Clinical Nephrology

Library of Congress catalog card No. 70-152433

ISBN 0-316-69046

4491-22J1-M09/71

First Edition

Published in Great Britain by J. & A. Churchill, London

Printed in the United States of America

NOTICE

The indications and dosages of all drugs in this book have been recommended in the medical literature and conform to practices at the University of Miami School of Medicine. The medications described do not necessarily have specific approval by the Food and Drug Administration for use in the diseases and dosages for which they are recommended. The package insert for each drug should be consulted for use and dosage as approved by the FDA. Because standards for usage change, it is advisable to keep abreast of revised recommendations, particularly those concerning new drugs.

Preface

One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.

FRANCIS WELD PEABODY

CLINICAL NEPHROLOGY has been written with the nonnephrologist in mind. I hope the book will also help serve some of the needs of the subspecialty trainee. As the title implies, the emphasis is clinical. An effort has been made to indicate controversy when it exists, but my own perspective is given and labeled for what it is; in this way, its inherent limitations should be apparent. The decision was made to select a relatively short list of suggested readings for each chapter. More detailed expositions of each subject, as well as reference materials, are available in several books, including, most recently, *Diseases of the Kidney* (2d ed.), edited by Strauss and Welt, published by Little, Brown, Boston, 1971. The last part of the book is a Handbook describing in detail methods for accomplishing many of the tests, procedures, and treatments mentioned in the text.

One of the pitfalls for author and reader in a subspecialty book is that the necessary emphasis may place an organ system

in sharper focus than the patient. It is, of course, the individual person who must be treated, with a thorough consideration of the spiritual, emotional, physical, and social phenomena which are man.

This book is personal in many ways and carries with it a permanent sense of deep appreciation to many people. To my wife and children, to whom this book is dedicated, for being who they are, and for the gift of love. To my parents and my brother, Dr. E. M. Papper, who have helped for almost a half century. To those teachers along the way who had the skill and who cared. To Dr. Maurice B. Strauss for his friendship, counsel, skill, wisdom, and knowledge, as well as for the educational opportunities he provided. To Dr. Jack D. Rosenbaum, who was the humane scholar and whose memory (and, I hope, influence) is always with me. To Dr. William B. Castle, who teaches by extraordinary example and whose insights and guidance have been generously shared and given through the years. To Dr. William J. Harrington, who gave when I had great need. And to all my students, house staff, and fellows, who allowed me the great privileges of teaching and learning together.

In the preparation of this text, I imposed on the friendship of experts to review and criticize each chapter. Their skill, interest, and willingness to help are greatly appreciated: Drs. Robert L. Barenberg, William B. Blythe, Neal S. Bricker, Murray Epstein, Carl Goldsmith, Charles R. Kleeman, John F. Maher, Barry J. Materson, Roger F. Palmer, Eliseo C. Perez-Stable, Victor A. Politano, Eric Reiss, John R. Richardson, Jr., Robert Schwartz, William N. Spellacy, Carlos A. Vaamonde, Liliana S. Vaamonde, and Robert Whang.

Since the book was written primarily for the nonnephrologist, I asked for review and guidance from: senior medical students (now physicians), Drs. Richard S. Kaplan, Homer L. Kirkpatrick, David H. Ornstein; residents in medicine, Drs. Jorge I. Presser, Douglas J. Stewart; and practicing physi-

cians who are not nephrologists, Drs. Chester Cassel, Thomas B. Gibbons, and Martin E. Liebling. Their advice and generosity of spirit are gratefully acknowledged.

Dr. Victoriano Pardo, my respected colleague in the Department of Pathology in Miami, gave unstintingly of his skill and efforts in the selection, description, and presentation of the material related to structure. The radiographs and radiographic guidance were thoughtfully provided by my distinguished friend Dr. Manuel Viamonte, Jr., Chairman of the Department of Radiology, University of Miami School of Medicine. The artwork was done by Mr. Marcelino Obaya, whose patience is appreciated.

My deep gratitude goes to two fine ladies: Miss M. Margaret Allshouse, CPS, whose devotion to and love of this book were expressed in enormous amounts of time, thought, and ability in editorial work and secretarial efforts; and Mrs. Margaret Wickline, whose sense of commitment, loyalty, and efficient operation of my office made it possible for me to arrive home nights and weekends in the mood to enjoy writing *Clinical Nephrology*.

Contents

I. GENERAL CONSIDERATIONS

1. Evaluation of the Patient

[The physician] will use scientific methods, he will for a time dismember his patient—isolate, for instance, his kidneys or his heart and observe their actions under very specialized conditions—but in the end he has to put these parts together in his "diagnosis." This "diagnosis" is his total conception of the relationships between the patient as a person, the disease as a part of the patient, and the patient as a part of the world in which he lives.

THOMAS ADDIS

PATIENTS with renal abnormalities present in a number of ways: they may have symptoms directly referable to the urinary tract, or urinalysis or a test for blood urea nitrogen concentration performed for other reasons may show abnormal findings. Other patients have nonrenal manifestations of some generalized illness which may involve the kidney (e.g., diabetes mellitus, tuberculosis, and systemic lupus erythematosus). Without prior knowledge of renal disease, patients may have symptoms and signs of renal failure (e.g., hypertension, anemia, Kussmaul breathing, and "uremic" symptoms). Edema may be the reason patients with the nephrotic syndrome originally seek medical advice.

Whatever the means of presentation, the physician is concerned with the following questions: (1) Does the patient have renal disease? (2) What is the nature of the renal lesion; is it reversible or treatable, or both? (3) What is the status of renal function? (4) What is the outlook for the patient?

Let us consider a general approach to finding the answers to these questions. This section deals mostly with highlights, more specific details being given in subsequent chapters.

As in virtually all aspects of clinical medicine, the search —that is, the problem-solving technique—begins with the history and physical examination.

Medical History

Obviously, symptoms directly referable to the urinary tract may provide clues to the nature and duration of illness. The implications of difficulty with urination, abnormal-appearing urine, frequency of urination, nocturia, or pain in the costovertebral angle, flank, or groin are well known. A detailed family history may be helpful, e.g., of hypertension, diabetes, gout, lupus, polycystic disease, hereditary nephritis (and/or the nerve deafness and visual symptoms that may occur in relatives of a patient with hereditary nephritis). A history of nephrotoxic agents, including antibiotics and combination analgesics, should be sought. Sometimes the patient has mild symptoms of systemic illness that afflict the kidney, e.g., gout and lupus. Concern with past pregnancies and possible urinary tract difficulties or instrumentation may provide clues.

In addition to these and other aspects, very commonly valuable data are submerged in past examinations done for purposes of insurance and employment or in the course of other illnesses. Often past blood pressure and the results of previous urinalyses, blood counts, and tests for blood urea nitrogen (BUN) can be determined. This aspect deserves considerable attention and potentially provides extraordinarily valuable information.

Physical Examination

Aside from the manifestations of uremia (page 106), which provide a clue to the presence of renal disease as well as to the level of renal function, other types of information may

be gained. For example, nerve deafness and cataracts might suggest hereditary nephritis. The presence of heart murmur, fever, and splenomegaly indicates that the proteinuria and hematuria are probably due to infective endocarditis. There may be evidence of generalized disease, e.g., sarcoid, scleroderma, or lupus, that may cause the renal disease. Tenderness in the costovertebral angle may be a helpful sign. We prefer to test for this with the patient supine, resting on the examiner's hands, while the examiner presses with one finger precisely in the angle. Bruits under the rib margin anteriorly may suggest renal vascular disease. One may feel a hydronephrotic kidney or polycystic kidneys. If the patient is a male, it is well to watch him void in order to assess possible difficulty in emptying the bladder. Prompt voiding of a strong stream of urine readily discontinued is normal. On the other hand, difficulty in initiating urination under direct scrutiny may be due to disease of the lower tract or to the patient's inability to urinate while being observed.

There are several ways of determining the presence of residual urine, including catheterization after voiding, as well as methods that do not require instrumentation. These are discussed in Part IV, the Handbook (pp. 457-500).

After the history and physical examination, and a search for past relevant information, certain laboratory procedures are valuable.

*Laboratory Examination**

This chapter considers only some principles along with certain selected aspects of laboratory examination. The Handbook contains more detailed descriptions of the various procedures, including urinalysis, the collection of a 24-hour urine, quantitative measurement of urinary protein, determination of renal function, urinary bacteriology, and others.

*Portions of this discussion are quoted with permission of the publisher from S. Papper, Proteinuria, *J. Florida Med. Ass.* 56:389, 1969.

The reader is urged to peruse the Handbook for specific technical aspects of the tests referred to in this and subsequent chapters.

Urinalysis is a simple, inexpensive test which generally reveals renal disease, if present, and in many instances directs the physician toward a specific diagnosis. However, the urine must be properly collected, the equipment must be accurate, and, most critically, the person performing the test must be skilled. It is commonplace to find the following urinalysis on a patient's record:

Urinalysis:	Color	Amber
	Sp. Gr.	qns
	pH	6
	Sugar	0
	Protein	Trace
	Sediment	Occ. RBC, 0-2 WBC, Occ. hyaline cast

I refer to it as the *all-purpose* urinalysis, because of its infinite scope (it may be associated with a normal urinary tract or one afflicted with a large spectrum of disease) and its possible aesthetic value in the patient's record. For the care of a patient, it is generally useless, while sometimes giving false comfort and denying the patient the potentially great value of a simple and extraordinarily helpful test.

The urine to be examined should be obtained following overnight dehydration (except in patients with known or suspected renal failure, in whom dehydration may be hazardous) in order to have some estimate of concentrating ability and to have a more meaningful setting for examining the sediment and testing for proteinuria.

While the urinalysis cannot provide a complete assessment of renal function, the *specific gravity* may serve as a guide before the results of more definitive tests are available. However, the specific gravity must be interpreted in the light of several factors: (1) Specific gravity is a measure of mass

and density rather than total solute concentration (osmolality), and we are really interested in the latter. The reason specific gravity has *any* relation to osmolality is that the types of material in urine are normally limited to urea and salts. Variations in the proportions of these substances limit the relationship of osmolality to specific gravity. A dilute urine is defined as having a total solute concentration lower than that of plasma (280 to 300 mOsm per kilogram H_2O), and a urine is regarded as concentrated when its osmolality exceeds that of plasma. The range of urinary osmolality is between 40 and 1200 mOsm per kilogram H_2O. In terms of specific gravity, a urine of 1.008 or less is generally dilute, and one of more than 1.020 is concentrated. Between 1.008 and 1.020, however, far less reliable information is available. (2) Specific gravity is greatly influenced by glycosuria, dextran, and contrast materials used in pyelography; it is relatively less influenced by protein in the urine. (3) Concentrating ability cannot be tested meaningfully in the presence of either water or solute diuresis (e.g., after diuretic drugs). (4) The hydrometer must be an accurate, calibrated instrument, reading 1.000 with distilled water. The failure to calibrate with each use of this instrument is a common omission.

Our hope is that more accurate and more directly interpretable tests of solute concentration will be used more generally in the near future. The osmometer, which measures solute concentration as a function of freezing point depression, is excellent but is a good deal more expensive than a urinometer. Recently, we have been using a refractometer* for routine purposes; it is simple, requires very small amounts of urine, needs no correction for temperature, costs considerably less than an osmometer, and gives more meaningful data than an ordinary urinometer. Although calibrated to read specific gravity, the instrument measures a property of solu-

*The refractometer (TS Meter, Model 10400) is available from the American Optical Company.

tions that is more closely related to, although not identical with, total solute concentration.

The following are two examples of the use of specific gravity as an index of renal function: (1) A patient with chronic pyelonephritis and a urinary specific gravity of 1.028 probably has good renal function. (2) If a dehydrated patient with strong stimulus to concentrate the urine has a specific gravity of 1.009, one can suspect renal functional impairment.

THE URINARY SEDIMENT

Addis, using a quantitative method, found that the normal adult during quiet activity might have as many as one million red blood cells (500,000 under age 12) per day (average 150,000 to 300,000), up to two million white blood cells per day (average 600,000 to 1,000,000), and 5000 to 10,000 casts per day (mostly narrow hyaline). With these figures in mind, it is evident that these elements will be found in normal urine, and the question resolves itself, at least in the case of the cells, into a determination of how many can be accepted as within the normal range. While a morning-voided, concentrated urine cannot provide quantitation, it is nevertheless of sufficient value so that more quantitative approaches are not generally needed. On occasion the semiquantitative data derived from the Addis count or its modifications are helpful, e.g., in following the recovery from acute poststreptococcal glomerulonephritis. There are data indicating that up to one, or possibly two, red blood cells per high-power field in a centrifuged sediment may be within the normal range. In the case of white blood cells, up to four per high-power field may be regarded as within normal limits. Arbitrary limits are pointless, and the very great error in sampling should not be ignored. In a concentrated urine the absence of white blood cells and red blood cells is reassuring; their presence above a very few per high-power field suggests an abnormality re-

quiring further evaluation. If a "random" urine is examined and it is *not* concentrated, a "normal" sediment gives no comfort and excludes nothing. Under the same circumstances, an abnormal urinalysis obviously has relevance.

Casts are molds of tubular lumina formed by the precipitation of protein. Hyaline casts are apparently pure protein and are without known clinical significance. Cellular casts identify the kidney parenchyma as the site of disease; the red blood cell cast is virtually diagnostic of active glomerulonephritis; the white cell cast usually means interstitial nephritis and often, more specifically, pyelonephritis. Granular casts may be degenerated cell casts and therefore should be regarded as abnormal, except perhaps after exercise. Waxy casts probably represent a further stage of degeneration of cellular casts. Fatty casts are granular casts containing lipoid material. They tend to be found in the nephrotic syndrome. Renal failure casts are very broad casts originating in large parts of the collecting system during urinary stagnation.

The term *telescoped urine* is used to refer to the evidence in the sediment of the presence of all stages of glomerular disease. For example, the sediment might contain red cell casts, indicating active glomerulonephritis; tubular epithelial cells filled with fat (oval fat bodies), suggesting the nephrotic phase; granular and waxy casts, indicating degeneration of cell casts; and renal failure casts.

In some patients it may be helpful to examine the voided urine in "segments" in an effort to determine the source of abnormalities and particularly to determine the site of bleeding that results in microscopic hematuria. A two-glass test for accomplishing this is quite useful.

URINARY pH

There are many determinants of urinary pH including diet, pH of extracellular fluid, the state of potassium within the

distal tubular cell, the ability of the distal tubule to form ammonia, and urinary tract infection with urea-splitting organisms. If one keeps these in mind, urinary pH may provide helpful information in individual patients. For example, if the urinary tract is infected and the pH is strongly alkaline, even before the organism is cultured it can be assumed to be one of the urea-splitting organisms—*Pseudomonas, Proteus,* or certain types of *Escherichia coli.* An alkaline pH in the absence of infection suggests alkalosis and, in a patient with hypertension, raises the question of an aldosterone-secreting tumor. It is important to recognize that these things are relative; one can have a slightly acid urine with hyperaldosteronism, but it is less acid than appropriate. The latter cannot be determined in any condition by simple assessment of urinary pH. The ability to acidify the urine may be tested further with a standard ammonium chloride load and measurement of urinary pH. If a patient has a low serum bicarbonate concentration and, on clinical grounds, it is uncertain whether or not this represents metabolic acidosis or respiratory alkalosis, an acid urine suggests acidosis, *provided* potassium depletion does not also exist. Obviously, blood pH is preferred.

PROTEINURIA

There is evidence that in animals some protein is normally present in glomerular filtrate and that filtered protein is reabsorbed by tubular cells. Experiments in dogs and observations in man indicate that some urine proteins are added to urine by renal tubular cells. The immunological similarity of some urine proteins to those in semen and prostatic fluid suggests that a small amount of protein is added to the urine in the lower urinary tract.

In renal disease associated with marked proteinuria, the major defect appears to be increased permeability of the