RENAL PHYSIOLOGY

JOSEPH P. GILMORE

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JOSEPH P. GILMORE, Ph.D.

Professor and Chairman
Department of Physiology and Biophysics
The University of Nebraska College of Medicine

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To Harry K

Preface

The purpose of this text is to provide a concise exposition of renal function. It is written for students and is not intended to be a reference text for serious workers in the field. Over the past several years there have been substantial changes in the medical school curriculum, with particular emphasis on decreasing the amount of time available for preclinical exposure. Unfortunately, what has happened in many instances, is that while the available time has been decreased, few teachers of renal physiology have taken the initiative to determine exactly what basic material the first year medical student should know in order to go on to the next step in the curriculum.

The author has made this decision as indicated by the contents of this text, which may also be suitable for college students who are interested in learning about the kidney. The author is not one who has been trained as a traditional renal physiologist, but rather is one who became interested in renal physiology as a result of his interest in the general area of the control of body salt and water. The contents of the text represent the results of teaching renal physiology for several years, the material and approach being modified from year to year on the basis of students' suggestions.

Few specific references will be found between the pages. Rather, at the end of each chapter general references are given for those who are interested in persuing the material in more depth. However, in instances in which there is a substantial difference in points of view, references substantiating each side are presented. It is apparent that in some cases it has been necessary to be somewhat dogmatic. When this is so, it will be indicated. It is the belief of the author that if this text is utilized for teaching renal physiology to first year medical students or to senior college students, the student contact hours can be utilized not for lecturing but for teaching, in that time can be spent in clarifying the material or going into further depth, depending on the students' interest. It is also hoped that this text will appeal to advanced medical students and residents who would like to have available a text which would provide them with a concise review of renal physiology.

The section on the control of micturition was written by Dr. Irving H. Zucker.

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JOSEPH P. GILMORE

Contents

1

The Structural Organization of the Kidney

SYNOPSIS An appreciation of the anatomy of the kidney is a prerequisite to an understanding of its function. Although the kidneys represent only one-half per cent of body weight, they receive approximately 25 per cent of the cardiac output. The nephron is the functional unit of the kidney, with each kidney containing approximately 1 million. The nephron, a U-shaped structure, begins at Bowman's capsule, which contains the glomerular capillaries across which filtration, the initial step in urine formation, occurs. Bowman's capsule leads into the proximal tubule, which then leads into the thin loop of Henle and then into the distal tubule. Finally, the distal tubule empties into the collecting duct. The ultrastructure of the cells of the proximal tubule, with their large number of microvilli which provide a large surface area, is histologically consistent with this portion of the nephron, carrying out extensive reabsorptive activity.

The structure of the thin loop of Henle is suited for countercurrent multiplication which provides for the high concentration of solute in the medulla. The structure of the vasa recta provides a low blood flow through the medulla as well as functioning as a countercurrent exchanger, thus contributing to the accumulation of solute in this area. The collecting duct passes through this area of high osmolality and provides a structural basis for the final concentration of the urine.

There are three capillary beds in the kidney that have important functional significance: (1) the glomerular capillary bed, which is interposed between the afferent arteriole that enters the capsule of the nephron and the efferent arteriole that leaves the capsule; (2) the peritubular capillary network, which originates from the efferent arteriole and is in close relation to the proximal and distal tubules; it carries the fluid that is reabsorbed by these segments of the nephron away from the kidney; (3) those nephrons that have long loops of Henle (juxtamedullary) penetrating deeply into the medulla have in association with them the vasa recta, which are essentially long extensions of the peritubular capillary network.

The kidneys receive an extensive sympathetic nerve supply which when stimulated can greatly reduce renal function owing to an effect upon afferent arteriolar tone. Although the kidney also contains parasympathetic nerves, their functional significance is not known.

The adult human kidneys appear as two smooth-surfaced, bean-shaped structures, located on either side of the spinal cord against the dorsal wall of the abdomen outside (retroperitoneal) the main body cavity. They are approximately 5 by 13 cm in size, with each kidney weighing approximately 120 to 160 g; together they constitute approximately 0.5 per cent of the total body weight. A longitudinal section showing the gross anatomy of the kidney is shown in Figure 1.1. The internal edge of the kidney has a large indentation, the hilus, which is the opening into the intrarenal cavity or sinus. It is here that the renal artery and nerves enter, and from which exit the renal vein, lymphatics, and ureter. The gross internal structure reflects the lobulations seen externally in the fetal kidney. The outermost portion or cortex is deep red; the inner portion, or medulla, is lighter in color. The calix appears as a funnel that receives urine from the papilla. Thus, the urine formed in the nephron drains into the collecting ducts and then passes through the papilla and out through the ducts of Bellini into one of the minor calices. It then flows into the major calix, the pelvis, and then through the ureter into the bladder.

The gross structure of the kidney is best regarded as consisting of several lobes, each containing a pyramid with its cortical sub-

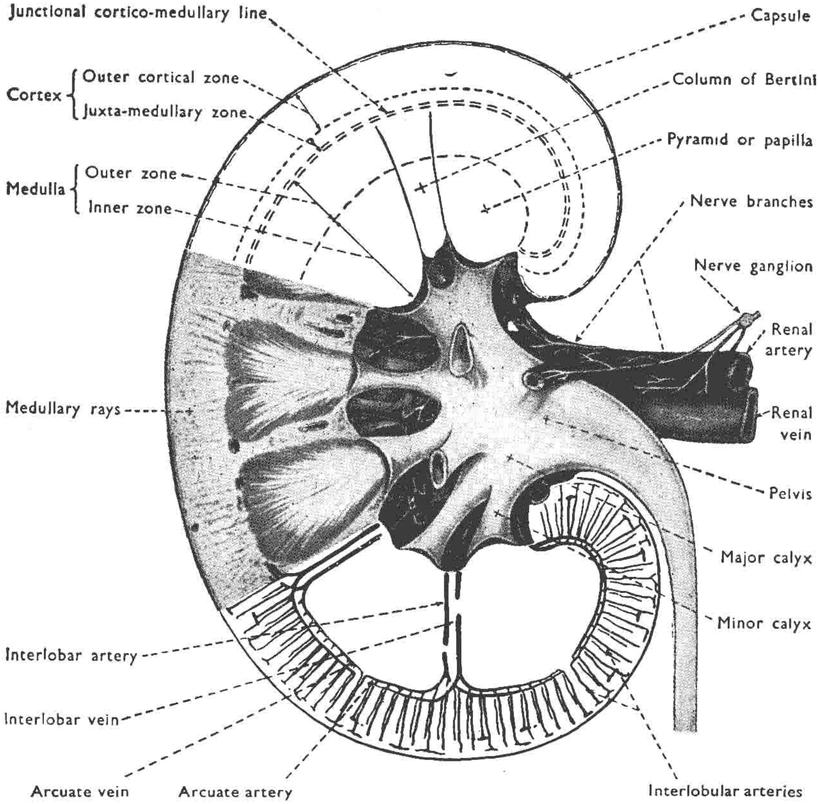

FIG. 1.1. Longitudinal section of human kidney. (From Garven, H. S. D.: *A Student's Histology*, E. & S. Livingstone, Edinburgh, 1957. Used with permission.)

stance. The difference in color between the cortex and medulla is due to the rich blood supply of the former relative to that of the latter. The cortex, which penetrates down between the pyramids of the individual lobules, has a granulated appearance; this is due to its content of renal corpuscles (see below) and the tortuous nature of the convoluted tubules. The medulla has a striated appearance because it contains primarily straight-running parts of the nephron such as the late proximal tubule, loop of Henle, early distal tubule, and collecting duct.

Each kidney contains approximately 1 million nephrons; these are the functional and anatomical units of the kidneys. The essential features of the nephron are shown in Figure 1.2. Embryologically and functionally, the nephron is considered to begin at Bowman's capsule. Although not considered part of the nephron anatomically, the glomerular capillaries together with Bowman's capsule are referred to as the Malpighian corpuscle, which is approximately 190 to 240 μ in diameter in adult man. The nature of the glomerulus and its relationship to Bowman's capsule will be discussed in more detail below. Bowman's capsule leads into

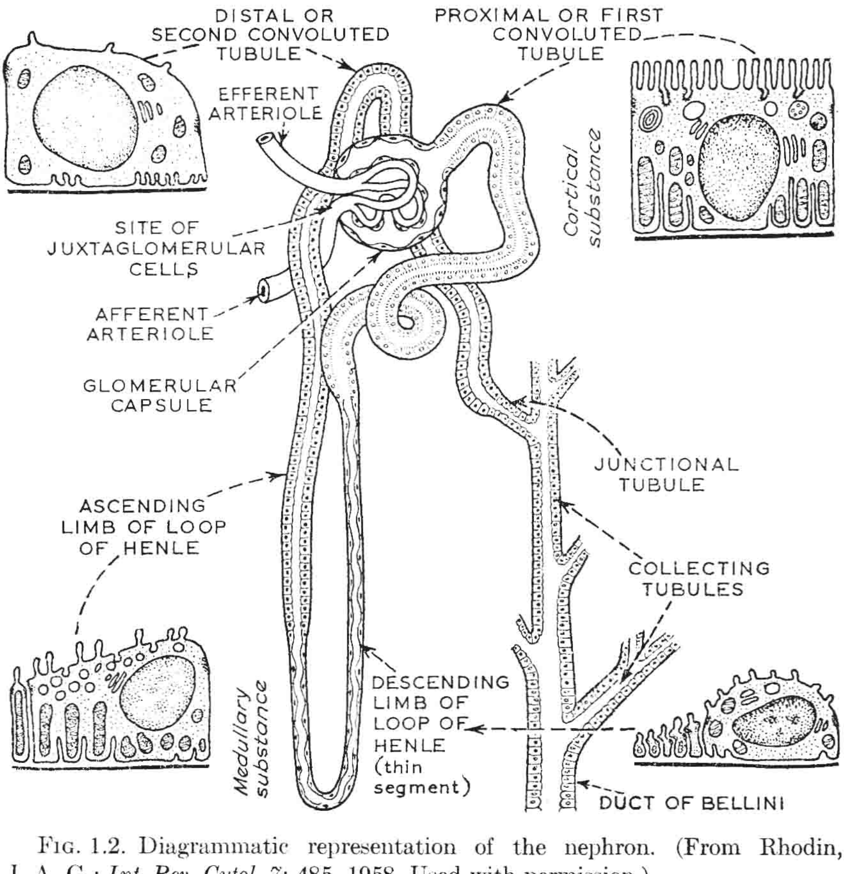

FIG. 1.2. Diagrammatic representation of the nephron. (From Rhodin, J. A. G.: *Int. Rev. Cytol. 7:* 485, 1958. Used with permission.)

the convoluted proximal tubule (pars convoluta), most of which is contained in the renal cortex. The convoluted tubule in turn becomes the thick descending portion of the loop of Henle (pars recta). Except for the specialized epithelial cells that line Bowman's capsule where it comes in contact with the glomerular capillary, the cells of the proximal tubule are best described as cuboidal.

In man the dimensions of the proximal tubule has been estimated to be 14 mm long and 57 μ wide. The epithelial cells of the proximal tubule resemble truncated pyramids which lie on the basement membrane. On cross section there is little lumen, to be seen, owing to the presence of the extensions or microvilli of the cellular luminal surface (sometimes referred to as the brush border). These microvilli presumably increase the surface area available for reabsorption and secretion. The basal surface of the cell has infoldings within which are long, large mitochondria. The functional significance of the basal infoldings is not clearly established. The microvilli of the proximal tubule cells apparently are phagocytic, because large molecules can be found within the cytoplasm after they are injected into the kidney. As the proximal tubule penetrates toward the medulla (pars recta) the number of microvilli and cell inclusions tends to decrease. Otherwise, the structure of these cells is similar to the structure of the cells found in the early part of the proximal tubule.

The pars recta forms the beginning of the loop of Henle. The thin limb of the loop of Henle contains flat squamous epithelial cells. The cells are clear and contain few inclusion bodies, suggesting that this area of the nephron contributes little to active reabsorption and secretion. The length of the thin limb is, in general, a function of the location of the nephron's glomerulus. The thin loop is short in those nephrons in which the glomeruli originate in the cortex, whereas those nephrons which originate at the cortical-medullary area have long, thin limbs that penetrate deeply into the medulla. (Fig. 1.3). Thus, depending upon the location, the dimensions of the thin limb vary in diameter from 10 to 15 μ, and in length from 0.5 to 20 mm.

In general, the distal tubule is shorter and narrower than the

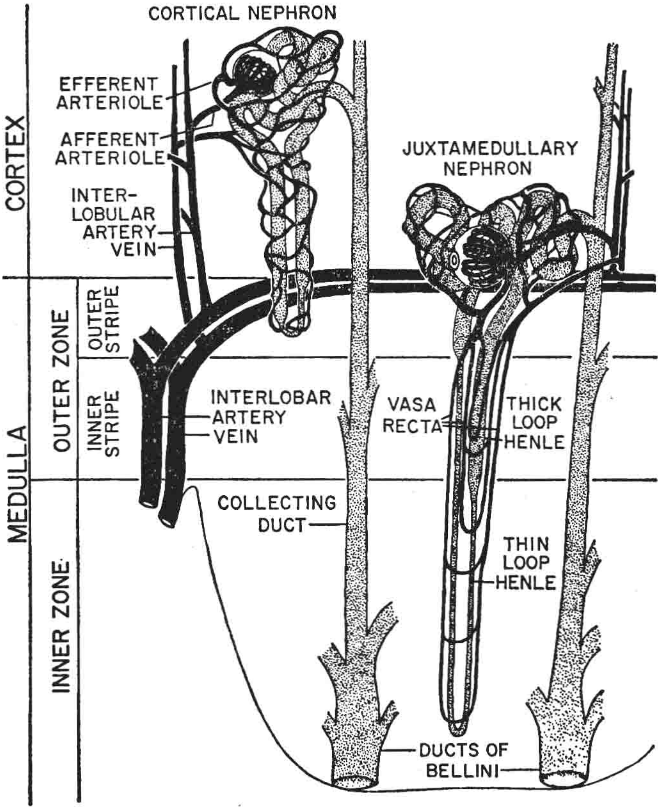

FIG. 1.3. Schematic representation of a cortical and juxtamedullary nephron with their blood supply. (From Pitts, R. F.: *Physiology of Kidney and Body Fluids*, Ed. 2. Year Book Medical Publishers, Inc., Chicago, 1968. Used with permission.)

proximal tubule. As the distal tubule courses from the outer portion of the medulla back to the cortex, it touches the afferent arteriole entering its own glomerulus. From here, the distal tubule courses through the renal parenchyma and finally empties into a collecting duct. The pars recta of the distal tubule is defined as that segment lying between the end of the thin limb of Henle's loop and the point at which the distal tubule touches the afferent arteriole. The area that touches the afferent arteriole is referred to as the macula densa. The distal tubule has cuboidal cells that are narrower than those of the proximal tubule and a lumen that is greater in diameter than that of the latter. This probably reflects the fact that the luminal surface of the distal tubule cell has very small microvilli as compared to those of the proximal tubule cell. Basal infoldings are also found in the cells of the distal tubule; however, the nuclei are smaller and appear to be rounder than those of the proximal tubule cells. Numerous mitochondria are found at the basal portion of the cell in the area of the interdigitations.

In the area of the macula densa the cells of the distal tubule become more columnar and densely packed. It is believed that the macula densa in some way can "sense" the amount or concentration of sodium in the tubular fluid. As the collecting duct courses from the cortex toward the medulla the cells are first cuboidal and then become columnar, with the number of mitochondria decreasing and the cytoplasm containing fewer inclusion bodies. The thickness of the collecting duct varies; in the cortex it is rather narrow, whereas as it penetrates down through the medulla it progressively increases in diameter. The average length of the collecting duct is approximately 20 mm.

BLOOD SUPPLY

The kidneys receive their blood supply from the renal arteries, which branch off from the abdominal aorta. In most instances the supply to each kidney is via a single artery, although the branching of the renal artery, which usually occurs at the hilus, in some instances occurs at the origin of the aorta, so that two renal arteries are not unusual. A schematic of the vascular anatomy of the kidney is shown in Figure 1.3. Upon entering the hilus (or in some instances as indicated before, outside the hilus), the first two branches of the main renal artery are referred to as the anterior and posterior vessels. From these originate five segmental arteries (referred to as the apical, upper, middle, lower, and posterior segmental arteries) that perfuse the respective parts of the kidney. From these main segmental arteries the interlobar arteries arise; they course along one or several pyramids, then divide again into the arcuate arteries. The arcuate arteries in turn course between the cortex and medulla parallel to the surface of the kidney. The interlobular artery usually originates from an arcuate artery, although it has been suggested that in some cases the interlobular artery may arise directly from an interlobar artery. In general, the interlobular artery gives rise to an afferent arteriole which in turn gives rise to the glomerular capillaries. The interlobular artery can divide into more than one afferent arteriole; it may become a cortical plexus of nutrient capillaries, the capillary network in the capsule, or a perirenal nutrient vessel. The afferent arteriole breaks up into a tuft of capillaries in Bowman's capsule and these capillaries then converge into the efferent arteriole. The efferent arteriole breaks up into a second network of capillaries called the peritubular capillary network. These vessels primarily envelop the proximal and distal convoluted tubules, although they also are in association with the thick descending and ascending loops of Henle. The peritubular capillary network then converges to form the interlobular vein, which becomes the arcuate vein, interlobar vein, segmental veins, and finally the main renal vein. In general, the course of these veins parallels that of the arteries. In the case of the nephrons which originate at the cortical medullary junction, the efferent arteriole breaks up not only into a peritubular capillary network but also into a second series of capillaries designated the vasa recta (Fig. 1.3). The latter are long loops of capillaries that penetrate deeply into the medulla in close association with the thin loops of Henle. Like other capillaries, the peritubular capillaries and vasa recta are composed of squamous epithelial cells and contain few mitochondria and inclusion bodies.

At the point where the afferent arteriole enters Bowman's capsule, and where the macula densa of the distal tubule abuts the afferent arteriole, there is a histologic change in the tunica media of the arteriole. The cells of the media become large, round, epithelioid cells which are closely packed and are called the juxtaglomerular cells. They stain clearly for granules which have renin activity. The juxtaglomerular cells and the macula densa cells of the distal tubule, together are referred to as the juxtaglomerular apparatus. Their functional significance will be discussed later.