prostaglandins, and regulating vitamin D metabolism. The physiologic mechanisms that the kidney has developed to carry out these functions require a high degree of structural complexity.

Renal diseases are responsible for a great deal of morbidity and mortality. When last surveyed in 2009, more than 570,000 Americans had end-stage renal disease (ESRD), of whom two thirds are maintained on dialysis, at a cost of approximately $42.5 billion. The 1-year mortality rate of ESRD, when the enhanced risk for cardiovascular disease conferred by ESRD is considered, exceeds that of most newly diagnosed cancers. Acute kidney injury occurs in more than 2 million people worldwide, and is a major risk factor for the development of chronic kidney disease (CKD) and ESRD. In addition, millions of people are affected annually by nonfatal kidney diseases, most notably infections of the kidney or lower urinary tract, kidney stones, and urinary obstruction. The availability of dialysis and the success of renal transplantation have improved the outlook for patients.

The study of kidney diseases is facilitated by dividing them into those that affect the four basic morphologic components: glomeruli, tubules, interstitium, and blood vessels. This approach is useful, since the early manifestations of disease affecting each of these components tend to be distinct. Further, some components seem to be more vulnerable to specific forms of renal injury; for example, **most glomerular diseases are immunologically mediated, whereas tubular and interstitial disorders are frequently caused by toxic or infectious agents**. However, some disorders affect more than one structure, and the anatomic and functional interdependence of the components of the kidney means that damage to one almost always secondarily affects the others. Primary disorders of the blood vessels, for example, inevitably affect all the structures supplied by these vessels. Severe glomerular damage impairs the flow through the peritubular vascular system; conversely, tubular destruction, by increasing intraglomerular pressure, may induce glomerular injury. Thus, whatever the origin, all forms of chronic kidney disease ultimately damage all four components of the kidney, culminating in what has been called *end-stage kidneys*. The functional reserve of the kidney is large, and much damage may occur before there is evident functional impairment. For these reasons the early signs and symptoms are of particular clinical importance.

Clinical Manifestations of Renal Diseases

The clinical manifestations of renal disease can be grouped into reasonably well-defined syndromes. Some are unique to glomerular diseases, and others are present in diseases that affect any one of the components.

- *Azotemia* is a biochemical abnormality that refers to an elevation of blood urea nitrogen (BUN) and creatinine levels, and is related largely to a decreased glomerular filtration rate (GFR). Azotemia is a consequence of many renal disorders, but it also arises from extrarenal disorders. It is a typical feature of both acute and chronic kidney injury. *Prerenal azotemia* is encountered when there is hypoperfusion of the kidneys (e.g., hypotension or excessive fluid losses from any cause, or if the effective intravascular volume is decreased due to shock, volume depletion, congestive heart failure or cirrhosis of the liver) that impairs renal function in the absence of parenchymal damage. *Postrenal azotemia* is seen whenever urine flow is obstructed distal to the kidney. Relief of the obstruction is followed by correction of the azotemia.

  When azotemia becomes associated with a constellation of clinical signs and symptoms and biochemical abnormalities, it is termed *uremia*. Uremia is characterized not only by failure of renal excretory function but also by a host of metabolic and endocrine alterations resulting from renal damage. Uremic patients frequently manifest secondary involvement of the gastrointestinal system (e.g., uremic gastroenteritis), peripheral nerves (e.g., peripheral neuropathy), and heart (e.g., uremic fibrinous pericarditis).
- *Nephritic syndrome* is a clinical entity caused by glomerular disease and is dominated by the acute onset of either grossly visible hematuria (red blood cells in urine) or microscopic hematuria with dysmorphic red cells and red cell casts on urinalysis, diminished GFR, mild to moderate proteinuria, and hypertension. It is the classic presentation of acute poststreptococcal glomerulonephritis. *Rapidly progressive glomerulonephritis* is characterized as a nephritic syndrome with rapid decline in GFR (within hours to days).
- The *nephrotic syndrome*, also due to glomerular disease, is characterized by heavy proteinuria (more than 3.5 gm/day), hypoalbuminemia, severe edema, hyperlipidemia, and lipiduria (lipid in the urine).
- *Asymptomatic hematuria or proteinuria*, or a combination of these two, is usually a manifestation of subtle or mild glomerular abnormalities.
- *Acute kidney injury* is characterized by rapid decline in GFR (within hours to days), with concurrent dysregulation of fluid and electrolyte balance, and retention of metabolic waste products normally excreted by the kidney including urea and creatinine. In its most severe forms, it is manifested by *oliguria* or *anuria* (reduced or no urine flow). It can result from glomerular, interstitial, vascular or acute tubular injury.
- *Chronic kidney disease* (previously called chronic renal failure) is defined as the presence of a diminished GFR that is persistently less than 60 mL/minute/1.73 m^2 for at least 3 months, from any cause, and/or persistent albuminuria. It may present with clinically silent decline in renal excretory function in milder forms, and in more severe cases, by prolonged symptoms and signs of uremia. It is the end result of all chronic renal parenchymal diseases.
- *In end-stage renal disease (ESRD)* the GFR is less than 5% of normal; this is the terminal stage of uremia.
- *Renal tubular defects* are dominated by polyuria (excessive urine formation), nocturia, and electrolyte disorders (e.g., metabolic acidosis). They are the result of diseases that either directly affect tubular structures (e.g., the nephronophthisis-medullary cystic disease complex) or cause defects in specific tubular functions. The latter can be inherited (e.g., familial nephrogenic