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Review Article

György Romhányi, the Hungarian Pioneer of Polarization Microscopy on his 120th Birth Anniversary

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György (George) Romhányi (Reichenbach until 1935) was born on September 15, 1905, in the village of Szár, at the foot of the Vértes Mountains in Fejér County. His father was a chief clerk. At home, they spoke German and Hungarian. He had four siblings: Dezső (1898-1960), Irén (1900-1990), Irma (1902-1988), György (1905-1991) and József (1908-1976). The boys graduated from the Cistercian grammar school in Székesfehérvár, where their maternal uncle, Antal Scheirich, the bishop's vicar, supervised them. The two sisters completed their teacher training in Pécs. The three boys became students at the medical faculty of Péter Pázmány University [1-5].

In his fifth year, György Reichenbach won the autopsy competition, and after passing his final exams with distinction, he was invited to join the Institute of Pathology by its director, Ernő Balogh nemes. He received his medical degree in 1929 and worked as a pathologist until his retirement. It became apparent in his early years that he was an excellent teacher, and with his method of counterstaining, he created an important component of education, macroscopic preparations, which included differential diagnoses in addition to clinical data.

He taught himself the method of polarisation microscopy based on the books of Albert Frey-Wyssling(Zürich) and Wilhelm Josef Schmidt (Giessen) Meanwhile, he studied in Berlin by Professor Rössle and in Wien by Professor Sternberg. After successfully completing his habilitation, he was awarded the title of private lecturer in 1939. Between 1939 and 1941, he studied amyloid deposits, and in 1942, he gave a lecture on the submicroscopic structure of amyloid at a meeting of the hungarian Pathological Society [6,7]. The German summary was also published in Zentrablatt in 1943.

At the end of November 1944, by ministerial ecree, he accompanied Hungarian medical students to Halle an der Saale in Germany, where he taught, examined, and performed autopsies. He was the most popular teacher: Lajos István, Jenö Ormos, Gyula Stenszky [51]. After the end of the war, he returned with his family to Budapest in July 1945. Meanwhile, his ched, the nobleman Ernő Balogh, was removed from the university, and Romhányi was demoted to assistant professor, where he finally resigned in 1946 [1,3,4,5].

In the summer of 1946, he was hoeing corn in Etyek. At that time, his younger brother, József Romhányi, was helping his family. Lajos István student helped him, and Romhányi was employed at the Szombathely County Hospital, first as a deputy head nurse [1,4,5]. He received his official appointment on October 19, 1946, as chief pathologist and laboratory director on a temporary basis, with his appointment becoming permanent in 1948. He organized a so-called private university in Szombathely.

Professor István Rusznyák, president of the Hungarian Academy of Sciences, supported Romhányi during these difficult years, who processed the extensive experimental renal pathology material of the First Internal Medicine Clinic of the University of Budapest using enzyme histochemistry and polarization optical methods. He received a polarizer from Straub f. Bruno. He obtained the current journals from the University Library in Budapest through Mr. Varjas. Romhányi often quoted Max Planck at this time: "We must try to overcome the difficulties of our lives! We must not forget our ideals and we must not give them up!" Professor Béla Entz, director of the Institute of Pathology at the University of Pécs, was officially retired.

György Romhányi took up the position of director of the Institute of Pathology at the University of Medicine in Pécs on October 15, 1951. Two people played an important role in his move from Szombathely to Pécs: Professors Jenő Ernst and János Szentágothai. Romhányi found it difficult to leave Szombathely, his secure home,

and it was only at the insistence of his friends and acquaintances that he finally decided to take over the department.

The Charismatic Personality

Romhányi was already a legendary teacher in Budapest, Halle, and Szombathely before his appointment in Pécs, where the number of university students participating in summer internships tripled. They spoke enthusiastically about Professor Romhányi, who had an excellent understanding of biochemistry and pathology. György Romhányi organized clinical pathology conferences and then a "private university" ("gittegylet") for medical students and young doctors, with afternoon lectures. The founders of this "private university" were Dezső Tanka, one of the founders of enzyme histochemistry in Hungary, Mihály Németh-Csóka, an internationally recognized connective tissue researcher, Béla Solymoss (János Selye's successor in Canada), and Lajos István, an internationally renowned hematologist in Szombathely and János Molnár, pathologist at the Einstein Collegium. They later became university professors. Kálmán Széll also belonged to this group. He first wanted to be a pathologist, then a surgeon, and later became chief anesthesiologist in Szombathely. They listened enthusiastically to Romhányi, performed autopsies during the summer holidays, and presented articles. It was here that Romhányi described the double fracture of the renal hilum and wrote his first comprehensive paper on amyloid, which Frey-Wissling immediately submitted for acceptance and publication.

For György Romhányi, his years at the University of Pécs represented the culmination of his scientific and teaching work. He always emphasized that he was "first and foremost a prosector, secondly a teacher, and thirdly a researcher." He also supported his theory of heart development with experiments [36]. He always remained faithful to and relied on traditional pathology teaching, emphasizing the unity of morphology and function. His work on the introduction of topo-optical reactions marked a renaissance in polarisation optics [38,39]. Together with Mihály Németh-Csóka, he researched collagen fibres, RNA and DNA with Kázmér Jobst [23]. He studied elastic fibers using the aniline reaction [38]. In the late 1960s and early 1970s, he worked on the acetylation and gentle sulfation of collagen fibers, the selective detection of sugar components, and the structure of biological membranes [20,43-50].

In the last years of his career, he worked on the polarization optical analysis of the double layer of red blood cell membranes and the anisotropic PAS reaction (aldehyde-bisulfite-toluidine blue reaction) to selectively examine the sugar components of plant cell walls, fungi, and bacteria. He described the charge-transfer reaction with eosin on the human erythrocyte membrane [19,20,47,49,50]. For amyloid research, as he said, "It remained an eternal love." Submicroscopic analysis of amyloid deposits proved that the green polarization color was indeed caused by Congo red-stained amyloid deposits [40-42]. The year 1967/1968 was a milestone in amyloid research. His name is associated with the separation of primary and secondary amyloid by potassium permanganate-trypsin digestion: primary amyloid was resistant to this treatment [8-14].

The Enthusiastic Teacher

Professor Romhányi hurried down Dischka Győző Street every morning around 8 o'clock, his small, quick steps making him difficult to follow. He took the stairs of the institute two at a time and, after saying "Good morning, good morning," in his characteristic manner, wearing a coat buttoned only at the top, he rushed down to the autopsy room, where he stopped among the group of medical students standing around the autopsy table and greeted them. He scanned the group: "You, what's your name? You look very pale, you must have been out partying," and without waiting for an answer, he asked for the case file. The instructor was about to tell the story, but he said, "Not you, him," and pointed to a student. Ten seconds later, he said, "Get to the point," and asked the next student, "What do you see in this chest?" He didn't rest until someone said that there was fibrinous exudate on the pericardium, or emphysematous bullae on the lungs, etc.

Often, without waiting for an answer, he would say, "Because you're just here to relax and not to study, I could die because of you," and then move on to the next question. He insisted that the clinician be present at the end of the autopsy. Senior colleagues always came, but for the more interesting, clinically critical cases, the professors came, and Professors István Környey, László Lajos, Artur Hámori, Lajos Schmidt, Ödön Kerpel-Fronius, Tihamér Karlinger were also present on several occasions. At such times, a small clinical pathology conference would take place. We watched with wide eyes and caught snippets of conversation. It is clear from the above that Romhányi was a proponent of dialectical, or what we would now call "interactive," training, and he immediately involved his surroundings, the medical students, in the conversation, the lecture, and the autopsy.

He then moved on to histology exercises, where the instructor would say no more than three sentences before Romhányi took over. He looked into the microscope: "Man, is this a skin cell? It's a leukocyte. What grade did you get in anatomy? I don't care, I can see you don't know much. You'll be a doctor who looks for the appendix on the left side. Don't cry in front of me. Will you start crying at the bedside if you can't recognize the disease? By the way, assistant professor, this section is not demonstrative, have a new one made immediately, I want to see it first. Hurry up, the lecture is about to begin!" And with a wave of his hand, he left the section room. Rokitansky's famous phrase was repeated almost every time in the dissection room: "hic mortui vivos docent"!-'The dead teach the living'!

The Lecturer

The lecture hall was always packed, with people even sitting on the stairs. Although we suspected that he prepared his lectures at home, we couldn't disturb him 20 minutes before the lecture began. At such times, he would close the door to his room. Professor Romhányi, the researcher and colorful pathologist, would leave with the classroom assistant. The late academic Károly Méhes, who spent several years performing this thankless but honorable task, could tell you more about this. Before the lecture, he would

announce what museum specimens to prepare, which he did not always manage to find ("because Makovitzky may have taken them"). During the lecture, with the list in his hand, he would discuss the day's dissections with the class. Questions flew around, and later he would call on students by name. "Even a shepherd knows his sheep!" he once said to his admiring colleague. He was a suggestive lecturer, and all the students felt that he was talking only to them because he maintained close "personal" contact with the students during the lecture. The patient and the lesson to be learned were always at the center of the discussion, because everyone can make mistakes. He never judged the clinician; at most he would say "one could have thought of that" if the diagnosis was incorrect. He conveyed the essence of the material in short, clear sentences and drew a lot [1,2,3,5,13].

He never used a projector, only circulated the relevant documents and illustrated the main points with drawings on the board using white chalk. Professor Romhányi taught pathology to medical students from a clinical-pathological perspective. There were no books or notes, and he did not want to write any, even though he was asked to do so several times. This meant that students had to pay attention and take notes. He always chose a current topic for the institute's lectures, which he would ask about again two to three weeks later.

What was the secret of Romhányi's charm? His style! The method he used to win the hearts of his students. He simplified complex problems and presented them in a clear and concise manner. Not only his students, but also his colleagues had to be on their intellectual toes. He did not like fraternizing or frivolity! [1,2,3,13]. He was the most popular lecturer at the University of Medicine in Pécs (between 1951 and 1976).

The Romhányi School

His successor in the department was Gábor Kelényi, who founded the internationally renowned Lymphoma Center at the institute. Kázmér Jobst, academician, founder and first director of the Institute of Laboratory Medicine at the Faculty of Medicine in Pécs. János Molnár is a professor at the Albert Einstein Collegium in the USA. Fedorina Horváth, László Kádas, István Kádas, Ottó Weiland, Károly Rajkovits, Béla Rohonyi, Gyula Kasza, István Orbán and György Deák became chief medical examiners. Károly Méhes, academician, became director of the Pécs Children's Clinic and a recognized expert in international genetic research; Árpád Németh became director of the Institute of Forensic Medicine at the University of Medicine in Pécs; János Fischer became professor of biochemistry in Szeged; and Péter Németh became the first director of the Institute of Immunology and Biotechnology. Kinga Karlinger became a professor of radiology, Lenke Molnár became an associate professor of internal medicine, János Szepesi became a university professor of orthopedics, Attila J. Horváth became an associate professor, László Melczer became an associate professor, Erzsébet Zombai became head of the histology laboratory at the Pécs Dermatology Clinic, and Károly Szilágyi became an associate professor. Judit Nagy became the first female professor at the University of Pécs.

Among the student circle, Professor András Guseo (Székesfehérvár) and Professor László Kisbenedek (Budapest) are worth mentioning, as well as Árpád Gógl, who was misitry of the Hungarian Medical Chamber and Minister of Health in the premier Victor Orbán government until 2000. Professor Péter Sótonyi, academician, studied partly with him in Pécs, which had a decisive influence on his career [48]. Gerhard Taubert, who learned the polarisation optical method in 1972, became professor of pathology at the University of Leipzig [57,58].

Professor László Módis, an anatomist (Debrecen), published two books on the results achieved using the Romhányi method [32,33]. Together with academician Miklós Kellermayer and Kázmér Jobst, he was one of the first to describe the cytoskeleton in 1975 [23,22]. Josef Makovitzky became a professor at the University of Halle-Wittenberg and later head of the histopathology laboratory at the Department of Obstetrics and Gynecology at the University of Rostock (1997-2007). Several doctoral dissertations and habilitation theses were written in Jena on the topic of the topo-optical reaction of human ertyhrocyte, as well as in Rostock on the topic of amyloid [24-35, 52-56, 59-63].

He described the difference between the membranes of T and B lymphocytes using a specific topo-optical reaction of sialic acid and O-acyl-sialic acid, which was confirmed by a Dutch/German team of chemists. He also described the differences between human red blood cell and lymphocyte membranes. Makovitzky worked in Rostock and Jena on human-. animal amyloid, bacterial amyloid, isolated amyloid fibers, and prion fibers. He described 2004 the helical structure of human and animal amyloid fibers, and animal amyloid fibers, which was confirmed by Steinbach et al. using confocal laser scanning microscopy [64]. He performed polarization optical analysis of different types of human and animal amyloids, bacterial amyloids, isolated human and animal amyloid fibers, and prion fibers in Rostock, Jena and Berlin

He analyzed the three components of Alzheimer's disease-amyloid plaques, neurofibrillary fibers, and amyloid angiopathy-using various topo-optical reactions and the Gallyas silver staining method. Bély, M. & Apáthy, Ágnes wrote a book entitled Differential Diagnosis of Amyloid Deposits by Light, Polarization and Electron Microscopy, published by Akadémia Publishing House in 2021 [64]. Ferenc Genzwein Director of the training high school at Eötvös Lóránd University (Budapest) a mathematics teacher. Prof. Dr. László Lovász, later president of the Hungarian Academy of Sciences, was his student.

Josef Makovitzky, Dezső Tanka, and Mayor Mihály Krupánszki organized the first Romhányi medical conference in Szár in 2000 [21]. Since 2001, university professor Miklós Kellermayer has been organizing Romhányi memorial conferences in the professor's birthplace, Szár [1,5]. In 2001, at the initiative of Makovitzky, a György Romhányi symposium was organized at the International Amyloid Forum in Budapest [12]. As a continuation of this, two Romhányi Amyloid Memorial symposia with international participation were held in Pécs in 2002 and 2004. Both symposia received

significant international acclaim [9,10,14], similar to the symposium held in Szeged in memory of Professor Romhányi's student, János Fischer [64].

In May 2005, at the Membrane Transport Congress held in Sümeg, in September at the ceremonial meeting of the Hungarian Academy of Sciences, and in October at the congress of the Hungarian Society of Pathologists in Pécs, the professor was commemorated with several presentations. On the 120th anniversary of György Romhányi's birth, Springer (Heidelberg and New York) published a comprehensive book on amyloid entitled "Analysis of Amyloid Using Various Methods" [64]. The statue of Professor György Romhányi, created by Sándor Rétfalvi (2006), stands opposite the Rector's Office on 48 Square, thanks to the organizational efforts of Miklós Kellermayer [15]. The auditorium of the Faculty of Medicine at the University of Pécs bears his name.

His memory is preserved by several awards named after him, four books, a monograph, several book chapters, commemorative plaques, a play, and countless students and listeners [15-20]. What are the central points of his scientific work? Romhányi had a broad range of interests, which is reflected in the diversity of his publications and his life achievements. He wrote more than 110 scientific articles.

i. Generations of physicians will remember the legendary Professor Romhányi and his unique style of teaching: the use of macroscopic preparations with regained colours, the synthesis of clinical history, the radiological photographs, and the data gathered in his laboratories. These preparations are still used in the teaching of medical students.

ii. He further studied the development of the heart and constructed a glass model of the folding of the cardiac tube to demonstrate the crossing of blood flows and the possible role of blood flow in determining the crossings of the large vessels. This model convincingly demonstrated the crossing of red and blue colored blood flows. He was convinced that the blood flow is responsible for the 180-degree spiral orientation of the arteric septum foldings (Romhányi 1952).

iii. Romhányi described and analysed the submicroscopic structure of amyloid deposits (1939-1941) with imbibition analysis and after Congo red staining, independent of Divry (1927) and Divry and Florkin (1927), who were the first to describe the phenomenon of birefringence of amyloid in senile plaques after Congo red staining.

Some authors questioned Romhányi's results about amyloid being the orientated structure which causes birefringency. They throught that the pre-existing collagen fibres, which are hidden by the amyloid, cause the birefringency (Missmahl and Hartwig 1953). Romhányi analysed the amyloid deposits using the von Ebner collagen specific reaction combined with Congo red staining. By means of this reaction, he found that the collagen fibres were linear negative while the amyloid deposits were still linear positive (Romhányi 1956 b). In the early 1970s, a clear differentiation of primary (AL) and secondary (AA) amyloid deposits was possible with the help of potassium permanganate-trypsin digestion. He showed for the first time the biological differences between the two kinds of amyloid. Thus, he created the basis for the further development of immunohistochemical reactions.

iv. He discovered the spiral-fibrillary structure of elastic fibres using the aniline reaction and the anisotropy caused by staining with Congo red.

v. He demonstrated the orented organisation of acidic mucopolysaccharides (glycosamino-glycans) in the matrix. The acid mucopolysaccharides form a structural unit together with collagenous fibres.

vi. With the selective visualisation of structural lipids in the microvillous border of epithelial cells of the kidney, first in their natural condition (Romhányi 1949) and later with the toluidine blue topo-optical staining reaction, he was able to carry out an optical analysis. As a result, he determined that the structural lipids are oriented vertically towards the axis of the microvilli.

vii. The charge transfer reaction: The visualisation of birefringence of the EP membrane system. The importance of a redox condition for topo-optical reactions of the ergastoplasmic membrane.

The oriented association of chlorpromazine with various biomembranes (blood cell membranes, bacteria and fungi) and successful oriented binding of eosin is a charge transfer reaction.

viii. The two topo-optical reactions (toluidine blue and rivanol precipitation methods which started a renaissance in the use of polarisation microscopy in the second half of the 20th century and was adopted by electronmicroscopy (Geyer et al. 1977, Németh et al. 1985, Sótonyi et al. 1981, 1983 a, b, 2009).

ix. The term "topo-optical reaction" of the inversive and the additive type.

x. The numerous collagen specific topo-optical staining reactions: such as the periodate-sulphation, the gentle sulphation reaction, or the inversive topo-optical reaction caused by Congo red staining.

xi. The two types of collagen fibres: steno- and porocollagen. The transition of stenocollagen into porocollagen.

xii. His method of aqueous Congo red staining for the selective visualisation of even smallest amounts of amyloid deposits in tissue preparations.

xiii. The aldehyde-bisulphite-toluidine blue topo-optical reaction (ABT-reaction) at pH 1, is "a polarization optical variant of the conventional PAS reaction" and the best method for the selective visualization and demonstration of linear ordered OH-groups of the sugar chains.

The following sentence rightly applies to Professor Romhányi: Those who are not forgotten remain among us even in death!

Acknowledgements

None.

Conflict of Interest

None.

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