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Preface

This revised Fifth Edition is intended to replace all earlier editions.

This manual was developed by the Committee on Drugs and Contrast Media, Commission on General and Pediatric Radiology of the American College of Radiology as a guide for radiologists in the use of iodinated contrast media. Suggestions for patient screening, premedication, recognition of adverse reactions, and emergency treatment of such reactions are emphasized in this manual. Its major purpose is to provide useful information regarding iodinated contrast media used in daily practice.

The committee offers this document to practicing radiologists as a consensus of scientific evidence and clinical experience concerning the use of iodinated contrast media. The general principles outlined here also pertain to the administration and systemic effects (e.g., adverse effects) of noniodinated contrast materials such as gadolinium or other compounds used for magnetic resonance imaging, radionuclides, and to gastrointestinal use of iodinated contrast media.

The committee wishes to express its sincere thanks to all who have contributed their knowledge and valuable time to this publication. Particular appreciation is extended to Dr. Arthur J. Segal for the primary effort of coordinating and assembling this document, as well as to the other significant contributors from the Committee: Drs. Michael A. Bettmann, William H. Bush, Jr., Kyongtae Tyler Bae, James H. Ellis, Kate A. Feinstein, Richard P. Gold, Jay P. Heiken, Richard W. Katzberg, and Bernard F. King. Special gratitude is expressed to Drs. Mark M. Mishkin and Bruce L. McClennan for their efforts in creating previous editions of this manual as well as their support and encouragement in the development of the fifth edition.

Finally, the Committee wishes to recognize the efforts of Ms. Christine Waldrip, Ms. Margaret Wyatt, and other supporting members of the ACR staff.

This document serves as a guide that may assist radiologists in their clinical evaluation and decision-making in regard to patient care in the administration of contrast media. It should not be deemed to include all proper methods of care that could be reasonably directed to obtain the same results. Adherence to this document will not assure a successful outcome in every situation. The radiologist given all clinical circumstances presented by the individual patient situation should make the ultimate judgment regarding the propriety of any specific medication, recommended dosage levels, or the course of conduct.
INTRODUCTION

Various forms of contrast media have been used to improve medical imaging. The value of contrast media has long been recognized, as attested by their common daily utilization in imaging departments worldwide. Like all other pharmaceuticals, however, these agents are not completely devoid of risk. The major purpose of this manual is to assist radiologists in recognizing and managing the small but real risks inherent in the use of contrast media.

Adverse side effects from the administration of contrast media vary from minor physiological disturbances to the rare severe, life-threatening situations. Preparation for prompt treatment of contrast media reactions must include preparation for the entire spectrum of potential adverse events and include prearranged response planning with availability of appropriately trained personnel, equipment, and medications. Therefore, such preparation is best accomplished prior to approving and performing these examinations. Additionally, an ongoing quality assurance and quality improvement program for all radiologists and technologists and the requisite equipment are recommended. Thorough familiarity with the presentation and emergency treatment of contrast material reactions must be part of the environment in which all intravascular iodinated contrast material is administered.

Millions of radiological examinations assisted by intravascular contrast media are conducted each year in North America. Although adverse side effects are infrequent (range: 5-12% of all intravenous injections with ionic high-osmolality contrast media or 1-3% with nonionic low-osmolality contrast media), a detailed knowledge of the variety of side effects, their likelihood in relationship to pre-existing conditions, and their treatment is required to insure optimal patient care. As would be appropriate with any diagnostic procedure, preliminary considerations for the referring physician and the radiologist include:

1. Assessment of patient risk versus potential benefit of the contrast-assisted examination.
2. Imaging alternatives that provide the same or better diagnostic information.
3. Assurance of a valid clinical indication for each contrast medium administration.

Because of the documented low incidence of adverse events, intravenous injection of contrast media may be exempted from the need for informed consent, but this decision should be based on state law and institutional policy, and departmental policy.

REFERENCES

ADVERSE EFFECTS

The majority of adverse side effects are mild or moderate, non-life-threatening events that require only observation, reassurance, and support. Severe adverse side effects, however, may have a mild or moderate beginning or prodrome. Virtually all life-threatening reactions occur immediately or within the first 20 minutes after contrast material injection.

The effects of dose, route, and rate of delivery of contrast media on adverse events are not entirely clear. Studies have shown that a “test injection” does not decrease the incidence of severe reactions and may actually increase it. In the past, it was widely believed that the incidence of adverse events overall was higher with intravenous than with intra-arterial injection, but data have shown the reverse to be true. Nevertheless, any contrast agent administration, regardless of route, may result in an adverse event, ranging from mild discomfort to a severe, life-threatening reaction.

Overall, the types of contrast reactions most threatening to patients are those unanticipated adverse events that result in sudden compromise of critical body functions, specifically anaphylactoid reactions or profound cardiovascular collapse.

Pathogenesis Mechanisms

The precise pathogenesis of most adverse events occurring after the administration of contrast agents is unknown. There are clearly multiple mechanisms. Some reactions may involve activation, de-activation, or inhibition of a variety of vasoactive substances or mediators. Histamine release must clearly have occurred when patients develop urticaria, but the precise cause and pathway of histamine release are not known.

The central nervous and cardiovascular systems are key target areas, as reflected in seizures or cardiovascular collapse. The mechanism may relate to the specific chemical formulation of the contrast agent (chemotoxicity), to hypertonicity, or perhaps even to binding of the small contrast agent molecule to activators, although binding of current contrast agents in the blood is minimal. Patient anxiety may contribute to adverse events. Additives such as calcium-chelating substances or substances leached from rubber stoppers in bottles or syringes have been suggested as contributory.

In general, accurate prediction of the occurrence of a contrast reaction is not yet possible, although it is clear that certain patients are at increased risk of a reaction. That is, allergy-like reactions, such as urticaria, are more frequent in patients with a strong history of active allergies.

Bronchospasm is a common reaction among patients with active asthma. Hemodynamic changes are more common among patients with significant cardiovascular disease, such as aortic stenosis or severe CHF. Perhaps most importantly, a prior reaction to contrast injection is the best predictor of a recurrent adverse event. It is not an absolute indicator, however, since the incidence of recurrent reactions is thought to range from eight percent too perhaps as high as 30 percent.

Obtaining a good history prior to the administration of contrast agents is clearly crucial. It is also imperative that all personnel who will administer contrast agents be prepared to recognize any adverse event that may occur, monitor it, and institute the appropriate measures. This may range from notifying the radiologist to administering medication to calling a code, depending on background and training. Knowledge about the effects of contrast agents is important since it can help to inform those caring for patients as to what specific therapy, if any, should be instituted.
In some cases, the cause of an adverse event can be clearly identified. The etiology of cardiovascular effects, for example, is complex but to some extent definable. Some effects, such as hypotension and tachycardia, are clearly related to hypertonicity. Others, such as the negative inotropy and chronotropy that occur with direct coronary injection, are related to both increased osmolality and ionic concentration. Still other effects, such as some arrhythmias seen in animal studies, are due to the absence of ions. Pulseless electrical activity, with associated cardiac arrest, has been shown to result from a sudden drop in serum-ionized calcium, which, in turn, may be caused by the specific contrast formulation or an additive. The incidence and severity of such events seem to decrease with the use of low-osmolality and isotonic contrast agents.

Further, cardiovascular effects are more frequent and more significant in patients with underlying cardiac disease. For example, patients with left heart failure are less able to compensate for the osmotic load and the minor negative chronotropic effects of contrast media, both because of the high osmolality of some contrast agents and because of the volume load. As a result, there is an increased risk of developing acute pulmonary edema. Patients with an acute increase in pulmonary vascular resistance, and thus an acute increase in right heart pressure (e.g., patients with massive pulmonary embolism), have an increased risk of developing right heart failure that may be irreversible.

Vasovagal reactions are relatively common, and are thought to be the result of increased vagal tone. The precise pathogenesis is unknown, but it is thought to be related to the central nervous system. The effects of increased vagal tone include depressed sinoatrial and atrioventricular nodal activity, inhibition of atrioventricular conduction, and peripheral vasodilatation (characterized by hypotension and bradycardia). Vasovagal reactions are in part related to anxiety, and they can occur while consent is being obtained, with placement of a needle or catheter for injection, or with the administration of contrast via any route. Such reactions generally present with a feeling of apprehension and accompanying diaphoresis.

Most vagal reactions are mild and self-limited, but if they are not observed and treated until they resolve fully, they may progress to cardiovascular collapse. (See Table 6 – Management of Acute Reactions in Adults.)

Special Circumstances

As outlined in drug package inserts, certain clinical circumstances require particular precautions to avoid adverse events (patients with known or suspected pheochromocytoma, thyrotoxicosis, dysproteinemias, or sickle cell disease, for example). (See the Section on Patient Selection and Preparation Strategies.)

Types of Reactions

1. Mild
2. Moderate
3. Severe
4. Organ-specific (see Table 2)

As all who are familiar with contrast agents know, reactions are most often mild but can be life threatening, and prediction is impossible, although there are some known risk factors. In general, it is not possible to classify the etiology of an adverse event following contrast agent administration, but it is possible to clarify and classify severity.
Mild Reactions

Some reactions, specifically nausea and vomiting, clearly increase in incidence with increasing osmolality. Urticaria also is increased with the use of high-osmolality ionic contrast media. Such reactions are almost always mild, although urticaria can progress to moderate severity. Mild reactions do not require treatment, but, as noted, they may presage a more severe reaction. Any patient with any reaction should, therefore, be carefully monitored for 20-30 minutes at least, to ensure that such worsening does not occur. Other mild reactions include warmth, which is really a physiologic response to the high-osmolality contrast agents, diffuse erythema, which can progress to a more severe reaction, and mild, transient hypotension. Pain on injection, particularly with injection into the arteries of the lower extremities or into the external carotid arteries, is largely a function of hypertonicity. It is, therefore, much decreased in both incidence and severity with the use of low-osmolality contrast agents.

Moderate Reactions

Moderate adverse events, by definition, are not immediately life threatening (although they may progress to be so) but are ones that require treatment. They include symptomatic urticaria, vasovagal reactions, bronchospasm, tachycardia, and mild laryngeal edema. Moderate reactions require close monitoring until they resolve completely. Treatment may include diphenhydramine for symptomatic hives, leg elevation for hypotension, use of a beta-agonist inhaler for bronchospasm, or epinephrine for laryngeal edema.

Severe Reactions

These are adverse events that are potentially or immediately life threatening. Although they are rare, it is imperative that all personnel who administer contrast agents be aware that they occur at a low but unpredictable rate and those they require prompt recognition and treatment. Patients may initially experience a variety of symptoms and signs, ranging from anxiety to diffuse erythema to sudden cardiac arrest.

Complete cardiovascular collapse requires cardiopulmonary resuscitation and advanced specialized life-support equipment and trained personnel. Cardiopulmonary collapse may occur very rapidly, so all patients receiving intravascular contrast must be carefully monitored. Since the outcome of cardiopulmonary arrest worsens as the response time increases, recognition of such reactions and prompt institution of treatment are crucial.

Severe adverse events include vasovagal reactions, moderate and severe broncho-spasm, moderate and severe laryngeal edema, loss of consciousness, seizures, and cardiac arrest. The initial presentation may be identical to an anaphylactic reaction to a drug or other allergen, but since an antigen-antibody response has never been identified, such a reaction is classified “anaphylactoid.” Treatment, however, is identical to that for an anaphylactic reaction, namely, the “ABCs” (airway assessment, breathing, circulation) followed by appropriate ACLS treatment. Pulmonary edema may also occur, particularly in patients with underlying cardiac compromise.

Seizures are a rare but serious adverse event. They are seen most often with intrathecal administration of contrast but can also occur with intravascular use.

Organ-Specific Effects

Some organ-specific adverse effects have been noted above. They include pulseless electrical activity (PEA), pulmonary edema, and seizures. The effect of extravasation of contrast during
Intravascular administration is generally mild, particularly if low-osmolality contrast is used, and is dealt with elsewhere.

Venous thrombosis can occur in response to infusion of contrast. This is clearly related to direct vascular endothelial damage, and it decreases with decreasing osmolality. Contrast agents are known to have an effect not only on vascular endothelial function but also on thrombosis and hemostasis. These complex interactions in general are not thought to be major or significant. Contrast agents are known to cause some alteration in red blood cell deformability and in platelet function, but these effects are not thought to be clinically relevant.

The renal effects of contrast agents have attracted increased attention over the last few years with the aging of the population and the increased utilization of studies such as CT and cardiac catheterization that require large volume injections. The pathogenesis of contrast damage to kidneys is unclear, and there are probably multiple mechanisms. It is clear that the risk, if any, is minimal in patients with normal renal function. The risk is also low in patients with normal serum creatinine, even in elderly persons with decreased body mass who are known to have a decrease in the glomerular filtration rate. In patients with elevated serum creatinine, the effects appear to be related primarily to dose. In most but not all cases, the elevation in serum creatinine that occurs is transient, with return to baseline at two to three weeks.

Despite the lack of clarity as to etiology, recent attempts to decrease the severity and incidence of contrast nephropathy have had some success, notably with use of an isotonic contrast agent and with a medication, N-acetylcysteine, which is thought to act as both a free-radical scavenger and a stimulus to intrarenal vasodilation.

In summary, contrast agents, acting through various mechanisms, most of which are not clearly defined, cause a variety of adverse events. These range from trivial to death and the prediction of such reactions are not currently possible. It is crucial that all who work with contrast agents be aware of the specific adverse events, of possible risk factors, and of the need for expeditious and appropriate treatment.

REFERENCES


INCIDENCE

The actual incidence of adverse effects after the administration of intravascular contrast media is difficult to determine since similar signs and symptoms may be due to concomitant medications, local anesthetics, needles, catheters, and anxiety, among other things. Under reporting or variation in the categorization or classification of reactions affects statistics regarding incidence. Most adverse effects are mild to moderate, do not require treatment, and are reported to occur in 5%-12% of all patients who receive ionic, high-osmolality contrast media. Many patients experience physiologic disturbances (i.e., warmth or heat), and this is often not recorded.

Use of low-osmolality ionic and nonionic contrast media is associated with a lower overall incidence of adverse effects, particularly non-life-threatening ones. Serious contrast reactions are rare and occur in 1 or 2 per 1,000 examinations using high-osmolality contrast media (HOCM) and in 1-2 per 10,000 examinations using low-osmolality contrast media (LOCM).

The precise incidence of fatal outcome from a contrast material reaction is also unknown for reasons similar to those mentioned previously. Additionally, resuscitative measures and treatment of adverse effects from contrast media have improved in the past two decades. Comparing published incidence rates from the use of HOCM, deaths are reported between 1 per 40,000 and 1 per 170,000 intravenous administrations. By the 1980s the incidence of fatal outcomes after a reaction to HOCM had decreased to 0.9 per 100,000, which is essentially equivalent to that observed with nonionic contrast media. This change likely reflects improvements in contrast media design (LOCM) and the increased use of LOCM for patients with risk factors, as well as the proper recognition and treatment of reactions.

Although most serious reactions occur in the immediate postinjection period, delayed reactions have been reported to occur with an incidence of approximately 2%. Most delayed reactions are cutaneous and, in turn, most of these are associated with the use of a nonionic contrast agent and were most often reported after the use of one specific nonionic dimer contrast agent (no longer available). The cutaneous reactions are usually mild and resolve within a week, but may be serious. Delayed pain at or near the site of injection may signal impending thrombophlebitis after intravenous injection or unrecognized extravasation.

Iodide “mumps” (salivary gland swelling) and a syndrome of acute polyarthropathy are two delayed reactions that can occur with either HOCM or LOCM and may be more frequent in patients with renal dysfunction. Delayed symptomatology, such as rash and itching, can occur as late as 1-7 days after the injection of contrast media. Patients treated with interleukin-2 immunotherapy, either concurrently or in the past (even 2 years after interleukin-2 therapy), can develop delayed reactions after the administration of contrast media that mimic the side effects associated with interleukin-2 therapy.

REFERENCES

PATIENT SELECTION AND PREPARATION STRATEGIES

GENERAL CONSIDERATIONS

The approach to patients has two general aims: to prevent a reaction from occurring and to be fully prepared to treat a reaction should one occur (see Table 4). Achieving these aims depends on obtaining an appropriate and adequate history for each patient, preparing the patient appropriately for the examination, having equipment available to treat reactions, and ensuring that expertise sufficient to treat even the most severe reactions is readily at hand. Although mild reactions to contrast media are relatively common, they are almost invariably self-limited and of no consequence. Severe, life-threatening reactions, although rare, can occur in the absence of any specific risk factors with any type of agent.

Current guidelines of the American College of Radiology regarding the choice of high- versus low-osmolality contrast media are shown in Appendix B. Radiologists should be aware of the warnings and guidelines for contrast agent use contained in the U.S. Food and Drug Administration approved package insert with each contrast agent.

The history obtained should focus on factors that may indicate either a contraindication to contrast media use or an increased likelihood of a reaction. General patient status is clearly important. This is supported by the observation that sick patients get sicker. Thus, hemodynamic, neurologic, and general nutritional status should be assessed.

In regard to specific risk factors, it is clear that a history of a prior allergy-like reaction to contrast media increases the likelihood of the patient experiencing a subsequent reaction. Additionally, an allergic diathesis predisposes individuals to reactions. The relationship is a difficult one to define, since many individuals have at least a minor allergy, such as seasonal rhinitis, and do not experience reactions. True concern should be focused on patients with significant allergies, such as a prior anaphylactic response to one or more allergens. A history of asthma indicates an increased likelihood of a contrast reaction.

The predictive value of specific allergies, such as those to shellfish or dairy products, previously thought to be helpful, is now recognized to be unreliable. Any patient who describes an “allergy” to a food or contrast agent should be questioned further to clarify the type and severity of the “allergy” or reaction, as these patients could represent atopic individuals who are at increased risk for reactions.

Another specific risk category is renal disease. Questions should address whether the patient has a history of renal dysfunction or diabetes mellitus. In patients with suspected renal dysfunction, baseline blood urea nitrogen and creatinine are useful. It is also important to ensure that all such patients are well hydrated before, during, and after the contrast study. In those patients with impaired renal function, the volume of contrast material should be limited if it is determined that an alternate examination (without the need for contrast media) cannot provide the necessary clinical information.

Cardiac status is an important consideration. Patients with significant cardiac disease seem to be at increased risk of reactions. These include symptomatic patients (e.g., patients with angina or congestive heart failure symptoms with minimal exertion) and also patients with problems such as severe aortic stenosis, primary pulmonary hypertension, or severe but well-compensated cardiomyopathy. In all such patients, particular attention should be paid to limiting the volume of the contrast agent.
A general category that deserves attention is emotional state. There is evidence that severe adverse effects to contrast media or to procedures can be mitigated at least in part by reducing anxiety. It is useful, therefore, to determine whether a patient is particularly anxious and to reassure and calm that patient before contrast injection.

There are several other specific risk factors that deserve attention. Paraproteinemias, particularly multiple myeloma, are known to predispose to irreversible renal failure after contrast administration due to protein precipitation in the renal tubules. This hazard is usually preventable with good hydration, so such patients should not have extensive enemas before procedures nor should they be restricted from drinking. Instead, oral and, if necessary, intravenous hydration should be encouraged, for example, beginning 6-12 hours before contrast medium use and continuing for at least 6-12 hours after.

Age, independent from the general health of the patient, is not a major consideration in patient preparation. In infants and neonates, contrast volume is an important consideration because of the low blood volume of the patient and the hypertonicity (and potentially detrimental cardiac affects) of even nonionic monomeric contrast media.

Some studies suggest that the use of beta-adrenergic blocking agents lowers the threshold for and increases the severity of contrast reactions. Others suggest that sickle cell trait or disease increases the risk to patients; however, in neither case is there evidence of significant clinical risk.

Concomitant use of certain intra-arterial injections, such as papaverine, is believed to lead to precipitation of contrast media during arteriography. There have been reports of thrombus formation during angiography using nonionic as opposed to ionic agents. In both cases, there are in vitro studies that suggest possible explanations.

Diabetic patients on the oral antihyperglycemic agent metformin or metformin combinations are at possible risk. The combination of contrast medium and metformin should be completely avoided in patients with renal dysfunction, hepatic dysfunction, alcohol abuse, or severe congestive heart failure because all of these conditions limit metformin excretion and/or increase lactate production and increase the likelihood of irreversible, possibly fatal, lactic acidosis. This issue is dealt with in more detail elsewhere in this manual.

Some patients with pheochromocytoma develop an increase in serum catecholamine levels after the intravenous injection of high-osmolality, conventional ionic contrast media. A subsequent study showed no elevation of catecholamine levels after the intravenous injection of low-osmolality, nonionic contrast media. Direct injection of either type of contrast medium into the adrenal or renal artery may cause a hypertensive crisis.

Some patients with hyperthyroidism or other thyroid disease (especially those who live in iodine-deficient areas) may develop iodine-provoked delayed hyperthyroidism. This effect may appear 4 to 6 weeks after the intravascular contrast administration in some of these patients. It can occur after the administration of either ionic, high-osmolality or nonionic, low-osmolality contrast. It is usually self-limited.

Patients with carcinoma of the thyroid deserve special consideration before the intravascular or oral administration of iodinated contrast media (ionic or nonionic). Uptake of I-131 in the thyroid becomes moderately decreased to about 50% at one week after iodinated contrast injection but seems to become normal within a few weeks. Therefore, if systemic radioactive iodine therapy is part of planned treatment, a pretherapy diagnostic study of the patient using iodinated
radiographic contrast medium (intravascular or oral) may be contraindicated; consultation with the ordering clinician prior to contrast administration in these patients is recommended.

Pain and extravasation are other considerations that deserve some preprocedural attention. (See sections on Injection of Contrast Media and on Contrast Reactions in Children.) Intravenous injections may cause heat and discomfort but rarely cause pain unless there is extravasation. Pain, however, can be minimal with extravasation of nonionic contrast. Intra-arterial injections into peripheral vessels in the arms, legs, or head can be quite painful, particularly with high-osmolality contrast media. For such injections, either low-osmolality contrast media (LOCM) or iso-osmolality contrast media (IOCM) or diluted high-osmolality contrast media are generally indicated. Even large extravasated volumes are generally not significant in most patients, but in the pediatric age group or in patients with poor perfusion at the injection site, extravasation can lead to skin slough or other tissue injury. The use of a nonionic agent does not in itself eliminate the potential sequelae of extravasation but does reduce the potential for injury.

General principles of patient selection and preparation require attention to the four Hs.

1. **History** – A careful, focused history is the necessary first step. Details about prior reactions and allergy history should be carefully evaluated.
2. **Hydration** – This should be adequate in all patients and is especially important in patients with renal dysfunction or paraproteinemias and in others (e.g., neonates, elderly, and debilitated individuals) who would be compromised by dehydration.
3. **Have equipment and expertise ready** – Serious reactions are rare, but establishing a method of how to react and treat them requires prior planning and cannot be left to the time at which they occur.
4. **Heads up!** – Be aware of specific risks, the patient’s status, possible reactions and the best response to them, and where and how to get help.

**Premedication**

The primary indication for premedication is pretreatment of “at-risk” patients who require contrast media. Such regimens have been shown in clinical trials to decrease the frequency of contrast medium reactions. However, no regimen has eliminated repeat reactions completely.

Perhaps because of the infrequency of severe life-threatening reactions, studies to date have demonstrated a decrease in adverse events after steroid premedication, but not a decrease in the incidence of severe adverse events.

Pretesting is not predictive, may itself be dangerous, and is not recommended.

Several premedication regimens have been proposed to reduce the frequency and/or severity of reactions to contrast media. Two frequently used regimens are:

1. **Corticosteroid/antihistamine**
   
   Prednisone 50 mg by mouth at 13 hours, 7 hours, and 1 hour before contrast medium injection, *plus*

   Diphenhydramine (Benadryl®) 50 mg intravenously, intramuscularly, or by mouth 1 hour before the contrast medium injection.

   Nonionic, low-osmolality contrast medium.
2. Corticosteroid alone
Methylprednisolone (Medrol®) 32 mg by mouth 12 hours and 2 hours before contrast medium injection.

An antihistamine (as in Option 1) can also be added to this regimen.

Nonionic, low-osmolality contrast medium.

For patients at increased risk of an adverse reaction to contrast medium injection, studies (albeit limited) indicate that low-osmolality, nonionic contrast media have a lower reaction rate than do the combination of premedication plus a conventional high-osmolality ionic agent. Lasser et al demonstrated that nonionic contrast media combined with a premedication strategy including corticosteroids showed a further reduction in reaction rates compared to other protocols for patients who had experienced a prior contrast media-induced reaction. However, no controlled studies are available to determine whether pretreatment alters the incidence of serious reactions.

Oral administration of steroids seems preferable to intravascular administration, and prednisone and methylprednisolone are equally effective. If the patient is unable to take oral medication, 200 mg of hydrocortisone intravenously may be substituted for oral prednisone in the Greenberger protocol.

One imperative is that steroids be given at least 6 hours prior to the injection of contrast medium regardless of the route of steroid administration. It is clear that administration for 3 hours or fewer prior to contrast does not decrease adverse reactions. Supplemental administration of an H-1 antihistamine (e.g., diphenhydramine), orally or intravenously, may reduce the frequency of urticaria, angioedema, and respiratory symptoms. In emergency situations, intravenous corticosteroid (e.g., 200 mg hydrocortisone) every 4 hours plus an H-1 antihistamine (e.g., 50 mg diphenhydramine) 1 hour before the procedure has been used. Additionally, ephedrine administration has been suggested to decrease the frequency of contrast reactions, but caution is advised in patients with unstable angina, arrhythmia, or hypertension. The use of ephedrine in a routine premedication protocol is not recommended. In one clinical study, addition of the H-2 antihistamine cimetidine to the premedication protocol resulted in a slight increase in the repeat reaction rate.

Corticosteroids are the essential component and should be included in any premedication protocol, unless there are very clear contraindications to their use. Antihistamines alone have not been shown to decrease severe reaction rate. Similarly, use of a low-osmolality, nonionic contrast medium is recommended for patients at risk of a reaction and when a premedication regimen is considered necessary.

In patients who have a prior, documented contrast reaction, the use of a different contrast agent has been advocated and may be protective. The switch to a different agent should be in combination with a pre-medication regimen.

No premedication strategy should be a substitute for the preadministration preparedness discussed in this manual. Contrast reactions occur despite premedication prophylaxis. The radiologist must be prepared and able to treat these reactions. To reiterate: a low-osmolality, nonionic contrast agent plus a corticosteroid premedication regimen should be considered for patients who are at risk for a second anaphylactoid reaction. For these patients, there is a slight chance that the recurrence may be more severe than the first reaction; however, it is more likely that the reaction will be the same or less or that there will be no recurrence.
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CONTRAST NEPHROTOXICITY

Definition

Nephrotoxicity is attributed to radiologic contrast media when there has been a sudden change in renal status after the administration of contrast medium and no other etiology appears likely from the clinical records. Renal failure due to the administration of contrast media has been reported to be the third most common cause of in-hospital renal failure, after hypotension and surgery.

There is no standard for reporting contrast media-induced nephrotoxicity, however, and the definition of “significant” changes varies considerably among studies: definitions used have included percent change in the baseline creatinine (e.g., 20-50% rise in serum creatinine) and absolute elevation from baseline (0.5-2.0 mg/dl). The time during which such changes were assessed has also varied widely. Porter defined contrast media-associated nephropathy as a serum creatinine increase of: (a) greater than 25%, if baseline serum creatinine is less than 1.5 mg/dl or (b) greater than 1.0 mg/dl, if baseline serum creatinine is greater than 1.5 mg/dl, when either occurs within 72 hours after the contrast administration. Solomon et al defined contrast media-induced nephrotoxicity as an acute decrease in renal function manifested by an increase in baseline serum creatinine of at least 0.5 mg/dl (44 µmol/l) within 48 hours of injection of contrast. The prevalence of contrast media-induced nephrotoxicity, therefore, varies depending on the definition that is used.

Serum creatinine has definite limitations as an accurate measure of renal function because it is influenced greatly by the patient’s gender, muscle mass, nutritional status, and age. Normal serum creatinine levels are maintained until the glomerular filtration rate (at least as reflected in creatinine clearance) is reduced to nearly 50%; that is, impaired renal function may exist even when serum creatinine levels are “normal.” Direct measurement of GFR would be most accurate in defining renal function before and after contrast administration, but such measurement is generally impractical. One viable alternative is to use a formula to calculate creatinine clearance, based on age, gender, body weight, and serum creatinine (e.g., Cockcroft-Gault formula). Even a 50% rise in serum creatinine in a patient with normal renal function may not be clinically significant, because it may not require intervention or affect prognosis if the change is transient, which is usually the case.

There is no uniform definition of renal dysfunction. When creatinine clearance is less than 60 ml/min (in a normal young adult equivalent to a serum creatinine of 133 mmol/l or 1.5 mg/dl) the term “renal insufficiency” has been used, and when creatinine clearance is less than 30 ml/min the term “renal failure” is often used.

Pathogenesis

The exact pathophysiology of contrast media-related nephrotoxicity and renal insufficiency/failure is not fully understood. Transient renal effects are seen with both conventional, high-osmolality ionic contrast media (HOCM) and low-osmolality contrast media (LOCM). Etiologic factors that have been suggested include: 1) renal hemodynamic changes and 2) direct tubular toxicity of the contrast material. Both osmotic and chemotoxic mechanisms may be involved and some investigations suggest agent-specific chemotoxicity.
Risk Factors

Numerous studies have attempted to isolate risk factors for contrast nephrotoxicity. The classic review by Byrd and Sherman listed predisposing factors for contrast media-induced acute renal failure as pre-existing renal insufficiency (serum creatinine level ≥1.5 mg/dl), diabetes mellitus, dehydration, cardiovascular disease and the use of diuretics, advanced age (≥70 years), myeloma, hypertension, and hyperuricemia. However, studies by Parfrey et al, and Schwab et al documented that the population at highest risk for developing contrast media-induced acute renal failure are patients with both diabetes and pre-existing renal insufficiency. These investigators found that, given equal states of hydration, neither diabetes alone nor renal insufficiency alone (although yielding a somewhat higher risk for renal failure than the normal population) resulted in a statistically greater incidence of renal dysfunction after contrast administration. The age threshold for a high risk of contrast-induced nephrotoxicity is not well established and actually seems to be changing, as people are healthier at older ages.

Barrett and Carlisle reported a meta-analysis of the literature concerning the relative nephrotoxicity of HOCM and LOCM. They concluded that LOCM are, generally, less nephrotoxic than HOCM in patients with underlying renal insufficiency. However, LOCM were not shown to confer a significant benefit in patients with normal renal function. Rudnick et al found similar results in a large prospective study.

For patients with pre-existing renal insufficiency, and more clearly for those with renal insufficiency and diabetes, nonionic LOCM are less nephrotoxic than ionic HOCM. Whether newer nonionic contrast media, particularly those that are isotonic to blood, have an advantage remains to be investigated thoroughly. One study suggests that nonionic iso-osmolality contrast media (IOCM) may be less nephrotoxic in diabetic patients with renal insufficiency when the contrast amount is also limited. A study in 2003 showed a lower incidence of elevation of serum creatine after the use of an isotonic, nonionic dimer as compared to a nonionic monomer in patients with elevated serum creatinine at baseline.

Patients with diabetes who are taking the antihyperglycemic agent metformin fall into a special category (See the section on Metformin Therapy and the Risk of Lactic Acidosis).

Consequence

The clinical course of contrast-associated nephrotoxicity depends on baseline renal function, co-existing risk factors, degree of hydration, and perhaps the dose of radiologic contrast media. Serum creatinine usually begins to rise within the first 24 hours, peaks within 96 hours (4 days), and usually returns to baseline within 7 to 10 days. It is rare for patients to require temporary or permanent dialysis.

Prevention or Amelioration

Hydration

Not all clinical studies have shown dehydration to be a major risk factor for contrast media-induced acute renal failure (ARF). However, in the dehydrated state, renal blood flow and glomerular filtration rate are decreased, the magnitude of the effects of contrast media on these parameters is accentuated, and there is the theoretical concern of prolonged tubular exposure to contrast material because of low tubular flow rates. Solomon et al studied patients with chronic renal insufficiency who underwent cardiac angiography. The incidence of contrast media-induced
ARF was decreased by hydration with 0.45% saline or 0.9% saline administered at a rate of 100 ml/hr beginning 12 hours before and continuing 12 hours after angiography.

**Diuretics: Mannitol and Furosemide**

In the same study by Solomon et al there were no beneficial effects from the osmotic diuretic mannitol when it was added to saline hydration in patients with or without diabetes. There was an exacerbation of contrast media-induced renal dysfunction when the loop diuretic furosemide was used in addition to saline hydration.

**Other Agents**

N-acetylcysteine, an antioxidant, has shown promise in recent clinical studies to reduce the incidence of contrast media-associated renal insufficiency. However, this agent should not be a substitute for close attention to renal function and adequate hydration. The evidence for other medications such as theophylline, endothelin-1, or intravenous infusion of fenoldopam is less convincing.

The regimen of oral acetylcysteine, 600 mg twice daily on the day before and on the day of administration of iodinated radiographic contrast, is simple and inexpensive, has few contraindications, and should be considered for patients at risk for contrast media-induced nephrotoxicity. Alternatively, a regimen of IV administration beginning 30 minutes prior to contrast administration may be considered (150 mg/kg over 30 minutes, followed by 50 mg/kg over 4 hours).

**Recommendations for Prevention of Contrast Media-Induced Acute Renal Failure**

Fortunately, patients with normal renal function are at extremely low risk for contrast media-induced acute renal failure. It may actually not occur if renal function (as opposed to serum creatinine) is truly normal. The fear of renal failure should not, therefore, dictate avoidance of diagnostic studies using contrast media. Radiologists should be attentive to the possibility of risk factors for renal injury, especially the combination of pre-existing renal insufficiency, diabetes, and dehydration.

The major precaution is adequate hydration. If the patient cannot take adequate oral hydration, consider intravenous infusion of 0.45% or 0.9% sodium chloride at 100 ml/hr, beginning 6-12 hours before and continuing 4-12 hours after the administration of contrast material. For patients with renal insufficiency, the substitution of a LOCM or IOCM is suggested.

Addition of a medication that may mitigate the nephrotoxic effect of iodinated radiographic contrast media, e.g., N-acetylcysteine, should be considered for patients at risk (i.e., exhibiting renal insufficiency, particularly when associated with diabetes mellitus), but not in lieu of adequate hydration and close surveillance of renal function. A good understanding of the particular patient and communication between radiologist and referring clinician are critically important.

For all patients with suspected renal dysfunction or those considered at risk for contrast nephrotoxicity, a baseline serum creatinine level should be obtained before the injection of contrast material. If renal dysfunction is identified, the referring clinician should be advised regarding alternative imaging approaches. Other precautionary recommendations are to increase the interval between contrast media examinations and reduce the contrast dose.
Recommended Indications for Serum Creatinine Measurement before Intravascular Administration of Iodinated Contrast Media

- History of “kidney disease” as an adult, including tumor and transplant.
- Family history of kidney failure.
- Diabetes treated with insulin or other medications for diabetes that are prescribed by a licensed physician.
- Paraproteinemia syndromes or diseases (e.g., myeloma).
- Collagen vascular disease.
- Certain medications:
  - Metformin or metformin-containing drug combinations.
  - Nonsteroidal anti-inflammatory drugs.
  - Regular use of nephrotoxic anti-biotics, such as aminoglycosides.

(Routine blood urea nitrogen may be useful as a reflection of hydration but should not be relied on solely in evaluating renal dysfunction).

Other patients who are scheduled for a routine intravascular study do not necessarily need a serum creatinine determination before the examination.

Chronic Renal Dialysis Patients and the Use of Contrast Media

In patients suffering from end-stage renal disease, the question arises as to the emergent need for dialysis after a contrast media examination. Because contrast agents are not protein-bound and possess relatively low molecular weights, they are readily cleared by dialysis. The primary concern about patients who are dialysis-dependent is the osmotic load of the contrast material, although direct chemotoxicity on the heart and blood-brain barrier is also of theoretical concern. Unless there is significant underlying cardiac dysfunction, or very large volumes of contrast media are used, there is no need for urgent dialysis. It is important, however, to limit the dose of contrast used in such patients and to consider the use of LOCM or IOCM if there is a risk of adverse effects of hypertonicity.

Patients with renal insufficiency who require only intermittent or occasional dialysis are at substantial risk for contrast media-induced nephrotoxicity with further permanent worsening of their renal function. Alternative imaging studies that do not require contrast media should be considered.

REFERENCES

METFORMIN THERAPY AND THE RISK OF LACTIC ACIDOSIS

Metformin is a biguanide oral antihyperglycemic agent used to treat patients with non-insulin-dependent diabetes mellitus. Metformin is available as a generic drug as well as in proprietary formulations, alone and in combination with other drugs (see Table at the end of the section for some of the brand-name formulations). The drug is relatively new in the United States, approved in December of 1994 for use as monotherapy or combination therapy in patients with non-insulin-dependent diabetes mellitus whose hyperglycemia is not controlled by diet or sulfonylurea therapy alone.

Metformin is thought to act by decreasing hepatic glucose production and enhancing peripheral glucose uptake as a result of increased sensitivity of peripheral tissues to insulin. Only rarely does it cause hypoglycemia.

The most significant adverse effect of metformin therapy is the potential for the development of metformin-associated lactic acidosis in the susceptible patient. Metformin-associated lactic acidosis is estimated to occur at a rate of 0–0.084 cases per 1,000 patient years. Patient mortality in reported cases is about 50%. However, in almost all reported cases, lactic acidosis occurred because one or more patient-associated contraindications for the drug were overlooked. In one extensive 13-year retrospective study of patients in Sweden, 16 cases were found and all patients had several co-morbid factors, most often cardiovascular or renal disease.

Metformin is excreted unchanged by the kidneys, probably by both glomerular filtration and tubular excretion. The renal route eliminates approximately 90% of the absorbed drug within the first 24 hours. Metformin seems to cause increased lactic acid production by the intestines. Any factors that decrease metformin excretion or increase blood lactate levels are important risk factors for lactic acidosis. Renal insufficiency, then, is a major consideration.

Also, factors that depress the ability to metabolize lactate, such as liver dysfunction or alcohol abuse, or increase lactate production by increasing anaerobic metabolism (e.g., cardiac failure, cardiac or peripheral muscle ischemia, or severe infection) are contraindications to the use of metformin. Iodinated X-ray contrast agents are not an independent risk factor for patients taking metformin but rather are a concern only in the presence of underlying renal dysfunction. Although contrast media-induced renal failure is very rare in patients with normal renal function, elderly patients with reduced muscle mass (and thus reduced ability to make creatinine) can have a “normal” serum creatinine level in the presence of a markedly depressed glomerular filtration rate.

Intravascular administration of iodinated contrast media to a patient taking metformin is a clinical concern. Of metformin-associated lactic acidosis cases reported worldwide between 1968 and 1991, 7 of the 110 patients received iodinated contrast agents before developing lactic acidosis. The U.S. Food and Drug Administration-approved metformin package insert states that metformin should be withheld temporarily for patients undergoing radiological studies using intravenous iodinated contrast media. If acute renal failure or a reduction in renal function were to be caused by the iodinated contrast media, an accumulation of metformin could occur, with resultant lactate accumulation. The major clinical concern, then, is confined to patients with known, borderline, or incipient renal dysfunction.

Limiting the amount of contrast medium administered and hydrating the patient lessen the risk of contrast media-induced dysfunction; both of these measures should be considered in patients with renal dysfunction. The efficacy of other measures thought to limit contrast nephrotoxicity (e.g.,
administration of N-acetylcysteine or fenoldopam) in preventing lactic acidosis related to metformin is not known.

Therefore, metformin should be discontinued at the time of an examination or procedure using intravascular contrast medium, withheld for 48 hours after the procedure, and reinstated only after renal function has been re-evaluated and found to be normal. The examination may proceed even if the patient took a dose of metformin on the morning of the examination.

Communication between the radiologist, the healthcare practitioner, and the patient will be necessary to establish the procedure for reassessing renal function and restarting metformin after the contrast examination. The exact method (e.g., serum creatinine measurement, clinical observation, hydration) will vary depending on the practice setting.

It is not necessary to discontinue metformin prior to gadolinium-enhanced MR studies when the amount of gadolinium administered is in the usual dose range of 0.1-0.3 mmol per kg of body weight. Although there are currently no relevant data, larger doses of gadolinium agents, such as might be used for angiography or CT scanning, can potentially cause nephrotoxicity. Metformin should be discontinued (as is recommended when administering intravascular iodinated contrast media) before such large-dose gadolinium procedures (see the section on Adverse Reactions to Gadolinium-Based Contrast Media).

Table 1

<table>
<thead>
<tr>
<th>Medications containing metformin*</th>
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<tbody>
<tr>
<td>Metformin (generic)</td>
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<tr>
<td>Avandamet®</td>
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<tr>
<td>Glucophage®</td>
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<tr>
<td>Glucophage XR®</td>
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<tr>
<td>Glucovance®</td>
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<tr>
<td>Metaglip®</td>
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</tbody>
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*As of April 2003. Additional medications containing Metformin may have become available since then.

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INJECTION OF CONTRAST MEDIA

General Considerations

Injection methods vary depending on vascular access, clinical problems, and type of examination. The mode and method of delivery, either by hand or power injector, also vary for the procedures listed. Subject to the requirements of state law, a radiologist, radiologic technologist, or nurse may administer contrast media. Stable intravenous access is necessary. Current American College of Radiology (ACR) recommendations regarding injection of contrast media (including radiopharmaceuticals) are as follows:

The ACR approves of the injection of contrast material and diagnostic levels of radiopharmaceuticals by certified or licensed radiologic technologists and radiologic nurses under the direction of a radiologist or his or her physician designee who is personally and immediately available, if the practice is in compliance with institutional and state regulations. There must be prior written approval by the medical director of the radiology department/service of such individuals. The approval process must have followed established policies and procedures, and the approved radiologic technologists and radiologic nurses need to have documentation of continuing medical education related to the materials being injected and to the procedures being performed. (ACR Council Policy – 1987; amended 1997)

Referring to the package insert may be appropriate in determining the contrast media dose and concentration (see Appendix A, Contrast Media Specifications). It is important to avoid prolonged admixture of blood and contrast media, especially nonionic agents, in syringes and catheters whenever possible; the same is true for admixture of contrast media and any medications except heparin.

Mechanical Injection of Intravenous Contrast Media

Bolus or power injection of intravenous contrast material is superior to drip infusion for enhancing normal and abnormal structures during body computed tomography (CT). Radiology personnel must recognize the need for proper technique to avoid the potentially serious complications of contrast medium extravasation and air embolism. When the proper technique is used, contrast medium can be safely administered intravenously by power injector, even at high flow rates.

Technique

To avoid potential complications, the patient’s full cooperation should be obtained whenever possible. Communicating with the patient before the examination and during the injection may reduce the risk of contrast medium extravasation. If the patient reports pain or the sensation of swelling at the injection site, injection should be discontinued.

Intravenous contrast material should be administered by power injector through a flexible plastic cannula. Use of metal needles for power injection should be avoided. In addition, the flow rate should be appropriate for the gauge of the catheter used. Although 22-gauge catheters may be able to tolerate flow rates up to 5 ml/sec, a 20-gauge or larger catheter is preferable for flow rates of 3 ml/sec or higher. An antecubital or large forearm vein is the preferred venous access site for power injection. If a more peripheral (i.e., hand or wrist) venipuncture site is used, a flow rate of no greater than 1.5 ml/sec may be more appropriate.
Careful preparation of the power injection apparatus is essential to minimize the risk of contrast medium extravasation or air embolism. Standard procedures should be used to clear the syringe and pressure tubing of air, after which the syringe should be reoriented with the tubing directed downward. Before initiating the injection, the position of the catheter tip should be checked for venous backflow. If backflow is not obtained, the catheter may need adjustment, and a saline test flush or special monitoring of the site during injection may be appropriate. If the venipuncture site is tender or infiltrated, an alternative venipuncture site should be sought. If venous backflow is obtained, the power injector and tubing should be positioned to allow adequate table movement without tension on the intravenous line.

A critical step in preventing significant extravasation is direct monitoring of the venipuncture site by palpation during the initial portion of the contrast medium injection. If no problem with the injection is encountered during the first 15 seconds of the injection, the individual monitoring the injection exits the CT scan room before the scanning begins. If extravasation is detected, the injection is stopped immediately. Communication between the technologist and the patient via an intercom or television system should be maintained throughout the examination.

Power injection of some central venous catheters can be performed safely, provided that certain precautions are followed. First, either the CT scout scan or a recent chest radiograph should be checked to confirm the proper location of the catheter tip. Before connecting the catheter to the injector system tubing, the catheter tip position should be tested for venous backflow. Occasionally backflow will not be obtained because the catheter tip is positioned against the wall of the vein in which it is located. If saline can be injected through the catheter without abnormal resistance, contrast material can be administered through the catheter safely. If abnormal resistance or discomfort is encountered, an alternative venous access site should be sought. Injection with large-bore (9.5-F to 10-F) central venous catheters using flow rates of up to 2.5 ml/sec has been shown to generate pressures below manufacturers’ specified limitations. For power injection of central venous catheters, the radiologist should consult manufacturers’ recommendations. Contrast media should not be administered by power injector through small-bore, peripheral (e.g., arm) access central venous catheters (unless permitted by the manufacturer’s specifications) because of the risk of catheter breakage.

Power injection of PICCs (peripherally inserted central catheters) may be problematic. Manufacturers rarely indicate safe maximal flow rates. These rates vary depending on catheter material, though a rate of 1 ml/sec is generally okay for use through PICCs.

**Extravasation**

Certain patients are at increased risk for extravasation, including those who cannot communicate adequately (e.g., the elderly, infants and children, and patients with altered consciousness), severely ill or debilitated patients, and patients with abnormal circulation in the limb to be injected. Patients with altered circulation include those with atherosclerotic peripheral vascular disease, diabetic vascular disease, Raynaud’s disease, venous thrombosis or insufficiency, or prior radiation therapy or extensive surgery (e.g., axillary lymph node dissection or saphenous vein graft harvesting) in the limb to be injected. Certain intravenous access sites (e.g., hand, wrist, foot, and ankle) are more likely to result in extravasation and should be avoided if possible. In addition, injection through indwelling peripheral intravenous lines that have been in place for more than 24 hours and multiple punctures into the same vein are associated with an increased risk of extravasation. When a patient with an increased risk of extravasation requires intravenous contrast material, use of a low-osmolality contrast media (LOCM) should be considered because extravasation of these agents is better tolerated than extravasation of high-osmolality contrast media (HOCM).
Extravasation can occur during hand or power injection. The reported incidence of intravenous contrast material extravasation related to power injection for CT has ranged from 0.1% to 0.9% (1/1,000 patients to 1/106 patients). The frequency of extravasation is not related to the injection flow rate. Extravasation occurring with dynamic bolus CT may involve large volumes of contrast media. Although most patients experience stinging or burning pain at the site of extravasation, some experience little or no discomfort, particularly if a LOCM is used.

Extravasated iodinated contrast media, particularly HOCM, are toxic to the surrounding tissues, particularly to the skin, producing an acute local inflammatory response that peaks in 24-48 hours. Most patients recover without sequelae, but in some this response may proceed to severe adverse events. Ulceration and tissue necrosis may result and can be identified as early as 6 hours after the injury. Acute inflammation is followed by a chronic inflammatory response that may be accompanied by fibrosis and adjacent muscle atrophy. The acute tissue injury resulting from extravasation of iodinated contrast material is related primarily to the hyperosmolality of the fluid. Extravasation of a large volume of contrast material can also produce a “compartment syndrome” as a result of mechanical compression.

Extravasation injury is more likely to be severe in patients with arterial insufficiency or compromised venous or lymphatic drainage in the affected extremity. In addition, extravasations involving large volumes of contrast media and those occurring in the dorsum of the hand, foot, or ankle are more likely to result in severe tissue damage. Extravasated LOCM are better tolerated than conventional HOCM.

**Evaluation and Treatment**

On physical examination, the extravasation site may be edematous, erythematous, and tender. Because the severity and prognosis of the injury are difficult to determine on initial evaluation of the affected site, close clinical follow-up for several hours is essential.

There is no clear consensus regarding the most effective treatment for contrast medium extravasation. Elevation of the affected extremity above the level of the heart to decrease capillary hydrostatic pressure and thereby promote resorption of extravasated fluid is recommended, but controlled studies demonstrating the efficacy of this treatment are lacking. There is no clear evidence favoring the use of either warm or cold compresses in cases of extravasation. As a result there are some radiologists who use warm compresses and some who use cold compresses. Those who have used cold have reported that it may be helpful for relieving pain at the injection site. Those who have used heat have found it helpful in improving absorption of the extravasation as well as in improving blood flow, particularly distal to the site.

When extravasation occurs, its location, the type and amount of contrast, and the clinical examination are all factors in determining a prudent course of action. When in doubt, a surgical consultation is recommended. Extravasation of 50 ml or more of HOCM and extravasation of 100 ml or more of LOCM will frequently be sufficient cause for such consultation. However, consultation should also be considered after extravasation of lesser amounts of contrast (30 ml of HOCM and 60 ml of LOCM) in the wrist, ankle, or dorsum of the hand. If the patient is totally asymptomatic, as is common with extravasation in the upper arm, careful evaluation and appropriate clinical follow-up are usually sufficient.

An immediate surgical consultation is indicated for any patient in whom one or more of the following signs or symptoms develops: increased swelling or pain after 2-4 hours, altered tissue perfusion as evidenced by decreased capillary refill at any time after the extravasation has
occurred, change in sensation in the affected limb, and skin ulceration or blistering. Outpatients who have suffered contrast medium extravasation should be released from the radiology department only after the radiologist is satisfied that any signs and symptoms that were present initially have improved or that new symptoms have not developed during the observation period. All extravasation events and their treatment should be documented in the medical record, and the referring physician should be notified.

**Air Embolism**

Clinically significant venous air embolism is a potentially fatal but extremely rare complication of intravenous contrast medium injection. Clinically “silent” venous air embolism, however, commonly occurs when intravenous contrast medium is administered by hand injection. Care when using power injection for contrast-enhanced CT minimizes the risk of this complication. On CT, venous air embolism is most commonly identified as air bubbles or air-fluid levels in the intrathoracic veins, main pulmonary artery, or right ventricle. Air embolism has also been identified in intracranial venous structures.

Inadvertent injection of large amounts of air into the venous system may result in air hunger, dyspnea, cough, chest pain, pulmonary edema, tachycardia, hypotension, or expiratory wheezing. Neurologic deficits may result from stroke due to decreased cardiac output or paradoxical air embolism. Patients with right-to-left intracardiac shunts or pulmonary arteriovenous malformations are at a higher risk of having a neurological deficit develop from small volumes of air embolism.

Treatment of venous air embolism includes administration of 100% oxygen and placing the patient in the left lateral decubitus position (i.e., left side down). Hyperbaric oxygen has been recommended to reduce the size of air bubbles, helping to restore circulation and oxygenation. If cardiopulmonary arrest occurs, closed-chest cardiopulmonary resuscitation should be initiated immediately.

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CONTRAST REACTIONS IN CHILDREN

Children have a lower frequency of contrast reactions than adults. They tend to have anaphylactoid reactions rather than cardiac problems. Infants and young children are unable to verbalize discomfort or symptoms mandating close observation and monitoring.

The intravenous contrast media dose is 2.0 – 3 ml of 280-300 mgl/ml per kg of body weight to a maximum of 150 ml in those weighing 50 kgs or greater. There is a reported minor reaction rate of 3% for ionic contrast material and 0.9% for low-osmolality contrast media (LOCM). In addition to fewer reactions, LOCM has the added benefit of decreased nausea and vomiting and diminished morbidity from soft-tissue extravasation. These are important factors in restrained and/or sedated infants and children who may have small veins and tenuous injection sites. LOCM is recommended for children who are sedated, are restrained, are younger than 1 year of age, have a history of asthma or allergies, have cardiac or renal disease, are critically ill, or need rapid injection of contrast.

Minor reactions to intravascular contrast media include hives, rhinorrhea, and sneezing. Trained medical personnel should evaluate these immediately. Treatment for minor reactions is usually with antihistamines such as diphenhydramine (Benadryl®). If the reaction progresses, subcutaneous epinephrine 1:1,000 may be needed (see section on Treatment).

Severe reactions include bronchospasm, laryngeal edema, anaphylactoid shock, pulmonary edema, and cardiac arrest. After prompt evaluation, help should be summoned and cardiopulmonary resuscitation initiated. Treatment should include intravenous fluids, intravenous epinephrine 1:10,000, and oxygen. For bronchospasm, an inhaled beta-agonist should be given. Patients with asthma may have an inhaler with them. Corticosteroids may be given parenterally. Steroids will not provide benefit in an acute reaction but may help with long-term stabilization. A pediatric medication chart with weight-based dosages on the emergency medication cart or posted in the room where contrast is injected is useful (see Table 5, Pediatric Dose Schedules).

Children’s airways are smaller and more easily compromised than adult’s airways. Pediatric emergency equipment should be available in all locations where intravascular contrast media are administered to children. Oxygen, suction equipment, and oxygen delivery devices are necessary, including facemasks to fit different size children. A separate box of pediatric airway equipment attached to the emergency cart may be useful in areas where both children and adults receive contrast media.

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IODINATED GASTROINTESTINAL CONTRAST MEDIA: 
INDICATIONS AND GUIDELINES

Conventional Fluoroscopy Indications

Barium sulfate contrast media continue to be the preferred agents for opacification of the gastrointestinal tract. These agents provide greater delineation of mucosal detail, are more resistant to dilution, and are less expensive than water-soluble iodinated contrast media. The current use of iodinated contrast media is primarily limited to those situations in which the administration of barium sulfate is contraindicated: 1) suspected or potential intestinal perforation or leak (including bowel abscess, fistula, or sinus tract); 2) administration before surgical or endoscopic procedures involving the bowel; and 3) confirmation of the position of percutaneously placed bowel catheters.

Aqueous contrast agents are absorbed rapidly from the interstitial spaces and peritoneal cavity, a feature that makes them uniquely useful in examining patients with a suspected perforation of a hollow viscus. No permanent deleterious effects from the presence of aqueous contrast media in the mediastinum, pleural cavity, or abdomen have been shown. Many authors recommend reevaluation with barium if an initial study with iodinated contrast medium fails to demonstrate a suspected perforation because small leaks, undetected with water-soluble media, may be more readily demonstrated by barium sulfate media.

Low-Osmolality Contrast Media

High-osmolality contrast media (HOCM) include very hypertonic ionic monomers (osmolality \( \approx \) 1500 mOsm/kg for 300 mgI/ml). Low-osmolality contrast media (LOCM) include hypertonic ionic dimers and nonionic monomers (osmolality \( \approx \) 600 mOsm/kg for 300 mgI/ml) and the nonionic dimers (osmolality \( \approx \) 300 mOsm/kg for 300 mgI/ml). In those patients for whom barium sulfate is contraindicated, guidelines for the use of LOCM rather than HOCM include the following:

1. Oral administration to children who are at risk for aspiration.
   LOCM cause less pulmonary edema than HOCM because of their lower osmolality. Isotonic nonionic contrast media may be used in children at risk for aspiration and for the evaluation of tracheoesophageal fistula. Water-soluble media are completely absorbed from the lungs, unlike barium that, if not completely expectorated, can remain indefinitely and may cause inflammation. While aspiration of full strength HOCM can cause severe morbidity and mortality, aspiration of isotonic or slightly hypertonic nonionic contrast media is well tolerated even in infants and children.

2. Infants and young children with potential bowel perforation.
   Although HOCM are well tolerated in the mediastinum and peritoneal cavity, LOCM are less irritating and are therefore recommended by several authors for use in young children.

3. Evaluation of the small bowel in infants and young children.
   Because the lower osmolality of LOCM (compared to HOCM) may result in less extravascular fluid shift and less risk of associated hypovolemia, LOCM is recommended for evaluation of the small bowel. Additionally, the lower osmolality of LOCM causes less dilution in the bowel lumen and thus improves small bowel opacification in patients of all ages.
Therapeutic Uses

Uncomplicated cases of meconium ileus and meconium plug syndrome may be treated with multiple iodinated contrast material enemas. A 100-175 mgI/ml HOCM solution is recommended for well-hydrated infants. Premature infants can be treated with isotonic nonionic contrast medium.

HOCM has been successfully used for the treatment of postoperative adynamic (or paralytic) ileus, barium impaction, and adhesive small-bowel obstruction (see dose under Administration section below).

Contraindications

Known prior moderate or severe reaction to iodinated contrast media is a contra-indication. A small percentage of iodinated contrast agent (approximately 1-2%) is normally absorbed and excreted in the urine after oral or rectal administration. Mucosal inflammation, mucosal infection, or bowel obstruction increases the amount absorbed by several fold. It is common to see opacification of the urinary tract in such patients.

Because anaphylactoid reactions are not considered to be dose related and can occur with less than 1 ml of intravenous contrast media, reactions can theoretically occur even from the small amount of contrast medium absorbed from the gastrointestinal tract. There are, however, only very rare reports of moderate or severe idiosyncratic reactions to orally or rectally administered iodinated contrast media.

HOCM are contraindicated for patients at risk for aspiration, whereas isotonic LOCM are safe for these patients.

HOCM should be avoided in patients with fluid and electrolyte imbalances, particularly the very young or elderly patients with hypovolemia or dehydration. The hypertonic HOCM solutions draw fluid into the lumen of the bowel, leading to further Hypovolemia. Isotonic LOCM preparations are preferable for these patients.

It has been theorized, although not shown, that a small amount of iodine can be absorbed from the contrast media and may interfere with studies involving protein-bound and radioactive iodine uptake, as well as with spectrophotometric trypsin assay.

Administration

Ionic and nonionic contrast media concentrations are expressed in milligrams of iodine per milliliter of solution (see Appendix A). A 290-367 mgI/ml solution is recommended for evaluation of the esophagus, stomach, or small bowel in adults. A 150-180 mgI/ml solution is effective for upper gastrointestinal examination in children up to 5 years of age. A 90-150 mgI/ml solution is effective for colon enema in adults and children.

Computed Tomography Indications

Water-soluble media are used for routine gastrointestinal opacification during abdominal computed tomography (CT). In contrast to conventional fluoroscopic imaging, there is no significant difference in the diagnostic quality of CT examinations obtained with HOCM, LOCM, or barium agents, all of which are administered at low concentration. In the United States, approximately 35% of abdominal CT examinations are currently performed using iodinated
gastrointestinal contrast media. Like conventional fluoroscopic imaging, there are a few specific clinical situations in which water-soluble contrast agents are strongly favored over barium agents: suspected gastrointestinal perforation, administration before bowel surgery, and as a bowel marker for percutaneous CT-guided interventional procedures.

**Contraindications**

The aqueous contrast solutions used for CT are very dilute and hypotonic (78 mOsm/kg for HOCLM). Therefore, aspiration and hypovolemia are not contraindications to their use. Idiosyncratic reactions remain a theoretical risk, more relevant to patients with active inflammatory bowel disease.

**Administration**

Various iodine concentrations of aqueous contrast media ranging from 4 to 48 mgI/ml have been suggested for bowel opacification with CT. Because the dilute, hypotonic contrast solutions become concentrated during their passage through the bowel, the concentration used for oral administration is a compromise between lower Hounsfield units opacity in the proximal bowel and higher Hounsfield units opacity in the distal bowel. A solution containing 13-15 mgI/ml is recommended for oral and rectal administration in adults. A 7-9 mgI/ml solution is recommended for oral and rectal administration in infants and small children.

**REFERENCES**

ADVERSE REACTIONS TO GADOLINIUM-BASED CONTRAST MEDIA

Gadolinium chelates have been approved for parenteral use since the late 1980s. Although these agents can be differentiated on the basis of stability, viscosity and osmolality, they cannot be differentiated on the basis of efficacy. These contrast media are extremely well tolerated by the vast majority of patients in whom they are injected. Adverse reactions are encountered with a much lower frequency than is observed after administration of iodinated contrast media.

Adverse Reactions to Gadolinium Contrast Agents

The frequency of all adverse events after an injection of 0.1 or 0.2 mmol/kg ranges from 0.07–2.4 percent. The vast majority of these reactions are mild, including coldness at the injection site, nausea with or without vomiting, headache, warmth or pain at the injection site, paresthesias, dizziness, and itching. Reactions resembling an “allergic” response are very unusual and vary in frequency from 0.004–0.7 percent. A rash, hives, or urticaria are the most frequent of this group, and very rarely there may be bronchospasm. Severe, life-threatening anaphylactoid reactions are exceedingly rare (0.001–0.01 percent). In an accumulated series of 687,000 doses there were only 5 severe reactions. In another survey based on 20 million administered doses there were 55 cases of anaphylactoid shock. It would appear that, to date, only one published death has been clearly related to the administration of gadolinium-based contrast. Other deaths in other series have been ascribed to other diseases or to other drugs, or were thought to be coincidental. Clearly, fatal reactions to gadolinium agents are very rare.

Risk Factors

The frequency of adverse reactions to gadolinium contrast agents is about 2.3–3.7 times higher in patients with a history of reactions to iodinated contrast material and about 8 times higher in patients with a previous reaction to gadolinium-based contrast agents. Second reactions to gadolinium-based compounds tend to be more severe than the first. Persons with asthma and various allergies are also at greater risk, with reports of adverse reaction rates as high as 3.7 percent.

In the absence of any widely accepted policy for dealing with patients with prior contrast reactions (especially to gadolinium-based compounds) and the need for subsequent exposure to MR agents, it does seem prudent to at least take precautions. It should be determined if contrast material is necessary, if a different MR contrast agent could be used, and if 12–24 hours of premedication with corticosteroids and antihistamines could be initiated. This is particularly applicable in patients with prior moderate to severe reactions.

Nephrotoxicity

Gadolinium agents are considered to have no nephrotoxicity at approved dosages for MR imaging. They can be used in azotemic patients and are dialyzable. MR with gadolinium has been used instead of contrast-enhanced CT in those at risk for developing worsening renal failure if exposed to iodinated contrast material.

Gadolinium agents are radiodense and can be used for opacification in CT and angiographic examinations instead of iodinated radiographic contrast agents. However, there is controversy over whether gadolinium contrast agents are less nephrotoxic at equal-attenuating doses. Caution should be used in extrapolating the lack of nephrotoxicity of intravenous gadolinium at MR
dosages to the use of gadolinium for angiographic procedures, including direct injection into the renal arteries. No assessment of gadolinium versus iodinated contrast nephrotoxicity by randomized studies of equal-attenuating doses is currently available.

**Pregnancy**

At doses considerably higher than recommended in humans, gadopentetate dimeglumine has been shown to retard fetal development in rats, double the incidence of post-implantation loss, and to increase the incidence of spontaneous abortion. It may also have an adverse effect on embryo-fetal development. Therefore, MR contrast using any chelate should only be performed if the potential benefit justifies the potential risk, and then only after obtaining written, informed consent.

**Treatment**

Treatment of moderate or severe adverse reactions to gadolinium-based contrast media is similar to that for moderate or severe reactions to iodinated contrast media (See Tables 3 and 6). In any facility where contrast material is injected, it is imperative that personnel trained in recognizing and handling reactions and the equipment and medications to do so be on site or immediately available. Most MR facilities take the position that patients requiring treatment should be taken immediately out of the imaging room and away from the magnet so that none of the resuscitative equipment becomes a hazard.

**Extravasation**

The incidence of extravasation in one series of 28,000 doses was 0.05 percent. Laboratory studies in animals have demonstrated that both gadopentetate dimeglumine and gadoteridol are much less toxic to the skin and subcutaneous tissues than are equal volumes of iodinated contrast media. For these reasons the likelihood of a significant injury resulting from extravasated MR contrast agent is extremely low.

**Serum Calcium Determinations**

Some evidence has developed that gadolinium-based MR contrast material might interfere with total serum calcium values determined with standard colorimetric methods (Roche, Dade and Olympus). This interference is not seen using dry slide technology (Vitros). A warning from Roche Diagnostics suggested that colorimetric determination might be erroneously low, especially in patients with impaired renal function who have recently received gadolinium. It appears that the linear chelates Gd-DTPA-BMA (gadodiamide) and Gd-DTPA bis (methoxyethyl) amide (gadoversetamide) are much more likely to cause this artifact than Gd-DTPA (gadopentetate dimeglumine) or the macrocyclic chelates such as Gd-DOTA (gadoterate meglumine).

If an unexpectedly low result for serum calcium is obtained, it should be repeated two days later or checked with atomic absorption spectroscopy which is not affected by gadolinium chelates.

**Off-Label Usage**

Radiologists commonly use contrast media for a clinical purpose not contained in the labeling and thus commonly use contrast media off-label. Examples include MR angiography, cardiac applications, pediatric applications in patients less than two years of age, and usage in patients
with renal failure. No gadolinium chelate is approved in the United States for use in a power injector.

REFERENCES

27. Witte RJ, Anzai LL. Life-threatening anaphylactoid reaction after intravenous gadoteridol administration in a patient who had previously received gadopentetate dimeglumine. AJNR 1994; 15:523–524.
ADMINISTRATION OF CONTRAST MEDIUM TO BREAST-FEEDING MOTHERS

Administration of either an iodinated or a gadolinium-based contrast agent occasionally is indicated for an imaging study on a woman who is breast-feeding. Both the patient and the patient’s physician may have concerns regarding potential toxicity to the infant from contrast media that is excreted into the breast milk.

The literature on the excretion into breast milk of iodinated and gadolinium-based contrast agents and the gastrointestinal absorption of these agents from breast milk is very limited. A review of the literature, however, reveals important facts: 1) less than 1% of the administered maternal dose of contrast agent is excreted into breast milk; and 2) less than 1% of the contrast medium in breast milk ingested by an infant is absorbed from the gastro-intestinal tract. Therefore, the expected dose of contrast medium absorbed by an infant from ingested breast milk is extremely low.

The Committee on Drugs and Contrast Media of the ACR has discussed this issue extensively and has prepared the following summary information and recommendations.

Iodinated X-ray Contrast Media (Ionic and Nonionic)

Background

The plasma half-life of intravenously administered iodinated contrast medium is approximately 2 hours, with nearly 100% of the agent cleared from the bloodstream within 24 hours. Because of its low lipid solubility, less than 1% of the administered maternal dose of iodinated contrast medium is excreted into the breast milk in the first 24 hours [1,2]. Because less than 1% of the contrast medium ingested by the infant is absorbed from its gastrointestinal tract [3], the expected dose absorbed by the infant from the breast milk is less than 0.01% of the intravascular dose given to the mother. This amount of contrast medium represents less than 1% of the recommended dose for an infant undergoing an imaging study, which is 2 mL/kg. The potential risks to the infant include direct toxicity and allergic sensitization or reaction, which are theoretical concerns but have not been reported.

Recommendation

Mothers who are breast-feeding should be given the opportunity to make an informed decision as to whether to continue or temporarily abstain from breast-feeding after receiving intravascularly administered iodinated contrast media. Because of the very small percentage of iodinated contrast medium that is excreted into the breast milk and absorbed by the infant’s gut, we believe that the available data suggest that it is safe for the mother and infant to continue breast-feeding after receiving such an agent. If the mother remains concerned about any potential ill effects to the infant, she may abstain from breast-feeding for 24 hours with active expression and discarding of breast milk from both breasts during that period. In anticipation of this, she may wish to use a breast pump to obtain milk before the contrast study to feed the infant during the 24-hour period following the examination.

Gadolinium-based Contrast Agents

Background

Gadolinium compounds are safe and useful as magnetic resonance imaging contrast agents. Although free gadolinium is neurotoxic when complexed to one of a variety of chelates, it is safe
for use in adults and children. These hydrophilic gadolinium chelate agents have pharmacokinetic properties very similar to those of iodinated X-ray contrast media. Like iodinated contrast agents, gadolinium contrast agents have a plasma half-life of approximately 2 hours and are nearly completely cleared from the bloodstream within 24 hours.

Less than 0.04% of the intravascular dose given to the mother is excreted into the breast milk in the first 24 hours [4-6]. Because less than 1% of the contrast medium ingested by the infant is absorbed from its gastrointestinal tract [7], the expected dose absorbed by the infant from the breast milk is less than 0.0004% of the intravascular dose given to the mother. Even in the extreme circumstance of a mother weighing 150 kg and receiving a dose of 0.2 mmol/kg, the absolute amount of gadolinium excreted in the breast milk in the first 24-hours after administration would be no more than 0.012 mmol. Thus, the dose of gadolinium absorbed from the gastrointestinal tract of a breast-feeding infant weighing 1,500 grams or more would be no more than 0.00008 mmol/kg, or 0.04% (four ten-thousandths) of the permitted adult or pediatric (2 years of age or older) intravenous dose of 0.2 mmol/kg. The potential risks to the infant include direct toxicity (including toxicity from free gadolinium, because it is unknown how much, if any, of the gadolinium in breast milk is in the unchelated form) and allergic sensitization or reaction, which are theoretical concerns but have not been reported.

**Recommendation**

Review of the literature shows no evidence to suggest that oral ingestion by an infant of the tiny amount of gadolinium contrast agent excreted into breast milk would cause toxic effects. We believe, therefore, that the available data suggest that it is safe for the mother and infant to continue breast-feeding after receiving such an agent.

If the mother remains concerned about any potential ill effects, she should be given the opportunity to make an informed decision as to whether to continue or temporarily abstain from breast-feeding after receiving a gadolinium contrast agent. If the mother so desires, she may abstain from breast-feeding for 24 hours with active expression and discarding of breast milk from both breasts during that period. In anticipation of this, she may wish to use a breast pump to obtain milk before the contrast study to feed the infant during the 24-hour period following the examination.

**REFERENCES**

ADMINISTRATION OF CONTRAST MEDIUM TO PREGNANT OR POTENTIALLY PREGNANT PATIENTS

Studies of low molecular weight water-soluble extracellular substances such as iodinated diagnostic and gadolinium-based magnetic resonance (MR) contrast agents in pregnancy have been limited, and effects on the human embryo or fetus are unknown. Iodinated diagnostic contrast media have been shown to cross the human placenta and enter the fetus in measurable quantities [1,2]. A standard gadolinium-based MR contrast agent has been shown to cross the placenta in primates and appear within the fetal bladder within 11 minutes after intravenous administration [3]. It must be assumed that all iodinated and gadolinium-based contrast media behave in a similar fashion and cross the blood-placental barrier into the fetus.

After entering the fetal blood stream, these agents will be excreted via the urine into the amniotic fluid and be subsequently swallowed by the fetus [4]. It is then possible that a small amount will be absorbed from the gut of the fetus and the rest eliminated back into the amniotic fluid, the entire cycle being repeated innumerable times.

In the study in primates, placental enhancement could be detected up to 2 hours following the intravenous administration of gadopentetate dimeglumine. When gadopentetate dimeglumine was injected directly into the amniotic cavity, it was still conspicuous at 1 hour after administration [3]. There are no data available to assess the rate of clearance of contrast agents from the amniotic fluid.

The ACR Committee on Drugs and Contrast Media has reviewed this issue extensively and has prepared the following summary of information and recommendations.

**Iodinated X-Ray Contrast Media (ionic and nonionic)**

Diagnostic iodinated contrast agents have been shown to cross the human placenta and enter the fetus when given in usual clinical doses. No adequate and well-controlled teratogenic studies of the effects of these agents in pregnant women have been performed.

In conjunction with the existing ACR policy for the use of ionizing radiation in pregnant women, we recommend that all imaging facilities should have polices and procedures to reasonably attempt to identify pregnant patients prior to the performance of any diagnostic examination involving ionizing radiation to determine the medical necessity for the administration of iodinated contrast media. If a patient is known to be pregnant, both the potential radiation risk and the potential added risks of contrast media should be considered before proceeding with the study.

While it is not possible to conclude that contrast agents present a definite risk to the fetus, there is insufficient evidence to conclude that they pose no risk. Consequently, the Committee recommends the following:

A. The radiologist should confer with the referring physician and document in the radiology report or the patient’s medical record the following:

1. That the information requested and the necessity for contrast material administration cannot be acquired via other means (e.g., ultrasonography).
2. That the information needed affects the care of the patient and fetus during the pregnancy.
3. That the referring physician is of the opinion that it is not prudent to wait to obtain this information until after the patient is no longer pregnant.

B. It is recommended that pregnant patients undergoing a diagnostic imaging examination with ionizing radiation and iodinated contrast material provide informed consent to document that they understand the risk/benefits of the procedure to be performed and the alternative diagnostic options available to them (if any), and that they wish to proceed.

**Gadolinium-Based Contrast Agents**

It is known that gadolinium-based MR contrast media cross the human placenta and into the fetus when given in clinical dose ranges. No adequate and well-controlled teratogenic studies of the effects of these agents in pregnant women have been performed. We recommend that all imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of the MR exam, and before the use of MR contrast media in these patients. The ACR has issued a White Paper on MR safety in pregnancy and related issues [4] that is also consistent with the ACR Committee on Drugs and Contrast Media’s recommendation for MR contrast media.

While there is no compelling evidence of teratogenicity or other adverse effect on the fetus of MR imaging or of gadolinium-based contrast agents, neither the safety of the MR environment nor the safety of the MR contrast agents in pregnant patients has been established. It is therefore prudent for pregnant patients at any stage of pregnancy to be informed of the risk-benefit ratio that may warrant the performance of an MR scan with or without contrast media. The radiologist should confer with the referring physician and document the following in the radiology report or the patient’s medical record:

- The information requested from the MR study cannot be acquired using other nonionizing radiation imaging modalities (e.g., ultrasonography).
- That the information needed affects the care of the patient and fetus during the pregnancy.
- That the referring physician is of the opinion that it is not prudent to wait to obtain this information until after the patient is no longer pregnant.

It is recommended that the pregnant patient undergoing an MR examination with contrast material provide informed consent to document that she understands the risk/benefits of the MR procedure to be performed, and the alternative diagnostic options available to her (if any), and that she wishes to proceed.

**REFERENCES**

TREATMENT of CONTRAST REACTIONS

Optimal treatment of contrast media reactions starts with a well-designed plan of action and a properly staffed and equipped imaging facility. Training of on-site personnel attending to patients receiving contrast media should include cardio-pulmonary resuscitation and/or advanced cardiac life support whenever possible. Ongoing quality assurance and quality improvement programs with in-service training and review sessions are recommended.

(See Tables 4 through 7 and the section on Contrast Reactions in Children.)

REFERENCES

### Table 1

**Indications for Use of Iodinated Contrast Media**

**Intravascular**

Intravenous  
- Computed tomography – head, body  
- Digital subtraction angiography  
- Intravenous urography  
- Venography (phlebography)  
  - Inferior vena cava and its tributaries  
  - Superior vena cava and its tributaries  
  - Extremities  
  - Other venous sites  
  - Epidural venography

Intra-arterial  
- Angiocardiography  
- Coronary angiography  
- Pulmonary angiography  
- Aortography  
- Visceral and peripheral arteriography  
- Digital subtraction angiography  
- Central nervous system  
  - Cerebral, vertebral, and spinal angiography

**Intrathecal**  
(Use U.S. Food and Drug Administration-approved contrast media only)  
- Myelography (myelographic nonionic only)  
- Cisternography (myelographic nonionic only)

**Other**  
- Oral, rectal, or ostomy – gastrointestinal tract  
  - Conventional fluoroscopy  
  - Computed tomography  
  - Therapeutic uses  
- Body cavity use  
  - Herniography  
  - Peritoneography  
  - Vaginography  
- Hysterosalpingography  
- Arthrography  
- Endoscopic retrograde cholangiopancreatography  
- Cholangiography  
- Nephrostography  
- Pyelography – antegrade, retrograde  
- Urethrography – voiding, retrograde  
- Cystography  
- Sialography  
- Ductography (breast)  
- Miscellaneous  
  - Sinus tract injection  
  - Dacryocystography  
  - Cavity delineation (including urinary diversions, such as loop and pouch)
Table 2

**Organ or System-Specific Adverse Effects**

Individual organs can manifest isolated adverse effects caused by the administration of contrast material.

**Adrenal**
Hypertension

**Central Nervous System**
Headache, confusion, dizziness, seizure, lost or diminished consciousness or vision

**Gastrointestinal Tract**
Nausea, vomiting, diarrhea, cramping

**Heart**
Hypotension
Dysrhythmia (asystole, ventricular fibrillation/ventricular tachycardia)
Pulseless electrical activity (PEA)
Acute congestive heart failure

**Kidney**
Oliguria
Hypertension

**Pancreas**
Swelling

**Respiratory System**
Bronchospasm (dyspnea); laryngeal edema
Pulmonary edema

**Salivary Glands**
Swelling

**Skin**
Pain, swelling, heat, erythema, urticaria, pruritus

**Thyroid**
Exacerbation of thyrotoxicosis
### Table 3

**Categories of Reactions**

**Mild**

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Appearance</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, vomiting</td>
<td>Altered taste</td>
<td>Sweats</td>
</tr>
<tr>
<td>Cough</td>
<td>Itching</td>
<td>Rash, hives</td>
</tr>
<tr>
<td>Warmth</td>
<td>Pallor</td>
<td>Nasal stuffiness</td>
</tr>
<tr>
<td>Headache</td>
<td>Flushing</td>
<td>Swelling: eyes, face</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Chills</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Shaking</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Signs and symptoms appear self-limited without evidence of progression (e.g., limited urticaria with mild pruritis, transient nausea, one episode of emesis).

**Treatment:** Requires observation to confirm resolution and/or lack of progression but usually no treatment. Patient reassurance is usually helpful.

**Moderate**

Moderate degree of clinically evident focal or systemic signs or symptoms including:

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Appearance</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia/bradycardia</td>
<td>Hypotension</td>
<td>Bronchospasm, wheezing</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Dyspnea</td>
<td>Laryngeal edema</td>
</tr>
</tbody>
</table>

**Pronounced cutaneous reaction**

**Treatment:** Clinical findings should be considered as indications for immediate treatment. These situations require close, careful observation for possible progression to a life-threatening event.

**Severe**

Life-threatening with more severe signs or symptoms, including:

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Appearance</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laryngeal edema</td>
<td>Profound hypotension</td>
<td>Unresponsiveness</td>
</tr>
<tr>
<td>Convulsions</td>
<td>Clinically manifest arrhythmias</td>
<td>Cardiopulmonary arrest</td>
</tr>
</tbody>
</table>

**Treatment:** Requires *prompt* recognition and treatment; almost always requires hospitalization.
Table 4

**ABCD Approach for Patient Evaluation and Treatment**

A
Assessment (severity and category of reaction); blood pressure and pulse (necessary); electrocardiogram monitor may be necessary for evaluation of cardiac rhythm.
Assistance (call for it).
Airway, oxygen.
Access (venous)-secure/improve intravenous line(s) – peripheral or central.

B
Breathing (begin cardiopulmonary resuscitation [CPR] if necessary); use mouth protective barrier.
Bag - valve-mask (e.g., “Ambu” bag) or mouth-mask.
Begin full resuscitation efforts (CPR) if necessary; call cardiopulmonary arrest response team.
Beware of paradoxical responses (e.g., beta-blockers may prevent tachycardic response).

C
Categorize reaction and patient status.
Circulatory assistance: use crystalloid (e.g., Ringer’s lactate, normal saline, or colloid replenishment), infuse rapidly, and may use pressure bag or forceful infusion.
Call cardiopulmonary arrest response team if necessary; CPR; continue to monitor.
Common denominators: assess cardiac output; capillary leak (third spacing); decreased venous return, decreased peripheral vascular resistance.

D
Drug therapies (Tables 5 and 6).
Do: monitor, assess, and reassure the patient; use correct dose (concentration) and route for drugs; push intravenous fluids and oxygen.
Don’t delay (call for help, if you need it); don’t use incorrect dose(s) and drugs.
## Table 5

**Pediatric Dose Schedules**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamine</td>
<td>Diphenhydramine (Benadryl®)</td>
<td>1-2 mg/kg intravenously, up to 50 mg</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Methylprednisolone (Solu-Medrol®)</td>
<td>2 mg/kg intravenously loading dose</td>
</tr>
<tr>
<td>Diuretic</td>
<td>Furosemide (Lasix®)</td>
<td>1 mg/kg per dose intravenously; maximum total dose of 40 mg</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Epinephrine (1:1,000)</td>
<td>0.01 ml/kg, repeat in 15-30 minutes maximum 0.3 ml/dose</td>
</tr>
<tr>
<td>Subcutaneously</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenously</td>
<td>Epinephrine (1:10,000)</td>
<td>0.1 ml/kg, repeat every 5-15 minutes (maximum 3 ml/dose)</td>
</tr>
<tr>
<td>Inhaled Beta Agonist</td>
<td>albuterol (Proventil®, Ventolin®)</td>
<td>5 mg nebulized in 2 ml saline; two puffs every 20-30 min as needed (90-180 µg)</td>
</tr>
<tr>
<td>Vagolytic</td>
<td>Atropine</td>
<td>0.02 mg/kg intravenously (of the 0.1 mg/ml solution) every 5 minutes as needed for persistent bradycardia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimum initial dose: 0.1 mg Maximum initial dose: 0.5 mg (infant/child) 0.5 mg (adolescent)</td>
</tr>
</tbody>
</table>

Conversion: kilograms (kg) ≈ pounds (lb) 2.2
### TABLE 6
Management of Acute Reactions in Adults

**Urticaria**
1. Discontinue injection if not completed
2. No treatment needed in most cases
3. Give H$_1$-receptor blocker: Diphenhydramine (Benadryl®) PO/IM/IV 25-50 mg
   - If severe or widely disseminated: Alpha agonist (arteriolar and venous constriction)
   - Epinephrine SC (1:1,000) 0.1-0.3 ml (=0.1-0.3 mg) (if no cardiac contraindications)

**Facial or Laryngeal Edema**
1. Give alpha agonist (arteriolar and venous constriction): Epinephrine SC or IM (1:1,000) 0.1-0.3 ml (=0.1-0.3 mg) or, if hypotension evident, Epinephrine (1:10,000) slowly IV 1 ml (=0.1 mg).
   - Repeat as needed up to a maximum of 1 mg.
2. Give O$_2$ 6-10 liters/min (via mask).
   - If not responsive to therapy or if there is obvious acute laryngeal edema, seek appropriate assistance (e.g., cardiopulmonary arrest response team).

**Bronchospasm**
1. Give O$_2$ 6-10 liters/min (via mask).
   - Monitor: electrocardiogram, O$_2$ saturation (pulse oximeter), and blood pressure.
2. Give beta-agonist inhalers [bronchiolar dilators, such as metaproterenol (Alupent®), terbutaline (Brethaire®), or albuterol (Proventil®)(Ventolin®) 2-3 puffs; repeat prn. If unresponsive to inhalers, use SC, IM or IV epinephrine.
3. Give epinephrine SC or IM (1:1,000) 0.1-0.3 ml (=0.1-0.3 mg) or, if hypotension evident, Epinephrine (1:10,000) slowly IV 1 ml (=0.1 mg).
   - Repeat as needed up to a maximum of 1 mg.

   *Alternatively:* Give aminophylline: 6 mg/kg IV in D5W over 10-20 minutes (loading dose), then 0.4-1 mg/kg/hr, as needed (caution: hypotension).

   Call for assistance (e.g., cardiopulmonary arrest response team) for severe bronchospasm or if O$_2$ saturation < 88% persists.

**Hypotension with Tachycardia**
1. Legs elevated 60° or more (preferred) or Trendelenburg position.
3. Give O$_2$ 6-10 liters/min (via mask).
4. Rapid intravenous administration of large volumes of isotonic Ringer’s lactate or normal saline.

   *If poorly responsive:* Epinephrine (1:10,000) slowly IV 1 ml (=0.1 mg) (if no cardiac contraindications).
   - Repeat as needed up to a maximum of 1 mg

   If still poorly responsive seek appropriate assistance (e.g., cardiopulmonary arrest response team).
Hypotension with Bradycardia (Vagal Reaction)
1. Monitor vital signs.
2. Legs elevated 60° or more (preferred) or Trendelenburg position.
3. Secure airway: give O₂ 6-10 liters/min (via mask).
4. Secure IV access: rapid fluid replacement with Ringer’s lactate or normal saline.
5. Give atropine 0.6-1 mg IV slowly if patient does not respond quickly to steps 2 – 4.
6. Repeat atropine up to a total dose of 0.04 mg/kg (2-3 mg) in adult.
7. Ensure complete resolution of hypotension and bradycardia prior to discharge.

Hypertension, Severe
1. Give O₂ 6-10 liters/min (via mask).
2. Monitor electrocardiogram, pulse oximeter, blood pressure.
3. Give nitroglycerine 0.4-mg tablet, sublingual (may repeat x 3); or; topical 2% ointment, apply 1 in. strip.
4. Transfer to intensive care unit or emergency department.
5. For pheochromocytoma—phentolamine 5 mg IV.

Seizures or Convulsions
1. Give O₂ 6-10 liters/min (via mask).
2. Consider diazepam (Valium®) 5 mg (or more, as appropriate) or midazolam (Versed®) 0.5-1 mg IV.
3. If longer effect needed, obtain consultation; consider phenytoin (Dilantin®) infusion – 15-18 mg/kg at 50 mg/min.
4. Careful monitoring of vital signs required, particularly of pO₂ because of risk to respiratory depression with benzodiazepine administration.
5. Consider using cardiopulmonary arrest response team for intubation if needed.

Pulmonary Edema
1. Elevate torso; rotating tourniquets (venous compression).
2. Give O₂ 6-10 liters/min (via mask).
3. Give diuretics – furosemide (Lasix®) 20-40 mg IV, slow push.
4. Consider giving morphine (1-3 mg IV).
5. Transfer to intensive care unit or emergency department.

Abbreviations: IM= intramuscular
IV=intravenous
SC=subcutaneous
PO=orally
### Table 7

**Equipment for Emergency Carts**

The phone or beeper number of the cardiopulmonary arrest response team phone should be clearly posted.

- Oxygen cylinders, flow valve, nasal prongs, tubing, partial non-rebreather oxygen masks** (adult and pediatric sizes).
- Suction: wall-mounted or portable; tubing and catheters.
- Oral airways: rubber/plastic; and/or protective breathing barriers.
- "Ambu® - type" bag – valve mask and mouth mask (adult and pediatric sizes) with protective barrier.
- Endotracheal tubes: laryngoscopes (adult and pediatric sizes).
- Stethoscope; sphygmomanometer, tourniquets, tongue depressor.
- Flashlight.
- Intravenous solutions and tubing.
- Normal saline, Ringer's lactate.
- Syringes: variety of sizes.
- Needles: variety of sizes, including cardiac needle.
- Tracheostomy set, cut-down trays with sterile instruments.
- Necessary drugs and medication.

The following items should be on the emergency cart or immediately available:

- Defibrillator
- Electrocardiogram
- Blood pressure/pulse monitor
- Pulse oximeter (optional)

* If in a hospital or clinic, the emergency cart should conform with hospital or departmental policies and procedures but usually includes these listed items.

** Although oxygen can be administered in a variety of ways, use of partial non-rebreather masks is preferred because of their ability to deliver more oxygen to the patient.

**Medications:**

- Epinephrine 1:10,000, 10 ml preloaded syringe
- Epinephrine 1:1,000, 1 ml preloaded syringe
- Atropine 1 mg in 10 ml preloaded syringe
- Beta-Agonist inhaler
- Diphenhydramine for IM/IV injection
- Nitroglycerin (NTG) – 0.4 mg tabs, sublingual
## Appendix A
### Contrast Media Specifications

<table>
<thead>
<tr>
<th>Product</th>
<th>Chemical Structure</th>
<th>Anion</th>
<th>Cation</th>
<th>% Salt Concentration</th>
<th>% Iodine Concentration</th>
<th>Iodine+ (mg/l/ml)</th>
<th>Visocosity+ 25° C (cps)</th>
<th>Viscosity+ 37° C (cps)</th>
<th>Osmolality (mOsm/kg H₂O)</th>
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<td>Nonionic</td>
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<td>≈1.5</td>
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<td>Nonionic</td>
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<td>270</td>
<td>12.7*</td>
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<td>% Iodine Concentration</td>
<td>Iodine+ (mgl/ml)</td>
<td>Viscoesity+ 25° C (cps)</td>
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<td>Sodium</td>
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### GASTROINTESTINAL

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<th>370</th>
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<td>Diatrizoate</td>
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### URORADIOLOGICAL

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<th>Meglumine</th>
<th>30 14.1</th>
<th>141</th>
<th>194</th>
<th>1.42</th>
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<td>Meglumine</td>
<td>17.2 8.1</td>
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<td>(Instill for retrograde cystography and cystourethrography)</td>
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<td>43 20.2</td>
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<td>≈2</td>
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## MR CONTRAST MEDIA

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<th>Cation</th>
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<th>Viscosity+ 37°C (cps)</th>
<th>Osmolality (mOsm/kg H₂O)</th>
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<td>Magnevist* (Berlex)</td>
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<td>DTPA</td>
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<td>Gadoverse-tamide</td>
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<td>2.0</td>
<td>1110</td>
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<td>None</td>
<td>250</td>
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</table>

+ Data from product package inserts, product brochures, or technical information services.
* Measured at 20°C.
° Viscosities of most products intended for oral administration are not reported by manufacturers.
APPENDIX B

Criteria for the Use of Water-Soluble Iodinated Contrast Media for Intravascular Injections

The American College of Radiology adopts as policy the attached report of the Committee on Drugs and Contrast Media entitled: Current Criteria for the Use of Water-Soluble Iodinated Contrast Media for Intravascular Injection: 1997.

I. Introduction

The American College of Radiology Committee on Drugs and Contrast Media was given the charge to advise College members regarding the appropriate use of contrast agents. In undertaking this task, the Committee’s objective was to thoroughly review the scientific literature to date.

Recommendations have been formulated to provide as much protection as possible to individual patients receiving iodinated contrast media, while at the same time being cognizant of the importance of economic issues and the potential for efficacious alternative uses of healthcare dollars.

The previous report of this Committee represented the Committee’s recommendations based on the scientific evidence through May 1990. This report represents the Committee’s view based on scientific evidence available since that time. It must be recognized that the conclusions reached in this report are subject to revision as more evidence becomes available.

II. General Considerations

There is now more scientific information available regarding the incidence of adverse reactions from the use of contrast media. The Committee wishes to re-emphasize some general principles:

1. Regardless of clinical site, appropriately trained medical personnel, emergency medical equipment, and medication should be readily available to treat any adverse reaction that might occur.
2. All patients referred for intravascular contrast examinations should be appropriately screened for the presence of risk factors that might increase the likelihood of adverse reactions.
3. All patients undergoing an iodinated contrast study should be adequately prepared prior to the examination, including adequate hydration and appropriate premedication when indicated.
4. If significant contraindications to intravascular contrast agents are present, it is prudent to seriously consider alternative diagnostic procedures that could provide the necessary information.
5. The American College of Radiology recognizes the appropriateness of the use of any approved contrast agent, in accordance with the radiologist’s best judgment.

When the decision is made to perform a contrast examination, the individual radiologist taking care of a specific patient must make a decision regarding the use of either high-osmolality contrast media (HOCM) or low-osmolality contrast media (LOCM). It cannot be emphasized too strongly that each patient undergoing each type of contrast examination requires consideration of the specific situation. In the final analysis, the radiologist (in consultation with the referring physician when necessary) is responsible for that patient and the radiological examination the patient is to undergo, and is in the best position to design the study, properly prepare the patient...
as indicated by the specific clinical circumstances, and select the appropriate contrast material.

III. High-Osmolality Contrast Media

Iodinated high-osmolality contrast media (HOCM) has been used in radiological examinations for approximately 70 years. Since they were first introduced, there has been progressive improvement in the quality of these agents in terms of usefulness and safety. They are regarded as safe and effective by the medical community (including radiology) and the FDA (See the section on Incidence of contrast reactions and subsection on Premedication under Patient Selection and Preparation Strategies).

IV. Low-Osmolality Contrast Media

Iodinated low-osmolality contrast media (LOCM), most of which are nonionic agents, have been shown to be associated with less discomfort and have a lower incidence of minor (1% versus 5% for HOCM) and severe (0.015% versus 0.1% for HOCM) adverse reactions. Because of this, some radiological facilities have decided to use LOCM on all patients. Other radiological facilities have decided on the selective use of LOCM in patients at increased risk.

These patients include:

1. Patients with a history of any previous adverse reaction to intravascular iodinated contrast material, with the exception of a sensation of heat, flushing, or a single episode of nausea or vomiting.
2. Patients with asthma.
3. Patients with a previous serious allergic reaction to materials other than contrast agents.
4. Patients with known cardiac dysfunction, including recent or potentially imminent cardiac decompensation, severe arrhythmias, unstable angina pectoris, recent myocardial infarction, and pulmonary hypertension.
5. Patients with renal insufficiency (particularly those with diabetes).
6. Patients with generalized severe debilitation, as determined by a physician.
7. Patients at high risk for contrast extravasation.
8. Any other circumstances in which, after due consideration, the radiologist believes there is a specific indication for the use of LOCM.

Examples of this include but are not restricted to:

a. Sickle cell disease.
b. Patients at increased risk for aspiration.
c. Patients who are very anxious about the contrast procedure or who request or demand the use of LOCM.
d. Patients in whom the risk factors cannot be satisfactorily established.

REFERENCES

The American College of Radiology, with more than 30,000 members, is the principal organization of radiologists, radiation oncologists, and clinical medical physicists in the United States. The College is a nonprofit professional society whose primary purposes are to advance the science of radiology, improve radiologic services to the patient, study the socioeconomic aspects of the practice of radiology, and encourage continuing education for radiologists, radiation oncologists, medical physicists, and persons practicing in allied professional fields.

The American College of Radiology will periodically define new practice guidelines and technical standards for radiologic practice to help advance the science of radiology and to improve the quality of service to patients throughout the United States. Existing practice guidelines and technical standards will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.

Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council. The practice guidelines and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice guideline and technical standard by those entities not providing these services is not authorized.

2001 (Res. 51)  
Revised 2006 (Res. 51,34,35,36)  
Effective 10/01/06

ACR PRACTICE GUIDELINE FOR THE USE OF INTRAVASCULAR CONTRAST MEDIA

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment.
Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

This guideline has been developed to establish guidelines for the safe administration of intravascular contrast media used for imaging studies.

Intravascular contrast media are used for a wide variety of imaging studies. The majority of intravascular contrast-enhanced imaging examinations involve iodinated contrast media, but other contrast media may be used for magnetic resonance imaging, ultrasonic imaging, and angiography.

II. GOAL

The goal of radiologists and other personnel administering intravascular contrast media should be to utilize these agents appropriately and properly so that imaging studies are optimized and risk to the patient is minimized.

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A. Supervising Physician

The supervising physician should be a licensed physician with the following qualifications:

1. Certification in Radiology, Diagnostic Radiology, or Radiation Oncology by the American Board of Radiology, the American Osteopathic Board of Radiology, the Royal College of Physicians and Surgeons of Canada, or Le College des Medecins du Quebec.
   or
2. Completion of an Accreditation Council for Graduate Medical Education (ACGME) approved residency program or an American Osteopathic Association (AOA) approved residency program including radiographic training on all body areas, and have documentation of a minimum of 6 months of formal dedicated training in the interpretation and formal reporting of general radiographs for patients of all ages.
   or
3. The physician whose residency or fellowship training did not include the above may still be considered qualified to administer contrast media provided he or she can demonstrate sufficient knowledge of the pharmacology, indications, and contraindications for the use of contrast media to enable safe administration and has the ability to recognize and initiate treatment for adverse reactions.
   and
4. The supervising physician should be familiar with the various contrast media available and the indications and contraindications for each. The physician should also be familiar with patient preparation for the examination, including any necessary hydration or bowel preparation. He/she should have an understanding about the volume and concentration of the appropriate contrast media required for a given examination (see the ACR Manual on Contrast Media).
5. Personnel familiar with the various risk factors, preparation, and any necessary premedication strategies should perform appropriate history and preprocedural screening. It is necessary for the supervising physician or designee to acquire familiarity with the patient history (to include indications and risk factors that might increase the likelihood of adverse effects from contrast media). The supervising physician must be specifically aware of relative contraindications and pertinent risk factors. The physician has the responsibility for reviewing all indications for the examination, and for specifying the type, use, dosage, and rate of administration of contrast media (see the ACR Manual on Contrast Media).

6. The supervising physician must have appropriate knowledge of alternative imaging methods.

7. The person responsible for the injection, who may be a technologist or registered nurse, must be aware of the signs and symptoms of an adverse effect and must monitor the patient for the development of these signs and symptoms during the examination. The supervising physician, or his or her physician designee, must be immediately available to respond promptly to an adverse effect.

8. The supervising physician, or his or her physician designee, must be knowledgeable in the recognition and treatment of adverse effects (e.g., idiosyncratic reactions, extravasations) of contrast media used for these supervised studies. Training and proficiency in cardiopulmonary resuscitation are recommended for those who attend to patients undergoing contrast-enhanced examinations.

Continuing Medical Education

The physician’s continuing medical education should be in accordance with the ACR Practice Guideline for Continuing Medical Education (CME).

B. Radiologist Assistant

A radiologist assistant is an advanced level radiographer who is certified and registered as a radiologist assistant by the American Registry of Radiologic Technologists (ARRT) after having successfully completed an advanced academic program encompassing an ACR/ASRT (American Society of Radiologic Technologists) radiologist assistant curriculum and a radiologist-directed clinical preceptorship. Under radiologist supervision, the radiologist assistant may perform patient assessment, patient management and selected examinations as delineated in the Joint Policy Statement of the ACR and the ASRT titled “Radiologist Assistant: Roles and Responsibilities” and as allowed by state law. The radiologist assistant transmits to the supervising radiologists those observations that have a bearing on diagnosis. Performance of diagnostic interpretations remains outside the scope of practice of the radiologist assistant. 2006 (Res. 34)

C. Radiologic Technologist

The technologist should be responsible for patient comfort as well as for preparing and positioning the patient for the examination. Qualifications for technologists performing
intravenous injections of contrast media should be in compliance with current ACR policy statements\(^1\) and existing operating procedures or manuals at the imaging facility.

Certification by the American Registry of Radiologic Technologists (ARRT) or an unrestricted state license is required.

IV. WRITTEN REQUEST FOR THE EXAMINATION

The written or electronic request for an examination using IV contrast media should provide sufficient information to demonstrate the medical necessity of the examination and allow for the proper performance and interpretation of the examination.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). The provision of additional information regarding the specific reason for the examination or a provisional diagnosis would be helpful and may at times be needed to allow for the proper performance and interpretation of the examination.

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient’s clinical problem or question and consistent with the state scope of practice requirements. 2006 (Res. 35)

V. INTRAVASCULAR CONTRAST MEDIA

A. Iodinated

1. For specific details (e.g., nephrotoxicity and drug interactions) refer to the ACR Manual on Contrast Media.

2. Types of iodinated contrast media: Conventional ionic high-osmolality contrast media (HOCM) and low-osmolality contrast media (LOCM) of both ionic and nonionic types are considered safe for intravascular use by the FDA. Iodinated LOCM, most of which are nonionic agents, has been shown to be associated with less discomfort and have a lower incidence of adverse effects. A single iso-osmolality iodinated contrast media (IOCM) is currently available. There are only preliminary data on this agent at this time, so decisions concerning how or when to use it (instead of LOCM) have not been clearly defined.

3. Patients considered likely to benefit from use of LOCM are those who are at increased overall risk for adverse effects. They include:

   a. Patients with a history of any previous adverse effect from intravascular iodinated contrast media, with the exception of a sensation of heat, flushing, or a single episode of nausea or vomiting.

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\(^1\)The American College of Radiology approves of the injection of contrast material and diagnostic levels of radiopharmaceuticals by certified and/or licensed radiologic technologists and radiologic nurses under the direction of a radiologist or his or her physician designee who is personally and immediately available, if the practice is in compliance with institutional and state regulations. There must be prior written approval by the medical director of the radiology department/service of such individuals; such approval process having followed established policies and procedures, and the radiologic technologists and radiologic nurses who have been so approved maintain documentation of continuing medical education related to the materials being injected and to the procedure being performed. (Res. 1-H, 1987, 1997)
b. Patients with asthma.

c. Patients with previous serious allergic reactions to materials other than contrast media.

d. Patients with known cardiac dysfunction, including patients with risks for or recent acute congestive heart failure, dysrhythmia, unstable angina pectoris, recent myocardial infarction, or pulmonary hypertension.

e. Patients with renal insufficiency (particularly those with diabetes).

f. Patients with generalized severe debilitation, as determined by a physician.

g. Patients at high risk for contrast extravasation.

h. Patients receiving contrast by power injector.

i. Any other circumstances in which, after due consideration, the radiologist believes there is a specific indication for the use of LOCM. Examples include, but are not restricted to:
   i. Patients with sickle cell disease.
   ii. Patients at increased risk for aspiration.
   iii. Patients with suspected or known pheochromocytoma.
   iv. Patients with suspected or known myasthenia gravis disease.
   v. Patients who are very anxious about the contrast procedure or who request or demand the use of LOCM.
   vi. Patients in whom the risk factors cannot be satisfactorily established.

B. MR Contrast Media

1. For specific details refer to the ACR Manual on Contrast Media.

2. Extracellular gadolinium chelate agents are extremely well tolerated by the vast majority of patients. Adverse reactions are encountered with a much lower frequency than is observed after administration of iodinated contrast media, but severe reactions can occur.

3. Adverse events, including some that are severe, have also been noted with other types of intravascular MR contrast media.

4. The supervising physician and radiologic technologists should adhere to the qualifications for administering intravascular contrast medium as stated in Section III.

C. The ACR recognizes the appropriateness of the use of any FDA-approved contrast media, in accordance with the supervising physician’s best judgment.

VI. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Guideline for Communication of Diagnostic Imaging Findings. The use of contrast media for radiation therapy planning should be documented in an appropriate record.
VII. EQUIPMENT SPECIFICATIONS

Appropriate medications and resuscitation equipment must be readily available to treat serious, potentially life-threatening adverse effects.

VIII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

ACKNOWLEDGEMENTS

This guideline was revised according to the process described in the ACR Practice Guidelines and Technical Standards book by the ACR Committee on Drugs and Contrast Media.

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REFERENCES