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# Effect of Thallium-201 Blood Levels on Reversible Myocardial Defects

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To determine if  $^{201}\text{Tl}$  plasma blood levels correlate with the presence of reversible myocardial defects during exercise testing, 14 patients with stable coronary artery disease underwent two separate exercise  $^{201}\text{Tl}$  stress tests. Between initial and delayed imaging, on one test the patients drank an instant breakfast drink (eating) and on the other they drank an equivalent volume of water as a control ( $\text{H}_2\text{O}$ ). Thallium-201 imaging was performed immediately postexercise, immediately after eating/ $\text{H}_2\text{O}$  and 210 min after eating/ $\text{H}_2\text{O}$ . Between initial and immediate post eating/ $\text{H}_2\text{O}$  images  $^{201}\text{Tl}$  reversible defects occurred in 27/38 regions in the  $\text{H}_2\text{O}$  test versus 15/38 regions in the eating test ( $p = 0.02$ ). Over this early time period, plasma  $^{201}\text{Tl}$  activity was significantly higher in the  $\text{H}_2\text{O}$  test than eating test ( $p < 0.05$ ). In conclusion, early reversal of  $^{201}\text{Tl}$  defects may, in part, be the result of higher plasma  $^{201}\text{Tl}$  activity early after initial postexercise  $^{201}\text{Tl}$  imaging.

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It has been previously shown that fasting thallium-201 ( $^{201}\text{Tl}$ ) exercise testing can enhance detection of reversible  $^{201}\text{Tl}$  defects compared to eating between initial and delayed  $^{201}\text{Tl}$  imaging (1,2). Animal experiments have demonstrated that glucose-insulin-potassium infusion can increase  $^{201}\text{Tl}$  myocardial clearance, especially in postischemic myocardium (3) and thereby attenuate the detection of reversible  $^{201}\text{Tl}$  defects (4). However, the mechanism(s) by which this effect occurs is unclear.

Thallium-201 myocardial content will depend on the avidity of the myocardial cell for the  $^{201}\text{Tl}$  and on the amount of  $^{201}\text{Tl}$  delivered to the myocardium by the blood. It has been postulated that higher blood levels of  $^{201}\text{Tl}$  may result in more "fill-in" of initial  $^{201}\text{Tl}$  defects between initial and delayed imaging (5). This study was designed with each patient acting as his own control to test the hypothesis that higher blood levels of  $^{201}\text{Tl}$  may be responsible at least in part for the reversibility of  $^{201}\text{Tl}$  defects. Accordingly, we sought to determine: (a) whether plasma  $^{201}\text{Tl}$  levels were different between eating and fasting  $^{201}\text{Tl}$  exercise tests, and (b) if these

differences in plasma  $^{201}\text{Tl}$  content were related to differences in the number of reversible  $^{201}\text{Tl}$  defects.

## METHODS

Fourteen patients with clinically stable angina performed two exercise tests within a 14-day period. They were chosen by the clinical criterion of stable exertional angina. The number of patients taking various medications were: digoxin (0), beta blockers (9), calcium channel blockers (10), and long-acting nitroglycerin (6). Between initial and delayed images, patients drank a commercially available instant breakfast preparation (Carnation Instant Breakfast in 12 oz. of whole milk) (eating) or an equivalent volume of water ( $\text{H}_2\text{O}$ ). Patients served as their own control since each underwent both eating and fasting ( $\text{H}_2\text{O}$ ) exercise tests. Initial and delayed thallium images and serial plasma samples were obtained on all patients during both studies (eating/ $\text{H}_2\text{O}$ ). There was no change in any of these medications and no change in anginal symptoms between the eating and fasting ( $\text{H}_2\text{O}$ ) exercise thallium tests. Ten of the 14 patients had clinical evidence of previous myocardial infarction based on significant Q-waves on the resting electrocardiogram, and/or cardiac enzyme elevation and region wall motion abnormalities at cardiac catheterization.

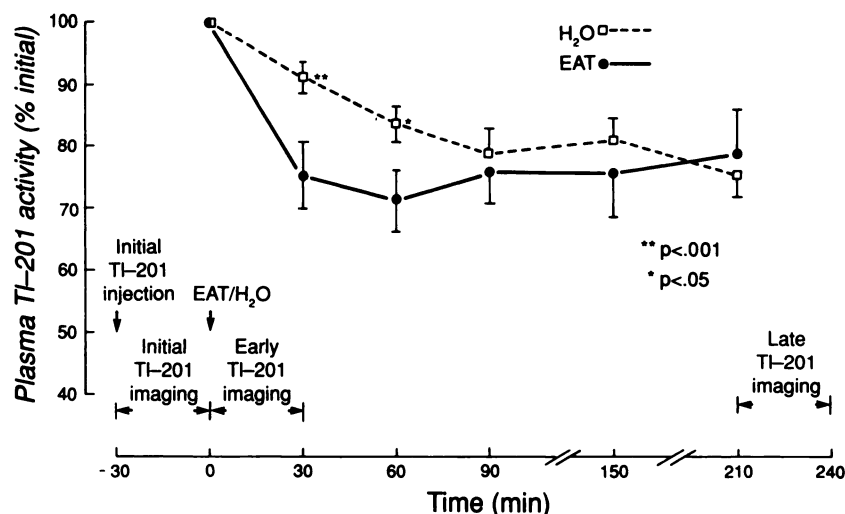
The protocol is shown in Figure 1. After an overnight fast, patients were exercised using a modified Bruce protocol. Near peak exercise  $^{201}\text{Tl}$ , 1.5 mCi (56 MBq) was injected intravenously and the patient exercised for an additional 30-60 sec. Three minutes after exercise, three planar myocardial images

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**FIGURE 1**  
Study protocol and plasma  $^{201}\text{Tl}$  activity over time for the eating and fasting ( $\text{H}_2\text{O}$ ) tests.

(anterior, 45° left anterior oblique, and left lateral) were acquired each for 10 min into a  $256 \times 256$  matrix (X2 zoom) using a standard gamma scintillation camera and a low-energy, general all purpose parallel hole collimator. Immediately after these initial images were obtained, the patients drank either a commercially available instant breakfast drink or an equivalent volume of water. To more clearly define the myocardial  $^{201}\text{Tl}$  activity at the time of the initial blood samples, and to determine an early effect of eating, the three images were repeated immediately after eating/ $\text{H}_2\text{O}$ , and 4 hr after exercise. Previous work has shown that significant reversal of initial  $^{201}\text{Tl}$  defects can occur very early (6).

An initial venous blood sample was obtained from an indwelling catheter (separate from the one used for  $^{201}\text{Tl}$  injection) 30 min after exercise and immediately before patients "ate" or drank  $\text{H}_2\text{O}$  and at 30, 60, 90, 150, and 210 min after eating/ $\text{H}_2\text{O}$ . Plasma  $^{201}\text{Tl}$  activity was measured in a well counter. After background subtraction (<1% of total counts), the remaining counts per gram of plasma were expressed as counts/min/g of plasma. Plasma  $^{201}\text{Tl}$  activity at the different times was expressed as a percent of the initial (pre-eating/ $\text{H}_2\text{O}$ )  $^{201}\text{Tl}$  activity. Serum glucose, potassium, and insulin levels were measured using standard glucose oxidase and radioimmunoassay techniques, respectively.

Initial and immediate post eating/ $\text{H}_2\text{O}$  and 4-hr image data were stored on floppy disks for quantitative interpretation images (blinded to patient identity and their eating or fasting test status).

To assess for reversible  $^{201}\text{Tl}$  defects, each patient's images were normalized to the peak pixel value for each image. Similar stress and rest image alignment was verified by visual inspection. Each of the three standard projections was divided into three regions for a total of nine regions per test. After background subtraction, quantitative regional analysis using the circumferential count profile method was applied to all nine regions (7). Initial  $^{201}\text{Tl}$  defects were recorded if regional counts were more than 2 s.d. below a mean value for a group of normal patients. A reversible defect was identified for regions where there was at least a 12% increase in  $^{201}\text{Tl}$  activity from stress to rest images over a minimum 18° of arc. For regions demonstrating reversible defects, regional  $^{201}\text{Tl}$  clearance per 4 hr was determined in the same arc before images

were count normalized. For normal regions, regional  $^{201}\text{Tl}$  clearance per 4 hr was determined as the clearance rate for the area which had the highest initial postexercise  $^{201}\text{Tl}$  activity.

#### Statistical Analysis

Eating/ $\text{H}_2\text{O}$  test differences in plasma  $^{201}\text{Tl}$ , glucose, insulin, and potassium were compared using one-way analysis of variance with multiple range testing. Differences in  $^{201}\text{Tl}$  regional myocardial clearance rates, peak heart rate, systolic blood pressure, double product, and exercise time between exercise tests were compared using a paired t-test. Comparisons between the frequency of reversible defects between eating and  $\text{H}_2\text{O}$  tests were analyzed using McNemar's test (8) or standard chi-square with Yates correction. Data are expressed as mean  $\pm$  s.e.m.

#### RESULTS

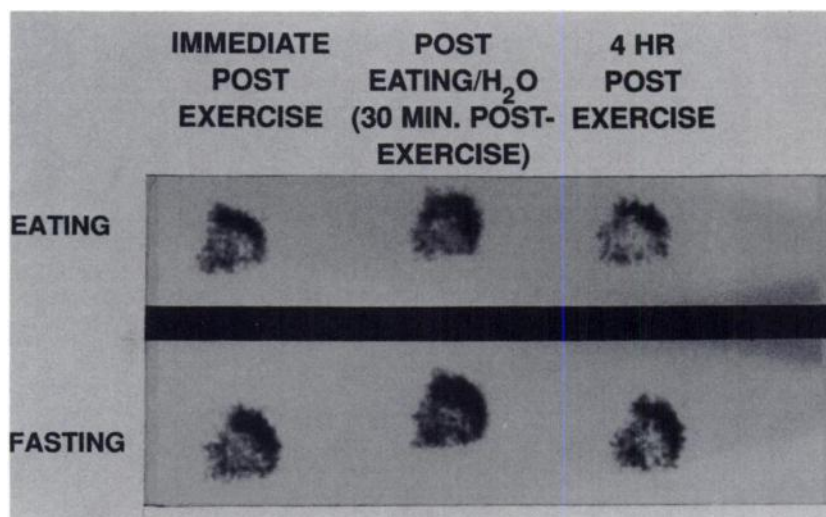
At 30 and 60 min after eating or fasting, significantly greater plasma  $^{201}\text{Tl}$  activity was detected in the fasting test ( $p < 0.001$ ,  $p < 0.05$ , respectively) (Fig. 1).

There were 41 areas of reversible  $^{201}\text{Tl}$  defects identified comparing initial to 4-hr images. There were 35/41 (85%) regions identified in  $\text{H}_2\text{O}$  studies, while only 17/41 (41%) were seen on eating examinations ( $p < 0.0001$ ). Thirty-eight of these 41 (92%) regions of reversible defects were identified comparing initial and immediate posteating/ $\text{H}_2\text{O}$  images: 27/38 (71%) on the  $\text{H}_2\text{O}$  studies, and 15/38 (39%) during the eating test ( $p = 0.02$ ). All nonreversible defects on one test that were reversible on the other test met the criteria for fixed defects. Thallium-201 blood levels were significantly higher in  $\text{H}_2\text{O}$  versus eating examinations early in the posteating/ $\text{H}_2\text{O}$  interval.

An example of early  $^{201}\text{Tl}$  reversible defect on the fasting ( $\text{H}_2\text{O}$ ) test and not in the eating test on the immediate posteating/ $\text{H}_2\text{O}$  images is shown in Figure 2. The initial and early postexercise images during eating and fasting tests in a patient with two-vessel

**FIGURE 2**

Patient example with a reversible  $^{201}\text{Tl}$  defect on the inferior wall seen on the early fasting, but not early eating images. No significant reversibility of the inferior wall defect was observed at 4 hr during the eating test. Plasma  $^{201}\text{Tl}$  levels early (60 min) after exercise were higher in the fasting than the eating test (98% vs. 77% of baseline, respectively).



coronary artery disease show a reversible inferior wall defect on the fasting test but a fixed inferior wall defect on the eating test. Plasma  $^{201}\text{Tl}$  levels at 60 min post-exercise remained higher in the fasting test than in the eating test (98% vs. 77% of baseline, respectively). Also, note that in this patient the reversible defect is not evident on the 4-hr delayed image on the eating test.

Thallium-201 regional myocardial clearance rates over 4 hr were significantly higher in the eating tests than the fasting test for the normal myocardial regions ( $47.4 \pm 1.7\%$  vs.  $41.7 \pm 2.3\%$ , respectively,  $p < 0.0001$ ) and for the 41 myocardial regions in which reversible defects were observed ( $41.4 \pm 2.0\%$  vs.  $30.6 \pm 2.1\%$ , respectively,  $p < 0.0001$ ).

There were no significant differences in peak heart rate, systolic blood pressure, or treadmill time between tests, though a slightly higher double product was reached during eating compared to fasting exercise tests ( $p = 0.04$ ) (Table 1). All patients had concordant outcomes on exercise ECG interpretation between eating/fasting examinations with six positive and eight negative or indeterminate test results.

Blood glucose and insulin levels were higher during

eating tests at 30, 60, 90, and 150 min after food intake compared to the  $\text{H}_2\text{O}$  test (Fig. 3) ( $p < 0.05$ ). No difference in potassium levels was detected over time or between eating and fasting tests.

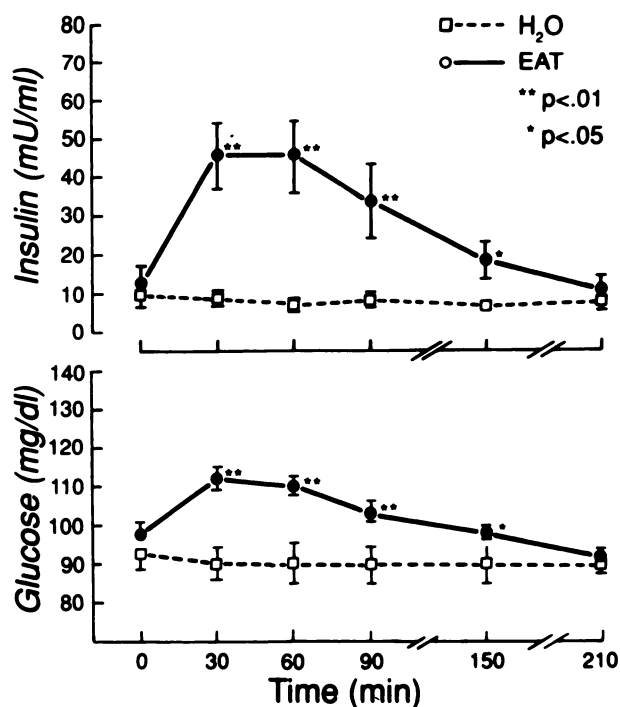
## DISCUSSION

It has been previously demonstrated that fasting between initial and delayed thallium imaging results in enhanced detection of reversible  $^{201}\text{Tl}$  defects (1,2). This study extends these observations and demonstrates that

**TABLE 1**  
Exercise Hemodynamic and  
Electrocardiographic Characteristics

	Eating	$\text{H}_2\text{O}$ (Fasting)	p
Heart rate (beats/min)	$117 \pm 7$	$112 \pm 7$	NS
Systolic blood pressure (mmHg)	$142 \pm 8$	$135 \pm 7$	NS
Double product (mmHg $\times$ beats/min)	$17240 \pm 1969$	$15519 \pm 1690$	0.04
Treadmill time (sec)	$588 \pm 58$	$556 \pm 58$	NS
ST segment depression	6/14	6/14	NS

Mean  $\pm$  s.e.m.



**FIGURE 3**

Blood glucose and insulin levels over time in the eating and the fasting ( $\text{H}_2\text{O}$ ) tests.

plasma  $^{201}\text{Tl}$  activity is increased in fasting patients 60 and 90 min after  $^{201}\text{Tl}$  injection (30 and 60 min after intervention) compared to patients who have eaten. Patients in this study performed both tests and served as their own control. This study also demonstrates that increased plasma thallium activity early in the rest period is associated with the detection of more reversible defects.

Significantly higher plasma thallium levels were demonstrated in fasting compared to eating tests 60 and 90 min postinjection (30 and 60 min post eating/ $\text{H}_2\text{O}$ ). These differences in plasma  $^{201}\text{Tl}$  activity suggest that the early and possibly late identification of  $^{201}\text{Tl}$  defects may, in part, be the result of increased availability of  $^{201}\text{Tl}$  in the plasma. Previous work by Rothendler et al. (6) has shown that early reversibility of  $^{201}\text{Tl}$  defects can occur. This observation was confirmed by this study. Thus, reversibility of  $^{201}\text{Tl}$  defects may depend in part on the plasma level of  $^{201}\text{Tl}$  that is available to attenuate the loss of  $^{201}\text{Tl}$  from the ischemic region during the time between initial, and early and later delayed images.

There was slightly higher double product achieved in the eating studies, which could have led to more prolonged ischemia in this group, favoring detection of more reversible defects in the fasting subjects. However, there was no difference in the number of initial scan defects between eating and fasting groups.

The mechanism by which eating accelerates  $^{201}\text{Tl}$  redistribution is unclear. Transient ischemia has been shown to decrease sodium-potassium ATPase activity (9,10), but insulin is known to stimulate sodium-potassium ATPase (11,12). In this study, eating stimulated endogenous insulin release. This may have resulted in stimulation of the ischemic myocardial cells' depressed sodium-potassium ATPase transport system. Since thallium (as opposed to potassium) can be transported out of the cell via the sodium channel of the sodium-potassium ATPase system (13), faster  $^{201}\text{Tl}$  myocardial clearance from the transiently ischemic region may have resulted during the eating test. The regional  $^{201}\text{Tl}$  myocardial clearance rates of the transiently ischemic region are more rapid during the eating test. The "normal" myocardial region also demonstrated more rapid  $^{201}\text{Tl}$  clearance in the eating test, but the increase in clearance from the transiently ischemic regions was even faster, resulting in less reversibility of the initial  $^{201}\text{Tl}$  defect.

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