Adverse Effects of Iodine-derived Intravenous Radiopaque Contrast Media

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Beginning with Resolution 91-4.04, and continuing through the current Standards of Practice, the American Society of Radiologic Technologists maintains that it is within the scope of practice and standard of care for a radiologic technologist to perform venipuncture and administer contrast media, radiopharmaceuticals, and intravenous (IV) medications where state law and institutional policy permit.1 Such actions must be undertaken only when a practitioner (eg, a radiologist) is immediately available to diagnose and treat allergic reactions.1,2

However, because “immediately available” and “present” are entirely different constructs, it is necessary for radiologic technologists to be aware of the ramifications of administering contrast media. This is especially important because adverse reactions to tri-iodinated benzoic-derived radiopaque contrast media (ROCM) occur randomly and are unpredictable. Although the use of nonionic low-osmolar agents has decreased the incidence of reactions, these contrast agents do not affect the possible severity of the reactions that do happen; furthermore, although most reactions are mild and self-limiting, severe reactions can occur with any patient at any time.3,4

Contrast Media History and Classification

The use of sodium iodide as a contrast medium began in clinical practice in the early 1920s. However, poor radiographic enhancement and high toxicity severely limited its use as a contrast medium. In the 1950s, the introduction of water-soluble sodium and meglumine salt derived from tri-iodinated benzoic acid greatly increased the daily use of radiographic contrast agents. Although these preparations were much less toxic than earlier preparations, they were hyperosmolar (with an average osmolality 5 to 8 times that of blood). By the 1970s, low-osmolality iodinated contrast media had been developed. The advent and prescription of both high-osmolar...
and low-osmolar contrast media have led to their being some of the most widely used drugs in the history of medicine. Each year approximately 70 million people worldwide receive IV iodinated contrast agents. In fact, iodinated contrast media are the most common IV pharmacologic agents of any type currently in use.

Osmolality and Ion State

ROCM typically are divided into categories based on their chemical composition and propensity to influence osmotic activity. These categories are defined as high or low osmolality and ionic or nonionic, depending on how they dissociate in solution. Ionic high-osmolality contrast agents dissociate into a cation (positively charged atom) and an anion (negatively charged particle) when in solution. The dissociation of ionic high-osmolality contrast agents is considered partially responsible for several of the adverse effects of contrast media. Nonionic low-osmolality contrast agents do not dissociate in solution. Regardless of whether a contrast medium has high or low osmolality and is ionic or nonionic, all of these substances have a high iodine content (11%-46%, on average).

Jensen and Peppers noted that the movement and distribution of water between body compartments is controlled by osmolality. Osmolality often is used interchangeably with osmolarity to define osmotic activity, but this is inappropriate. Osmolality is the measure (concentration) of molecules by weight, while osmolarity is the measure (concentration) of molecules by volume. Although both can affect osmotic activity, or the transfer of water across a permeable or semipermeable membrane, ROCM are defined by the number of milliosmoles per kilogram of water. Therefore, osmolality should be used to describe ROCM.

High-osmolality contrast agents are those that attract water across a semipermeable or permeable membrane, such as cell walls. When highly osmotic ROCM are injected into the bloodstream, the body’s response is to transfer fluid from the extravascular space to the intravascular space in an effort to restore equilibrium in the osmotic pressure of the body. The effect of this action is to dilute the normal intravascular constituents and increase intravascular pressure. This normal osmotic transfer contributes to the adverse effects experienced with ROCM. High-osmolar contrast agents are ionic monomers containing 3 iodine atoms per molecule. These agents dissociate into a cation and an anion in solution. The anion, coupled with the positively charged cation, arises from a monomeric molecule that has 3 iodine atoms; the result is a 3:2 ratio compound (3 iodine atoms plus 2 charged particles) defined by the ratio of iodine atoms to osmotically active particles. Typically, high-osmolality ionic ROCM are derived from meglumine salts, sodium salts, or both, and they have an osmolality of around 1500 mOsm/kgH2O.

Low-osmolality contrast agents are defined by a sliding scale (low osmolality being relative) and typically have osmolalities ranging from 290 to 860 mOsm/kgH2O. All ROCM have a higher osmolality than blood, so high or low measures are used only to differentiate one ROCM from another and not from the substance into which they are being injected.

Low-osmolality contrast agents exist in 3 primary forms: nonionic monomers, ionic dimers, and nonionic dimers. The primary standard by which low-osmolality contrast agents are measured is the outcome of their injection; they all result in one osmotically active particle per 3 iodine atoms. Therefore, low-osmolality contrast media result in a ratio 3:1 (sometimes referred to as a ratio 3.0) media.

Nonionic monomers were the initial attempt to reduce the osmotically induced adverse effects of contrast media and make them safer. Nonionic monomers have a single tri-iodinated benzene ring but lack a carboxyl side group; furthermore, they have an added hydrophilic hydroxyl group on one of the organic side chains. The effect of these chemical changes is that the monomers dissolve in water but do not dissociate (ionize) into a cation and an anion; therefore, they render a ratio 3:1 media with 3 iodine particles and one osmotically active particle.

Low-osmolality ionic contrast agents were the next major iteration in contrast media. These contrast media are formed from 2 benzene rings chemically joined and as such are considered dimers. Dimetric contrast media are formed when 2 ionic monomers are combined through elimination of (and sharing of) one carboxyl group. These contrast media exist with 6 iodine atoms and dissociate in the body into 2 osmotically active particles. Upon dissociation, the contrast media have...
2 particles per 6 iodine atoms, which results in a ratio 6:2 contrast media. A ratio 6:2 medium, simplified, is a ratio 3:1 medium. The only commercially available ionic dimer is ioxaglate (Hexabrix).²,¹²,¹⁴ A major characteristic of low-osmolality ionic dimers is their exceptionally high viscosity. Of the commonly used contrast media, ioxaglate derivatives are the most viscous.

Viscosity is a measure of the resistance of a liquid to flow. This is sometimes categorized as the relative amount of friction a liquid causes. Viscous liquids are thicker than nonviscous liquids. Viscosity is measured in centipoises (cps), with water being the standard of reference, equal to 1 cps.¹ Viscosity can be influenced by several external factors; heat is the one most applicable to ROCM. Heating the contrast media to body temperature prior to injection lowers the relative viscosity of the contrast media and makes it easier to inject. Less viscous contrast media can be injected more quickly than contrast media with a higher viscosity. The rate of injection, coupled with the viscosity of the contrast media, is associated with the flushing (warmth) that patients feel upon being administered contrast media. This is not a pharmacologic adverse effect, and warming the contrast media to body temperature before injection helps to reduce patient discomfort.²,¹⁴

The most recent innovation in contrast media is the use of nonionic dimers. Joining 2 nonionic monomers forms these contrast media. Nonionic monomers do not dissociate in situ, and when joined to form a dimer they remain connected following injection. The result is that there are 6 iodine atoms for every one particle. The iodine concentration is much higher per particle, but much lower within the bloodstream because of the decreased volume necessary to opacify tissue.²,¹³,¹⁴ The major effect of this is that, “for a given concentration, the nonionic dimers have the lowest osmolality of all the contrast agents.”²⁴ The result of this lack of dissociation is a virtually iso-osmolar contrast medium with osmolality measuring up to 300 mOsm/kgH₂O.² The Table lists some of the most commonly used contrast media by category.

### Distribution and Excretion

Intravascular ROCM have a high molecular weight—generally between 600 and 1700. They also have very poor lipid solubility. The result of these 2 physical traits is that iodinated ROCM do not cross cellular membranes easily and stay primarily within the bloodstream. Typically, the blood-brain barrier prevents ROCM from being distributed into the normal central nervous system; however, in some cases trace amounts of ROCM enter the cerebrospinal fluid by crossing through the choroid plexus, a nerve complex in the brain.² ROCM typically diffuse rapidly in the presence of relatively normal biophysical function. As a result of the rapid process of glomerular filtration, the primary means of ROCM excretion, 70% of the injected dose is cleared from the blood plasma within 2 to 5 minutes.²,⁶ Additional reverse diffusion takes place, moving fluid from the extracellular spaces into the plasma, diluting the contrast further. About 2 hours following injection, complete equilibrium takes place between plasma and the interstitial spaces. Four hours after injection, 75% of the dose will be excreted; over the subsequent 24 hours, between 90% and 100% of the measurable IV dose will be excreted by the kidneys.²,⁶,¹⁶ Generally, less than 1% of ROCM is excreted extrarenally. The exception is iodamide meglumine (Renovue), which is excreted principally through the hepatobiliary system.²,⁶

### Table

<table>
<thead>
<tr>
<th>Common Iodinated Contrast Agents²,⁵,¹²</th>
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<tbody>
<tr>
<td><strong>Generic Name</strong></td>
<td><strong>Proprietary Names</strong></td>
</tr>
<tr>
<td>Ionic monomers:</td>
<td></td>
</tr>
<tr>
<td>sodium amidotrizoate</td>
<td>Urografin, Hypaque</td>
</tr>
<tr>
<td>meglumine ioxithalamate</td>
<td>Telebrix</td>
</tr>
<tr>
<td>Conray</td>
<td></td>
</tr>
<tr>
<td>Nonionic monomers:</td>
<td></td>
</tr>
<tr>
<td>iohexol</td>
<td>Omnipaque</td>
</tr>
<tr>
<td>iopromide</td>
<td>Ultravist</td>
</tr>
<tr>
<td>ioversol</td>
<td>Optiray</td>
</tr>
<tr>
<td>Ionic dimer:</td>
<td></td>
</tr>
<tr>
<td>ioxaglate</td>
<td>Hexabrix</td>
</tr>
<tr>
<td>Nonionic dimers:</td>
<td></td>
</tr>
<tr>
<td>iodixanol</td>
<td>Visipaque</td>
</tr>
<tr>
<td>iotrolan</td>
<td>Isovist</td>
</tr>
</tbody>
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Reactions to ROCM derived from tri-iodinated benzoic acid occur in up to 54% of injected patients. Adverse effects can be anticipated in 2% to 17% of routine patients receiving ROCM; adverse effects approach 60% in patients who have exhibited a previous adverse reaction. Severe, life-threatening reactions occur in 0.1% to 0.4% of patients, with a mortality rate of approximately 1:75,000.5,8,17,18

Reactions to ROCM fall into 2 major categories: systemic (idiosyncratic) and chemotoxic (nonidiosyncratic). Other, noncategorized reactions also occur and typically are associated with the act of administering the media (eg, air embolism) or contaminants in the media, rather than contrast media itself.

Idiosyncratic reactions are the most common and can be either immediate (acute) or delayed (latent). Immediate reactions are anaphylactoid in nature and do not involve the release of immunoglobulin E (IgE) antibodies; delayed reactions are anaphylactic in nature and do involve the release of IgE. Anaphylactoid and anaphylactic reactions are random. Both involve mast cell mediator release, and both escalate in severity without decisive intervention.18,19

Typically, allergy-like reactions to contrast media are anaphylactoid in nature and do not arise from the iodine content of the contrast; indeed, numerous studies have demonstrated no correlation between seafood allergy and contrast allergy. Therefore, radiologic technologists should not perpetuate the myth that seafood allergy correlates with iodine or radiopaque contrast allergy.20,21

Chemotoxic adverse effects generally are predictable and can be averted in most cases. These effects are directly related to the dose of contrast given and the physiochemical properties of the contrast agent used. Physiochemical properties include the osmolality, viscosity, salt content, calcium binding properties, and hydrophilicity of the contrast media. Some of these characteristics are beyond the control of the radiologic technologist; however, if the technologist is aware of them, they can be suppressed.1

Systemic/Idiosyncratic Reactions

Systemic reactions typically occur following mast cell decomposition (degranulation) and release of their inherent mediators. Mast cells are connective tissue cells that contain a number of substances, some of which are preformed and stored, and others that are rapidly produced by submembrane phospholipids once the membrane of the cell is triggered. Mast cells are found throughout the body in skin, synovia, mesentery, surrounding blood vessels, and the gastrointestinal tract.2,19

Histamine is the most prevalent preformed granule in mast cells. Histamine release also is the major early concern in mast cell degranulation. Histamine release results in smooth muscle contraction. Because of the locations of mast cells in the body, the action of histamine on surrounding tissue can be problematic. For example, smooth bronchial muscular contraction results in bronchospasm. Histamine release also increases capillary permeability, and in the respiratory system this might lead to laryngeal edema and stridor. People with asthma are at increased risk of respiratory compromise as a result of the action of histamine on the respiratory system. Histamine interacting with receptors in cardiac muscle can cause arrhythmias.

Histamine release in the skin leads to pruritis, and redness is an adverse effect of histamine release in superficial capillaries near the skin’s surface. Pruritis is the cardinal symptom of a histamine-mediated reaction, and any report of itchiness by the patient should immediately alert the technologist to take decisive action.1,19,22

In addition to histamine release, mast cell degranulation results in the discharge of many other substances. These substances are primarily the lipid mediators produced by the submembrane phospholipids in mast cells. They are produced very rapidly following mast cell triggering and are responsible for a host of secondary signs and symptoms associated with allergy-like reactions. Leukotrienes (commonly referred to as the slow-reacting substance of anaphylaxis), eosinophil and neutrophil chemotactic factors, kinogenase, bradykinin, platelet activating factor, and prostaglandins are produced and released during mast cell degranulation.

Leukotrienes, specifically LTD4 and LTC4, cause bronchospasms that might lead to stridor, coughing, wheezing, and dyspnea in addition to those same symptoms caused by histamine; therefore, the symptoms become more pronounced and longer lasting. Platelet activating factor and the remaining lipid mediators
cause warmth, redness, and various cardiac effects, including decreased output and tachycardia; the cardiac effects resulting from the lipid mediators lead to syncope and shock. Box 1 lists some common organ-specific and system-specific adverse effects of ROCM.

Anaphylactoid Reactions
Acute anaphylactoid contrast media reactions are those that occur within 60 minutes following injection. Typically, these reactions fall into one of 3 categories: minor, moderate or intermediate, and severe. Some authors specify death as a fourth category; however, it more accurately falls in the category of severe reactions because death is an outcome of an adverse reaction and not a spontaneous event. Anaphylactoid reactions do not require any previous exposure or sensitivity to an allergen (ie, iodine, in this case).

Minor reactions to iodinated radiographic contrast are the most common clinical manifestation. Minor reactions typically include any or all of the following:
- Flushing.
- Nausea.
- Vomiting.
- Pruritus.
- Headache.
- Mild urticaria.
- Arm pain.

Minor reactions do not generally require any therapeutic intervention beyond routine patient care, comfort, and monitoring. Most patients exhibiting only minor signs and symptoms fully recover within several hours.

Box 1
Organ-specific and System-specific Adverse Effects From Iodine-based or Gadolinium-based Contrast Agents

<table>
<thead>
<tr>
<th>Organ</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal Glands</td>
<td>Hypertension — in patients with pheochromocytoma after intra-arterial injection</td>
</tr>
<tr>
<td>Brain</td>
<td>Headache</td>
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<tr>
<td></td>
<td>Confusion</td>
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<td></td>
<td>Dizziness</td>
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<td></td>
<td>Seizure</td>
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<td></td>
<td>Rigors</td>
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<tr>
<td></td>
<td>Lost or diminished consciousness</td>
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<tr>
<td></td>
<td>Lost or diminished vision</td>
</tr>
<tr>
<td>Gastrointestinal Tract</td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
</tr>
<tr>
<td></td>
<td>Intestinal cramping</td>
</tr>
<tr>
<td>Heart</td>
<td>Hypotension</td>
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<tr>
<td></td>
<td>Dysrhythmia — asystole, ventricular fibrillation/ventricular tachycardia</td>
</tr>
<tr>
<td></td>
<td>Pulseless electrical activity (PEA)</td>
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<tr>
<td></td>
<td>Acute congestive heart failure</td>
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<tr>
<td>Kidney</td>
<td>Oliguria</td>
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<tr>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>Contrast-induced nephropathy (CIN)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Swelling — pancreatitis</td>
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<tr>
<td>Respiratory System</td>
<td>Laryngeal edema</td>
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<tr>
<td></td>
<td>Bronchospasm</td>
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<tr>
<td></td>
<td>Pulmonary edema</td>
</tr>
<tr>
<td>Salivary Glands</td>
<td>Swelling — parotitis</td>
</tr>
<tr>
<td>Skin and Soft Tissues</td>
<td>Pain</td>
</tr>
<tr>
<td></td>
<td>Edema</td>
</tr>
<tr>
<td></td>
<td>Flushing</td>
</tr>
<tr>
<td></td>
<td>Erythema</td>
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<tr>
<td></td>
<td>Urticaria</td>
</tr>
<tr>
<td></td>
<td>Pruritus</td>
</tr>
<tr>
<td></td>
<td>Compartment syndrome — from extravasation</td>
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<tr>
<td></td>
<td>Nephrogenic systemic fibrosis (NSF)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Exacerbation of thyrotoxicosis</td>
</tr>
<tr>
<td>Vascular System</td>
<td>Hemorrhage — due to direct vascular trauma from contrast injection or from the reduction in clotting ability</td>
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<tr>
<td></td>
<td>Thrombophlebitis</td>
</tr>
</tbody>
</table>


Moderate reactions include any or all of the signs and symptoms found in mild reactions but to a heightened or more developed degree; mild signs and symptoms that progress become moderate reactions. In addition to the mild symptoms, patients undergoing an intermediate-level reaction might exhibit bronchospasm, moderate urticaria, chest pain, dyspnea, hypotension or hypertension, tachycardia or bradycardia, and other vasovagal responses. Patients exhibiting any signs of a moderate reaction generally require therapeutic intervention, but not admission.
to the hospital. Generally, these patients have a favorable outcome following pharmacologic intervention.²,⁶,¹⁴

Severe reactions occur in fewer than 1% of patients who receive iodinated contrast media. Generally, if a patient is going to develop a severe reaction to ROCM, the reaction is quite acute without a significant delay following administration. Indeed, the signs and symptoms of a severe reaction manifest within 20 to 30 minutes following injection in 95% of patients exhibiting this elevated response; virtually every fatal contrast reaction begins within 20 minutes.¹¹,¹⁴ Patients who develop a severe reaction require rapid intervention because of life-threatening effects of the reaction. In addition to the signs and symptoms of mild and moderate reactions, severe reactions include laryngeal edema, severe bronchospasm, seizures, convulsions, paralysis, unresponsiveness, and cardiovascular collapse resulting in cardiopulmonary arrest. Without immediate and decisive intervention, death is the outcome of severe reactions to ROCM.¹⁷,¹⁹,²³

Anaphylactic Reactions

Although the majority of contrast-induced reactions are pseudoallergic anaphylactoid reactions, there is no clear demonstration of the exact pathogenesis for contrast-induced reactions; therefore, the possibility that patients might exhibit a true anaphylactic response to contrast media should be addressed. The radiologic technologist should be reminded that anaphylaxis following contrast media injection is likely not a reaction to the iodine content of the ROCM but to some other substance in the contrast media, the injection solution, or to one of the tools of administration.²⁰,²¹ The primary difference between an anaphylactoid reaction and an anaphylactic response is that anaphylactic reactions require a previous exposure to an antigen, whereas no previous exposure is required for anaphylactoid reactions. In the case of anaphylactic events, exposure to an antigen occurs during an initial sensitizing event (ie, the patient’s first exposure to the antigen iodine either via administration of ROCM or some other means). As a response to the sensitizing event, mast cells generate an antibody. This antigen-antibody complex response requires about 2 weeks to mature. Following this period, subsequent exposure to the antigen will result in catastrophic mast cell degranulation. The sequence of events, including the signs and symptoms previously discussed, are identical to an anaphylactoid response with one important difference: in the absence of intervention, true anaphylactic events almost always result in death.²,¹⁹,²²

There have been few demonstrated true anaphylactic reactions to contrast media (as defined by the antigen-antibody complex), but studies have confirmed allergies to the contrast media solutions. Skin testing can confirm that the reaction response was anaphylactic in nature and define the antigen (which has never been shown to be iodine).¹⁹,²⁴

Chemotoxic Reactions

Chemotoxic reactions are much easier to quantify than idiosyncratic reactions; they are predictable and can be partially managed—or even completely suppressed—in most circumstances. Chemotoxic effects generally result from the physical make-up and composition of the contrast (eg, viscosity), but they also might arise following faulty injection technique or because of unrelated patient pathophysiology. These types of adverse effects are the only outcomes that might be controllable by the radiologic technologist and that are foreseeable or predictable. Although all patients are at risk for chemotoxic reactions, individuals with debilitating disease and those who are medically unstable are the most likely to exhibit these effects.¹⁶ Of primary concern are patients with a recent or ongoing history of seizures, cardiovascular disease, renal dysfunction, or renovascular compromise.⁵,¹⁸

Effects that result from the ionic activity of contrast media arise from the cation content of the various agents. Hypotension and tachycardia, in the absence of other allergy-like signs and symptoms, are common adverse effects of contrast hypertonicity. Sickling of red blood cells in patients who have sickle cell disease also has been linked to hypertonicity. Myasthenia gravis, a chronic autoimmune neuromuscular disease, can be exacerbated as a result of the neurotoxicity of certain contrast media. Patients suffering from a pheochromocytoma, a rare tumor of the adrenal gland, are at increased risk of hypertension as a result of IV contrast media administration.⁴,¹⁹
Anecdotal evidence suggests contrast-induced nephrotoxicity is a direct effect of osmotic and chemotoxic interactions. Furthermore, there is evidence to infer that the probability of nephrotoxic events increases proportionally with dose.\(^{17}\) Regardless, it is known that nephrotoxicity averages 15% to 25% in patients with debilitating medical histories and might approach 90% in patients with multiple pre-existing conditions. Therefore, radiologic technologists should ensure that the pre-examination history includes renal function, blood pressure (to evaluate cardiovascular and/or renal vascular health), age, uric acid levels, hydration status, and recent previous contrast administration.\(^{18}\) The American College of Radiology (ACR) lists the following as risk factors for nephrotoxicity\(^{23}\):

- Age older than 60 years – increased likelihood of contrast-induced nephrotoxicity.
- History of renal disease – including dialysis, renal transplant, having only a single kidney, history of renal cancer, or any type of renal surgery. Renal impairment is the most compelling risk factor for nephrotoxicity.
- History of hypertension requiring medical care.
- History of diabetes mellitus.
- Currently taking metformin or metformin combinations.

The ACR noted that metformin does not confer an increased risk of nephrotoxicity, but that metformin might lead to lactic acidosis in patients with renal failure. A patient with any of the previously described conditions should undergo preprocedural renal function testing (specifically an evaluation of serum creatinine) to stratify their risk of continuing an IV contrast-enhanced examination.\(^{23}\) A risk-benefit analysis always should be completed on these patients to confirm that the diagnostic information obtained from the examination will outweigh the risk of adverse effects.

The most significant adverse effects that might be directly correlated to the iodine in ROCM are hyperthyroidism and thyroid storm.\(^{4}\) Both of these diseases are clinical diagnoses arising from an increase in circulating thyroid hormones. Alkhua et al noted that thyroid storm is a life-threatening condition associated with mortality rates as high as 30% and characterized by hemodynamic abnormalities, hyperpyrexia, dysrhythmias, and delirium.

Thyroid storm typically is caused by a major stressful event or an increased iodine load, such as that following iodinated contrast administration.\(^{25}\)

Vasovagal Reactions

Vasovagal reactions occur for a variety of reasons and are not uniquely associated with IV administration of contrast. They can occur as a result of anxiety and have been known to happen before radiographic examinations (eg, when obtaining the informed consent). Vasovagal reactions commonly occur as a result of IV injections of all types.\(^{5,23}\)

Vasovagal reactions occur when baroreceptors and chemoreceptors located at the bifurcation of the aortic arch and carotid arteries are stimulated, typically in response to pain or fear. When stimulated, the baroreceptors and chemoreceptors cause the autonomic nervous system to induce bradycardia and produce a commensurate drop in aortic pressure. Typically, the drop in aortic pressure is a result of peripheral vasodilation which, when coupled with the bradycardia, produces hypotension. Hypotension coupled with bradycardia is the cardinal sign of a vasovagal response.\(^{2,5,23}\)

Vasovagal reactions typically self-rectify but should be treated seriously because signs and symptoms might escalate. Close patient observation allows the radiologic technologist to determine whether the hypotension is progressing. Progressive hypotension leads to loss of consciousness, cardiovascular collapse, angina, seizures, and ultimately cardiopulmonary arrest.\(^{5,23}\)

Treatment of vasovagal reactions, if warranted, focuses on fluid replacement and the administration of atropine. Antihistamines and epinephrine have no effect on this type of reaction, so it is imperative that it be identified as vagal and not systemic. Treatment should:

**[B]egin with 0.6 mg to 0.8 mg of atropine given intravenously, followed by repeated doses every minute (while monitoring pulse rate) until a maximum total dosage of atropine (3 mg for adults) is administered. Fluids should then be given intravenously as well.**\(^{23}\)
Pulse rate should be used to determine the efficacy of the atropine dosage, because the patient might remain hypotensive for several hours. Diaphoresis and anxiety or apprehension are clinical manifestations of vagal reactions, and the decrease in these signs and symptoms might signal the rectification of the event.23,26

**Noncategorized Adverse Effects**

Extravasation

Extravasation is a well-known complication following parenteral administration of any substance, particularly radiographic contrast media. Any material that is injected or attempted to be injected intravenously can cause rupture or leakage of the substance from the selected vessel into the surrounding tissue; the leakage of this material into the surrounding fascia constitutes extravasation. Although all extravasation is painful, extravasated contrast media is toxic to extravascular tissue and produces an acute local inflammatory response. The response typically peaks within 24 to 48 hours.23 Research data are lacking for extravasation injuries in all modalities except computed tomography; however, studies in that field indicate extravasation rates approaching 1% even when proper injection techniques are applied.23,27,28 Therefore, it is important to understand the mechanism of extravasation injuries as a physiologic adverse effect of radiographic contrast injection.

Extravasation injuries are typically limited to the tissues immediately surrounding the injection site. As a result, the clinical experience is widely varied; however, swelling or tightness, and stinging or burning are cardinal signs of extravasation injury. If not treated, or if the amount of extravasated contrast is not minimized or the contrast media is high-osmolar, the consequences can progress from minimal swelling and erythema to skin ulcerations, soft tissue necrosis, or compartment syndrome. Compartment syndrome is an extremely painful mechanical compression of tissue as a result of the extravasated material that exerts pressure on blood vessels and limits blood supply.23,29

The severity of contrast media extravasation is determined by the clinical manifestations and the treatment protocols necessary to rectify the situation. In mild extravasation cases, patients experience pain, tenderness, swelling, mild erythema, and limited range of motion. Mild cases occur as a result of minimal amounts of extravasation, or in cases where the patient does not exhibit new signs or progression of initial signs after a period of observation. Patients with mild extravasation should be watched closely for 2 to 4 hours following the event and, in the absence of other issues, may be released under orders to report any change in their status immediately. Typically, mild extravasations resolve within 2 to 4 days and the patient has no lingering effects beyond minor tenderness.24-30

Clinically moderate cases of extravasation are defined by pain that persists or increases beyond 2 to 4 hours, or any of the following signs and symptoms:
- Skin ulcerations.
- Skin blistering.
- Altered tissue perfusion.
- Clinical worsening with persistent or increased swelling, firmness, or paresthesias.

Without treatment, moderate cases progress to severe cases of extravasation. In any case where surgical intervention is required or permanent deficits occur, the event is defined as severe. The worst adverse effect of extravasation, compartment syndrome, is exceptional.23,28,29

Compartment syndrome typically arises following large extravasations, but it is known to occur in the presence of smaller extravasations when they occur in less spacious compartments of the body such as the wrist (see Figure).23 In addition to the volume of contrast extravasated, the primary factors that influence the development of compartment syndrome are the osmolality and ionic or nonionic nature of the compound.27

Treatment for extravasation injuries varies widely. There are no clear-cut guidelines or recommendations on how best to treat these types of injury.23 As much contrast media as possible should be aspirated from the injury site prior to removing the cannula. Reintroduction of an aspiration cannula might be merited, depending on the volume of contrast present; however, success with both aspiration approaches has been limited. Elevating the affected limb (typically the arm) above the level of the heart decreases capillary hydrostatic pressure and allows more rapid resorption of the media, with a consequent decrease in edema around the injection site. No data has been collected in controlled
studies to support the efficacy of elevation, so the usefulness of this approach is anecdotal. 23,28

A common approach to treating extravasation injuries is the application of a moist cloth. Again, no experimental evidence exists to support the efficacy of either warm or cool cloths, but they work equally well in treating some of the manifestations of extravasation. Warm cloths increase absorption of the extravasated contrast and improve blood flow distal to the site by causing vasodilation. Cool cloths increase vasoconstriction, decreasing pain and swelling at the site. 23,28 The only recommendation that exists for the use of either warm or cold cloths is presented by the Oncology Nursing Society, specifically for chemotherapy extravasation. This group endorses the use of cold compresses 3 times a day for 15 to 60 minutes following extravasation. 28

Surgical consultation and intervention is merited in the presence of severe incidents or with any of the following clinical manifestations 23,27,28:

- Change in sensation in the affected limb.
- Skin ulceration.
- Blistering.

Surgical consultation might be merited in cases of extravasation involving 100 mL or more of contrast, although this guideline was recently revised by the ACR to include surgical consultation anytime there is concern for extravasation injury, regardless of the volume of extravasated fluid. 23,28 If surgery is warranted, typical procedures might include incision and drainage, excision of any hematoma, and fasciotomy. 27

Although there is no definitive method of treating anything other than severe cases of extravasation, early diagnosis and intervention lead to positive outcomes. Therefore, identifying individuals who might be more prone to extravasation injuries could be of some help to the radiologic technologist. Patients at increased risk of extravasation include those who are incapable of timely, concise, and adequate communication, such as infants and small children, patients with altered consciousness, those of advanced age, and individuals for whom language might be a barrier. Individuals who are obese or who have had radiation therapy or chemotherapy also are at increased risk as a result of small-caliber or fragile veins. Injections that take place through indwelling peripheral IV lines that have been in place for longer than 24 hours also have demonstrated an increased risk for extravasation. Injecting into veins with multiple recent puncture sites also increases the risk of injury to the patient. Finally, injection into the hand, wrist, foot, or ankle has been shown to increase the risk of extravasation. 23,28 Although administering contrast to all patients who could be at increased risk of extravasation cannot always be avoided, the technologist might limit these types of injuries by avoiding compromised injection sites.

Air Embolism

Air emboli are a known—and relatively common—adverse effect of IV injections of all types. Indeed, the first known death resulting from air embolism occurred in 1850. 31 Clinically significant air emboli are potentially fatal; however, they are extremely rare and generally arise following the use of power injectors. Most insignificant air emboli arise following hand injection and are measured...
in a few milliliters of fluid. Although typically asymptomatic, the frequency with which air emboli occur and the possible catastrophic outcomes warrant further examination of the phenomenon.\textsuperscript{23,31}

Air emboli can occur in one of 2 ways: through either manipulation or use of a peripheral catheter. Manipulation, including the introduction or removal of a catheter, is the least common means of inducing an air embolism, and little is known about the microemboli that formed as a result of this mechanism. Manipulation-induced air emboli often are referred to as passive emboli. Most clinically significant air emboli form following use of a peripheral catheter; typically power injectors account for most (if not all) of the catastrophic embolic events that occur in this manner. Injection emboli are considered to be active in their origin.\textsuperscript{23,31,32}

When an air embolus forms, it is the result of a pressure gradient that occurs between the vascular space and ambient atmospheric air. The severity of the embolism depends on several factors, including the volume of air, the rate of air entry, and the patient’s relative position at the time of injection. In general, 50 mL of air is considered lethal, but emboli as small as 20 mL (at an extremely rapid injection rate) have proven fatal. The typical mechanism for death is precipitous cardiovascular collapse or myocardial infarction. However, fatalities also occur when neurologic deficits arise from stroke secondary to decreased cardiac output or paradoxical air emboli (ie, when the air embolus crosses from the right side of the heart to the left and enters systemic circulation).\textsuperscript{23,31,32}

Common clinical manifestations of air emboli include dyspnea, chest pain, pulmonary edema, tachycardia, hypotension, and expiratory wheezing.\textsuperscript{23} Less common symptoms can include shoulder pain, light-headedness, and nausea.\textsuperscript{33} Patients with compromised cardiac outflow might be at higher risk for catastrophic complications resulting from smaller air emboli; right to left intracardiac shunts and pulmonary arteriovenous malformations are the most common bloodflow problems that cause neurologic deficits arising from minute air emboli.\textsuperscript{23,32}

Treatment of air emboli requires immediate action. Injection should be stopped immediately, and if passive air entry is occurring, the opening should be occluded prior to any other intervention. Sterility of the catheter or site should not be a primary concern; in one published case study, the nurse used a wet wash cloth to occlude a tri-lumen catheter that was inadvertently cut at the skin surface and could not be removed. The cloth effectively formed an air-proof seal.\textsuperscript{32} The patient should be placed on 100% oxygen immediately; hyperbaric oxygen can be used in an effort to reduce the size of air bubbles, but it might not be immediately available. Furthermore, the patient should, if possible, be placed on his or her left side in a Trendelenburg position. If the patient cannot tolerate the Trendelenburg position, left lateral decubitus positioning has been shown to be only slightly less effective. Both of these positions reduce the differential pressure gradient between the vascular and atmospheric pressures while holding the trapped air bubbles in the apex of the right atrium. Holding the air in the apical portion of the right atrium prevents occlusion of the pulmonary artery.\textsuperscript{23,32} In all cases, cardiopulmonary arrest should be treated immediately with closed-chest cardiopulmonary resuscitation.

**Radiographic Contrast and Special Populations**

Radiographic contrast is a widely used diagnostic tool and is preferred in imaging vascular structures; however, it is not completely safe and always should be used only after a risk-benefit analysis. The radiologic technologist, as the administering health care provider, provides the final safeguard against injecting individuals who are at increased risk or who are contraindicated to receive radiopaque IV iodinated contrast media. Patient screening is essential to minimize adverse effects.

**Pregnant or Possibly Pregnant Patients**

The interaction of iodinated contrast media with human fetuses is incompletely understood; no large studies on the interaction of iodinated contrast with placental barriers, fetuses, and birth mothers have been undertaken. However, gadolinium-based contrast agents have been shown to cross the placental barrier and arrive in the fetal bladder of primates within a short time in controlled trials.\textsuperscript{23} It also has been clinically demonstrated that iodinated contrast crosses the
placental barrier in measurable quantities. Although no definitive evidence links low-osmolality iodinated contrast to mutagenic or teratogenic effects, reports of hypothyroidism have been linked to fetal doses of ROCM in newborn infants. Therefore, it is best to err on the side of caution when dealing with pregnant or possibly pregnant patients.

All patients who fall into this category should be approved for examination by a supervising radiologist after it has been determined that the information requested by the ordering provider cannot be acquired without the administration of contrast media; the information directly affects the care of the patient, her fetus, or both during the pregnancy; and the referring physician believes it would be imprudent to delay obtaining the diagnostic information until after delivery. The approval to continue should be given in writing by the supervising radiologist.

**Pediatric Patients**

Pediatric and adult patients share the same risks relative to the administration of ROCM; however, some unique considerations should be addressed when imaging a pediatric patient. Neonates and young children have an increased susceptibility to osmotically induced fluid shifts, which might lead to an increased risk of pulmonary edema or cardiac failure; therefore, isosmotic contrast agents should be considered in these populations.

Because of the small-caliber needles used in younger patients, contrast viscosity is a primary concern. This is particularly true when large volumes or high rates of administration are required. The radiologic technologist should be cognizant of the catheter size to avoid vessel rupture or catheter failure.

The final difference the technologist should keep in mind is the physiologic effects that contrast has and the manifestations these can exhibit in children. In adults, warmth or minor pain at the injection site might be easily tolerated; in children these might result in movement to the detriment of the study or dislodgment of the IV access point. The former could result in the need for additional imaging, increasing the patient’s radiation dose; the latter might result in repeated venous access, increasing patient discomfort and psychological distress.

**Breastfeeding Women**

Literature discussing the excretion of iodinated contrast media into breast milk is extremely limited; however, studies have confirmed that breast milk does contain trace amounts of ROCM. The low lipid solubility of contrast media limits the amount of contrast media transferred into breast milk to less than 1% of the total administered dose. Furthermore, because of lipid solubility, less than 1% of an ingested dose is absorbed from the gastrointestinal tract; this results in a systemic dose to the infant of less than 0.01% of the IV dose given to the mother.

The ACR noted that the primary concerns resulting from this infant systemic dose are direct toxicity, allergic sensitization, or anaphylactoid reaction. However, these are theoretical concerns only; none have been clinically reported. Nevertheless, a breastfeeding woman might choose to limit or stop breastfeeding for 24 hours after the IV injection. Because of the excretion time of contrast media, cessation of breastfeeding for longer than 24 hours is not necessary. Mothers might consider expressing and storing breast milk before contrast administration for use during this period.

**Patients With Pre-existing Medical Conditions**

Many reasons might preclude a patient from receiving ROCM; however, there are fewer reasons a patient should always be excluded. Radiologic technologists must use their discretion regarding the decision about whether patients should or must be excluded, and always use every resource available, including nursing staff, physicians, and radiologists, to make an informed decision. Ultimately, the responsibility for injecting any material lies with the person controlling the injector or syringe.

Multiple risk factors might increase the likelihood that iodinated media will elicit an adverse reaction in a patient. The patients at greatest risk are patients with asthma and those who have a history of severe allergic or allergy-type reactions to contrast or any other allergen. Box 2 lists predisposing risk factors for adverse reactions following contrast media administration.

Patients taking certain medications are at increased risk of acute adverse reactions to ROCM. In the absence of complicating factors, metformin is not one of these medications and is not contraindicated in patients receiving ROCM. Risky drugs include those that interact...
Box 2

Predisposing Conditions for Adverse Effects From Iodine-based Contrast Agent Administration

- History of severe adverse reaction to previous contrast media administration.
- Asthma.
- Dehydration.
- Hay fever.
- Renal insufficiency.
- Heart disease.
- Renal disease.
- Cirrhosis.
- Sickle cell anemia.
- Polycythemia.
- Multiple myeloma.
- Interleukin-2 therapy.
- Mastocytosis.
- β-blocker therapy.
- Malignancy or malignant tumors.

*This list is not exhaustive but includes the most commonly encountered predisposing conditions.

with the contrast to create a synergistic effect and drugs that interact with contrast to form crystals and precipitates (see Box 3). If it is necessary to comingle these medications through a shared IV access line, extreme care should be taken to flush the line completely prior to each administration; such activity should be undertaken only under the direct supervision of a physician."

Demographic Considerations

Certain demographic groups have shown a higher incidence of acute adverse reactions to ROCM. For example, women and girls tend to have more reactions, and more severe reactions, than do men and boys. Individuals of Eastern Indian descent have a greater risk of adverse effects than individuals of European or African descent. The incidence of acute adverse reactions also is higher in individuals aged between 20 and 50 years; the fewest reactions occur in people aged less than 20 years."

Treating Iodinated Contrast Media Reactions

The best means of ensuring a successful outcome following an acute contrast reaction is early detection and decisive intervention. Early recognition of reactions requires the use of less medication to inhibit the reaction and results in a more positive outcome. Anyone

Box 3

Common Medications Contraindicated for Patients Receiving Radiopaque Contrast Media

| Drugs that increase coagulation time: 
| Antithrombin III 
| Dicoumarol 
| Heparin 
| Warfarin |
| Drugs that might lead to lactic acidosis: 
| Metformin |
| Drugs that intensify and prolong hypotensive effects: 
| Calcium channel blockers, including diltiazem, nifedipine, verapamil |
| Drugs that increase the release of anaphylactoid mediators: 
| β-blockers, including atenolol, metoprolol, propanolol, timolol |
| Drugs that might increase the risk of nephropathy: 
| Diuretics, including acetazolamide, furosemide, spironolactone |
| Drugs that might increase the risk of adverse reactions: 
| Interferon 
| Aldesleukin 
| Interleukin-2 |
| Drugs that are thrombolytic and increase coagulation time: 
| r-TPA – intravenous tissue plasminogen activator (alteplase) 
| Streptokinase 
| Urokinase |
| Drugs that may inhibit platelet formation: 
| Aspirin 
| Nonsteroidal anti-inflammatory drugs |
| Drugs that crystallize and form precipitates: 
| Cimetidine 
| Diazepam 
| Diphenhydramine 
| Ethanol 
| Meperidine hydrochloride 
| Papaverine 
| Promethazine 
| Protamine sulfate |
who administers contrast or cares for patients following contrast administration should be well-informed about the adverse effects of ROCM and managing acute reactions to these substances. \(^3,11\) Facilities where iodinated contrast is administered should have well-stocked emergency response carts readily accessible in examination rooms; furthermore, standard treatment protocols should be in place for managing patients who exhibit signs and symptoms of an adverse reaction. The following guidelines do not replace the positions, policies, or procedures of individual facilities.

**Prophylaxis**

The likelihood of an adverse reaction can be minimized in at-risk patients through the timely use of prophylactic premedication. Typically, corticosteroids are recommended for patients with a previous history of adverse reaction to ROCM and patients with a medical history that might predispose them to an acute reaction. Corticosteroids should be administered during the 24 hours prior to the study; at a minimum, 2 doses of corticosteroids should be administered beginning no later than 12 hours before the study. Single doses of corticosteroids given immediately prior to the study (ie, within 2 hours) have been shown to have no effect on minimizing the risk of contrast media reactions. Typically, 3 doses of 50 mg each of oral prednisone are suggested in the 24 hours preceding the study, with 50 mg of diphenhydramine given one hour before the study. \(^3,11,14\)

**Patient Evaluation**

The sooner a reaction occurs after injection, the more likely it will be severe. \(^14\) Therefore, patients should be evaluated continuously following contrast administration and this evaluation should continue for at least 20 minutes postinjection; an additional 1-hour evaluation is recommended, if possible. Evaluation always should be predicated on the patient’s current status compared with previous evaluations. Ongoing assessments should include an analysis of the patient’s:

- General appearance.
- Ability to speak (and if so, the quality of that speech).
- Breathing.
- Cardiovascular status (ie, pulse strength and pulse rate).
- Blood pressure.

The severity of a reaction can be immediately assessed by evaluating these 5 items. Any degradation of the patient’s physiologic state could indicate that an adverse reaction is taking place. If the radiologic technologist believes this to be the case, he or she should immediately seek assistance. \(^11,23\)

**Emergency Treatment**

When an adverse reaction occurs, getting help is the first and most important thing a radiologic technologist should do; everything else should be secondary to getting assistance as quickly as possible. Once help has been sought, the next steps depend on the patient’s condition, and many of these can and should be completed concurrently: \(^11\):

- Assess the patient to determine the progression of the reaction.
- Ensure or establish a patent airway, as needed.
- Ensure IV access.
- Prepare appropriate medications.

These treatment directions apply to both adult and pediatric patients. The radiologic technologist should chart all therapeutic treatments delivered to the patient, including oxygen.

After the radiologic technologist has ensured that help is on the way and has begun a secondary evaluation of the patient’s status, the technologist should be most concerned with the ABCs of cardiopulmonary resuscitation. The patient’s airway, breathing, and circulation should be evaluated and re-established if there is not a positive indication of cardiorespiratory effort. Every member of the radiology care team should be familiar with and certified to perform cardiopulmonary resuscitation. \(^3,11\)

**Oxygen Therapy**

If the patient has patent cardiopulmonary effort, administration of oxygen at a high flow rate should be considered. Oxygen is the immediate, first-line drug of choice for treating bronchospasm, laryngeal edema, hypotension without bradycardia, vagal reactions, and anaphylactoid reactions. Every patient who exhibits
signs of a reaction of any type should be administered oxygen, previous medical history notwithstanding. High-flow oxygen must be administered via a face mask; nasal cannulas are insufficient to deliver the rates of oxygen needed in emergency situations. Typical flow rates for oxygen delivery during the treatment of reactions should be greater than or equal to 6 to 10 L/minute delivered via face mask or partial rebreather mask. Some treatment protocols suggest even higher flow rates, up to 100% oxygen using rebreather masks.

**Intravenous Fluid Therapy**

Although oxygen is the first-line treatment for any reaction, hypotensive situations require advanced treatment, including fluid replacement. IV fluid delivery should begin immediately following the administration of oxygen therapy; fluid replacement has repeatedly been shown to be the most effective treatment for hypertension. Multiple studies have shown that fluid replacement alone is sufficient to treat most hypotensive events. In adults, 1000 mL of lactated Ringer’s or 0.9% (normal) saline solution should be infused rapidly to treat hypotensive emergencies. In pediatric patients, a maximum of 500 mL to 1000 mL of lactated Ringer’s or normal saline, calculated at the rate of 10 mL/kg to 20 mL/kg, should be infused. In all cases, IV fluid administration should be initiated prior to delivering any drugs.

**Pharmaceutical Intervention**

Pharmaceutical intervention is well within the scope of practice for radiologic technologists. The standards of practice, educational curricula, and national examining bodies of the radiologic sciences professions support the administration of medications in an emergent situation, so long as an independent practitioner (eg, a physician) is immediately available. The American Society of Radiologic Technologists issued opinion statements supporting the applicability of technologists injecting medications as needed “where federal or state law and/or institutional policy permits.” It is important to note that a physician does not have to be present, only immediately available, for a technologist to administer therapeutic medications; however, radiologic technologists should exercise extreme caution when making such a decision. The most commonly used drugs in the treatment of adverse reactions are epinephrine and diphenhydramine.

**Epinephrine**

Epinephrine is the first-line drug of choice for treating contrast reactions in all patients except pregnant women. It is unique in its ability to simultaneously invoke α-agonistic and β-agonistic pharmacodynamic effects. Alpha-agonists increase blood pressure by reversing vasoconstriction. Beta-agonists increase cardiac output and rate while reversing bronchoconstriction and inhibiting mast cell degranulation through the triggered release of cyclic adenosine monophosphate at the cellular level. Epinephrine comes in many forms, varieties, and concentrations; however, most emergency response carts contain 1:10 000 dilutions of epinephrine for IV use. Epinephrine diluted at 1:10 000 contains 1 mg of epinephrine per 10 mL of fluid.

The ACR has a specific treatment protocol for administering epinephrine in case of contrast reactions, and radiologic technologists should be familiar with the protocol. According to the ACR, pediatric patients should not be administered more than 0.01 mg/kg (0.1 mL/kg), to a maximum of 0.15 mg (1.5 mL) in patients weighing less than 30 kg, or a maximum of 0.30 mg (3.0 mL) in patients weighing more than 30 kg. The dose may be repeated every 5 to 15 minutes to a maximum of 1 mg cumulative total. Doses for adult patients are easier to calculate; the standard epinephrine dose for an adult patient is 1 mL to 3 mL of 1:10 000 dilution repeated every 5 to 10 minutes, up to a cumulative total of 10 mL.

Epinephrine also is available for intramuscular (IM) use. IM epinephrine is diluted at 1:1000, or 1 mg/mL. Dosing calculations are substantially easier using IM epinephrine. Standard dose rates are 0.5 mg for adults, 0.3 mg in children aged 6 to 12 years (more than 30 kg), and 0.15 mg in children younger than 6 years of age (less than 30 kg). However, the use of IM epinephrine is less common in radiology departments.

**Antihistamines**

Antihistamines are not effective in the treatment of acute life-threatening contrast reactions; however, they
are effective in treating skin reactions and delayed secondary reactions. Diphenhydramine is the drug of choice in the treatment of skin reactions.\textsuperscript{24,38} Dosage is standard, regardless of route (oral, IM, or IV), at 1 mg/kg to a maximum of 50 mg.\textsuperscript{23} In the absence of life-threatening signs and symptoms, the technologist should delay administering antihistamine medications until ordered to do so by a physician or advanced practitioner.

**Conclusion**

Iodinated ROCM are regularly used in the diagnosis and treatment of vascular structures. However, they can be dangerous and acute adverse reactions should be expected from every patient. A consequence of the propensity of radiographic contrast to cause severe, life-threatening reactions is that injection of these materials should never be taken lightly, nor should they be used in isolated settings or in the absence of the appropriate tools and knowledge to treat any possible adverse effects.

Radiologic technologists should be knowledgeable about the contrast media they are using, including the possible adverse effects of these drugs. Technologists also should understand relevant contraindications and patient histories that might indicate increased risk of reaction following injection.

Individuals who inject contrast should be trained in emergency life-saving measures and be prepared to take decisive action following every contrast media injection. All personnel engaged in patient care in radiology departments should know the location of emergency treatment tools (eg, emergency response carts, oxygen), be familiar with treatment protocols for adverse contrast reactions, and receive annual training in basic life support. These simple measures reduce the risks of contrast media injection and help increase favorable outcomes if an acute adverse reaction does occur.

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**References**

Adverse Effects of Iodine-derived Intravenous Radiopaque Contrast Media

1. When state and institutional policy permit, it is within a radiologic technologist’s scope of practice to administer contrast media only when:
   a. a practitioner is physically present in the imaging department to supervise the procedure.
   b. a practitioner is immediately available to diagnose and treat allergic reactions.
   c. he or she has completed advanced training and certification in contrast administration.
   d. his or her supervisor determines that the technologist is capable.

2. Among intravenous (IV) pharmacologic agents currently in use, iodinated contrast media are the _______ common.
   a. most
   b. second most
   c. fifth most
   d. least

3. Categories of radiopaque iodinated contrast media (ROCM) include all of the following except:
   a. high osmolarity.
   b. low osmolality.
   c. ionic.
   d. nonionic.

4. Intravenous ROCM are typically highly lipid soluble.
   a. true
   b. false

5. Seventy percent of the injected dose of ROCM is cleared from the blood plasma within _______ minutes.
   a. 1 to 3
   b. 2 to 5
   c. 5 to 10
   d. 10 to 15

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6. One difference between anaphylactoid and anaphylactic reactions is the release of:
   a. IgE antibodies.
   b. histamine.
   c. slow-reacting substance of anaphylaxis (SRSA).
   d. leukotrienes.

7. Seafood allergies correlate with iodine or ROCM allergies.
   a. true
   b. false

8. ______ adverse effects are predictable.
   a. Chemotoxic
   b. Anaphylactic
   c. Anaphylactoid
   d. Idiosyncratic

9. ______ release is the major early concern in mast cell degeneration, which leads to systemic reactions.
   a. Histamine
   b. SRSA
   c. Prostaglandin
   d. Leukotriene

10. Which of the following is not a sign or symptom of minor anaphylactoid reactions?
    a. flushing
    b. nausea
    c. vomiting
    d. dyspnea

11. Which of the following is not a sign or symptom of severe anaphylactoid reactions?
    a. hyperosmia
    b. laryngeal edema
    c. paralysis
    d. seizures

12. ______ reactions require a previous exposure to an antigen.
    a. Anaphylactoid
    b. Chemotoxic
    c. Idiosyncratic
    d. Anaphylactic

13. The antigen-antibody complex required to elicit a true anaphylactic response requires approximately ______ week(s) to mature.
    a. 1
    b. 2
    c. 3
    d. 4

14. Chemotoxic effects can result from which of the following?
    1. the physical make-up and composition of the contrast (eg, viscosity)
    2. faulty injection technique
    3. unrelated patient pathophysiology
    a. 1 and 2
    b. 1 and 3
    c. 2 and 3
    d. 1, 2, and 3

15. The American College of Radiology lists which of the following as risk factors for nephrotoxicity?
    1. age older than 60 years
    2. history of hypertension requiring medical care
    3. history of lung cancer
    a. 1 and 2
    b. 1 and 3
    c. 2 and 3
    d. 1, 2, and 3

continued on next page
16. Extravasated contrast media is toxic to surrounding tissue and produces an inflammatory response; this response usually peaks within _______ hours.
   a. 6 to 8
   b. 12 to 24
   c. 24 to 36
   d. 24 to 48

17. Which of the following are signs of extravasation?
   1. swelling
   2. limited range of motion
   3. pain
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

18. Mild extravasation cases typically resolve within:
   a. a day.
   b. 2 to 4 days.
   c. 3 to 5 days.
   d. a week.

19. A pressure gradient between vascular space and ambient atmospheric air results in a(an):
   a. extravasation.
   b. catheter fragment.
   c. air embolus.
   d. hematologic deficit.

20. Which of the following are mentioned in the article as particular concerns for pediatric patients receiving ROCM?
   1. increased susceptibility to osmotically induced fluid shifts
   2. smaller-caliber needles and contrast viscosity
   3. dislodgement of the IV due to patient movement
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

21. Which of the following medications are contraindicated in patients receiving ROCM?
   1. streptokinase
   2. aspirin
   3. diphenhydramine
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

22. Acute adverse reactions to ROCM are most common in which of the following age groups?
   a. infants and children from birth to age 3 years
   b. older children and teenagers
   c. adults aged 20 to 50 years
   d. people older than 75 years

23. The first thing a technologist should do when a contrast reaction occurs is:
   a. administer oxygen.
   b. locate, reposition, and access an emergency response cart.
   c. seek assistance.
   d. administer diphenhydramine.
24. The first drug of choice for anaphylactoid reactions in the presence of patent cardiopulmonary effort is:
   a. diphenhydramine.
   b. corticosteroids.
   c. epinephrine.
   d. oxygen.

25. The standard dosage of diphenhydramine is _______ to a maximum of _______.
   a. 1 mL/kg; 25 mL
   b. 1 mL/kg; 50 mL
   c. 1 mg/kg; 25 mg
   d. 1 mg/kg; 50 mg