emission computered tomography: 5. Physical-anatomical effects. *J Comput Assist Tomogr* 1981;5:734–743.
15. Bendriem B, Dewey SL, Schlyer DJ, Wolf AP, Volkow ND. Quantitation of the human basal ganglia with positron emission tomography: a phantom study of the effect of contrast and axial positioning. *IEEE Trans Med Imag* 1991;5:203–213.
16. Hoffman EJ, Huang SC, Phelps ME. Quantitation in positron emission computed tomography. 1. Effect of object size. *J Comput Assist Tomogr* 1979;3:299–308.
17. Kessler R, Ellis JR, Eden M. Analysis of emission tomography scan data: limitations composed by resolution and background. *J Comput Assist Tomogr* 1984;8:514–522.
18. Gjedde A, Reith J, Kuwabara H, Dyve S. Determining dopa decarboxylase activity in the human brain in vivo: the complete fluoro-dopa model. *J Nucl Med* 1990;31:720.
19. Eidelberg D, Moeller JR, Dhawan V, et al. The metabolic anatomy of Parkinson's disease complementary [F-18]fluorodeoxyglucose and [F-18]fluorodopa positron emission tomography studies. *Movement Disorder* 1990;5:203–213.
20. Rottenberg DA, Moeller JR, Strother SC, Dhawan V, Sergi ML. Effects of percent thresholding on the extraction of [F18]fluorodeoxyglucose positron emission tomographic region-of-interest. *J Cereb Flow Metab* 1991;11:A83–A88.
21. Gambhir SS. Quantitation of the physical factors affecting tracer kinetic modeling of cardiac positron emission tomography data, PhD Dissertation Thesis, University of California, Los Angeles; 1991.
22. Abramowitz M, Stegun IA. *Handbook of mathematical functions.* New York: McGraw-Hill; 1972.
23. Huang SC, Carson RE, Phelps ME, Hoffman EJ, Schelbert HR, Kuhl DE. A boundary method for attenuation correction in positron computed tomography. *J Nucl Med* 1981;22:627–637.
24. Carson RE, Huang SC, Phelps ME. BLD: a software system for physiological data handling and model analysis. *The 5th Annual Symposium on Computer Applications in Medical Care* 1981;562–565.
25. Miller TM, Wallis JW, Grothe RA Jr. Design and use of PET tomography: the effect of slice spacing. *J Nucl Med* 1990;31:1732–1739.
26. Yu DC, Huang SC, Melega WP, et al. Evaluation of various graphical analysis for estimating influx constant in F-DOPA PET studies. *J Nucl Med* 1991;32 suppl:1004.
27. Pate BD, Snow BJ, Hewitt KA, Morrison KS, Ruth TJ, Calne DB. The reproducibility of striatal uptake data obtained with positron emission tomography and fluorine-18-L-6-fluorodopa tracer in nonhuman primates. *J Nucl Med* 1991;32:1246–1251.
28. Doudet DJ, McLellan CA, Carson RE, et al. Distribution and kinetics of 3-O-methyl-6-[F-18]fluoro-L-DOPA in the Rhesus monkey brain. *J Cereb Blood Flow Metab* 1991;11:726–734.
29. Gambhir SS, Schwaiger M, Huang SC, et al. Simple noninvasive quantification method for measuring myocardial glucose utilization in human employing positron emission tomography and fluorine-18-deoxyglucose. *J Nucl Med* 1989;30:359–366.
30. Choi Y, Hawkins RA, Huang SC, et al. Parametric images of myocardial metabolic rate of glucose generated from dynamic cardiac PET and 2-[^{18}F]fluoro-2-deoxy-d-glucose studies. *J Nucl Med* 1991;32:733–738.
31. Brooks DJ, Ibanez V, Sawle GV, et al. Differing pattern of striatal ^{18}F-dopa uptake in Parkinson's disease, multiple system atrophy and progressive supranuclear palsy. *Ann Neurol* 1990;28:547–555.
32. Kak AC, Slaney M. *Principles of computerized tomographic imaging.* New York: IEEE Press; 1987.
33. Huesman RH, Mazoyer BM. Kinetic data analysis with a noisy input function. *Phys Med Biol* 1987;32:1569–1579.
34. Chen K, Huang SC, Yu DC. The effect of measurement errors in the plasma radioactivity curve on parameter estimation in positron emission tomography. *Phys Med Biol* 1991;36:1183–1200.
35. Draper NR, Smith H. *Applied regression analysis*, 2nd edition. New York: Wiley; 1981.

SELF-STUDY TEST

Gastrointestinal Nuclear Medicine

Questions are taken from the *Nuclear Medicine Self-Study Program 1,* 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 694.

True statements concerning scintigraphy for detection of Meckel's diverticulum include which of the following?

1. Pretreatment with cimetidine increases the frequency of false-negative studies.
2. Uterine blood-pool activity occasionally causes false-positive studies.
3. Small bowel duplication is usually distinguishable from Meckel's diverticulum.
4. Technetium-99m pertechnetate is selectively concentrated in parietal cells of ectopic gastric mucosa.

True statements regarding Meckel's diverticula in adults include which of the following?

5. Most are symptomatic.
6. Two-thirds of affected elderly patients present with melena.
7. Technetium-99m pertechnetate imaging has a sensitivity of greater than 80%.

A 35-year-old man was admitted with abdominal pain, melena, and orthostatic hypotension. Upper gastrointestinal endoscopy to the second portion of the duodenum was normal. Melena persisted and the patient required multiple transfusions. Colonoscopy to the hepatic flexure demonstrated melena, but no actively bleeding lesion. The colonoscope could not be advanced further because of spasm. Scintigraphy with ^{99m}Tc-labeled red blood cells was performed (Fig. 1). Images were taken at 5, 10, 15, and 20 minutes.

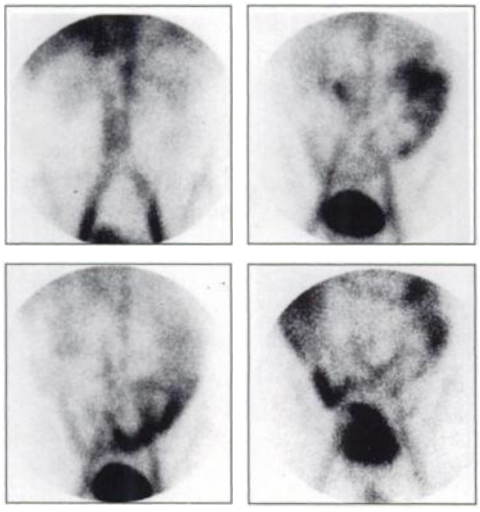

Figure 1

(continued on page 694)

marrow cellularity using volume-localized proton NMR spectroscopy. *Magnetic Reson Med* 1991;19:85–95.
17. Eary JF, Matthews D, Appelbaum F, et al. Bone marrow radiation absorbed dose estimation for ^{131}I radioimmunotherapy of leukemia [Abstract]. *J Nucl Med* 1992;33:941.
18. Ganong WF. *Review of medical physiology*, 12th edition. Los Altos: Lange; 1985:830.
19. International Commission on Radiological Protection. *Report of the task group on reference man.* ICRP Publication 23. New York: Pergamon Press; 1975.

(continued from page 688)

SELF-STUDY TEST
Gastrointestinal Nuclear Medicine

QUESTIONS *(continued)*

True statements concerning this patient include which of the following?

8. There is excessive free ^{99m}Tc pertechnetate as a result of poor red blood cell labeling efficiency.
9. A small bowel enteroclysis study would not be helpful in this patient.
10. A bleeding site would have been better localized by scintigraphy with ^{99m}Tc sulfur colloid.
11. An intravenous injection of glucagon prior to imaging would have reduced free ^{99m}Tc pertechnetate activity in the small bowel.

True statements concerning red blood cell labeling techniques with ^{99m}Tc include which of the following?

12. When the modified in vivo ("in vivtro") method is used, heparin rather than acid citrate dextrose (ACD) is preferred as the anticoagulant.
13. Stanous pyrophosphate and ^{99m}Tc should be injected through the same indwelling catheter when either the in vivo or the modified in vivo technique is used.
14 The bladder is the organ receiving the highest radiation exposure when the in vivo method of red blood cell labeling is used.
15. Technetium-99m binds predominantly to the red blood cell membrane.

SELF-STUDY TEST
Gastrointestinal Nuclear Medicine

ANSWERS

Items 1-4: Scintigraphy for Meckel's Diverticula

Answers: 1, F; 2, T; 3, F; 4, F

The histamine-2 receptor antagonist, cimetidine, enhances imaging of Meckel's diverticulum by causing continued accumulation of ^{99m}Tc pertechnetate in ectopic gastric mucosa and by reducing secretion of ^{99m}Tc activity into the bowel. By decreasing the amount of pertechnetate entering the small bowel, cimetidine helps to reduce the frequency of false-positive studies.

Up to 73% of menstruating women have been shown to demonstrate a uterine "blush" following ^{99m}Tc pertechnetate administration during the menstrual or secretory phase of their menstrual cycle. This may lead to a false-positive interpretation. In general, premenarchal, postmenopausal, and menstruating patients in the proliferative phase do not show this uterine "blush."

Small bowel duplications occasionally contain ectopic gastric mucosa and may simulate Meckel's diverticulum on scintigraphy with ^{99m}Tc pertechnetate. Because the position within the abdomen of a small bowel duplication can mimic that of Meckel's diverticulum and because both anomalies contain ectopic gastric mucosa, it usually is not possible to distinguish Meckel's diverticulum from a small-bowel duplication by ^{99m}Tc pertechnetate imaging.

Autoradiographic studies have shown that, after intravenous administration, ^{99m}Tc pertechnetate is selectively concentrated by the mucous-producing cells of gastric mucosa, rather than by parietal cells or chief cells. Experimental animal studies have demonstrated that at least 2 cm of functioning ectopic gastric mucosa is necessary for visualization.

References

1. Baum S. Pertechnetate imaging following cimetidine administration in Meckel's diverticulum of the ileum. *Am J Gastroenterol* 1981;76:464-465.
2. Chaudhuri TK, Polak JJ. Autoradiographic studies of distribution in the stomach of ^{99m}Tc pertechnetate. *Radiology* 1977;123:223-224.
3. Fink-Bennett D. The uterine blush. A potential false-positive in Meckel's scan interpretation. *Clin Nucl Med* 1982;7:444-446.

Items 5-7: Meckel's Diverticula in Adults

Answers: 5, F; 6, F; 7 F

Although Meckel's diverticulum is the most common congenital anomaly of the gastrointestinal tract, with a prevalence of approximately 1%, most are not symptomatic. Additionally, those that cause symptoms usually do so in the first 2 years of life. Ectopic gastric mucosa is more frequently encountered in symptomatic Meckel's diverticula, but may also be present in asymptomatic Meckel's diverticula. Lower gastrointestinal bleeding is the most frequent presentation of symptomatic Meckel's diverticulum in the pediatric population. In adults, the most common presentation is acute inflammation (Meckel's diverticulitis). Obstruction is seen less often and gastrointestinal bleeding occurs rarely. Several studies have clearly shown that the sensitivity of ^{99m}Tc pertechnetate scintigraphy for Meckel's diverticulum is greater than 80% in the pediatric population. In adults, however, the sensitivity of Meckel's scintigraphy is approximately 60%. The precise reasons for this are unclear.

References

1. Mackey WC, Dineen P. A 50-year experience with Meckel's diverticulum. *Surg Gynecol Obstet* 1983;156:56-64.

(continued on page 713)

16. Rutland MD. An analysis of the uptake of ^{99m}Tc sulphur colloid by liver and spleen. *Nucl Med Commun* 1984;5:593–602.
17. Decostre PL, Salmon Y. Temporal behavior of peripheral organ distribution volume in mammillary systems. A new tool for tracer analysis. *J Nucl Med* 1990;31:1702–1709.
18. Peters AM. Measurement of microvascular permeability to small solutes in man. Limitations of the technique. *Cardiovasc Res* 1990;24:504–509.
19. Peters AM, Brown J, Crossman D, et al. Noninvasive measurement of renal blood flow with ^{99m}Tc DTPA in the evaluation of patients with suspected renovascular hypertension. *J Nucl Med* 1990;31:1980–1985.
20. Carpani de Kaski M, Peters AM, Knight D, Stuttle AWJ, Lavender JP, Hodgson HJ. Indium-111 whole body retention: a new method for quantification of disease activity in inflammatory bowel disease. *J Nucl Med* 1992;33:756–762.
21. Currie DC, Saverymuttu SH, Peters AM, et al. Indium-111-labeled granulocyte accumulation in the respiratory tract of patients with bronchiectasis. *Lancet* 1987;1:1335–1339.
22. Merrick MV, Eastwood MA, Anderson JR, Ross HM. Enterohepatic circulation in man of a gamma-emitting bile acid conjugate 23-selena-25-homotaurocholic acid (SeHCAT). *J Nucl Med* 1982;23:126–130.
23. Hawkins PN, Wootton R, Pepys MB. Metabolic studies of radioiodinated serum amyloid P component in normal subjects and patients with systemic amyloidosis. *J Clin Invest* 1990;86:1862–1869.

(continued from page 694)

SELF-STUDY TEST
Gastrointestinal Nuclear Medicine

ANSWERS *(continued)*

2. Schwartz MJ, Lewis JH. Meckel's diverticulum: pitfalls in scintigraphic detection in the adult. *Am J Gastroenterol* 1984;78:611-618.

Items 8-11: Bleeding from a Rest of Ectopic Gastric Mucosa
Answers: 8, F; 9, F; 10, F; 11, F
This patient's images (Fig. 1) demonstrate active upper gastrointestinal bleeding, which is first seen on the 10-minute view (upper right image). A film from an upper gastrointestinal barium study (Fig. 2) demonstrates a 2-cm mucosal abnormality (white arrow) in the third portion of the duodenum. This was removed at surgery and histologically confirmed to be a site of bleeding in a focus of ectopic gastric mucosa.

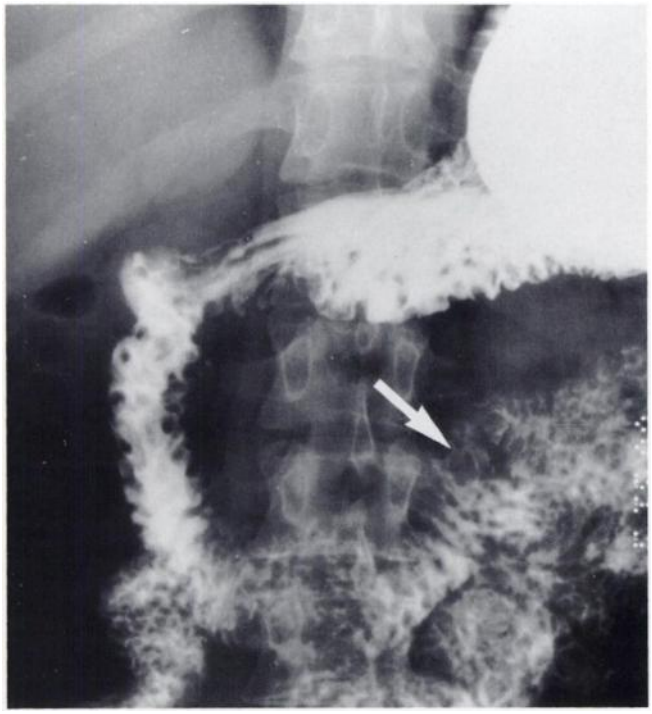

Figure 2. Upper gastrointestinal barium study of the patient whose ^{99m}Tc red blood cell scintigrams are shown in Test Figure 1. There is a filling defect in the barrium column in the third portion of the duodenum (arrow). This mass proved to be a rest of ectopic gastric mucosa.

This study was performed with red blood cells labeled by the "in vivtro" (modified in vivo) technique. The initial view at 5 minutes (upper left image) demonstrates tracer in the blood pool structures without significant gastric activity to suggest a large amount of free ^{99m}Tc pertechnetate or any area of active bleeding. By 10 minutes (upper right image), labeled red blood cells are now seen to have accumulated in the second and third portions of the duodenum. Over the next 20 minutes, extravasated activity moves quickly through the small bowel. Again, there is little gastric mucosal activity to suggest that small bowel activity is derived from free ^{99m}Tc pertechnetate. While the "in vivtro" method of red blood cell labeling is easy to perform and generally results in better labeling efficiency than the in vivo technique, 100% red blood cell labeling does not occur. When heparin is used as the anticoagulant during red blood cell labeling, ^{99m}Tc heparin complexes can accumulate in the kidney and urinary bladder (as in this patient). The bladder activity is not primarily due to free ^{99m}Tc pertechnetate. Excessive urinary activity is usually not a problem when the in vitro labeling method is used.

While gastrointestinal bleeding scintigraphy primarily has been used to identify sites of lower intestinal bleeding, sources of upper tract bleeding can be identified, as was true in this patient. This is one of the theoretical advantages of scintigraphy with labeled red blood cells versus that with ^{99m}Tc sulfur colloid; the latter has limited use in detecting upper gastrointestinal bleeding because hepatic and splenic activity often obscure sites of active bleeding in the upper abdomen.

Use of intravenous glucagon as an antispasmodic has been advocated by some to enhance visualization of bleeding sites in the small bowel. By decreasing small bowel motility, glucagon decreases the translocation of blood within the small bowel and, thus, the actively bleeding focus is more readily identifiable. The enhanced detection of bleeding sites may also be related to a vasodilatory effect of glucagon.

Occasionally, barium examination of the small bowel may be useful in identifying sites of gastrointestinal bleeding. The small bowel enteroclysis study is a specialized barium examination in which a gastric tube is fluoroscopically placed into the third or fourth portion of the duodenum and barium is instilled, followed by a mixture of saline and methyl cellulose. By precisely controlling the column of barium, optimal small bowel distention can be achieved and small bowel lesions, such as tumors, polyps, or Meckel's diverticula can be identified more readily.

References

1. Froelich JW, Juni J. Glucagon in the scintigraphic diagnosis of small bowel hemorrhage by Tc-99m-labeled red cells. *Radiology* 1984;151:239-243.
2. Maglinte DDT, Elmore MF, Isenberg M, Dolan PA. Meckel diverticulum: radiologic demonstration by enteroclysis. *AJR* 1980;134:925-933.

(continued on page 716)

calculations for patients undergoing nuclear medicine procedures continue to be made in terms of the radiation absorbed dose (in units of grays or rads).

REFERENCES

1. International Commission on Radiological Protection. Recommendations of the ICRP, ICRP Publication 26. *Annals of the ICRP, volume 1, no. 3.* Oxford: Pergamon Press; 1977.
2. International Commission on Radiological Protection. Recommendations of the ICRP. ICRP publication 60. *Annals of the ICRP, volume 21, no. 1–3.* Oxford: Pergamon Press; 1991.
3. International Commission on Radiological Protection. Statement from the 1978 Stockholm meeting of the International Commission on Radiological Protection, 1978.
4. International Commission on Radiological Protection. Problems involved in developing an index of harm. ICRP Publication 27. *Annals of the ICRP, volume 1, no. 4.* Oxford: Pergamon Press; 1977.
5. Pochin EE. Why be quantitative about radiation risk estimates? Lauriston S. Taylor Lecture Series in Radiation Protection and Measurements, National Council on Radiation Protection and Measurements, Bethesda, MD, March 15, 1978.
6. Title 10 Code of Federal Regulations Part 20. U.S. Nuclear Regulatory Commission, Washington, DC, May 21, 1991.

(continued from page 713)

SELF-STUDY TEST

Gastrointestinal Nuclear Medicine

ANSWERS *(continued)*

Items 12-15: Red Blood Cell Labeling with ^{99m}Tc

Answers:12, F; 13, F; 14, T; 15, F

In vivo red blood cell labeling is the most frequently utilized method because it is the simplest approach. It is not the most satisfactory method, however, for gastrointestinal bleeding scintigraphy. Because of the variability in labeling efficiency, significant amounts of unbound, free ^{99m}Tc can be secreted into the stomach and bowel, causing false-positive studies. Additionally, much of the activity not bound to red blood cells is excreted by the kidney as labeled small proteins and reduced technetium complexes. This urinary activity may cause problems in interpretation e.g., a rectal bleeding site may be obscured and renders the bladder as the critical organ with this labeling method approximately 2.4 rads/20 mCi. When in vivo techniques are used, the "cold" stannous pyrophosphate should be injected directly into a vein. The precise reason for this is unclear, but if the cold pyrophosphate is injected via an indwelling catheter, poor red blood cell labeling can occur, and this may result in a nondiagnostic examination.

The basic theory underlying red blood cell labeling with ^{99m}Tc is as follows. The stannous ion complex freely diffuses into the red blood cell and binds to cellular components. Pertechnetate ion also freely diffuses into and out of red cells. Once the pertechnetate ion is inside the red blood cell, the stannous ion (Sn^{2+}) reduces it, and the reduced technetium species binds to hemoglobin. Once bound, it remains intracellular. If any stannous ion is present outside the red blood cell, any free extracellular pertechnetate will be reduced. This free reduced technetium will degrade the images (increased background activity and increased urinary excretion).

The in vitro method provides the optimal red blood cell labeling, because of its uniformly high labeling efficiency. The most recent modification of the in vitro method uses whole blood and does not require centrifugation or the removal of blood into multiple sterile containers. The Brookhaven-modified red blood cell labeling kit achieves high labeling efficiency by stopping the premature extracellular reduction of ^{99m}Tc pertechnetate. By the addition of an oxidizing agent sodium hypochlorite, which cannot pass through the red-blood cell membrane, extracellular stannous ion is oxidized to stannic ion (Sn^{4+}). This prevents extra cellular reduction of pertechnetate ion.

The modified in vivo ("in vivtro") technique of red blood cell labeling has been developed as a compromise between the in vivo method and the original in vitro method (which required a long incubation period, multiple handling steps, and written patient consent, because of its investigational status.) When the "in vivtro" technique is used, heparin is often used as the anticoagulant. Unfortunately, ^{99m}Tc heparin complexes can be excreted in the urine and accumulated in the bladder. For this reason, some investigators recommend that ACD solution be used as the anticoagulant, which yields a slightly higher labeling efficiency and reduced urinary activity.

References

1. Porter WC, Dees SM, Freitas JE, Dworkin HJ. Acid-citrate-dextrose compared with heparin in the preparation of in vivo/in vitro technetium-99m red blood cells. *J Nucl Med* 1983;24:383-387.
2. Srivastava SC, Chervu LR. Radionuclide-labeled red blood cells: current status and future prospects. *Semin Nucl Med* 1984;14:6882.

For further in-depth information, refer to the syllabus pages in Nuclear Medicine Self-Study I.