Early Detection of Rejection and Assessment of Cyclosporine Therapy by $^{111}$In Antimyosin Imaging in Mouse Heart Allografts

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**Background.** Mice ($n=58$) with abdominal heterotopic heart transplants were studied to examine the effectiveness of $^{111}$In-labeled antimyosin scintigraphy in the detection of rejection and to determine the consequence of cyclosporine therapy on the results.

**Methods and Results.** Allografts from B10D2 donors were transplanted into B6AF1 recipients. Of the 49 allografted mice, 19 were treated with cyclosporine (15 mg/kg-day). Nine isografted mice served as controls. Scintigraphy was performed by injecting 100 μCi $^{111}$In antimyosin monoclonal antibody 2–15 days after transplantation. An increase in the ratio of percent dose of antimyosin injected per gram (% dose/g) of the graft heart (G) to that of the autologous heart (A) (G/A) as well as the increasing percent dose per gram of antimyosin in the grafts reflected the severity of histopathological rejection regardless of the presence or absence of cyclosporine. Scintigraphic images demonstrated unequivocally intense accumulation of $^{111}$In in rejected allografts as confirmed by histologically demonstrable myocyte necrosis. The G/A ratio in allografted mice with mildly deteriorated mechanical activity (4.2±1.0, mean±SD) was greater than that in mice with normal contractility (1.8±0.7) ($p<0.001$), and the necrosis correlated with this modest decline in mechanical function could be scintigraphically identified. Of mice with normally contracting allografts, the G/A ratio was greater in animals with demonstrated myocyte necrosis (2.6±0.5) than in those without necrosis (1.5±0.5) ($p<0.001$). In contrast, isografted mice or a subset of allografted mice treated with cyclosporine and not showing evidence of rejection did not manifest any significant change in G/A ratio, nor did they have scintigrams positive for rejection as late as 15 days after transplantation.

**Conclusions.** These findings suggest that antimyosin scintigraphy is a sensitive and early indicator of cardiac transplant rejection and that it could be useful as a noninvasive method for assessing the efficacy of cyclosporine treatment. (*Circulation* 1991;84:1246–1255)

Early detection of allograft rejection is crucial in the care of patients after heart transplantation. A definitive diagnosis of rejection currently requires repeated endomyocardial biopsies as well as their interpretation by a highly experienced pathologist.1,2 To avoid risk and discomfort to the patient, a variety of noninvasive approaches for assessing cardiac allograft rejection have been explored, including echocardiography,3 cytoimmunologic monitoring,4 nuclear magnetic resonance imaging,5,6 nuclear scintigraphy with radiolabeled lymphocytes,7,8 and scintigraphy with radiolabeled antimyosin monoclonal antibody.9–13

We previously demonstrated that cardiac localization of monoclonal antimyosin antibodies is correlated with myocardial necrosis, whether caused by acute myocardial infarction14,15 or myocarditis.16,17 Because cardiac allograft rejection is also associated with histologically apparent myocyte necrosis,2 it was logical to explore the applicability of this method in the diagnosis of rejection, which has been done in both an experimental model10 and patients.9,12 Although some studies in dogs10 and rats13 showed antimyosin accumulation in rejecting cardiac allografts, other investigations did not support this finding.11 Furthermore, the reported experiments did not define whether antimyosin imaging could be used as an early marker of acute rejection, or whether cyclosporine, apart from its effect on the rejection process, affected accumula-
tion of the antibody in cardiac allografts. Therefore, the present study was designed to evaluate the relation between uptake of labeled antimyosin and histological degree of rejection, determine whether antimyosin imaging can detect rejection at a stage earlier than the decline of mechanical activity in the transplanted heart, and evaluate whether the immunosuppressive effects of cyclosporine therapy alter antimyosin uptake in the rejecting heart.

Methods

Animals
Male, inbred B10D2 and B6AF1 mice were obtained from the Jackson Laboratory (Bar Harbor, Me.). CD-1 mice were purchased from Charles River Breeding Laboratory (Boston).

Organ Grafting
Heterotopic cardiac transplantation was performed in 75 mice. The B10D2 donor/B6AF1 recipient combination was used for 63 allografts. B10D2 (n=5), B6AF1 (n=4), or CD-1 (n=3) hearts were also isografted. Hearts were transplanted to the abdomen of the recipients as primary vascularized grafts by the microvascular technique described by Ono and Lindsey and Corry et al, with some modifications.

Donor preparation. Mice (15–25 g) were anesthetized with 3.6% chloral hydrate i.p. at a dose of 0.1 ml/10 g, and the abdominal skin was cleaned with 70% ethanol. The operation was performed under clean but nonsterile conditions. After a midline abdominal incision had been made and the abdominal aorta was cut to allow the animal to exsanguinate, the incision was extended cephalad to open the chest wide. The following procedures were performed under an operating microscope. The inferior vena cava was isolated, and 0.5–1 ml of a cold, 7.5% solution of heparin in cardioplegia solution (7 g glucose and 24 meq KCl dissolved in 1 l lactated Ringer’s solution, pH 7.8 adjusted by Tris) was intermittently infused into the vessel with a 30-gauge needle. The inferior and superior venae cavae were then ligated with 6–0 silk and cut away. The hilum of the right and left lungs were ligated and transected independently, and the aorta and pulmonary arteries were separated and cut with microscissors. A ligature was then placed around the mass of pulmonary veins. The heart, which at that point was detached from the chest wall, was placed into cold (4°C) cardioplegia solution. The entire procedure was completed within 10 minutes.

Recipient preparation. The recipient mice were prepared as described above. The abdomen was shaved, and a midline abdominal incision was made. The intestine was then exteriorized and wrapped with wet gauze. The abdominal aorta and inferior vena cava were gently separated below the branching of the renal vessels using cotton-tipped applicators and forceps. All small lumbar vessels were ligated with 6–0 silk. Proximal control of the inferior vena cava was obtained by ligature with 6–0 silk, and the abdominal aorta was secured with a Yasargil artery clamp. Distal control was established en masse with 6–0 silk ligature. After closely adjacent venotomy and aortotomy were effected by microscissors, the donor heart was placed within the abdominal cavity. An end-to-side anastomosis was then made by running suture with a 10–0 nylon strand (Ethilon) tipped with a BV75-3 needle. After the anastomoses had been completed, the distal and proximal ligatures and a clamp were loosened, in this order, slowly and carefully. At this point, the grafted hearts became pink and began to contract within a few seconds of reperfusion, after which rhythmic contraction was restored. Warm saline was then dripped onto the graft. After the confirmation of continuous strong beats in the graft, the abdominal wall was closed with 6–0 silk. The animal was then warmed under a heat lamp. The ischemic time was defined as the interval between the injection of cardioplegia solution into the donor heart and reperfusion.

Experimental Groups
Cyclosporine (Sandoz, Inc., Basel, Switzerland) (15 mg/kg) was injected subcutaneously daily beginning on the day of surgery in 26 allografted mice. Four of 37 allografted mice without cyclosporine, three of 26 allografted mice with cyclosporine, and one of 12 isografted mice died within 2 days after transplantation and were excluded from the analysis.

Heartbeat
The function of the transplanted hearts was assessed daily by direct palpation, and mechanical activity was graded independently by two examiners. One examiner was blinded to the animal’s treatment group, and interobserver agreement was more than 90%. Our preliminary experience and a report from another laboratory show that a sharp decline in the intensity of the cardiac impulse is a reliable sign of rejection. The quality of the heartbeats was graded from 0 to 4+ (4+ being optimal and 0 being complete arrest). Grades 4+ and 3+ were considered normal, and grades 2+, 1+, and 0 were interpreted as signs of rejection.

Scintigraphy
The preparation of antimyosin monoclonal antibody 2G42D7 has been reported previously. Diethylaminoethylacetate (DTPA) was covalently attached to the antibody according to the procedures of Krejcirek and Tucker and Khaw et al. Coupled to antimyosin antibody was labeled with 111In. Mice were randomly chosen for scintigraphy 2–15 days after the transplantation. Approximately 100 μCi of labeled antimyosin was injected into the tail vein 24–48 hours before imaging. Scintigraphy was performed after intraperitoneal injection of chloral hydrate. Planar images were obtained with a gamma camera (Ohio Nuclear 100) equipped with a 3-mm-diameter pinhole collimator. From 100,000 to 300,000 counts were obtained in a presetting of 5
minutes for each image. For each scintigram, the intensity of radioactivity in the graft was measured in comparison with that in the native heart after an area of interest had been set by computer planimetry.

**Tissue Analysis**

Mice were killed after scintigraphy, and venous blood was withdrawn from the inferior vena cava. The autologous heart, transplanted heart, liver, spleen, kidneys, lungs, and small intestine were excised. Both hearts were washed thoroughly with saline and immersed in 10% formalin. Each organ was weighed, and the biodistribution of radioactivity in the organ was determined by gamma scintillation counting. Localization was expressed as the percent injected dose per gram of wet tissue (% dose/g). The ratio of percent dose per gram of the graft heart (G) to that of the autologous heart (A) was determined for each mouse and designated G/A ratio. We regarded $^{131}$I-labeled antimyosin activity in the autologous heart as background antibody uptake by normal myocardium.

**Duration of Ischemia and Antimyosin Uptake**

The duration of ischemia in the donor heart has been shown to be a crucial factor of myocyte necrosis in the murine ectopic heart transplantation model.23–25 The effect on antimyosin uptake of myocyte necrosis resulting from ischemia during surgery was investigated in 20 isografted mice (B10D2 or B6AF1). Heart transplantation was performed as described above. Mice were randomly assigned to one of four groups (A, B, C, and D) containing five mice each. Reperfusion was performed 30 minutes after resection of the donor hearts in group A, 60 minutes in group B, 90 minutes in group C, and 120 minutes in group D. Five minutes after reperfusion, the mice were injected with approximately 100 μCi of $^{131}$I-labeled antimyosin. Fifteen minutes later, grafted and autologous hearts were resected, and the G/A ratio was determined for each mouse.

**Histopathology**

A broad spectrum of histological findings was present among the 49 allografts, ranging from nearly normal to severe rejection (Figure 1). Regardless of the time after transplantation and the presence or absence of cyclosporine therapy, antibody uptake increased with increasing severity of rejection (Table 1 and Figures 2 and 3). Mouse with mild or moderate rejection in the absence of necrosis showed no statistical increase in G/A ratio or percent dose per gram compared with mice determined to be normal by histology. However, mice with severe or moderate rejection and the presence of necrosis showed significant increases in both G/A ratio and percent dose per gram of grafted heart compared with mice with no, mild, or moderate rejection without necrosis.

Sensitivity and specificity (G/A ratio of more than 2.0 [mean value for isografts + 1 SD] was considered positive) for the detection of myocyte necrosis in all mice were 86% and 91%, respectively. Regarding the detection of rejection (regardless of degree), sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy were 57%, 91%, 96%, 33%, and 64%, respectively. Sensitivity and specificity for discrimination between rejecting grafts without myocyte necrosis and normal grafts were 11% and 91%, respectively. In cyclosporine-treated animals, sensitivity and specificity for the detection of myocyte necrosis were each 100%.

Three of the allografts among the 19 mice that were treated with cyclosporine showed histologically severe rejection. Both G/A ratio (3.79, 2.78, and 7.14) and percent dose per gram of grafted heart (14.7%, 10.3%, and 11.2%, respectively) in these three mice were greater than those of any other allografted mice with cyclosporine therapy or those of isografted mice.

**Statistical Analysis**

The Bonferroni method was used for multiple comparisons.26 A probability value of less than 0.05 was considered nonsignificant in comparisons between multiple groups of data. All data are expressed as mean ± SD. Linear regression was computed by the least-squares method.
In contrast, the G/A ratio of mice treated with cyclosporine but without histological evidence of necrosis was 1.81 or less, which was as low as that of the isografted mice.

**Time Course of \(^{111}\)In Antimyosin Uptake**

The G/A ratio increased progressively with time in allografted mice that did not receive cyclosporine therapy \((r=0.64, p<0.001)\) (Figure 4). In contrast to the progression in the G/A ratio in these allografted mice, the isografted mice showed no significant increase in the G/A ratio as late as 14 days after transplantation. Figure 5 shows the time course of the G/A ratio in cyclosporine-treated allografts.

Allografted animals not treated with cyclosporine were divided into three groups according to the time between transplantation and tissue counting: 2–4 days \((n=8)\), 5–9 days \((n=11)\), and 10–14 days \((n=11)\). As shown in Table 2, the G/A ratio in the group that was killed early \((2–4 \text{ days})\) was not significantly different from that of the isografted group. However, in the 5–9- and 10–15-day groups, the G/A ratio was significantly greater than that of the isografted animals \((p<0.001\) and \(p<0.01\), respectively).

**Heartbeat**

In all nine isografted mice, 16 of 19 allografted mice treated with cyclosporine, and 16 of 30 non-treated allografted mice, the heartbeat was normal.
(3+ to 4+) in the grafts when the animals were killed. The G/A ratio in the six allografted mice that showed mildly impaired contraction (2+) (4.2±1.0) was greater than that in allografted mice with normal contraction (1.8±0.7) (p<0.001) (Figure 6). The G/A ratio was more than 2.0 in all 17 mice with a grade 1+ or 2+ heartbeat and less than 2.0 in 30 of 41 mice with a grade 3+ or 4+ heartbeat, regardless of the presence or absence of cyclosporine therapy. Sensitivity, specificity, and accuracy for detecting deterioration in the mechanical activity of a graft were 100%, 73%, and 81%, respectively.

All 17 grafts with a grade 1+ or 2+ heartbeat and nine of 41 grafts with normal contractility revealed myocyte necrosis. When allografted mice with normal contractility were divided into two groups according to the presence or absence of histological evidence of necrosis, the G/A ratio in mice with no necrosis (1.5±0.5) was significantly lower than that in mice with necrosis (2.6±0.5) (p<0.001) (Figure 7).

**Scintigraphy**

Antimyosin scans showed unequivocal accumulation of the tracer in allografts with high G/A ratios. A good correlation was observed between the G/A ratio measured by tissue counting and the ratio measured by computer planimetry from the scintigrams (P=0.42×G/A+1.3, r=0.87, n=49, p<0.001, where P is ratio of radioactivity in the graft to that in the autologous heart measured by computer planimetry). (Nine mice in which images of the grafts overlay those of the kidneys were excluded from this evaluation.) Correlation between the intensity of radiotracer signal from the scintigram and the percent injected dose per gram (%ID) was also good (P=0.12×%ID+1.45, r=0.79, n=49, p<0.001). Representative images are shown in Figures 8–11. Allografted mice treated with cyclosporine without histological evidence of rejection showed no specific accumulation of radiolabeled antimyosin at any time after transplantation, whereas three mice with histological evidence of rejection as well as increased G/A ratios showed considerable uptake of radioactivity.
Biodistribution of Injected Antimyosin

The biodistribution of $^{111}$In antmyosin (% dose/g) in all organs was as follows: autologous heart (3.1±0.9%), liver (25.6±11.0%), spleen (7.7±3.8%), right kidney (17.1±7.9%), right lung (3.8±2.5%), bowel (3.4±1.4%), and blood (3.0±4.6%). There was no statistical difference in the percent dose per gram of these organs among nontreated allografted, treated allografted, and isografted mice. The percent dose per gram of grafted hearts is listed in Table 2.

### Discussion

Results from the present study demonstrate that scintigraphy with $^{111}$In-labeled antimyosin antibody accurately detects the existence of acute cardiac rejection. The degree of accumulation of $^{111}$In-labeled antimyosin in rejected hearts also reflects the magnitude of rejection by histological criteria. Antimyosin uptake precedes the decline in mechanical activity of the transplanted heart. Furthermore, the degree of uptake is not affected by cyclosporine therapy but rather reflects the extent of myocyte necrosis resulting from rejection. These findings are reflected in the gamma scintigram.

The ability to detect cardiac allograft rejection noninvasively could play an important role in the

**TABLE 2. Uptake of Labeled Antimyosin in Transplanted Hearts, Autologous Hearts, and Blood**

<table>
<thead>
<tr>
<th></th>
<th>Isografted mice</th>
<th>Allografted mice (no treatment)</th>
<th>Allografted mice treated with cyclosporine</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>9</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Grafted hearts</td>
<td></td>
<td>4.3±1.7</td>
<td>7.2±2.8</td>
</tr>
<tr>
<td>Autologous hearts</td>
<td></td>
<td>2.6±0.8</td>
<td>3.3±0.8</td>
</tr>
<tr>
<td>Ratio of grafted hearts to autologous hearts</td>
<td>1.7±0.3</td>
<td>2.1±0.6</td>
<td>3.3±1.2*</td>
</tr>
<tr>
<td>Blood</td>
<td></td>
<td>2.6±4.6</td>
<td>3.5±4.9</td>
</tr>
<tr>
<td>Radioactivity measured from scintigram</td>
<td>2.0±0.5</td>
<td>2.4±0.8</td>
<td>2.9±1.1*</td>
</tr>
<tr>
<td>($n=8$)</td>
<td></td>
<td>(n=8)</td>
<td>(n=10)</td>
</tr>
</tbody>
</table>

Values are expressed in % dose/g of organ except for the ratio.

$^*p<0.01$, $^+p<0.001$, and $^§p<0.05$ compared with isografted mice.

$^§p<0.01$ compared with isografted mice and cyclosporine-treated mice, and $p<0.05$ compared with mice with 2–4-day-old allografts.
management of patients who undergo heart transplantation. Rejection should be detectable before a decline in mechanical activity, and the diagnosis should be sensitive, specific, and effective even in the presence of immunosuppressive therapy with cyclosporine. Although several scintigraphic approaches for the diagnosis of rejection, such as $^{99m}$Tc-pyrophosphate,$^{27,28}$ $^{201}$TI,$^{26,29}$ or $^{111}$In lymphocytes,$^{7,8}$ have been reported, none has proved clinically satisfactory.$^{30-32}$

We previously showed that radiolabeled antimyosin antibody localizes in histochemically delineated regions of myocyte necrosis.$^{14,33}$ Because myocardial necrosis is an obligatory component of rejection, it is reasonable to apply this method for detection of acute cardiac rejection. The results of two clinical studies involving relatively small numbers of patients$^{9,12}$ suggested the usefulness of antimyosin scanning for detecting rejection. Although some experimental studies have been reported, there is a lack of full agreement.$^{10,11,13}$ Ueda et al$^{11}$ indicated that antimyosin may not be a sensitive marker of rejection in a rat heart transplant model. The difference between their study and ours may be related to the exclusion of all animals with myocyte necrosis of more than 5% by histological criteria to avoid distortion of their results by ischemic necrosis resulting from surgery. In the course of excluding this subset of animals, they may have also excluded those with necrosis that resulted from the rejection process. In our study, we were able to demonstrate that ischemic necrosis did not occur if perfusion was interrupted for less than 60 minutes. By including only animals with shorter periods of ischemia, we were able to assess necrosis caused by transplant rejection alone. Prolonged storage of donor hearts in a cold solution has been shown to cause mechanical dysfunction.$^{25}$ The results of our acute experiment using antimyosin clearly indicated that storage of donor hearts in a cold solution causes significant ischemic myocyte necrosis. Grafts with an ischemic time of more than 90 minutes showed significantly increased antimyosin uptake in comparison with grafts with an ischemia time of less than 60 minutes. Therefore, it is reasonable to exclude mice with an ischemic time of more

**Figure 7.** Bar graph of ratio of percent dose of antimyosin of grafted heart (G) to that of autologous heart (A) (G/A) in mice that show normal allograft contraction compared with G/A ratio in mice with and without histological evidence of myocyte necrosis. Eight of 24 mice with apparently normal mechanical activity had evidence of myocyte necrosis; G/A ratio in these eight mice is significantly greater than G/A ratio in the remaining 16 mice that did not show myocyte necrosis.

**Figure 8.** Scintigrams of nontreated allografted mice 3 days (left panel) and 4 days (right panel) after transplantation. Ratios of percent dose of antimyosin of grafted heart to that of autologous heart determined immediately after scintigraphy are 1.7 and 1.9, respectively. Faint uptake is visible in right panel in region of allograft. L, liver; K, kidney; A, autologous heart; G, graft.
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FIGURE 9. Scintigrams of nontreated allografted mice 10 days (left panel) and 14 days (right panel) after transplantation. Ratios of percent dose of antimyosin of grafted heart to that of autologous heart are 7.4 and 10.7, respectively. Strong, unequivocal accumulation of antimyosin is visible in regions of allografts in both panels. L, liver; K, kidney; A, autologous heart; G, graft.

than 60 minutes to minimize the effect of antimyosin uptake caused by intraoperative ischemic myocyte necrosis. The fact that isografts or nonrejected allografts showed no increase in antimyosin uptake as late as 15 days indicates that antibody uptake correlates with rejection-associated myocyte necrosis. Thus, the potential for false-positive scans caused by perioperative infarction could be excluded in our experiment.

As shown by Corry et al,19 B10D2 mice rapidly reject hearts from B6AF1 mice. In their study of seven mice with transplanted hearts, a sharp decline in impulse was observed between 7 and 22 days (median±SD time of sharp decline, 11.5±1.1 days) after surgery. In the present study, allografted mice were killed 2–15 days after transplantation. Although some mice showed significant reduction in the intensity of cardiac impulse at the time of termination, none showed a complete absence of impulse.

Uptake of antimyosin (percent dose of 125I antimyosin per gram of grafted heart and G/A ratio) generally reflected the degree of rejection by histological criteria.

FIGURE 10. Scintigrams of isografted mice 8 days (left panel) and 9 days (right panel) after transplantation. Ratios of percent dose of antimyosin of grafted heart to that of autologous heart are 1.5 and 1.4, respectively. L, liver; K, kidney; A, autologous heart; G, graft.
In nontreated cardiac allografts, antimyosin antibody accumulated progressively during the course of rejection. Reflecting the demonstrated antibody accumulation, antimyosin scintigraphy proved to be a sensitive indicator of myocyte necrosis.

Ballester-Rodés et al.12 studied the usefulness of antimyosin scintigraphy in detecting cardiac rejection in patients. They used a ratio of cardiac graft to adjacent lung background to quantitate uptake in sequential scans and regarded a heart-to-lung ratio of more than 1.6 as a positive scan. In experimental models of cardiac allograft rejection in dogs10 and rats,13 an uptake G/A ratio was used as the parameter for quantitation. These investigations showed that a ratio of more than 1.4 or 2.3 predicted the presence of moderate or severe histological rejection, respectively, which corresponds closely to the results reported here. It is of interest that regardless of differences in species studied or methods used, mild and moderate rejection are defined at similar graft-to-background antibody uptake ratios.

Mechanical dysfunction in the transplanted heart is the most serious outcome of cardiac rejection. However, the relation between deterioration in mechanical activity in allografts and uptake of labeled antimyosin has not been investigated previously. Antimyosin uptake is significantly increased in rejecting allografts with deteriorating mechanical activity compared with allografts with normal mechanical activity. We found that some mice with histological evidence of necrosis resulting from acute rejection showed apparently normal cardiac contractility. Even in these mice, the G/A ratio was significantly greater than the ratios in mice with histologically normal grafts. Although it should be noted that the direct palpation of grafts is a rough, subjective estimate of mechanical performance, these results suggest that accumulation of antimyosin is a more sensitive early detector of rejection than is decline in mechanical activity.

Cyclosporine (15 mg/kg-day) suppressed rejection in the majority of allografted mice. As shown in Figure 5, the G/A ratio remained low as late as 15 days after transplantation, with the exception of three mice. Histological examination revealed severe rejection in these three allografts. Scintigrams in these three animals showed significant accumulation of radioactivity in the allografts in comparison with cyclosporine-treated allografted mice without histological evidence of necrosis. The absence of nonspecific positive scan or false-negative scan during the period of cyclosporine administration attests to the usefulness of antimyosin scintigraphy during cyclosporine therapy. These results suggest that despite the limited scope of this evaluation, antimyosin scanning may be helpful in monitoring the effects of cyclosporine therapy.

Our experiments demonstrate that antimyosin scintigraphy can be used to detect cardiac rejection in the presence of myocyte necrosis, that the efficiency of antimyosin scintigraphy is not affected by cyclosporine treatment, and that antimyosin scintigraphy reflects the degree of severity of rejection by histological assessment. Myocyte necrosis is a relatively advanced indicator of acute cardiac transplant rejection, yet because many transplant patients receive intensive immunosuppressive therapy only after myocardial necrosis has been demonstrated by endomyocardial biopsy,34,35 a noninvasive test that clearly demar-

**Figure 11.** Scintigrams of allografted mice treated with cyclosporine 14 days (left panel) and 10 days (right panel) after transplantation. Histological examinations showed severe rejection in mouse shown in left panel and nearly normal findings in mouse shown in right panel. Ratios of percent dose of antimyosin of grafted heart to that of autologous heart are 7.2 (left panel) and 1.3 (right panel). L, liver; K, kidney; A, autologous heart; G, graft.
ulates myocyte necrosis could benefit these patients. It appears that clinical trials of antimyosin scintigraphy in the monitoring of patients who have undergone heart transplantation are indicated.

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References

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