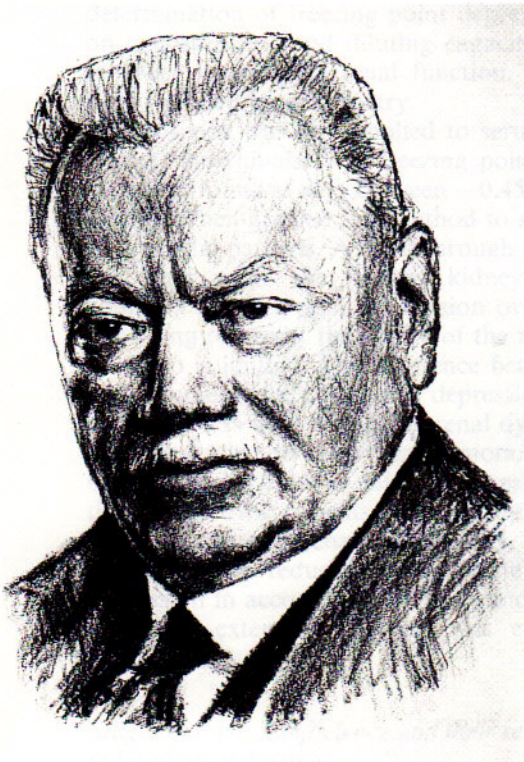


Special Feature

Sándor Korányi (1866–1944)



Sándor Korányi was a distinguished Hungarian physiologist and clinician who opened the door to studies of kidney function in renal disease. In this respect he was a pioneer of the modern era of clinical nephrology. For various reasons his work has largely been forgotten today. On an annual basis, the Hungarian Society of Nephrology awards a Korányi Prize and the Sándor Korányi Society awards a Korányi Memorial Medal with an accompanying lecture. This brief review introduces the life and work of Sándor Korányi to the non-Hungarian nephrological community. It emphasizes his two main contributions to modern nephrology, i.e. the introduction of physicochemical methods into the analysis of renal function, and the provision of a rational basis for dietary treatment of renal disease.

His life

Sándor Korányi was born in Budapest in 1866. His father, Frigyes Korányi, was a renowned professor in charge of the First Internal Clinic in Budapest. Sándor Korányi started as a student of anatomy (1884–1885) and subsequently pathology (1887–1888). He immedi-

ately showed his talent by publishing three papers and presenting one of them to the Hungarian Academy of Sciences (15 June 1885). He obtained his medical diploma in 1898 and turned to Strasbourg, then one of the leading German universities, to start a career in the Department of Physiology (under Professor Goltz). He was introduced into the methodology of experimental medicine and collaborated with, and became a friend of, Jacques Loeb. In August 1889 Sándor Korányi returned to Budapest. He was first resident in the clinic of his father and was appointed as assistant to the professor in 1895. His interest in physiology prompted him to lecture on physiology, physics and histology at the veterinary college, where he then became a lecturer and submitted a thesis on the subject 'Experimental and practical pathology and therapy of the nervous system'. In 1900 he was made Honorary Professor of Neurology and was promoted to full Professor in Internal Medicine in 1907. He had only a small clinic with two wards, but had a laboratory in which his ground-breaking scientific studies were performed. After the retirement of his father, he was appointed Professor of Internal Medicine at the Third Clinic of Internal Medicine in Budapest.

Major scientific contributions in nephrology

His major achievement was that he tried to apply physico-chemical methods to practical clinical and to research problems in an effort to understand renal disease from their repercussions on excretory renal function. This line of research led him to the concept of renal insufficiency. He was convinced that changes in renal function influenced the disease process (a concept with a modern ring in the age of progression research).

Functional studies on healthy and pathological kidneys

It all started with an anecdotal observation. During a gynaecological operation in 1890 the ureter of a patient was damaged. The surgeon stitched the ureteral stub to the abdominal wall and asked Korányi to determine whether the kidney was healthy or whether it could be safely removed. Korányi performed detailed studies on the function of both kidneys. The function of the kidney with the intact ureter proved to be normal, while tests on urine from the ureter stitched to the abdominal wall indicated impaired function, i.e. decreased sodium, chloride, phosphate and urea concentrations. Consequently, the kidney was removed

and histology showed marked sclerosis [1]. This unusual case prompted a series of studies on renal function which culminated in the concept of renal insufficiency. The use of ureteral diversion was introduced, half a century later, as a model to study experimental renal disease [2].

Introduction of the freezing point method

Sándor Korányi applied the method of cryoscopy, i.e. determination of freezing point depression, to studies on concentrating and diluting capacity of the kidney in order to evaluate renal function. Cryoscopy was later replaced by gravimetry.

Cryoscopy was first applied to serum and urine of normal individuals. The freezing point depression of urine was found to vary between -0.45°C and -2.4°C . Korányi then applied this method to serum and urine of nephritic patients. A breakthrough was his recognition that while the healthy kidney is capable of adapting freezing point depression over a wide range according to needs, the ability of the nephritic patient to do so is limited. The difference between maximum and minimum freezing point depression became progressively less with advancing renal dysfunction.

He proceeded to show that osmotic pressure in the blood of highly evolved animals is constant. He showed that in nephritic patients, independent of the cause of renal disease and renal morphology, the capacity of the kidney is reduced to modulate freezing point depression in accordance with salt and water load. To a certain extent this defect was compensated by polyuria.

Stages of renal insufficiency and their relation to reduced renal function

Korányi introduced the term 'renal insufficiency' in 1896: 'If the organism is unable to compensate, a state ensues when demands of the organism cannot be met any more.' He stated that in healthy individuals daily urinary excretion exceeds the potential minimum urine volume, suggesting the presence of a 'safety reserve'. He argued that if kidneys lose reserve capacity, the function can be maintained by recruiting compensating mechanisms, so that a new balanced steady state ensues. Sixty years before this subject raised widespread interest, Korányi recognized the importance of residual parenchymal function for the progression of renal disease.

He observed that in advanced renal failure, freezing point depression of blood and urine approached each other, suggesting limitation of the osmotic function of the kidney. The adapting capacity of the kidney appeared to cease, i.e. freezing point depression of blood and urine did not change following loads of water, saline or nitrogen. This state was later called isostenuria by Volhard.

Korányi recognized that in the advanced stage of renal insufficiency, retention of nitrogenous products is characteristic and freezing point depression of blood

changes from -0.56°C to -0.6°C . He ascribed this increase to organic decomposition products which he called 'residual nitrogen'. This work was appreciated by Volhard, who wrote in 1942 'the main result of lasting value is the recognition that variability of renal function is lost in renal failure' [3].

Dietary treatment of renal insufficiency

Korányi tried to translate these insights into practical advice for the treatment of renal patients. He proposed that the diet should be tailored to the capacity of the kidney: 'We would greatly ease the life of patients if we could adapt the diet in such a way that the number of dissolved molecules released through metabolism does not exceed the capacity of the kidney to discharge molecules.' The results and observations of this approach were published in a monography 'Funktionelle Pathologie und Therapie der Nierenkrankheiten' [Functional Pathology and Therapy of Renal Disease] [4].

To do full justice to his scientific *oeuvre*, it must be mentioned that his investigations were not only limited to renal disease. He also worked on such diverse topics as oedema formation (as recently reviewed by Richet [5]), digitalis therapy in heart disease, pathogenesis of arrhythmias, relationship of high blood pressure to cardiac disturbances, treatment of typhoid fever and tuberculosis. He even proposed the concept of cyto-static treatment in malignant haematological diseases. He also recognized the importance of statistical evaluation of therapeutic results and published on this issue.

As a representative of the Medical Faculty of the University of Budapest he was member of the Upper House of Parliament. He castigated the shortcomings of Hungarian medical science, medical care and medical training. He called for improvement, with some success. He was member of the Hungarian Academy of Sciences, but his scientific merits were also acknowledged on an international level. He was honorary member of the Academia Leopoldina (Deutsche Naturforscher) and of the Interstate Postgraduate Medical Association of North America. He retired in 1936 at age 70. The last years of his life were clouded by myocardial infarction and stroke. He died on 12 April 1994. He is rightly considered the Nestor of Hungarian nephrology.

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References

1. Korányi A. *Funktionelle Pathologie und Therapie der Nierenkrankheiten*. Berlin: 1929
2. Masaki Z, Ferrario CM, Bumpus FM. Cutaneous tubeless ureterostomy as a procedure to study renal function in conscious dogs. *Invest Urol* 1978; 16: 224–228

3. Volhard F. *Nierenkrankungen und Hochdruck*. Leipzig: 1942
4. Springer 1929
5. Richet G. Edema and uremia from 1827 to 1905: the first faltering steps of renal pathophysiology. *Kidney Int* 1993; 43: 1385–1306
6. Korányi S. (with coauthor Jacques Loeb). Über den Einfluss der Schwerkraft auf den zeitlichen Verlauf der geradlinigen Willkürbewegung unseren Armes, *Pflüg Arch Ges Physiol* 1889; 46: 101
7. Korányi S. (with coauthor Jacques Loeb). Über Störungen der compensatorischen und spontanen Bewegungen nach Verletzung des Grosshirns. *Pflüg Arch Ges Physiol* 1891; 48: 423
8. Korányi S. Physikalisch-chemische Methoden und Gesichtspunkte in ihrer Anwendung auf die pathologische Physiologie des Kreislaufes, *Z Physiol* 1897
9. Korányi S. *Vom diagnostischen Werte der Niereninsuffizienz auf Grund klinischen Erfahrungen*. Ung. Med. Presse, 1898; 13