MANUAL

ON

CONTRAST

MEDIA

VERSION 6
2008

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Preface

This Sixth Edition of the ACR Manual on Contrast Media replaces all earlier editions. It is being published as a Web-based document only so it can be updated as frequently as needed.

This manual was developed by the Committee on Drugs and Contrast Media of the ACR Commission on General, Small and/or Rural Radiology as a guide for radiologists to enhance the safe and effective use of contrast media. Suggestions for patient screening, premedication, recognition of adverse reactions, and emergency treatment of such reactions are emphasized. Its major purpose is to provide useful information regarding 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 media such as gadolinium or other compounds used for magnetic resonance imaging, as well as to the use of iodinated contrast media for gastrointestinal imaging.

The editorial staff sincerely thanks all who have contributed their knowledge and valuable time to this publication.

Members of the committee at the time of this edition are:

Arthur J. Segal, MD, Chair and Editor
James H. Ellis, MD, Vice Chair
Bruce R. Baumgartner, MD
Peter L. Choyke, MD
Richard H. Cohan, MD
Mervyn Cohen, MD
Kate A. Feinstein, MD
Julia R. Fielding, MD
Richard Jenkins, MD
Karl N. Krecke, MD
Carl M. Sandler, MD
David J. Spinosa, MD
David B. Spring, MD
Neil F. Wasserman, MD

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

INTRODUCTION

Various forms of contrast media have been used to improve medical imaging. Their value has long been recognized, as attested to by their common daily use 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 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 media reactions must be part of the environment in which all intravascular contrast media are administered.

Millions of radiological examinations assisted by intravascular contrast media are conducted each year in North America. Although adverse side effects are infrequent, 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 would 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, institutional policy, and departmental policy.

Usage Note: In this manual, the term “lower-osmolality” in reference to radiographic iodinated contrast media is intended to encompass both low-osmolality and iso-osmolality media, the former having osmolality approximately twice that of human serum, and the latter having osmolality approximately that of human serum. Also, unless otherwise obvious in context, this manual focuses on issues concerning radiographic iodinated contrast media.

PATIENT SELECTION AND PREPARATION STRATEGIES

General Considerations

The approach to patients about to undergo a contrast-enhanced examination has three general goals: 1) to assure that the administration of contrast is appropriate for the patient and the indication; 2) to minimize the likelihood of a contrast reaction; and 3) 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 media.

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 important. This is supported by the observation that sick patients are more likely to get sicker. Thus, hemodynamic, neurologic, and general nutritional status should be assessed.

In regard to specific risk factors, a history of a prior allergy-like reaction to contrast media is associated with an increased 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 major anaphylactic response to one or more allergens. A history of asthma may indicate 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 media should be questioned further to clarify the type and severity of the “allergy” or reaction, as these patients could be atopic and at increased risk for reactions.

Another specific risk category is renal failure. Questions should address whether the patient has a history of renal dysfunction (especially diabetic nephropathy and multiple myeloma-associated nephropathy) or is taking concurrent nephrotoxic medications (including aminoglycosides and amphotericin B). Contrast-induced nephropathy (CIN) is defined in terms of percentage or absolute rise in serum creatinine**.** Thus, testing of baseline blood urea nitrogen (BUN) and creatinine levels or calculation of an estimated glomerular filtration rate is useful in patients with suspected renal dysfunction. It is also important to ensure that all such patients are well-hydrated before, during, and after the contrast study. In patients with impaired renal function, the volume of contrast media should be limited if it is determined that an alternate examination (without the need for contrast media) cannot provide the necessary clinical information. More discussion of CIN can be found in the chapter on Contrast Nephrotoxicity.

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, attention should be paid to limiting the volume of the contrast media.

A general category that deserves attention is emotional state. There is anecdotal 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 patients to irreversible renal failure after contrast administration due to tubular protein precipitation and aggregation. This hazard may be prevented with good hydration; 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 to 12 hours before contrast medium use and continuing for at least 6 to 12 hours after.

Age, apart from the general health of the patient, is not a major consideration in patient preparation. In infants and neonates, contrast volume is an important consider-ation because of the low blood volume of the patient and the hypertonicity (and potentially detrimental cardiac effects) 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.

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 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. This can occur after the administration of any iodinated contrast media. 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 an iodinated radiographic contrast medium (intravascular or oral) may be contraindicated; consultation with the ordering clinician prior to contrast administration in these patients is recommended.

Intravenous injections may cause heat and discomfort but rarely cause pain unless there is extravasation. 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, low-osmolality contrast media or

iso-osmolality contrast media are generally indicated.

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

1. **H**istory – A careful, focused history is the necessary first step. Details about prior reactions and allergy history should be carefully evaluated.
2. **H**ydration – 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. **H**ave equipment and expertise ready – Serious reactions are rare, but establishing a method of reacting to and treating them requires prior planning and cannot be left to the time at which they occur.
4. **H**eads 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. In this context, "at risk" means at higher risk for an acute allergic-like reaction. Such regimens have been shown in clinical trials to decrease the frequency of contrast media 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.

Cortiocosteroids are the essential component and should be included in any premedication protocol, unless there are very clear contraindications to their use.

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

1. Prednisone – 50 mg by mouth at 13 hours, 7 hours, and 1 hour before contrast media injection, *plus*

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

2. Methylprednisolone (Medrol®) – 32 mg by mouth 12 hours and 2 hours before contrast media injection. An antihistamine (as in option 1) can also be added to this regimen.

Lasser et al have demonstrated that use of nonionic contrast media combined with a premedication strategy including cortico-steroids results in a 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 media 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. Supple-

mental 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.

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 premedication 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. For these patients, there is a slight chance that a recurrent reaction may be more severe than the first reaction; however, it is more likely that the reaction will be the same or less severe or that there will be no recurrence of adverse symptoms at all.

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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 by 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. For current American College of Radiology (ACR) recommendations regarding injection of contrast media (including radiopharmaceuticals) see the ACR Practice Guideline for the Use of Intravascular Contrast Media.

Referring to the FDA-mandated package inserts may be appropriate in determining the contrast media doses and concentrations (see Appendix A, Contrast Media Specifications). It is important to avoid prolonged admixture of blood and contrast media, in syringes and catheters whenever possible, due to the risk of clots forming. In general, unless known to be safe, the admixture of contrast media and *any* medication should be avoided. However, heparin may be combined with contrast media..

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. (See the Chapter on Extravasation of Contrast Media.) 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 media 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 (e.g., 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 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 is encountered during the first 15 seconds, 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 contrast media through 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 media 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 limits. For power injection of contrast media through some 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.

Recent studies demonstrate that current PICCs (peripherally inserted central catheters) vary in their ability to tolerate power injection of CT contrast media for non-CT angiography studies. Data suggest that standard PICCs can tolerate injections of contrast media at rates up to 2 ml/sec. Certain specifically designed PICCs can tolerate injection rates up to 5 m/sec. The manufacturer's recommendations should be followed.

Air Embolism

Clinically significant venous air embolism is a potentially fatal but extremely rare complication of intravenous contrast media injection. Clinically "silent" venous air embolism, however, commonly occurs when an 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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EXTRAVASATION OF CONTRAST MEDIA

Frequency

The reported incidence of intravenous contrast media extravasation related to power injection for CT has ranged from 0.1% to 0.9% (1/1,000 patients to 1/106 patients). Extravasation can occur during hand or power injection. 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.

Initial Signs and Symptoms

Although most patients complain of initial swelling or tightness, and/or stinging or burning pain at the site of extravasation, some experience little or no discomfort. On physical examination, the extravasation site may be edematous, erythematous, and tender.

Sequelae of Extravasations

Extravasated iodinated contrast media are toxic to the surrounding tissues, particularly to the skin, producing an acute local inflammatory response that peaks in 24-48 hours. The acute tissue injury resulting from extravasation of iodinated contrast media is possibly related primarily to the hyper-osmolality of the extravasated fluid. Despite this, the vast majority of patients in whom extravasations occur recover without significant sequelae. Only rarely will a LOCM extravasation injury proceed to a severe adverse event.

Most extravasations are limited to the immediately adjacent soft tissues (typically the skin and subcutaneous tissues). Usually there is no permanent injury, but skin ulceration and tissue necrosis can occur as severe manifestations and can be encountered as early as six hours after the extravasation has occurred. A compartment syndrome may be produced as a result of mechanical compression. A compartment syndrome is more likely to occur after extravasation of larger volumes of contrast media; however, it also has been observed after extravasation of relatively small volumes, especially when this occurs in less capacious areas (such as over the ventral or dorsal surfaces of the wrist). The most commonly reported severe injuries after extravasation of LOCM are compartment syndromes.

A recent study has illustrated the infrequency of severe injuries after LOCM extravasation. In a 2007 report by Wang et al only one of 442 adult LOCM extravasations resulted in a severe injury (a compartment syndrome), although three other patients developed blisters or ulcerations that were successfully treated locally.

Evaluation

Because the severity and prognosis of a contrast medium extravasation injury are difficult to determine on initial evaluation of the affected site, close clinical follow-up for several hours is essential for all patients in whom extravasations occur.

Treatment

There is no clear consensus regarding 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.

There is no consistent evidence that the effects of an extravasion can be mitigated effectively by trying to aspirate the extravasated contrast medium through an inserted needle or angiocatheter, or by local injection of other agents such as corticosteroids or hyaluronidase.

Outpatients who have suffered contrast media 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. Clear instructions should be given to the patient to seek additional medical care, should there be any worsening of symptoms, skin ulceration, or the development of any neurologic or circulatory symptoms, including paresthesias.

Surgical Consultation

Surgical consultation prior to discharge should be obtained whenever there is concern for a severe extravasation injury. 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. It is important to note that initial symptoms of a compartment syndrome may be relatively mild (such as limited to the development of focal paresthesia).

In a previous edition of this manual, it was suggested that surgical consultation should be obtained automatically for any large volume extravasations, particularly those estimated to be in excess of 100 ml; however, more recently it has been suggested that reliance on volume threshold is unreliable and that the need for surgical consultation should be based entirely on patient signs and symptoms. 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.

Patients at Increased Risk for Extravasations

Certain patients have been found to be at increased risk for extravasations, 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.

Patients at Increased Risk for a Severe Extravasation Injury Once an Extravasation Occurs

A severe extravasation injury is more likely to result from an extavasation in patients with arterial insufficiency or compromised venous or lymphatic drainage in the affected extremity. In addition, extravasations involving larger 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.

Documentation

All extravasation events and their treatment should be documented in the medical record, especially in the dictated imaging report of the obtained study, and the referring physician should be notified.

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INCIDENCE OF ADVERSE EFFECTS

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. Underreporting 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% to 12% of all patients who receive ionic, high-osmolality contrast media (HOCM). Many patients experience physiologic disturbances (e.g., warmth or heat), and this is often not recorded. The use of HOCM for intravascular use is now uncommon.

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 HOCM and in 1 or 2 per 10,000 examinations using low-osmolality contrast media (LOCM). Cochran reported an overall incidence of 0.2% for non-ionic contrast administered at a single institution. Severe reactions totaled 0.05%. A slightly higher overall incidence (0.7%) was reported from a second institution upon review of 29,508 patients given iopromide over a 2-year period.

The incidence of fatal outcome from a contrast media injection is not known with precision. Older literature from the HOCM era cited rates of fatal outcome from contrast media injections as high as 1 per 40,000 intravenous administrations. However, in the large Japanese study [Katayama et al.] of the late 1980s, no fatal reactions were attributed to either HOCM or LOCM despite over 170,000 injections of each. The conservative estimate of 1 fatality per 170,000 contrast media administrations is thus often quoted, but the exact incidence is not known. Current low fatality rates likely reflect the widespread use of LOCM with its lower rate of severe reactions as well as improvements in treatment of reactions when they occur.

Although most serious reactions occur in the immediate postinjection period, delayed reactions have been reported to occur with an incidence of up to 2% (see following section on Adverse Effects of Iodinated Contrast Media).

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ADVERSE EFFECTS OF IODINATED CONTRAST MEDIA

The general frequency of adverse events related to the administration of contrast media has decreased considerably with changes in usage from high-osmolality agents to lower-osmolality agents. While the incidence of mild and moderate reactions have decreased, severe and life-threatening adverse events continue to occur unpredictably, and appropriate training of, and vigilance by, health care workers are necessary in areas where contrast media are administered.

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

The effects of dose, route, and rate of delivery of contrast media on the incidence of 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. Any contrast media administration, regardless of route, may result in an adverse event, ranging from mild discomfort to a severe, life-threatening reaction.

Pathogenesis Mechanisms

Presentations appear identical to an anaphylactic reaction to a drug or other allergen, but since an antigen-antibody response has not been identified, such a reaction is classified as "anaphylactoid." Or as "non-allergic anaphylactic". Treatment, however, is identical to that for an allergic anaphylactic reaction.

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

Physiologic mechanisms may relate to the specific chemical formulation of the contrast media, most notably chemotoxicity and hypertonicity, or to binding of the small contrast media molecule to activators. Patient anxiety may contribute to adverse events. Additives or contaminants 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 a contrast reaction is not yet possible, although it is clear that certain patients are at increased risk of a reaction.

In some cases, the cause of an adverse event can be identified. The etiology of cardiovascular effects, for example, is complex but to some extent definable. Some effects, such as hypotension and tachycardia, are 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 media.

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 media 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 characterized by hypotension with bradycardia. Pathogenesis is unknown, but the response is thought to be the result of increased vagal tone arising from the central nervous system. The effects of increased vagal tone include depressed sinoatrial and atrioventricular nodal activity, inhibition of atrioventricular conduction, and peripheral vasodilatation. Vasovagal reactions are related to anxiety and 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 should be treated and observed closely until they resolve fully, as they may progress to cardiovascular collapse or be associated with angina or seizure secondary to clinically significant hypo-tension. (See Table 6 – Management of Acute Reactions in Adults.)

Obtaining a focused patient medical history prior to the administration of contrast media is critically important. 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 may range from 8% to perhaps as high as 30%. Pre-existing medical conditions can also foreshadow adverse events. Urticarial reactions 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 cardio-vascular disease, such as aortic stenosis or severe congestive heart failure.

It is very important that all personnel who administer contrast media be prepared to recognize the variety of adverse events that may occur, monitor the patient, and institute the appropriate measures. These measures may range from notifying the radiologist, to administering medication, to calling a code. Knowledge about the varying adverse effects of contrast media is important, as it will guide the choice of therapy.

Special Circumstances

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

Types of Reactions

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

Reactions are most often mild but can be life threatening. Prediction of occurrence or severity is impossible, although there are some known risk factors, and anticipation and vigilance are critical. In general, it is not possible to classify the etiology of an adverse event following contrast media administration, but it is possible to clarify and classify severity and begin supportive measures.

Mild Reactions

Some reactions, specifically nausea and vomiting, increase in incidence with increasing osmolality. For example, the frequency of urticarial reactions was increased with the use of high-osmolality ionic contrast media. Urticarial reactions are almost always mild, although it can progress to moderate severity. Mild reactions do not require treatment, but, as noted, they may presage or evolve into a more severe reaction. Any patient with any reaction should, therefore, be observed for 20 to 30 minutes, or as necessary, to ensure clinical stability and recovery.

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 lower-osmolality contrast agents. Similarly, sensations of warmth or flushing are an unpleasant physiologic response of very short duration and not indicative of an adverse event.

Moderate Reactions

Moderate adverse events, by definition, are not immediately life threatening (although they may progress to be so) but often require treatment. These events include symptomatic urticaria, vasovagal reaction, mild bronchospasm, and tachycardia secondary to transient mild hypotension. Moderate reactions require close monitoring until they resolve completely. Treatment may include diphenhydramine for symptomatic hives, use of a beta-agonist inhaler for bronchospasm, or leg elevation and/or fluid therapy for hypotension. It is appropriate to consider securing IV access and providing oxygen.

Severe Reactions

Severe adverse events are potentially or immediately life threatening. Although they are rare, it is imperative that all personnel who administer contrast media be aware that they occur unpredictably and that they require prompt recognition and treatment. Patients may initially experience a variety of symptoms and signs, ranging from anxiety to respiratory distress, diffuse erythema, or sudden cardiac arrest.

Complete cardiopulmonary 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 observed closely during the procedure. Since the outcome of cardiopulmonary arrest worsens as the response time increases, prompt recognition of such reactions and rapid institution of treatment are crucial.

Severe adverse events also include profound vasovagal reactions, moderate and severe bronchospasm, laryngeal edema, seizure, severe hypotension, and cardiac arrest. Pulmonary edema may also occur, particularly, but not exclusively, in patients with underlying cardiac compromise.

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 specific therapies are dealt with elsewhere.

Venous thrombosis can occur in response to infusion of contrast. This is related to direct vascular endothelial damage and is more of a problem with high-osmolality media. Contrast media 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 media 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.

Renal effects of contrast media have attracted increased attention over the last few years with the aging of the population and the increased use 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 patients with decreased body mass who are known to have a decrease in their 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.

In summary, contrast media, acting through various poorly understood mechanisms, can be associated with a variety of adverse events. These events range from trivial to profound and reliable prediction of such reactions is not currently possible. The health care team should be knowledgeable about specific adverse events, risk factors, and signs and symptoms, as well as the need for routine thoughtful patient observation. Personnel must be similarly prepared for expeditious and appropriate treatment when indicated.

Delayed Reactions to Contrast Media

Reactions that are not acute have long been a source of concern with both iodinated and gadolinium-based contrast media. Currently, delayed reactions to gadolinium media in the form of nephrogenic systemic fibrosis (NSF, also known as nephrogenic fibrosing dermopathy) are a major concern, and are dealt with in detail elsewhere in this manual.

Many different symptoms and signs have been reported as delayed reactions associated with iodinated contrast media. Some relatively common ones are nausea, vomiting, drowsiness, headache, and pruritus without urticaria, all of which are self-limited and usually do not require therapy. Delayed cardiopulmonary arrest has also been reported, but this and other severe systemic reactions are probably related to etiologies other than the contrast media.

Currently, other than contrast-induced nephropathy, the delayed reactions to contrast media that are of most frequent concern are the cutaneous ones. These are important for several reasons: they occur more often than is generally recognized; they may recur; they may have serious sequellae; and, perhaps most importantly, they are often ascribed to causes other than contrast media.

The incidence of delayed adverse cutaneous reactions has been reported to range from 0.5% to 9%. Some are moderate to severe in distribution and associated symptoms. Delayed cutaneous reactions are more common in patients treated with interleukin-2 (IL-2) therapy.

The onset of delayed cutaneous reactions ranges from 3 hours to 7 days following the administration of a contrast agent. For several reasons (lack of awareness of such adverse events, usual practice patterns, relatively low frequency of serious outcomes), they are often not brought to the attention of the radiologist and are ascribed to other causes because contrast agents have a biologic half-life of less than one hour, are too small to function unbound as antigens, and are minimally protein bound.

Delayed cutaneous reactions present with an exanthem that varies widely in size and distribution. The manifestations are often macular but may be maculopapular or pustular or may resemble angioneurotic edema, and are usually associated with pruritus. They are generally self limited and require only minimal symptomatic therapy. They may, however, progress to severe

symptomatology with wide distribution. Cases have been reported that resemble Stevens-Johnson syndrome, toxic epidermal necrolysis, or cutaneous vasculitis, and one fatality has even been described. When the rash is limited, symptomatic therapy such as corticosteroid creams can be used; if it is progressive or widespread, or if there are significant associated symptoms, consultation with allergy or dermatology services is an appropriate early step.

These adverse events are also unusual in that there is a high rate of recurrence, particularly if the same contrast medium is used but also with a different specific contrast. The true recurrence rate is not known, but anecdotally it is greater than 25%. Delayed cutaneous reactions are not, however, associated with other acute adverse events such as bronchospasm or laryngeal edema. The etiology, as with most significant contrast-related complications, is not clear. Because of the tendency to recur and because of the associated symptomatology, these reactions are thought to be T-cell mediated. The effectiveness of prophylaxis, particularly with oral corticosteroids, is unknown.

In summary, delayed cutaneous reactions are relatively frequent and are often mistakenly thought to be caused by another inciting media, in part because of the physiology of contrast media, and in part because many radiologists are (not surprisingly) unaware that such reactions occur. Their overall incidence appears to be increased after the use of a non-ionic dimer, as is the likelihood that such reactions will be moderate or severe. These adverse events appear to be true delayed-hypersensitivity reactions and tend to recur if a contrast medium is administered again, particularly if the same agent is used. Their onset ranges from three hours to a week after contrast administration. These reactions should be followed closely, documented thoroughly, and treated symptomatically with the realization that symptoms and signs may be clinically significant.

Other Adverse Effects

Iodide “mumps” (salivary gland swelling) and a syndrome of acute polyarthropathy are two delayed reactions that can occur with either high-osmolality or low-osmolality contrast media and that may be more frequent in patients with renal dysfunction.

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CONTRAST NEPHROTOXICITY

Definition

Nephrotoxicity is attributed to radiologic iodinated contrast media when there has been a sudden change in renal status after the administration of a contrast medium and no other etiology appears likely from the clinical records. The risk of nephrotoxicity is related to the degree of pre-existing renal disease and hydration. Clinically significant nephrotoxicity after administration of iodinated contrast media is highly unusual in patients with normal renal function.

There is no standard definition for reporting contrast media-induced nephrotoxicity (CIN); definitions used have included percent change in the baseline serum creatinine (e.g., a 20% to 50% rise in serum creatinine) and absolute elevation from baseline (0.5 to 2.0 mg/dl). Studies also vary in the length of time and number of data points over which serum creatinine was obtained following contrast media administration, but few studies have followed patients for more than 72 hours. Porter defined CIN 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 CIN 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 CIN, therefore, varies depending on the definition used. The clinical significance of these definitions remains open to debate. 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.

Serum creatinine has 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 (GFR) — 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." Although direct measurement of GFR with inulin or a similar clearance marker would be most accurate in defining renal function before and after contrast administration, this 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 or Modification of Diet in Renal Disease [MDRD] formula; calculators are available on various Web pages), however a 2006 survey of radiologists indicated that this is rarely done in practice. Furthermore, the clinical benefit of using calculated creatinine clearance in assessing CIN risk is uncertain because much of our published knowledge comes from studies that used only serum creatinine measurements. Indeed, the threshold values at which different clinical actions should be taken (e.g., active intravenous hydration, avoidance of contrast material administration) are neither proven nor generally agreed upon for either serum creatinine measurement or calculated creatinine clearance.-

Another confounding variable in the literature is whether the contrast media were injected intravenously or intra-arterially. Many of the studies of CIN are obtained from patients undergoing cardiac catheterization. Such patients are more likely to have diabetes and hypertension and are thus at higher risk. Many of these studies investigate contrast media effects in patients who are sick enough to be inpatients long enough to obtain the postcontrast creatinine measurements. Additionally, there may be nephrotoxic effects from the angiography procedure itself (e.g., atherosclerotic emboli). Therefore data from cardiac angiography studies may be applicable in that situation but may not predict how the

general population of patients undergoing computed tomography (CT) studies will do when the contrast media are injected intravenously.

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 CIN is not fully understood. Renal effects are seen with high-osmolality ionic contrast media (HOCM), low-osmolality contrast media (LOCM), and iso-osmolality contrast media (IOCM). Etiologic factors that have been suggested include: 1) renal hemodynamic changes (vasoconstriction) and 2) direct tubular toxicity of the contrast material. Both osmotic and chemotoxic mechanisms may be involved, and some investigations suggest agent-specific chemotoxicity. Regardless, it does appear that the nephrotoxicity of contrast media is related to the dose administered.

Risk Factors

Numerous studies have attempted to isolate risk factors for CIN. The classic review by Byrd and Sherman listed predisposing factors for radiologic contrast media-induced acute renal failure as pre-existing renal insufficiency (serum creatinine level $\geq$1.5 mg/dl), diabetes mellitus, dehydration, cardiovascular disease and the use of diuretics, advanced age ($\geq$70 years), myeloma, hypertension, and hyperuricemia. However, studies by Parfrey et al and Schwab et al documented that the patients at highest risk for developing contrast media-induced acute renal failure are those with both diabetes *and* pre-existing renal insufficiency. These investigators did not find that, given equal states of hydration, either diabetes alone or 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 seems to be changing, as people are becoming healthier at older ages.

Consequence

The clinical course of contrast-associated nephrotoxicity depends on baseline renal function, coexisting risk factors, degree of hydration, and the dose of radiologic contrast medium. 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 unusual for patients to develop permanent renal failure, and this usually occurs in the setting of multiple risk factors. However, when chronic renal failure develops it is associated with lifelong morbidity.

Patients who are taking the antihyperglycemic agent metformin are not at increased risk of CIN compared to other similar patients not on metformin. However, there is the risk of metformin-related complications if such patients were to develop CIN and their renal excretion of metformin were to diminish (see section on Metformin).

Prevention or Amelioration

Avoidance of Iodinated Contrast Media

The risk of developing CIN is not an absolute but a relative (and often weak relative) contraindication to the administration of intravascular iodinated contrast media. Indeed, with the use of the maneuvers described below to reduce risk, and the usual short clinical course of CIN, the risk of clinically relevant renal dysfunction is very low in many situations. In other cases, the risk may be sufficiently great, and the information that may be obtained by using alternative or no contrast media (e.g., carbon dioxide angiography, noncontrast CT) or by other modalities (e.g.,

ultrasound or magnetic resonance imaging [MRI]) may be sufficiently useful, that intravascular iodinated contrast may be avoided. (See the chapter on Adverse Reactions to Gadolinium-Based Contrast Media for a discussion on the risk of development of nephrogenic systemic fibrosis (NSF) following administration of gadolinium chelates to patients with renal disease). In some clinical situations, the use of iodinated contrast media may be necessary regardless of CIN risk. The use of the minimum dose of radiographic iodinated contrast media that provides sufficient diagnostic information may reduce risk.

Choice of Iodinated Contrast Media

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 where the risk is low. 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 that are isotonic to blood have an additional advantage remains to be investigated thoroughly. Various studies, with differing LOCM as the comparison agent to an IOCM and different routes of administration (intra-arterial vs. intra-venous), have produced differing results, some positive and some negative. All studies (at present) have been small in patient numbers.

Aspelin et al were among the first to suggest that the isosmolality contrast agent iodixanol was associated with a lower risk of CIN. Subsequent reports (Barrett 2006, Feldkamp, Liss, Solomon 2007) have failed to establish a clear advantage of iodixanol over the other lower-osmolality contrast media with regard to CIN whether administered intravenously or intra-arterially.

Hydration

Not all clinical studies have shown dehydration to be a major risk factor for CIN. 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 media because of low tubular flow rates. Solomon et al studied patients with chronic renal insufficiency who underwent cardiac angiography. The incidence of CIN 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. In another study, intravenous 0.9% saline hydration was shown to reduce CIN risk more than 0.45% saline hydration. Hydration with sodium bicarbonate may be more effective than using 0.9% saline, but the data are limited at present.

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

The efficacy of N-acetylcysteine, an antioxidant, to reduce the incidence of contrast media-associated renal insufficiency is controversial. A number of individual studies, and a number of meta-analyses, have disagreed as to whether this agent reduces the risk of CIN. There is evidence that it reduces serum creatinine in normal volunteers without changing cystatin C (said to be a better marker of GFR than serum creatinine). This raises the possibility that N-acetylcysteine might be simply

lowering serum creatinine so patients do not meet the laboratory criteria for CIN but not preventing any renal damage. Considerably more investigation is needed. Therefore, 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 popular 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, and has few contraindications (although allergic reactions have been reported). However, higher doses may be more effective if the agent is effective at all, and there is controversy over whether solid (not currently available in the USA) or liquid preparations are equally effective. Alternatively, a regimen of intravenous 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 CIN. It may actually not occur if renal function (as opposed to serum creatinine) is truly normal. Indeed, Rao and Newhouse have argued that few properly controlled studies of intravenous use of iodinated contrast media have been published; in a literature review they found only two properly controlled studies and neither demonstrated renal damage from intravenous iodinated contrast media. 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.

There is no universally agreed upon threshold of serum creatinine elevation (or degree of renal dysfunction) beyond which iodinated contrast media should not be administered. In a survey of radiologists by Elicker et al published in 2006, it was clear that policies regarding the cutoff value for serum creatinine varied widely among radiology practices. Thirty-five percent of respondents used 1.5 mg/dL, 27% used 1.7 mg/dL, and 31% used 2.0 mg/dL (mean, 1.78 mg/dL) as a cutoff value in patients with no risk factors other than elevated creatinine; threshold values were slightly lower in diabetics (mean 1.68 mg/dL). Patients in end-stage renal disease who have no remaining natural renal function are no longer at risk for CIN and may receive LOCM or IOCM (but see "Renal Dialysis Patients and the Use of Contrast Media" below in this section).

The major preventive action against CIN is to ensure adequate hydration. If the patient cannot be hydrated orally, one should consider intravenous infusion of 0.9% saline at 100 ml/hr in adults, beginning 6 to 12 hours before and continuing 4 to 12 hours after the administration of contrast media. For patients with renal insufficiency, only LOCM or IOCM should be used.

Addition of a medication that may mitigate the nephrotoxic effect of iodinated radiographic contrast media, e.g., N-acetylcysteine, can 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 media. 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.
- Prior renal surgery.
- Certain medications:
  - Metformin or metformin-containing drug combinations.
  - Nonsteroidal anti-inflammatory drugs.
  - Regular use of nephrotoxic antibiotics, such as aminoglycosides.

(Routine blood urea nitrogen (BUN) testing 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.

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 have 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 media, 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 use LOCM or IOCM (rather than HOCM) to reduce the 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.

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METFORMIN

Metformin is a biguanide oral antihyperglycemic agent used to treat patients with non-insulin-dependent diabetes mellitus. It is available as a generic drug as well as in proprietary formulations, alone and in combination with other drugs (see Table A at the end of the section for some of the brand-name formulations). The drug was approved in the United States 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. This condition is estimated to occur at a rate of 0 to 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 comorbid factors, most often cardiovascular or renal disease. There are no documented cases of metformin-associated lactic acidosis in properly selected patients.

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 (see Table B). Iodinated X-ray contrast media are not an independent risk factor for patients taking metformin but 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 potential clinical concern. Of metformin associated lactic acidosis cases reported worldwide between 1968 and 1991, 7 of the 110 patients received iodinated contrast media before developing lactic acidosis. The metformin package insert approved by the U.S. Food and Drug Administration 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 known or incipient 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.

Management

The management of patients taking metformin should be guided by the following:

1. Evidence suggesting clinically significant CIN induced by intravenous contrast injection is weak to nonexistent in patients with normal renal function [4].
2. Iodinated contrast is not an independent risk factor for patients taking metformin, but it is a concern in the presence of underlying conditions delaying renal excretion of metformin or decreased metabolism of lactic acid or increased anaerobic metabolism.
3. There have been no reports of lactic acidosis following intravenous contrast injection in properly selected patients.
4. In elderly patients, preliminary estimates of renal function relying on serum creatinine levels may be misleading and overestimate the adequacy of renal function.

Category I

In patients with normal renal function and no known comorbidities (see Table B), there is no need to discontinue metformin prior to intravenously administering iodinated contrast media, nor is there a need to check creatinine following the test or procedure before instructing the patient to resume metformin after 48 hours.[1]

Category II

In patients with multiple comorbidities (see Table B) who apparently have normal renal function, metformin should be discontinued at the time of an examination or procedure using intravascular iodinated contrast media and withheld for 48 hours. Communication between the radiologist, the health care 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. A repeat serum creatinine measurement is not mandatory.[1] If the patient had normal renal function at baseline, was clinically stable, and had no intercurrent risk factors for renal damage (e.g., treatment with aminoglycosides, major surgery, heart failure, sepsis, repeat administration of large amounts of contrast media), metformin can be restarted without repeating the serum creatinine measurement.

Category III

In patients taking metformin who are known to have renal dysfunction, metformin should be suspended at the time of contrast injection, and cautious follow-up of renal function should be performed until safe reinstitution of metformin can be assured.

Metformin and Gadolinium

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.

[1]The ACR Committee on Drugs and Contrast Media recognizes that the U.S. Food and Drug Administration (FDA) guidelines for metformin advise that for patients in whom an intravascular contrast study with iodinated materials is planned, metformin should be temporarily discontinued at the time of or before the study, and withheld for 48 hours after the procedure and reinstituted only after renal function has been re-evaluated and found to be normal. However, the committee concurs with the prevailing weight of clinical evidence on this matter that deems such measures unnecessary.

Table A

Medications containing Metformin*

Generic Ingredients	Trade names
Metformin	Glucophage
	Glucophage XR
	Fortamet
	Glumetza
	Riomet
Glyburide/metformin	Glucovance
Glipizide/metformin	Metaglip
Pioglitazone/metformin	ActoPlus Met
Rosiglitazone/metformin	Avandamet

*As of February, 2007. Additional medications containing metformin may have become available since then.

Table B

Comorbidities for Lactic Acidosis with use of Metformin

Decreased Metabolism of Lactate
- Liver dysfunction
- Alcohol abuse

Increased Anaerobic Metabolism
- Cardiac failure
- Myocardial or peripheral muscle ischemia
- Sepsis or severe infection

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REACTIONS TO IODINATED CONTRAST MEDIA IN CHILDREN

Children have a lower frequency of contrast reactions than adults. They tend to have anaphylactoid or non-allergic anaphylactic 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 to 3.0 ml of 280 to 300 mgI/ml per kg of body weight to a maximum of 150 ml in those weighing 50 kg or greater. There is a reported minor reaction rate of 3% for ionic contrast media and 0.9% for low-osmolality contrast media (LOCM). In addition to fewer reactions, LOCM have 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 have become the conventional agents for intravascular inject, but in any event, LOCM are 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 reactions immediately. Treatment for minor reactions is usually observation or administration of anti-histamines such as diphenhydramine (Benadryl®). If the reaction progresses, subcutaneous epinephrine 1:1,000 may be needed (see Table 5).

Severe reactions include bronchospasm, laryngeal edema, hypotension, pulmonary edema, and, very rarely, cardiac arrest. After prompt evaluation, help should be summoned and appropriate resuscitation initiated. Treatment depends on the type of reaction. Oxygen administration is vital and needs to be initiated immediately along with monitoring of the electro-cardiogram, oxygen saturation by pulse oximeter, and blood pressure. For bronchospasm, an inhaled beta-agonist should be given. Patients with asthma may have an inhaler with them. Corticosteroids may be administered 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, Management of Acute Reactions in Children). For pulmonary edema, a diuretic should be given intravenously. In patients who have hypotension, the legs should be elevated. Blankets, heat lamps, and/or heat packs should be used to provide warmth. Intravenous or intraosseous fluids should be administered. In those with hypotension and bradycardia, atropine is recommended.

Children's airways are smaller and more easily compromised than adults' 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 children of different sizes. 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. They 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.

Water soluble contrast media 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 re-evaluation with barium if an initial study with iodinated contrast medium fails to demonstrate a suspected perforation, because small leaks that are undetected with water-soluble media may be more readily demonstrated by barium sulfate media.

In those patients for whom barium sulfate is contraindicated, guidelines for the use of lower-osmolality contrast media (LOCM) rather than high osmolality contrast media (HOCM) for aqueous contrast media include the following:

1. Oral administration to children and adults who are at risk for aspiration.

   When aspirated, LOCM are much less likely to cause pulmonary edema than HOCM because of their lower osmolality. Iso-osmolality nonionic contrast media may be used in children at risk for aspiration and for evaluation of tracheo-esophageal fistula. Water-soluble media are completely absorbed from the lungs, unlike barium which 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 lower-osmolality 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, their use is recommended for evaluating the small bowel in infants and young children. Additionally, the lower osmolality of lower-osmolality contrast media 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 media enemas. A 100-175 mgI/ml HOCM solution is recommended for well-hydrated infants. Premature infants can be treated with

isotonic nonionic contrast media.

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

Contraindications

Known prior moderate or severe reaction to iodinated contrast media is a contra-indication. A small percentage of iodinated contrast media (approximately 1% to 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 nonionic LOCM are safer for these patients.

HOCM in hypertonic concentrations 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. Preparations made from nonionic LOCM are preferable for these patients because for any given required radiographic density, the LOCM version will have lower osmolality. In addition, when there is a risk of aspiration, nonionic contrast is safer than ionic contrast.

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 to 367 mgI/ml solution is recommended for evaluating the esophagus, stomach, or small bowel in adults. A 150 to 180 mgI/ml solution is effective for upper gastrointestinal examination in children up to 5 years of age. A 90 to 150 mgI/ml solution is effective for colon enema in adults and children.

Computed Tomography Indications

Orally administered contrast 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 for use in CT 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 HOCM). Therefore, aspiration and

hypovolemia are not specific contra-indications 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 unit opacity in the proximal bowel and higher Hounsfield unit opacity in the distal bowel. A solution containing 13 to 15 mgI/ml is recommended for oral and rectal administration in adults. A 7 to 9 mgI/ml solution is recommended for oral and rectal administration in infants and small children.

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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. Gadolinium chelates are extremely well tolerated by the vast majority of patients in whom they are injected. Acute **a**dverse reactions are encountered with a much lower frequency than is observed after administration of iodinated contrast media.

Adverse Reactions

The frequency of all acute adverse events after an injection of 0.1 or 0.2 mmol/kg of gadolinium chelate ranges from 0.07% to 2.4%. 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% to 0.7%. A rash, hives, or urticaria are the most frequent of this group, and very rarely there may be bronchospasm. Severe, life-threatening anaphylactoid or non-allergic anaphylactic reactions are exceedingly rare (0.001% to 0.01%). 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 severe reactions. Fatal reactions to gadolinium chelate agents occur but are extremely rare.

Gadolinium chelates administered to patients with acute renal failure or severe chronic kidney disease can result in a syndrome of nephrogenic systemic fibrosis (NSF) (See chapter on NSF).

Risk Factors

The frequency of acute adverse reactions to gadolinium contrast media is about 8 times higher in patients with a previous reaction to gadolinium-based contrast media. Second reactions to gadolinium-based media 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%. Although there is no cross-reactivity, patients who have had previous allergic-like reactions to iodinated contrast media are also in this category.

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

Nephrotoxicity

Gadolinium agents are considered to have no nephrotoxicity at approved dosages for MR imaging. 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 media. However in view of the risk of NSF in patients with severe renal dysfunction, this practice should only be considered after reviewing the recommendations for use of gadolinium-based contrast in this group of patients.

Gadolinium agents are radiodense and can be used for opacification in CT and angiographic examinations instead of iodinated radiographic contrast media. However, there is controversy about whether

gadolinium contrast media are less nephrotoxic at equally attenuating doses. Caution should be used in extrapolating the lack of nephrotoxicity of intravenous gadolinium at MR dosages to its use for angiographic procedures, including direct injection into the renal arteries. No assessment of gadolinium versus iodinated contrast nephrotoxicity by randomized studies of equally attenuating doses is currently available. Initially, radiographic use of high-doses of gadolinium agents was proposed as an alternative to nephrotoxic iodinated contrast media in patients with renal insufficiency. However, because of the risk of NSF following gadolinium-based contrast material administration, especially in patients with acute renal failure or severe chronic kidney disease, and because of the unknown nephrotoxicity of high-doses of gadolinium agents, use of these contrast media for conventional angiography is no longer recommended.

Treatment

Treatment of moderate or severe acute adverse reactions to gadolinium-based contrast media is similar to that for moderate or severe acute reactions to iodinated contrast media (see Tables 3 through 6). In any facility where contrast media are 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 out of the imaging room immediately and away from the magnet so that none of the resuscitative equipment becomes a magnetic hazard.

Extravasation

The incidence of extravasation in one series of 28,000 doses was 0.05%. 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. The small volumes typically injected for MR studies limit the chances for a compartment syndrome. For these reasons the likelihood of a significant injury resulting from extravasated MR contrast media is extremely low. Non-ionic contrast media are less likely to cause symptomatic extravasation than hypertonic agents such as gadopentate dimeglumine.

Serum Calcium Determinations

Some gadolinium-based MR contrast media interfere with total serum calcium values determined with standard colorimetric methods (Roche, Dade, and Olympus). It should be emphasized that the MR contrast media do not cause actual reductions in serum calcium, only that the contrast media interferes with the test, leading to falsely low serum calcium values. 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. By definition, such usage is not approved by the Food and Drug Administration and the legal ramifications are unclear. Physicians have some latitude in

using gadolinium chelates off label as guided by clinical circumstances but must be prepared to justify such usage in individual cases. Examples include MR angiography, cardiac applications, and pediatric applications in patients younger than two years of age. No gadolinium chelate is approved in the United States for use in a power injector.

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NEPHROGENIC SYSTEMIC FIBROSIS (as of 5/1/2008)

Definition

Nephrogenic systemic fibrosis (NSF) is a fibrosing disease, primarily identified in the skin and subcutaneous tissues but also known to involve many other organs, such as the lungs, esophagus, heart, and skeletal muscles. Initial symptoms typically include skin thickening and/or pruritis. Symptoms and signs may develop and progress rapidly, with some affected patients developing contractures and joint immobility. Death may result in some patients, presumably as a result of visceral organ involvement.

Associations

When first described in 1997 the disease was noted to occur predominantly in patients with severe chronic kidney disease (CKD), particularly in patients on chronic dialysis. Initially, no other association was identified; however, in 2006 several groups noted a strong association between gadolinium-based contrast media (GBCM) administration and the disease. In fact, all patients in the two earliest reports [1,2] had been injected with one of the GBCM: gadodiamide. Subsequently, although the majority of affected patients still appear to have been exposed to gadodiamide (Omniscan – General Electric Healthcare), additional reports have implicated all of the other GBCM available in the United States: gadopentetate dimeglumine (Magnevist® – Bayer HealthCare Pharmaceuticals), gadoversetide (Optimark® – Covidien), gadobenate dimeglumine (MultiHance® – Bracco Diagnostics), and gadoteridol (ProHance® – Bracco Diagnostics), but at lower rates [3-5].

In a 2007 survey by the American College of Radiology, 156 cases of NSF were reported by 27 responding institutions; 140 of these 156 patients were known to have received GBCM. In 78 patients, the specific GBCM was known. Forty-five of them received gadodiamide, 17 gadopentetate dimeglumine, 13 gadoversetamide, and three gadobenate dimeglumine. (ACR unpublished data.) NSF following gadoteridol administration has been reported elsewhere. Many of the cases in which agents other than gadodiamide and gadopentetate dimeglumine were utilized are confounded by the fact that affected patients were injected with other agents as well.

It must be emphasized that the frequency with which NSF has been associated with different GBCM likely reflects a combination of differences in agent toxicity and market share.

At this time very few pediatric cases of NSF have been reported, and no cases have been reported in children under the age of 7 years. It is not safe, however, to assume that NSF is any less likely to occur in children than in adults. It is therefore prudent to follow the guidelines for adults, described in the remainder of this document on NSF, for all pediatric patients.

Interval between GBCM Administration and Symptom Onset

A number of studies have noted the time between injection of GBCM and the onset of symptoms to be within days to six months in the vast majority of patients [1,2,58].

Incidence

Based on current knowledge it is estimated that patients with severe CKD have a 1% to 7% chance of developing NSF after exposure to gadodiamide [1-3,5-8], although in one series, the incidence was even higher [9]. It is important to note that NSF has been encountered in patients who have severe acute as well as severe chronic renal dysfunction.

Additional Risk Factors

Many of the published series have suggested that patients are at highest risk when they are exposed to high doses or multiple doses of GBCM. Nonetheless, there are reported instances of NSF occurring in patients who have been exposed to standard (0.1 mmol/kg) single doses of GBCM [8,10], or who have no known GBCM exposure [11]. Conversely, some patients with severe CKD who have received many doses of GBCM have not developed NSF [8]. Some researchers have also observed that a disproportionate number of affected patients have had severe liver as well as renal dysfunction. Indeed, many of the reported cases have been liver transplant candidates or recent liver transplant recipients [7,8].

A number of other comorbidities have been postulated to explain why some patients with severe CKD who are exposed to GBCM develop NSF and some do not. These include increasing cumulative GBCM exposure [12], metabolic acidosis or medications that predispose patients to acidosis [1,4], increased iron, calcium, and/or phosphate levels [4,12,13], high-dose erythropoietin therapy [12], immuno-suppression [5], vasculopathy [14], an acute pro-inflammatory event [7,15], and infection alone [16], all at the time of GBCM exposure. None of these potential risk factors has been demonstrated consistently to be present in all affected patients in all studies. Therefore, at the present time, none of these risk factors can be considered to have been established as a true comorbidity with a high degree of confidence.

Postulated Mechanism

The exact mechanism of NSF is unknown; however, the most widely held theory is that the gadolinium ion dissociates from its chelate in patients with severe CKD, due to the prolonged clearance of the GBCM in CKD patients as well as to other metabolic factors associated with CKD. This dissociation occurs by a process known as transmetallation, whereby other cations replace the gadolinium on the chelate. Suspected cations include protons (in acidic environments), calcium, and rare metals. The free gadolinium then binds with other anions (such as phosphate), and the resulting insoluble precipitate is deposited in the skin and subcutaneous tissues (as well as at other locations) via a process that is still poorly understood [3,17]. A fibrotic reaction ensues, involving the activation of circulating fibrocytes [17,18].

This process may explain why some GBCM seem to be associated with the development of NSF with greater frequency (although relative market share of the different GBCM may also play a part). The GBCM that dissociate at higher rates in acidic solutions, for example, appear to be associated with NSF more often [3].

Recommendations for Identifying High-Risk Groups

A number of precautions have been recommended by the Food and Drug Administration (FDA) and the American College of Radiology (ACR) Committee on MR Safety in patients who have severe renal failure (generally defined as patients who have estimated glomerular filtration rates of less than 30 ml/min/1.73m^2) [19,20]. In order to identify these patients, it is recommended that all patients be questioned for a history of renal disease. According to the FDA http://www.fda.gov/cder/drug/infopage/gcca/default.htm this could be accomplished by obtaining a history and/or laboratory tests. The ACR Committee on MR Safety www.acr.org/SecondaryMainMenuCategories/quality_safety/MRSafety/safe_mr07.aspx recommends obtaining an estimated GFR within six weeks of an anticipated GBCM-enhanced study in patients with renal disease (including a solitary kidney, renal transplant, or renal neoplasm), in anyone over 60 years of age, or in patients with hypertension, diabetes mellitus, or a history of severe liver disease (including prior liver

transplantation), with strong consideration of contemporaneous assess-ment in this last group as well as in patients who present acutely, including hospital inpatients.

Recommendations for Imaging High-Risk Patients

Once a high risk patient is identified, a number of additional recommendations can be made [19,20], including considering alternative studies, informing such patients about the potential risks of GBCM-enhanced magnetic resonance imaging (MRI) studies should such studies be deemed necessary despite the risks, using the lowest possible dose of GBCM required to obtain the needed clinical information, avoiding double or triple dose studies if at all possible, and avoiding those GBCM that have been most frequently associated with NSF.

Specific Recommendations for High-Risk Groups

Patients with end-stage renal disease on chronic dialysis

If a contrast-enhanced cross-sectional imaging study is required in this group of patients, it would be reasonable to consider administering iodinated contrast media and performing a CT rather than an MR when such a substitution is deemed possible. If a contrast-enhanced MR examination must be performed, the ACR Committee on MR Safety has recommended that GBCM-enhanced MRI exams could be performed shortly before dialysis, as prompt post-procedural dialysis may reduce the likelihood that NSF will develop, although this has not been proved definitively to date. For example, in one study, three patients who developed NSF received dialysis for three consecutive days beginning at 9, 17, and 18 hours after GBCM administration [21]. Because it may be difficult for a busy dialysis center to alter dialysis schedules at the request of imaging departments, it may be more feasible for the imaging studies to be timed to precede a scheduled dialysis session.

Patients with CKD 4 or 5 (eGFR < 30 ml/min/1.73m^2) not on chronic dialysis

The correct course of action in this patient group is most problematic, as administration of iodinated contrast media for CT could worsen renal function and lead to the need for dialysis, while administration of GBCM for MRI could lead to NSF. Recent data suggests that the risk of NSF may be greatest of all in patients with an eGFR of < 15 ml/min/1.73m^2 and much less in patients with eGFRs that are higher. Accordingly, it is recommended that any contrast media administration be avoided if at all possible. If MRI contrast media administration is needed, judicious use of the lowest possible doses (needed to obtain a diagnostic study) of selected GBCM is probably safest. Currently, it is suggested that until or unless there is additional evidence to the contrary, the use of gadodiamide is to be avoided in such high risk patients. Macrocyclic media may be safest [22]. In this setting, the patient and his or her referring physician must be informed of the risks of GBCM administration and must give their consent to proceed.

Patients with CKD 3 (eGFR 30 to 59 ml/min/1.73m^2)

Assuming an accurate assessment of renal function can be made and that the patient is stable, this group can be considered to be at extremely low or no risk for developing NSF (as long as a dose of GBCM of 0.1 mmol/kg or less is utilized).

Patients with CKD 1 or 2 (eGFR 60 to 119 ml/min/1.73m^2)

Currently, there is no evidence that patients in these groups are at increased risk of developing NSF. GBCM can be administered safely to these patients. Some have argued, however, that gadodiamide should be avoided in these groups as well.

Patients in acute renal failure

Administration of iodinated contrast media for CT is to be avoided in this group, as there may be otherwise recoverable renal function. GBCM should only be administered if absolutely necessary. The lowest dose necessary to achieve a diagnostic study should be administered. Again, current evidence suggests that gadodiamide should be avoided in these patients.

Other

The ACR Committee on MR Safety has also advised that GBCM generally should not be administered to patients who have fluid in spaces in which the GBCM may reside for long periods of time (such as the peritoneal cavity in patients with ascites or the amniotic cavity in pregnant women).

Caveat

It must be stressed that information on NSF and its relationship to GBCM administration is still very preliminary, and the summary included here represents only the most recent opinions of the ACR Committee on Drugs and Contrast Media (as of May 1, 2008). As additional information becomes available our understanding of causative events leading to NSF and recommendations for preventing it will likely change.

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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. Rapid recognition, assessment, and diagnosis are crucial to the effective implementation of treatment. 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, 5, 6 and 7 and the chapter on Reactions to Iodinated Contrast Media in Children.)

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ADMINISTRATION OF CONTRAST MEDIA 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 media in pregnancy have been limited, and their effects on the human embryo or fetus are incompletely understood. Iodinated diagnostic contrast media have been shown to cross the human placenta and enter the fetus in measurable quantities. A standard gadolinium-based MR contrast medium has been shown to cross the placenta in primates and appear within the fetal bladder within 11 minutes after intravenous administration. 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. 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. There are no data available to assess the rate of clearance of contrast media from the amniotic fluid.

Iodinated X-Ray Contrast Media (Ionic and Nonionic)

Diagnostic iodinated contrast media have been shown to cross the human placenta and enter the fetus when given in usual clinical doses. In-vivo tests in animals have shown no evidence of either mutagenic or teratogenic effects with lower osmolality contrast media. No adequate and well-controlled teratogenic studies of the effects of these media 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 attempt to identify pregnant patients prior to the performance of any 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 iodinated contrast media present a definite risk to the fetus, there is insufficient evidence to conclude that they pose no risk. Consequently, the Committee on Drugs and Contrast Media 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 cannot be acquired without contrast administration or via another image modality (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 media provide informed consent to document that they understand the risk and 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 media in pregnant women have been performed. A single cohort study of 26 women exposed to gadolinium chelates during the first trimester of pregnancy showed no evidence of teratogenesis or mutagenesis in their progeny.

Gadolinium chelates may accumulate in the amniotic fluid and remain there for an indefinite period of time, with potential dissociation of the toxic free gadolinium ion from the chelate; the significance of this exposure to the fetus is uncertain, and its potential association with NSF in the child or mother is unknown. Therefore, gadolinium chelates should not be routinely used in pregnant patients.

The ACR Guidance Document for Safe MR Practices www.acr.org/SecondaryMainMenuCategories/quality_safety/MRSafety/safe_mr07.aspx also covers use of MR contrast media in pregnant patients, and its recommendations are consistent with those in this Manual. See also the preceding chapter on nephrogenic systemic fibrosis.

Because it is unclear how gadolinium-based contrast agents will affect the fetus, these agents should be administered only with extreme caution. Each case should be reviewed carefully and gadolinium based contrast agent administered only when there is a potential overwhelming benefit to the patient or fetus that outweighs the possible risk of exposure of the fetus to free gadolinium ions**.** The radiologist should confer with the referring physician and document the following in the radiology report or the patient's medical record:

1. That information requested from the MR study cannot be acquired without the use of intravenous contrast or by using other imaging modalities.
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.

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

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ADMINISTRATION OF CONTRAST MEDIA TO BREAST-FEEDING MOTHERS

Administration of either an iodinated or a gadolinium-based contrast media 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 media and the gastrointestinal absorption of these agents from breast milk is very limited however, several studies have shown that 1) less than 1% of the administered maternal dose of contrast medium 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 gastrointestinal tract. Therefore, the expected dose of contrast medium absorbed by an infant from ingested breast milk is extremely low.

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 media 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. Because less than 1% of the contrast medium ingested by the infant is absorbed from its gastrointestinal tract, 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 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 media. Although free gadolinium is neurotoxic, when complexed to one of a variety of chelates it is safe for use in most adults and children. These hydrophilic gadolinium chelate agents have pharmacokinetic properties very similar to those of iodinated X-ray contrast media. Like iodinated contrast media, gadolinium contrast media 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. Because less than

1% of the contrast medium ingested by the infant is absorbed from its gastrointestinal tract, 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 medium 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 medium. 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.

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Table 1
Indications for Use of Iodinated Contrast Media

Intravascular
- Intravenous
  - Computed tomography
  - 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
  - Computed tomography
  - 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)
- Cysternography (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
  - Cavity delineation (including urinary diversions, such as loop and pouch)

Table 2
Organ-Specific or System-Specific Adverse Effects

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

Adrenal Glands
Hypertension (in patients with pheochromocytoma after intra-arterial injection)

Brain
Headache, confusion, dizziness, seizure, rigors, 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
Contrast-induced nephropathy (CIN)

Pancreas
Swelling / pancreatitis

Respiratory System
Laryngeal edema, bronchospasm
Pulmonary edema

Salivary Glands
Swelling / parotitis

Skin and Soft Tissues
Pain, swelling, flushing, erythema, urticaria, pruritus
Compartment syndrome (from extravasation)

Thyroid
Exacerbation of thyrotoxicosis

Vascular System
Hemorrhage (from the procedure of administration or from the reduction in clotting ability)
Thrombophlebitis

Table 3
Categories of Reactions

Mild

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

Nausea, vomiting
Cough
Warmth
Headache
Dizziness
Shaking
Altered taste
Itching
Pallor
Flushing
Chills
Sweats
Rash, hives
Nasal stuffiness
Swelling: eyes, face
Anxiety

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

Moderate

Signs and symptoms are more pronounced. Moderate degree of clinically evident focal or systemic signs or symptoms, including:

Tachycardia/bradycardia
Hypertension
Generalized or diffuse erythema
Dyspnea
Bronchospasm, wheezing
Laryngeal edema
Mild hypotension

Treatment: Clinical findings in moderate reactions frequently require prompt treatment. These situations require close, careful observation for possible progression to a life-threatening event.

Severe

Signs and symptoms are often life-threatening, including:

Laryngeal edema
(severe or rapidly progressing)
Unresponsiveness
Cardiopulmonary arrest
Convulsions
Profound hypotension
Clinically manifest arrhythmias

Treatment: Requires *prompt* recognition and aggressive treatment; manifestations and treatment frequently require hospitalization.

Table 4
ABCD Approach for Patient Evaluation and Treatment

A

Airway, oxygen

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)

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 atypical manifestation (e.g., beta-blockers may prevent tachycardic response)

C

Circulatory assistance: as appropriate, administer isotonic fluid (e.g., Ringer's lactate, normal saline), infuse rapidly, and may use pressure bag or forceful infusion

Categorize reaction and patient status

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; pulmonary edema

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
Management of Acute Reactions in Children

Urticaria

1. No treatment needed in most cases
2. Give H_1-receptor blocker: Diphenhydramine (Benadryl®) PO/IM/IV 1 to 2 mg/kg, up to 50 mg.
3. If severe or widely disseminated: give alpha agonist: epinephrine SC (1:1,000) 0.01mL/kg.

Facial Edema

1. Give O_2 6-10 liters/min (via mask, face tent, or blow-by stream). Monitor: electrocardiogram, O_2 saturation (pulse oximeter), and blood pressure.
2. Give alpha agonist: epinephrine SC or IM (1:1,000) 0.01 mL/kg, up to 0.3 mL/dose. Repeat in 15 to 30 minutes as needed.
3. Give H_1-receptor blocker: Diphenhydramine (Benadryl®) IM/IV 1 to 2 mg/kg, up to 50 mg.

If not responsive to therapy, seek appropriate assistance (e.g., cardiopulmonary arrest response team).

Laryngeal Edema or Bronchospasm

1. Give O_2 6 to 10 liters/min (via mask, face tent, or blow-by stream). 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®) or (Ventolin®)] 2 to 3 puffs; repeat as necessary.
3. Give epinephrine SC or IM (1:1,000) 0.01 mL/kg , maximum 0.3 mL/dose OR epinephrine (1:10,000) IV 0.1 mL/kg, maximum 3mL/dose. Repeat in 3 to 5 minutes as needed.

Call for assistance (e.g., cardiopulmonary arrest response team) for severe bronchospasm or if O_2 saturation < 88% persists.

Pulmonary Edema

1. Give O_2 6 to 10 liters/min (via mask, face tent, or blow-by stream). Monitor: electrocardiogram, O_2 saturation (pulse oximeter), and blood pressure.
2. Give diuretic – furosemide (Lasix®) IV 1 to 2 mg/kg.

Call for assistance (e.g., cardiopulmonary arrest response team).

Hypotension with Tachycardia

1. Give O_2 6 to 10 liters/min (via mask). Monitor: electrocardiogram, O_2 saturation (pulse oximeter), and blood pressure.
2. Legs elevated 60° or more (preferred) or Trendelenburg position.
3. Keep patient warm.
4. Give IV or IO normal saline or Ringer's lactate 20 mL/kg over 5 to 10 minutes. Bolus infusion over 10 to 20 minutes in patients with myocardial dysfunction.

Seek appropriate assistance (e.g., cardiopulmonary arrest response team).

Hypotension with Bradycardia (Vagal Reaction)

1. Give O_2 6-10 liters/min (via mask). Monitor: electrocardiogram, O_2 saturation (pulse oximeter), and blood pressure.
2. Legs elevated 60° or more (preferred) or Trendelenburg position.
3. Keep patient warm.
4. Give IV or IO normal saline or Ringer's lactate 20 mL/kg over 5 to 10 minutes. Give infusion over 10 to 20 minutes in patients with myocardial dysfunction.
5. Give atropine IV 0.02 mg/kg if patient does not respond quickly to steps 2, 3, and 4. Minimum initial dose of 0.1 mg. Maximum initial dose of 0.5 mg (infant/child), 1.0 mg (adolescent).
6. Atropine dose may be doubled for second administration.

Seek appropriate assistance (e.g., cardiopulmonary arrest response team).

Abbreviations: IM= intramuscular
IO= intraosseous
IV=intravenous
SC=subcutaneous
PO=orally

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 to 50 mg.

If severe or widely disseminated: give alpha agonist (arteriolar and venous constriction): epinephrine SC (1:1,000) 0.1 to 0.3 ml (=0.1 to 0.3 mg) (if no cardiac contraindications).

Facial or Laryngeal Edema

1. Give O_2 6 to 10 liters/min (via mask).
2. Give alpha agonist (arteriolar and venous constriction): epinephrine SC or IM (1:1,000) 0.1 to 0.3 ml (=0.1-0.3 mg) or, especially if hypotension evident, epinephrine (1:10,000) slowly IV 1-3 ml (=0.1-0.3 mg).
   Repeat as needed up to a maximum of 1 mg.

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 to 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® or Ventolin®)] 2 to 3 puffs; repeat as necessary. If unresponsive to inhalers, use SC, IM, or IV epinephrine.
3. Give epinephrine SC or IM (1:1,000) 0.1- to 0.3 ml (=0.1-0.3 mg) or, especially if hypotension evident, epinephrine (1:10,000) slowly IV 1-3 ml (=0.1-0.3 mg).
   Repeat as needed up to a maximum of 1 mg.

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.
2. Monitor: electrocardiogram, pulse oximeter, blood pressure.
3. Give O_2 6 to 10 liters/min (via mask).
4. Rapid intravenous administration of large volumes of Ringer's lactate or normal saline.

If poorly responsive: epinephrine (1:10,000) slowly IV 1 ml (=0.1 mg)-
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 Secure airway: give O_2 6 to 10 liters/min (via mask)
2. Monitor vital signs.
3. Legs elevated 60° or more (preferred) or Trendelenburg position.
4. Secure IV access: rapid administration of Ringer's lactate or normal saline.
5. Give atropine 0.6-1 mg IV slowly if patient does not respond quickly to steps 2 to 4.
6. Repeat atropine up to a total dose of 0.04 mg/kg (2 to 3 mg) in adult.
7. Ensure complete resolution of hypotension and bradycardia prior to discharge.

Hypertension, Severe

1. Give O_2 6 to 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 inch strip.
4. If no response, consider labetalol 20 mg IV, then 20 to 80 mg IV every 10 minutes up to 300 mg.
5. Transfer to intensive care unit or emergency department.
6. For pheochromocytoma: phentolamine 5 mg IV. (may use labetalol if phentolamine is not available)

Seizures or Convulsions

1. Give O_2 6 to 10 liters/min (via mask).
2. Consider diazepam (Valium®) 5 mg IV (or more, as appropriate) or midazolam (Versed®) 0.5-1 mg IV.
3. If longer effect needed, obtain consultation; consider phenytoin (Dilantin®) infusion – 15 to 18 mg/kg at 50 mg/min.
4. Careful monitoring of vital signs required, particularly of pO_2 because of risk to respiratory depression with benzodiazepine administration.
5. Consider using cardiopulmonary arrest response team for intubation if needed.

Pulmonary Edema

1. Give O_2 6 to 10 liters/min (via mask).
2. Elevate torso.
3. Give diuretics: furosemide (Lasix®) 20-40 mg IV, slow push.
4. Consider giving morphine (1 to 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 contact 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.
- 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).

Medications:

- Epinephrine 1:10,000, 10 ml preloaded syringe.
- Epinephrine 1:1000, 1 ml preloaded syringe – optional.
- Atropine 1 mg in 10 ml preloaded syringe.
- Beta-agonist inhaler.
- Diphenhydramine for IM/IV injection.
- Nitroglycerin (NTG) – 0.4 mg tabs, sublingual.
- Aspirin 325 mg.

* 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.

Appendix A
Contrast Media Specifications
(The following information has been updated and validated by the appropriate drug manufacturers)

Product	Chemical Structure	Anion	Cation	% Salt Concen-tration	% Iodine Concen-tration	Iodine+ (mgl/ml)	Viscosity+ 25° C (cps)	Viscosity+ 37° C (cps)	Osmolality (mOsm/kg H2O)
INTRAVASCULAR									
Omnipaque® 140 (GE Healthcare)	Iohexol	Nonionic	Nonionic	None	14	140	2.3*	1.5	322
Conray™ 30 (Covidien)	Ionic	Iothalamate	Meglumine	30	14.1	141	2	1.5	600
Reno-DIP® (Bracco)	Ionic	Diatrizoate	Meglumine	30	14.1	141	2.0	1.5	607
Ultravist® 150 (Bayer HealthCare)	Iopromide	Nonionic	Nonionic	<0.1	15	150	2.3*	1.5	328
Optiray™ 160 (Covidien)	Ioversol 34%	Nonionic	Nonionic	None	16	160	2.7	1.9	355
Isovue®-200 (Bracco)	Iopamidol 40.8%	Nonionic	Nonionic	None	20	200	3.3*	2.0	413
Conray™ 43 (Covidien)	Ionic	Iothalamate	Meglumine	43	20.2	202	3	2	1000
Omnipaque® 240 (GE Healthcare)	Iohexol 51.8%	Nonionic	Nonionic	None	24	240	5.8*	3.4	520
Optiray™ 240 (Covidien)	Ioversol 51%	Nonionic	Nonionic	None	24	240	4.6	3.0	502
Ultravist® 240 (Bayer Healthcare)	Iopromide	Nonionic	Nonionic	<0.1	24	240	4.9*	2.8	483
Isovue® -250 (Bracco)	Iopamidol 51%	Nonionic	Nonionic	None	25	250	5.1*	3.0	524
Visipaque® 270 (GE Healthcare)	Iodixanol	Nonionic	Nonionic	None	27	270	12.7*	6.3	290
Reno® -60 (Bracco)	Ionic	Diatrizoate	Meglumine	60	28.2	282	6.4	4.3	1404
Conray™ (Covidien)	Ionic	Iothalamate	Meglumine	60	28.2	282	6	4	1400
Renografin® -60 (Bracco)	Ionic	Diatrizoate	Meglumine Sodium	52 8	29.25	292.5	6.2	4.2	1450
Isovue® -300 (Bracco)	Iopamidol 61.2%	Nonionic	Nonionic	None	30	300	8.8*	4.7	616
Omnipaque® -300 (GE Healthcare)	Iohexol 64.7%	Nonionic	Nonionic	None	30	300	11.8*	6.3	672
Optiray™ 300 (Covidien)	Ioversol 64%	Nonionic	Nonionic	None	30	300	8.2	5.5	651
Oxilan® 300 (Guerbet)	Ioxilan 62.3%	Nonionic	Nonionic	None	30	300	9.4*	5.1	585
Ultravist® 300 (Bayer Healthcare)	Iopromide	Nonionic	Nonionic	<0.1	30	300	9.2*	4.9	607
Hexabrix™ (Covidien)	Ionic	Ioxaglate	Meglumine Sodium	39.3 19.6	32	320	15.7*	7.5	≈600
Optiray™320 (Covidien)	Ioversol 68%	Nonionic	Nonionic	None	32	320	9.9	5.8	702
Visipaque® -320 (GE Healthcare)	Iodixanol	Nonionic	Nonionic	None	32	320	26.6	11.8	290

Product	Chemical Structure	Anion	Cation	% Salt Concen-tration	% Iodine Concen-tration	Iodine+ (mgl/ml)	Viscosity+ 25° C (cps)	Viscosity+ 37° C (cps)	Osmolality (mOsm/kg H2O)
INTRAVASCULAR									
Optiray™ 350 (Covidien)	Ioversol 74%	Nonionic	Nonionic	None	35	350	14.3	9.0	792
Omnipaque® -350 (GE Healthcare)	Iohexol 75.5%	Nonionic	Nonionic	None	35	350	20.4*	10.4	844
Oxilan® 350 (Guerbet)	Ioxilan 72.7%	Nonionic	Nonionic	None	35	350	16.3*	8.1	695
Isovue® -370 (Bracco)	Iopamidol 75.5%	Nonionic	Nonionic	None	37	370	20.9*	9.4	796
MD-76™ R (Covidien)	Ionic	Diatrizoate	Meglumine Sodium	66 10	37	370	16.4	10.5	1551
Ultravist® 370 (Bayer Healthcare)	Iopromide	Nonionic	Nonionic	<0.1	37	370	22.0*	10.0	774
Conray™ 400 (Covidien)	Ionic	Iothalamate	Sodium	66.9	40	400	7	4.5	2300
Cholografin® (Bracco)	Ionic	Iodipamide	Meglumine	52	25.7	257	6.6	5.6	664
GASTROINTESTINAL – Oral Contrast									
Gastrografin® (Bracco)	Ionic	Diatrizoate	Meglumine Sodium	66 10	37	370		8.4	1940
MD-Gastroview™ (Covidien	Ionic	Diatrizoate	Meglumine Sodium	66 10	37	370			2000
Omnipaque® 180 (GE Healthcare)	Iohexol	Nonionic	None	18	18	180	3.1*	2.0	331
Omnipaque® 240 (GE Heathcare)	Iohexol	Nonionic	None	24	24	240	5.8*	3.4	520
Omnipaque® 300 (GE Healthcare)	Iohexol	Nonionic	None	30	30	300	11.8*	6.3	672
Omnipaque® 350 (GE Healthcare)	Iohexol	Nonionic	None	35	35	350	20.4*	10.4	844
Cholografin* (Bracco)	Ionic	Iodipanide	Meglumine	52	25.7	257	8.0	5.3	522
URORADIOLOGICAL									
Cystografin® (Bracco)	Ionic	Diatrizoate	Meglumine	30	14.1	141	2.0	1.5	556
Cystografin® Dilute (Bracco)	Ionic	Diatrizoate	Meglumine	18	8.5	85	1.4	1.1	349
Cysto-Conray™ II (Covidien)	Ionic	Iothalamate	Meglumine	17.2	8.1	81	(Instill for retrograde cystography and cystourethrography)		
Conray™ 43 (Covidien)	Ionic	Iothalamate	Meglumine	43	20.2	202	3	2	1000
Omnipaque® 240 (GE Healthcare)	Nonionic	Nonionic	None	24	240		5.8*	3.4	520
Omnipaque® 300 (GE Healthcare)	Iohexol	Nonionic	None	30	30	300	11.8*	6.3	672
Omnipaque® 350 (GE Healthcare)	Iohexol	Nonionic	None	35	35	350	20.4*	10.4	844

Product	Chemical Structure	Anion	Cation	% Salt Concen-tration	% Iodine Concen-tration	Iodine+ (mgl/ml)	Viscosity+ 25° C (cps)	Viscosity+ 37° C (cps)	Osmolality (mOsm/kg H2O)
URORADIOLOGICAL									
Visipaque® 270 (GE Heathcare)	Iodixanol	Nonionic	None	27	27	270	12.7*	6.3	290
Visipaque 320 (GE Healthcare)	Iodixanol	Nonionic	None	32	32	320	26.6	11.8	290
INTRATHECAL									
Omnipaque* 180 (GE Healthcare)	Iohexol	Nonionic	Nonionic	None	18	180	3.1*	2.0	408
Omnipaque® 240 (GE Healthcare)	Iohexol	Nonionic	None	24	24	240	5.8*	3.4	520
Omnipaque® 300 (GE Healthcare)	Iohexol	Nonionic	None	30	30	300	11.8*	6.3	672
Isovue[M] 200 (Bracco)	Iopamidol	Nonionic	Nonionic	None	20	200	3.3*	2.0	413
Isovu[M] 300	Iopamidol	Nonionic	Nonionic	None	30	300	8.8*	4.7	616
BODY CAVITY									
Onmipaque* 180 (GE Healthcare)	Iohexol	Nonionic	None	None	18	180	3.1*	2.0	408
Omnipaque® 240 (GE Healthcare)	Iohexol	Nonionic	None	24	24	240	5.8*	3.4	520
Omnipaque® 300 (GE Healthcare)	Iohexol	Nonionic	None	30	30	300	11.8*	6.3	672
Omnipaque® 350 (GE Healthcare)	Iohexol	Nonionic	None	35	35	350	20.4*	10.4	844

MR CONTRAST MEDIA						
Product	**Chemical Structure**	**Anion**	**Cation**	**Viscosity+ 25° C (cps)**	**Viscosity+ 37° C (cps)**	**Osmolality (mOsm/kgH_2 O)**
Magnevist® (Bayer Healthcare)	Ionic Linear	Gadopen tetate	Dimegl-umine	4.9*	2.9	1960
Prohance® (Bracco)	Nonionic GD-HP-DOTA Gadoteridol			2.0	1.3	630
Multihance® (Bracco)	Ionic Linear	Gadoben ate	Dimegl-umine	9.2*	5.3	1970
Omniscan® (GE Healthcare)	Gd-DTPA-BMA Linear	Nonionic		2.0	1.4	789
Optimark™ (Covidien)	Nonionic Gd-DTPA-BMEA Gadoversetamide			2.8**	2.0	1110
Feridex® (Bayer Healthcare)	Ferrous-ferric oxide ferumoxides	None	None	1.3*		340
Gastromark™ (Covidien) Oral Suspension	Nonionic Ferrous-ferric oxide ferumoxsil	None	None			

+Data from product package inserts, product brochures, or technical information services.
*Measured at 20° C.
**Data on file with Covidien
***Hexabrix is licensed by a registered trademark of Guerbet, S.A. and sold by Covidien in the U.S.
oViscosities of most products intended for oral administration are not reported by manufacturers

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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 promote the safe and effective 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 (MRI), 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

The healthcare professional performing the injection may be a certified and/or licensed radiologic technologist, nurse, physician assistant, physician, or other appropriately credentialed healthcare professional under the direct supervision[2] of a radiologist or his or her physician designee if the practice is in compliance with institutional and state regulations. Training and proficiency in cardiopulmonary resuscitation are recommended for those who attend to patients undergoing contrast-enhanced examinations.

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 can 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 or she should have knowledge of the volume and concentration of the appropriate contrast media required for a given examination (see the ACR Manual on Contrast Media).

5. Physicians should have sufficient patient history to determine the indications for the study. The supervising physician or his or her physician designee must be aware of specific relative contraindications and pertinent risk factors that might increase the likelihood of adverse effects from contrast administration, and must have appropriate knowledge of alternative imaging methods. The physician has the responsibility for reviewing indications for the examination and for specifying the type, timing, dosage, rate, and route of administration of contrast media (see the ACR Manual on Contrast Media).

6. 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 studies.

Continuing Medical Education

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

B. Registered Radiologist Assistant

A registered 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 - ACR Resolution 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 injections of contrast media

[2]For the purpose of this guideline, direct supervision means that the physician must be present and immediately available to furnish assistance and direction throughout the performance of the procedure. It does not mean that the physician must be present in the room where the procedure is performed.

should be in compliance with existing operating polices and procedures at the imaging facility.

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

D. Nurse or Other Healthcare Professional

The certified and/or licensed nurse or other appropriately credentialed healthcare professional performing injections of contrast media should be in compliance with the existing operating policies and procedures at the imaging facility.

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 its proper performance and interpretation.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). 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 - ACR Resolution 35)

V. INTRAVASCULAR CONTRAST MEDIA

A. Iodinated Contrast Media

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

2. Types of iodinated contrast media: 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 Food and Drug Administration. Iodinated LOCM, most of which are nonionic agents, are associated with less discomfort and have a lower incidence of adverse effects. Iso-osmolar iodinated contrast media (IOCM) are also currently available. At this time there are only preliminary data on this agent, so indications for its use (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.

   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. Physicians and other healthcare professionals should be aware that certain gadolinium based contrast agents used in MRI examinations have been associated with nephrogenic systemic fibrosis (NSF) in patients with advanced or moderate kidney failure.

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

4. The same qualifications for injecting, monitoring and/or supervising iodinated contrast media pertain to physicians, nurses, radiologist assistants, radiologic technologists, and other healthcare professionals administering intravascular MR contrast media, 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. PROCEDURE

Each facility or department should have written policies and procedures.

Personnel familiar with the various risk factors, preparation, and any necessary premedication strategies should perform appropriate history and preprocedural screening. Relevant history should be brought to the attention of the supervising physician prior to contrast injection.

All imaging facilities should have policies and procedures to identify pregnant patients prior to imaging, and to consider any possible risks to the fetus of any planned administration of contrast material, taking into consideration the potential clinical benefits of the examination.

Vascular access should be established using the facility's protocol. Adequate flow should be ascertained prior to injection.

The healthcare professional performing the injection must be aware of the signs and symptoms of an adverse reaction and must monitor the patient for the development of these signs and symptoms during the examination. Patients should be monitored during and after contrast injection.

The supervising physician, or his or her physician designee, must be immediately available to respond promptly to an adverse effect.

Protocols should be in place for treating patients with adverse contrast effects. After a reaction there must be documentation of the effect and treatment, reporting to the appropriate healthcare personnel, counseling about future contrast administration, and flagging of the patient's medical and/or radiological record.

VII. 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.

VIII. EQUIPMENT SPECIFICATIONS

Appropriate emergency equipment and medications must be immediately available to treat adverse reactions associated with administered contrast media. The equipment and medications should be monitored for inventory and drug expiration dates on a regular basis.

IX. 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.

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Principal Reviewers: Arthur J. Segal, MD
James H. Ellis, MD

ACR Committee on Drugs and Contrast Media
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David B. Spring, MD
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Comments Reconciliation Committee
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E. Kent Yucel, MD

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