Disclosures
Kara Weatherman discloses research support from Teva Pharmaceuticals

The American Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Learning Objectives
1. Describe nuclear medicine and molecular imaging use of adjunct agents.
   1. Review nuclear medicine and molecular imaging
   2. Discuss the clinical approach for using various pharmaceuticals in diagnostic imaging
   3. Review common radiopharmaceuticals and pharmaceuticals that are used in nuclear medicine departments
   4. Highlight examples of potential adverse reactions / complications that arise with the use of pharmaceuticals in nuclear medicine
   5. Outline potential collaborative effects between pharmacy and nuclear medicine
2. List examples of best practices for pharmacy provided care in nuclear medicine and molecular imaging.
   1. Patient examples

Pharmacist Provider’s Guide to Nuclear Medicine and Molecular Imaging
Kara D. Weatherman, PharmD, BCNP, FAPhA
Clinical Associate Professor of Pharmacy Practice
Director, Nuclear Pharmacy Programs
Purdue University College of Pharmacy
West Lafayette, IN

• Target Audience: Pharmacists
• ACPE#: 0202-0000-17-061-L04-P
• Activity Type: Knowledge-based

1. How many medical imaging procedures are performed annually in the United States?
   A. 50 million
   B. 200 million
   C. 400 million
   D. 800 million
2. Currently, courses in radiologic pharmaceuticals and their uses is a REQUIRED academic course in any college of pharmacy curriculum

A. True
B. False

3. Which of the following is TRUE regarding non-radioactive pharmaceuticals used in nuclear medicine studies

A. They are administered in sub-pharmacologic quantities
B. They are generally given as multiple doses over the course of the imaging study
C. They have a much greater incidence of adverse reactions as compared to radiopharmaceuticals themselves
D. All of the above are true

Before We Start....

Radiology and Nuclear Medicine

- Nearly 400 million medical imaging procedures performed annually in the US
  - X-ray / CT
  - MRI
  - Ultrasound
  - Nuclear medicine
- How does that fit into pharmacy?
  - Diagnosis
  - Therapeutic decision making
  - Evaluating / monitoring therapeutic choices
  - Updating therapeutic choices

Pharmaceuticals in Radiology

- CT
  - Contrast media
  - Ionic / nonionic iodine compounds
  - Barium oral compounds
- MRI
  - Contrast media
  - Heavy metal paramagnetic compounds
  - Ultrasound
  - Contrast media

Patient Presentation
Pharmaceuticals in Radiology

- Nuclear medicine
  - Diagnostic tracers
  - FD approved radioactive pharmaceuticals
- Therapeutic agents
  - FDA approved radioactive pharmaceuticals
- Interventional agents
  - FD approved NON-RADIOACTIVE pharmaceuticals used to enhance nuclear medicine studies

Pharmacy Training in Radiology

- Pharmacy training in radiology
  - How many colleges of pharmacy offer specific training in radiology based pharmaceuticals
- Purdue University experience
  - Radiopharmaceuticals: yes, only if taking elective series
    - 30-50 / 150 students annually
  - Contrast media: no
    - Diagnostic pharmaceutical course d/c with most recent curriculum revision
- Other universities?

Why Does It Matter?

- Pharmacovigilance
  - Adverse drug reactions
  - Off label uses
  - Safety updates
- The Joint Commission
- Medication Therapy Management

Nuclear Medicine / Pharmacy

Pharmacy Involvement

- Pharmacists generally don’t have much interaction in the nuclear medicine department
- Review the progression of any given patient through the imaging procedure
  - Pre-study prep
  - Radiopharmaceutical administration
  - Mid-study enhancement with nonradioactive pharmaceutical
  - Post-study recovery

Nuclear Medicine

1. Pre-study prep
Pre-Study Prep

- Medication review
  - Any drugs that interfere with potential outcome of the study?
  - Any limitations/issus with the planned pharmaceuticals/radiopharmaceuticals used in the study?
- Patient review
  - Any conditions that might impact the outcome of the study?

Nuclear Medicine

1. Pre-study prep
2. Radiopharmaceutical administration

Radiopharmaceutical Administration

- Pharmaceuticals which are formulated to contain radioactivity
- Used as a radiotracer for diagnostic imaging studies, as well as for therapeutic applications
- Molecular imaging:
  - Enables visualization of cellular function and molecular processes
  - Probes known as biomarkers are labeled with radioactive materials
  - Biomarker interact chemically with their surroundings and provide information on the molecular changes that are occurring

Radiopharmaceuticals and Use

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Clinical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tc-99m Neurosite</td>
<td>Brain Imaging</td>
</tr>
<tr>
<td>Tc-99m Concor (exametazime)</td>
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<tr>
<td>Tc-99m DTPA (pentetate)</td>
<td></td>
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<tr>
<td>I-123 DaTscan (ioflupane)</td>
<td></td>
</tr>
<tr>
<td>In-111 DTPA (pentetate)</td>
<td>CNS imaging</td>
</tr>
<tr>
<td>F-18 Neuraceq (florbetaben)</td>
<td></td>
</tr>
<tr>
<td>F-18 Amyvid (florbetapir)</td>
<td></td>
</tr>
<tr>
<td>V-18 Vizamyl (fluciclovine)</td>
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<tr>
<td>F-18 Fluorodeoxyglucose (FDG)</td>
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</tbody>
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</thead>
<tbody>
<tr>
<td>Tc-99m MDP</td>
<td>Bone Imaging</td>
<td></td>
</tr>
<tr>
<td>Tc-99m HDP</td>
<td></td>
<td></td>
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<tr>
<td>Tc-99m PYP</td>
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<tr>
<td>F-18 Sodium fluoride</td>
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<tbody>
<tr>
<td>Tc-99m Cardiolite (sestamibi)</td>
<td>Cardiac Imaging</td>
<td></td>
</tr>
<tr>
<td>Tc-99m Myoview (tetrofosmin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tl-201 Thallous chloride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tc-99m RBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N-13 Ammonia</td>
<td>Cardiac imaging</td>
<td></td>
</tr>
<tr>
<td>Rb-82 Cardiogen (rubidium)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F-18 Fludeoxyglucose (FDG)</td>
<td>Cardiac metabolism</td>
<td></td>
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<tr>
<td>Tc-99m Sodium pertechnetate</td>
<td>Gastric Imaging</td>
</tr>
<tr>
<td>Tc-99m Sulfur colloid</td>
<td></td>
</tr>
<tr>
<td>C-14 Pytest (urea)</td>
<td></td>
</tr>
<tr>
<td>Tc-99m Choletec (mebrofenin)</td>
<td>Hepatobiliary Imaging</td>
</tr>
<tr>
<td>Tc-99m Hepatolite (disoferin)</td>
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<th>Radiopharmaceutical</th>
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<tr>
<td>Ga-67 Gallium citrate</td>
<td>Infection Imaging</td>
</tr>
<tr>
<td>Tc-99m Ceretec labeled WBC</td>
<td></td>
</tr>
<tr>
<td>In-111 Oxine labeled WBC</td>
<td></td>
</tr>
<tr>
<td>Tc-99m Sulfur colloid</td>
<td>Lymphatic Imaging</td>
</tr>
<tr>
<td>Tc-99m Lymphoseek (tilmanocept)</td>
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</tr>
<tr>
<td>Tc-99m Sulfur colloid</td>
<td>Reticuloendothelial System Imaging</td>
</tr>
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<tr>
<td>Tc-99m MAA (Macroaggregated albumin)</td>
<td>Pulmonary Imaging</td>
</tr>
<tr>
<td>Tc-99m DTPA (pentetate)</td>
<td></td>
</tr>
<tr>
<td>Xe-133 Xenon gas</td>
<td></td>
</tr>
<tr>
<td>Tc-99m MAG-3 (meristatide)</td>
<td>Renal Imaging</td>
</tr>
<tr>
<td>Tc-99m DTPA (pentetate)</td>
<td></td>
</tr>
<tr>
<td>Tc-99m DMSA (succimer)</td>
<td>Thyroid Imaging</td>
</tr>
<tr>
<td>I-123 Sodium iodide</td>
<td></td>
</tr>
<tr>
<td>I-131 Sodium iodide</td>
<td></td>
</tr>
<tr>
<td>Tc-99m Sodium pertechnetate</td>
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</table>

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<tbody>
<tr>
<td>In-111 ProstaScint (capromab)</td>
<td>Tumor Imaging</td>
</tr>
<tr>
<td>Ga-67 Gallium citrate</td>
<td></td>
</tr>
<tr>
<td>I-123 AdreView (ioseguan)</td>
<td>Tumor Imaging - PET</td>
</tr>
<tr>
<td>In-111 Octreoscan (pentetotecide)</td>
<td></td>
</tr>
<tr>
<td>C-11 Choline</td>
<td></td>
</tr>
<tr>
<td>Ga-68 Netspot (dotatate)</td>
<td></td>
</tr>
<tr>
<td>F-18 Axumin (fluciclovine)</td>
<td></td>
</tr>
<tr>
<td>F-18 Fludeoxyglucose (FDG)</td>
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</tr>
</tbody>
</table>

Radiopharmaceuticals

- Imaging
  - **TRACER principle**
    - Small, non-pharmacologic quantities of material used
    - TRACER a physiologic process, not alter it (positively or negatively)
    - Also minimizes adverse reactions to these drug products – DOES NOT eliminate them
  - Therapy
    - Utilization of types of radiation that impart toxic effects to cells (alpha, beta)
    - Intentionally impart damage to desired cells, but will also lead some damage to other cells

- Radiopharmaceuticals
- Imaging
- Therapy
- TRACER principle
Nuclear Medicine

1. Pre-study prep

2. Radiopharmaceutical administration

3. Mid-study enhancement with nonradioactive pharmaceutical

Non-Radioactive Pharmaceuticals

• Many nuclear medicine studies utilize some type of adjunct pharmaceutical agent to contribute to the overall quality of the study
• These pharmaceuticals are rarely supplied by commercial radiopharmacies, but are obtained from internal sources
• For some studies, the nonradioactive pharmaceutical is required for successful completion of the study
• In some cases, the pharmaceutical is utilized to mitigate a problem or is used based on factors determined during the progression of the study

Non-Radioactive Pharmaceuticals and Use

<table>
<thead>
<tr>
<th>Pharmaceutical</th>
<th>Clinical Use</th>
<th>Pharmaceutical</th>
<th>Clinical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetazolamide</td>
<td>Brain imaging</td>
<td>Furosemide</td>
<td>Renal imaging</td>
</tr>
<tr>
<td>Adenosine</td>
<td>Cardiac imaging</td>
<td>Glucagon</td>
<td>Gastric imaging</td>
</tr>
<tr>
<td>Atropine</td>
<td>Cardiac imaging</td>
<td>Glucose</td>
<td>PET cardiac imaging</td>
</tr>
<tr>
<td>Captopril</td>
<td>Renal imaging</td>
<td>Insulin</td>
<td>PET cardiac imaging</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Gastric imaging</td>
<td>Morphine</td>
<td>Hepatobiliary imaging</td>
</tr>
<tr>
<td>Contrast media</td>
<td>Tumor/PET imaging</td>
<td>Regadenoson</td>
<td>Cardiac imaging</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Cardiac imaging</td>
<td>Sinalide</td>
<td>Hepatobiliary imaging</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>Cardiac imaging</td>
<td>Thyrotropin</td>
<td>Thyroid imaging</td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>Renal imaging</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Post-Study Recovery

• Since interventional pharmaceuticals are given in doses that are intended to induce a pharmacologic effect, their use may lead to complications / risks to patient safety
• Non-radioactive “reversal agents” can be used to counteract certain pharmacologic effects, ideally reducing the complications that the patient experiences during the imaging procedure

Examples

• Since interventional pharmaceuticals are given in doses that are intended to induce a pharmacologic effect, their use may lead to complications / risks to patient safety
• Non-radioactive “reversal agents” can be used to counteract certain pharmacologic effects, ideally reducing the complications that the patient experiences during the imaging procedure
Pre-Study Prep

- The distribution and uptake of radiopharmaceuticals can be impacted by drug therapy on board at the time of administration

- In some cases, the pre-administration of non-radioactive drugs is essential for adequate imaging

Pre-Study Prep

Y-90 Zevalin

- Monoclonal antibody radiolabeled with beta emitting isotope for the treatment of non-Hodgkins lymphoma

- Specific for CD20 antigen on B-cells

- How do you protect normal cells and maximize tumor cell uptake?

Pre-Study Prep

- Rituximab
  - Non-radioactive antibody
  - Infuse pre-imaging to block 'normal' B-cell antigen sites
  - Must also consider Rituximab black box warning
    - Severe infusion reactions occur after multiple administrations
    - Severe and prolonged cytopenias

Pre-Study Prep

- Normally, cardiac muscle uses fatty acids for fuel, but in absence of fatty acids (or excess of glucose), it can utilize glucose as well

- To evaluate glucose metabolism in heart muscle, we must force the heart to switch to glucose for fuel

  - Decreased FDG uptake in myocardium = nonviable myocardial tissues

Pre-Study Prep

- Prior to cardiac PET imaging, we want to boost blood glucose levels to ensure FDG uptake by the heart is maximized

- In patients with fasting blood glucose < 250 mg/dl we load with 25-100 mg of glucose

  - Once the blood glucose is sufficiently high, we must force glucose into the tissues

  - Insulin promotes adsorption of glucose from the blood into fat, liver and muscle (including myocardium)

  - 1-5 units regular insulin, depending on the glucose levels after administration of oral glucose load

Radiopharmaceutical Administration

- Radiopharmaceuticals are administered via several routes of administration, depending on the study being performed
  - Intravenously
  - Orally
  - Inhalation
  - Intrathecally

- Most radiopharmaceuticals are sterile products, and are prepared / radiolabeled / dispensed following USP <797> sterile product guidelines
**Mid-Study Enhancement**

- Non-radioactive pharmaceuticals can be used as enhancements for common nuclear medicine studies
  - To be effective, the dose administered will be at pharmacologic levels
  - May result in extensive adverse reactions as a result of administration
- Goal:
  - Change physiologic process in a manner that benefits the nuclear medicine study

**Cardiac Interventions**

- Coronary flow reserve: the maximal increase in coronary flow above resting level for a given pressure when coronary vasculature is maximally dilated
  - Ratio of maximal blood velocity to resting blood velocity
  - Coronary flow at rest remains fairly normal until significant stenosis (>90%) occurs
  - In stress situations, the ability to increase flow in response to increased oxygen demand becomes impaired
  - This fundamental difference allows for myocardial perfusion imaging

**Cardiac Intervention**

- Pharmacologic vasodilators increase adenosine concentration at adenosine receptors in smooth muscle
  - Leads to vasodilation of coronary vasculature
    - Increased blood flow
    - Increased oxygen delivery to tissues
    - Done without physically requiring patient to exercise

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**RP Adverse Reactions**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Radiopharmaceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>Ga-67, In-DTPA, Octreoscan, Iodine, Bicisate, SC, MAA, MDP, MIBI, Metiodiben, MAG-3, OTRA, Ti-99m,</td>
</tr>
<tr>
<td>Pruritis / Rash / Erythema</td>
<td>Ga-67, Iodine, Bicisate, IMMO, SC, MAA, MDP, MIBI, Metiodiben, OTRA, Ti-99m, MIBI, Tl-201</td>
</tr>
<tr>
<td>Facial swelling</td>
<td>Ga-67, IMMO</td>
</tr>
<tr>
<td>Dizziness/Bradycardia</td>
<td>Ga-67, IMNO, SC, MAA, MDP, OTRA, Ti-99m</td>
</tr>
<tr>
<td>Fever</td>
<td>In-WBC, In-DTPA, Octreoscan, Sr-89, IMNO, SC, MAA, MDP</td>
</tr>
<tr>
<td>Headache</td>
<td>In-DTPA, Octreoscan, Iodine, SC, MDP, OTRA, Ti-99m, MIBI</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Octreoscan, SC, MAA, MDP, OTRA, Ti-201</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Bicisate, MAA</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>IMNO, SC, MAA, MDP, OTRA</td>
</tr>
</tbody>
</table>

- Adverse reactions to radiopharmaceuticals are uncommon and generally mild and transient
  - Only a few reported per 100,000 administrations
  - Small amount (mass) of drug administered
  - Lack of pharmacologic action
  - Lack of repeat exposure
- Adverse reactions are most likely not well documented
  - Allergic / hypersensitivity / anaphylactoid / idiosyncratic reactions may not present while patient is in department – may go unreported
  - “Adverse reaction” or “common side effect”
Cardiac Intervention

- Regadenoson Phase 4 Post Marketing Surveillance led to package insert warnings:
  - Cardiovascular
  - Central Nervous System
  - Gastrointestinal
  - Hypersensitivity
  - Musculoskeletal
  - Respiratory

Post-Study Recovery

- A final use of pharmaceuticals in nuclear medicine is as recovery agents, to counteract the effects of drugs administered, specifically the non-radioactive adjunct agents that are used as adjunct study enhancements.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Aminophylline</td>
<td>Cardiac stress perfusion studies</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Cardiac stress perfusion studies</td>
</tr>
<tr>
<td>Esmolol</td>
<td>Cardiac stress perfusion studies</td>
</tr>
<tr>
<td>Naloxone</td>
<td>Hepatobiliary morphine enhancement</td>
</tr>
</tbody>
</table>

Drug Reporting and Tracking

- Where are nuclear medicine agents / interventional agents / reversal agents documented and recorded in patient medication record?
  - Electronic medical record?
  - Who has access to that information?
- Adverse reaction reporting
  - Adverse reactions in nuclear medicine very often go unreported, even when a problem is noted:
    - Ignorance, time constraints, liability issues, lack of knowledge of reporting process, adverse reaction or side effect, lack of interest.

Why Report?

- For nuclear medicine, there are many reasons why reporting issues is essential:
  - Radiopharmaceuticals are given as a single dose
  - Can not use multiple administrations to "verify"
  - The incidence of adverse reactions is too low to observe trends within a single institution
  - Many adverse reactions go unnoticed because patient leaves nuclear medicine
  - Delayed reactions may not occur for several hours of days after administration

Other Pharmacy Considerations
Conclusion

- Nuclear medicine, as well as other areas of radiology, frequently utilize various pharmaceuticals in the course of carrying out imaging procedures.
- The drugs being used have the potential for contributing significantly to various aspects of the patient, both positively and negatively.
- There are multiple places where pharmacists can have an active role in patient care as it relates to patients undergoing typical diagnostic imaging procedures.

Questions?

kdwan@purdue.edu

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