Pathophysiology of Persistently Positive Myocardial Scintigrams

It was with great interest that we read the Journal's recent articles by Malin et al. (1) and Botvinick et al. (2) concerning persistently positive technetium-99m stannous pyrophosphate (Tc-PPi) myocardial scintigrams. Several possible causes for this were discussed, including the misinterpretation of blood-pool activity, ventricular aneurysms, and dystrophic calcification. Another cause that should be considered is ongoing myocardial damage. Autoradiographic studies (3) in experimental acute myocardial infarcts have shown that tracer concentration occurs predominantly in frankly necrotic cells and a small population of severely damaged border-zone muscle cells admixed with necrotic cells.

We have recently reviewed the pathologic findings of 41 patients with positive Tc-PPi myocardial scintigrams (4). Twenty-nine of the 41 patients with scintigrams, history, and laboratory data indicating acute myocardial infarction were studied at necropsy. All had histologic evidence of myocardial necrosis that corresponded, both temporally and in location, with the abnormal uptake seen on scintigram. Each of five additional patients with unstable angina and positive scintigrams showed small multifocal lesions consisting of coagulation necrosis or myocytolysis at an irreversible stage. Most importantly, seven patients with scintigrams persistently positive 2½-9 nine mo after myocardial infarction were examined, four at necropsy, and three with surgical specimens. All seven showed focal coagulation necrosis, irreversible myocytolysis, or fibrosis consistent with acute damage at the time of scintigraphic study. We note that the three surgical specimens were ventricular aneurysms, but irreversible myocytolysis was also present histologically in each. No evidence of dystrophic calcification in scar tissue or in a mural thrombus was present in any of the patients examined.

Our group has previously reported (5) a worse prognosis in 19 patients with persistently positive scintigrams compared with 27 patients whose scintigrams reverted to normal following an acute myocardial infarction. The worse prognosis in the persistently positive group is, we feel, the clinical counterpart of the progressive myocardial necrosis seen pathologically.

We therefore suggest that ongoing cellular damage in chronically ischemic myocardium be considered as an explanation for persistently positive myocardial scintigrams.

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In response to the letter of Datz et al., we agree that, on the basis of the evidence presented in the literature thus far, one possible cause for persistently positive Tc-99m pyrophosphate scintigrams could relate to continued foci of myocardial necrosis (1). The pathologic location and state of necrosis in specimens studied correlate closely with those expected from the findings of scintigraphic study. However, pathologic correlations with persistently positive scintigrams have been sparse. As noted by Datz et al., each of seven such cases studied pathologically by Buja et al. (1) has indeed documented the presence of acute necrosis. The difficulty lies in the fact that four of these seven patients were studied at necropsy. It is likely that some of these patients died of primary cardiac causes, whereas the remainder could conceivably have suffered preterminal myocardial cell death. Similarly, the preoperative symptoms are not clearly stated for the remaining three patients with persistently positive scintigrams and surgical demonstration of acute necrosis. It would not be surprising to find limited scintigraphic and acute pathologic abnormalities in these patients if they had unstable angina or suffered some complication during surgery (2).

Although such continued or renewed necrosis may be the cause of persistently positive Tc-PPi scintigrams, there are two factors that would make this an unlikely possibility in the patients studied in our series (3). First, the overwhelming majority of our patients and of those demonstrating persistently positive uptake were either entirely asymptomatic when studied or had chest pain that was found to be unrelated to any clinical or laboratory evidence of acute myocardial necrosis. Many of the
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patients were asymptomatic, and the remainder had known stable angina or some other noncardiac-pain syndrome without evidence of any ongoing myocardial necrosis. None of these patients died, and many were not hospitalized but were simply asked to undergo repeat scintigraphy as part of the research protocol. All those patients hospitalized during the period of scintigraphy were discharged shortly thereafter, following complete evaluation of their pain syndrome or following coronary bypass graft surgery. Certainly, ischemic disease was in a relatively benign, quiescent phase in all patients studied during the period of examination, and it would be surprising indeed if a large percentage of these patients demonstrated pathologic evidence of myocardial necrosis. The second point involves the distribution of radioactivity in persistently positive scintigrams. Our study and those of Malin et al. (4) and others (5) document the frequent occurrence of the 2+ and diffuse pattern of radionuclide uptake in persistently positive scintigrams. Although the exact reason for this, and for the 2+ diffuse pattern of uptake in general, remains in doubt, we and others (6,7) have established the nonspecificity of such scintigraphic findings. In the current study, we observed such 2+ diffuse uptake in nine of 11 patients with persistently positive scintigrams. This distribution of uptake cannot easily be explained in terms of ongoing myocardial necrosis, especially in a group of patients with minimal or totally absent symptoms. Indeed, the seven patients with persistently positive scintigrams studied pathologically by Buja et al. (1) have shown a relationship between pathologic and scintigraphic localization. However, in each of these cases, scintigraphy showed discrete, well-localized myocardial uptake, and the pathologic correlate of the 2+ diffuse pattern of uptake remains to be defined. Although we agree, then, that continued myocardial necrosis may be one explanation for persistently positive Tc-99m scintigrams, the evidence to date is suggestive but incomplete, and leaves a fertile area for future investigation.

Possibly more important are the areas of general agreement noted in the studies thus far performed evaluating the frequency and clinical significance of persistently positive scintigrams. Paralleling other studies (4,5) we have noted the occurrence of persistently positive scintigrams that often are found in patients who have suffered large infarctions and, frequently, aneurysm formation. This is consistent with past findings relating persistently positive scintigrams with an increased frequency of complications following infarction (1). Most observers would also agree that persistently positive scintigrams are frequently of low intensity—generally less intense than in an earlier study performed in the same patient. Furthermore, many of such persistently positive scintigrams demonstrate a 2+ and diffuse pattern of uptake. Unless this pattern is further clarified by the findings of serial scintigrams, our current study supports our previous findings (6), indicating the lack of diagnostic specificity of this 2+ diffuse scintigraphic pattern. However, from the findings in our current study and from those related in the literature and in the letter by Dr. Datz, it appears that the discrete pattern of Tc-99m scintigraphy remains a satisfactorily specific indicator of acute myocardial necrosis, even at a time remote from the event.

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A Clinical Comparison of Tc-99m HEDP and Tc-99m MDP

Drs. Fogelman et al. have published a very useful clinical comparison of the performance of Tc-99m-tagged HEDP and MDP in patients with bone metastases (1). In their Table 1, the bone image quality on a 1-3 scale is determined by three observers and expressed as the mean. In Table 2, the numbers of detected metastases per patient are again tabulated as the mean. Taking arithmetic means of small numerical values can unknowingly mask a pattern of differences among numbers making up the mean. Despite the correlation coefficients presented, there could be significant interobserver difference in the image-quality scores and the numbers of bone lesions determined. This becomes important when a small laboratory is choosing between competitive products for the same clinical indication: it is often necessary for one person to compare products objectively. That single evaluator would not necessarily know what to expect should he repeat the authors' study.

In Tables 1 and 2, therefore, if the statistical analyses were performed on each observer's findings individually, would the results be consistent among the observers and qualitatively as published?

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We thank Drs. Coupal and Kim for their interest in and comments on our paper. We accept their implied criticism that a scan-quality scale of only 1-3 is rather coarse for precise intercomparison, although we do not believe that a more precise subjective judgment of scan quality is valid. It was for this reason that we took the three observers together, giving an effective seven-point scale of 3-9, thereby removing a good proportion of the tied scores between imaging agents. The lesion count was also aggregated over the three observers, although