THE KIDNEY

An Outline of Normal and Abnormal Structure and Function

By

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With 74 Illustrations

To

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PREFACE

THE purpose of this book is to present an outline of renal function and structure of the normal and diseased kidney. It is intended for students, but I hope it may also be useful to others who wish to know more about the subject.

At the beginning there is a short description of normal structure and function; and the methods used to obtain information about each are discussed. There then follows a description of the four main syndromes which occur in renal disease, i.e. the nephrotic syndrome, acute renal failure, chronic renal failure, and the acute nephritic syndrome; there is also a section on the relationship between disturbances of renal function and electrolyte disorders. The second half of the book consists principally of an account of renal diseases, including the renal manifestations of some generalised diseases. These are discussed in terms of the patterns of functional disturbance which have been described in the previous sections. Unless, therefore, the reader is already familiar with the subject it is best that he should start at the beginning or at least read the sections on the four syndromes and electrolyte disturbances before those on specific renal disorders.

For the sake of clarity, I have to confess that I have over-simplified many controversial subjects and in some instances given only one explanation where several exist. I have not attempted a comprehensive classification of renal disease, for in the present state of knowledge I doubt whether it is possible to arrive at a classification whose subdivisions are at the same time mutually exclusive and collectively exhaustive. Renal tuberculosis, hydronephrosis, calculi, renal tumours and certain other predominantly surgical conditions have been excluded.

I am indebted to the many workers and writers who have preceded me and I should like particularly to mention the following sources of information; Homer Smith's textbooks of renal physiology; A. C. Allen's histological textbook, "The Kidney"; A. M. Fishberg's "Hypertension and Nephritis"; T. Addis' "Glomerular Nephritis"; R. W. Lippman's "Urine and the Urinary Sediment"; G. W. Pickering's "High Blood Pressure"; and, finally, J. R. Robinson's lucid "Reflections on Renal Function," which anyone interested in the kidney should read at least once. As a guide to more detailed reading there is a list of references at the end of each section.

I am grateful to Drs. B. E. Miles, R. R. McSwiney, D. M. Nut-

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London

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THE STRUCTURE OF THE KIDNEY

A KIDNEY contains about 1,000,000 nephrons. Each nephron is a thin tube approximately 20–50 μ wide and 50 mm. long with one end closed and the other opening into a collecting duct. The total length of the tubules in the two kidneys is about 70 miles, or more than the distance between London and Brighton. The blind upper end of each nephron lies in the cortex, invaginated and expanded by a cluster of capillaries (the glomerulus); next to the glomerulus the tube is

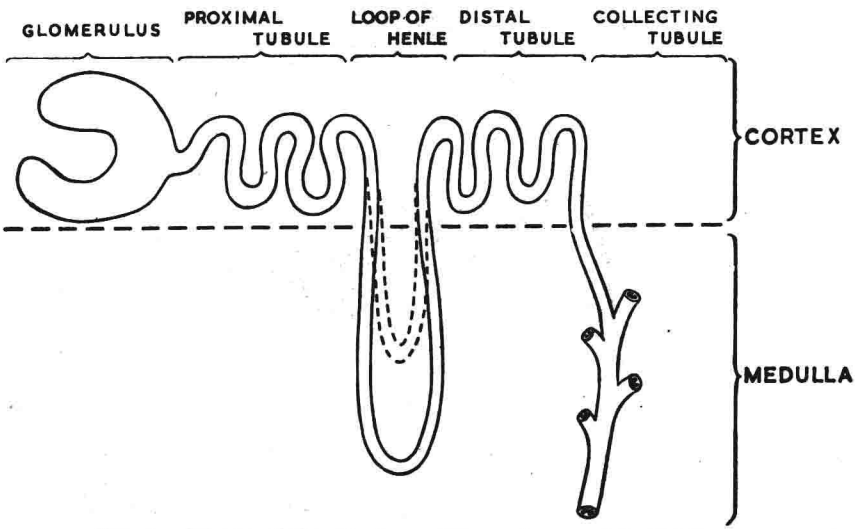

FIG. 1. Schema of the structure of the nephron and its distribution between the cortex and medulla.

coiled into a compact mass (the proximal tubule); it then plunges straight towards the hilum of the kidney, sometimes reaching into the medulla for a variable distance; it turns back in a tight hairpin bend (the loop of Henle) and once again lies in a coil (the distal tubule) next to its own glomerulus. Finally it straightens out and together with several other distal tubules joins a collecting duct, either in or near the medulla. Several collecting ducts join together and empty their contents into larger tubes called the papillary ducts which open directly on the surface of the pyramids (Fig. 1).

Most of the proximal and distal tubules lie in the cortex, while the loops of Henle and the collecting ducts form the bulk of the medulla.

Glomerular Structure

The glomerulus is composed of 4–6 capillary loops which spring from the afferent arteriole and end in the efferent arteriole ; they lie within a space whose peripheral wall is known as the glomerular capsule (or Bowman's capsule). This cluster of capillaries shares a stalk of endothelial cells ; the cytoplasm of the outer part of the stalk is hollowed out to form the lumens of the capillary loops, while the inner part contains the nuclei (Fig. 2). There does not appear to be

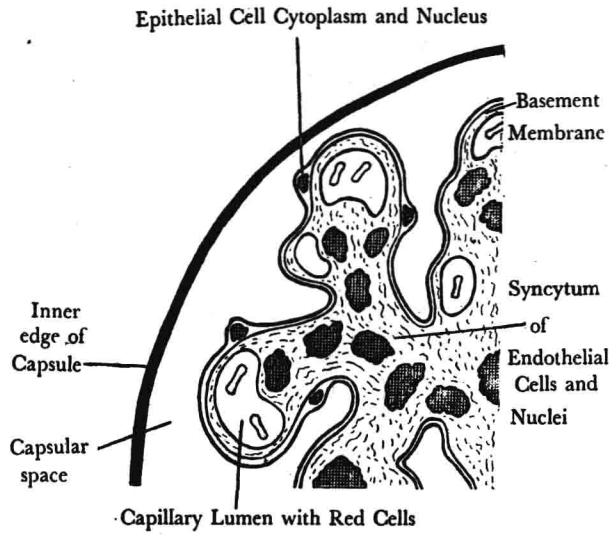

FIG. 2. Glomerulus. High magnification schema of a portion of the glomerulus to show that the lumens of the glomerular capillaries penetrate the periphery of a syncytium of endothelial cells. The inner surface of the capillary is formed from a prolongation of endothelial cell cytoplasm while the peripheral outer surface is covered by epithelial cell cytoplasm : basement membrane lies between.

any intercapillary substance, the central core of endothelial cells forming one continuous syncytium. The capillary loop is covered by a basement membrane which is continuous with that of the glomerular capsule and of the tubule ; the glomerular capillary basement membrane is itself covered by a layer of epithelial cells (Fig. 3). The latter are a continuous extension of the cells of the proximal tubule and the glomerular capsule. The surface area of the loops of the glomeruli in both kidneys is about 1·5 square metres.

Electron microscopy has demonstrated that the cytoplasm of the

epithelial cells is divided peripherally into numerous thin extensions, and that these lie in contact with the basement membrane covering the capillary loops. The surface of the loops is therefore covered by a vast number of interdigitating processes between which there are potential spaces (Fig. 3). This is an arrangement which would seem to permit a relatively large area of basement membrane to be exposed directly to the lumen of the capsular space which would not be possible if

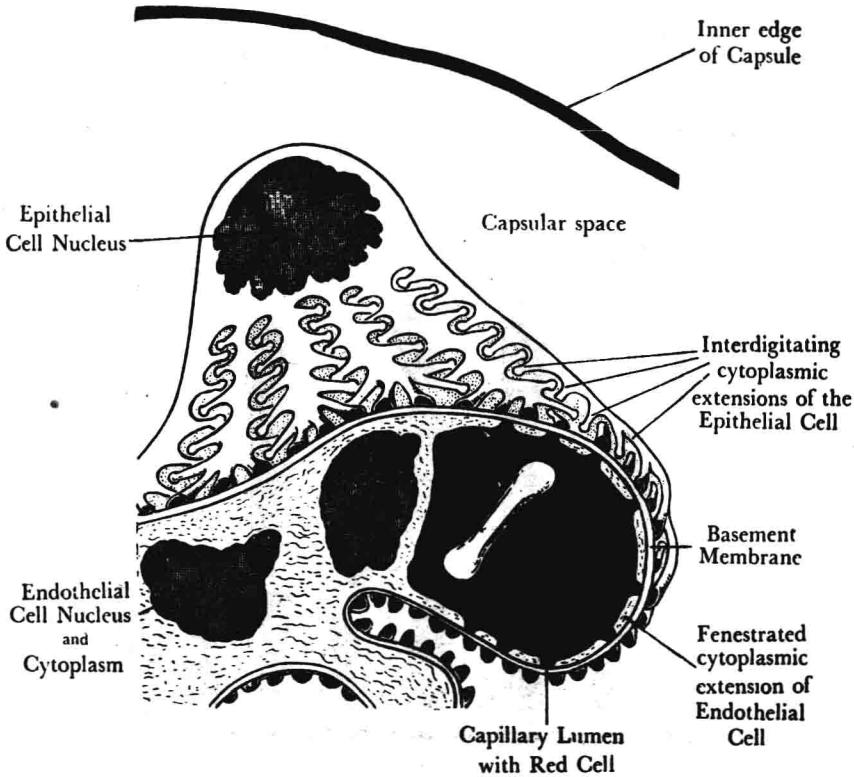

FIG. 3. Glomerulus. Schema of the electron microscopy appearances of a cross-section of a single glomerular capillary.

instead, the loops were covered by a thin, flat continuous layer of cytoplasm. Electron microscopy has also shown that the cytoplasm of the endothelial cells, where it forms the inner surface of the capillary loops, is pierced by relatively large holes about 0·1 μ wide. There is also some equivocal evidence that there are smaller apertures (100 Å) in the basement membrane. It is possible therefore that glomerular filtrate may pass directly from the lumen of the capillary into that of the capsular space without diffusion being necessary.

Structure of the Tubule

The outer surface of the whole nephron is covered by a continuous layer of basement membrane. The proximal tubule is composed of irregularly cuboidal cells with coarse granular cytoplasm and ragged inner margins (the brush border). The cells of the loops of Henle are

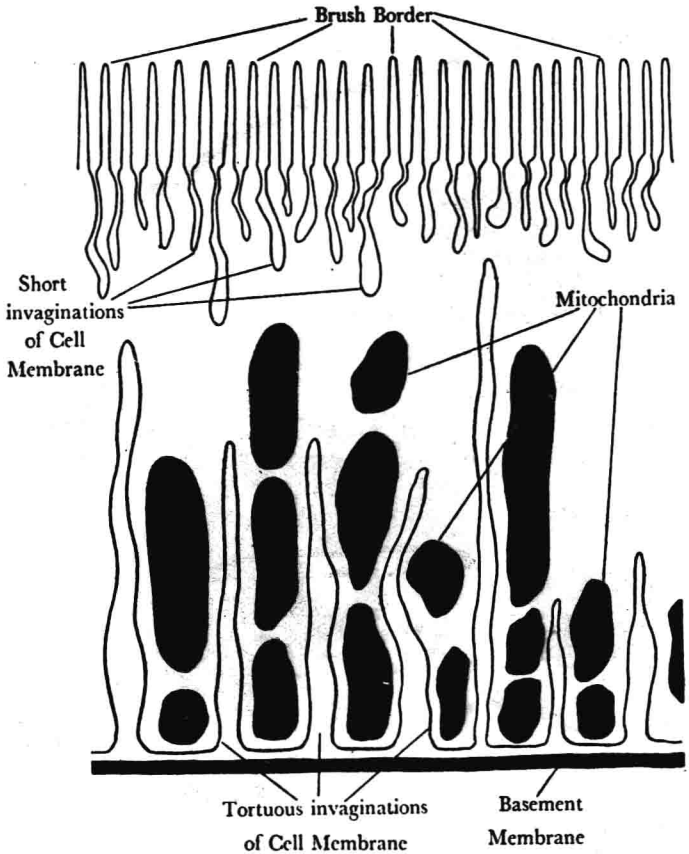

FIG. 4. Tubule. Schema of the electron microscopy appearances of a proximal tubule cell ; the nucleus has been omitted.

extremely thin and flat and have clear cytoplasm. The length of the loops varies greatly ; those that originate from glomeruli near the cortico-medullary junction are the longest and penetrate deeply into the medulla. The cells of the distal tubules are cuboidal but they are smaller than those in the proximal tubules ; they have clear cytoplasm and sharp margins.

With the electron microscope the brush border of the proximal

tubule cells is seen to consist of multiple projections of cell cytoplasm covered by surface membrane. Between these projections invaginations of the surface membrane penetrate into the cell cytoplasm and extend towards the mitochondria. These projections and invaginations increase enormously the area of contact between the tubular fluid and the contents of the cells. The membrane of the surface which lies next to the peritubular venous capillaries is also invaginated into a number of pockets which lie between the basal mitochondria (Fig. 4).

Cortico-medullary Junction

At the junction of the cortex with the medulla there is a thick, wide-meshed fibrous net to which the renal pelvis is attached and through which the medulla and pyramids project. The vessels and lymphatic channels lie outside the lumen of the pelvis and have to travel up to the cortico-medullary junction before they can enter into the renal parenchyma.

Renal Vasculature

At the cortico-medullary junction, the branches of the renal artery divide and lie in the long axis of the kidney. These branches are known as the arcuate arteries and contrary to original descriptions, they are only linked together by capillary connections (Fig. 5). The

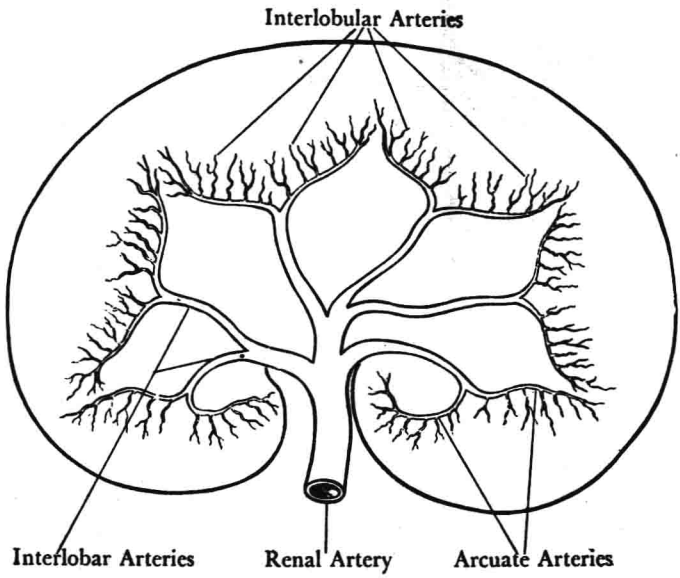

FIG. 5. Main branches of the renal arterial tree illustrating that the arcuate arteries are only connected by a capillary anastamosis.

interlobular arteries branch off at right angles to these arcades, and penetrate straight into the cortex, where they give rise to short afferent glomerular arterioles, so that even the most distal glomerulus receives its afferent arteriole direct from a relatively large artery. Beyond the glomerulus the blood flows into the efferent arteriole and then into a capacious intercommunicating plexus of capillaries situated between

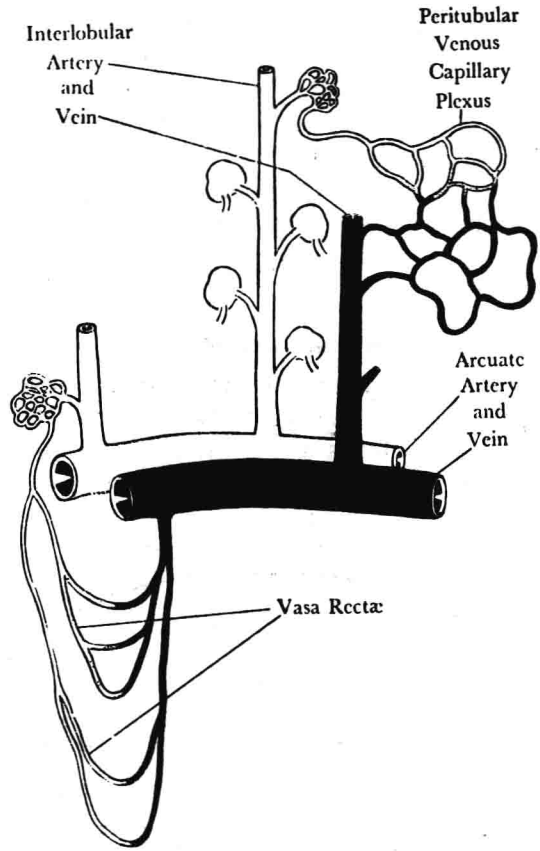

FIG. 6. Schema illustrating the renal circulation of the cortex and medulla.

the tubules (the peritubular venous capillaries) which empties into the interlobular veins (Fig. 6).

The blood supply to the medulla passes through those glomeruli which are nearest to the medulla ; these are sometimes known as juxta-medullary glomeruli. Anatomically they are distinguished by large arterioles, and it is probable that they can accommodate relatively large blood flows. Subsequently the blood travels down long, looped venous capillaries which penetrate towards the apex of the pyramids

and double back to the cortico-medullary junction to empty into the arcuate veins.

The striking differences between the blood vessels of the cortex and medulla therefore are : (*a*) that the medulla has no direct arterial supply and (*b*) that whereas the peritubular venous capillaries in the cortex form one vast network, the peritubular venous capillaries in the medulla are individual parallel channels with little or no intercommunication.

The Interstitial Space

The cortex is almost free of connective tissue and in an ordinary histological preparation the peritubular venous capillaries and the tubules are contiguous, which suggests that there is no interstitial space. It is by no means certain however that this is true in life. Electron microscopy has revealed that there are apertures about 0·05 μ wide in the cytoplasm of the endothelial cells which line the peritubular venous capillaries ; and that on the outer surface of this perforated cytoplasm there lies an extremely thin basement membrane. The porosity of this membrane is not known, but it may be considerable. Sections from kidneys which have been frozen instantaneously, after being excised from living animals, show that there exists a clear area around each tubule, between the tubule and the peritubular capillary. It is also well established that the blood that drains from a kidney which has just been excised from a living animal has a much lower hæmatocrit than the hæmatocrit of that animal's arterial or venous blood. It is probable that the extra plasma lies in the clear areas around the tubules. Usually these spaces are not visible, for the plasma they contain escapes with the blood in the capillaries via the cut renal artery and vein.

The presence of an interstitial space in the medulla is certain, for the many parallel tubes that it contains are separated by a lagging of connective tissue which is particularly thick towards the apex of the pyramids.

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2

TESTS OF RENAL STRUCTURAL INTEGRITY

THE following methods are used to obtain information about the structure of the kidney :

Clinical Examination of the Abdomen.
Straight X-ray of the Abdomen.
Intravenous Pyelography.
Retrograde Pyelography.
Renal Arteriogram.
Renal Biopsy.

Clinical Examination of the Abdomen

Obviously this is most helpful in thin patients and may give information about the presence of a tumour, hydronephrosis and polycystic kidneys ; if the kidneys are easily palpable it is usually easy to decide whether or not they are much larger than normal. To obtain the best results from this examination it is essential that the patient move his diaphragm well down with each inspiration, while relaxing the anterior abdominal muscles. Some patients seem unable to do this, but may be taught to do so by being told to place their hands palm downwards on the surface of their abdomen while they practice. Tenderness in the renal angle or over the kidney anteriorly indicates that there is inflammation which may be due either to infection, infarction or an allergic reaction.

A distended bladder is often an invaluable clue to the presence and cause of renal failure.

Straight X-ray of the Abdomen

Such an X-ray is less revealing than an intravenous pyelogram, but it has certain advantages. It can be performed at short notice and it is painless. Often the outline of the kidneys may be distinguished so that their size, shape and position can be determined, and it may also be possible to decide whether there are any shadows consistent with the presence of calculi or renal calcification.

Intravenous Pyelography (I.V.P.)

This is achieved by the intravenous administration of sodium diatrizoate (Hypaque) or sodium acetrizoate (Diaginol) at a time when the rate of flow of the urine is minimal. These two substances consist of large molecules containing three radio-opaque iodine atoms, and although they are filtered at the glomerulus the amount filtered is greatly exceeded by the amount that is actively secreted by the proximal tubule cells into the tubular fluid. If large quantities reach the kidney therefore, the tubular fluid and the urine contain high concentrations of radio-opaque material ; radiologically the kidney's parenchyma becomes faintly visible while the calyces and pelves are densely shadowed.

Intestinal gas and movements, fæces and fat may considerably obscure and confuse the results. An aperient should be taken the preceding evening and, if it has failed to act, a small enema should be given. It is best to allow the patient to be up and about for 24 hours before the examination, and a low-residue diet and no medicine containing bismuth or similar radio-opaque substances should be taken for at least two days previously. Intestinal gas can sometimes be dispelled by an injection of aqueous pitressin or neostigmine methyl-sulphate.

The density of the pelvic shadow is dependent upon the following :

(i) The anterior-posterior depth of the iodine-containing urine which the X-rays have to penetrate.

(ii) The rate of urine flow, or in other words, the volume of urine into which the iodine is excreted.

(iii) The rate at which the kidneys can secrete the iodine, which in turn depends on the secretory capacity of the tubule cells and their total number.

To increase the amount and depth of the urine in the pelves and ureters they are forcibly distended by partially obstructing the lower ureters by compression of the lower abdomen with an inflatable rubber balloon. This is best done about 5–10 minutes after the injection of the contrast solution, when its concentration in the pelves has reached a plateau. The rate of urine flow is reduced as much as possible by fluid deprivation or the administration of pitressin tannate in oil. Nothing can be done to increase the rate at which the tubules secrete contrast medium beyond making sure that this is occurring at the tubules' maximum capacity, i.e. that the amount of contrast medium presented to the kidney per minute greatly exceeds its capacity to transfer it from the blood into the tubular lumen. In many ways the technique is comparable to that used when estimating a Tm (p 58)