Teaching Editorial

Pharmacologic Reactions in Interventional Nuclear Medicine

HISTORICAL PERSPECTIVE

Nuclear medicine has not been thought of as an interventional or invasive diagnostic procedure; in fact, it was just this simplicity that was the selling point of this modality in the past. As the field of nuclear medicine continued to advance and a better understanding of the organ systems we were investigating emerged, it became clearer that we could extract even more information from these procedures if we dared to become more interventional or invasive. Let us, for a moment, review some of the procedures that we have; and in particular, pay attention to the simplicity of the following examinations: 1) iodine-123 thyroid uptake and scan; 2) ventilation and perfusion scan; 3) liver/spleen scan; 4) bone scans; and 5) iodine-131-hippuran renograms, to name just a few.

With new interventional approaches to nuclear medicine, we have introduced certain risks to the patients. These risks are small but are risks nonetheless. Each of the examinations listed were simple enough to perform and carried little or no risk. However, these examinations can be enhanced to provide additional information by provoking a pharmacologic response by the administration of a nonradioactive pharmaceutical.

NUCLEAR MEDICINE INTERVENTIONS

Pharmacologic and physiologic interventions are becoming more important in diagnostic nuclear medicine. Intervention is either the administration of a drug or a physical maneuver for a diagnostic purpose.

Listed are some of the more common nuclear medicine procedures that require an interventional approach before the conclusion of the procedure: myocardial imaging with dipyridimole (persantine), lasix renogram, hepatobiliary imaging with cholycystokinin (CCK) and phenobarbital premedication, salivary gland imaging with atropine or lemon, ice bath stress testing, pediatric cystograms, gastric emptying with metaclopramide and anticholinergics, and thyroid imaging using thyroid extract stimulation or suppression. On examination of the manufacturer's package inserts that accompany most or all medications, it becomes evident that these medications are not to be used without some degree of concern, which brings us to the purpose of this editorial. If your nuclear medicine department is anything like many of the departments in which we have worked or visited, then most of these interventions and medications are administered by senior staff technologists, often without a physician or nurse in attendance. If this is the case in your department, then it behooves you to pay particular attention to your patient's responses or reactions to "your interventional methods." Let us stress again the *minimal risk* involved in the use of many of these medications; but who among us wants to be responsible for not being able to recognize the patient who experiences adverse reactions and not be informed enough to respond correctly. *Correct interpretation* of any adverse reaction listed in the package insert could help to minimize the effects of an *idiosyncratic/allergic reaction*. Before we continue to discuss the various medications associated with interventional nuclear medicine, let us briefly review an allergic reaction and some of the speculation of what might be the causative factors.

Allergic Reactions

Without question, an allergic reaction is one of the most serious adverse reactions your patient can experience. What provokes such a reaction? No one knows all of the answers, but a review of the normal immune response provides some clues. Take a moment to consider what follows. As you will recall, an antigen is a substance that provokes an immune response. Normally, the body produces antibodies (also called immunoglobulins) to combat specific antigens that enter into the system. Some antibodies bind to mast cells throughout the body and to basophils circulating in the blood. When an antibody encounters its corresponding antigen, it binds with it to form a macro-molecule called an antigen-antibody complex (Ag-Ab complex). Of the five classes of possible antigen/antibody complexes, IgE is by far the most dangerous. The Ag-Ab complex causes the mast cell or basophil to break apart and release a vasoactive substance, which includes histamine, that help destroy the antigen. This is one of the processes called the *immune response*. It is the body's way of protecting itself from harmful invaders. In an *allergy*, however, the body mistakingly recognizes a *benign* substance as a threat. The resulting antigen-antibody reaction causes the symptoms of an allergic reaction, which varies in clinical appearance and intensity according to the individual system and the patient's individual response. In short, the immune

For reprints contact: Vincent Cherico, CNMT, Dept. of Diagnostic Imaging, Rhode Island Hospital, 593 Eddy St., Providence, RI 02908.

system goes awry, causing an abnormal and possibly dangerous overreaction. A drug allergy occurs when a drug provokes an antibody formation, as we have just discussed, causing an adverse reaction that is unrelated to the drug's pharmacologic action. Drug allergy can be caused by an almost limitless number of usually benign substances, which can trigger allergic reactions in susceptible individuals.

Stage I Allergic Reaction. Stage I occurs when an allergy-producing drug first enters the body of a susceptible individual. It is unlikely to cause any symptoms; nevertheless, it may cause trouble. For reasons not fully understood, the body recognizes the drug as an antigen and begins making antibodies. This process takes from several days to more than a week. Most likely, the drug has been eliminated from the patient's system by then, which explains why the patient does not experience an allergic reaction on first exposure to the drug. However, when exposed to the offending drug again, the patient is almost certain to experience an allergic reaction of some sort.

Stage II Allergic Reaction. As in a normal immune response, an allergic response triggers release of histamine and other vasoactive substances from mast cells and basophils. Because an allergic response is abnormal and excessive, this process causes adverse reactions that can range from a rash or hives to anaphylactic shock. (Generalized anaphylaxis in humans will start within 5–30 min after administration of the antagonist, with flushing, urticaria, paroxysmal cough, dyspnea, wheezing, vomiting, cyanosis, circulatory collapse, and shock.) Major causes of death are laryngeal edema, massive airway edema, and cardiac arrhythmias. The major causes of generalized anaphylaxis in humans are drugs, biologicals (e.g., animal sera), insect stings (e.g., bee or wasp venom), and foods. These reactions may appear within seconds (following an i.v. injection), or days later. Allergic reactions to a drug can vary from one individual to the next. Penicillin may give one person a mild rash and another anaphylactic shock, with no apparent reason for the difference. Even the same patient may react differently at various times. Once an allergy has appeared, the individual is likely to experience an allergic response of some sort every time there is exposure to the drug itself or other substances of similar chemical structure.

Idiosyncratic reactions. An idiosyncratic reaction is unlike an allergic reaction. Idiosyncrasy does not result from Ag-Ab production following first exposure to a drug. Instead, it apparently stems from a genetically determined intolerance of a particular drug. A patient may develop an idiosyncratic reaction without warning on his first exposure to only a small amount of the drug.

Anaphylactic Shock. Anaphylactic shock is a life-threatening systemic allergic response, and it is one of the most alarming experiences imaginable for your patient and you. Learning about this condition also includes knowing how to recognize it immediately. Anaphylactic shock occurs when an antigen such as a drug, a food-derived dye, snake or insect venom, or an antigen present in a blood transfusion reacts with an antibody to trigger a generalized, severe allergic reaction. The vasoactive substances released cause smooth muscle contractions, especially in the lungs, leading to bronchospasm. They also cause increased vascular permeability and vasodilation; these effects lower blood pressure and lead to shock. Respiratory distress develops rapidly; death can follow within minutes. Find out what you, a nuclear medicine technologist, as the first person on the scene can do to intervene and possibly reverse this disaster. The patients in our care expect nothing less than this (*1*).

POTENTIAL ADVERSE REACTIONS

The following is a partial sampling of some of the listed side effects noted in the manufacturer's package inserts. The purpose of this abbreviated list is to draw your attention to the manufacturer's package inserts and to familiarize you with the possible side effects or potential adverse reactions that have been reported in the past.

Iodine-123

Adverse Reactions. There were nine adverse reactions reported in a series of 1,393 administrations. None of these were attributed to ^{123}I. Five adverse reactions, consisting of gastric upset and vomiting, were attributed to a filler in the capsule. Two cases of headache and one case of nausea and weakness were attributed to the fasting state. One case of garlic odor on the breath was presumed to be attributable to the presence of tellurium (*2*).

Technetium-99m Albumin Aggregated

Adverse Reactions. Although adverse reactions specifically attributable to ^{99m}Tc albumin aggregated injections have not been noted, the literature contains reports of deaths occuring after the administration of albumin aggregated to patients with pre-existing severe pulmonary hypotension. Instances of hemodynamic or idiosyncratic reactions to the preparations of the technetium ^{99m}Tc albumin aggregated have been reported (*3*).

INTERVENTIONAL NUCLEAR MEDICINE PHARMACEUTICALS

The following is a partial listing of some interventional nuclear medicine techniques and the pharmaceuticals used. The listing is used to underline the intent and purpose of this article.

Hepatobiliary Imaging with Morphine Sulfate or Cholycystokinin

Morphine sulfate. The most serious side effect resulting from use of this pharmaceutical is respiratory depression. Because of a delay in maximum central nervous system effect with an intravenously administered drug (30 min), rapid administration may result in overdosing. Miscellaneous side effects include constipation, headache, anxiety, depression of cough reflex, interference with thermal regulation, and oliguria. Evidence of histamine release such as uticaria, wheals and/or local tissue irritation may occur (*4*).

Cholycystokinin (Kinevac, Sincalide). Gastrointestinal symptoms such as abdominal discomfort or pain and an urge to defecate frequently accompany the injection of sincalide. Nausea, dizziness, and flushing occur occasionally (*5*).

Cardiac Imaging

Dipyridimole (persantine). Adverse reactions are minimal and transient at recommended dosages. However, instances of headache, dizziness, flushing, weakness, syncope, mild gastrointestinal distress, and skin rash have been noted during therapy. Rare cases of what appeared to be an aggravation of angina pectoris have been reported, usually at the initiation of therapy (*6*).

Renogram

Lasix (furosemide). Adverse reactions listed on the inserts are probably the result of extended therapy. In addition to nine possible gastrointestinal system reactions, there are seven possible central nervous system reactions, five possible hematologic reactions, and eight possible dermatologic reactions, as well as cardiovascular reactions (*7*).

In conclusion, new interventional approaches to nuclear medicine have introduced certain risks to the patient. The technologist who is aware of the possible adverse reactions of these pharmaceuticals can intervene in a crisis situation and maintain the health and safety of the patient.

Vincent V. Cherico, CNMT
Stephan I. Frater, MD
Rhode Island Hospital
Providence, Rhode Island

REFERENCES

1. Deiglin JH, Walters JK. Drug interactions. In: *Nursing now*. Springhouse, PA: Springhouse Corp; 1984:29–37.

2. Medi+Physics, I-123, package insert, April 1979.

3. Squibb Diagnostic, MACROTEC, package insert J3-436F. July 1984 (revised).

4. Physicians' desk reference, 41st ed. Oradell, NJ: Medical Economics Co, 1987:923.

5. Kastrup IK, ed. *Facts and comparisons*. Philadelphia: JB Lippincott; 1982:949B

6. Physicians' desk reference, 40th ed. Oradell, NJ: Medical Economics Co; 1986:717

7. Physicians' desk reference, 41st ed. Oradell, NJ: Medical Economics Co; 1987:617