Abstract

Acute Kidney Injury (AKI)

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Background

Acute kidney injury (AKI)—or acute renal failure (ARF), is defined as an abrupt or rapid decline in renal filtration function. This condition is usually marked by a rise in serum creatinine concentration or by azotemia (a rise in blood urea nitrogen [BUN] concentration). However, immediately after a kidney injury, BUN or creatinine levels may be normal, and the only sign of a kidney injury may be decreased urine production.

Categories of AKI

AKI may be classified into 3 general categories, as follows:

- Prerenal - As an adaptive response to severe volume depletion and hypotension, with structurally intact nephrons
- Intrinsic - In response to cytotoxic, ischemic, or inflammatory insults to the kidney, with structural and functional damage
- Postrenal - From obstruction to the passage of urine

Patients who develop AKI can be oliguric or nonoliguric, can have a rapid or slow rise in creatinine levels, and may have qualitative differences in urine solute concentrations and cellular content. (Approximately 50-60% of all causes of AKI are nonoliguric.) This lack of a uniform clinical presentation reflects the variable nature of the injury.
Classifying AKI as oliguric or nonoliguric on the basis of daily urine excretion has prognostic value. Oliguria is defined as a daily urine volume of less than 400 mL and has a worse prognosis.
Anuria is defined as a urine output of less than 100 mL/day and, if abrupt in onset, suggests bilateral obstruction or catastrophic injury to both kidneys.
Stratification of renal injury along these lines helps in diagnosis and decision-making (eg, timing of dialysis) and can be an important criterion for patient response to therapy.

RIFLE classification system

In 2004, the Acute Dialysis Quality Initiative work group set forth a definition and classification system for acute renal failure, described by the acronym RIFLE (Risk of renal dysfunction, Injury to the kidney, Failure or Loss of kidney function, and End-stage kidney disease). Investigators have since applied the RIFLE system to the clinical evaluation of AKI, although it was not originally intended for that purpose. AKI research increasingly uses RIFLE. See Table below.

RIFLE Classification System for Acute Kidney Injury

Stage	GFR** Criteria	Urine Output Criteria	Probability
Risk	SCreat† increased × 1.5 or GFR decreased >25%	UO‡< 0.5 mL/kg/h × 6 h	High sensitivity (Risk >Injury >Failure)
Injury	SCreat increased × 2 or GFR decreased >50%	UO < 0.5 mL/kg/h × 12 h	
Failure	SCreat increased × 3 or GFR decreased 75% or SCreat ≥4 mg/dL; acute rise ≥0.5 mg/dL	UO < 0.3 mL/kg/h × 24 h (oliguria) or anuria × 12 h	
Loss	Persistent acute renal failure: complete loss of kidney function >4 wk		High specificity
ESKD*	Complete loss of kidney function >3 mo		

Acute Kidney Injury Network classification system

The Acute Kidney Injury Network (AKIN) has developed specific criteria for the diagnosis of AKI. The AKIN defines AKI as abrupt (within 48 hours) reduction of kidney function, manifested by any 1 of the following:

- An absolute increase in serum creatinine of 0.3 mg/dL or greater (≥26.4 µmol/L)
- A percentage increase in serum creatinine of 50% or greater (1.5-fold from baseline)
- A reduction in urine output, defined as less than 0.5 mL/kg/h for more than 6 hours

AKIN has proposed a staging system for AKI that is modified from RIFLE. In this system, either serum creatinine or urine output criteria can be used to determine stage. See Table 2, below.

Table 2. Acute Kidney Injury Network Classification/Staging System for AKI

Stage	Serum Creatinine Criteria	Urine Output Criteria
1	Increase of ≥0.3 mg/dL (≥26.4 µmol/L) or 1.5- to 2-fold increase from baseline	< 0.5 mL/kg/h for >6 h
2	>2-fold to 3-fold increase from baseline	< 0.5 mL/kg/h for >12 h
3*	>3-fold increase from baseline, or increase of ≥ 4.0 mg/dL (≥35.4 µmol/L) with an acute increase of at least 0.5 mg/dL (44 µmol/L)	< 0.3 mL/kg/h for 24 h or anuria for 12 h
*Patients who receive renal replacement therapy (RRT) are considered to have met the criteria for stage 3 irrespective of the stage they are in at the time of RRT.		

Pathophysiology

The driving force for glomerular filtration is the pressure gradient from the glomerulus to the Bowman space. Glomerular pressure depends primarily on renal blood flow (RBF) and is controlled by the combined resistances of renal afferent and efferent arterioles. Regardless of the cause of AKI, reductions in RBF represent a common pathologic pathway for decreasing glomerular filtration rate (GFR). The etiology of AKI consists of 3 main mechanisms: prerenal, intrinsic, and obstructive.

In prerenal failure, GFR is depressed by compromised renal perfusion. Tubular and glomerular function remain normal.

Intrinsic renal failure includes diseases of the kidney itself, predominantly affecting the glomerulus or tubule, which are associated with the release of renal afferent vasoconstrictors. Ischemic renal injury is the most common cause of intrinsic renal failure. Patients with chronic kidney disease may also present with superimposed AKI from prerenal failure and obstruction, as well as intrinsic renal disease.

Obstruction of the urinary tract initially causes an increase in tubular pressure, which decreases the filtration driving force. This pressure gradient soon equalizes, and maintenance of a depressed GFR then depends on renal efferent vasoconstriction.

Depressed renal blood flow

Depressed RBF eventually leads to ischemia and cell death. This may happen before frank systemic hypotension is present and is referred to as normotensive ischemic AKI. The initial ischemic insult triggers a cascade of events, including production of oxygen free radicals, cytokines and enzymes; endothelial activation and leukocyte adhesion; activation of coagulation; and initiation of apoptosis. These events continue to cause cell injury even after restoration of RBF.

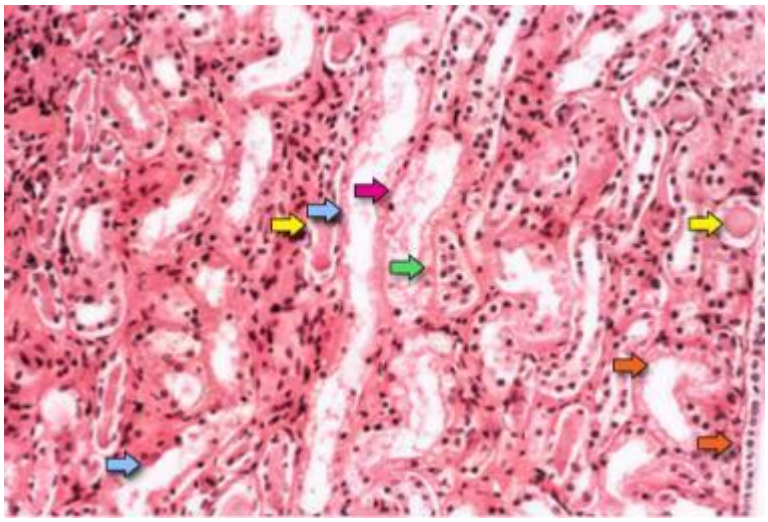
Tubular cellular damage results in disruption of tight junctions between cells, allowing back leak of glomerular filtrate and further depressing effective GFR. In addition, dying cells slough off into the tubules, forming obstructing casts, which further decrease GFR and lead to oliguria. During this period of depressed RBF, the kidneys are particularly vulnerable to further insults; this is when iatrogenic renal injury is most common. The following are common combinations:

- Radiocontrast agents, aminoglycosides, or cardiovascular surgery with preexisting renal disease (eg, elderly, diabetic, jaundiced patients)
- Angiotensin-converting enzyme (ACE) inhibitors with diuretics, small- or large-vessel renal arterial disease
- NSAIDs with chronic heart failure, hypertension, or renal artery stenosis

Acute tubular necrosis

Frank necrosis is not prominent in most human cases of ATN and tends to be patchy. Less obvious injuries include the following (see the image below):

- Loss of brush borders
- Flattening of the epithelium
- Detachment of cells
- Formation of intratubular casts
- Dilatation of the lumen



Photomicrograph of a renal biopsy specimen shows renal medulla, which is composed mainly of renal tubules. Features suggesting acute tubular necrosis are the patchy or diffuse denudation of the renal tubular cells with loss of brush border (blue arrows); flattening of the renal tubular cells due to tubular dilation (orange arrows); intratubular cast formation (yellow arrows); and sloughing of cells, which is responsible for the

formation of granular casts (red arrow). Finally, intratubular obstruction due to the denuded epithelium and cellular debris is evident (green arrow); note that the denuded tubular epithelial cells clump together because of rearrangement of intercellular adhesion molecules.

Apoptosis

In contrast to necrosis, the principal site of apoptotic cell death is the distal nephron. During the initial phase of ischemic injury, loss of integrity of the actin cytoskeleton leads to flattening of the epithelium, with loss of the brush border, loss of focal cell contacts, and subsequent disengagement of the cell from the underlying substratum.

Inflammatory response

Many endogenous growth factors that participate in the process of regeneration following ischemic renal injury have not been identified. However, administration of growth factors exogenously has been shown to ameliorate and hasten recovery from AKI.
Depletion of neutrophils and blockage of neutrophil adhesion reduce renal injury following ischemia, indicating that the inflammatory response is responsible, in part, for some features of ATN, especially in postischemic injury after transplant.

Vasoconstriction

Intrarenal vasoconstriction is the dominant mechanism for reduced GFR in patients with ATN. The mediators of this vasoconstriction are unknown, but tubular injury seems to be an important concomitant finding. Urine backflow and intratubular obstruction (from sloughed cells and debris) are causes of reduced net ultrafiltration. The importance of this mechanism is highlighted by the improvement in renal function that follows relief of such intratubular obstruction.
In addition, when obstruction is prolonged, intrarenal vasoconstriction is prominent in part due to the tubuloglomerular feedback mechanism, which is thought to be mediated by adenosine and activated when there is proximal tubular damage and the macula densa is presented with increased chloride load.
Apart from the increase in basal renal vascular tone, the stressed renal microvasculature is more sensitive to potentially vasoconstrictive drugs and otherwise-tolerated changes in systemic blood pressure. The vasculature of the injured kidney has an impaired vasodilatory response and loses its autoregulatory behavior.
This latter phenomenon has important clinical relevance because the frequent reduction in systemic pressure during intermittent hemodialysis may provoke additional damage that can delay recovery from ATN. Often, injury results in atubular glomeruli, where the glomerular function is preserved, but the lack of tubular outflow precludes its function.

Isosthenuria

A physiologic hallmark of ATN is a failure to maximally dilute or concentrate urine (isosthenuria). This defect is not responsive to pharmacologic doses of vasopressin. The

injured kidney fails to generate and maintain a high medullary solute gradient, because the accumulation of solute in the medulla depends on normal distal nephron function.
Failure to excrete concentrated urine even in the presence of oliguria is a helpful diagnostic clue in distinguishing prerenal from intrinsic renal disease. In prerenal azotemia, urine osmolality is typically more than 500 mOsm/kg, whereas in intrinsic renal disease, urine osmolality is less than 300 mOsm/kg.

Restoration of renal blood flow and associated complications

Recovery from AKI is first dependent upon restoration of RBF. Early RBF normalization predicts better prognosis for recovery of renal function. In prerenal failure, restoration of circulating blood volume is usually sufficient. Rapid relief of urinary obstruction in postrenal failure results in a prompt decrease of vasoconstriction. With intrinsic renal failure, removal of tubular toxins and initiation of therapy for glomerular diseases decreases renal afferent vasoconstriction.
Once RBF is restored, the remaining functional nephrons increase their filtration and eventually undergo hypertrophy. GFR recovery depends on the size of this remnant nephron pool. If the number of remaining nephrons is below a critical threshold, continued hyperfiltration results in progressive glomerular sclerosis, eventually leading to increased nephron loss.
A vicious cycle ensues; continued nephron loss causes more hyperfiltration until complete renal failure results. This has been termed the hyperfiltration theory of renal failure and explains the scenario in which progressive renal failure is frequently observed after apparent recovery from AKI.

History

A detailed and accurate history is crucial for diagnosing acute kidney injury (AKI) and determining treatment. Distinguishing AKI from chronic kidney disease is important, yet making the distinction can be difficult; chronic kidney disease is itself an important risk factor for AKI. [32] A history of chronic symptoms—months of fatigue, weight loss, anorexia, nocturia, sleep disturbance, and pruritus—suggests chronic kidney disease. AKI can cause identical symptoms, but over a shorter course.
It is important to elicit a history of any of the following etiologic factors:

- Volume restriction (eg, low fluid intake, gastroenteritis)
- Nephrotoxic drug ingestion (eg, nonsteroidal anti-inflammatory drugs [NSAIDs], aminoglycosides) [32]
- Exposure to iodinated contrast agents within the past week [32]
- Trauma or unaccustomed exertion
- Blood loss or transfusions
- Exposure to toxic substances, such as ethyl alcohol or ethylene glycol
- Exposure to mercury vapors, lead, cadmium, or other heavy metals, which can be encountered in welders and miners

People with the following comorbid conditions are at a higher risk for developing AKI:

- Hypertension
- Chronic heart failure
- Diabetes
- Liver disease

- Obesity
- Multiple myeloma
- Chronic infection
- Myeloproliferative disorder
- Connective tissue disorders
- Autoimmune diseases

Physical Examination

Obtaining a thorough physical examination is extremely important when collecting evidence about the etiology of AKI. Clues may be found in any of the following:

- Skin
- Eyes
- Ears
- Cardiovascular system
- Abdomen
- Pulmonary system

Kidney Function Studies

Although increased levels of blood urea nitrogen (BUN) and creatinine are the hallmarks of renal failure, the rate of rise depends on the degree of renal insult and, with respect to BUN, on protein intake. BUN may be elevated in patients with gastrointestinal (GI) or mucosal bleeding, steroid treatment, or protein loading.

The ratio of BUN to creatinine is an important finding. The ratio can exceed 20:1 in conditions in which enhanced reabsorption of urea is favored (eg, in volume contraction); this suggests prerenal AKI.

Assuming that the patient has no renal function, the rise in BUN over 24 hours can be roughly predicted using the following formula:

(24-hour protein intake in milligrams × 0.16) ÷ total body water

The result is expressed in mg/dL and added to the baseline BUN value to yield the predicted BUN.

Assuming no renal function, the rise in creatinine can be predicted using the following formulas:

- For males: Weight in kilograms × [28 - 0.2(age)] ÷ total body water, with the result in mg/dL added to the creatinine value
- For females: Weight in kilograms × [23.8 - 0.17(age)] ÷ total body water, with the result in mg/dL added to the creatinine value

As a general rule, if serum creatinine increases to more than 1.5 mg/dL/day, rhabdomyolysis must be ruled out.

In September 2014 the US Food and Drug Administration (FDA) approved NephroCheck, the first laboratory test to evaluate the risk of developing moderate to severe AKI in hospitalized, critically ill patients. The test identifies the presence of two AKI-associated proteins (insulinlike growth-factor binding protein 7, tissue inhibitor of metalloproteinases) in urine. Based on the level of these proteins, a score is derived that indicates the likelihood that a patient will develop AKI within the next 12 hours.

CBC, Peripheral Smear, and Serology

The peripheral smear may show schistocytes in conditions such as hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP). A finding of increased rouleaux formation suggests multiple myeloma, and the workup should be directed toward immunoelectrophoresis of serum and urine.

The presence of the following, along with related findings, may help to further define the etiology of AKI:

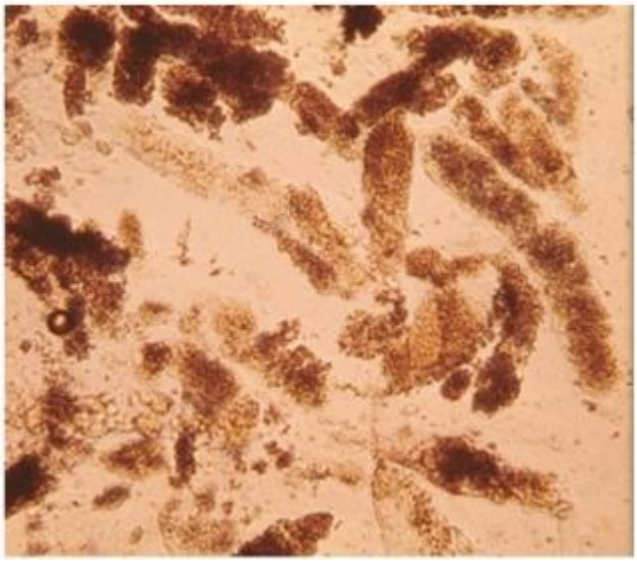
- Myoglobin or free hemoglobin - Eg, pigment nephropathy
- Increased serum uric acid level - Eg, tumor lysis syndrome
- Serum lactate dehydrogenase (LDH) - Eg, renal infarction

Although serologic tests can be informative, the costs can be prohibitive if these tests are not ordered judiciously. Possible tests include the following:

- Complement levels
- Antinuclear antibody (ANA)
- Antineutrophil cytoplasmic antibody (ANCA)
- Anti-glomerular basement membrane (anti-GBM) antibody
- Hepatitis B and C virus studies
- Antistreptolysin (ASO)

Urinalysis

Findings of granular, muddy brown casts in urine sediment are highly suggestive of tubular necrosis (see the image below). The presence of tubular cells or tubular cell casts also supports the diagnosis of ATN. Often, oxalate crystals are observed in cases of ATN.



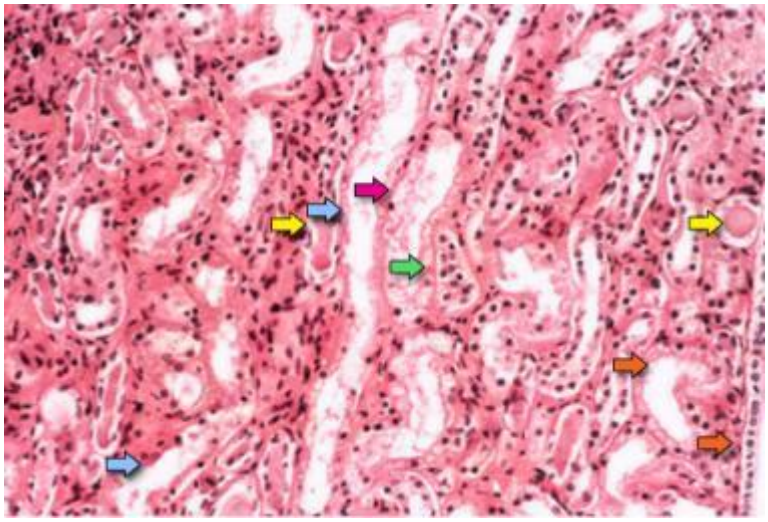
Pigmented, muddy brown, granular casts are visible in the urine sediment of a patient with acute tubular necrosis (400x magnification).

Reddish brown or cola-colored urine suggests the presence of myoglobin or hemoglobin, especially in the setting of a positive dipstick for heme and no red blood cells (RBCs) on the microscopic examination. The dipstick assay may reveal significant proteinuria as a result of tubular injury.

The presence of RBCs in the urine is always pathologic. Eumorphic RBCs suggest bleeding along the collecting system. Dysmorphic RBCs or RBC casts indicate glomerular inflammation, suggesting glomerulonephritis is present.
The presence of white blood cells (WBCs) or WBC casts suggests pyelonephritis or acute interstitial nephritis. The presence of urine eosinophils is helpful in establishing a diagnosis but is not necessary for allergic interstitial nephritis to be present.
The presence of eosinophils, as visualized with Wright stain or Hansel stain, suggests interstitial nephritis. However, this finding can also be seen in urinary tract infections, glomerulonephritis, and atheroembolic disease.
The presence of uric acid crystals may represent ATN associated with uric acid nephropathy. Calcium oxalate crystals are usually present in cases of ethylene glycol poisoning.

Renal Biopsy

A renal biopsy can be useful in identifying intrarenal causes of AKI and can be justified if the results may change management (eg, initiation of immunosuppressive medications). See the image below. A renal biopsy may also be indicated when renal function does not return for a prolonged period and a prognosis is required to develop long-term management. In as many as 40% of cases, renal biopsy results reveal an unexpected diagnosis.
Acute cellular or humoral rejection in a transplanted kidney can be definitively diagnosed only by performing a renal biopsy.



Photomicrograph of a renal biopsy specimen shows renal medulla, which is composed mainly of renal tubules. Features suggesting acute tubular necrosis are the patchy or diffuse denudation of the renal tubular cells with loss of brush border (blue arrows); flattening of the renal tubular cells due to tubular dilation (orange arrows); intratubular cast formation (yellow arrows); and sloughing of cells, which is responsible for the formation of granular casts (red arrow). Finally, intratubular obstruction due to the denuded epithelium and cellular debris is evident (green arrow); note that the denuded tubular epithelial cells clump together because of rearrangement of intercellular adhesion molecule

Treatment

Dietary Modification

Dietary changes are an important facet of AKI treatment. Restriction of salt and fluid becomes crucial in the management of oliguric renal failure, wherein the kidneys do not adequately excrete either toxins or fluids.

Because potassium and phosphorus are not excreted optimally in patients with AKI, blood levels of these electrolytes tend to be high. Restriction of these elements in the diet may be necessary, with guidance from frequent measurements. In the polyuric phase of AKI, potassium and phosphorus may be depleted, so that patients may require dietary supplementation and IV replacement.

Calculation of the nitrogen balance can be challenging, especially in the presence of volume contraction, hypercatabolic states, GI bleeding, and diarrheal disease. Critically ill patients should receive at least 1 g/kg/day protein but should avoid hyperalimentation, which can lead to an elevated blood urea nitrogen (BUN) level and water loss resulting in hypernatremia.

Vasodilators

The rationale for vasodilator therapy in AKI is that improved renal perfusion may reduce renal damage. Strong evidence in support of this approach is lacking, however.

A meta-analysis of 16 randomized studies concluded that the vasodilator fenoldopam reduces the need for renal replacement therapy and lowers the mortality rate in patients with AKI. [47] However, larger trials need to be conducted before the use of fenoldopam can be recommended.

Dopamine in small doses (eg, 1-5 mcg/kg/min) causes selective dilatation of the renal vasculature, enhancing renal perfusion. Dopamine also reduces sodium absorption; this enhances urine flow, which helps to prevent tubular cast obstruction. However, most clinical studies have failed to establish this beneficial role of low-dose dopamine infusion, and one study demonstrated that low-dose dopamine may worsen renal perfusion in patients with AKI.

Dialysis

Dialysis, especially hemodialysis, may delay the recovery of patients with AKI. Most authorities prefer using biocompatible membrane dialyzers for hemodialysis. Indications for dialysis (ie, renal replacement therapy) in patients with AKI are as follows:

- Volume expansion that cannot be managed with diuretics
- Hyperkalemia refractory to medical therapy
- Correction of severe acid-base disturbances that are refractory to medical therapy
- Severe azotemia (BUN >80-100)
- Uremia

Timing and intensity

Great controversy exists regarding the timing of dialysis. Older studies suggested decreased mortality with early, versus late, initiation of dialysis, but timing of dialysis

initiation has not been assessed in large, randomized, controlled trials. [48] Approaches vary widely at present.
The Acute Renal Failure Trial Network (ATN) Study found that increasing the intensity of dialysis (either intermittent or continuous) did not improve clinical outcomes (morbidity/mortality). [49] The best evidence suggests that patients with dialysis-dependent AKI should receive at least 3 hemodialysis treatments per week with a delivered Kt/V value of 1.2, or continuous hemodialysis (continuous venovenous hemodialysis or hemofiltration) of 20 mg/kg/h (prescribed).

CRRT

There seems to be no difference in outcome between the use of intermittent hemodialysis and continuous renal replacement therapy (CRRT), but this question is currently under investigation. CRRT may have a role in patients who are hemodynamically unstable and who have had prolonged renal failure after a stroke or liver failure. Such patients may not tolerate the rapid shift of fluid and electrolytes caused during conventional hemodialysis.

Diuretics, Loop

Class Summary

Although diuretics seem to have no effect on the outcome of established AKI, they appear to be useful in fluid homeostasis and are used extensively. They have also been used to reduce the requirement for renal replacement therapy. The use of isotonic sodium chloride solution in conjunction with diuretics is debatable.

Furosemide (Lasix)

Furosemide increases the excretion of water by interfering with the chloride-binding cotransport system, which, in turn, inhibits sodium and chloride reabsorption in the thick ascending loop of Henle and the distal renal tubule. It is a potent and rapid-acting agent with peak action at 60 minutes and a 6- to 8-hour duration of action.
In renal failure, higher doses must be used for greater diuretic effect. Doses as high as 600 mg/day may be needed under monitored conditions.
Frequently, IV doses are needed in AKI to maintain urine output. IV infusions are often helpful in intensive care settings, in which larger doses are necessary. This method promotes a sustained natriuresis with reduced ototoxicity compared with conventional intermittent bolus dosing.

Inotropic Agents

Class Summary

Dopamine in small doses (eg, 1-5 mcg/kg/min) causes selective dilatation of the renal vasculature, enhancing renal perfusion. Dopamine also reduces sodium absorption, thereby decreasing the energy requirement of the damaged tubules. This enhances urine

flow, which, in turn, helps to prevent tubular cast obstruction. The clinical benefit of low-dose dopamine remains uncertain.

Dopamine (Intropin)

Dopamine stimulates adrenergic and dopaminergic receptors. Its hemodynamic effect is dose dependent. Lower doses (0.5-3.0 mcg/kg/min) predominantly stimulate dopaminergic receptors, which, in turn, produce renal and mesenteric vasodilation. Higher doses produce cardiac stimulation and renal vasodilation. Potential complications of dopamine use include cardiac arrhythmias, myocardial ischemia, and intestinal ischemia.

Vasodilators

Class Summary

Fenoldopam decreases systemic vascular resistance and increases renal blood flow to the cortex and medullary regions in the kidney. It has been noted to improve renal function in patients with severe hypertension.

Fenoldopam (Corlopam)

Fenoldopam is a selective dopamine-receptor agonist that acts as a rapid-acting vasodilator. It is 6 times more potent than dopamine in producing renal vasodilation. It increases diuresis and has minimal adrenergic effects. Fenoldopam is indicated for the treatment of severe hypertension, including patients with renal compromise

Calcium Channel Blockers

Class Summary

These drugs are effective in animal models of AKI, but their efficacy has not been proven in humans. The effects of calcium channel blockers are believed to be mediated through vasodilation, and they are increasingly used to enhance the function of transplanted kidneys.

Nifedipine (Adalat, Procardia, Afeditab CR, Nifediac CC, Nifedical XL)

Nifedipine relaxes smooth muscle and produces vasodilation, which, in turn, improves blood flow and oxygen delivery.

Complications :

Cardiovascular complications

Cardiovascular complications (eg, heart failure, myocardial infarction, arrhythmias, cardiac arrest) have been observed in as many as 35% of patients with AKI. Fluid overload secondary to oliguric AKI is a particular risk for elderly patients with limited cardiac reserve. In cardiac patients who experience AKI either in the setting of acute decompensated heart failure or cardiac surgery, AKI is associated with worse morbidity and mortality.
Pericarditis is a relatively rare complication of AKI. When pericarditis complicates AKI, consider additional diagnoses, such as systemic lupus erythematosus (SLE) and hepatorenal syndrome.
AKI also can be a complication of cardiac diseases, such as endocarditis, decompensated heart failure, or atrial fibrillation with emboli. Cardiac arrest in a patient with AKI always should arouse suspicion of hyperkalemia. Many authors recommend a trial of intravenous calcium chloride (or gluconate) in all patients with AKI

who experience cardiac arrest.

Pulmonary complications

Pulmonary complications have been reported in approximately 54% of patients with AKI and are the single most significant risk factor for death in patients with AKI. In addition, diseases exist that commonly present with simultaneous pulmonary and renal involvement, including the following:

- Goodpasture syndrome
- Granulomatosis with polyangiitis (Wegener granulomatosis)
- Polyarteritis nodosa
- Cryoglobulinemia
- Sarcoidosis

Hypoxia commonly occurs during hemodialysis and can be particularly significant in the patient with pulmonary disease. This dialysis-related hypoxia is thought to occur secondary to white blood cell (WBC) lung sequestration and alveolar hypoventilation.

GI complications

Nausea, vomiting, and anorexia are frequent complications of AKI and represent one of the cardinal signs of uremia. GI bleeding occurs in approximately one third of patients with AKI. Most episodes are mild, but GI bleeding accounts for 3-8% of deaths in patients with AKI.
Pancreatitis
Mild hyperamylasemia commonly is seen in AKI (2-3 times controls). Elevation of baseline amylase concentrations can complicate diagnosis of pancreatitis in patients with AKI. Measurement of lipase, which commonly is not elevated in AKI, often is necessary to make the diagnosis of pancreatitis. Pancreatitis has been reported as a concurrent illness with AKI in patients with atheroemboli, vasculitis, and sepsis from ascending cholangitis.

Jaundice

Jaundice has been reported to complicate AKI in approximately 43% of cases. Etiologies of jaundice with AKI include hepatic congestion, blood transfusions, and sepsis.

Hepatitis

Hepatitis occurring concurrently with AKI should prompt consideration of the following disorders in the differential diagnosis:

- Common bile duct obstruction
- Fulminant hepatitis B
- Leptospirosis
- Acetaminophen toxicity
- Amanita phalloides poisoning

Infectious complications

Infections commonly complicate the course of AKI and have been reported to occur in as many as 33% of patients with AKI. The most common sites of infection are the pulmonary and urinary tracts. Infections are the leading cause of morbidity and death in patients with AKI. Various studies have reported mortality rates of 11-72% in infections complicating AKI.

Neurologic complications

Neurologic signs of uremia are a common complication of AKI and have been reported in approximately 38% of patients with AKI. Neurologic sequelae include lethargy, somnolence, reversal of the sleep-wake cycle, and cognitive or memory deficits. Focal neurologic deficits are rarely caused solely by uremia.

The pathophysiology of neurologic symptoms is still unknown, but these symptoms do not correlate well to levels of BUN or creatinine.

A number of diseases express themselves with concurrent neurologic and renal manifestations, including the following:

- SLE
- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)
- Endocarditis
- Malignant hypertension