Diagnosis & Treatment of Contrast Reactions & Contrast Extravasations

M. Victoria Marx, MD
LAC+USC Department of Radiology
Non-Interpretive Curriculum
Iodinated Contrast

- Benzene ring + iodine
- 1950’s – HOCM
- 1980’s – LOCM
- Millions of doses per year, one of safest drugs in existence
Iodinated Contrast

Physiologic effects: predictable

- Renal: brief ↑ renal blood flow followed by prolonged ↓ in renal blood flow
- Cardiac: decrease in contractility, bradycardia
- Neuro: ↓ blood-brain barrier, ↓ seizure threshold, vaso-vagal reaction
- Vascular: peripheral vasodilation, ↓ PVR which leads to increase heart rate and cardiac output
Iodinated Contrast

• Anaphylactoid effects (unpredictable)
  – No detectable IgE antibodies, therefore not strictly anaphylaxis. Antigen not known (benzene ring, side chains, preservative?)
  – Contrast administration ® release of vasoactive peptides in some people
    • Histamine
    • Bradykinin
    • Leukotrienes
    • Complement cascade
Anaphylactoid Reaction

- Peptide release \( \circ \) vasodilatation
- Clinical manifestations depend on affected capillary bed
  - Skin: urticaria
  - Hypopharynx / Larynx: laryngeal edema
  - Airways: bronchospasm
  - Peripheral vasculature: circulatory collapse
Anaphylactoid Reaction

- 70% of reactions begin within 5 minutes of contrast injection
- Nearly 100% of severe reactions begin within 20 minutes of injection
- Rare delayed reactions occur but are typically mild
Risk Factors

- Prior history of contrast reaction
- Hx asthma / atopy
- Anxiety
- ??shellfish??
- COPD
Outcomes

- Over 95% of patients with severe reactions will recover with aggressive treatment
- Early intervention is key to good outcome
- We need to be prepared to recognize contrast reaction and initiate treatment
Contrast Reaction Data
IONIC
Katayama, Radiology 1990

• 10%  - some type of reaction
• 0.5%  - severe (requiring rx)
• 0.05% - very severe
Contrast Reaction Data
NONIONIC
Katayama, Radiology 1990

- 2% - some type of reaction
- 0.1% - severe (requiring rx)
- 0.01% - very severe
HOCM or LOCM

- Death is rare
- 1/40,000
Major Reaction Types

- Urticaria
- Bronchospasm
- Larygospasm
- Cardiovascular collapse
- Vaso-vagal
- Anxiety
Major Reaction Types

- Any reaction can progress to cardiovascular collapse requiring BLS and ACLS
- Aggressive early treatment can prevent progression
- Severe respiratory reaction can be preceded by sneezing!
Treatment of Reactions to Contrast Media

- Screen patients well prior to administering contrast so you know their risk factors.
- Stay calm as you recognize that something is wrong.
Treatment of Reactions to Contrast Media

• A: assess, access, airway, assistance
• B: breathing – oxygen, apparatus
• C: circulation – trendelenberg, IV fluid
• D: drugs – know what to use, when to use it and where they are located. Rxion type determines algorithm.
Assessment

• Talk to the patient
  – Can the patient talk?
  – What are his/her symptoms?

• Vital signs
  – take pulse and respiratory rate/effort while you talk

• Call for help
Oxygen

- At least 10L/min
- Mask

- No nasal cannula – max delivery with nc is 6L/min.
IV Fluid

• Isotonic solution is best:
  – Normal saline
  – Lactated Ringers

• Always begin by giving a bolus of at least 500cc

• Requires an IV ≥ 20g
Presentation:

itching, redness, hives
Urticaria

- Welts, hives, no breathing problems
- Another skin reaction can be diffuse skin erythema (lobster red)
- Severe third-spacing of fluid can lead to hypotension
Urticaria

- Maintain IV access – give fluid bolus if lightheaded or hypotensive
- Observe until resolution
- No medication if mild (no itching, <10 hives)
- 25-50 mg diphenhydramine (PO, IM, IV) if symptoms are troublesome to patient
- Subcutaneous epinephrine if doesn’t respond or progresses despite antihistamine 1/1,000 concentration 0.1 – 0.3cc
Angioedema

- A variant of urticaria affecting mucous membranes – manifests as swelling around eyes, tongue, mouth
- May quickly progress to laryngeal edema
- Treat aggressively (like laryngeal edema)
For non-urticarial reactions:

- Assess
- Oxygen
- IV fluid – isotonic, bolus, fast
- Get help
  - Meds
  - Monitoring Equipment
  - Crash Cart

Benedryl is a primary rx only for urticaria!!
Presentation:
difficulty breathing
Diagnosis:

Bronchospasm vs.
Laryngospasm / Angioedema
Lower Airway = Bronchospasm

- wheezing
- tightness in chest
- anxiety
- tachypnea, tachycardia
- wants to sit up
Isolated Bronchospasm
(not rapidly accelerating, no airway edema, normal bp)

• beta agonist inhaler
  – albuterol
  – metaproterenol
  – terbutaline
• 2-3 deep inhalations with breath hold over 3-5 min
Isolated Bronchospasm
(not rapidly accelerating, no airway edema, normal bp)

- Some people can’t use an inhaler or don’t respond to inhaler
Isolated Bronchospasm
(not rapidly accelerating, no airway edema, normal bp)

• Epinephrine 1:1,000
  – 0.3 cc (0.3mg) subcutaneous q 15 min
  – can also squirt onto mucous membranes in persons without IV access

• Epinephrine 1:10,000, slowly
  – 1cc IV if patient hypotensive
  – Repeat q 3 – 5 min
Effects of Epinephrine

• Alpha adrenergic:
  – vasoconstriction

• Beta adrenergic:
  – bronchodilation
  – positive chronotropic & inotropic cardiac effects
IV Epinephrine

- Alpha effects predominate with rapid administration.
- Beta effects predominate with slow administration.
Patients already using beta agonists may be resistant to inhalers and the beta adrenergic effects of epinephrine.
Upper Airway = Laryngospasm or Angioedema

- Inspiratory stridor
- Hoarseness / change in voice / whisper
- Tightness in throat
- Drooling
Laryngospasm / Angioedema

- Oxygen: 10L / mask
- IV access: isotonic fluid*
- Epinephrine: 1 ml 1:10,000 IV slowly (repeat as needed)

*will need large volumes if also hypotensive
Epinephrine for Upper Airway Reactions

- Use it early in Rx
- 1:10,000 IV
- 1-3 ml over 5-10 minutes
- Repeat as needed
Laryngospasm / Angioedema Unresponsive to Epinephrine

- More epinephrine
- Code Blue
- Antihistamines
  - diphenhydramine: 25-50 mg IV
  - H2 blocker
Presentation:
light-headed, feels faint
Presentation:
light-headed, feels faint

Hypotension til proven otherwise
Differential Diagnosis of Hypotension

- Vasovagal reaction
- Early cardiovascular collapse
- Anxiety
Hypotension DDx

- **Bradycardic (P < 60)**
  - Vasovagal reaction
  - Anaphylactoid reaction with impending circulatory collapse on beta blockers

- **Tachycardic (P > 100)**
  - Anaphylactoid reaction with impending circulatory collapse
  - Primary cardiac event
Rx of Vasovagal Reaction: Hypotension + Bradycardia

- Oxygen
- Fluid bolus – NS or LR
- Trendelenberg position / raise legs
- Atropine 0.6-1.0 mg IVP
  - (repeat q 3-5 min up to 2-3 mg)

Atropine treats bradycardia not hypotension
Atropine = parasympathetic blocker

Paradoxical effect of low dose atropine
– may exacerbate bradycardia
If unresponsive......

- Call a Code Blue
- Consider pressors: dopamine, isoproterenol
- Consider transcutaneous pacing
Rx of Impending Circulatory Collapse

- Oxygen
- Fluid bolus – NS or LR
- Trendelenberg position
- Monitoring – EKG, oximetry
- Open the crash cart
Continued Rx of Circulatory Collapse

• If BP does not respond to initial measures:
  – Dopamine 2-5mg/kg/min
  – Code Blue
  – Treat arrhythmias
Life Threatening Arrhythmias

- Ventricular fibrillation
- Pulseless V-tach
- Pulseless Electrical Activity
- Asystole
Rhythm?
Asystole

CPR
Intubate
IV Access
Epinephrine 1 mg IV q 3-5 min
Atropine 1 mg IV q 3-5 min
Rhythm?
Ventricular Fibrillation

- Debrillate
- Continue CPR, intubate
- Epinephrine 1 mg IV q 3-5 min
- Defibrillate (360 J)
- ACLS algorithms
Rhythm?
Pulseless Ventricular Tachycardia

Cardiovert
Continue CPR, intubate
Epinephrine 1 mg IV q 3-5 min
Cardiovert
ACLS algorithms
Pulseless Electrical Activity

CPR
Intubate
IV access, fluids
Epinephrine 1 mg IV q 3-5 min
Atropine 1 mg IV q 3-5 min for bradycardia
ACLS algorithms
Anxiety Reaction

- Diagnosis of exclusion
- Talk to patient
- Vital signs
- Reassure patient
Presentation:

disoriented, agitated or unresponsive
Differential Diagnosis

• Anaphylactoid reaction
• Patient works in health care industry and has seen a contrast reaction
• Patient is a senior radiology resident 1 month before oral boards
Contrast Reactions

• Don’t just reach for the Benadryl
• Don’t delay in calling for help
Prevention of Contrast Reactions

• Lasser Approach:
  Medrol - 32 mg p.o. 12 hr and 2 hr prior to IV contrast administration

• Greenberger regimen:
  Prednisone – 50 mg p.o. 13, 7, and 1 hr prior to IV contrast administration
  Benadryl – 50 mg p.o. 1 hr prior
  Ephedrine - 25 mg p.o. 1 hr prior
  \((\text{contraind in people with cardiac disease})\)
Prevention of Contrast Reactions

- LAC / USC Approach:
  - Prednisone – 50 mg p.o. 13, 7, and 1 hr prior to IV contrast administration
  - Benadryl – 50 mg p.o. Or IV at time of exam

OR

- Hydrocortisone - 100 mg IV q 12 hrs x 2 doses prior to exam
Prevention of Contrast Reactions

- If a patient states s/he has a history of contrast reaction, you must premedicate prior to administration of iodinated intravascular contrast.
- Have a consistent plan for prophylaxis.
Gadolinium-based Agents

- Allergic type reactions almost unheard of but have occurred
  - Nausea / vomiting
  - Anaphylaxis
  - Death

- Growing concern over ill-effects in persons with renal insufficiency

Murphy et al, AJR 1996; 167:847-849
Nephrogenic Systemic Fibrosis

- Over 200 reports worldwide
- Consists of fibrosis and calcification of skin, skeletal muscle, heart, lung, kidney (clinically similar to scleroderma)
- Risk ↑ with GFR <60mL/min/1.73m²
- Gadolinium deposition has been found in affected tissue
- No effective treatment
Gadolinium Transmetallation

- Free Gadolinium is very toxic
- Chelated Gado is safe
- MR contrast agents are all chelates but prolonged presence in vivo (i.e. due to renal insufficiency) may allow chelated gado to be replaced by endogenous cation such as zinc, calcium, iron or copper
Open chain compounds more susceptible to transmetallation than cyclic compounds

- **Open chain:**
  - Omniscan, GE
  - Magnevist, Berlex
  - OptiMARK, Mallinckrodt

- **Cyclic**
  - ProHance, Bracco
  - MultiHance, Bracco
FDA Recommendations (2006): Gadolinium Use

- Use of gadolinium in the setting of moderate to severe renal insufficiency be reconsidered
- If use is necessary, use lowest possible dose
- Dialysis patients should be dialyzed as soon as possible after administration
- Intrathecal, intraarticular, and intraperitoneal administration should be discontinued until safety guidelines are established
Major Extravasation Injuries

- Tendency to underestimate severity of major extravasation injury
- Radiologist wants to assume everything will be ok!
- Worst case scenario: skin loss requiring grafting; neurologic damage due to untreated compartment syndrome
Most Common Therapeutic Error

- Failure to follow patient after extravasation
- Failure to facilitate consultation with plastic surgery / orthopedics
Result

- Prolonged pain
- Anxiety
- Confusion
Immediate Care of Extravasation

- Assess Patient
- Elevate Extremity
- Apply Ice Packs
- Observe 2 hours in radiology dept
Immediate Care of Extravasation

• Surgical consultation if:
  — Increasing Pain after 2 hrs.
  — Altered Perfusion / tense arm
  — Skin Blistering/Ulceration
  — Altered Sensation
  — ≥ 30 ml ionic, ≥ 100 ml nonionic
Follow up Care of Extravasation

- Call the patient in 24 hours
- Follow-up until resolution (at least every 24 hr)
- Most symptoms resolve in 24 hours
- If you think the patient’s symptoms are worsening have the patient return to radiology
Increased Risk of Extravasation

- Use of needles rather than catheters
- Small bore catheters
- Atypical injection rates
- Injection outside of antecubital fossa
MR Agents

- Gadopentetate dimeglumine is capable of producing skin ulceration and necrosis (in animal studies).
MR Agents

• Since volumes of injected MR contrast agents are small, serious injuries due to extravasation are rare
Other Local Contrast Reactions

- Flare
- Koebner
- Acute pain
- Delayed pain
Flare Reaction

• Rare
• 6-8 cm long pruritic red streak along vein being injected
• No pain or swelling
• Transient (30-90 min)
Koebner Phenomenon

- Skin reaction at sites of prior trauma (i.e., surg. scar)
- Often consists of urticaria or rash
Acute Arm Pain

- 2 - 5%
- May be severe
- Transient
- No swelling
- Probably due to endothelial irritation
Delayed Arm Pain

- 0.1 - 14%
- May be severe
- mean = 3 days (1-30)
- No swelling
- Probably due to endothelial irritation
Conclusion

• **Contrast Reaction:**
  - Physical Exam: mental status, breathing pattern, pulse rate, skin
  - Urticaria: observation / antihistamine
  - All others: oxygen, fluid, monitors, crash cart, call for help
    - Bronchospasm: inhaler, subcutaneous epi
    - Laryngospasm: IV epi
    - Circulatory Collapse: IV Dopamine
    - Vasovagal: IV Atropine
Conclusion

• **Contrast Extravasation:**
  - Elevation
  - Ice
  - Observation 2 hours
  - Follow up in 24 hours
  - Blistering or tense arm: surgical consult
Resources

• Bush WH, Krecke KN, King BF, Bettman MA. Radiology Life Support, New York, Oxford University Press, 1999

• Mayo Clinic DVD Series Advanced Radiology Life Support. 2002. CMEinfo.com