LETTERS TO THE EDITOR

Technetium-99m Pyrophosphate Uptake

To the Editor:

Except for temporal correlation between the localization of \(^{99m}\text{Tc}\) pyrophosphate (\(^{99m}\text{Tc-PYP}\)) and a few granules of calcium phosphate in mitochondria of infarcted myocardium observed under electron microscopy,\(^1,2\) no proof has been demonstrated that calcium phosphate in infarcted myocardium and other cardiac abnormalities is the only reason for the localization of \(^{99m}\text{Tc-PYP}\). All the experiments that we have performed in our laboratory to investigate the mechanism provide proof contrary to this hypothesis.\(^2,3\) Although \(^{99m}\text{Tc-PYP}\) is a bone scanning agent, the binding of \(^{99m}\text{Tc-PYP}\) with calcium phosphate on a weight basis is eight to nine times higher than that of soluble proteins, but the redistribution of \(^{99m}\text{Tc-PYP}\) in the infarcted myocardium depends on extracellular protein, intracellular proteins and enzymes of leaky dead cells, and mitochondrial or cytoplasmic particles of calcium phosphate or fibrin deposits. We have also determined the intensity of nonspecific binding of \(^{99m}\text{Tc-PYP}\) as shown by the sequence: calcium phosphate > soluble proteins and enzymes > dextran > myosin > cellulose.

The contribution of soluble proteins and calcium phosphate\(^4\) for the uptake of \(^{99m}\text{Tc-PYP}\) in infarcted myocardium is shown in table 1.

On the assumption that all of the calcium ion in the infarcted myocardium are converted to calcium phosphates, less than 1% of \(^{99m}\text{Tc-PYP}\) uptake could be accounted for by calcium phosphate. \(^{99m}\text{Tc-PYP}\) is strongly adsorbed into calcium phosphate granules. If calcium phosphate in infarcted tissue responsible for uptake of \(\text{Tc-PYP}\), autoradiography could be easily performed, but minor amounts of residual radioactivity are observed after fixing and staining the tissue. If calcium phosphate is responsible for the uptake, we should be able to quantify the infarct with \(\text{Tc-PYP}\). The three-dimensional reconstruction of infarcted lesion with \(\text{Tc-PYP}\) always overestimates the size of the true lesion by a factor of 1.5:2.

We have also found that the presence of free calcium ion is not necessary for the protein binding of \(\text{Tc-chelate}\), Ca ion does not increase the protein binding of \(\text{Tc-PYP}\); only calcium phosphate granules retain \(^{99m}\text{Tc-PYP}\).

If calcium phosphate is responsible for the uptake of \(\text{Tc-PYP}\), we should see the uptake only in the presence of large amounts of calcium phosphate in soft tissue. However, we also see uptake in the following conditions in which calcium phosphate is present in minor amounts: inflammatory diseases, unstable angina, cardioversion, after radiation therapy and amyloid diseases. Thus, the binding of \(\text{Tc-PYP}\) in the soluble muscle proteins and enzymes in different cardiac abnormalities probably plays a major role and calcium phosphate has only a minor role. Showing just the presence of calcium phosphate is inadequate; the amount of this agent must be quantified. In the absence of direct proof to counter these arguments, the previous hypothesis regarding the role of calcium phosphate should be seriously questioned.

Mrinal K. Dewanjee, Ph.D.
Mayo Clinic
Rochester, Minnesota 55901

References


The authors reply:

To the Editor:

We do not agree with Dr. Dewanjee’s conclusion that uptake of technetium-99m stannous pyrophosphate (\(^{99m}\text{Tc-PYP}\)) in infarcted myocardium results from calcium-independent binding of \(^{99m}\text{Tc-PYP}\) with organic molecules, particularly soluble proteins, to the exclusion of complexing with inorganic calcium phosphate deposits. Following the initial observation that \(^{99m}\text{Tc-PYP}\) concentrates in experimental myocardial infarcts,\(^1\) our clinical studies showed that \(^{99m}\text{Tc-PYP}\) scintigraphy could be used successfully for the detection of myocardial infarction.\(^2,3\) We also realized that detailed experimental work was needed to test the original hypothesis regarding \(^{99m}\text{Tc-PYP}\) uptake in infarcted myocardium and also to evaluate the specificity of cardiac localization of \(^{99m}\text{Tc-PYP}\) in irreversibly injured myocardium.\(^4,5\) From these studies we have reached the general conclusion that uptake of \(^{99m}\text{Tc-PYP}\) and related phosphates in infarcted myocardium and other tissues is a multifactoral phenomenon in which concentration of the agents results from complexing with various soluble and insoluble forms of tissue calcium stores, including amorphous calcium phosphate, crystalline hydroxyapatite and calcium complexed with organic macromolecules, possibly supplemented by calcium-independent complexing with tissue constituents.\(^6\)

We have serious reservations about Dr. Dewanjee’s new observations, including: 1) the omission of details regarding the infarct model used; 2) the omission of actual levels of \(^{99m}\text{Tc-PYP}\) measured in the tissue samples; 3) the high value of 62.58 micromgs for calcium content of normal myocardium;\(^6\) 4) the apparent lack of a significant increase above the reported normal value for the calcium content of infarcted myocardium, and 5) the direct extrapolation of relative in vitro binding affinities to in vivo concentration. In dogs

Table 1. Contribution of Soluble Proteins and Calcium Phosphate to the Uptake of \(^{99m}\text{Tc-PYP}\) in Infarcted Myocardium

<table>
<thead>
<tr>
<th></th>
<th>Normal myocardium</th>
<th>Infarcted myocardium</th>
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<tbody>
<tr>
<td>Calcium ion (µ mole/g of muscle)</td>
<td>0.6 ± 0.03</td>
<td>0.8 ± 0.04</td>
</tr>
<tr>
<td>Calcium phosphate (µg)</td>
<td>62.58</td>
<td>83.44</td>
</tr>
<tr>
<td>Soluble proteins and enzymes (mg)</td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>Soluble proteins and enzymes calcium phosphate</td>
<td>719</td>
<td>963</td>
</tr>
<tr>
<td>Percent uptake by calcium phosphate in infarcted myocardium</td>
<td>—</td>
<td>&lt;0.08</td>
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Technetium-99m pyrophosphate uptake.
M K Dewanjee

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