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The History of Renal Physiology in Czechoslovakia

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The beginnings of renal physiology in Czechoslovakia date back to the end of 1950s and the man behind it all was undoubtedly Jan Brod. Although a clinician himself, Brod was endowed with the ability to think like a physiologist. He thereby had a marked effect on the whole of Czechoslovak nephrology, which underwent rapid development and modernization under his influence. In addition, Brod lectured on renal physiology at the Medical Faculty of Prague Charles University and wrote tutorial texts on this subject. In the Institute of Cardiovascular Diseases, of which he was a co-founder and later director, he promoted the development of modern nephrology on a sound physiological basis (Jirka, Hejl, Ulrych, Hornych, Prát and others), directly recruited renal physiologists (Fencl, Heller, Nováková) and welcomed workers from abroad (Cort, etc.). Brod conceived the institute as a team of specialists with a wide range of qualifications (morphology, biochemistry, physiology, pharmacology, epidemiology and clinical medicine), all working together under the same roof – in those days a rather unique idea, but one which turned out to be very rewarding. In 1968 the development of the institute was interrupted, when Brod was forced into exile. Brod is further known from his monographs on the kidneys, which were published in Czech as well as in English (Brod 1962, 1978) and were probably the last monographs of this type written by a single author.

Two more research centers, closely associated with renal problems, were founded during the 1950s. One was a team in the Institute of Physiology of the Czechoslovak Academy of Sciences, working under J. Křeček, which began to investigate developmental aspects of water and electrolyte balance. Renal problems were studied by Čapek, Martínek, Friebová and others. A further group was formed in the Institute of Endocrinology of the Slovak Academy of Sciences in Bratislava, where long-term research on natriuretic factors was started under B. Lichardus.

O. Schück, the present president of the Czech Nephrological Society, is another representative of Czech clinical nephrology with a strong inclination to physiology. He began to perform animal experiments at the end of 1950s in which he studied the reabsorption of various substances from the urine across the wall of the urinary bladder. His best known experimental study concerned the distribution of substances in the renal parenchyma, with a special reference to the medullary countercurrent system. Since 1970s he investigated the pharmacokinetics of various drugs (chiefly antibiotics).

R. Dzúrik, the president of the Slovak Nephrological Society, is a well-known biochemist. Some of the studies carried out by his team naturally include physiological aspects, especially those performed in the 1970s, when he looked for a factor inhibiting the utilization of glucose in the blood of patients with uraemia. Subsequently, he studied the accumulation of hippurate in experimental renal failure.

In the 1950s, it was practically impossible to do any work in the field of pure renal physiology at the Department of Physiology of the Medical Faculty in Prague, as the department was "consecrated" to the Pavlovian school of thought. I therefore studied the mechanisms of conditioned reflex changes in diuresis. It was found that repeated water administration through a stomach tube in dogs naturally promoted a water diuresis, i.e. led to the production of hypotonic urine. After about the thirtieth dose, when the tube was introduced, but no water was administered, the dog again reacted by diuresis, but the urine was hypertonic and not hypotonic. In the following years I looked in vain for an explanation, which today presents itself quite logically. After water has been poured into the stomach and then reabsorbed, the resultant expansion of extracellular fluid volume led to the secretion of an atrial natriuretic peptide and hence to natriuresis and diuresis. This, of course, was masked by massive water diuresis, but when the administration of water was only simulated, natriuresis with diuresis induced by the atrial natriuretic peptide took place.

For a few years I studied the antidiuretic hormone. Štulc and I developed a relatively sensitive biological titration method allowing to detect the antidiuretic activity of human and animal plasma under normal conditions (i.e. without dehydration). In this way, for the first time, we described ADH levels not only in man (in infants detectable amounts were not found until the age of 4 months, i.e. when urine actually starts to be concentrated), but also in various experimental animals.

In 1965, I learnt the micropuncture technique from Prof. J. Ullrich in the Department of Physiology of the Free University in Berlin. I and V. Horáček were then the first workers east of the river Elbe to employ this technique. We measured proximal resorption after expansion of extracellular fluid volume, after vasodilatation induced by different substances and at different blood pressures. The limitation of these experiments was that in rats there it was impossible to achieve changes in only a single parameter. For instance, the injection of dopamine is followed by the desired vasodilatation in the kidneys but the blood pressure falls at the same time. The impossibility (in those days) to measure the renal blood flow with a flowmeter was likewise felt to be a serious disadvantage. Consequently, we began to work in dogs. To enable direct measurement of the pressure in the glomerular capillaries, we developed a method for thin-layer (0.5 – 1.0 mm) ablation of the cortex corticis, thereby gaining access to the more superficially localized glomeruli. The injection of radioactively labelled chick red blood cells, followed by their measurement in single glomeruli, allowed us to measure the glomerular blood flow. At first, we worked on an isolated dog kidney preparation perfused under constant pressure with blood from a dog (the perfusor), without even the slightest interruption of kidney blood flow. This method had great advantages, but its extremely exacting nature made it liable to failure. We therefore tried a simpler technique, which we still use today. We work with beagles of the same age, weighing 13 ± 1 kg and eating the same amount of food, so that they are highly standardized.

The kidney is prepared for micropuncture by a standard technique, but after decapsulation a small portion of the surface (about 1 x 1 cm) is sliced away as described above, thereby providing access to the glomeruli. We can then measure – and not just calculate – all the parameters needed for determination of the afferent and efferent resistance. These measurements led us to the conclusion that the great majority of vasoconstrictors preferentially constrict the vas efferens. We believe this to be an advantage, since efferent constriction restricts the renal blood flow (if blood is needed at important sites, such as the brain) but does not curtail glomerular filtration.

All models of experimental hypertension known so far – with the exception of Dahl rats, which is a salt-dependent model – are known to lack a good control line. In 1982 we therefore began with the inbreeding of the Prague Hypertensive Rat (PHR) which, unlike others, has a normotensive counterpart (PNR). Both lines stem from the same pair of parents and are thus blood relatives. This, *inter alia*, has the advantage that, even after 20 generations, kidneys can be transplanted from one animal to another without any significant signs of rejection. At present, we are still working to obtain as exact definition of this strain as possible.

References

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