ASSESSMENT OF GFR

Monitoring the GFR is important in both hospital and outpatient settings, and several different methodologies are available. GFR is the primary metric for kidney "function," and its direct measurement involves administration of a radioactive isotope (such as inulin or iothalamate) that is filtered at the glomerulus into the urinary space but is neither reabsorbed nor secreted throughout the tubule. GFR—i.e., the clearance of inulin or iothalamate in milliliters per minute—is calculated from the rate of appearance of the isotope in the urine over several hours. In most clinical circumstances, direct GFR measurement is not feasible, and the plasma creatinine level is used as a surrogate to estimate GFR. Plasma creatinine (P_{Cr}) is the most widely used marker for GFR, which is related directly to urine creatinine (U_{Cr}) excretion and inversely to P_{Cr}. On the basis of this relationship (with some important caveats, as discussed below), GFR will fall in roughly inverse proportion to the rise in P_{Cr}. Failure to account for GFR reductions in drug dosing can lead to significant morbidity and death from drug toxicities (e.g., digoxin, aminoglycosides). In the outpatient setting, P_{Cr} serves as an estimate for GFR (although much less accurate; see below). In patients with chronic progressive renal disease, there is an approximately linear relationship between $1/P_{Cr}$ (*y* axis) and time (*x* axis). The slope of that line will remain constant for an individual; when values deviate, an investigation for a superimposed acute process (e.g., volume depletion, drug reaction) should be initiated. Signs and symptoms of uremia develop at significantly different levels of P_{Cr}, depending on the patient (size, age, and sex), underlying renal disease, existence of concurrent diseases, and true GFR. Generally, patients do not develop symptomatic uremia until renal insufficiency is severe (GFR <15 mL/min).

A significantly reduced GFR (either acute or chronic) is usually reflected in a rise in P_{Cr}, leading to retention of nitrogenous waste products (defined as azotemia) such as urea. Azotemia may result from reduced renal perfusion, intrinsic renal disease, or postrenal processes (ureteral obstruction; see below and Fig. 61-1). Precise determination of GFR is problematic, as both commonly measured indices (urea and creatinine) have characteristics that affect their accuracy as markers of clearance. Urea clearance may underestimate GFR significantly because of urea reabsorption by the tubule. In contrast, creatinine is derived from muscle metabolism of creatine, and its generation varies little from day to day.

Creatinine clearance (CrCl), an approximation of GFR, is measured from plasma and urinary creatinine excretion rates for a defined period (usually 24 h) and is expressed in milliliters per minute: $CrCl = (U_{vol} \times U_{Cr})/(P_{Cr} \times T_{min})$. Creatinine is useful for estimating GFR because it is a small, freely filtered solute that is not reabsorbed by the tubules. P_{Cr} levels can increase acutely from

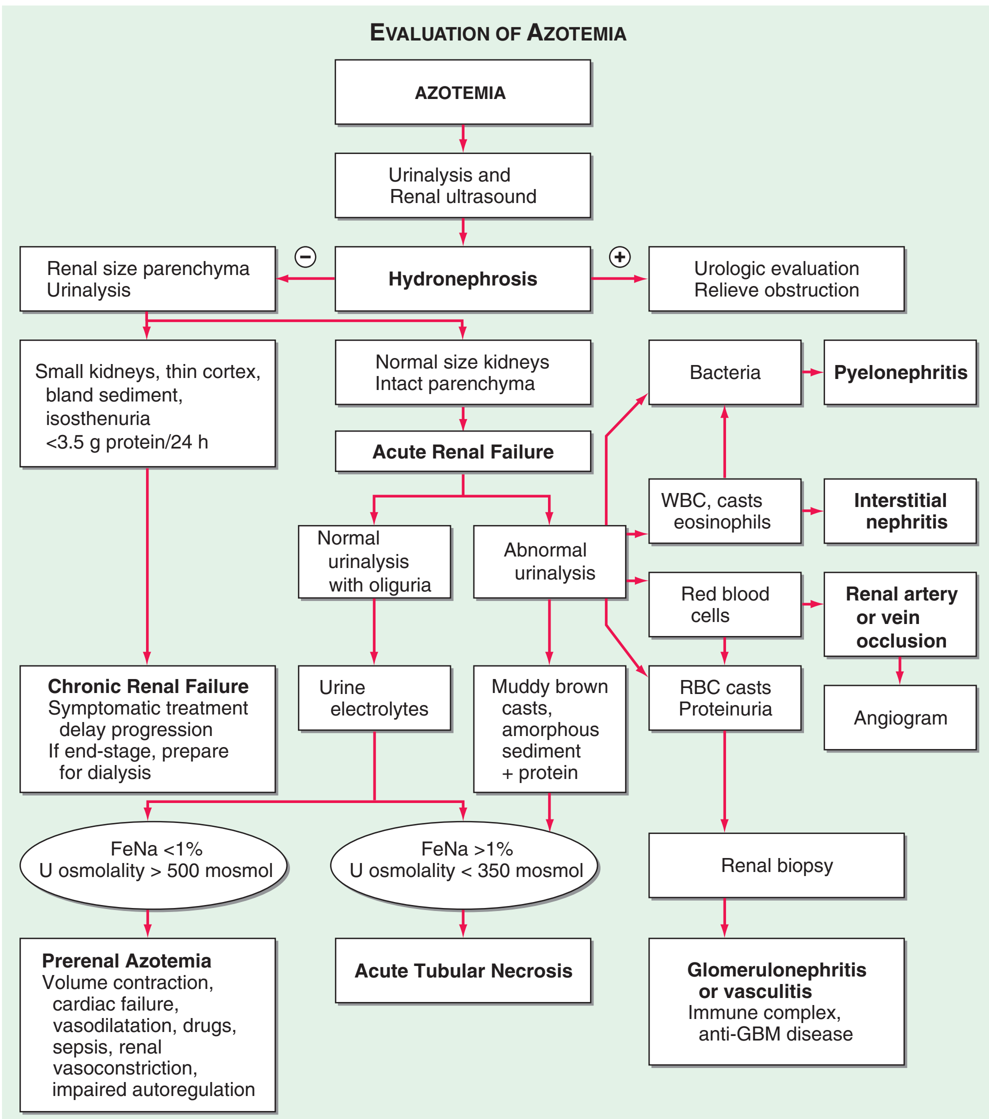

FIGURE 61-1 Approach to the patient with azotemia. FeNa, fractional excretion of sodium; GBM, glomerular basement membrane; RBC, red blood cell; WBC, white blood cell.