Contrast Media and Contrast Reactions

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Malpractice Issues

- Incorrect use of contrast media
- Extravasation (primarily HOCM)
- Failure to use safer imaging option
- SUBSTANDARD TREATMENT OF A CONTRAST REACTION
Contrast Media

- Iodinated contrast media
  - HOCM vs LOCM
  - Precautions & premedications
  - Adverse effects
- Gadolinium-based contrast media
- Enteric contrast media
Iodinated Contrast: Compounds

- **Ionic monomer:** Tri-iodinated benzene with 3 simple amide chains. Dissociate in solution.
- **Ionic dimer:** 2 rings connected by amide chain
- **Nonionic monomer:** Side chains modified with hydroxyl groups.
- **Nonionic dimer:** Contains up to 12 hydroxyl groups

From R. Older, internet tutorial
## Iodinated Contrast: Properties

<table>
<thead>
<tr>
<th>Compound</th>
<th>[Iodine] mg/mL</th>
<th>mOsm/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionic monomer</td>
<td>up to 400</td>
<td>1400-2100</td>
</tr>
<tr>
<td>Ionic dimer</td>
<td>320</td>
<td>600</td>
</tr>
<tr>
<td>Nonionic mono</td>
<td>up to 350</td>
<td>600-800</td>
</tr>
<tr>
<td>Nonionic dimer</td>
<td>320</td>
<td>290</td>
</tr>
</tbody>
</table>

Human serum: 290 mOsm/kg water
Iodixanol

- Nonionic dimer, iso-osmolar
- Less nephrotoxic, fewer reactions?
- NEPHRIC study (NEJM 348:491-499, 2003)
  - Patients with creatinine 1.5 – 3.5 mg/dL had angiography
    - Iohexol: nephropathy in 26%
    - Iodixanol: nephropathy in 3%
## Incidence of Reactions

<table>
<thead>
<tr>
<th>Reaction</th>
<th>HOCM</th>
<th>LOCM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>5-8%</td>
<td>1-2%</td>
</tr>
<tr>
<td>H/O Allergy</td>
<td>10%</td>
<td>3-4%</td>
</tr>
<tr>
<td>Severe</td>
<td>.1%</td>
<td>.01%</td>
</tr>
<tr>
<td>Fatal</td>
<td>1/40k-170k</td>
<td>1/200k-300k</td>
</tr>
</tbody>
</table>

Indications for LOCM: previous reaction, asthma, atopy or allergies, cardiac disease, children, patient request, no history, renal insufficiency, extravasation risk, physician discretion.
Types of Reactions

• Anaphylactoid
• Nonanaphylactoid
• Delayed
Anaphylactoid Reactions

- Urticaria
- Facial/laryngeal edema
- Bronchospasm
- Circulatory collapse
Nonanaphylactoid Reactions

- Nausea/vomiting
- Cardiac arrhythmia
- Pulmonary edema
- Seizure
- Renal failure
Delayed Reactions

- Fever, chills
- Rash, flushing, pruritis
- Arthralgias
- Nausea, vomiting
- Headache
Risk Factors and Precautions

• **Risks**
  • Allergy
  • Renal failure
  • Other

• **Precautions**
  • Premedication
  • Hydration
  • Dose limitation
Allergic Risk

Patients with hx of major allergy, asthma

- 50 mg prednisone PO 13, 7, and 1 hr prior
- 50 mg Benadryl PO/IM 1 hour prior

- If urgent: 200mg hydrocortisone IV q 4 hrs
  - Consider ephedrine (NOT if HTN, angina, arrhythmia)
  - At least 6 hours from first dose
Elevated creatinine, especially with diabetes, or paraproteinemia such as myeloma

- Hydration
- Limit dose
- Consider premedication
Metformin

Risk of lactic acidosis

• Discontinue for 48 hrs after contrast
• Check creatinine before resuming
• If Metformin+CRI+IVC → LA

50% mortality
Cardiac Risk

- Angina/CHF with minor exertion
- Aortic stenosis
- Primary pulmonary hypertension
- Severe cardiomyopathy

➤ Limit dose
Other Risks

- **Pregnancy:** category B
- **Breast-feeding:**
  - Package insert: may substitute with bottle for 24 hrs, not necessary
  - 1% excreted in milk, of which 2% absorbed by baby
Other Risks

Pheochromocytoma  
Sickle cell disease  
Untreated hyperthyroid  
Myasthenia gravis  
Interleukin-2 therapy

Hypertensive crisis*  
Sickle cell crisis  
Thyroid storm  
Exacerbation*  
Delayed reaction

*Doubtful risk with nonionic agents
Acute Reactions

• ALWAYS
  • ABC’s
  • Vitals
  • Physical exam

• OFTEN
  • Oxygen 10L/min
  • IV Fluids: NS or Ringer’s
Nausea

• Common with ionics
• OBSERVE
• Can be a precursor of more severe reaction
Urticaria

- OBSERVE
- Listen to lungs
- Benadryl 25-50mg PO/IM/IV
- Zantac 50mg PO or slowly IV
- Epi SC (1:1000) .1-.3ml = .1-.3mg
Laryngeal Edema

- EPINEPHRINE IV slow, 1.0ml*
  - May repeat up to 1mg*
- O2 10L/min via mask*
- NO BRONCHODILATORS

*Consider calling code
Bronchospasm

- **O2 10L/min**
- Monitor: ECG, O2 sat, BP
- **ALBUTEROL INHALER**
- Epinephrine SC .1-.3ml*
- Epinephrine IV 1.0 ml, may repeat*
Bronchospasm on $\beta$-Blockers

May get pure alpha response to epi: HTN

- **ISUPREL INHALER**
- **ISOPROTERENOL IV 1:5000 0.5-1 ml in 10 cc NS**
- If HTN severe, glucagon 1 mg IM/IV, 1-2mg
  - Reverses $\beta$ blockade
  - Side effects: nausea, vomiting, hypoglycemia
Hypotension with Bradycardia (Vagal Reaction)

- Legs elevated, Monitor vital signs
- O2 10L/min
- Ringer's lactate or normal saline
- ATROPINE 0.6-1.0mg IV slow, repeat to 0.04mg/kg
Hypotension with Tachycardia

- Legs elevated > 60 degrees, head down
- Monitor ECG, O2 sat, BP
- O2 10L/min
- Ringer's lactate or normal saline
- Epinephrine IV 1.0ml slowly, up to 1mg
- DOPAMINE 1600 ug/ml: 2-5 ug/kg/min IV
- Consider ICU transfer
Severe Hypertension

- Monitor ECG, O2 sat, BP
- NITROGLYCERINE 0.4mg SL (x3) or 1" topical 2%
- Sodium nitroprusside, must dilute with D5W
- Transfer to ICU or ED
- For pheochromocytoma: PHENTOLAMINE 5mg IV
Chest Pain

- ECG
- O2 10 L/min
- Vitals, physical exam: ?CHF
- NITROGLYCERINE, SL
- Discuss with primary MD
- Transfer to ED/ICU
**Pulmonary Edema**

- Elevate torso, rotating turniquets
- O₂ 6-10L/min
- LASIX 40mg IV, slow push
- Consider morphine
- ICU or ED
Seizures or Convulsions

- O2 10L/min, monitor vitals
- VALIUM 5mg or VERSED 2.5mg IV
- Consider Dilantin 15-18mg/kg at 50mg/min*
Severe Anaphylactoid Reaction

Sx: angioedema, bronchospasm or laryngospasm, hypotension*

- Epinephrine 1:10,000 1ml IV over 3-5 min
- O2 10L/min
- NS or Ringer’s
- Benadryl 25-50 mg IV
- Hydrocortizone 1g IV push/30 sec
Autonomic Dysreflexia
(High Cord Injury)

Irritant below level of injury e.g., overdistension of bowel or bladder

- Vasoconstriction: HTN, pallor, goosebumps, splanchnic vasoconstriction
- Vasodilation (above cord level): headache, congestion, diaphoresis
  - Decompress viscus (colon or bladder)
  - Raise head
  - Lower BP: hydralazine 10 mg IV, repeat up to 40 mg
Contrast-Induced Nephrotoxicity

• Due to renal vascular effects and direct toxicity to tubular cells
• Third most common cause of in-hospital renal failure, after hypotension and surgery
• Definition: elevation of creatinine 25% or 0.5-1.0 mg/dL within 72 hours
Contrast-Induced Nephrotoxicity

- Usually asymptomatic: creatinine peaks 3-5 days, in severe oliguric renal failure: peaks 5-10 days
- Incidence:
  - 7-8% arterial injections
  - 2-5% venous injections
  - ~0% venous injections if no risk factors
Nephrotoxicity: Risk Factors

• Byrd and Sherman, 1979:
  • Renal insufficiency (creat > 1.5)
  • Diabetes
  • Dehydration
  • Cardiovascular dz and diuretics
  • Age > 70
  • Myeloma
  • Hypertension
  • Hyperuricemia

Highest risk (Parfey et al., 1989):
RENAL INSUFFICIENCY AND DIABETES
Creatinine measurement recommended:

- Hx of kidney dz
- Family hx of kidney failure
- IDDM for 2 years
- NIDDM for 5 years
- Paraproteinemia
- Collagen vascular dz
- Medications: NSAIDs, aminoglycosides
Nephrotoxicity: Prevention

- **HYDRATION**
  100 ml/hr at least 4 hours before and 12 hours after
  - Mannitol
  - Furosemide
  - Dopamine
  - Theophylline
  - ANP

- **FENOLDOPAM**: may help; requires infusion, titration
- **HEMOFILTRATION**: works; expensive, complicated
Nephrotoxicity: Prevention

- **N-Acetylcysteine (Mucomyst):** Antioxidant with vasodilatory properties
  - *NEJM 2000;343(3) 180-183:* nephrotoxicity occurred in 9/42 patients receiving placebo and 1/41 patients receiving acetylcysteine after 75 ml iopromide

- **For premedication**
  - 600mg PO BID day before and of study
  - Alternative: 150mg/kg IV over 30 min prior to study, then 50mg/kg over 4 hours
N-Acetylcysteine

- Mobilizes mucus in COPD & cystic fibrosis
- Prevents liver damage after Tylenol overdose
- Protective effects in ARDS
- Decreases incidence of cancers in vivo
- Inhibits cardiac damage & reperfusion injury
- Blocks HIV virus production
- Blocks DNA damage
- Shown to reduce toxicity of:
  - heavy metals, carbon tetrachloride, carbon monoxide, doxorubicin, ifosfamide, valproic acid, E. coli, alcohol…
- Decreases frequency & severity of the flu
Nephrotoxicity

Image from R. Older, MD: internet tutorial
Injection of Contrast

- 20g IV recommended for rates of 3 ml/s or higher in large antecubital or forearm vein
- In hand or wrist, rate no greater than 1.5 ml per second
- ACR recommends direct monitoring for first 15 seconds
Extravasation

- **At risk:** Peripheral vascular disease, Raynaud's, XRT, LN dissection, any IV in hand, wrist, foot, ankle, or > 24 hours

- **Prevention:** good IV access best, extravasation detectors (FP, FN cases)

- **Diagnosis:** PE, can use scanogram if uncertain, estimate volume
Extravasation

- **Therapy**: elevation recommended, warm or cold compress, +/- hyaluronidase
  - warm: speed tissue absorption
  - cold: decrease inflammatory response

- **Surgical consult**:
  - LOCM>100ml AC fossa, >60ml in hand, wrist, ankle, OR increased swelling over 2-4 hours, decreased capillary refill, change in sensation, blistering
Extravasation

UCSD Guidelines

<20ml (minor): elevate, observe

>20 ml (major): aspirate, intermittent ice, elevation, consider hyaluronidase (consult plastics prior to using): 50-250 units at extrav site with tuberculin syringe. Add 1ml sterile saline to vial of 150u.
Extravasation

>100cc: same

Immediate plastics consult if:
- blistering
- altered perfusion
- pain worse after 2-4 hours
- change in sensation distally

Radiology faculty must evaluate patient
Extravasation

• Explain and reassure patient / family

• Provide detailed patient instructions: what to look for and what to do

• Call patient q 24 hrs until asymptomatic

• If major: call referring MD, plastics if appropriate
Extravasation

- **Progress note**: type, volume, management

- **QVR Form**: submit to CQI

- **Contrast Extravasation Form**: submit to Quality Resource Management
Central Lines

• ACR recommends scout or CXR
• Test catheter with normal saline
• Rates of up to 2.5 ml/s shown safe
• Do not power inject a PICC
Air Embolism

- Clinically silent air embolism not uncommon: air bubbles in the thoracic veins, MPA or RV

- Significant air embolism potentially fatal but extremely rare

- Symptoms: air hunger, dyspnea, cough, pulm edema, tachycardia, HTN, wheezing

- Treatment: 100% O2, LLD, hyperbaric O2, CPR if arrest occurs
Other Routes of Administration

Retrograde urological studies
- Ionic is standard
- Risks:
  - Irritation from contrast (transient)
  - Other reactions rare
  - Consider premedication & nonionic if high risk patient
Other Uses of Iodinated Media

- **Myelography**
  - Nonionic FDA-approved for myelography
  - DO NOT use ionic:
    - Ascending myoclonic spasms, rhabdomyolysis.
    - Tx: elevation of the head, remove CSF, anticonvulsants, diuresis, sedation, neuromuscular blockade

- **Hysterosalpingography**
Gadolinium-Based Contrast

- Paramagnetic agent
- Decreases T1 relaxation times
- Toxic in free state

Gadodiamide (Omniscan)
Gadolinium-Based Contrast

Excretion
- Glomerular filtration 95%
- Hepatobiliary excretion 5%
- Slower excretion in renal failure
- No nephrotoxicity at approved doses (up to 0.3 mmol/kg)
Gadolinium-Based Contrast

- **Pregnancy**
  - Category C; readily crosses placenta

- **Breast-feeding**
  - Effect not known
  - .011% excreted over 33 hours, .8% absorbed from oral dose
  - Stop for 48 hours
Gadolinium Contrast: Reactions

- **Incidence:** 1-2.4%, nearly half > 1 hr later
- **Most common:**
  - Nausea 25-42%
  - Warmth/pain 13-27%
  - Headache 18%
  - Parasthesias 8-9%
  - Dizziness 7-8%
  - Urticaria 3-7% (33% in one study)
  - Cardiovascular 3.5%
  - Airway 2.5%
- Anaphylaxis can occur; at least one death reported
- **Risk factors:** prior reaction to MR contrast or iodinated contrast, allergies, asthma. May premedicate with steroids, occasionally antihistamines
Feridex

- Superparamagnetic iron oxide particle
- Taken up by reticuloendothelial cells
- Used to increase conspicuity of nonhepatocellular lesions
- Thick dark fluid diluted and delivered over 30min
- Pregnancy category C: Teratogenic in rabbits at all doses studied (smallest was 6 times human dose)
Ferumoxides: Potential Side Effects

Adverse reactions in up to 9.4% (clinical trials)

- Nausea: 11 (0.7%)
- Back/Leg Pain: 56 (3.6%)
- Headache: 13 (0.8%)
- Chest Pain: 10 (0.7%)
- Vasodilation: 33 (2.1%)
- Urticaria: 12 (0.7%)
- Rash/Dyspnea: 8 (0.5%)

www.radinfonet.com
Ultrasound Contrast Agents

- **IMAGENT**: perflexane (stable gas) lipid microspheres
  - Do not give to patients with cardiac shunts
  - 14% reported AE (compare to 11% with saline): headache, nausea most common

- **OPTISON**: human albumin microspheres with octafluoropropane
  - Contraindicated if hypersensitivity to blood products
  - 17% reported AE: headache, nausea, flushing, dizziness

- Pregnancy category C
- Few SAEs
Enteric Contrast

- **Barium sulfates**
  - Better, cheaper than water-soluble iodinated
  - Mild reactions 1/100k, severe reactions 1/500k
  - Complications:
    - Exacerbation of pre-existing LBO
    - Extravasation leads to extensive fibrosis

- **Use iodinated if barium contraindicated:**
  - Bowel perforation, fistula, sinus tract
  - Prior to bowel surgery
  - Check position of percutaneous bowel catheters
Enteric Contrast

- **HOCM**: 1500 mOsm/kg for 300 mg I/ml
  - Cx: aspiration pneumonitis, diarrhea, hypovolemic shock if undiluted in kids
- **LOCM**: 300-600 mOsm/kg for 300 mg I/ml
  - Aspiration risk: less pulmonary edema
  - Infants, children potential bowel perforation
  - Small bowel: better opacification, less dilution
- Reactions: rare, same risks factors as IV
Summary

- Premedicate MAJOR allergies and severe asthma
- Urgent high risk cases: IV CORTICOSTEROIDS
- Renal risk: HYDRATE, consider Mucomyst
- Consider DECREASING DOSE
Summary

- For abd CT in pregnancy, USE IV CONTRAST
- For MR in pregnancy, try NOT to use IV CONTRAST
- For EXTRAVASATION, know institutional protocol
Summary

- Familiarize yourself with emergency supplies
- Be able to recognize and treat contrast reactions
- Don’t hesitate to call a code