Differentiation of Transiently Ischemic from Infarcted Myocardium by Serial Imaging after a Single Dose of Thallium-201

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SUMMARY Myocardial $^{201}$TI uptake and regional blood flow by the microsphere technique were determined in anesthetized dogs undergoing either 20 min of coronary occlusion and 100 min of reperfusion (N = 10) or 120 min of occlusion (N = 4). In both groups, $^{201}$TI was injected intravenously after 10 min of occlusion. In transiently occluded dogs, regional flow at the time of $^{201}$TI administration was reduced to $8 \pm 3\%$ of normal flow in endocardial layers of the central ischemic zone. After 100 min of reperfusion, flow values were not significantly different from normal. $^{201}$TI activity after reperfusion rose to $56 \pm 5\%$ of normal, demonstrating that redistribution of the radionuclide occurred during the reflow period. In animals with persistent occlusion, there was a significant relationship between $^{201}$TI uptake and flow ($r = 0.95$) and no evidence of redistribution of $^{201}$TI during the two hour occlusion period. In another five dogs receiving $^{201}$TI, serial gamma camera images obtained during reperfusion showed increasing uptake of the tracer in apical defects which returned to normal by 4 hours of reflow.

Thirteen patients with stable angina received 2 mCi of $^{201}$TI intravenously at peak exercise, and multiple gamma camera images obtained serially. All demonstrated zones of diminished $^{201}$TI uptake 10 min after exercise. Defects which partially or completely disappeared within 1-6 hours postexercise corresponded to areas supplied by coronary arteries with significant stenoses. Persistent defects were present in regions of old myocardial infarction. Six additional patients with acute myocardial infarction demonstrated $^{201}$TI myocardial defects which showed no significant change over 6 hours.

Thus, redistribution of $^{201}$TI into ischemic myocardium was demonstrated during transient coronary occlusion in dogs and after exercise stress in man. Sequential imaging after a single dose of $^{201}$TI at the time of exercise may provide a means for distinguishing between transient perfusion abnormalities or ischemia and myocardial infarction or scar.

IN RECENT YEARS the technique of imaging the heart using radiopharmaceutical agents for the assessment of regional myocardial perfusion, and for the detection and localization of myocardial infarcts has improved considerably. The existence of active transport mechanisms for concentrating monovalent cations in normal myocardium has led to the use of radioisotopes of potassium, rubidium, cesium and thallium for myocardial imaging. Uptake of these agents in myocardium is related to nutrient blood flow, and structural and functional integrity of the myocardial cell membrane. Areas of ischemic or infarcted myocardium appear as regions of diminished radioactivity in gamma camera images.

Thallium-201, a transitional metallic element, has recently been introduced as an agent for myocardial imaging with a gamma camera. It appears to concentrate in myocardium in a manner similar to potassium or rubidium but to a somewhat greater degree. Imaging after $^{201}$TI administration has also been employed for delineation of myocardial defects induced by exercise stress and these defects have correlated with regions of myocardium supplied by coronary arteries with significant obstructive lesions. Because of the rather long physical half-life of $^{201}$TI (73.5 hours) a rest imaging study at least 3 days later using another tracer injection is necessary to differentiate transient perfusion abnormalities or ischemia from old infarction.

In the present study, a new method for differentiating transient perfusion abnormalities or ischemia from infarc-
tion is described utilizing sequential imaging after a single intravenous dose of $^{201}$TI. This technique is based on the observation that there is redistribution of $^{201}$TI over time into areas of transient relative underperfusion or ischemia, whereas areas of infarction demonstrate persistent reduction in thallium activity.

**Methods**

**Animal Studies**

In this series of experiments myocardial $^{201}$TI distribution was compared in animals undergoing persistent coronary occlusion and animals subjected to 20 min of occlusion followed by reperfusion. Myocardial $^{201}$TI activity in ischemic and normal myocardium in both groups was related to blood flow as determined by microsphere distribution utilizing in vitro well-counting techniques. Similar studies were undertaken in dogs with persistent or transient coronary occlusion in which change in $^{201}$TI distribution over time was assessed by serial imaging with a gamma scintillation camera.

**Experimental Canine Model**

Transient or sustained coronary occlusion was induced in 19 open chest dogs as described previously. Briefly, animals were anesthetized with intravenous pentobarbital (30 mg/kg) and ventilated with a Harvard respirator with an FIO$_2$ of 0.4. The arterial pO$_2$ ranged between 81 and 106 mm Hg in these animals. Following a left thoracotomy, the heart was suspended in a pericardial cradle. Antero-apical myocardial injury was produced by serial snaring or ligation of multiple confluent branches of the left coronary system with 2-0 mersilene at 3 min intervals. Coronary venous branches remained intact. In 15 animals, reperfusion was instituted by release of snares after 20 min of coronary occlusion. In the remaining four animals, occlusions were maintained throughout the study period.

**Regional Blood Flow Measurements**

In all experiments in which regional flow was measured, an 8 inch polyethylene cannula was inserted into the left atrium through a stab wound in the left atrial appendage and held in place with a purse string suture. Nutrient blood flow to ischemic and nonischemic myocardium during occlusion and reperfusion periods was measured utilizing 15±5 micron carbonized radioactive microspheres as previously described. Microspheres were obtained as 1 mCi of nuclide suspended in 10 ml of 10% Dextran with 1 drop of Tween-80 added to minimize clumping (3M Co.). Prior to withdrawing a dose, vials containing microspheres were shaken in a Vortex mixer set at full speed for 5 min, after which the vials were agitated in an ultrasonic bath for 10 min. Bolus doses of approximately 4 million microspheres labeled with strontium-85 or cerium-141 were injected into the left atrium over a period of several seconds. We and others have previously shown that this dose of microspheres produces no alteration in systemic hemodynamics or in the epicardial electrogram. At the completion of each experiment, animals were sacrificed and microsphere distribution determined in multiple specimens from ischemic and non-ischemic zones as outlined in further detail in the next section.

**Control Experiments: Sustained Coronary Occlusion**

Four dogs underwent left coronary arterial branch occlusions as described above. Ten minutes after the last ligation each animal received 1.0 mCi of $^{201}$TI administered intravenously. Five minutes later a bolus of $4 \times 10^6$ $^{85}$Sr-labeled microspheres was injected into the left atrium via the indwelling cannula. Two hours later, after occlusion, a second bolus of microspheres labeled with $^{141}$Ce was injected and several minutes later animals were sacrificed, the hearts were excised, and multiple tissue specimens from ischemic and nonischemic zones divided into endocardial and epicardial halves. The weighed samples (0.75 to 1.5 g) were placed in plastic tubes and counted in a gamma well scintillation counter (Nuclear Chicago) at the appropriate energy windows for the three radionuclides with correction of counts in each channel for spill from other channels. Relative uptake of $^{201}$TI in ischemic myocardium was calculated as percent of nonischemic uptake. Regional blood flow in these samples was expressed as percent of non-ischemic posterior wall flow.

**Reperfusion Experiments**

Another 10 dogs underwent snaring of coronary arterial branches as described above. As was done in the control group, ten minutes after the last occlusion, 1 mCi of $^{201}$TI was administered intravenously. Five minutes later $4 \times 10^6$ $^{85}$Sr-labeled microspheres were injected into the left atrium to determine regional blood flow values during the initial distribution of thallium. Ten minutes after thallium administration (20 min after occlusion), coronary reperfusion was instituted by sequential release of snares, and another dose of microspheres labeled with $^{141}$Ce was injected 100 min later. Animals were then sacrificed, and microsphere and $^{201}$TI activities measured in multiple specimens of ischemic and nonischemic myocardium.

**Imaging Studies in Dogs**

In another two control dogs and five reperfused dogs serial imaging of the heart after $^{201}$TI administration was performed over a 4-6 hour period in the left lateral projection with a Pho-Gamma III HP camera (Searle Radiographics). Two hundred thousand count images were collected with a Hewlett Packard Gamma Computer System, displayed, and photographed on Polaroid film. In the reperfusion group, imaging was begun 10 min after $^{201}$TI administration, just prior to and immediately after release of the coronary arterial snares, and every 30 min during the subsequent reperfusion period. In control dogs, images were obtained serially during four hours of permanent occlusion.

**Patient Studies**

Serial imaging studies were undertaken in ten patients with angina pectoris after exercise stress and in six patients with acute myocardial infarction to assess changes in $^{201}$TI distribution over time. A defect which was present on initial myocardial images and which subsequently disappeared completely was defined as demonstrating "total redistribution," whereas a defect which displayed incomplete filling in with $^{201}$TI activity on delayed images was defined as "partial redistribution."
Exercise Thallium-201 Imaging

Ten patients in the fasting state, with chronic stable angina pectoris, and ages ranging from 40 to 65, underwent conventional exercise stress testing on a treadmill or stationary bicycle. Incremental exercise was continued until anginal chest pain, 2 mm or more of ST-segment depression on monitor leads (II, III, or V5), fatigue, or maximal exercise occurred, at which time 2 mCi of Thallium-201 chloride was given intravenously and exercise continued for another 60 sec. Ten to fifteen minutes later, gamma camera imaging was begun. A Searle Pho Gamma III HP camera equipped with a low energy all purpose (LEAP) collimator was used for imaging. Each 200,000 count image required 5–10 min to collect. Anterior and 30°, 50°, and 70° left anterior oblique images were obtained.

The initial imaging sequence as described above was completed in approximately 40 min after Thallium-201 administration. Afterwards, imaging was repeated in the anterior projection and the left anterior oblique (LAO) projection which best demonstrated the filling defect. Images in the same projection were also obtained 4–6 hours after exercise. Data were collected in the core of a PDP-9 computer, subjected to contrast enhancement and displayed on a 128 × 128 matrix oscilloscope with 64 levels of gray.16 Polaroid photographs of each image were obtained. Photographs of computer-processed images were reviewed independently by two of the authors and presence and location of regions of diminished uptake were noted.

Thallium-201 Imaging after Myocardial Infarction

Six patients hospitalized for acute myocardial infarction underwent myocardial imaging after intravenous administration of 2 mCi of Thallium-201 chloride. Patients were studied 24–96 hours after admission. Imaging commenced 15 min after injection. Images were obtained in the anterior and 30°, 50°, and 70° LAO projections. Serial images were obtained as described above at 45 min to 1 hour and 4–6 hours after injection.

Cardiac Catheterization Studies

All ten patients with stable angina pectoris and five of the six patients with acute myocardial infarction underwent coronary angiography and left ventriculography without complication. The coronary angiograms and left ventriculograms were reviewed to determine the extent and location of coronary artery disease and wall motion abnormalities. Angiographic and ventriculographic findings were correlated with the presence or absence of Thallium-201 redistribution in defects observed on myocardial images.

Statistical Methods

All data are presented as mean values ± standard error of the mean (SEM). The significance of differences was assessed by the paired t-test using a two-tailed distribution.17

Results

Animal Studies

Control Group

Regional blood flow measurements and Thallium-201 activity in four control dogs occluded for 2 hours and not reperfused are shown in figure 1. After 20 min of occlusion (10 min after Thallium-201 administration) regional flow in the center of the ischemic zone was reduced to 6 ± 3% (SEM) of nonischemic flow in endocardial and 19 ± 5% in epicardial layers (P < 0.001 by paired t-test). At the end of 2 hours of occlusion, regional flow values were not significantly different from those obtained after 10 min of occlusion. Thallium-201 uptake was significantly reduced to 15 ± 5% of nonischemic uptake in endocardial and 34 ± 7% in epicardial layers, both values slightly but significantly higher (P < 0.05) than regional flow 10 min after Thallium-201 administration, perhaps suggesting increased extraction of the radionuclide in low flow areas. As shown in figure 1, qualitatively similar findings were observed in the periphery of the ischemic zone.

Figure 2 shows the relationship between Thallium-201 uptake and regional myocardial blood flow in all myocardial samples (N = 50) from the control group of four dogs occluded for two hours. A linear relationship between Thallium-201 uptake and regional blood flow is evident (r = 0.95). Thus, in animals occluded for 2 hours, Thallium-201 uptake in ischemic myocardium was reduced in proportion to regional blood flow.

Reperfusion Group

Figure 3 summarizes regional blood flow measurements and Thallium-201 uptake in the ten dogs occluded for 20 min and reperfused. Regional blood flow during the occlusion period, when Thallium-201 was administered, was significantly reduced to 8 ± 3% of nonischemic flow in endocardial (P < 0.001) and 29 ± 6% in epicardial (P < 0.001) layers of the central ischemic zone. These values were not significantly different from the early regional flow reductions in this zone observed in control animals. After 100 min of reperfusion flow returned to normal or near normal values (fig. 3), Thallium-201 activity in the central ischemic zone after reperfusion was 56 ± 5% of nonischemic posterior wall activity in endocardial and 63 ± 5% in epicardial layers, both substantially higher (P < 0.001) than corresponding flow values at the time of Thallium-201 administration, suggesting that redistribution

![Figure 1. Regional myocardial blood flow (% normal flow) and Thallium-201 uptake (% normal) in epicardial and endocardial samples from central and peripheral ischemic zones in 4 dogs undergoing 2 hours of coronary occlusion. Thallium-201 was administered after 10 min of occlusion.](image-url)
of the isotope occurred into previously ischemic myocardium. Similar findings were observed in the periphery of the ischemic zone.

Figure 4 shows a linear relationship between $^{201}$TI activity at the end of 2 hours of reperfusion and regional blood flow during occlusion derived from measurements in all myocardial samples ($N = 134$) obtained in these dogs ($r = .81$). It can be seen that both the slope and the intercept of this relationship are different from that observed in control animals, reflecting greater $^{201}$TI activity relative to flow, attributed to redistribution of the radionuclide during the reperfusion period.

**Animal Imaging Studies**

The experiments described above using *in vitro* counting techniques to determine myocardial tracer uptake demonstrated a significant redistribution of $^{201}$TI into ischemic myocardium after transient coronary occlusion. Similar experiments employing sequential imaging after the intravenous administration of 1 mCi of $^{201}$TI was undertaken in another seven anesthetized dogs. In two dogs with permanent occlusions persistent absence of activity was demonstrated in the left ventricular apex in the distribution of the occluded coronary vessels over the 4 hour imaging period. In five with transient coronary occlusion, similar apical defects were apparent 10 min after $^{201}$TI administration during the occlusion phase. After reperfusion

**Figure 2.** Relationship between $^{201}$TI uptake and relative regional myocardial blood flow in all myocardial samples from the control group of 4 dogs occluded for 2 hours. The ordinate indicates $^{201}$TI activity as percent of nonischemic $^{201}$TI activity. The abscissa indicates relative flow (% normal flow) as determined by microsphere distribution. A strong linear relationship between $^{201}$TI uptake and regional flow is evident.

**Figure 3.** Regional myocardial blood flow (% normal flow) and $^{201}$TI uptake (% normal) in epicardial and endocardial samples from central and peripheral ischemic zones in 10 dogs undergoing 20 min of coronary occlusion and 100 min of reperfusion. $^{201}$TI was administered after 10 min of occlusion. $^{201}$TI uptake in ischemic zones is significantly higher than flow (stippled bars) at the time of thallium administration, reflecting redistribution of the radionuclide during the 100 min reperfusion period.

**Figure 4.** Relationship between $^{201}$TI uptake and relative regional myocardial blood flow after 20 min of coronary occlusion and 100 min of reperfusion derived from measurements obtained in all myocardial samples from these dogs. The ordinate indicates $^{201}$TI activity as percent of nonischemic $^{201}$TI activity. The abscissa indicates relative flow (% normal flow) as determined by microsphere distribution. Both the slope and intercept of this relationship are different from that observed in control animals (fig. 2), reflecting greater $^{201}$TI activity relative to flow, attributed to thallium redistribution during reperfusion.
progressive filling in of the defects occurred. After 4 hours of reflow these defects were no longer evident. The final image showed homogeneous distribution of $^{201}$TI activity in the left ventricular myocardium. Figure 5 shows serial images obtained in representative animals from the permanently occluded and reperfused groups.

**Patient Studies**

*Exercise Thallium-201 Myocardial Imaging*

Table 1 summarizes the clinical and catheterization data in the ten patients with stable angina pectoris who underwent $^{201}$TI exercise imaging. All patients had coronary artery disease documented by coronary angiography. Left ventriculograms were within normal limits in three while the remaining seven patients demonstrated wall motion abnormalities appropriate to their coronary cineangiographic anatomy. Six of these ten patients had unequivocally positive stress electrocardiograms (i.e., 2 mm or more of flat ST-segment depression). In three patients the stress electrocardiogram was negative.

All patients demonstrated defects reflecting regions of diminished $^{201}$TI activity in myocardial images obtained 10–15 min after exercise stress. Eight had regional defects on initial stress scans which filled in during the 4–6 hour postexercise imaging period. For example, in patient J.M. (fig. 6) with a negative stress electrocardiogram, severe three vessel coronary disease and a normal left ventriculogram, an apical defect demonstrable immediately after cessation of exercise was not evident in the 6 hour postexercise image. In the three patients with previous myocardial infarction, defects corresponding to the regions of scar persisted during the 4–6 hour study period. In one of these patients (AG) with a previous anteroseptal myocardial infarction, an occluded left anterior descending coronary artery and severe circumflex disease, exercise-induced anterolateral and posterior wall defects filled in while an upper septal defect persisted (fig. 7). The remaining two patients had old inferior wall myocardial damage and absent $^{201}$TI uptake in this region in the immediate postexercise images. Serial images obtained 4–6 hours after exercise stress showed persistence of these defects.

Comparison of serial images at rest was undertaken in three of the ten patients who had serial imaging after exercise. Serial rest images demonstrated mildly inhomogeneous uptake of $^{201}$TI which did not change significantly over the 6 hour imaging interval. These rest images appeared similar to the 4–6 hour postexercise images previously obtained.

**Myocardial Infarction Thallium-201**

myocardial imaging (table 2)

Six patients with clinical and electrocardiographic evidence of acute myocardial infarction underwent serial

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**Figure 5.** Left lateral images obtained serially over a 4 hour period in a transiently occluded (panel A) and permanently occluded (panel B) dog. A perfusion defect is evident at the apex in early images of both sequences (A and B). Sequence A was obtained prior to (initial image) and after release of coronary ligatures. Redistribution of $^{201}$TI activity can be seen only in sequence A with total filling in of the apical defect at 4 hours, whereas persistence of the defect is noted in Sequence B.
Myocardial imaging after intravenous administration of 2 mCi of $^{201}$TI. All patients were studied 24-96 hours after admission. Five patients had anterior or apical transmural infarction and the remaining patient had an anterolateral subendocardial infarction. Five of these six patients also underwent cardiac catheterization with coronary angiography and left ventricular cineangiography without complications. The four patients with transmural infarction who underwent catheterization demonstrated akinesis of the anterolateral and apical segments. The patients with anterolateral subendocardial infarction and normal coronary arteries demonstrated anterolateral wall hypokinesis. Areas of diminished $^{201}$TI uptake corresponded to regional wall motion abnormalities demonstrated by ventriculography.

Images obtained 10-30 min after $^{201}$TI administration demonstrated diminished or absent activity in the apical region in all patients, as well as in the anterolateral wall in two, septum in three, and inferior wall in two. Forty-five to sixty minute and 4-6 hour images demonstrated no change in thallium distribution in any of these patients. Serial images in one of these patients (AL) with an acute anterior myocardial infarction are shown in figure 8. Thus, patients with acute myocardial infarction demonstrated defects in thallium uptake that persisted over 4-6 hours of sequential imaging.

**Discussion**

Myocardial imaging after the intravenous administration of radioactive potassium or its analogs has been employed for detection of maldistribution of blood flow or detection of regions of myocardial ischemia during exercise stress.$^5,^7$ In patients with angina pectoris and significant coronary artery

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**Table 1. Clinical, Catheterization and Imaging Data in Ten Patients with Stable Angina Pectoris**

<table>
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<tr>
<th>Pt</th>
<th>Age</th>
<th>Rest ECG</th>
<th>Stress ECG</th>
<th>Coronary Stenoses</th>
<th>LV wall motion abn</th>
<th>$^{201}$TI perfusion defects 10-15 min post-exercise</th>
<th>$^{201}$TI Redistribution*</th>
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<td>52</td>
<td>WNL</td>
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<td>AL, AP</td>
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<td>++</td>
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<tr>
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<td>40</td>
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<td>AP</td>
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<td>AP</td>
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<td>LAD, RCA</td>
<td>None</td>
<td>AP</td>
<td>0: none; +: partial; ++: total</td>
</tr>
</tbody>
</table>

*Abbreviations: Pt = patients; ECG = electrocardiogram; WNL = within normal limits; ASMI = anteroseptal myocardial infarction; NSTWA = nonspecific T wave abnormalities; IMI = inferior myocardial infarction; LAD = left anterior descending; CFx = circumflex; LMCA = left main coronary artery; RCA = right coronary artery; AL = anterolateral; AP = apex; P = posterior; S = septum; CF = circumflex; LMCA = left main coronary artery; RCA = right coronary artery; AL = anterolateral; AP = apex; I = inferior; P = posterior; S = septum; IMI = inferior myocardial infarction; WNL = within normal limits; Negative = no abnormality; Positive = abnormality.*

$^{201}$TI Redistribution:

- **Partial Redistribution**: Incomplete filling in of defect.
- **Total Redistribution**: Complete filling in of defect.
disease demonstrated by coronary angiography, perfusion defects may not be apparent when the radionuclide is administered during the resting state. However, when the tracer is administered during exercise stress, regions of decreased tracer uptake frequently become apparent. Customarily, control images are obtained with a second injection of the radiopharmaceutical after an appropriate time interval allowing for physical decay and disappearance of radionuclide activity present from the first injection.

201TI has been the most promising radionuclide for myocardial imaging with the gamma camera. Its physical characteristics are superior to 42K and 86Rb for gamma camera imaging. It has been shown that blood clearance of thallium is rapid, similar to 42K or 86Rb, with maximum myocardial-to-blood ratios achieved 10–15 min after intravenous injection. Myocardial imaging with 201TI has been employed for detection of areas of relative underperfusion or areas of ischemia induced by exercise testing. As previously shown for 42K and 86Rb, regions of diminished tracer activity after exercise have correlated well with areas of myocardium supplied by significantly diseased coronary arteries. Gamma camera imaging with 201TI has also been employed for detection of regions of acute myocardial infarction.

Immediately after exercise, a region of diminished 201TI uptake on a single image may represent transient relative underperfusion or old myocardial infarction. Imaging after a second dose of thallium-201 conventionally given one week later is necessary to distinguish between the two. Results of the present study suggest that transient underperfusion or myocardial ischemia may be distinguished from old infarction by sequential imaging over a 4–6 hour period after a single dose of 201TI. This is based upon our observation that there is gradual redistribution of 201TI into exercise-induced defects corresponding to regions of myocardium supplied by coronary arteries with significant stenoses.

The results of our animal experiments indicate that when 201TI is administered intravenously to dogs with permanent coronary artery occlusion, the uptake of the tracer is directly proportional to regional myocardial blood flow as measured by the radioactive microsphere technique. In these animals, thallium distribution in epicardial and endocardial layers of the central infarct zone was slightly higher than regional flow to this area at the time thallium was injected, suggesting either increased extraction of the cation in low flow regions or some redistribution of the tracer via collateral flow during the two hour occlusion period. The finding of increased 201TI extraction in areas of severely diminished blood flow is similar to that reported in studies using radioactive potassium as the tracer. On the other hand, when 201TI was given during a 20 min occlusion period in animals that were subsequently reperfused, 201TI uptake in the central ischemic

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**Figure 7.** Representative sequence of thallium-201 myocardial images 15 min, 45 min and 6 hr after cessation of exercise in a patient with an old anteroseptal myocardial infarction. Anterior (AP) and left anterior oblique (LAO) views demonstrate complete filling in of anterolateral and posterior wall defects (total redistribution), whereas an upper septal defect (in region of old infarct) persists during the 6 hour imaging period. The anterolateral defect demonstrates partial redistribution by 45 min.
zone significantly increased to approximately 50% of non-ischemic uptake after only two hours of reflow. Thallium activity in the ischemic zone in these dogs was strikingly higher than flow at the time of thallium administration. Serial images obtained during reperfusion in another group of animals demonstrated progressive increase in thallium activity into the apical defect. By four hours of reperfusion thallium images had returned to normal in all dogs. On the other hand, animals which had permanent coronary artery occlusion demonstrated no redistribution into the apical defect over a 4 hour period. These experiments suggest that myocardium rendered ischemic for 20 min accumulates $^{201}$TI after regional flow is restored, whereas myocardium supplied by persistently occluded vessels shows no significant $^{201}$TI accumulation over time.

In order to explore the clinical utility of serial imaging after a single dose of $^{201}$TI, studies were carried out in patients undergoing exercise stress testing and in patients with stable acute myocardial infarctions. Early images in patients who received $^{201}$TI during peak exercise demonstrated perfusion defects in all patients who developed ischemic electrographic changes. Serial imaging in multiple oblique projections over a four hour period demonstrated redistribution of the tracer within myocardium which initially demonstrated a reduction in thallium uptake. Defects in $^{201}$TI uptake were demonstrable in the regions of myocardium supplied by stenotic coronary vessels. In several patients with old infarctions manifested by Q waves on the electrocardiogram and akinetic segments on the ventriculogram, no redistribution was observed into early defects during the 4–6 hour imaging period. This does not imply that some $^{201}$TI may not have been taken up initially by remaining viable cells in the region of scar. Serial images in these patients merely demonstrate that these regions do not show increasing $^{201}$TI activity over time. These exercise studies suggest that areas of reduced thallium activity seen immediately after exercise, and which subsequently fill in totally, reflect the presence of transient relative underperfusion or transient ischemia. On the other hand, regions of diminished activity that did not fill in represent persistently injured myocardium.

In patients with stable acute myocardial infarctions, thallium images showed "cold spots" in the areas of acute myocardial damage as defined electrocardiographically and by coronary and left ventricular cineangiography. Serial imaging over a four hour period in these patients did not show any significant change. This finding may have been predicted by the results of our animal studies in which no redistribution into regions of myocardium supplied by permanently occluded vessels was evident.

Preliminary data suggest that filling in of transiently underperfused or ischemic myocardial defects with $^{201}$TI may be explained by gradual extraction of the cation from the minimal concentration within the blood pool. When $^{201}$TI was selectively injected into the circumflex coronary artery of intact anesthetized dogs, serial images over a 6 hour period demonstrated appearance of $^{201}$TI activity into the remainder of the left ventricular myocardium and simultaneously into the splanchic viscera.

Redistribution of $^{201}$TI activity may be helpful in exercise imaging studies. First, it is important to be aware of this phenomenon and to begin imaging shortly after $^{201}$TI administration. Myocardial defects may be missed if imaging is delayed for more than one hour. If multiple oblique views are obtained, later images may demonstrate less of a defect than was present in earlier views, lessening the potential sensitivity of the technique. Next, improvement in the sensitivity of stress-imaging may be expected by using the serial imaging technique. Defects which show accumulation of $^{201}$TI activity after exercise may represent zones of relative underperfusion or ischemia rather than scar. Comparison of the 4–6 hour images with ones obtained earlier might afford easier resolution of perfusion defects which were not clearly evident with the initial image alone. Finally, since the entire exercise imaging study may be performed after a single dose of $^{201}$TI, patient radioactive exposure is lessened and expense of a repeat dose of radiopharmaceutical is eliminated.

Acknowledgments

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