Myocardial Thallium-201 Kinetics in Normal and Ischemic Myocardium

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SUMMARY The initial myocardial uptake of thallium-201 depends on myocardial blood flow distribution. The phenomenon of delayed thallium redistribution after transiently or chronically altered myocardial perfusion has been described. The net myocardial accumulation of thallium-201 after injection depends upon the net balance between continuing myocardial extraction from low levels of recirculating thallium in the blood compartment and the net rate of efflux of thallium from the myocardium into the extracardiac blood pool. These experiments were designed to measure separately the myocardial extraction and intrinsic myocardial efflux of thallium-201 at normal and at reduced rates of myocardial blood flow. The average myocardial extraction fraction at normal blood flow in 10 anesthetized dogs was 82 ± 6% (±SD) at normal coronary arterial perfusion pressures and increased insignificantly, to 85 ± 7%, at coronary perfusion pressures of 10–35 mm Hg. At normal coronary arterial perfusion pressures in 12 additional dogs, the intrinsic thallium washout in the absence of systemic recirculation had a half-time (T½) of 54 ± 7 minutes. The intrinsic cellular washout rate began to increase as distal perfusion pressures fell below 60 mm Hg and increased markedly to a T½ of 300 minutes at perfusion pressures of 25–30 mm Hg. A second, more rapid component of intrinsic thallium washout (T½ 2.5 minutes) representing approximately 7% of the total initially extracted myocardial thallium was observed. The faster washout component is presumed to be due to washout of interstitial thallium unextracted by myocardial cells, whereas the slower component is presumed due to intracellular washout. The net clearance time of thallium measured after i.v. injection is much longer than the intrinsic myocardial cellular washout rate because of continuous replacement of myocardial thallium from systemic recirculation. Myocardial redistribution of thallium-201 in states of chronically reduced perfusion cannot be the result of increased myocardial extraction efficiency, but rather, is the result of the slower intrinsic cellular washout rate at reduced perfusion levels.

DELPHU the widespread use of thallium-201 perfusion scintigraphy in clinical situations, there remain significant gaps in our knowledge concerning the kinetics of the radionuclide in normal and ischemic myocardium. The initial distribution of thallium in the myocardium immediately after i.v. injection is the result of both blood flow delivery of the tracer to the heart and the extraction of the tracer by the myocardium.1 2 The delayed or equilibrium distribution, particularly under conditions of altered perfusion, is less well understood. The determination of relative myocardial thallium concentration as a function of time in sequential imaging studies is being used increasingly to detect and evaluate coronary artery disease.3 4 5 The clinical use of delayed thallium redistribution imaging has brought about an acute need for an improved understanding of the mechanism of thallium kinetic exchange and redistribution. Many groups are now using delayed redistribution approach in exercise scintigraphy as a means to improve sensitivity and specificity in the detection of coronary artery disease and suggesting that there is a relationship between thallium redistribution patterns on delayed images and the functional severity of myocardial perfusion abnormalities.

It has been widely assumed that delayed thallium redistribution is primarily a reflection of changing myocardial perfusion between the stress state when thallium is administered and the resting state when delayed images are performed. There is now convincing evidence from studies in humans and animals showing thallium redistribution during resting states with stable myocardial blood flow.6 7 10 11 Clearly, thallium redistribution is not simply blood-flow-dependent, but rather reflects a transition from an initial blood-flow-related distribution to a delayed distribution that reflects a compartmental exchange equilibrium.

The determinant of the net compartmental exchange of thallium in the myocardium is the balance between continued myocardial extraction from systemic recirculation and the intrinsic myocardial loss of thallium into the systemic pool. Net loss of thallium from the myocardium occurs when thallium efflux exceeds uptake and, conversely, accumulation of thallium over time may occur if uptake exceeds efflux. Accordingly, the aims of this study were to determine the myocardial extraction of thallium and how it is influenced by altered myocardial perfusion and to measure the intrinsic myocardial washout rate of thallium in the absence of systemic recirculation and to determine if it related to myocardial perfusion. Determination of these two factors is necessary to understand the cause of altered myocardial thallium kinetics after i.v. injection under conditions of abnormal perfusion and the consequent redistribution of myocardial thallium.

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Methods
Myocardial Extraction Fraction of Thallium-201 at Normal and Reduced Coronary Perfusion Pressures

The relationship between myocardial extraction fraction for thallium-201 and blood flow must be determined before a quantitative relationship can be established between thallium uptake and myocardial perfusion. These canine experiments were undertaken to measure the extraction fraction for thallium-201 at different levels of blood flow reduction. The method for measuring thallium-201 extraction fraction is similar to the one described by Weich et al. Ten adult mongrel dogs (mean weight 27 ± 4 kg) were anesthetized with sodium pentobarbital (30 mg/kg), intubated, and placed on a Harvard Apparatus respirator at a rate of 13 respirations/min and a tidal volume of 500 ml. Lead II of the ECG was continuously monitored throughout the experiments. After a cutdown, a polyethylene catheter was inserted in the right femoral vein for administration fluids. Another catheter (Intramedic #7450) was advanced to the aortic arch via the right femoral artery for continuous monitoring of central aortic pressure. The third catheter was introduced into the left femoral artery and advanced to the distal aorta for collection of reference blood samples.

After a left thoracotomy, a 0.5-cm-long segment of the left anterior descending coronary artery (LAD) just distal to the bifurcation of the left coronary artery was dissected free of the epicardium and a hydraulic occluder was placed around the vessel (Rhodes Medical Instruments, Model VO-3). A Desseret 22-gauge angiocath was then inserted into the lumen of the LAD, just distal to the occluder, and sutured into place. This angiocath was then connected to a Hewlett-Packard 1280 pressure transducer to monitor distal LAD pressure continuously.

The coronary sinus was catheterized according to the method of Carlson and Utley, using a Bardac #5 infant feeding tube. A Harvard infusion pump was attached to the coronary sinus catheter and adjusted to withdraw blood at a rate of approximately 4 ml/min. An isotope mixture containing 3 μCi of ¹²⁴I-albumin and 12 μCi of thallium-201 per milliliter of saline was prepared and diluted 20-fold. The volume of the first injection was 0.4 ml. Subsequent injections of 0.8, 1.2 and 2.0 ml were administered directly into the LAD. The rationale for doubling the activity of the injectate for each injection is to compensate for the accumulation of background activity in the blood. The experimental protocol was as follows:

Control Extraction Fraction Measurements

Control extraction fraction measurements at normal coronary flow were undertaken by withdrawing blood from the coronary sinus for 5 seconds before the injection of the isotope mixture and continued while the isotope mixture was administered via the intracoronary cannula over a period of 10 seconds and flushed with 3 ml of saline. Coronary sinus blood was withdrawn for another 20 seconds after this bolus injection, after which the entire blood sample was transferred into preweighed plastic tubes (Falcon #2054) for subsequent analysis.

Extraction Fraction Measurements at Reduced Flow

To measure the extraction fraction for thallium at reduced flow, the hydraulic coronary occluder was inflated in a graded fashion to reduce the distal LAD pressure in the ranges of 70–80 mm Hg, 40–65 mm Hg and 10–35 mm Hg. At each level of diminished distal LAD perfusion pressure, extraction fraction was measured by injecting the isotope mixture distal to the occluder. After each decrement in LAD perfusion pressure, the bolus administration of the isotope mixture was preceded by a 10-minute stabilization period.

Analysis of Samples

The collected samples were weighed and counted in a gamma well counter (Packard Autogamma Scintillation Spectrometer, model #9601). Energy windows of 25–35 keV were used for ¹²⁴I-albumin, and 130–180 keV for thallium-201 (using the 135- and 167-keV gamma lines, which are better resolved by the well counter than the 80-keV x-rays used for scintiphoto imaging). The extraction fraction was calculated using the formula:

\[ 1 - \frac{Tl \text{(coronary sinus)} \times I \text{(injectate)}}{Tl \text{(injectate)} \times I \text{(coronary sinus)}}. \]

Measurement of Intrinsic Thallium-201 Washout as a Function of Coronary Perfusion Pressure

The goal of these experiments was to determine the rate of intrinsic thallium output from the myocardium in a way as to exclude the continuous reintroduction of thallium to the myocardium from the systemic pool. The intrinsic washout rate depends solely upon factors intrinsic to the myocardium, whereas the net thallium clearance time, which is determined after i.v. injection, depends upon how rapidly the tracer is being recirculated back to the heart from extracardiac organs and, therefore, will depend upon factors extrinsic to the myocardium, predominantly the blood pool concentration. It is essential to consider these two washout rates independently. The intrinsic washout rate of thallium-201 must be determined after direct intracoronary injection of the radiotracer. By this mode of administration, as will be shown, there is almost no systemic recirculation of thallium to the myocardium, which permits assessment of the true efflux rate from myocardium into the systemic pool. In these experiments, measurements of the intrinsic myocardial washout rate of thallium-201 were made under normal and low-flow conditions.

Twelve adult mongrel dogs (mean weight 26 ± 4 kg) were fasted for 24 hours before surgery. The dogs were anesthetized with sodium pentobarbital (30 mg/kg), intubated, and placed on a Harvard Ap-
paratus respirator with an average tidal volume of 500 ml at a rate of 13 respirations/min and with 10 cm of positive end-expiratory pressure. A 25-cm polyethylene catheter (Intramedic #7450, 0.066 i.d. × 0.095 o.d.) was inserted into the right femoral artery through a cutdown and advanced to the aortic arch. An identical catheter was inserted into the femoral vein for administration of fluids. The arterial catheter was used to monitor central aortic pressure continuously. Lead II of the ECG was also recorded continuously. As in the previous protocol, the LAD was dissected free from the epicardium, 0.5 cm from the bifurcation of the left coronary artery, and the hydraulic balloon occluder was placed around the vessel at that site. The LAD was then cannulated with a 22-gauge intracath (Dessereit Angiocath) and secured to the epicardium with a suture in such a way that the tip of the catheter was distal to the occluder within the artery.

After baseline steady-state hemodynamic measurements were obtained, an external gamma-detector probe (Nuclear Chicago Model 8742 pulse-height analyzer) was positioned over the heart 25 cm above the epicardial surface. Thirty microCuries of thallium-201 were then administered through the intercath into the LAD and flushed with 4 ml of normal saline. Absolute isotopic disintegrations were recorded and printed every 30 seconds by interfacing the gamma probe with a scaler-timer (Hewlett-Packard Model 5202 L) and an automated digital strip recorder (Hewlett-Packard Model H-43 562A). Control thallium counts were recorded in this manner for 15 minutes. The balloon occluder was then activated until an occlusion resulted in the desired decrease in distal LAD perfusion pressure. Steady-state hemodynamic measurements and electrocardiographic recordings were then obtained. The thallium-201 isotopic activity was again recorded over the same cardiac area under low perfusion pressure conditions as described above. Thallium activity was recorded every 30 seconds for another 15 minutes. After the second recording, the balloon occluder was deflated and after a brief recording of blood pressure and cardiac rhythm, a third 15-minute period of thallium activity recording over the myocardium was accomplished as above. Before the dogs were sacrificed, arterial blood samples were obtained for determination of thallium-201 activity. Myocardial samples were obtained from regions in the distribution of LAD and left circumflex coronary arteries. Biopsy samples from lung tissue were also obtained.

The thallium-201 washout rates were obtained from the data by standard least-squares curve-fitting methods using exponential functions. After calculation of the half-time (T½) of the intrinsic thallium washout rate, these values for each dog were plotted against the LAD perfusion pressure from which they were derived. Twenty-four points were obtained in the 12 experimental dogs, one control value and one value at the reduced perfusion pressure for each. These washout rates were then plotted against the perfusion pressure on a single graph.

Comparison of Intrinsic Thallium Washout Rate Measurements Obtained from External Probe vs Direct Coronary Sinus Sampling

To validate the measurements of intrinsic myocardial washout thallium-201 from data collected by the external gamma probe, we compared these measurements with those calculated in the same dogs from direct coronary sinus samplings. This was undertaken to ascertain whether myocardial geometric changes after reduced flow (i.e., systolic expansion of the ischemic segment) could alter the measurements alone when the probe was used. Accordingly, five additional mongrel dogs (mean weight 24 ± 2 kg) were anesthetized, mechanically ventilated and surgically prepared as before. After baseline steady-state hemodynamic measurements were obtained, the external gamma probe was again positioned 25 cm above the epicardial surface of the left ventricle. Thirty microCuries of thallium-201 were administered directly into the LAD. The isotopic disintegrations in counts per 30 seconds as detected by this probe were recorded on the automated strip-chart recorder for 45 minutes after thallium injection.

Simultaneously, 2.0-ml blood samples were withdrawn through a previously implanted coronary sinus catheter at 1-minute intervals for the 15 minutes and thereafter at 5-minute intervals. The collected coronary sinus samples were weighed and counted in a gamma scintillation counter (Packard Autogamma Scintillation Spectrometer, Model 9601) at the appropriate energy window for thallium-201 (130–180 keV). Thallium-201 washout rates (T½) were measured from the probe data and from the coronary sinus samples and compared. The intrinsic washout rate was calculated from the coronary sinus data by plotting counts over time on semilogarithmic paper. Using the monoeponential decay function C(t) = Coe−Kt, where C(t) is the myocardial thallium concentration at time t and K = 0.693/T½, which represents the intrinsic clearance coefficient, we solved for T½ for the entire 45-minute experimental period. The same method was used to calculate T½ using the probe data.

Results

Extraction Fraction Measurements

The extraction fractions for thallium-201 at normal and reduced LAD perfusion pressures for the 10 dogs are summarized in figure 1. There were no significant differences in thallium-201 extraction fractions at various levels of reduced perfusion compared with the control values. There was a slight but not statistically significant increase in extraction fraction when the perfusion pressure was reduced to 10–35 mm Hg. The extraction fraction at this level of reduced perfusion was 85 ± 7%, compared with 82 ± 6% at perfusion.
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pressures of 100–125 mm Hg. Thus, the extraction of thallium by the myocardium is not significantly altered at various levels of flow reduction.

Intrinsic Myocardial Thallium-201 Washout

The intrinsic washout rate for thallium-201 in a representative dog from this group is plotted in figure 2. The net clearance rate obtained after i.v. injection of 1.5 mCi of thallium-201 is shown on the same graph for comparison. The latter measurement was made 1 week after the intracoronary injection study. The washout rate after the intracoronary injection of the isotope is significantly more rapid, as shown by the significantly steeper slope of thallium-20 activity over time.

In the 12 dogs that underwent transient partial occlusion of the LAD, mean aortic pressures at control, during LAD occlusion and reflow periods were 110 ± 20 mm Hg, 110 ± 19 mm Hg and 110 ± 20 mm Hg, respectively. There was no significant alteration in systemic arterial pressure during the experimental protocol. The mean LAD perfusion pressure was 110 ± 20 mm Hg during the control period and reduced to levels in the range of 25–63 mm Hg for each of the 12 dogs during occlusion. During the reflow period, the LAD pressure returned to baseline (110 ± 19 mm Hg). The control and reflow LAD pressures were, as expected, identical to aortic pressure measurements. The mean heart rates during each of the three 15-minute periods were 150 ± 20 beats/min, 154 ± 19 beats/min and 147 ± 20 beats/min. There is no significant difference between these values.

Thallium-201 activity vs time was plotted on semilogarithmic paper. Using the monoequation function $C(t) = C_0 e^{-Kt}$, where $C(t)$ is the myocardial thallium concentration at time $t$, and $K = 0.693/T_{1/2}$, which represents the intrinsic clearance coefficient, the $T_{1/2}$ of thallium washout during each 15-minute period was calculated. Figure 3 shows the washout plot during the control, occlusion and reflow periods in a representative dog from this group after intracoronary thallium injection. In this instance, the $T_{1/2}$ of thallium washout was 52 minutes and markedly increased to 311 minutes after coronary occlusion. After reflow, the $T_{1/2}$ returned to 66 minutes. The mean arterial blood thallium-201 activity was 5 ± 2 disintegrations/sec (dps)/g, which was not significantly different from background, which was approximately 2 dps for these experiments. Mean thallium-201 activity was 75 ± 28 dps/g in lung tissue, 176 ± 176 dps/g in circumflex-perfused myocardium, and 6371 ± 3461 dps/g in LAD-perfused myocardium. These values indicate that there is negligible blood pool activity after intracoronary injection, in contrast to findings observed after i.v. injection of the radionuclide.

Thallium-201 washout ($T_{1/2}$) was plotted as a function of the mean LAD distal perfusion pressure (fig.

![Figure 1](http://circ.ahajournals.org/download/figure/1595204158692.png)

**Figure 1.** Extraction fraction for thallium-201 as a function of left anterior descending coronary artery (LAD) perfusion pressure.

![Figure 2](http://circ.ahajournals.org/download/figure/1595204158692.png)

**Figure 2.** The intrinsic thallium washout rate and net thallium clearance rate in a representative dog. The intrinsic washout rate after the intracoronary injection of the radionuclide is significantly more rapid than the net clearance of thallium from the myocardium measured after i.v. injection.
by some mechanical means. Nevertheless, the T½ values measured by the probe and by serial coronary sinus thallium concentrations were comparable, indicating that the probe method for measuring intrinsic thallium washout after intracoronary injection is valid.

Components of the Intrinsic Thallium Washout Curve

Differences in the appearance of thallium washout curves obtained from monitoring myocardial thallium activity by the probe and that obtained by monitoring the venous concentration, particularly with respect to the early washout phase (figs. 5A–C), are apparent. This is caused by the striking appearance of the early component, with a T½ of 2.25 minutes (fig. 5C), in the samples of venous concentration and is attributed to

<table>
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<th>Experiment</th>
<th>Mean LAD pressure (mm Hg)</th>
<th>T½ probe (min)</th>
<th>T½ coronary sinus (min)</th>
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<tr>
<td>1</td>
<td>95</td>
<td>96</td>
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<tr>
<td>5</td>
<td>85</td>
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Mean ± SD 91 ± 17 100 ± 19 104 ± 23

Abbreviation: LAD = left anterior descending coronary artery; T½ = washout rate.
early washout of thallium from the interstitial compartment. This component of the curve is rapid and therefore contributes greatly to the early venous concentration because the rapid egress of a small amount of thallium early in the washout constitutes a large percentage of the thallium leaving the myocardium during that period. However, by comparing the total area beneath the extrapolated portion of the 2.2-minute component with the total area of the extrapolated portion of the longer curve component, which is taken to represent intracellular washout, this interstitial component represents only 7% of the total injected thallium in the example. Because 93% of the total thallium remains in the myocardium, which is sampled by the probe, this early interstitial component is barely detectable by the probe measurement (fig. 5A). The probe merely monitors the thallium that remains in the myocardium, in contrast to the venous sampling method, which measures thallium that is leaving the myocardium.
Discussion

The results of this study show that there is no significant alteration in the extraction fraction for thallium-201 at significantly reduced myocardial perfusion pressures (25–50 mm Hg). Second, the intrinsic washout rate of thallium-201 is markedly prolonged when the coronary perfusion pressure is reduced. These observations now permit us to formulate an explanation for thallium-201 redistribution that occurs in the absence of a change in coronary blood flow between the initial distribution and the delayed distribution.

The results of our extraction fraction studies show that the capacity of the myocardium to extract thallium is remarkably constant over a wide range of coronary perfusion pressures. In the dogs we studied, 82% of the thallium-201 was extracted from the blood at normal central aortic pressures during the first passage through the coronary circulation. This average value is comparable to that described previously under normal flow conditions. When the LAD was partially occluded to lower the perfusion pressure to levels of 30 mm Hg, the extraction fraction increased only slightly, to 85% (NS vs control). This small increase in the capacity of severely hypoperfused myocardium to extract thallium-201 cannot account for the relative increase in thallium-201 activity observed as redistribution during fixed reduction in blood flow.

In contrast to the observed constancy of extraction fraction for thallium-201 at reduced coronary perfusion pressures, the present study shows that the intrinsic washout rate for thallium-201 is markedly prolonged when coronary perfusion pressure is diminished. At coronary perfusion pressures above 55 mm Hg, the T½ for intrinsic thallium washout averaged 55 minutes. As the distal LAD pressure was reduced in a graded manner below this level, the washout T½ increased markedly, approaching 300 minutes when the vessel was obstructed to a degree that approached the coronary critical closing pressure. Two distinct components to the intrinsic washout curve were observed. The first was a rapid component immediately after intracoronary injection, which represents the myocardial clearance of unextracted thallium-201 from the interstitial space. The T½ for this component averaged approximately 2.5 minutes. Approximately 5 minutes after intracoronary thallium-201 administration, the intrinsic washout curve was monoexponential from 5 minutes to 2 hours after injection. The washout rates were monitored for no more than 2 hours because of the eventual occurrence of systemic recirculation, which would interfere with the measurement of intrinsic washout rate at later time points. As the coronary perfusion pressure is reduced, the intrinsic washout rate for thallium-201 changes dramatically and slows markedly when hypoperfusion becomes more severe. The explanation for this slowing of thallium-201 efflux with reduction in coronary perfusion pressure is not entirely clear, but may reflect either altered metabolic activity in the cell membrane, alteration in thallium-201 diffusion kinetics between the plasma compartment and the myocardial cell in low-flow regions, or undetermined causes. Interestingly, the washout rate was immediately restored to normal by coronary reperfusion that resulted in restoration of normal LAD perfusion pressures and presumably regional myocardial blood flow.

The data from these and other studies support the concept that after i.v. injection, thallium-201 does not simply remain fixed in the myocardium, but continuously exchanges with new thallium from systemic recirculation. This process of continuous exchange readily leads to an explanation for thallium-201 redistribution after transient hypoperfusion. Under these conditions, thallium-201 is injected and initially extracted during a period of relative hypoperfusion resulting in an initially decreased intracellular thallium-201 concentration. If, subsequently, the perfusion and cellular kinetic transport return to normal, as with reperfusion after a brief coronary occlusion, the continuous extraction of thallium by systemic recirculation will eventually result in a normal equilibrium intracellular thallium-201 concentration. The time course of this delayed normalization of myocardial thallium concentration after transient LAD occlusion has recently been reported. In these latter experiments, thallium-201 activity was reduced by 80% compared to the normal zone during LAD occlusion. Near-equalization of activity between normal and ischemic zones occurred by 4 hours, although significant redistribution was observed at 20 minutes after flow restoration. Continuous extraction of thallium from systemic recirculation also accounts for disappearance of defects after stress-induced ischemia or when the radionuclide is administered during an episode of transient spasm of a major coronary vessel. Under these conditions, a maldistribution of blood flow occurs at the time of thallium-201 injection. However, because of restored perfusion and assuming the preservation of cell membrane function, myocardial cells initially deprived of thallium-201 continue to extract thallium-201 being recirculated through the blood pool from the extracardiac compartments. Eventually, the intracellular thallium concentration will normalize and all viable myocardial cells will reach a stable value of intracellular thallium-201 concentration.

The situation after chronic reduction of regional myocardial blood flow is slightly more complex. Consider, for example, a myocardial region that is persistently perfused at 50% of its normal level. The rate of thallium-201 delivery to this myocardial region will therefore also be reduced by 50% compared with the normal region. Even if the extraction efficiency in the underperfused region approached 100%, the rate of thallium-201 delivery to myocardial cells in this region would remain far below that of the normally perfused region. If the intrinsic washout rate of thallium-201 were to remain constant, the intracellular concentration of thallium-201 in the underperfused region would necessarily be reduced by an amount nearly in
proporition to the decreased blood flow. However, the observation of thallium-201 redistribution in this situation (fixed reduction in coronary blood flow) clearly indicates that the intracellular concentration tends to normalize rather than remaining persistently decreased. The only other possibility to explain redistribution without an increase in flow or thallium extraction is that the intrinsic washout rate must decrease in the region of hypoperfusion. This creates a situation in which both the input rate and the output rate are chronically reduced, so as to allow an increasing intracellular concentration. The experimental data from this study indicate that this must be the case, because the intrinsic washout rates were strikingly prolonged under conditions of reduced myocardial perfusion.

The experimental data recently described by Gewirtz et al. are in total agreement with this concept, although their approach and model were substantially different from ours. Gewirtz et al. administered thallium-201 intravenously and allowed it to distribute throughout the body under conditions of normal perfusion. Then, transient hypoperfusion was achieved by occluding the LAD and the venous thallium-201 concentration was continuously monitored from the coronary sinus thallium-201 concentration during the time of transiently reduced coronary blood flow. Gewirtz et al. observed that after coronary artery occlusion, the net myocardial thallium concentration and the venous concentration of thallium were unchanged. This observation gave rise to the apparently contradictory statement that the myocardial washout rate of thallium-201 was independent of blood flow. Actually, as the rate of input of thallium from systemic recirculation is decreased by the coronary occlusion, the intrinsic washout rate of thallium is proportionately reduced, and there is no net change in thallium concentration in the occluded segment. Moreover, the intrinsic myocardial washout rate is given as the product of blood flow times concentration of the venous outflow. The data of Gewirtz showed that when the flow was reduced, the concentration of venous outflow remained unchanged. This observation necessarily implies that the intrinsic washout rate must have decreased in proportion to the decreased blood flow at the time of coronary occlusion. These findings are entirely consistent with our results, which show a decrease in intrinsic myocardial washout rate with decreasing perfusion pressure. Confusion arose when Gewirtz et al. interpreted their data as indicating that myocardial washout rate was independent of flow. His data showed no change in net washout under those particular circumstances, but in fact the same data prove that intrinsic washout rate must have changed in accordance with our measurements. The ramifications of this finding and the interpretation we have applied result in a model that explains not only why thallium-201 redistribution occurs in regions of chronic hypoperfusion when thallium-201 is injected intravenously during hypoperfusion, but also why the intracellular thallium-201 concentration, once established during normal blood flow, will not change in response to subsequent hypoperfusion.

In conclusion, from the experimental data obtained in these and previous animal studies, and from clinical experience of serial rest imaging in patients, a better understanding of thallium-201 kinetics has evolved. Clearly, the initial distribution of thallium-201 in the myocardium is proportional to regional myocardial blood flow at the time of injection. Redistribution begins immediately and proceeds continuously until an equilibrium distribution is reached, which is determined by a net balance between thallium-201 input and intrinsic thallium-201 washout. It is now clear from the washout measurements made in these experiments, and from measurements made of the thallium-201 extraction coefficients, that redistribution cannot be explained simply on the basis of different rates of myocardial accumulation. At least in the instance of persistently diminished perfusion, delayed thallium-201 accumulation and redistribution must be associated with a delayed intrinsic myocardial thallium-201 washout rate. Finally, these studies suggest the kinetic exchange rates might be used as a means of quantitating the functional degree of severity of coronary artery stenosis.

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Identification of Pulmonary Emboli in the Dog: Comparison of Angioscopy and Perfusion Scanning

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SUMMARY Fifteen dogs were studied by perfusion scan, angioscopy and autopsy. In 10, emboli were formed in leg veins and released before study; five dogs were not embolized and served as controls. In controls, angioscopy disclosed no emboli, perfusion scans were normal after angioscopy and autopsy disclosed no emboli. Among the embolized dogs, 23 emboli were identified at autopsy. Perfusion scans disclosed 23 defects, but in three dogs there was a disparity between scan and autopsy localization. Angioscopy identified 21 of the 23 autopsy-defined emboli and localized them correctly; two emboli in vessels less than 1 mm in diameter were not visualized. Angioscopy may provide a useful new approach in animal investigations of pulmonary embolism and perhaps, after additional study, in selected patients.

THE SPECIFICITY, sensitivity and risk/benefit ratio of techniques for diagnosing pulmonary embolism are controversial. Direct in vivo visualization of emboli might help resolve certain elements of this controversy in animal investigations and in selected patients. We have described development of a fiberoptic device, the angioscope, for direct, in vivo visualization of the right-heart chambers and the pulmonary vasculature. Among the potential diagnostic applications of this device is the direct visualization of pulmonary emboli. To evaluate this application, we studied 10 dogs with experimentally induced emboli and five nonembolized controls with angioscopy, lung perfusion scans and autopsy.

Methods

Ten dogs were sedated with pentobarbital (25 mg/kg), intubated and mechanically ventilated at tidal volumes of 15 ml/kg. To produce thrombi, we occluded the femoral vein by inflating the balloon of a Swan-Ganz catheter passed retrograde from the paw and injecting 10 NIH units of bovine thrombin proximal to the balloon. After “aging” in situ for 30 minutes, the thrombi were embolized by deflating the balloon and gently milking the leg manually. This technique consistently (> 95%) produces thrombi and emboli.

Within 10–15 minutes after embolization, the angioscope was inserted through a right jugular venotomy and guided to the pulmonary arterial system under direct visualization. Its position was periodically confirmed by fluoroscopy. The locations of all emboli were recorded by the angiographer during the procedure, and the angioscope was removed. The entire procedure, from venotomy to angioscope removal, lasted approximately 20 minutes.

Next, 1 mCi of $^{99m}$Tc-albumin microspheres was injected intravenously and perfusion scans were obtained in anterior, posterior and both lateral positions. The scans were interpreted by one of the authors, who was unaware of the angiographic results.

Finally, the dogs were heparinized and sacrificed, and postmortem examination was performed immediately. Dissection was carried down to arterial branches of 1 mm in diameter, and the presence of all emboli was recorded by a third member of the investigative team.

Five control dogs were studied in the same way as the embolized dogs, except that venous thrombi were not induced. The control scans were interpreted along with those from the embolized dogs.

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