Managing Adverse Events
Part III: Contrast Enhanced MRI

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Purpose of Contrast Media

• To alter the inherent property of selected tissues
• To provide imaging “signal,” thus giving them greater image contrast vs. adjacent tissues
• For MR, this means altering the relaxation of blood and certain tissues.
• Structures that enhance with IV contrast media in MRI will also enhance on CT images and visa-versa.

Outline

1. MR Contrast Agents
   • This module will discuss contrast agents that are used in magnetic resonance imaging (MRI).
2. Properties of contrast media (CM) in MRI
   • Next, properties of contrast agents in MRI will be discussed.
3. Patient interaction with CM in MRI
   • In addition, MR contrast agent interaction with patients will be explained.
4. Managing adverse events in MRI
   • Finally, how to manage adverse events in MRI will be explained.

Objectives

Upon completion of this course, the learner should be able to:

• Discuss what contrast agents are used in MRI.
• Describe the properties of contrast agents used in MRI.
• Explain patient interactions with contrast media.
• Recognize how to manage adverse events in MRI.

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Contrast Characteristics in MR & CT

Axial T1 Weighted Image
Axial T1 Weighted Image
Axial CT Pre-contrast
Axial CT Post-contrast (lodinated)

Pre Injection T1WI Post Injection T1WI

Unenhanced CT Enhanced CT

Perfusion Images

White Structure On White Background White Structure On Grey Background
White Structure On Dark Grey Background White Structure On Black Background
Black Structure On Black Background
Elemental Components of MRI Contrast Media

- Radiographic contrast media are chosen for their ability to attenuate (block) x-rays:
  - Ba – Barium
  - I – Iodine

- MRI contrast media are chosen for their ability to exert a paramagnetic effect:
  - Gd – Gadolinium
  - Mn – Manganese
  - Fe – Iron

Gadolinium-Based Contrast Agents (GBCA)

- Gadolinium is used in its Gd$^{3+}$ form, which has 7 unpaired electrons and is paramagnetic (can affect the behavior of charged particles in a magnetic field)
- Gadolinium alters (speeds up) relaxation rates of water-based hydrogen nuclei in tissues; so it
  - Shortens T1-Relaxation Time
    - Bright on T1 weighted images
    - Used for lesions of the brain, spine, body, breast, etc...
  - Shortens T2-Relaxation Time
    - But the T2 shortening is less commonly used!
    - Used for perfusion imaging in the brain.

How Does It Work?

Relaxation times are mostly dependent on molecular tumbling rates

The bigger the molecule, the slower it tumbles and the faster it relaxes

Gadolinium is a big, slow-tumbling magnet

When gadolinium is close to a water molecule it slows its molecular tumbling rate which results in faster relaxation rates

The amount of change is given by the relaxivity ($r_1$, $r_2$) of the agent

Mechanisms of Action – Summary

- Gadolinium-based contrast agents (GBCA)
  - Alter relaxation rates proportional to their relaxivity
    \[ \frac{1}{T_1} = r_1[Gd] \]
  - To improve their effect
    - Increase dose
    - Increase relaxivity

Comparing MR Images – an Example

Different MR techniques, which involve different manipulations of the magnetic field, result in different types and strengths of signal from different tissues.

Axial T2
- Water is white

Axial FLAIR
- Edema is white

Axial T1
- Fat is white

Axial T1 Post-Gd
- Fat and GBCA are white

Which allows you to see the actual lesion better?

Gadolinium Will Have Different Effects on Different Sequences

Pre-Injection T1WI
Post-Injection T1WI
Perfusion Dynamic T2*
What Is Gadolinium?

It is an element that is a “rare earth” metal of the “lanthanide” series.

Free gadolinium is toxic. So GBCA must hold onto gadolinium atoms by a chemical process known as “chelation.” The chelate is the holding molecule.

A macrocyclic chelate completely surrounds the gadolinium atom—it is a “stronger claw.”

GBCA Stability vs. Characteristics

In general, certain physicochemical characteristics indicate greater vs. lesser stability.

- Ionic: Higher Stability
- Non-Ionic: Lower Stability

But, there’s no difference in general adverse events (AEs).

- Dillman, et. al.: AJR 189 Dec 2007
- Murphy, et. al.: AJR 196 Oct 1996
- Runge VM: *Invest Radiol* 2006 Vol 41, Num 6, 65-71
Injection Reflection…

Gadolinium-based contrast agents (GBCA):

a. Shorten T1 relaxation only
b. Shorten T2 relaxation only
c. Shorten both T1 & T2
d. Has no affect on T1 or T2

If you had difficulty answering this “Injection Reflection” question correctly, or if you would like to re-review this concept: Click back to slide 11-12 on the table of contents.

Remember, you are NOW on slide 20. Click slide 20 to continue with this lecture.

Injection Reflection…

Gadolinium-based contrast agents (GBCA):

a. Shorten T1 relaxation only
b. Shorten T2 relaxation only
c. **Shorten both T1 & T2**
d. Has no affect on T1 or T2

Injection Reflection…

Gadolinium is a ‘rare earth’ metal:

a. **True**
b. False

If you had difficulty answering this “Injection Reflection” question correctly, or if you would like to re-review this concept: Click back to slide 8 on the table of contents.

Remember, you are NOW on slide 22. Click slide 22 to continue with this lecture.

Injection Reflection…

Gadolinium is a ‘rare earth’ metal:

a. **True**
b. False

Adverse Reactions to Contrast Media

• Chemotoxic
  – Taste
  – Warmth
  – Nausea
• Allergoid
  – Mild
  – Moderate
  – Severe

**How can we interpret “what went wrong” if we did not know the patient status at the beginning of the exam?**

First, know your patient.

Then, know about your contrast agent.

Before We Begin…

Unfortunately, we get ‘caught up’ in the day-to-day challenges, and tend to become complacent.

• We forget that we are caring for ‘sick’ people.
• We forget that we are injecting ‘drugs’.
• We do not remember what we learned about the biochemistry & physiology of the human body.
• We do not understand the interactions of ‘medications’ with the human body.
• We forget that …

**There usually is more to the story than meets the eye!**
**GBCA Adverse Reactions**

- The same types of general adverse reactions can occur with GBCA as with any other contrast agents
  - Chemotoxic - Nausea / vomiting, flushing, metallic taste
  - Allergoid – Severity ranges from urticaria to anaphylaxis

**Adverse Reactions**

- Adverse reactions are less common with GBCA than with iodinated CM because the doses are so much lower.
- Minor reactions occur with all agents, in a low percentage of cases.
- The current 5 agents approved for CNS MRI have similar general safety profiles.
- Anaphylactoid reactions are rare, and have occurred with all agents.
- Death from anaphylaxis is preventable, but may occur if treatment is not prompt and effective – all imaging sites should be prepared to treat a severe reaction.

**Timing of Adverse Reactions with CM**

- Early reactions
  - Most reactions occur within 5 minutes of administration, when most of the CM is still in the body, and in fairly high concentrations in the blood and tissues
- Delayed adverse reactions
  - Are rare because the CM is a single dose that is excreted from the body fairly quickly
  - But they can rarely occur

**Adverse Events – Then & Now**

- **Then in CT**
  - Happened every day
  - In every type of patient
  - In- and out-patients
  - Same chemotoxic and allergoid reactions
  - Severity varied
  - We were prepared
  - Antihistamines
  - Steroids
  - Epinephrine

- **Now in MRI**
  - Still rarely happen
  - Seem like more often, because we change GBCA often, and are always anxious
  - Drug are locked up
  - Key is ???

- **Then in MRI**
  - Rarely happened
  - We didn’t notice much, because we were comfortable with same old GBCA we always used
  - Severity varied
  - We were not prepared
  - Drugs were locked up
  - Key is ???

**Adverse Events vs. Adverse Reactions**

- **Adverse Event** – a harmful or otherwise undesired effect occurring after the administration of a drug or the use of a medical device; *causal relationship is not implied*
- **Adverse Reaction** – a harmful or otherwise undesired effect that is thought to be *caused* by the administration of a drug or the use of a medical device

**Adverse Reactions to GBCA**

- The most common chemotoxic reactions are a warm or hot "flushed" sensation during the injection, and a "metallic" taste in the mouth, which usually last less than a minute or so. These can vary depending on the type of CM used, the rate at which it is administered, and individual patient sensitivity. No treatments are necessary.
- A common mild allergoid reaction is urticaria (hives), consisting of wheals (bumps) and flares (flushed patches) on the skin, associated with pruritus (itching). This can last from several minutes to several hours after the injection. This type of reaction by itself requires no treatment, but for patient comfort is often treated with antihistamines and corticosteroids.
- Serious reactions, although much less likely, can be caused by the allergoid physiology of vasodilation and bronchoconstriction, leading to breathing difficulty, hypotension, and other respiratory and cardiovascular symptoms. These reactions can be life-threatening or fatal if not recognized and properly treated immediately.
**Classification of Severity of Adverse Events**

- **Mild** – DOES NOT require treatment
  - Mild skin/mucosal effects or brief sensations
  - E.g., itchy eyes; a few hives; brief nausea
- **Moderate** – OFTEN requires treatment
  - Not considered life-threatening
  - May (or may not) progress to a more severe reaction if not treated; watch closely
  - E.g., widespread edema, wheezing
- **Severe** – DOES require timely, effective treatment
  - Are life-threatening
  - May lead to permanent injury or death

**What to watch for in MRI**

- Transient nausea / vomiting
- Warmth / flushing
- Headache
- Lightheadedness
- Hives/urticaria
- Itching
- Mild Hypotension

NOTE: A true drug-induced rash is a different phenomenon, with a delayed time course, somewhat similar to the poison ivy reaction.

**Moderate Adverse Events**

What to watch for in MRI

- More severe degree of previously mentioned signs and symptoms – or
- Systemic signs & symptoms including:
  - Multiple areas of angioedema
  - Tachycardia
  - Hypotension (moderate)
  - Bronchospasm (mild)
  - Laryngeal edema (mild)
  - Dyspnea / wheezing
- Close observation
- Treatment often indicated

**Severe Adverse Events**

What to watch for in MRI

- Life-threatening
  - Moderate to severe laryngeal edema
  - Moderate to severe bronchospasm
  - Unresponsiveness
  - Ventricular arrhythmias
  - Shock (severe hypotension with organ failure)
  - Respiratory arrest
  - Cardiac arrest
- Require prompt recognition and timely, appropriate, and effective treatment
- Almost always require hospitalization

**“Allergoid” (Allergic-Like) Reactions**

What to watch for in MRI

- Idiosyncratic (unpredictable) reactions to contrast media have the same manifestations as type I hypersensitivity reactions, but they are not true hypersensitivity reactions, because antibodies are not involved.
  - Therefore, prior sensitization does not occur, so:
    - They are not predictable in occurrence or recurrence.
    - They are not predictable in severity.
- For these reasons, idiosyncratic reactions to CM are called allergoid reactions, and when life-threatening are called anaphylactoid reactions.

**Histamine Release**

- Histamine is released by specialized circulating white blood cells (WBCs) called mast cells and basophils.
  - Its purpose is to help create the inflammatory response, which helps the body to fight local infection and to heal local trauma
  - The inflammatory response is:
    - Vasodilation – to bring more blood to the region
    - Increased blood vessel permeability – to bring more fluid, nutrients and WBCs to the tissue
    - Bronchoconstriction – to shut down air flow to the injured or sick area of the lungs
**"Allergoid" Reactions**

**Histamine Release**
- The inflammatory response "makes perfect sense" in the setting of local injury or infection.
- BUT, the release of histamine unfortunately also occurs in unwanted/unnecessary immunological responses, which we call allergic reactions.
- But with contrast media, there is no true immunological response. So why is histamine released by mast cells and basophils in some patients who receive CM?
- Theory: in sensitive individuals, the CM bolus directly induces the mast cells and basophils to release histamine.
- But by what means do CM exert this effect? Is it their ionicity? Osmolality? Viscosity? And, if it is one or more of these physico-chemical properties, at what point can they initiate such an effect? NO ONE KNOWS.

**Vasovagal Reaction**
- Must be distinguished from allergoid reactions
- Is the result of stimulation of the vagus nerve
  - In evolutionary terms, it is the "diving reflex", which slows oxygen consumption in diving mammals (e.g., whales, dolphins, seals).
  - The hallmark is bradycardia, which results in hypotension and sometimes fainting or GI symptoms
- Usually caused by pain/discomfort and anxiety
  - Often associated with fear of needles and the sharp pain of the needle stick, but can be related to claustrophobia, or fear of the CM.
- Treatment
  - Symptomatic treatment for hypotension (elevate legs, give IV fluids)
  - If severe, can give atropine to reverse the bradycardia
  - Close observation until recovery

** Reported Incidence of Most Frequent AEs**

<table>
<thead>
<tr>
<th>Contrast Agent</th>
<th>No. of Patients</th>
<th>Headache (%)</th>
<th>Nausea (%)</th>
<th>Taste Perversion (%)</th>
<th>Urticaria (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnevist</td>
<td>1,068</td>
<td>3.6</td>
<td>1.5</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>ProHance</td>
<td>1,709</td>
<td>0.4</td>
<td>1.1</td>
<td>1.2</td>
<td>0.4</td>
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<tr>
<td>Omniscan</td>
<td>439/700</td>
<td>1.8/4.4</td>
<td>0.9/3.6</td>
<td>0.9/2.1</td>
<td>0.70/1.1</td>
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<tr>
<td>OptMARK</td>
<td>1,663</td>
<td>7.5</td>
<td>2.6</td>
<td>5.7</td>
<td>N/A</td>
</tr>
<tr>
<td>MultiHance</td>
<td>2,367</td>
<td>1.9</td>
<td>1.3</td>
<td>1.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>


**MultiHance/Magnevist Safety Paper**
- 287 patients enrolled in intra-individual crossover trials (each patient received both agents in a blinded manner)
  - Received MultiHance and Magnevist in 2 separate examinations within 14 days
- Adverse events rate in these patients was comparable
  - 8% for MultiHance
  - 9% for Magnevist
  - Post marketing survey AE rate: 0.05%

Saline (control): 17% AE

According to the ACR Manual on Contrast Media, adverse events after the intravenous injection of GBCA seem to be more common in patients who had previous reactions to CM, or are "reactors" in general to external antigens.

- In one study, 16 (21%) of 75 patients who had previous adverse reactions to MR contrast agents reacted to subsequent injections of gadolinium.
- Patients with asthma seem to be more likely to have an adverse reaction to the administration of a GBCA.
- Patients with allergies also seemed to be at increased risk (approx 2 - 3.7 times compared with patients without allergies).
- Patients who have had adverse reactions to iodinated contrast media are more than twice as likely to have an adverse reaction to gadolinium (6.3% of 857 patients).

Patients with asthma seem to be more likely to have an adverse reaction to the administration of a GBCA.

- Patients with allergies also seemed to be at increased risk (approx 2 - 3.7 times compared with patients without allergies).

Patients who have had adverse reactions to iodinated contrast media are more than twice as likely to have an adverse reaction to gadolinium (6.3% of 857 patients).

The decision to administer a gadolinium-based contrast agent (GBCA) to pregnant patients should be accompanied by a well-documented and thoughtful risk–benefit analysis. This analysis should be able to defend a decision to administer the GBCA based on overwhelming potential benefit to the patient or fetus, outweighing the theoretical but unproven risk. Studies have demonstrated that gadolinium-based MR contrast agents pass through the placental barrier and enter the fetal circulation. From there, they are filtered in the fetal kidneys and then excreted into the amniotic fluid. In this location, the GBCA molecules are in a relatively protected space and may remain in the amniotic fluid for an indeterminate amount of time before finally being reabsorbed and eliminated. As with any equilibrium situation involving any dissociation constant, the longer the GBCA molecule remains in this space, the greater the potential for dissociation of the potentially toxic gadolinium ion from the chelating molecule. The uncharged gadolinium ion might then be released in any quantity in the amniotic fluid. Cations, diffusion into the developing fetus would raise concerns of possible secondary adverse effects. The risk to the fetus of GBCA remains unclear, and they may be harmful.

Injection Reflection…

Adverse reactions are classified as Mild, Moderate and/or Severe. Severe reactions:
- Do not require intervention
- Sometimes require intervention
- Always require intervention
- Are not noticeable

If you had difficulty answering this "Injection Reflection" question correctly, or if you would like to re-review this concept, click back to slide 34 on the table of contents. Remember, you are NOW on slide 47. Click slide 47 to continue with this lecture.

When we discuss general adverse events (AEs), all GBCAs have a similar safety profile:
- True
- False
**Injection Reflection…**

When we discuss general adverse events (AEs), all GBCAs have a similar safety profile:

a. True  
b. False

If you had difficulty answering this “Injection Reflection” question correctly, or if you would like to re-review this concept, click back to slide 34 on the table of contents.

**GBCA Nephrotoxicity … Yes or No?**

- Standard IV use/doses
  - Not nephrotoxic (usually), because those doses are small
- Doses equivalent to those of iodinated CM (as was the case when GBCAs were used in intra-arterial x-ray angiography)
  - Nephrotoxicity has been reported
  - Debatable if GBCAs are safer than low osmolar iodinated CM in such uses
- The modern risk dilemma with moderate-to-severe renal failure
  - Contrast enhanced MR – Nephrogenic systemic fibrosis
  - Contrast enhanced CT/angiogram – Contrast induced nephropathy

**Does the Chelate Really Matter?**

- A new disease – What is it?
- Original findings reported in 1998

Scleromyxoedema-like cutaneous diseases in renal-dialysis patients

Shawn E. Cowper, Howard S. Robin, Steven M. Steinberg, Lyndon D. Su, Samantweep Gupta, Philip E. LeBolt

**What’s in a Name?**

This disease was...

- First described in 1997, in 15 patients on dialysis
- Resembled another illness (scleromyxedema)
- So it was mislabeled at first
  - First named NFD (nephrogenic fibrosing dermalapathy), indicating a skin-only condition
  - Then changed to NSF (nephrogenic systemic fibrosis), indicating organ system involvement
- Is caused by activated circulating fibrocytes
  - So the question is – What’s activating them?
- Should be diagnosed by both skin biopsy + clinical presentation

**What Are the Symptoms?**

- Sometime after administration of a GBCA...
  - Skin develops burning, itching, reddened/darkened patches and/or inflammation, hardening and/or tightening
  - Sclerosing lesions
    - Yellow raised spots on sclera
  - “Orange-peel” skin
  - Systemic component
    - Joint stiffness
    - Limited peripheral movement
    - Deep hip/rib pain
    - Muscle weakness
    - Sclerosed organs

**Nephrogenic Systemic Fibrosis (NSF)**

Symptoms can occur...

Anywhere from several weeks to months later

Sadowski, E. A. et al.  
Radiology 2007;0:2431062144  
Broome DR et al.  
AJR:188, Feb 2007 586-92
There Is No Known Cure...

- No actual cure
- Early treatment (particularly improving renal function) helps
- Physical therapy (PT)
- Photopheresis

Who’s at Risk for NSF?

- End-stage renal disease (ESRD) – highest risk
  - Peritoneal dialysis > Hemodialysis
- Chronic kidney disease (CKD) stage 4-5
  - No dialysis, but severe renal dysfunction (glomerular filtration rate (GFR) less than 30 ml/min/1.73 m²)
- Other high-risk patients
  - Acute renal injury
  - Hepato-renal syndrome
  - Perioperative renal transplant period
  - Neonates and infants under 1 year

To date...

NO cases have been reported in patients with normal renal function.

Differences in Chelates

- OptimARK
  - Non-ionic
- Magnevist
  - Ionic
- Omniscan
  - Non-ionic
- MultiHance
  - Ionic
- Eovist
  - Ionic
- ProHance
  - Non-ionic
- Linear
- Macro cyclic

Stability and Transmetallation

Concerns regarding stability of GBCA chelates are not new.

Laurent S, Elst LV, Muller RN Contrast Media Mol Imaging. 2006 May;1(3):128-37

Concerns regarding stability of GBCA chelates are not new.

GBCA Stability

There are two categories of gadolinium chelates: the macrocyclic molecules where Gd³⁺ is capped in the pre-representation cavity of the ligand and linear molecules. Gadolinium chelates differ in their thermodynamic stability constants and in their kinetic stability. In general, macrocyclic chelates are more stable than linear molecules. Probing linear agents, differences can be found. The lowest stability is reached with Gd-DTPA-BMA and (g-d-DTPA-BMEA, Fundam Clin Pharmacol. 1998 Dec;32(4):383-76).

Gd-DTPA-BMA = Omniscan™
Gd-DTPA-BMEA = OptimARK®

GBCA | Thermodynamic Stability Constant (log Keq) | Conditional Stability Constant at pH 7.4
---|---|---
ProHance | 23.8 | 17.1
MultiHance | 22.6 | 18.4
Magnevist | 22.1 | 18.1
Omniscan | 16.9 | 14.9
OptiMARK | 16.6 | 15
Stability Measurements

**Kinetic Stability**
(rate of dissociation of Gd from its chelate)

<table>
<thead>
<tr>
<th>Chelate</th>
<th>4x10^(-5)</th>
<th>2x10^(-5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omniscan</td>
<td>2.3 x 10^(-5)</td>
<td>2.0 x 10^(-5)</td>
</tr>
<tr>
<td>Magnevist</td>
<td>1.2 x 10^(-5)</td>
<td>1.0 x 10^(-5)</td>
</tr>
<tr>
<td>ProHance</td>
<td>6.3 x 10^(-5)</td>
<td>5.0 x 10^(-5)</td>
</tr>
<tr>
<td>GdDOLA</td>
<td>2.1 x 10^(-5)</td>
<td>2.0 x 10^(-5)</td>
</tr>
</tbody>
</table>

**Excess Chelate (Suggests Stability Issues)**

<table>
<thead>
<tr>
<th>GBCAs</th>
<th>Excess Chelate</th>
</tr>
</thead>
<tbody>
<tr>
<td>MultiHance (gadobenate dimeglumine)</td>
<td>0.0 mg/mL</td>
</tr>
<tr>
<td>ProHance (gadoteridol)</td>
<td>0.23 mg/mL</td>
</tr>
<tr>
<td>Magnevist (gadopentetate dimeglumine)</td>
<td>0.4 mg/mL</td>
</tr>
<tr>
<td>Omniscan (gadodiamide)*</td>
<td>12 mg/mL</td>
</tr>
<tr>
<td>OptiMARK (gadoversetamide)*</td>
<td>28.4 mg/mL</td>
</tr>
</tbody>
</table>

*Linear nonionic;

One Consequence of Gd Dissociation

- Gadodiamide administration causes spurious hypocalcemia.
- CONCLUSION: Gadodiamide administration causes spurious hypocalcemia, particularly at doses of 0.2 mmol/kg or higher and in patients with renal insufficiency.

Gd Dissociation and Bone Deposition

Comparison of Gd DTPA-BMA (Omniscan) versus Gd HP-DO3A (ProHance) retention in human bone tissue by inductively coupled plasma atomic emission spectroscopy.

**RATIONALE AND OBJECTIVES:** Human bone tissue was collected following administration of a clinical dose of gadolinium chelate (0.1 mmol per kg) to patients undergoing hip joint replacement surgery to determine if measurable differences in Gd deposition occur between two widely available magnetic resonance contrast agents.

**CONCLUSION:** Omniscan (Gd DTPA-BMA) left 2.5 times more Gd behind in bone than did ProHance (Gd HP-DO3A).

NSF – Are GBCM (GBCAs) Equal in Risk?

- **ACR 2010:** “…empirical data and theoretical lines of reasoning suggest that not all GBCM are associated with an identical risk of NSF in at-risk patients”
- **ACR 2010:** GBCM are categorized into 3 groups re risk of NSF
  - **Group I:** Agents associated with the greatest number of NSF cases:
    - Gadodiamide (Omniscan™)
    - Gadopentetate dimeglumine (Magnevist®)
    - Gadoversetamide (OptiMARK®)
  - **Group II:** Agents associated with few, if any, unconfounded cases of NSF:
    - Gadobenate dimeglumine (MultiHance®)
    - Gadoteridol (ProHance®)
    - Gadoteric acid (Dotarem®)*
    - Gadobutrol (Gadovist®)*
- **Group III** are recently approved agents with limited data (Ablavar®, Eovist®)

**NOTE:** Group III are recently approved agents with limited data (Ablavar®, Eovist®)

**NSF – Are GBCM (GBCAs) Equal in Risk?**

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    - Gadobutrol (Gadovist®)*
  - **NSF – Are GBCM (GBCAs) Equal in Risk?**

FDA Regulations as of September 2010

- **FDA – September 2010**
  - Contraindications for…
  - Group I agents Magnevist, Omnican, OptiMark
  - In patients with:
    - AKI (acute kidney injury)
    - Chronic Renal disease
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ACR Recommendations

- ACR Manual on Contrast Media V7.0 (2010)
  - "If a contrast-enhanced MR examination must be performed in a patient with end-stage renal disease on chronic dialysis, avoidance of Group I agents is recommended."
  - For patients with stage 4 or 5 CKD (eGFR < 30) not on dialysis – “…it is recommended that Group I agents be avoided is GBCM is deemed necessary.”
  - For patients with stage 3 CKD (eGFR 30-59)
    - Stage 3a (eGFR=45-59) – “…a decision to administer a Group I agent to these patients should be made only following appropriate risk-benefit assessment.
    - Stage 3b (eGFR=30-44) – “…similar precautions as those mentioned for CKD (stage) 4 and CKD (stage) 5 … could be considered…”
  - For patients with acute kidney injury – “When GBCM administration is required, avoidance of agents associated with the greatest apparent NSF-associated risk (Group I agents) is preferred.”

Minimizing Risk of NSF

- Screen patients
  - Obtain an eGFR
  - Serum creatinine (SCr) not good enough
- Reduce dose / Avoid repeat doses
- Understand the stability of GBCA used
- Counsel patients at risk
- Consider alternative imaging methods

Stages of Kidney Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (ml/min/1.73 m²)</th>
<th>N (thousands)</th>
<th>% of US Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>≥ 90</td>
<td>5,900</td>
<td>3.3</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with modest ↓ GFR</td>
<td>60 - 89</td>
<td>5,300</td>
<td>3.0</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30 - 59</td>
<td>7,600</td>
<td>4.3</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15 - 29</td>
<td>400</td>
<td>0.2</td>
</tr>
<tr>
<td>5</td>
<td>Kidney Failure</td>
<td>&lt; 15 or dialysis</td>
<td>300</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Do Patients Know About Their Kidneys?

- National Health and Nutrition Examination Survey (N-HaNES) – awareness of CKD graph
- Similar unpublished study by Christiana Care Imaging System (CCIS) found similar results

% of Patients Who Are Aware of Their CKD in the United States

<table>
<thead>
<tr>
<th>Stage</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>1.1</td>
</tr>
<tr>
<td>Stage 2</td>
<td>1.4</td>
</tr>
<tr>
<td>Stage 3</td>
<td>2.9</td>
</tr>
<tr>
<td>Stage 4</td>
<td>4.2</td>
</tr>
<tr>
<td>Stage 5</td>
<td>15.6</td>
</tr>
</tbody>
</table>

eGFR Calculator

- eGFR - Estimated Glomerular Filtration Rate
- Web-based eGFR calculators are available!

eGFR: iPhone / iPod Touch

And, they've got an “APP” for that!
When we discuss NSF [and patients with severe renal dysfunction], all gadolinium-based contrast media have a similar safety profile:

a. True
b. False

The disease known as Nephrogenic Systemic Fibrosis (NSF) is likely to be related to:

a. Patients with normal kidney function and injection of saline.
b. Patients with normal kidney function and injection of any gadolinium agent.
c. Patients with severe kidney dysfunction and injection of a GBCM with lower stability.
d. No particular patients.

1. MR Contrast Agents
   • This Module will discuss contrast agents that are used in magnetic resonance imaging (MRI)?
2. Properties of contrast media (CM) in MRI
   • Next, properties of contrast agents in MRI will be discussed.
3. Patient interaction with CM in MRI
   • In addition, MR contrast agent interaction with patients will be explained.
4. Managing adverse events in MRI
   • Finally, how to manage adverse events in MRI will be explained.
Objectives

Upon completion of this course, the learner should be able to:

• Discuss what contrast agents are used in MRI.
• Describe the properties of contrast agents used in MRI.
• Explain patient interactions with contrast media.
• Recognize how to manage adverse events in MRI.

Thank you for your attention!

Managing Adverse Events
Part III: Contrast Enhanced MRI

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