1. 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." —ACR Manual on Contrast Media- Version 10.1, 2015

The majority of the following guidelines and policies are derived, many times verbatim, from the ACR Manual on Contrast Media Version 10.1, 2015. Additional references will be provided as needed or requested.

The major purpose of these guidelines and policies is to assist attending and resident radiologists, technologists, and referring clinicians in recognizing and managing the small but real risks inherent in the use of intravenous iodinated contrast media utilized at the University of Toledo Medical Center. The following applies to patients >14 years of age unless indicated. Please see separate section regarding patients ≤ 14 years of age.

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.

The term "low-osmolality" (LOCM) 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 at conventionally used iodine concentrations for intravenous injection.

Arterial use of the iso-osmolality, iodinated contrast agents such as iodixanol (Visipaque) will follow the guidelines of the cardiovascular, interventional and neuroradiology departments/ divisions.
2. Intravenous Use of Iodinated Contrast

2.1. Policy for Steroid Preparations for Allergic-Like Reactions

A. Background
The overall incidence for acute allergic-like reactions is very low with LOCM. With regard to specific risk factors, a history of a prior allergy-like reaction to iodinated contrast is associated with a fivefold increased likelihood of the patient experiencing a subsequent reaction.

There is a 2 to 3 times increased likelihood of an acute contrast reaction in atopic individuals (more than two severe allergies to different classes of substances) compared to non-atopic individuals, however the benefit of premedication regimens is not felt to outweigh the risk to sufficiently warrant the routine use. There is no evidence to support premedication for allergies to shellfish or dairy products.

B. Purpose
Improve patient safety by identifying at risk patients for allergic-like reactions and recommend standardized premedication regimens when such a patient is identified.

C. Scope
All health care professionals involved in caring for patients in whom intravenous iodinated contrast is administered.

D. Procedure
1. The technologist will screen all patients for any prior allergic-like reaction to iodinated contrast prior to iodinated contrast administration.
   a. Allergic-like reactions include any mild to severe reactions as follows:
      i. Skin Reactions (Hives, rash, erythema, itching, nasal congestion)
      ii. Facial or body edema
      iii. Bronchospasm
      iv. Laryngeal edema
      v. Difficulty breathing
      vi. Anaphylaxis (Tachycardia and hypotension)
      vii. Any reaction requiring hospitalization or ER visit
      viii. Cardiopulmonary Arrest
   b. This does not include:
      i. Vasovagal reactions
      ii. Nausea
      iii. Vomiting
      iv. Contrast Induced Renal Dysfunction
II. Any patient found to have an above prior allergic-like reaction to iodinated contrast is suggested to have a premedication regimen (see examples below) prior to intravenous administration.

III. In circumstances where the ordering physician requests iodinated contrast without a premedication regimen despite a known allergic-like reaction, the injection will need to be directly supervised by the radiologist (attending or resident) or ordering physician/resident.

IV. In circumstances where premedication is required, consideration should be given to performing the examination without intravenous iodinated contrast if diagnostic information can be obtained or considering alternate imaging such as US or MRI.

V. Health care providers may choose to provide premedication regimens in other circumstances but that is at their discretion and not required for iodinated contrast administration in the department of radiology.

2.1.1. Recommended Premedication Regimens

Standard Oral Preparation Regimen:
- Prednisone – 50 mg PO, 13, 7, and 1 hour prior
- Diphenhydramine – 50 mg PO 1 hour prior

Alternate Intravenous Preparation Regimen:
- Hydrocortisone – 200 mg IV 13, 7, and 1 hour prior
- Diphenhydramine - 50 mg IM or IV 1 hour prior

Urgent Preparation Regimen:
- Diphenhydramine – 50 mg PO, IV or IM 1 hour prior; if blood pressure permits

Notes:
If a clinician prefers, methylprednisolone 40 mg IV can be substituted for hydrocortisone, dose for dose.

If an outpatient requires diphenhydramine, they will need to arrange for transportation, due to the possibility of drowsiness

2.2. Policy for Decreasing Risk of CIN from Iodinated Contrast Exposure

A. Background
Contrast induced nephrotoxicity (CIN) is a sudden deterioration in renal function following recent intravascular administration of iodinated contrast in the absence of another nephrototoxic event. CIN is a controversial topic with few published studies adequately isolating patients’ exposure from nephrototoxic events, with some recent studies suggesting it “may not be the causative agent in diminished renal function”. The pathophysiology is poorly understood. There are no standard criteria for diagnosis.
There is no agreed open threshold of renal dysfunction beyond which iodinated contrast should not be administered. Serum creatinine is the most commonly used measure of renal function but has limitations as an accurate measure of eGFR. Therefore, our department will use eGFR calculated from the MDRD formula as a threshold to administer contrast safely. See Appendix A.

There is no longer evidence to support the use of intravenous iodixanol (Visipaque) in chronic kidney disease to decrease the risk of CIN. There is no significant evidence to support the use of any regimen except hydration in an attempt to decrease CIN.

B. Purpose

Improve patient safety by identifying at risk patients for CIN through eGFR screening, subsequently decreasing their exposure to iodinated contrast and recommend standardized hydration regimens when such a patient is identified that requires iodinated contrast.

C. Scope

All health care professionals involved in caring for patients in whom intravenous iodinated contrast is administered.

D. Procedure

I. The technologist will screen all patients (exceptions below) for any of the following CIN risk factors:
   i. Age > 60
   ii. History of hypertension requiring medical therapy
   iii. History of diabetes mellitus
   iv. History of renal disease, solitary kidney, renal cancer, renal surgery, kidney transplant, or prior dialysis
   v. Acute kidney injury or Acute renal failure

II. If NONE of the above risk factors are identified an eGFR will NOT be required prior to intravenous iodinated contrast administration.

III. If ANY of the following risk factors are identified an eGFR will be REQUIRED within 60 days (outpatient) or 2 days (ER, inpatient) prior to intravenous iodinated contrast administration.

IV. If the eGFR is < 30ml/min/1.73 m² consider changing from a contrasted enhanced study to a noncontrast study or the use of alternate tests should be considered. The technologist or radiologist will inform the ordering physician of the low eGFR.

V. If contrast is given in the setting of a GFR < 30 ml/min/1.73m² the technologist will screen for concurrent Metformin use and recommendations to discontinue the medication will be made by the radiologist to the referring clinician.

VI. If the patient is on chronic dialysis, whether anuric or oliguric, an eGFR screening and urgent dialysis are not required prior to or after intravenous contrast administration, respectively.
VII. If a patient requires intravenous contrast despite the above considerations a hydration regimen is suggested (see below).

VIII. In the setting of suspected or known acute kidney injury, iodinated contrast should be avoided unless absolutely necessary despite the current serum creatinine/eGFR.

E. Trauma Patients or Emergent Life Threatening Conditions

I. An eGFR screening is NOT required prior to contrast administration. The benefit of contrast media under these circumstances will almost certainly outweigh the theoretical risk of contrast induced renal dysfunction.

II. The list of conditions includes but is not limited to pulmonary embolism, aortic aneurysm rupture, aortic dissection and stroke.

2.2.1. Recommended Hydration Regimens

Standard Inpatient Intravenous Regimen:
- 0.45% to 0.9% saline IV at 1 ml/kg/hr beginning at least 2 to 12 hours prior to the contrast administration and continuing for 24 hours total

Standard Outpatient Intravenous Regimen:
- 0.9% saline IV at 1 ml/kg/hr beginning 1 hour prior to the contrast administration and continuing for 6 hours total.

Standard Oral Regimen:
- Water PO at 1 ml/kg/hr for 24 hours, beginning 12 hours before the procedure and continuing for 24 hours total
- Please note evidence suggests an oral regimen is less effective

2.3. Increased Risk from Specific Underlying Diseases

A. Asthma
During an acute asthma attack there is possibly an increased risk of an iodinated contrast reaction. Non-contrast studies are suggested or an above premedication regimen.

B. Sickle Cell Anemia
There is no evidence of increased risk to patients, particularly with LOCM. No precautions are recommended at this time.

C. Pheochromcytoma
There is no evidence that nonionic increases catecholamine levels. No precautions are recommended at this time.

D. Cardiac Status
Patients with significant cardiac disease may be at risk for contrast reactions, but evidence does not support premedication regimens at this time. Volume should be limited.

E. Hyperthyroidism or Autonomous Functioning Nodule
In iodine deficient patients iodine-provoked delayed hyperthyroidism may develop. This effect may be delayed occurring 4-6 weeks after iodinated contrast administration. It is usually self-limited. No precautions are recommended at this time.
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F. Multiple Myeloma
There is no evidence that LOCM causes renal dysfunction. No precautions are recommended at this time.

G. Myasthenia Gravis
LOCM may cause disease-related symptom exacerbations within 24 hours. Myasthenia Gravis is considered a relative contraindication in this patient population. The ordering physician will be notified prior to proceeding with contrast.

H. Thyroid Carcinoma
Thyroid uptake on I-131 is decreased about 50% one week following iodinated contrast administration. This should be taken into consideration if contrast administration is given prior to using systemic radioactive iodine therapy.

2.4. Guidelines for Large Intravenous Doses
Sometimes the question arises of how much total iodinated contrast media can be safely administered intravenous in a short time frame. (An example might be a patient who received a CT scan at another institution or a cardiac catheterization and a repeat CT is desired, all within the same day.) Unfortunately, there is very little evidence available to answer this question.

As the volume of contrast administered goes up, the risk of nephrotoxicity probably increases. (Allergic-like reactions are independent of dose.) It is believed that a total dose of 200 ml or less of any of the department’s iodinated contrast agents is well within the safety zone for patients without specific risk factors for nephrotoxicity.

The question of a “maximum” allowed dose is more difficult, as the risk-benefit ratio must always be taken into account (i.e., there is no fixed maximum if the potential benefit outweighs the potential risk). The FDA package insert for Ultravist-370 states that the “maximum recommended total dose of iodine in adults is 86 grams”. The FDA package insert for Visipaque states that the “maximum recommended total dose of iodine is 80 grams”. Using these recommendations, it is suggested that the approximate maximum volumes of iodinated contrast in should be as follows:

- 285 ml of Omnipaque-300
- 245 ml of Omnipaque-350

These volumes are not rigid and may be adjusted as warranted by the clinical situation and patient condition, including risk factors for nephrotoxicity.

These recommendations don’t specify the time frame over which the contrast is given. Except in unusual circumstances, it is probably best to stay within the recommended maximums within any 24-48 hour period. It is generally accepted that contrast material can again be administered after 72 hours if renal function remains unaltered, but this based on limited data.

Dose adjustments and alternate studies should be considered for patients who are at risk for nephrotoxicity (see prior CIN guidelines). It is not advisable to use such a low dose as to result in an inadequate study because then the patient has taken on the extra risk and received no benefit.
In the event of overdose, it is unlikely that hemodialysis will reduce the risk of nephrotoxicity once the kidneys have been exposed, but it can be considered after consultation with nephrology. Prophylactic hemodialysis after contrast administration in patients with renal insufficiency is potentially harmful.

2.5. Pregnant or Potentially Pregnant Patients
A. Background
Diagnostic iodinated contrast has been to cross the placenta and enter the fetus. No mutagenic or teratogenic effects have been demonstrated during in-vivo animal testing.

Intravenous iodinated contrast does not affect short-term neonatal TSH, likely because it is transient and a low dose. To date there is no report of neonatal hypothyroidism from maternal administration of iodinated contrast.

Recognize that the examination’s radiation is a greater risk than the contrast material.

The least attractive clinic decision is when the fetus or neonate is exposed to radiation yet the diagnostic information is substantially compromised by lack of contrast material.

B. Purpose
Improve patient safety by minimizing exposure of the pregnant or potentially pregnant patient to intravenous iodinated contrast.

C. Scope
All health care professionals involved in caring for pregnant or potentially pregnant patients in whom intravenous iodinated contrast is administered.

D. Procedure
I. The technologist will screen all patients prior to imaging for the potential of pregnancy (see separate policy details).
II. If a patient is found to be pregnant an attending or resident radiologist should confer with the requesting physician and document the indications for iodinated contrast in the report.

2.6. Breast Feeding Women
Imaging studies with iodinated contrast may be needed in breast-feeding women. Iodinated contrast has a half-life of two hours with nearly 100% clearance by 24 hours in the setting of normal renal function.

The infant through the GI tract absorbs less than 0.01% of the administered mother’s dose, which is less than 1% of the recommended dose for infants. The risk for toxic or allergic-like reactions resulting from the ingested contrast is therefore extremely low.

Therefore, it is believed to be safe for mothers to continue breast-feeding after receiving intravenous iodinated contrast agents.

If the patient wishes to abstain from breast-feeding despite the above facts, stopping for a period longer than 24 hours has no benefit.
3. **Intravenous Iodinated Contrast Media in Children**

   **A. Background**
   Principles regarding iodinated contrast media in children and their adverse events are similar to the above adult recommendations as it relates to allergic-like reactions, extravasations, and CIN.

   **B. Purpose**
   Improve pediatric patient (defined as ≤ 14 years of age) safety prior to intravenous iodinated contrast administration.

   **C. Scope**
   All health care professionals involved in caring pediatric patients in whom intravenous iodinated contrast agents may be administered.

   **D. Procedure**
   I. The technologist will screen for pregnancy, prior allergic-like reactions, and risk factors associated with CIN as already detailed above.
   II. Given the limited number of neonatal and pediatric cases performed at the University of Toledo Medical Center, all patients 14 years or younger that a contrast (iodinated or GBCA) study is requested will be need approval by the attending or resident radiologist prior to intravenous contrast administration. See separate Standard Operating Procedure P-02.
   III. Standard dosing of intravenous contrast agents per the package inserts will be followed.
   IV. Premedication regimens for prior allergic-like reactions will require weight based dosing.

See separate document for the patient questionnaire form.
Appendix A

**MDRD equation:**

\[ eGFR (\text{ml/min/1.73} \text{ m}^2) = 175 \times (\text{serum creatinine in mg/dl})^{-1.154} \times (\text{age in years})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American}) \]

Appendix B

**Table A**

**Medications containing Metformin**

<table>
<thead>
<tr>
<th>Generic Ingredients</th>
<th>Trade Names</th>
</tr>
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<tbody>
<tr>
<td>Metformin</td>
<td>Glucophage</td>
</tr>
<tr>
<td></td>
<td>Glucophage XR</td>
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<tr>
<td></td>
<td>Fortamet</td>
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<td></td>
<td>Glumetza</td>
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<tr>
<td></td>
<td>Riomet</td>
</tr>
<tr>
<td>Glyburide/metformin</td>
<td>Glucovance</td>
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<tr>
<td>Glipizide/metformin</td>
<td>Metaglip</td>
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<tr>
<td>Pioglitazone/metformin</td>
<td>ActoPlus Met</td>
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<tr>
<td></td>
<td>ActoPlus Met XR</td>
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<tr>
<td>Repaglinide/metformin</td>
<td>Prandimet</td>
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<tr>
<td>Rosiglitazone/metformin</td>
<td>Avandamet</td>
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<tr>
<td>Saxagliptin/metformin</td>
<td>Kombiglyze XR</td>
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<tr>
<td>Sitagliptin/metformin</td>
<td>Janumet</td>
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<tr>
<td></td>
<td>Janumet XR</td>
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</tbody>
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(Metformin and several of the combination drugs also available in generic versions)

*List as of June, 2012.

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Review/Revision Date:
1/15/2009
5/20/2011
9/28/2012
5/5/2014
9/28/2015

Next Review Date:
10/1/2018