

# Effects of Stress Management Training and Dietary Changes in Treating Ischemic Heart Disease

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• To evaluate the short-term effects of an intervention that consists of stress management training and dietary changes in patients with ischemic heart disease (IHD), we compared the cardiovascular status of 23 patients who received this intervention with a randomized control group of 23 patients who did not. After 24 days, patients in the experimental group demonstrated a 44% mean increase in duration of exercise, a 55% mean increase in total work performed, somewhat improved left ventricular regional wall motion during peak exercise, and a net change in the left ventricular ejection fraction from rest to maximum exercise of +6.4%. Also, we measured a 20.5% mean decrease in plasma cholesterol levels and a 91.0% mean reduction in frequency of anginal episodes. In this selected sample, short-term improvements in cardiovascular status seem to result from these adjuncts to conventional treatments of IHD.

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THE ROLES of both emotional stress and diet have long been suspected in the pathogenesis of ischemic heart disease (IHD).<sup>1</sup> Some emotions and behaviors are associated with IHD in a variety of populations; these include intense anxiety, depression, feelings

of helplessness, and "type A behavior," characterized by ambitiousness, competitiveness, impatience, and a sense of time urgency.<sup>2</sup> Biobehavioral techniques, eg, meditation, yoga, and progressive relaxation, may elicit what Benson has termed the "relaxation response," which may reduce cardiovascular risk factors, eg, BP<sup>3</sup> and plasma cholesterol levels,<sup>4,5</sup> independent of dietary changes.

The evidence linking elevated lipid levels, particularly plasma cholesterol levels, to the development of IHD is well established.<sup>6</sup> Studies of vegan subgroups in this country have disclosed lower levels of plasma cholesterol, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and triglyceride, a higher high-density lipoprotein (HDL)-LDL ratio, and lower BPs when compared with matched controls from the Framingham study; as the intake of animal products increased, the plasma cholesterol level rose.<sup>7,8</sup> Case reports have

suggested that changing to a vegan diet may reduce the frequency of angina.<sup>9</sup>

We report the results of a randomized, controlled study to determine if a combination of training in stress management and an essentially vegan diet may produce short-term improvements in the cardiovascular status of patients with IHD.

## PATIENTS AND METHODS

### Patient Selection

We audited all patient records (1977 to 1980) in the files of the nuclear cardiology and cardiac catheterization laboratories at St Luke's Episcopal Hospital, The Methodist Hospital, and the Kelsey-Seybold Clinic in Houston as well as the entire office records of two groups of cardiologists. We selected patients (aged 45 to 75 years) who had evidence of IHD with (1) greater than 50% stenosis in one or more major coronary arteries by cardiac catheterization or (2) positive exercise radionuclide ventriculography, defined as a resting ejection fraction that fails to rise more than 5% with exercise and/or with regional wall-motion abnormalities during exercise.<sup>10</sup> We excluded patients for any of the following reasons: a resting ejection fraction of less than 40%, cardiomyopathy, a myocardial infarction or changes in cardiac medications within the preceding six months, carcinoma, a cerebral vascular accident, psychosis, or previous coronary artery bypass surgery, unless there was angiographically verified evidence of graft occlusion.

Using these criteria, 125 patients were eligible. Each was sent a letter that described the intervention (which began six weeks later) and a statement of informed consent. Fifty-one patients volunteered and were pretested during Au-

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gust 1980. Three patients had a resting ejection fraction less than 40% and were excluded from the study. The remaining 48 patients were randomly assigned to the experimental and control groups (24 patients each), using random number tables in a balanced randomization.<sup>12</sup> During the study, one patient withdrew from each group (before posttesting), and their results are excluded from all the analyses.

### Study Design

The experimental group participated in a program of stress management training and dietary changes from Sept 3 to 27, 1980, while the control group continued their routine activities at work and home. Patients in the experimental group were housed together in a rural environment to maximize compliance with the intervention and as a component of the stress management training. The project staff prepared and served all meals at this site and trained the patients in stress management. Patients were required to consume only the food and beverages that were served to them; this was further reinforced by the relative inaccessibility of other food. (To reduce confounding influences, aerobic exercise was not a component of this intervention.)

Both groups were retested on all preintervention measures between Sept 27 and Oct 13 according to the exact preintervention protocols. All tests were conducted at the Texas Medical Center in Houston. Technicians who processed the data and physicians who interpreted the results were blinded to patient identity, testing time (before or after intervention), and group membership (experimental or control). The protocol was approved by the Human Subjects Committees of Baylor College of Medicine, Houston, St Luke's Episcopal Hospital, and the Kelsey-Seybold Clinic.

### Dependent Variables

**Exercise Radionuclide Ventriculography.**—The protocol for exercise radionuclide ventriculography has been described in detail in other publications.<sup>12</sup> Our protocol differed only slightly—we discontinued all medications for 12 hours before testing, and we tested patients in a sitting position rather than in a supine position. In brief, 30 mCi of sodium pertechnetate Tc 99m was injected into an antecubital vein 20 minutes after the injection of 6 mg of stannous pyrophosphate to label RBCs. All radioactive emissions were collected with the patient in the 45° sitting position using a scintillation camera. A 30° resting right anterior oblique gated image and a 45° resting left anterior oblique (LAO) gated image were collected for 2½ minutes each. Electrocardiographic gating was used by a computer to organize the

acquired data into a series of images that span an average cardiac cycle. Images were displayed in rapid sequence as an endless-loop flicker-free movie so that wall motion could be evaluated. Globular ventricular function was assessed by a determination of the ejection fraction, which is calculated from the ratio of the radioactive emissions (counts) after background correction collected from the left ventricle in end-diastole (ED) minus end-systolic (ES) counts to end-diastolic counts (ED), or (ED-ES)/ED. The BP was obtained in the right brachial artery using an audible BP cuff that uses an electronic transducer. After resting measurements were completed, the patient pedaled a bicycle ergometer at a load of 300 kpm/min (approximately 50 W), and this load was increased in 100-kpm increments in three-minute stages until stopping. After an initial 30-s period to reset the RR interval that was accepted by the computer, sequential LAO images were recorded during the remaining 2½ minutes of each stress period. Heart rate and BP were recorded at three-minute intervals to calculate the rate-pressure product. Reasons for stopping exercise included exhaustion, severe chest pain, shortness of breath, attainment of maximum heart rate, ECG changes (ST-segment displacement of 2 mm or more if flat or downsloping or if the J point is depressed 2 mm or more and the return to baseline is 80 ms or longer), complex ventricular arrhythmias, a systolic BP greater than 250 mm Hg or a diastolic BP greater than 140 mm Hg or a falling BP with increasing exercise. Three nuclear cardiologists reached a consensus on global ejection fraction and regional wall motion by viewing each patient's preintervention and postintervention study together as a random A-B comparison.

**Other Measurements.**—Plasma lipids were drawn after a 14-hour fast, during which nothing but water was ingested. Blood samples were analyzed under laboratory conditions standardized for the Lipid Research Clinics.<sup>13</sup> Angina frequency, smoking history, and medication usage were determined by questionnaire.

### Intervention

**Stress Management Training.**—Stress management techniques were taught and practiced five hours per day; this time was divided equally among the different techniques. Each technique was presented as having the common purpose of increasing a patient's sense of relaxation, concentration, and awareness of internal states to retrain physiological responsiveness to emotional stress.<sup>14,15</sup> Techniques included the following.

**1. Stretching/Relaxation Exercises.**—Patients were taught simple, nonaerobic

stretching exercises. They were advised to stretch slowly and gently and were carefully monitored to avoid injury or strain. Patients were directed to focus their attention on the areas being stretched and while resting to concentrate on their breathing. At the end of each class, each patient was instructed to tense and relax muscle groups sequentially from feet to head, ending with a meditation.

**2. Meditation.**—Each patient was asked to sit in a comfortable position and to breathe slowly and deeply while focusing his attention on his breathing, returning to it when attention wandered.

**3. Applied Meditation (Visualization).**—Each class began with a lecture on basic physiology and anatomy of the cardiovascular system and the pathophysiology of IHD to aid in constructing and maintaining a mental image. After the lecture, each patient was instructed to meditate, as previously described. After several minutes of meditation, each patient was asked to visualize his heart and coronary arteries, referring, whenever necessary, to drawings based on prior coronary angiography. With eyes closed, each patient was asked to visualize the atherosclerotic plaques being removed from the coronary arteries using an image of their choice. Each class ended with the patients visualizing themselves as healthy, doing an activity that they enjoyed when they were without the physical limitations of IHD.

**4. Environment.**—The primary reason for housing patients together in a rural environment was to ensure compliance to the intervention. Approximately half the patients reported that the investigative setting contributed to their perceived reduction in stress, but the others said that it was more stressful for them to be away from their work, home, and family and to be living in close quarters with a new group of persons.

**Diet.**—Patients were served a vegan diet (devoid of animal products) except for minimal amounts of nonfat yogurt. Also excluded in the diet were salt, sugar, alcohol, and caffeine. They were served fresh fruits and vegetables, whole grains, legumes, tubers, and soybean products. The diet was verified for nutritional adequacy, with an average daily intake of 1,400 calories, 325 mg of sodium, and 5.2 mg of cholesterol. Particular attention was given to making the food attractive and appetizing. Daily classes were given in food purchasing, preparation, and nutrition.

### Statistical Analysis

To compare the experimental and control groups before intervention, we used Student's *t* test (two tailed) on the interval data and Fisher's exact probability test on the categorical measures. To assess whether the experimental group improved rela-

Table 1.—Characteristics of Patients at Entry Into Trial*			
Characteristics	Experimental Group (n=23)	Control Group (n=23)	Significance
Age, yr (mean ± SEM)	58.3 ± 1.3 (47-68)	60.0 ± 1.8 (45-72)	NS
Men	17	19	NS
Previous myocardial infarction	9	7	NS
Previous coronary bypass surgery	1	1	NS

\*Values in parentheses are ranges; NS indicates  $P > .05$  by Student's *t* test.

Table 2.—Exercise Radionuclide Ventriculography*				
Index	Period	Mean ± SEM		Significance
		Experimental Group	Control Group	
Duration of exercise, s	Before intervention	392.1 ± 41.7	489.3 ± 39.3	$P < .001$
	After intervention	564.3 ± 54.0	483.9 ± 45.9	
Total work performed, kpm	Before intervention	2682.8 ± 392.7	3556.7 ± 500.3	$P < .0001$
	After intervention	4952.7 ± 542.4	3427.4 ± 443.5	
Maximum rate-pressure product, $\text{HR} \times \text{BP} \times 10^{-3}$ (beats/min × mm Hg)	Before intervention	250.5 ± 10.2	223.5 ± 9.4	NS
	After intervention	251.0 ± 13.7	229.8 ± 12.9	

\*Changes in the experimental group were compared with changes in the control group using an analysis of covariance. The values of preintervention-dependent measures were the covariates for the postintervention measures. NS indicates  $P > .05$ ; HR, heart rate.

Table 3.—Plasma Lipid and Lipoprotein Levels*				
Measurement	Period	Mean ± SEM		Significance
		Experimental Group	Control Group	
Plasma cholesterol level, mg/dL	Before intervention	229.0 ± 9.3	220.9 ± 10.3	$P < .0001$
	After intervention	182.0 ± 8.4	215.2 ± 9.7	
Plasma triglyceride level, mg/dL	Before intervention	188.9 ± 21.2	245.8 ± 67.7	$P < .01$
	After intervention	159.7 ± 13.1	248.0 ± 48.2	
High-density lipoprotein level (HDL), mg/dL	Before intervention	47.1 ± 2.2	38.8 ± 3.3	$P < .0001$
	After intervention	39.2 ± 1.8	38.2 ± 3.0	
Total cholesterol/HDL	Before intervention	5.06 ± 0.35	6.34 ± 0.50	NS
	After intervention	4.65 ± 0.22	6.27 ± 0.54	

\*Changes in the experimental group were compared with changes in the control group using an analysis of covariance. The preintervention-dependent measures were the covariates for the postintervention measures. NS indicates  $P > .05$ .

tive to the control group after intervention, we conducted analyses of covariance<sup>16</sup> on all interval data; the values of preintervention-dependent measures were the covariates for the postintervention measures. The ejection fraction response data were further analyzed using a three-way analysis of variance; the factors were (1) group (experimental *v* control), (2) time (before intervention *v* after intervention), and (3) condition (rest *v* maximal exercise).<sup>17</sup> Group data are expressed as mean ± SEM. Percentage changes reflect differences in mean values of the raw data.

## RESULTS

### Baseline Characteristics

There were no statistically significant preintervention differences ( $P > .05$ ) between the experimental and control groups in age, sex, previous myocardial infarction, or previous coronary bypass surgery (Table 1).

Also, there were no significant preintervention differences in any of the reported measures, with the exception of the serum HDL level, which was slightly higher in the experimental group. Eighteen patients in the experimental group and 21 patients in the control group had prior coronary angiography; they averaged 1.8 and 2.4 occluded arteries ( $\geq 50\%$ ) ( $P > .05$ ). In the experimental group, seven persons had one-vessel disease, seven persons had two-vessel disease, and four persons had three-vessel disease; in the control group, six persons had one-vessel disease, eight persons had two-vessel disease, and seven persons had three-vessel disease.

### Exercise Tolerance

In the experimental group, the total duration of exercise (bicycle ergome-

try) increased 44% ( $F = 20.1$ ,  $P < .001$ ), and the total work performed increased 55% ( $F = 16.0$ ,  $P < .0001$ ), whereas the control group was essentially unchanged in both measurements (Table 2). Both groups achieved approximately the same rate-pressure products (systolic BP × heart rate at peak exercise) after intervention as before intervention, but the experimental group performed at a much higher work load before achieving the preintervention rate-pressure product (Table 2). The resting heart rate did not change significantly in either group.

### Plasma Lipid Levels

Changes in plasma lipids are outlined in Table 3. Overall, the experimental group showed a 20.5% reduction in plasma cholesterol levels (22 of 23 patients had reductions, even though most were not hypercholesterolemic), while the control group did not change ( $F = 19.6$ ,  $P < .0001$ ). Triglycerides also were significantly reduced in the experimental group but not in the control group ( $F = 6.5$ ,  $P < .01$ ). While the HDL levels decreased in the experimental group, the total cholesterol/HDL ratio showed no significant differences between the groups. Studies of vegetarian subgroups in this country and elsewhere have shown both a lower total plasma cholesterol and a lower HDL level, yet a lower incidence of coronary heart disease than the general population. The total cholesterol/HDL ratio may be a better indicator of coronary risk than the HDL level per se.<sup>18</sup>

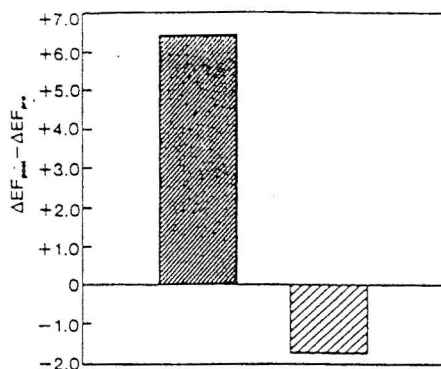
### Frequency of Angina

In the experimental group, the reported frequency of angina episodes per week decreased from  $10.1 \pm 2.0$  before intervention, to  $1.6 \pm 0.5$  after two weeks of the intervention, to  $0.9 \pm 0.3$  after intervention stopped. The control group remained essentially unchanged from  $8.0 \pm 2.1$  episodes per week before intervention to  $7.5 \pm 2.1$  after intervention ( $F = 25.1$ ,  $P < .0001$ ).

### Exercise Radionuclide Ventriculography

This test provides an accurate, non-invasive measure of left ventricular function at rest and during exercise. In interpreting the global left ventric-





Changes in left ventricular ejection fraction in percent from rest to maximum exercise ( $\Delta EF$ ) before and after intervention. Each bar is obtained by subtracting  $\Delta EF_{pre}$  from  $\Delta EF_{post}$ , where  $\Delta EF$  equals change in ejection fraction from rest to peak exercise. Experimental group, narrow diagonal lines; control group, wide diagonal lines.

ular ejection fraction data, the change in ejection fraction from rest to peak exercise ( $\Delta EF$ ) is more reflective of the degree of myocardial ischemia than the absolute values of ejection fraction at rest or at peak exercise. Most patients with multivessel IHD are unable to increase their ejection fraction more than 5 absolute percent from rest to peak exercise ( $\Delta EF$ ) and/or they exhibit new regional wall-motion abnormalities during exercise that are not present at rest.<sup>10,12</sup>

### Ejection Fraction Response

Before intervention, the ejection fraction response to exercise was abnormal for both the experimental and control groups. In the experimental group, there was a slight decrease in the mean ejection fraction from rest ( $58.5 \pm 2.2\%$ ) to maximal exercise ( $57.9 \pm 2.1\%$ ),  $\Delta EF_{pre} = -0.6 \pm 1.5\%$ ; in the control group, there was a slight rise from rest ( $58.5 \pm 1.7\%$ ) to maximal exercise ( $61.4 \pm 2.2\%$ ),  $\Delta EF_{pre} = +2.6 \pm 1.5\%$  (Figure). These intergroup preintervention differences were not statistically significant ( $P > .05$ ).

However, after intervention, the mean ejection fraction response to exercise ( $\Delta EF$ ) of the experimental group was significantly improved when compared with the control group ( $F=16.0$ ,  $P < .0001$ , three-way analysis of variance). In the experimental group, there was an increase in the mean ejection fraction from rest ( $53.8 \pm 2.4\%$ ) to maximal exercise ( $59.6 \pm 2.7\%$ ),  $\Delta EF_{post} = +5.8\%$ . In the

Medication	Discontinued	Reduced Dosage	No Change	Not Taking
<b>Diuretics</b>				
Experimental group	2	0	7	13
Control group	0	0	5	18
<b>Other antihypertensives</b>				
Experimental group	2	1	7	13
Control group	0	0	2	21
<b><math>\beta</math>-Blockers</b>				
Experimental group	4	8	3	8
Control group	0	0	17	6

control group, there was less rise from rest ( $56.3 \pm 1.6\%$ ) to peak exercise ( $57.2 \pm 2.4\%$ ) than in the preintervention studies,  $\Delta EF_{post} = +0.9\%$ .

In the experimental group,  $\Delta EF_{post} - \Delta EF_{pre} = (+5.8) - (-0.6) = +6.4\%$ . Of these 23 patients, 19 showed improvement, one was unchanged, and three showed a slight decline ( $-1\%$ ,  $-1\%$ , and  $-2\%$ ) in the mean ejection fraction response from rest to peak exercise. In the control group,  $\Delta EF_{post} - \Delta EF_{pre} = (+0.9) - (+2.6) = -1.7\%$ . Of these 23 patients, nine showed improvement, one was unchanged, and 13 showed a decline ( $F=12.5$ ,  $P < .0001$ , analysis of covariance, Fig 1) in the mean ejection fraction response from rest to peak exercise.

Before the intervention, 20 patients in the experimental group and 15 patients in the control group demonstrated abnormal responses in the left ventricular ejection fraction to peak exercise ( $\Delta EF < 5\%$ ). After the intervention, only ten patients in the experimental group showed abnormal ejection fraction responses to exercise compared with 17 patients in the control group.

### Regional Wall Motion

The experimental group also showed some improvements in regional wall motion at peak exercise after intervention when compared with the control group. Before intervention, there were 13 patients in the experimental group with new regional wall-motion abnormalities during peak exercise (not present at rest). After intervention, despite a much higher level of exercise, five of these patients displayed some improvement in regional wall motion when compared with their preintervention studies, seven were unchanged, and one was worse ( $P < .05$ ). Before intervention, 15 patients in the control group had new regional wall-motion

abnormalities during maximal exercise; after intervention, two of these abnormalities were somewhat improved, six were unchanged, and seven were worse ( $P > .05$ ).

### Medication Changes

It was necessary to discontinue antihypertensive medications and/or  $\beta$ -blockers in eight patients and reduce dosages in ten others in the experimental group (Table 4) because of the appearance of medication side effects and/or hypotension (diastolic BP  $< 70$  mm Hg), although none reported an increase in compliance with medication regimens during the intervention. No medication changes were made in control group patients. In the experimental group, propranolol hydrochloride therapy was reduced in those taking it from a mean dosage of 80.7 to 40.7 mg/day; mean dosage in the control group remained unchanged (91.2 mg/day).

### Multivariate Analysis

In the experimental group, there was a significant reduction in weight during the intervention, from  $78.5 \pm 3.1$  to  $73.9 \pm 2.9$  kg, whereas the control group remained essentially unchanged from  $82.5 \pm 2.9$  to  $83.2 \pm 3.0$  kg ( $F=79.3$ ,  $P < .0001$ ). Four of nine smokers in the experimental group and one of nine smokers in the control group quit smoking during the intervention, although they were not asked to do so. To assess whether weight and smoking reductions accounted for the observed improvements in the experimental group, we performed stepwise multiple regression analyses<sup>16</sup> individually with weight change and reduction in smoking as possible predictors of the observed changes (variance). Weight change as a predictor accounted for only 2% of the variance in ejection fraction changes, 9% of the variance in resting systolic

BP, 3% of the variance in total cholesterol, and none of the variance in total duration of exercise, total work performed, or diastolic BP. Smoking cessation as a predictor accounted for 8% of the variance in total cholesterol and was not a significant predictor for the variance in the other measured outcomes. Also, neither systolic nor diastolic BP changes were significant predictors of the variance in ejection fraction response, total duration of exercise, or total work performed.

#### COMMENT

Our study indicates that stress management training and a diet low in animal fat, cholesterol, and salt produced short-term improvements in patients with IHD when compared with a nonintervention control group. We measured statistically significant improvements in frequency of angina, total work performed, total duration of exercise, global left ventricular ejection fraction response to exercise, and regional wall-motion response to exercise. The patients' cardiovascular risk status also improved, as evidenced by reductions in levels of plasma cholesterol and triglycerides, when compared with the control group. Confidence in these findings is increased because patients were randomly assigned to each group, medical tests were conducted by technicians blind to condition, and the conditions of the control patients did not improve. The data are consistent with our earlier pilot study.<sup>19</sup> The clinical importance of these changes remains to be determined. Regional wall motion and frequency of angina are subjectively assessed and are, thus, less rigorous than the other reported measures.

Many important questions remain unanswered. Our study was designed only to assess whether short-term improvements in cardiovascular function would result from these ancient and rather simple adjuncts to conventional treatments of IHD. Our aim was to determine first if a combined intervention was effective in the short term before undertaking more extensive and costly long-term studies. It remains to be determined what the long-term effects would be. Also, our two-group design does not allow us to determine the relative contribution of each component of the

intervention or the mechanisms of improvement. Further studies seem justified to explore these areas.

It is of particular interest from a cost-effectiveness point of view to learn if the intervention can be equally effective and whether compliance can be maintained when taught on an outpatient basis rather than in a residential program. A recent report suggests that the effects of psychosocial environment in cardiovascular disease need to be considered. In this context, the group support, the close attention and encouragement given by the staff, and the pleasant environment may have contributed to the measured improvements.<sup>20</sup>

The improvements in global and regional left ventricular response to exercise occurred even though measured at much higher levels of exercise after intervention. In patients with IHD, propranolol improves exercise tolerance and ventricular performance during exercise,<sup>21</sup> yet the measured improvements occurred despite a substantial reduction in propranolol therapy in many of the participants. Also, these changes were not correlated with reductions in BP, weight, or smoking.

The possibility that changes in ejection fraction are caused by factors other than an improvement in myocardial perfusion or performance should be considered. The ejection fraction change in the experimental group was caused more by a reduction in resting ejection fraction after intervention than an increase in the ejection fraction at peak exercise. However, the control group also displayed a reduction in resting ejection fraction in the postintervention studies (although somewhat less); when compared with this, the reduction in the resting ejection fraction in the experimental group was not significant ( $P > .05$ ). Other studies have demonstrated that the resting ejection fraction tends to be lower when it is measured a second time, whether by radionuclide ventriculography<sup>22</sup> or by coronary angiography.<sup>23</sup> This biologic variability may be related to greater familiarity with the procedures at the second study. Also, if the increase in the postintervention change in the ejection fraction from rest to peak exercise were caused only by the decrease in resting ejection fraction, then the control group

should have displayed a similar increase in the postintervention change in the ejection fraction from rest to peak exercise, but it did not. The changes are not likely to be because of changes in BP (afterload), since neither systolic or diastolic BP changes were significant predictors of the variance in ejection fraction response. It is possible that the change in ejection fraction response may be caused by factors other than a reduction in myocardial ischemia.

Aerobic exercise was not a component of this intervention, although some patients began to walk more as they became less symptom-limited. This may be responsible in part for the increases that we measured in total duration of exercise and total work performed. Although aerobic exercise has many cardiovascular benefits, it is not likely to be a factor in the short-term improvements in exercise radionuclide ventriculography that we measured.<sup>24</sup>

We do not know why the conditions of the patients improved. There is some evidence to speculate that the apparent improvements in the experimental group may have occurred through currently accepted mechanisms of IHD, although we did not study this. Emotional stress may lead to myocardial ischemia both by way of coronary artery spasm and by increased platelet aggregation within coronary arteries.<sup>25</sup> Stress may lead to coronary spasm mediated either by direct  $\alpha$ -adrenergic stimulation or secondary to the release of thromboxane  $A_2$  from platelets, perhaps through increasing circulating catecholamines or other mediators.<sup>26-28</sup> Both thromboxane  $A_2$  and catecholamines are potent constrictors of arterial smooth muscle and powerful endogenous stimulators of platelet aggregation.<sup>29</sup>

Even a single high-fat, high-cholesterol meal may cause short-term enhancement of platelet reactivity.<sup>30</sup> These changes may result from a shift in the thromboxane/prostacyclin balance to favor thromboxane production; some evidence supports this. Cholesterol-enriched platelets release more arachidonic acid from platelet phospholipids than cholesterol-depleted platelets, and the conversion of released arachidonic acid to platelet thromboxane is higher in cholesterol-rich platelets than in

those that are cholesterol depleted.<sup>31</sup> In animals with atherosclerosis induced by high-cholesterol diets, platelets synthesize thromboxane A<sub>2</sub> in increased amounts.<sup>32</sup> Since cholesterol is contained only in foods of animal origin, a vegan diet may shift the balance away from thromboxane formation, which would make both coronary spasm and platelet aggregation less likely to occur.

In general, animal protein has been found to increase the level of plasma cholesterol, even in experiments in which the cholesterol and fat have been removed from the protein.<sup>33</sup> Some studies suggest that plant protein may be hypocholesterolemic.<sup>34</sup>

Changes in free fatty acid (FFA) metabolism may have contributed to the observed improvements. Myocardial oxygen consumption is influenced by the substrate supply to the heart. Use of excess FFAs increases myocardial oxygen consumption and decreases left ventricular work, left ventricular systolic pressure, aortic pressure, epicardial motion, and exercise duration; these effects also are seen during myocardial ischemia.<sup>35</sup> Excess FFAs during ischemia result in even greater deteriorations in hemodynamic and metabolic functions.<sup>36</sup> A diet that contains a large proportion of animal products results in high blood levels of FFAs. The opposite is true with diets low in animal products, probably by shifting from noncarbohydrate to carbohydrate energy sources during physical or emotional stresses.<sup>37</sup> Emotional stress also increases blood levels of FFAs, primarily by way of catecholamine stimulation; furthermore, catecholamines sensitize the heart to the oxygen-wasting effects of FFAs.<sup>38</sup>

A combination of stress management training and an essentially vegan diet produced short-term improvement in cardiovascular status (as measured by a variety of endpoints) when compared with a nonintervention control group. Interpretation and generalization of these findings must be tempered with caution, since the patient population is selected and the sample size is relatively small. The intervention is safe and compatible with conventional treatments of IHD.

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