The Treatment of Renal Failure

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Therapeutic Principles in the Management of Acute and Chronic Uremia

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The Treatment of Renal Failure

This Book is Dedicated
to the Memory of

DR. JOHN T. HODGEN
(1884–1954)

PREFACE

THIS MONOGRAPH is intended to serve as a guide to the treatment of renal insufficiency and renal failure. By renal *insufficiency* is meant the inability of the renal mechanisms to respond in normal fashion to abnormal demands and to functional tests. Renal *failure* is implied when these mechanisms are inadequate for the ordinary excretory and metabolic needs. The concept of therapy of renal insufficiency also deserves elaboration. This concept embodies a knowledge of "what to do" and, equally important, "what not to do," or perhaps "when to do nothing." The attitude of the student of renal disease toward therapy is well summarized by the following: "In 1836 Richard Bright wrote, 'It is indeed an humiliating confession that although much attention has been directed to this disease for nearly ten years, . . . yet little or nothing has been done toward devising a method for permanent relief when the disease has been confirmed; and no fixed plan has been laid down, as affording a tolerable certainty of cure in the more recent cases.' A hundred years later we must amplify this apology of Bright with the equally humiliating confession that we today cannot cure the disease." [174]

While this evaluation is true of the therapy of chronic glomerular nephritis and other forms of renal disease where the disease process is characterized by fibrosis, scarring and permanent destruction of nephrons, it is not true of all renal disease. Acute pyelonephritis, obstructive uropathy, and some forms of renal calcinosis as well as the nephrotic syndrome, may be reversible, at least temporarily, with specific therapy. Furthermore, even when the parenchymatous change is irreversible, the *structural* damage to the kidney in itself seldom causes difficulty. The signs and symptoms of renal failure result rather from lack of functioning nephrons or inadequate function in parts thereof, no matter how this deficiency has been brought about. The consequent chemical and metabolic abnormalities resulting therefrom are susceptible to "cure" only by restitution of adequate functioning renal tissue, and this we can only infrequently accomplish.

Diabetes mellitus, however, cannot be "cured" either, but an understanding of the abnormalities resulting from the absence of islet tissue and the institution of adequate replacement and dietary therapy do much for the clinical syndrome caused by the deficiency. While we have no replacement therapy in renal disease as specific as insulin, nevertheless the analogy is a valid one in many other respects.

An understanding of the abnormalities resulting from renal failure requires some familiarity with renal physiology and with the etiology and pathophysiology of renal disease. In the chapters that follow these aspects will be dealt with in outline so that they may serve as a framework on which to build the rationale for therapy. If in these presentations hypotheses are presented as facts, it is not with the intent of misleading the reader but because the establishment of such hypotheses gives a better understanding of therapeutic principles which the author believes *are* firmly based in fact. In such a discussion of therapy, it is the author's conviction that it is valuable to do more than recommend forms of treatment which he believes are beneficial. Equally important is a critical evaluation of therapeutic measures which many physicians have conscientiously recommended and which the author does *not* believe to be of value. The reader may thus obtain a specific opinion on a subject in which he may be interested, rather than a condemnation inferred by omission.

Since, in large part, the picture in renal failure is determined not by the nature of the lesion but by the disturbance in the chemical pattern of body fluids which results from this lesion, an understanding of renal failure requires some familiarity with first principles of biochemistry. However, while the biochemist can frequently explain to us the origin of the chemical changes, he cannot explain the frequent lack of correlation between them and the clinical signs and symptoms. Nor can he explain why the correction of chemical abnormalities may fail to improve the clinical situation. He can, however, point out that what may be abnormal for the patient with good kidney function may not necessarily represent a defect requiring correction in the chronic compensated uremic patient. It is for this reason that the interpretation of the results of treatment depends on the clinical results to a greater degree than upon the chemical changes, and upon the opinion of the clinician rather than the interpretation of the laboratory data alone.

There is no rule of thumb, no formula for the treatment of renal failure. In the final analysis its successful accomplishment depends more frequently upon experience and the clinical trial than upon the slide rule.

J. P. M.

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J. P. M.

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CHAPTER I

Normal Renal Function

Anatomy of the Nephron

The functional unit of the kidney is the nephron, of which each normal human adult kidney contains about one million. The nephron itself consists of two anatomically and functionally distinct entities, the glomerulus and the tubule. We may trace the structure of the glomerulus by beginning with the renal artery as it enters the hilus of the kidney. It then divides into interlobar vessels from which transverse arcuate branches are given off. From these in turn spring vessels running in the axis from hilus to cortex between the renal lobules (Fig. 1). These latter vessels are the interlobular vessels and from them arise the small arterial twigs (afferent arterioles) supplying the individual glomeruli. The glomerulus itself is a roughly spheric network of capillaries invaginated into the closed end of the renal tubule in such a way that the epithelium of the tubule buckles inward into its own lumen, thus enclosing the glomerular tuft in a spheric double-walled capsule (Bowman's capsule). The capsular layer in contact with the glomerular capillary is the *visceral layer*; the outer portion of tubular epithelium is the *parietal* layer. A space exists between the visceral and parietal layer (the capsular space), into which passes filtrate from the glomerulus, to begin its journey down the lumen of the renal tubule. Recent evidence[139a] suggests that between the basement membrane of the capillary endothelial cell and that of the basement membrane of the epithelial cell (visceral layer) is interposed a potential connective tissue space, the pericapillary space. This pericapillary space may not be evident in the normal because of the close apposition of the two basement membranes. However, with proliferation of the connective tissue therein, it may be very much in evidence. Thus, water and solutes gaining entry from the capillary lumen to the tubular lumen must traverse, (1) capillary endothelium, (2) capillary basement membrane, (3) pericapillary space, (4) epithelial basement membrane, and (5) capsular epithelium. The basement membrane of the glomerulus is particularly significant in that patho-

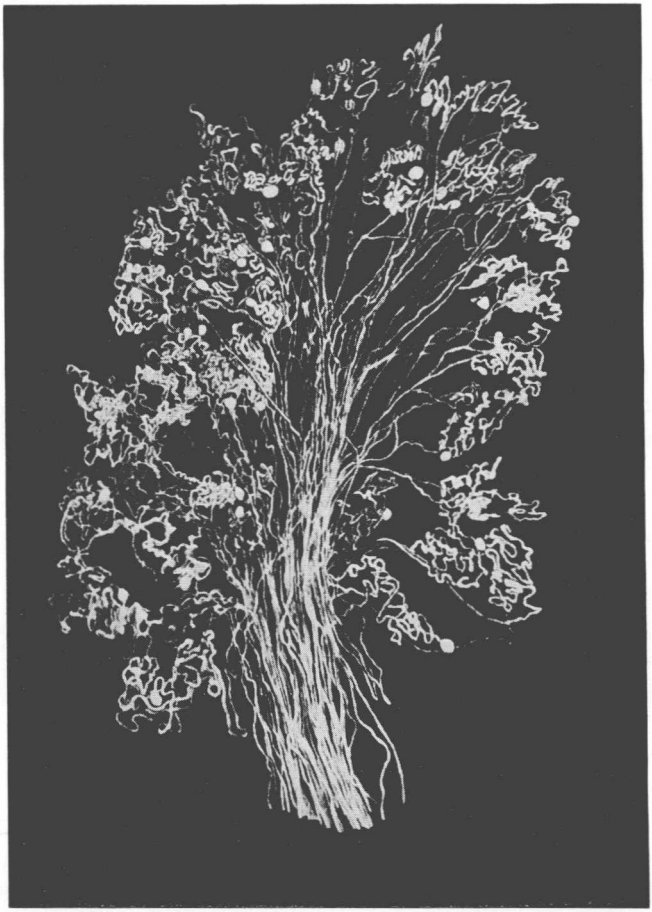

FIG. 1.—Arrangement of nephrons in the lobule of a normal human kidney.[222] The nephrons have been teased free by microdissection from macerated renal tissues. The glomeruli are seen as the spheric objects in the periphery of the lobule surrounded by the convolutions of the tubules. The descending, thin, and ascending limbs are clustered centrally in the "stalk." (Oliver, J.: When is the kidney not a kidney? J. Urol. 63: 373, 1950.)

logic changes in it appear to be the fundamental lesion in certain renal diseases characterized by inflammatory change in the glomerulus. Connective tissue proliferation both in the pericapillary space and in the intercapillary space may cause the scarred fibrotic glo-

meruli seen in chronic diseases. Blood entering the glomerulus by way of the afferent arteriole passes through the glomerular capillaries, during which time the process of glomerular filtration occurs. Blood leaves the glomerulus by way of the efferent arteriole formed by the junction of the glomerular capillaries. The efferent arteriole then divides into a second capillary network supplying the convoluted tubules. This capillary network drains into a venous system analogous to the renal arteriolar system. As the afferent arteriole enters the glomerulus, there may be seen cells resembling smooth muscle cells, whose importance may lie in the fact that, by affecting vascular tone and the width of the lumen at this point, they may play a role in the regulation of renal circulation and the filtering mechanism.

The foregoing description pertains to the vascular system supplying the majority of glomeruli in the outer portion of the renal cortex. However, in the inner portion of the cortex, at the beginning of the medullary portion of the kidney, the efferent vessel of these "juxtamedullary glomeruli" is seen as a single large vessel proceeding into the medulla where it divides into large, straight parallel vessels (vasa recta) which continue through the medulla toward the renal papilla, then loop back toward the cortex to drain into an arcuate or interlobar vein. Unlike the postglomerular capillaries of the cortex, they do not invest the tubules in a fine network of branching capillaries. The significance of these vessels is stressed by some observers who believe that they offer a pathway for blood to pass from the arterial to the venous system, thus by-passing and rendering ischemic the nephrons in the cortex.

The renal tubule, shortly after its beginning at Bowman's capsule, undergoes a series of marked convolutions near the glomerulus and then, decreasing somewhat in caliber, descends into the medullary portion of the kidney in a relatively straight course. It then makes a sharp turn and returns, somewhat increased in caliber, and again in a straight line toward its own glomerulus, near which occurs another series of contortions (distal convoluted tubules). Shortly it terminates, along with a number of other tubules, in a large collecting duct which eventually drains into the renal calyces. The "hairpin" portion has been referred to as the loop of Henle. However, as pointed out by Smith,[266] this anatomic entity serves several different functions, so that a more proper division of the renal tubule would be into (1)