Contrast-induced nephropathy (CIN) is a major adverse event that occurs during studies that require contrast medium. Almost 10% of all hospital-acquired instances of renal insufficiency are directly attributed to contrast material, with significantly higher mortality and morbidity than cases that do not involve contrast material. Contrast material causes an acceleration of the renal vasoconstrictive response, which results in a cascade of events that affect the vasoregulatory system. Multiple prophylactic measures must be instituted when considering a patient for a contrast study. Critical care nurses are pivotal in identifying patients’ risk factors and potential nephrotoxic agents in order to avoid contrast-induced nephropathy. This article outlines the pathophysiology and definitions of normal kidney function, nephropathy, and chronic kidney disease. (Critical Care Nurse. 2012;32[3]:41-48)
by protein or water intake or by exercise. Age, however, does affect the level. Beyond the age of 40 years creatinine clearance decreases by 1 mL/min per year.6

The GFR is a measure of renal function, indicating the clearance of creatinine by the kidneys. By knowing the GFR, kidney function can be assessed and managed and progression of disease can be monitored. Two of the most widely used equations to quickly and accurately measure GFR are the Cockcroft formula and the Modification of Diet in Renal Disease (MDRD) equation.7

In the Cockcroft formula, creatinine level, body weight, age, and sex are used to determine the rate. With the MDRD, initially 6 variables were used: creatinine level, age, urea nitrogen level, albumin level, sex, and African descent (Table 1). A calculation with 4 variables—age, serum creatinine level, ethnic background, and sex—is also reliable. The National Kidney Disease Education Program, the Kidney Disease Outcomes Quality Initiative, and the US Food and Drug Administration have determined that the MDRD calculation is best used to stage chronic kidney disease; the Cockcroft is recommended to determine the dose of medications.7

**Kidney Disease as a Risk Factor for CIN**

ARF is defined as the sudden loss of renal function accompanied by azotemia. Azotemia is the accumulation of waste products in the blood due to a lack of renal filtration. Uremia is the development of systemic disorders and signs and symptoms of the neurological, hematological, and metabolic systems in response to renal dysfunction.8

Chronic kidney disease develops over months to years. Anemia occurs in both acute and chronic kidney disease associated with altered erythropoietin production. Erythropoietin is a growth factor necessary for the maturation of erythroid cells in the bone marrow to red blood cells. With normal renal function, when hemoglobin levels decrease to less than 12 g/dL, more erythropoietin is produced. In renal dysfunction, renal tubular cells cease to function, and erythropoietin production is decreased. The chronic anemia that ensues because of a lack of oxygen-rich red blood cells induces hypoxia in all organ systems.9 Administering contrast material to a patient whose kidneys are already dysfunctional leads to an acute worsening of chronic kidney disease.6

A history of chronic kidney disease is the foremost predictor of ARF after studies that require contrast material. In a study by Hsu et al.,5 74% of patients with ARF who required dialysis were patients with a GFR less than 60 mL/min. In the Cardiac Angiography in Renally Impaired Patients (CARE) study,9 4 major adverse events were used as end points: death, myocardial infarction, stroke, and end-stage renal disease. Of the 294 patients with moderate to severe renal impairment who had cardiac angiograms, 13% went on to experience a major adverse event.

Chronic kidney disease is classified according to the presence and extent of kidney damage. Any patient with a GFR less than 60 mL/min for 6 months or longer has chronic kidney disease.10 The stage of the chronic disease helps define a patient’s risk for CIN: the risk increases as the severity of preexisting renal disease increases. Chronic kidney disease has 5 stages; each stage indicates a progressive decrease in renal function (Table 2).

**Risk Factors for CIN and Nursing Interventions**

Risk factors for CIN consist of 2 major categories: patient risk factors...
and nephrotoxic medications (Table 3). Nurses should assess each patient for factors that predispose the patient to ARF induced by contrast material. Attempts should be made to determine the patient’s previous baseline renal function, not just the creatinine level at the time of admission to the hospital; the current level may be falsely high or low because of acute factors. Compared with patients with a GFR greater than 60 mL/min, patients with mild impairment of renal function, a GFR of 45 to 59 mL/min, have a 2-fold increased risk for ARF. Other factors to consider are age and sex, which are used in calculating the GFR. Major risk factors for ARF include preexisting diabetes, proteinuria, and hypertension. Anemia is another risk factor. The National Kidney Foundation recommends hemoglobin levels of 11 to 12 g/dL and hematocrit levels of 33% to 36% in patients with chronic kidney disease. Red blood cells transport oxygen; anemia therefore creates a chronic hypoxic state that affects all body systems. The chronic hypoxia and stress are further aggravated by contrast medium. Other comorbid conditions, congestive heart failure, low ejection fraction, multiple myeloma, and acute myocardial infarction, particularly if accompanied by cardiogenic shock, decrease renal perfusion and potentiate renal ischemia. Dehydration activates the renin-angiotensin cascade, leading to vasoconstriction. Patients’ hydration status should be assessed before any procedure that requires contrast material. Diuretics, vomiting, 

### Table 2

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR, mL/min</th>
<th>Risks</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, disease diagnosed</td>
<td>≥90</td>
<td>GFR normal but comorbid conditions affect kidneys</td>
<td>Cardiovascular risk education to stop progression of renal decline</td>
</tr>
<tr>
<td>2, mild</td>
<td>60-89</td>
<td>Marked kidney damage, heightened risk of death with only mild decrease in renal function</td>
<td>Continued cardiovascular risk education, treatment of comorbid conditions of hypertension</td>
</tr>
<tr>
<td>3, moderate</td>
<td>30-59</td>
<td>Half of kidney function has been lost, 74% of cases of acute renal failure requiring dialysis were in patients with GFR &lt;60&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Aggressive treatment of comorbid conditions with lifestyle changes, medications, surgical interventions</td>
</tr>
<tr>
<td>4, severe</td>
<td>15-29</td>
<td>Severely decreased renal function, &gt;30% die when acute renal failure progresses to dialysis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Discussion of dialysis options, continued management of comorbid conditions to slow decline in renal function</td>
</tr>
<tr>
<td>5, end stage</td>
<td>&lt;15</td>
<td>Kidney failure with uremia</td>
<td>Initiation of or continued dialysis</td>
</tr>
</tbody>
</table>

<sup>a</sup> Based on information from Solomon et al.<sup>3</sup>

### Table 3

<table>
<thead>
<tr>
<th>Type of risk factor</th>
<th>Risk factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related to patient</td>
<td>History of chronic kidney disease, glomerular filtration rate &lt; 60 mL/min</td>
</tr>
<tr>
<td></td>
<td>Age &gt; 75 y, kidney function decreases normally with aging</td>
</tr>
<tr>
<td></td>
<td>Low cardiac output states: congestive heart failure, hypotension shock states, acute myocardial infarction</td>
</tr>
<tr>
<td></td>
<td>Preexisting conditions that compromise renal function and cause oxidative stress: anemia, diabetes with neuropathy, multiple myeloma, hypotension, dehydration</td>
</tr>
<tr>
<td>Related to medication</td>
<td>Contrast media, greater volumes of contrast media equate with higher incidence of contrast-induced nephropathy; low-osmolar agents less toxic</td>
</tr>
<tr>
<td></td>
<td>Angiotensin-converting enzymes</td>
</tr>
<tr>
<td></td>
<td>Nonsteroidal anti-inflammatory agents</td>
</tr>
<tr>
<td></td>
<td>Antibiotics: aminoglycosides, penicillins, vancomycin, sulfonamides</td>
</tr>
<tr>
<td></td>
<td>Diuretics: predispose to dehydration</td>
</tr>
<tr>
<td></td>
<td>Metformin: potential for lactic acidosis</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine, potentiation of decrease in kidney function</td>
</tr>
</tbody>
</table>

<sup>a</sup> Based on information from Anderson and Smith.<sup>2</sup>
Diarrhea, and fever can cause dehydration and result in elevation of even a baseline normal creatinine level. Diuretics should be discontinued if possible, and rehydration with intravenous fluids should be considered if a patient’s clinical condition permits.

**Nephrotoxic Effects of Contrast Media**

The number of nephrotoxic agents is considerable (Table 4). Contrast medium itself causes an acceleration of the renal vasoconstriction response. The regulatory system of the kidney is normally responsive to changes in blood flow and sodium concentration. Renin, an enzyme formed in the juxtaglomerular apparatus, is released in response to decreased renal perfusion. Renin converts angiotensinogen, a liver plasma protein, to angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin-converting enzyme. Angiotensin-converting enzyme is present on the surface of all blood vessels, but the highest concentrations are in the highly vascular pulmonary capillary beds. Angiotensin II stimulates the release of aldosterone, a mineralocorticoid released from the adrenal cortex, causing vasoconstriction. Aldosterone enhances sodium reabsorption and potassium excretion. It also stimulates release of corticotropin from the pituitary gland. Corticotropin causes sodium and water retention, leading to vasoconstriction. When contrast material is injected, sodium is retained to maintain plasma osmolarity, and vasoconstriction is initiated.

A hyperosmolar effect on the juxtaglomerular apparatus also occurs. In addition to activating the feedback mechanism of the glomerular system, the viscosity of the contrast material increases hydrostatic pressure in the renal tubules. The feedback mechanism and the increased hydrostatic pressure cause a decrease in GFR and renal blood flow. In response to changes in osmolarity, as occurs with injection of contrast material, release of antidiuretic hormone, also known as vasopressin, from the posterior lobe of the pituitary gland is increased. Antidiuretic hormone induces renal tubules to retain water and causes vasoconstriction.

Vascular endothelium, a cell layer that lines blood vessels, produces vasoregulatory substances. This cell layer is highly responsive to shifts in osmolarity and volume. In response to decreased blood flow, as occurs with injection of contrast material, the vasodilatory compounds nitric oxide and prostaglandin are inhibited. The vasoconstrictive compound endothelin is released from the vascular endothelium. These vasoregulatory responses cause decreased oxygen transport, further exacerbating renal medullary hypoxia, necrosis, and renal cell tubular collapse.

The greater the volume of contrast medium used for a study, the

<table>
<thead>
<tr>
<th>Table 4 Effects of contrast media, pathophysiology&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regulatory agents</strong></td>
</tr>
<tr>
<td>Renin (formed in juxtaglomerular apparatus)</td>
</tr>
<tr>
<td>Angiotensin I</td>
</tr>
<tr>
<td>Angiotensin II</td>
</tr>
<tr>
<td>Aldosterone, a mineralocorticoid (released from adrenal cortex)</td>
</tr>
<tr>
<td>Sodium</td>
</tr>
<tr>
<td>Vascular endothelin</td>
</tr>
<tr>
<td>Antidiuretic hormone released by posterior lobe of pituitary gland</td>
</tr>
</tbody>
</table>

<sup>a</sup> Based on information from Solomon et al<sup>9</sup> and National Kidney Foundation.<sup>10</sup>
greater is the risk for CIN. Staging or performing procedures on separate days will limit the volume of contrast medium given in a single day and allow the kidneys to recover. Schweiger et al noted that use of less than 30 mL of contrast material for a diagnostic study and less than 100 mL for an interventional study has decreased risk of CIN. Contrast agents have become less nephrotoxic over the years. High-osmolar agents were the first agents used, but low-osmolar and iso-osmolar agents have since been formulated. In one study, high-osmolar agents were 3.3 times more likely to have nephrotoxic effects than were low-osmolar agents. Low-osmolar agents create greater osmotic diuretic effects than do iso-osmolar agents, thus causing renal hypoxia and volume depletion. The initial impact of contrast material occurs 3 to 5 days after injection of the material. Nurses should consult with the medical team to ensure that iso-osmolar or low-osmolar agents are used for high-risk patients.

Other Nephrotoxic Agents

High-dose gadolinium used in magnetic resonance imaging can cause CIN and is also a risk factor for nephrogenic systemic fibrosis. First reported in 2006, this fibrotic hardening of the skin, joints, and organs has occurred in patients with advanced renal disease who were injected with gadolinium. Nephrogenic systemic fibrosis occurs 24 hours to as long as 3 months after exposure to gadolinium. Use of this agent should be limited in patients who have advanced chronic kidney disease.

Nonsteroidal anti-inflammatory agents can cause interstitial nephritis, renal papillary necrosis, and toxic effects on the kidneys. Diuretics and inhibitors of angiotensin-converting enzyme inhibitors have the same effects. Many antibiotics are potentially nephrotoxic, including penicillins, sulfonamides, aminoglycosides, and vancomycin. Alternative antibiotics that are effective against the infectious organism should be chosen. Cyclosporine, commonly used in transplant recipients and patients with rheumatoid arthritis, potentiates renal decline. Metformin, which can cause lactic acidosis if given with contrast medium, should not be given the day before and for 48 hours after the procedure. All of these medications can be restarted when renal function has returned to normal.

Prevention of CIN

Hydration is considered the gold standard in CIN prevention. Hydration counteracts the renin-angiotensin cascade. Lowering the osmolarity of plasma and increasing renal blood flow leads to inhibition of vasoconstrictive substances, such as renin, vasopressin, and aldosterone. Fluids dilute contrast medium, thereby decreasing direct nephrotoxic effects of inflammation and necrosis on renal cells.

Hydration is necessary the day before and for 24 hours after a procedure that requires contrast material. Isotonic saline is the preferred intravenous fluid. Various protocols exist, but Schweiger et al recommend 1 L of normal saline solution; the infusion should start 3 hours before a procedure and continue for 6 to 8 hours after the procedure. Adjustments should be made for patients with low cardiac ejection fractions and history of congestive heart failure, but infusion rates of 100 to 150 mL/h are standard. Mueller et al compared the use of normal saline with half-normal saline and found a significant advantage in using normal saline (incidence of CIN, 0.7% vs 2%). The dose used in studies has been 1 mL/kg. Simply forcing fluids did not produce the same effects that intravenous fluids did. If possible, diuretics and any nephrotoxic drugs should be avoided 1 to 2 days before a planned procedure that requires contrast material. The medications can be resumed safely once the creatinine level has returned to baseline. A second preventive therapy that has been studied for its vasodilator and antioxidant effects is N-acetylcysteine (Mucomyst; commonly used to treat bronchospasm and acetaminophen poisoning). The compound acts as an antioxidant of oxygen free radicals and is a vasodilator of the kidney bed. Its use in combination with intravenous fluids has had positive outcomes. Doses of 600 to 1200 mg twice daily starting the day before a study that requires contrast material and continuing the day of the study have been effective.

The proven efficacy of N-acetylcysteine is controversial. In an early study by Tepel et al, patients who received intravenous saline along with N-acetylcysteine had only a 2% occurrence of nephropathy, whereas the occurrence was 21% in patients who received only normal saline for 12 hours before and after a study that required contrast material. Fishbane, however, noted the inconsistency of findings among the various
studies. Additionally, most studies had used small sample sizes with fewer than 500 participants, thus decreasing the strength of conclusions. The study by Tepel et al had only 83 participants. In a study of 354 patients who were being prepared for cardiac angioplasty after myocardial infarction, Marenzi et al used placebo vs standard dose of N-acetylcysteine vs high dose of N-acetylcysteine. Results were dramatically impressive: a 54.5% reduction in CIN in patients given the standard dose of N-acetylcysteine and a 75.8% reduction in patients given the high dose. These results have not been replicated. Fishbane noted that compared with studies that indicated positive results with N-acetylcysteine, twice as many studies indicated no benefit. In his study, results in the placebo group and the N-acetylcysteine group were comparable: 26.3% vs 22%, respectively. Fishbane also pointed out that a trial with a much larger sample size of 457 participants was stopped before completion because treatment with N-acetylcysteine had no benefits.

N-acetylcysteine is economical, has no serious adverse effects, and may prevent CIN. Although multicenter, larger scale studies are indicated before proven efficacy is established, N-acetylcysteine is widely used as a preventive strategy. This medication is considered a cornerstone of prevention at my institution in Philadelphia and is used on a daily basis. The potential benefits of N-acetylcysteine in preserving kidney function far outweigh any harm.

The third therapy that has had positive outcomes is sodium bicarbonate. In some studies, it has been more effective than normal saline, possibly eliminating the vasoconstriction and free radicals that are formed with administration of contrast material. In a study in which sodium bicarbonate was compared with normal saline, the reductions in the occurrence of CIN were 1.7% and 13.6%, respectively. Doses of 3 mL/kg per hour for 1 hour before the procedure that required contrast material combined with doses of 1 mL/kg per hour for 6 hours after the procedure limited the increase in the serum level of creatinine to just 0.5 mg greater than baseline. Tamura et al investigated standard hydration plus a single injection of sodium bicarbonate just before coronary angioplasty with standard hydration alone. Serum creatinine levels were significantly lower in the bicarbonate group, with a CIN rate of 1.4% vs a rate of 12.5% in the group given hydration alone.

Tamura et al acknowledged that 2 recent studies indicated no superiority of sodium bicarbonate with hydration vs hydration alone.

As with N-acetylcysteine, further studies with sodium bicarbonate are indicated. The sodium load as well as the volume loads must be considered when used in patients who are prone to pulmonary edema or have low ejection fractions and/or congestive heart failure. The combination of sodium bicarbonate plus hydration is commonly used as prophylaxis.

### Conclusions

Interventional studies are becoming increasingly common for all patients. Nurses play a vital role in assessing for and preventing the increased morbidity and mortality associated with CIN. Critical care nurses must assess risk factors of patients and plan prophylaxis with physicians and pharmacists (Table 5). Consideration must be given to determining a patient’s baseline serum creatinine level and kidney function and his or her hydration state, as well as assessing any nephrotoxic medications that might need

---

**Table 5** Prevention of contrast-induced nephropathy*  

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prevention Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administer N-acetylcysteine, 600 mg orally x 4 doses</td>
<td></td>
</tr>
<tr>
<td>Use sodium bicarbonate prophylaxis as volume status permits</td>
<td></td>
</tr>
<tr>
<td>Use low-osmolar or iso-osmolar contrast agents in minimal quantities</td>
<td></td>
</tr>
<tr>
<td>Consider other imaging studies or staging, postponing studies with contrast material</td>
<td></td>
</tr>
<tr>
<td>Determine serum creatinine levels 1 to 5 days after procedure with contrast material</td>
<td></td>
</tr>
<tr>
<td>If contrast-induced nephropathy develops, continue to avoid nephrotoxic drugs, consult renal specialist, and consider dialysis if needed</td>
<td></td>
</tr>
</tbody>
</table>

* Based on information from National Kidney Foundation.
to be changed. Teaching patients and their family members about why the patients are not getting their medications and why they are receiving hydration, N-acetylcysteine, and sodium bicarbonate are essential components of a nurse’s role.

After a study that requires contrast material, critical care nurses should be alert for an increase in the serum level of creatinine during the next 3 to 5 days. If a patient is discharged shortly after a study that required contrast material and is at high risk for CIN, nurses can play a key role in ensuring that the patient has good follow-up care to monitor the creatinine level. Patients should be taught to watch for indications of decreased renal function, such as changes in the amount of urine and a darker color of urine. Polyuria and nocturia may develop in early ARF because the kidneys are unable to concentrate urine. As renal function worsens, urine output will decrease.8

A key component in CIN is the nurse’s role in risk stratification, prevention, and follow-up. Maintaining the quality of a patient’s life is the core of these preventive measures. The potential devastating aftermath of CIN can be averted if forethought is instituted. [CCN]

Financial Disclosures
None reported.

References
Contrast-Induced Nephropathy: Nursing Implications

Facts

Contrast-induced nephropathy (CIN) is a major adverse event that occurs during studies that require contrast medium. Almost 10% of all hospital-acquired instances of renal insufficiency are directly attributed to contrast material, with significantly higher mortality and morbidity than cases that do not involve contrast material. Contrast material causes an acceleration of the renal vasoconstrictive response, which results in a cascade of events that affect the vasoregulatory system. Multiple prophylactic measures must be instituted when considering a patient for a contrast study. Nurses play a vital role in assessing for and preventing the increased morbidity and mortality associated with CIN. Critical care nurses must assess risk factors of patients and plan prophylaxis with physicians and pharmacists (see Table).

Risk factors for CIN consist of 2 major categories: patient risk factors and nephrotoxic medications. Nurses should assess each patient for factors that predispose the patient to acute renal failure (ARF) induced by contrast material. Attempts should be made to determine the patient’s previous baseline renal function, not just the creatinine level at the time of admission to the hospital. Compared with patients with a glomerular filtration rate (GFR) greater than 60 mL/min, patients with mild impairment of renal function, a GFR of 45 to 59 mL/min, have a 2-fold increased risk for ARF. Major risk factors for ARF include preexisting diabetes, proteinuria, and hypertension.

Anemia is another risk factor. Red blood cells transport oxygen; anemia therefore creates a chronic hypoxic state that affects all body systems. The chronic hypoxia and stress are further aggravated by contrast medium. Other comorbid conditions, congestive heart failure, low ejection fraction, multiple myeloma, and acute myocardial infarction, particularly if accompanied by cardiogenic shock, decrease renal perfusion and potentiate renal ischemia.

Patients’ hydration status should be assessed before any procedure that requires contrast material. Diuretics, vomiting, diarrhea, and fever can cause dehydration and result in elevation of even a baseline normal creatinine level. Diuretics should be discontinued if possible, and rehydration with intravenous fluids should be considered if a patient’s clinical condition permits.

Teaching patients and their family members about why the patients are not getting their medications and why they are receiving hydration, N-acetylcysteine, and sodium bicarbonate are essential components of a nurse’s role.

Table Prevention of contrast-induced nephropathy

- Assess risk factors related to patient and medications
- Avoid nephotoxic medications 24 to 48 hours before procedure with contrast material and resume when renal function stabilizes
- Hydrate with saline as tolerated
- Administer N-acetylcysteine, 600 mg orally × 4 doses
- Use sodium bicarbonate prophylaxis as volume status permits
- Use low-osmolar or iso-osmolar contrast agents in minimal quantities
- Consider other imaging studies or staging, postponing studies with contrast material
- Determine serum creatinine levels 1 to 5 days after procedure with contrast material
- If contrast-induced nephropathy develops, continue to avoid nephrotoxic drugs, consult renal specialist, and consider dialysis if needed

References
Contrast-Induced Nephropathy: Nursing Implications
Susan Isaac

Crit Care Nurse 2012;32 41-48 10.4037/ccn2012516
©2012 American Association of Critical-Care Nurses
Published online http://ccn.aacnjournals.org/

Personal use only. For copyright permission information:
http://ccn.aacnjournals.org/cgi/external_ref?link_type=PERMISSIONDIRECT

Subscription Information
http://ccn.aacnjournals.org/subscriptions/

Information for authors
http://ccn.aacnjournals.org/misc/ifora.xhtml

Submit a manuscript
http://www.editorialmanager.com/ccn

Email alerts
http://ccn.aacnjournals.org/subscriptions/etoc.xhtml