ELSEVIER
SAUNDERS

Michael R. Clarkson
Barry M. Brenner

Pocket Companion to Brenner & Rector's The Kidney

Seventh Edition

Pocket Companion to Brenner & Rector's THE KIDNEY

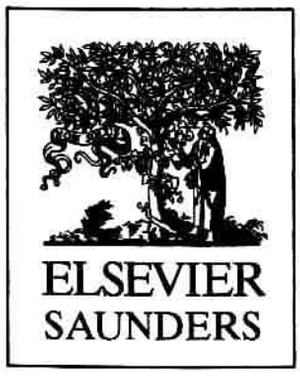
SEVENTH EDITION

Michael R. Clarkson, M.B., M.R.C.P.I.

Instructor in Medicine, Harvard Medical School;
Instructor in Medicine, Renal Division, Department of Medicine,
Brigham and Women's Hospital, Boston, Massachusetts

Barry M. Brenner, M.D., A.M. (Hon.), D.Sc. (Hon.), D.M.Sc. (Hon), M.D. (Hon.), Dipl. (Hon.), F.R.C.P. (Lond., Hon.)

Samuel A. Levine, Professor of Medicine, Harvard Medical School;
Director Emeritus, Renal Division, and Senior Physician,
Department of Medicine, Brigham and Women's Hospital, Boston,
Massachusetts



ELSEVIER
SAUNDERS

The Curtis Center
170 S Independence Mall W 300E
Philadelphia, Pennsylvania 19106

POCKET COMPANION TO BRENNER & RECTOR'S THE KIDNEY
SEVENTH EDITION 0-7216-0559-1

Acquisitions Editor: Susan F. Pioli
Assistant Editor: Laurie Anello
Production Manager: David Saltzberg

Printed in the United States of America

Last digit is the print number: 9 8 7 6 5 4 3 2 1

To sharing the inherent elegance
of
renal pathophysiology and clinical nephrology
with physicians
of
today and tomorrow.

Preface

Given the dramatic expansion in the number of patients being treated for chronic kidney disease and end-stage renal failure over the past three decades a working knowledge of renal medicine is a prerequisite for the practicing physician. Nephrology is often perceived as being among the more challenging and complex areas of internal medicine, and the major nephrology textbooks can appear daunting at first glance to the uninitiated. Therefore, in designing this concise first edition of *Pocket Companion to Brenner & Rector's The Kidney* we have endeavored to provide a readily accessible and current source of information on clinical renal disease for medical students, residents, renal fellows, primary care physicians, internists, pediatricians and urologists, and trainees in these specialties. To ensure that the text meets the requirement of the busy clinician, we have chosen the most clinically relevant chapters from *Brenner & Rector's The Kidney* and distilled the essence of the pathophysiologic, diagnostic, and treatment issues pertaining to the practice of clinical nephrology. The goal of the *Pocket Companion* is not to replace the main textbook but rather to provide a source of immediate clinical information at the bedside and to act as a starting point for further in-depth reading of *Brenner and Rector's The Kidney* and its companion volumes *Therapy in Hypertension and Nephrology*, *Acute Renal Failure*, *Dialysis and Transplantation*, *Hypertension*, and *Acid-Base and Electrolyte Disorders*.

We wish to express our sincere gratitude to the professional staff at Elsevier and in particular to Susan Pioli for her encouragement, guidance, and support.

Contents

I

Approach to the Patient with Renal Disease

Clinical Assessment of the Patient with Kidney Disease

1

ACUTE RENAL FAILURE

Acute renal failure (ARF) is defined as a sudden decrease in kidney function (hours to weeks). The distinction between acute and chronic kidney disease is an important factor in the management of the patient with renal failure (Table 1–1). Early manifestations of renal failure vary and depend in part on context and underlying cause (Table 1–2).

History

The history should initially focus on two key areas: renal hypoperfusion and nephrotoxins.

Table 1–1: Differentiation of Acute from Chronic Kidney Disease

History	Long-standing history suggests chronic kidney disease
Renal osteodystrophy	Radiographic evidence of osteitis fibrosa cystica, osteomalacia suggest chronic kidney disease
Renal size (length)	
Small kidneys (e.g., <9 cm)	Chronic kidney disease
Normal (9–12 cm)	Acute kidney disease
Enlarged kidneys (>12 cm)	Human immunodeficiency virus nephropathy Diabetic nephropathy Amyloidosis Autosomal dominant polycystic kidney disease Tuberous sclerosis Obstructive nephropathy
Renal biopsy	Histologic diagnosis

Table 1–2: Presentations of Renal Failure

Symptomatic presentation

General
- Fatigue
- Weakness

Cardiovascular
- Hypertension
- Pulmonary congestion
- Cough
- Dyspnea
- Hemoptysis

Neurologic
- Encephalopathy
- Seizure
- Peripheral neuropathy

Gastrointestinal
- Anorexia
- Nausea
- Vomiting
- Abdominal pain
- Bleeding

Musculoskeletal
- Muscle weakness
- Periarticular or articular pain
- Bone pain

Genitourinary
- Hematuria
- Dysuria

Cutaneous
- Pruritus
- Necrosis
- Vasculitis
- Bruising

Asymptomatic presentation
- Hypertension
- Proteinuria
- Hematuria
- Abnormal renal imaging findings

A meticulous review of the medical record should include a careful search for ischemic and nephrotoxic insults. Common causes of volume depletion such as vomiting, diarrhea, excessive sweating, burns, and renal salt wasting (e.g., diabetic ketoacidosis) must be investigated. Evidence of "effective" circulating volume depletion should also be evaluated (e.g., congestive heart failure or cirrhosis). A history of recent trauma with or without overt blood loss or muscle trauma should raise the possibility of ischemia, myoglobin-induced tubular necrosis, or both. Fever, rash, and joint pains are associated with lupus nephritis, vasculitides, endocarditis, drug allergy, and infectious diseases that cause intrinsic acute renal failure. A history of dyspnea or hemoptysis may be a sign of pulmonary vasculitis but typically results from pulmonary edema due to volume overload. Obstructive uropathy and acute inflammation of the kidney can cause painful stretching of the renal capsule. Upper quadrant pain is also a sign of acute renal infarction (e.g., renal artery emboli). Prominent neurologic signs are often observed in thrombotic thrombocytopenic purpura, toxic nephropathies,

and poisonings. Constitutional and nonspecific symptoms, such as malaise, weakness, fatigue, anorexia, nausea, and vomiting, are common in patients with ARF but do not alone establish an underlying diagnosis.

A history of nephrotoxin exposure is an extremely important component of the evaluation of a patient with ARF. Both endogenous and exogenous toxins can cause renal failure (Table 1–3). A thorough review of the patient's history and medical record for evidence of nephrotoxin exposure is essential. The potential toxicity of over-the-counter drugs and poisons should be considered in all patients in whom the cause of ARF is not readily apparent. Endogenous toxins include myoglobin, hemoglobin, uric acid, paraproteins, and calcium-phosphorus complexes. Tumor lysis, usually occurring in patients with bulky abdominal lymphomas, can be caused by acute uric acid nephropathy or deposition of calcium and phosphorus and can lead to severe, even anuric ARF. Cancers, including solid tumors and lymphoma, may also cause intrinsic renal failure as a result of hypercalcemia or tumor infiltration.

A history of the color and volume of the patient's urine as well as the pattern of urination can be useful in some settings. For example, abrupt anuria suggests urinary obstruction or vascular obstruction due to renal artery emboli or atherosclerotic occlusion of the aortorenal bifurcation. A history of gradually diminishing

Table 1–3: Nephrotoxins Reported to Cause Acute Renal Failure

Endogenous substances
- Myoglobin
- Uric acid
- Calcium phosphorus
- Light chains
- Atheroemboli

Exogenous substances
Antibiotics
- Aminoglycosides
- Penicillins
- Cephalosporins
- Fluoroquinolones
- Sulfa drugs
- Pentamidine

Continued

Table 1–3: (cont'd)

- Foscarnet
- Cidofovir
- Acyclovir

Angiotensin-converting enzyme inhibitors
Angiotensin II receptor 1 antagonists
Analgesics and nonsteroidal anti-inflammatory drugs
Acetaminophen
Aspirin
Nonselective cyclooxygenase inhibitors
Cyclooxygenase-2 inhibitors
Calcineurin inhibitors

- Cyclosporin
- Tacrolimus

Chemotherapeutic agents

- Cisplatin
- Mitomycin C
- Methotrexate
- Cytosine arabinoside
- Interleukin-2

Reverse transcriptase inhibitors

- Indinavir
- Stavudine

Mannitol
Immunomodulatory agents

- Interferon-α
- Therapeutic immunoglobulins

Radiocontrast agents
Heavy metals and poisons

- Mercury
- Arsenic
- Cadmium
- Lead
- Ethylene glycol

Antidepressants and anticonvulsants

- Citalopram (Celexa)
- Phenytoin
- Carbamazepine

urine output may indicate urethral stricture or in an older man bladder outlet obstruction due to prostate enlargement. Gross hematuria in the setting of ARF suggests acute glomerulonephritis or ureteral obstruction by tumor, blood clots, or sloughed renal papillae.

Physical Examination

The physical examination can provide many clues to the underlying cause of and potential therapy for ARF.

Skin

Petechiae, purpura, and ecchymoses suggest inflammatory or vascular causes of kidney failure. Cutaneous infarcts may result from embolic phenomena, and cutaneous vasculitis manifesting as palpable purpura occurs in patients with septic shock, atheroembolic disease, systemic vasculitis, and infective endocarditis.

Eye

Eye manifestations include uveitis (interstitial nephritis and necrotizing vasculitis), ocular muscle paralysis (ethylene glycol poisoning and necrotizing vasculitis), signs of severe hypertension, atheroembolic lesions, Roth spots (endocarditis), and cytoid bodies (cotton-wool exudates are seen in acute lupus nephritis). Conjunctivitis can be a result of vasculitis or drug toxicity or a manifestation of end-stage renal disease (ESRD) ("red eyes of renal failure"), the latter being due to conjunctival calcium deposition.

Cardiovascular and Volume Status

Meticulous assessment of cardiovascular and volume status is the most important aspect in the diagnosis and initial management of ARF. Evidence for volume depletion, including orthostatic hypotension, dry mucous membranes, and decreased skin turgor, as well as signs of sepsis, congestive heart failure, and cardiac tamponade, should be sought in patients with low blood pressure or overt hypotension. However, often it is difficult to assess the volume status from physical findings alone, and in some patients it may be necessary to place a central venous catheter or pulmonary artery catheter to measure right heart pressures, cardiac output, and systemic vascular resistance. If severe hypertension is present, ARF may be due to malignant nephrosclerosis (e.g., scleroderma), glomerulonephritis, or atheroembolic disease. Cardiac murmurs are associated with endocarditis or atrial myxoma, which can cause ARF due to fulminant glomerulonephritis. A pericardial friction rub in a patient with newly diagnosed renal failure may be a sign of impending cardiac tamponade and is an indication for emergency dialysis. In this situation, progressive hypotension is dramatic but blood pressure can be temporarily stabilized by a rapid intravenous bolus infusion of fluids.

Abdomen

Abdominal examination may reveal a palpable bladder (urinary obstruction). Also, tenderness in the upper quadrants can be associated with ureteral obstruction or renal infarction. Ascites may be observed in fulminant hepatic failure, severe nephrotic syndrome, and Budd-Chiari syndrome, all of which are associated with ARF. Abdominal bruit evokes the diagnosis of severe atherosclerotic disease, which can engender renal failure from renal artery stenosis, thrombosis of the aortorenal bifurcation, or atheroembolic renal disease. A flank mass can be a sign of renal obstruction from tumor or retroperitoneal fibrosis. In addition, a tense distended abdomen in a patient who has just undergone surgery raises the possibility of abdominal compartment syndrome.

Extremities

Examination of the extremities for signs of edema, evidence of tissue ischemia, muscle tenderness (e.g., rhabdomyolysis causing myoglobinuric renal failure), and arthritis (e.g., systemic lupus erythematosus) may provide clues to the diagnosis of renal failure.

Neuropsychiatric Features

Neuropsychiatric abnormalities range from signs of uremic encephalopathy (e.g., confusion, somnolence, stupor, coma, and seizures) to focal neurologic abnormalities in specific diseases such as the vasculitides. Cranial nerve palsies can be seen in patients with ethylene glycol poisoning or vasculitides. Altered and changing mental status is common in thrombotic microangiopathies and systemic atheroembolism.

Urinalysis

The urinalysis is essential in the evaluation of ARF (Table 1–4). An abnormal urinary sediment strongly suggests intrarenal kidney failure. Reddish brown urine or "Coca-Cola" urine is characteristic of acute glomerulonephritis, myoglobinuria, and hemoglobinuria. Bilious urine in patients with combined liver and renal disease appears yellow-brown owing to bile pigments.

Qualitative assessments for proteinuria and heme pigment are helpful in identifying glomerulonephritis, interstitial nephritis, and toxic and infectious causes of tubular necrosis. Microscopic examination of urine sediment after centrifugation is extremely helpful for differentiating prerenal from intrarenal causes of kidney failure. The urine sediment in acute tubular necrosis (ATN)

Table 1–4: Urine Tests in the Differential Diagnosis of Acute Renal Failure

Diagnosis	*Urinalysis*	*Urine-to-Plasma Osmolality*	*UNa (mEq/L)*	*Fractional Excretion of Na*
Prerenal	Normal	>1.0	<20	<1.0
Acute tubular necrosis	Granular casts, epithelial cells	≤1.0	>20	>1.0
Interstitial necrosis	RBCs WBCs, ± eosinophils, granular casts	≤1.0	>2.0	>1.0
Glomerulonephritis	RBCs, RBC casts, marked proteinuria	>1.0	<20	<1.0
Vascular disorders	Normal or RBCs, proteinuria	>1.0	<20	<1.0
Postrenal	Normal or RBCs, casts, pyuria	<1.0	>20	>1.0

RBC, red blood cell; UNa, urine sodium concentration; WBC, white blood cell.

typically has granular "muddy" casts and renal tubular cells. Interstitial nephritis is often accompanied by pyuria, microhematuria, and eosinophiluria. Glomerulonephritis is heralded by hematuria and red blood cell casts. In addition, granular casts, fat globules, and oval fat bodies may be seen in glomerulopathies associated with heavy proteinuria. Uric acid crystals suggest ATN associated with acute uric acid nephropathy from tumor lysis syndrome. Calcium oxalate crystals may be present in ethylene glycol poisoning with ARF due to nephrocalcinosis, and acetaminophen crystals may be observed in acute acetaminophen poisoning.

Blood Tests

Increases in blood urea nitrogen (BUN) and serum creatinine (Cr) levels are hallmarks of renal failure. The normal BUN/Cr ratio of 10:1 is usually maintained in cases of intrinsic ARF. The ratio is usually elevated (>20/1) in prerenal conditions and in some patients with obstructive uropathy. Also, in patients with