CHAPTER

24

Renal Failure

Renal failure is a condition in which the kidneys fail to remove metabolic end-products from the blood and regulate the fluid, electrolyte, and pH balance of the extracellular fluids. The underlying cause may be renal disease, systemic disease, or urologic defects of nonrenal origin. Renal failure can occur as an acute or a chronic disorder. Acute renal failure is abrupt in onset and often is reversible if recognized early and treated appropriately. In contrast, chronic renal failure is the end result of irreparable damage to the kidneys. It develops slowly, usually over the course of a number of years.

ACUTE RENAL FAILURE

Acute renal failure represents a rapid decline in renal function sufficient to increase blood levels of nitrogenous wastes and impair fluid and electrolyte balance. It is a common threat to seriously ill persons in intensive care units, with a mortality rate ranging from 42% to 88%.[1] Although treatment methods such as dialysis and renal replacement methods are effective in correcting life-threatening fluid and electrolyte disorders, the mortality rate associated with acute renal failure has not changed substantially since the 1960s.[2,3] This probably is because acute renal failure is seen more often in older persons than before, and because it frequently is superimposed on other life-threatening conditions, such as trauma, shock, and sepsis.

The most common indicator of acute renal failure is *azotemia*, an accumulation of nitrogenous wastes (urea nitrogen, uric acid, and creatinine) in the blood. In acute renal failure the glomerular filtration rate (GFR) is decreased. As a result, excretion of nitrogenous wastes is reduced and fluid and electrolyte balance cannot be maintained. Persons with acute renal failure often are asymptomatic, and the condition is diagnosed by observation of elevations in blood urea nitrogen (BUN) and creatinine.

Types of Acute Renal Failure

Acute renal failure can be caused by several types of conditions, including a decrease in blood flow without ischemic injury; ischemic, toxic, or obstructive tubular injury; and obstruction of urinary tract outflow. The causes of acute renal failure commonly are categorized as prerenal (55% to 60%), postrenal

KEY CONCEPTS

ACUTE RENAL FAILURE

- Acute renal failure is caused by conditions that produce an acute shutdown in renal function.
- It can result from decreased blood flow to the kidney (prerenal failure), disorders that interfere with the elimination of urine from the kidney (postrenal failure), or disorders that disrupt the structures in the kidney (intrinsic or intrarenal failure).
- Acute renal failure, although it causes an accumulation of products normally cleared by the kidney, is a reversible process if the factors causing the condition can be corrected.

(<5%), and intrinsic (35% to 40%).[3] Causes of renal failure within these categories are summarized in Chart 24-1.

Prerenal Failure

Prerenal failure, the most common form of acute renal failure, is characterized by a marked decrease in renal blood flow. It is reversible if the cause of the decreased renal blood flow can be identified and corrected before kidney damage occurs. Causes of prerenal failure include profound depletion of vascular volume (*e.g.*, hemorrhage, loss of extracellular fluid volume), impaired perfusion caused by heart failure and cardiogenic shock, and decreased vascular filling because of increased vascular capacity (*e.g.*, anaphylaxis or sepsis). Elderly persons are particularly at risk because of their predisposition to hypovolemia and their high prevalence of renal vascular disorders.

Some vasoactive mediators, drugs, and diagnostic agents stimulate intense intrarenal vasoconstriction and induce glomerular hypoperfusion and prerenal failure.[3] Examples include hypercalcemia, endotoxins, and radiocontrast agents such as those used for cardiac catheterization.[3] Many of these agents also cause acute tubular necrosis (discussed later). In addition, several commonly used classes of drugs impair renal adaptive mechanisms and can convert compensated renal hypoperfusion into prerenal failure. Angiotensin-converting enzyme (ACE) inhibitors reduce the effects of renin on renal blood flow; when combined with diuretics, they may cause prerenal failure in persons with decreased blood flow caused by large-vessel or small-vessel renal vascular disease. Prostaglandins have a vasodilatory effect on renal blood vessels. Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce renal blood flow through inhibition of prostaglandin synthesis. In some persons with diminished renal perfusion, NSAIDs can precipitate prerenal failure.

Normally, the kidneys receive 20% to 25% of the cardiac output.[4] This large blood supply is required to remove metabolic wastes and regulate body fluids and electrolytes. Fortunately, the normal kidney can tolerate relatively large reductions in blood flow before renal damage occurs. As renal blood flow is reduced, the GFR drops, the amount of sodium and other substances that is filtered by the glomeruli is reduced, and the need for energy-dependent mechanisms to reabsorb these substances is reduced. As the GFR and urine output approach zero, oxygen consumption by the kidney approximates that required to keep renal tubular cells alive.[4] When blood flow falls below this level, which is about 20% of normal, ischemic changes occur. Because of their high metabolic rate, the tubular epithelial cells are most vulnerable to ischemic injury. Improperly treated, prolonged renal hypoperfusion can lead to ischemic tubular necrosis with significant morbidity and mortality.

Acute renal failure is manifested by a sharp decrease in urine output and a disproportionate elevation of BUN in relation to serum creatinine levels. The kidney normally responds to a decrease in the GFR with a decrease in urine output. An early sign of prerenal failure is a sharp decrease in urine output. BUN levels also depend on the GFR. A low GFR allows more time for small particles such as urea to be reabsorbed into the blood. Creatinine, which is larger and nondiffusible, remains in the tubular fluid, and the total amount of creatinine that is filtered, although small, is excreted in the urine. Thus, there also is a disproportionate elevation in the ratio of BUN to serum creatinine to greater than 20:1 (normal, approximately 10:1).

CHART 24-1 Causes of Acute Renal Failure

Prerenal

Hypovolemia
- Hemorrhage
- Dehydration
- Excessive loss of gastrointestinal tract fluids
- Excessive loss of fluid due to burn injury

Decreased vascular filling
- Anaphylactic shock
- Septic shock

Heart failure and cardiogenic shock

Decreased renal perfusion due to vasoactive mediators, drugs, diagnostic agents

Intrinsic or Intrarenal

Acute tubular necrosis
- Prolonged renal ischemia
- Exposure to nephrotoxic drugs, heavy metals, and organic solvents
- Intratubular obstruction resulting from hemoglobinuria, myoglobinuria, myeloma light chains, or uric acid casts
- Acute renal disease (acute glomerulonephritis, pyelonephritis)

Postrenal

Bilateral ureteral obstruction

Bladder outlet obstruction

Postrenal Failure

Postrenal failure results from obstruction of urine outflow from the kidneys. The obstruction can occur in the ureter (*i.e.*, calculi and strictures), bladder (*i.e.*, tumors or neurogenic bladder), or urethra (*i.e.*, prostatic hypertrophy). Prostatic hyperplasia is the most common underlying problem. Because both ureters must be occluded to produce renal failure, obstruction of the bladder rarely causes acute renal failure unless one of the kidneys already is damaged or a person has only one kidney. The treatment of acute postrenal failure consists of treat-

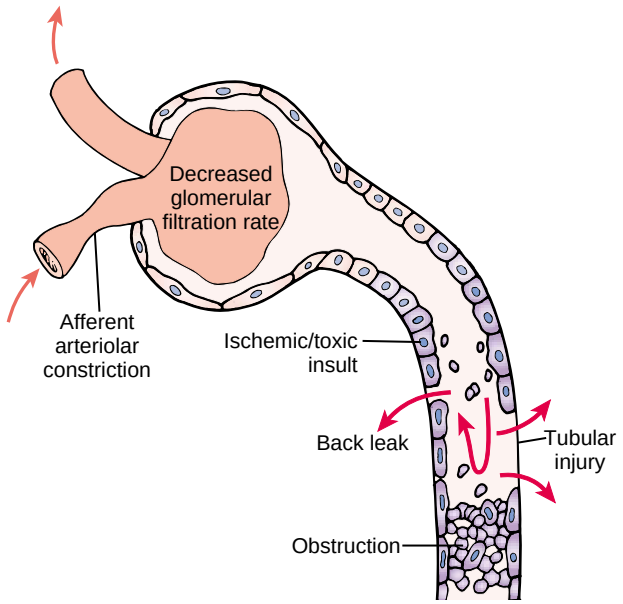
ing the underlying cause of obstruction so that urine flow can be re-established before permanent nephron damage occurs.

Intrinsic Renal Failure

Intrinsic or intrarenal renal failure results from conditions that cause damage to structures within the kidney—glomerular, tubular, or interstitial. Injury to the tubules is most common and often is ischemic or toxic in origin. The major causes of intrarenal failure are ischemia associated with prerenal failure, toxic insult to the tubular structures of the nephron, and intratubular obstruction. Acute glomerulonephritis and acute pyelonephritis also are intrarenal causes of acute renal failure.

Acute Tubular Necrosis. Acute tubular necrosis (ATN) is characterized by destruction of tubular epithelial cells with acute suppression of renal function (Fig. 24-1).[3,5] It is the most common cause of intrinsic renal failure. ATN can be caused by a variety of conditions, including acute tubular damage caused by ischemia, the nephrotoxic effects of drugs, tubular obstruction, and toxins from a massive infection. The tubular injury that occurs in ATN frequently is reversible. The process depends on the recovery of the injured cells, removal of the necrotic cells and intratubular casts, and regeneration of renal cells to restore the normal continuity of the tubular epithelium. However, if the ischemia is severe enough to cause cortical necrosis, irreversible renal failure occurs.

Ischemic ATN occurs most frequently in persons who have major surgery, severe hypovolemia, overwhelming sepsis, trauma, and burns.[3] Sepsis produces ischemia by provoking a combination of systemic vasodilation and intrarenal hypoperfusion. In addition, sepsis results in the generation of toxins that sensitize renal tubular cells to the damaging effects of ischemia. ATN complicating trauma and burns frequently is multifactorial in origin and caused by the combined effects of hypovolemia and myoglobin or other toxins released from damaged tissue. In contrast to prerenal failure, the GFR does not improve with the restoration of renal blood flow in acute renal failure caused by ischemic ATN.



■ **FIGURE 24-1** ■ Pathogenesis of acute tubular necrosis. Sloughing and necrosis of tubular epithelial cells leading to obstruction and increased intraluminal pressure, which reduces glomerular filtration. Afferent arteriolar vasoconstriction, caused in part by tubuloglomular feedback, results in decreased glomerular capillary filtration pressure. Tubular injury and increased intraluminal pressure cause fluid to move from the tubular lumen into the interstitium (backleak). (Modified from Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 901]. Philadelphia: Lippincott Williams & Wilkins)

Nephrotoxic ATN complicates the administration of or exposure to many structurally diverse drugs and other toxic agents. Nephrotoxic agents cause renal injury by inducing varying combinations of renal vasoconstriction, direct tubular damage, or intratubular obstruction. The kidney is particularly vulnerable to nephrotic injury because of its rich blood supply and ability to concentrate toxins to high levels in the medullary portion of the kidney. In addition, the kidney is an important site for metabolic processes that transform relatively harmless agents into toxic metabolites. Pharmacologic agents that are directly toxic to the renal tubule include antimicrobial agents such as the aminoglycosides, chemotherapeutic agents such as cisplatin and ifosfamide, and the radiocontrast agents used during cardiac catheterization and other diagnostic procedures.[5,6] Radiocontrast media-induced nephrotoxicity is thought to result from direct tubular toxicity and renal ischemia.[7] The risk of renal damage caused by radiocontrast media is greatest in elderly persons, in persons with diabetes mellitus, and in persons who, for various reasons, are susceptible to kidney disease.[3] Heavy metals (*e.g.*, lead, mercury) and organic solvents (*e.g.*, carbon tetrachloride, ethylene glycol) are other nephrotoxic agents.

Myoglobin, hemoglobin, uric acid, and myeloma light chains are the most common cause of ATN attributable to intratubular obstruction. Deposits of immunoglobulins and urine acid crystals usually are seen in the setting of widespread malignancy or massive tumor destruction by therapeutic agents.[3] Hemoglobinuria results from blood transfusion reactions and other hemolytic crises. Skeletal and cardiac muscles contain myoglobin, which accounts for their red color. Myoglobin corresponds to hemoglobin in function, serving as an oxygen reservoir in the muscle fibers. Myoglobin normally is not found in the serum or urine. Myoglobinuria most commonly results from muscle trauma but may result from extreme exertion, hyperthermia, sepsis, prolonged seizures, potassium or phosphate depletion, and alcoholism or drug abuse. Both myoglobin and hemoglobin discolor the urine, which may range from the color of tea to red, brown, or black.

Clinical Course

The course of acute renal failure can be divided into three phases: the *onset* or *initiating phase*, the maintenance phase, and the recovery or convalescent phase.[3] The onset or initiating phase, which lasts hours or days, is the time from the onset of the precipitating event (*e.g.*, ischemic phase of prerenal failure or toxin exposure) until tubular injury occurs.

The *maintenance phase* is characterized by a marked decrease in the GFR, causing sudden retention of endogenous metabolites such as urea, potassium, sulfate, and creatinine that normally are cleared by the kidneys. The urine output usually is lowest at this point. Fluid retention gives rise to edema, water

intoxication, and pulmonary congestion. If the period of oliguria is prolonged, hypertension frequently develops and with it signs of uremia. When untreated, the neurologic manifestations of uremia progress from neuromuscular irritability to seizures, somnolence, coma, and death. Hyperkalemia usually is asymptomatic until serum levels of potassium rise above 6.0 to 6.5 mEq/L, at which point characteristic electrocardiographic changes and symptoms of muscle weakness are seen.

The *recovery phase* is the period during which repair of renal tissue takes place. Its onset usually is heralded by a gradual increase in urine output and a fall in serum creatinine, indicating that the nephrons have recovered to the point where urine excretion is possible. Diuresis often occurs before renal function has fully returned to normal. Consequently, BUN and serum creatinine, potassium, and phosphate levels may remain elevated or continue to rise even though urine output is increased. In some cases, the diuresis may result from impaired nephron function and may cause excessive loss of water and electrolytes. Eventually, renal tubular function is restored with improvement in urine concentrating ability. At about the same time, the BUN and creatinine begin to return to normal. In some cases, mild to moderate kidney damage persists.

Diagnosis and Treatment

Given the high morbidity and mortality rates associated with acute renal failure, attention should be focused on prevention and early diagnosis. This includes assessment measures to identify persons at risk for the development of acute renal failure, including those with pre-existing renal insufficiency and diabetes. Elderly persons are susceptible to all forms of acute renal failure because of the effects of aging on renal reserve.

Careful observation of urine output is essential for persons at risk for the development of acute renal failure. Urine output and urine osmolality or specific gravity should be carefully monitored. One of the earliest manifestations of tubular damage is the inability to concentrate the urine. Further diagnostic information that can be obtained from the urinalysis includes evidence of proteinuria, hemoglobinuria, and casts or crystals in the urine. Blood tests for BUN and creatinine provide information regarding the ability to remove nitrogenous wastes from the blood.

A major concern in the treatment of acute renal failure is identifying and correcting the cause (*e.g.*, improving renal perfusion, discontinuing nephrotoxic drugs). Fluids are carefully regulated in an effort to maintain normal fluid volume and electrolyte concentrations. Adequate caloric intake is needed to prevent the breakdown of body proteins, which increases the need for elimination of nitrogenous wastes. Parenteral hyperalimentation may be used for this purpose. Because secondary infections are a major cause of death in persons with acute renal failure, constant effort is needed to prevent and treat such infections.

Dialysis or continuous renal replacement therapy (CRRT) may be indicated when nitrogenous wastes and the water and electrolyte balance cannot be kept under control by other means.

In summary, acute renal failure is an acute, reversible suppression of kidney function. It is a common threat to seriously ill persons in intensive care units and is associated with a high mortality rate. Acute renal failure is characterized by an accumulation of nitrogenous wastes in the blood (*i.e.*, azotemia) and alterations in body fluids and electrolytes. Acute renal failure is classified as prerenal, postrenal, or intrarenal in origin. Prerenal failure is caused by decreased blood flow to the kidneys; postrenal failure by obstruction to urine output; and intrinsic renal failure by disorders in the kidney itself. ATN, caused by ischemia or nephrotoxic agents, is a common cause of acute intrinsic renal failure. Acute renal failure typically progresses through three phases: the initiation phase, during which tubular injury is induced; the maintenance phase, during which the GFR falls, nitrogenous wastes accumulate, and urine output decreases; and the recovery or reparative phase, during which the GFR, urine output, and blood levels of nitrogenous wastes return to normal.

Because of the high morbidity and mortality rates associated with acute renal failure, identification of persons at risk is important to clinical decision making. Acute renal failure often is reversible, making early identification and correction of the underlying cause (*e.g.*, improving renal perfusion, discontinuing nephrotoxic drugs) important. Treatment includes the judicious administration of fluids and dialysis or CRRT.

CHRONIC RENAL FAILURE

Unlike acute renal failure, chronic renal failure represents progressive and irreversible destruction of kidney structures. As recently as 1965, many patients with chronic renal failure pro-

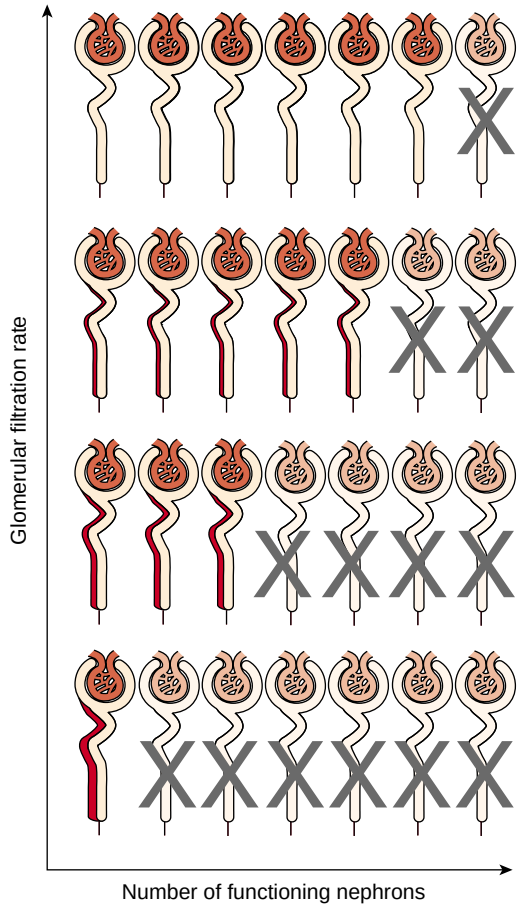
KEY CONCEPTS

CHRONIC RENAL FAILURE

- Chronic renal failure represents the end result of conditions that greatly reduce renal function by destroying renal nephrons and producing a marked decrease in the glomerular filtration rate (GFR).
- Signs of renal failure begin to appear as renal function moves from renal insufficiency (GFR 50% to 20% normal), to renal failure (20% to 5% normal), to end-stage renal disease (<5% normal). When the GFR decreases to less than 5% of normal, dialysis or kidney transplantation is necessary for survival.
- The manifestations of chronic renal failure represent the inability of the kidney to perform its normal functions in terms of regulating fluid and electrolyte balance, controlling blood pressure through fluid volume and the renin-angiotensin system, eliminating nitrogenous and other waste products, governing the red blood cell count through erythropoietin synthesis, and directing parathyroid and skeletal function through phosphate elimination and activation of vitamin D.

gressed to the final stages of the disease and then died. The high mortality rate was associated with limitations in the treatment of renal disease and with the tremendous cost of ongoing treatment. In 1972, federal support began for dialysis and transplantation through a Medicare entitlement program.[8] Technologic advances in renal replacement therapy (*i.e.*, dialysis therapy and transplantation) have improved the outcomes for persons with renal failure. In the United States, there are approximately 400,000 persons with end-stage renal disease who are living today, a product of continued research and advances in treatment methods.[9]

Chronic renal failure can result from a number of conditions that cause permanent loss of nephrons, including diabetes, hypertension, glomerulonephritis, and polycystic kidney disease. Typically, the signs and symptoms of renal failure occur gradually and do not become evident until the disease is far advanced. This is because of the amazing compensatory ability of the kidneys. As kidney structures are destroyed, the remaining nephrons undergo structural and functional hypertrophy, each increasing its function as a means of compensating for those that have been lost (Fig. 24-2). It is only when the few remaining nephrons are destroyed that the manifestations of renal failure become evident.



■ **FIGURE 24-2** ■ Relation of renal function and nephron mass. Each kidney contains 1 million tiny nephrons. A proportional relation exists between the number of nephrons affected by disease and the resulting glomerular filtration rate.

Regardless of cause, chronic renal failure results in progressive deterioration of glomerular filtration, tubular reabsorptive capacity, and endocrine functions of the kidneys. All forms of renal failure are characterized by a reduction in the GFR, reflecting a corresponding reduction in the number of functional nephrons.

Stages of Progression

The rate of nephron destruction differs from case to case, ranging from several months to many years. The progression of chronic renal failure usually occurs in four stages: diminished renal reserve, renal insufficiency, renal failure, and end-stage renal disease.[5]

Diminished Renal Reserve

Diminished renal reserve occurs when the GFR drops to approximately 50% of normal. At this point, the serum BUN and creatinine levels still are normal, and no symptoms of impaired renal function are evident. This is supported by the fact that many persons survive an entire lifetime with only one kidney. Because of the diminished reserve, the risk for development of azotemia increases with an additional renal insult, such as that caused by nephrotoxic drugs.

Renal Insufficiency

Renal insufficiency represents a reduction in the GFR to 20% to 50% of normal. During this stage, azotemia, anemia, and hypertension appear. Signs and symptoms of renal insufficiency do not begin to appear until more than 50% of the function in both kidneys is lost. As nephrons are destroyed, the remaining nephrons compensate for those that are lost by filtering more solute particles from the blood. Because the solute particles are osmotically active, they cause additional water to be lost in the urine. One of the earliest symptoms of renal insufficiency is isosthenuria or polyuria with urine that is almost isotonic with plasma.[4]

Conservative treatment during this stage includes measures to retard the deterioration of renal function and assist the body in managing the effects of impaired function. Because the kidneys have difficulty eliminating the waste products of protein metabolism, a restricted-protein diet usually produces fewer symptoms and slows progression of renal failure. The few remaining nephrons that constitute the functional reserve of the kidneys can be easily disrupted; at that point, renal failure progresses rapidly.

Renal Failure

Renal failure develops when the GFR is less than 20% of normal. At this point, the kidneys cannot regulate volume and solute composition, and edema, metabolic acidosis, and hyperkalemia develop. These alterations affect other body systems to cause neurologic, gastrointestinal, and cardiovascular manifestations.

End-Stage Renal Disease

End-stage renal disease (ESRD) occurs when the GFR is less than 5% of normal. Histologic findings of an end-stage kidney include a reduction in renal capillaries and scarring in the glomeruli. Atrophy and fibrosis are evident in the tubules. The mass of the kidneys usually is reduced. At this final phase of

renal failure, treatment with dialysis or transplantation is necessary for survival.

Clinical Manifestations

The clinical manifestations of renal failure include alterations in water, electrolyte, and acid-base balance; mineral and skeletal disorders; anemia and coagulation disorders; hypertension and alterations in cardiovascular function; gastrointestinal disorders; neurologic complications; disorders of skin integrity; and immunologic disorders (Fig. 24-3). *Uremia*, which literally means "urine in the blood," is the term used to describe the clinical manifestations of ESRD. Uremia differs from azotemia, which merely indicates the accumulation of nitrogenous wastes in the blood and can occur without symptoms.

There currently are four target populations that comprise the entire population of persons with chronic renal failure: persons with chronic renal insufficiency, those with ESRD being treated with hemodialysis, those being treated with peritoneal dialysis, and renal transplant recipients. The manifestations of renal failure are determined largely by the extent of renal function that is present (*e.g.*, renal insufficiency, ESRD), coexisting disease conditions, and the type of renal replacement therapy the person is receiving.

Accumulation of Nitrogenous Wastes

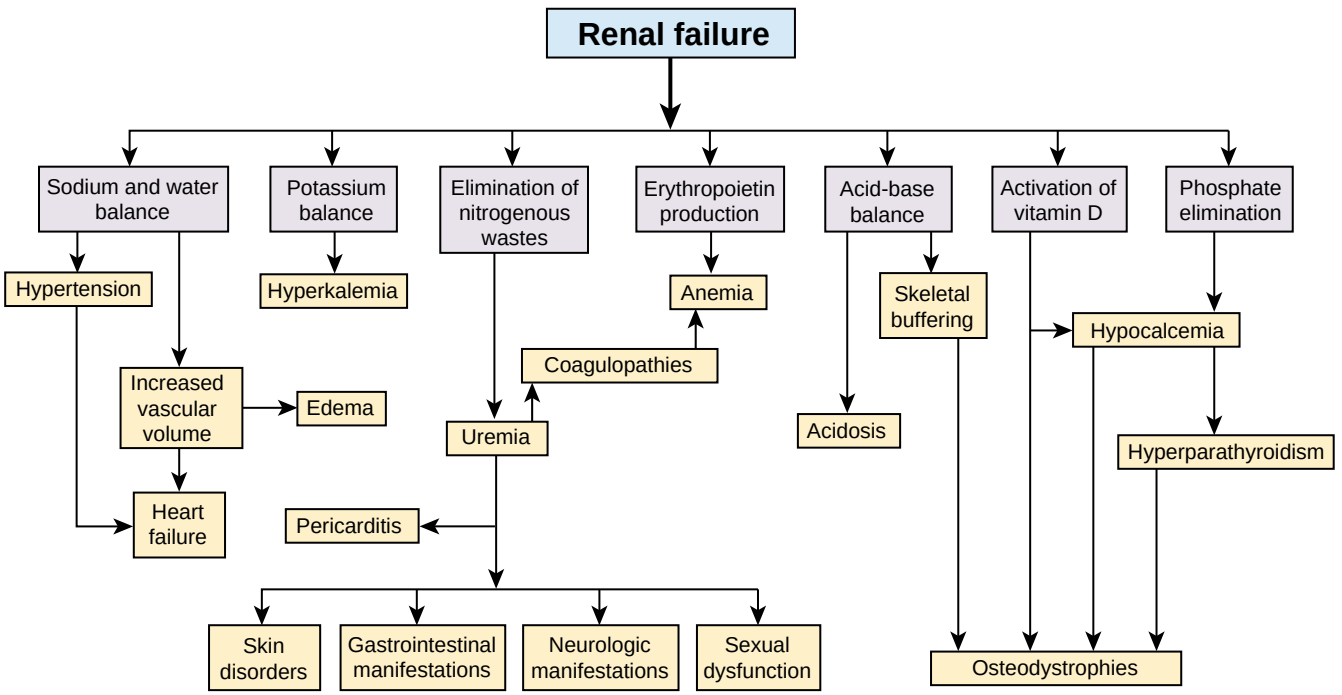
The accumulation of nitrogenous wastes is an early sign of renal failure, usually occurring before other symptoms become evident. Urea is one of the first nitrogenous wastes to accumulate in the blood, and the BUN level becomes increasingly elevated as renal failure progresses. The normal concentration of urea in the plasma is usually less than 20 mg/dL. In renal failure, this level may rise to as high as 800 mg/dL.

Creatinine, a by-product of muscle metabolism, is freely filtered in the glomerulus and is not reabsorbed in the renal tubules. Creatinine is produced at a relatively constant rate, and any creatinine that is filtered in the glomerulus is lost in the urine, rather than being reabsorbed into the blood. Thus, serum creatinine can be used as an indirect method for assessing the GFR and the extent of renal damage that has occurred in renal failure. Because creatinine is a by-product of muscle metabolism, serum values vary with age and muscle mass. An increase in serum creatinine to three times its normal value suggests that there is a 75% loss of renal function, and with creatinine levels of 10 mg/dL or more, it can be assumed that 90% of renal function has been lost. (See Chapter 22, Fig. 22-12.)

Disorders of Water, Electrolyte, and Acid-Base Balance

The kidneys function in the regulation of extracellular fluid volume. They do this by either eliminating or conserving sodium and water. Chronic renal failure can produce dehydration or fluid overload, depending on the pathology of the renal disease. In addition to volume regulation, the ability of the kidneys to concentrate the urine is diminished. With early losses in renal function, the specific gravity of the urine becomes fixed (1.008 to 1.012) and varies little from voiding to voiding. Polyuria and nocturia are common.

As renal function declines further, the ability to regulate sodium excretion is reduced. There is impaired ability to adjust to a sudden reduction in sodium intake and poor tolerance of an acute sodium overload. Volume depletion with an accompanying decrease in the GFR can occur with a restricted sodium intake or excess sodium loss caused by diarrhea or vomiting. Salt wasting is a common problem in advanced renal failure because of impaired tubular reabsorption of sodium. Increas-



■ **FIGURE 24-3** ■ Manifestations of renal failure.

ing sodium intake in persons with chronic renal failure often improves the GFR and whatever renal function remains. In patients with associated hypertension, the possibility of increasing blood pressure or production of congestive heart failure often excludes supplemental sodium intake.

Approximately 90% of potassium excretion is through the kidneys. In renal failure, potassium excretion by each nephron increases as the kidneys adapt to a decrease in the GFR. As a result, hyperkalemia usually does not develop until renal function is severely compromised. Because of this adaptive mechanism, it usually is not necessary to restrict potassium intake in patients with chronic renal failure until the GFR has dropped below 5 mL/minute. In persons with ESRD, hyperkalemia often results from the failure to follow dietary potassium restrictions and ingestion of medications that contain potassium, or from an endogenous release of potassium, as in trauma or infection.

The kidneys normally regulate blood pH by eliminating hydrogen ions produced in metabolic processes and regenerating bicarbonate. This is achieved through hydrogen ion secretion, sodium and bicarbonate reabsorption, and the production of ammonia, which acts as a buffer for titratable acids (see Chapter 6). With a decline in renal function, these mechanisms become impaired, and metabolic acidosis results. In chronic renal failure, acidosis seems to stabilize as the disease progresses, probably as a result of the tremendous buffering capacity of bone. However, this buffering action is thought to increase bone resorption and contribute to the skeletal defects present in chronic renal failure.

Mineral Metabolism and Skeletal Disorders

Abnormalities of calcium, phosphate, and vitamin D occur early in the course of chronic renal failure.[10] They involve the renal regulation of serum calcium and phosphate levels, activation of vitamin D, and regulation of parathyroid hormone (PTH) levels.

The regulation of serum phosphate levels requires a daily urinary excretion of an amount equal to that absorbed from the diet. With deteriorating renal function, phosphate excretion is impaired, and as a result, serum phosphate levels rise. At the same time, serum calcium levels fall because serum calcium is inversely regulated in relation to serum phosphate levels (see Chapter 6). The drop in serum calcium, in turn, stimulates PTH release, with a resultant increase in calcium resorption from bone. Most persons with ESRD develop secondary hyperparathyroidism, the result of chronic stimulation of the parathyroid glands. Although serum calcium levels are maintained through increased PTH function, this adjustment is accomplished at the expense of the skeletal system and other body organs.

The kidneys regulate vitamin D activity by converting the inactive form of vitamin D [25(OH) vitamin D_3] to its active form (1,25-OH_2 vitamin D_3). Decreased levels of active vitamin D lead to a decrease in intestinal absorption of calcium with a resultant increase in parathyroid hormone levels. Vitamin D also regulates osteoblast differentiation, thereby affecting bone matrix formation and mineralization.

Skeletal Disorders. The term *renal osteodystrophy* is used to describe the skeletal complications of ESRD.[10,11] Several factors are thought to contribute to the development of renal osteodystrophy, including elevated serum phosphate levels, decreased serum calcium levels, impaired renal activation of vitamin D, and hyperparathyroidism. The skeletal changes that occur with renal failure have been divided into two major types of disorders: high-turnover and low-turnover osteodystrophy.[5] Inherent to both of these conditions is abnormal reabsorption and defective remodeling of bone.

High–bone-turnover osteodystrophy, sometimes referred to as *osteitis fibrosa*,[11] is characterized by increased bone resorption and formation, with bone resorption predominating. The disorder is associated with secondary hyperparathyroidism; altered vitamin D metabolism along with resistance to the action of vitamin D; and impaired regulation of locally produced growth factors and inhibitors. There is an increase in both osteoblast and osteoclast numbers and activity. Although the osteoblasts produce excessive amounts of bone matrix, mineralization fails to keep pace, and there is a decrease in bone density and formation of porous and coarse-fibered bone. Cortical bone is affected more severely than cancellous bone. Marrow fibrosis is another component of osteitis fibrosa; it occurs in areas of increased bone cell activity. In advanced stages of the disorder, cysts may develop in the bone, a condition called *osteitis fibrosa cystica*.[12]

Low–bone-turnover osteodystrophy is characterized by decreased numbers of osteoblasts and low or reduced numbers of osteoclasts, a low rate of bone turnover, and an accumulation of unmineralized bone matrix.[12] There are two forms of low-turnover osteodystrophy: osteomalacia and adynamic osteodystrophy. *Osteomalacia*, sometimes referred to as *renal rickets*, is characterized by a slow rate of bone formation and defects in bone mineralization. Until the 1980s, osteomalacia in ESRD resulted mainly from aluminum intoxication. Aluminum intoxication causes decreased and defective mineralization of bone by existing osteoblasts and more long-term inhibition of osteoblast differentiation. During the 1970s and 1980s, it was discovered that accumulation of aluminum from water used in dialysis and aluminum salts used as phosphate binders caused osteomalacia and adynamic bone disease.[13] This discovery led to a change in the composition of dialysis solutions and substitution of calcium carbonate for aluminum salts as phosphate binders. As a result, the prevalence of osteomalacia in persons with ESRD is declining.

The second type of low-turnover osteodystrophy, *adynamic osteodystrophy*, is characterized by a low number of osteoblasts, the osteoclast number being normal or reduced.[12] In persons with adynamic bone disease, bone remodeling is greatly reduced, and the bone surfaces become hypocellular. Adynamic bone disease is associated with an increased fracture rate. The disease is associated with a "relative hypothyroidism." It has been suggested that hypersecretion of parathyroid hormone may be necessary to maintain normal rates of bone formation in persons with ESRD. Thus, this form of renal osteodystrophy is seen more commonly in persons with ESRD who do not have secondary hyperparathyroidism (*i.e.*, those who have been treated with parathyroidectomy) or have been overtreated with calcium and vitamin D.

The symptoms of renal osteodystrophy, which occur late in the disease, include bone tenderness and muscle weakness. Proximal muscle weakness in the lower extremities is common, making it difficult to get out of a chair or climb stairs.[11] Fractures are more common with low-turnover osteomalacia and adynamic renal bone disease.

Early treatment of hyperphosphatemia and hypocalcemia is important to prevent or slow long-term skeletal complica-

tions.[14] Activated forms of vitamin D and calcium supplements often are used to facilitate intestinal absorption of calcium, increase serum calcium levels, and reduce parathyroid hormone levels. Milk products and other foods high in phosphorus content are restricted in the diet. Oral phosphate-binding agents such as calcium carbonate may be prescribed to decrease absorption of phosphate from the gastrointestinal tract. Aluminum-containing antacids can contribute to the development of osteodystrophy and their use should be avoided except in acute situations.

Hematologic Disorders

Chronic anemia is the most profound hematologic alteration that accompanies renal failure. Anemia first appears when the GFR falls below 40 mL/minute and is present in most persons with ESRD.[15] Several factors contribute to anemia in persons with chronic renal failure, including a erythropoietin deficiency, uremic toxins, and iron deficiency. The kidneys are the primary site for the production of the hormone *erythropoietin*, which controls red blood cell production. The accumulation of uremic toxins further suppresses red cell production in the bone marrow, and the cells that are produced have a shortened life span. Iron is essential for erythropoiesis. Many persons receiving maintenance hemodialysis also are iron deficient because of blood sampling and accidental loss of blood during dialysis. Other causes of iron deficiency include factors such as anorexia and dietary restrictions that limit intake.

When untreated, anemia causes or contributes to weakness, fatigue, depression, insomnia, and decreased cognitive function. There is also increasing concern regarding the physiologic effects of anemia on cardiovascular function. The anemia of renal failure produces a decrease in blood viscosity and a compensatory increase in heart rate. The decreased blood viscosity also exacerbates peripheral vasodilatation and contributes to decreased vascular resistance. Cardiac output increases in a compensatory fashion to maintain tissue perfusion. Echocardiographic studies after initiation of chronic dialysis have shown ventricular dilatation with compensatory left ventricular hypertrophy.[15] Anemia also limits myocardial oxygen supply, particularly in persons with coronary heart disease, leading to angina pectoris and other ischemic events.[16] Thus, anemia, when coupled with hypertension, may be a major contributing factor to the development of left ventricular dysfunction and congestive heart failure in persons with ESRD.

A remarkable advance in medical management of anemia in persons with ESRD occurred with the availability of recombinant human erythropoietin (rhEPO). Secondary benefits of treating anemia with rhEPO, previously attributed to the correction of uremia, include improvement in appetite, energy level, sexual function, skin color, and hair and nail growth, and reduced cold intolerance. Frequent measurements of hematocrit are necessary. Worsening hypertension and seizures have occurred when the hematocrit was raised too suddenly. Because iron deficiency is common among persons with chronic renal failure, iron supplementation often is needed. Iron can be given orally or intravenously. Intravenous iron may be used for treatment of persons who are not able to maintain adequate iron status with oral iron.

Bleeding disorders, which are manifested by epistaxis, menorrhagia, gastrointestinal bleeding, and bruising of the skin and subcutaneous tissues, are also common among persons with chronic renal failure. Although platelet production often is normal in ESRD, platelet function is impaired. Platelet function improves with dialysis but does not completely normalize, suggesting that uremia contributes to the problem. Anemia may accentuate the problem by changing the position of the platelets with respect to the vessel wall. Normally the red cells occupy the center of the bloodstream, and the platelets are in the skimming layer along the endothelial surface. In anemia, the platelets become dispersed, impairing the platelet-endothelial cell adherence needed to initiate hemostasis.[17]

Cardiovascular Disorders

Cardiovascular disorders, including hypertension, left ventricular hypertrophy, and pericarditis, are a major cause of morbidity and mortality in patients with ESRD. Hypertension commonly is an early manifestation of chronic renal failure. The mechanisms that produce hypertension in ESRD are multifactorial; they include an increased vascular volume, elevation of peripheral vascular resistance, decreased levels of renal vasodilator prostaglandins, and increased activity of the renin-angiotensin system.[18] Early identification and aggressive treatment of hypertension has been shown to slow the rate of renal impairment in many types of renal disease. Treatment involves salt and water restriction and the use of antihypertensive medications to control blood pressure. Many persons with renal insufficiency need to take several antihypertensive medications to control blood pressure (see Chapter 16).

The spectrum of heart disease includes left ventricular hypertrophy and ischemic heart disease. People with ESRD tend to have an increased prevalence of left ventricular dysfunction, both with a depressed left ventricular ejection fraction, as in systolic dysfunction, as well as impaired ventricular filling, as in diastolic failure (see Chapter 18).[19] There are multiple factors that lead to development of left ventricular dysfunction, including extracellular fluid overload, shunting of blood through an arteriovenous fistula for dialysis, and anemia. These abnormalities, coupled with the hypertension that often is present, cause increased myocardial work and oxygen demand, with eventual development of heart failure. Coexisting conditions that have been identified as contributing to the burden of cardiovascular disease include anemia, diabetes mellitus, dyslipidemia, and coagulopathies. Anemia, in particular, has been correlated with the presence of left ventricular hypertrophy.

Pericarditis occurs in approximately 20% of persons receiving chronic dialysis.[20] It can result from metabolic toxins associated with the uremic state or from dialysis. The manifestations of uremic pericarditis resemble those of viral pericarditis, with all its complications, including cardiac tamponade (see Chapter 17).

Gastrointestinal Disorders

Anorexia, nausea, and vomiting are common in patients with uremia, along with a metallic taste in the mouth that further depresses the appetite. Early-morning nausea is common. Ulceration and bleeding of the gastrointestinal mucosa may develop, and hiccups are common. A possible cause of nausea and vomiting is the decomposition of urea by intestinal flora, resulting in a high concentration of ammonia. Parathyroid hormone increases gastric acid secretion and contributes to gastrointestinal problems. Nausea and vomiting often

improve with restriction of dietary protein and after initiation of dialysis and disappear after kidney transplantation.

Disorders of Neural Function

Many persons with chronic renal failure have alterations in peripheral and central nervous system function. Peripheral neuropathy, or involvement of the peripheral nerves, affects the lower limbs more frequently than the upper limbs. It is symmetric and affects both sensory and motor function. Neuropathy is caused by atrophy and demyelination of nerve fibers, possibly caused by uremic toxins. Restless legs syndrome is a manifestation of peripheral nerve involvement and can be seen in as many as two thirds of patients on dialysis. This syndrome is characterized by creeping, prickling, and itching sensations that typically are more intense at rest. Temporary relief is obtained by moving the legs. A burning sensation of the feet, which may be followed by muscle weakness and atrophy, is a manifestation of uremia.

The central nervous system disturbances in uremia are similar to those caused by other metabolic and toxic disorders. Sometimes referred to as *uremic encephalopathy*, the condition is poorly understood and may result, at least in part, from an excess of toxic organic acids that alter neural function. Electrolyte abnormalities, such as sodium shifts, also may contribute. The manifestations are more closely related to the progress of the uremic disorder than to the level of the metabolic end-products. Reductions in alertness and awareness are the earliest and most significant indications of uremic encephalopathy. This often is followed by an inability to fix attention, loss of recent memory, and perceptual errors in identifying persons and objects. Delirium and coma occur late in the course; seizures are the preterminal event.

Disorders of motor function commonly accompany the neurologic manifestations of uremic encephalopathy. During the early stages, there often is difficulty in performing fine movements of the extremities; the gait becomes unsteady and clumsy with tremulousness of movement. Asterixis (dorsiflexion movements of the hands and feet) typically occurs as the disease progresses. It can be elicited by having the person hyperextend his or her arms at the elbow and wrist with the fingers spread apart. If asterixis is present, this position causes side-to-side flapping movements of the fingers.

Altered Immune Function

Infection is a common complication and cause of hospitalization and death of patients with chronic renal failure. Immunologic abnormalities decrease the efficiency of the immune response to infection. All aspects of inflammation and immune function may be affected adversely by the high levels of urea and metabolic wastes, including a decrease in granulocyte count, impaired humoral and cell-mediated immunity, and defective phagocyte function. The acute inflammatory response and delayed-type hypersensitivity response are impaired. Although persons with ESRD have normal humoral responses to vaccines, a more aggressive immunization program may be needed. Skin and mucosal barriers to infection also may be defective. In persons who are receiving dialysis, vascular access devices are common portals of entry for pathogens. Many persons with ESRD do not experience fever with infection, making the diagnosis more difficult.

Disorders of Skin Integrity

Skin manifestations are common in persons with ESRD. The skin often is pale because of anemia and may have a sallow, yellow-brown hue. The skin and mucous membranes often are dry, and subcutaneous bruising is common. Skin dryness is caused by a reduction in perspiration caused by the decreased size of sweat glands and the diminished activity of oil glands. Pruritus is common; it results from the high serum phosphate levels and the development of phosphate crystals that occur with hyperparathyroidism. Severe scratching and repeated needlesticks, especially with hemodialysis, break the skin integrity and increase the risk for infection. In the advanced stages of untreated renal failure, urea crystals may precipitate on the skin as a result of the high urea concentration in body fluids. The fingernails may become thin and brittle, with a dark band just behind the leading edge of the nail, followed by a white band. This appearance is known as *Terry's nails*.

Sexual Dysfunction

Alterations in physiologic sexual responses, reproductive ability, and libido are common. The cause probably is multifactorial and may result from high levels of uremic toxins, neuropathy, altered endocrine function, psychological factors, and medications (*e.g.*, antihypertensive drugs).

Impotence occurs in as many as 56% of male patients receiving dialysis.[21] Derangements of the pituitary and gonadal hormones, such as decreases in testosterone levels and increases in prolactin and luteinizing hormone levels, are common and cause erectile difficulties and decreased spermatocyte counts. Loss of libido may result from chronic anemia and decreased testosterone levels. Several drugs, such as exogenous testosterone and bromocriptine, have been used in an attempt to return hormone levels to normal.

Impaired sexual function in women is manifested by abnormal levels of progesterone, luteinizing hormone, and prolactin. Hypofertility, menstrual abnormalities, decreased vaginal lubrication, and various orgasmic problems have been described.[22] Amenorrhea is common among women who are receiving dialysis therapy.

Elimination of Drugs

The kidneys are responsible for the elimination of many drugs and their metabolites.[6] Renal failure and its treatment can interfere with the absorption, distribution, and elimination of drugs. The administration of large quantities of phosphate-binding antacids to control hyperphosphatemia and hypocalcemia in patients with advanced renal failure interferes with the absorption of some drugs. Many drugs are bound to plasma proteins, such as albumin, for transport in the body; the unbound portion of the drug is available to act at the various receptor sites and is free to be metabolized. A decrease in plasma proteins, particularly albumin, that occurs in many persons with ESRD results in less protein-bound drug and greater amounts of free drug.

Decreased elimination by the kidneys allows drugs or their metabolites to accumulate in the body and requires that drug dosages be adjusted accordingly. Some drugs contain unwanted nitrogen, sodium, potassium, and magnesium and must be avoided in patients with renal failure. For example, penicillin contains potassium. Nitrofurantoin and ammonium chloride

add to the body's nitrogen pool. Many antacids contain magnesium. Because of problems with drug dosing and elimination, persons with renal failure should be cautioned against the use of over-the-counter remedies.

Treatment

During the past several decades, an increasing number of persons have required renal replacement therapy with dialysis or transplantation. The growing volume is largely attributable to the improvement in treatment and more liberal policies regarding who is treated. Between 1980 and 1992, there was a twofold reported increase in treatment for ESRD.[23] In 1998, almost 245,910 persons were receiving dialysis therapy in the United States, and another 13,272 underwent kidney transplantation.[24]

Medical Management

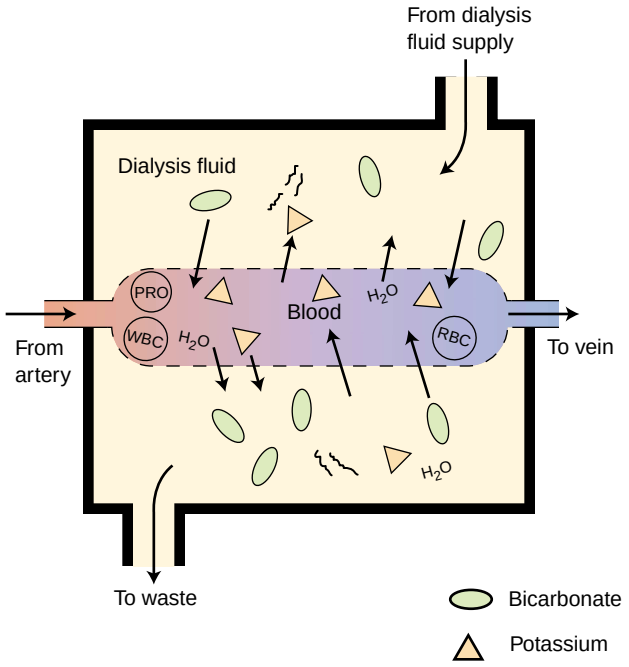
Chronic renal failure can be treated by conservative management of renal insufficiency and by renal replacement therapy with dialysis or transplantation. Conservative treatment consists of measures to prevent or retard deterioration in remaining renal function and to assist the body in compensating for the existing impairment. Interventions that have been shown to significantly retard the progression of chronic renal insufficiency include dietary protein restriction and blood pressure normalization. Various interventions are used to compensate for reduced renal function and correct the resulting anemia, hypocalcemia, and acidosis. These interventions often are used in conjunction with dialysis therapy for patients with ESRD.

Dialysis and Transplantation

Dialysis or renal replacement therapy is indicated when advanced uremia or serious electrolyte imbalances are present. The choice between dialysis and transplantation is dictated by age, related health problems, donor availability, and personal preference. Although transplantation often is the treatment preference, dialysis plays a critical role as a treatment method for ESRD. It is life sustaining for persons who are not candidates for transplantation or who are awaiting transplantation. There are two broad categories of dialysis: hemodialysis and peritoneal dialysis.

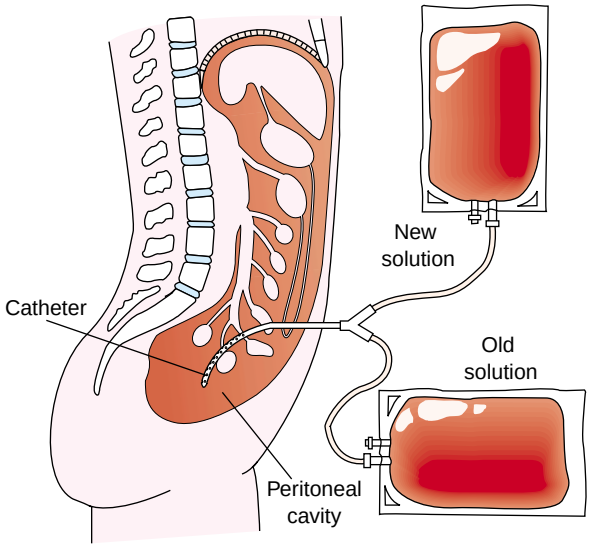
Hemodialysis. The basic principles of hemodialysis have remained unchanged throughout the years, although new technology has improved the efficiency and speed of dialysis.[25] A hemodialysis system, or artificial kidney, consists of three parts: a blood compartment, a dialysis fluid compartment, and a cellophane membrane that separates the two compartments. The cellophane membrane is semipermeable, permitting all molecules except blood cells and plasma proteins to move freely in both directions—from the blood into the dialyzing solution and from the dialyzing solution into the blood. The direction of flow is determined by the concentration of the substances contained in the two solutions. The waste products and excess electrolytes in the blood normally diffuse into the dialyzing solution. If there is a need to replace or add substances, such as bicarbonate, to the blood, these can be added to the dialyzing solution (Fig. 24-4).

During dialysis, blood moves from an artery through the tubing and blood chamber in the dialysis machine and then back into the body through a vein. Access to the vascular system is accomplished through an external arteriovenous shunt (*i.e.*, tubing implanted into an artery and a vein) or, more commonly, through an internal arteriovenous fistula (*i.e.*, anastomosis of a vein to an artery, usually in the forearm). Heparin is used to prevent clotting during the dialysis treatment; it can be administered continuously or intermittently.



■ **FIGURE 24-4** ■ Schematic diagram of a hemodialysis system. The blood compartment and dialysis solution compartment are separated by a cellophane membrane. This membrane is porous enough to allow all the constituents, except the plasma proteins and blood cells, to diffuse between the two compartments.

Peritoneal Dialysis. Peritoneal dialysis uses the same principles of diffusion, osmosis, and ultrafiltration that apply to hemodialysis. The thin serous membrane of the peritoneal cavity serves as the dialyzing membrane. A silastic catheter is surgically implanted in the peritoneal cavity below the umbilicus to provide access. The catheter is tunneled through subcutaneous tissue and exits on the side of the abdomen (Fig. 24-5). The dialysis process involves instilling a sterile dialyzing solution (usually 2 L) through the catheter during a period of approximately 10 minutes. The solution then is allowed to remain, or dwell, in the peritoneal cavity for a prescribed amount of time, during which the metabolic end-products and extracellular fluid diffuse into the dialysis solution. At the end of the dwell time, the dialysis fluid is drained out of the peritoneal cavity by gravity into a sterile bag. Glucose in the dialysis solution accounts for water removal. Commercial dialysis solution is available in 1.5%, 2.5%, and 4.25% dextrose concentrations. Solutions with higher dextrose levels increase osmosis, causing more fluid to be removed. The most common method is continuous ambulatory peritoneal dialysis (CAPD), a self-care procedure in which the person manages the dialysis procedure and the type of solution (*i.e.*, dextrose concentration) used at home.



■ **FIGURE 24-5** ■ Peritoneal dialysis. A semipermeable membrane, richly supplied with small blood vessels, lines the peritoneal cavity. With dialysate dwelling in the peritoneal cavity, waste products diffuse from the network of blood cells into the dialysate.

Transplantation. Greatly improved success rates have made kidney transplantation the treatment of choice for many patients with chronic renal failure. The availability of donor organs continues to limit the number of transplantations performed each year. Donor organs are obtained from cadavers and living related donors (*e.g.*, parent, sibling). The success of transplantation depends primarily on the degree of histocompatibility, adequate organ preservation, and immunologic management.[26]

In summary, chronic renal failure results from the destructive effects of many forms of renal disease. Regardless of the cause, the consequences of nephron destruction in ESRD are alterations in the filtration, reabsorption, and endocrine functions of the kidneys. The progression of chronic renal failure usually occurs in four stages: diminished renal reserve, renal insufficiency, renal failure, and ESRD. Renal insufficiency represents a reduction in the GFR to approximately 20% to 50% of normal; renal failure, a reduction to less than 20% to 25% of normal; and ESRD, a decrease in GFR to less than 5% of normal.

End-stage renal disease affects almost every body system. It causes an accumulation of nitrogenous wastes (*i.e.*, azotemia), alters sodium and water excretion, and alters regulation of body levels of potassium, phosphate, calcium, and magnesium. It also causes skeletal disorders, anemia, alterations in cardiovascular function, neurologic disturbances, gastrointestinal dysfunction, and discomforting skin changes.

The treatment of ESRD can be divided into two types: conservative management of renal insufficiency and renal replacement therapy with dialysis or transplantation. Conservative treatment consists of measures to prevent or retard deterioration in remaining renal function and to assist the body in compensating for the existing impairment.

RENAL FAILURE IN CHILDREN AND ELDERLY PERSONS

Although the spectrum of renal disease among children and elderly persons is similar to that of adults, several unique issues affecting these groups warrant further discussion.

Chronic Renal Failure in Children

The true incidence of chronic renal failure in infants and children is unknown. The data indicate that 2500 people in the United States who are younger than 20 years of age begin treatment for chronic renal failure each year; 100 of these children are younger than 2 years of age.[27] The most common cause of chronic renal failure in children is glomerulonephritis and congenital malformations, such as renal hypoplasia or dysplasia, obstructive uropathy, and reflux nephropathy.[28]

Features of renal disease that are marked during childhood include severe growth impairment, developmental delay, delay in sexual maturation, bone abnormalities, and development of psychosocial problems.[27,29] Critical growth periods occur during the first 2 years of life and during adolescence. Physical growth and cognitive development occur at a slower rate as consequences of renal disease, especially among children with congenital renal disease. Puberty usually occurs at a later age in children with renal failure, partly because of endocrine abnormalities. Renal osteodystrophy is more common and extensive in children than in adults because of the presence of open epiphyses. As a result, metaphyseal fractures, bone pain, impaired bone growth, short stature, and osteitis fibrosa cystica occur with greater frequency. Some hereditary renal diseases, such as medullary cystic disease, have patterns of skeletal involvement that further complicate the problems of renal osteodystrophy. Factors related to impaired growth include deficient nutrition, anemia, renal osteodystrophy, chronic acidosis, and cases of nephrotic syndrome that require high-dose corticosteroid therapy.

The success of treatment depends on the level of bone maturation at the initiation of therapy. Nutrition is believed to be the most important determinant during infancy. During childhood, growth hormone is important, and gonadotropic hormones become important during puberty.[30] Parental heights provide a means of assessing growth potential. For many children, catch-up growth is important because a growth deficit frequently is established during the first months of life. Recombinant human growth hormone therapy has been used to improve growth in children with ESRD.[30] Success of treatment depends on the level of bone maturation at the initiation of therapy.

All forms of renal replacement therapy can be safely and reliably used for children. Children typically are treated with CAPD or transplantation to optimize growth and development.[28] An alternative to CAPD is continuous cyclic peritoneal dialysis. The procedure reverses the schedule of CAPD by providing the exchanges at night, rather than during the day. The exchanges are performed automatically during sleep by a simple cycler machine. Renal transplantation is considered the best alternative for children.[31] Early transplantation in young children is regarded as the best way to promote physical growth, improve cognitive function, and foster psychosocial

development.[31] Immunosuppressive therapy in children is similar to that used in adults. All of these immunosuppressive agents have side effects, including increased risk of infection. Corticosteroids, which have been the mainstay of chronic immunosuppressive therapy for decades, carry the risk of hypertension, orthopedic complications (especially aseptic necrosis), cataracts, and growth retardation.

Chronic Renal Failure in Elderly Persons

Since the mid-1980s, there have been increasing numbers of elderly persons accepted to ESRD programs. In 2001, 20.1% of persons being treated for ESRD were 65 to 74 years of age, and 14.4% were older than 75 years of age.[32] Among elderly persons, the presentation and course of renal failure may be altered because of age-related changes in the kidneys and concurrent medical conditions.

Normal aging is associated with a decline in the GFR and subsequently with reduced homeostatic regulation under stressful conditions.[33] This reduction in GFR makes elderly persons more susceptible to the detrimental effects of nephrotoxic drugs, such as radiographic contrast compounds. The reduction in GFR related to aging is not accompanied by a parallel increase in the serum creatinine level because the serum creatinine level, which results from muscle metabolism, is significantly reduced in elderly persons because of diminished muscle mass and other age-related changes. Evaluation of renal function in elderly persons should include a measurement of creatinine clearance along with the serum creatinine level.

The prevalence of chronic disease affecting the cerebrovascular, cardiovascular, and skeletal systems is higher in this age group. Because of concurrent disease, the presenting symptoms of renal disease in elderly persons may be less typical than those observed in younger adults. For example, congestive heart failure and hypertension may be the dominant clinical features with the onset of acute glomerulonephritis, whereas oliguria and discolored urine more often are the first signs in younger adults. The course of renal failure may be more complicated in older patients with numerous chronic diseases.

Treatment options for chronic renal failure in elderly patients with ESRD include hemodialysis and peritoneal dialysis. Neither hemodialysis nor peritoneal dialysis has proven to be superior in the elderly. Many transplantation centers have increased the age for acceptance on transplant waiting lists, so renal transplantation provides another option. The general reduction in T-cell function that occurs with aging has been suggested as a beneficial effect that increases transplant graft survival.

In summary, there is approximately a 2% per year incidence of renal failure in children, most frequently resulting from congenital malformations and glomerulonephritis. Problems associated with renal failure in children include growth impairment, delay in sexual maturation, and more extensive bone abnormalities than in adults. Although all forms of renal replacement therapy can be safely and reliably used for children, CAPD or transplantation optimize growth and development.

Adults 65 years of age and older account for close to one half of the new cases of ESRD each year. Normal aging is associated with a decline in the GFR, which makes elderly persons more susceptible to the detrimental effects of nephrotoxic drugs and other conditions that compromise renal function. Treatment options for chronic renal failure in elderly patients are similar to those for younger persons.

REVIEW QUESTIONS

- Compare acute and chronic renal failure in terms of reversibility.
- Differentiate the prerenal, intrinsic, and extrarenal forms of acute renal failure in terms of the mechanisms of development and manifestations.
- Cite the two most common causes of acute tubular necrosis and describe the course of the disease in terms of the initiation, maintenance, and recovery phases.
- State the definitions of renal impairment, renal insufficiency, renal failure, and end-stage renal disease.
- List the common problems associated with end-stage renal disease, including alterations in fluid and electrolyte balance and disorders of skeletal, hematologic, cardiovascular, immune, neurologic, skin, and sexual function, and explain their physiologic significance.
- Describe the scientific principles underlying dialysis treatment, and compare hemodialysis with peritoneal dialysis.
- List the causes of renal failure in children and describe the special problems of children with ESRD.
- Explain why renal failure is so common in the elderly, and describe measures to prevent or delay the onset of ESRD in this population.

Visit the Connection site at connection.lww.com/go/porth for links to chapter-related resources on the Internet.

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