Can Myocardial Ischemia Be Imaged with Technetium-99m-Sn-2\(^{+}\)-pyrophosphate?

To the Editor:

Olson et al.\(^1\) report in Circulation that pyrophosphate imaging is uniquely sensitive for the detection of "scattered" areas of myocardial necrosis undiagnosed by serial enzyme assays.\(^2\) They found that one-third of their patients with unstable angina had positive scintigrams. The recorded scintiscans were predominantly of the diffuse type. Positive scans correlated with ST-segment depression. I believe that their interpretation of these data is incorrect.

Creatine kinase (CK) analysis has been regarded as a reference technique for identification of acute cardiac necrosis, and in fact, enzyme levels roughly correlate with pyrophosphate infarct areas.\(^3\) Thus, these investigators need to prove that diffuse cardiac necrosis can be present with no changes in CK levels.

It is hard to understand how scattered areas of myocardial necrosis, which cannot be identified by enzymes, can, on planar imaging, appear as zones of diffuse pyrophosphate accumulation. First, acute myocardial infarction in the one-major-vessel-occlusion model is not an entity showing a random pattern. Quite the opposite: The biology of an acute cardiac infarct is one of high order.\(^4\) Forty minutes after coronary occlusion, the endocardial layer in the area at risk dies. The lateral boundary of this endocardial layer is sharply demarcated; only a few millimeters separate it from the uninvolved cardiac muscle. Over the ensuing 3-6 hours, necrosis advances as a wave front to involve the area at risk in an expected transmural fashion. However, a parallel phenomenon occurs simultaneously: A network of collateral flow develops in the epicardium.\(^5\) Ten to 40% of the area at risk is spontaneously salvaged, largely where collateral flow develops.\(^6\) These events appear to be the rule in both the dog\(^7\) and in man.\(^8\)

Although many aspects of pyrophosphate imaging remain controversial,\(^6\) one may advance some calculated guesses. It is likely that pyrophosphate gains access to the infarcted myocardium (and perhaps to functionally ischemic myocardium) through the developed collateral pathways just described. Two days after the onset of acute myocardial infarction, epicardial flow is still at subnormal levels.\(^6\) The radiophosphate uptake will then be predominantly epicardial. In some patients, this uptake is predominantly in the perinfarction regions — the so-called doughnut pattern.\(^3\)

Olson et al. should provide an explanation for their postulated hypothesis, which, at first glance, is unsubstantiated.

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References

3. Reimer KA, Jennings RB: The "wave front phenomenon" of myocardial ischemic cell death. Lab Invest 40: 633, 1979

The author replies:

To the Editor:

The present study was not designed to settle the controversy of whether pyrophosphate concentrates in ischemic as well as necrotic myocardial cells. Although we have no definitive answer to this controversy, we feel that pyrophosphate imaging in unstable angina provides useful prognostic information. Unstable angina patients with positive scintigrams have a more fulminant clinical course than patients with negative scintigrams. Based on the work of others, we believe the most likely explanation is myocardial necrosis.\(^1,4\) Other possible mechanisms include persistently positive scintigrams after myocardial infarction,\(^4\) ventricular aneurysm,\(^7\) and persistent blood pool activity.\(^8\) In support of myocardial necrosis, we refer to experimental animal studies which indicate that myocardial uptake of technetium-99m pyrophosphate requires myocardial necrosis. Also, autopsy studies of patients with consistently positive scintigrams after myocardial infarction show local ongoing necrosis in the area of previous infarction.\(^1,4\)

CK-MB isoenzyme analysis is clinically the most sensitive and specific technique for diagnosing myocardial necrosis. A recent study showed that myocardial necrosis is most likely present in patients with an elevated CK-MB in the presence of normal serum CK.\(^7\) Jaffe and associates showed that the majority of unstable
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