Prospective Study of Magnetic Resonance Imaging and SPECT Bone Scans in Renal Allograft Recipients: Evidence for a Self-Limited Subclinical Abnormality of the Hip

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We recently reported that typical abnormalities of avascular necrosis (AVN) in magnetic resonance images (MRI) of the hips of asymptomatic renal transplant recipients whose plain radiographs are normal may improve spontaneously and even disappear completely. We present the results of serial bone scans, most of which were performed with single-photon emission computed tomography obtained over periods as long as 24 mo after transplantation in 72 of these patients. Three paired imaging studies (i.e., MR and bone scan performed within 30 days of each other) were available for each of these patients. In three patients, both the MR images and the bone scans showed changes consistent with bilateral AVN within 4 mo after transplantation. All three patients developed hip pain which was bilateral in two and unilateral in one. Two patients (three hips) required surgical intervention at which time AVN was found on pathologic examination of all three hips. None of the remaining 69 patients developed hip pain during the study. However, in nine patients whose MR studies were consistently normal, at least one bone scan was abnormal (13 hips). The presence of AVN was pathologically confirmed in each of the hips subjected to surgery. Where the imaging findings were identical to those in the asymptomatic patients as well as those in whom the imaging abnormality regressed, we suggest that the subclinical imaging abnormalities represent mild AVN, which is reversible in some cases. Since the process was identified in 10 hips by MRI and in 13 hips by bone scan, both studies are needed to detect subclinical AVN. This may be important if treatment of subclinical disease is clearly shown to prevent progression to symptomatic AVN.

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The reported prevalence of avascular necrosis (AVN) of the femoral head in patients who receive corticosteroids for immunosuppression after renal transplantation ranges from 4% to 29% (*1–6*). Although the pathogenesis of AVN in patients treated with glucocorticoids is not known, suppression of osteoblastic activity and fat microemboli may play a role (*7,8*). Extrinsic compression of the sinusoidal vascular bed due to an increase in the size of the surrounding fat cells, which in experimental models exhibits an increase in volume as great as 25% (*9*), also has been implicated. This may compromise blood flow to the microarchitecture of the femoral head by increasing intraosseous venous pressure (*10*).

Among patients who develop AVN after renal transplantation, 80% become symptomatic within 2 yr after transplantation (*2–4*). Since there is some evidence that early surgical core decompression of the femoral head may arrest the progress of the disease and prevent collapse of the head (*8*), early diagnosis may be important. Bone scintigraphy with single-photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI) have been found useful in the detection of early or mild AVN of the hip in some patients whose plain radiographs are normal (*8,11–13*). We recently reported that some asymptomatic renal allograft recipients with MRI evidence of AVN of the hip exhibit spontaneous improvement of the imaging abnormalities and in some cases the MRI abnormality disappeared (*14*). Here we report the findings of paired MR images and SPECT bone scintigraphs in a subgroup of the transplant recipients described in our earlier report.

PATIENTS AND METHODS

As indicated previously (*14*), between October 1986 and December 1989, 104 renal allograft recipients were enrolled in the

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study (58 males, 46 females). The mean age at the time of transplantation was 36 yr (range, 14–59 yr). The protocol called for baseline MRI study and SPECT bone scintigraphy within 1 wk of transplantation and follow-up imaging 1, 3, 6, 12 and 24 mo after transplantation or as close to these intervals as possible.

MRI was performed with a 1.5 Tesla superconducting magnet (Vista 2055 HP, Picker International, Mayfield Village, OH). Contiguous 10 mm thick coronal images were obtained with relative T1 weighing (repetition times (TR) of 450–900 msec and echo times (TE) of 15–26 msec) and with relative T2 weighing (TR 2000/TE 90). The field of view was 35 cm and images were reconstructed using a 192 × 256 matrix.

The MR images were interpreted by three radiologists (EMB, ECK, KKK) who were "blinded" to the presence of symptoms or clinical course. The MRI was read as normal if the signal intensity was uniform throughout the femoral head. Criteria for the diagnosis of AVN included low signal intensity crescents in the weight-bearing portion of the femoral head, rings of low intensity, low signal dark bands with high signal intensity inner margins on high TR, high TE images, i.e., the "double line sign" (*15*), or collapse of the femoral head. Each lesion detected by MRI was measured in two dimensions on the image in which it appeared largest and the area of the lesion was calculated using the formula for the area of an ellipse: area = $\pi r_1 r_2$.

For bone scintigraphy, the Apex SP/6 Elscint (Boston, MA), Raytheon Spectrum 150 DT (Hudson, OH) or Siemens Dual-head Rotacamera (Des Plaines, IL) was used. Scintigraphy was performed after intravenous injection of 1110 MBq (30 mCi) of technetium-99m-methylene diphosphonate. Beginning at the time of injection, serial 2-sec images of the pelvis and hips were obtained in the anterior projection for 1 min, following which serial 1-min images of the same region were obtained for 20 min. Three hour delayed planar and SPECT images of the hips were then obtained with the patient in the supine position. Data were acquired in 360 degrees with a 128 × 128 matrix using 120 stops, each with a 10-sec acquisition. Butterworth filters with appropriate cutoff were employed during reconstruction. The bone scans were interpreted by three nuclear medicine physicians (HMP, ARS, HNW) who were unaware of the clinical status of the patients and a consensus reading was derived for each study. The activity in the femoral head was compared with that in the shaft and any decrease or increase in activity in the femoral head was considered abnormal.

All MRI studies were read in joint sessions of the three radiologists. All studies in each patient were read at one time in chronological order. No specialized scoring or weighting system was used and each study was read only as positive or negative for AVN. All disagreements were resolved by discussion or by using the majority opinion, however, no record of these discussions was kept. The same format was used for the bone scans.

For analysis, paired MR and bone scans (i.e., both the MRI study and the bone scan in each pair had been performed, by definition, within 30 days of each other) were compared.

RESULTS

As noted in our recent report, 413 MRI studies were performed in 103 patients (*14*). During the study period, 414 bone scans were performed in these subjects. Because of patient refusal due to the additional examination time required or equipment failure, 16 of these scans were obtained without SPECT. In a few cases in which an MRI study and bone scan were not obtained within 30 days of each other, neither imaging study was included in the analysis. Thus, data were available from 384 pairs of scans (both MRI study and bone scan) from 101 patients (202 hips). For 72 patients, at least three paired studies (maximum = 8, mean = 4.7) were available. Some asymptomatic patients had extra studies between 12 and 24 mo when, during the day of their routine clinic visit, MRI and bone scan times were available. The vast majority of the paired imaging studies were obtained on the same day (range 0–28 days, mean 1.44 days, s.d. 4.0).

TABLE 1
Results of the Paired Imaging Studies

Bone scan	MRI	No. of hips	Symptomatic	Total joint arthroplasty
Normal	Normal	115	0	0
Normal	Abnormal	10	0	0
Abnormal	Normal	13	0	0
Abnormal	Abnormal	6	5	3

Normal Bone Scan and Normal MRI

For 53 patients (106 hips), bone scans and MRI studies of both hips were normal throughout the study. In nine others, one hip was normal by both imaging techniques but the contralateral hip became abnormal on one or both imaging procedures (Table 1). None of the 115 hips that were normal by both MRI and bone scan became painful during the study.

Normal Bone Scan and Abnormal MRI

Bone scans of 10 hips (7 patients) were normal, although at least one MRI study showed evidence of AVN (Fig. 1). In eight of these hips, the MRI abnormality appeared within 4 mo after transplantation. In two hips (Patient VB, Fig. 1), the MRI abnormality was not seen until 13 mo after surgery. However, in this patient, no MRI studies were available between the fourth and twelfth months after surgery. None of the patients in this group developed hip pain.

In 6 of these 10 hips, the MRI abnormality was resolved 3–15 mo (mean, 8.5 mo) after it was first noted. In the other four, it remained stable over a mean follow-up period of 20 mo (range, 18–24 mo).

Abnormal Bone Scan and Normal MRI

For 13 hips (9 patients), serial MRI scans were normal but at least one bone scan exhibited findings consistent with AVN. In 11 hips (7 patients), the scan abnormality appeared within 2 mo after transplantation. In the remaining two subjects (Patients CS and ML, Fig. 2), the scan abnormality was first noted 12 mo and 14 mo, respectively, after surgery. None of these patients became symptomatic.

In each of these 13 hips, the lesion on bone scan was "hot," i.e., it was characterized by increased uptake of the radiopharmaceutical. In one subject, the plain radiograph revealed a large bone island in the femoral neck which was probably the cause of the increased uptake of radiopharmaceutical.

Over a follow-up period of 3–18 mo following appearance of the lesion (mean, 10 mo), the bone scan abnormality in 6 of the 13 hips resolved completely and in two others it improved markedly (Fig. 2). In five hips, the "hot" lesion remained unchanged over a mean interval of 15 mo (range, 5–23 mo) following its appearance.

Abnormal Bone Scan and Abnormal MRI

In three patients (6 hips), at least one bone scan and one MRI study developed abnormalities consistent with AVN (Fig. 3). In these cases, the imaging changes appeared within 4 mo after transplantation. In two patients (LP and MR, Fig. 3), whose imaging studies showed bilateral hip abnormalities, defects were seen first on the bone scan, which showed a "cold" defect in each case. The MRI studies in these two patients first became abnormal 2 and 5 mo later, respectively, at which time the bone scans of three of these hips were now "hot," while that of the fourth hip had become normal (right hip of Patient LP, Fig. 3). Six months later, however, a bone scan of that hip showed increased uptake of the radiopharmaceutical.

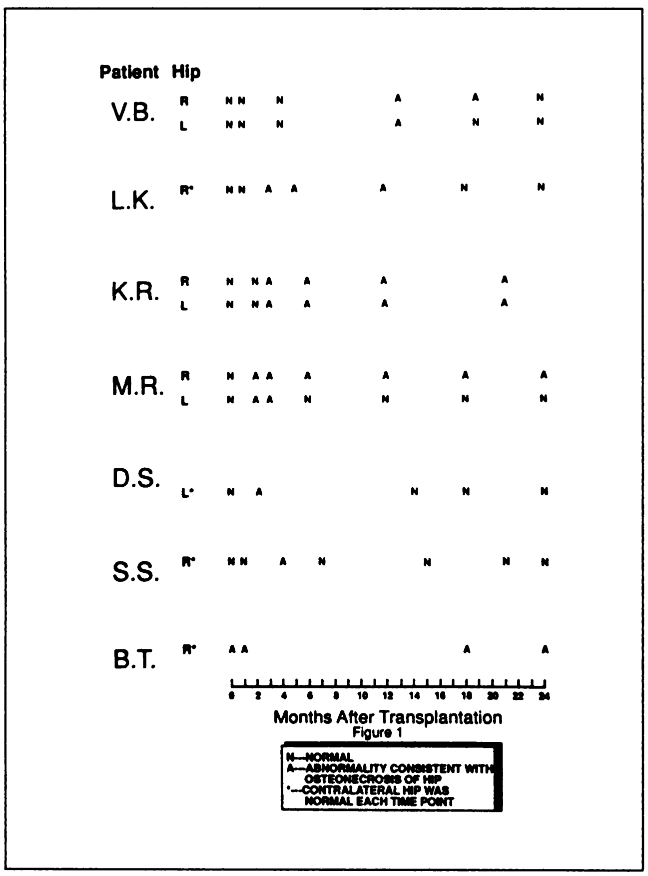

FIGURE 1. Clinical course and results of imaging studies in seven patients in whom bone scans were normal but MRI studies showed changes of AVN of the hip.

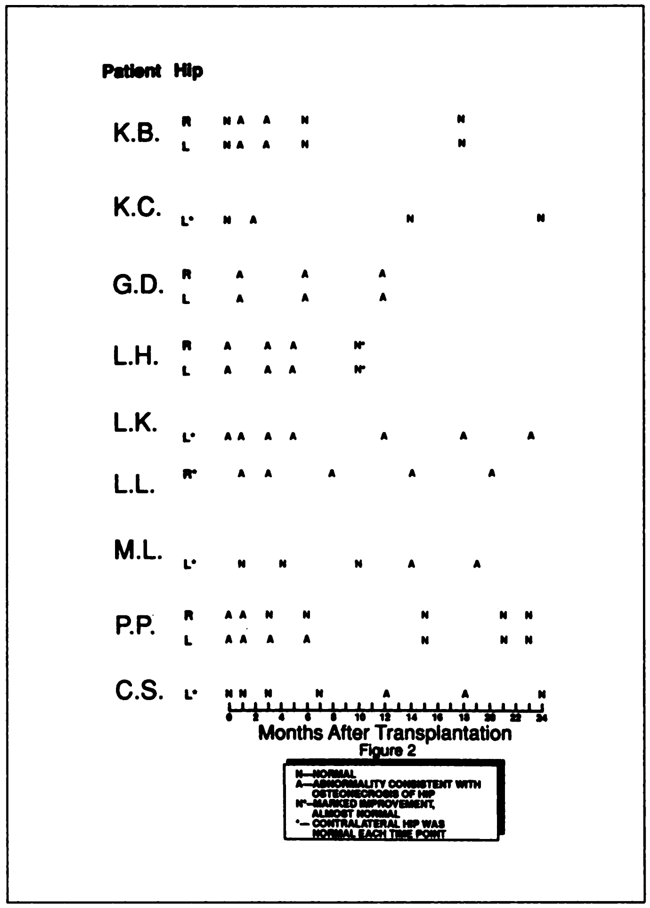

FIGURE 2. Clinical course and results of imaging studies in nine patients in whom MRI studies were normal but bone scans developed changes of AVN of the hip.

In the remaining patient in this group (Patient BS, Fig. 3), the bone scan and MRI study both exhibited bilateral abnormalities one month after transplantation. Both hips were "hot" on the bone scan. Although the bone scan of the left hip showed an abnormality indistinguishable from that seen on the initial scan 18 mo after transplantation, a repeat scan of the left hip 6 mo later was normal. In contrast, the scan abnormality in the right hip remained unchanged over the duration of the study.

In all six hips that exhibited abnormality, both bone scan and MRI persisted (mean follow-up after appearance of the lesion, 12 mo; range, 6–24 mo) (Fig. 3). Five hips became symptomatic during the study, three of which required joint arthroplasty. In each case the pathological findings were consistent with AVN.

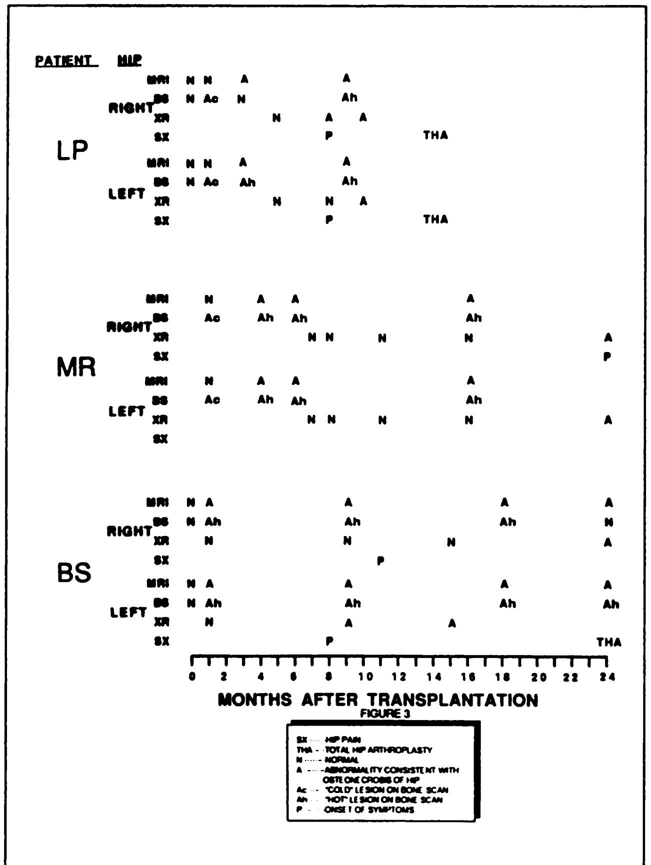

FIGURE 3. Clinical course and results of imaging studies in three patients in whom both MRI studies and bone scan developed changes of AVN of the hip.

Planar Bone Scans Without SPECT

As indicated above, 16 bone scans (32 hips) were obtained without SPECT. These studies were normal with two exceptions: in one patient, the planar images showed a "hot" hip 2 mo after surgery which was resolved in 12 mo and no MRI abnormalities were seen. In another individual, bilateral "cold" hips were seen one month after transplantation, at which time the MRI study was normal (patient MR, Fig. 3). Both "cold" hips became "hot" 2 mo later, at which time MRI studies now also exhibited changes consistent with AVN.

Bone Scintigraphy and Lesion Size on MRI

For all 46 hips that showed an abnormality on the MRI study, the area of the lesion was calculated. A strong correlation ($p < 0.001$, logistic regressive analysis) existed between the size of the lesion on the MRI and the abnormal bone scan. Fourteen of 16 MRI lesions larger than 500 mm^2 were accompanied by an abnormality on the bone scan. In each of these cases the bone scan lesion was "hot" (Table 2).

Patients Without Paired Studies

The 29 patients (58 hips) in whom fewer than three paired imaging studies were available were analyzed separately. Among these individuals, 14 hips (8 patients) were abnormal by MRI study, bone scan or both. For 9 of these 14 hips (5 patients), the bone scan was normal but at least one MRI study was abnormal. In each of these cases, the MRI abnormality developed within 10 mo after transplant surgery. Three of these hips (2 patients) became symptomatic, leading to total hip arthroplasty. Pathologic examination confirmed the presence of AVN in each case. In the remaining 6 hips (3 patients), the MRI abnormality remained stable and no symptoms of hip disease developed during the follow-up period of 3–9 mo.

For three hips (2 patients), MRI studies were normal but a "hot" bone scan abnormality was seen 1 mo (2 hips) and 24 mo (1 hip) after transplantation. Neither of these patients underwent follow-up imaging procedures and neither had symptoms. Both were lost to follow-up. In another patient in this group, both hips showed abnormality in the MRI study 2 mo after transplantation at which time the bone scan was normal. However, 8 mo later the bone scan showed increased uptake in one hip. The patient did not become symptomatic over a follow-up period of 9 mo.

DISCUSSION

Both MRI and scintigraphy can detect AVN of the femoral head prior to the appearance of changes on the plain radiographs (*16,17*). Although the natural history of AVN is not well known, aggressive surgical therapy has been advocated for management of AVN at this stage (*18*). In the past, spontaneous regression of preradiographic AVN was considered to be rare (*19*). Recent data, however, suggest that it may be relatively common (*14,17,20*).

In this prospective study, 10 patients (14 femoral heads) developed lesions seen by MRI and/or scintigraphy that were subsequently resolved (Fig. 1 VB, MR, DS, SS; Fig. 2 KB, KL, LH, PP, CS). Although a tissue diagnosis confirming AVN was not obtained, the imaging findings in these hips were identical to those in the three patients who had surgically proven AVN and corresponded to the pattern for AVN reported in the literature (*8,12,13*). This supports the concept of subclinical AVN

TABLE 2
Relationship of Lesion Size on MRI to Findings on Bone Scan

Bone scan results	Lesion size on MRI	
	<500 mm^2	>500 mm^2
Abnormal*	2	14
Normal	28	2

*All abnormal bone scans were "hot," i.e., they showed increased uptake of the radiopharmaceutical in the hip.

associated with corticosteroid administration after renal transplantation which may be reversible in some cases.

Insufficiency fractures associated with corticosteroids can produce "hot" lesions on the bone scintigraphy but they are almost always symptomatic. Another explanation of these findings could be some form of undefined self-limited "corticosteroid osteopathy." Whatever these findings may mean, one thing is clear: the decision to intervene surgically should not be based solely on the results of the MRI or SPECT images.

Most reports suggest that the sensitivity of MRI in the diagnosis of AVN of the femoral head ranges from 85% to 100% (*17,21–24*). In addition to its high sensitivity in the detection of AVN, MRI has the advantage of demonstrating specific anatomic detail of both bone and soft tissue which may lead to a diagnosis of septic arthritis, insufficiency fracture or some other cause of hip pain.

On the bone scan, the earliest finding in AVN is a "cold" defect, due to impaired vascular supply of the femoral head. This occurs prior to the radiographic evidence of AVN and has been described extensively (*25*). Over the course of the disorder, weeks to months after appearance of the "cold" defect, increased uptake of the radiopharmaceutical occurs (i.e., a "hot" lesion) due to hyperemia and ingrowth of osteoblasts (*26*). In our study, "cold" defects were seen in four hips in two patients (one had only a planar study) 2 to 3 mo before the MRI became abnormal.

As our data show, increased accumulation of the radiopharmaceutical in the hips was dependent upon the size of the lesion seen in the MRI study. The larger the lesion, the greater the likelihood of a "hot" lesion on the bone scan.

Since bone scintigraphy creates an image of the entire skeleton, areas of silent AVN at other sites may be demonstrated in patients who present with hip pain due to AVN of the femoral head (*27,28*). Also, information about renal function may be obtained if the allograft is imaged during the first few minutes after injection, since MDP is excreted by the kidneys in the same fashion as the conventional renal imaging agent, diethylene triamine pentaacetic acid (DTPA) (*29*).

Both of the imaging studies utilized in this study have their advantages. Since biopsies were not performed in asymptomatic patients, the data cannot be used to recommend one imaging procedure over the other. There were 24 asymptomatic hips with abnormalities detected only by MRI in 10 hips and only by bone scan in 14 hips. This suggests that both imaging studies should be performed if one wants to detect subclinical AVN in as many patients as possible, which may be important if treatment of subclinical disease is shown to prevent development of clinical AVN. However, if one's goal is only to diagnose AVN in symptomatic patients at risk for the disease, then either MRI or scintigraphy is sufficient, because in our experience all symptomatic hips were correctly diagnosed by both imaging studies.

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REFERENCES

1. Farge D, Parfrey PS, St Andre C, Kuo Y-l, Guttmann RD. Aseptic necrosis following renal transplantation: a 25-year experience. *Transplant Proc* 1985;17:1947–1950.
2. Elmstedt E. Avascular bone necrosis in the renal transplant patient: a discriminate analysis of 144 cases. *Clin Orthop* 1981;158:149–157.
3. Ibels LS, Alfrey AC, Huffer WE, Weil R III. Aseptic necrosis of bone following renal transplantation: experience in 194 transplant recipients and review of the literature. *Medicine* 1978;57:25–45.
4. Susan LP, Braun WE, Banowsky LH, Straffon RA, Bergfeld JA. Avascular necrosis following renal transplantation: experience with 449 allografts with and without high dose steroid therapy. *Urology* 1978;11:225–229.
5. Andersen J, Nielsen HE. Osteonecrosis and spontaneous fractures following renal transplantation: a longitudinal study of radiological bone changes and metacarpal bone mass. *Acta Orthop Scand* 1981;52:397–404.
6. Brazil M, Linderer RJ, Dickhans MJ, Garvin PJ. Aseptic necrosis after renal transplantation. *Arch Surg* 1986;121:803–805.
7. Zizic TM, Hungerford DS, Stevens MB. Ischemic bone necrosis in systemic lupus erythematosus I. The early diagnosis of ischemic necrosis of bone. *Medicine* 1980;59:134–142.
8. Gillespy T III, Genant HR, Helms CA. Magnetic resonance imaging of osteonecrosis. *Rad Clin North Am* 1986;24:193–208.
9. Wang G-J, Sweet DE, Reger SI, Thompson RC. Fat cell changes as a mechanism of avascular necrosis of the femoral head in cortisone treated rabbits. *J Bone Joint Surg* 1977;59-A:729–735.
10. Wang G-J, Dughman SS, Reger SI. The effect of core decompression on femoral head blood flow in steroid-induced avascular necrosis of the femoral head. *J Bone Joint Surg* 1985;67A:121–124.
11. Spencer JD, Maisey M. A prospective scintigraphic study of avascular necrosis of bone in renal transplant patients. *Clin Orthop* 1985;194:125–135.
12. Collier BD, Carrera CF, Johnson RP, et al. Detection of femoral head avascular necrosis in adults by SPECT. *J Nucl Med* 1985;26:979–987.
13. Miller IL, Savory CG, Polly DW Jr, Graham GD, McCabe JM, Callaghan JJ. Femoral head osteonecrosis: detection by magnetic resonance imaging versus single photon emission computed tomography. *Clin Orthop* 1989; 247:152–162.
14. Kopecky KK, Braunstein EM, Brandt KD, et al. Apparent avascular necrosis of the hip: appearance and spontaneous resolution of MR findings in renal allograft recipients. *Radiology* 1991;179:523–527.
15. Mitchell DG, Rao VM, Dalinka MK, et al. Femoral head avascular necrosis: correlation of MRI, radiographic staging, radionuclide imaging and clinical findings. *Radiology* 1987;162:709–715.
16. Coleman BG, Kressel HY, Dalinka MK, Scheibler ML, Burk DL, Cohen EK. Radiographically negative avascular necrosis: detection with MRI. *Radiology* 1988;168:525–528.
17. Stulberg BN, Levine M, Bauer TW, et al. Multimodality approach to osteonecrosis of the femoral head. *Clin Orthop* 1989;240:181–193.
18. Ficat RP. Idiopathic bone necrosis of the femoral head: early diagnosis and treatment. *J Bone Joint Surg* 1985;67B:3–9.
19. Boettcher WC, Bonfiglio M, Smith K. Nontraumatic necrosis of the femoral head. II. Experiences in treatment. *J Bone Joint Surgery* 1970; 52A:322–329.
20. Bassett LW, Gold RH, Reicher M, Bennett LR, Tooke SM. Magnetic resonance imaging in the early diagnosis of ischemic necrosis of the femoral head. *Clin Orthop* 1987;214:237–248.
21. Camp JF, Colwell CW. Core decompression of the femoral head for osteonecrosis. *J Bone Joint Surg* 1986;68A:1313–1319.

22. Markisz JA, Knowles RJR, Altchek DW, Schneider R, Whalen JP, Cahill PT. Segmental patterns of avascular necrosis of the femoral heads: early detection with MRI. *Radiology* 1987;162:717–720.
23. Beltran J, Herman LJ, Burk JM, et al. Femoral head avascular necrosis: MRI with clinical-pathologic and radionuclide correlation. *Radiology* 1988;166:215–220.
24. Glickstein MF, Burk DL Jr, Schiebler ML, et al. Avascular necrosis versus other diseases of the hip: sensitivity of MRI. *Radiology* 1988;169: 213–215.
25. Collier BD Jr, Hellman RS, Krasnow AZ. Bone SPECT. *Semin Nucl Med* 1987;17:247–266.
26. D'Ambrosia RD, Shoji H, Riggnis RS, Stadalnik RC, DeNardo GL. Scintigraphy in the diagnosis of osteonecrosis. *Clin Orthop* 1978;130:139–143.
27. Davidson JK, Tsakiris D, Briggs JD, Junor BJR. Osteonecrosis and fractures following renal transplantation. *Clin Radiology* 1985;36:27–35.
28. Burt RW, Matthew TJ. Aseptic necrosis of the knee: bone scintigraphy. *AJR* 1983;138:571–573.
29. Siddiqui AR, Cohen M, Moran DP. Abdominal masses in children: multiorgan imaging with ^{99m}Tc methylene disphosphonate. *AJR* 1982;139:35–38.

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 below.

Drugs that typically slow gastric emptying include which of the following?

1. nicotine
2. verapamil
3. isoproterenol
4. levodopa
5. metoclopramide
6. domperidone

True statements concerning Barrett's esophagus include which of the following?

7. More than half of patients with Barrett's esophagus will develop squamous cell cancer of the esophagus.
8. The radiologic appearance on upper gastrointestinal radiography is diagnostic in most patients.
9. In patients with gastroesophageal reflux, an increase in symptoms suggests development of Barrett's esophagus.
10. Sequential ^{99m}Tc pertechnetate imaging in patients with Barrett's esophagus is helpful in determining which patients will develop malignancy.

True statements concerning scintigraphic evaluation of peritoneovenous shunt patency include which of the following?

11. Because of its low specificity, it is not helpful in most cases.
12. When ^{99m}Tc MAA is injected intraperitoneally, nonvisualization of the efferent limb of the shunt indicates shunt malfunction.
13. The afferent portion of the shunt is the most frequent site of shunt malfunction.
14. Congestive heart failure occasionally causes false-positive studies.
15. Direct puncture of the efferent limb of the shunt occasionally is necessary to precisely locate the site of malfunction.

SELF-STUDY TEST

Gastrointestinal Nuclear Medicine

ANSWERS

Items 1-6: Effect of Drugs on Gastric Emptying

Answers:1, T; 2, T; 3, T; 4, T; 5, F; 6, F

Many drugs have been shown to slow gastric emptying,and their effects must be considered in reporting the results of gastric emptying studies. The nicotine associated with cigarette smoking has been shown to slow gastric emptying. In addition, calcium channel blockers have been shown to decrease the amplitude and duration of contractions of smooth muscle throughout the gastrointestinal tract. Calcium channel blockers either decrease the number of calcium channels nifedipine, verapamil, diltiazem and/or decrease the rate of calcium transport in the remaining channels verapamil, diltiazem. Adrenergic agonists, especially beta agonists such as isoproterenol, all tend to delay gastric emptying. Dopamine is a neural transmitter, which appears to be involved primarily in gastric relaxation. Dopamine agonists, such as levodopa, will slow gastric emptying. The D-receptor antagonist metoclopramide stimulates gastric contractions and, thus, increases the rate of gastric emptying. It is also felt to have a central antiemetic effect. Domperidone is another dopaminergic antagonist, which also accelerates gastric emptying and has been shown to increase gastric antral contractions.

References

1. Berkowitz DM, McCallum RW. Interaction of levodopa and metoclopramide on gastric emptying. *Clin Pharmacol Ther* 1980;27:414-420.
2. Broekaert A. Effect of domperidone on gastric emptying and secretion. *Postgrad Med J* 1979;55:11-14.
3. Jacob H, Brandt LJ, Farkas P, Frishman W. Beta-adrenergic blockade and the gastrointestinal system. *Am J Med* 1983;74:1042-1051.

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