Effect of Coronary Blood Flow on Uptake and Washout of Tc-99m DMPE and Tl-201

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After intravenous administration of Tc-99m DMPE the flow-dependent kinetics were studied in dogs during induced ischemia and during induced maximal reactive hyperemia. A control group was also studied. Mean time-activity curves obtained from the myocardial wall were compared within the same intervention group and also with other groups. During reactive hyperemia, there was a rapid and absolute increase in uptake followed by a rapid washout, whereas during ischemia there was a slow and decreased uptake followed by a slow washout. The magnitude of Tc-99m DMPE uptake during reactive hyperemia was slightly less than that of Tl-201, but the decreased uptake with ischemia was about equal for the two agents. Following maximal uptake in the myocardium the effective half-life of Tc-99m DMPE was one-third to one-fourth that of Tl-201. The similar kinetics of Tc-99m DMPE compared to Tl-201 suggests its usefulness in the evaluation of ischemic heart disease.

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The design and development of Tc-99m-labeled myocardial imaging agents, resulting in the water-insoluble Tc-99m DIARS (*1*), and water-soluble Tc-99m DMPE (*2*) have recently been reported from our laboratories, and has been extensively studied as a myocardial imaging agent in the anesthetized dog (*3*).

The usefulness of a myocardial imaging agent is clearly dependent upon its ability to distribute proportionally in the myocardium over a wide range of regional coronary blood-flow rates during exercise, and its ability to redistribute with time (*4*). This study deals with Tc-99m DMPE kinetics in the dog under conditions of varying coronary blood flow produced by regional transient ischemia and reactive hyperemia in the initial phase, and followed by continuous assessment of time-activity curves to evaluate regional washout. The results of all studies were compared with the Tl-201 data obtained in an earlier study using an identical experimental design (*5*), which was designed to help explain the redistribution phenomenon observed with Tl-201.

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MATERIALS AND METHODS

Preparation. The preparation and quality control of Tc-99m DMPE has been described (*2,3*). Seven mongrel dogs weighing 28–35 kg were anesthetized with sodium pentobarbital in a dose of 30 mg/Kg. Respiration was controlled with a mechanical respirator. Through a left thoracotomy, a Gould electromagnetic flow probe was placed around the proximal part of the circumflex coronary artery, and an hydraulic occluder was placed immediately distal to the flow probe. The ends of the occluder and the lead wires of the flow probe were tunneled dorsally to the base of the neck. The dog was allowed to recover for 2–3 days. Three of these dogs served as their own controls for both the ischemia and reactive-hyperemia studies, separated by intervals of one week. Two additional dogs were studied only during ischemia, and

another two only during reactive hyperemia, because of problems resulting from persistent kinking of the artery by the flow probe. Thus, data for the ischemia and reactive-hyperemia studies were obtained from a total of five dogs in each group. Six dogs weighing 26–35 kg underwent no surgical intervention and served as controls (*3*).

Data collection. The anesthetized dogs were placed in the right decubitus position under a gamma camera equipped with a parallel-hole, high-resolution collimator, which was angled for a 60° left anterior oblique view to visualize the anteroseptal wall (control area) and the posterolateral wall (ischemic or hyperemic area). During the data collection, arterial blood pH and p_{CO_2} were maintained at 7.40 ± 0.05 and 30 ± 5 mm Hg, respectively.

Zero flow was determined at the beginning of the study by 5–10 sec occlusion of the artery. The ischemia experiments were designed to validate zero flow in the circumflex coronary artery when the imaging agent was given. The reactive hyperemia experiments were designed so that the imaging agent was administered during the maximal flow, expressed as a percentage increase over baseline flow rather than as absolute flow. Thus, the flow was continuously recorded from the baseline, occlusion to the subsequent flow after release of the occlusion.

Five to seven mCi (185–259 MBq) of Tc-99m DMPE was administered intravenously as a bolus at the onset of a 2-min occlusion of the circumflex coronary artery during the ischemia study, and 30 sec after release of a 2-min occlusion in the reactive-hyperemia study. These times coincided with either zero or maximal circumflex coronary blood flow, respectively. Time zero was designated as the time of intravenous Tc-99m DMPE administration for all groups. Data beginning at time zero were stored in a computer in a 64 × 64 matrix. The data were accumulated in 1-min frames continuously during the initial 30 min, then for two successive 1-min frames at 10-min intervals, for a total of 120 min. Frequent blood samples were also obtained from four dogs in each group for the clearance study through the preinserted catheter, beginning 1 min after dose (*3*).

Data analysis. Regions of interest were defined over the anterior and posterior left-ventricular walls as shown in Fig. 1. Justification for defining the lung background as an area between the aorta and ventricular cavities has been offered previously (*5–7*). The normalized counts, in the 50 pixels over the region of interest and the background area, were generated as a function of time from the stored data. The net counts in the myocardium were obtained by subtracting the lung background from the counts obtained from the region of interest. During the initial 30 min, the net count represented the counts accumulated within the preceding 1 min. Thereafter, two 1-min intervals of counts were averaged to represent the

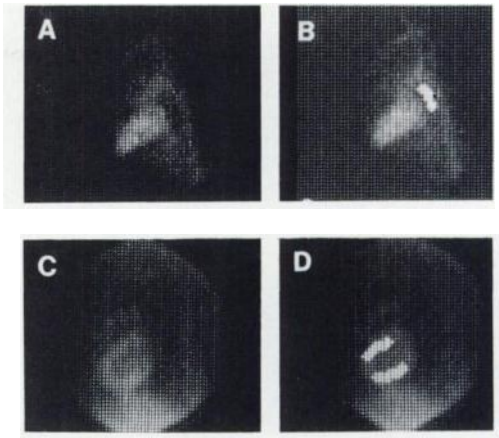

FIG. 1. Digitized initial blood-pool (A) and late (C) images were used to define lung background (B) and cardiac (D) regions of interest. Both anterior and posterior myocardial walls were defined by large areas of interest (D), excluding mainly basal and apical regions.

1-min value at each data point. In all three groups, the maximal net count observed in the uninvolved anterior wall was designated as 100% activity. The remainder of the activities in the anterior and posterior walls, lung, and liver background were expressed relative to the 100% anterior-wall value in each dog. A mean value ± 1 s.d. was calculated for each data point. Thus these time-activity curves were directly comparable, since all the values were expressed relative to the value obtained in the anterior wall (*5*). Decay correction was not made for these calculations unless noted.

From a baseline value of circumflex coronary artery blood flow, the percent change at various time intervals was calculated in each dog. The mean percent change of the coronary blood flow was then calculated to correlate with changing uptake rates of the agent in the myocardium. Subsequently, linearity of the flow measurement was verified by timed blood-collections with the probe in situ before the dog was sacrificed.

The blood clearance was calculated by methods described (*3,8*). For statistical evaluation, the paired Students t-test was used.

RESULTS

Blood clearance. The blood clearance of Tc-99m DMPE in either the ischemia or reactive-hyperemia groups was compared with that of the control group, and showed no statistically significant differences throughout the 120-min observation period. Thallium-201, on the other hand, showed a significantly delayed clearance in the ischemia group at 1 min when compared with either the control or reactive-hyperemia groups ($p < 0.025$) (*5*), but not thereafter. Table 1 shows the blood clearance of Tc-99m DMPE in the control group, with and without Tc-99m decay correction, compared with Tl-201 data for control and ischemia groups without decay correc-

TABLE 1. BLOOD CLEARANCE OF Tc-99m DMPE AND Tl-201* (% REMAINING IN BLOOD POOL)

Time (min)	Tc-99m DMPE (control: n = 4) (decay not corrected)	(decay corrected)	Tl-201 (control: n = 3) (ischemia: n = 5) (decay not corrected)	
0	100	100	100	100
1	32.4 (27.2–37.0)†	32.5 (27.3–37.1)	23.9 (20.5–27.2)†	46.8 (32.4–69.8)
3	8.0 (7.1–8.9)	8.0 (7.1–9.0)	12.0 (8.5–17.2)‡	16.6 (9.7–22.0)‡
5	5.3 (5.0–5.8)	5.4 (5.0–5.9)	8.1 (5.9–11.4)	10.5 (6.7–12.5)
10	3.7 (3.4–4.1)	3.8 (3.5–4.2)	4.1 (3.5–5.2)	5.3 (3.6–6.1)
20	3.0 (2.7–3.3)	3.1 (2.8–3.4)	2.4 (2.2–2.7)	2.8 (2.3–3.4)
30	2.7 (2.3–3.1)	2.9 (2.4–3.3)	2.1 (2.0–2.3)	2.2 (1.8–2.6)
40	2.5 (2.0–2.9)	2.7 (2.2–3.1)	1.9 (1.8–2.1)	1.9 (1.7–2.3)
60	2.2 (1.8–2.5)	2.5 (2.0–2.8)	1.7 (1.6–1.8)	1.6 (1.3–1.8)
80	2.0 (1.6–2.3)	2.4 (1.9–2.7)	1.5 (1.4–1.7)	1.4 (1.1–1.7)
100	1.9 (1.5–2.2)	2.3 (1.8–2.7)	1.5 (1.4–1.7)	1.4 (1.0–1.7)
120	1.8 (1.5–2.0)	2.3 (1.9–2.6)	1.4 (1.2–1.6)	1.4 (1.1–1.7)

* Mean value and range
† $p < 0.05$
‡ $p < 0.025$

tion, obtained in the same manner (*5*). The difference between the two agents in the blood clearance rates observed in the control groups was statistically significant only at 1 min ($p < 0.05$).

Control group. Figure 2 shows the time-activity curves of Tc-99m DMPE in the anterior and posterior walls within the control group. The peak anterior-wall activity, on the average, was observed 15 min after dose, and decreased to 49% of the maximum at 120 min (*3*). The 60° LAO view in the right decubitus position suggested higher counts in the posterior wall, but the difference was not statistically significant. These differences were likely due to geometrical effects (*5*). The amount of cardiac muscle tangentially projected toward the gamma camera differed slightly depending upon the relative positions of the heart and the gamma camera, due to attenuation by both distance and overlying tissue.

Figure 3 shows the Tc-99m DMPE time-activity curves with and without decay correction. Comparable mean values of the Tl-201 data without decay correction are also shown. The decay-corrected data show that the rapid myocardial washout of Tc-99m DMPE was not due mainly, to the 6-hr physical half-life of Tc-99m; thus, at 120 min the decay-corrected activity was, on the average, 60.8% compared with 49.0% without decay correction. On the other hand, Tl-201 uptake was slow, with a maximum at 40 min, followed by a slow washout. The decay of Tl-201 during the 120-min data collection was negligible, and the remaining Tl-201 activity in the myocardium was 90.3% at 120 min (*5*). This value was over 30% higher at 120 min than that of Tc-99m DMPE (with decay correction).

Total counts/min/view using 5–7 mCi (185–259 MBq) of Tc-99m DMPE with a parallel-hole, high resolution collimator ranged from 241,752 to 306,097 with a mean value of 203,986 when the maximal myocardial uptake was observed; i.e., 15 min after dose. Corresponding values, using 2–3 mCi (74–111 MBq) of Tl-201 with a parallel-hole, high sensitivity collimator, ranged from 61,888 to 110,331 with a mean value of 79,040 at 40 min after dose when the maximal myocardial uptake was observed. These values will vary depending upon the activity used, size of the dog; and degree of liver inclusion within the field of view. The data indicate, however, that to obtain an image using Tc-99m DMPE an approximately three times faster count collection can be ex-

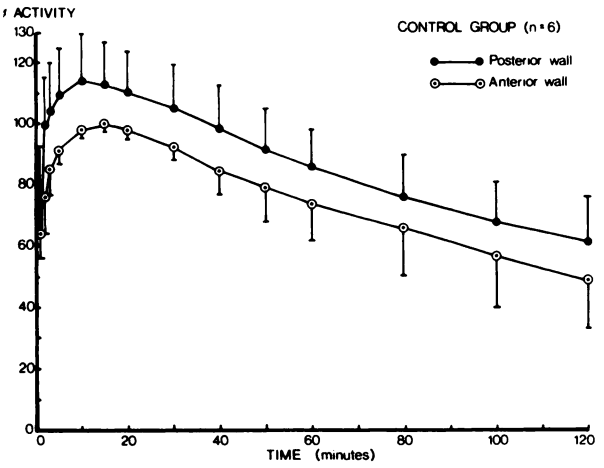

FIG. 2. Time-activity curves of Tc-99m DMPE in control group. On average, maximal uptake was observed 10–15 min after dose, and 49% of maximal activity in anterior wall remained at 120 min. Higher activity in posterior wall was likely due to geometrical effects (see text). Each data point was expressed as mean ±1 s.d. No decay correction was made.

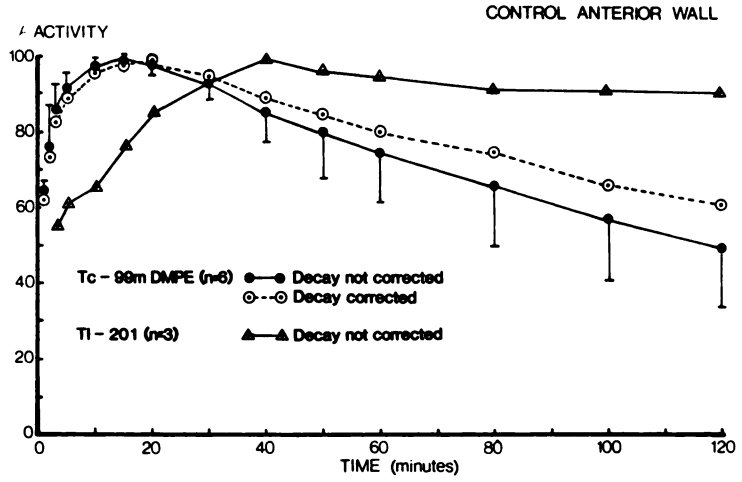

FIG. 3 Comparative time-activity curves of Tc-99m DMPE and Tl-201 in control group. When Tc-99m decay was corrected, value at 120 min was raised about 20%. Maximal uptake of Tl-201 was at 40 min, and 90.3% of maximum remained at 120 min.

pected when compared with Tl-201 under the condition described above.

Reactive-hyperemia group. This study was designed so that the Tc-99m DMPE would be administered at peak coronary blood flow after a 2-min transient occlusion of the circumflex coronary artery. Peak flow was generally observed 30 sec after release, so a bolus of Tc-99m DMPE was administered intravenously at that time. Time-activity curves observed in the posterior and anterior walls are shown in Fig. 4. The anterior wall seemed to show slightly faster washout relative to the control anterior wall, shown in Fig. 2, but there was no statistical difference at individual data points. The peak activity in the anterior wall was observed at a mean of 10 min after dose, and 40% of the maximum activity remained at 120 min. The posterior wall showed its peak activity at 5 min after dose; this was followed by a rapid washout until about 40 min after dose. The washout rate thereafter was similar to that from the anterior wall. There was a significant difference of activity between the anterior and posterior walls at all data points except at 1 min after dose. Increasingly larger statistical variations were found with time in both anterior and posterior walls ($p < 0.01$ at 80 min, $p < 0.025$ at 100 min, and $p < 0.05$ at 120 min). These findings suggest the likelihood that had data been collected beyond 120 min, with time there would have been no significant difference in activity between the anterior and posterior walls; in other words, an equilibrium state would be achieved.

Whether increased coronary blood flow to the posterior wall paralleled the increased uptake of Tc-99m DMPE was examined and the results are shown in Fig. 5. The mean baseline coronary blood flow in five dogs with an average weight of 32 kg was 70.6 ml/min ±21.2 ml (mean ±1 s.d.). The magnitude of increased coronary blood flow varied greatly between dogs, and the mean

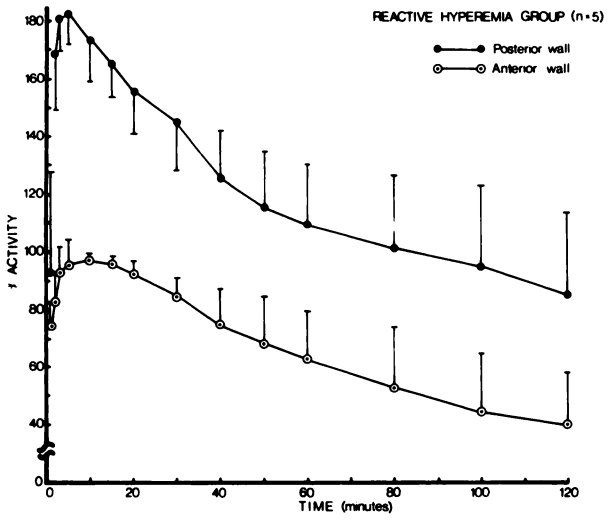

FIG. 4. Time-activity curves from reactive-hyperemia group. Increased circumflex coronary blood flow produced by reactive hyperemia was demonstrated by increased Tc-99m DMPE activity in posterior wall compared with activity in anterior wall. Percentage difference in activity between anterior and posterior walls was 87.5% at 3 min and 86.4% at 5 min.

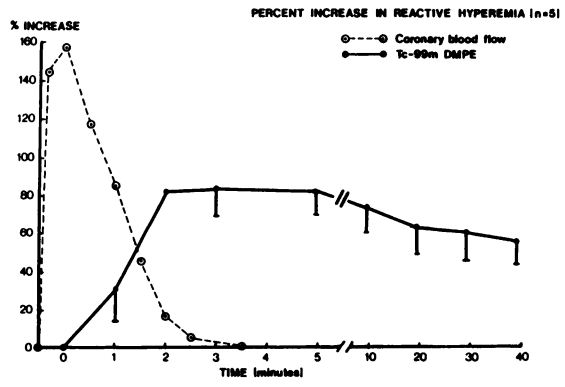

FIG. 5. Relationship between coronary blood flow and percent Tc-99m DMPE uptake. Tc-99m DMPE during reactive hyperemia was expressed as mean ±1 s.d. of activity in posterior wall relative to activity in anterior wall. Coronary flow had increased 156.8% at 30 sec after release (time 0). Mean maximal uptake of 84.4% was observed at 3 min, followed by steady washout to 57.0% at 40 min.

percent increase was characterized by large standard deviations: at 10 sec after release, 144.6% ± 94.7; 30 sec, 156.8 ± 104.8; 1 min, 116.7 ± 97.8; 1.5 min, 85.0 ± 50.6; 2 min, 45.8 ± 40.0; 2.5 min, 17.2 ± 19.5; 3 min, 5.3 ± 6.0; and 4 min, 1.2 ± 2.0. Variability in peak flow reflects in large part, the variability in the extent of collateral circulation and the amount of myocardium supplied by the coronary artery. The percent increase of Tc-99m DMPE uptake was calculated by subtracting the value of the anterior wall from that of the posterior wall in each of the five dogs. The maximal percent increase in Tc-99m DMPE uptake was (84.8 ± 15.4)% (mean ±1 s.d.) at 3 min followed by a steady decline of the activity until 40–50 min. The difference between anterior and posterior walls then remained essentially unchanged (see also Fig. 4). These data indicated that the percent increase of Tc-99m DMPE was proportional to the increased coronary blood flow on a relative scale, but it underestimated the increased regional coronary blood flow, as has been noted with Tl-201 (*9*). That is, the mean maximal percent increase in coronary blood flow was 156.8% at 30 sec after release, but the mean maximal percent increase of Tc-99m DMPE activity was only 84.8%, and was delayed.

The time-activity curves were examined in an attempt to determine which of the two imaging agents, Tc-99m DMPE or Tl-201, represented more accurately the increased regional coronary blood flow in the imaging procedure. Thallium-201 data for this comparison were based on an earlier study (*5*). The technique for producing reactive hyperemia was identical with both agents. The mean percent differences at each data point were calculated by subtracting the mean value of the control group from the mean value of the reactive-hyperemia group for each agent. The results are shown in Fig. 6. Although the peak uptake of Tc-99m DMPE was

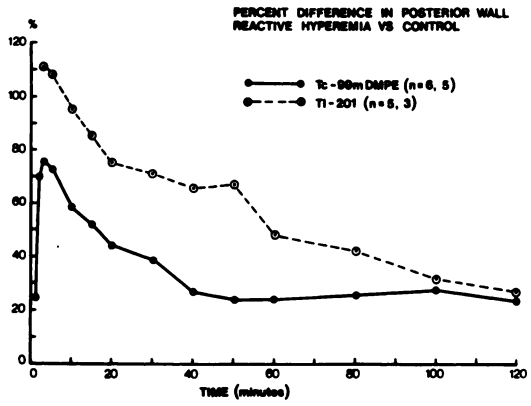

FIG. 6. Percent difference in activity in posterior walls in reactive-hyperemia group compared with control group, for Tc-99m DMPE and Tl-201. Maximal differences occurred at 3 min: 75.5% for Tc-99m DMPE and 111.3% for Tl-201. Thallium-201 response to increased regional flow is greater than that of Tc-99m DMPE. Numbers in parentheses indicate, first, number of control dogs, then number of reactive-hyperemia dogs.

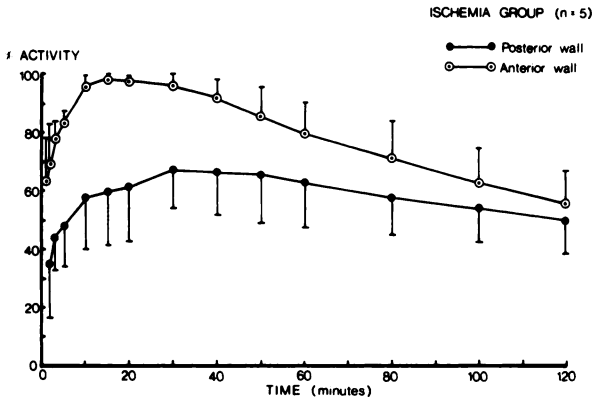

FIG. 7. Tc-99m DMPE time-activity curves for ischemia group. Note significant difference of activity between anterior and posterior walls up to 40 min, and relatively faster washout from anterior wall, indicating ultimate equality.

observed at 5 min in the posterior wall of the reactive-hyperemia group, the maximal percent difference (increase) was 75.5%, which was observed at 3 min. Similarly, the maximal percent difference (increase) of Tl-201 was 111.3% at 3 min. Following the maximal uptake, a steady washout curve was observed with Tl-201. With Tc-99m DMPE this trend was observed until 40–50 min and no further accelerated washout rate was observed. With thallium-201, uptake was 35.8% higher in response to maximal reactive hyperemia compared with maximal Tc-99m DMPE uptake. Thus, Tl-201 uptake appears to follow increased regional coronary blood flow better than does Tc-99m DMPE.

Ischemia group. In the ischemia study, Tc-99m DMPE was administered at the beginning of the 2-min transient occlusion, when the regional coronary blood flow was zero. The time-activity curve for the posterior wall showed slower uptake and washout compared with that for the anterior wall (Fig. 7). Activities observed in the anterior and posterior walls were significantly different at 2 min after dose ($p < 0.05$) to 40 min after dose ($p < 0.01$) and at 50 min the difference was marginally significant ($\cong 0.05$). No statistical difference was observed at 60 min and thereafter. These data indicate a definite trend towards an equilibrium state between the activities of anterior and posterior walls with time. That is, the initial deficit in the posterior wall due to the transient ischemia is corrected with time, leading to the similar activity observed in the anterior wall—as was seen with Tl-201 (*5*).

A comparison of the ischemia data for Tc-99m DMPE and Tl-201 (*5*) was made, based on the percent difference (decrease) in the mean activities observed in the posterior walls of the control and the ischemia groups. Figure 8 shows the percent difference obtained by subtracting, at each data point, the mean posterior-wall activity of the ischemia study from that of the control study. The maximal percent difference for Tc-99m DMPE was 65.2% at 2 min, after which it steadily de-

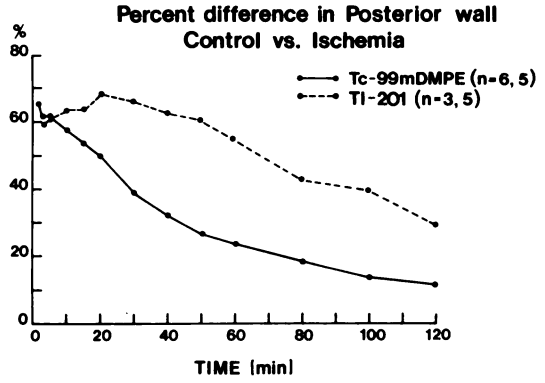

FIG. 8. Percent differences in activity in posterior walls in ischemia group compared with control group, for Tl-201 and Tc-99m DMPE. Maximal percent difference was 65.2% for Tc-99m DMPE at 2 min, compared with 68.4% for Tl-201 at 20 min. More rapid decrease of the percent difference with Tc-99m DMPE indicates its more rapid uptake in ischemic region. Numbers in parentheses refer first to number of controls, second to number of ischemic dogs.

creased to approach the equilibrium state with time. For Tl-201, the maximal percent difference was 68.4% at 20 min, followed by a relatively slow equilibration thereafter. The data indicate that the ischemic region should be equally well visualized with either agent, but at different times after dose. The faster equilibration of Tc-99m DMPE is more than compensated for by its faster imaging time relative to Tl-201, since an equal number of counts per view in the dog are obtained 2–3 times faster with 5 mCi of Tc-99m DMPE than with 2 mCi of Tl-201.

Effective and biological half-times ($t_{1/2}$ eff. and $t_{1/2}$ biol.). Based on the time-activity curves observed in the control, ischemia, and reactive-hyperemia studies, the $t_{1/2}$ eff. and $t_{1/2}$ biol. of Tc-99m DMPE and Tl-201 were calculated using the data points after the respective agent reached its peak concentration in the organs by the described method (*3*). The results are shown in Table 2. The half-times of these agents in the myocardium were calculated from activities in the posterior walls, where comparable flow changes were achieved with Tc-99m DMPE and Tl-201. Both $t_{1/2}$ eff. and $t_{1/2}$ biol. for the lung and liver were calculated from data obtained from the control group, since there was no statistical difference among groups using either agent (*3*).

These data support the observation of faster kinetics of Tc-99m DMPE, compared with Tl-201, at different levels of regional myocardial blood flow. The substantially different $t_{1/2}$ eff. and $t_{1/2}$ biol. of the two agents suggest that they follow different biological pathways. Furthermore, clearly different effective half-times of the myocardium in control, reactive-hyperemia, and ischemia groups indicate that the initial overload of the agent in reactive hyperemia tends to correct itself through an accelerated washout rate, and that the initial deficit in ischemia tends to correct with a slow washout rate. The uptake and washout kinetics of Tc-99m DMPE clearly demonstrate its flow dependency at the time of administration, as was seen also with Tl-201 (*5*). As shown in Fig. 9, the three groups showed significantly different degrees of uptake and washout until 50 min ($p < 0.025$); at 60 min the difference between the control and reactive hyperemia groups was not significant ($p < 0.10$). The difference between the ischemia and control groups was significant up to 60 min ($p < 0.02$), but not at 80 min ($p < 0.10$) and thereafter. The ischemia and reactive-hyperemia groups continue to show a significant difference, but it tends to be less significant with time: $p < 0.01$ at 80 min, $p < 0.02$ at 100 min, and $p < 0.05$ at 120 min.

TABLE 2. EFFECTIVE AND BIOLOGICAL HALF-TIMES (HR)

Organ condition	Tc-99m DMPE		Tl-201*	
	$t_{1/2}$ eff.	$t_{1/2}$ biol.	$t_{1/2}$ eff.	$t_{1/2}$ biol.
Myocardium				
control	1.9	2.8	7.2	8.0
ischemia	3.0	6.1	12.8	15.6
reactive hyperemia	1.1† (1.9)	1.3† (2.8)	3.6	3.8
Lung	2.6	4.5	6.8	7.5
Liver	6.1	∞‡	—	—

* Because of slow kinetics, calculations were based on data obtained up to 180 min for control and up to 240 min for reactive-hyperemia study.

† Calculation from 15–40 min after dose. See also Fig. 4.

‡ Limited data points are probably the reason for infinity. Tc-99m DMPE appeared invariably in gall bladder and intestine after 2–3 hr.

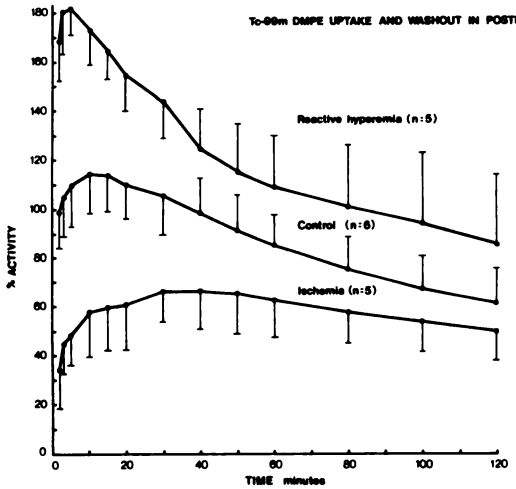

FIG. 9. Time-activity curves for Tc-99m DMPE observed in ischemia, control, and reactive-hyperemia groups. There were statistically significant differences between groups up to 50 min.

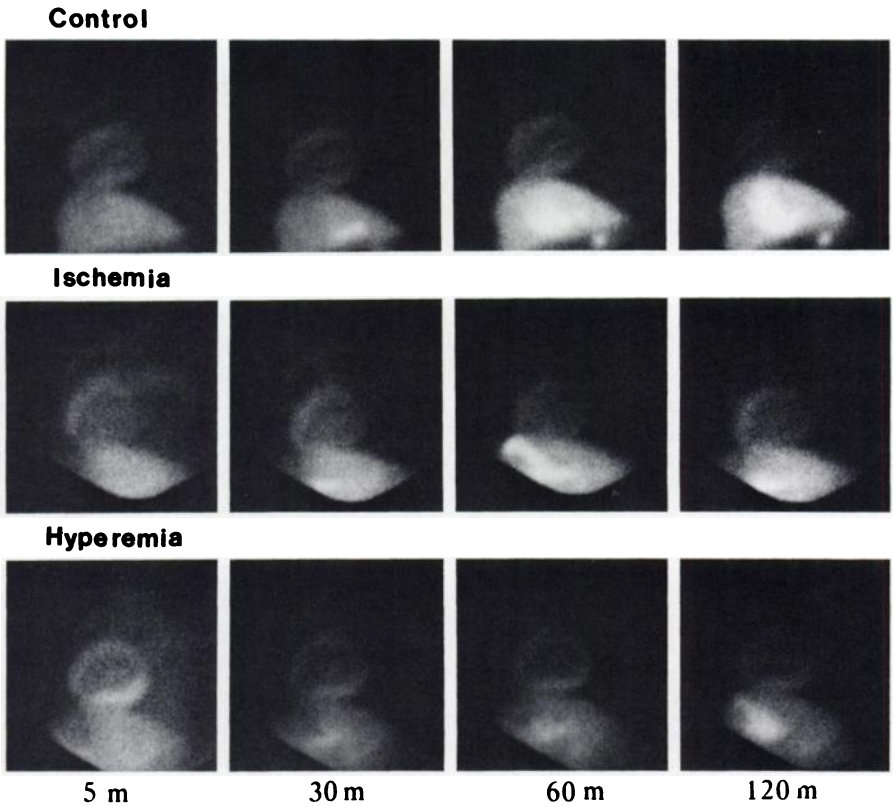

FIG. 10. Selected images of control (top), ischemia (middle), and reactive-hyperemia (bottom) studies with Tc-99m DMPE. Although deteriorating image quality was apparent after 60 min in each group, images under both ischemia and reactive hyperemia tend to show equilibration between anterior and posterior walls.

Figure 10 shows myocardial images of the three groups obtained at intervals of 5 min until 120 min after dose. The images demonstrate the qualitative kinetics of Tc-99m DMPE as a function of time, and are comparable to the time-activity curves shown in Figs. 2, 4, and 7. Good-quality images were consistently obtained starting as early as 3–5 min after dose and continued up to 60 min. The image quality usually declined thereafter because of the short myocardial retention time and the longer lung and liver retention times, as evidenced by the $t^1/_2$ eff. shown in Table 2. Since the functional recovery after transient ischemia could be markedly delayed after restoration of coronary blood flow (*10*), the short $t^1/_2$ eff. of Tc-99m DMPE could preclude observation of the redistribution phenomenon (*4*), as is possible with Tl-201.

DISCUSSION

Although our experimental models of ischemia and reactive hyperemia differ from the regional ischemia and exercise-induced hyperemia encountered in patients, these models were designed as reasonable compromises to study the relationship between major changes in regional myocardial blood flow and the distribution of a myocardial imaging agent (*5*). The ischemia and hyperemia models appear to undergo equilibration of activities of the affected and unaffected areas of myocardium with time, a process that simulates the redistribution phenomenon previously described using Tl-201 (*5*). Since the mechanisms of uptake and washout of Tc-99m DMPE are unknown, we have referred to this process as equilibrium rather than redistribution.

In spite of zero flow shown by the flow probe placed around the proximal circumflex coronary artery during the 2-min occlusion in the ischemia model, activity was seen in the posterior wall, as shown in Fig. 7. This discrepancy is likely a result of the extensive but variable collateral circulation found in the dog, the manner in which counts are collected in a one-min frame, and the probable inclusion of adjacent regions supplied by other than the circumflex coronary artery. Similar effects of coronary collateral circulation in humans undergoing a Tl-201 exercise study are well documented (*11*), and their development is directly proportional to the degree and time course of coronary obstruction (*12*).

Kinetic studies during dynamic changes in regional blood flow as reported here show that Tc-99m DMPE and Tl-201 have different biological properties. These differences can be summarized as follows: Tc-99m DMPE exhibits (a) faster overall kinetics, (b) an equal flow dependency in a transiently ischemic region, but (c) a slightly less sensitive flow dependency in a transiently hyperemic region, and (d) that the tendency to correct

the initial overload or deficit may be incomplete due to its short effective half-time. The findings suggest that while Tc-99m DMPE cannot be utilized in exactly the same fashion as Tl-201, its unique kinetic properties could complement those of Tl-201.

The mechanism of myocardial uptake of Tc-99m DMPE is unknown, whereas the continuous influx and efflux of Tl-201 between the cellular and extracellular spaces via the sodium-potassium pump appears to be well established (*13*). The net Tl-201 activity in the myocardium probably parallels K^+ and Na^+ ATPase activity. Tracer kinetics are governed by regional perfusion, especially at the time of administration (*5,14,15*). The increased myocardial uptake of Tl-201 that results from increased coronary blood flow is followed by accelerated washout (*5*). Decreased myocardial uptake in an ischemic region is associated with decreased efflux of Tl-201 in the early states of washout (*5,16*). All of these kinetic findings for Tl-201 appear to be applicable to Tc-99m DMPE, and suggest the usefulness of this new agent in evaluating ischemic heart disease.

Recognition of the redistribution phenomenon has enhanced the clinical usefulness of Tl-201 (*4*). Its long $t^1/_2$ eff. in the myocardium probably plays an important role in the evaluation of exercise-induced regional ischemia, and the short $t^1/_2$ eff. of Tc-99m DMPE would be a disadvantage in this respect. In addition, a faster washout from the myocardium and a relatively slower clearance from the lung and liver have made prolonged observations difficult at times. In order to overcome this disadvantage, we have administered a booster dose of Tc-99m DMPE to the dog following the 120-min observation. In practice, a booster dose with about half of the initial activity appeared to be satisfactory, with equilibrium images usually observed in 10–15 min. An alternative approach is the two-stage procedure initially proposed for Tl-201 (*9,17*). That is, the resting and exercise Tc-99m DMPE studies could be carried out at two separate sessions. Advantages to using Tc-99m DMPE in this mode are a faster imaging time at each study, and the ability to repeat the study as early as 24–48 hr later due to the short physical half-life of Tc-99m. The predicted minimal additional cost relative to that of Tl-201 is another advantage.

The reactive-hyperemia study indicates that Tc-99m DMPE will respond to changing coronary blood flow, but that the activity observed in the myocardium may not be as closely proportional to increased coronary blood flow as is observed for Tl-201 (*5,15,16*). Our comparable Tc-99m DMPE and Tl-201 data indicate that the regional increased myocardial blood flow is monitored slightly better with Tl-201 than with Tc-99m DMPE.

CLINICAL IMPLICATIONS

The major disadvantages of Tl-201 result largely from its physical characteristics and production methods (*18,19*). A further disadvantage is the tissue attenuation of the Tl-201 radiation, which results not only in artifactual defects by attenuation in breast and diaphragm, but also in scatter from the lung and chest wall. The 140-keV gamma rays of Tc-99m are close to ideal for detection by current gamma cameras and are far superior to the 69–80 keV x-rays from the Hg-201 daughter of Tl-201. Technitium-99m DMPE demonstrated transient ischemia as clearly as Tl-201, but myocardial uptake with transient hyperemia was slightly less than with Tl-201. The kinetic characteristics of Tc-99m DMPE suggest that some of the established roles of Tl-201 could be replaced by this new agent, or an analog, and that both comparable and even complementary roles could evolve as further understanding of this new agent is obtained. Furthermore, the ready availability of Tc-99m makes it a better suited agent for an unexpected study. Our current procedure requires 30–40 min of preparation time and the in vitro stability of Tc-99m DMPE at room temperature is also excellent (*3*).

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