treatment-monitoring test.

For a measurement to be useful as a *screening* test, it should accurately reflect risk (of fracture). True prospective evaluation of risk by accepted epidemiologic methods is wholly dependent upon fracture incidence data (*1*). To our knowledge, there is no published data which prospectively relates BMC to purely fracture incidence, and OHTA also indicates that they have not received such data. (It should be noted that previous comparisons of BMC for "fracture cases" compared with "normals" do not recognize that BMC, like blood pressure, is a continuum; in addition, age-related BMC does not define "normal.")

However, in October, 1984, we presented at the Western Regional Meeting of the SNM in Monterey, California data relating BMC measurements at four different skeletal sites to prospective fracture incidence (*2*). The good news is that we were able to predict future fracture risk from BMC measurements, and this is the essential message which OHTA needs to receive. However, our data indicates that the strongest determinant of successful risk prediction is the *skeletal site*, and not the specific technique used to measure BMC at that site. We have found that all four of our measurement sites (spine, os calcis, distal radius, proximal radius) predict risk to some degree, but that the os calcis does it best.

Thus, there is not good rationale for pitting dual- against single-photon absorptiometry. Once we know which skeletal site is most useful for screening (risk prediction), the next question is which technique is necessary to measure that site accurately. Of course, it is necessary to use dual photon technology for the spine, but it has no advantage over single-photon for most appendicular measurements.

We are concerned that an inappropriate distinction between the two gamma photon absorptiometry techniques has weakened the position of both, especially with respect to far more expensive x-ray CT techniques that have no proven advantage for this specific clinical use. There is no published data relating CT measurements to fracture incidence, and even if it can be done, it would have to be shown cost-effective.

If we are collectively able to present information on screening and monitoring to OHTA, and if we also take the lead in addressing *cost*, we believe that we would improve the chances of both types of gamma photon absorptiometry being approved for their proper, respective clinical applications.

The preventive management of osteoporosis would be greatly transformed by the availability of a practical technique which can prospectively screen for fracture risk. The impact upon national fracture incidence, and its associated costs, could begin within a few years. However, attempts to introduce x-ray CT for this purpose are inappropriate; even if it is found to be capable of risk prediction, its inherent higher cost would likely be a deterrent to its use, which would in turn delay initiation of rational osteoporosis prevention programs.

References

1. Basic concepts in the assessment of risk. In *Case Controls Studies; Design, Conduct Analysis*, Schlesselmann, JJ Oxford Univ Press, 1982, pp 27-68
2. Wasnich RD, Ross PD, Heilbrun LK, Vogel JM. Prediction of postmenopausal fracture risk with bone mineral measurements. Am J Obstetrics and Gynecology, in press.

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Three Mile Island—Six Years Later

TO THE EDITOR: In the March 1985 *Newsline*, a report I prepared on radiation doses from the Three Mile Island (TMI) accident was discussed. One critic, Sydney Porter, was quoted as follows:

> *Essentially, what the Beyea report says is that the NRC, the DOE, the EPA, the FDA, the utility, and the states of Pennsylvania and Maryland didn't know what they were doing when they measured radiation in the environment. It impunes hundreds of scientists, and some of the finest health physicists in the country.*

These remarks are not an adequate characterization of my report. To make measurements of radiation, it is usually necessary to have equipment available and functioning. As is well known, this was not the case at the start of the Three Mile Island Accident. The situation was so unusual that the staff of the Kemeny Commission task force on health physics and dosimetry was moved to make the following criticisms:

> *The task group was disturbed repeatedly by general problem areas at TMI that are not subject to quantitative evaluation by NRC/I&E [Nuclear Regulatory Commission, Office of Inspection and Enforcement] and that, in general, should not need to be regulated in a formal manner; they are normally handled as an aspect of health physics professionalism. These problem areas include the following: An exceptional percentage (well over half) of health physics and monitoring instruments were not functional at the time of the accident . . . The staff of this task group is of the opinion that the high percentage of inoperable instruments could have contributed to the difficulties in getting data during the first several hours of the accident before the Radiological Assistance Program teams began to arrive . . .(1)*

If Sydney Porter, who was a consultant to the utility before the accident, has a complaint about criticism of health physicists, he is directing it at the wrong person. I made no *professional* criticism of him or anyone else who made analyses of radiation doses. In outlining the status of TMI dosimetry, I stated:

> *Problems remain, it should be emphasized, not because investigators have been incompetent. On the contrary, the investigators reviewed in this study were found to have been extremely clever in using a combination of inference and science to extract information from limited data. Problems remain because a great deal of crucial data does not exist. (2)*

If the critical part of my report, which represents the first peer review for most of the early studies, is to be condensed into one sentence, it would be this: The large uncertainty in the

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

1. Auxier JA, et al: Report of the public health and safety task force on health physics and dosimetry. In *Reports of the Public Health and Safety Task Force on Public Health and Safety Summary, Health Physics and Dosimetry, Radiation Health Effects, Behavioral Effects, Public Health and Epidemiology.* United States President's Commission on the Accident at Three Mile Island, Washington, 1979, p 64
2. Beyea J: A Review of Dose Assessments at Three Mile Island and Recommendations for Future Research, distributed by the Three Mile Island Public Health Fund, 1622 Locust Street, Philadelphia, PA 19103, p 2, 1984

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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