Acute Renal Failure: A Practical Update

ROBERT C. ALBRIGHT, JR, DO

Acute renal failure (ARF) affects almost all medical specialties. Its occurrence seems to be increasing in hospitalized patients. A structured approach to the evaluation and management of ARF would facilitate rapid diagnosis and treatment in most patients. Appreciation for the multiple drugs that affect renal function is especially important. Exclusion of urinary outflow obstruction and administration of therapies that improve renal perfusion should be given top priority with respect to managing ARF. Dialytic intervention for ARF is required when otherwise irreversible pathophysiologic derangements of electrolyte homeostasis, fluid balance, and uremic solute control are imminent. This article provides a brief review and update on the clinical evaluation and management of ARF.


ACE = angiotensin-converting enzyme; ARF = acute renal failure; ATN = acute tubular necrosis; ICU = intensive care unit; NSAIDs = nonsteroidal anti-inflammatory drugs

EPIDEMIOLOGY

Rigorous study of ARF is complicated by the lack of a uniform definition. More than 20 definitions have been published in both basic science and clinical trials. Despite these difficulties, ARF occurs in approximately 1% of hospitalized patients, in as many as 20% of patients treated in ICUs, and as many as 4% to 15% of patients after cardiovascular surgery. Approximately 30% of patients who experience ARF will require renal replacement therapy. Community-acquired ARF occurs in approximately 209 patients per 1 million population, and the frequency of this syndrome appears to be increasing in hospitalized patients.

ASSESSMENT OF THE PATIENT WITH ARF

Because of the various causes of ARF, effective use of history and medical chart review, physical examination, and laboratory testing are essential to recognize and correct the factors quickly that cause ARF. Results of these evaluations will help to classify patients into 1 of 3 major diagnostic categories of ARF: traditional prerenal, postrenal, and intrinsic renal.

Medical Chart Review and Physical Examination

A thorough review of the patient’s history often reveals possible contributing factors of ARF, such as nephrotoxin exposure, episodes of blood pressure swings, and predisposing conditions for renal damage (hypertension and diabetes). Determination of a familial history of renal disease and a personal history of urolithiasis or urinary outlet symptoms is often helpful in the evaluation of ARF.

Intravascular volume status is perhaps the most important factor in the evaluation of ARF. Extracellular volume depletion is often suggested by tachycardia, orthostatic blood pressure changes, dry mucous membranes, or hypotension. However, obtaining serial weights of hospitalized patients often proves crucial in determining volume status. Physical examination findings suggestive of congestive heart failure or cirrhosis that leads to functional renal hypoperfusion deserve special attention. Skin condi-
tions such as cutaneous exanthems, purpura, livedo reticularis, microinfarctions, stigma of endocarditis, and limb ischemia often provide valuable clues in ascertaining causes of ARF. A distended bladder, costovertebral angle tenderness, or prostatic hypertrophy is suggestive of obstructive uropathy.

A decrease in urinary volume is often one of the initial clinical findings in ARF. Categorization of renal failure into oliguric or nonoliguric is of diagnostic importance. Oliguria is defined as a urinary output of less than 400 mL/d. Anuria (<50 mL of urinary output per day) suggests acute cortical necrosis, obstructive uropathy, or a vascular catastrophe causing cessation of renal perfusion.

Laboratory Testing

The diagnosis of ARF is primarily determined by increasing levels of nitrogenous-based waste products, such as creatinine or blood urea nitrogen, often along with a decline in urinary production. Unfortunately, a well-accepted common definition of ARF does not exist. Generally, a decline in renal function occurring over hours to days involving an increase in nitrogenous-based waste products such as a serum creatinine level by more than 0.5 mg/dL, an increase of 50% or more in serum creatinine over the baseline serum creatinine level, and a decline of calculated or measured creatinine clearance by more than 25% are accepted as indicators of ARF. Pseudoacute renal failure may occur when substances (ketoacids, cefoxitin) are falsely analyzed as creatinine, when creatinine production is increased (mild muscle protein breakdown), or when a substance (trimethoprim, cimetidine) inhibits renal tubular creatinine secretion.

Determination of serum electrolytes offers valuable information, such as potassium levels, clues about volume status (high bicarbonate, elevated blood urea nitrogen-creatinine ratio, hypernatremia), acidosis, and anion gap. Therefore, an electrolyte panel should be part of the required evaluation of all patients with ARF. Additionally, determination of calcium, phosphorus, albumin, uric acid, and creatine kinase levels as well as liver function tests often add important information.

Arguably, the most important laboratory test for a patient with ARF is urinalysis. Both the urinary sediment and the urinary indices in combination with serum values can often be extremely helpful in determining the cause of ARF. Conceptually, these indices are designed to determine whether tubular function is intact. A low fractional excretion of sodium (<1%) suggests that oliguria (and perhaps azotemia) is likely due to decreased renal perfusion, and the nephron is responding appropriately by decreasing the excretion of filtered sodium to improve plasma volume and perfusion. The various serum and urinary findings used in diagnosing the major causes of ARF are shown in Table 1.

Discovery of an active urinary sediment should lead to a focused set of serologic tests to determine whether an autoimmune diathesis is present. Renal biopsy should be considered when no apparent cause of ARF is found or to achieve tissue diagnosis of a suspected glomerulonephritis associated with ARF.

Radiologic Evaluation

A renal ultrasound study is key in the evaluation of ARF. Valuable information about renal size, echotexture (parenchymal density), and renal vascular status (with Doppler evaluation) is obtained with this noninvasive test. Specifically, renal ultrasonography is most often performed to rule out obstructive uropathy as the cause of ARF. Unfortunately, renal ultrasonography is neither highly sensitive nor specific for obstructive uropathy (see subsequent discussion), but accuracy increases with serial examinations. Computed tomograms (without contrast) and nuclear perfusion scans have a limited role in the evaluation of ARF.

Categorization of ARF

More than 50 identified pathophysiologic pathways are responsible for ARF. Traditionally, the evaluation of ARF has focused on the determination of whether the cause of renal failure is prerenal (a condition resulting in decreased “effective renal perfusion”), postrenal (an obstruction to urinary outflow), or intrinsic renal (due to pathophysiologic derangements in the renal tubules, interstitium, vascularity, or glomeruli). This designation has not yet been improved.

PRERENAL CAUSES

Overall, 60% of cases of community-acquired ARF are due to prerenal conditions. Frequently, this disorder is caused by excessive, nonreplaced fluid deficits due to gastrointestinal, renal, or cutaneous losses. However, hospital-acquired prerenal renal failure is primarily due to decreased effective renal perfusion. Often, congestive heart failure, cirrhosis, or sepsis (hyperdynamic vasodilated hypotensive states with cytokinemia) is noted. A continuum exists between prerenal renal failure and ischemic acute tubular necrosis (ATN); thus, prompt recognition and therapy for prerenal conditions is necessary before irreversible ischemic tubular necrosis develops. Commonly, prerenal conditions that otherwise would not progress to frank ATN do so in the setting of acute multisystemic illness and ongoing additional renal insults. Of importance, many medications induce a functional prerenal state because of alterations in glomerular hemodynamics.
Table 1. Laboratory Evaluation of Acute Renal Failure*

<table>
<thead>
<tr>
<th>Test</th>
<th>Prerenal</th>
<th>Intrinsic renal</th>
<th>Postrenal</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN/Cr ratio</td>
<td>&gt; 20</td>
<td>10-20</td>
<td>10-20</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>&gt;1.020</td>
<td>~1.010</td>
<td>&gt;1.010 early, &lt;1.0101 late</td>
</tr>
<tr>
<td>Uosm (mOsm/kg)</td>
<td>&gt;350</td>
<td>~300</td>
<td>&gt;400 early, ~300 late</td>
</tr>
<tr>
<td>UNa (mEq/L)</td>
<td>&lt;20</td>
<td>&gt;30</td>
<td>&lt;20 early, &gt;40 late</td>
</tr>
<tr>
<td>FeNa (%)</td>
<td>&lt;1†</td>
<td>2-3</td>
<td>&lt;1 early, &gt;3 late</td>
</tr>
<tr>
<td>UCr/PCr ratio</td>
<td>≥40</td>
<td>≤20</td>
<td>&gt;40 early, ≤20 late</td>
</tr>
<tr>
<td>Urine microscopy</td>
<td>Normal</td>
<td>hyaline casts, renal epithelial cells/casts</td>
<td>Normal hyaline, granular casts</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GN: RBCs, dysmorphic RBC (&gt;20%), RBC casts, WBC/WBC casts, proteinuria</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>AIN: urine eosinophilia, WBC, WBC casts, hyaline casts (consider CES)</td>
<td></td>
</tr>
</tbody>
</table>

*AIN = acute interstitial nephritis; ATN = acute tubular necrosis; BUN = blood urea nitrogen; CES = cholesterol emboli syndrome; Cr = creatinine; FeNa = fractional excretion of sodium (calculated as UNa/PNa × PCr/UCr × 100); GN = glomerulonephritis; PCr = plasma creatinine; PNa = plasma sodium; RBC = red blood cell; UCr = urinary creatinine; UNa = urinary sodium; Uosm = urinary osmolality; WBC = white blood cell.
†Falsely low FeNa seen occasionally with acute GN, radiocontrast-induced nephropathy, rhabdomyolysis.

Nonsteroidal Anti-inflammatory Drugs
Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin-mediated afferent arteriolar vasodilation in the glomerulus. These prostaglandins are essential for patients who rely on preglomerular capillary vasodilation to maintain glomerular capillary pressure. Predisposing factors for NSAID-induced ARF include congestive heart failure, cirrhosis, nephrotic syndrome, chronic renal failure, severe atherosclerotic disease of the renal arteries, and hypovolemia. Additionally, NSAIDs have been implicated in acute allergic interstitial nephritis, membranous nephritis, and minimal change nephropathy; occasionally, they cause hyperkalemia, hyponatremia, and sodium and water retention.

Angiotensin-Converting Enzyme Inhibitors
Angiotensin-converting enzyme (ACE) inhibitors were recently shown to be particularly useful in the treatment of chronic renal diseases. However, these agents continue to be recognized for their ability to induce ARF. Primarily, ACE inhibitors can cause ARF by inhibiting the ability of the glomerular efferent arteriole to vasoconstrict to maintain a glomerular filtration rate constant within the autoregulatory range. The risk factors with ACE inhibitors are similar to those with NSAIDs. Acute renal failure associated with administration of ACE inhibitors should prompt investigation to rule out bilateral renal artery stenosis or severe renal artery stenosis in a solitary functioning kidney.

Calcineurin Inhibitors
Calcineurin inhibitors (tacrolimus and cyclosporine) are used in an increasing number of solid organ transplant recipients who are often treated by primary care clinicians. These immunosuppressive agents may induce a prerenal state due to preglomerular vasoconstriction. Hypovolemia, a complication associated with calcineurin inhibitor use, is an often-recognized cause of ARF in recipients of solid organ transplants. Of importance, the interaction between several antihypertensive and anti-infective agents must be remembered in regard to the possibility of these drug-drug interactions causing elevated levels of calcineurin inhibitors, thereby inducing renal failure. Additionally, calcineurin inhibitors have occasionally been implicated in inducing microangiopathic hemolytic anemia causing ARF.

Amphotericin B
Amphotericin B primarily causes distal tubular derangements that lead to decreasing urinary concentration, distal renal tubular acidosis, potassium wasting, magnesium wasting, and occasionally profound renal vasoconstriction. Patients of advanced age with a history of diuretic use (when use induces hypovolemia or electrolyte imbalance), high doses of amphotericin therapy, preexisting advanced renal insufficiency, hypokalemia (due to induction of impaired renal concentration capacity), and decreased effective renal perfusion are particularly at risk for amphotericin B nephrotoxicity. Prevention of amphotericin B nephrotox-
icity is best accomplished by preadministration of intravenous saline solution. Liposomal preparations of amphotericin B have been demonstrated to be less nephrotoxic in patients with neutropenic fever. However, widespread use is limited because of expense.

Contrast-Induced Nephropathy
Contrast-induced nephropathy causes ARF predominantly via acute vasoconstriction. Additionally, after decreased renal perfusion, the sluggish flow of filtered contrast material often causes intratubular precipitation and ongoing generation of free oxygen radicals.

Risk factors for contrast-induced nephropathy are generally accepted to be a glomerular filtration rate of less than 35 mL/min, diabetic nephropathy, severe heart failure, administration of large amounts of contrast, or preexisting hypokalemia or hypotension.

Despite multiple trials involving numerous therapeutics, administration of crystalloid (1-1.5 mL·kg⁻¹·h⁻¹ for 8-12 hours before a procedure) remains the safest, most efficacious, and cost-effective method of preventing contrast-induced nephropathy. Recently, Tepel et al showed prevention of radiographic-contrast–induced nephrotoxicity by administering acetylcysteine in two 600-mg doses the day before along with saline infusion for patients with stable chronic renal insufficiency (creatinine >2.0 mg/dL).

Immunostimulant Agents
Immunostimulant agents (interleukin 2, tumor necrosis factor receptor agonists) have rarely been implicated in causing a capillary leak syndrome, which causes decreased “effective circulating volume” similar to sepsis.

Cocaine
Cocaine induces ARF via multiple pathways. Acute vasoconstriction of both afferent and efferent arterioles has been documented in experimental studies of cocaine nephrotoxicity. Additionally, cocaine has been implicated in causing malignant hypertension, rhabdomyolysis, antilglomerular basement membrane nephropathy, thrombotic microangiopathy, renal infarction, and multiple acid base and electrolyte derangements (metabolic acidosis, respiratory alkalosis, hypokalemia, and hyperkalemia-rhabdomyolysis). In many urban centers, cocaine-induced nephrotoxicity is the most common cause of ARF.

POSTRENAL CAUSES
Postrenal causes account for 5% to 15% of cases of community-acquired ARF. A history of prostatism, urolithiasis, retroperitoneal disease, or use of medications known to cause crystalluria should prompt a thorough evaluation to rule out obstruction. Elderly and young patients are most commonly affected. Renal ultrasonography is an essential part of the work-up of any patient with ARF. However, ultrasonography is neither highly sensitive nor specific (sensitivity may be only 80%-85%); when the clinical situation suggests a high probability of postrenal ARF, serial ultrasound studies may be necessary. Alternatively, spiral computed tomography (without contrast) may often be of benefit in delineating obstructive uropathy due to urolithiasis. A patent urinary catheter is obviously a required first step in the work-up of any patient with ARF.

Medication-induced crystalluria causing tubular or ureteral obstruction has been known to occur with multiple drugs. The most common agents that cause this phenomenon are acyclovir, the sulfonamides, methotrexate, and protease inhibitors (indinavir).

RENAL CAUSES
Although the most common cause of ARF in the hospitalized patient is intrinsic renal failure due to ATN, the terms acute tubular necrosis and intrinsic renal failure are not synonymous. Delineating intrinsic ARF into the 4 distinct anatomical compartments of the kidney facilitates the most accurate categorization.

Vascular Causes of Intrinsic ARF
The incidence of renal failure due to vascular disease is increasing. Epidemic atherosclerotic vascular disease in the aging population, widespread use of vasoactive drugs, and the increased frequency of invasive vascular procedures have led to a general increase in the incidence of vascular causes of intrinsic ARF. Small-vessel vascular diseases that cause renal failure, including atheroembolic renal disease, scleroderma, malignant hypertension, hemolytic uremic syndrome-thrombotic thrombocytopenic purpura, and acute cortical necrosis, are being diagnosed with much more frequency. These disorders may lead to only mild prerenal azotemia; however, frequently they lead to frank tubular damage and necrosis resulting in ARF.

Atheroemboli may also be increasing in frequency. Acute renal failure in the setting of recent intravascular intervention or anticoagulation associated with livedo reticularis, hypocomplementemia, eosinophilia (occasionally with eosinophiluria), blue toe syndrome, or cutaneous infarctions should prompt consideration of atheroemboli. Thrombotic or embolic disease and renal arterial dissection, which may present as anuria and flank pain, are accurately diagnosed with nuclear perfusion scans and angiography.

Renal Interstitial Diseases
Polypharmacy is common among most patients with chronic diseases and hospitalized patients. Allergic inter-
stitial nephritis should be strongly considered in all patients with ARF. A nonexclusive list of agents that have been firmly implicated in causing allergic interstitial nephritis include the penicillins, cephalosporins, sulfonamides, rifampin, ciprofloxacin, NSAIDs, thiazide diuretics, furosemide, cimetidine, phenytoin, and allopurinol. Recently, Chinese herb nephropathy was recognized as an important cause of fibrotic interstitial nephritis. Chinese herb nephropathy often occurs in patients who use “slimming teas,” often labeled Han Fang Ji or Quang Fang Ji. The causative agent implicated in this disorder is aristolochic acid. The syndrome of Chinese herb nephropathy is characterized by progressive renal failure with a bland urinary sediment, shrunken hyperechoic kidneys with low-grade proteinuria, and an association with uroepithelial cancers.10

Often, the characteristic eosinophilia, rash, and urinary eosinophilia are absent in allergic interstitial nephritis. Therefore, a high index of suspicion is necessary to diagnose this disorder. Allergic interstitial nephritis is classically nonoliguric, which may aid in the diagnosis.

Glomerulonephritis
Acute glomerulonephritis as a cause of ARF is rarely subtle. Urinary findings including prominent moderate to severe proteinuria (nephrotic category), hemoglobinuria, erythrocytes, leukocytes, and erythrocyte casts with dysmorphic erythrocytes (nephritic category) are characteristic features. Often, constitutional signs and symptoms, specifically an influenza-like syndrome, are noted. Frequently, urine is smoky in color, and a rash accompanies many syndromes of glomerulonephritis.

Acute glomerulonephritis often accompanies systemic disorders such as lupus, hepatitis, vasculitis, and pulmonary renal syndromes. Serologic assays (notably lupus serologies, antineutrophil cytoplasmic antibodies, and complement levels) and immunopathologic examination of the kidneys will identify most causes of rapidly progressive glomerulonephritis. Recognition of this syndrome is extremely important because it is often reversible with immunosuppressive therapy.

Tubular Disorders
The most common cause of hospital-acquired ARF is ATN. As previously mentioned, prerenal azotemia and ischemic ATN represent a continuum. Multiple pathways and clinical conditions lead to renal ischemia. Numerous factors commonly contribute to the occurrence of ischemic ATN.

Dramatic advances were made recently in the understanding of the cellular mechanisms involved in glomerular and renal tubular cell damage and death, interstitial fibrogenesis, and apoptosis. Increased cytosolic calcium levels, decreased adenosine triphosphate levels, derangements in cytoskeletal functions, increased intracellular phospholipase levels, increased generation of apoptotic signals, and increased levels of intracellular reactive oxygen species have all been experimentally well documented to contribute to ARF due to ATN.1,11

Patients at risk for ATN include those with prolonged systemic hypotension and those with decreased effective renal perfusion for prolonged periods. Additionally, multiple medications and toxins may induce tubular damage. Aminoglycoside antibiotics, cisplatin, cyclosporine, tacrolimus, mannitol, amphotericin B, methotrexate, foscarinet, pentamidine, organic solvents, heavy metals, cocaine, intravenous immunoglobulin, and radiocontrast agents are often implicated in tubular dysfunction and damage. Intrinsic toxins such as heme pigments (as in rhabdomyolysis), myeloma light chain proteins, and uric acid crystals frequently cause tubular obstruction and damage.

Rhabdomyolysis induced by combination antihyperlipidemic therapy or by antihyperlipidemic therapy in combination with immunosuppressive agents (especially calcineurin inhibitors) has been recognized. Additionally, the epidemic of cocaine use has caused an increase in the incidence of cocaine-induced rhabdomyolysis. Clinical hallmarks of rhabdomyolysis are often present in patients with ARF and include muscle tenderness, signs of extremity compartment syndrome, and characteristic elevation in serum creatine kinase and urinary myoglobin levels.

ARF IN THE RENAL TRANSPLANT RECIPIENT
The assessment of patients with ARF who have a renal allograft does not differ from that for the general population. Serum, urine, and radiographic studies are indicated. Therapeutic levels of immunosuppressive agents should be determined at the trough period.

Obstructive uropathy due to trauma, ureteral stenosis, or compression by lymphocele is often seen; therefore, ultrasonography is a necessary first step in the evaluation. Doppler flow studies of the transplant’s vascular supply are easily performed because of the position of the graft. The diagnosis and management of prerenal causes are complicated by the known vasoconstrictive effects of the calcineurin inhibitors (cyclosporine, tacrolimus), which are often injurious in situations of volume depletion. Close attention to possible drug-drug interactions, which may potentiate calcineurin toxicity by inhibition of hepatic metabolic pathway, is extremely important.

Rejection of the transplant is one of the renal parenchymal causes of ARF. Again, a review of the medication history to determine whether induction of the hepatic meta-
bolic pathways has been stimulated by pharmacologic agents (thereby decreasing immunosuppressive agent levels) is necessary, as is an assessment of compliance with the medication regimen. Transplant biopsy is frequently performed to determine presence and/or extent of the rejection process.

**THERAPY**

The goal of any focused evaluation of ARF is immediate correction of its reversible causes. Recognition and relief of urinary outlet obstruction should be given the highest priority, especially for patients with anuria. Support of renal perfusion with either volume infusion or therapeutics that improve renal oxygen delivery should be considered before any attempt to improve urinary flow. Urinary indices should be examined before diuretic intervention.

Therapy to correct the pathophysiologic derangements of ARF can be broadly categorized into nondialytic and dialytic.

**Nondialytic Therapy**

Paramount in the initial treatment of ARF is ensuring that renal perfusion is maximized by volume infusion and/or correction of the underlying pathophysiologic process that has caused ARF. Additionally, a recent growth in the understanding of the molecular biology of ARF has led to several clinically based targeted therapeutic trials.

**Growth Factors.**—As the most common cause of hospital-acquired ARF is ATN, prompt recovery from ATN requires tubular cell regeneration. Multiple animal studies have shown promise in stimulating regrowth of the ischemic injured tubular cells by growth factors such as insulin-like growth factor, hepatocyte growth factor, and transforming growth factor α. However, thus far, human trials have been disappointing in their ability to document any pronounced change in the course of ARF with directed therapy with insulin-like growth factor or hepatocyte growth factor.

**Atrial Natriuretic Peptide.**—Atrial natriuretic peptide has been shown in small studies to improve urinary flow. Animal trials have suggested that, because of the vasodilatory activities of atrial natriuretic peptides, the severity of ARF may be attenuated with their use. However, a recent randomized controlled multicenter trial of atrial natriuretic peptide in oliguric ARF failed to show any benefit with this agent.

**Intracellular Adhesion Molecules.**—Recently, it was well documented that intracellular adhesion molecules have an essential role in leukocyte adhesion, rolling, and diapedesis in the ongoing injury model. Inhibition of intracellular adhesion molecules is the subject of current animal studies.

**Antioxidant Therapy.**—Several indirect and direct lines of evidence suggest that free oxygen radical damage is a prominent etiologic factor in ongoing renal parenchymal damage. Whether up-regulation of intrinsic cellular protective antioxidant mechanisms may be stimulated by previous ischemic insults and whether supplementation of antioxidant compounds affords protection from ARF is intriguing hypotheses. Studies of several antioxidant compounds are currently under way to assess their ability to decrease the severity and length of injury in ARF.

**Dopamine.**—Traditionally, dopamine has been a mainstay of the therapeutic armamentarium in all patients with ARF. This is primarily due to its putative ability to vasodilate splanchnic vasculature selectively at "renal doses" (1-3 µg·kg⁻¹·min⁻¹). While dopamine has certainly been proved in humans to be natriuretic and phosphaturic, no evidence shows, despite many clinical trials, that dopamine favorably affects the course of ARF.

**Diuretics.**—In many clinical settings, there is little evidence that use of diuretics to change a patient’s condition from oliguric to nonoliguric renal failure has any effect on clinical outcome. Use of diuretics for patients with ARF complicated by volume overload or for patients who need “intravascular space” for therapeutic parenteral medications is certainly warranted. However, their use specifically to affect the course and outcome of ARF has not been shown to be advantageous. Therefore, diuretics should be considered only after renal perfusion has been maximized.

Certain clinical situations may warrant the use of diuretics early in the course of renal failure, such as in volume-replete patients with endogenous heme pigment injury; forced diuresis in the setting of renally excreted toxins such as lithium, theophylline, and salicylates and toxic alcohol ingestions; or in patients with tumor lysis syndrome.

**Adjuvant Measures.**—A nutrition program with an energy prescription of 126 to 147 kJ/kg per day and restriction of potassium (60 mEq/d), sodium (90 mEq/d), and phosphorus (800 mg/d) should be recommended for most patients with ARF. Protein supplementation of 0.6 to 1.4 g/kg per day is required for most patients with hospital-acquired ARF to minimize protein catabolism, depending on whether dialysis is required. Severe protein restriction, prescribed to avoid dialysis, is controversial at best. A patient’s current medical regimen, especially medication doses, should be adjusted to their residual renal function, and patients should be told to avoid further potential nephrotoxins.

Agents whose renally excreted metabolites may become toxic must be closely monitored. Meperidine’s metabolite...
normeperidine accumulates in ARF and has been linked to seizure activity, as has the antibiotic imipenem. Digoxin should be administered cautiously with close attention to serum levels, as with nitroprusside and its metabolites. NSAIDs should be avoided in the setting of ARF because of their previously described adverse effects on renal perfusion.

Life-threatening hyperkalemia may complicate ARF. Urgent measures to stabilize cardiac cellular membrane repolarization with intravenous calcium gluconate or chloride for patients with electrocardiographic changes should be the first priority. Until removal of potassium is possible, induction of intracellular shifting of potassium is the next priority. These shifts can be facilitated by intravenous insulin and dextrose administration, as well as β-agonist therapy. However, the required dose of β-agonist to effect transcellular potassium shifting is about 10 to 20 times the usual nebulized dose for reactive airway disease, and therefore β-agonists are often impractical. Parenteral bicarbonate therapy may be of use, although this has been questioned recently. Potassium removal may be achieved via the kidneys, if oliguria is not present, with high-dose loop diuretics. If oliguria occurs, enteric removal by administration of exchange resins (sodium polystyrene sulfonate) may be considered. Recently, several case reports and series demonstrated colonic necrosis associated with the use of sodium polystyrene sulfonate in critically ill and hemodynamically unstable patients. Therefore, many clinicians think that sodium polystyrene sulfonate should be used cautiously in the ICU. Hemodialysis after placement of suitable vascular access allows rapid removal of potassium and should be considered early in the presentation of life-threatening hyperkalemia.

**Dialysis**

Initiation of renal replacement therapy (peritoneal dialysis, intermittent hemodialysis, continuous dialysis-hemofiltration) has traditionally been recommended when severe derangements in electrolyte concentrations (potassium, sodium), volume overload, acid-base imbalance, pronounced azotemia (blood urea nitrogen >100 mg/dL), or florid symptoms of uremia (pericarditis, encephalopathy, bleeding, nausea-vomiting, pruritus) are noted. Few patients with ARF are treated with peritoneal dialysis primarily because of poor delivery of dialysis dose and difficulty managing ultrafiltration. In the United States, most patients with ARF who require renal replacement therapy are treated with intermittent hemodialysis.

A link between the delivered dose of dialysis and outcome has been firmly established in patients with end-stage renal disease receiving outpatient maintenance dialysis. Recent data have suggested a similar relationship in patients with ARF. Furthermore, initiation of hemodialysis before severe pathophysiologic derangements occur has been suggested to benefit the patient with multiorgan failure and ARF.

The extracorporeal circuit obviously has an important role in renal replacement therapies. Pivotal studies performed in the mid-1990s documented improved mortality and recovery of renal function with the use of biocompatible dialysis membranes.

Continuous renal replacement therapies likely offer several potential benefits for critically ill patients with ARF. These benefits are suggested by an increased hemodynamic tolerance of dialysis, improved ability to manage fluid and electrolyte balance, improved dialytic dose delivery, and use of synthetic (more biocompatible) membranes.

**SUMMARY**

Acute renal failure is a multisystemic disorder that affects patients cared for by nearly all health care professionals. Its occurrence seems to be increasing in hospitalized patients. A structured approach to the evaluation of ARF will result in a quick diagnosis of the cause and facilitate rapid effective therapy. The clinician should recognize the growing list of medications and potential nephrotoxins that cause ARF. Although morbidity statistics remain unacceptably high in patients with hospital-acquired ARF, ongoing efforts to improve both dialytic and nondialytic therapies are being explored.

**REFERENCES**


Questions About ARF

1. Which one of the following would not be associated with an elevated serum creatinine level, which may not reflect a decline in renal function?
   a. Hypovolemia
   b. Elevated serum ketone levels
   c. Administration of select types of cephalosporin antibiotics
   d. Elevated serum creatine kinase levels
   e. Administration of cimetidine

   Correct answers: 1. a, 2. c, 3. b, 4. d, 5. c

2. Which one of the following is not an indication for urgent dialysis therapy?
   a. Pericarditis associated with severe azotemia
   b. Hyperkalemia
   c. Oliguria
   d. Volume overload (congestive heart failure)
   e. Nausea, vomiting, mental status changes, and bleeding associated with severe azotemia

3. Which one of the following urinary findings is inconsistent with intrinsic renal causes of ARF?
   a. Dysmorphic erythrocytes, erythrocyte casts
   b. Fractional excretion of sodium, 0.58%
   c. Fractional excretion of sodium, 5.8%
   d. Urinary creatinine-plasma creatinine ratio, 15:1
   e. Dark granular “muddy brown” casts

4. Which one of the following medications does not cause a functional decrease in renal perfusion?
   a. NSAIDs
   b. Cyclosporine
   c. Cocaine
   d. Cisplatin
   e. ACE inhibitors

5. Which one of the following strategies has been shown in human clinical trials to prevent or ameliorate ARF?
   a. Dopamine at renal dose (1-4 µg·kg⁻¹·min⁻¹)
   b. Infusion of atrial natriuretic peptide
   c. Infusion of saline before radiographic contrast exposure (1 mL·kg⁻¹·min⁻¹ 12 hours before)
   d. High-dose intravenous loop diuretics
   e. Infusion of insulin-like growth factor