Technetium-99m Stannous Pyrophosphate Imaging of Experimental Infective Endocarditis

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SUMMARY Technetium-99m stannous pyrophosphate (99mTc-PYP) cardiac scintigraphy was performed in 15 rabbits with experimental Streptococcus sanguis aortic valve infective endocarditis. The animals were imaged five to seven days after the administration of bacteria, and in each case abnormal accumulation of the tracer was visualized in the region of the aortic valve. Three types of cardiac scintigraphic patterns were demonstrated: focal, multifocal and extensive, each correlating well with the anatomical extent of the lesion as defined by gross pathology. Tissue distribution studies demonstrated a 30 ± 5.3 (mean ± SEM) fold excess of radionuclide uptake in the infective endocarditis lesion compared with that of normal myocardium. Imaging of excised hearts from four animals showed an excellent correlation with in vivo imaging as well as gross pathology.

Five animals with nonbacterial thrombotic aortic valve endocarditis demonstrated similar scintigraphic and tissue distribution results. In contrast, four normal animals failed to demonstrate abnormal 99mTc-PYP cardiac scintigrams or tissue uptake.

This study demonstrates that 99mTc-PYP cardiac scintigraphy is a sensitive technique to detect experimental aortic valve endocarditis.

THE DIAGNOSIS OF infective endocarditis is challenging. A suspected clinical diagnosis requires at least 24 hours for bacteriologic confirmation. Furthermore, blood cultures may be negative in up to 20% of cases. Culture negativity is especially common in patients in whom prior antimicrobial therapy has been instituted and in patients with fungal or anaerobic bacterial infections. Evaluation also is made difficult by variable febrile responses and inconsistent cardiac auscultatory findings. Since a delayed or incorrect diagnosis has serious clinical implications, a rapid and sensitive noninvasive method for detecting infective endocarditis is needed.

This report describes our initial experience with the development of a noninvasive radionuclide imaging technique for detecting infective endocarditis in an animal model. The approach utilized technetium-99m stannous pyrophosphate (99mTc-PYP) cardiac scintigraphy, a technique widely used for imaging myocardial necrosis. This radionuclide initially was chosen for study because of the frequent occurrence of myocarditis and myocardial necrosis in clinical and experimental infective endocarditis. However, we immediately observed that maximal radionuclide uptake occurred in the verrucous endocardial lesion itself, rather than in the surrounding left ventricular myocardium. This phenomenon, demonstrated by in vivo imaging and confirmed by tissue distribution studies, indicates the potential of radionuclide techniques for imaging infective endocarditis.

Methods
Preparation of the Experimental Model of Infective Endocarditis

Aortic valve infective endocarditis was established in 15 New Zealand white rabbits using the technique of Durack, Beeson and Petersdorf. Each rabbit was anesthetized with 200 mg of intramuscular ketamine. An incision was made in the neck slightly to the left of the midline and the left carotid artery was isolated. A 1.0 mm diameter polyethylene catheter filled with sterile saline and connected to a Statham physiologic pressure transducer was placed in the carotid artery. Under pressure monitoring, the catheter was advanced into the left ventricle and then passed back and forth across the aortic valve five times in order to abrade the endocardium. The catheter was then withdrawn to a position immediately above the aortic valve cusps, tied in place and buried in the subcutaneous tissues by closing the incision. Aseptic technique was not necessary for this procedure, and no localized infections occurred. Twenty-four to 48 hours later, each rabbit was injected via a marginal ear vein with approximately 10^7 colony forming units of Streptococcus sanguis. The bacteria were maintained on blood agar and transferred daily in a candle extinction jar maintained at 37°C. Before administration, the microorganisms were suspended in Brain Heart Infusion broth supplemented with 5% sucrose. Following induction of infection, the animals were isolated and observed closely. In each case, the rabbits became restless, anorectic and lost weight.

Two additional groups of animals were evaluated. Nonbacterial thrombotic endocarditis was produced in five rabbits by repeating the above catheterization without the subsequent intravenous injection of
bacteria. Four healthy, noncatheterized animals served as additional controls.

Radionuclide Imaging

Each rabbit received 4-6 mCi of $^{99m}$Tc-PYP (Mallinckrodt Nuclear, Inc.) intravenously five and seven days after the induction of infective and nonbacterial thrombotic endocarditis, respectively. Blood pool scintigrams obtained immediately after radionuclide administration provided an anatomic reference for any subsequent focal $^{99m}$Tc-PYP localization in the aortic valve and outflow tract. Any abnormal $^{99m}$Tc-PYP activity could then be correlated with the location of the heart chambers and ascending aorta. Cardiac imaging was performed two to four hours after radionuclide administration, using the same positioning of the animal as for the blood pool scan. Initial studies were obtained in multiple positions. It became evident at an early stage that abnormal focal aortic valve accumulation could best be visualized in a 30-45° left anterior oblique position. The majority of imaging procedures, therefore, were performed only in this position. Cardiac images were obtained on Polaroid film using a Searle Radiographics Pho Gamma IV or HP scintillation camera fitted with a 5 mm pinhole collimator. At least 150,000 counts were accumulated for each image at the energy peak of 140 KeV, using a 20% window. All scintigrams were interpreted independently by two observers unaware of the experimental conditions. Focal abnormal uptake of the tracer was considered present in the region of the aortic valve if the localization had an intensity equal or greater than the overlying ribs, was anatomically distinct when correlated with the cardiac blood pool scan and was located in the region of the aortic outflow tract.

Analysis of Tissue Radionuclide Uptake

Upon completion of in vivo imaging, each animal was sacrificed with a lethal dose of intravenous sodium pentobarbital. The heart was excised intact and washed free of blood and clot. It was examined grossly for the presence of aortic valvular, aortic endothelial and left ventricular endocardial vegetations. The excised hearts from four of the animals with infective endocarditis were imaged again after the aortic outflow tract and left ventricular wall were cut open. The images of the excised hearts were directly compared to both the in vivo imaging and gross pathology.

Samples of the vegetations and normal appearing left ventricular myocardium from each animal with endocarditis were excised, washed and dried. In each animal, careful dissection was used to remove vegetative material grossly free of adjacent valvular endocardial, aortic endothelial and left ventricular myocardial tissue. In the healthy animals, samples of normal aortic valvular structures and left ventricular myocardium were similarly handled. Each sample was weighed and counted in a well-type scintillation counter. Sample activities were expressed as counts/min per gram of tissue per mCi of radionuclide injected (corrected for physical decay). A mean normal value of myocardial radioactive uptake for each heart was calculated by averaging at least three samples obtained from normal appearing left ventricular myocardium remote from the lesion. The average activity of two or three samples of pure vegetative lesions from each heart was compared to the myocardial uptake in that heart and expressed as a radioactivity uptake ratio. Uptake within the immediate perivalvular myocardial tissue was not analyzed.

Pathology and Microbiology

Lesions from six randomly selected animals with infective endocarditis were submitted for microbiological analysis. A sample of the lesion was excised

![Figure 1. The heart from a rabbit with experimental infective endocarditis five days after the injection of Streptococcus sanguis. The anterior wall of the left ventricle and ascending aorta have been removed. Friable, amorphous vegetations are present on the aortic valve and proximal ascending aorta.](image-url)
using sterile techniques and placed in Brain Heart Infusion broth supplemented with 5% sucrose. The culture was incubated in a candle extinction jar maintained at 37°C for at least five days or until turbidity was noted. Any evident bacterial growth was plated out on blood agar, cultured and the organism subsequently confirmed with appropriate biochemical tests.

Nine of the hearts with infective endocarditis and all of those with nonbacterial thrombotic endocarditis were suspended in formalin and samples were obtained for histological analysis. Samples of the lesion and their supportive endocardium and normal appearing left ventricular myocardium remote from the lesion were stained with hematoxylin and eosin and Brown-Brenn dyes and microscopically examined.

Results

Pathology and Microbiology

Gross pathological evidence of infective endocarditis was present in each rabbit injected with bacteria (fig. 1). Friable, round, greyish-white vegetations varying in size from 2–5 mm were present either on the aortic valve or adjacent aortic endothelium. In most cases, one or more aortic valve cusps were destroyed by vegetations. Occasionally, the mitral valve and supportive structures, papillary muscles and left ventricular endocardium were spotted with similar lesions. Massive necrosis of contiguous sections of left ventricular myocardium was rarely seen. Those animals with nonbacterial thrombotic endocarditis contained less extensive, bland vegetations. Small, rough, whitish nodules 2–5 mm in size were present at points of contact between the catheter and the endocardium.

Histologic analysis in selected cases confirmed the diagnosis of infective endocarditis noted on gross examination. Each lesion contained mononuclear cells, polymorphonuclear leukocytes and platelets embedded within a collagen fibrin framework. Focal infiltration of leukocytes appeared on the valve surfaces and along the supporting collagenous zones. Occasionally, particularly in animals with extensive involvement, there was extension of the inflammatory process with localized areas of necrosis and fibrous proliferation deep in the subendocardial regions. Myocardial tissue remote from the lesion contained focal collections of leukocytes and spotty areas of necrosis.

Bacterial staining demonstrated streptococcal organisms enmeshed deep within the vegetation. Pure *Streptococcus sanguis* was isolated from lesions obtained from five of six hearts with infective endocarditis. The microscopic appearance of the noninfectious lesions was qualitatively similar but there was less leukocytic infiltration. Brown-Brenn staining of the nonbacterial thrombotic endocarditic lesions showed no bacteria.

Radionuclide Imaging

In each of the 15 rabbits with infective endocarditis, abnormal 99mTc-PYP uptake was visualized in the region of the aortic valve or contiguous structures in a pattern anatomically distinct from the remainder of the heart as defined by the blood pool scan (fig. 2). No such uptake was seen in normal control animals. In the 15 infected animals, three separate image patterns were seen (fig. 3). Nine animals demonstrated a focal area of uptake which correlated well with isolated aortic valve or contiguous aortic endothelial involvement (figs. 2 and 3). Three animals demonstrated multifocal uptake with abnormal discrete accumulation both in the aortic valve and either the proximal aorta or left ventricle (fig. 3). Extensive uptake was seen in three animals containing diffuse endocardial lesions extending into the left ventricle and proximal aorta (fig. 3). One animal had massive necrosis of the subvalvular myocardium. Images of four randomly selected excised hearts showed an excellent correlation with both the grossly observed

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**Figure 2.** Left anterior oblique 99mTc-PYP scintigrams showing the cardiac blood pool immediately after injection (BP) and findings in a normal control (NL) and in a rabbit with infective endocarditis (IE). Note the absence of cardiac uptake in the normal rabbit with activity seen only in bony structures. In contrast, in the IE rabbit abnormal focal 99mTc-PYP uptake is present in the region of the aortic valve, which is distinct in location from the blood pool activity. These and all subsequent images were obtained with a pinhole collimator, which produces a good deal of magnification.
lesions and in vivo imaging (figs. 4 and 5), and confirmed that the maximal tracer uptake was confined to the lesion itself and not the surrounding subendocardial tissues. Tracer uptake was not seen in endocardial areas which were lacking vegetations, but which were nevertheless in contact with the catheter. It appeared, therefore, that endothelial damage by catheter abrasion alone was not sufficient to cause significant tracer uptake to permit detection by external imaging.

The vegetations were far less extensive in animals with nonbacterial thrombotic endocarditis. Cardiac scintigraphy in each case demonstrated a focal area of uptake in the region of the aortic valve (fig. 6). Gross examination of each heart demonstrated small bland vegetations either on the aortic valve or proximal aortic endothelium.

**Tissue Distribution Studies (Figure 7, Table 1)**

Animals with infective endocarditis exhibited a 30 ± 5.3 (mean ± SEM) fold excess (range 4–72) of 99mTc-PYP uptake in the vegetative lesion compared with normal-appearing left ventricular myocardium (table 1). Animals with the lowest ratios tended to have extensive endocarditis and relatively high radionuclide uptake in the left ventricular myocardium. Tracer uptake in the nonbacterial thrombotic endocarditic lesions averaged 44 ± 14.3 (mean ± SEM) (range 23–100) times greater than than of remote, normal-appearing left ventricular myocardium. The difference between the mean activity ratios of the two groups was not statistically significant by the Wilcoxin Rank Sum test. The four healthy rabbits failed to show any abnormal cardiac tissue uptake, and the radioactivity concentrations were comparable in aortic valve structures and left ventricular myocardium (mean activity ratio 1.2 ± 0.2, range 0.7–1.6).

**Discussion**

The results of this study demonstrate that 99mTc-PYP cardiac scintigraphy is an extremely sensitive technique for detecting acute aortic valve endocarditis in the experimental animal. Both infectious and nonbacterial thrombotic endocarditic lesions selectively concentrate 99mTc-PYP thus allowing external recognition by in vivo imaging. In all animals with endocarditis, 99mTc-PYP cardiac scintigraphy revealed focal areas of increased uptake in the region of the aortic valve which correlated well with the pathological extent of the lesion. The in vivo scintigraphic results were supported by radionuclide tissue uptake studies, and comparison of images of the excised heart with lesion location as observed on the pathological gross specimen. Thus, 99mTc-PYP scintigraphy may prove valuable in assessing endocarditis, and its utility may extend beyond detection of acute myocardial infarction.

Previous studies in experimental animals and man have indicated that 99mTc-PYP is an extremely sensitive technique for detecting acute myocardial infarction. Focal uptake of the radionuclide occurs predominantly in patients with a recent myocardial infarction. Discrete myocardial uptake is also seen in instances of left ventricular aneurysm,12 pericarditis,13 left ventricular metastases,14 experimental and human myocardial contusion,15 and following repeated thoracic direct current countershock.16, 17 Well-localized 99mTc-PYP in our experimental model differs...
from previously reported patterns in that it was confined primarily to the aortic outflow tract. While perivalvular and subendocardial uptake secondary to endocarditis associated necrosis could not be entirely excluded, the results of the excised heart images demonstrated that the predominant uptake in this model is confined to the lesion itself, since the resulting “hot spot” images conformed exactly to the anatomic extent of the lesion.

Diffuse cardiac uptake outlining the entire ventricular silhouette has been noted in patients with stable and unstable angina pectoris, subendocardial myocardial infarction, and patients with presumably normal hearts. Faintly positive diffuse uptake probably frequently reflects either delayed radionuclide blood pool clearance or uptake of the tracer in scattered nests of myocardial necrosis not detected by conventional techniques. Three animals in our series demonstrated extensive \textsuperscript{99mTc}PYP cardiac uptake corresponding to massive endocardial vegetations occurring in vivo.

**FIGURE 4.** Relationship of in vivo imaging to the corresponding excised heart image and gross pathology in an animal with multifocal involvement. Three separate areas of discrete uptake are seen in the in vivo image obtained in the right anterior oblique position. Three distinct “hot spots” are visualized on the excised heart image. On gross pathology, there are three separate noncontiguous endocardial lesions identified in the aorta, aortic valve and left ventricular apex (arrows).

**FIGURE 5.** Similar correlation as in figure 4 in an animal with extensive involvement. Extensive cardiac uptake is present on in vivo imaging. The excised heart image conforms exactly to what is seen on the in vivo image and gross pathology demonstrates massive endocardial lesions and necrosis involving the aortic valve, contiguous left ventricular septum and proximal ascending aorta.

**FIGURE 6.** \textsuperscript{99mTc}PYP cardiac scintigraphy in an animal with nonbacterial thrombotic endocarditis. A focal area of uptake (arrow) is seen in the region of the aortic outflow tract. The gross specimen demonstrated a hemorrhagic bland lesion in the proximal ascending aorta.
patients with a calcified valve detected by fluoroscopy revealed increased uptake. In a second study, 12 of 14 patients with either calcific aortic or mitral valvular heart disease had positive 99mTc-PYP cardiac scintigrams. The uptake was predominantly focal in the patients with calcified aortic valves; 75% of such patients demonstrated focal accumulation in the region of the aortic valve. Resected calcified valves demonstrated three times greater uptake in the valve compared to skeletal muscle. Their control group consisted of six patients with noncalcified valves, two of whom had infective endocarditis. All had normal cardiac 99mTc-PYP scintigraphy and in three resected valves (one with infective endocarditis), there was no abnormal uptake. The clinical details of the patients with infective endocarditis were not specified. It is possible that the disease was inactive or in a healing phase at the time of study. Alternatively, the lesions in the human endocarditis may have been too small compared with the animal model and beyond the limits of resolution using conventional collimation. The diagnostic accuracy of the present method in patients with calcified valves and suspected infective endocarditis may be limited by the uptake of 99mTc-PYP in both conditions; however, the uptake appears to be of a much greater magnitude in endocarditis.

The mechanism by which 99mTc-PYP accumulates in the lesion of experimental infectious endocarditis requires further study. Insight into potential mechanisms may be gained from recent studies in acute myocardial infarction. In experimental myocardial infarction, a temporal and topographic relationship exists between abnormal calcium deposition in the mitochondria of necrotic myocardial cells and 99mTc-PYP uptake. Buja and associates demonstrated that 99mTc-PYP selectively localizes in tissue sites with elevated calcium levels, although not in a linear fashion. Concentration of the tracer was felt to result from selective absorption with various forms of tissue calcium such as amorphous calcium phosphate, crystalline hydroxyapatite and calcium complexed with macromolecules. On the other hand, Dewanjee has proposed that 99mTc-PYP uptake in necrotic cells results primarily from complexing with cytoplasmic macromolecules as a result of protein denaturation in damaged tissue. The majority of radionuclide uptake occurs in the nonmitochondrial fraction of necrotic myocardial cells. However, such intracellular distribution studies may not be entirely valid, since mitochondrial calcium and radionuclide in necrotic cells may be released during tissue homogenization.

99mTc-PYP uptake in the vegetative endocardial lesion may be related to the presence of both calcium and denatured protein macromolecules in the necrotic debris. This mechanism is partly supported by the occasional occurrence of dystrophic calcification in infective endocardial lesions. Clearly, bacteria are not essential for radionuclide binding, since similar uptake was seen in infective as well as nonbacterial thrombotic lesions. This latter observation indicates that 99mTc-PYP also may be of value in demonstrating the

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**Figure 7.** Mean activity ratios of 99mTc-PYP uptake in the endocardial lesions or normal aortic valves compared to normal-appearing left ventricular myocardium in control (open bar), infective endocarditis (IE, stippled bar) and nonbacterial thrombotic endocarditis (NBTE, striped bar) animals. The difference in activity ratios between animals with infective and nonbacterial thrombotic endocarditis is not statistically significant.

cupying a large proportion of the entire outflow tract and contiguous left ventricle. This pattern of extensive uptake may be discriminated from a more diffuse pattern of myocardial uptake by comparison with the blood pool scan.

Myocardial lesions occur in more than 90% of patients with infective endocarditis, and such involvement was recently reported in 100% of rabbits with experimentally induced infective endocarditis. Analysis of left ventricular myocardium in the present study likewise showed focal areas of myocarditis. In addition, perivalvular tissues revealed focal necrosis with cellular and bacterial infiltration. If 99mTc-PYP uptake in the experimental infective endocarditis model depended solely on myocardial and valvular necrosis, then scintigraphy should have resulted in a diffuse pattern rather than the focal uptake demonstrated.

Valvular uptake of 99mTc-PYP also has been noted in man. However, in this instance, uptake was related to calcification rather than infection. Righetti et al. reported abnormal 99mTc-PYP images in three patients with calcified valves. After valve replacement, postoperative scans were negative in two patients. In one excised valve, radionuclide uptake was four times higher than in adjacent myocardium. The sensitivity of 99mTc-PYP imaging of calcified valves was limited, however, since only three of seven...
presence of intravascular or intracardiac thrombosis. In fact, abnormal \( ^{99m} \text{Tc-PYP} \) scintigrams in some patients with left ventricular aneurysm may be due to radionuclide concentration within associated mural thrombosis rather than within the aneurysmal wall itself.

The necrotic and cellular process resulting from infective endocarditis makes it a potential model for further study of the mechanism of \( ^{99m} \text{Tc-PYP} \) cardiac uptake. Preliminary work in our laboratory utilizing in vitro methods has shown that the infective endocarditis vegetation itself selectively binds \( ^{99m} \text{Tc-PYP} \). In this experiment, the tracer was incubated for 90 minutes at 37\(^\circ\)C separately with endocardial vegetations from one animal, normal left ventricular myocardium and postmortem blood clot. After three vigorous saline washes followed by one hour of dialysis against normal saline, the bacterial endocarditis lesion retained 8.5% of the tracer, compared with 1.2% for normal left ventricular myocardium and 0.4% for postmortem clot. These results support our imaging and tissue distribution studies and reconfirm that the vegetative lesion concentrates \( ^{99m} \text{Tc-PYP} \).

Further detailed analyses will be necessary to clarify the exact mechanism by which \( ^{99m} \text{Tc-PYP} \) is an in vivo biochemical marker of endocardial vegetations.

One previous study approached the problem of detecting infective endocarditis by radionuclide imaging. Wiseman and associates performed gallium-67 citrate cardiac scintigraphy in 11 patients with clinically evident bacterial endocarditis. Seven patients demonstrated uptake in the region of the heart. This was confirmed in three patients by postmortem imaging and tissue analysis. Although this study demonstrated the potential feasibility of radioisotopic imaging of human infective endocarditis, the poor localization and imaging characteristics of gallium-67, and slow blood clearance, severely limit its usefulness. More recently, a preliminary report demonstrated positive valvular scintigrams, and increased lesion uptake of \( ^{99m} \text{Tc-pertechnetate} \) labeled antistaphylococcal antibody in experimental \textit{Staphylococcus aureus} endocarditis.

This technique, however, is limited by the difficulty in tracer preparation, by the need to administer heterologous protein and by the vast number of specific antibacterial antibodies required. Until a more general bacterial antigen can be found, this tech-

### TABLE 1. \( ^{99m} \text{Tc-PYP} \) Cardiac Scintigraphy and Tissue Uptake in Normal Rabbits and Those with Infective and Nonbacterial Thrombotic Endocarditis

<table>
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<tr>
<th>Animal No.</th>
<th>Scintigrams</th>
<th>Anatomic Involvement (gross pathology)</th>
<th>Lesion ( ^{99m} \text{Tc-PYP} ) Activity (cpm/gm/mCi ( \times 10^9 ))</th>
<th>LV ( ^{99m} \text{Tc-PYP} ) Activity (cpm/gm/mCi ( \times 10^9 ))</th>
<th>Lesion/LV ( ^{99m} \text{Tc-PYP} ) Activity Ratio</th>
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In normal rabbits, the radioactivity uptake of normal aortic valve structures was compared to normal left ventricular myocardium. Abbreviations: \( F = \) focal; \( M = \) multifocal; \( E = \) extensive; \( AV = \) aortic valve; \( AO = \) aorta; \( MV = \) mitral valve; \( LV = \) left ventricle.
ni cue will have minimal clinical diagnostic relevance unless the specific bacterium can be implicated before study.

Echocardiography has been the only available and widely applied noninvasive technique for detecting infective endocarditis.\textsuperscript{29-31} Although some reported findings have been dramatic, the overall sensitivity of conventional M-mode echocardiography has recently been shown to be limited to 34\% of patients with endocarditis.\textsuperscript{32} Cross-sectional echocardiography may prove to be more sensitive;\textsuperscript{33} however, no prospective evaluation has been reported. Valvular lesions of 2 mm have been detected by echocardiography,\textsuperscript{29} but it is not known whether all lesions of this size can be accurately assessed. Lesions of this magnitude resulted in focal areas of \textsuperscript{99m}Tc-PYP cardiac uptake, and cardiac scintigraphy revealed discrete uptake in all animals with nonbacterial thrombotic endocarditis whose lesions were all very small.

The marked sensitivity of \textsuperscript{99m}Tc-PYP imaging of infective endocarditis, at least in the experimental model, offers great promise as a reliable noninvasive method for detecting this process. The present findings provide a basis upon which radionuclide imaging may be applied to man. However, differences in relative lesion size between experimental and clinical conditions, and both the increased scattering medium and greater radioactivity attenuation potential of the human thorax compared to the rabbit, may make extrapolation of these experimental results to man difficult. Nevertheless, the fact that relatively small lesions were effectively defined in the rabbit is encouraging. The studies described in this report were performed during the acute phase of infective endocarditis. The exact time at which images will first become positive and the time during which an untreated lesion will remain positive has not been determined. Finally, the infective endocarditis lesion is composed of platelets, white blood cells, bacteria, fibrinogen and antibacterial substances. Labeling these components with radioactive tracers may also be interesting and valuable in imaging infective endocarditis.

\textbf{Acknowledgment}

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Pressure and Sound Correlates of the Mitral Valve Echocardiogram in Mitral Stenosis

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SUMMARY The pressure and sound correlates of the mitral valve echocardiogram (MVE) were investigated in 10 patients with mild to moderate mitral stenosis using high fidelity catheter tip micromanometers. Slow and rapid phases of the MVE anterior motion at the time of opening are associated with the slow and rapid phases of the left atrial y descent. The slow MVE motion and the slow y descent begin during isovolumic left ventricular relaxation when left ventricular pressure still exceeds left atrial pressure. The rapid MVE anterior motion and the rapid y descent begin with pressure crossover. Posterior motion of the MVE at the time of closure also occurs in two phases. After the onset of left ventricular pressure rise at end-diastole, a slow posterior motion is associated with a falling left atrial c wave. Rapid posterior motion begins with pressure crossover and is completed near the peak of the c wave. The fall in left atrial pressure during valve opening can be related to movement of the mitral valve away from the left atrium with the fall in left ventricular (LV) pressure. During valve closure, the rising left atrial (LA) pressure can be related to the ascent of the mitral valve toward the left atrium. Both the mitral component of the first heart sound and the opening snap occur at points of maximum MVE excursion and after LV-LA pressure crossover.

ALTHOUGH THE SOUND and pressure correlates in mitral stenosis using high fidelity micromanometer pressures have previously been described,1, 2 the valve motion correlates of these parameters have been limited to angiographic studies.3-4 Since the introduction of echocardiography and the recognition of characteristic patterns of valve motion, this method has been used to study instantaneous valve motion in normal and abnormal states.5 Because of the ease with which the anterior mitral leaflet can be visualized by echocardiography, this structure has been the most extensively studied. The echo pattern has been particularly useful in the evaluation of patients with mitral stenosis.6-7 Although several investigators have described the relationship of echocardiographic mitral valve motion to the production of heart sounds and murmurs,8-13 there have been few studies correlating the mitral echocardiogram with hemodynamic events. Recently, investigators have described the pressure and motion correlates of the normal mitral valve echocardiogram in experimental animals.14, 15 In man, fluid-filled catheter pressures have been used for pressure and motion correlates,16 except in one patient with an atrial septal defect where micromanometer catheters were used.17 This study describes the sound and pressure correlates of echocardiographic mitral valve motion in mitral stenosis using simultaneous high fidelity left atrial (LA) and left ventricular (LV) catheter tip micromanometer pressures recorded with the mitral valve echocardiogram.

Materials and Methods
Ten patients with mitral stenosis were studied during diagnostic cardiac catheterization. Informed consent was obtained from all patients.
Technetium-99m stannous pyrophosphate imaging of experimental infective endocarditis.
A L Riba, J Downs, M L Thakur, A Gottschalk, V T Andriole and B L Zaret

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