II. INTRARENAL SITES OF SALT AND WATER EXCHANGE

Chairman: Robert F. Pitts, Ph.D., M.D.

INTRODUCTION

By Robert F. Pitts, Ph.D., M.D.

In all vertebrates except, perhaps, the marine fishes and birds, total body content and concentration of salt and water are regulated primarily by the kidneys. Precision of regulation and the ability to meet the stresses of deprivation or of gross excess of intake are dependent on osmoreceptor–antidiuretic hormone and volume receptor–adrenocortical mechanisms of control. Our topic this afternoon is “Intrarenal Sites and Mechanisms of Salt and Water Exchange.” Extrarenal regulatory mechanisms will be considered tomorrow.

Over the past 30 years or more, an extensive body of knowledge has accumulated describing the gross over-all operation of these renal mechanisms. We are at present entering an exciting phase of increasing understanding of the renal processes at a cellular level. The foundation for this understanding was laid nearly 30 years ago, by Dr. A. N. Richards and his associates in their pioneering studies with micropuncture techniques on the amphibian, and later, on the mammalian kidney.

Further development of knowledge and the testing of hypotheses on intact animals and man depended in major part on the clearance methods and concepts developed largely by Dr. Homer Smith. And yet, despite a mass of descriptive information, there has been no very satisfactory understanding of mechanisms of excretion or of reabsorption of salt and water at a cellular level.

I propose that the major developments of understanding which occur periodically at some 10- to 15-year intervals depend on 3 factors: first, the gradual accumulation of a critical mass of basic information; second, the new concept or way of viewing the problem; and third, the new method, or adaptation of the old, which permits a more precise testing of the concept.

Our first topic this afternoon is “Osmotic Concentration and Dilution in the Mammalian Nephron.” Ten to 15 years ago, our understanding was reasonable, though not profound. In water deprivation, antidiuretic hormone stimulated the active pumping of water in the distal convoluted portion of the nephron. Solutes remaining in the tubule were concentrated by the extraction of water. A concentrated urine of small volume was formed. Then, it became evident from micropuncture studies that the urine within the distal tubule is hypo- or isotonic even when the final urine is markedly hypertonic. The pumping of water was shifted to the collecting ducts.

Some began to grumble about the pumping of water. Can any cell transport water actively? Based on this and far more background information, a new concept originated with the chemists, Hargitay and Kuhn, and the physiologist, Wirz; ions were pumped actively by the loops of Henle to establish an osmotic gradient between cortex and medulla. Water diffused passively down this osmotic gradient as urine flowed along the collecting ducts. No pumping of water was necessary.

At first, little credence was accorded this concept in this country. Perhaps it was not
clearly explained. Our first 2 speakers, Drs. Gottschalk and Ullrich have contributed significantly to this thesis of osmotic concentration and dilution of the urine. They have used different approaches. Dr. Gottschalk, with a background of experience in micropuncture techniques obtained in a study of intratubular and peritubular capillary pressures, has provided impressive data in support of this view of formation of a concentrated urine. Dr. Ullrich, working with ureteral microcatheterization in the hamster, has done much to clarify the role of the collecting ducts in forming a concentrated and a dilute urine.

The second part of the program this afternoon deals more specifically with the mechanisms of transport of ions, although there will be continuing reference to the transport of water as well. The first speaker, Dr. Giebisch, could qualify as the grandson, scientifically speaking, of Dr. A. N. Richards—if Dr. Phyllis Bott will permit me to call her his mother. (Laughter) The reason why I say this is that Dr. Giebisch learned the technic of micropuncture through the kindness of Phyllis Bott who took him into her laboratory and devoted time to his training. His presentation will be concerned with the measurements of electrical potentials and ion fluxes in single nephrons. The second speaker, Dr. Berliner, is really a perfect example of one who needs no introduction. His basic and fundamental work, not only on ion exchange but also on other aspects of renal function, are well known to all of you. He will deal with mechanisms involved in ion exchange in the nephron. The final paper on this afternoon’s program is by Drs. Malvin and Wilde. They will consider the role of “stop-flow” studies in elucidating ion and water reabsorption in the nephron. As many of you know, Dr. Malvin and Dr. Wilde have pioneered in a new method of study of renal tubular functions, a sort of a poor man’s micropuncture technic, as I like to look upon it. I say this in no derogatory sense, since I am a poor man myself and have used their method extensively. At the close of these papers, the participants will have the opportunity to appraise the information and concepts which have been derived from these diverse sources.
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