Nonradioactive Pharmaceuticals in Nuclear Medicine

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Objective: Pharmacologic interventions play an important role in nuclear medicine by providing additional information which may help diagnose diseases, evaluate functional reserve and reduce diagnostic imaging time. However, the nonradioactive pharmaceuticals used in nuclear medicine are not without adverse effects which must be familiar to those who administer them.
Methods: Although not all-encompassing, the following is a listing of the most common nonradioactive pharmaceuticals used in nuclear medicine.
Results: Included are the mechanisms of action, indications, dosages and adverse effects of each agent, organized alphabetically for easy reference.
Conclusions: This listing should provide an easy reference for the nuclear medicine technologist when using these pharmaceuticals.
Key Words: acetazolamide; adenosine; bothanechol; captopril; cholecystokinin; cimetidine; dipyridamole; dobutamine; enalaprilat; furosemide; glucagon; morphine; pentagastrin; phenobarbital; vitamin B-12

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Radiopharmaceutical imaging is an important noninvasive modality in the diagnosis and work-up of diseases. In general, diagnostic radiopharmaceuticals monitor a physiological process without altering this process. Unfortunately, however, the information obtained is sometimes insufficient to answer the clinical questions. To overcome this shortfall, interventional pharmaceuticals have been employed. These agents cause alterations in the physiological processes being studied. When used in conjunction with a nuclear medicine procedure, the amount of information which can be obtained is greatly enhanced. Pharmacologic intervention can not only provide additional information about the physiological process studied, but also increase the specificity and sensitivity of the study, or shorten the time of the imaging process itself.

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The list of pharmaceuticals used in nuclear medicine is expanding. A comprehensive listing of the most commonly used agents, indications, doses and side effects would be beneficial to nuclear medicine practitioners as a basic reference. We have attempted to provide such a list. Frequently used nonradioactive pharmaceuticals are discussed, and summarized in Table 1.

ACETAZOLAMIDE (DIAMOX®)

Cerebral perfusion evaluation using blood flow agents can be enhanced with the use of the carbonic anhydrase inhibitor acetazolamide. This agent, commonly used to treat glaucoma and as a diuretic, has also been shown to increase cerebral blood flow following intravenous administration (*1*). Cerebral vasodilatation which results from acetazolamide administration can increase the blood flow by as much as 50% with an average increase of 23% ± 8% (*2*). Normal vessels can easily dilate; however, diseased vessels cannot. As a result, the disparity in the amount of blood flow through normal versus stenosed vessels will be enhanced and better recognized.

Nuclear Medicine Indication

Acetazolamide is used in cerebral perfusion studies to enhance the differentiation between the areas of the brain supplied by normal vessels and those supplied by diseased vessels. It is indicated for patients with transient ischemic attack, carotid artery disease or cerebrovascular accident to determine areas of the brain at risk of infarct. Acetazolamide is also used for other conditions where the cerebral perfusion is typically decreased such as Alzheimer's disease, multi-infarct dementia and complex partial seizure (interictal stage).

Dosage and Administration

One gram of acetazolamide is diluted in 10 cc of sterile water and injected slowly over 2 min. The cerebral blood flow imaging agent is administered 25 min later to take advantage of the peak action of acetazolamide at 20–30 min (*3*). Image acquisition starts 15 min later.

TABLE 1
Nonradioactive Pharmaceuticals in Nuclear Medicine

Pharmaceutical	Indication	Dose	Adverse effects
Acetazolamide (Diamox®)	Brain perfusion imaging (*1–3*)	1 g in 10 ml sterile water, IV over 2 min	Tingling sensations in extremities and mouth, flushing, lightheadedness, blurred vision, headache
Adenosine (Adenocard®)	Cardiac stress imaging (*4–7*)	140 μg/kg/min for 6 min, or 50 μg/kg/min increased to 75, 100 and 140 μg/kg/min each min to 7 min	Chest, throat, jaw or arm pain, headache, flushing, dyspnea, ECG changes
Bethanechol (Urecholine®)	Gastric emptying	2.5–5 mg subcutaneously	Abdominal discomfort, salivation, flushing, sweating, nausea, fall in blood pressure
Captopril (Capoten®)	Renovascular Hypertension Evaluation (*8*)	25–50 mg orally 1 hr prior to study	Orthostatic hypotension, rash, dizziness, chest pain, tachycardia, loss of taste
Cholecystokinin (Kinevac®)	Hepatobiliary imaging (*9–12*)	0.02 μg/kg in 10 ml saline, IV over 5 min	Abdominal pain, urge to defecate, nausea, dizziness and flushing
Cimetidine (Tagamet®)	Meckel's diverticulum imaging (*13–16*)	Adult: 300 mg/kg Pediatric: 20 mg/kg in 20 ml saline, IV over 2 min with imaging 1 hr later	Diarrhea, headache, dizziness, confusion and bradycardia
Dipyridamole (Persantine®)	Cardiac stress imaging (*7,17*)	0.57 mg/kg IV over 4 min (0.142 mg/kg/min)	Chest pain, nausea, headache, dizziness, flushing, tachycardia, shortness of breath and hypotension
Dobutamine (Dobutrex®)	Cardiac function reserve	Incremental dose rate of 15 μg/kg/min up to 15 (child), and up to 40 μg/kg/min every 3 min (adult)	Angina, tachyarrhythmia headache, nausea and vomiting
Enalaprilat (Vasotec I.V.®)	Renovascular hypertension evaluation (*20,21*)	0.04 mg/kg in 10 ml saline, IV over 5 min	Orthostatic hypotension, dizziness, chest pain, headache, vomiting and diarrhea
Furosemide (Lasix®)	Renal imaging (*22*)	Adult: 20 to 40 mg Pediatric: 0.5 to 1 mg/kg given IV over 1–2 min	Nausea, vomiting, diarrhea, headache, dizziness and hypotension
Glucagon	Meckel's diverticulum imaging (*13*)	Adult: 0.5 mg (range 0.25 to 2 mg) Pediatric: 5 μg/kg, given IV or IM	Nausea, vomiting
Morphine (Astramorph®, Duramorph®)	Hepatobiliary imaging (*10,12,23*)	0.04 mg/kg, diluted in 10 ml saline, IV over 2 min (range 2–4.5 mg)	Respiratory depression, nausea, sedation, lightheadedness, dizziness and sweating
Pentagastrin (Peptavalon®)	Meckel's diverticulum imaging (*13,24*)	6 μg/kg subcutaneously	Abdominal discomfort, urge to defecate, nausea, flushing, headache, dizziness, tachycardia and drowsiness
Phenobarbital (Luminal®)	Hepatobiliary imaging (*25,26*)	5 mg/kg/day orally for 5 days	Respiratory depression, nausea, vomiting, dizziness, drowsiness, headache and paradoxical excitement in children
Vitamin B-12 (Cyanoject®, Cyomin®)	Schilling's test	1 mg IM 2 hr after radioactive B-12 dose	None

Contraindications and Adverse Effects

Acetazolamide is a sulfonamide which may provoke an allergic reaction in patients with sulfa allergy or intolerance (*3*). Due to its diuretic action, patients with severe electrolyte imbalances should not receive this agent. Acetazolamide may precipitate hyperglycemia in diabetics, and may potentiate nephrotoxicity in patients with severe renal disease. An absolute contraindication is used in patients with hepatic cirrhosis because of the risk of developing hepatic encephalopathy. Use in patients with increased cerebral pressures or with frequent transient ischemic attacks should be carefully considered.

Adverse effects are generally mild and subside within 10–15 min (*3*). They include tingling sensations in the extremities and around the mouth, lightheadedness, blurred vision, headache and mild confusion. A flushed feeling in the face and neck may also be a complaint, along with taste alteration, nausea, tinnitus and urinary urgency. Adverse effects can be minimized by administering the dose slowly over 2 min.

ADENOSINE (ADENOCARD®)

Adenosine is a potent coronary vasodilator with an ultrashort half-life of <10 sec, which makes it ideal for use in combination with myocardial perfusion imaging agents. Adenosine may increase coronary blood flow up to four to five times that at rest, while the blood flow through stenosed arteries will increase to a lesser extent, if at all (*4*). This differential is less obvious in rest or nonchallenged baseline status. Dipyridamole raises adenosine indirectly by inactivating adenosine deaminase and has a longer half-life and frequent (up to 50% of patients) side effects which require administration of the antidote aminophylline. Although not presently approved by the Food and Drug Administration (FDA), adenosine is expected to be released soon for use in stress testing.

Nuclear Medicine Indication

Adenosine is used in cardiac imaging as an alternative to treadmill stress in patients who are unable to exercise. These are patients with peripheral or cerebral vascular disease, chronic respiratory disease, orthopedic problems or severe arthritis, patients on beta blockers or calcium channel blockers and patients who are poorly motivated.

Dosage and Administration

Prior to an adenosine stress study, theophylline- and caffeine-containing agents (Table 2) should be discontinued and the patient should fast overnight. Adenosine is administered as either a 6-min infusion of 140 μg/kg/min with the radiopharmaceutical injected at the end of the third minute, or as a 7-min titrated dose, with 50 μg/kg/min for 1 min followed by increases each minute to 75, 100 and 140 μg/kg/min (*5,6*), with the radiopharmaceutical injected at the end of the fourth minute. The titrated infusion is ideal for those patients at increased risk for side effects.

Adverse Effects

Adverse effects of adenosine are relatively common and most frequently include chest pain, pain in the throat, jaw or arm, headache, flushing and dyspnea, while ECG changes and AV block occasionally occur (*7*). However, due to the short half-life of adenosine, these adverse effects generally disappear within 1–2 min of the discontinuation of the infusion. If needed, the antidote aminophylline can be used.

BETHANECHOL (URECHOLINE®)

Bethanechol is a cholinergic agent with many effects on the gastrointestinal (GI) tract which mimic parasympathetic nervous system stimulation. Bethanechol increases gastric motility, gastric tone and lower esophageal sphincter pressure and restores impaired peristalsis. It also promotes urination. Generally, bethanechol is used to treat urinary retention, enhance gastric emptying and treat gastroesophageal reflux. However, due to the availability of other agents which promote gastric motility such as erythromycin, metoclopramide (Reglan®) and cisapride (Propulsid®), the use of bethanecol has decreased, mainly due to its side effect profile.

Nuclear Medicine Indication

Bethanechol can be used in nuclear medicine gastric emptying studies to see if the patient will respond to bethanechol therapy.

Dosage and Administration

Bethanechol is administered subcutaneously to prevent cholinergic over-stimulation which may be seen if given intramuscularly or intravenously. Usually, doses between 2.5 and 5 mg will produce the desired effect. Doses >5 mg are used only if lower doses are not effective. The onset of action is 5–15 min following administration, and effects can last up to 2 hr.

Contraindications and Adverse Effects

There are many contraindications to using bethanechol. Bethanechol may increase gastric acid secretion, which limits its use in patients with gastric ulcers. Patients with severe bradycardia or hypotension may experience a significant decrease in blood pressure. Asthmatics or patients with chronic obstructive pulmonary disease should not be given bethanechol since its cholinergic stimulatory properties may exacerbate these conditions. Hyperthyroidism, epilepsy and Parkinsonism are also contraindications for use. Finally, patients with questionable GI or bladder wall integrity should not be given bethanechol since it has a direct action on the muscles of these organs. Common adverse reactions with bethanechol are abdominal cramping, blurred vision, urinary urgency, diarrhea, flushing, sweating, nausea and a decrease in blood pressure with reflex tachycardia. Atropine is the antidote.

TABLE 2
Methylxanthine-Containing Compounds Affecting Dypyridamole Studies (Partial Listing)

Caffeine

Coffee/Tea
Cocoa/Chocolate
Soft Drinks:
- Coca-Cola
- Dr. Pepper
- Mellow Yellow
- Mountain Dew
- Pepsi Cola
- Tab

Over-the-Counter Drugs

Anacin
Anacin Maximum Strength
Appedrine, Maximum Strength
Aqua-Ban
Excedrin

Prescription Drugs

Cafergot (all forms)
Darvon compound
Fiorinal
Prolamine
Synalgos DC
Wigraine (all forms)

Theophylline (prescription drugs)

Aerolate	Slo-bid Gyrocaps	Theo-Dur
Bronkodyl S-R	Slo-phyllin Gyrocaps	Theo-Dur Sprinkle
Constant-T	Somophyllin-CRT	Theolair-SR
Duraphyl	Sustaire	Theophyl-SR
Elixophyllin SR	Theo-24	Theophyllin SR
LaBID	Theobid Duracaps	Theospan SR
Lodrane	Theobid Jr. Duracaps	Theo-Time
Quibron-T S/R	Theochron	Theovent Long-Acting
Respbid	Theoclear LA	Uniphyl

CAPTOPRIL (CAPOTEN®)

Captopril belongs to the class of drugs known as angiotensin converting enzyme (ACE) inhibitors. These agents are used in the treatment of hypertension and congestive heart failure. Captopril blocks the conversion of angiotensin I to angiotensin II and prevents vasoconstriction of, particularly, the efferent arterioles in the kidney, causing decreased glomerular filtration pressure in the affected kidney (*8*).

Nuclear Medicine Indication

Captopril intervention is used to help diagnose renovascular hypertension in hypertensive patients with abdominal bruits, worsening of renal function and poorly controlled hypertension with medication. It may be used to select candidates for successful angioplasty or surgical bypass in patients with known renal artery stenosis.

Dosage and Administration

Patient preparation for the study requires the discontinuation of ACE inhibitor therapy 2 days prior to imaging. In addition, the patient is encouraged to increase fluid intake. The usual dose of captopril is 25 or 50 mg orally. Some recommend crushing the tablet before administering it for better absorption.

Adverse Effects

Single-dose captopril administration may produce transient adverse effects which include orthostatic hypotension, dizziness, tachycardia, chest pain, development of rash and loss of taste. Rare adverse effects which are generally seen with long-term therapy include proteinuria, neutropenia and thrombocytopenia.

CHOLECYSTOKININ (KINEVAC®)

In a normal subject, hepatobiliary imaging agents are extracted by the hepatocytes, cleared through the biliary system into the gallbladder and then move through the common bile duct and into the small intestine. Pharmacologic intervention with a cholecystokinin (CCK) analog can be used not only to enhance the specificity of a gallbladder study in the diagnosis of cholecystitis, but also to shorten the time required to obtain the information. Acute cholecystitis is usually associated with an obstruction of the cystic duct, which occurs in 95%–98% of cases (*9*). During a hepatobiliary study, filling of the gallbladder effectively excludes acute cholecystitis. Unfortunately, nonvisualization of the gallbladder is not necessarily indicative of acute cholecystitis, since several other circumstances such as prolonged fasting, total parenteral nutrition, severe illness or chronic cholecystitis may also cause delayed visualization or nonvisualization of the gallbladder (*10*). In these conditions, administration of CCK can be helpful.

Nuclear Medicine Indication

In performing a hepatobiliary study, the patient should fast for approximately 4 hr prior to the administration of the hepatobiliary imaging agent. This prevents endogenous CCK release due to food in the stomach or in the small bowel. Endogenous CCK has a half-life of 45 min (*11*) and results in gallbladder contraction which prevents the radioactive bile from entering the gallbladder. On the other hand, if the patient has fasted for more than 24 hr or is on hyperalimentation, there is no stimulus to contract the gallbladder and it will stay full, preventing the new bile from entering.

Cholecystokinin is used to empty the gallbladder in patients whose gallbladder is full prior to starting a hepatobiliary study and to determine the gallbladder ejection fraction when the gallbladder has been visualized during the study.

Dosage and Administration

The recommended dose of CCK is 0.02 μg/kg given intravenously over 3 min (*12*). This recommendation amounts to 2 μg/100 kg of body weight and is in compliance with the manufacturer's indications. The dose may be diluted to 10 ml

or more of saline for slower infusion over 5 min to reduce the side effects. Following CCK administration, the gallbladder starts emptying in 2 min with a duration of approximately 11 min (*11*). In a patient whose gallbladder is visualized, CCK is used to calculate the gallbladder ejection fraction and quantitatively assess gallbladder function. Generally, 35% emptying or more indicates normal gallbladder function (*11*). If a satisfactory ejection does not occur in 15 min, a larger, second dose (0.04 μg/kg) of CCK may be administered.

Contraindications and Adverse Effects

CCK is contraindicated in patients who have a history of hypersensitivity and in patients with intestinal obstruction. The adverse effects of CCK are frequent and include nausea, abdominal pain and discomfort, and an urge to defecate. Dizziness and flushing have also been noted. Usually, the adverse effects develop immediately following injection and last only a few minutes. The adverse effects can be minimized by a slower (5 min) infusion of CCK diluted in 10 cc or more of normal saline.

CIMETIDINE (TAGAMET®)

Meckel's diverticulum is a congenital anomaly of the gastrointestinal tract which affects 2% of the population (*13*). It generally presents in the pediatric age group with symptoms of rectal bleeding and abdominal pain occurring in 25%–30% of the cases (*14*). Meckel's diverticulum is an abnormal remnant of the developing GI tract which contains gastric mucosa that can bleed abnormally. The gastric mucosa in the Meckel's diverticulum concentrates ^{99m}Tc-pertechnetate just as the normal gastric mucosa does. The usefulness of cimetidine in Meckel's diverticulum imaging stems from its mechanism of action as a histamine-H2 receptor antagonist.

Cimetidine administration results in a reduction in the volume and concentration of hydrochloric acid produced by the stomach (*15*). In a Meckel's study, following cimetidine administration, the cells of the gastric mucosa continue to accumulate ^{99m}Tc-pertechnetate, but the secretion into the gastric lumen is reduced or prevented. This allows for continued ^{99m}Tc-pertechnetate accumulation in the gastric mucosa with little transit through the intestinal tract (*16*). As a result, the ability to visualize the small area of ectopic gastric mucosa is greatly enhanced.

Nuclear Medicine Indication

Cimetidine is used to enhance the visualization of ectopic gastric mucosa in a Meckel's diverticulum imaging study.

Dosage and Administration

Ideally, cimetidine should be given orally or parenterally for at least 24 hr prior to the study. However, since this is not always possible, it can be given intravenously at doses of 300 mg in adults and 20 mg/kg in children 1 hr before the study (*16*). The dose is diluted in total volume of 20 ml using normal saline, and injected over a period of not less than 2 min.

Adverse Effects

Administration of cimetidine is associated with relatively few adverse effects. Dizziness, confusion, headache, bradycardia and diarrhea may occur. These effects are usually self-limiting and may be minimized by administering the dose over 20 min.

DIPYRIDAMOLE (PERSANTINE®)

The most likely mechanism of action of dipyridamole in producing coronary artery vasodilatation is indirect elevation of adenosine by inactivation of adenosine deaminase, the enzyme responsible for the degradation of adenosine. Dipyridamole has a peak effect at 2–3 min after infusion and a plasma half-life of 15–30 min (*7*).

Nuclear Medicine Indication

In nuclear medicine, dipyridamole is used as an alternative to treadmill stress in cardiac imaging studies. Candidates for dipyridamole cardiac imaging are patients with vascular, respiratory or orthopedic problems, patients on beta blockers or calcium channel blockers and patients with poor motivation, all of which prohibit treadmill exercise.

Dosage and Administration

The protocol for dipyridamole testing has had many modifications since first described in 1978, but the dose, 0.57 mg/kg over 4 min, has not changed (*17*). The patient preparation includes discontinuation of xanthines (theophylline for 36 hr, caffeine for 2–4 hr, Table 2), and nothing by mouth for 4–6 hr. The proper dose of dipyridamole is diluted in approximately 50 cc and administered over 4 min. Four minutes following the completion of the dipyridamole infusion, the radiopharmaceutical is injected.

Contraindications and Adverse Effects

Caution must be used when administering dipyridamole to patients with severe hepatic dysfunction, as its metabolism is almost entirely hepatic (*17*). In addition, risk-benefit assessment must be done in patients with angina, hypotension and asthma.

In general, dipyridamole is safe, however, adverse effects do occur and may require intervention. Chest pain, headache and dizziness occur most frequently while ECG changes, nausea, flushing, tachycardia, shortness of breath and hypotension can also be seen. Aminophylline can be given intravenously to reverse the effects of dipyridamole. If necessary, nitroglycerine can also be given to relieve chest pain. The usual loading dose is the equivalent of 5 mg of anhydrous theophylline per kilogram of body weight administered over 28 min.

DOBUTAMINE (DOBUTREX®)

Unlike the coronary vasodilators, dobutamine is a positive inotrope, which, through stimulation of beta-1 receptors, produces an increase in heart muscle contraction. The increased force of contraction and resulting increase in oxygen

demand produces a stressed state. Dobutamine doses >20 μg/kg/min also have chronotropic effects on the heart. High doses of dobutamine (40 μg/kg/min) produce an increase in heart rate from 70 ± 16 to 121 ± 23 bpm (*18*). As a result, dobutamine infusion has been studied as an alternative cardiac stress agent.

Nuclear Medicine Indication

Dobutamine is used to induce stress in cardiac imaging studies in patients who cannot exercise or who are unable to tolerate other pharmacological stress agents, including patients who suffer from bronchospastic disease which may be exacerbated by administration of these agents. It is also used in the assessment of ventricular function in infants and children with cardiomyopathy and for assessment of cardiac reserve for those on anthracycline chemotherapy (*19*).

Dosage and Administration

Prior to the study, the patient should have nothing by mouth for 3–4 hr, and beta-blocker drug therapy should be discontinued for 24–48 hr to allow full effect of the dobutamine beta stimulation. Dobutamine has a short half-life in serum of 2 min, requiring it to be delivered as a continuous infusion. The dose is diluted in 50 ml of 5% dextrose/water, or normal saline.

The infusion starts at a rate of 5 μg/kg/min for 3 min with increases to 10, 20, 30 and 40 μg/kg/min every 3 min. The infusion can be decreased to the maximum tolerated dose if side effects occur. The radiopharmaceutical is injected 1 min after titration to the highest dose. The dobutamine infusion is continued for 2 min after the radiopharmaceutical injection (*6*). In children, dobutamine infusions range from 5 to 15 μg/kg/min (*19*).

Adverse Effects

The most prevalent adverse effects associated with dobutamine infusions are angina, palpitations, headache, nausea and tachycardia, which can be seen in as many as 70% of patients (*18*). If necessary, administration of an intravenous beta blocker such as esmolol can be used to reverse dobutamine effects.

ENALAPRILAT (VASOTEC IV®)

Enalaprilat is the active metabolite of enalapril, an ACE inhibitor. Enalaprilat has the same mechanism of action as captopril, however, since it is an intravenous form, it eliminates problems such as variable absorption and delayed onset of action which is normally seen with oral captopril. This allows a more complete response and a much shorter study time for the detection of renovascular hypertension.

Nuclear Medicine Indication

Enalaprilat is used in conjunction with renal scintigraphy in the diagnosis of renovascular hypertension in patients with moderate to high probability of renal artery stenosis. It is also used to select candidates for interventional procedures such as renal angioplasty or bypass surgery among patients with hypertension and renal artery stenosis.

Dosage and Administration

The procedure starts with an open intravenous line using normal saline. The recommended dose of enalaprilat is 0.04 mg/kg in 10 ml of normal saline administered intravenously through the intravenous line. The injection should be done slowly over 5 min (*20,21*) in order to avoid adverse effects such as a precipitous drop in blood pressure. Generally, a fall in blood pressure is seen at 10–15 min. If the blood pressure falls below 30% of the baseline, the saline infusion should be increased. The renal imaging agent is injected 10 min after completion of enalaprilat administration.

Adverse Effects

An expected adverse effect of intravenous enalaprilat is a rapid fall in blood pressure. If the blood pressure falls too low, the rate of the concurrent saline infusion can be increased. Caution should be used in allowing the patient to stand up or move around after the study since orthostatic hypotension may be severe. Other less common adverse effects include dizziness, chest pain, headache, dry cough, electrolyte disturbances, fatigue, abdominal pain, vomiting and diarrhea.

FUROSEMIDE (LASIX®)

Furosemide is a loop diuretic which inhibits reabsorption of electrolytes, primarily sodium, in the ascending limb of the loop of Henle, as well as in the proximal and distal tubules. This results in increased excretion of sodium, chloride, potassium and water. Generally, furosemide is used as a diuretic in patients with edema associated with congestive heart failure. Intravenous injection produces diuresis within 5 min, a peak at 20–60 min and a duration of 2 hr.

Nuclear Medicine Indication

Furosemide is administered to confirm or rule out mechanical obstruction during renal scintigraphy when there is significant retention of radioactivity noted in the renal pelvis. In an obstructed kidney, furosemide diuresis will have little effect on the clearance of the radioactivity retained in the kidney. A nonobstructed kidney will rapidly clear the radioactivity into the bladder following furosemide administration. In addition, the renograms produced over the course of the study will show rapid emptying with a steeply declining curve if there is no obstruction. Progressive accumulation even after the administration of furosemide is indicative of obstruction (*22*).

Dosage and Administration

Usual adult doses of 20–40 mg and pediatric doses of 0.5–1 mg/kg are given intravenously, slowly over 1–2 min. Furosemide is usually administered after 20 min of renal imaging if there is retention of radioactivity in the renal pelvis.

Contraindications and Adverse Effects

Furosemide is contraindicated in patients who are anuric as well as those who are dehydrated since the resulting diuresis could further compound the problem. Also, in posturologic procedure situations, extreme care must be exercised since the increased urine flow may tear the fresh sutures. It is important to adequately hydrate the patient before the study. Although the adverse effects from a single furosemide dose are mild, one should be aware of possible reactions that can occur, including nausea, vomiting, diarrhea, dizziness, hypotension, headache, tinnitus, rash, electrolyte depletion and dehydration.

GLUCAGON

One of the problems with the ^{99m}Tc-pertechnetate study for Meckel's diverticulum is the difficulty in visualizing the small area of ectopic mucosa with the large amount of radioactivity present in the GI tract. Glucagon is utilized as an adjunct to Meckel's diverticulum imaging due to its effect on GI motility. Glucagon has a direct effect on the GI tract, producing relaxation of the smooth muscle of the stomach, duodenum, small bowel and colon. This allows the radioactivity secreted by the Meckel's diverticulum and the stomach to remain confined for easy recognition when imaging (*13*). Since glucagon decreases ^{99m}Tc-pertechnetate uptake in the gastric mucosa, pentagastrin is given to improve the uptake (see Pentagastrin).

Nuclear Medicine Indication

Glucagon is used as an adjunct to Meckel's diverticulum imaging to enhance visualization of the ectopic gastric mucosa.

Dosage and Administration

Glucagon can be administered intravenously or intramuscularly at doses ranging from 0.25 to 2 mg in adults, and 5 μg/kg in children. Usually, a dose of 0.5 mg produces a sufficient decrease in GI motility with few side effects. If used intravenously, smooth muscle relaxation begins in 1 min with a peak at 2–4 min. The onset of action is approximately 10 min when given intramuscularly. The duration of action is 20–30 min. Glucagon is administered 10 min after the dose of ^{99m}Tc-pertechnetate.

Adverse Effects

The adverse effects of glucagon are very few. Nausea and vomiting may occasionally occur, as well as allergic reactions producing respiratory distress and hypotension. Treatment is symptomatic.

MORPHINE (ASTRAMORPH®, DURAMORPH®)

Morphine is a Schedule II substance which is primarily used for analgesia. Morphine also exerts an effect on the GI tract by increasing biliary tract pressure. As a result, intravenous morphine has been utilized in hepatobiliary imaging to aid in the visualization of the gallbladder.

In a normal biliary system, bile enters the gallbladder before it passes through the common bile duct into the duodenum. There are many reasons why hepatobiliary imaging agents may not fill the gallbladder and instead empty directly into the small intestine. These include acute and chronic cholecystitis, total parenteral nutrition, the presence of food in the upper GI tract and prolonged fasting (*23*).

Morphine causes contraction of the sphincter of Oddi, increasing bile duct pressure and causing diversion of the flow of bile into the gallbladder if the cystic duct is patent. In acute cholecystitis, the cystic duct is obstructed and the gallbladder will not fill even after the administration of morphine. The use of morphine has improved the specificity of the study and shortened the procedure time from many hours to 90 min (*12*).

Nuclear Medicine Indication

Morphine is used in hepatobiliary imaging studies to aid in the diagnosis of acute cholecystitis when the bile activity is seen in the small bowel but not in the gallbladder.

Dosage and Administration

During a hepatobiliary study, if the gallbladder does not visualize in 60 min, 0.04 mg/kg of morphine may be given intravenously over 3 min (*10*). Imaging continues for an additional 30 min. If the gallbladder fails to visualize 30 min following morphine administration, the most probable diagnosis is acute cholecystitis.

Contraindications and Adverse Effects

Morphine is contraindicated in patients allergic to morphine, in patients with respiratory depression, and in premature infants. Generally, patients with head injuries, seizures, chronic pulmonary disease, renal insufficiency or hepatic dysfunction should be carefully monitored when receiving morphine. Also, morphine administration increases plasma amylase concentrations which may aggravate pancreatitis. Morphine should not be used if the GI tract is not visualized.

Adverse effects of morphine can be severe, the most important to consider being respiratory depression. Other common adverse effects include dizziness, sedation, nausea, vomiting, sweating and constipation. Naloxone, a narcotic antagonist, can be given if the adverse effects are severe. The usual dose of naloxone is 0.4 mg intravenously.

PENTAGASTRIN (PEPTAVLON®)

False-negative results in ^{99m}Tc-pertechnetate imaging for Meckel's diverticulum are encountered in approximately 15% of the patients who undergo this study (*24*). Pentagastrin is an agent which can be used to improve this study's sensitivity. Pentagastrin is a synthetic compound which contains the active portion of gastrin, a naturally produced hormone which stimulates gastric acid secretion. Pentagastrin administration increases uptake of ^{99m}Tc-pertechnetate by the gastric mucosa. In addition, the ectopic gastric mucosa found in the Meckel's diverticulum will also concentrate

more ^{99m}Tc-pertechnetate following pentagastrin, allowing easier recognition of the ectopic site.

Nuclear Medicine Indication

Pentagastrin is used in Meckel's diverticulum studies to enhance visualization of the site of ectopic gastric mucosa.

Dosage and Administration

Pentagastrin is given subcutaneously, 15 min before the radiopharmaceutical administration. The usual dose is 6 μg/kg (*24*). Gastric secretion enhancement occurs approximately 10 min after the subcutaneous injection with a peak response at 20–30 min and a duration of 60–80 min.

There are many factors which must be considered when using pentagastrin which may contribute to difficulty in interpreting the study results. Pentagastrin also stimulates GI motility due to a direct effect on the smooth muscle. The increase in peristalsis may move the activity away from the ectopic site. The enhanced movement of radioactivity through the GI tract may make it difficult to differentiate between the ectopic site and the surrounding loops of bowel (*19*). Thus, glucagon is often used in conjunction with pentagastrin in Meckel's diverticulum imaging (see Glucagon).

Contraindications and Adverse Effects

A contraindication to the use of pentagastrin is hypersensitivity to the agent. Caution should be used in patients with pancreatic, hepatic or biliary disease, as pentagastrin may stimulate pancreatic enzyme secretion and increase biliary flow.

Adverse effects of pentagastrin generally involve the GI tract. Abdominal pain, nausea and vomiting are common, as is the urge to defecate. Flushing, tachycardia, dizziness, headache and drowsiness may also be seen. In some cases, allergic reactions may occur, producing shortness of breath, tingling fingers, chills and a heavy sensation in the arms and legs, all of which can be treated symptomatically.

PHENOBARBITAL (LUMINAL®)

Phenobarbital is used as an adjunct to imaging of the hepatobiliary system in patients with the differential diagnosis of biliary atresia or neonatal hepatitis. These are the main considerations in neonates with jaundice and conjugated hyperbilirubinemia which persists beyond the first month of life. The diagnosis is difficult since there are similar clinical, biochemical and histologic features associated with both diseases (*25*).

Phenobarbital is an inducer of hepatic microsomal enzymes leading to increased bilirubin conjugation and excretion. It also increases the uptake and excretion of other compounds by the liver. Administration of phenobarbital will enhance the excretion of hepatobiliary imaging agents in patients with cholestatic jaundice who have patent biliary ducts. In patients with biliary atresia, there will be no excretion into the small bowel (*26*). The use of phenobarbital pretreatment with hepatobiliary imaging is sensitive, specific and accurate in differentiating between these two diseases (*25*).

Nuclear Medicine Indication

Phenobarbital is used in pediatric hepatobiliary studies to aid in the differentiation of neonatal jaundice and biliary atresia.

Dosage and Administration

Pretreatment with phenobarbital is necessary to achieve the most information from the hepatobiliary study. Patients are given 5 mg/kg/day orally for at least 5 days (*26*). This allows for induction of the hepatic enzymes which will aid in the movement of the hepatobiliary imaging agent through the liver and biliary system. Scintigraphy is performed in the usual manner following the pretreatment.

Contraindications and Adverse Effects

Phenobarbital is contraindicated in patients allergic to barbiturates, as well as in patients with severe respiratory diseases since respiratory depression is a major concern in these patients. The most common adverse effects associated with phenobarbital are respiratory depression, drowsiness, lethargy, hyperexcitability in children, rash, nausea and vomiting.

VITAMIN B-12 (CYANOJECT®, CYOMIN®)

Vitamin B-12, a water-soluble vitamin, is found in many foods in the daily diet such as meat, eggs and milk. In the stomach, vitamin B-12 is released from food and is bound to intrinsic factors. The intrinsic factor-vitamin B-12 complex is absorbed from the ileum and stored in the liver. Vitamin B-12 is excreted in the urine once the storage capacity is exceeded. If there is a deficiency in vitamin B-12, either due to the lack of the vitamin in the diet, or due to an inadequate absorption, pernicious anemia develops.

Nuclear Medicine Indication

Schilling's test is used to determine if the patient can absorb radioactive vitamin B-12 from the intestine. This test requires an intramuscular injection of nonradioactive vitamin B-12 to "flush out" the absorbed radioactive vitamin B-12 from the storage sites into circulation and out in urine.

Dosage and Administration

One milligram of nonradioactive B-12 is given intramuscularly two hours after ^{57}Co-labeled vitamin B-12 is administered. This large dose saturates the storage sites and helps flush the absorbed radiolabeled B-12 out into the urine.

The excreted radioactivity reflects the amount absorbed. Normally, urinary excretion of B-12 ranges between 15% and 40%, however, if the excretion is <5%, this is diagnostic of B-12 malabsorption. The test can be repeated using an intrinsic factor in addition to the vitamin B-12. If urinary B-12 excretion returns to normal, this is indicative of an intrinsic factor deficiency.

Adverse Effects

Vitamin B-12 is water soluble and nontoxic, even in large doses. However, rare incidences of diarrhea, itching, urticaria and anaphylaxis have been reported.

OTHER MEDICATIONS THAT AFFECT NUCLEAR MEDICINE STUDIES

There are numerous pharmacologic agents or food that may adversely affect nuclear medicine studies, particularly dipyridamole studies, radioiodine thyroid uptake and radioiodinated metaiodobenzylguanidine (MIBG) studies.

Table 2 lists methylxanthine-containing compounds which may interfere with dipyridamole studies. Table 3 lists the most common iodine-containing pharmaceuticals which interfere with thyroid studies. Table 4 includes medications which are known to affect and which will most likely affect MIBG imaging for neuroblastomas, pheochromocytomas and cardiac denervation.

When evaluating a patient for these studies, it is imperative to check for these agents and discontinue them for a proper period of time to avoid misinterpretation of the results.

TABLE 3
Pharmaceuticals Affecting Radioiodine Thyroid Uptake

Thyroid hormones
- Levothyroxine (T4)—(Synthroid, Levoxine)
- Triiodothyronine (T3)—(Cytomel)
- T4 + T3 Combination Drug—(Euthroid, Thyrolar, Armour-Thyroid)
- Thyroglobulin—(Proloid)
- D-Thyroxine—(Choloxin)

Antithyroid drugs
- Propylthiouracil
- Methimazole
- Carbimazole

Perchlorates
- $KClO_4$
- $NaClO_4$

Iodine-containing drugs*
- Oral:
  - Amiodarone (Cordarone)
  - Diiodohydroxyquin (Yodoxin)
  - Iodine-containing vitamins
  - Iodinated glycerol (Iophen, Organidin)
  - Iodinated expectorants (KIE, Calcidrine)
  - Isopropamide iodide (Darbid)
  - Lugol's solution
  - Potassium iodide
- Topical:
  - Diiodohydroxyquin cream (Vytone)
  - Iodine tincture
  - Iodine gauze (NuGauze)
  - Iodochlorhydroxyquin cream (Vioform)
  - Povidone iodine (Betadine)

Iodinated contrast agents
Some examples include:
- Iohexol (Omnipaque)
- Metrizamide (Amipaque)
- Iothalamate (Angio-Conray)
- Diatrizoate meglumine sodium (Renografin)

*Adapted from reference 27

TABLE 4
Pharmaceuticals Affecting Metaiodobenzylguanidine Studies*

Known to reduce uptake	
Antihypertensive/cardiovascular	Sympathomimetics
Labetalol	Ephedrine
Reserpine	Phenylephrine
	Phenylpropanolamine
	Pseudoephedrine
Calcium channel blockers	
Diltiazem	
Nifedipine	Others
Verapamil	Cocaine
Tricyclic antidepressants	
Amitriptyline	
Amoxapine	
Doxepin	
Imipramine	
Loxapine	
Expected to reduce uptake	
Cardiovascular	Tranquilizers
Bretylium	Chlorpromazine
Dobutamine	Fluphenazine
Dopamine	Haloperidol
Guanethidine	Promethazine
Metaproterenol	Prochlorperazine
	Thioridazine
	Trazolone
Sympathomimetics	
Amphetamine	
Albuterol	
Methylphenidate	
Terbutaline	

*Adapted from reference 28

SUMMARY

The use of pharmaceutical interventions is an essential part of nuclear medicine practice. Over time, more and more agents will likely be added to the list as we learn more about the benefits of using them. Although there may be many variations in the use of nonradioactive pharmaceuticals depending on the institutions and the nuclear medicine specialists who use them, the compilation should provide information that can be used in any practice or by any member of the nuclear medicine team. The beneficial results produced through the use of these agents make this an important and growing aspect of nuclear medicine that everyone should become familiar with.

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