LETTERS TO THE EDITOR

Technetium-99m Pyrophosphate Uptake

To the Editor:

Except for temporal correlation between the localization of 99mTc-PYMP (99mTc-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 99mTc-PYP. All the experiments that we have performed in our laboratory to investigate the mechanism provide proof contrary to this hypothesis.3,4 Although 99mTc-PYP is a bone scanning agent, the binding of 99mTc-PYP with calcium phosphate on a weight basis is eight to nine times higher than that of soluble proteins, but the redistribution of 99mTc-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 99mTc-PYP as shown by the sequence: calcium phosphate > soluble proteins and enzymes > dextran > myosin > celluose.

The contribution of soluble proteins and calcium phosphate1 for the uptake of 99mTc-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 99mTc-PYP uptake could be accounted for by calcium phosphate. 99mTc-PYP is strongly adsorbed into calcium phosphate granules. If calcium phosphate in infarcted tissue responsible for uptake of 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 Tc-PYP. The three-dimensional reconstruction of infarcted lesion with 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 Tc-chelate, Ca ion does not increase the protein binding of Tc-PYP; only calcium phosphate granules retain 99mTc-PYP.

If calcium phosphate is responsible for the uptake of 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 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. Shewing just the presence of calcium phosphate is inadequate; the amount of this agent must be quantified. In the absence of direct proof to count these arguments, the previous hypothesis regarding the role of calcium phosphate should be seriously questioned.

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References


The authors reply:

To the Editor:

We do not agree with Dr. Dewanjee's conclusion that uptake of technetium-99m stannous pyrophosphate (99mTc-PYP) in infarcted myocardium results from calcium-independent binding of 99mTc-PYP with organic molecules, particularly soluble proteins, to the exclusion of complexing with inorganic calcium phosphate deposits. Following the initial observation that 99mTc-PYP concentrates in experimental myocardial infarcts,1 our clinical studies showed that 99mTc-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 99mTc-PYP uptake in infarcted myocardium and also to evaluate the specificity of cardiac localization of 99mTc-PYP in irreversibly injured myocardium.4,5 From these studies we have reached the general conclusion that uptake of 99mTc-PYP in infarcted myocardium and related phosphates in infarcted myocardium and other tissues is a multifactorial 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 99mTc-PYP measured in the tissue samples; 3) the high value of 62.58 micromgrams for calcium content of normal myocardium;4,5 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 99mTc-PYP in Infarcted Myocardium

<table>
<thead>
<tr>
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<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 (mg)</td>
<td>719</td>
<td>963</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>percent uptake by calcium phosphate in infarcted myocardium</td>
<td>≤ 0.08</td>
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</table>

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Technetium-99m pyrophosphate uptake.
M K Dewanjee

Circulation. 1978;58:186-187
doi: 10.1161/01.CIR.58.1.186

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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