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Editor

L. TAKÁCS

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(Each volume is available separately.)

FOREWORD

This volume is one of the series published by Akadémiai Kiadó, the Publishing House of the Hungarian Academy of Sciences in coedition with Pergamon Press, containing the proceedings of the symposia of the 28th International Congress of Physiology held in Budapest between 13 and 19 July, 1980. In view of the diversity of the material and the "taxonomic" difficulties encountered whenever an attempt is made to put the various subdisciplines and major themes of modern physiology into the semblance of some systematic order, the organizers of the Congress had to settle for 14 sections and for 127 symposia, with a considerable number of free communications presented either orally or as posters.

The Congress could boast of an unusually bright galaxy of top names among the invited lecturers and participants and, naturally, the ideal would have been to include all the invited lectures and symposia papers into the volumes. We are most grateful for all the material received and truly regret that a fraction of the manuscripts were not submitted in time. We were forced to set rigid deadlines, and top priority was given to speedy publication even at the price of sacrifices and compromises. It will be for the readers to judge whether or not such an editorial policy is justifiable, for we strongly believe that the value of congress proceedings declines proportionally with the gap between the time of the meeting and the date of publication. For the same reason, instead of giving exact transcriptions of the discussions, we had to rely on the introductions of the Symposia Chairmen who knew the material beforehand and on their concluding remarks summing up the highlights of the discussions.

Evidently, such publications cannot and should not be compared with papers that have gone through the ordinary scrupulous editorial process of the international periodicals with their strict reviewing policy and high rejection rates or suggestions for major changes. However, it may be refreshing to read these more spontaneous presentations written without having to watch the "shibboleths" of the scientific establishment.

September 1, 1980 J. Szentágothai

President of the
Hungarian Academy of Sciences

INTRODUCTION

This volume intends to summarize scientific material of Invited Lectures and Symposia of Section 06 "Kidney and Body Fluids" of the 28th International Congress of Physiological Sciences held in Budapest, July 13–19, 1980.

Selection of Invited Lecturers, topics and Invited Speakers of Symposia preceded the Congress by about one and a half years and arrangements were made after having consulted with the IUPS Council, and having considered the opinions of prominent nephrologists and, finally, according to the viewpoints of the local Section Organizing Committee. Chairmen of Symposia were invited with similar circumspection who, thereafter, suggested persons to be Invited Speakers of Symposia after careful multilateral exchange of ideas. Accordingly, we organized the Programme of the Section and compiled this Volume with the hope of giving a material representing promising research trends. May we hope that participants of the Congress and readers of this book will meet with their expectations.

The Symposia were organized by a uniform schedule: chairmen's introduction was usually followed by four Invited Papers and complemented by five Free Communications. This procedure rendered possible completion of selection on the basis of invitation as well as correction of errors in organization. Chairmen were asked to give a brief summary of main results and discussions.

Actually, this Volume comprises 80 papers of 93 presented. To our sincere regret, a part of the papers lacking could not be submitted because of copyright difficulties while others have not reached us for unknown reasons. In the latter cases the Abstract Volume will be helpful for general survey of the Section's Programme.

Finally, we would like to apologize for possible faults and errors in preparing this Volume, but our primary aim and intention was – similarly to all other volumes in this Series – to make it available in a published form as soon as possible.

Lajos Takács
editor

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NEURAL CONTROL OF RENAL FUNCTION*

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This morning I wish to consider the role of the renal nerves in maintaining the homeostasis of the body fluids. I will discuss the efferent control of excretory activity and the nature of the renal receptors that send afferent impulses to the neural axis when stimulated. I will also consider the possibility of a neural mechanism, a renorenal reflex, being responsible for the coordination of the excretory activity of the two kidneys that occurs when the function of one of the kidneys is altered.

Claude Bernard (1859) was the first to report that acute section of the splanchnic nerves in an anesthetized dog results in an increase in urine production by the ipsilateral kidney. This observation has been repeatedly confirmed over the subsequent years. The two problems addressed by most investigators have been, (first) whether the effect is exclusively hemodynamic in origin due to an increase in glomerular filtration rate and renal blood flow, or whether there is also an effect on the tubular mechanisms for reabsorption, and secondly, whether the effect, whatever its mechanism, is evident only under the abnormal circumstances of anesthesia and surgery, and thus should not be considered a response to "physiological" alterations. Until recently the answer to the first question was that the effect was exclusively hemodynamic, but I will review the compelling evidence that the sympathetic efferent inflow to the kidney has a direct effect on tubular reabsorptive mechanisms which may under certain circumstances

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be magnified by hemodynamic factors, although the latter need not occur. I do not believe that the answer to the second question has yet been completely resolved. Almost all of the published evidence favors the view that it is apparent only when the animal is severely stressed. More recent studies, however, indicate that the effects of denervation may be seen in conscious animals.

The neural efferent mechanism for control of salt and water excretion has been intensively investigated in recent years in 3 laboratories, by Dr. Takacs and his colleagues at Semmelweis University here in Budapest, by Dr. DiBona and colleagues at the University of Iowa, and by my associates in the Chapel Hill Micropuncture Laboratory. The results obtained in these laboratories have been complementary.

The recent description of a tubular innervation provides an anatomical basis for the tubular functional effects reported by these 3 laboratories. It has been known since the studies of Bradford (1889) that there is a rich sympathetic innervation of the blood vessels of the kidney; although there have been periodic reports of a direct tubular innervation there have been at least as many reports denying this. In the early 1970's Barajas and Mueller presented for the first time convincing evidence for a direct innervation of the tubular cells in the cortex of monkey and rat kidneys (Barajas and Mueller 1973 and Mueller and Barajas 1972). Using electron microscopic and histochemical methods these investigators demonstrated adrenergic nerve terminals separated from proximal and distal tubular cells only by basement membrane material. This relationship is identical to that observed between similar vesiculated varicosities and vascular smooth muscle, a site where synaptic transmission is thought to occur.

MICROPUNCTURE AND CLEARANCE EXPERIMENTS

Although a proximal tubular effect was first reported by Bencsath et al. (1972), the Chapel Hill group was the first to provide extensive micropuncture documentation for such a result. Bello-Reuss et al. (1975) characterized the renal response to acute unilateral denervation in an extensive study of sham denervated and denervated kidneys. Denervation of a kidney was accomplished by stripping the renal artery of its adventitia and coating it with a solution of 10% phenol in alcohol. For a variety of reasons the functional changes observed cannot be attributed to a direct effect of phenol on kidney function: no norepinephrine could be detected in the kidneys several days after denervation; incomplete denervation from splanchnic nerve crushing produced similar, but quantitatively smaller results than the apparently complete chemical denervation, and these effects were reversed by electrical stimulation of the distal end of the cut splanchnic nerve. Coating the artery with lidocaine instead of phenol produced similar but transitory effects.

No changes were observed in any function of either kidney of sham-denervated rats. Following unilateral denervation in hydropenic animals urine volume from the denervated kidney increased to about twice its control value, and urinary sodium excretion increased sixfold. There was no change in urine volume or sodium excretion from the innervated kidney. Glomerular filtration rate (GFR) and renal plasma flow (RPF) remained unchanged in both kidneys after the procedure. SNGFR remained unchanged after denervation. The fluid-to-plasma ratio of inulin decreased in samples of fluid collected from late proximal tubules of denervated kidneys indicating a 60% decrease in water and sodium reabsorption by the proximal tubule. Absolute water and sodium reabsorption increased in the loop of Henle, distal convolution, and collecting ducts, but not enough to compensate for the 60% decrease in the proximal tubule.

Denervation caused no change in estimated glomerular capillary or efferent arteriolar pressure. There were very small increases in hydrostatic pressure in proximal and distal convolutions and in small peritubular capillaries. Since there was no change in whole kidney or single nephron GFR and renal plasma flow was unchanged, it is unlikely that there was a change in overall or superficial nephron colloid osmotic pressure or significant redistribution of renal blood flow. It thus appears that the physical factors did not play an important role in the observed changes in tubular reabsorption.

Similar results were observed in animals expanded 10% above their body weight by an infusion of isotonic saline solution (Bello-Reuss et al. 1977). There was no change in GFR or RPF in either kidney after unilateral denervation or sham denervation. Urine flow and sodium excretion by denervated kidneys was doubled. Simultaneously urine flow and sodium excretion by the contralateral innervated kidneys fell by half so that there was little change in total salt and water excretion. I will return to this striking finding shortly. After denervation SNGFR remained unchanged. The F/P inulin ratio in fluid from late proximal tubules decreased, indicating a fall in water and sodium reabsorption in the proximal tubule of more than 50%. Absolute water and sodium reabsorption increased after denervation in the loop of Henle, distal convolution and collecting ducts but not enough to prevent the natriuresis and diuresis.

In another series of experiments in anesthetized rats the natriuresis and diuresis resulting from unilateral crushing of the greater splanchnic nerve was reversed by electrical stimulation of the distal portion of the cut nerve with square wave pulses of 0.5 msec duration, voltage twice threshold, and 1 or 2 Hz frequency (Bello-Reuss et al. 1976). Kidney GFR and RPF and SNGFR remained unchanged during stimulation. Nerve stimulation produced a reduction of approximately 25% in urine flow and sodium excretion due to increased water reabsorption in the proximal tubule. In 5 of 6 animals, stimulation at 1