Manual of Nephrology

Diagnosis and Therapy

Third Edition

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Edited by
Robert W. Schrier, M.D.
Professor and Chairman, Department of Medicine, University of Colorado School of Medicine, Denver

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本书首版于1981年，1985年第2版。本版运用最新资料，主要阐述了肾脏、液体与电解质、酸碱平衡及高血压等各种疾病的诊断与治疗的最新途径。本书的最大特点是：观点新颖，叙述简明扼要，并讲求其实用性。可供医学院校师生、临床专科医师和进修医生参考。

目次摘译：水肿病人；低钠血症病人；低钾血症病人；动脉血pH、P_{CO_2}及碳酸氢盐；血清钙及磷疾病患者；肾结石疾病；尿道感染患者；尿的微镜检查；急性氮血症患者；慢性氮质血症患者及慢性肾衰患者；药物中毒肾脏透析的实用方法；妊娠期间的肾脏疾病与高血压；高血压患者；放射性技术在肾脏疾病方面的运用。索引。

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Preface

The third edition of *Manual of Nephrology: Diagnosis and Therapy* has been written explicitly for the primary care physician. This edition has been substantially revised, but the purpose of the manual is still to provide a practical approach for diagnosis and treatment of renal, fluid and electrolyte, acid-base, and hypertensive disorders.

The first chapter on edematous disorders has been written for this edition by the editor and includes a new unifying hypothesis for body fluid volume regulation in health and disease. A decrease in arterial filling, determined by either a decrease in cardiac output or peripheral arterial vasodilation, is proposed to be the major factor that initiates an extrarenal reflex leading to renal sodium and water retention in edematous disorders. Baroreceptor-mediated increased sympathetic tone, which stimulates the nonosmotic release of vasopressin and the renin-angiotensin-aldosterone system, is involved in this extrarenal reflex.

In the revised second chapter on disorders of water metabolism, the controversial issue of the optimal rate of correction of hyponatremia is addressed as well as newer methods now used to determine serum sodium concentration and diagnose pseudohyponatremia. The classic approach to diagnosing and treating hyponatremic and hypernatremic disorders is again a central focus of this important chapter.

In this edition of the manual, Robert G. Narins, a renowned educator, joins Richard L. Tannen in authoring the chapter on abnormalities of potassium metabolism. William D. Kaehny, an expert in the field of acid-base disorders, again writes a lucid chapter that allows the primary care physician to diagnose and treat simple and mixed metabolic and respiratory disorders. Zalman S. Agus and colleagues have extensively revised their chapter on calcium and phosphorus disorders to include the state-of-the-art knowledge in this area. Fredric L. Coe presents a practical approach to the diagnostic evaluation and treatment of the patient with renal stones, an extremely important and common clinical problem.

Richard A. Wright joins L. Barth Reller in updating the chapter on urinary tract infections. Single-dose antibiotic treatment without pre- or post-treatment urine cultures is presented as a cost-effective means of treating uncomplicated lower urinary tract infections and differentiating these infections from those of the upper urinary tract.

What constitutes a practical approach to the evaluation of the patient with hematuria and/or proteinuria is discussed by Kenneth F. Fairley. For example, the question of which patients with hematuria should have cystoscopy, renal biopsy, or renal angiogram is examined. Acute and chronic renal failure are areas handled in a clinically relevant and lucid manner by Robert E. Cronin and Ronald B. Miller and colleagues, respectively.

How the physician should alter drug therapy in the patient with renal disease is discussed by George R. Aronoff and Steven R. Abel. Marshall D. Lindheimer and Adrian I. Katz present a practical approach to management of the pregnant patient who has hypertension, renal disease, or both. They also discuss which pa-

tients the physician should advise not to become pregnant because of either danger to the mother or the prospect of worsening the renal disease.

Michael J. Dunn, a prominent expert in hypertension, and his associate, Michael C. Smith, present an excellent and authoritative approach to evaluating and treating the patient with primary and secondary hypertension.

Finally, many sophisticated and expensive radiologic procedures in addition to excretory urography including ultrasonography, computerized tomography, cyst puncture, renal scan, and renal angiography are now available. Michael D. Parker, Robert A. Older, Daniel E. Wertman, Jr., Larry M. Crane, and Hector J. Hidalgo present a practical and systematic approach to the use of these procedures in the evaluation of the patient with a renal mass, renal failure, urinary tract obstruction, hematuria, renal transplant, renal and perirenal infection, or renal hypertension.

I invited the authors of these chapters to contribute to the manual not because of their sophistication in the science of medicine, although sophisticated scientists they are, but because they are physicians who are able to use their scientific knowledge in a practical way to allow for a focused and cost-effective plan of diagnosis and treatment that is in the best interests of their patients. In this same spirit, I would like once again to dedicate this book to Professor Hugh de Wardener, a humane physician, a man of science, and above all, a practical man whose uncanny ability to focus on important issues in many areas, including sodium and water metabolism, bone disease, chronic dialysis, and hypertension, has benefited medical science and his patients for over 40 years.

R.W.S.

Contributing Authors

Steven R. Abel, Pharm.D.	Affiliate Assistant Professor of Clinical Pharmacy, Purdue University School of Pharmacy, West Lafayette, Indiana; Assistant Director of Pharmacy, Clinical/Education Services, Indiana University Hospitals, Indianapolis
Zalman S. Agus, M.D.	Professor of Medicine, University of Pennsylvania School of Medicine; Attending Physician, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia
George R. Aronoff, M.D.	Professor of Medicine and Pharmacology, University of Louisville School of Medicine; Chief, Division of Nephrology, Department of Medicine, University of Louisville Hospitals, Louisville, Kentucky
Fredric L. Coe, M.D.	Professor of Medicine and Physiology, University of Chicago Pritzker School of Medicine; Chief, Nephrology Program, Department of Medicine, University of Chicago Medical Center, Chicago
Larry M. Crane, M.D.	Chief, Division of Ultrasound, and Chairman, Department of Radiology, Durham County General Hospital, Durham, North Carolina
Robert E. Cronin, M.D.	Associate Professor of Internal Medicine, University of Texas Southwestern Medical School; Chief, Renal/Hypertension Clinic, Veterans Administration Medical Center, Dallas
Michael J. Dunn, M.D.	Professor of Medicine, Case Western Reserve University School of Medicine; Director of Nephrology, University Hospitals, Cleveland
Kenneth F. Fairley, M.D., F.R.C.P., F.R.A.C.P.	Professorial Associate, Department of Medicine, University of Melbourne; Senior Physician, Royal Melbourne Hospital, Melbourne, Australia

Michael Heifets, M.D.	Assistant Professor of Medicine, Temple University School of Medicine; Attending Physician, Department of Medicine, Temple University Hospital, Philadelphia
Hector J. Hildago, M.D.	Clinical Assistant Professor of Radiology, Duke University School of Medicine, Durham, and University of North Carolina at Chapel Hill School of Medicine, Chapel Hill; Attending Radiologist, Durham County General Hospital, Durham, North Carolina
William D. Kaehny, M.D.	Associate Professor of Medicine, University of Colorado School of Medicine; Assistant Chief, Medical Service, Veterans Administration Medical Center, Denver
Adrian I. Katz, M.D.	Professor of Medicine, University of Chicago Pritzker School of Medicine; Attending Physician, Department of Medicine, University of Chicago Medical Center, Chicago
Ellie Kelepouris, M.D.	Assistant Professor of Medicine, University of Pennsylvania School of Medicine; Attending Physician, Renal Section, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia
Marshall D. Lindheimer, M.D.	Professor of Medicine and Obstetrics and Gynecology, University of Chicago Pritzker School of Medicine and University of Chicago Medical Center; Director, Medical High Risk Clinic, Lying-in Hospital, Chicago
Ronald B. Miller, M.D., F.A.C.P.	Clinical Professor of Medicine and Director, Program in Medical Ethics, University of California, Irvine, College of Medicine; Division of Nephrology and Department of Medicine, University of California, Irvine, Medical Center, Orange, California
Robert G. Narins, M.D.	Professor and Chief, Renal Section, Department of Medicine, Temple University School of Medicine; Senior Attending Physician, Temple University Hospital, Philadelphia

Robert A. Older, M.D.	Clinical Associate Professor of Radiology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill; Chief, Section of Uroradiology, Durham County General Hospital, Durham, North Carolina
Michael D. Parker, M.D.	Associate Professor of Radiology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill
L. Barth Reller, M.D.	Professor of Medicine and Pathology, Duke University School of Medicine; Director of Clinical Microbiology, Duke University Medical Center, Durham, North Carolina
Robert W. Schrier, M.D.	Professor and Chairman, Department of Medicine, University of Colorado School of Medicine, Denver
Jerald F. Sigala, M.D., Dr. P.H.	Assistant Clinical Professor of Medicine, University of California, Irvine, College of Medicine, Irvine, California
Michael C. Smith, M.D.	Associate Professor of Medicine, Case Western Reserve University School of Medicine; Associate Physician, Department of Medicine, University Hospitals, Cleveland
Richard L. Tannen, M.D.	Professor and Chairman, Department of Medicine, University of Southern California School of Medicine; Chairman, Department of Medicine, Los Angeles County/USC Medical Center, Los Angeles
A. Tyler Upham, M.D.	Assistant Clinical Professor of Medicine, University of California, Irvine, College of Medicine; Medical Director, Dialysis Unit, Hoag Memorial Hospital, Newport Beach, California
Alan Wasserstein, M.D.	Associate Professor of Medicine, University of Pennsylvania School of Medicine; Attending Physician, Hospital of the University of Pennsylvania, Philadelphia
Daniel E. Wertman, Jr., M.D.	Chief of Vascular and Interventional Radiology, Durham County General Hospital, Durham, North Carolina

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Notice

The indications and dosages of all drugs in this book have been recommended in the medical literature and conform to the practices of the general medical community. 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.

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1 The Edematous Patient

Robert W. Schrier

I. Body fluid distribution. Of the total fluids in the human body, two-thirds reside inside the cell (i.e., intracellular fluid), and one-third resides outside the cell (i.e., extracellular fluid [ECF]). The patient with generalized edema by definition has an excess of ECF. The ECF resides in two compartments—the vascular compartment (i.e., plasma fluid) and the fluid that resides between the cells of the body but outside of the vascular compartment (i.e., interstitial fluid). In the vascular compartment, 85 percent of the fluid resides on the venous side of the circulation and 15 percent on the arterial side (Table 1-1). An excess of interstitial fluid constitutes edema. With digital pressure the interstitial fluid can generally be moved from the area of pressure and thus has been described as "pitting." This observation demonstrates that the excess interstitial fluid can move freely within its space between the body's cells and the vascular compartment. If digital pressure does not cause pitting in the edematous patient (i.e., nonpitting edema), then the free movement of the interstitial fluid is not present. Such nonpitting edema can occur with lymphatic obstruction (i.e., lymphedema) or regional fibrosis of subcutaneous tissue, which may occur with chronic venous stasis.

Although generalized edema always signifies an excess of ECF, specifically in the interstitial compartment, the intravascular volume may be decreased, normal, or increased. Since two-thirds of ECF resides in the interstitial space and only one-third in the intravascular compartment, a rise in total ECF volume may occur as a consequence of excess interstitial fluid (i.e., generalized edema), even though intravascular volume is decreased.

Starling's forces, namely capillary hydrostatic and oncotic pressures, govern the movement of fluid between the interstitial space and the vascular compartment. Since serum albumin is the major determinant of capillary oncotic pressure, the Starling force that maintains fluid in the capillary, hypoalbuminemia can lead to excess transudation of fluid from the vascular to interstitial compartment. In this setting the kidney retains sodium and water in an effort to normalize intravascular volume. However, because of the diminished plasma albumin and oncotic pressure, fluid continues to move from the vascular compartment into the interstitium with resulting edema formation and expansion of total ECF volume. Proteinuria (>3.5 gm/day), dermal losses of protein (e.g., burns), severe malnutrition (e.g., kwoshiorkor disease), protein-losing enteropathy (e.g., malabsorption), and impaired hepatic synthesis of albumin (e.g., cirrhosis) are causes that can lead to a hypoalbuminemic state and generalized edema.

As shown in Fig. 1-1, fluid leaves the capillary at the arterial end because hydrostatic pressure exceeds oncotic pressure and returns at the venous end of the capillary because oncotic pressure exceeds hydrostatic pressure. The interstitial fluid that is not returned to the capillaries by virtue of these Starling forces is returned to the vascular compartment by lymphatic drainage into the jugular veins. In fact, in cirrhosis where hepatic fibrosis causes high capillary hydrostatic pressures in association with low capillary oncotic pressures, the lymphatic flow can increase 20-fold from 1 to 20 liters per day in an effort to diminish the increase in accumulating interstitial fluid. Nevertheless, in decompensated cirrhosis excess interstitial fluid accumulates, with a predilection for the abdominal

Table 1-1. Body fluid distribution

Compartment	Amount	Volumes in 70-kg man
Total body fluid	60% of body weight	42 liters
Intracellular fluid	40% of body weight	28 liters
Extracellular fluid (ECF)	20% of body weight	14 liters
Interstitial fluid	Two-thirds of ECF	9.4 liters
Plasma fluid	One-third of ECF	4.6 liters
Venous fluid	85% of plasma fluid	3.9 liters
Arterial fluid	15% of plasma fluid	0.7 liters

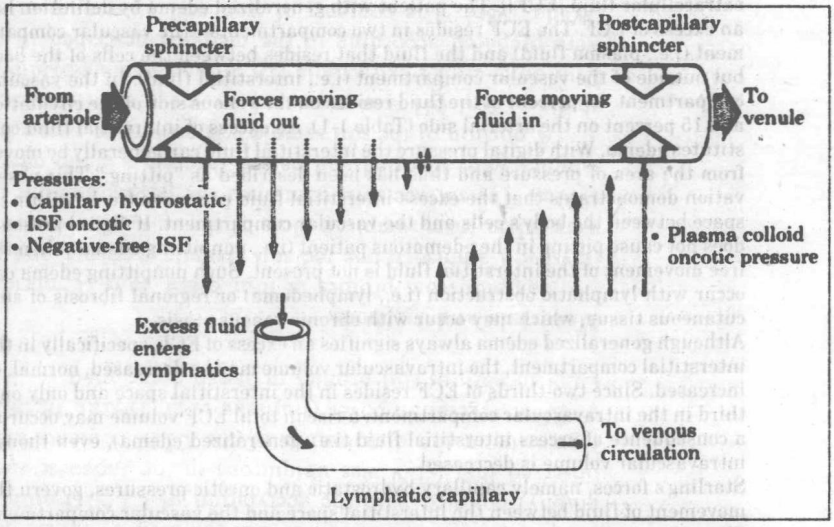

Fig. 1-1. Effect of Starling forces on fluid movement across capillary wall. (ISF = interstitial fluid.)

interstitial space (i.e. ascites) because of portal and splanchnic venous hypertension causing an elevation in capillary hydrostatic pressure.

From this foregoing discussion, it should also be clear that lymphatic obstruction (e.g., malignancy) can also cause excessive accumulation of interstitial fluid and thus edema. Another factor that must be borne in mind as a cause of edema is an increase in fluid permeability of the capillary wall. This is the cause of edema in association with hypersensitivity reactions and angioneurotic edema and may be a factor in edema associated with diabetes mellitus and idiopathic cyclic edema. The factors that may cause edema, either alone or in concert, are summarized in Table 1-2.

Although the preceding comments refer to generalized edema (i.e., an increase in total body interstitial fluid), it should be noted that such edema may have a predilection for specific areas of the body for various reasons. The formation of ascites because of portal hypertension has already been mentioned. With the normal hours of upright posture, accumulation of the edema fluid in the dependent parts of the body should be expected, whereas excessive hours at bed rest in the supine position will predispose to edema accumulation in the sacral and perior-

Table 1-2. Factors that may cause edema

Increased capillary hydrostatic pressure
Decreased capillary oncotic pressure
Lymphatic obstruction
Increased capillary permeability

bital areas of the body. The physician must also be aware of the potential presence of localized edema, which must be differentiated from generalized edema. Although generalized edema may have a predilection for certain body sites, it is nevertheless a total-body phenomenon of excessive interstitial fluid. On the other hand, localized edema is due to local factors and therefore is not a total-body phenomenon. Venous obstruction, as occurs in thrombophlebitis, may cause localized edema of one lower extremity. The physical examination in a patient with ankle edema therefore should include a search for venous incompetence—e.g., varicose veins. It should be recognized, however, that deep venous disease may not be detectable on physical examination and thus may necessitate other diagnostic approaches (e.g., venography). Thus, if the venous disease is bilateral, the physician may mistakenly search for causes of generalized edema (e.g., cardiac failure and cirrhosis), when indeed the bilateral ankle edema is due to local factors. Pelvic lymphatic obstruction (e.g., malignancy) can also cause bilateral lower extremity edema and thereby mimic generalized edema. Trauma, burns, inflammation, cellulitis, and angioedema are other causes of localized edema.

II. **Body fluid volume regulation.** The edematous patient has presented a challenge in the understanding of body fluid volume regulation for several decades. In the normal subject, if ECF is expanded by the administration of isotonic saline, the kidney will excrete the excessive amount of sodium and water in the urine, thus returning ECF volume to normal. Such an important role of the kidney in volume regulation has been recognized for many years. What has not been understood, however, is why in the edematous patient the kidneys continue to retain sodium and water. Certainly in circumstances where kidney disease is present and renal function is markedly impaired (i.e., acute or chronic renal failure) it is understandable why the kidney continues to retain sodium and water even to the degree of causing hypertension and pulmonary edema. However, much more perplexing are those circumstances where the kidneys are known to be normal and yet continue to retain sodium and water in spite of expansion of ECF and edema formation (e.g., cirrhosis, congestive heart failure). For example, if the kidneys from a cirrhotic patient are transplanted to another environment (e.g., a patient without liver disease), excessive renal sodium and water retention no longer occurs. The conclusion therefore emerged that neither total ECF nor its interstitial component, both of which are expanded in the patient with generalized edema, are the modulators of renal sodium and water excretion. Rather, Peters suggested in the 1950s that another body fluid compartment other than total ECF or interstitial fluid volume must be the regulator of renal sodium and water excretion. The term *effective blood volume* was coined to describe this undefined, enigmatic body fluid compartment that was signaling, through unknown pathways, the kidney to retain sodium and water in spite of expansion of total ECF and interstitial volumes with edema formation in the patient with cardiac or liver disease. It was then suggested that the kidney must be responding to cardiac output, thus providing an explanation for sodium and water retention in low-output cardiac failure. This concept, however, did not provide a universal explanation for generalized edema because many patients with decompensated cirrhosis, who were avidly retaining sodium and water, were found to have normal or elevated cardiac outputs.