estimates made for individual and population doses was not recognized in the official studies.

However, the best way for a reader of *The Journal of Nuclear Medicine* to determine what my report says is to send for a copy of either the four-page summary or the full 300-page report. Copies can be obtained from the Three Mile Island Public Health Fund, 1622 Locust St, Philadelphia, PA 19103.

References

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Electrophoretic Analysis of Technetium-99m MDP Complexes

TO THE EDITOR: In a recent journal article (*1*), Najafi and Hutchinson addressed a very important question: "what is the explanation for the occasional liver uptake in bone scintigraphy which is not readily explained by findings on paper chromatography?" The approach by the authors to answer this question and their subsequent conclusions are the subject of this correspondence.

As the authors stated, it is difficult to do preparative work with electrophoresis to study the biological behavior of each complex individually. Their goal of using electrophoresis to find conditions for the formation of a single technetium-99m (Sn) methylene diphosphonate (^{99m}Tc(Sn)MDP) complex appears naive to us, and several points should be considered in interpretating their data.

Electrophoresis separates on the basis of charge. The charge on the ^{99m}Tc (Sn) MDP complex is a function of the pH of the solvent. Unfortunately, acetate (pKa = 4.75) is not a buffer at pH 7, so it is difficult to know the pH during electrophoresis. The authors' titration of MDP shows that the pKa_3 is ~7. At 0.02M, MDP likely was acting as its own buffer during electrophoresis. However, MDP would only be an effective buffer over the range of pH 6–8, with the buffering capacity greatest at pH 7 and weakest at the extreme of the range.

The authors followed the electrophoretic movements of radioactive complexes and showed that ^{99m}Tc (Sn) MDP is the major complex. Addition of almost equimolar amounts of competing cations, phosphate, and methylphosphonate, will disrupt this complex. Their peaks C and D are likely the +2 and +3 complexes of ^{99m}Tc (Sn) MDP. Assuming the pH of the preparation is the pH of electrophoresis, the presence of equal amounts of C and D at pH 6 would indicate a pKa_3 of ~6 for the ^{99m}Tc (Sn) MDP. It is also reasonable to expect similar images (Figs. 7 and 8) using radiopharmaceuticals containing only C or D because they are different ionic species of the same chelate and would probably be identical in blood.

One of the main reasons that MDP has wide-spread use for bone imaging is that it is much less likely to be hydrolized than pyrophosphate. If the authors' hydrolysis scheme can be documented, a reference would be most helpful. Their hydrolysis of MDP shows the formation of methylphos*phonate* and their reference for synthesis is for methylphos*phonate*, but the text refers only to methylphos*phate*. This is quite confusing. It is reasonable to assume that adding almost equimolar amounts of a competing cation would disrupt the ^{99m}Tc (Sn) MDP complex but the authors have not shown that hydrolysis happens in their kit (solution) or in commercial kits (lyophilized).

Although pH probably plays an important role in bone imaging with Tc-labeled diphosphonates, the authors neglected the role of the stannous ion and the effects of aging on stannous ion. The authors give no information on the pH of the commercial kit preparations. It should be noted that the Squibb kit contains ascorbic acid as a stabilizer while the Mallinckrodt kit does not.

The authors do state that high performance liquid chromatographic analysis would have been a much more informative system for the characterization of these complexes.

We, then, would urge readers to be skeptical in their conclusions of this report. To state that the reason for the occasional liver uptake seen in bone scintigraphy is due to the presence of methylphos*phate* or methylphos*phon*ate in MDP kits, we feel, is not warranted from the data reported.

References

1. Najafi A, Hutchinson N: Electrophoretic analysis of different technetium-99m (SnC12) methylene diphosphonate complexes. *J Nucl Med* 26:524–530, 1985

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REPLY: We thank Drs. Shafer, and Elson for their comments concerning our recent article (*1*) in this Journal.

In this article we have *tried* to address and explore the reasons of occasional liver uptake in bone scintigraphy not readily explained by findings on paper chromatography. Indeed, at no place in this article did we attempt to show that this issue is solved nor that our effort to solve this problem has ceased. We have shown, however, in this article that the presence of methylphosphonate (which was stated methylphosphate incorrectly) in MDP kits will give rise to an increase in concentration of peak A according to our electrophoretic analysis which ultimately gives rise to accumulation of activity in the liver of a rabbit. Trace amounts of peak A were found in most of our technetium-99m ($SnCl_2$) methylene diphosphonate preparations including those that were prepared by using Mallinckrodt or Squibb MDP kits. In addition high performance liquid chromatography (HPLC) analysis on a 5-mo-old solution of methylene diphosphonate pH = 7 revealed the presence of methylphosphonate. We agree that the carbon-phosphorus bond is