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*Drugs Used as Interventional Agents in Nuclear Medicine*

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# DRUGS USED AS INTERVENTIONAL AGENTS IN NUCLEAR MEDICINE

## STATEMENT OF OBJECTIVES

The primary purpose of this lesson is to provide a basic understanding of drugs used as interventional agents in the practice of nuclear medicine.

*Upon successful completion of this material, the reader should be able to:*

1. Identify the indications for interventional agents used in various nuclear medicine studies.
2. Know the dosage ranges for the interventional drugs.
3. Discuss the proposed mechanism(s) of action for each of these pharmaceuticals.
4. Describe the precautions and contraindications associated with these drugs.
5. With selected interventional pharmaceuticals, know the treatment if an adverse reaction occurs.

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## DRUGS USED AS INTERVENTIONAL AGENTS IN NUCLEAR MEDICINE

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### INTRODUCTION

In many nuclear medicine studies, pharmacologic interventional agents are essential components. Care must be exercised with dosage determination and administration of these pharmaceuticals since there is a risk of causing adverse drug reactions. The severity of these reactions varies with the different drugs.

In this lesson, the pharmaceuticals are categorized according to the type of imaging study; the focus is on traditional nuclear medicine rather than PET imaging. Various aspects of these conventional drugs are discussed in terms of their use as adjuncts to nuclear medicine studies.

### MYOCARDIAL PERFUSION IMAGING

Myocardial perfusion imaging with the injection of a radiopharmaceutical during stress can demonstrate the presence of myocardial ischemia. The uptake of radiopharmaceuticals used in myocardial perfusion scintigraphy is proportional to the regional blood flow. Differences in regional cardiac blood flow result in nonhomogeneous uptake of the radiopharmaceutical which is the primary criterion used to diagnose coronary artery disease. During exercise-induced vasodilation, blood flow in myocardial regions supplied by stenotic coronary arteries does not increase to the extent that it does in areas supplied by normal coronary arteries. Pharmacologic stress agents offer an alternative to exercise in patients who are unable to attain an acceptable level of exertion or who are unable to exercise due to physical limitations. The three pharmacologic stress agents covered in this unit are adenosine, dipyridamole, and dobutamine.

#### Adenosine

*Mechanism of Action.* Adenosine is an endogenous nucleoside found in all cells of the body, and it is a potent coronary vasodilator. It is reported to exert its pharmacological effects by activating specific cell surface receptors  $A_1$  and  $A_2$ . Once adenosine interacts with  $A_2$ -receptors, there is enhanced production of

adenylate cyclase and cyclic adenosine monophosphate with a reduction of sarcolemmic calcium uptake. This results in coronary vasodilation.<sup>7,12,13</sup>

Once adenosine is transported into cells, it is rapidly metabolized to inosine via deamination by adenosine deaminase in the cytosol or via phosphorylation to adenosine monophosphate by adenosine kinase. The rapid inward cellular transport and metabolism of adenosine yields an ultra-short half-life which has been reported to be less than 2 seconds. It follows, then, that adenosine must be administered as a constant infusion when used for its vasodilator effects for nuclear cardiac imaging purposes.<sup>1,12,13,14</sup>

**Methodology.** Patient preparation requires nothing by mouth for a minimum of 4 hours with caffeine-containing beverages and foods stopped for at least 12 hours prior to the study. Long acting aminophylline or theophylline preparations should be discontinued for 48 to 72 hours prior to the study. The exception to this is pentoxifylline since it does not inhibit the action of adenosine. Since dipyridamole blocks the cellular uptake of adenosine which could significantly increase its level in the blood and tissues, it is recommended that patients taking dipyridamole chronically should not receive adenosine until 24 hours after the last dose of dipyridamole. The recommended adult dosing regimen is 140 µg/kg/min intravenously infused continuously over 6 minutes using an infusion pump (for a total dose of 0.84 mg/kg). The radiopharmaceutical is injected at 3 minutes into the infusion. Except when severe adverse reactions prohibit, it is recommended to continue the adenosine infusion for at least 1 minute after the radiopharmaceutical is injected. In some cases of severe adverse reactions, the cardiologist may request that the infusion rate be decreased rather than stopped.<sup>3,4,6,7,13,14</sup>

Since <sup>201</sup>Tl undergoes redistribution, imaging should begin immediately after the termination of the adenosine infusion; however, imaging with <sup>99m</sup>Tc-tetrofosmin or <sup>99m</sup>Tc-sestamibi can be delayed for 30 minutes after cessation of the infusion because they only minimally redistribute. During the adenosine infusion and for a minimum of 5 minutes after termination of the infusion, the patient's ECG should be monitored continuously with blood pressure measurements obtained every minute.<sup>3,14,74,75</sup>

**Contraindications.** The following are contraindications to the use of adenosine: 2nd- or 3rd-degree atrioventricular block (except in patients having a functioning artificial pacemaker); sinus node disease, such as symptomatic bradycardia or sick sinus syndrome (except in patients having a functioning artificial pacemaker); known or suspected bronchoconstrictive or bronchospastic lung disease, such as asthma; known hypersensitivity to adenosine; unstable angina; oral

dipyridamole use; and hypotension (< 80 mm Hg systolic pressure).<sup>3,12,13,14</sup>

**Precautions.** When adenosine is administered to patients receiving drugs which have depressant effects on the SA and AV nodes, caution should be exercised because of the potential for additive or synergistic effects of these agents.<sup>12</sup>

**Adverse Effects.** Among 1421 patients in U.S. clinical trials, the following reactions were reported with an incidence of 1% or greater: flushing (44%); chest discomfort (40%); dyspnea or the urge to breathe deeply (28%); headache (18%); throat, neck, or jaw discomfort (15%); gastrointestinal discomfort (13%); lightheadedness/dizziness (12%); upper extremity discomfort (4%); ST segment depression (3%); 1st degree AV block (3%); 2nd degree AV block (3%); paresthesia (2%); hypotension (2%); nervousness (2%); and arrhythmias (1%). Even though adenosine has a very short half-life, 10.6% of the side effects occurred several hours after termination of the infusion rather than during the infusion. It was also reported that 8.4% of adverse effects beginning during the infusion persisted for up to 24 hours after cessation of the infusion; however in many cases, it was not possible to determine whether these late adverse reactions were due to the adenosine infusion or some other factor. In this same group of patients, some of the adverse reactions listed with an incidence of less than 1% were nonfatal myocardial infarction, life-threatening ventricular arrhythmia, third-degree AV block, and bradycardia. The package insert also reports that fatal cardiac arrest and sustained ventricular tachycardia (requiring resuscitation) had been reported coincident with the infusion of adenosine, but it did not provide a percent incidence.<sup>12</sup>

Clinically it has been observed that the adverse effects of adenosine disappear within 1 or 2 minutes when the infusion is discontinued. The package insert reports that in controlled clinical trials, aminophylline (theophylline 50-125 mg via slow intravenous administration) was needed to abort the side effects of adenosine in less than 2% of the patients. Even though it is generally not necessary to administer aminophylline, the standard adenosine antagonist, it still should be available in all cases.<sup>3,12,14</sup>

## Dipyridamole

**Mechanism of Action.** Dipyridamole is a potent coronary vasodilator, and it is used to evaluate the coronary flow reserve. This agent can increase coronary blood flow in the range of 3.5 to 5 times. It is believed that dipyridamole's pharmacological effect is the result of an augmentation of endogenous adenosine either by the blockade of adenosine receptors or by inhibiting the activity of the enzyme adenosine deaminase. An increase in adenosine in the myocardial arterial walls produces

vasodilation.<sup>1,2,7</sup>

**Methodology.** The patient should fast for at least 4 hours prior to dipyridamole infusion. Also, the patient should abstain from caffeine-containing beverages and foods for a minimum of 12 hours prior to the study and should discontinue long-acting theophylline (methylxanthine) preparations for 48 to 72 hours prior to dipyridamole infusion. This is because methylxanthines are pharmacological antagonists of adenosine. The exception to this is pentoxifylline since it does not inhibit the coronary hyperemia induced by dipyridamole.<sup>3,6</sup>

According to the package insert, the dose for dipyridamole is 0.57 mg/kg body weight to a maximum of dose of 60 mg infused intravenously at the rate of 0.142 mg/kg/min for 4 minutes. The myocardial perfusion scintigraphy radiopharmaceutical is injected 3 to 5 minutes after the completion of the dipyridamole infusion or earlier, if significant hemodynamic or side effects exceed the patient's tolerance or threaten the safety of the patient.<sup>3,5,7,8</sup>

**Contraindications.** Hypersensitivity to dipyridamole and an allergy to aminophylline are both considered contraindications to the use of dipyridamole. It has also been reported that this drug is contraindicated in patients with severe bronchospastic lung disease since there is a potential for provoking bronchospasm. Leppo's recommendation is to perform dipyridamole testing only on those patients who would otherwise be referred for exercise testing except for their physical limitations. He also stated that the patient selection should be limited to patients who are free of angina and relatively stable.<sup>3,5,9,10</sup>

**Precautions/Warnings.** If the patient does not abstain from xanthine derivatives such as caffeine and oral maintenance theophylline medications, a false negative cardiac perfusion study could result. As mentioned previously, this is due to the fact that the methylxanthines can abolish dipyridamole's coronary vasodilation effect.

Patients having severe coronary artery disease or abnormalities of cardiac conduction/impulse formation may be at increased risk for serious adverse events.<sup>5</sup>

**Adverse Effects.** In a study of 3911 patients receiving intravenous dipyridamole as an alternative to exercise in thallium myocardial perfusion imaging, two types of serious adverse reactions were noted: (1) four cases of myocardial infarction, two fatal and two non-fatal and (2) six cases of severe bronchospasm. The most frequent adverse events were chest pain/angina pectoris (19.7%), electrocardiographic changes [most commonly ST-T changes] (15.9%), headache (12.2%), and dizziness (11.8%). If necessary to reverse adverse effects, aminophylline can be administered by slow IV infusion at a dose of 50 - 100 mg (depending on the severity of symptoms) over a time period of 30 to 60 seconds. This aminophylline dose can be repeated, usually within 5

minutes if symptoms persist. (Note: The maximal total aminophylline dose reported by Johnston et al. was 400 mg). If chest pain persists, sublingual nitroglycerin can be administered. If possible, do not administer the aminophylline until at least 3 minutes after the radiopharmaceutical injection. This will permit radiopharmaceutical perfusion imaging to be conducted prior to the reversal of dipyridamole's pharmacologic effects on the coronary circulation. In patients with severe side effects, monitoring should be continued for at least 5 minutes (monitoring should be continued longer if symptoms persist) post aminophylline administration.<sup>1,3,5,7,8,11,77</sup>

## Dobutamine

**Mechanism of Action.** Dobutamine is a beta-receptor agonist possessing both positive inotropic and chronotropic effects. This agent produces a dose-dependent increase in heart rate and systolic blood pressure, but it causes a decrease in diastolic blood pressure. Dobutamine's hemodynamic effects imitate those seen with submaximal exercise, but the heart rate response of the drug predominates over systolic blood pressure changes. Dobutamine exhibits advantageous characteristics for the pharmacologic manipulation of myocardial oxygen demand in the provocation of ischemia during the study of coronary artery disease. Dobutamine's plasma half-life is 2 minutes, thus it has a rapid onset and cessation of action allowing easy control of blood levels. An alternative to dobutamine is arbutamine which is a synthetic catecholamine developed for pharmacologic stress testing.<sup>15,16,17,76</sup>

Patients with bronchospastic disease, in whom pharmacologic stress is necessary and in whom adenosine or dipyridamole is contraindicated, are candidates for dobutamine. Other candidates are those who are taking oral dipyridamole or who have ingested caffeine or a xanthine preparation within the previous 12 hours.<sup>3</sup>

**Methodology.** The pharmacologic stress produced by dobutamine is similar to exercise and indirectly assesses flow reserve. The dobutamine can be diluted with either saline or 5% dextrose solution to obtain a final concentration of 1 mg/mL. It is administered with the use of an infusion pump system through a peripheral intravenous line at doses of 10, 20, 30, and 40 µg/kg/min at 3 minute intervals. Variations of this method exist, such as a starting dose of 5 µg/kg/min and time intervals of 5 minutes between stepped increases. In some cases the maximum tolerated dose will be less than 40 µg/kg/min. The patient's ECG, heart rate, and blood pressure are monitored throughout the dobutamine infusion and until the heart rate returns to < 100 beats/minute and all symptoms resolve. The radiopharmaceutical is injected after 1 minute of

maximum (or maximally tolerated) dose, and the dobutamine infusion is continued for another 2 minutes.<sup>3,7,15,18,19</sup>

The following are criteria for the dobutamine infusion to be terminated early: (1) a systolic blood pressure >220 mm Hg or a diastolic blood pressure >120 mm Hg, or both; (2) a decrease in systolic blood pressure to < 80 mm Hg; (3) >2 mm ST segment depression beyond the initial baseline ECG; (4) nonsustained or sustained ventricular tachycardia; (5) supraventricular tachycardia; (6) severe angina; (7) dyspnea or other intolerable symptoms.<sup>15,20</sup>

**Contraindications.** The use of dobutamine is contraindicated in patients who have demonstrated previous manifestations of hypersensitivity to this drug. Also, patients who are currently taking beta-blockers or who have hypertrophic cardiomyopathy, uncontrolled hypertension (systolic pressure > 200 mm Hg, diastolic pressure > 110 mm Hg), unstable angina, or ventricular arrhythmias should not undergo a dobutamine pharmacologic stress study.<sup>3,15,18,20</sup>

**Precautions/Warnings.** Because the potential side effects include nausea and vomiting, the patient should fast for at least 3 hours prior to dobutamine administration. The patient should continue to be monitored for 5 minutes after the conclusion of the dobutamine infusion. If severe side effects occur, the physician can terminate the dobutamine infusion early; the side effects should resolve within several minutes of terminating the infusion. Esmolol, a fast acting beta-blocker, can be used to treat the adverse effects, if necessary. Patients who have a sulfite sensitivity may have allergic-type reactions when receiving dobutamine hydrochloride preparations containing sodium bisulfite. Asthmatics demonstrate sulfite sensitivity more frequently than nonasthmatic people.<sup>3,15,18</sup>

**Adverse Effects.** In a study involving 144 patients, Hays et al. reported the incidence of chest pain and palpitation as being 31% and 29%, respectively. Some of the other adverse effects reported include cardiac arrhythmias, headache, ischemic ECG changes, and flushing. The majority of dobutamine's adverse effects are transient, but esmolol should be available to counteract any adverse effects of dobutamine when necessary.<sup>3,15</sup>

## RADIONUCLIDE RENAL STUDIES

Pharmacological interventional agents in combination with renal imaging radiopharmaceuticals are employed to assess the functional integrity of the kidney. The renal nuclear medicine studies utilizing pharmacologic intervention are diuresis renography and angiotensin-converting-enzyme inhibitor (ACEI) scintigraphy.

Diuresis renography, utilizing furosemide, is indicated in the diagnosis of obstructive uropathy. ACEI scintigraphy, employing captopril or enalaprilat, is used in the diagnosis of renovascular hypertension. Furosemide can also be used in ACEI scintigraphy for the purpose of emptying the renal collecting system and increasing the accuracy of the comparative measurements in the residual cortical activity between the baseline (BSL) and ACEI scintigraphy studies.<sup>21</sup>

Renal scans should be delayed for 24 hours whenever the patient has undergone a contrast study. This is because intravenous radiographic contrast medium may cause a transient reduction in renal function. In the case of renal angiography or angioplasty, it has been recommended to defer the nuclear medicine renal study for 3 days.<sup>24,31</sup>

### Furosemide

**Mechanism of Action.** Furosemide induces diuresis by primarily inhibiting the reabsorption of sodium and chloride in the proximal tubule, the distal tubule, and in the loop of Henle. The fundamental principle of diuretic renography is that the prolonged retention of radioactivity observed in nonobstructed, dilated systems is the result of a reservoir effect. With any type of renal obstruction, delayed excretion and retention of urine results. Obstruction results in varying degrees of reduced flow and function as well as an abnormal renogram. Because delayed excretion and retention of urine are nonspecific, diuretic renography is indicated in the diagnosis of obstruction. Diuresis causes fast emptying of a nonobstructed kidney, but it has minimal effect on a kidney that is obstructed.<sup>21-23</sup>

**Methodology.** Different dosing protocols exist for furosemide, one based on serum creatinine and creatinine clearance, and another based on body weight. An example using body weight: intravenous furosemide (0.5 to 1 mg/kg, maximum of 40 mg in normal function, 80 mg in renal insufficiency) is intravenously administered over 1 to 2 minutes. It is recommended to flush the furosemide dose with saline. It is given either more than 15 minutes prior to, within 3 minutes, or 20 to 30 minutes after the radiopharmaceutical injection. One of the most commonly used radiopharmaceuticals to evaluate renal function is <sup>99m</sup>Tc-mercuric diethylenetriamine.<sup>21,23,24</sup>

When furosemide is used in combination with ACEI scintigraphy, furosemide (maximum of 40 mg in the absence of renal insufficiency, 80 mg in renal insufficiency) is intravenously administered 3 to 5 minutes after the radiopharmaceutical administration. Furosemide is injected slowly over a time period of 1 to 2 minutes.<sup>21,24</sup>

**Contraindications.** The package insert states that furosemide is contraindicated in patients who have a

history of hypersensitivity to furosemide and in patients with anuria.<sup>22</sup>

**Precautions.** Good hydration is necessary so that fluid is available for mobilization in response to diuresis and to prevent dehydration. When managing fluid intake, the patient's other medical conditions must always be considered. If hydration is not sufficient, the patient should drink 300 to 500 mL of water or juice. After 20 to 30 minutes, the hydration status should be evaluated again. If an indwelling catheter is not present, a blunted diuretic effect may result since increased pressure from bladder filling can be transmitted. This can be interpreted as a false positive study. In patients with outlet obstruction or obstruction of the ureterovesical junction, an indwelling catheter may be beneficial. For this study it is necessary to catheterize infants and children as well as patients unable to void voluntarily. When a catheter is not used, the patient should void prior to the study.<sup>23,24</sup>

**Adverse Effects.** It is rare for the patient to experience side effects from furosemide when the patient is well hydrated. Syncope rarely occurs. When furosemide is administered over a time period of less than 1 to 2 minutes, the patient may experience some degree of nausea.<sup>21,23,25</sup>

## Captopril

**Mechanism of Action.** In renal artery stenosis (RAS), angiotensin II produces constriction of the efferent arterioles of the glomerulus resulting in elevation of the filtration pressure which maintains glomerular filtration rate (GFR). There are limits to this normal compensatory mechanism. ACEI blocks the conversion of angiotensin I to angiotensin II which prevents this normal compensatory mechanism. In kidneys with renin-dependent, hemodynamically significant RAS, the result is a decrease in postglomerular resistance resulting in a drop in the transcapillary driving force which maintains glomerular filtration. Thus, glomerular filtration is reduced in the affected kidney. This short-term ACE inhibition serves as a pharmacologic probe to analyze the patient's renin-angiotensin-aldosterone system. Delayed uptake and cortical retention of the radiopharmaceutical demonstrates reduced GFR on renal scintigraphy. Likewise, the renogram curve shows a decrease in the function of the affected kidney.<sup>23,26</sup>

**Methodology.** Different protocols are available for performing ACEI scintigraphy studies. Many centers obtain ACEI scintigraphy studies without first performing a baseline study. If the ACEI study demonstrates a compromised GFR and scintigraphic signs of RAS, a subsequent baseline study without captopril should be performed for comparison. (As an alternative to performing the baseline study, the

physician may proceed directly to renal angiography if there is a high clinical index for suspicion of renovascular hypertension.) When obtaining an ACEI scintigraphy study, captopril in a dose of 25 or 50 mg is given orally 1 hour prior to starting the radionuclide study. Often intravenous furosemide is administered simultaneously with the radiopharmaceutical for the purpose of clearing the collecting system activity, which could have an effect on the visual and renographic interpretation of the study.<sup>23,26</sup>

**Contraindications.** Patients who are hypersensitive to captopril or any other ACEI should not receive this product. Patients with high renin levels, or who are dehydrated, salt depleted, or who have recently had dialysis should not have this product administered since potentially dangerous hypotension may result.<sup>24,27</sup>

**Precautions.** In order to ensure captopril absorption, the drug should be administered on an empty stomach. For all renal studies, the patient should be adequately hydrated especially if diuretics are also being administered. If the patient's hydration status is not satisfactory, the patient can drink 300 to 500 mL of water or juice. After 20 to 30 minutes, the hydration status is evaluated again. An alternative method is to administer, over a time period of 1 hour, normal saline in a dose of 10 mL/kg (maximum of 500 mL) prior to the radionuclide injection. It is best to withhold ACEI for 2 to 5 days prior to the test in order to decrease the possibility of a false negative study that can be observed with long-term ACE inhibition. The blood pressure should be frequently monitored, and the patient should void immediately prior to the injection of the radiopharmaceutical.<sup>23,24,26,28</sup>

**Adverse Effects.** After captopril, the patient rarely becomes symptomatically hypotensive. When this does occur, the patient usually responds quickly to being placed in the recumbent position. Volume expansion with saline may be used if the patient continues to be symptomatic.<sup>29</sup>

## Enalaprilat

**Mechanism of Action.** Refer to the mechanism of action for captopril.

**Methodology.** Some centers have used intravenous enalaprilat because it has a more rapid onset of action. Sfakianakis et al. has used two different protocols: (1) sequentially performing BSL and ACEI studies; (2) conducting the test without interrupting ACEI treatment. This latter method is conducted as a single phase study; however, if the study is abnormal, a BSL study is performed later without the ACEI on board. Any other antihypertensive drugs and those with a potential for hypotensive effects are withheld overnight.<sup>21,23,27</sup>

With the sequential method, a BSL scintigraphic study



is performed after the administration of 1 mCi of  $^{99m}\text{Tc}$ -mercatide. Furosemide may be injected at both BSL and after administration of ACEI; however Sfakianakis et al. recommends relying on good hydration alone for the BSL study rather than injecting a diuretic. An image is acquired after the patient voids. At this point, blood pressure monitoring begins at 5 minute intervals. Intravenous enalaprilat at a dose of 0.04 mg/kg (maximum dose of 2.5 mg) is infused over 5 minutes. At 10 minutes after the initiation of the enalaprilat infusion, 9 mCi of  $^{99m}\text{Tc}$ -mercatide and 40 mg of furosemide are administered intravenously for the post-ACEI scintigraphy. (In renal insufficiency 80 mg of furosemide may be given.) Images are acquired for 22 minutes following radiopharmaceuticals administration. Interpretation follows the same guidelines as for captopril studies.<sup>21</sup>

**Contraindications.** This drug is contraindicated in patients who are hypersensitive to any component of this product, as well as in patients exhibiting a history of angioedema related to prior ACEI treatment. When undergoing a BSL and an ACEI study, the patient should initially be off ACEI therapy for a minimum of 48 hours.<sup>21,30</sup>

**Precautions.** A complication that may develop with ACEI inhibition is severe hypotension, and it characteristically occurs in patients with intravascular volume depletion. Prior to the study, the patient should be hydrated orally with 10 mL/kg of water. Also, an IV infusion of 500 mL of normal saline at a rate of 4 mL/min should be started at the beginning of the test and continued throughout the study. After the postvoid image is acquired for the BSL part of the study, the patient's blood pressure should be monitored every 5 minutes. The saline is infused until the blood pressure stabilizes or a rebound is demonstrated. The patient should empty his/her bladder at the beginning of each part of the scintigraphy procedure since a false positive study may result when starting with a full bladder. In patients with prostatic hypertrophy or in renal transplant patients, a urinary catheter may be required.<sup>21,26</sup>

**Adverse Effects.** Fast saline infusion is recommended to prevent complications if there is more than a 30% drop in blood pressure or anuria develops in susceptible patients. Some patients may need up to 1 liter or more of saline. In some cases it may be necessary to administer vasoconstrictors.<sup>21</sup>

## HEPATOBIILIARY IMAGING

Adjunctive pharmaceuticals are utilized to enhance the diagnostic sensitivity of  $^{99m}\text{Tc}$ -labeled iminodiacetic acid (IDA) derivatives used in hepatobiliary scintigraphy. Sincalide and morphine are often helpful in the

assessment of acute cholecystitis while phenobarbital is used in pediatric patients to aid in differentiating neonatal hepatitis from biliary atresia.

### Sincalide

**Mechanism of Action.** Cholecystokinin, whether produced endogenously or synthetically, causes contraction of the gallbladder, relaxation of the sphincter of Oddi, augmentation of pyloric sphincter tone, and enhancement of the motility of the small and large bowel. The physiologic action of cholecystokinin is confined to the C-terminal portion, and sincalide is a synthetically-prepared C-terminal octapeptide of this 33-amino-acid polypeptide hormone.<sup>32-39</sup>

**Methodology.** Patients should fast a minimum of 4 hours prior to the administration of  $^{99m}\text{Tc}$ -IDA; however, patients fasting longer than 48 hours or undergoing intravenous total parenteral nutrition (TPN) are at risk for a false-positive hepatobiliary study, meaning nonvisualization of gallbladder despite patency of the cystic duct. Nonvisualization of the gallbladder is due to increased intraluminal gallbladder pressure developing due to biliary stasis or sludge, and this reduces the flow of  $^{99m}\text{Tc}$ -IDA into the gallbladder. Cholecystokinin cholescintigraphy is a means of evaluating patients suspected of having acute cholecystitis who have fasted for longer than 48 hours and/or who are undergoing TPN. Cholecystokinin or sincalide produces gallbladder contraction which ejects and cleans the gallbladder of its sludge resulting in elimination of increased intraluminal pressure within the gallbladder. The radiopharmaceutical is then free to flow into the gallbladder if the cystic duct is patent. Sincalide, in a dose of 0.02  $\mu\text{g}/\text{kg}$  of body weight, is intravenously administered approximately 30 minutes prior to the radiopharmaceutical. The infusion is administered over a 2-3 minute time period.<sup>33,35,40,41,42,43</sup>

Gallbladder ejection fraction is used in the diagnosis of chronic acalculous biliary disease. A procedure described by Fink-Bennett requires that the patient fast after midnight prior to the injection of  $^{99m}\text{Tc}$ -IDA. Hepatobiliary images are acquired every 10 minutes for 1 hour or until the gallbladder is maximally filled (little or no radioactivity remaining within the major hepatic biliary radicles). At this point sincalide is administered over a 3-minute time period. The sincalide can be administered manually (diluted with normal saline) or by an infusion pump. It is important that sincalide not be given as a bolus injection since this could cause spasm of the neck of the gallbladder resulting in a falsely reduced maximal gallbladder ejection fraction response to sincalide. After the sincalide infusion, hepatobiliary images are acquired every 5 minutes for a total of 4 images. The gallbladder ejection fraction is then determined by comparing pre-sincalide images (counts)

to post-sincalide images (counts).<sup>42</sup>

**Contraindications.** The package insert states that sincalide is contraindicated in patients hypersensitive to this agent and in patients with intestinal obstruction.<sup>32</sup>

**Precautions/Warnings.** Sincalide should not be administered after morphine sulfate since morphine sulfate can counteract the effect of sincalide. Morphine sulfate has a relatively long and variable serum half-life ranging from 3 to 6 hours. There is a possibility in patients having small gallbladder stones that stimulation of gallbladder contraction could cause evacuation of the stones from the gallbladder, resulting in the stones lodging in the cystic duct or in the common bile duct.<sup>32,44</sup>

**Adverse Effects.** Usually the adverse effects to sincalide are mild and of short duration. The most frequently reported adverse reactions are abdominal discomfort or pain and nausea. With rapid intravenous injection of sincalide in a dose of 0.04 µg/kg body weight, there is transient abdominal cramping. Usually, these effects are manifestations of the physiologic actions of the drug, such as delayed gastric emptying and/or increased intestinal motility. These adverse effects are not to be interpreted as necessarily indicating an abnormality of the biliary tract unless there is other clinical or diagnostic evidence of disease. Other reported adverse reactions include dizziness, vomiting, flushing, sweating, rash, hypotension, hypertension, shortness of breath, urge to defecate, headache, diarrhea, sneezing, and numbness. The package insert states that the intestinal side effects can be reduced by administering the intravenous solution, at a dose of 0.12 µg/kg in 100 mL 0.9% Sodium Chloride Injection USP, at a rate of 2 mL per minute.<sup>32,34</sup>

## Morphine

**Mechanism of Action.** Morphine constricts the sphincter of Oddi (increasing the pressure within the sphincter) and increases the intraluminal common bile duct pressure after the intravenous administration of as little as 0.04 mg/kg. The elevated pressure in the lumen of the common bile duct is great enough to overcome the increased resistance to bile flow within a functionally-obstructed, sludge-filled gallbladder and diverts <sup>99m</sup>Tc-IDA into gallbladder if there is patency of the cystic duct.<sup>35,42</sup>

**Methodology.** If there is nonvisualization of the gallbladder up to 60 minutes post radiopharmaceutical administration, provided there is radioactivity in the small bowel, morphine-augmented cholescintigraphy can be performed. When this occurs, morphine is slowly administered intravenously over 1 to 3 minutes. The dose is 0.04 mg/kg of morphine sulfate diluted in 10 mL of normal saline. A positive diagnosis of abnormal gallbladder function can be suggested when the

gallbladder is not visualized by 60 minutes but it is seen with morphine augmentation after 60 minutes. This dose of morphine sulfate is safe and well tolerated by the patient.<sup>35,42</sup>

**Contraindications.** The contraindications to the use of morphine are a known allergy to it or codeine, a history of drug abuse, and the presence of pancreatitis. It is also contraindicated in patients in whom the physician does not want morphine to obscure the patient's clinical symptoms.<sup>33,43,45</sup>

**Precautions/Warnings.** When performing morphine-augmented cholescintigraphy in the detection of acute cholecystitis, care must be exercised because both false-negative and false-positive studies can occur. False-negative morphine-augmented cholescintigraphy may occur, particularly in patients having acute acalculous cholecystitis, unless the increased pressure in the edematous cystic duct and the gallbladder are great enough to prevent the radiopharmaceutical from entering it after morphine administration. A false-positive study may occur if the cystic duct is patent but there is not a sufficient amount of <sup>99m</sup>Tc-IDA present within the intrahepatic biliary system to permit gallbladder visualization after morphine administration. If this is suspected, the patient should be re-injected with <sup>99m</sup>Tc-IDA and then augmentation with morphine can be performed approximately 20 to 30 minutes post radiopharmaceutical administration.<sup>42</sup>

Morphine-augmentation should probably not be performed in patients demonstrating a "dilated cystic duct sign." The elevated pressure created within the common bile duct due to the contraction of the sphincter of Oddi can and has resulted in the production of enough intrabiliary ductal pressure to dislodge a cystic duct stone.<sup>42</sup>

**Adverse Effects.** When morphine is used as described above, no significant complications were reported. Also, exacerbation of gallbladder pain was not associated with morphine when using this low dose. In the event that morphine's effects need to be reversed, naloxone can be intravenously administered.<sup>33,37, 43,46,47</sup>

## Phenobarbital

**Mechanism of Action.** Phenobarbital used in conjunction with <sup>99m</sup>Tc-IDA imaging improves the accuracy of cholescintigraphy in differentiating neonatal hepatitis from biliary atresia. Phenobarbital is a potent inducer of hepatic microsomal enzymes, and it increases bilirubin conjugation and excretion. It also enhances the uptake and excretion of bile components, particularly those utilizing the hepatic transport system for organic anions. The IDA-radiolabeled substrates are in this class of organic anions. By augmenting <sup>99m</sup>Tc-IDA uptake and excretion, the compromised liver is better demonstrated,

its function more readily evaluated, and the underlying etiology of neonatal jaundice more accurately diagnosed.<sup>42,48,49</sup>

**Methodology.** In one protocol for this study, the patient is premedicated orally with 5 mg/kg of phenobarbital in 2 divided doses for at least 5 days prior to the radiopharmaceutical administration. Another protocol has a phenobarbital dosing schedule of 1 - 2 mg/kg orally every day for 2 weeks to promote biliary excretion. The diagnosis of biliary atresia is excluded if the hepatobiliary study shows passage of the radiopharmaceutical into the bowel. If <sup>99m</sup>Tc-IDA is not observed in the small bowel, the distinction between biliary atresia and severe hepatocellular disease cannot be made with certainty. Persistent nonvisualization of the bowel occurs when the liver cells are severely damaged and are not able to extract and excrete the radiopharmaceutical. Other types of diagnostic procedures may be necessary to determine the underlying cause of the persistent icterus and conjugated hyperbilirubinemia.<sup>42,48,51</sup>

**Contraindications.** Phenobarbital is contraindicated in patients having a hypersensitivity to barbiturates, patients with a history of manifest or latent porphyria, and in patients having respiratory disease in which dyspnea or obstruction is evident.<sup>50</sup>

**Precautions.** In some patients, especially pediatric patients, barbiturates repeatedly produce excitement instead of depression. It has been noted that premature infants are particularly susceptible to barbiturates' depressant effects.<sup>50</sup>

**Adverse Effects.** Barbiturates have been known to cause irritability and hyperactivity in children. The package insert reports on data collected on thousands of hospitalized patients receiving barbiturates, and some of the reactions noted are somnolence, agitation, CNS depression, hypoventilation, apnea, bradycardia, hypotension, nausea, vomiting, constipation, hypersensitivity reactions, and fever.<sup>50</sup>

## MECKEL'S DIVERTICULUM IMAGING

Meckel's diverticulum is the most common congenital anomaly of the gastrointestinal tract affecting 1% to 3% of the population. This anomaly results from the failure of closure of the omphalomesenteric duct of the embryo. The umbilical cord connects the omphalomesenteric duct to the primitive foregut. These diverticula are found on the antimesenteric side of the terminal ileum. Gastric mucosa can be found in 10% to 30% of all cases, in about 60% of symptomatic patients, and in 98% of those with bleeding. Just as normal gastric mucosa concentrates <sup>99m</sup>Tc-pertechnetate so does the ectopic gastric mucosa of Meckel's diverticula. Pharmacologic

intervention has been used in combination with <sup>99m</sup>Tc-pertechnetate to improve the detection of Meckel's diverticula. The three agents which will be covered in this section are cimetidine, pentagastrin, and glucagon.<sup>53,54</sup>

### Cimetidine

**Mechanism of Action.** Cimetidine is a histamine H<sub>2</sub>-receptor antagonist that competitively inhibits histamine's action at the histamine H<sub>2</sub> receptors of the parietal cells. It has been shown that it causes an inhibition of both daytime and nocturnal basal gastric acid secretion. Also, it inhibits the gastric acid secretion stimulated by food, histamine, caffeine, pentagastrin, insulin, and sham feeding. Cimetidine causes a reduction in the volume of secreted gastric juice and pepsin. This pharmacologic agent is used as a means of improving the detection of Meckel's diverticulum by blocking the secretion of pertechnetate from gastric mucosa, thus improving the lesion to background ratio.<sup>52-55</sup>

**Methodology.** Cimetidine may be administered orally or parenterally. In adults, the oral dose is 300 mg 4 times a day for 48 hours prior to the study. For intravenous administration, the dose is 300 mg diluted in 100 mL of D<sub>5</sub>W. The intravenous dose is administered over 20 minutes; imaging is started 1 hour later. The oral dose for pediatric patients is 20 mg/kg/day for 2 days before the study.<sup>53,54,56</sup>

**Contraindications.** Cimetidine is contraindicated in patients who have a hypersensitivity to this agent.<sup>52</sup>

**Precautions.** Apparently through an effect on certain microsomal enzyme systems, cimetidine has been reported to decrease the hepatic metabolism of warfarin-type anticoagulants, phenytoin, propranolol, nifedipine, chlordiazepoxide, diazepam, certain tricyclic antidepressants, lidocaine, theophylline and metronidazole. Thus, there is a delay in the elimination and an increase in the blood levels of these pharmaceuticals.<sup>52</sup>

**Adverse Effects.** Some of the adverse effects reported in the package insert are diarrhea (usually mild), reversible confusional states, and hypersensitivity reactions. When used in the dosage for this study, cimetidine has been reported to be without significant risks or side effects.<sup>52,54,57</sup>

### Pentagastrin

**Mechanism of Action.** Pentagastrin is a synthetic polypeptide containing the active N-terminal 5-amino acid residue of gastrin. Gastrin is a natural hormone, produced by the gastric mucosa lining the antrum; and it stimulates gastric mucosal blood flow. Pentagastrin, likewise, stimulates blood flow in the gastric mucosa. Pentagastrin is a potent stimulator of gastric acid

secretion and increases the levels of pepsin and intrinsic factor. It has been shown that gastric secretion of pertechnetate correlates more closely with gastric secretion volume as opposed to acid output.<sup>53</sup>

Sfakianankis et al. studied the effect of gastrointestinal hormones on pertechnetate imaging of ectopic gastric mucosa in experimental Meckel's diverticulum by using dogs implanted with vascularized patches of gastric wall onto the distal ileum. They found that pentagastrin accelerated the accumulation of the radiopharmaceutical but the end result was a decrease in the target-to-background ratio. When pentagastrin administration was used in combination with glucagon, there was an enhancement of the target-to-background ratio.<sup>53,58</sup>

**Methodology.** Pentagastrin is administered subcutaneously at a dose of 6 µg/kg 5 to 15 minutes prior to the injection of <sup>99m</sup>Tc-pertechnetate.<sup>54-56</sup>

**Contraindications.** Hypersensitivity or idiosyncrasy to pentagastrin is considered a contraindication to the use of this pharmaceutical.<sup>59</sup>

**Precautions/Warnings.** Pentagastrin should not be used in combination with cimetidine because cimetidine antagonizes the stimulation of pertechnetate uptake by pentagastrin. Pentagastrin has the potential of causing re-bleeding since it increases acid secretion.<sup>53</sup>

Pentagastrin not only stimulates the uptake and secretion of pertechnetate in the Meckel's diverticulum but also in the stomach. The peak pertechnetate activity, which could be obtained, is decreased due to the secretion from the ectopic gastric mucosa into the ileum. It is also a potent stimulator of gastrointestinal motility by a direct effect on smooth muscle; thus, peristalsis rapidly moves pertechnetate away from the ectopic mucosa site. This, in combination with dilution in the increased volume of gastric and intestinal juices caused by pentagastrin, further reduces the radiopharmaceutical activity at the ectopic site. Also, the Meckel's site can be obscured due to the gastric pertechnetate secreted by the stomach moving distally via the enhanced peristalsis.<sup>53,56</sup>

**Adverse Effects.** Nausea, vomiting, and tachycardia can be caused by the administration of pentagastrin.<sup>53</sup>

## Glucagon

**Mechanism of Action.** Glucagon is a single-chain polypeptide consisting of 29 amino acid residues, and parenteral administration produces relaxation of the smooth muscle of the stomach, duodenum, small bowel, and colon. The stomach is the least sensitive organ to glucagon's action, and the duodenum is the most sensitive. It also reduces gastric and pancreatic secretions. Glucagon's antiperistaltic effect has been used to prevent washout of <sup>99m</sup>Tc-pertechnetate from the stomach and from Meckel's diverticulum.<sup>53,54,60</sup>

It has been used with pentagastrin in order to enhance

the effects of the latter. Glucagon, by decreasing peristalsis, permits activity secreted by the Meckel's diverticula in response to pentagastrin to continue to accumulate at the abnormal site. Glucagon decreases background activity by inhibiting pertechnetate secreted by the stomach from moving distally.<sup>53,54,56,58</sup>

**Methodology.** Different dosing protocols exist for the administration of glucagon. One protocol stated that the drug is intravenously administered in a dose of 50 µg/kg 10 minutes after the beginning of the study while another one called for glucagon (50 µg/kg) to be intravenously administered at 1 minute after the injection of pertechnetate.<sup>56,58</sup>

**Contraindications.** The package insert states that glucagon is contraindicated in patients who have a hypersensitivity to the drug and in patients having pheochromocytoma.<sup>60</sup>

**Precautions/Warnings.** The package insert recommends that glucagon be administered cautiously to patients having a history suggestive of insulinoma and/or pheochromocytoma. Also, it states that the effectiveness of this pharmaceutical as a diagnostic aid has not been established in pediatric patients.<sup>60</sup>

**Adverse Effects.** Occasional nausea and vomiting, which may occur with hypoglycemia, have been reported as adverse reactions. Also generalized allergic reactions have been reported in patients receiving parenterally administered glucagon.<sup>60</sup>

## CENTRAL NERVOUS SYSTEM IMAGING

Acetazolamide is used as an adjunct in brain perfusion SPECT and PET to evaluate cerebrovascular hemodynamic reserve. Acetazolamide increases cerebral blood flow approximately 30% to 40% over baseline in normal subjects or patients. Ischemic areas have decreased reserve and thus have a lower response to acetazolamide as compared to normal areas. Demonstration of heterogeneity in radiopharmaceutical uptake between affected and unaffected regions of the brain can be used to identify cerebrovascular disease that is at risk of infarcting.<sup>61-64</sup>

### Acetazolamide

**Mechanism of Action** Acetazolamide (ACZ) is a potent carbonic anhydrase inhibitor, and it is a nonbacteriostatic sulfonamide. Acetazolamide's mechanism of action responsible for cerebral vasodilatation is not fully understood. One proposed mechanism is that there is a temporary increase in CO<sub>2</sub> tension in the brain arterioles from the altered enzyme metabolism controlling pO<sub>2</sub>. Others postulate a direct, if unknown, effect on the brain arterioles.<sup>61,65</sup>

**Methodology.** Different protocols exist for the use of

ACZ in combination with radiopharmaceuticals for brain imaging. Burt et al. recommends that if the rest study (without ACZ) is conducted within 24 to 36 hours of the ACZ study, there should be a 1 minute acquisition of lateral images of the head for background correction. Datz presents a method which calls for 1 gram of ACZ to be administered IV over 2 minutes with  $^{99m}\text{Tc}$ -exametazime (HMPAO) administered 25 minutes later and cerebral SPECT imaging conducted 15 to 25 minutes after injection. Either before or after the pharmacologic examination, a rest study is acquired for differentiation of ischemia from infarct. Asenbaum et al. describes a protocol in which two  $^{99m}\text{Tc}$ -HMPAO SPECT studies were acquired with one week separation between the two. Patients were instructed to close their eyes and relax prior to the administration of  $^{99m}\text{Tc}$ -HMPAO. Imaging started 10 minutes later with 60 projections acquired within 30 minutes. The first study is without ACZ, and one week later the second study is performed with ACZ if no new neurological event has occurred. In the second SPECT study, 1 gram of ACZ is intravenously administered approximately 13 to 15 minutes prior to the injection of  $^{99m}\text{Tc}$ -HMPAO. Mullan described a protocol using  $^{99m}\text{Tc}$ -bicisate (ECD) and 1 gram of ACZ. The ACZ is intravenously administered over a 5-minute time period with the patient in the supine position.  $^{99m}\text{Tc}$ -ECD is administered 20 minutes after the ACZ injection, and imaging is started 10 to 15 minutes later. The rest study (without ACZ) is on a different day using the same dose of  $^{99m}\text{Tc}$ -ECD. As with the ACZ study, imaging is started 10 to 15 minutes after the radiopharmaceutical injection. For both the ACZ and rest studies, the same gamma camera should be used.<sup>63,64,66,67</sup>

**Contraindications.** The package insert states that acetazolamide is contraindicated in patients having depressed serum levels of sodium and/or potassium, in cases of significant kidney and liver disease or dysfunction, in suprarenal gland failure, and in hyperchloremic acidosis. This drug is also contraindicated in patients having cirrhosis since there is a risk of developing hepatic encephalopathy.<sup>65</sup>

**Precautions/Warnings.** In patients with acute strokes, vasodilators should be used with caution. It has been reported that when used as therapeutic agents in patients with acute strokes, there has been no effect or deterioration in the clinical status of the patient. The package insert states that fatalities, though rare, have occurred as a result of severe reactions to sulfonamides. Also, caution is advised in patients who are receiving concomitant high-dose aspirin and ACZ since anorexia, tachypnea, lethargy, coma, and death have been reported.<sup>65,68</sup>

**Adverse Effects.** The following side effects to ACZ have been reported in some patients as slight discomfort:

lightheadedness, paresthesias in the distal limbs and around the mouth, and a short-acting diuretic effect. Matsuda et al. reported that mild headache occurred in 4 of 19 patients after ACZ administration.<sup>65,68,69</sup>

## SCHILLING TEST

The Schilling test is conducted in patients having a vitamin B<sub>12</sub> (cyanocobalamin) deficiency, and it involves measurement of urinary excretion of radioactive B<sub>12</sub>. In this procedure, the patient is administered a radioactive B<sub>12</sub> capsule by mouth, and the urine is collected to determine the amount of radioactive B<sub>12</sub> absorbed via ileal intrinsic factor receptors. Nonradioactive cyanocobalamin is parenterally administered for the purpose of blocking all potential tissue sites of vitamin B<sub>12</sub> binding. This nonradioactive dose of vitamin B<sub>12</sub> serves as the flushing dose. The radioactive cyanocobalamin, absorbed through the GI tract, will be flushed out via the urinary system.<sup>70,71</sup>

### Cyanocobalamin

**Mechanism of Action.** After intramuscular or subcutaneous injection, nonradioactive cyanocobalamin is rapidly absorbed; within 1 hour post intramuscular injection, peak plasma levels are reached. This parenterally administered vitamin B<sub>12</sub> saturates the binding proteins which transport cyanocobalamin to the various tissues. Thus, the absorbed radioactive B<sub>12</sub> will not be bound by the saturated transport proteins and will undergo urinary excretion.<sup>70,72</sup>

**Methodology.** There are different variations of the test procedure. One procedure calls for the patient to receive the oral dose of radioactive B<sub>12</sub> at the same time the flushing dose of nonradioactive B<sub>12</sub> is administered. Another method requires that the flushing dose be administered 2 hours after the radioactive cyanocobalamin. The flushing dose is 1000 µg of nonradioactive B<sub>12</sub>, and it is either administered intramuscularly or subcutaneously.<sup>70,71,72</sup>

**Contraindications.** Cyanocobalamin is contraindicated in patients who are sensitive to vitamin B<sub>12</sub> or cobalt.<sup>70</sup>

**Precautions/Warnings.** Anaphylactic shock and death have been documented after parenteral administration of vitamin B<sub>12</sub>. In patients suspected of being sensitive to this pharmaceutical, it is recommended to administer an intradermal test dose prior to cyanocobalamin being administered. When hematocrit, reticulocyte count, vitamin B<sub>12</sub>, folate, and/or iron levels are ordered, they should be obtained prior to the injection of cyanocobalamin.<sup>70</sup>

**Adverse Effects.** As previously stated, anaphylactic shock and death have been reported as well as pulmonary

edema, congestive heart failure, peripheral vascular thrombosis, polycythemia vera, mild transient diarrhea, itching, transitory exanthema, and the feeling of swelling of the entire body.<sup>70,73</sup>

## CASE STUDIES

*Adenosine Case Study.* A 48-year-old male, with an abnormal ECG and hypercholesterolemia (252 mg/dL), was referred to nuclear medicine for a stress/rest myocardial perfusion study. The patient denied having any symptoms, and he was on no medications. He is 5'11" and weighs 245 pounds, and he does not use tobacco products. His past medical history is negative for myocardial infarction, hypertension, and diabetes mellitus. He does not have a family history of coronary artery disease.

The physician was concerned that the patient would not achieve maximum exercise, and therefore, chose to use pharmacologic stress rather than exercise. For the stress study the patient was administered 88.2 mg of adenosine and 4.4 mCi of <sup>201</sup>Tl. With the pharmacologic stress study, the patient's heart rate increased from 76 to 106 beats per minute, and his blood pressure decreased from 130/86 to 118/80. Upon receiving the adenosine, the patient did complain of a tingling in the head and a flushing sensation; but the symptoms subsided after termination of the adenosine infusion. For the rest (redistribution) study, an additional 1.1 mCi of <sup>201</sup>Tl was administered.

Please refer to Figure 1. Tomographic (SPECT) images demonstrated a moderate to severe reversible perfusion decrease throughout the mid and basilar thirds of the inferior wall of the left ventricle. In the mid third of the inferior wall, small regions of incomplete reversibility were demonstrated, but this appeared to involve the external surface (rather than the endocardial region) of the heart, which implied that artifact is more likely than scar. Otherwise, the left ventricle showed normal perfusion. The nuclear medicine physician's impression was that this patient most likely had right coronary artery disease with myocardium at risk from decreased coronary flow reserve in the mid and basilar regions of the inferior wall of the left ventricle.

To determine the degree of stenosis in the right coronary artery, the patient could undergo cardiac catheterization and angiography.

*Cholescintigraphy Case Study.* A 54-year-old female was referred to nuclear medicine for a hepatobiliary study with ejection fraction determination. She presented with a three to four month history of right upper quadrant pain, but no nausea. Her past history was negative for cholecystectomy and cholelithiasis. The pain did not increase with the ingestion of food. Her oral medications included mefenamic acid 400 mg twice a day, potassium

chloride 20 mEq 3 times a day, conjugated estrogens 1.25 mg daily, medroxyprogesterone acetate 5 mg daily 7 days out of the month, fluoxetine HCl 20 mg daily, amitriptyline HCl 50 mg daily, labetalol HCl 20 mg twice daily, iron and liver combination (iron, liver fraction 1, vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, and B<sub>12</sub>) 3 tsp. daily, propoxyphene napsylate and acetaminophen tablet as needed (usually 1 per day). She also receives 1000 mcg of vitamin B<sub>12</sub> IM twice a week. She was NPO after midnight prior to the study. For the hepatobiliary study, she was administered approximately 1.5 µg of sincalide (diluted in normal saline) over 30 minutes and 5 mCi of <sup>99m</sup>Tc-mebrofenin. The sincalide was administered 60 minutes after the radiopharmaceutical administration. The study revealed a patent biliary system with a normal ejection fraction of the gallbladder.

Please refer to figure 2 for the study images and graph. The images demonstrate normal visualization of the liver, gallbladder, common bile duct and small bowel; therefore, the entire biliary system is patent. Following intravenous administration of sincalide, the patient's highest ejection fraction was 80% which is within normal limits. An abnormal response to sincalide is a maximal gallbladder ejection fraction of less than 35%. Since this study is normal and does not identify the source of patient's complaint, further evaluation of the patient could include an upper GI study and/or an ultrasound study.

*Renal Case Study.* A 77-year-old female was referred to nuclear medicine for a renal scan with flow to rule out renal obstruction. Her history included carcinoma of the colon with urosepsis and a serum creatinine of 3.2 mg/dL. An ultrasound 5 days earlier demonstrated mild to moderate bilateral hydronephrosis with left ureteral dilation. For the study she received 40 mg of furosemide by slow I.V. injection 30 minutes prior to the injection of 9.6 mCi of <sup>99m</sup>Tc-meritide.

Please refer to Figure 3a, 3b. The study demonstrated renal dysfunction, and the findings were consistent with either left renal artery stenosis or more severe parenchymal disease in the left kidney. The study did not suggest obstructive uropathy.

With total ureteral obstruction greater than 24 hours in duration, a nonfunctioning kidney may result. In a high-grade but lesser obstruction, the study will reveal poor blood flow, decreased function, and no evidence of radiopharmaceutical entering the collecting system. In a lower-grade obstruction, the kidney has good blood flow and function; the radiopharmaceutical empties into a hydronephrotic collecting system. Although, there is no pelvic or calyceal clearance occurring during the 30-minute duration of the study. During this time period, a differentiation often cannot be made between nonobstructed and obstructed hydronephrosis. Delayed

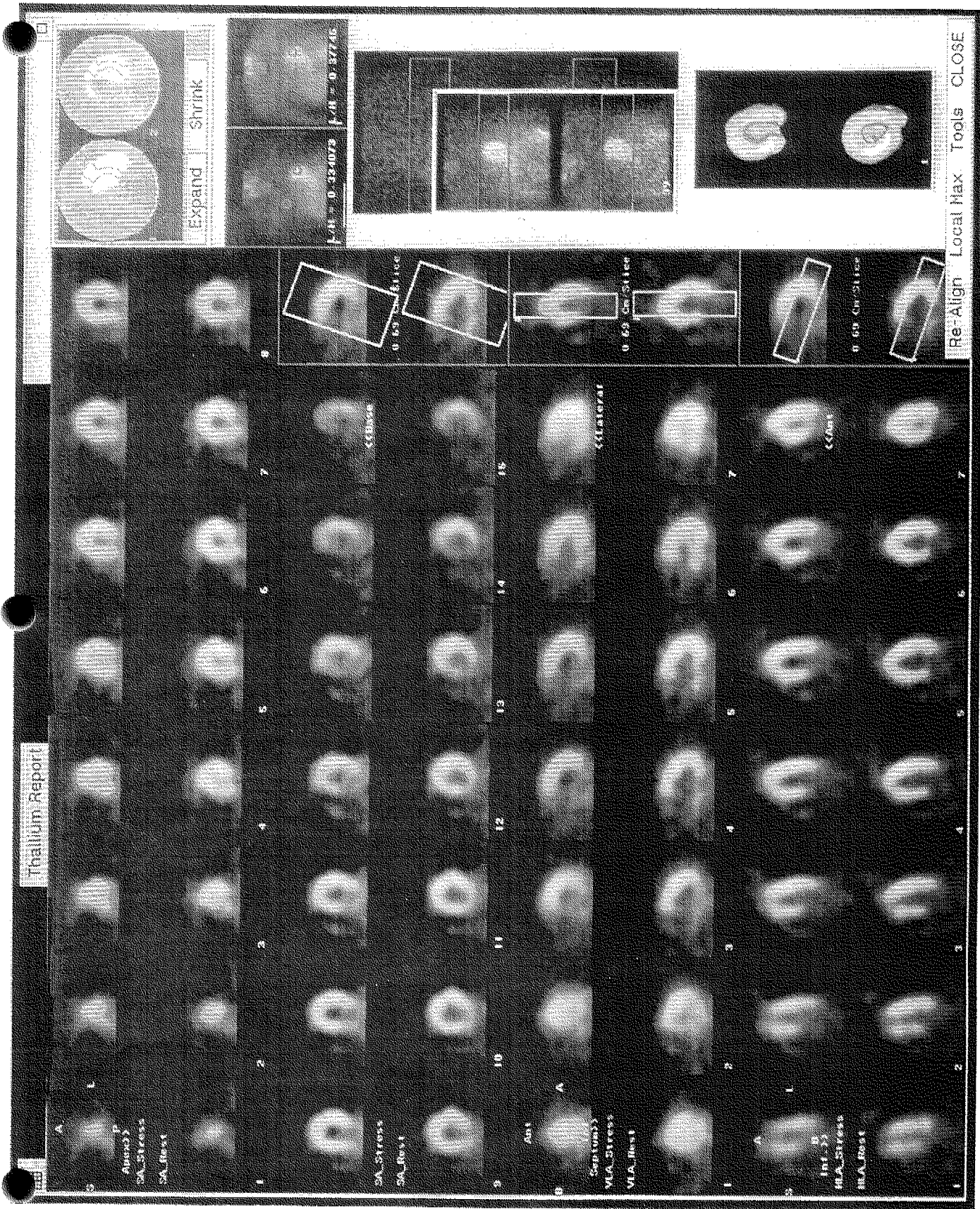
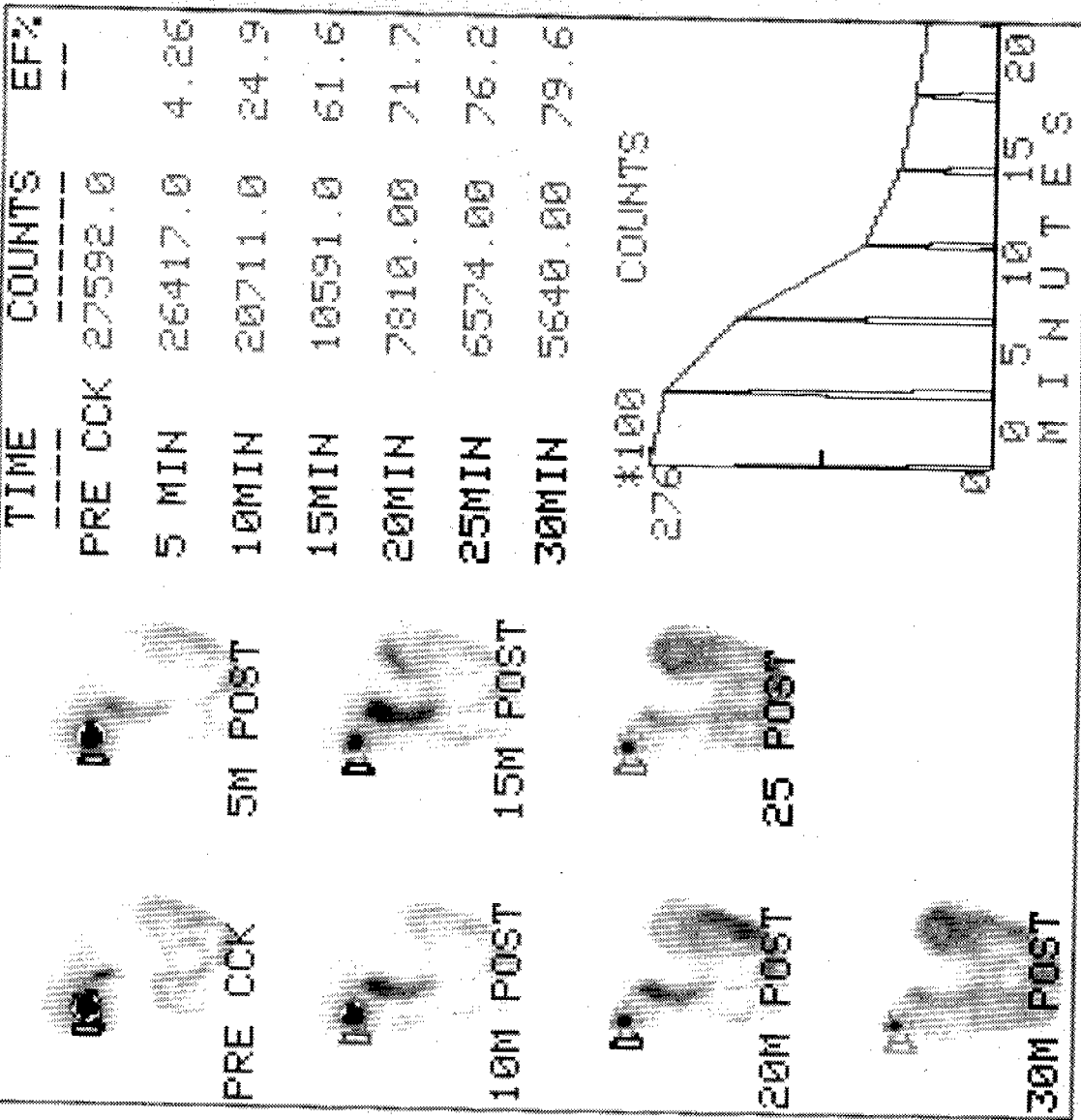


Figure 1. Abnormal cardiac study using <sup>201</sup>Tl and adenosine as demonstrated by moderate to severe reversible perfusion decrease throughout the mid and basal thirds of the inferior wall of the left ventricle.

HIDA



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Figure 2. Hepatobiliary study using <sup>99m</sup>Tc-mebrofenin and sincalide (CCK) demonstrates normal visualization of liver, gallbladder, common bile duct, and small intestine. The graph represents a normal ejection fraction of the gallbladder.



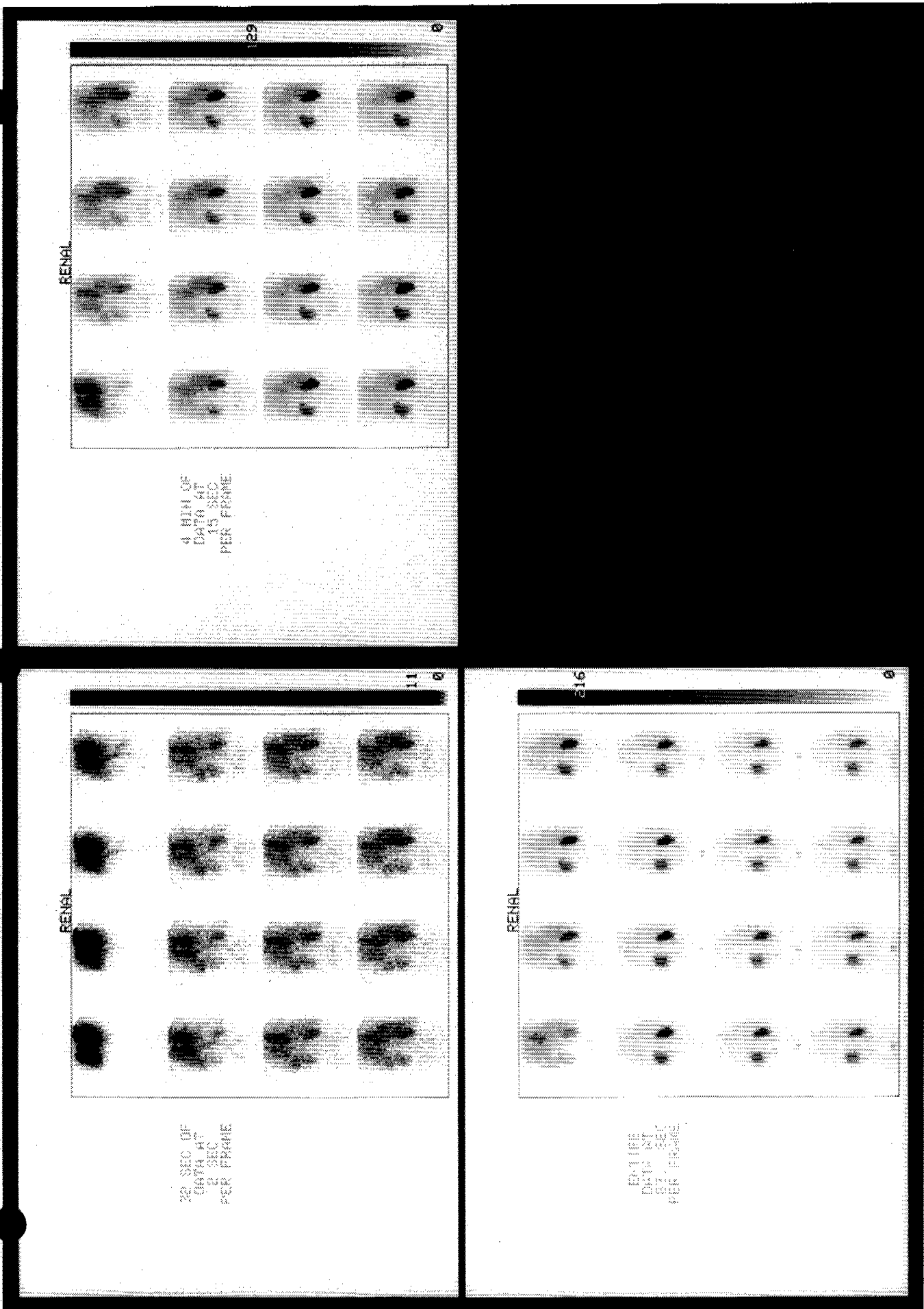
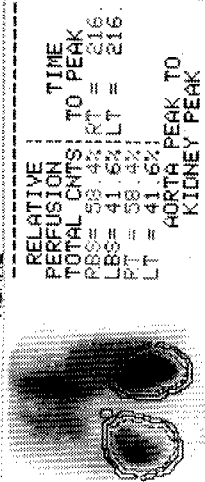


Figure 3a. Serial renal images obtained with <sup>99m</sup>Tc-meritide and furosemide reveals asymmetric perfusion in the kidneys with delayed visualization on the left.

FLOW INITIAL FUNCTION REPORT

RENAL



AORTA WIDTH AT 59.4% OF MAX 12.0 S

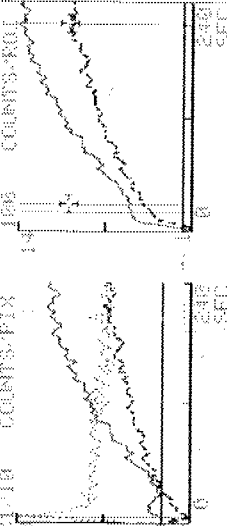
RELATIVE BLOOD FLOW RT K= 66.0% LT K= 34.0%

AORTA PEAK TO INITIAL FUNCTION RT K= 23.26 LT K= 14.78

#PIXELS/ROI AORTA 24.00 RT K= 459.0 LT K= 571.0 RT/LT .8214

AORTA=DOTTED RT K=SOLID LT K=DASHED

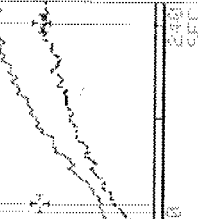
ROI NORMALIZED RIGHT, LEFT & AORTA



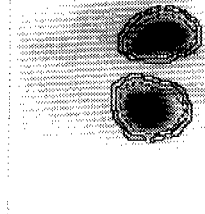
RELATIVE PERFUSSION TOTAL CNTS TO PEAK ABS= 58.4% RT = 216. LBS= 41.6% LT = 216. RT = 58.4% LT = 41.6% AORTA PEAK TO KIDNEY PEAK

RT K= 210.8 LT K= 210.8

BACKGROUND SUBTRACTED RIGHT & LEFT



WHOLE KIDNEY RENOGRAM REPORT



NON BKG SUB TIME TO FIRST PEAK RT= 4.5 M

#PIXELS/ROI RT K= 469. LT K= 571. RT/LT .821

RELATIVE RENAL FUNCT AT 1ST PEAK RT= 58.2% LT= 42.2%

% EMPTY AT END FROM KIDNEY PEAK RT= 39.9% LT= 26.3%

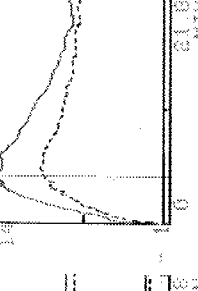
RT K=SOLID LT K=DASHED BACKGROUND

BACKGROUND SUBTRACTED TIME TO FIRST PEAK RT= 4.5 M

% EMPTY AT END FROM KIDNEY PEAK RT= 43.1% LT= 29.3%

RELATIVE RENAL FUNCT AT 1ST PEAK RT= 58.2% LT= 42.2%

% BACKGROUND SUBTRACTED RIGHT & LEFT CURVES



SELECTIVE RENOGRAM REPORT



KIDNEYS TIME TO MAX CNTS RT= 4.50 M LT= 5.25 M

RELATIVE FUNCTION ANALYSIS (INTEGRAL) RT= 59.7% LT= 40.3%

PELVIS TIME TO MAX CNTS RT= 3.20 M LT= 3.50 M

% EMPTY AT END FROM PELVIS PEAK RT= 39.5% LT= 22.3%

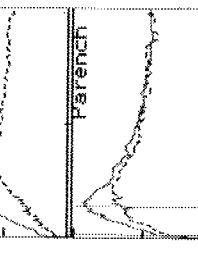
RT=> SOLID LT=> DASHED

Cortex Ratio 21min/Max RSCA= .396 LRCA= .567

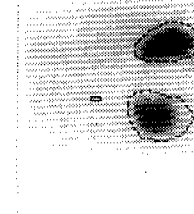
25-75% OF 1ST PEAK RELATIVE FUNCTION ANALYSIS (INTEGRAL)

KIDNEYS PARENCHYMA RT= 59.7% LT= 40.3%

PELVIS PARENCHYMA RT= 39.5% LT= 22.3%



DECONVOLUTION REPORT



DECONVOLUTION ANALYSIS

RENAL BLOOD CURVE & RENOGRAMS RT= 4.5 M LT= 5.25 M

LEFT KID RETENTION RT= 4.5 M LT= 5.25 M

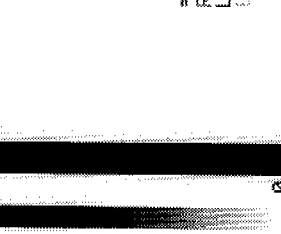


Figure 3b. Images with renograms show delayed excretion of radioactivity from both the kidneys due to renal dysfunction.

imaging obtained at approximately 4 hours can be useful since an obstructed kidney will demonstrate little change while a nonobstructed kidney will have cleared the radiopharmaceutical. However, this observation is not quantitative, delays diagnosis, and is variable. Diuretic renography study can demonstrate prompt clearance in a nonobstructed kidney and an absence of clearance in an obstructed kidney. Time-activity curves can be important for interpretation of this study since it is often not an all-or-none occurrence.<sup>23</sup>

## SUMMARY

This lesson includes some of the more common pharmaceuticals used as adjuncts in nuclear medicine; however, there are others that may also be used. Even though radiation dose is not a concern with these conventional agents, it is imperative to recognize the significance of their pharmacologic actions and accompanying adverse effects. These drugs have an important role in selected nuclear medicine studies. Their use makes the performance of some studies possible and increases the sensitivity, specificity, and diagnostic accuracy of others.

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## QUESTIONS

1. Dipyridamole's mechanism of action is based on its ability to
  - A. constrict stenosed coronary vessels.
  - B. vasodilate normal coronary vessels.
  - C. significantly increase oxygen demand.
  - D. decrease the amount of endogenous adenosine.
2. What is the recommended total dosage of dipyridamole for a patient weighing 250 pounds?
  - A. 60 mg
  - B. 65 mg
  - C. 95 mg
  - D. 142 mg
3. When pharmacologic stress testing for coronary artery disease is indicated, which of the following patients would benefit from dipyridamole testing?
  - A. those with acute bronchospastic lung disease
  - B. patients with unstable angina
  - C. those taking beta blockers
  - D. patients who have been off theophylline less than 8 hours
4. Which of the following would pose a problem with adenosine stress testing of a patient for coronary artery disease?
  - A. chronic use of pentoxifylline
  - B. last dose of theophylline 72 hours prior to the study
  - C. ingestion of a Diet Coke 6 hours prior to the study
  - D. daily dose of propranolol
5. What is the recommended adult dose of adenosine for a patient weighing 200 pounds?
  - A. 52 mg
  - B. 60 mg
  - C. 76 mg
  - D. 91 mg

6. Adverse reactions to adenosine
- usually require administration of aminophylline.
  - routinely last several hours.
  - may include chest discomfort.
  - include a high incidence of mortality.
7. Which of the following characterize dobutamine's mechanism of action as a pharmacologic stress agent?
- negative inotropic effect
  - negative chronotropic effect
  - increase in heart rate
  - decrease in systolic blood pressure
8. Patients, in whom pharmacologic stress testing is indicated, would be candidates for dobutamine testing if
- ingested coffee 8 hours prior to the study.
  - currently taking theophylline preparations.
  - last dose of oral dipyridamole was morning of study.
  - all of the above
9. Which pharmaceutical would be best to treat the side effects of dobutamine?
- esmolol
  - aminophylline
  - adenosine
  - captopril
10. Which is true concerning diuretic renography?
- Delayed excretion and retention of urine is nonspecific.
  - Diuresis has maximal effect on emptying of an obstructed kidney.
  - Renogram is normal with obstructed kidney.
  - Reservoir effect is seen in an obstructed kidney.
11. Administration of furosemide should be based on
- body weight.
  - creatinine clearance.
  - serum creatinine.
  - any of the above.
12. Furosemide should be administered
- as a bolus.
  - over less than 30 seconds.
  - over 1 to 2 minutes.
  - as a constant infusion over 30 minutes.
13. Which of the following can pose a problem with the use of furosemide in renography studies?
- good hydration
  - indwelling catheter
  - used in combination with captopril
  - none of the above
14. In renal artery stenosis, angiotensin II
- produces constriction of the efferent arterioles of the glomerulus.
  - produces constriction of the afferent arterioles of the glomerulus.
  - has no effect on glomerular filtration rate.
  - reverts back to angiotensin I.
15. When performing ACEI scintigraphy, the usual dose of captopril is
- 0.5 - 1.0 mg/kg body weight.
  - 0.57 mg/kg body weight.
  - 2.5 mg.
  - 25 or 50 mg.
16. Which of the following is true concerning enalaprilat?
- administered orally
  - slower onset of action than captopril
  - indicated with a systolic blood pressure of 130 mm Hg or less
  - patient should be off ACEI for 48 hours with baseline study
17. A complication that may occur with ACEI is
- hypertension.
  - hypotension.
  - intestinal cramping.
  - spasm of sphincter of Oddi.

18. In a Schilling study, nonradioactive cyanocobalamin
- A. serves as a flushing dose.
  - B. is administered orally.
  - C. blocks renal elimination of radioactive B<sub>12</sub>.
  - D. dose is 100 mg.
19. Sincalide's pharmacologic action includes:
- A. spasm of the sphincter of Oddi
  - B. relaxation of pyloric sphincter tone
  - C. decreased motility of small bowel
  - D. contraction of the gallbladder
20. Which is true concerning sincalide administration?
- A. administered rapidly over less than 30 seconds
  - B. dosage is 0.2 mg/kg
  - C. administered orally after radiopharmaceutical dose
  - D. useful for patients who have fasted longer than 48 hours
21. The mechanism of action of morphine sulfate is:
- A. constriction of the sphincter of Oddi
  - B. decreases intraluminal common bile duct pressure
  - C. produces spasm of cystic duct
  - D. increases flow of bile from common bile duct to small intestine
22. Which pharmaceutical is used to evaluate the possibility of biliary atresia?
- A. morphine sulfate
  - B. cimetidine
  - C. phenobarbital
  - D. pentagastrin
23. Which of the following is NOT routinely used to evaluate Meckel's diverticulum?
- A. cimetidine
  - B. phenobarbital
  - C. glucagon
  - D. pentagastrin
24. Parenteral administration of glucagon produces
- A. relaxation of smooth muscle of duodenum.
  - B. constriction of smooth muscle of stomach.
  - C. spasm of the small bowel.
  - D. an increase in gastric secretions
25. Caution should be exercised when acetazolamide is used with
- A. high doses of acetaminophen.
  - B. high doses of antihistamines.
  - C. high doses of vasoconstrictors.
  - D. high doses of aspirin.