist consultants of leading hospitals. They established the specialty of Clinical Laboratory Medicine and organized the Society. Co-ordination of professional development was the responsibility of the Ministry of Health. Initially, Pharmacy and Medical graduates were trained in the theory and practice of clinical chemistry, hematology and microbiology for 3 years at laboratories of medical schools, then, from 1951, they could take the state examination to become qualified specialists of clinical laboratory medicine. Now the specialist residency program for pharmacists and medics in clinical laboratory diagnostics is 5 years long, and has a polyvalent character. Further specialist qualifications can be gained in the fields of hematology and immunology, and molecular diagnostics. From 2006, non-medical graduates (biologists, chemists, molecular biologists, clinical laboratory scientists) can take part in a 4 year long, complex, disease-oriented training, followed by a specialist exam in clinical biochemistry. This exam certifies their status as specialists in clinical biochemistry.

A retrospective view of Hungarian higher education, especially medical education:

In the 1000 year old historical Hungary, our kings established universities in Veszprém (1185), Pécs (1367), Óbuda (1410) and Pozsony (1465). These universities did not go beyond the level of „studium generale”, were destroyed in the turmoil of history before medical education could have been started. The lack of medical doctors in Medieval Hungary was alleviated by priest-monk doctors educated abroad. The first Hungarian university which has been working without disruption since its establishment is the University of Nagyszombat (now in Slovakia). Its medical school started medical education and patient care in 1769/1770. The university was moved to Buda in 1777, then to Pest in 1784. Later it was named Péter Pázmány University. Its medical school became the Semmelweis University of Budapest. The universities established from 1910 to 1930 in Debrecen, Pécs and Szeged have had medical schools from the beginning. In our country, training of undergraduate medical students in clinical chemistry (now termed laboratory medicine) started only in 1980. Before 1910, medical students studying in Budapest received a short introduction to clinical laboratory diagnostics during the course named „Chemistry of Life and Disease”. Later, many internists, pediatricians and pathologists, some of them trained abroad, did the chemical and hematological diagnostic work at hospitals, some of them to a high scientific standard. Others were not in the limelight of their era, but the history of our specialty requires that we acknowledge their significance.

### **Pál Plósz (1844-1902)**

As a young physician, he spent several years at German hospitals, e.g. in Hoppe-Seyler's laboratory in Strassburg. There he realized that the lack of chemical knowledge severely obstructed his work. In 1876, he translated Hoppe-Seyler's book „Chemistry of Life and Disease” into Hungarian. The book was the only text available for Hungarian physicians for decades. Their main work was protein assay in serum and urine, iron and urea detection in blood samples, Trommer assay, polarimetric analysis. Pál Plósz laid down the grounds of clinical chemistry of our times. He had many students, one of them; László Udránszky became his successor as head of the Pathochemical Institute.

**László Udránszky (1862-1914)**

He received his medical degree in Budapest in 1883. Before starting his studies in the chemistry of life and disease, he spent a year at Hoppe-Seyler's laboratory in Strassburg, then, in 1877, another year at Baumann's chemical laboratory in Freiburg. The main result of his experiments done there that furfural, forming when carbohydrates are treated with concentrated sulfuric acid, is responsible for color development. The essence of Molisch's reaction and the formerly used Molisch-Udránszky reaction to detect carbohydrates in urine with alfa naphthol is also the formation of furfural. Udránszky sensitized the Pettenkoffer reaction used for the detection of biliary acids by the addition of furfural. For years he led the laboratory of the University Hospital of Internal Medicine I headed by Frigyes Korányi. Among others, Bernát Vas and Géza Gara worked there in 1894, who edited the first „manual of laboratory work” written in Hungarian. Udránszky made significant discoveries in physiology as well. He was especially interested in sensation of heat and pain. The theme of his inaugural lecture at the Hungarian Academy of Sciences was also the field of pain sensation.

**Mihály Somogyi (1883-1971)**

He graduated from József Nádor University of Technology at Budapest as a chemical engineer in 1905, and then he received his doctorate degree in chemistry from Péter Pázmány University in 1914. After 1905 he worked as a biochemical assistant at the University of Technology for a year, and then took a position at the Institute of Food Science in Budapest. He spent 2 years in the USA in between: first he worked as laboratory technologists, then at the Biochemical Department of Cornell University. From 1922 he worked in the biochemistry department of Washington University in St. Louis, then from 1926 till his retirement he was head of the first biochemistry laboratory of the city's Jewish hospital. Based on his experiences with the treatment of 5000 diabetic patients, he found that diet is a requirement for successful insulin therapy. He published his results in a widely acclaimed lecture. He described the diabetogenic effect of hyperinsulinemia that is hypoglycemia triggered by an overdose of insulin leads to hyperglycemia. This phenomenon is known in the literature as the „Somogyi effect”.

Together with Nobel Laureate A. Dossy (discoverer of vitamin K), he developed a method for the isolation and production of insulin, still used in industry. He updated his first iodometric method of blood glucose assay (described in 1926) several times. Nelson replaced iodide-iodate with arseno-molibdate in 1944, making the method suitable for photometry (Somogyi-Nelson blood glucose assay). The method became popular mainly in the overseas countries. Somogyi's name is well known in professional circles in the west. In Hungary, HSLM made professionals aware of his significance by the establishment of the Somogyi Prize. We should be proud of the „laboratory specialist”, who was both a diabetologist and a clinical chemist.

**Kálmán Pándy (1868-1945)**

One of the most serious diseases of the 1900-s was syphilis with its neurological manifestation: progressive paralysis. Clinically the disease was well characterized. As the method of collecting cerebrospinal fluid (CSF) was already known, the elevated protein (including globulin) level of the CSF could be detected in progressive paralysis. After his studies in Germany and France, he became interested in the Nonne-Appel ammonium-sulphate method of CSF protein assay. After performing hundreds of such assays, he found the method too sensitive, giving false positive results in numerous cases, indicating disease in clinically healthy individuals. He never let anyone else to perform CSF analysis in the laboratory, he did them all. Once he accidentally knocked over the phenol bottle, and the spilt phenol mixed with a drop of CSF on the bench, producing a bluish-white, smoke-like cloud, a fine precipitate

with the bigger globulin molecules. This reaction did not escape his attention, and Pándy's method of selective detection of globulins using a 6.6 % phenol solution was born. Later he tried numerous phenol derivatives but he could not find anything better than phenol itself. Several decades ago his method was still in use as a rapid test in many countries. „In the field of observation, chance favors only the prepared mind.” The saying holds true for Pándy's case as well.

**Loránd Jendrassik (1896-1970)**

He received his medical degree from Péter Pázmány University in 1921. He got interested in physiological sciences early, in his student years. In 1925 and 1926 he studied modern biochemical methods and developed his skills in precise laboratory work in Dutch and German physiology and pharmacology departments, including the Nobel Prize winner (1922) Mayerhof's. The widely traveled, promising young research physician did not feel below him to accept the invitation of the professor of the University Hospital of Internal Medicine in Pécs. He was responsible for setting up the routine laboratory of the hospital, where he stayed as leader till 1940.

In accordance with the spectrum of methods available at the time, he focused his attention to reliable assays of metabolites, proteins and electrolytes. He „micronised” the formerly required ml-size samples. At the same time he started the revision of methodologies used for quantitative analysis of biliary pigments/bilirubin in blood and urine samples. The method of Ehrlich that was widely used till that time, such as adding sulfanilic acid to urine samples to produce azobilirubin, was modified by van der Bergh in 1924. He used caffeine – sodium-benzoate mixture as a catalyst to intensify color development. Jendrassik already adopted this modification in 1927. His most successful contribution was using the then state-of-the-art Pulfrich photometer to improve the accuracy of the rather unreliable bilirubin assays. Working together with R. A. Cleghorn who was on study leave from Aberdeen, he further improved his photometric method first published in 1936. Following other minor modifications, he published two review articles about the Jendrassik method of photometric bilirubin assay, with the medical student Pál Gróf as co-author. Between 1922 and 1940 he published 76 articles, 61 of them in international journals. Fifty percent of the papers were in the field of clinical laboratory diagnostics. He became habilitated doctor in 1927 based on his thesis „Clinical application of chemical and physico-chemical methods”. It was also the title of the 3 lectures a week course he presented to 4th year medical students.

Jendrassik’s articles are still cited in papers about bilirubin assays. In fact he did not invent an entirely new method; instead he adapted van der Bergh’s method to the then state-of-the-art Pulfrich photometer, making accurate bilirubin quantization possible. This „discovery” might not seem to be very significant today, but in 1938 it resulted in a dramatic improvement in diagnostics based on bilirubin levels. Jendrassik’s contribution was widely acknowledged and made his name known all over the world. What is not known about he and Somogyi is that they were Hungarians.

The Hungarian Society of Laboratory Medicine established the Loránd Jendrassik Memorial Plaque in his honor. The Plaque was first given in every year, now it is given bi-annually. The long list of names of scholars from all over the world who have received it is evidence of the high prestige of the Plaque: E. Kaiser, T.R. Niederland, D.S. Young, R. Haschen, H. Greiling, I. Pentilla, M.M. Müller, J. Todorov, H. Wisser, H. Bidlingmaier, H. Reinauer, L. Sárközi, M. McQueen, C.A. Burtis, P. Bonini, O. Zinder, I. Vermes, V. Blaton, S. Sandberg, E. Topic, G. Bodor.

#### **Gábor Szász (1933-1979)**

He received his chemistry degree from Loránd Eötvös University in 1959. He was mainly interested in enzymes significant in diagnostics. His first and last employer in Hungary was the laboratory of the Pál Heim Children’s Hospital, where he developed the beta-glucuronidase and cholin-esterase methods, which were published internationally. Thanks to these results, he was able to get positions in Frankfurt am Main in 1963, then in the department of the physician-chemist and hematologist László Róka, (a native of Transsylvania) in Giessen, where he later became head of department. He developed the diagnostic methods for leucine-aminopeptidase, gamma-glutamyl-transpeptidase and creatinine-kinase in Giessen. Boehringer Mannheim, the chemical company which supported Szász’s research, later marketed these diagnostic methods. The German Society of Clinical Chemistry and the IFFC officially accepted the CK method. In spite of his incurable disease, he accepted our invitation, and was the guest of HSLM in Budapest in the year prior to his death. The German Society of Clinical Chemistry established a Gábor Szász Memorial Plaque, awarded once in each year. The HSLM placed a commemorative plaque in Gábor Szász’s honor in the Pál Heim Hospital where he used to work.

During its 66 years of history, HSLM gave two internationally recognized researchers to the world of routine laboratory diagnostics: M. Somogyi and L. Jendrassik. There were, however, two Hungarian Nobel Prize Winners, dedicated to basic research, whose discoveries were not far from the field of laboratory medicine. Both of them were born in Budapest, received their first degrees from the universities of Budapest, and died abroad. A typical fate for many gifted Hungarians.

#### **György Hevesy (1885, Budapest, 1966. West-Germany, Nobel Prize 1943)**



György Hevesy was a chemical engineer. He played a crucial role in the development of using radioactive isotopes as tracers in biomedical research and also in RIA in laboratory hormone diagnostics, so his contributions to laboratory diagnostics are also significant.

**Albert Szent-Györgyi (1893. Budapest, 1986. USA; Nobel Prize 1937)**

Szent-Györgyi was a physician and biochemist. He was working on cellular respiration, the role of dicarboxylic acids in metabolism and the role of the reducing agent ascorbic acid in the peroxidase system. He was prescient when he said in 1946 that clinical and pathobiochemistry should be taught to medical students in their clinical years, because it would help to connect students to patients. Recently this practice is being developed.

In the past decades Iván Nagy, Kázmér Jobst, László Muszbek, Mihály Németh-Csóka, Andrea Rita Horváth and Gábor L. Kovács, all members of HSLM Executive Board, were working in various committees of IFCC. Andrea Rita Horváth (now living in Australia) was president of the European Federation of Clinical Chemistry and Laboratory Medicine, and Gábor L. Kovács played a crucial role in the Executive Board of the Forum of the European Societies of Clinical Chemistry (FESCC).

**Wine-tasting after a long-lasting executive board meeting of the HSLM, Pécs, 2004**

*(from left to right: M. Fekete, G.L: Kovacs, A.R. Horvath, F. Farago†, K. Hetyesy and K. Jobst).*

Specialists of Laboratory Medicine play important roles in the organization of scientific life. There are three laboratory diagnostic scientists working in Hungary who are members of the Hungarian Academy of Sciences: Kázmér Jobst, László Muszbek and Gábor L. Kovács. In addition, one honorary member: Matthias M. Müller, and one external member: István Vermes contributes to scientific life.