

8. Lin LI. A concordance correlation coefficient to evaluate reproducibility. *Biometrics* 1989;45:225-268.
9. Donner A, Eliasziw M. Sample size requirements for reliability studies. *Statistics in Medicine* 1987;6:441-448.
10. Zar JH, ed. Simple linear correlation. In: *Biostatistical analysis*, Second edition, Englewood Cliffs, NJ: Prentice-Hall; 1984:323-324.
11. Hoiland-Carlson PF, Laritzen SL, Marving J, et al. The reliability of measuring left ventricular ejection fraction by radionuclide cardiography: evaluation by the method of variance components. *Br Heart J* 1988;58:653-662.
12. Lindquist EF, ed. *Design and analysis of experiments in psychology and education*. New York: Houghton Mifflin; 1953:357-382.
13. Dixon WJ, ed. *BMDP statistical software, Volumes 1 and 2*. Berkeley: University of California Press; 1985.
14. SAS Institute Inc. Cary, North Carolina, 1985.
15. Rerych SK, Scholz PM, Newman GE, et al. Cardiac function at rest and during exercise in normals and in patients with coronary heart disease: evaluation by radionuclide angiography. *Ann Surg* 1978;198:449-464.
16. Tamaki N, Gill JB, Moore RH, et al. Cardiac response to daily activities and exercise in normal subjects assessed by an ambulatory ventricular function monitor. *Am J Cardiol* 1987;59:1164-1169.
17. Kostuk WJ, Chamberlain MJ, Sang HC. Radionuclide angiocardiography, a noninvasive method for evaluating left ventricular ejection fraction and regional wall motion: comparison with contrast left ventricular angiography. *Can Med Assoc J* 1978;119:877-884.
18. Altman DG, Bland JM. Measurement in medicine: the analysis of method comparison studies. *The Statistician* 1983;32:307-317.
19. Okada RD, Kirshenbaum HD, Kushner FG, et al. Observer variance in the qualitative evaluation of left ventricular wall motion and quantification of left ventricular ejection fraction using rest and exercise multigated blood pool imaging. *Circulation* 1980;61:128-136.
20. Allen RD, Gettes LS, Phalan C, Avington MD. Painless ST-segment depression in patients with angina pectoris: correlation with daily activities and cigarette smoking. *Chest* 1976;69:467-473.
21. Northcote RJ, Cooke MBD. How useful are the cold pressor test and sustained isometric handgrip exercise with radionuclide ventriculography in the evaluation of patients with coronary artery disease? *Br Heart J* 1987;57:319-328.
22. Breisblatt WM, Weiland FL, McLain JR, et al. Usefulness of ambulatory radionuclide monitoring of left ventricular function early after acute myocardial ischemia. *Am J Cardiol* 1988;62:1005-1010.
23. Kayden DS, Wackers FJTh, Zaret BL. Silent left ventricular dysfunction during routine activity after thrombolytic therapy for acute myocardial infarction. *J Am Coll Cardiol* 1990;15:1500-1507.

## **SELF-STUDY TEST**

# **Gastrointestinal Nuclear Medicine**

Questions are taken from the *Nuclear Medicine Self-Study Program I*, published by The Society of Nuclear Medicine

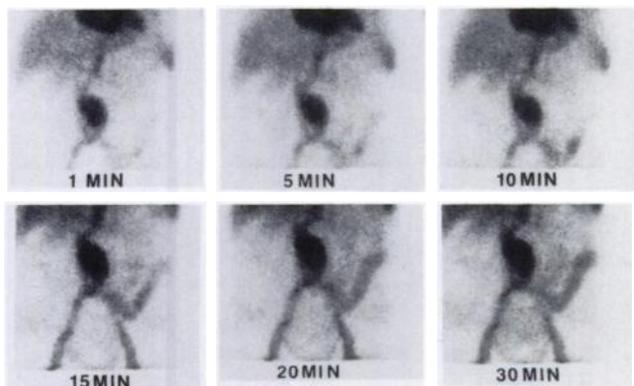
### **DIRECTIONS**

The following items consist of a heading followed by lettered options related to that heading. Select the *one* lettered option that is best for each item. Answers may be found on page 824.

- 1.** A 2-month-old infant has conjugated hyperbilirubinemia. Hepatobiliary scintigraphy with <sup>99m</sup>Tc-iminodiacetic acid shows no evidence of excretion into the bowel by 24 hr. Evaluation of which *one* of the following features of the early images would be most useful in distinguishing biliary atresia from neonatal hepatitis?

- A. hepatic perfusion during the initial angiographic phase
- B. the amount of renal excretion and early bladder activity
- C. the delineation of intrahepatic bile ducts
- D. the degree of hepatic extraction of the tracer
- E. nonvisualization of the gallbladder

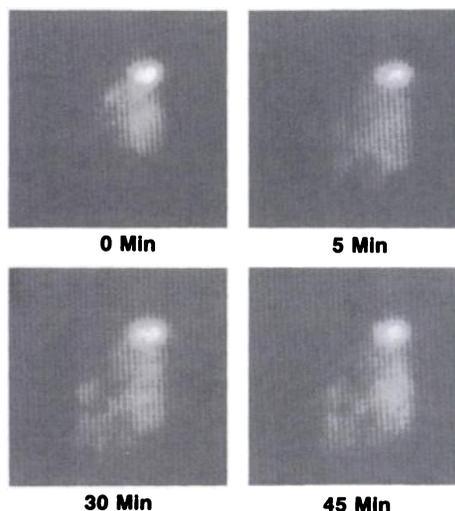
- 2.** A 65-year-old man is admitted to the emergency room because of hematochezia. His blood pressure is 90/60 mm/Hg and his heart rate is 100 bpm. Figure 1 shows sequential anterior images from a <sup>99m</sup>Tc-red blood cell study. Which *one* of the following is the most likely cause for the patient's bleeding?



**Figure 1**

- A. duodenal ulcer
- B. aortoenteric fistula
- C. diverticulum in the descending colon
- D. diverticulum in the splenic flexure
- E. leiomyoma of the small bowel

- 3.** This 48-year-old woman has nausea, vomiting, and abdominal pain 8 months following vagotomy, hemigastrectomy, and Billroth II gastrojejunostomy. There was no history of bilious vomiting. A gastric emptying study done with <sup>111</sup>In-labeled solid egg (Fig. 2A) and a concurrently performed <sup>99m</sup>Tc-disofenin hepatobiliary study (Fig. 2B) are shown. Which *one* of the following statements concerning this clinical situation and these scintigraphic results is correct?



**Figure 2A**

(continued on p. 824)

- 1989:343-358.
23. Levin VA. Relationship of octanol/water partition coefficient and molecular weight to rat brain capillary permeability. *J Med Chem* 1980;23:682-684.
  24. Tislar U, Kloster G, Ritzl F, Stöcklin G. Accumulation of radioiodinated L-alpha-methyltyrosine in pancreas of mice: concise communication. *J Nucl Med* 1979;20:973-976.
  25. Kloster G, Coenen HH, Szabo Z, Ritzl F, Stöcklin G. Radiohalogenated L-alpha-methyltyrosine as potential pancreas imaging agents for PECT and SPECT. In: Cox PH, ed. *Progress in radiopharmacology, volume 3*. Den Haag: Martinus Nijhoff; 1982:97-107.
  26. Bockslaff H, Kloster G, Stöcklin G, et al. Studies on L-3-[<sup>123</sup>I]iodo-methyl tyrosine: a new potential melanoma-seeking compound. *Nuklearmedizin* 1980;(suppl 17):179-182.
  27. Bockslaff H, Kloster G, Dausch D, et al. First clinical results using L-3-<sup>123</sup>I-alpha-methyl tyrosine for non-invasive detection of intraocular melanoma. *Nuklearmedizin* 1981;(suppl 18):840-844.
  28. Bockslaff H, Spitznas M, Hahn I, Kloster G. Noncontact detection of experimental amelanotic ocular melanoma with L-3-<sup>123</sup>I-iodo-alpha-methyltyrosine. *Albrecht v Graefes Arch Klin Ophthal* 1981;217:255-266.
  29. Biersack HJ, Coenen HH, Stöcklin G, et al. Imaging of brain tumors with L-3-[<sup>123</sup>I]iodo-alpha-methyltyrosine and SPECT. *J Nucl Med* 1989;30:110-112.
  30. Langen KJ, Coenen HH, Roosen N, et al. SPECT studies of brain tumors with L-3-[<sup>123</sup>I]iodo-alpha-methyltyrosine: comparison with PET, <sup>124</sup>IMT, and first clinical results. *J Nucl Med* 1990;31:281-286.

(continued from page 802)

## SELF-STUDY TEST

### Gastrointestinal Nuclear Medicine

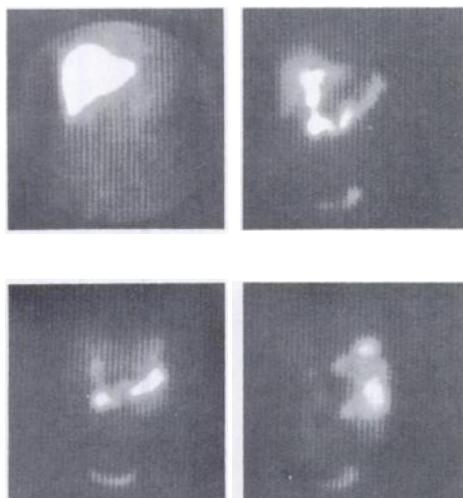


Figure 2B

- A. There is evidence for obstruction of the afferent (proximal) limb of the Billroth II reconstruction
- B. On the basis of the images alone, it can be concluded that entero gastric reflux is responsible for the patient's symptoms.
- C. A calculated peak entero gastric reflux index of 64% indicates that the patient's symptoms are likely to be relieved by surgical diversion of bile with a 45-cm Roux-en-Y limb.
- D. The patient's symptoms are likely related to post-operative gastroesophageal reflux.
- E. The absence of bilious vomiting makes it unlikely that the patient's symptoms are related to alkaline reflux gastritis.

### ANSWERS

#### ITEM 1: Neonatal Jaundice

ANSWER: D

The initial angiographic phase with rapid sequential imaging is a useful component of hepatobiliary scintigraphy, in that unsuspected abnormalities, such as an arteriovenous malformation in the liver or renal inflammatory lesion, may occasionally be demonstrated. Avascular, photon-deficient areas within the liver may suggest cysts, dilated bile ducts as in Caroli's disease, or a choledochal cyst. There is no specific alteration in hepatic perfusion useful for distinguishing hepatocyte dysfunction from biliary atresia, however.

The kidneys are the alternate route of excretion of the <sup>99m</sup>Tc-IDA derivatives. Renal and bladder activity is prominent with either poor hepatic uptake and excretion (e.g., hepatitis), or good hepatic extraction but no excretion (biliary atresia). Normally, some renal and bladder activity is expected because, depending on the specific iminodiacetic acid derivative, 5%-15% of the injected dose will be excreted by the kidneys. The degree of renal excretion cannot be used to differentiate hepatocellular disease from an obstructive process.

In the newborn period, it is not usual to see good definition of the intrahepatic ducts, and visualization of the gallbladder is infrequent. When the gallbladder is seen, however, *intrahepatic* biliary atresia can be excluded. *Extrahepatic* obstruction is still possible, but dilatation of the bile ducts will often be evident by ultrasonography. Nonvisualization of the gallbladder is usual with impaired hepatocyte function and prolonged hepatic transit of the radiopharmaceutical. Thus, nonvisualization of the intrahepatic bile ducts and gallbladder may be seen with both hepatitis and biliary atresia, and these features cannot serve to distinguish these disorders.

In infants less than 3 months of age, assessing the degree of hepatic extraction may aid in differential diagnosis. Good extraction with a high liver-to-heart activity ratio at 5 minutes is suggestive of biliary atresia. Visually, there is rapid clearance from the blood pool with prominent hepatic uptake. Evaluation of the time-activity curves will confirm prompt uptake of tracer by the liver with either no washout over 60 minutes or a slight decrease after reaching peak activity. This is in keeping with the relatively good hepatocyte function at this stage. Beyond the age of 3 months, the effect of the prolonged obstruction on liver function becomes evident as hepatic extraction decreases. If the initial hepatic uptake is poor, then the patient is more likely to have neonatal hepatitis (or some other cause of hepatocellular dysfunction). Typically, the time-activity curve shows an early peak due to vascular activity. The shape of the curve parallels that of the cardiac blood pool, because there is minimal active uptake by the liver. With less severe hepatitis the extraction ratio is decreased. The curves show delayed uptake by the liver with a washout rate equal to or slightly greater than the rate of decrease in blood-pool activity. In the latter instance, excretion into the bowel may be anticipated in the delayed images. Thus, an evaluation of the early hepatic extraction and washout during the first 60 minutes may suggest the presence of biliary atresia or neonatal hepatitis, provided the patient is less than 3 months old.

#### References

1. Gerhold JP, Klingensmith WC II, Kuni CC, et al. Diagnosis of biliary atresia with radionuclide hepatobiliary imaging. *Radiology* 1983;146:499-504.
2. Majd M, Reba RC, Altman RP. Effect of phenobarbital on <sup>99m</sup>Tc-IDA scintigraphy in the evaluation of neonatal jaundice. *Semin Nucl Med* 1981;11:194-204.

(continued on p. 829)

radioactive waste disposal problems. Thus, the new Ga-IRMA system appears likely to provide a solution to some of the problems inherent in the current  $^{125}\text{I}$  assay systems.

## REFERENCES

1. Krejcarek GE, Tucker KL. Covalent attachment of chelating groups to macromolecules. *Biochem Biophys Res Commun* 1975;256:495-497.
2. Hnatowich DJ, Layne WW, Childs RL, et al. Radioactive labeling of antibody: a simple and efficient method. *Science* 1983;220:613-615.
3. Yokoyama A, Ohmono Y, Horiuchi K, et al. Deferoxamine, a promising bifunctional chelating agent for labeling proteins with gallium: Ga-67-DF-HSA: concise communication. *J Nucl Med* 1982;23:909-914.
4. Childs RL, Hnatowich DJ. Optimum conditions for labeling of DTPA-coupled antibodies with technetium-99m. *J Nucl Med* 1985;26:293-299.
5. Arano Y, Yokoyama A, Magata Y, et al. Synthesis and evaluation of a new bifunctional chelating agent for  $^{99\text{m}}\text{Tc}$  labeling proteins, p-carboxy-ethylphenylglyoxal-di (N-methylthiosemicarbazone). *Int J Nucl Med Biol* 1985;12:425-430.
6. Takahashi K, Ueda N, Hazue M, et al. Preparation and biodistribution of  $^{67}\text{Ga}$ -labeled fibrinogen conjugated with a water-soluble polymer containing deferoxamine, a potential thrombus imaging agent. In: *Radiopharmaceuticals and labeled compounds*. Vienna: IAEA: 1985:471-482.
7. Fritzberg AR, Berninger RW, Hadlew SW, Wester DW. Approaches to radiolabeling of antibodies for diagnosis and therapy of cancer. *Pharm Res* 1988;5:325-334.
8. Kunimatsu M, Endo K, Nakashima T, et al. Development of new immunoradiometric assay for CA125 antigen using two monoclonal antibodies produced by immunizing lung cancer cells. *Ann Nucl Med* 1988;2:73-79.
9. Furukawa T, Fujibayashi Y, Fukunaga M, Yokoyama A. Ga-labeling of IgG with high specific radioactivity. *Chem Pharm Bull* 1990;38:2285-2286.
10. Furukawa T, Endo K, Ohmomo Y, et al. Radioimmuno-detection of tumor with Ga-67-labeled antibodies: effect of radiolabeling on the antibody activities. *Jpn J Nucl Med* 1986;23:337-343.
11. Eckelman WC, Paik CH, Reba RC. Radiolabeling of antibodies. *Cancer Res* 1980;40:3036-3042.

(continued from p. 824)

# SELF-STUDY TEST

## Gastrointestinal Nuclear Medicine

### ANSWERS

#### ITEM 2: Colonic Bleeding

ANSWER: C

The images in Figure 1 demonstrate a faint focus of abnormal  $^{99\text{m}}\text{Tc}$ -red blood cell accumulation in the left lower quadrant, which is first seen at 1 minute but becomes more intense with time and conforms with the descending colon. A bleeding diverticulum in the descending colon was found at colonoscopy.

There is no gastric, duodenal, or proximal jejunal activity present to suggest a bleeding duodenal ulcer, nor are small bowel loops seen on the images to suggest a bleeding leiomyoma. The activity in the left upper quadrant is the spleen, which is always seen normally, but may have unusually prominent activity if the patient has been transfused recently. This splenic activity remains stable with time and should not be confused with bleeding from the splenic flexure, which generally should increase with time and move distally.

The  $^{99\text{m}}\text{Tc}$ -red blood cell scan demonstrates an abdominal aortic aneurysm, but there is no evidence for a bleeding aortoenteric fistula. Spontaneous aortoenteric fistulae are rare, occurring in approximately seven of 10,000 autopsy cases. The most common area of fistula formation is between the aorta and duodenum, which is the case in 80% of patients. Atherosclerotic aneurysms of the iliac arteries can erode into the bowel, as well. In the current case, no aneurysm is seen in either iliac artery.

#### Reference

1. Yen CK, Pollycove M, Parker H, Nalls G. Rupture of a spontaneous aortoduodenal fistula visualized with Tc-RBC scintigraphy. *J Nucl Med* 1983;24:332-333.

#### ITEM 3: Symptomatic Alkalkine Reflux Gastritis

ANSWER: C

No esophageal reflux of tracer is identified in any of the images in Figures 2A-B to suggest that the patient's symptoms are due to reflux esophagitis. Furthermore, the patient's symptoms following vagotomy, hemigastrectomy, and Billroth II gastrojejunostomy are not typical of those experienced in patients with simple reflux esophagitis.

Clinical symptoms associated with the postgastrectomy syndrome of

"alkaline reflux gastritis" include epigastric pain, nausea, vomiting, bilious vomiting, and weight loss. Ritchie has reported that, in general, it is not possible on clinical grounds alone to predict which patients will benefit from surgical procedures to divert bile flow. In his series of patients, the frequency of symptoms was no different between patients with documented "excessive" reflux compared to those with "normal" reflux. Bilious vomiting was the only symptom found more frequently in the "excessive" reflux group. However, bilious vomiting was absent in some symptomatic "excessive" refluxers who responded to surgical diversion. The absence of bilious vomiting cannot be used, therefore, to conclude that the patient does not have alkaline reflux gastritis.

While there is some early "pooling" of the hepatobiliary agent in the afferent loop of bowel, there is no significant retention in the later images to suggest obstruction of the afferent loop of the Billroth II reconstruction.

It is not abnormal to see bile reflux in patients following Billroth II reconstruction. In fact, the presence of reflux is a typical postoperative finding. Symptoms, however, are best correlated with the amount of reflux, which needs to be determined quantitatively and not merely by visual assessment. In this case, there is excessive reflux quantitated by an enterogastric reflux index of 64%. Values elevated into this range have been best correlated with the patient's symptoms. In Ritchie's study, asymptomatic postgastrectomy patients without excessive reflux had a mean reflux index of  $16\% \pm 9\%$ , while for symptomatic, "excessive" refluxers the mean value was  $81\% \pm 15\%$ .

Ritchie also reported surgical correction of reflux documented by objective criteria (e.g., measurement of gastric bile-acid concentrations, net bile-acid reflux, scintigraphic enterogastric reflux, and histologic evidence of gastritis) in all of 14 patients with excessive reflux following diversion with a 45-cm Roux-en-Y limb. This patient, therefore, has excessive bile reflux that is the likely cause for her symptoms. She would be expected to obtain relief of her symptoms following surgical diversion.

#### Reference

1. Ritchie WP. Alkaline reflux gastritis: an objective assessment of its diagnosis and treatment. *Ann Surg* 1980;192:288-298.