

# Contrast Media and Contrast Reactions



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# Malpractice Issues

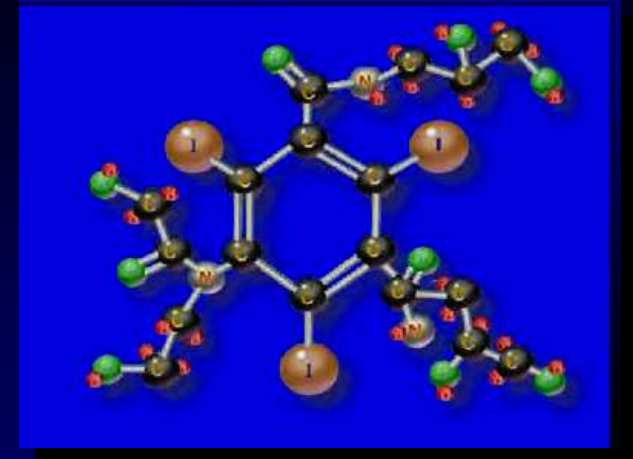
- Incorrect use of contrast media
- Extravasation (primarily HOOCM)
- Failure to use safer imaging option
- **SUBSTANDARD TREATMENT OF A CONTRAST REACTION**

# Contrast Media

- Iodinated contrast media
  - HOICM vs LOICM
  - Precautions & premedications
  - Adverse effects
- Gadolinium-based contrast media
- Enteric contrast media

# Iodinated Contrast: Compounds

Nonionic monomer



*From R. Older,; internet tutorial*

- **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

# Iodinated Contrast: Properties

<u>Compound</u>	<u>[Iodine] mg/mL</u>	<u>mOsm/kg</u>
Ionic monomer	up to 400	1400-2100
Ionic dimer	320	600
Nonionic mono	up to 350	600-800
Nonionic dimer	320	290

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

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

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

# Renal Risk

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

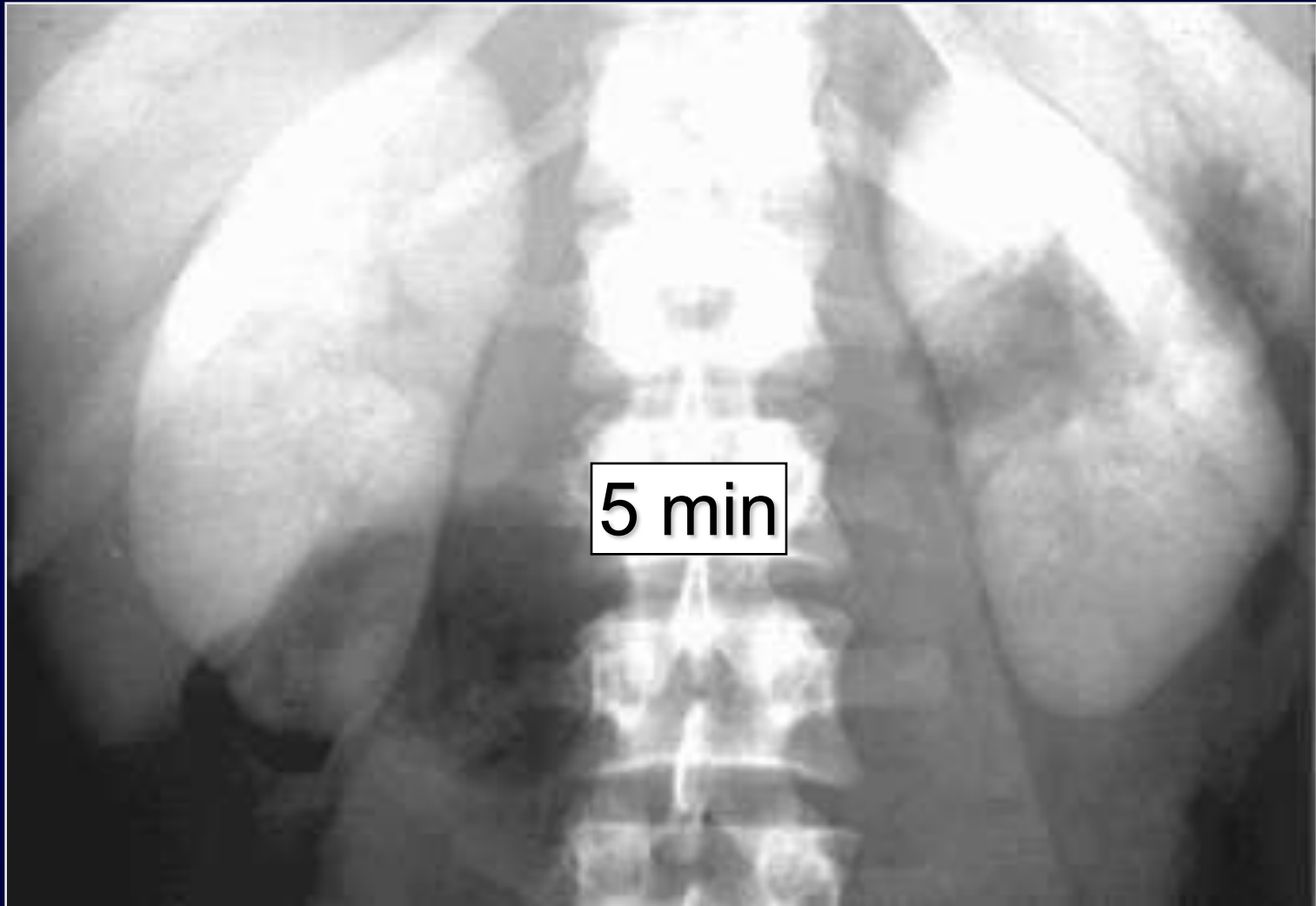
- O<sub>2</sub> 10L/min
- Monitor: ECG, O<sub>2</sub> sat, BP
- ALBUTEROL INHALER
- Epinephrine SC .1-.3ml\*
- Epinephrine IV 1.0 ml, may repeat\*

# 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





*Image from R. Older, MD: internet tutorial*

# Hypotension with Bradycardia (Vagal Reaction)

- Legs elevated, Monitor vital signs
- O<sub>2</sub> 10L/min
- Ringer's lactate or normal saline
- ATROPINE .6-1.0mg IV/ slow, repeat to .04mg/kg

# Hypotension with Tachycardia

- Legs elevated  $> 60$  degrees, head down
- Monitor ECG, O<sub>2</sub> sat, BP
- O<sub>2</sub> 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 tourniquets
- O<sub>2</sub> 6-10L/min
- LASIX 40mg IV, slow push
- Consider morphine
- ICU or ED

# Seizures or Convulsions

- O<sub>2</sub> 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 .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**

# Nephrotoxicity: Risk Factors

## 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

} disappointing in  
clinical trials

- 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, ifosphamide, valproic acid, E. coli, alcohol...
- Decreases frequency & severity of the flu



# Nephrotoxicity



*Image from R. Older, MD: internet tutorial*

Dec 18



Dec 19



Dec 21



# 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

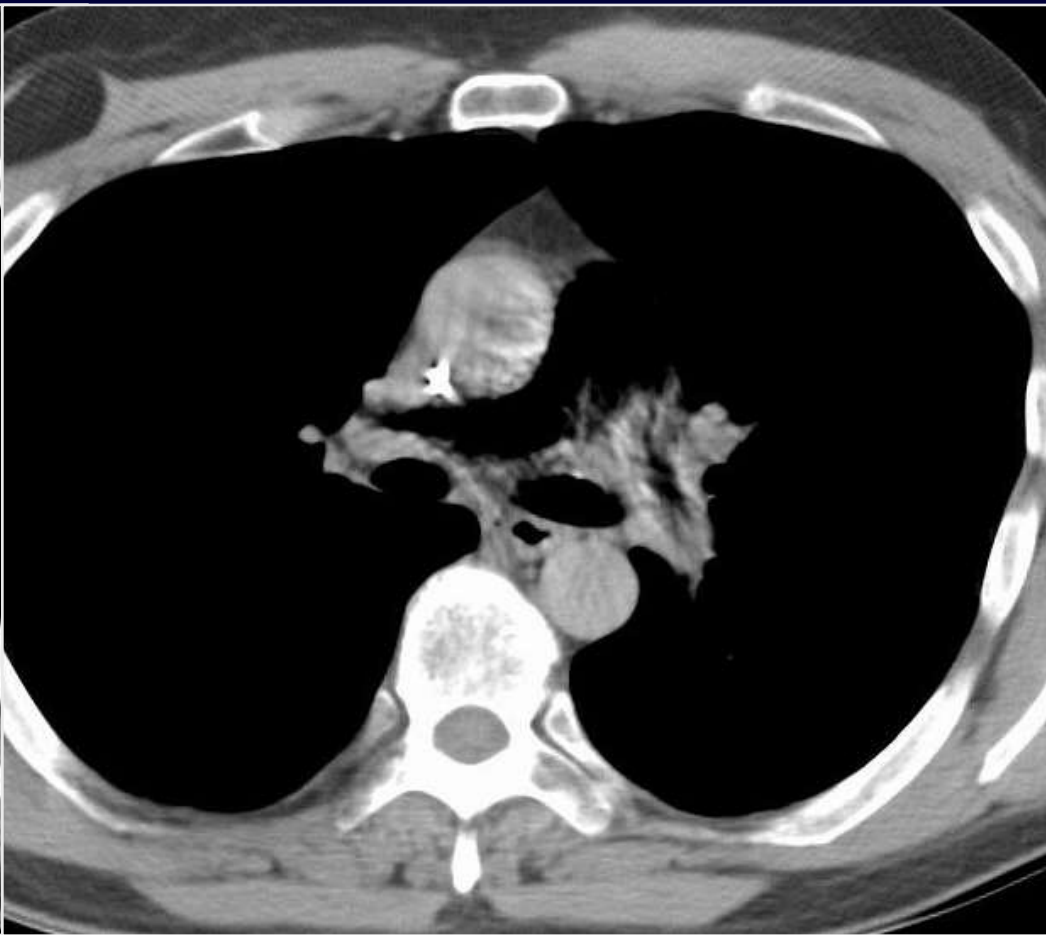
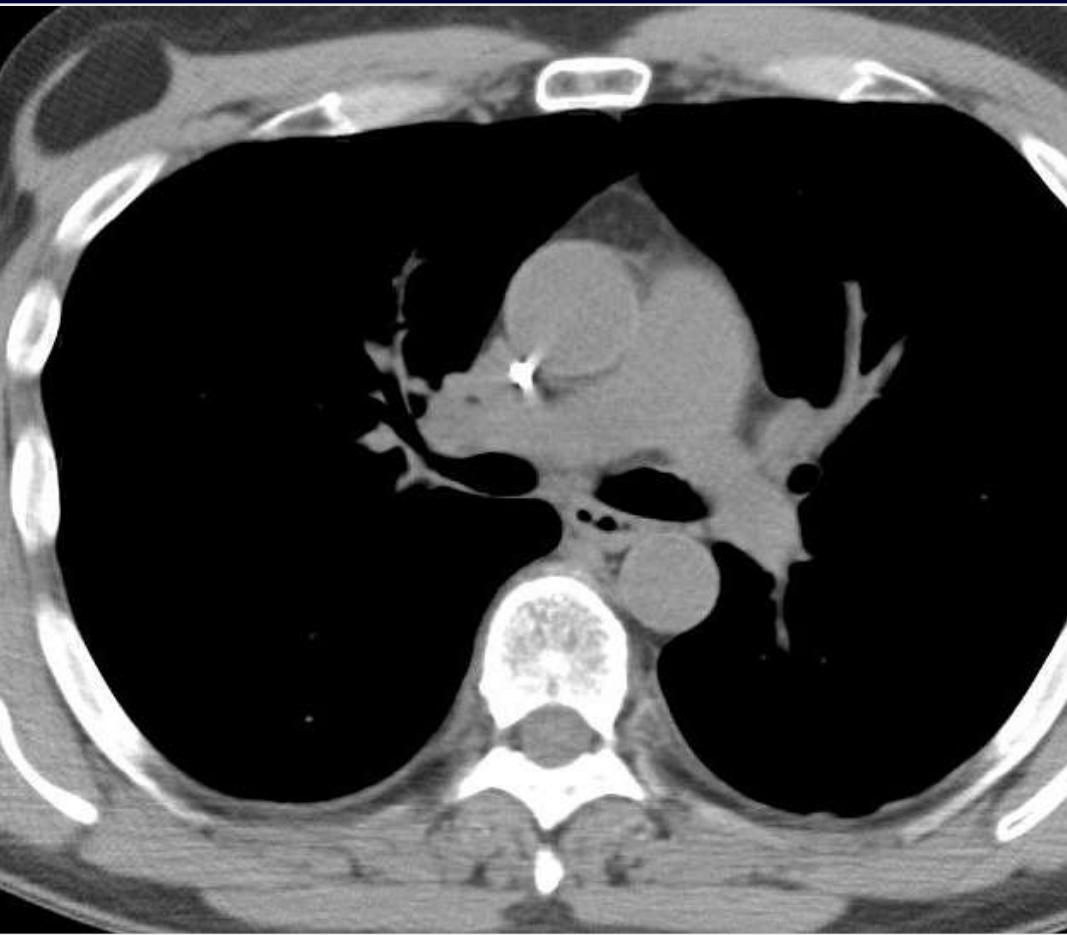


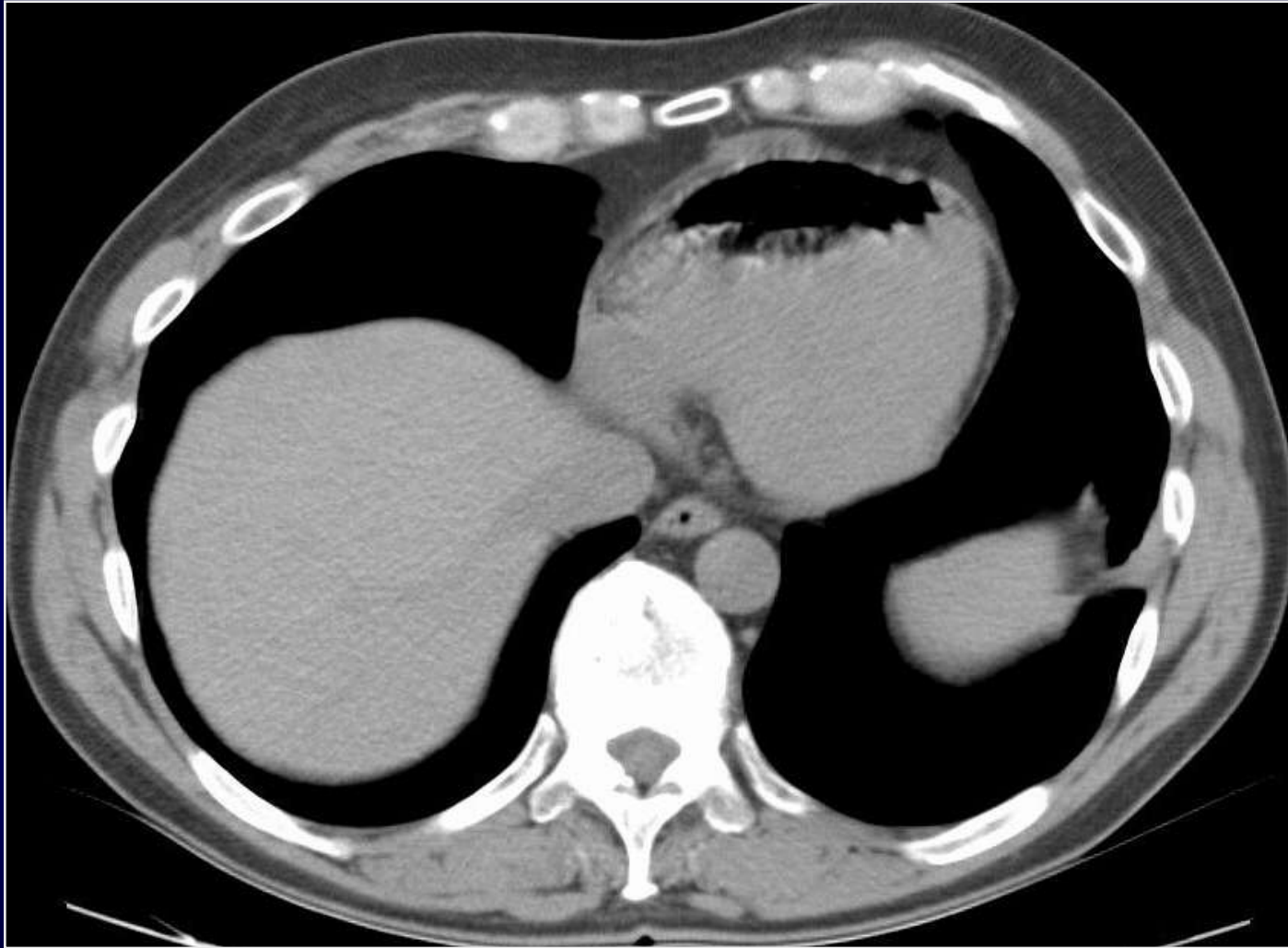
# Extravasation

- **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% O<sub>2</sub>, LLD, hyperbaric O<sub>2</sub>, CPR if arrest occurs

# Other Routes of Administration

## Retrograde urological studies

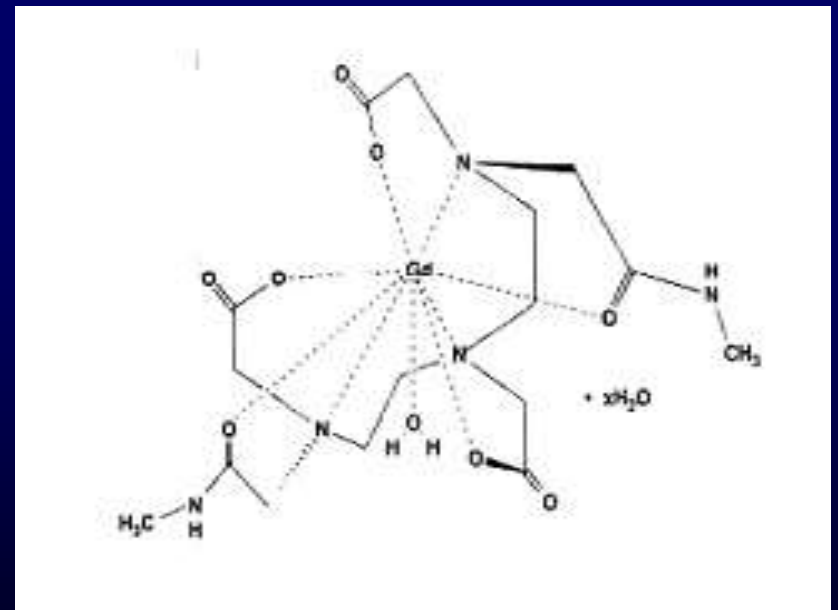
- Ionic is standard
- Risks:
  - Irritation from contrast (transient)
  - Other reactions rare
  - Consider premedication & nonionic if high risk patient

# 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

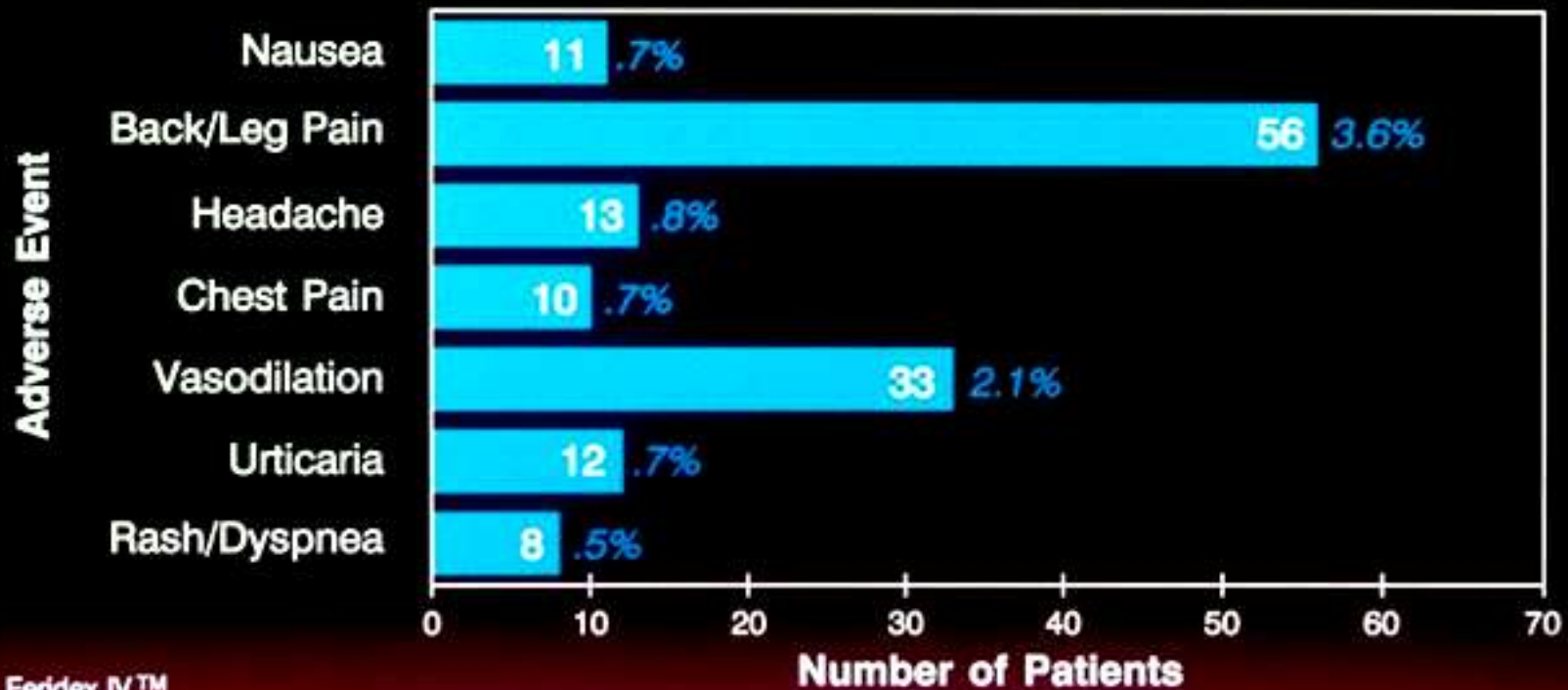
# Feridex

- 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)

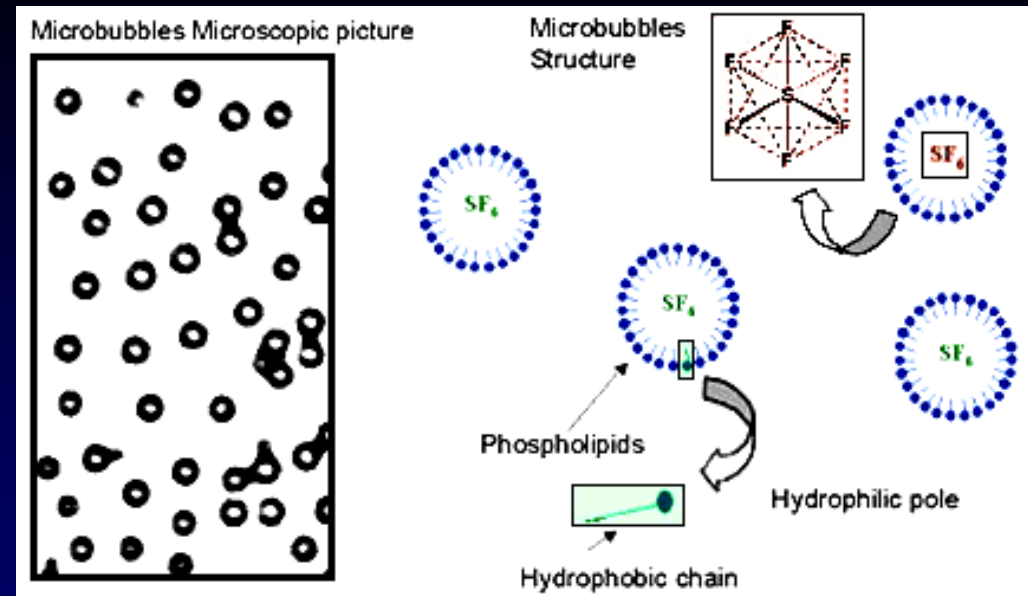
# Feridex

## Ferumoxides: Potential Side Effects

*Adverse reactions in up to 9.4% (clinical trials)*



# Ultrasound Contrast Agents



Sonovue

- IMAGENT: perflorane (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