Acute Kidney Injury

Acute kidney injury (AKI) occurs in up to 2% to 20% of non-intensive care unit (ICU) hospitalized patients and in as many as 67% of patients treated in ICUs. Regardless of the underlying etiology, AKI is associated with increased in-hospital morbidity, mortality, and costs as well as increased long-term mortality and morbidity. Patients with AKI who are treated with renal replacement therapy (RRT) have a mortality rate between 40% and 70% despite advances in technology and RRT. Evidence suggests that even in patients who survive AKI and approach normal kidney function by hospital discharge are at increased risk for later development of chronic kidney disease (CKD) and should have longitudinal monitoring of their kidney function.

AKI was previously known as acute renal failure (ARF). More than 35 different definitions of ARF were contained in the medical literature. The lack of a standard definition resulted in variations in the reported incidence of ARF and conflicting reports regarding morbidity and mortality. This situation had an adverse effect on research studies. Consequently, in 2004, a group of expert intensivists and nephrologists formed the Acute Dialysis Quality Initiative (ADQI) to develop a consensus definition for ARF/AKI. The consensus definition formulated by the ADQI is known as the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) classification. As defined by the RIFLE classification, there are three increasing grades of severity of AKI—risk, injury, and failure—based on a relative increase in serum creatinine or a period of decreased urine output. Also, two outcome criteria—loss and end-stage kidney disease—are defined by duration of loss of kidney function, 4 weeks and 3 months, respectively.

In 2007, the RIFLE criteria were modified by the Acute Kidney Injury Network (AKIN), which included the ADQI group as well as other representatives from nephrology and intensive care societies. The AKIN-proposed diagnostic criteria for AKI are an abrupt (within 48 hours) increase in the serum creatinine of 0.3 mg/dL or more from baseline, a percentage increase in the serum creatinine concentration of 50% or more, or a urine output of less than 0.5 mL/kg/h for more than 6 hours. Most recently, the Kidney Disease/Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury further revised the definition of AKI. KDIGO is a nonprofit international foundation established in 2003 with the mission to develop global practice guidelines to improve kidney disease care and outcomes. The main change in the KDIGO definition is the extension of the timeframe for a 50% or more increase in serum creatinine to 7 days. In the future, it is likely that functional markers of renal failure (urine output and serum creatinine) will be replaced or augmented by biologic injury markers, analogous to how troponin is now used to help diagnose an acute myocardial infarction (MI). It is hoped that such markers of kidney cellular injury will not only define AKI but will also offer the potential to diagnose the disorder before functional decline.

Urine output patterns in AKI can manifest as oliguria (less than 500 mL/d), nonoliguria (greater than 500 mL/d), or anuria (less than 50 mL/d). Categorization of AKI as oliguric or nonoliguric is diagnostically significant because the oliguric form is associated with higher morbidity and mortality. This may be mediated in part by the more pronounced fluid retention in oliguric versus nonoliguric patients. Anuria is rare and is most often seen in two conditions: shock and...
Chapter 31
Acute Kidney Injury and Chronic Kidney Disease

**Causes of Acute Kidney Injury**

Many pathophysiologic pathways may lead to the syndrome of AKI. To aid in establishing a diagnostic and management plan, AKI is organized into three general categories according to precipitating factors and the symptoms manifested (Box 31-1).

**Prerenal Acute Kidney Injury**

Prerenal AKI is characterized by any physiologic event that results in renal hypoperfusion. Most commonly, precipitating events include hypovolemia and cardiovascular failure; however, any other event that leads to an acute decrease in "effective renal perfusion" can fall into this category (see Box 31-1). For example, in sepsis, a systemic inflammatory response triggers a cascade of events that results in a vasodilated hypotensive state despite no net loss in body fluids.

**Postrenal Acute Kidney Injury**

Any obstruction in the flow of urine from the collecting ducts in the kidney to the external urethral orifice can result in postrenal AKI. Postrenal obstruction can result from ureteral blockage (as with bilateral renal stones), urethral blockage (as from stricture and benign prostatic hypertrophy), or an extrinsic source, such as a retroperitoneal tumor or fibrosis. Another source of postrenal AKI is a dysfunctional bladder (as might be caused by ganglionic blocking agents that interrupt autonomic supply to the urinary system). Elderly men and the young are populations particularly susceptible to postrenal AKI. Children are at risk secondary to congenital anomalies, and elderly men are at risk because of the high prevalence of benign or malignant prostate hypertrophy.

**Interpretation of Results**

Complete bilateral urinary tract obstruction. Any sudden and complete cessation of urinary flow in a patient with a Foley catheter should alert the nurse to inspect, flush, or change the urinary catheter.

**TABLE 31-1 Acute Kidney Injury Staging Criteria**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Creatinine Criteria</th>
<th>Urine Output Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RIFLE Criteria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Injury</td>
<td>Creatinine increase of 1.5–2 times baseline value</td>
<td>&lt;0.5 mL/kg/h × 6 h</td>
</tr>
<tr>
<td>Failure</td>
<td>Creatinine increase of 2–3 times baseline value</td>
<td>&lt;0.5 mL/kg/h × 12 h</td>
</tr>
<tr>
<td>Loss</td>
<td>Creatinine increase of 3 or more times baseline value or a creatinine value &gt;4 mg/dL with an acute increase of 0.5 mg/dL or more</td>
<td>&lt;0.3 mL/kg/h × 24 h or anuria × 12 h</td>
</tr>
<tr>
<td>End-stage kidney disease</td>
<td>Persistent ARF for &gt;4 wk</td>
<td>Persistent ARF for &gt;3 mo</td>
</tr>
<tr>
<td><strong>AKIN Criteria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Creatinine increase of 1/5–2 times baseline value or increases in creatinine of 0.3 or more mg/dL</td>
<td>&lt;0.5 mL/kg/h × 6 h</td>
</tr>
<tr>
<td>2</td>
<td>Creatinine increase of 2–3 times baseline value</td>
<td>&lt;0.5 mL/kg/h × 12 h</td>
</tr>
<tr>
<td>3</td>
<td>Creatinine increase of 3 or more times baseline value or a creatinine value &gt;4 mg/dL with an acute increase of 0.5 mg/dL or more</td>
<td>&lt;0.3 mL/kg/h × 24 h or anuria × 12 h</td>
</tr>
<tr>
<td><strong>KDIGO Criteria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Creatinine increase of 1.5–1.9 times baseline** or ≥0.3 mg/dL***</td>
<td>&lt;0.5 mL/kg/h × 6 h</td>
</tr>
<tr>
<td>2</td>
<td>Creatinine increase of 2–2.9 times baseline</td>
<td>&lt;0.5 mL/kg/h × 12 h</td>
</tr>
<tr>
<td>3</td>
<td>Creatinine increase of 3 or more times baseline or a creatinine value of ≥4 mg/dL or initiation of RRT</td>
<td>&lt;0.3 mL/kg/h × 24 h or anuria × 12 h</td>
</tr>
</tbody>
</table>

*Reduction in renal function must occur within 48 h.
**Serum creatinine increase is known or presumed to have occurred within the prior 7 days.
***Serum creatinine increase within any 48-h period.
### BOX 31-1 Precipitating Causes of Acute Kidney Injury

**Prerenal**
- Decreased intravascular volume
  - Dehydration
  - Hemorrhage
  - Hypovolemic shock
  - Hypovolemia (gastrointestinal losses, diuretics, diabetes insipidus)
  - Third-spacing (burns, peritonitis)
- Cardiovascular failure
  - Heart failure
  - Myocardial infarction
  - Cardiogenic shock
  - Valvular heart disease
  - Renal artery stenosis or thrombosis
- Drugs
  - ACE inhibitors
  - NSAIDs—block prostaglandin-mediated afferent arteriolar vasodilation
  - Calcineurin inhibitors (e.g., tacrolimus, cyclosporine)—cause preglomerular vasoconstriction
- Decreased “effective renal perfusion”
  - Sepsis
  - Cirrhosis
  - Neurogenic shock

**Intrarenal**
- Acute glomerulonephritis
  - Immune complex–mediated (postinfectious, lupus nephritis, cryoglobulinemia, immunoglobulin A nephropathy)
  - With vasculitis (Wegener’s granulomatosis, antiglomerular basement membrane disease, polyarteritis nodosa)
- Vascular disease
  - Malignant hypertension
  - Microangiopathic HUS
  - TTP

### BOX 31-2 Common Causes of Acute Tubular Necrosis

**Ischemic Causes**
- Hemorrhagic hypotension
- Severe volume depletion
- Surgical aortic cross-clamping
- Cardiac surgery
- Defective cardiac output
- Septic shock
- Pancreatitis
- Immunosuppression (cyclosporine, tacrolimus)
- NSAIDs

**Nephrotoxic Causes**
- Drugs, including antimicrobials (aminoglycosides, amphotericin), cyclosporine, anesthetics, chemotherapeutic agents
- Heavy metals (mercury, lead, cisplatinum, uranium, cadmium, bismuth, arsenic)
- Radiologic contrast agents
- Heme/pigments (myoglobin, hemoglobin)
- Organic solvents (carbon tetrachloride)
- Fungicides and pesticides
- Plant and animal substances (mushrooms, snake venom)

### Pathophysiology of Acute Kidney Injury

**Prerenal Acute Kidney Injury**

The pathophysiology of prerenal AKI is centered on the kidneys’ response to inadequate perfusion. A decrease in renal perfusion results in the release of the enzyme renin from juxtaglomerular cells in the walls of the afferent arterioles. This activates the renin–angiotensin–aldosterone cascade, the end result being the production of angiotensin II and the release of aldosterone from the adrenal cortex. Angiotensin II causes profound systemic vasoconstriction, and aldosterone induces sodium and water retention. These effects help the body preserve circulatory volume to maintain adequate blood flow to essential organs such as the heart and brain. In the kidneys, angiotensin II also helps maintain the GFR by increasing efferent arteriolar resistance and by stimulating intrarenal vasodilator prostaglandins (which dilate the afferent arteriole), increasing hydrostatic pressure in the glomeruli. In this way, the kidneys can preserve the GFR over a wide range of mean arterial pressures. However, when renal
perfusion is severely compromised, the capacity for autoregulation is overwhelmed, and the GFR decreases.

Even with moderate hypovolemia or congestive heart failure, certain drugs, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and nonsteroidal anti-inflammatory drugs (NSAIDs), can overwhelm the kidney’s ability to autoregulate. These drugs disrupt some of the autoregulatory mechanisms, such as prostaglandin-mediated afferent arterial vasodilation, in the case of NSAIDs, and increased efferent arterial resistance, in the case of ACE inhibitors and ARBs. Predisposing factors for NSAID- and ACE inhibitor–induced prerenal failure are hypovolemia, baseline renal insufficiency, liver disease, heart failure, and diseases of the renal arteries. Concomitant use of diuretics, ACEI, or ARBS with NSAIDS may also increase the risk of NSAID-induced AKI, even in the absence of other risk factors.12

In prerenal AKI, once autoregulatory capacity is overwhelmed and the GFR decreases, changes in urinary composition and volume occur in a predictable pattern. When the GFR decreases, the amount of tubular fluid is reduced, and the fluid travels through the tubule more slowly. This results in increased sodium and water reabsorption. Because of the reduced renal circulation, the solutes reabsorbed from the tubular fluid are removed more slowly than normal from the interstitium of the renal medulla. This results in increased medullary toniccy, further augmenting water reabsorption from the distal tubular fluid. As a result of these events, the urinary volume is reduced to less than 400 mL/d (less than 17 mL/h), the urine specific gravity is increased, and the urine sodium concentration is low (usually less than 5 mEq/L; Fig. 31-1). Because of these characteristic changes associated with renal underperfusion, measurement of urinary volume, urinary sodium, and specific gravity is a simple method for determining the effect of management on renal perfusion.

An increase in systemic BP does not necessarily imply improvement in renal perfusion. This may be especially evident when drugs such as norepinephrine are used to correct the hypotension associated with states of volume depletion. These drugs may be associated with further reduction in renal blood flow as a consequence of constriction of the renal arteries. This is manifested by a further fall in urinary volume and rise in specific gravity. In turn, if the hypoperfusion state is more appropriately and specifically treated by replacement of volume, improvement of cardiac output, correction of dysrhythmias, or a combination of these approaches, the improved renal perfusion is manifested as an increased urinary volume and urine sodium concentration and as a decreased specific gravity of the urine. This ability to reverse prerenal AKI is the key to its diagnosis.

**Intrarenal Acute Kidney Injury**

Just as there are many causes of intrarenal AKI, there are also many pathophysiologic mechanisms that lead to it (Fig. 31-2). Because ATN is the most common hospital-acquired form of intrarenal AKI, this discussion focuses on the pathophysiology of ATN, which is complex, but intense and ongoing research has increased understanding of the factors contributing to this condition. Ischemia and nephrotoxicity are two major underlying causes of ATN (Fig. 31-3).

**Ischemic Acute Tubular Necrosis**

Ischemic ATN results from prolonged hypoperfusion. Thus, prerenal AKI and ischemic ATN are actually a continuum, a fact that underscores the importance of prompt recognition and treatment of the prerenal state. When renal hypoperfusion persists for a sufficient time (the exact duration of which is unpredictable and varies with clinical circumstances), renal tubular epithelial cells become hypoxic and sustain damage to the point that restoration of renal perfusion no longer causes an improvement in glomerular filtration.

Ischemia results in an inflammatory response and decreased adenosine triphosphate production in renal cell mitochondria. Inflammatory mediators produced by activated leukocytes and tubular epithelial cells promote inflammation in a positive feedback loop, causing further kidney injury. Decreased adenosine triphosphate production robs the cells of a needed energy supply. Part of this energy is used to keep the proper concentration of electrolytes in the cell through electrolyte exchange channels. Some of the cellular electrolyte disturbances from ischemia are decreased intracellular potassium, magnesium, and phosphate and increased intracellular sodium, chloride, and calcium. Increased intracellular calcium specifically has been shown to predispose the cells to injury and dysfunction.13

During reperfusion, cellular insults also occur from the formation of oxygen free radicals. Eventually, these cellular
FIGURE 31-2  Potential mechanisms of intrarenal AKI include decreased filtration pressure because of constriction in the renal arterioles (A), decreased glomerular capillary permeability (B), increased permeability of the proximal tubules with back leak of filtrate (C), obstruction of urine flow by necrotic tubular cells (D), and increased sodium delivery to the macula densa (E), which causes an increase in renin–angiotensin production and vasoconstriction at the glomerular level.

insults cause the tubular cells to swell and become necrotic. The necrotic cells then slough off and may obstruct the tubular lumen. These sloughed cells also allow back leak of tubular fluid because of altered function of their basement membrane, which contributes to the decreased GFR seen in this disorder.

A final contributor to the pathophysiology of ischemic ATN is profound renal vasoconstriction and reduced renal blood flow. These hemodynamic disturbances further compromise renal oxygen delivery and add to the ischemic damage. Vasconstrictors involved include norepinephrine from sympathetic nervous system activation, angiotensin II, thromboxane A₂, adenosine, leukotrienes C₄ and D₄, prostaglandin H₂, and endothelin. Release of endothelin, a powerful vasoconstrictor, by damaged vascular endothelial cells free radicals augment renal vasoconstrictor responses, and cellular swelling can further compromise renal blood flow. The necrotic cells then slough off and may obstruct the tubular lumen. These sloughed cells also allow back leak of tubular fluid because of altered function of their basement membrane, which contributes to the decreased GFR seen in this disorder.

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Toxic Acute Tubular Necrosis
The pathophysiology of toxic ATN begins with a concentration of a nephrotoxin in the renal tubular cells, which causes necrosis. These necrotic cells then slough off into the tubular lumen, possibly causing obstruction and impairing glomerular filtration in a manner similar to that of ischemic ATN. However, there are significant differences between toxic ATN and ischemic ATN. In toxic ATN, the basement membrane of the renal cells usually remains intact, and the injured necrotic areas are more localized. In addition, nonoliguria occurs more often with toxic ATN, and the healing process is often more rapid.

Although the potential nephrotoxins in toxic ATN are many (see Box 31-2), aminoglycoside antibiotics and radiographic contrast dye deserve special mention because of the frequency with which they are seen as causes of toxic ATN in hospitalized patients. Nephrotoxicity occurs in 10% to 25% of patients treated with aminoglycosides. The onset of AKI secondary to aminoglycosides is usually delayed, often beginning 5 to 10 days after the onset of therapy. The toxicity of these agents is dose dependent, and because these agents are primarily eliminated by the kidneys, dosage must be adjusted in patients with preexisting renal impairment. To ensure that the correct therapeutic range is being achieved, blood is drawn frequently for peak and trough level analysis. Several studies have suggested that a single daily dose of an aminoglycoside may result in less nephrotoxicity than giving the same total amount of medication in three daily doses. According to the KDIGO Practice Guideline for AKI recommends both once-daily dosing and close monitoring of drug levels. Other risk factors for aminoglycoside toxicity are volume depletion, advanced age, diabetes, concurrent use of other nephrotoxic agents, and hepatic dysfunction. If feasible, using alternative antibiotics with decreased associated nephrotoxicity is the best prevention of aminoglycoside-induced nephrotoxicity.

Contrast-induced nephropathy (CIN), the sudden decline of renal function following intravascular injection of contrast media, accounts for a significant number of hospital-acquired cases of AKI. In critically ill patients, the frequency of CIN is 2% to 23%. It usually begins within 24 to 48 hours of intravenous (IV) radiocontrast administration and peaks within 3 to 7 days. Typically, CIN is nonoliguric, transient, and reversible; however, in high-risk patients, dialysis may be required on an intermittent or permanent basis. Patients at greatest risk for CIN are those with diabetes and those with underlying renal impairment. In these patients, the incidence of CIN may be as high as 50%. Other patients at risk are elderly patients; those with intravascular volume depletion, heart failure, therapy, or concomitant use of nephrotoxic drugs; and those who receive a large contrast load.

The only proven way to reduce the risk for CIN is by aggressive volume expansion with isotonic crystalloids (normal saline solution) before and after contrast agent administration. Because CIN is believed to involve the production of oxygen free radicals, it is postulated that alkalization of the urine with sodium bicarbonate may confer greater protection than IV fluids alone. However, multiple trials comparing the use of sodium bicarbonate with normal saline for prophylaxis have yielded inconsistent results, and meta-analyses have been inconclusive. Accordingly, the KDIGO AKI Guideline recommends volume expansion with either isotonic sodium chloride or sodium bicarbonate solutions in patients with increased risk of CIN-AKI. Recently, there has been increased clinical trial activity revolving around the concept of forced diuresis (combining diuretics to augment urine output while given crystalloids to maintain euvolemia) for CIN prevention. Although some studies have shown promise, further research is needed.

Other interventions to reduce the incidence of CIN include using the minimal necessary dose of contrast media, using low or iso-osmolar nonionic contrast media instead of ionic hyperosmolar agents, stopping the intake of nephrotoxic drugs 24 hours before contrast media injection, and avoiding short intervals between contrast procedures. N-Acetylcysteine (NAC), an antioxidant and a potent vasodilator, is part of the protocol in many hospitals to prevent CIN based on clinical trials demonstrating its renoprotective effects in patients receiving IV contrast media. However, NAC has been the subject of many trials and meta-analyses, and overall there has been insufficient evidence to support...
Radiocontrast, particularly when used in small doses. This has led to the use of gadolinium-based contrast agents (GBCAs) as alternatives to iodinated contrast agents for digital subtraction angiography or interventional procedures, especially in patients with iodinated contrast allergies. However, one important caveat regarding the use of GBCA in patients with AKI or severe CKD (GFR < 30 mL/min) is the rare but serious risk for developing nephrogenic systemic fibrosis (NSF). NSF, a fibrosing disorder seen only in patients with kidney disease, is characterized by thickening and hardening of the skin overlying the extremities and trunk. Occasionally, fibrosis of deeper structures (such as joints, muscles, the testes, dura, kidneys, and the heart) occurs as well. Because the condition can be devastating to a patient (resulting in significant loss of mobility and...
Table 31-2  ACR Classifications of GBCAs

<table>
<thead>
<tr>
<th>GBCA</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group I: Agents with greatest number of NSF cases</strong></td>
<td></td>
</tr>
<tr>
<td>Gadodiamide</td>
<td>Omniscan</td>
</tr>
<tr>
<td>Gadopentetate dimeglumine</td>
<td>Magnevist</td>
</tr>
<tr>
<td>Gadoversetamide</td>
<td>OptiMARK</td>
</tr>
<tr>
<td><strong>Group II: Agents associated with few, if any, unconfounded cases of NSF</strong></td>
<td></td>
</tr>
<tr>
<td>Gadobenate dimeglumine</td>
<td>MultiHance</td>
</tr>
<tr>
<td>Gadoteridol</td>
<td>ProHance</td>
</tr>
<tr>
<td>Gadoteric acid</td>
<td>Dotarem</td>
</tr>
<tr>
<td>Gadobutrol</td>
<td>Gadovist</td>
</tr>
<tr>
<td><strong>Group III: Agents that have only recently appeared on the market in the United States</strong></td>
<td></td>
</tr>
<tr>
<td>Gadofosveset</td>
<td>Ablavar</td>
</tr>
<tr>
<td>Gadoxetic acid</td>
<td>Evovist</td>
</tr>
</tbody>
</table>

Box 31-3  CONSIDERATIONS for the Older Patient

Physiologic Changes Affecting the Renal System

As the body ages, physiologic systemic and kidney-specific changes occur that are important to take into consideration when addressing the kidney:

- **Vascular changes:** At 30 years of age, arteriosclerosis starts to develop, including in the renal arteries; this can result in significant damage.
- **Musculoskeletal changes:** In elderly people, there is a decreased muscle mass and body weight. These changes must be kept in mind when assessing renal function because of the possibility of a consequent decreased baseline serum creatinine value. A minimum rise in serum creatinine value in elderly patients, which may be within normal limits for a young adult, may actually signify major renal impairment.
- **Kidney-specific changes:** With aging, there is a decrease in the total number of functioning glomeruli, a decrease in renal blood flow, and a decrease in GFR of about 0.75 mL/min/1.73 m² per year after 30 years of age.

In view of these systemic and kidney-specific changes, an accurate assessment of GFR using a 24-hour urine study or an isotopic study is essential. The Cockcroft-Gault formula or the Modification of Diet in Renal Disease (MDRD) formulas below, which take into account gender and age, can also be used. It is important to realize that these formulas are not extensively validated in patients older than 70 years. After true GFR is realized, therapy (eg, drug dosages) can be guided more safely.

**Cockcroft-Gault Formula for Creatinine Clearance (mL/min)**

Men = (140 – age) × weight in kg/72 × serum creatinine

Women = 0.85 × creatinine clearance for men

**MDRD Formula for GFR (adults; mL/min)**

175 × Serum creatinine concentration⁻¹\(^{1.54}\) × Age⁻⁰\(^{.203}\) × 0.742 (if female) × 1.210 (if black)

Diagnosis of AKI begins with a determination of whether the AKI is prerenal, intrarenal, or postrenal. The assessment tools used to make this determination include the history and physical examination, laboratory tests, and diagnostic studies. Special considerations for assessing renal function in older patients are given in Box 31-3.

History and Physical Examination

Essential to any assessment is the health history and physical examination. By taking a detailed history, clues to the categorization and exact cause of the AKI can be obtained. Important indications in the history that suggest prerenal AKI include any event or condition that may have contributed to decreased renal perfusion (eg, acute MI, cardiovascular surgery, cardiac arrest, high fever, any shock state, and the use of certain drugs, such as NSAIDs). Also, a history of atherosclerotic disease may be a clue to renal artery stenosis, another precipitant of prerenal AKI. Clues to an intrarenal cause provided by the history include any prolonged prerenal event or condition as well as exposure to nephrotoxins, especially aminoglycoside antibiotics and radiocontrast media. It is
Laboratory assessment, critical to the diagnosis and categorization of AKI, includes both serum and urinary values. For a basic comparison of laboratory values in prerenal AKI, postrenal AKI, and ATN, see Table 31-3. In addition to helping differentiate between prerenal, intrarenal, and postrenal AKI, blood and urine tests are also helpful for diagnosing the underlying etiology of the AKI (Box 31-4).

**URINARY VALUES.** Obtaining a urine specimen for diagnostic evaluations is invaluable in establishing the diagnosis and determining the type of AKI. The urine specimen should be obtained before a diagnostic challenge dose of...
Consequently, the urine sodium level and the fractional excretion of sodium and water in an attempt to increase circulatory volume. In prerenal failure, the hypoperfused kidney actively reabsorbs sodium and water in an attempt to increase circulatory volume. Consequently, the urine sodium level and the fractional excretion of sodium (FENa) are low (less than 20 mEq/L and less than 1%, respectively), whereas the urine osmolality and concentration of nonreabsorbable solutes are high. In contrast, in ATN in which parenchymal damage affects the kidney, the tubular cells can no longer effectively reabsorb sodium or concentrate the urine. As a result, the urine sodium concentration is often greater than 40 mEq/L, the FENa is greater than 1%, and the urine osmolality is close to that of plasma (isosthenuria). Unfortunately, there is a limit to the usefulness of these indices because of overlap in these values for prerenal AKI and ATN (ie, urine sodium concentration values in the 20 to 40 mEq/L range). Values at the extremes are thus the most useful. The sediment in a urinalysis is also very helpful in diagnosing and distinguishing the types of AKI. In prerenal AKI, the urinary sediment is normal with only a few hyaline casts, whereas in ATN, coarse, muddy-brown granular casts and tubular epithelial cells are typically found. In postrenal AKI, the sediment is often normal but can be helpful in diagnosing kidney stones.

**BLOOD UREA NITROGEN AND CREATinine LEVELS.** Serum tests for BUN and creatinine are essential not only for diagnosing AKI but also for helping to distinguish between prerenal AKI and ATN or postrenal AKI. In prerenal AKI, the BUN-to-creatinine ratio is increased from the normal ratio of 10:1 to more than 20:1. This finding is caused by a state of dehydration and by the fact that, as the tubules become more permeable to sodium and water in prerenal AKI, urea is also passively reabsorbed. In ATN and postrenal AKI, when the concentrating ability of the kidneys is impaired, both the BUN and creatinine increase proportionally, maintaining the normal 10:1 ratio.

**Diagnostic Studies**

Renal ultrasonography, an important diagnostic test in the evaluation of AKI, is especially useful in ruling out an obstruction, and has the advantage of being noninvasive. With a high-grade obstruction, dilation of the urinary collecting system is detectable on ultrasonography within 1 to 2 days of the onset of the obstruction. Ultrasonography may also reveal proximal renal calculi as a cause of postrenal obstruction. In addition, it can be used to estimate renal size, which is helpful in distinguishing between AKI and advanced CKD. Oftentimes in advanced CKD, the kidneys are small (less than 9 cm) and echogenic. Other studies that may be useful in diagnosing AKI are CT and MRI to evaluate for masses, vascular disorders, and filling defects in the collecting system, and renal angiography to evaluate for renal artery stenosis. It is notable that the iodinated contrast media used in some studies are allergenic and nephrotoxic, and that GBCAs can cause NSF in patients with severe kidney disease (GFR < 30 mL/min). For any diagnostic test, the benefits of the study must be weighed against potential risks. If available, alternative technology, such as the use of carbon dioxide gas in digital subtraction angiography, should be considered for patients allergic to iodinated agents or with advanced kidney failure. Finally, renal biopsy may be helpful in patients thought to have in-renal AKI that is not ATN, especially if significant proteinuria or unexplained hematuria is revealed on urinalysis. In addition to having diagnostic value, the results of a biopsy may help determine prognosis and therapy.

**Chronic Kidney Disease**

CKD is a slow, progressive, irreversible deterioration in renal function that results in the kidney’s inability to eliminate waste products and maintain fluid and electrolyte balance. Ultimately, it leads to end-stage renal disease (ESRD) and the need for RRT or renal transplantation to sustain life. Currently, there are more than 615,000 dialysis and renal transplant recipients in the United States, which is a 26% increase in prevalence since the year 2000. In 2011 alone, more than 115,000 patients were newly diagnosed with ESRD. Among ESRD patients, incidence rates are higher in men than in women and are higher with increasing age. The incidence rates in the African American population are 3.4 times greater than in the white population. Hispanics and Native Americans also have higher incidence rates than whites, but the difference in rates is not as dramatic. These differences in incidence rates are important when considering patient risk factors and target populations for health education.

Factors postulated to contribute to the increasing prevalence of ESRD include changes in the demographics of the population, differences in disease burden among racial groups, under-recognition and undertreatment of earlier stages of CKD, under-recognition of the risk factors for CKD, and increased survival of patients with ESRD. Increasing evidence shows that early detection and treatment of CKD may prevent, or at least delay, progression to ESRD. Consequently, it is important that opportunities to prevent and treat CKD are not lost secondary to underdiagnosis or undertreatment.

**Definition and Classification**

In an effort to address the growing public health problem of CKD, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) published clinical practice guidelines for CKD in 2002. The goals of the working group that developed these guidelines were to define CKD and classify its stages, to evaluate laboratory measurements for clinical assessment of kidney disease, to associate the level of kidney function with the complications of CKD, and to stratify risk for the loss of kidney function and the development of cardiovascular disease. The KDOQI defines CKD as either kidney damage with or without decreased GFR for 3 or more months or a GFR of less than 60 mL/min/1.73 m² for greater than 3 months (Box 31-5). Markers of damage include abnormal findings in the blood or urine tests or imaging studies. Examples are proteinuria, abnormalities in the urine sediment, increased serum creatinine, and multiple renal cysts detected on ultrasound in a patient with a family history of polycystic kidney...
Definition of Chronic Kidney Disease

1. Kidney damage for greater than or equal to 3 months as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifested by either:
   a. Pathologic abnormalities; or
   b. Markers of kidney damage, including abnormalities in the composition of the blood and urine, or abnormalities in imaging tests
2. GFR less than 60 mL/min/1.73 m², with or without kidney damage


Acute Kidney Injury and Chronic Kidney Disease

Poly cystic Kidney Disease

- Polycystic kidney disease is one of the most common disorders caused by mutations in a single gene. It affects about 500,000 people in the United States. The autosomal-dominant form of the disease is much more common than the autosomal-recessive form. Autosomal-dominant polycystic kidney disease affects 1 in 500 to 1,000 people, while the autosomal-recessive type occurs in an estimated 1 in 20,000 to 40,000 people. Clusters of fluid-filled sacs, called cysts, develop in the kidneys and interfere with their ability to filter waste products from the blood.
- Mutations in the PKD1, PKD2, and PKHD1 genes cause polycystic kidney disease.
- Mutations in either the PKD1 or PKD2 gene can cause autosomal-dominant polycystic kidney disease. These genes provide instructions for making proteins whose functions are not fully understood. Researchers believe that they are involved in transmitting chemical signals from outside the cell to the cell’s nucleus. The two proteins work together to promote normal kidney development, organization, and function. Mutations in the PKD1 or PKD2 gene lead to the formation of thousands of cysts, which disrupt the normal functions of the kidneys and other organs.
- Genetic tests for autosomal-dominant and autosomal-recessive type of polycystic kidney disease are available.

G-Stages

- G1 is characterized by the lack of a clear filtration deficit and is defined as normal or increased kidney function (GFR ≥ 90 mL/min/1.73 m²) in association with evidence of kidney damage.
- G2 is defined as a mild reduction in kidney function (GFR 60 to 89 mL/min/1.73 m²) that occurs in association with kidney damage.
- G3a is defined as mildly to moderately decreased kidney function (GFR 45 to 59 mL/min/1.73 m²).
- G3b is defined as moderately to severely decreased kidney function (GFR 30 to 44 mL/min/1.73 m²).
- G4 is defined as severely decreased kidney function (GFR 15 to 29 mL/min/1.73 m²).
- G5 is defined as a GFR of less than 15 mL/min/1.73 m² or the need for dialysis therapy. The term ESRD, widely used in regulatory and administrative circles, correlates to G5 CKD and represents those patients receiving or eligible for RRT by dialysis or transplantation.

Albuminuria—A Stages

- A1 is defined as an ACR < 30 mg/g.
- A2 is defined as an ACR 30 to 299 mg/g.
- A3 is defined as an ACR ≥ 300 mg/g.

Causes

The causes of CKD are numerous (Box 31-6). By far, the two most common causes are diabetes mellitus and hypertension, which account for more than 44% and 28% of incident cases of ESRD, respectively. Other causes include glomerulonephritis (both primary and secondary to systemic diseases),
interstitial nephritis, congenital malformations, genetic disorders, neoplasms, hepatorenal syndrome, obstructive uropathy, and microangiopathic etiologies, such as scleroderma and atheroembolic disease.

**Pathophysiology**

Although many diseases can cause CKD, there appear to be common pathophysiologic pathways for disease progression. The outstanding common morphologic features seen in CKD include fibrosis, loss of native renal cells, and infiltration by monocytes and macrophages. The mediators of the process are many and include abnormal glomerular hemodynamics, hypoxia, proteinuria, and vasoactive substances such as angiotensin II.34,35

In discussing glomerular hemodynamics, it is important to understand intact nephron theory. Because each of the more than 1 million nephrons in each kidney is an independent functioning unit, as renal disease progresses nephrons can lose function at different times. When an individual nephron becomes diseased, nephrons in close proximity increase their individual filtration rates by increasing the rate of blood flow and hydrostatic pressure in their glomerular capillaries. This hyperfiltration response in the nondiseased nephrons enables the kidneys to maintain excretory and homeostatic functions, even when up to 70% of the nephrons are damaged. Eventually, however, the intact nephrons reach a point of maximal filtration, and any additional loss of glomerular mass is accompanied by an incremental loss in GFR and subsequent accumulation of filterable toxins.

Although hyperfiltration is an adaptive measure to nephron loss, over time it can actually accelerate the loss of nephrons, because the hyperfiltration causes endothelial injury, stimulation of profibrotic cytokines, infiltration by monocytes and macrophages, and detachment of glomerular epithelial cells. In addition, hypertrophy of the nondiseased nephrons caused by hyperfiltration leads to increased wall stress and even more injury.37 This is why many interventions to slow down the progression of renal failure involve measures that reduce glomerular hydrostatic pressure. One such example is the use of ACE inhibitors and ARBs, which prevent angiotensin II–mediated efferent arteriolar vasoconstriction and subsequent nephron hyperfiltration.

Other possible mediators of CKD progression are hypoxia and angiotensin II. In CKD, the loss of peritubular capillaries by various causes results in reduced capillary perfusion of the tubules. The resultant hypoxia favors the release of proinflammatory and profibrotic cytokines, leading to fibrosis and cell injury. Angiotensin II stimulates growth factors and cytokines that contribute to fibrosis aside from its hemodynamic effects on the glomerulus.38,39

Proteinuria, the result of glomerular hypertension and abnormal glomerular permeability, also contributes to CKD progression. Abnormally filtered protein is reabsorbed by proximal tubular cells through endocytosis and accumulates in the cells, causing the production of cytokines. These proinflammatory factors ultimately cause fibrosis and scarring of the tubulointerstitium.40 Proteinuria is a very strong predictor of CKD progression, consistent with its role in the

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**Table 31-4: 2002 National Kidney Foundation Kidney Disease Outcome Quality Initiative Stages of Chronic Kidney Disease**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>90 or more</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild or decreased GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

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**Figure 31-4** Risk of CKD progression according to KDIGO staging.
pathophysiology of CKD and as evidenced by its inclusion in the new KDIGO CKD staging.

**Diabetic Nephropathy**

Because of the extremely high prevalence of diabetes and hypertension as causes of CKD, an understanding of the renal pathophysiology specific to these entities, and knowledge of interventions designed to slow down or prevent progression to stage 5 CKD, is imperative. Diabetic nephropathy is a major complication of diabetes, with an incidence of approximately 20% to 40%.41

In diabetes, the microvasculature in the organ systems of the body, including the kidneys, is damaged. In the kidneys, primarily the afferent and efferent arterioles and the glomerular capillaries are affected. Glomerular changes include thickening of the basement membrane, mesangial expansion from overproduction and underdegradation of extracellular matrix proteins, and diffuse glomerulosclerosis. Late in diabetic nephropathy, tubular atrophy and interstitial fibrosis also occur. The exact physiologic mechanism for these structural alterations is unclear, but hyperglycemia is a major contributor. In the classic Diabetes Control and Complications Trial (DCCT)—a prospective, randomized, multicenter trial performed to assess the effectiveness of tight blood glucose control on the complications of type 1 diabetes—researchers found that strict blood glucose control delayed, and possibly even prevented, the progression of diabetic nephropathy.45 The follow-up study to the DCCT, called the Epidemiology of Diabetes Interventions and Complications (EDIC) study, revealed that the benefits of tight control persist for a number of years.43 Most recently, it has also been shown that intensive diabetes therapy in type 1 diabetics improve renal outcomes even after the development of persistent microalbuminuria (urine albumin excretion rate of 30 to 300 mg/24 h).44 In addition, the classic United Kingdom Prospective Diabetes Study (UKPDS) reached conclusions about people with type II diabetes that were similar to those of the DCCT.45

At the onset of diabetic nephropathy, patients may have an increased GFR (as high as 140 mL/min) because of hyperfiltration, slightly enlarged kidneys, and microalbuminuria (30 to 300 mg/dl of albumin in the urine). Over the course of approximately 10 to 15 years, hypertension and protein leakage increase. Eventually, protein leakage is massive, with consequent hypoalbuminemia and edema as well as mild azotemia. At this point kidney damage is extensive, often requiring dialysis therapy within a few years.

**Hypertensive Nephrosclerosis**

Systemic hypertension may result in a condition known as nephrosclerosis. Hypertensive nephrosclerosis involves the development of sclerotic lesions in the renal arterioles and glomerular capillaries that cause them to become thickened, narrowed, and eventually necrotic. Hypertensive nephrosclerosis can be benign or malignant. In benign nephrosclerosis, associated with chronic mild or moderate hypertension, renal impairment occurs over many years. Malignant nephrosclerosis, associated with malignant hypertension, can lead to permanent renal failure rapidly if BP is not immediately reduced. Often, symptoms such as blurred vision and a severe headache accompany this crisis situation.

Because hypertensive nephrosclerosis is directly caused by hypertension, its incidence is greater in populations with a higher incidence of primary hypertension (eg, elderly people, African Americans). Among African Americans younger than 75 years, the incidence rate for hypertension-induced ESRD is between 6 and 11 times that of Caucasians.33 The signs of hypertensive nephrosclerosis vary depending on the severity of the renal damage and the acuteness of the hypertension. Some signs that may be present include proteinuria, azotemia, and hematuria with red blood cell casts. Unfortunately, like those with hypertension, patients often remain asymptomatic until extensive damage has occurred. To prevent or delay the progression of hypertensive nephropathy, BP control is essential, and often multiple antihypertensive medications are required. This is an area in which patient education can have a great impact in decreasing the incidence of ESRD. Educating patients about the complications of uncontrolled hypertension is particularly important and may foster the patient’s active involvement in controlling his or her BP.

**Preventing the Progression of Chronic Kidney Disease**

An important characteristic of CKD is continuous progression. Slowing the rate of progression after CKD is diagnosed is a focus of extensive and ongoing research. Regardless of the primary cause of CKD, specific identifiable secondary insults to the kidney can rapidly accelerate the loss of nephrons. Such secondary insults include an alteration in renal perfusion, as observed in congestive heart failure or intravascular volume depletion; the administration of nephrotoxic agents; urinary obstruction; and urinary infections. Consequently, monitoring for and avoiding these insults and aggressively treating them if they occur are paramount.

It is also important to educate patients and their families about the dangers of these insults. Patients and families should be instructed, for instance, about the signs and symptoms of urinary infections and the need for prompt treatment, as well as common nephrotoxic drugs to avoid. Common over-the-counter and prescription analgesics, such as NSAIDs, can...
cause rapid deterioration in renal function and should be avoided in patients with CKD.

Strict control of blood glucose levels is critical to preventing and retarding the progression of renal failure in people with diabetes. The targets for key parameters of glucose control set by the American Diabetes Association for people with diabetes are a glycosylated hemoglobin of less than 7.0%, a preprandial plasma glucose of 70 to 130 mg/dL, and a peak postprandial plasma glucose of less than 180 mg/dL.

BP control is also essential for preventing the progression of renal failure from almost any primary etiology, not just hypertension or diabetes. According to the KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease and the Eighth Joint National Committee (JNC 8) 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults, the target of therapy is a BP of less than 140/90 mm Hg. KDIGO, however, recommends a lower target of less than 130/80 mm Hg in CKD patients with an ACR ≥ 30 mg.35,36 A more severe protein restriction of 0.6 to 0.8 g/kg/d is indicated.35 Contradictions include patients with salt-wasting states or those who have previously been treated with a high-protein diet (1.3 g/kg/d) to avoid proteinuria.35 A more severe protein restriction of 0.6 to 0.8 g/kg/d is recommended by some renal nutritionists, but this has not been shown to decrease proteinuria or delay progression of CKD.34,35,46,47

A protein-restricted diet as a means to slow the progression of renal failure is controversial. The KDIGO Clinical Practice Guideline recommends lowering protein to 0.8 g/kg/d in adults with diabetes or in adults with a GFR < 30. KDIGO also suggested that a high-protein diet (1.3 g/kg/d) be avoided in any CKD patient at risk for progression.35 A more severe protein restriction of 0.6 to 0.8 g/kg/d is recommended by some renal nutritionists, but this has not been shown to decrease proteinuria or delay progression of CKD.34,35,46,47

Management of Renal Failure

Although some distinct differences exist in how AKI and CKD are managed, many of the clinical manifestations and complications encountered are the same. Thus, the general management of renal failure is addressed here, noting any differences between AKI and CKD as necessary. In either type of renal failure, management begins with treating the primary insult. An overview of the management of patients with AKI is provided in the accompanying Collaborative Care Guide (Box 31-7).

Managing Fluid Balance Alterations

Clinical management of fluid balance is of primary importance in patients with renal failure, and is the area in which differences in the management of AKI and CKD are perhaps most dramatic.

Fluid Balance Changes in Acute Kidney Injury

In prerenal AKI and the early stages of ischemic ATN, the cause of the renal failure is inadequate renal perfusion, often from intravascular volume deficits. After using laboratory, physical assessment, and hemodynamic clues to make a rapid diagnosis of intravascular volume depletion, therapy involves prompt administration of replacement fluids, such as blood and crystalloids. The replacement solutions used should reflect the type of losses (eg, for a patient with a hemorrhagic condition, blood would be the replacement fluid of choice). Often in AKI, even if signs and symptoms of intravascular volume deficits are not present, large boluses of IV fluids are given. Reversal of AKI after such a bolus is therapeutic as well as diagnostic of prerenal AKI.

Fluid administration in AKI is also indicated for the prevention or alleviation of tubular obstruction seen in obstructive causes of AKI, including ATN and many postrenal etiologies. However, in any oliguric state, caution must be taken to prevent fluid overload. In a sustained oliguric state, such as the oliguric stage of ATN, fluid is restricted to the previous day’s urine output amount plus 500 to 800 mL to account for insensible losses.

Diuretics are often used in AKI to increase urinary flow and thereby help alleviate conditions of fluid overload or to prevent tubular obstruction. Furosemide, a loop diuretic, and mannitol, an osmotic diuretic, are often used with hydration to prevent tubular obstruction in certain obstructive causes of AKI, such as acute ureter nephropathy, and in hemolysis; nephropathy, such as rhabdomyolysis. In states of fluid overload, such as pulmonary edema and heart failure, diuretics are also useful. Often in these situations, furosemide is administered every 6 hours, with the initial dose ranging between 20 and 100 mg depending on whether the patient has previously been treated with furosemide or a continuous furosemide drip. In addition, a thiazide diuretic, such as chlorothiazide, may be administered with furosemide because of the synergistic action of these diuretics in promoting urinary excretion.

With the use of diuretics, caution must be taken to avoid complications of dehydration, electrolyte imbalances, and...
Chapter 31  Acute Kidney Injury and Chronic Kidney Disease

Outcomes Interventions

### Coordination of Care

All appropriate team members and disciplines will be involved in the plan of care

- Develop the plan of care with the patient, family, primary physician, nephrologist, pulmonologist, cardiologist, registered nurse, advanced practice nurse, social worker, respiratory therapist, physical therapist, occupational therapist, dietitian, chaplain, and dialysis staff

### Ineffective breathing pattern

**Impaired gas exchange**

Patient will have adequate gas exchange as evidenced by:

- ABGs within normal limits
- Functional oxygen saturation (SpO₂) >92%
- Clear breath sounds
- Normal respiratory rate and depth
- Normal chest x-ray

- Monitor ABGs and continuous pulse oximetry
- Monitor acid–base status
- Monitor for signs and symptoms of pulmonary distress from fluid overload
- Provide routine pulmonary toilet, including the following:
  - Airway suctioning
  - Chest percussion
  - Incentive spirometer
  - Frequent turning
- Mobilize out of bed to chair
- Support patient with oxygen therapy, mechanical ventilation, or both as indicated. Involve respiratory therapist

### Decreased cardiac and peripheral tissue perfusion

**Patient’s BP, heart rate, and hemodynamic parameters will be within normal limits.**

Patient will have adequate tissue perfusion as evidenced by:

- Adequate hemoglobin levels
- Euvolemic status
- Optimal urine output depending on phase of AKI
- Appropriate level of consciousness

- Monitor vital signs every 1 to 2 hours
- Monitor PAOP, right atrial pressure, cardiac output, systemic vascular resistance, and peripheral vascular resistance every 4 hours or as ordered if pulmonary artery catheter is in place
- Assess vital signs continuously or every 15 minutes during dialysis
- Monitor hemoglobin and hematocrit levels daily
- Assess evidence of tissue perfusion (pain, pulses, color, temperature, and signs of decreased organ perfusion such as an altered level of consciousness, ileus, and decreasing urine output)
- Administer intravascular crystalloids or blood products as indicated

### Excess fluid volume related to decreased kidney function

**Ineffective renal perfusion**

Patient will be euvolemic

Patient will achieve normal electrolyte balance

Patient will achieve optimal renal function

- Monitor fluid status, including input and output (fluid restriction), daily weight, urine output trends, vital signs, CVP, and PAOP
- Monitor for signs and symptoms of hypervolemia (hypertension, pulmonary edema, peripheral edema, jugular venous distention, and increased CVP)
- Monitor serum electrolytes daily
- Monitor renal parameters, including urine output, BUN, serum creatinine, acid–base status, urine electrolytes, urine osmolality, and urine specific gravity
- Administer fluids and diuretics to maintain intravascular volume and renal function, per order
- Replace electrolytes as ordered
- Treat patient with, and monitor response to, dialysis therapies if indicated
- Monitor and maintain dialysis access for chosen intermittent or continuous dialysis method:
  - Continuous Veno–Veno Dialysis
    - Monitor and regulate ultrafiltration rate hourly based on patient’s response and fluid status
    - Provide fluid replacements as ordered
    - Assess and troubleshoot hemofilter and blood tubing hourly
    - Protect vascular access from dislodgment
    - Change filter and tubing per protocol
    - Monitor vascular access for infection
  - Peritoneal Dialysis
    - Slowly infuse warmed dialysate
    - Drain after appropriate dwell time
    - Assess drainage for volume and appearance
    - Send cultures daily or as ordered
    - Assess access site for infection
  - Intermittent Hemodialysis
    - Assess shunt for thrill and buzzing sound (bruit) every 12 hours
    - Avoid constrictions (ie, BPs), phlebotomy, and IV fluid administration in arm with shunt
    - Assess for infection
    - Monitor perfusion of related extremity

<table>
<thead>
<tr>
<th>Box 31-7</th>
<th>COLLABORATIVE CARE GUIDE for the Patient With Acute Kidney Injury</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coordination of Care</td>
<td>All appropriate team members and disciplines will be involved in the plan of care</td>
</tr>
</tbody>
</table>

- Develop the plan of care with the patient, family, primary physician, nephrologist, pulmonologist, cardiologist, registered nurse, advanced practice nurse, social worker, respiratory therapist, physical therapist, occupational therapist, dietitian, chaplain, and dialysis staff |

### Ineffective breathing pattern

**Impaired gas exchange**

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- ABGs within normal limits
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- Clear breath sounds
- Normal respiratory rate and depth
- Normal chest x-ray

- Monitor ABGs and continuous pulse oximetry
- Monitor acid–base status
- Monitor for signs and symptoms of pulmonary distress from fluid overload
- Provide routine pulmonary toilet, including the following:
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  - Incentive spirometer
  - Frequent turning
- Mobilize out of bed to chair
- Support patient with oxygen therapy, mechanical ventilation, or both as indicated. Involve respiratory therapist

### Decreased cardiac and peripheral tissue perfusion

**Patient’s BP, heart rate, and hemodynamic parameters will be within normal limits.**

Patient will have adequate tissue perfusion as evidenced by:

- Adequate hemoglobin levels
- Euvolemic status
- Optimal urine output depending on phase of AKI
- Appropriate level of consciousness

- Monitor vital signs every 1 to 2 hours
- Monitor PAOP, right atrial pressure, cardiac output, systemic vascular resistance, and peripheral vascular resistance every 4 hours or as ordered if pulmonary artery catheter is in place
- Assess vital signs continuously or every 15 minutes during dialysis
- Monitor hemoglobin and hematocrit levels daily
- Assess evidence of tissue perfusion (pain, pulses, color, temperature, and signs of decreased organ perfusion such as an altered level of consciousness, ileus, and decreasing urine output)
- Administer intravascular crystalloids or blood products as indicated

### Excess fluid volume related to decreased kidney function

**Ineffective renal perfusion**

Patient will be euvolemic

Patient will achieve normal electrolyte balance

Patient will achieve optimal renal function

- Monitor fluid status, including input and output (fluid restriction), daily weight, urine output trends, vital signs, CVP, and PAOP
- Monitor for signs and symptoms of hypervolemia (hypertension, pulmonary edema, peripheral edema, jugular venous distention, and increased CVP)
- Monitor serum electrolytes daily
- Monitor renal parameters, including urine output, BUN, serum creatinine, acid–base status, urine electrolytes, urine osmolality, and urine specific gravity
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    - Assess and troubleshoot hemofilter and blood tubing hourly
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    - Assess drainage for volume and appearance
    - Send cultures daily or as ordered
    - Assess access site for infection
  - Intermittent Hemodialysis
    - Assess shunt for thrill and buzzing sound (bruit) every 12 hours
    - Avoid constrictions (ie, BPs), phlebotomy, and IV fluid administration in arm with shunt
    - Assess for infection
    - Monitor perfusion of related extremity
### COLLABORATIVE CARE GUIDE for the Patient With Acute Kidney Injury (continued)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Interventions</th>
</tr>
</thead>
</table>
| **Impaired physical mobility**    | - Initiate deep venous thrombosis prophylaxis  
- Reposition frequently  
- Mobilize to chair when possible  
- Consult physical therapist  
- Conduct range-of-motion and strengthening exercises                                                                                                                                 |
| **Risk for injury**               |                                                                                                                                                                                                            |
| **Risk for falls**                |                                                                                                                                                                                                            |
| Patient will be protected from possible harm | - Assess need for wrist restraints if patient is intubated, has a decreased level of consciousness, is unable to follow commands, or is acutely agitated, or for affected extremity during hemodialysis. Explain need for restraints to patient and family members. If restrained, assess response to restraints and check every 1 to 2 hours for skin integrity and impairment in tissue perfusion. Follow hospital protocol for use of restraints  
- Use siderails on bed and safety belts on chairs as appropriate  
- Follow seizure precautions                                                                                                                                 |
| **Impaired skin integrity**       |                                                                                                                                                                                                            |
| Patient will have intact skin     | - Assess skin integrity and all bony prominences every 4 hours  
- Turn every 2 hours  
- Consider a pressure relief/reduction mattress. Use Braden Scale to assess risk for skin breakdown  
- Use superfatted or lanolin-based soap for bathing and apply emollients for pruritus  
- Treat pressure ulcers according to hospital protocol. Involve enterostomal nurse in care                                                                                                                                 |
| **Imbalanced nutrition**          |                                                                                                                                                                                                            |
| **Electrolyte imbalance**         |                                                                                                                                                                                                            |
| Patient will be adequately nourished as evidenced by: | - Consult dietitian to direct and coordinate nutritional support  
- Observe sodium, potassium, protein, and fluid restriction as indicated  
- Provide small, frequent feedings  
- Provide parenteral or enteral feeding as ordered  
- Monitor albumin, prealbumin, total protein, hematocrit, hemoglobin, and white blood cell counts, and monitor daily weights to assess effectiveness of nutritional therapy                                                                                                                                 |
| Stable weight not <10% below, or >20% above, ideal body weight |                                                                                                                                                                                                            |
| An albumin level of 3.5 to 4.0 g/dL |                                                                                                                                                                                                            |
| A total lymphocyte count of 1,000 to 3,000 x 10⁶/L |                                                                                                                                                                                                            |
| A total protein level of 6 to 8 g/dL |                                                                                                                                                                                                            |
| **Impaired comfort**              |                                                                                                                                                                                                            |
| Patient will be as comfortable and as pain free as possible as evidenced by: | - Monitor for signs and symptoms of respiratory distress related to fluid overload and support oxygenation as needed. Keep head of bed elevated and teach breathing techniques to minimize oxygen distress, such as pursed-lip breathing  
- Plan fluid restrictions over 24 hours, allowing for periodic sips of water and ice chips to minimize thirst  
- Provide frequent mouth and skin care  
- Assess quantity and quality of discomfort  
- Provide a quiet environment and frequent reassurance  
- Observe for complications that may cause discomfort, such as infection of vascular access device, peritonitis or inadequate draining during peritoneal dialysis, and gastrointestinal disturbances (nausea, vomiting, diarrhea, constipation)  
- Administer analgesics, antiemetics, antidiarrheals, laxatives (non–magnesium and non–phosphate containing), stool softeners, antihistamines, sedatives, or anxiolytics as needed and monitor response                                                                                                                                 |
| No complaints of discomfort |                                                                                                                                                                                                            |
| No objective indicators of discomfort |                                                                                                                                                                                                            |
| **Ineffective coping**            |                                                                                                                                                                                                            |
| Patient will demonstrate a decrease in anxiety as evidenced by: | - Assess vital signs  
- Explore patient and family concerns  
- If the patient is intubated, develop interventions for effective communication  
- Arrange for flexible visitation to meet needs of the patient and family  
- Provide for adequate rest and sleep  
- Provide frequent information and updates on condition and treatment, and explain equipment. Answer all questions  
- Consult social services and clergy as appropriate  
- Administer sedatives and antidepressants as appropriate and monitor response                                                                                                                                 |
| Vital signs within normal limits  |                                                                                                                                                                                                            |
| Level of consciousness within normal limits |                                                                                                                                                                                                            |
| Subjective reports of decreased anxiety levels |                                                                                                                                                                                                            |
| Objective assessment of decreased anxiety level |                                                                                                                                                                                                            |

(continued)
Fluid Balance Changes in Chronic Kidney Disease

In CKD, fluid and salt restriction is a mainstay of therapy to prevent fluid overload. Sodium is restricted to less than 2,000 mg/d, and fluid intake is limited to 500 mL plus the patient’s previous day’s 24-hour urine output. Diuretics are also used to manage volume overload. Patients are usually able to respond to diuretics until their GFR falls below 10 to 15, at which point extensive renal damage prevents an adequate response. By the time CKD progresses to stage G5, oliguria is typically manifested, and signs and symptoms of fluid overload, such as edema, hypertension, pulmonary edema, heart failure, and jugular vein distention, occur unless dialysis therapy is instituted. In these patients, an ongoing assessment of fluid status, including obtaining accurate intake and output measurements with daily weights and monitoring for fluid complications, is imperative.

Managing Acid–Base Alterations

AKI and CKD typically result in metabolic acidosis because of the nephrons’ inability to secrete and excrete hydrogen ions and reabsorb bicarbonate ions as renal failure progresses. In critically ill patients, this acid–base disturbance may be intensified because of concurrent conditions, such as lactic acidosis or diabetic ketoacidosis, and because such patients are in a high-catabolic state, which increases the release of intracellular acids into the circulation. Clinical manifestations of metabolic acidosis include headaches, nausea and vomiting, deep and rapid respirations (Kussmaul respirations), altered mental status, hyperkalemia, and tachycardia. In severe metabolic acidosis, bradycardia and hypotension may manifest because of myocardial depression and vasodilation. There is also a dramatic depression of the patient’s level of consciousness, often resulting in stupor or coma.

In CKD, metabolic acidosis begins to manifest as the patient reaches G stage 3A and the GFR falls below 60 mL/min/1.73 m². Although the metabolic acidosis associated with CKD is usually mild (CO₂ 16 to 22 mEq/L), it is associated with many adverse consequences, including fatigue, protein catabolism, and bone demineralization. The bones become demineralized because bone phosphate and carbonate are used as buffers against excess hydrogen ions.

Laboratory assessments of acid–base status using arterial blood gas (ABG) values and venous carbon dioxide content guide therapy. Patients with a plasma bicarbonate level less than 22 mEq/L warrant treatment. Therapy involves...
the administration of alkaline medications (eg, Bicitra, sodium bicarbonate tablets), dialysis, or both. When using citrate-containing medications, such as Bicitra, it is important that these medications not be given with aluminum-containing phosphate binders. Using these agents together would put the patient at risk for aluminum toxicity because citrate significantly increases aluminum absorption from the gastrointestinal tract.

The use of IV sodium bicarbonate is reserved for severe acidosis (evidenced by a blood pH < 7.2 or a plasma bicarbonate level less than 12 to 14 mEq/L) because of potential complications of extracellular volume excess, metabolic alkalosis, and hypokalemia. Intractable acidosis is an indication for dialysis, which removes excess hydrogen ions and adds a buffer to the body. In hemodialysis the buffer is bicarbonate, and in peritoneal dialysis it is lactate, which is metabolized to bicarbonate. When correcting metabolic acidosis, caution is advised. Rapid correction may result in a suppressed respiratory drive and hypoventilation. Rapid correction can also lead to acute hypocalcemia and tetany, because the amount of ionized calcium decreases in an alkaliotic state owing to increased binding of calcium with albumin and inorganic substances such as phosphate. Throughout any kind of acid–base therapy, it is necessary to monitor serum bicarbonate, pH, and calcium and potassium levels closely.

Managing Cardiovascular Alterations

Alterations in the cardiovascular system can cause or accelerate AKI and CKD. In addition, cardiovascular complications can arise as a result of renal failure itself. Common cardiovascular complications in AKI and CKD include hypertension and hyperkalemia. Pericarditis, another cardiovascular complication of renal disease, is primarily seen with CKD.

Hypertension

Hypertension as a complication of renal failure results from excess retention of water and sodium, overactivation of the sympathetic nervous system, and stimulation of the renin–angiotensin–aldosterone system. Because controlling BP is essential to prevent end-organ damage and reduce the risk for life-threatening cardiovascular events, adequate treatment is necessary. Management may include fluid and sodium restrictions, diuretic administration, antihypertensive therapy, and dialysis to remove excess fluid. Extensive patient teaching regarding nonpharmacologic and pharmacologic treatment and the potential complications of uncontrolled hypertension is an integral part of management.

Hyperkalemia

Hyperkalemia is a life-threatening condition seen in patients with AKI and CKD. As the GFR decreases, the ability of the kidneys to excrete excess potassium diminishes. In critically ill patients, this renal impairment is frequently compounded by states of increased catabolism, acidosis, cellular injury, administration of potassium-based medications, and blood transfusions, all of which can raise serum potassium levels. If not recognized and treated, hyperkalemia leads to fatal dysrhythmias.

Assessment of hyperkalemia involves close monitoring of serum potassium levels as well as monitoring the effects of potassium on the electrical conduction system of the heart. Characteristically, electrocardiogram (ECG) changes occur as potassium levels rise (Fig. 31-5). The first ECG changes that occur, usually when serum potassium is in the range of 6 to 7 mEq/L, are the appearance of tall, tented T waves and a prolonged PR interval. Next, there is a loss of the P wave and a slight widening of the QRS complex. At this point, the serum potassium is usually in the range of 8 to 9 mEq/L. From here, the QRS complex continues to widen until a sine wave (wavy line) pattern develops. This ominous sign is closely followed by ventricular fibrillation or standstill.

When evaluating hyperkalemia, note that patients with long-standing elevations in serum potassium are more refractory to its effects on the heart than patients in whom hyperkalemia develops suddenly. Thus, potassium and ECG changes must be evaluated together to determine the acuteness of the situation. Other effects of hyperkalemia that are monitored include paresthesias, hyporeflexia, and muscle weakness (which typically begins in the lower extremities and ascends to the trunk and upper extremities).

Mild hyperkalemia (a serum potassium level less than 6 mEq/L without ECG changes) may be treated with dietary potassium restriction, diuretics, and potassium-binding resins (eg, sodium polystyrene sulfate [SPS]). SPS is given orally,
with or without sorbitol, or as an enema without sorbitol. The oral dose is 15 to 30 g every 4 to 6 hours as needed. The rectal dose is 50 g in 150 mL of tap water; it should be retained in the colon for at least 30 to 60 minutes. This drug must be used with extreme caution in critically ill patients with decreased colonic motility, such as postsurgical patients and patients taking large amounts of opiates, because of its association with colonic necrosis in this population. The risk of colonic necrosis may be increased when SPS is mixed with sorbitol.55 Use should be discontinued in patients who develop constipation, and repeated doses should not be administered if a patient has not passed stool. It is recommended that a cleansing enema with 250 to 1,000 mL tap water at body temperature be given after rectal administration. Sodium polystyrene should never be used in a patient with a gastrointestinal obstruction or ileus, and bowel sounds should always be assessed before its administration.

Treatment of life-threatening hyperkalemia entails taking steps to antagonize the effects of potassium on the heart, promote intracellular shifting of potassium, and remove potassium from the body. Antagonizing the effects of potassium on the heart is achieved with IV calcium gluconate or chloride, and is the first priority for patients with substantial ECG changes. Intracellular shifting of potassium is done next to bridge the gap until potassium removal from the body can be executed. Means to shift potassium into the cell include IV insulin and dextrose administration and IV bicarbonate administration. β2-Adrenergic therapy can also effect transcellular potassium shifting, but is less commonly used because of the requirement for 10 to 20 times the dose used for reactive airway disease. Removal of potassium from the body entails, as previously mentioned, diuretic administration and the use of potassium exchange resins. If these measures do not control hyperkalemia, dialysis must be initiated. Obviously, in a patient who has stage G5 CKD, and who is likely already receiving dialysis therapy, dialysis is initiated immediately along with other emergent therapy in life-threatening hyperkalemia.

Pericarditis

Pericarditis resulting from uremia (uremic pericarditis) is a complication that can be seen primarily in stage G5 CKD. This type of pericarditis is characterized by an inflammation of the pericardial membrane, which causes the pericardial capillaries to become permeable to fluid, red blood cells, fibrinogen, and albumin. In most cases, the inflammation is aspecific, although it may also result from bacterial or viral infections. The consequent serous or serosanguineous fluid in the pericardial cavity (pericardial effusion) can increase the intrapericardial pressure and compromise ventricular contractility, stroke volume, and cardiac output. Pericardial tamponade, which results when the accumulation of pericardial fluid is so large that adequate cardiac output cannot be maintained, is a life-threatening emergency. The exact etiology of uremic pericarditis is unknown, but it is associated with prolonged inadequate dialysis therapy, uremic toxins, infectious agents, treatment with the antihypertensive agent minoxidil, and heparin administration.

Chest pain, fever, and a pericardial friction rub are the classic triad of findings associated with pericarditis. The chest pain is characteristically sharp and steady, and is relieved by sitting forward and intensified by breathing deeply. The pericardial friction rub (a harsh, leathery sound heard over the precordial area) may precede the pain, may persist after the pain has subsided, and may disappear when the volume of effusion increases. The typical ECG changes in pericarditis are new-onset atrial dysrhythmias and widespread ST elevations with an upward concavity (versus the upward convexity typical in an acute MI). However, the widespread ST wave elevations are not consistently present in uremic pericarditis because its etiology is metabolic in nature, and injury is uncommon. In a large pericardial effusion, signs and symptoms are more dramatic and include dyspnea, tachycardia, mental confusion, weakness, increased jugular vein distention, peripheral edema, and a paradoxical pulse greater than 10 mm Hg during inspiration. Tamponade results in distended neck veins, tachypnea, a narrowed pulse pressure, an increased PAOP, muffled heart sounds, diminished peripheral pulses, and a decreased level of consciousness.

Therapy for uremic pericarditis includes aggressive dialysis therapy, usually daily, until symptoms disappear. Also, because anticoagulation during dialysis may precipitate or enhance bleeding into the pericardial space, low-dose, regional, or no heparin may be prescribed. Systemic steroids and NSAIDs, such as indomethacin, may also be used but have had variable results. Cardiac tamponade is an emergency that requires urgent pericardiocentesis to relieve the pressure on the heart. For the patient in whom recurrent pericarditis develops or in whom the pericardium becomes constrictive, surgical creation of a pericardial window or pericardectomy may be necessary.

Cardiovascular Disease in Chronic Kidney Disease

CKD is associated with high cardiovascular morbidity and mortality. In fact, patients with CKD are much more likely to suffer from cardiac disease resulting in cardiovascular death than to eventually require RRT.35,50 The predominant cardiac disorders in CKD are left ventricular hypertrophy, coronary artery disease, dysrhythmias, cardiomyopathy, congestive heart failure, and valvular dysfunction. Because most of these cardiovascular disorders develop over a period of at least a few years, they usually present early in CKD and continue to progress as renal function declines. This association between CKD and cardiovascular disease may occur for the following reasons: (1) cardiovascular disease causes renal dysfunction (ie, heart failure); (2) CKD causes an increased risk for cardiovascular disease; or (3) other factors (eg, hypertension, diabetes mellitus, anemia, or hyperlipidemia) cause or accelerate both renal dysfunction and cardiovascular disease. In any case, monitoring for cardiovascular disease, reducing modifiable risk factors, and treating specific cardiovascular conditions when present are essential to decrease mortality in patients with CKD.

Diagnostic tests useful in assessing for cardiovascular disease in these high-risk patients include routine ECGs, echocardiography, and cardiac stress testing. Pharmacologic rather than exercise stress testing is the stress test of choice because patients with CKD are often unable to attain the level of exercise needed to make exercise stress tests useful. More invasive tests for symptomatic patients include a thallium scan and coronary angiography. Regarding blood testing, in patients with a GFR < 60, cardiac biomarkers (troponins and...
B-type natriuretic peptides) must be interpreted with caution as their diagnostic value becomes less reliable. Modifiable risk factors that can contribute to cardiovascular disease, and that should be addressed as part of managing patients with CKD, include hypertension, obesity, hyperlipidemia, hypervolemia, anemia, smoking, hyperglycemia, calcium and phosphate imbalances, vitamin D deficiency, and metabolic acidosis. Statin therapy is recommended for lipid lowering in CKD, to decrease all-cause and cardiovascular mortality for patients not yet on dialysis; benefits are less clear for patients already on dialysis. As with the general population, disease-specific treatment (eg, antiplatelet therapy and β-blocker administration for coronary artery disease) must be instituted as appropriate.

Managing Pulmonary Alterations

A frequent complication in patients with oliguric AKI or stage G5 CKD is the development of pulmonary edema. This complication results from fluid overload, heart failure, or both. Clinical manifestations include dyspnea; crackles on auscultation; the production of pink, frothy sputum; tachypnea; tachycardia; decreased arterial oxygen saturation (SaO2); and evidence of fluid overload on chest radiograph. Management involves fluid and sodium restriction, treating underlying cardiac disease, and possibly diuretic medications if the patient’s kidneys can respond to them. Frequently, pulmonary edema becomes life threatening, necessitating intubation, emergent dialysis, or both to improve arterial oxygenation and restore fluid balance.

Other pulmonary complications in renal failure include pleural effusions, pleuritic inflammation and pain, uremic pneumonitis, and pulmonary infections. Pleuritic inflammation and uremic pneumonitis occur more frequently with stage G5 CKD and are due to the effect of uremic toxins on the lungs and inadequate dialysis. Pulmonary infections, on the other hand, are common in both AKI and CKD, especially in critically ill patients. Factors associated with renal failure that contribute to pulmonary infections include decreased pulmonary macrophage activity, a generalized immunocompromised state, tenacious sputum, and a depressed cough reflex. Collaborative management includes culturing sputum, administering broad-spectrum antibiotics until organism-specific sensitivities are available, and teaching and encouraging pulmonary hygiene measures (ie, coughing and deep breathing).

Managing Gastrointestinal Alterations

A potentially life-threatening gastrointestinal complication in both AKI and CKD is gastrointestinal bleeding. Proposed etiologies for gastrointestinal bleeding as it relates to renal failure include platelet and blood-clotting abnormalities; anticoagulation with dialysis, access patency, or both; ingestion of irritating drugs (eg, NSAIDs, aspirin); arteriovenous malformations (with CKD), and increased ammonia production in the gastrointestinal tract from urea breakdown. Ammonia is known to be irritating to mucosal surfaces. CKD patients with high urea levels are prone to develop gastritis, ulcerative esophagitis, and duodenitis as evidenced by biopsy. Physiologic stress, especially in critically ill patients, is another proposed contributor. Assessment parameters include examining all vomit and stool for gross and occult blood; monitoring iron, hemoglobin, hematocrit, and red blood cell indices; and paying close attention to signs of intravascular volume depletion. If gastrointestinal bleeding is suspected, radiographic and endoscopic examinations are often required to diagnose and treat specific lesions. Management depends on the specific lesion, but often includes volume restoration with crystalloids and blood products as well as administration of histamine-2 receptor (H2) blockers, proton-pump inhibitors (PPIs), or both.

Other gastrointestinal complications associated with renal failure occur primarily in CKD and include anorexia, nausea, vomiting, diarrhea, constipation, gastroesophageal reflux disease (GERD), and oral cavity alterations, such as stomatitis, a metallic taste in the mouth, and uremic fetor (the smell of urine and ammonia on the breath). Oral alterations and symptoms of anorexia, nausea, and vomiting are partially attributable to high levels of uremic toxins, which affect the intestinal mucosa and stimulate vomiting centers in the brain. The reason GERD is common is unclear, but it may be due to delayed gastric emptying, increased gastrin production, and use of medications that affect lower esophageal sphincter tone (ie, calcium-channel blockers). Collaborative management involves initiating (or providing) adequate dialysis, providing prophylactic antacids and H2 blockers or PPIs, and administering antiemetics. Good oral hygiene is also essential.

The complication of constipation is seen frequently in patients with renal failure owing to decreased bulk and fluid in the diet and the administration of oral iron supplements and calcium-based phosphate binders. Diarrhea may also occur as a result of intestinal irritation from uremia. Collaborative management includes increasing dietary bulk; administering bulk-forming laxatives, stool softeners, or both; administering antidiarrheal agents; or a combination of these therapies. For patients with stage G5 CKD, magnesium-containing medications, including cathartics such as magnesium citrate, should be avoided because of the risk of hypermagnesemia in these patients. In addition, Fleet enemas, which contain large amounts of phosphate that could be absorbed systemically, should not be used.

Managing Neuromuscular Alterations

Neuromuscular alterations include sleep disturbances, cognitive process disturbances, lethargy, muscle irritability, and peripheral neuropathies, including restless leg syndrome and burning feet syndrome. Restless leg syndrome is characterized by a discomfort in the legs, especially at night, which is sometimes relieved by continuous movement of the extremities. Burning feet syndrome consists of paresthesias and numbness in the soles of the feet and lower parts of the legs. These neuromuscular complications are associated primarily with stage G4 and G5 CKD and are thought to be the result of electrolyte imbalances, metabolic acidosis, and the effect of uremic toxins on motor and sensory nerves. Cognitive process disturbances, such as difficulty concentrating and impaired short-term memory, are linked to elevations of BUN in the cerebral vasculature, which can result in cerebral edema. Extensive cerebral edema can result in seizures, projectile vomiting, and even coma or death.
Frequent assessments for cognitive disturbances, seizure activity, and other neuromuscular alterations are important. In addition to thorough neuromuscular examinations, nerve conduction studies and diagnostic tests, including electroencephalograms and head CT scans, may be used. Collaborative management involves implementing emergency treatment, as in the case of sustained seizure activity; maintaining electrolyte balance; correcting metabolic acidosis; using regular dialysis; and providing extensive patient teaching. Specific points that need to be included during patient teaching are the importance of preventing injury to the extremities by heat or trauma when paresthesias are present, and that alterations in neuromuscular function often improve with regular dialysis or transplantation. However, if components of the patient’s neuropathies are due to other comorbid conditions, such as diabetes, the problem may respond only minimally to dialysis or renal transplantation.

It is important to be aware of possible cognitive alterations during patient teaching. Because the patient may have difficulties concentrating and impairments in short-term memory, teaching should be provided in short, frequent sessions with reinforcement of material, and should include the family as much as possible. This is especially true for critically ill patients who are, by definition, in a crisis situation.

Managing Hematologic Alterations

Hematologic system alterations are major complications in AKI and CKD. These alterations include an increased bleeding tendency, an impaired immune system, and anemia.

Increased Bleeding Tendency

The increased bleeding tendency in renal failure is attributable to impaired platelet aggregation and adhesion and an altered platelet–vessel wall interaction. These alterations are thought to be due to uremia, but their exact pathophysiologic mechanisms are unknown. Assessment involves the monitoring of platelet counts, coagulation studies, and assessing for bleeding, especially gastrointestinal bleeding. Collaborative management includes administering blood products as needed, protecting the patient from injury, and avoiding medications that alter platelet function, such as NSAIDs and aspirin. Often heparin (for dialysis) and aspirin (for MI prevention) are indicated in patients with renal failure; in such cases, the effects of these medications on platelets must be closely monitored. One potential and serious complication of heparin is heparin-induced thrombocytopenia; the development of this complication mandates discontinuation of the drug.

Impairments in the Immune System

Patients with renal failure are in an immunocompromised state, which sets the stage for infections (a major cause of mortality in AKI and CKD). The impairments in the immune system are thought to be due to malnutrition and the effects of uremia on white blood cells. These effects include depressed T cell–mediated and antibody-mediated immunity, impaired phagocytosis, and decreased chemotaxis and adherence of white blood cells.

Assessing the patient for infection and monitoring laboratory indicators of infection must be done continuously. The baseline body temperature in uremic patients is decreased, and thus any increase in temperature above baseline is significant as a gauge of infection. Collaborative management includes frequent hand washing, removing invasive catheters as soon as possible (or avoiding their use altogether), and culturing blood and other body fluids that may be infected to identify specific organisms and determine appropriate antimicrobial therapy.

Anemia

Anemia associated with renal failure is attributable to three main mechanisms: erythropoietin deficiency, decreased red blood cell survival time, and blood loss from an increased bleeding tendency. Of these three mechanisms, erythropoietin deficiency has the most dramatic effect.

More than 90% of the hormone erythropoietin is produced in the kidneys. It is a glycoprotein that stimulates red blood cell production in response to hypoxia, and it is essential to maintaining normal red blood cell counts. As kidney disease progresses and nephrons are damaged, this hormone is inadequately synthesized, and a hypoproliferative anemia occurs, resulting in normocytic normochromic red blood cells. Before the production of erythropoietin by human recombinant techniques, this hormone deficiency caused most patients with CKD to be in a severely anemic state, requiring frequent blood transfusions.

Decreased red blood cell survival time in renal failure occurs in the form of a mild hemolysis. The exact mechanism for this hemolysis is unclear, but it may be related to dialysis therapy or the effect of uremia on red blood cells. The average survival of red blood cells in uremia is only 70 days, which contrasts with the normal 120-day life span of a red blood cell in the general population.

In addition to the three aforementioned mechanisms of anemia, other factors can contribute to anemia in patients with renal failure, particularly those who are critically ill. Examples are malnutrition, frequent laboratory blood sampling, dialyzer malfunction and sequestration of blood in the dialyzer, and infectious states. Treating anemia in patients with renal failure is extremely important for many different reasons, including increasing the oxygen-carrying capacity of the blood, increasing intravascular volume, and preventing the negative consequences of anemia on the cardiovascular system. Anemia exacerbates myocardial, cerebral, and peripheral ischemia and increases the risk for development (or acceleration) of left ventricular hypertrophy. Correcting anemia has also been shown to have a positive impact on quality-of-life issues in patients with renal failure, including increases in appetite, energy, and work capacity.

A thorough evaluation of anemia involves diagnostic studies and a history and physical examination. Diagnostic metabolic parameters that should be obtained and monitored include hemoglobin, hematocrit, red blood cell indices, and reticulocyte counts. In addition, the stool or vomit should be tested for occult blood. Iron studies also need to be obtained, because iron deficiency itself can cause anemia, and because adequate iron stores are needed for erythropoietin to be effective. Specific iron indices that should be obtained include total serum iron, total iron-binding capacity, and serum ferritin levels. Finally, nutritional parameters and levels of folic acid, pyridoxine, and vitamin B12, all of which affect red blood cell production, need to be monitored.
A thorough history and physical examination involve questioning patients about potential sites of bleeding (eg, by asking about stool color), assessing for signs and symptoms of anemia (eg, angina, tachycardia, skin and mucous membrane pallor, appetite suppression, weight loss, decreased energy levels, fatigue), assessing for sources of blood loss, assessing for inflammation or infection, and assessing for other diseases that can cause anemia (eg, lupus, sickle cell anemia).

Collaborative management of anemia includes minimizing blood loss, administering oral or IV iron supplements, providing vitamin supplementation, aggressively treating infections, ensuring adequate nutrition, and administering erythropoietin-stimulating agents (ESAs), such as human erythropoietin or darbepoetin, blood products, or both. The KDIGO Guideline suggests iron administration in CKD patients when transferrin saturation is ≤30% and serum ferritin level is ≤500 ng/mL.65 Goals for ESA therapy are less concrete owing to potential cardiovascular risks when targeting normal hemoglobin levels. These cardiovascular risks prompted the Federal Drug Administration (FDA) to issue a warning in all package inserts of ESAs. Hemoglobin goals should be individualized, based on patient symptoms and comorbidities, using the lowest ESA dose to reduce the need for red blood cell transfusions. The KDIGO Guideline advises not to use ESAs to intentionally increase Hgb concentration greater than 11.5 mg/dL, or recommend against their use in patients with active cancer or a recent history of malignancy.35

Certain points regarding ESA therapy and the management of anemia deserve special mention. One is that the full effect of these medications takes weeks to achieve, and hence in patients with profound anemia, blood administration is indicated. In addition, ESA administration may result in an elevation of BP; in some cases, modification of antihypertensive therapy may be needed. When there is an inadequate response to ESAs despite increased dosages, reasons for erythropoietin resistance need to be explored. These include occult infections, inflammatory states, human immunodeficiency virus infection, hyperparathyroidism, aluminum toxicity, malnutrition, iron deficiency, and bone marrow malignancy.

Important clinical features regarding iron preparations should also be considered. Oral iron is poorly absorbed if taken with phosphate binders, antacids, H2 blockers, or PPIs, all of which are commonly prescribed to patients with renal failure. On the other hand, IV iron has much better bioavailability but carries the risk of an allergic, sometimes life-threatening, reaction. This risk has significantly decreased with newer, more biocompatible IV preparations.

Extensive patient teaching about anemia is crucial. At minimum, teaching should include information about medication therapy; timing of iron supplements; potential causes, signs, and symptoms of worsening anemia; and energy conservation techniques. Instruction about measures to decrease bleeding, such as use of a soft toothbrush and avoidance of NSAIDs, is also helpful.

Managing Alterations in Drug Elimination

Because many pharmacologic agents, their metabolites, or both are excreted by the kidneys, extreme caution must be used when administering medication to patients with renal failure. Depending on the patient’s GFR, adjustments may need to be made in drug dosage, the interval between drug dosages, or both. Important to consider, especially in AKI, is that the GFR is often unstable, and thus the GFR must be monitored frequently to determine dosages accurately. As in patients without renal failure, monitoring serum levels of certain medications to be sure they are within the therapeutic range is essential. For patients receiving dialysis, the health care team must be cognizant of which drugs are removed during dialysis therapy to ensure appropriate timing of drug administration.

Managing Skeletal Alterations

In renal failure, disturbances in calcium and phosphate balance set the stage for secondary hyperparathyroidism and high-turnover renal osteodystrophy (renal bone disease). As the GFR declines, glomerular filtration of phosphate also decreases, and serum phosphate levels begin to rise. This results in decreased serum ionized calcium levels because of binding of the calcium with the phosphate. Calcium levels also decrease because of the failing kidneys’ inability to convert vitamin D to its active form (1,25-dihydroxycholecalciferol, or vitamin D3), which is needed for adequate intestinal absorption of calcium. In response to decreased ionized calcium levels, elevations in serum phosphorus levels, and reduced vitamin D3 synthesis, the parathyroid glands secrete parathyroid hormone (PTH). Over time, the continuous PTH stimulation leads to hyperplasia and proliferation of the parathyroid cells, resulting in secondary hyperparathyroidism. PTH causes the reabsorption of calcium and phosphate salts from bones, thus increasing the serum calcium level at the expense of bone density and mass. PTH also causes calcium reabsorption and phosphate excretion in the kidneys; however, as renal failure progresses, this effect of PTH is not realized. Eventually, as calcium and phosphate continue to be reabsorbed from bones, both levels rise in the serum concomitantly. This results in an elevation in the normal calcium–phosphate product (serum calcium multiplied by serum phosphate) of less than 40 mg/dL. When the product exceeds 55 mg/dL, calcium phosphate crystals can form and precipitate in various parts of the body (a condition known as metastatic calcifications), including the brain, eyes, gums, valves of the heart, myocardium, lungs, joints, blood vessels, and skin. Other insults to bones that can occur in renal disease include bone demineralization in response to metabolic acidosis and low-turnover renal osteodystrophy from aluminum deposits in the bone or overdose of vitamin D3 therapy. The events related to high-turnover renal osteodystrophy in renal failure are summarized in Figure 31-6.

Complications from renal bone disease include bone pain, fractures, pseudogout from deposits of calcium oxalate in synovial fluid, periartthritis from calcifications of the joints, proximal muscle weakness, spontaneous tendon rupture, and pruritus. Metastatic calcifications can result in calcified blood vessels and valves, skin lesions, red-eye syndrome from crystal deposition in the conjunctiva, and, most seriously, ischemic ulcers. Laboratory data, including levels of calcium, phosphate, aluminum, alkaline phosphatase, and intact PTH, help make the diagnosis. Radiographic findings also may be helpful, particularly in high-turnover bone disease; images may reveal subperiosteal bone thinning, most easily
According to the KDIGO Clinical Practice Guideline, calcium levels should be maintained in the normal range. This is accomplished with diet and calcium supplements. If calcium levels exceed 10.2 mg/dL, therapies that may be contributing to hypercalcemia (eg, administering calcium or vitamin D supplements) should be adjusted to reduce the risk for extraskeletal calcifications.

Vitamin D supplements are administered to suppress PTH secretion. Besides causing a decrease in PTH indirectly through the elevation of serum calcium, active vitamin D also directly inhibits PTH secretion by binding to vitamin D receptors on the parathyroid gland. Active vitamin D may be given orally (calcitriol) or intravenously (Calcijex). In either case, caution must be exercised with the administration of these agents to avoid hypercalcemia and hyperphosphatemia as well as to avoid oversuppression of the parathyroid gland. Two synthetic analogs of active vitamin D that can also be used are paricalcitol (Zemplar) and doxercalciferol (Hectorol). These drugs have the advantage of causing less dramatic increases in serum calcium and phosphate levels while still causing PTH suppression.

The most recent therapeutic agents developed to help suppress PTH and the development of secondary hyperparathyroidism are calcimimetics, which work by increasing the sensitivity of the calcium-sensing receptor in the parathyroid gland to extracellular calcium. In the United States, the Food and Drug Administration approved the calcimimetic cinacalcet hydrochloride (Sensipar) for patients with ESRD. It has been shown to be both safe and effective, with the most common side effects being nausea and vomiting and hypocalcemia. Rarely, a parathyroidectomy may be necessary for patients who are refractory to available treatments for secondary hyperparathyroidism, including vitamin D therapy and calcimimetics.

Patient teaching concerning bone disease and its management is complex and needs to be continually reinforced. Particular areas that should be included are the purpose and timing of medications (eg, phosphate binders must be given with meals to be effective), dietary modifications, and the complications of untreated bone disease.

### Managing Integumentary Alterations

Alterations in the integumentary system in renal failure include xerosis (dryness), pruritus, pallor, ecchymosis and purpura, and pigmentation changes. Pigment changes include hyperpigmentation, especially at sun-exposed sites, or a yellow discoloration to the skin. CKD is also associated with hair loss and nail changes, such as the absence of the lunula, splinter hemorrhages, Beau lines (white lines across the fingernails), and onychomycosis. Possible contributing factors to these alterations are iron deficiency anemia, decreased activity of sweat and sebaceous glands, retained skin pigments, platelet dysfunction and capillary fragility, deposition of calcium phosphate crystals into the skin, hyperparathyroidism, hyperphosphatemia, increased vitamin A levels in the epidermis, and impaired cellular immunity.

Uremic frost, a white powdery substance composed of urates on the skin, is due to crystallization of urate; it is usually seen only in severely uremic patients for whom needed dialytic therapy is being withheld. These skin alterations, particularly pruritus...
and xerosis, may lead to localized infection from excoriation and secondary skin changes, such as lichen simplex and keratic papules. In addition, substantial patient discomfort and psychological disturbances from skin disfigurement may occur.

Collaborative management for skin alterations includes phosphate regulation, nutritional supplementation, correction of anemia, antihistamine medications, and meticulous skin care and turning to prevent skin breakdown. Dialysis therapy helps as well by removing metabolic waste products. However, because of potential allergies to the dialysis system components, dialysis therapy can also aggravate some conditions, such as pruritus. Patient education should include information on factors contributing to skin alterations, the importance of keeping the skin clean and well moisturized, and ways to avoid excoriation (such as keeping the fingernails trimmed).

### Managing Alterations in Dietary Intake

The goals of nutritional therapy in renal failure are to minimize uremic symptoms; reduce the incidence of fluid, electrolyte, and acid–base imbalances; minimize symptoms of anemia; decrease the patient’s vulnerability to infections; and limit catabolism. Dietary restrictions related to managing comorbid conditions and reducing cardiovascular risk also need to be considered. Because of the complexity of achieving a nutritional therapy plan that meets these goals, a collaborative health care team approach, including the ongoing participation of a dietitian, is essential. This is particularly the case in critical care, where patients are usually in a catabolic state and are at risk for substantial malnutrition.

Renal diet prescriptions include restrictions in fluid, sodium, potassium, and phosphate intake, and may include supplementation of iron, vitamins, and calcium. Calorically, critically ill patients with renal disease need a high-calorie diet with a total of 20 to 30 kcal/kg/d, most of which should come from a combination of carbohydrates and lipids. In addition, adequate protein intake must be administered to prevent catabolism, and at least 50% of protein intake should be of high biologic value to ensure that the minimal intake requirements of essential amino acids are met. Protein restriction to decrease symptoms of uremia and slow the progression of renal failure is controversial (refer to the section on preventing the progression of CKD) but may be beneficial. However, protein restriction should never compromise meeting anabolic goals, exposing the patient to the risk of malnutrition. In AKI patients, the KDIGO 2012 Guideline does not recommend protein restriction as it has not been shown to delay the need for RRT.

In critically ill patients, parenteral nutrition may need to be instituted because of impaired bowel function or severe malnutrition, but the enteral route is preferred if feasible. In oliguric patients, the high hourly volume requirements needed for parenteral or enteral nutrition often must be offset by dialysis or isolated ultrafiltration.

To determine the effectiveness of nutritional therapy, continual laboratory monitoring of serum protein, cholesterol, albumin and prealbumin, electrolytes, hemoglobin, hematocrit, and urea and creatinine levels is essential. Patient weight, volume status, and energy levels are additional monitoring parameters. Nutritional education, including information on dietary restrictions, the use and timing of phosphate binders, vitamin and mineral supplements, and measures of nutritional status should be provided.

### Managing Alterations in Psychosocial Functioning

Patients in AKI and CKD often experience feelings of fear, anxiety, and powerlessness. In addition, patients frequently have an alteration in self-concept as well as body image disturbances because of both physical and functional changes that occur in renal failure. Patients and their families may have difficulty coping owing to stress, limited resources or support, inadequate or ineffective coping mechanisms, interruptions in usual family roles, or a combination of these factors. It is important that the health care team attend to these and other psychosocial complications of renal failure to treat the patient and family holistically. Specific interventions include thorough patient and family teaching, active involvement of the patient and family members in managing the condition, ensuring adequate rest and sleep for the patient, exploring the patient’s and family’s feelings and concerns, providing support, and obtaining the active involvement of social services and clergy as appropriate.

### Clinical Applicability Challenges

**Case Study**

Mr. X., a 63-year-old white man, was admitted for ST elevation MI. He was in his normal state of health until 6 hours before admission, when he developed substernal chest pain (SSCP) with radiation to his left arm. Pain was accompanied by mild diaphoresis. After self-administering antacids without relief, he asked his wife to take him to the emergency department (ED).

In the ED, he was found to be anxious and diaphoretic, and he complained of dyspnea and 9/10 SSCP. Initial vital signs were as follows: temperature 37.5°C, BP 90/60, pulse 105, respiratory rate 24, peripheral capillary oxygen saturation 92% on 4 L nasal cannula. The physical exam was significant for an elevated jugular venous pressure and pulmonary crackles halfway up bilaterally. Mr. X. did not have any peripheral edema. His past medical history included hypertension for 22 years with variable control, hyperlipidemia, CKD (baseline serum creatinine of 1.8 mg/dL), and type II diabetes mellitus for 15 years.

Initial labs in the ED were notable for a serum creatinine of 1.9 mg/dL, an elevated troponin, and 2+ protein on urinalysis. EKG revealed 3 mm ST elevation in leads II and AVF. Chest x-ray revealed moderate pulmonary
artery prominence. Home medications include aspirin 81 mg QD, Lisinopril 20 mg QD, Lantus 15 units QHS, Lasix 20 mg, and atorvastatin 20 mg QHS. Aside from supplemental oxygen, Mr. X received aspirin 325 mg and nitroglycerin SL 0.4 mg in the ED. Post SL nitroglycerin, his chest pain remained unchanged and his BP decreased to 85/50; HR 110.

The patient was evaluated by the cardiology department and emergently taken to the catheterization laboratory; coronary angiography revealed a 95% stenotic lesion in the mid-right coronary artery. The remaining arteries showed no flow limiting. The patient underwent percutaneous transluminal angioplasty and placement of a bare metal stent. He received 175 mL of IV contrast dye. Following the procedure, the patient started on Plavix, SSI, beta-blocker therapy, and continued on daily aspirin.

On postprocedure day 1, the patient was feeling well and chest pain free. BP was 140/85, HR 70, SPO2 95% on RA. Urine output was 1,100 mL and serum creatinine was 1.8 mg/dL. On postprocedure day 2, urine output had decreased to 600 mL. Serum creatinine was 1.9 mg/dL. By postprocedure day 3, the patient was oliguric with a total urine output of 200 mL and required 4 L nasal cannula supplemental oxygen to maintain SPO2 over 92%. Serum creatinine was 2.7 mg/dL. Chest x-ray revealed pulmonary edema, and retained contrast could be seen in the visible portion of the kidneys.

1. What information supports the diagnosis of AKI in Mr. X. versus progression of his CKD?
2. What makes Mr. X. at risk for contrast-induced nephropathy?
3. In caring for Mr. X., what fluid and electrolyte and acid–base alterations may be anticipated?