Issues in the Use of Contrast Media in Patients at High Risk for Contrast-Induced Nephrotoxicity (CIN)

Release date: June 2003
Expiration date: June 2004
Estimated time to complete activity: 1.0 hours
Target Audience

This activity has been designed to meet the educational needs of radiologists, including interventional radiologists, interventional cardiologists, nephrologists, and radiologic technologists.

Statement of Need/Program Overview

The use of contrast media in radiologic procedures has continued to expand. The availability of both ionic and nonionic (including isosmolar) contrast has generated interest in reassessing the association of contrast with nephrotoxicity, particularly in high-risk patients, and evaluating clinically useful prophylactic measures.

Educational Objectives

Upon completion of this activity, participants should be better able to:

- Identify issues in patients at high risk for CIN
- Describe prophylactic strategies to lower the risk of CIN
- Discuss recently published data on the use of contrast media in patients at high risk for CIN

Method of Participation

There are no fees for participating and receiving CME credit for this activity. During the period June 2003 through June 30, 2004 participants must:

- Read the learning objectives and faculty disclosures
- Study the educational activity
- Complete the Post-Test by recording the best answer to each question in the answer key on the Evaluation Form
- Complete the Evaluation Form
- Fax the Evaluation Form with answer key to the Postgraduate Institute for Medicine
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Accreditation Statement
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Issues in the Use of Contrast Media in Patients at High Risk for Contrast-Induced Nephrotoxicity (CIN)

Introduction
Intravascular radiopaque contrast media (RCM) are used globally for the performance of a wide variety of diagnostic and interventional procedures such as urography, computed tomography (CT), digital subtraction angiography, and cardiac catheterization. Over 16 million examinations using intravascular RCM were done in the United States alone in 1994. Although the vast majority of radiographic examinations are completed without incident, adverse reactions to RCM can be, at least, unpleasant and, at worst, potentially life-threatening. One such adverse reaction is CIN, which can increase hospital costs and, in some high-risk patients, lead to dialysis and/or permanent renal damage.

This program will focus on CIN, the patients who are at increased risk of CIN, and clinical approaches to reduce its occurrence.

Characteristics of RCM
Ionic vs nonionic. Since the first description of intravenous contrast use in humans in 1919, contrast agents have gradually evolved from early, relatively toxic products such as sodium iodopyridone or sodium iodomethamate to the new nonionic isosmolar ioxanol. RCM are typically divided into categories—ionic contrast media are salts of sodium and/or meglumine, nonionic contrast media are organic compounds that do not dissociate in solution. Ionic contrast media require two molecules to deliver the same number of iodine atoms as nonionic contrast media deliver with one molecule (Figure 1).
Osmolality. The number of ions of a solute (e.g., contrast medium) dissolved in a solution determines its osmolality. The osmolality of normal human serum is 285 mOsm/L. High osmolar contrast media (HOClM) have an osmolality range of approximately 1,400 to 3,000 mOsm/L; low osmolar contrast media (LOCM) have an osmolality range of approximately 400 to 850 mOsm/L. With one exception all LOCM are nonionic monomeric compounds. The lone ionic LOCM is ioxaglate. Recently, a nonionic isosmolar dimer, iodixanol, has been introduced that has an osmolality of 290 mOsm/L, essentially the same osmolality as that of human serum.

Figure 1. Chemical structure of contrast agents.

Ideally, RCM should be water soluble, chemical and heat stable, biologically inert (nonantigenic), of low viscosity, and low or isosmolar, excreted selectively through the kidney, safe, and inexpensive.\(^3\) Selected properties of RCM are shown in Tables 1–2. Lower osmolality may decrease some adverse effects, hence the rationale to produce nonionic agents. Higher osmolality may not only increase pain and other symptoms, but may also increase adverse effects affecting the heart and kidney.\(^1,3\) While the wide variety of contrast agents available in the marketplace today continues to improve, physicians still must address the risk of adverse effects and find ways to mitigate them.
Table 1. Ionic Radiopaque Contrast Media* (ACR 4.1, pp41–42)

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Composition</th>
<th>% Salt</th>
<th>Iodine 240–320 (mg/mL)</th>
<th>Viscosity at 37°C</th>
<th>Osmolality (mOsm/kg H$_2$O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypaque Diatrizoate Meglumine 60% (Amersham Health)</td>
<td>Diatrizoate Meglumine</td>
<td>60</td>
<td>282</td>
<td>4.1</td>
<td>1,415</td>
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<td>Reno®-60 (Bracco)</td>
<td>Diatrizoate Meglumine</td>
<td>60</td>
<td>282</td>
<td>4.0</td>
<td>1,404</td>
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<tr>
<td>Conray-60 (Mallinckrodt)</td>
<td>Iothalamate Meglumine</td>
<td>60</td>
<td>282</td>
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<tr>
<td>Renograffin-60 (Bracco)</td>
<td>Diatrizoate Meglumine Sodium</td>
<td>52 8</td>
<td>292.5</td>
<td>4.0</td>
<td>1,450</td>
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<tr>
<td>Hypaque Sodium 50% (Amersham Health)</td>
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<td>300</td>
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<tr>
<td>Hexabrix (Mallinckrodt)</td>
<td>Ioxaglate Meglumine Sodium</td>
<td>39.3 19.6</td>
<td>320</td>
<td>7.5</td>
<td>600</td>
</tr>
<tr>
<td>Trade Name</td>
<td>Composition</td>
<td>Iodine 200–320 (mg/mL)</td>
<td>Viscosity at 37°C</td>
<td>Osmolality (mOsm/kg H₂O)</td>
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<tr>
<td>Omnipoque® 240</td>
<td>Iohexol 51.8%</td>
<td>240</td>
<td>3.4</td>
<td>520</td>
<td></td>
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<tr>
<td>(Amersham Health)</td>
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<tr>
<td>Optiray® 240</td>
<td>Ioversol 50.9%</td>
<td>240</td>
<td>3.0</td>
<td>502</td>
<td></td>
</tr>
<tr>
<td>(Mallinckrodt)</td>
<td></td>
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<tr>
<td>Ultravist®-240</td>
<td>Iopromide</td>
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<td>3.0</td>
<td>502</td>
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<td>(Berlex)</td>
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<tr>
<td>Isovue®-250</td>
<td>Iopamidol 51%</td>
<td>250</td>
<td>3.0</td>
<td>524</td>
<td></td>
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<tr>
<td>(Bracco)</td>
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<tr>
<td>Visipaque®-270</td>
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<tr>
<td>Isovue®-300</td>
<td>Iopamidol 61.2%</td>
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<td>4.7</td>
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<tr>
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<td>5.5</td>
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<td>(Amersham Health)</td>
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<td></td>
</tr>
<tr>
<td>Optiray® 300</td>
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<td>Oxilan® 300</td>
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<td>(Cook)</td>
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<tr>
<td>(Berlex)</td>
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<td></td>
</tr>
<tr>
<td>Optiray® 320</td>
<td>Ioversol 67.8%</td>
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<td>5.8</td>
<td>702</td>
<td></td>
</tr>
<tr>
<td>(Mallinckrodt)</td>
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<tr>
<td>Visipaque®-320</td>
<td>Iodixanol</td>
<td>320</td>
<td>11.8</td>
<td>290</td>
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<tr>
<td>(Amersham)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
### Table 3. Radiopaque Contrast Media Typically Used in Cardiac Procedures

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Composition</th>
<th>% Salt</th>
<th>Iodine (mg/mL)</th>
<th>Viscosity at 37°C</th>
<th>Osmolality (mOsm/kg H₂O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omnipoque–350 (Amersham Health)</td>
<td>Nonionic iohexol 75.5%</td>
<td>—</td>
<td>350</td>
<td>10.4</td>
<td>844</td>
</tr>
<tr>
<td>Isovue–370 (Bracco)</td>
<td>Nonionic iopamidol 75.5%</td>
<td>—</td>
<td>370</td>
<td>9.4</td>
<td>796</td>
</tr>
<tr>
<td>Hypaque–76 (Amersham Health)</td>
<td>Ionic diatrizoate meglumine sodium</td>
<td>—</td>
<td>370</td>
<td>8.32</td>
<td>2016</td>
</tr>
</tbody>
</table>

*Note: Tables 1–2 are not a complete listing of currently available ionic and nonionic contrast media.

**Adverse Effects of RCM**

Adverse reactions to intravascular HOCM occur in 5% to 12% of patients compared with a 1% to 3% incidence in those receiving LOCM. Reactions to RCM may include anaphylactoid, or pseudoallergic reactions (eg, urticaria, nasal congestion, laryngeal edema, bronchospasm); chemotoxic reactions (eg, cardiac depression, arrhythmia, renal tubular or vascular damage); osmotoxic reactions (eg, changes in plasma volume, vascular permeability, vasodilation, blood–brain barrier); and vasovagal reactions (eg, bradycardia, hypotension). Severe reactions, which include dyspnea (shortness of breath), sudden drop in blood pressure, cardiac arrest, and loss of consciousness occur in <0.004% of procedures with ionic RCM and in 0.001% of procedures with nonionic RCM.

CIN is an adverse effect associated with RCM that continues to receive considerable attention—particularly because it is relatively common in high-risk patients and has the potential for serious sequelae.
Clinical Features of Contrast Nephrotoxicity

Definition of CIN. The first challenge in evaluating CIN is to determine what defines significant nephrotoxicity. In most studies, an increase in serum creatinine of at least 0.5 mg/dL or 25% above baseline during the 48- to 72-hour period following contrast media exposure is considered clinically significant, although not all clinicians are in agreement. However, outcomes that represent clinically more severe forms of CIN such as the need for dialysis or prolonged hospitalization due to renal toxicity, are uncommon, and are generally not selected to define CIN clinically.

Historical perspective. CIN was first reported in 1928 when acute renal failure was observed in some patients after the administration of iodopyridone. Subsequently, it was demonstrated that pre-existing renal insufficiency was a risk factor for this complication. In the early 1950s, the first RCM to use the benzene ring, Urokon, was introduced and was soon followed by tri-iodinated agents that were less nephrotoxic. The advent of low osmolar agents has further improved the safety profile of these agents. However, nephrotoxicity still occurs in a number of patients, so an understanding of its clinical course and what measures can be taken to prevent or reduce it is important.

Clinical course. The clinical course of CIN typically shows an increase in serum creatinine levels within 24 to 48 hours after intravascular contrast administration with peak values occurring between 3 to 5 days. There is usually complete return of the serum creatinine value to its precontrast baseline value by 10 days. In more severe cases, the serum creatinine may continue to rise for 5 to 10 days and, in rare cases, dialysis may be needed. Although most cases of CIN are nonoliguric, oliguric CIN can occur and is most typically seen in patients with diabetes and severe pre-existing renal insufficiency. A rise in serum creatinine that occurs more than 48 hours after contrast exposure should suggest a cause for acute renal failure other than CIN, such as cholesterol embolization.
Pathogenesis of CIN
Although no one has clearly established what physiochemical property of contrast media has the most effect on the kidney, renal medullary hypoxia and direct cytotoxicity have been identified as key causes of CIN. As shown in Figure 2, there are several factors that affect medullary oxygenation: prostaglandins (PGs) and atrial natriuretic peptide (ANP) are known to increase renal medullary blood flow while endothelin, vasopressin, adenosine, and reductions in prostacyclin (PGI₂) decrease blood flow. If there is systemic hypoxemia or increased blood viscosity, oxygen delivery to the renal medulla may also be reduced.¹¹

**Figure 2. The effect of contrast media on acute renal failure.**


**Effect of osmolality on the kidney.** With one exception, iodixanol, all currently available radiopaque contrast media for intravascular use are hyperosmolar relative to human serum. Administration of hyperosmolar RCM increases delivery of NaCl to the ascending limb of the loop of Henle (ie, RCM act as "osmotic diuretics"). This may result in increased active reabsorption of NaCl, a process which requires increased oxygen expenditure thus further contributing to medullary hypoxia.¹¹,¹² The increase in NaCl reabsorption also leads to adenosine triphosphate (ATP) hydrolysis and increased adenosine production, which can cause renal vasoconstriction and hence CIN.¹³
In addition, there is in vitro evidence that hyperosmolality can increase programmed cell death (apoptosis) of kidney cells, which also contributes to the pathogenesis of CIN. These observations may explain why the incidence of CIN is lower with LOCM than with HOCM and possibly lower still with isosmolar media than with LOCM.

**Risk Factors for CIN: Impact on Incidence**

CIN is uncommon in “low-risk” patients who are defined as not having pre-existing renal insufficiency. The mean incidence of CIN in the low-risk population is approximately 3%, based on data from both retrospective and prospective studies.

Nephrotoxicity almost exclusively occurs in patients with pre-existing renal insufficiency. In patients with pre-existing renal insufficiency with or without diabetes mellitus (“high-risk” patients), the incidence of CIN is much greater, reaching 9% to 50% in patients with both comorbidities. In a study of patients undergoing coronary angiography, CIN occurred in 21.6% of high-risk patients and in 7.9% of low-risk patients. Diabetes mellitus alone is probably not a significant risk factor; however, the incidence of CIN is much higher in azotemic patients with diabetes than in azotemic patients without diabetes (Table 4).

Thus, patients with chronic renal insufficiency and diabetes mellitus are at the greatest risk for CIN.
Table 4. CIN in Patients Who Have Renal Insufficiency (RI) With and Without Diabetes Mellitus (DM)

<table>
<thead>
<tr>
<th>Reference</th>
<th>(+) RI (-) DM n/N (%)</th>
<th>(+) RI (+) DM n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rudnick et al, 8 1994</td>
<td>15/296 (5)</td>
<td>43/213 (20)</td>
</tr>
<tr>
<td>Harris et al, 10 1991</td>
<td>5/76 (7)</td>
<td>3/25 (12)</td>
</tr>
<tr>
<td>Barrett et al, 34 1992</td>
<td>6/213 (3)</td>
<td>6/36 (17)</td>
</tr>
<tr>
<td>Moore et al, 28 1992</td>
<td>4/117 (3)</td>
<td>8/43 (19)</td>
</tr>
</tbody>
</table>

Other factors that may be implicated in the development of CIN include: dehydration and absence of preventative measures, large volume of injected contrast medium, severe congestive heart failure, and prior history of contrast media-associated acute renal failure (Figure 3).

Figure 3. CIN: contributing factors.

It has also been shown that the incidence of CIN increases as serum creatinine levels increase: 0% at <1.5 mg/dL (normal)\textsuperscript{18,19}; 50% to 75% at 1.6 to 4.5 mg/dL (moderate CIN)\textsuperscript{18-20}; 90% to 100% at >4.5 mg/dL (severe CIN).\textsuperscript{18,20}
Effect of CIN on Mortality

As with any medical procedure or adverse reaction, the key issue is the ultimate effect on patient outcome. In a large analysis (>16,000 patients) of in-hospital patients who underwent RCM procedures, 183 developed CIN. The mortality rate was 34% compared with only 7% in a matched cohort of patients without CIN. Increased mortality in patients who develop CIN versus those who do not has been substantiated in several additional studies. However, due to the association of higher cardiovascular comorbidities in patients who developed CIN versus those who did not, it is not possible at this time to determine if CIN directly contributes to mortality or is simply a marker for patients with severe illnesses.

Role of Osmolality in CIN

HOCM versus LOCM. Although high or low osmolar contrast media (CM) have not been conclusively shown to differentially affect the kidneys in patients with normal renal function, the osmolality of contrast agents may be a factor in patients with pre-existing renal insufficiency. The data strongly support a kidney-sparing effect with LOCM (Figure 4).

Figure 4. Incidence of CIN (SCr ≥1 mg%) stratified by risk factor.

(SCr=serum creatinine; RI=renal insufficiency; DM=diabetes mellitus)
A meta-analysis of 25 trials revealed that the risk of having more than a 0.5 mg/dL increase in serum creatinine level following contrast exposure was 40% lower with LOCM than with HO CM. In patients with pre-existing renal insufficiency, the odds ratio was even greater.29

**Isosmolar contrast media versus LOCM.** The recent development of the isosmolar nonionic contrast agent iodixanol has led to additional comparative studies to demonstrate reduced renal effects.15,30 In a recently published report (the NEPHRIC study), 129 patients with diabetes and impaired renal function were prospectively randomized to receive either iodixanol or iohexol for coronary angiography.15 Iodixanol was shown to be less nephrotoxic than iohexol based on both the standard definition of CIN (SCr >0.5 mg/dL) and a more rigorous definition of CIN (SCr >1.0 mg/dL) (Figure 5). The risk of developing CIN was 11 times higher with iohexol compared with iodixanol, using the standard definition.

Although data are still limited, these studies suggest that the isosmolar nonionic RCM iodixanol may be less nephrotoxic than low osmolar agents for the “high-risk” patient.

**Figure 5. The effect of iodixanol (isosmolar, nonionic) vs iohexol (LOCM, nonionic) on CIN (the NEPHRIC study).**

Prophylactic Strategies to Reduce CIN

Type, Volume, and Timing of Contrast Media
The type and volume of contrast media are important factors that affect the incidence of CIN. Logically, the less volume used the better, but more concentrated contrast media should not necessarily be chosen simply to reduce the volume without considering the effects of the higher concentration. It is important to select the lowest concentration that will provide adequate radiopacity for the type of procedure being performed. As previously noted, in patients with normal renal function, there is little effect on the incidence of CIN with use of either HOCM or LOCM. Conversely, in patients with pre-existing renal insufficiency, the use of LOCM, and possibly isosmolar contrast is beneficial. When multiple procedures are needed in 1 patient, increasing the time between procedures will help give the kidneys more recovery time and reduce the incidence and severity of CIN. If a patient is taking nonsteroidal anti-inflammatory drugs (NSAIDs), the NSAIDs should be discontinued prior to a contrast procedure to also help reduce nephrotoxicity.

Hydration
Hydration is the simplest and least expensive treatment to reduce the incidence of CIN. The value of hydration as a prophylactic strategy may be due to increased beneficial effects on the kidneys, such as decreased activity of the renin–angiotensin system, augmentation of diuresis and sodium excretion, and reduction in renal vasoconstriction by dilution of contrast media. Although hydration is generally well accepted, there are few clinical data to support timing, amount, or type of hydration. Most studies have used either normal or half-normal saline at a rate of 1 mL/kg/hr starting 12 hours before contrast and continuing for 12 hours after contrast. Studies have shown that normal saline is superior to half-normal and that normal saline is also superior to unrestricted oral fluids. Hydration is recommended for all patients and is particularly important in patients who have pre-existing impaired renal function in the presence or absence of diabetes as well as in patients who have had previous episodes of CIN.
Mannitol and Furosemide

Although mannitol and furosemide were at one time considered to be potentially useful in the prevention of CIN, a prospective study demonstrated that saline alone was superior to either agent as a prophylactic strategy in CIN. Based on findings such as these, neither agent is recommended today.

Acetylcysteine

As indicated in preclinical studies, an antioxidant such as acetylcysteine (NAC) may help reduce CIN by decreasing the presence of oxygen-free radicals generated by contrast media and/or by its ability to reduce renal vasoconstriction.

Reported clinical data have been inconsistent regarding the ability of NAC to reduce the incidence of CIN. In the studies that showed benefit, patients with renal insufficiency who underwent radiographic procedures using LOCM and hydration as prophylaxis, received NAC (600 mg; total of 4 doses) both before and after RCM administration.

Other studies, however, that used similar study designs to those described, have not been able to demonstrate a clinically beneficial role for NAC in CIN. NAC was unable to prevent or minimize renal dysfunction compared with either saline alone or placebo.

Reasons for the lack of consistent findings in these studies are unclear at the present time. However, a large, randomized trial primarily designed to evaluate the prophylactic value of NAC will be needed before any definitive statements can be made. Despite the conflicting data, the relative safety and inexpensive cost of NAC favor its use at the present time.
Dopamine and Fenoldopam

Dopamine. Stimulation of renal arterial dopamine D1 receptors results in vasodilation of these vessels. Therefore, several studies have evaluated dopamine as a prophylactic agent to prevent CIN, although with inconsistent results. The failure to demonstrate a consistent benefit may be due to the nonselectivity of dopamine for the D1 receptors.

Fenoldopam. Fenoldopam is a selective D1 receptor agonist that is approved for the management of severe hypertension. Although initial studies suggested a potential benefit for fenoldopam in preventing CIN, the results of a large, double-blind, randomized trial that compared fenoldopam with placebo in high-risk patients demonstrated that fenoldopam was unable to prevent CIN.

Theophylline

Experimental and clinical studies have demonstrated that the nonselective adenosine receptor antagonist, theophylline, inhibits contrast media-induced renal vasoconstriction. Furthermore, several studies suggest a beneficial effect of theophylline in reducing CIN. Patients who received oral theophylline starting at least one hour before contrast administration demonstrated prevention or attenuation of reductions in creatinine clearance induced by both HOCM and LOCM compared with placebo. The possibility of theophylline causing tachyarrhythmias in this setting is of potential concern especially in patients with coronary artery disease undergoing coronary angiography.
**Gadolinium as an Alternative Agent**

In patients with renal insufficiency or severe allergy to iodinated contrast media, gadolinium can be considered as a substitute for use in angiography.\(^5\) Although typically considered only for magnetic resonance imaging, gadolinium—a rare earth paramagnetic material—is mildly radiopaque and can be used as a substitute for low-concentration iodinated contrast media. Gadolinium-DTPA at a concentration of 0.5 mmol/mL is equivalent to a 12.5% to 25% dilution of standard iodinated contrast material (e.g., iohexol). Although it is extremely rare to see severe reactions to gadolinium, headache, nausea, and flushing can occur.\(^4\) The attractiveness of gadolinium in patients with renal insufficiency is its relative lack of nephrotoxicity.\(^4,50\)

At the present time, investigators who advocate the use of gadolinium during angiography in patients with renal insufficiency recommend that the total dose of gadolinium not exceed 0.3 to 0.4 mmol/kg body weight (about 40 to 50 mL for a 70-kg patient),\(^50\) which is adequate for many types of angiographic examinations. Studies that require larger volumes of contrast can still be accomplished when gadolinium is supplemented with \(\text{CO}_2\).

**Summary**

Physicians must carefully assess each patient who undergoes an intravascular procedure that uses iodinated RCM. Patients at increased risk of adverse clinical events such as nephrotoxicity must be recognized and appropriate strategies for mitigating this risk must be implemented. Currently, hydration is the most widely recommended prophylactic measure to reduce the incidence of CIN. Patients who are at highest risk for developing CIN are those with existing renal insufficiency and diabetes mellitus. The development of LOCM has significantly reduced adverse reactions compared with HOCM and the availability of new isosmolar contrast media may have an even better tolerability and reduced nephrotoxicity profile. As new products and clinical management strategies emerge and with careful further study, the incidence and severity of adverse sequelae will hopefully continue to diminish, resulting in improved patient care.
References


1. Nonionic contrast media require only 1 molecule to deliver the same number of iodine atoms as ionic contrast media deliver with 2 molecules.  
A) true  B) false

2. Which of the following statements about osmolality are true?  
a) High osmolar contrast media (HOCM) have an osmolality range of approximately 1,400 to 3,000 mOsm/L.  
b) Low osmolar contrast media (LOCM) have an osmolality range of 400 to 850 mOsm/L.  
c) Human serum has an osmolality of approximately 285 mOsm/L.  
A) a and b  B) b and c  C) a and c  D) a, b, and c

3. Which of the following observations may explain why the incidence of CIN is lower with LOCM than with HOCM, and possibly lower still with an isosmolar contrast medium than with LOCM?  
Hyperosmolality may:  
a) Increase apoptosis of kidney cells  
b) Decrease delivery of NaCl to the ascending limb of the loop of Henle  
c) Increase reabsorption of NaCl, resulting in increased adenosine production and subsequent renal vasconstriction  
d) Contribute to medullary hypoxia, as a result of reabsorption of NaCl  
A) b and c  B) a, b, and c  C) a and c  D) a, b, and d

4. In most studies, an increase in serum creatinine of at least ____ mg/dL during the 48- to 72-hour period following contrast media exposure is considered a clinically significant indicator of nephrotoxicity.  
A) 0.05  B) 0.2  C) 0.5  D) 0.10

5. Although it has not been clearly established what physiochemical property of contrast media has the most effect on the kidney, _______ and _______ have been identified as key causes of CIN.  
A) Renal medullary hypoxia/direct cytotoxicity  
B) Renal medullary hypoxia/indirect cytotoxicity  
C) Renal cortical hypoxia/direct cytotoxicity

6. In patients with pre-existing renal insufficiency with or without diabetes mellitus, the incidence of CIN is much greater in patients with both comorbidities.  
A) true  B) false

7. In addition to pre-existing renal insufficiency and diabetes mellitus, which of these factors can also contribute to CIN?  
a) Dehydration  
b) The use of HOCM in chronic renal failure patients  
c) Severe congestive heart failure  
d) Large volume of injected contrast medium  
A) a, b, and c  B) b, c, and d  C) a, c, and d  D) a, b, c, and d

8. The risk of having more than a 0.5 mg/dL increase in serum creatinine level following contrast exposure was significantly ________ with LOCM than with HOCM.  
A) higher  B) lower

9. Which of the following statements about the NEPHRIC study are true?  
a) The study included 129 patients with diabetes and impaired renal function prospectively randomized to receive either ioxanol or iohexol for coronary angiography.  
b) The risk of developing CIN was 11 times higher with ioxanol than with iohexol, based on the standard definition of CIN (Scr >0.5 mg/dL) and a more rigorous definition of CIN (Scr >1.0 mg/dL).  
c) Although data are still limited, the study suggests that the isosmolar, nonionic radiopaque contrast media (RCM) ioxanol may be less nephrotoxic than low osmolar agents for high-risk patients.  
d) The NEPHRIC study data were published in the New England Journal of Medicine (Aspelin et al), Volume 348, No. 6.  
A) a and b  B) a, b, and c  C) a, b, and c  D) a, b, c, and d

10. Which of the following statements about the use of hydration as a treatment to reduce the incidence of CIN are true?  
a) Hydration increases the activity of the renin–angiotensin system.  
b) Hydration augments diuresis and sodium excretion.  
c) Hydration reduces renal vasoconstriction by dilution of contrast media.  
d) Hydration is recommended for all patients, and is particularly important in patients who have pre-existing impaired renal function or those who have had previous episodes of CIN.  
A) a, b, and c  B) a, b, c, and d  C) a, b, c, and d  D) a, b, c, and d

11. Although mannitol and furosemide were once considered potentially useful for preventing CIN, a prospective study demonstrated that saline alone was superior to either agent as a prophylactic strategy.  
A) true  B) false

12. Which of the following statements about the use of gadolinium as an alternative contrast agent are true?  
a) Gadolinium can be considered as a substitute for use in angiography in patients with renal insufficiency or severe allergy to iodinated contrast media.  
b) Gadolinium-DTPA at a concentration of 0.5 mmol/mL is equivalent to a 12.5% to 25% dilution of standard iodinated contrast material (iohexol).  
c) Although it is extremely rare to see severe reactions to gadolinium, headache, nausea, and flushing can occur.  
d) Studies that require larger volumes of contrast can still be accomplished when gadolinium is supplemented with CO2.  
A) a and b  B) b, c, and d  C) a, b, and d  D) a, b, c, and d

13. Which of the following statements about other prophylactic strategies for reducing the risk of CIN are true?  
a) Several studies have evaluated dopamine, a D1 agonist, as a prophylactic agent to prevent CIN, although with inconsistent results, possibly due to the nonselectivity of dopamine for the D1 receptors.  
b) Results of a large, double-blind, randomized trial that compared fenoldopam to placebo in high-risk patients demonstrated that fenoldopam was unable to prevent CIN.  
c) Several studies suggest that theophylline may have a beneficial effect in reducing CIN; however, it may cause tachyarrhythmias in patients with coronary artery disease undergoing coronary angiography.  
A) a and b  B) b and c  C) a, b, and c

14. An antioxidant such as acetylcysteine (NAC) may help reduce CIN by decreasing the presence of oxygen-free radicals generated by contrast media; however, clinical data have been inconsistent regarding the ability of NAC to reduce the incidence of CIN.  
A) true  B) false
CME BOOKLET—EVALUATION FORM (PHYSICIAN CREDIT)

PIM Project ID # 021167-ES-5 Issues in the Use of Contrast Media in Patients at High Risk for Contrast-Induced Nephrotoxicity (CIN)

The Postgraduate Institute for Medicine (PIM) respects and appreciates your opinions. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few minutes to complete this evaluation form. Please note that a certificate of completion is issued only upon receipt of your completed evaluation form.

Please answer the following questions by circling the appropriate rating: 5 = Outstanding 4 = Good 3 = Satisfactory 2 = Fair 1 = Poor

Extent to Which Program Activity Met the Identified Objectives

Upon completion of this activity, participants should be able to:

• Identify issues in patients at high risk for contrast-induced nephrotoxicity (CIN)  5 4 3 2 1
• Describe prophylactic strategies to lower the risk of CIN  5 4 3 2 1
• Discuss recently published data on the use of contrast media in patients at high risk for CIN  5 4 3 2 1

Overall Effectiveness of the Activity

Objectives were related to overall purpose/goal(s) of activity  5 4 3 2 1
Related to my practice needs  5 4 3 2 1
Will influence how I practice  5 4 3 2 1
Will help me improve patient care  5 4 3 2 1
Stimulated my intellectual curiosity  5 4 3 2 1
Material was clearly and thoroughly presented  5 4 3 2 1
Support materials/references were useful  5 4 3 2 1
Overall, the activity met my expectations  5 4 3 2 1
Avoided commercial bias or influence  5 4 3 2 1

Will the information presented cause you to make any changes in your practice?  ____Yes  ____ No
If Yes, please describe any change(s) you plan to make in your practice as a result of this activity.
________________________________________________________________________________________________________________________________________
________________________________________________________________________________________________________________________________________

How committed are you to making these changes?  (Very committed)  5 4 3 2 1 (Not at all committed)

Additional comments about this activity?
________________________________________________________________________________________________________________________________________
________________________________________________________________________________________________________________________________________

Do you feel future activities on this subject matter are necessary and/or important to your practice?
____Yes  ____No  Comment: _____________________________________________________________

Please list any other topics that would be of interest to you for future educational activities:
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3. A  B  C  D  10. A  B  C  D
5. A  B  C  12. A  B  C  D

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