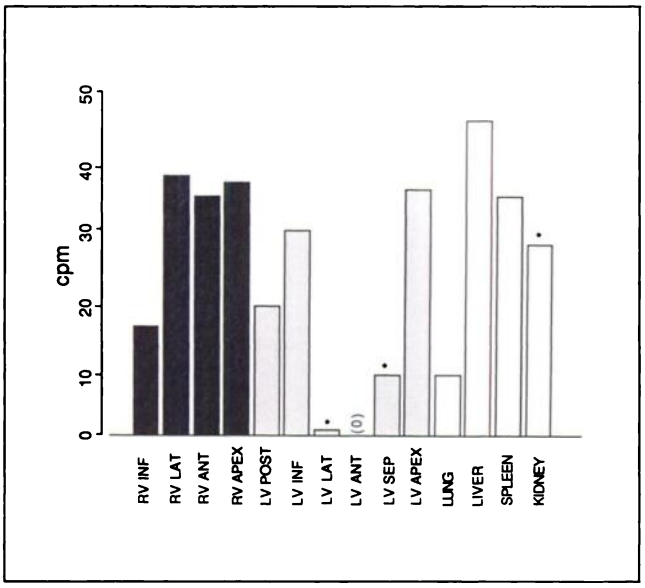

FIGURE 3. Biodistribution of ^{111}In eight days after administration of ^{111}In-antimyosin Fab. Closed columns = activities in the right ventricle; dotted columns = activities in the left ventricle; and open columns = activities in the other organs. *Values are presented as the mean of two or three tissue samples. ANT = anterior, INF = inferior, LAT = lateral, LV = left ventricular, POST = posterior, RV = right ventricular, and SEP = septal.

sumably, upon the antigenicity of the remaining cardiac myosin. During the reparative process of infarcted myocardium, cardiac myosin gradually disappears and is replaced by scar tissue over several weeks (*9,10*), suggesting that this tracer would be less sensitive during the later stages of acute myocardial infarction. However, there is little information on the effect of infarct age on the sensitivity of this agent. Jain et al. (*7*) reported a positive antimyosin image of a 6-day-old infarction and a recent study by Tamaki et al. (*8*) showed that antimyosin Fab scintigraphy detected infarction at various stages from 3 days to 9 mo after myocardial infarction in humans. The present study confirms previous reports (*7,8*) demonstrating that ^{111}In-antimyosin Fab can be used to identify 7-day-old infarcted myocardium with a high degree of specificity. However, it is not clear how well acutely necrotic tissue can be differentiated from that infarcted much earlier. Further clinical studies are necessary to define the interval during which the technique is useful, to establish a method for identifying the age of infarct, and to confirm its utility in detecting right ventricular infarction.

In conclusion, the present report demonstrates that ^{111}In-antimyosin Fab localization can identify myocardial necrosis of the left and also the right ventricle with a high degree of specificity and that this tracer may support the diagnosis of infarctions several days, but not years, old.

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EDITORIAL

Of Antimyosin Imaging and Histopathology of Myocardial Infarction: When, Where, and Why?

Antimyosin antibodies bind specifically to myosin exposed in myocardial cells that have lost their sarcolemmal integrity, thereby providing a noninvasive approach for the diagnosis of myocyte necrosis associated with acute myocardial infarction (MI) (*1–7*), acute myocarditis (*8,9*), and heart transplant rejection (*9,10*). This principle was demonstrated with cultured neonatal murine myocytes subjected to ischemic condition. Antimyosin antibody covalently linked to polystyrene spheres selectively adhered to necrotic cells that had intracellular contents herniating through

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the membrane defects but did not bind to those cells with intact cell membranes (*11*).

Experimental studies have validated the feasibility of in vivo assessment and quantitation of myocyte necrosis associated with acute MI by gamma imaging and histopathology (*12–17*). Clinical studies (*1–7,18,19*) utilizing antimyosin scintigraphy have reported a sensitivity and specificity of approximately 90% for detection of acute MI. Postmortem evidence of antimyosin antibody localization in human myocardial infarcts has been described in three case reports. In vivo antimyosin uptake was compared to ex vivo images of the heart slices as well as to histopathologic infarcts in patients who died within a few days of antimyosin administration (*20–22*). In these reported cases, regions of acute left ventricular infarcts delineated by antimyosin corresponded to the histopathologic infarcts. In the case report of Nakata and co-workers (*23*), a triad of pathologic conditions was present in the same patient:

1. A remote anterior MI.
2. An acute inferior MI.
3. An acute right ventricular MI.

The questions pertaining to the specificity of antimyosin localization for acute or remote left ventricular infarcts and right ventricular infarct can be answered simultaneously.

These investigators have compared the in vivo imaging data of pyrophosphate scans to the ex vivo counting data obtained 30 days (11 half-lives) after ^{111}In-antimyosin administration, in what appeared to be a hindsight experiment. Reinfarction in the inferior wall was reported to have occurred 24 hr after antimyosin antibody administration (when approximately 20% of the injected antimyosin dose is still circulating) and 5 days after pyrophosphate scan. No clinical, electrocardiographic, or pathologic evidence of reinfarction was provided in the report. Therefore, it is uncertain whether the inferior wall was ischemic, stunned, infarcted, or reperfused at the time the pyrophosphate images were acquired relative to the subsequent antimyosin distribution data. Figure 1B of the case report of Nakata and co-workers (*23*) showed extensive septal ^{99m}Tc-pyrophosphate uptake equal in intensity to that of the apex, whereas the antimyosin distribution data in Figure 3 showed minimal septal activity and maximal apical activity. The investigators did not provide an explanation for this discrepancy. This difference could be due to the propensity of ^{99m}Tc-pyrophosphate to also localize in severely ischemic but viable myocardium and the inability of ^{111}In-antimyosin to demarcate ischemic cells with intact cell membrane. An alternative interpretation, although unlikely, is that the septal infarct delineated by pyrophosphate did not permit free access of antimyosin into this zone following the seventh day of infarction. Despite this confusion, the study demonstrated unequivocally that there was no antimyosin activity in the remote anterior MI, whereas antimyosin activity was detected in the acute infarction of the inferior and apical wall of the left ventricle and in the right ventricle.

Postmortem studies provide evidence of right ventricular infarction in up to 50% of patients dying from inferior wall MI (*24,25,30*). ST-segment elevation in right ventricular precordial leads is a sensitive (>80%) but less specific (40%–90%) finding (*27–30*). When severe right ventricular dysfunction occurs as a result of extensive MI, cardiogenic shock and typical physical and hemodynamic findings are present (*30–32*). Pyrophosphate scintigraphy of the right ventricular myocardium may confirm the presence of the infarct but failure of myocardial uptake does not exclude the diagnosis (*26–28,30*). Impairment of right ventricular function or regional wall motion abnormalities has been shown frequently in patients with inferior MI (*26,33,34*). A clearer understanding of the role of antimyosin in the differentiation and diagnosis of right and left ventricular infarction would have been achieved had the investigators obtained in vivo images, or better delineation of the infarcted regions would have been possible with macro-autoradiography of the heart slices. Nevertheless, the investigators were able to demonstrate that necrosis in the right ventricle was antimyosin-avid. As realized by the investigators (*23*), whether these observations can be translated into successful right ventricular infarct imaging must await additional studies.

Indium-111-antimyosin Fab can image acute MIs up to about 14 days after the acute event. No uptake of antimyosin antibody was observed in the old infarcts (*1,2,19*). However, recent reports have presented evidence that antimyosin may localize at sites of necrosis long after an acute event, reducing the specificity of this modality for imaging acute onset of myocyte necrosis (*35*). Similarly, reports of pyrophosphate uptake weeks to months after the acute event are rare or represent clinically inapparent ongoing myocyte necrosis (*36–38*). Due to the specific mechanism of localization of antimyosin, brief but not prolonged positivity would be understandable (*12*). Studies of the evolution of MIs have not produced histopathologic evidence of necrotic myocytes in any infarcts that were 36–90-days-old (*39*). However, necrosis was observed in 35% of the infarcts that were 22–35-days-old (*39*). Large MIs and subendocardial infarcts healed less rapidly (*40*). The rate of healing also depended on the competency of the remaining circulation (*40*). In rare instances, islands of necrotic myocytes may remain longer (mummified myocytes) in the midst of thick, strong, fibrous tissue of the scar (*40*). Whether antimyosin can diffuse through fibrous scar tissues to react with myosin of mummified myocytes, or for that matter, whether mummified myosin is still antimyosin-avid is unknown.

Further, the introduction of thrombolytic therapy may facilitate the heal-

ing of necrotic tissue due to restoration of blood flow, however, it may also permit survival of pockets of myocardial tissue that may be amenable to intermittent ischemic insults, resulting in prolonged antimyosin positivity. It is logical to expect that intense localization of ^{111}In-antimyosin would occur in a fresh infarct and that this intensity would decrease with the diminution of the antigenic determinants as the infarct undergoes the process of healing. The present report demonstrated that freshly infarcted zones had high count density indices, whereas no significant ^{111}In-antimyosin localization was observed in the remote anterior infarct that was about two years old (*15*). Further sequential studies with multiple antimyosin scans and clinical follow-up will be required to address the issue of the length of antimyosin positivity and its implications in the retrospective evaluation of the age of an infarct.

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