Diagnostic approach to acute renal failure

**STEP I**
- ACUTE
  - Normal recent function
  - Normal renal size on ultrasound
  - Normal Hct

- CHRONIC
  - Prior renal dysfunction
  - Small kidneys on ultrasound
  - Anemia

**STEP II**
- History, physical exam
- Prerenal
  - Edema
  - CHF
  - Cirrhosis
  - ECFV contraction
  - Drugs
- Intrinsic renal
  - Hypotension
  - Nephrotoxins
  - Systemic symptoms
  - Trauma/surgery
- Postrenal
  - Distended bladder
  - Pelvic mass (♀)
  - Enlarged kidney(s)
  - Flank pain
  - Prostatism (♂)

**STEP III**
- Urinalysis
- RBC casts and/or dysmorphic RBCs
- Uric acid crystals
- Myoglobin
- Hemoglobin
- Epithelial cells
- Granular, pigmented casts
- Dipstick-negative proteinuria
- Anuria
- Bilateral cortical necrosis
- Bilateral renal artery or vein occlusion
- Orthotolidine positive on dipstick but RBC negative in sediment

**STEP IV**
- Other blood studies
  - Blood chemistry
    - BUN/creatinine ratio
    - Calcium
    - Uric acid
    - Phosphorus
    - CPK, aldolase
- Other blood studies
  - SPE—M spike
  - C3/C4 (complement)
  - Haptoglobin
  - Eosinophilia

**STEP V**
- Urinary diagnostic indices
- Blood chemistry
- Blood chemistry
- Acute uric acid nephropathy
- Light chain cast nephropathy
- Acute tubular necrosis
- Prerenal or postrenal

**FIGURE 5-18**
Diagnostic approach to acute renal failure. Acute renal failure developing in a patient with malignancy may be due to diverse causes. It is important to employ an organized diagnostic approach to define the specific cause in a cost-effective manner. The approach outlined in this figure involves five steps. Step I addresses the distinction between acute and chronic renal failure, and step II lists the various causes of prerenal, intrinsic, and postrenal acute renal failure (see Figs. 5-2, 5-4, and 5-16) according to data obtained from the history and physical examination.

Urinalysis is very useful in the workup of a patient with acute renal failure, particularly due to intrinsic renal disease, as outlined in step III. The presence of red blood cell (RBC) casts or dysmorphic RBCs in the urine sediment is suggestive of glomerulonephritis, while eosinophiluria is indicative of acute interstitial nephritis. Step IV involves obtaining blood chemistry and other blood studies, abnormalities that may strongly support a given diagnosis. Step V is employed in the presence of oliguric acute renal failure. Urinary diagnostic indices are used to distinguish between prerenal acute renal failure and glomerulonephritis, as opposed to acute tubular necrosis or acute obstruction. Evaluation of the urine is also helpful in detecting the presence of light chains of immunoglobulins, which may be diagnostic of multiple myeloma-induced acute renal failure. Also, an increased urinary uric acid/creatinine ratio may indicate acute uric acid nephropathy. In the patient who is anuric (<50 mL of urine per day), it is particularly important to rule out obstruction. Bilateral cortical necrosis or glomerulonephritis must be considered in this setting; a renal biopsy may be necessary for definitive diagnosis. If bilateral renal artery or vein occlusion is a consideration, angiography may be indicated. ATN—acute tubular necrosis; BUN—blood urea nitrogen; CHF—congestive heart failure; CPK—creatine phosphokinase; ECFV—extracellular fluid volume; FEna—fractional extraction of sodium; Hct—hematocrit; SPE—serum protein electrophoresis; Una—urine sodium; Uosm—urine osmolality; UPE—urine protein electrophoresis.
Hematuria and/or the Nephrotic Syndrome

CAUSES OF HEMATURIA AND/OR THE NPHROTIC SYNDROME

- Paraneoplastic glomerulonephritis
- Membranous glomerulonephritis
- Minimal change nephrotic syndrome
- Crescentic glomerulonephritis
- Membranoproliferative glomerulonephritis
- Primary or metastatic renal cancer
- Chemotherapy agents causing nephrotic syndrome
  - Mitomycin C
  - Gemcitabine
  - Interferon

FIGURE 5-19
Causes of hematuria and/or the nephrotic syndrome may occur in association with malignancy without causing acute or chronic renal failure. Causes may include one of the many paraneoplastic types of glomerulonephritis, with proteinuria and often the nephrotic syndrome resulting from the glomerular injury; hematuria is also noted in some cases. In contrast, isolated hematuria is the predominant feature when primary or metastatic renal cancer erodes the intrarenal vasculature. Proteinuria, and in some cases the nephrotic syndrome, may be the presenting nephrotoxicity of cancer chemotherapy agents.

FIGURE 5-20
Membranous glomerulonephritis and the nephrotic syndrome in a patient with bronchogenic carcinoma. A 76-year-old veteran presented with ankle edema and weight gain of 8 weeks’ duration. He was noted to have the nephrotic syndrome with 5 grams of proteinuria per day. A chest radiograph revealed a perihilar mass. A bronchoscopic biopsy of the mass was diagnostic of malignancy. He was managed conservatively with diuretics and radiotherapy for the chest mass. He died 10 months later.

A, Light microscopic study of the kidney of this patient. Note the thickening of capillary walls and spikes (PAM stain).

B, Immunofluorescence microscopy of renal tissue showing peripheral glomerular capillary deposition of IgG in a granular pattern indicative of immune-complex-mediated glomerulonephritis.

(Continued on next page)
5.12 Systemic Diseases and the Kidney

**FIGURE 5-20** (Continued)

C, Electron microscopy of the glomerulus showing subepithelial electron-dense deposits along the capillary walls. There is effacement of the epithelial cell foot processes, which is a common finding in patients with nephrotic syndrome. D, Bronchogenic carcinoma noted at autopsy in this patient (hematoxylin and eosin stain).

Membranous glomerulonephritis is an immune-complex–mediated glomerular disease, often resulting in nephrotic syndrome as a clinical manifestation. In adults older than the age of 50, a coexisting malignancy, usually a carcinoma, may be present in up to 10% of cases [5]. Although a variety of malignancies have been observed to be associated with membranous glomerulonephritis, the most common sites are the breast, the lung, and the colon. In some instances, the tumor antigen or antitumor antibodies have been detected in the glomeruli. Development of the nephrotic syndrome has been temporally related to the malignancy in several instances, and successful cure of the malignancy has led to a remission in the nephrotic syndrome. Relapses have been associated with reappearance of proteinuria [46].

**FIGURE 5-21**

Minimal change nephrotic syndrome in Hodgkin's disease. A, Light microscopic study of a renal biopsy specimen from a 57-year-old man with nephrotic syndrome of 3 months' duration. Urine protein excretion was 7.1 g/d. The serum creatinine concentration was 1.3 mg/dL. The patient also had cervical lymphadenopathy, biopsy of which revealed Hodgkin's disease of the mixed cellularity type. He was treated with irradiation to the upper mantle region with resolution of the lymphadenopathy. Proteinuria also declined to 2 g/d in 2 weeks and was absent in 8 weeks. The glomerulus was normocellular with delicate capillary walls diagnostic of minimal change nephrotic syndrome (PAM stain).

B, Electron microscopy of a glomerulus from the same patient showing glomerular capillaries with extensive effacement of the epithelial foot processes but without electron-dense deposits.

In patients with Hodgkin's disease and other malignancies arising from lymph nodes as well as different types of chronic leukemias, the occurrence of glomerular diseases has been noted [5,46]. Several histologic types of glomerular diseases have been documented in these instances; the most common type has been minimal change nephrotic syndrome [47]. The glomeruli of these patients are normal on light microscopic study and are devoid of hypercellularity or capillary wall thickening. No immunoglobulins are noted in the glomeruli on immunofluorescence microscopy. On electron microscopy, effacement of the epithelial cell foot processes is the only abnormality present. Proteinuria has been noted to remit with cure of lymphoma (with use of surgery, radiotherapy, or chemotherapy) in some cases; relapses in nephrotic syndrome occur with recurrence of the tumor. This has been documented to occur several times in some patients [47]. The pathogenesis of minimal change nephrotic syndrome in patients with malignancy remains unknown. It is possible that a cytokine or tumor cell product may be responsible for the increase in glomerular permeability with resultant proteinuria [48].