gradient ("diffusive" clearance) and/or along with the movement of plasma water ("convective" clearance). The choice of modality is often dictated by the immediate availability of technology and the expertise of medical staff. Peritoneal dialysis is performed through a temporary intraperitoneal catheter. It is rarely used in the United States for AKI in adults but has enjoyed widespread use internationally, particularly when hemodialysis technology is not available. Dialysate solution is instilled into and removed from the peritoneal cavity at regular intervals in order to achieve diffusive and convective clearance of solutes across the peritoneal membrane; ultrafiltration of water is achieved by the presence of an osmotic gradient across the peritoneal membrane achieved by high concentrations of dextrose in the dialysate solution. Because of its continuous nature, it is often better tolerated than intermittent procedures like hemodialysis in hypotensive patients. Peritoneal dialysis may not be sufficient for hypercatabolic patients due to inherent limitations in dialysis efficacy.

Hemodialysis can be used intermittently or continuously and can be done through convective clearance, diffusive clearance, or a combination of the two. Vascular access is through the femoral, internal jugular, or subclavian veins. Hemodialysis is an intermittent procedure that removes solutes through diffusive and convective clearance. Hemodialysis is typically performed 3–4 h per day, three to four times per week, and is the most common form of renal replacement therapy for AKI. One of the major complications of hemodialysis is hypotension, particularly in the critically ill.

Continuous intravascular procedures were developed in the early 1980s to treat hemodynamically unstable patients without inducing the rapid shifts of volume, osmolarity, and electrolytes characteristic of intermittent hemodialysis. Continuous renal replacement therapy (CRRT) can be performed by convective clearance (continuous venovenous hemofiltration [CVVH]), in which large volumes of plasma water (and accompanying solutes) are forced across the semipermeable membrane by means of hydrostatic pressure; the plasma water is then replaced by a physiologic crystalloid solution. CRRT can also be performed by diffusive clearance (continuous venovenous hemodialysis [CVVHD]), a technology similar to hemodialysis except at lower blood flow and dialysate flow rates. A hybrid therapy combines both diffusive and convective clearance (continuous venovenous hemodiafiltration [CVVHDF]). To achieve some of the advantages of CRRT without the need for 24-h staffing of the procedure, some physicians favor slow low-efficiency dialysis (SLED) or extended daily dialysis (EDD). In this therapy, blood flow and dialysate flow are higher than in CVVHD, but the treatment time is reduced to 12 h or less.

The optimal dose of dialysis for AKI is not clear. Daily intermittent hemodialysis and high-dose CRRT do not confer a demonstrable survival or renal recovery advantage, but care should be taken to avoid undertreatment. Studies have failed to show that continuous therapies are superior to intermittent therapies. If available, CRRT is often preferred in patients with severe hemodynamic instability, cerebral edema, or significant volume overload.

OUTCOME AND PROGNOSIS

The development of AKI is associated with a significantly increased risk of in-hospital and long-term mortality, longer length of stay, and increased costs. Prerenal azotemia, with the exception of the cardiorenal and hepatorenal syndromes, and postrenal azotemia carry a better prognosis than most cases of intrinsic AKI. The kidneys may recover even after severe, dialysis-requiring AKI. Survivors of an episode of AKI requiring temporary dialysis, however, are at extremely high risk for progressive CKD, and up to 10% may develop end-stage renal disease. Postdischarge care under the supervision of a nephrologist for aggressive secondary prevention of kidney disease is prudent. Patients with AKI are more likely to die prematurely after they leave the hospital even if their kidney function has recovered.

335 Chronic Kidney Disease

Joanne M. Bargman, Karl Skorecki

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). Figure 335-1 provides a recently updated classification, in which stages of CKD are stratified by both estimated GFR and the degree of albuminuria, in order to predict risk of progression of CKD. Previously, CKD had been staged solely by the GFR. However, the risk of worsening of kidney function is closely linked to the amount of albuminuria, and so it has been incorporated into the classification.

The pathophysiologic processes, adaptations, clinical presentations, assessment, and therapeutic interventions associated with CKD will be the focus of this chapter. The dispiriting term *end-stage renal disease* represents a stage of CKD where the accumulation of toxins, fluid, and electrolytes normally excreted by the kidneys results in the *uremic syndrome*. This syndrome leads to death unless the toxins are removed by renal replacement therapy, using dialysis or kidney transplantation. These interventions are discussed in Chaps. 336 and 337. *End-stage renal disease* will be supplanted in this chapter by the term *stage 5 CKD*.

PATHOPHYSIOLOGY OF CHRONIC KIDNEY DISEASE

The pathophysiology of CKD involves two broad sets of mechanisms of damage: (1) initiating mechanisms specific to the underlying etiology (e.g., genetically determined abnormalities in kidney development or integrity, immune complex deposition and inflammation in certain types of glomerulonephritis, or toxin exposure in certain diseases of the renal tubules and interstitium) and (2) a set of progressive mechanisms, involving hyperfiltration and hypertrophy of the remaining viable nephrons, that are a common consequence following long-term reduction of renal mass, irrespective of underlying etiology (Chap. 333e). The responses to reduction in nephron number are mediated by vasoactive hormones, cytokines, and growth factors. Eventually, these short-term adaptations of hypertrophy and hyperfiltration become maladaptive as the increased pressure and flow within the nephron predisposes to distortion of glomerular architecture, abnormal podocyte function, and disruption of the filtration barrier leading to sclerosis and dropout of the remaining nephrons (Fig. 335-2). Increased intrarenal activity of the renin-angiotensin system (RAS) appears to contribute both to the initial adaptive hyperfiltration and to the subsequent maladaptive hypertrophy and sclerosis. This process explains why a reduction in renal mass from an isolated insult may lead to a progressive decline in renal function over many years (Fig. 335-3).

IDENTIFICATION OF RISK FACTORS AND STAGING OF CKD

It is important to identify factors that increase the risk for CKD, even in individuals with normal GFR. Risk factors include small for gestation birth weight, childhood obesity, hypertension, diabetes mellitus, autoimmune disease, advanced age, African ancestry, a family history of kidney disease, a previous episode of acute kidney injury, and the presence of proteinuria, abnormal urinary sediment, or structural abnormalities of the urinary tract.

Many rare inherited forms of CKD follow a Mendelian inheritance pattern, often as part of a systemic syndrome, with the most common in this category being autosomal dominant polycystic kidney disease. In addition, recent research in the genetics of predisposition to common complex diseases (Chap. 82) has revealed DNA sequence variants at a number of genetic loci that are associated with common forms of CKD. A striking example is the finding of allelic versions of the *APOL1* gene, of West African population ancestry, which contributes to the several-fold higher frequency of certain common etiologies of nondiabetic CKD (e.g., focal segmental glomerulosclerosis) observed among African and Hispanic Americans. The prevalence in West African populations seems to have arisen as an evolutionary adaptation conferring protection from tropical pathogens. As in other common diseases