previously received diphosphonate compounds. Other patients injected from the same vial developed no symptoms. Pyrogenic and nonsterile reactions were excluded. According to the package insert the kit did not contain additives except tin and MDP. The temporal relationship between [^{99m}Tc]MDP injection and these symptoms is suggestive for a reaction to the radiopharmaceutical. Those patients with reactions have not returned for a second bone scan.

Few data are available on the nature of the reactions to [^{99m}Tc]MDP. The most common reaction seems to be a skin rash 2 to 24 hr after injection (*2,3,4*). Our patients, however, did not show cutaneous manifestations. Ramos-Gabatin et al. (*4*) described a case with a certain similarity to our patients, the symptoms consisted of nausea, headache, cough, myalgias and fever. It was discovered that the patient had a similar but milder reaction one month earlier when an initial bone scan was performed. Spicer et al. (*3*) reported a case with a mucocutaneous reaction and also a more severe reaction following repeated [^{99m}Tc]MDP injection. In neither report was there evidence of previous sensitization to the radiopharmaceutical. Both authors stated that an allergic response was responsible for these reactions which is very likely in the case of a late mucocutaneous reaction (*3*) but is very difficult to establish with certainty even by skin testing (*4,5*). The symptoms in our patients may also be explained by nonimmunologic histamine release such as probably occurs in reactions to radiographic contrast media (*5*).

An important question is how to deal with a repeat bone scan in those patients with a reaction from a previous injection of [^{99m}Tc]MDP. It is likely that there is cross reactivity to several diphosphonate compounds from different manufacturers (*4*). Technetium-99m pyrophosphate may be a safe substitute as a bone imaging agent as has been shown in two patients (*3,4*). Alternatively, repeated administration of [^{99m}Tc]MDP may be considered after pretreatment with antihistamines and corticosteroids which is a recommended strategy in cases of a previous reaction to radiographic contrast media (*5*).

The reported incidence of adverse reactions to radiopharmaceuticals may not only be biased by failure to report reactions but also because moderate symptoms are ignored or not associated with radiopharmaceutical administration. The present report suggests that mild adverse reactions to [^{99m}Tc]MDP occur more frequently than officially documented. Possibly repeated injections may cause reactions of increasing severity. More awareness and registration of any adverse reactions is needed.

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Kinetics of Interstitially Administered Monoclonal Antibodies for Purposes of Lymphoscintigraphy

TO THE EDITOR: We read with interest the article "Kinetics of Interstitially Administered Monoclonal Antibodies for Purposes of Lymphoscintigraphy" by Wahl, Geatti, Liebert, et al. (*1*). They report little difference in clearance rate between intact IgG and IgM monoclonal antibodies from a subcutaneous injection site in mice.

We (*2*) and others (*3*) have found a significant difference in clearance rates from a subcutaneous injection site between indium-111- (^{111}In) labeled IgG and IgM monoclonal antibodies. Our study showed that in rabbits maximum clearance from the injection site occurred by 24 hr postinjection, with IgG antibody clearing more rapidly (86%) than IgM antibody (66%). The study by Halpern et al. (*3*) also showed that in mice ^{111}In-labeled IgM antibody cleared much slower from a subcutaneous injection site than IgG antibody.

There are a number of differences between our study and that of Wahl et al. which may explain these results. First, there may be differences in clearance rates between different subclasses of IgG antibodies. Our study compared IgG_1 monoclonal antibody with IgM whereas the study by Wahl et al. compared IgG_{2ak} antibody with IgM. Second, there may even be differences in clearance rate between different antibodies of the same isotype and subclass. For example, we have found differences in hepatic uptake and clearance rates between different ^{111}In-labeled IgG_1 antibodies. There may also be species differences in clearance rates. Our study used a rabbit model to study the clearance of subcutaneously injected murine antibodies whereas the study by Wahl et al. used a mouse model. However, it should be noted that the study by Halpern (*3*) also used a mouse model. Finally, although both ^{111}In- and iodine-131- (^{131}I) labeled antibodies are referred to in the "Methods" section of the paper by Wahl most of the data reported in the "Results" section pertain to ^{131}I-labeled antibodies. However they report no significant difference in clearance from a subcutaneous injection site at 6 hr postinjection between ^{111}In- and ^{131}I-labeled antibodies. In our study we found that clearance is very similar between ^{111}In-labeled IgG and IgM antibodies up to 4 hr postinjection with much more marked differences observed at later time points.

It appears that further study may be necessary to fully understand the clearance kinetics of different isotypes and subclasses of monoclonal antibodies from a subcutaneous injection site.

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REPLY: We appreciate the comments of Reilly regarding our manuscript Kinetics of Interstitially Administered Monoconal Antibodies for Purposes of Lymphoscintigraphy (*1*). In that manuscript we observed, in addition to faster injection site clearance of an Fab fragment (when there was no ambulation) than of its intact parent, that a radioiodinated IgM monoclonal antibody cleared from the injection site at a rate comparable to that of the intact IgG antibody studied (as determined by external scintigraphy). By contrast, Reilly has observed slower clearance (by gamma camera imaging) from the injection site in five rabbits for an Indium 111 labeled IgM than for a comparably labeled IgG (*2*). While in his abstract, no indication of the variability of the data is provided, so assessment of the statistical significance of this difference is not possible; his results are similar to those of Halpern who has reported slower clearance of indium-111 (^{111}In) IgM antibodies from the injection site in mice (by tissue counting) than for IgG's (*3*). Our studies differ methodologically from both of these in that we evaluated an iodine-131 (^{131}I) IgM, but did not evaluate ^{111}In IgM as did the other investigators. Certainly, as we mentioned, some of our results could be due to deiodination, though our comparative study of the ^{111}In and ^{131}I labeled IgG did show slower clearance of the iodinated IgG even to 24 hr after injection. We certainly agree with Reilly that there can be significant differences in biological behavior among antibodies of the same class and even of the same isotypes, and it may be a combination of these two factors that account for our different results. We also observed continued clearance of radioantibody from the injection site after 24 hr, apparently in contrast to the results of Reilly. This continued clearance is certainly desirable from a dosimetric standpoint.

Of what may be of equal or greater importance than injection site egress rate is that we, and Reilly, both observed higher normal nodal uptake of IgM than of IgG (*1,2*). Additional studies we have since conducted have shown normal node/blood ratios significantly higher for IgM than for several different intact IgGs (*4*). These higher normal nodal uptakes of IgM than of IgG may be a major limitation to the use of IgMs for immunolymphoscintigraphy, regardless of the rate of clearance from the injection site, in that it may be more difficult to detect an antigen-specific signal if nodal background activity is too high. Further study of IgM injection site clearance and in particular, nodal uptake will be of interest due to the possibility of biologic variability among members of the IgM class. We thank Mr. Reilly for his interest in our work.

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Correction: Duplication of Figures

In the article by Weinberg et al., "Validation of PET-Acquired Input Functions for Cardiac Studies" (*J Nucl Med* 1988; 29:241–247), duplicate figures were submitted for Figures 6 and 7. The correct Figure 6 is shown below.