MEDICAL DISEASES OF THE KIDNEY

J. F. A. McMANUS

MEDICAL DISEASES OF THE KIDNEY

(An Atlas and Introduction)

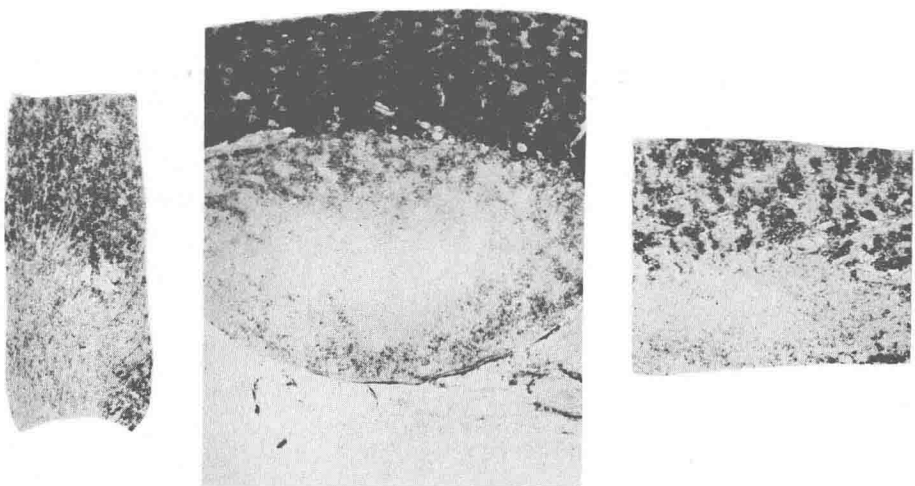
by

J. F. A. McMANUS, M. D.

Associate Professor of Pathology, The Medical College of Alabama, Birmingham, Alabama; late Beit Memorial Fellow in Medical Research, the University Museum, Oxford, England.

100 ILLUSTRATIONS

LONDON
HENRY KIMPTON
25 BLOOMSBURY WAY, W.C.1



Alkaline Phosphatase on Sections:

Center—Normal Kidney.
Left —"Crush" failure.
Right —Acute Hypertension.

MEDICAL DISEASES OF THE KIDNEY

(An Atlas and Introduction)

by

J. F. A. McMANUS, M. D.

Associate Professor of Pathology, The Medical College of Alabama, Birmingham, Alabama; late Beit Memorial Fellow in Medical Research, the University Museum, Oxford, England.

100 ILLUSTRATIONS

LONDON
HENRY KIMPTON
25 BLOOMSBURY WAY, W.C.1

PRINTED IN AMERICA

For
Norma

FOREWORD

IT was in 1914 that Volhard and Fahr published their book on Bright's disease, which was at once a monograph and an atlas. After thirty-five years Dr. McManus has given us another atlas and monograph. The author is a pathologist with a clinical outlook and a keen appreciation of physiologic and chemical problems. His outlook is essentially original, and he has studied his microscopic sections not only with the seeing eye but with the understanding mind. An admirable balance is maintained throughout between structure, function, and the manifestations of disease. Even a cursory perusal of the text will show how up-to-date is the treatment of the entire subject. The description of the normal histology could not be bettered, and it is refreshing to find a morphologist so deeply versed in the chemistry of the cell.

An element of novelty is imparted to the work by the extensive use of recent technical methods, more particularly the periodic acid—Schiff's reagent stain for bringing out intimate glomerular structure and Gomori's method for demonstrating alkaline phosphatase in the renal tubules. Thus figure 87 (hematoxylin and oesin) and figure 88 (periodic acid stain) form a dramatic contrast, and demonstrate in a striking manner the value of the latter method for emphasizing basement membranes.

However familiar the reader may be with renal structure in health and disease, it is safe to say that he will learn new facts and be stimulated to think along new lines by the perusal of these pages and examination of these pictures. How many of us, for example, are familiar with the variations of the position of the Golgi apparatus in the cells of the macula densa under conditions of disease?

These 100 pictures, which are a delight to the eye, and recall the work of that master of pathologic histology, the late F. B. Mallory, tell the whole story of the medical diseases of the kidney.

The work appears to be designed for the clinician as much as for the pathologist, because the author is not satisfied with demonstrating mere alterations in structure but seeks always to uncover the underlying physiologic and clinical significance of these changes. The division of the text into acute renal failure and chronic renal failure is particularly stimulating.

Actually a good book needs no Foreword, and this is true in the present instance.

WILLIAM BOYD

PREFACE

"Do not stop to question whether these ideas are new or old but ask, more properly, whether they harmonize with Nature. And be assured of one thing, that I never reached my ideas of the structure of the kidney by the aid of books but by the long, patient and varied use of the microscope." MARCELLO MALPIGHI—"DE VISCERUM STRUCTURA" (1666)

THIS is a pictorial introduction to the study of the diseased kidney. I have tried to orient the pathologist to the patient and the clinician to the pathology by an alternating discussion of clinical and pathologic details. Acute renal failure and chronic renal failure are the two main groupings under which kidney diseases are discussed here. These two headings comprise the majority of cases which clinician and pathologist alike encounter.

Most of the photomicrographs are taken from sections prepared by the periodic acid-Schiff's reagent technique. This method demonstrates the renal basement membrane and other carbohydrates in section. Its use has permitted the recognition, separation, and illustration of the process of glomerular injury in arteriosclerosis, in pyelonephritis, and in glomerulonephritis. Tubular atrophy in these three main disease processes is nonspecific but the glomerular changes allow the evaluation of the degree to which each is operating in the diseased kidney studied histologically.

The approximation of functional ability in sections of the kidney is possible by the use of Gomori's method for alkaline phosphatase. The interpretation of a number of kidney diseases in the light of Trueta's studies on the renal circulation allow a reappraisal of the overall picture in shock and in the "crush" lesion. Including the description of "pattern" glomerular obsolescence there is much that is new in this treatise.

The limited bibliography is explained in part by the newness of the data and concepts. Also I have restricted intentionally the references to key articles or first descriptions. I should like to mention my dependence upon the standard textbooks of Pathology and the monographs of Bell, Fishberg, Oliver, Addis and Christian for isolated data.

Grateful acknowledgement is made to: Dr. James Miller, now Emeritus Professor of Pathology, Queen's University Faculty of Medicine, Kingston, Canada, who started my interest in the kidney; to the late W. G. MacCallum and Sam S. Blackman, Jr., who continued it; to Drs. William Boyd, John Fisher, J. A. Cunningham, Louis C. Posey, J. D. Bush, A. E. Casey, Paul Kimmelstiel and others for interesting slides and tissues; to John Ledbetter and Edith Gay Jones for the photomicrographs, a few being made by Jon Franzke; to Sara Howell and her staff of technicians for the sections; to Dr. Roger Baker, Professor of Pathology, and my other colleagues of the Medical College of Alabama who have been unsparing with

their help and information; to Drs. G. L. Rutledge, Jr., and R. W. Mowry who have collaborated in the sections on the Crush Kidney and the Phosphatase studies respectively. J. C. Saunders was associated in the studies of the chemical constitution of the renal basement membrane. Miss Charleane Everett did most of the typing. Miss Mildred Crowe and her library staff at the Medical College of Alabama have been most helpful. A few illustrations have been reproduced by the courtesy of the editors of the American Journal of Pathology, the Lancet, the Quarterly Journal of Microscopical Science, and the Bulletin of the International Association of Medical Museums. Credit is given in the legend in each case.

A portion of the studies was done on a Beit Memorial Fellowship in Medical Research in the Department of Zoology and Comparative Anatomy, the University Museum, Oxford. At the Medical College of Alabama funds from the Life Insurance Medical Research Fund were used in a study of the histochemistry of arteriosclerosis, some results of which are included

J. F. A. McMANUS

BIRMINGHAM, ALABAMA

CONTENTS

Part I. Gross and Microscopic Anatomy in Health

Chapter 1

INTRODUCTION; PHYSIOLOGY; NEPHRON IN GENERAL

THE normal human kidney can be best understood as a collection of a number of similar units, each unit being called a nephron. Supporting these nephrons there is a minimum amount of connective tissue. The one arterial supply and venous drainage nourishes the interstitial connective tissue as well as determining the production of the specific fluid elaborated by the nephron—the urine.

The nephron has a constant number of continuous portions. It begins at the glomerulus, a capillary tuft invaginated into the closed end of an epithelial tube. The nephron ends in a large duct system connecting with the pelvis of the kidney. Between the capillary loops of the glomerulus and the collecting tubule—the beginning of the duct system—the epithelial tubule undergoes a number of contortions. One may recognize in order a proximal convoluted portion, a descending loop extending down toward the pelvis, an ascending loop returning to the glomerulus of origin about which the distal convoluted tubule is seen to twine, before ending in the collecting tubule which receives a number of these distal tubules.

The capillary tuft of the glomerulus delivers a filtrate of blood plasma into the epithelial tube at the beginning of the first or proximal convoluted tubule. A selective process of reabsorption of certain materials and the addition of other substances occurs in the passage of the glomerular filtrate down the tubule to the collecting duct. The duct conveys the final product—urine—to the exterior as represented by the renal pelvis.

In terms of function as well as structure, the nephrons appear to be a homogeneous unit group. We have no evidence that the different nephrons do different tasks, but it appears that the parts of the individual nephrons possess separate functions.

The efficiency and quantity of the urine production depend in final analysis upon the integrity of the individual nephrons. The acid-base balance of the blood, the calcium and phosphorous content of blood and tissue, the sugar content of the blood, the water content of the body and the excretion of many products of metabolism are functions of the kidney and eventually of the individual nephrons. In most of these regulations and controls the kidney represents a single link in a complicated body mechanism, but in each the rôle of the kidney is an important one. Disease of the kidneys may be reflected in disturbances of these balances.

Besides these chemical relationships with the blood, the tissues and the cells of the body, the kidney may have an important part in the control of vascular tonus and in regulating blood pressure. Changes in the blood pressure more commonly follow diseases of the kidney than of any other organ. In many cases of disturbed blood pressure, characteristic changes can be found in the kidney.

QUANTITATIVE FEATURES OF THE KIDNEYS

Each kidney normally contains between 1 and 1½ million nephrons. The glomeruli have a total filtering surface of over twice the body surface area. The length of the individual capillaries in a glomerulus totals about 25 mm. or 1 inch, so that the total of all the loops in both kidneys is about 60 kilometers or 37 miles plus.

The kidney at birth has a volume of 6.5 cc. There is a gradual increase to the adult volume of 120 cc. at about the age of sixteen. The diameter of the glomerulus is about 85 mu at birth while the adult glomerulus has a diameter up to 200 mu, usually 180 to 190 mu.

Some interesting figures (Policard) result from the calculation of total glomerular surface as a function of the body weights, glomerular surface in cm_2 per gram of body weight. There is a species difference in the length

Mouse	0.458	Pig	0.089
Rabbit	0.144	Human	0.070
Cow	0.06		

of the various segments of the nephrons. The loop of Henle is short or lacking in reptiles and in some avians in which a semi-solid urine is produced. Comparative physiology has not progressed to the point where differences of function can be correlated with differences in structure. It may be that the lack of spontaneous glomerulonephritis in animals and the failure of its experimental production may be related to structural differences.

THE NORMAL PRODUCTION OF URINE

In twenty-four hours about 200 liters of fluid are filtered into the tubules by the glomeruli. Nearly 99 per cent of this must be reabsorbed since the daily urine volume is something between 1 and 3 liters. The main features of tubular activity are shown in figure 1.

It appears fairly definite in the frog, and probable in the human, that 65 per cent of the fluid is reabsorbed in the proximal convoluted tubule, along with all the sugar, some of the sodium, the phosphate and part of the chloride. The loop of Henle has no certain function; its variation in length within the kidney from nephron to nephron suggest no constant activity. In the distal tubule, the remainder of the water is reabsorbed with the rest of the chloride. At this level of the tubule the reaction of the urine becomes acid. It is now hypotonic, suggesting some addition of water.

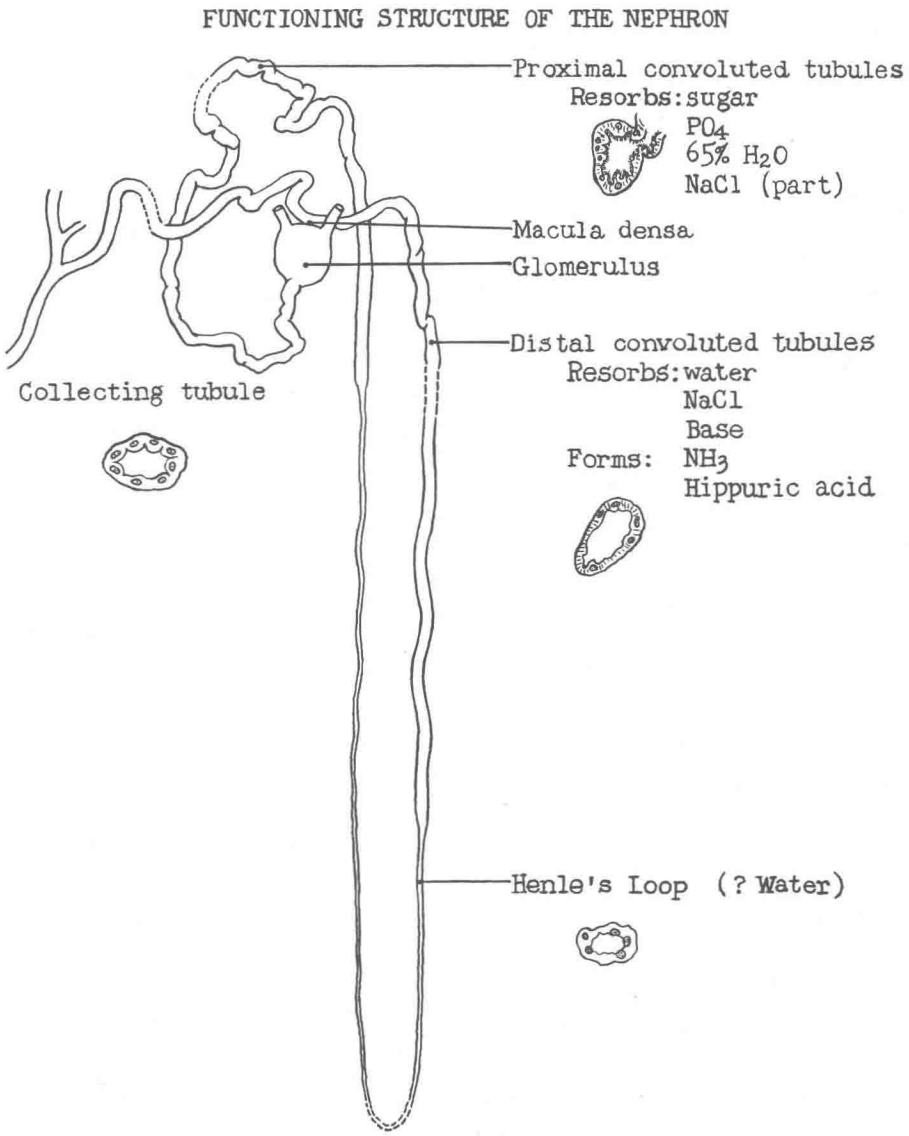


Figure 1

Diagram of Nephron.

This diagram shows the continuous portions of the nephron. The suspected functions of the portions or levels of the tubule are indicated.

Some of the factors controlling reabsorption are tabulated in the following:

Material Reabsorbed	*Site Reabsorbed*	*Controlling Factor*
Sodium	Proximal Tubule	Posterior Pituitary Inhibits
Sodium	Distal Tubule	Posterior Pituitary Increases
Sodium	Proximal & Distal Tubule	Adrenal Cortex Inhibits
*Water	Proximal & Distal Tubule	Posterior Pituitary
Phosphate	Proximal Tubule	Parathormone Increases

The acid-base balance has one of its important regulating mechanisms in the excretion of urine. The fixed base of the body—sodium, potassium, magnesium, and calcium—is preserved by rearranging the balance between NaH_2PO_4 and Na_2HPO_4. The filtrate of blood plasma formed by the glomerulus has a pH of 7.4. The urine has normally a pH from 5 to 7 with a mean of 6.0. The excretion of an acid urine conserves the base for re-use by the body.

The proportion of acid phosphate to basic phosphate in the original filtrate in about 1 to 4, in the final urine the proportion is normally 9 to 1 and may reach as high as 50 to 1 in a very acid urine. The decrease in basic phosphate is probably produced by reaction with bicarbonate in the following fashion:

$$Na_2HPO_4 + H_2CO_3 \longrightarrow NaH_2PO_4 + NaHCO_3$$

Reabsorbed by tubular epithelum.

The reabsorption of the sodium bicarbonate conserves base, as does the excretion of organic acids such as uric acid as free acids while they exist in the blood in combined forms. The formation of ammonia ion by the kidney epithelium and its addition to the urine serves as another method by which the base is conserved.

Ammonia formation largely derives from glutamine rather than from urea. The problem of disposal of endogenous ammonia is a complicated one.† In the kidney ammonia is formed from glutamine by the enzyme glutaminase. Some of the ammonia may be formed as well from amino acids and from adenosine phosphate. Ammonia formation and excretion by the kidney is a defense against acidosis since the acid urine appears to be one stimulus for NH_3 formation.

Certain features of urine volume must be remembered for the later appreciation of the changes of disease. The normal twenty-four hours of output of urine ranges from 1000 to 3000 cc. with the day to night proportion ranging from 2 to 1 as high as 4 to 1. The increase of night urine production is called nocturia. Polyuria is the term used to describe any increase in urine production. Oliguria denotes decrease in urine volume, while anuria describes complete cessation of urine production.

* The reabsorption of water in the distal tubule is variable or "facultative," according to posterior pituitary control (Smith).

† cf discussion in Peters.[88]

The specific gravity of the urine usually ranges in health as high as 1.015 or 1.025 and as low as 1.001 after fluid ingestion of high quantity. The production of urine of specific gravity equivalent to blood plasma—1.010—is called isosthenuria.* The meanings of hypersthenuria as in diabetes, and hyposthenuria in some renal disease, will be understood easily.

THE NEPHRON IN GENERAL

The Glomerulus.—The glomerulus of the kidney was first seen by Malpighi[68] some time before 1666. Malpighi was able to inject the glomeruli either from the arterial or the venous side and he described them as resembling apples hung on the vascular tree. He believed he had found the "glands" which secreted the urine but he was unable to see the connections between the glomeruli and tubules to the exterior. Bowman[11] in 1842 rediscovered and redescribed the glomeruli as round masses of minute vessels invested by a cyst or capsule. "The capsule is seen to pass into the basement membrane of the tube as the body of a Florence flask into its neck." Bowman suggested part of the modern theory of function when he says, "It is difficult to conceive the disposition of parts more calculated to favor the escape of water from the blood than that of the Malpighian body."

It has already been mentioned that somewhere between 1 and $1\frac{1}{2}$ million glomeruli are found in each kidney. The number is constant from birth. Each glomerulus has an oval shape and a diameter close to 200 micra. The peripheral glomeruli of the cortex are probably larger than the more centrally situated (Peters). Each glomerulus is seen in relation to one afferent arteriole but double (bifid) glomeruli are not too rare in the human.

The glomerulus is a tuft of capillaries invaginating the blind end of the tubular portion of the nephron. It is, in a real sense, a capillary bed between the afferent arteriole and the efferent arteriole, compactly contorted and covered by basement membrane. The capillary tuft of the glomerulus is unique in lacking anastomoses between the capillaries, as Vimtrup[105] has shown by injection experiments. It would be easy to comprehend the structure of the glomerulus in sections if it were not for the contortions which the capillaries pursue in the elaboration of maximum filtration surface for each capillary. The difference produced by contortion can be expressed as AwwwB instead of A——B.

The arteriole which gives origin to the capillaries of the glomerulus is called the afferent to distinguish it from the efferent arteriole which drains the capillaries. The afferent arteriole connects with a dilated space within the glomerulus, the atrium or infundibulum, from which the capillaries originate. The capillaries course in the glomerulus to terminate directly in the efferent arteriole.

The glomerular tuft of capillaries can be seen in the newborn and fetal kidney, and in some lower animals, to be completely covered by cuboidal

* Isosthenuria also is used to mean fixed specific gravity.