Renal Function:
Mechanisms Preserving Fluid and Solute Balance in Health

Heinz Valtin

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The cover design, representing two kidneys on a background of the world, is based on the official emblem of the V International Congress of Nephrology, Mexico City, 1972. The symbol is used with the kind permission of Dr. Herman Villarreal, President of the Congress.

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To

Nancy

and

Tom and Alison

Preface

With the advent of new curricula, virtually every medical educator has had to try to define the basic material in his particular discipline. This book represents my view of the essential elements in renal, fluid, and electrolyte physiology, which every medical student should master. These are necessarily personal choices, and thus most teachers in this field may find some fault with them or, what is more likely, will point out omissions.

Problems. Many chapters are supplemented by one or more quantitative problems that amplify the material in the text. The answers — as well as explanations of how the answers were obtained — are given in the section Answers to Problems following the text.

A note to students. This textbook has been prepared with a certain amount of hesitation, for fear that its concise style may tend to underplay the importance of mastering basic scientific principles. I firmly believe that the basic sciences are the foundation of excellence in medicine. The references at the end of each chapter are meant to underscore this conviction by encouraging those individuals whose curiosity has been aroused to read further. In selecting the references, I have tried to fulfill three purposes: (1) to list some classic contributions; (2) to cite original experiments, especially when their results conflict with those of other studies; and (3) to list review articles in which many further references can be located. As a result, these reference lists, although selective, are somewhat long, and I advise students to enlist the help of their instructors in selecting the particular works that are appropriate to their purpose.

A request for critique. I shall appreciate suggestions from any reader — be he student or teacher — on how this text might be improved.

H. V.

Acknowledgments

Every chapter was reviewed by at least one person who is an expert on the topic treated in that chapter. I shall not name these individuals here, not only because I might inadvertently omit some of them, but also because any errors should not be blamed on them. I trust that I have thanked them all personally for their very real help.

I am grateful to many authors and publishers for permission to reproduce their work. I have tried to acknowledge this debt — especially in the case of original photographs — in the legends to the figures.

Special thanks are due Mrs. Grace E. McCann for her invariably cheerful patience in typing the manuscript, from first draft to final copy. Mrs. Ethel B. Garrity kindly proofread the entire manuscript. Valma and Henry Page and Genevieve Zyskowski diligently prepared all the illustrations. The librarians of the Dana Biomedical Library at Dartmouth College provided an amiable atmosphere and much thoughtful and expert help. It was a real pleasure to work with the superb staff at Little, Brown and Company through all phases of production.

Finally, I was greatly aided by the on-the-spot advice of a number of colleagues at Dartmouth Medical School, especially S. Marsh Tenney, Gilbert H. Mudge, William O. Berndt, John T. Gatzy, Howard H. Green, and Richard D. Mamelok.

H. V.

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Contents

1 : Components of Renal Function

The lay view of renal function is that the kidneys remove waste liquids and potentially harmful end products of metabolism, such as urea, uric acid, sulfates, and phosphates. While this is true, it should be emphasized that an equally important function is the conservation of substances that are essential to life. Such substances include water, sugars, amino acids, and electrolytes such as sodium, potassium, bicarbonate, and chloride. Therefore, the kidneys should be viewed as regulatory organs that selectively excrete and conserve water and numerous chemical compounds and thereby help to preserve the constancy of the internal environment.

A castaway at sea may survive for three weeks without drinking water, and a man lost in the desert may survive from two to four days without water or salt. Conversely, a healthy individual frequently tolerates dietary excesses of fluid and salt. The reason that such extreme conditions can be endured lies primarily in the renal control of salt and water excretion and conservation. It is obvious that the renal adjustments must be relatively rapid if they are to preserve life. In fact they are brought into play within minutes or at most a few hours after the individual has been subjected to the environmental challenge.

Anatomy

The major gross anatomical features of the mammalian kidney are illustrated in Figure 1-1. The kidney consists of cortical and medullary substances and a pelvis that connects with the ureter. The medullary substance is divided into an outer and inner zone (Fig. 1-2a), the latter comprising one or more papillae, depending on the species. The renal artery enters the kidney alongside the ureter, branching to become progressively the interlobar artery, the arciform or arcuate artery, the interlobular artery, and then the afferent arteriole that leads to the glomerular capillary network. The venous system has subdivisions with similar designations, terminating in the renal vein, which also courses beside the ureter.

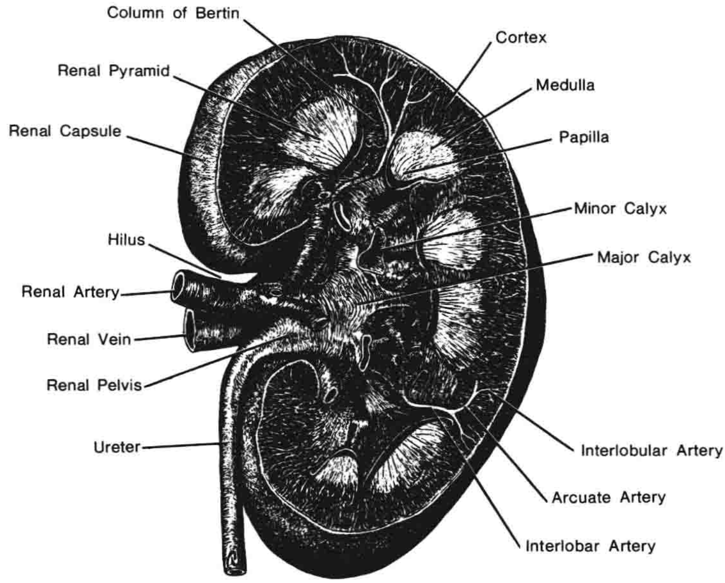


Figure 1-1
Sagittal section of a human kidney, showing the major gross anatomical features. The renal columns are extensions of cortical tissue between the medullary areas. Redrawn and very slightly modified from Braus, H. *Anatomie des Menschen*, vol. 2. Springer, Berlin, 1924.

By *renal blood flow* (RBF), we mean the total amount of blood that traverses either the renal artery or the renal vein per unit time. The difference between flow in the renal artery and flow in the vein is the urine flow, which is negligibly small compared to the total blood flow. In adult man about 1,300 ml of blood (i.e., about 25% of the cardiac output) flows through the two kidneys each minute, even though they constitute less than 0.5% of the total body weight. About 1,299 ml of blood leaves through the renal veins each minute, so a normal urine flow is about 1 ml per minute. *Renal plasma flow* (RPF) refers to the amount of plasma that traverses either the renal artery or the renal vein per unit time. Obviously, if the systemic hematocrit is 45%, RPF constitutes 55% of RBF.

The Nephron

The nephron, or functional unit of the kidney, consists of a glomerular capillary network that is surrounded by Bowman's capsule, a proximal convoluted tubule, a loop of Henle, a distal convoluted tubule, and a collecting duct (Fig. 1-2a). Together, the adult human kidneys comprise roughly two million such functional units, which provide tremendous reserve. Man at rest can survive on about one-tenth this amount of functioning renal tissue, and he can continue an active life even though about 75% of the tissue has been destroyed.

Superficial Cortical and Juxtamedullary Nephrons. As is illustrated in Figure 1-2(a) and (b), two types of nephron have been described. The superficial cortical nephron has a short loop of Henle that reaches varying distances into the outer medulla, and its efferent arteriole branches into the peritubular capillary network that surrounds the tubular segments belonging to its own and other nephrons. This capillary network nourishes the tubular cells, picks up substances that have been reabsorbed from the tubules, and brings substances to the tubules for secretion.

The juxtamedullary nephron arises from the deep cortical regions. Its glomerulus is larger than that of a superficial cortical nephron, and its loop of Henle extends varying distances into the inner medulla, sometimes all the way to the papillary tip. Its efferent arteriole continues not only as a peritubular capillary network but also as a series of vascular loops called the vasa recta. The vasa recta descend in bundles to varying depths in the inner medulla, or papilla. There they break up into capillary networks that surround the collecting ducts and ascending limbs of Henle. The blood then returns to the cortex in ascending vasa recta that run within the vascular bundles. The ratio of superficial cortical to juxtamedullary nephrons varies with the species of mammal. In man, about seven-eighths of all nephrons are superficial cortical and one-eighth are juxtamedullary.

Ultrastructural Differences of Various Nephron Segments. Epithelial cells lining the various nephron segments differ in many respects, such as size, number and length of microvilli at the apical (mucosal) surface, number of mitochondria, number and extent of basal infoldings, and many others. The major differences are shown in Figure 1-3. Although the functional significance of some of these variations has not yet been clarified, many fruitful correlations between structure and function have been drawn, and these will be referred to when appropriate.

The Juxtaglomerular Apparatus (JGA)

This apparatus (Fig. 1-3) consists of specialized epithelial cells in the very early distal tubule, the macula densa cells, and specialized secretory or granular cells at the vascular pole where the afferent and efferent arterioles enter and leave the glomerulus. The JGA thus is a combination of specialized tubular and vascular cells. The macula densa cells always come into intimate

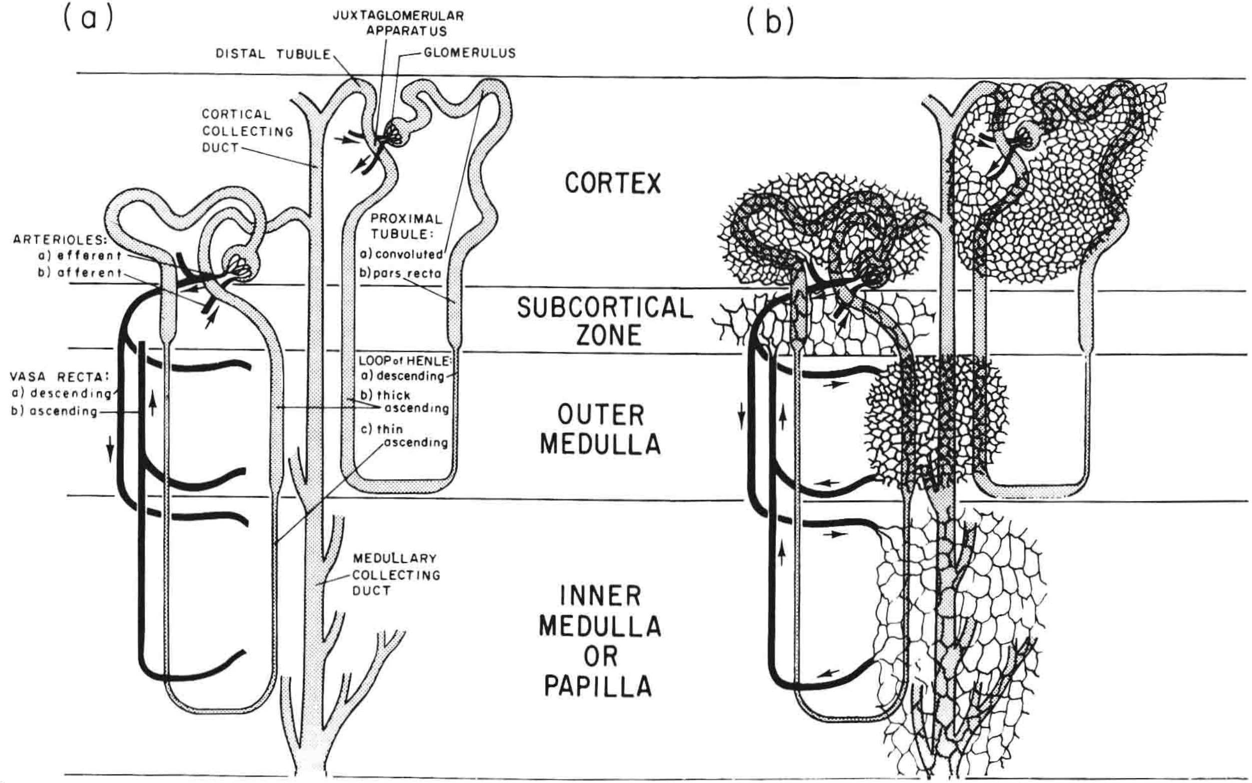
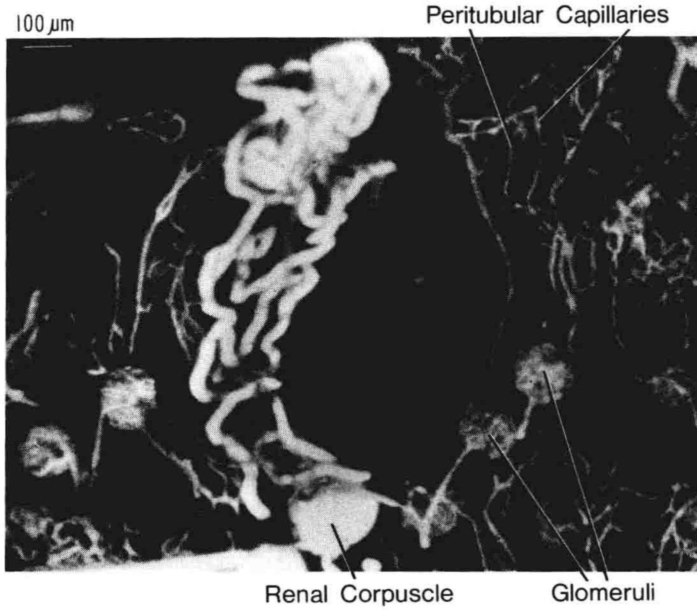


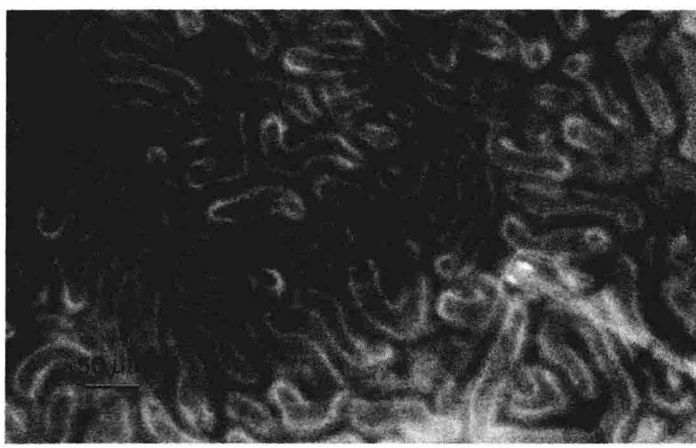
Figure 1-2

(a) Superficial cortical and juxtamedullary nephrons, and their vasculature. The glomerulus plus the surrounding Bowman's capsule are known as the "renal corpuscle." The beginning of the proximal tubule – the so-called urinary pole – lies opposite the vascular pole, where the afferent and efferent arterioles enter and leave the glomerulus. The early distal tubule is always closely associated with the vascular pole belonging to the same nephron; the juxtaglomerular apparatus is located at the point of contact.

(b) Capillary networks have been superimposed on the nephrons illustrated in (a). Note that the capillary network that is interposed between descending and ascending vasa recta surrounds primarily the collecting duct and the ascending limb of Henle. In the outer and inner medulla, the vasa recta run in bundles, closely associated with the descending limb of Henle. Parts (a) and (b), slightly modified, are from Kriz, W., and Lever, A. F. *Amer. Heart J.* 78:101, 1969.



(c) The cortex of a dog kidney (photomicrograph) illustrating the highly convoluted course of the proximal tubule. A micropipet (white streak at the lower left) was inserted into Bowman's space, and the convolutions were filled with a silicone rubber compound ("Microfil"). Other glomeruli, as well as peritubular capillaries, were partially filled with Microfil through an intra-arterial injection. Photograph courtesy of R. Beeuwkes and A. C. Barger.



(d) The surface of a rat kidney as seen during micropuncture. The so-called bag of worms consists mainly of segments of proximal convolutions as they repeatedly rise to the surface. A few segments of distal convolutions are also visible, but glomeruli are not usually found at the surface of a mammalian kidney. Each tubular segment is surrounded by peritubular capillaries. The light, linear streak in the lower right is a micropipet that has been inserted into a tubular segment. The pipet is out of focus because its shaft lies above the renal surface. Photograph courtesy of J. Schnermann.

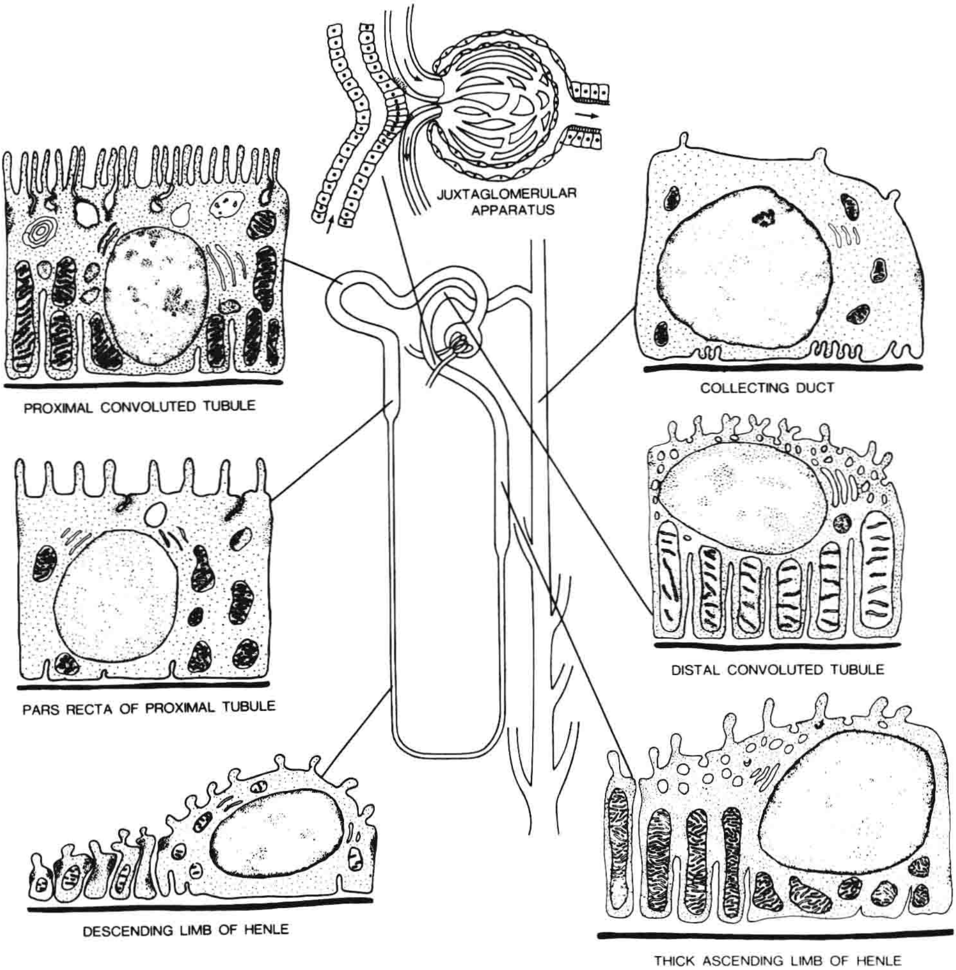


Figure 1-3
Diagrams illustrating some of the ultrastructural differences of the major segments of the nephron. Also shown is the juxtaglomerular apparatus, which lies at the point of contact between the distal tubule and the vascular pole of its own glomerulus. Adapted from Rhodin, J. *Int. Rev. Cytology* 7:485, 1958.