NEW TITLE: IMAGING THE HEPATOBILIARY SYSTEM

OBJECTIVES

Upon completion of this course, you will be able to complete the tasks listed here:

- Describe the anatomy and physiology of the hepatobiliary system.
- Compare the commercially available hepatobiliary imaging agents and their mechanism of localization.
- Explain the role of interventional agents in hepatobiliary imaging.
- Recognize the indication for hepatobiliary imaging.

HEPATOBILIARY ANATOMY AND PHYSIOLOGY

The hepatobiliary system consists of the hepatocytes (or polygonal cells of the liver), bile canaliculi, interlobular bile ducts, hepatic ducts, cystic duct, gallbladder, common bile duct, sphincter of Oddi.

Bile flows through the bile canaliculi into the interlobular bile ducts which come together to create the hepatic ducts. The right and left hepatic ducts unite to make the common hepatic duct. Once the bile is in the common bile duct, it can move through a patent cystic duct into the gallbladder where it undergoes concentration and storage.

The principal hormone that causes the contraction of the gallbladder is cholecystokinin. Once the gallbladder contracts, the stored bile is ejected through the cystic duct into the common bile duct. From the common bile duct, the bile flows into the duodenum under the control of the sphincter of Oddi.

Figure 1 – Hepatobiliary system
RADIOPHARMACEUTICALS

APPROVED RADIOPHARMACEUTICALS

Hepatobiliary imaging or cholescintigraphy with $^{99m}$Tc iminodiacetic acid (IDA) analogs was introduced in the 1970s.

The first $^{99m}$Tc-IDA analog approved for hepatobiliary imaging was $^{99m}$Tc-lidofenin. Because of its high hepatic extraction, it was known by the acronym HIDA. $^{99m}$Tc-lidofenin is no longer commercially available.

The three $^{99m}$Tc-IDA radiopharmaceuticals approved by the Food and Drug Administration are $^{99m}$Tc-lidofenin, $^{99m}$Tc-disofenin, and $^{99m}$Tc-mebrofenin.

Please refer to Table 1 for the names of the commercially available $^{99m}$Tc-IDA radiopharmaceuticals.

<table>
<thead>
<tr>
<th>RADIOPHARMACEUTICAL</th>
<th>MANUFACTURER</th>
<th>BRAND NAMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>disofenin</td>
<td>Pharmalucence</td>
<td>Hepatolite®</td>
</tr>
<tr>
<td>mebrofenin</td>
<td>Bracco</td>
<td>Choletec®</td>
</tr>
<tr>
<td></td>
<td>Pharmalucence</td>
<td>-</td>
</tr>
</tbody>
</table>

*Table 1 – Manufacture package inserts*

MECHANISM OF LOCALIZATION

The IDA complex is a bifunctional chelate with $^{99m}$Tc attaching to one end of the IDA complex and the other end attaching to acetanilide (analog of lidocaine). The acetanilide provides the biologic function.²

The $^{99m}$Tc-IDA radiopharmaceuticals mimic the behavior of bilirubin by having the same uptake by hepatocytes and by using the same transport and excretion pathways.¹

When bilirubin levels are elevated above normal, the extraction of these radiopharmaceuticals by the liver is competitively decreased since the $^{99m}$Tc-IDA analogues share the same extraction site with bilirubin.³

Prompt liver uptake and a lack of renal visualization is the biological excretion pattern of $^{99m}$Tc-mebrofenin in normal subjects.⁴

In a study involving normal subjects, $^{99m}$Tc-mebrofenin cleared rapidly from the circulation after intravenous administration. At 10 minutes post injection, 17% was the mean percent injected dose still in the blood. The liver was seen by 5 minutes with the maximal uptake observed at 11 minutes after injection.⁵
Because of the speed by which $^{99m}$Tc-mebrofenin enters the bile ducts, a high count density in the ducts is obtained which ensures a clear image of them.\(^4\)

Refer to Figure 2 for the structure of mebrofenin.

By 10 to 15 minutes post-injection in individuals having normal hepatobiliary function, the hepatic duct and gallbladder were demonstrated; demonstration of intestinal activity was seen by 30 – 60 minutes in this group.

During the first 3 hours after radiopharmaceutical administration in normal subjects, 1% was the mean percent of the administered dose appearing in the urine. Renal excretion of $^{99m}$Tc-IDA radiopharmaceuticals increases when serum bilirubin levels are elevated.

The percent administered dose still in the blood of jaundiced patients at 10 minutes may be increased two times or more as compared to normal subjects. The image quality can be inferior in jaundiced patients due to the prolongation of hepatobiliary transit, resulting in delay of visualization times.\(^5\)

After intravenous injection of $^{99m}$Tc disofenin, there is rapid clearance from the circulation of normal subjects.

At 30 minutes after injection, approximately 8% of the administered activity is still in the circulation.

During the first 2 hours after administration, approximately 9% of the activity appears in the urine.

The balance of the activity undergoes hepatobiliary clearance. The maximum liver accumulation is seen by 10 minutes after injection with maximal gallbladder uptake by 30 to 40 minutes in normal, fasting subjects.

In subjects with normal hepatobiliary function, visualization of the gallbladder and intestinal activity is demonstrated by 60 minutes after administration of this radiopharmaceutical.\(^6\)
When comparing both radiopharmaceuticals for hepatic uptake in normal subjects, the uptake of *mebrofenin* and *disofenin* is reported to be 98% and 88%, respectively.¹

Mebrofenin demonstrates lower urinary excretion at high bilirubin levels than disofenin does at normal bilirubin levels.

This illustrates mebrofenin’s greater organ specificity and increased resistance to bilirubin.⁴ Thus, mebrofenin is preferred in hepatic dysfunction patients.¹

**PREPARATION OF RADIOPHARMACEUTICALS**

The preparation of $^{99m}$Tc-mebrofenin entails aseptically adding up to 100 mCi of sterile, preservative free sodium pertechnetate$^{99m}$Tc in a volume of 1 to 5 mL. If it is necessary to dilute the sodium pertechnetate$^{99m}$Tc eluate in the reconstitution process, the only approved diluent is preservative free sodium chloride Injection USP.

During reconstitution, the nitrogen atmosphere in the vial must be maintained by preventing the introduction of air. The product can be stored at room temperature and used within 18 hours of reconstitution if it passes radiochemical purity testing. During the process of preparing the kit and withdrawing doses, appropriate shielding of the radioactivity should be utilized.⁵

Radiolabeling of disofenin involves the aseptic addition of 12 to 100 mCi of sterile, preservative free sodium pertechnetate$^{99m}$Tc in a volume of 4 to 5 mL. As with the preparation of mebrofenin, the only approved diluent is preservative free sodium chloride Injection USP, and the nitrogen atmosphere must be maintained during reconstitution.

The radiolabeled product can be stored at room temperature but it must be used within 6 hours of preparation. Also, appropriate shielding must be used during the reconstitution process and withdrawing of doses.⁶

**QUALITY CONTROL**

In the determination of radiochemical quality of IDA compounds, the chromatographic system uses dual solvents as the mobile phases and instant thin-layer *chromatography* (ITLC) *glass microfiber mesh sheets* for the solid support.

The radiochemical impurities that can be present are the free $^{99m}$Tc pertechnetate species and hydrolyzed-reduced (H-R) species. To determine the per cent free $^{99m}$Tc sodium pertechnetate, the solvent system is 20% sodium chloride, and the solid support system is ITLC-SA (polysilicic acid impregnated ITLC strip).

The per cent H-R species can be determined using water as the solvent phase and ITLC-SC (silica gel-impregnated ITLC sheet) as the solid support system. The per cent radiolabeled IDA complex can be calculated by totaling the radiochemical impurities and subtracting from 100%.⁷,⁸

The minimal acceptable radiochemical purity for both IDA compounds is 90%.⁸ As with all $^{99m}$Tc radiopharmaceuticals, the sodium pertechnetate$^{99m}$Tc used in the reconstitution of the
IDA compounds must meet the requirement of $^{99}$Mo contamination being less than 0.15 µCi/mCi of $^{99m}$Tc.  

INTERVENTIONAL AGENTS

A number of pharmaceuticals are useful for augmented cholescintigraphy. The pharmacologic agents presented in this article are sincalide, morphine, and phenobarbital.

Depending upon the pharmaceutical employed, pharmacologic intervention can aid in validating the referring physician’s clinical impression of the items listed here:

- Symptomatic chronic acalculous biliary disease.
- In providing a better perpective of the pathophysiology of gallstone formation.
- In diagnosing acute cholecystitis.
- In increasing the diagnostic accuracy of differentiating neonatal hepatitis from biliary atresia.

SINCALIDE

Cholecystokinin (CCK) is an amino acid polypeptide hormone released from the mucosa of the duodenum and upper jejunum as a result of ingestion of a meal containing fat. The biologic activity can be found in the C-terminal octapeptide portion of the hormone. A synthetic peptide consisting of the terminal eight amino acids of cholecystokinin is available commercially as sincalide (CCK-8). Some of cholecystokinin’s actions include contracting and emptying the gallbladder as well as causing the sphincter of Oddi to relax.

When a patient has been fasting for greater than 24 hours, the gallbladder may be filled with viscous bile or sludge thus preventing the radiopharmaceutical from entering the gallbladder. With the administration of sincalide, the gallbladder temporarily contracts expelling the bile and allowing the radiopharmaceutical to enter.

Other indications for the infusion of sincalide include diagnosing dysfunction of the sphincter of Oddi, differentiating obstruction of the common bile duct from functional causes, ruling out acute acalculous (without stones) cholecystitis, diagnosing chronic acalculous cholecystitis, and confirming or excluding chronic calculous (stone) cholecystitis.

Both the infusion rate and the administered dose of sincalide have varied among different institutions. The administered dose has varied from 0.01 to 0.04 µg of sincalide per kilogram of body weight; however, 0.02 µg/kg is the most routinely used administered dose.

The infusion rate has varied from 1 minute to 60 minutes. When sincalide is administered over 1 to 3 minutes, studies have demonstrated unsuccessful gallbladder emptying in up to one third of normal subjects. Although when these same subjects were administered the drug over 30 to 60 minutes, good contraction of the gallbladder was achieved.

When the sincalide is diluted in 10 mL of normal saline and infused over 30 to 60 minutes, there is a decrease in the number of adverse symptoms. Since sincalide has a brief serum half-life of only 2.5 minutes, it can be administered prior to the injection of the radiopharmaceutical for gallbladder
emptying and then given again at 60 minutes post radiopharmaceutical injection for calculation of gallbladder ejection fraction. \(^1,^{12}\)

Adverse effects are common with the administration of sincalide, and their onset is usually soon after infusion; however, their duration is only a few minutes. Please see Table 2 for a list of adverse effects.\(^{12}\)

When a patient has received morphine sulfate, caution should be used in injecting this patient with sincalide. Sincalide’s effects may be counteracted due to the pharmacological effect of morphine being 4 to 6 hours.\(^1\)

Sincalide is contraindicated in patients having a known hypersensitivity to this drug or those with intestinal obstruction.\(^{12}\)

<table>
<thead>
<tr>
<th>ADVERSE EFFECTS OF SINCALIDE</th>
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<tbody>
<tr>
<td>Dizziness</td>
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<td>Flushing</td>
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<tr>
<td>Nausea</td>
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<tr>
<td>Urge to Defecate</td>
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</table>

Table 2

MORPHINE

After intravenous administration of morphine sulfate in a dose as little as 0.04 mg/kg, there is augmentation of the tone of the sphincter of Oddis as well as an increase in the intraluminal common bile duct pressure. The increase in intraluminal common bile duct pressure is sufficient to overcome the increased resistance to bile flow within a sludge filled gallbladder thus allowing the radiopharmaceutical to enter the gallbladder if the cystic duct is not obstructed.\(^9\)

When the gallbladder is not demonstrated within 40 to 60 minutes post radiopharmaceutical administration, morphine sulfate may be intravenously administered as an option to delayed cholecintigraphy. If the gallbladder is visualized after morphine sulfate administration, acute cholecystitis is excluded since acute cholecystitis is routinely associated with obstruction of the cystic duct.\(^{12}\)

Morphine sulfate in a dose of 0.04 – 0.1 mg/kg is diluted in 10 mL of normal saline and administered intravenously over 3 minutes when the gallbladder is not demonstrated up to 60 minutes but activity is observed in the small bowel.\(^9,^{11}\)

Some of the possible adverse effects are dizziness, sedation, nausea, vomiting, and sweating. Morphine is contraindicated in patients with a morphine allergy.\(^{12}\) A relative contraindication to the administration of morphine is pancreatitis.\(^{11}\)
If scintigraphic findings indicate biliary obstruction, such as delayed biliary-to-bowel passage and/or considerable radiopharmaceutical retention in the biliary ducts, morphine sulfate should not be administered. Because morphine causes a functional partial obstruction in the common duct, scintigraphy cannot distinguish between an obstruction due to a stone or stricture or the effects of morphine. Therefore, a diagnosis of biliary obstruction cannot be established once morphine is injected.

Morphine should not be injected if biliary obstruction has not been ruled out by 60 minutes post radiopharmaceutical administration. Also a false positive study may occur if insufficient radiopharmaceutical is present within the intrahepatic biliary system to allow gallbladder visualization after morphine administration in a patient with a patent cystic duct. This can be prevented by viewing the hepatobiliary study prior to morphine injection to ensure sufficient radiopharmaceutical is localized within the hepatocytes and/or biliary system.

**PHENOBARBITAL**

In conjunction with cholescintigraphy, phenobarbital is used to improve the accuracy in differentiating between biliary atresia and other causes of neonatal jaundice. As a powerful inducer of hepatic enzymes, phenobarbital augments bilirubin conjugation and excretion.

It also enhances the uptake and excretion of bile components, including the radiolabeled IDA compounds, in patients with patent bile ducts. When the radiolabeled IDA complex’s uptake and excretion is increased, there is better visualization of the compromised liver. This allows the liver’s function to be more readily assessed as well as a more accurate determination of the principal cause of neonatal jaundice.

The patient is pretreated with 5 mg/kg of phenobarbital in 2 divided doses for 5 days prior to administration of the radiopharmaceutical. It is advisable to check the serum phenobarbital level for a therapeutic level prior to initiating the hepatobiliary study. Some of the potential adverse effects are drowsiness, hyperexcitability in pediatric patients, rash, nausea, and vomiting.
IMAGING PROCEDURE

INDICATIONS

Hepatobiliary scintigraphy is useful for the evaluation of a variety of acute and chronic diseases of the biliary tract. Refer to Table 3 for a list of indications.

<table>
<thead>
<tr>
<th>CLINICAL INDICATIONS</th>
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<tbody>
<tr>
<td>Acute cholecystitis</td>
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<td>Biliary tract obstruction</td>
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<tr>
<td>Evaluation of biliary system post surgery</td>
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<tr>
<td>Evaluation of cold defects identified on 99mTc-sulfur colloid imaging</td>
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<tr>
<td>Gallbladder ejection fraction calculation</td>
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<tr>
<td>Enterogastric bile reflux</td>
</tr>
<tr>
<td>Pediatric applications: biliary atresia vs. neonatalhepatitis; identification of choledochal cysts</td>
</tr>
</tbody>
</table>

TABLE 31,12,13

PATIENT PREPARATION

Prior to initiating cholescintigraphy the patient’s medical history should be thoroughly reviewed. Information to be obtained includes the patient’s suspected diagnosis and/or the indication for the procedure, the serum bilirubin level, whether the patient has had gallbladder surgery or any other gastrointestinal surgery, pharmaceuticals that could interfere with the radiopharmaceutical transit through the biliary tract, and the time as well as the content of the patient’s last meal.1,12

For 6 to 12 hours prior to the hepatobiliary study, all morphine-related pharmaceuticals must be discontinued since they can produce a functional partial biliary obstruction that cannot be distinguished from a true obstruction. Before radiopharmaceutical injection the patient should fast for 3 to 4 hours.1,11,12 This is to prevent the gallbladder from being in a contracted state which would not allow entry of the radiopharmaceutical.1

However, the patient should not be in fasting state for more than 24 hours because this would cause the gallbladder to be most likely filled with viscous bile or sludge thus preventing entry of the radiopharmaceutical. If the patient has fasted for more than 24 hours, sincalide should be administered 30 minutes prior to the injection of the IDA complex to empty the gallbladder of the sludge thus allowing the entry of the radiopharmaceutical.9
TECHNIQUE

The $^{99m}$Tc radiolabeled IDA compound is intravenously administered in a dosage range of 1 to 8 mCi, which can be based on the serum bilirubin level.\textsuperscript{12}

Immediately after radiopharmaceutical administration, imaging of the abdomen begins with the patient in the supine position, and serial images at 5 minute intervals are obtained for 45 to 60 minutes.\textsuperscript{11,12}

The study can be stopped at one hour if both the gallbladder and duodenum are demonstrated at this time because this indicates a normal study. However, if the gallbladder is not observed by 1 hour post radiopharmaceutical administration, this suggests acute or chronic cholecystitis.

Specificity for acute cholecystitis is increased when there is nonvisualization of the gallbladder on the 2-hour and 4-hour images. In a patient with severe hepatic dysfunction, it may be necessary to carry out imaging to 24 hours.\textsuperscript{11}

An alternative to delayed imaging would be the administration of morphine sulfate over a time period of 2 to 3 minutes in order to determine if the cystic duct is obstructed. This reduces the exam time to 60 to 90 minutes and yet provides a high degree of specificity.\textsuperscript{11}

As stated previously regarding a patient who has been fasting for more than 24 hours, sincalide can be administered to prevent a false-positive study.\textsuperscript{9} Sincalide can also be used in the determination of the gallbladder ejection fraction. When performing this procedure, it is advisable to infuse the sincalide over a period of 30 to 45 minutes because too rapid an administration may cause the gallbladder to spasm resulting in an ejection fraction that is falsely low. An ejection fraction can also be quantified by the patient ingesting a fatty meal which causes the gallbladder to contract.\textsuperscript{11}

In the differentiation of biliary atresia from other causes of neonatal jaundice, the patient should be premedicated with 5 mg/kg of phenobarbital daily (in 2 divided doses) for 5 days before injection of the radiopharmaceutical. The $^{99m}$Tc-IDA complex dosage may be based on 200µCi/kg (5 mCi/1.7m$^2$), with the minimal amount of activity being 1 mCi.\textsuperscript{1,9}

PITFALLS

If the patient has a recent meal, the gallbladder may be contracted resulting in nonvisualization of the gallbladder, thus suggesting acute cholecystitis.\textsuperscript{11}

In order to alleviate this problem, the patient must fast for 3 to 4 hours, except for non-narcotic pharmaceuticals and water, prior to radiopharmaceutical administration.\textsuperscript{1,11}

In contrast, if the patient has fasted for greater than 24 hours, the gallbladder may be filled with sludge thus preventing the radiolabeled IDA complex from entering the gallbladder. The radiopharmaceutical, in this case, would traverse the common bile duct and go directly into the duodenum, again suggesting acute cholecystitis.

This false study can be prevented by pretreating a patient, who has fasted for longer than 24 hours, with sincalide, thus allowing the gallbladder to contract so the radiopharmaceutical may enter.\textsuperscript{11}
Imaging the Hepatobiliary System

Thirty minutes must elapse after completion of the sincalide infusion before radiopharmaceutical injection so the gallbladder will have adequate time to relax after contraction.¹

When conducting a gallbladder ejection fraction with sincalide, it is critical not to inject the sincalide as a bolus. The neck of the gallbladder may spasm when sincalide is administered as bolus, and this would cause a falsely decreased maximal ejection fraction in response to sincalide. Sincalide can be diluted in 10 to 20 mL of normal saline in order to facilitate a slow intravenous injection.⁹,¹²

Morphine-related medications can constrict the sphincter of Oddi, resulting in a functional partial obstruction that simulates a true obstruction.¹ This can be prevented by discontinuing these medications for 6 to 12 hours prior to radiopharmaceutical administration.

Additional causes of false-positive hepatobiliary studies can include chronic cholecystitis, unknown prior cholecystectomy, severe intercurrent disease, rapid biliary to bowel transit, severe hepatocellular disease, and hyperalimentation.¹¹

False negative studies can occur by mistaking the duodenum, renal pelvis, and the cystic or common bile duct for the gallbladder. If this is a possibility, additional views or other maneuvers can be utilized.¹¹

**DIAGNOSIS**

In a normal hepatobiliary study, the radiopharmaceutical appears within the hepatic ducts and gallbladder by 15 to 30 minutes.¹² The gallbladder is routinely filled by 30 to 40 minutes, however the standard time interval for a normal study is 60 minutes.¹

Also, in a normal study radioactivity appears in the small intestine by 30 minutes post radiopharmaceutical administration.¹² With acute cholecystitis the gallbladder does not visualize by 4 hours post radiopharmaceutical injection even though the liver, common bile duct, and gastrointestinal tract are demonstrated within 60 minutes.

Lack of gallbladder visualization can be due to anatomic or functional obstruction of the cystic duct. However with chronic cholecystitis, the gallbladder may be seen after 60 minutes post injection (commonly 2 to 4 hours) although the liver, common bile duct, and gastrointestinal tract are observed by 60 minutes.

When the gallbladder is not seen by 60 minutes post radiopharmaceutical administration, cystic duct obstruction can be ruled out if the gallbladder visualizes after administering either sincalide or morphine sulfate.¹³

The determination of the maximal gallbladder ejection fraction in response to intravenous administration of sincalide is one method used to aid in the diagnosis of symptomatic chronic acalculous biliary disease.⁹

When activity is observed in the liver, common bile duct, and gallbladder but not in the intestinal tract by 60 minutes, this is indicative of either functional or anatomic common bile duct obstruction.¹³

Bile leaks can be demonstrated as an increasing accumulation of radioactivity in the area of the gallbladder fossa or hepatic hilum. The radiopharmaceutical may move into the subdiaphragmatic space into the colonic gutters or be visualized as free bile in the abdomen. Positioning maneuvers and delayed imaging are helpful in making the diagnosis.¹
Imaging the Hepatobiliary System

Hepatobiliary imaging can determine whether or not cold defects seen on $^{99m}$Tc-sulfur colloid imaging are due to normal biliary anatomic structures.\textsuperscript{13}

With nonobstructive causes of neonatal jaundice, the radiopharmaceutical will usually be excreted into the bowel during the first 24 hours post radiopharmaceutical administration. However in patients with biliary atresia, the radiopharmaceutical will not be excreted into the bowel by 24 hours.\textsuperscript{1,12}

PATIENT STUDIES

Shown here in figure 4 is an example of a normal study.

![Figure 4: Normal Cholescintigraphy](image)

A normal gallbladder ejection fraction:

![Figure 5: Normal Gallbladder Ejection Fraction](image)
An abnormal gallbladder ejection fraction:

![Image of gallbladder ejection fraction](image)

**Figure 6: Abnormal Gallbladder Ejection Fraction**

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### QUIZ

**QUESTION #1**

Following intravenous administration, $^{99m}$Tc labeled IDA compounds are extracted from the blood by:

- [ ] Kupffer cells
- [ ] Hepatocytes
- [ ] Reticuloendothelial cells
- [ ] Leukocytes

**QUESTION #2**

Which of the following pharmaceuticals may be administered to facilitate the uptake of $^{99m}$Tc-mebrofenin into gallbladder to differentiate between chronic and acute cholecystitis?

- [ ] Furosemide
- [ ] Dipyridamole
- [ ] Phenobarbital
- [ ] Sincalide
QUESTION #3
A major cause of focal biliary obstruction in a neonate is:

- Acute cholecystitis
- Biliary atresia
- Hepatic fibrosis
- Neonatal hepatitis

QUESTION #4
Which sincalide dose would be suitable for a 265 lb patient?

- 0.5 µg
- 2.4 µg
- 0.6 mg
- 5 mg

QUESTION #5
Which interventional agent would be indicated in patient whose gallbladder is not demonstrated within 60 minutes post radiopharmaceutical administration even though intestinal activity is observed?

- Furosemide
- Morphine
- Phenobarbital
- Sincalide

QUESTION #6
In preparation for a hepatobiliary study, what is the minimum time the patient should fast prior to radiopharmaceutical administration in order to minimize a false positive study?

- 1 hour
- 3 to 4 hours
- 6 to 12 hours
- 24 hours
QUESTION #7

The minimal acceptable radiochemical purity for $^{99m}$Tc labeled IDA compounds is:

- 85%
- 90%
- 95%
- 99%

QUESTION #8

The actions of morphine include:

- Enhancement of the flow of radiopharmaceutical into the duodenum
- Functional blockage of the cystic duct
- Spasm of the sphincter of Oddi
- Contraction of the gallbladder

QUESTION #9

After disofenin is radiolabeled with $^{99m}$Tc, it should be used within:

- 30 minutes
- 1 hour
- 6 hours
- 18 hours

QUESTION #10

The actions of phenobarbital includes:

- Inhibits the action of hepatic enzymes in pediatric patients with neonatal jaundice
- Prevents the uptake of bile components
- Enhances excretion of $^{99m}$Tc disofenin in patients with patent bile ducts
- Blocks bilirubin conjugation and excretion

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REFERENCES