absence of pertechnetate in the preparation, and a scan of the lungs and the liver (10 min. p.i.) will establish the integrity of the lipophilic ^{99m}Tc-HMPAO in the administered solution.

The correct diagnosis of cerebral death will be much safer using these quality control procedures, especially with regard to the fast and easy handling of the methods mentioned above.

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REPLY: We agree that radiopharmaceutical quality assurance is especially important in the case of ^{99m}Tc-HMPAO because of its short half-life. This quality assurance takes the form of both chromatography and assessment of the in-vivo distribution. With such a short-lived radiopharmaceutical, the chromatographic assessment may, in our view, be properly performed after the fact analogous to common practice with short-lived positron pharmaceuticals. The cases presented by Brandau et al. demonstrate the importance of attention to the extra-cranial biodistribution and we thank them for pointing that out.

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Synthesis of ^{18}F-6-FD

TO THE EDITOR: In a recent report in *The Journal of Nuclear Medicine*, Chen et al. (*1*) reported a "Quality Control Procedure for 6-[^{18}F]-fluoro-L-DOPA (6-FD)." Although the radiosynthetic method (*2*) used by these authors has been superseded by more regioselective synthesis (*3,4*), we found their studies on the stability of 6-FD to be very useful to the routine production of this radiotracer.

We synthesize ^{18}F-6-FD in our institution using L-ethyl-N-trifluoroacetyl-[β-3,4-dimethoxy-6-mercuric-trifluoroacetyl-phenyl)]alaninate (obtained from BIS Chem. Inc., Quebec, Canada) and ^{18}F-acetylhypofluorite produced from ^{18}F-F_2 made from proton reaction on ^{18}O-O_2 (*5*). Purification of the ^{18}F-6-FD product essentially followed the method by Adam and Jivan (*4*) except the semi-prep HPLC mobile phase we used was 0.02*M* NaOAc pH 3.5. As Chen et al. (*1*) and others have observed, we found that shortly after neutralization to pH 6-7, the HPLC purified ^{18}F-6-FD solution turned brownish in color which further darkened with time. In light of the finding by Chen et al. (*1*) that the addition of 0.15% Na_2EDTA prevented or at least significantly slowed decomposition of ^{18}F-6-FD, we included 0.15% Na_2EDTA to the HPLC mobile phase used without affecting the separation of ^{18}F-6-FD. However, even with this added EDTA, slight darkening of the solution containing the ^{18}F-6-FD HPLC peak was observed within an hour after neutralization even though the solution was kept in ice and in the dark as recommended by Chen et al. (*1*).

Due to the known instability of L-DOPA at pH 7 and above (*6*), we suspected pH to be a most critical factor in the decomposition of ^{18}F-6-FD. To test this hypothesis, we divided a dose of ^{18}F-6-FD (8 mCi, 500 mCi/mmol, 10 ml 0.02*M* NaOAc pH 3.5 + 0.15% Na_2EDTA) into four sterile and capped vials. Two vials were neutralized to pH 7 using 1*M* NaOH while the other two were kept at pH 3.5. One pH 7 sample and one pH 3.5 sample were bubbled with He gas while another pH 3.5 sample was bubbled with O_2 gas. These vials were kept overnight in ice and in a dark room. As seen in the photograph (Fig. 1), low pH is indeed critical to the stability of ^{18}F-6-FD while the effect of oxygen is more pronounced at neutral pH. HPLC analysis using three detectors, UV = 254nm, electrochemical = +0.9V, and a pair of coincidence detectors, showed unchanged ^{18}F-6-FD in both pH 3.5 samples. On the other hand, more complicated chromatograms were seen in the UV and radioactivity tracings for both pH 7 samples. No electrochemical trace was seen in the pH 7 sample under ambient air while a late eluting peak was seen for the pH 7 sample under He. Further studies to identify the products are under way to elucidate the mechanism of

FIGURE 1
Effect of pH and oxygen on the stability of ^{18}F-6-FD. 6-FD samples from left to right are: (1) pH 7 under ambient air; (2) pH 7 under helium gas; (3) pH 3.5 under helium gas; and (4) pH 3.5 under oxygen gas. Note that samples (3) and (4) are clear, sample (2) is slightly colored, while sample (1) is dark.

this decomposition with the aim of routinely preparing stable ^{18}F-6-FD parenteral solutions. Nonetheless, based on these observations, in addition to the inclusion of EDTA, we recommend that the pH of ^{18}F-6-FD solution be kept at around 3.5 and adjusted, if desired, immediately prior to administration. We found pH to be most critical to stability since an uncapped ^{18}F-6-FD sample kept at pH 3.5 but under ambient temperature and light was found by HPLC (UV + EC detectors) analysis to be unchanged after two weeks.

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SELF-STUDY TEST
Skeletal Nuclear Medicine

ANSWERS

(continued from p. 2028)

With both acute rheumatoid arthritis and septic arthritis, there is increased uptake of ^{99m}Tc-MDP and ^{67}Ga. On average, the degree of ^{67}Ga uptake is higher in septic arthritis, but the overlap in concentration between the two conditions is considerable, so that in any given individual a distinction is not readily made by scintigraphy. Aspiration of the joint with culture of synovial fluid is the best method of diagnosis

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ITEM 4: Sacroiliac Joint Scintigraphy

ANSWERS: **A:** *T;* **B:** *F;* **C:** *T;* **D:** *T;*

Low-grade, symmetrical increases in ^{99m}Tc-MDP concentration about the sacroiliac joints are difficult to evaluate subjectively. It is for this reason that various computer-assisted approaches have been devised for quantifying sacroiliac joint uptake. Most of these are successful in separating groups of normal subjects from those with ankylosing spondylitis or other inflammatory spondyloarthropathies, but the overlap has been found to be too great for these techniques to qualify as screening procedures.

Metabolic bone disease and osteoarthritis are characterized also by high periarticular concentrations of ^{99m}Tc-MDP and cannot be distinguished reliably from ankylosing spondylitis. Diffuse idiopathic skeletal hyperostosis typically has shown normal uptake in lumbar vertebrae and the sacroiliac joints, presumably because the disease has stabilized and become metabolically inactive by the time it is recognized radiographically.

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ITEM 5: Scintigraphic Evaluation of Total-Hip Prostheses

ANSWERS: **A:** *F;* **B:** *F;* **C:** *F;* **D:** *T;* **E:** *F*

Increased uptake of ^{99m}Tc-MDP about the stem of the femoral component of a hip prosthesis is a normal occurrence in the first 8–12 months postimplant. Continued uptake beyond this time frame is strong evidence of loosening. Normally, increased activity in the acetabulum, greater trochanter, and femoral stem tip may persist for up to 2 years after surgery. A persistent focal uptake at the tip of the femoral stem, with no other associated abnormalities, beyond 12 months, is not a pathognomonic sign of prosthetic loosening because it may occur in 10%–20% of asymptomatic patients. It has been attributed to micromovement of the tip, which does not constitute clinically significant loosening.

There may be some ^{67}Ga uptake surrounding the femoral stem in the same distribution as ^{99m}Tc-MDP for several months after implantation. Beyond that time, accumulation of ^{67}Ga in a distribution congruent with ^{99m}Tc-MDP is an indeterminate finding with respect to the presence of infection. If the intensity of ^{67}Ga uptake approximates or exceeds that of ^{99m}Tc-MDP, then infection is more likely. Incongruent distribution of ^{67}Ga or ^{111}In-leukocytes indicates a high probability for infection involving soft tissue, bone, or both.

Persistently increased uptake of ^{99m}Tc-MDP in heterotopic bone, i.e., higher than that in the shaft of the femur, occurs in the majority of patients with hip prostheses, even though the radiographic manifestations of maturity (bone cortication and trabeculation) are present. This appears to be contrary to the observations in patients with heterotopic bone formation secondary to parapelgia; in such patients, the ^{99m}Tc-MDP uptake decreases as the bone matures.

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Note: For further in-depth information, please refer to the syllabus pages included at the beginning of *Nuclear Medicine Self-Study Program I: Part I.*