RRH, Lavender JP. Autologous granulocyte scanning of painful prosthetic joints. *J Bone Joint Surg [Br]* 1986; 68-B:647–652.
15. Mountford PJ, Hall FM, Wells CP, Coakley AJ. ^{99m}Tc-MDP, ^{67}Ga-citrate and ^{111}In-leukocytes for detecting prosthetic hip infection. *Nucl Med Comm* 1986; 7:113–120.
16. Pring DJ, Henderson RG, Keshavarzian A, et al. Indium-granulocyte scanning in the painful prosthetic joint. *AJR* 1986; 146:167–172.
17. Prchal CL, Kahen HL, Blend MJ, Barmada R. Detection of musculoskeletal infection with the indium-111-leukocyte scan. *Orthopedics* 1987; 10:1253–1257.
18. Ouzounian TJ, Thompson L, Grogan TJ, Webber MM, Amstutz HC. Evaluation of musculoskeletal sepsis with indium-111-white blood cell imaging. *Clin Orthop* 1987; 221:304–311.
19. Wukich DK, Abreu SH, Callaghan JJ, et al. Diagnosis of infection by preoperative scintigraphy with indium-labeled white blood cells. *J Bone Joint Surg [Am]* 1987; 69-A:1353–1360.
20. Gomez-Luzuriaga MA, Galan V, Villar JM. Scintigraphy with Tc, Ga, and In in painful total hip prostheses. *Int Orthop* 1988; 12:163–167.
21. Johnson JA, Christie MJ, Sandler MP, Parks PF Jr, Homra L, Kaye JJ. Detection of occult infection following total joint arthroplasty using sequential technetium-99m-HDP bone scintigraphy and indium-111-WBC imaging. *J Nucl Med* 1988; 29:1347–1353.
22. Magnuson JE, Brown ML, Hauser MF, Berquist TH, Fitzgerald RH Jr, Klee GG. In-111-labeled leukocyte scintigraphy in suspected orthopedic prosthesis infection: comparison with other imaging modalities. *Radiology* 1988; 168:235–239.
23. Fink-Bennett D, Stanisavljevic S, Blake D, Weber K, Weir J, Mayne B. Improved accuracy for detecting an infected hip arthroplasty (HA): sequential technetium-99m-sulfur colloid (TSC)/indium-111(In-111) WBC imaging [Abstract]. *J Nucl Med* 1988; 29:P887.
24. Palestro CJ, Charalel J, Vallabhajosula S, Greenberg M, Goldsmith SJ. In-WBC as a bone marrow imaging agent [Abstract]. *J Nucl Med* 1987; 27:P574.
25. Feigin DS, Strauss HW, James AE. Detection of osteomyelitis by bone marrow scanning [Abstract]. *J Nucl Med* 1974; 15:P490.
26. Thakur ML, Lavender JP, Arnot RN, Silverstein DJ, Segal AW. Indium-111-labeled autologous leukocytes in man. *J Nucl Med* 1977; 18:1014–1021.
27. Harris WH. Total joint replacement. *N Engl J Med* 1977; 297:650–651.
28. Charnley J, Eftekar N. Postoperative infection in total prosthetic replacement arthroplasty of the hip joint: with special reference to the bacterial content of the air of the operating room. *Br J Surg* 1969; 56:641–649.
29. Andrews HJ, Arden GP, Hart GM, Owen JW. Deep infection after total hip replacement. *J Bone Joint Surg [Br]* 1981; 63B:53–57.
30. Lidwell OM, Lowbury EJL, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultra clean air in operating room on deep sepsis in the joint after total hip or knee replacement: a randomized study. *Br Med J* 1982; 285:10–14.
31. Maderazo EG, Judson S, Pasternak H. Late infections of total joint prostheses. A review and recommendations for prevention. *Clin Orthop* 1988; 229:131–142.
32. Hunter GA, Welsh RP, Cameron HU, Bailey WH. The results of revision of total hip arthroplasty. *J Bone Joint Surg [Br]* 1979; 61-B:419–421.
33. Weissman BN. The radiology of total joint replacement. *Orthop Coin North Am* 1983; 14:171–191.
34. Skeletal Scintigraphy. In: Galasko CSB, ed. *Orthopaedics.* Edinburgh: Churchill Livingstone; 1984;135–162.
35. Utz JA, Lull RJ, Galvin EG. Asymptomatic total hip prosthesis: natural history determined using Tc-99m-MDP bone scans. *Radiology* 1986; 161:509–512.
36. Merkel KD, Fitzgerald RH Jr, Brown ML. Scintigraphic examination of total hip arthroplasty: comparison of indium with technetium-gallium in the loose and infected canine arthroplasty. In: Welch RB, ed. *The hip. Proceedings of the twelfth open scientific meeting of the Hip Society.* Atlanta; 1984:163–192.
37. Van Dyke D, Shkurkin C, Price D, Yano Y, Anger HO. Differences in distribution of erythropoeitic and reticuloendothelial marrow in hematologic disease. *Blood* 1967; 30:364–374.
38. Custer RP. *An atlas of the blood & bone marrow.* 2nd edition. Philadelphia: WB Saunders; 1974:33–42.
39. Oswald SG, Van Nostrand D, Savory CG, Callaghan JJ. Three-phase bone scan and indium white blood cell scintigraphy following porous-coated hip arthroplasty: a prospective study of the prosthetic tip. *J Nucl Med* 1989; 30:1321–1331.

Editorial
Diagnosing Prosthetic Joint Infection

For the past 17 years, we have been studying the problem of how to best diagnose infection in a prosthetic joint by nuclear imaging. We have studied prosthetic joints with various combinations of technetium bone scans, gallium, indium leukocytes, indium chloride, and newer infection imaging formulations including indium-labeled gamma globulin and ^{99m}Tc-HMPAO. Palestro et al. in this issue of *JNM* presents the case for the combination of ^{111}In-labeled leukocytes and ^{99m}Tc-colloid bone marrow imaging. To better understand why this has been so problematic a clinical diagnostic imaging challenge, we need to review our past history in imaging infected prosthetic joints, including the hows and whys of the various radiopharmaceuticals used.

Between 1973 and 1979, Reing et al. and Bauer et al. (*1,2*) reported results of trials of bone scans and gallium scans in patients suspected of having infection or loosening of prostheses. Conclusions often stated that a normal bone scan excluded the possibility of need for surgical

Received Aug. 29, 1990; accepted Aug. 29, 1990.
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intervention to correct loosening or infection as a cause for the patient's pain. Abnormal scans, bone and gallium, could not reliably distinguish between infection and loosening. In fact, we have all seen strikingly abnormal gallium scans that were not associated with infection, but rather, with "abundant granulation tissue" related to chronic loosening. Rosenthall et al. reported in 1979 that incongruent gallium-technetium uptake was the hallmark for infection in prosthetic joints (*3*).

Later studies confirmed these earlier conclusions (*4–6*). For example, Schauwecker (*4*) studied 56 patients suspected of having osteomyelitis with gallium-technetium bone scans and reported that, when normal, it was excellent for ruling out osteomyelitis. The gallium-technetium scans were reliable indicators of osteomyelitis when the relative uptake of gallium exceeded that of technetium or the distribution of gallium was different from that of technetium (incongruence). However, only 28% of patients with osteomyelitis showed the patterns of gallium exceeding bone scan uptake or incongruence. Tumeh et al. (*5*) reported a similar comparative study in which the authors emphasized defining the various patterns of gallium-bone scan uptake in patients with suspected osteomyelitis. They described five patterns and noted that only the patterns of (a) gallium uptake exceeding bone scan uptake and/or (b) incongruence of gallium and bone scan uptake correlated well with the presence of osteomyelitis. Tumeh et al. further found that only about one-fourth of patients with osteomyelitis showed those patterns on their scans. Schauwecker and Tumeh concluded similarly that although gallium could be relied upon to exclude osteomyelitis when normal, the Ga-Tc combination was a good indicator of infection in only about one-fourth to one-third of patients who had infection.

The results with ^{111}In-leukocytes were much more appealing. When correlated with bone scans, several studies showed sensitivities of greater than 88% and similar specificities (*7,8*), but the following difficulties were noted:

1. Because of image resolution problems, soft-tissue uptake was sometimes not separable from abnormal bone uptake.
2. Because indium leukocytes are concentrated in some arthritides (e.g., rheumatoid arthritis, which may be the underlying disease process which led to the prosthesis), abnormal indium uptake was seen without infection.
3. Because as Palestro points out, indium activity is normally seen in marrow and can be misleading in evaluating infection.
4. Because the presence of heterotropic bone containing marrow adjacent to the prosthetic joint can confuse the interpretation of infection.
5. Because as Schauwecker has shown, indium-leukocytes have a decreasing sensitivity for demonstrating infection in bones that are more central than peripheral in location and infections that are more chronic. For chronic hip infection, indium-leukocyte sensitivity may be decreased to as low as 50%.

The hallmark of positive indium-leukocyte studies is migration of polymorphonuclear leukocytes to a site of infection. While acute infection is indeed characterized by that migration, chronic inflammation shows migration of mononuclear cells, lymphocytes, and fibroblasts. Since we inject a mixed population of indium-labeled cells, the success of the scan depends somewhat on the white count differential in the patient's blood. Using ^{99m}Tc-colloid for bone marrow imaging makes sense for diagnosis of osteomyelitis. The pathophysiology of osteomyelitis involves "sluggish" blood flow through the marrow with stasis, which may result in infarctive changes and predisposition to infection. Thus, typically, the bone marrow scan is "cold," giving the incongruent pattern with indium-leukocytes. One problem, not addressed by Palestro, is that the presence of the prosthesis displaces normal marrow, and even in the absence of infection, the marrow scan will therefore show photopenia in the regions of concern.

For evaluating prosthetic joints for infection, radionuclide approaches are clearly preferred over other imaging, such as magnetic resonance (MR) or computed tomography (CT). MR images are degraded by metal, usually a component of the prostheses, and CT does not visualize cortical bone well. The cost of radionuclide imaging to assess presence of infection is substantial. An alternative procedure would be needle aspiration and culture. The cost of the test, with cultures and laboratory processing, is about $288.00 at my institution. Several reports (*10,11*) have advocated aspiration and culture of joint fluid in cases where infection is considered following plain radiographs and bone scan.

Another major concern about indium-labeled leukocytes is the handling of whole blood to separate cells, label cells, and reinjection. The process offers several opportunities for iatrogenic errors. In this era of HIV positive prevalences, we should be concerned with minimizing work with blood and blood products. Even strict adherence to quality assurance measures as mandated by JCAHO principles and good medical practices to maintain the lowest misadministration incidences (approaching the unavoidable human error levels), will not totally eliminate a rare misadministration. Misadministration statistics in nuclear medicine demonstrate impressively low incidences of diag-

nostic misadministrations for the past years (about 1 in 10,000 administrations according to NRC data). The prevalence of HIV-positive blood poses a risk which unfortunately will manifest as a rare, tragic misadministration. Therefore, although the indium-leukocyte study is the best test available, in view of the multitude of problems attached to indium-leukocyte imaging, we may wish to continue to pursue alternatives for infection imaging.

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REFERENCES

1. Reing MC, Richin PI, Kenmore PL. Differential bone scanning in the evaluation of a painful total joint replacement. *J Bone Joint Surg Am* 1979; 61:933–936.
2. Bauer GCH, Lindberg L, Naverstein Y, Sjöstrand LO. Radionuclide scintimetry in infected total hip arthroplasty. *Acta Orthop Scand* 1973; 44:439–450.
3. Rosenthall L, Lisbona R, Hernandez M, Hadkipavlov A. ^{99m}Tc-PP and ^{67}Ga imaging following insertion of orthopedic devices. *Radiology* 1979; 133:717–721.
4. Schauwecker DS, Park HM, Mock BH, et al. Evaluation of complication osteomyelitis with Tc-99m-MDP, In-111-granulocytes, and Ga-67-citrate. *J Nucl Med* 1984; 25:849–853.
5. Tumeh SS, Aliabadi P, Weissman BN, McNeil JB. Chronic osteomyelitis: bone and gallium scan patterns associated with active disease. *Radiology* 1986; 158:685–688.
6. Merkel KD, Brown ML, Dewanjee MK, Fitzgerald RH. Comparison of indium-labeled leukocyte imaging with sequential technetium-gallium scanning in the diagnosis of low-grade musculoskeletal sepsis. *J Bone Joint Surg Am* 1985; 67A:465–476.
7. Magnuson JE, Brown ML, Hauser MF, et al. In-111-labeled leukocyte scintigraphy in suspected orthopedic prosthesis infection: comparison with other imaging modalities. *Radiology* 1988; 168:235–239.
8. Johnson JA, Christie MJ, Sandler MP, et al. Detection of occult infection following total joint arthroplasty using sequential technetium-99m-HDP bone scintigraphy and indium-111-WBC imaging. *J Nucl Med* 1988; 29:1347–1353.
9. Chafetz N, Hattner RS, Ruarke WC, Helms CA, Genant HK, Murray WR. Multinuclide digital subtraction imaging in symptomatic prosthetic joints. *AJR* 1985; 144:1255–1258.
10. Aliabadi P, Tumeh S, Weissman BN, McNeil B. Cemeted total-hip prosthesis: radiographic and scintigraphic evaluation. *Radiology* 1989; 173:203–206.