Best Practices in the Use of Iodinated Contrast Media in the Clinical Setting: What the Pharmacist Needs to Know

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Presented as a Live Webinar

Thursday, February 4, 2016
1:00 p.m. – 2:00 p.m. ET

On-demand Activity

Live webinar recorded and archived to be watched at your convenience
Available after March 28, 2016

www.ashpadvantage.com/contrastmedia

Planned by ASHP Advantage and supported by an educational grant from GE Healthcare

Activity Overview

This educational activity will review currently available iodine-based contrast agents in terms of use, dosing, route of administration, and safety profile. Specific clinical situations for which use of a particular agent would be advantageous will also be explained. Effective approaches to screening and managing patients at risk of developing adverse effects will be discussed. The activity will conclude with a description of safe handling and storage processes for contrast media that should be employed by the pharmacy department.

Learning Objectives

At the conclusion of this knowledge-based educational activity, participants should be able to

- Review currently available iodinated contrast agents with respect to use, dosing, and safety profile in adults and children.
- Review the routes of administration of available iodinated contrast media.
- Explain how to screen and manage patients at risk of adverse effects with iodinated contrast agents.
- Describe safe handling and storage processes that should be employed when handling contrast agents.

Continuing Education Accreditation

ASHP is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity provides 1.0 hour (0.1 CEU – no partial credit) of continuing pharmacy education credit (ACPE activity #0204-0000-16-414-L05-P for the live activity and ACPE activity #0204-0000-16-414-H05-P for the on-demand activity).

Participants will process CPE credit online at http://elearning.ashp.org/my-activities. CPE credit will be reported directly to CPE Monitor. Per ACPE, CPE credit must be claimed no later than 60 days from the date of the live activity or completion of a home-study activity.

Webinar Information

Visit www.ashpadvantage.com/contrastmedia to find

- Webinar registration link
- Group viewing information and technical requirements
- CPE webinar processing information

Additional Educational Activities

- On-demand activity based on the live webinar (1 hour CPE, available after March 28, 2016) – Please note that individuals who claim CPE credit for the live webinar are ineligible to claim credit for the on-demand activity.

www.ashpadvantage.com/contrastmedia

Activity Faculty

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Senior Consultant, Vizient Performance Services
Billings, Montana

Ed Kent is Director, VHA Mountain States (VHAMS) Pharmacy RxNetwork, which represents 51 hospitals across a ten-state region. Pharmacy directors and clinical coordinators from 35 affiliated member organizations formed the Integrated Delivery Network (IDN), which resulted in the regional formulary standardization and clinical process improvement in all pharmacy service areas. Ed's primary responsibilities include identifying formulary standardization and clinical process improvement opportunities; analyzing and assessing the potential for savings; contacting vendor's national account managers; developing and requesting proposals; negotiating contract enhancements; developing strategies for successful implementation; auditing all partner's performance; identifying any/all remaining opportunities for conversion; and reporting the financial impact to all key stakeholders. Overall Member satisfaction exceeds 92%.

Ed received his B.S. Pharmacy degree from the University of Iowa. Ed is a member of the American Society of Health-System Pharmacists and is a past member of the *Novation Pharmacy Executive Strategic Planning Council* (2007).

Prior to joining VHA, Ed worked 10 years as the Pharmacy Manager/Director of Billings Clinic (formerly Deaconess Billings Clinic), in Billings, Montana. In 2004, Billings Clinic and Ed accepted a *VHA Mountain States and National Leadership Award for Clinical Effectiveness: Cardiac Care (CHF/MI)*. In 2005, Ed was recognized by *VHA Mountain States with an Excellence Award for Supply Chain Management: Pharmacy ADA Consolidation Initiative.* Since 2002, seven of his pharmacy staff members were nominated and received *Billings Clinic Excellence Awards for Personal Service Excellence.*

At VHA, Ed's performance has been recognized with several awards and recognition, including a 2009 *Member Engagement Satisfaction Award*, *1Q 2010 WOW Award, 2010 Business Unit Plan Achievement and Financial Stewardship Awards.*

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- The faculty and planners report no financial relationships relevant to this activity**.**

Best Practices in the Use of Iodinated Contrast Media in the Clinical Setting:

WHAT THE PHARMACIST NEEDS TO KNOW

Ed Kent, B.S.Pharm.
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1.0 hr. CPE

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ashp Advantage

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Learning Objectives

After the conclusion of this knowledge-based educational activity participants should be able to

- Review currently available iodinated contrast agents with respect to use, dosing, and safety profile in adults and children.
- Review the routes of administration of available iodinated contrast media.
- Explain how to screen and manage patients at risk of adverse effects with iodinated contrast agents.
- Describe safe handling and storage processes that should be employed when handling contrast agents.

Pharmacy Oversight – Collaboration with Radiology

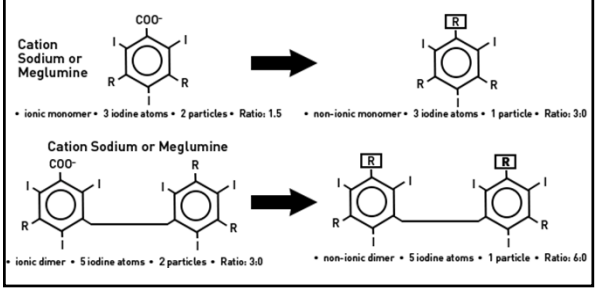
- 2004: The Joint Commission (TJC) defined diagnostic agents and radiopharmaceuticals as a "drug" – MUST comply with Medication Management standards
  - **Director of Pharmacy is responsible for oversight of all medication-related areas**
- Centers for Medicare and Medicaid Services (CMS) Condition of Participation (COP)
  - Preparation of radiopharmaceuticals included in Pharmaceutical Services standards in the Code of Federal Regulations (42 CFR 482.25) and Nursing Services standards (42 CFR 482.23(c))
- All CMS "deemed" Accrediting Organizations base their standards on CMS' COP:
  - The Joint Commission (TJC); The American Osteopathic Association's Healthcare Facilities Accreditation Program (HFAP); Det Norske Veritas (DNV's) National Integrated Accreditation for Healthcare Organizations (NIAHO)
- State Department of Health, State Board of Pharmacy, FDA

Radiocontrast Media

- Purpose: improve the visibility of x-ray images of internal body structures
  - Computed tomography (CT or CAT scan)
  - Radiography
  - Fluoroscopy
- Types:
  - Barium, which is administered orally or rectally
  - Iodine, which is administered orally, rectally, body cavity, and intravascularly
- How it Works
  - Iodine "dye" absorbs X-ray radiation preventing it from passing through which changes the appearance of surrounding tissue – "contrast-enhanced"

Iodinated Contrast Media - Classification

- Categorized by chemical structure (monomer and dimer), Ionization, and osmolality
- Structure based on modifications of the 2, 4, 6-tri-iodinated benzene ring structure



Iodinated Contrast Media: Classification and Use

See page 14 for enlarged view

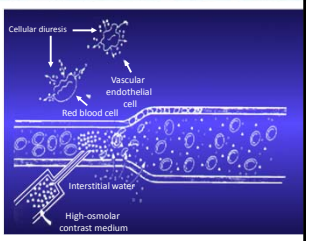
Iodinated Contrast Media – Osmolality

- Osmolality is a measure of the number of dissolved particles per Kilogram (Osmolarity is per Liter) of water
  - Normal human plasma: 270–300 mOsm/Kg
  - Normal cerebrospinal fluid: 280–300 mOsm/Kg
- Osmolality depends on concentration and ionicity
  - Higher osmolality relates to some of the adverse events of ICM
- Magnitude (and duration) of osmolality deviation from "normal" are important along with size and blood flow of the vasculature
- Osmolality has a threshold phenomenon for causing pain and ultimately tissue damage
  - Peripheral vein: < 600 mOsm/Kg - no injection site pain
    > 900 mOsm/Kg - injection site burning and pain
  - D5NS, D5LR, and D10W all have an osmolality of ~ 600 mOsm/Liter
  - Adult patients: Osmolality of an IV solution administered via peripheral vein should be below 900 mOsm/L

mgI/mL = milligrams iodine per milliliter

High-osmolality Iodinated Contrast Media

- Greater than 1000 mOsm/Kg (5 – 8X Normal Plasma Osmolality)
- 100% Ionic (two generic names: anion and cation)
- **NOT** routinely given intravascularly due to adverse physiological effects
- **Restricted to GI tract (oral/rectal), bladder, gallbladder, uterus and fallopian tubes**
- **Store HOCM (oral/other) separate from i.v. formulations**



Immediate effects of a High-Osmolar ICM on vascular physiology

Solomon R. Kidney Int. 2005;68:2256-2263.
Fischer HW. *Radiology*. 1968;91:66-73.

Low-osmolality Iodinated Contrast Media

- Broad Use: intravascularly, intra-arterially, oral, rectal, gastrointestinal, bladder, intra-articularly, intrauterine
- General Properties:
  - Osmolality ranges 290 to 844 mOsm/Kg
  - Normally used concentration: 200 to 370 mgI/mL (300 mgI/mL most often used)
  - Cost is approximately 10x higher than HOCM
  - Associated with lower incidence of adverse drug reactions compared to HOCM
- LOCM sub-categories
  - Ionic Dimer: osmolality ≈ 600 mOsm/Kg (ioxaglate recently withdrawn from U.S.)
  - Non-Ionic Monomer: osmolality = 322 to 844 mOsm/Kg
  - Non-Ionic Dimer: osmolality = 290 mOsm/Kg (marketed as "Iso-Osmolar Contrast")
    - ~ 50% the osmolality of non-ionic monomers at the same iodine concentration
    - Only "iso-osmolar contrast" is iodixanol
    - Due to higher expense – Do to cost; use is limited

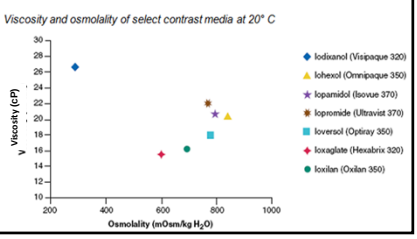
Iodinated Contrast Media – Concentration

- Iodine is Iodine to all X-ray scanners; equivalent milligrams concentrations of iodine are viewed the same, regardless of the carrier molecule
- X-ray radiopacity is directly proportional to the organically bound Iodine per mL or organically bound iodine infused per milliliter per second
  - "mgI/mL" in a body cavity/space or
  - "mgI/mL/sec" when infused intravascularly
- Iohexol 300 mgI/mL = iopamidol 300 mgI/mL ≈ 320 mgI/mL iodixanol
  - 85 mL of iopamidol 370 mgI/mL delivers the same amount of iodine as 100 mL of iodixanol 320 mgI/mL and iopamidol, at this concentration, is more radiopaque if administered at an equivalent infusion rate
- Deeper, visceral internal body structures require a greater concentration of iodine to obtain clear X-ray images

mgI/mL = milligrams iodine per milliliter

Iodinated Contrast Media – Viscosity

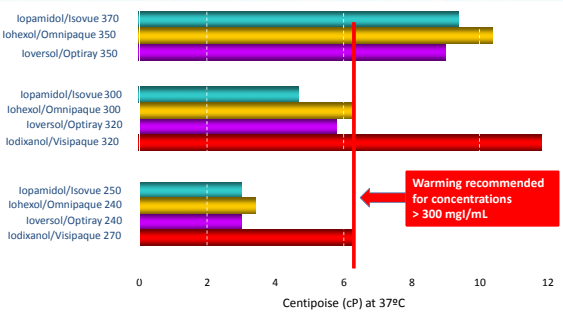
- High viscosity generally means lower miscibility (mixing with blood). As molecular size, shape, weight and iodine concentration increases; viscosity increases
- Normal Plasma Viscosity is 1.4 to 1.8 cP (or mPas) at 37°C
- Higher viscosity agents require higher injection pressures to initiate and maintain the necessary iodine delivery rates
- Increased risk of catheter damage and vascular trauma



Warming Iodinated Contrast Media

- Warming from room (25°C) to body temperature (37°C) reduces viscosity by 50%
- Warming reduces injection pressures needed for higher injection rates needed to improve vascular opacification
  - Warming (to 37°C) has NO EFFECT on adverse event rates with LOCM at 300mgI/mL or lower concentrations at injection speeds less than 6 mL/sec
  - Warming of concentrations above 300 mgI/mL - 3X reduction of extravasation and incidence of adverse events
    - Viscosity of Iodixanol at 25°C = 26.6cP ~ 15x normal; viscosity of iodixanol at 37°C = 11.8cP ~7x normal - so warming to body temperature reduces viscosity by 50%
    - At equivalent iodine concentrations, the viscosity of the non-ionic dimer, remains two times greater than non-ionic monomers
- Warming of ICM is recommended as follows:
  - High rate i.v. LOCM power injectors (>5 mL/sec)
  - Injections of viscous LOCM iodinated contrast media with concentrations above 300 mgI/mL
  - Direct arterial injections through small-caliber catheters (5 French or smaller)
  - Intravenously injected arterial studies in which timing and peak enhancement are critical

Viscosity of Low-osmolality Iodinated Contrast Media



Normal Plasma viscosity = 1.4 -1.8 cP at 37^{0}C

Polling Question

Which of the following statements is **FALSE**?

a. HOCM is associated with a higher incidence of adverse drug events

b. ICM with an osmolality >900 mOsm/Kg causes injection site burning, pain and potentially cellular and tissue damage

c. HOCM should be stored separate from intravascular LOCM

d. Products with equivalent concentrations of iodine produce the same X-ray results regardless of the ICM carrier molecule

e. Warming to body temperature (37C) is needed to reduce injection pressures and the inherent risk of extravasation and other adverse reactions for all LOCM ICM

Dosing: Concentration and Volume

Iodinated Contrast Media: Barium or HOCM or LOCM

- GI Tract Imaging: HOCM or LOCM?
  - IF previous allergic reaction to barium (rare: 1/750,000 exams) use HOCM or LOCM ICM
  - IF barium is unavailable, generally use HOCM, unless LOCM is clinically preferred or less expensive
  - "Injectable" LOCM is clinically preferred over barium and HOCM if:
    - Potential perforation of GI tract (e.g., abdominal trauma)
    - Neonates and patients at risk for aspiration
- Recent HOCM drug shortages (e.g., Gastrografin®/Gastroview®) and price changes have led to more oral and rectal administration of "injectable LOCM"
  - All LOCM can be administered orally/rectally - diluted or full strength
  - Iohexol (Omnipaque®) is only FDA approved LOCM for oral use
    - Better taste than HOCM
    - Less risk for aspiration ADE
    - Generally, a diluted solution containing 13 to 15 mgI/mL is recommended
    - Omnipaque ORAL Preparation protocol : See FDA package insert

Iodinated Contrast Media: Concentration and Dosing

- FDA-approved range for adult low-osmolar contrast media enhanced CT head and body exams: 30 to 60 grams iodine
  - Infants and young children: dosing is weight-based (i.e., mg iodine per Kg)
- General guidelines: "Use minimum dose necessary to achieve adequate visualization"
- Factors that determine how much iodinated contrast media a patient receives:
  - Scanner technology (strength and speed) and radiologist's preference
  - Patient's clinical condition and procedure(s) being performed
- Concentration influences image quality - depends on location or depth of the area of interest and equipment employed
  - Surface features (e.g., veins) lower concentrations used (e.g., 200-250 mgI/mL)
  - Deep features (e.g., arteries/coronary angiogram) higher concentrations necessary
    - 300 mgI/mL (child) to 300 to 370mgI/mL (adult)
  - Myelogrophy: adults 180 to 300 mgI/mL; child 180mgI/mL
- Volume
  - Depends on the number and size of the vessels or size of the cavity imaged
  - Myelography: adults/children NOT TO EXCEED 20 mL in intrathecal space
  - Dual injector technology – saline "chaser" following ICM infusion can reduce wasted ICM left in infusion lines

Intra-arterial Doses for Adult Patients

INTRA-ARTERIAL			
Procedure (ICM Concentration)	**Injection Site**	**Adult Dose**	**Max Dose**
Cerebral Arteriography (300 – 320 mg I/mL)	Carotid Arteries, Vertebral Arteries, Aortic Arch Injection (4 vessel study)	3–12 mL 4–12 mL 20–50 mL	150 mL (45 G iodine)
Peripheral Arteriography (300 mg I/mL)	Subclavian or Femoral Artery Aortic Bifurcation (distal runoff)	5–40 mL 25–50 mL	200 mL (60 G iodine)
Coronary Arteriography and Left Ventriculography (300–370 mg I/mL)	Right Coronary Artery Left Coronary Artery Left Ventricle	3–14 mL 3–14 mL 30–60 mL	200 mL (60 G iodine)

mgI/mL = milligrams iodine per milliliter

Intraveneous Doses for Adult Patients

INTRA-VENOUS			
Procedure (ICM Concentration)	**Injection Site**	**Adult Dose**	**Max Dose**
Peripheral Venography (240-250 mg I/mL)	Peripheral Venography	Minimum volume necessary to visualize structures	250 mL (60 G iodine)
Excretory Urography (300 mg I/mL)	Excretory Urography	Approximately 300 mgI/Kg body weight (Adults with normal renal function)	100 mL (30 G iodine)
Contrast Computed Tomography (300 mg I/mL)	Head	50–200 mL	200mL (60 G iodine)
Contrast Computed Tomography (300-320 mg I/mL)	Body Bolus Injection Rapid Infusion	50–200 mL 100–200 mL	200mL (60 G iodine)
Contrast Computed Tomography (350-370 mg I/mL)	Head	41–162 mL	200mL (60 G iodine)
Contrast Computed Tomography (350-370 mg I/mL)	Body Bolus Injection Rapid Infusion	41–162 mL 81–162 mL	200mL (60 G iodine)

mg I/mL = milligrams iodine per milliliter

Pharmacokinetics of Commonly Used Injectable ICM

PHARMACOKINETICS					
Chemical Name (Trade Name)	**Protein Binding (%)**	**Volume Distribution**	**Metabolism**	**Elimination Half-life**	**Route Elimination**
Iodixanol (Visipaque®)	0%	0.28 L/kg	None	120-130 min (23 hrs renal insufficiency)	98% renal
Iopromide (Ultravist®)	1%	0.2 L/kg	None	6.2–40 hours	94% renal
Iopamidol (Isovue®)	1%	0.35 L/kg	Minimal	2 hours	92-98% renal, 10% feces
Iohexol (Omnipaque®)	Low	0.108–0.219 L/kg	Minimal	2 hours	100% renal
Ioversol (Optiray®)	0%	Not Reported	None	1.6–2 hours	95% or greater
Ioxilan (Oxilan®)	Negligible	10 L	None	137 minutes	94% renal
Ioxaglate (Hexabrix®)	Low	0.12–0.3 L/kg	None	61–140 minutes	90% renal

- Primary mode of elimination: Kidney, via glomerular filtration
  - Normal renal elimination half-life: 2 hours; 100% cleared in 24 hours
- Severe renal impairment: Elimination half-life: 16 to 84 hours
  - Secondary mode: Liver metabolism with biliary excretion – slow and limited
  - Dialysis effectively removes ICM
- Low plasma protein binding
- Low volume of distribution due to low lipid solubility

See page 15 for enlarged view

Polling Question

Which of the following statements is **FALSE**?

a. FDA-approved ADULT dose for LOCM enhanced CT head and body exams is 30 to 60 grams Iodine

b. Myelography imaging (i.e., intrathecal injections) dosage volumes should not exceed 20 mL

c. Injectable ICM is primarily eliminated via liver metabolism and biliary excretion. It half-life is 24 hours in patients with normal renal function

d. For GI tract imaging; oral LOCM is the preferred if there is a risk of GI tract perforation

Safety Considerations
Incidence, Risk Factor Assessment, Prevention & Treatment

- Acute adverse reactions
- Delayed adverse reactions
- Allergic reactions
- Post-contrast acute kidney injury (AKI) and contrast-induced nephropathy (CIN)
- Special populations
- Extravasation

Adverse Reactions Overview

- Adverse drug reactions (ADR) categorized based as: Acute or Delayed, based on time of onset
  - Acute adverse reactions occur **within** 1 hour of the injection
  - Delayed adverse reactions occur **after** 1 hour to 1 week after the injection
- Severity of ADRs range from minor physiological disturbances to rare, severe events
- Incidence varies with class of contrast used[1,2]
  - Any ADR: 12.7% HOCM (Ionic) vs. 3.1% LOCM (Non-Ionic)
  - Severe (non-fatal) ADR: 0.157% HOCM vs. 0.031% LOCM
    - *Incidence reduced 80% using LOCM vs. HOCM*
  - Incidence of Fatal ADR: 1:100,000 patients (0.0001%) with LOCM or HOCM
  - No clinically significant difference in the incidence and severity of acute ADRs between LOCM products currently marketed in the United States

HOCM: High-Osmolar Contrast Medium
LOCM: Low-Osmolar Contrast Medium

1. Katayama H et al. Radiology. 1990 Jun;175(3):621-8.
2. Caro JJ, et al. Am J Roentgenol. 1991 Apr; 156(4):825-32.

Acute Adverse Reactions Classification

- **Mild Symptoms** (self-limiting)
  - Treatment: Observation and reassurance (minimize patient anxiety)
  - Symptoms: Nausea, mild vomiting, urticaria, itching
- **Moderate Symptoms** (potential to be severe)
  - Treatment: Responds to symptomatic treatment. Continue to treat and monitor to ensure symptoms abate.
  - Symptoms: Severe vomiting, marked urticaria, bronchospasm, facial/laryngeal edema, and vasovagal symptoms
- **Severe Symptoms** (potential morbidity/death)
  - Treatment: CPR/code cart, usually hospitalization
  - Symptoms: Hypotensive shock, respiratory arrest, cardiac arrest or severe arrhythmia, convulsion

American College of Radiology. *Manual on Contrast Media. Version 10.1* 2015.

Iodinated Contrast Media: Physiologic Reactions

- Anxiety[1,2,3]
  - Screening and prophylaxis is recommended. Anxiety can evoke and potentiate the severity of contrast reactions
  - May be necessary to pre-medicate some patients with oral or IV benzodiazepine
- Vasovagal
  - Hypotension with bradycardia and/or nausea/vomiting, generally mild and self-limited
  - Cause unknown; increased vagal tone from CNS - most likely fueled by anxiety
  - Treatment: observation, calm and reassurance
- Cardiovascular toxicity
  - More common during angiocardiography than intravenous administration
    - No difference between LOCM and IOCM
  - Heart failure patients – increased risk of pulmonary edema due to osmotic load and vasovagal effects of ICM
- Neurotoxicity - direct chemotoxic effects; primarily seen with HOCM

1. American College of Radiology. *Manual on Contrast Media. Version 10.1* , 2015.
2. Lalli AF. Radiology 1974; 112:267-271.
3. University of Wisconsin, Contrast Media Tutorial, Jessica B. Robbins, MD and Myron A. Pozniak, MD (Dec 2015).

Iodinated Contrast Media – Allergic-like Reactions

- Allergy Myth: "True allergy to iodine is not possible" [1,2]
- Iodine is an essential trace element (thyroid hormone); NOT an allergen
- No cross-reactivity between ICM and iodine-rich substances
  - Allergy to "iodine-rich" seafood (e.g., shellfish) are due to proteins, not iodine
  - Relative risk of cross-reactivity to ICM in patients with various food allergies[4]: 3.0 – seafood; 2.9 – eggs, milk, or chocolate; 2.6 – fruit and strawberries; 2.2 – asthmatics
- Reactions to iodinated solutions or ointments (e.g., povidone iodine) are unrelated to iodine (due to irritant or allergic dermatitis reaction to the formulation)
- "Allergic-Like" reactions to ICM are due to an inflammatory cytokine response to irritating hyperosmolar, ionic agents
- Replace "Iodine allergy" with more accurate, specific, and descriptive terms
  - "Iodinated contrast media sensitivity"
  - "Seafood intolerance
  - "Povidone-iodine dermatitis"

1. Shehadi WH. AJR 1975;24: 145-152. 2. Katelaris CH, Smith WB. Austr Prescr 2009;32 125-8. 3. American College of Radiology. *Manual on Contrast Media. Version 10.1* 2015. 4. UCSF Dept Radiology, Iodine Allergy and Contrast Administration, http://bit.ly/20CGqID (Dec 2015).

Acute Adverse Reactions: Risk Factor Screening

- Product Specific
  - High-osmolality ionic contrast media: avoid or minimize intravascular use for all patients (e.g., isothalamate meglumine 60% w/v (Conray® 60) = 1,400 mOsm/L)
- Patient-Related
  - Previous history of ICM reaction: 7-17% increased rate of mild reactions; mild reactions not shown to increase the rate of severe reactions
  - Previous moderate or severe acute ICM reaction – 5X increased rate of subsequent acute reactions. But, previous severe reaction not shown to increase the rate of subsequent severe reactions
  - Any severe allergic response to medications or food that required medical treatment
  - Hereditary predisposition (atopic syndrome): asthma, hay fever, allergic rhinitis, or dermatitis (eczema/psoriasis).
    - Note seasonal phenomenon of increased acute reactions during high pollen counts

1. European Society of Urogenital Radiology, ESUR Guidelines on Contrast Media v8.1 (Dec 2015).
2. American College of Radiology. *Manual on Contrast Media. Version 10.1* , 2015.
3. Schabelman E, Witting M. J Emerg Med. 2010 Nov;39(5):701-7.

Acute Adverse Reactions: Prevention

- Consider an alternative test not requiring ICM
- Use a different ICM agent (than before)
- Test dose "offers no value"
- Premedication[1,2]
  - Elective procedure
    - Oral prednisone preferred over i.v. administration – must begin oral doses at least 6 hours prior
    - H-1 antihistamine oral or i.v. 1 hr prior (e.g. diphenhydramine 50 mg)
  - Emergency procedure
    - Methylprednisolone 40 mg i.v. or hydrocortisone 200 mg i.v. every 4hrs prior to ICM (or omit entirely and give only H-1 antihistamine i.v.)
    - Diphenhydramine 50 mg i.v. 1 hr prior to ICM

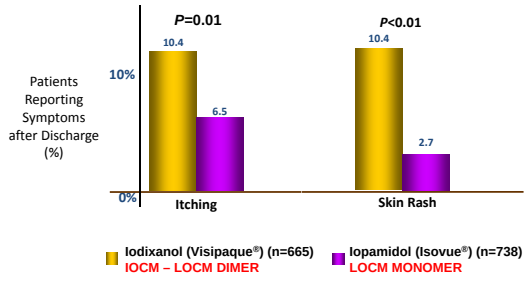
1. European Society of Urogenital Radiology, ESUR Guidelines on Contrast Media v8.1 (Dec 2015).
2. American College of Radiology. *Manual on Contrast Media. Version 10.1* , 2015.
3. Schabelman E, Witting M. J Emerg Med. 2010 Nov;39(5):701-7.

Delayed Adverse Reactions

- Definition: An event occurring more than 1 hour to 1 week after ICM injection; majority occur between 3 hrs and 2 days[1]
- Incidence: 0.5%–14%
  - More common with iso-osmolar dimer (IOCM): Iodixanol (Visipaque®): 10 – 14%[3,4,5,6]
  - Even more common in patients treated with Interleukin-2 (up to 2 yrs)[2]
- Clinical features
  - Seldom reported to Radiologist
  - Majority cutaneous adverse events (persistent skin rash with or without itching)
  - Usually mild to moderate severity, rarely requires hospitalization or is life-threatening
  - May require symptomatic treatment (antihistamines and/or corticosteroids; antipyretics; anti-emetics; fluids)

1. American College of Radiology. *Manual on Contrast Media. Version 10.1* 2015.
2. Univ of Wisc Contrast Agent Tutorial. http://bit.ly/1nB4mO3 (Dec 2015).
3. Christiansen C, et al. Eur Radiol 2000; 10:1965-1975.
4. Loh S, et al. *Radiology* 2010; 255:764-771.
5. Sutton AG et al. *J Invasive Cardiol.* 2003;15:133-138 .
6. Schild HH et al. *Radiology* 2006; 240:56-64.

Delayed Adverse Reaction: Incidence of Symptoms



Sutton AG et al. *J Invasive Cardiol.* 2003;15:133-138.

Delayed Adverse Reactions: Recurrence and Prophylaxis

- Recurrence rates are 25% or higher[3,4]
- T-Cell mediated hypersensitivity – efficacy of corticosteroid and/or H1- antihistamine prophylaxis is unknown[1]
- Premedication prophylaxis is not currently recommended with only a history of mild delayed cutaneous reactions - recommend alternative LOCM be used[1]

1. American College of Radiology. *Manual on Contrast Media. Version 10.1* 2015.
2. Univ of Wisc Contrast Agent Tutorial. http://bit.ly/1nB4mO3 (Dec 2015).
3. Christiansen C, et al. Eur Radiol 2000; 10:1965-1975.
4. Loh S, et al. *Radiology* 2010; 255:764-771.
5. Sutton AG et al. *J Invasive Cardiol.* 2003;15:133-138.
6. Schild HH et al. *Radiology* 2006; 240:56-64.

Polling Question

Which of the following statements is **FALSE**?

a. Anxiety is a risk factor for contrast media reactions and should be assessed and pretreated, if appropriate
b. ICM should not be used in patients reporting an allergy to povidone-iodine
c. Delayed adverse reactions are more common with the iso-osmolar dimer, iodixanol, than with LOCM monomers

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Post-Contrast Acute Kidney Injury (PC-AKI) and Contrast-Induced Nephropathy (CIN)

Post-contrast Acute Kidney Injury and Contrast-induced Nephropathy: Definition

- **Post-contrast acute kidney injury** (PC-AKI): A general term for sudden deterioration in renal function that occurs *within 48 hours following* intravascular administration of iodinated contrast medium
  - PC-AKI may occur regardless of whether the contrast media was the cause
  - PC-AKI is a correlative diagnosis
- **Contrast-induced nephropathy** (CIN): a specific term for sudden deterioration in renal function *that is caused by* the intravascular administration of iodinated contrast media
  - CIN is a subgroup of PC-AKI
  - CIN is a causative diagnosis
- ACR (2015) "Unfortunately, very few published studies have a suitable control group to permit the separation of CIN from PC-AKI"
  - "At present, the position of ACR is that CIN is a real, albeit rare entity – true incidence of CIN requires further study"
  - Prior to 2007, CIN studies failed to include a control group of patients not receiving contrast and failed to adjust for normal fluctuations in serum creatinine

1. American College of Radiology (ACR). Manual on Contrast Media. Version 10.1 2015.
2. Solomon, R. www.appliedradiology.org/CIN-CE June 2014.

Post-contrast Acute Kidney Injury and Contrast-induced Nephropathy: Pathogenesis

- PC-AKI may be caused by ANY nephrotoxic event (including CIN) that is **coincident to** intravascular administration of ICM
  - Note there is a normal physiologic fluctuation in serum creatinine (SCr)
  - Patients with an elevated SCr at baseline have a greater variance in daily measurements than normal patients
- CIN Pathophysiology is not well understood but is believed to be caused by
  - Renal vasoconstriction causing renal medullary ischemia
    - Osmotic and direct chemotoxic mechanisms
  - Direct tubular toxicity
    - Direct cytotoxic effect of ICM on tubular epithelial cells

Morcos SK, European Society of Urogenital Radiology (ESUR) Guidelines on Contrast Media Eur Radiol 2007;6 17-25.

Contrast-induced Nephropathy: Incidence and Patient Harm

- 3rd leading cause of hospital-acquired acute kidney injury
- Overall incidence of CIN ~ 6.5% among patients with risk factors
  - Primary Risk Factor: Stage III and IV chronic kidney disease (CKD)
    - eGFR between 15 to 45mL/min/1.73m^2
  - ~6 million US adults (2.5% of population) are at 5-10X increased risk for CIN
  - Diabetics with CKD have the greatest risk
- Patient harm:
  - Increased length of stay (LOS): 2 days (average)
    - 0.4 to 1% of patients require dialysis – increases LOS by 17 days[2]
  - Increased in-hospital mortality[2]
    - 22% mortality during index hospitalization vs. 1.4% w/o CIN[2]
  - Increased post-discharge mortality and morbidity
    - 1 year mortality: 12.1% w/CIN vs. 3.7% w/o CIN
    - 5 year mortality: 44.6% w/CIN vs. 14.5% w/o CIN
    - All have a much higher incidence of renal, cardiac, and neurological events

1. Solomon, R. www.appliedradiology.org/CIN-CE June 2014.
2. Levy EM et al. JAMA. 1996;275:1489-1494.
3. Gruberg L et al. J Am Coll Cardiol. 2000;36(5):1542-1548.
4. Rihal CS et al. Circulation. 2002;105:2259-2264.

Contrast-Induced Nephropathy: Risk Factors

- Chronic kidney disease is the most important risk factor for the development of CIN[1]
  - Calculated eGFR using the modification of diet in renal disease (MDRD) equation
    - eGFR is more reliable than serum creatinine (SCr) for assessing CIN risk
- Diabetes Mellitus
- Acute Kidney Injury
- Dehydration (Any condition associated with hypovolemia)
- Large ICM dosage volumes – proportional nephrotoxic effect; no evidence of dose-toxicity following i.v. administration when administered at recommended doses
- Cardiac Angiography – due to intra-arterial and supra-renal; dose is large and less dilute
- ICM repeated within the last week
- Acute gout
- Paraproteinemias: multiple myeloma
- **Concurrent nephrotoxic medications**
  - ACE inhibitors; Angiotensin II receptor blockers; aminoglycosides, amphotericin B; beta-lactam antibiotics; cyclosporine, diuretics (and/or combination with ACEI/ARB), gold salts, iodinated contrast media, numerous chemotherapy agents, NSAIDs, vancomycin, etc.

1. American College of Radiology (ACR). Manual on Contrast Media. Version 10.1 2015.
2. Davenport, MS et al. Radiology 2013 268:3, 719-728.
3. McDonald, JS, et al. Radiology 2014 271:1, 65-73.

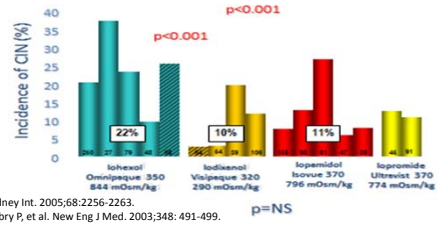
Contrast-induced Nephropathy: Relative LOCM Risk

- 42 trial, meta-analysis (n = 10,048) of controlled trials of LOCM and iso-osmolar iodinated contrast media (IOCM)
- **Aim**: Determine if there is a difference in nephrotoxic potential between commonly used LOCM and IOCM products
- **Purpose**: perform a systematic review and network (mixed treatment comparison) meta-analysis of randomized trials focusing on renal safety of LOCM or IOCM ICM
- **Conclusions:**
  - Iodixanol, iomeprol (not US approved), iopamidol and ioversol – similar renal safety profile
  - Iohexol and ioxaglate have a poorer renal safety profile
  - Iopromide - further data is required

Biondi-Zoccai et al. International Journal of Cardiology 172 (2014) 375–380.

Contrast-induced Nephropathy: Cardiac Arterial Angiography

- Preferentially use lower risk IV LOCM[1-5] for larger volume and/or cardiac angiography studies
  - Iohexol (Omnipaque®)
    - eGFR 15 to 30 mL/min/1.73m^2 with no additional risk factors – avoid use of iohexol
    - eGFR 30 to 45 mL/min/1.73m^2 with multiple risk factors – avoid use of iohexol



1. Solomon R. Kidney Int. 2005;68:2256-2263.
2. Aspelin PA, Aubry P, et al. New Eng J Med. 2003;348: 491-499.
3. Sharma SK, Kini A. Cathet Cardiovasc Interv. 2005;65: 386-393.
4. Laskey, W., Aspelin P et al. American Heart Journal, Nov 2009;158(5):822-8.
5. Solomon R. Kidney Int. 2005;68:2256-2263.

See page 15 for enlarged view

CIN High Risk Patient: Risk Reduction Strategies

- Determine eGFR prior to procedure; if not possible, follow eGFR ≤ 45 mL/min protocols
  - Diabetic (higher risk) than non-diabetic
- Consider alternative imaging strategies (ultrasound, non-contrast MRI)[1]
- Use the least nephrotoxic LOCM at the lowest effective dose (concentration and volume)[2]
  - Iodixanol (Visipaque®), Iopamidol (Isovue®), Ioversol (Optiray®)
  - Iopromide (Ultravist®) – need more clinical data
- Stop nephrotoxic drugs[1]
- Routine/emergency hydration protocols[1]
  - Scheduled exam: encourage oral fluids (1-2 L 6hr before and after) and i.v. normal saline or i.v. sodium bicarbonate (154 mEq/L in Dextrose 5% Water)
  - Emergency exam: i.v. sodium bicarbonate
    - Mannitol has no benefit
    - Furosemide, routine use, may be harmful
- Antioxidants
  - Acetylcysteine oral (scheduled) –insufficient evidence of efficacy[1]

1. American College of Radiology. *Manual on Contrast Media. Version 10.1*, 2015.
2. Biondi-Zoccai et al. International Journal of Cardiology 172 (2014) 375–380.
3. Aspelin PA, Aubry P, et al. New Eng J Med. 2003;348: 491-499.
4. Laskey, W., Aspelin P et al. American Heart Journal, Nov 2009;158(5):822-8.
5. Sharma SK, Kini A. Cathet Cardiovasc Interv. 2005;65: 386-393.
6. Solomon R. Kidney Int. 2005;68:2256-2263.

CIN High Risk Patient: Risk Reduction Strategies

DIABETIC		
Agent	**Creatinine**	**eGFR**
Iohexol	< 1.4	≥ 45
Iodixanol	1.4 – 2	45 – 30
No i.v. contrast	> 2	< 30

NON-DIABETIC		
Agent	**Creatinine**	**eGFR**
Iohexol	< 1.8	> 30
Iodixanol	1.8 – 3	30 – 15
No i.v. contrast	> 3	< 15

Contrast-induced Nephropathy: Screening Guidelines When is a Baseline Serum Creatinine Needed

- Baseline serum creatinine (SCr) required prior to ICM injection for patients with CIN risk factors
- Patients without the following risk factors DO NOT REQUIRE a baseline SCr [1,2]
  - Age > 60
  - History of renal disease (i.e., eGFR ≤ 60 mL/min/1.73m^2)
  - History of hypertension requiring medical therapy
  - History of diabetes mellitus
  - Intra-arterial ICM injection[3] or CT angiography exam[3]
- No agreed upon maximum interval between baseline renal function assessment and ICM administration in at-risk patients[2]
  - Outpatients: typically 30 to 60 day interval (some 6 months)
  - Inpatients: typically 1 to 2 weeks
  - Shorter interval recommended for patients with a new risk factor or heightened risk of renal dysfunction (e.g. abdominal trauma)

1. American College of Radiology. Manual on Contrast Media. Version 10.1, 2015.
2. European Society of Urogenital Radiology, ESUR Guidelines on Contrast Media v8.1 (Dec 2015).
3. Choyke PL, et al. Tech Urol.1998;4(2):65-69.

Metformin

- Metformin does not increase risk of CIN
- Patients who develop PC-AKI while taking metformin are susceptible to lactic acidosis
  - Normally, 90% of metformin is excreted unchanged by the kidneys in 24 hrs.
- Incidence of lactic acidosis (Radiology): 0 to 0.084 cases per 1,000 patient years[1,2]
  - Patient mortality : Metabolic acidosis ~ 50%
- Patient Management is risk-based[1,2]
  - **Category I**: Patients with no evidence of AKI and eGFR ≥30 mL/min/1.73m^2, there is NO need to discontinue metformin either prior to or following ICM administration, nor is there an obligatory requirement to reassess the patient's renal function following the procedure
  - **Category II**: Patients with acute kidney injury or moderate to severe chronic kidney disease (defined as eGFR < 30), or are undergoing arterial catheter studies that might result in emboli to the renal arteries, metformin should be temporarily discontinued at the time of the procedure, withheld for 48 hours, and reinstituted ONLY after renal function has found to be normal

1. American College of Radiology. Manual on Contrast Media. Version 10.1, 2015.
2. European Society of Urogenital Radiology, ESUR Guidelines on Contrast Media v8.1 (Dec 2015).

Patient Screening for Other Medication Risk Factors

- Other medication risk factors NOT related to CIN:
  - Myelography: Anticoagulants and antiplatelets
    - Warfarin – stop within 4 days
    - Novel oral anticoagulants and dual antiplatelets should be held and resumed per protocol
  - Interleukin-2 (within 2 years): increased risk of delayed skin reactions
  - Beta-Blockers: May impair the management of bronchospasm and response to epinephrine (use should be documented and assessed)

1. European Society of Urogenital Radiology, ESUR Guidelines on Contrast Media v8.1 (Dec 2015).
2. American College of Radiology. *Manual on Contrast Media. Version 10.1* , 2015.

Patient Screening: Special Populations

- **Pregnancy category B**[1] – Routine pregnancy screening is not recommended
  - Use if clinically necessary (In-vivo tests (rats/rabbits ~100x human doses) report no mutagenic or teratogenic effects)
- **Breast feeding**[1] – Low risk. Use supplemental breast milk for 24 hrs – If desired
  - < 0.01% of the intravascular maternal ICM dose is absorbed systemicallyby infant
- **Neonates**
  - Use caution if less than 12 months of age; SCr ≥ 1.5 mg/dl, CHF, or asthma
- **Myasthenia gravis**
  - Historically considered a relative contraindication only for HOCM; but 2013 study[2] reported significant disease-related symptom exacerbations (weakness, dyspnea) within 24 hours after LOCM vs. no contrast
- **Thyrotoxicosis**
  - Untreated Graves' Disease
  - Multinodular goiter and thyroid autonomy and/or live in area of dietary iodine deficiency
  - Refer to Endocrinologist

1. American College of Radiology. Manual on Contrast Media. Version 10.1 2015.
2. Somashekar DK, et al. Radiology. 2013 Jun;267(3):727-34.

Patient Screening: Unique Considerations for Children

- Unique Considerations ('strange' sensations coupled with anxiety or fear)
- Injection-related physiological effects or side-effects more significant in young children
  - Sensation of warmth, burning, and nausea – "unusual feeling" for an infant or young child
  - Recommend sedation to avoid:
    - Crying/Moving – Necessitating repeated exposure to ICM and radiation
  - Use lowest effective LOCM/IOCM iodine concentration to reduce osmolality and viscosity (i.e. risk of extravasation)
    - Osmolality - small children particularly susceptible to osmotic loads and fluid shifts
    - Viscosity - small vessels influence catheter size and increase injection pressures
- Assessing Renal Function: estimated GFR better than serum creatinine
  - Bedside Schwartz Equation:

    eGFR (mL/min/1.73 m^2) = (0.41 × height) / serum creatinine

    Height in cm; Serum creatinine in mg/dL

1. American College of Radiology. *Manual on Contrast Media. Version 10.1* , 2015.

Patient Screening: Unique Considerations for Children

LOCM Agent	Concentration mg I/mL	Increase Iodine Concentration (%)	Osmolality (mOsm/Kg)	Increase Osmolality (%)	Viscosity (cp @ 37 C)	Increase Viscosity (%)
Iohexol 240	240	Baseline	520	Baseline	3.4	Baseline
Iohexol 300	300	25%	672	29%	6.3	85%
Iohexol 350	350	46%	844	62%	10.4	206%
Iopamidol 250	250	Baseline	524	Baseline	3	Baseline
Iopamidol 300	300	20%	616	18%	4.7	57%
Iopamidol 370	370	48%	796	52%	9.4	213%

- Recommend IOCM - iodixanol (not shown in table) or LOCM at lowest effective iodine concentration
  - Reducing iodine concentration disproportionally reduces osmolality and to a greater extent viscosity

1. American College of Radiology. *Manual on Contrast Media. Version 10.1* , 2015.

See page 16 for enlarged view

Extravasation

- Incidence: LOW
  - Intravenous ICM extravasation: 0.1 to 0.9% (1/1,000 to 1/106 patients)
- Sequelae
  - Usually non-eventful
  - Acute local inflammatory response peaks in 24 to 48 hrs - rarely a severe event, no permanent injury
- Best prevented by proper technique, vascular access device, and patient communication
  - Intra-arterial contrast injections into peripheral vessels of the arm, legs, or head can be quite painful - IOCM/LOCM are preferred
  - Avoid small vessels (hand, wrist, foot, ankle); LOCM/IOCM (lowest viscosity) are preferred
- Treatment
  - Observation – several hours prior to discharge
    - Elevation of affected extremity above the heart
    - Hot or cold compresses – no evidence favoring one over other
    - No evidence of benefit or harm: aspiration of fluid and/or local injection of corticosteroids or hyaluronidase
  - Surgical consultation if prolonged pain or tissue injury

1. Wang, CL et al. Radiology. 2007 Apr; 243:1;80-87.
2. American College of Radiology. Manual on Contrast Media. Version 10.1 2015.

Polling Question

For an adult patient with an eGFR between 15 to 30 mL/min/1.73m^2 who is undergoing a cardiac angiography exam with contrast, which iodinate contrast media should be used to minimize the risk of contrast-induced nephropathy?

a. Iodixanol (Visipaque®) 320
b. Iodixanol (Visipaque®) 320, Iopamidol (Isovue®) 370, or Ioversol (Optiray®) 350
c. Iodixanol (Visipaque®) 320, Iohexol (Omnipaque®) 350, Iopamidol (Isovue®) 370, Ioversol (Optiray®) 350
d. Iodixanol (Visipaque®) 320, Iohexol (Omnipaque®) 350, Iopamidol (Isovue®) 370, Iothalamate meglumine (Conray®) 60% 300 mgI/mL, Ioversol (Optiray®) 350

Safe Handling - CDC Safe Injection Practices

- ICM are super-saturated solutions: Do not mix ICM with other drugs or solutions
- Aseptic and USP 797 Sterile Compounding guidelines must be followed. Applies to all areas
  - BUD assigned: Inside ISO Class 5: Can be stored up to 3 days at room temperature
    Outside ISO Class 5: Use immediately (≤ 1 hour)
- CDC Safe Injection Practices guidelines* - Incorporate into policies and procedure
  - Do not administer medications from single-dose vials or ampules to multiple patients
    - Propofol, contrast media
  - Do not use bags or bottles of i.v. solution as a common source for multiple patients
  - Do not "pre-spike IV bags"
  - Multi-dose vial (MDV) used for multiple patients
    - Medication from MDV must be drawn up outside of immediate treatment area or MDV must be discarded after treatment (i.e., used for only one patient)
    - Use a revised 28 day BUD from the date of opening or puncture except when:
      - Original BUD is shorter
      - Manufacturer specifies in package insert

BUD = Beyond Use Date; MDV = Multi-Dose Vial

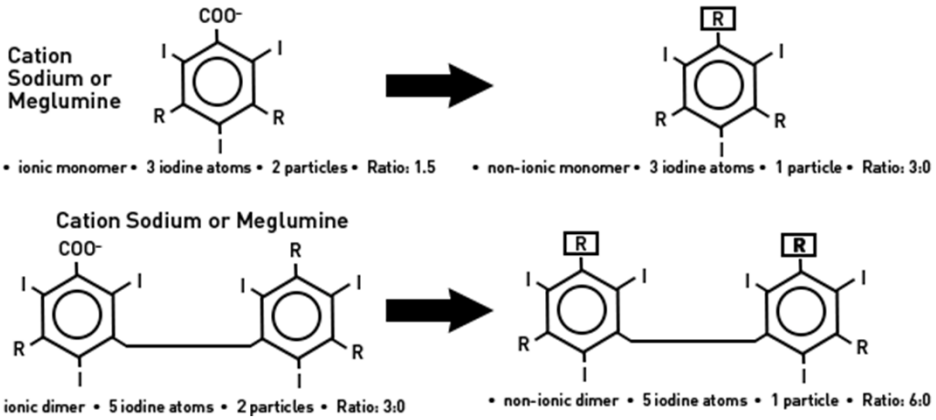
*Direct Impact EP (Non-compliance is likely to create an immediate risk to patient safety or quality of care)

Summary

- Director of Pharmacy is responsible for compliance with medication management standards, including the Radiology Department – with few, notable, exceptions
- Non-ionic, low-osmolar iodinated contrast media (LOCM) are the safest agents for intravascular and intrathecal administration
- "Injectable" LOCM should be substituted for barium and HOCM for patients at risk for aspiration or GI tract perforation
- Iodine allergy is a "medical myth." However, patients should be screened for sensitivities that put them at risk for adverse reactions
- Chronic kidney disease is the most important risk factor for developing CIN
- CIN prevention is essential to reduce in-hospital length of stay, morbidity and mortality
- Estimated Glomerular Filtration Rate (eGFR) is a more accurate predictor for assessing CIN risk than serum creatinine
- There is no agreed-upon eGFR threshold below which the risk of CIN is considered so great that intravascular ICM should never be administered
- LOCM used for contrast-enhanced imaging of non-communicative patients (neonates/young children) should be carefully selected – using minimum concentrations and balancing the physical properties of osmolality and viscosity

Iodinated Contrast Media - Classification

- Categorized by chemical structure (monomer and dimer), Ionization, and osmolality
- Structure based on modifications of the 2, 4, 6-tri-iodinated benzene ring structure



Iodinated Contrast Media: Classification and Use

IONIC HIGH-OSMOLALITY CONTRAST MEDIA (HOCM) >1,000 mOsm/Kg
Use: Oral or Gastrointestinal[1], Intrauterine, Bladder

Ionic Monomers
Oral/GI: diatrizoate sodium/diatrizoate meglumine (Gatrografin®, Gastroview®), diatrizoate sodium (Hypaque®)
Intrauterine: iodipamide meglumine/diatrizoate meglumine (Sinografin®)
Bladder: iothalamate meglumine (Conray®, CystoConray®), diatrizoate meglumine (Cystografin®)

Use: Arteriography Only

Ionic Dimer
Ioxaglate (Hexabrix®) – *withdrawn from U.S. Sept. 2015*

NON-IONIC LOW-OSMOLALITY CONTRAST MEDIA (LOCM) <900 mOsm/Kg
Use: Intravascular, Intrathecal[2], Intrauterine, Bladder, Oral/Rectal[1]

Nonionic Monomers
Iohexol (Omnipaque®), Iopamidol (Isovue®), Iopromide (Ultravist®), Ioversol (Optiray®)

Nonionic Dimers (iso-osmolar contrast)
Iodixanol (Visipaque®)

Higher Osmolality

Goal is to lower osmolality

Lower Osmolality

[1]Oral/Rectal: Iohexol only FDA approved; others off-label use
[2]Intrathecal: Iohexol, Iopamidol only FDA approved; 180-300 mgI/mL concentrations only, 10–20 mL max

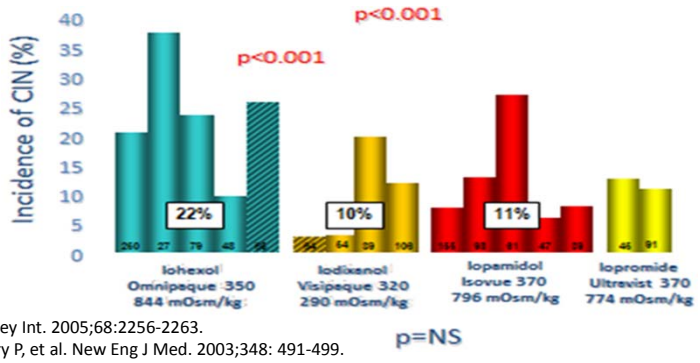
Pharmacokinetics of Commonly Used Injectable ICM

PHARMACOKINETICS					
Chemical Name (Trade Name)	Protein Binding (%)	Volume Distribution	Metabolism	Elimination Half-life	Route Elimination
Iodixanol (Visipaque®)	0%	0.28 L/kg	None	120-130 min (23 hrs renal insufficiency)	98% renal
Iopromide (Ultravist®)	1%	0.2 L/kg	None	6.2–40 hours	94% renal
Iopamidol (Isovue®)	1%	0.35 L/kg	Minimal	2 hours	92-98% renal, 10% feces
Iohexol (Omnipaque®)	Low	0.108–0.219 L/kg	Minimal	2 hours	100% renal
Ioversol (Optiray®)	0%	Not Reported	None	1.6–2 hours	95% or greater
Ioxilan (Oxilan®)	Negligible	10 L	None	137 minutes	94% renal
Ioxaglate (Hexabrix®)	Low	0.12–0.3 L/kg	None	61–140 minutes	90% renal

- Primary mode of elimination: Kidney, via glomerular filtration
  - Normal renal elimination half-life: 2 hours; 100% cleared in 24 hours
- Severe renal impairment: Elimination half-life: 16 to 84 hours
  - Secondary mode: Liver metabolism with biliary excretion – slow and limited
  - Dialysis effectively removes ICM
- Low plasma protein binding
- Low volume of distribution due to low lipid solubility

Contrast-induced Nephropathy: Cardiac Arterial Angiography

- Preferentially use lower risk IV LOCM[1-5] for larger volume and/or cardiac angiography studies
  - Iohexol (Omnipaque®)
    - eGFR 15 to 30 mL/min/1.73m^2 with no additional risk factors – avoid use of iohexol
    - eGFR 30 to 45 mL/min/1.73m^2 with multiple risk factors – avoid use of iohexol



1. Solomon R. Kidney Int. 2005;68:2256-2263.
2. Aspelin PA, Aubry P, et al. New Eng J Med. 2003;348: 491-499.
3. Sharma SK, Kini A. Cathet Cardiovasc Interv. 2005;65: 386-393.
4. Laskey, W., Aspelin P et al. American Heart Journal, Nov 2009;158(5):822-8.
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Iopamidol 250	250	Baseline	524	Baseline	3	Baseline
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- Recommend IOCM - iodixanol (not shown in table) or LOCM at lowest effective iodine concentration
  - Reducing iodine concentration disproportionally reduces osmolality and to a greater extent viscosity

1. American College of Radiology. *Manual on Contrast Media. Version 10.1* , 2015.

Resources

American College of Radiology

- www.acr.org

ACR Manual on Contrast Media, version 10.1, 2015

- http://www.acr.org/~/media/37D84428BF1D4E1B9A3A2918DA9E27A3.pdf

Association for Professionals in Infection Control and Epidemiology

- www.apic.org

APIC 2010: Safe Injection, Infusion, and Medication Vial Practices in Health Care

- http://apic.org/Resource_/TinyMceFileManager/Position_Statements/2016APICSIPPositionPaper.pdf

Centers for Disease Control

- www.cdc.gov

CDC Guidelines: Safe Injection Practices to Prevent Transmission of Infections to Patients

- http://www.cdc.gov/injectionsafety/IP07_standardPrecaution.html
- http://www.cdc.gov/injectionsafety/unsafePractices.html

CDC Infection Prevention Checklist for Outpatient Settings

- http://www.cdc.gov/hai/pdfs/guidelines/Ambulatory-Care+Checklist_508_11_2015.pdf

Centers for Medicare and Medicaid (CMS)

- www.cms.gov

Conditions of Participation: Hospitals (Survey, Certification, and Compliance)

- https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/CertificationandComplianc/Hospitals.html

CMS Memorandum: Safe Use of Single Dose/Single Use Medications to Prevent Healthcare-associated Infections

- https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/downloads/Survey-and-Cert-Letter-12-35.pdf

European Society of Urogenital Radiology

- www.esur.org

- ESUR Guidelines – 8.1 Contrast Media
  www.esur.org/esur-guidelines/

- ESUR Guidelines – 9.0 Contrast Media Guidelines (order direct via email to:raymond.oyen@uzleuven.be)

ISMP Medication Safety Alert!

- www.ismp.org

- ISMP Medication Safety Alert!® Acute Care edition (biweekly email subscription)

http://ismp.org/newsletters/acutecare/default.aspx

- **The Joint Commission**
  - www.jointcommission.org
    - FAQ for current standards
    - FAQ for current NPSG
    - Current and Past Copies of:
    - Sentinel Event Alert
    - Sentinel Event Alert Issue 52: Preventing Infection from the Misuse of Vials
    - http://www.jointcommission.org/sea_issue_52/
    - Pre-publication standards

- **University of Wisconsin, Contrast Media Tutorial, Jessica B. Robbins, MD and Myron A. Pozniak, MD (Dec 2015)**
  - http://docplayer.net/7254603-Contrast-media-tutorial-ct-contrast-agents.html
  - ESUR Guidelines – 8.1 Contrast Media

  - Myron A. Pozniak, MD
    mpozniak@uwhealth.org

Intravascular Iodinated Contrast Media Specifications - US (Dec 2014)

Product	Generic name (concentration in mg contrast/ml	Ionicity	Iodine+ (mg/ml)	Viscosity+ 25° C (cp or mPa.s)	Viscosity+ 37° C (cp or mPa.s)	Osmolality (mOsm/kg H2O)
INTRAVASCULAR						
Omnipaque™ 140 (GE Healthcare)	Iohexol 302	Nonionic	140	2.3*	1.5	322
Conray™ 30 (Covidien)	iothalamate (300)	Ionic	141	2	1.5	600
Ultravist* 150 (Bayer HealthCare)	iopromide	Nonionic	150	2.3*	1.5	328
Omnipaque™ 180 (GE Healthcare)	iohexol (388)	Nonionic	180	3.1*	2	408
Isovue*-200 (Bracco)	iopamidol (408)	Nonionic	200	3.3*	2.0	413
Conray™ 43 (Covidien)	iothalamate (430)	Ionic	202	3	2	1000
Omnipaque™ 240 (GE Healthcare)	iohexol (518)	Nonionic	240	5.8*	3.4	520
Optiray™ 240 (Mallinckrodt)	ioversol (509)	Nonionic	240	4.6	3.0	502
Ultravist* 240 (Bayer Healthcare)	iopromide	Nonionic	240	4.9*	2.8	483
Isovue* 250 (Bracco)	iopamidol (510)	Nonionic	250	5.1*	3.0	524
Visipaque™ 270 (GE Healthcare)	iodixanol (550)	Nonionic	270	12.7*	6.3	290
Conray™ (Covidien)	iothalamate (600)	Ionic	282	6	4	1400
Isovue* 300 (Bracco)	iopamidol (612)	Nonionic	300	8.8*	4.7	616
Omnipaque™ -300 (GE Healthcare)	iohexol (647)	Nonionic	300	11.8*	6.3	672
Optiray™ 300 (Mallinckrodt)	ioversol (640)	Nonionic	300	8.2	5.5	651
Oxilan* 300 (Guerbet)	ioxilan (623)	Nonionic	300	9.4*	5.1	610
Ultravist* 300 (Bayer Healthcare)	iopromide	Nonionic	300	9.2*	4.9	607
Hexabrix™**** (Guerbet)	ioxaglate meglumine/ sodium (589)	Ionic	320	15.7*	7.5	=600
Optiray™320 (Mallinckrodt)	ioversol (680)	Nonionic	320	9.9	5.8	702
Visipaque™ 320 (GE Healthcare)	iodixanol (652)	Nonionic	320	26.6	11.8	290
Optiray™ 350 (Mallinckrodt)	ioversol (740)	Nonionic	350	14.3	9.0	792
Omnipaque™ 350 (GE Healthcare)	iohexol (755)	Nonionic	350	20.4*	10.4	844
Oxilan* 350 (Guerbet)	ioxilan (727)	Nonionic	350	16.3*	8.1	721
Isovue* 370 (Bracco)	iopamidol (755)	Nonionic	370	20.9*	9.4	796
MD-76™ R (Mallinckrodt)	diatrizoate/ meglumine/ sodium (760)	Ionic	370	16.4	10.5	1551
Ultravist* 370 (Bayer Healthcare)	Ioprokoi98mide	Nonionic	370	22.0*	10.0	774
Cholografin* (Bracco)	iodipamide (520)	Ionic	257	6.6	5.6	664

+ Data from product package inserts, product brochures, technical information services and Rohrer, M, et al., Comparison of Magnetic Properties of MRI Contrast Media Solutions at Different Field Strengths. Investigative Radiology 2005;40:715-724.

* Measured at 20o C.

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1

Self-assessment Questions

1. Which of the following is a not risk factor for contrast-induced nephropathy?

    a. Diabetes mellitus.
    b. Hypervolemia.
    c. Gout.
    d. Chronic kidney disease.

2. Which of the following is **not** a risk factor for adverse reactions to iodinated contrast media?

    a. Psoriasis.
    b. Allergic response to medications or food that requires medical treatment.
    c. Use of low-osmolality iodinated contrast media.
    d. Previous moderate or severe acute reaction to iodinated contrast media.

3. Which of the following statements is **FALSE**?

    a. X-ray radiopacity is directly proportional to the organically bound iodine.
    b. X-ray response to iodine concentration varies among iodinated contrast media products with equal concentrations of iodine.
    c. Low-osmolality contrast media is associated with lower incidence of adverse drug reactions compared to high-osmolality contrast media.
    d. Low-osmolality contrast media are non-ionic dimers or monomers.

4. Which of the following statements is **FALSE**?

    a. Iodinated contrast media with an osmolality above 900 mOsm/L is not approved for peripheral vascular administration.
    b. Low-osmolarity contrast media is approved by the FDA for peripheral vascular administration.
    c. High-osmolality contrast media is restricted for use in the GI tract and body cavities.
    d. Patients at risk for GI performation should receive barium or high-osmolality contrast media.

5. Which of the following is NOT a possible acute adverse reactions to iodinated contrast media?

    a. Urticaria.
    b. Bronchospasm.
    c. Nausea.
    d. Allergic reaction to iodine.

6. Which of the following regarding contrast-induced Nephropathy (CIN) is **FALSE**?

a. Is caused by the intravascular administration of iodinated contrast media.
b. Has an incidence of approximately 6.5% in patients with risk factors.
c. Patients on beta blockers have an increased risk for CIN.
d. Determining an eGFR prior to a procedure is a recommended risk reduction strategy.

Answers

1. b
2. c
3. b
4. d
5. d
6. c