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Dear Colleague:

We enclose the reprint that you requested of our short synthesis of the relationship of physical activity to coronary heart disease risk. Since publication, two other relevant articles have been published, both from the Lipid Research Clinics Group. In the first, from the LRC/CPPT Trial, the experience among 1,500 hypercholesterolemic men, having an average total cholesterol value of 290 mg/dl, was reported as indicating "no protective effect of physical activity" (Siscovick et al., AJPH, 1988;28:1428). This analysis is based on response to only one question: "Do you regularly engage in strenuous exercise or hard physical labor?" This sort of question fails to discriminate classes of habitual physical activity within the light and moderate intensity categories. The study had sufficient power to detect only a 30% or greater risk difference. On the basis of such a limited assessment, the results may be questioned. They were not confirmatory of the MRFIT experience among high risk men (Leon et al., JAMA 1987;258:2388). They are consistent with the Seven Countries findings in Finland where high physical activity was not protective in the presence of mass hypercholesterolemia and atherosclerosis, however, it is likely that most of the U.S. men who answered "yes" to the single LRC question were substantially less active than the Finns.

A second article about fitness rather than habitual activity, also comes from the Lipid Research Clinics but from its mortality study of 4,276 men ages 30-69 followed for 8 1/2 years, with analyses made among the 3,106 men free of cardiovascular disease, with some co-authors from the other paper (Ekelund et al., NEJM, 1988;319:1379). Based on objective classes of heart rate response to submaximal exercise, the risk ratio for all CVD deaths in the least fit men compared with others was 2.7, and, based on time spent on the treadmill, the ratio was 3.0. The risk ratios were similar for risk of coronary death. The authors concluded that lower level fitness, adjusted for cardiovascular risk factors, is independently associated with higher risk of CVD death. They apparently did not adjust for habitual physical activity level which was measured by the same LRC question responded to in the Siscovick paper. Again, we observe generally, that the better the study design, and the more precise the measures, the greater the predictive value of activity and fitness for CHD and CVD death.

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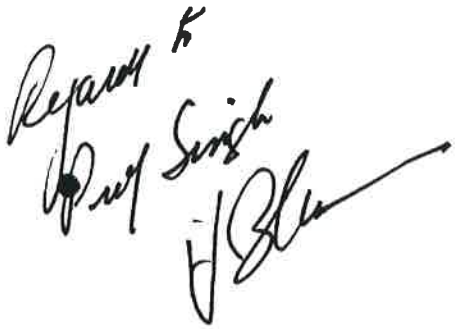

PHYSICAL ACTIVITY AND THE RISK OF CORONARY HEART DISEASE

In this issue of the *Journal*, Wood and colleagues[1] at Stanford report on a clinical trial comparing two methods of weight loss: restricting energy intake and increasing energy expenditure. Each method was equally effective in reducing fat weight, raising plasma levels of high-density lipoprotein cholesterol, and decreasing triglyceride concentrations. This excellent study improves our understanding of mechanisms of weight loss and sets the stage for pragmatic tests of optimal programs for treating obesity while simultaneously modifying plasma lipid levels and improving functional capacity.

In addition to the findings of Wood et al., there is much evidence for a favorable influence of regular physical activity on each link in the causal chain of atherosclerosis and coronary heart disease (CHD).[2,3] Thus, the Stanford experiment may be viewed in a broader context that includes all that is known about physical activity and the prevention of CHD. Here, we join others[2-5] who have attempted to synthesize the findings of many studies of primary and secondary prevention of CHD, using statistical summaries that provide estimates of effects based on the whole body of evidence.

Trials of cardiac rehabilitation after myocardial infarction (secondary prevention), including studies of exercise training, have had samples too small to allow definite conclusions to be drawn. Oldridge and colleagues have carried out a useful meta-analysis of the better-designed studies, noting first that many trials demonstrate an effect of exercise on levels of risk factors and exercise tolerance.[4] They then used rigorous criteria for the inclusion of 10 trials in a statistical summary. That analysis found an estimated 24 percent reduction in deaths from all causes in patients undergoing cardiac rehabilitation, and a 25 percent reduction in cardiovascular mortality — both estimates clinically important and statistically significant. The incidence of nonfatal myocardial infarction, however, was 15 percent higher (no significant difference) in all the treatment groups combined and 32 percent higher ($P = 0.058$) in the groups in which cardiac rehabilitation was begun early, within eight weeks after infarction. Thus, cardiac rehabilitation had no overall effect on nonfatal infarction, and when initiated early, it may even have increased the incidence of nonfatal infarction. Oldridge and colleagues addressed a number of the uses and limitations of such summaries by meta-analysis. Interpretation is strengthened by results that are in the same direction in many studies and over different periods, and that are obtained with various protocols, populations, and investigators. Thus, we conclude that physical activity, as a major component of cardiac rehabilitation, probably has a preventive effect on postinfarction deaths due to cardiovascular causes and all causes. A prudent approach would be to avoid instituting vigorous exercise as a component of rehabilitation too soon.

A larger issue is the effectiveness of physical activity in the primary prevention of CHD. This important question is not likely to be tested rigorously, because compliance with exercise protocols is often poor and the cost of such a study would be enormous. Thus, our primary sources of information are observational studies involving attempts to identify the confounding effects of life-style characteristics other than physical activity, and experiments, such as that of Wood and colleagues, on the effects of physical activity and energy intake on known coronary risk factors.

A recent synthesis by Powell and colleagues[5] concluded that the majority of observational studies meeting their criteria found a significant and graded relation between physical inactivity and the risk of CHD, and that studies with a stronger design were more likely to show an effect. These authors calculated a median risk ratio of 1.9 — that is, a 90 percent excess risk of CHD among physically inactive persons.

We analyzed the subset of 16 studies from the review of Powell et al. that measured individual physical activity, and added recent studies from the Multiple Risk Factor Intervention Trial and a study of U.S. railroad workers.[6,7] We found that all 18 studies showed that habitual physical activity was inversely related to death from CHD or death from all causes. The more recent studies adjusted for confounding risks, and this adjustment usually diminished but did not abolish the risk associated with physical inactivity. Several studies found that the relation was largely "explained" by the level of physical fitness, in that the gradient of risk with the level of physical activity largely disappeared when measures of fitness were controlled for.[8,9]

The duration, frequency, and intensity of physical activity that may be protective against CHD remain at issue. Recent studies suggest that an energy expenditure of 150 to 300 kcal daily, in activity of moderate intensity such as walking and working around the house, has a beneficial effect, as does a moderate amount of vigorous physical activity.[6,7] Anthropologic observations suggest that farmers and herdsmen the world over rarely work at a pace that would lead to a

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shortness of breath. More systematic observations with colleagues in the Seven Countries study[10] indicate that even a large amount of regular, vigorous physical activity does not protect an individual or a population if hypercholesterolemia is present. In that study, subjects in eastern Finland were found to be the most physically active, yet had the highest rates of CHD, with little reduction in risk among the physically active within that population.[10]

Our interpretation of all these observations is that physical activity protects against coronary death, at least in middle-aged men. A basic uncertainty that nevertheless remains after all these studies is whether the effect is due to environment (activity) or constitution (genes). People exercise if they feel good when they exercise. Fitness, with its strong constitutional component, may be a major contributor to the apparent protective effect of physical activity. It is possible that fitness determines both who will be active and who will be protected from clinical CHD. At least two pieces of evidence are related to this question. Any protective effect of once having been a college athlete, and presumably constitutionally superior, disappears over time after graduation, whereas current physical activity is apparently effective.[11] Moreover, constitutional factors are likely to be less important to participation in moderate exercise than to participation in vigorous exercise, and the association of activity of moderate intensity with a lower risk of CHD suggests that constitution is not the major operant.

Finally, safety is foremost, both in prescribing exercise for the individual and making recommendations for the public health. Siscovick et al. found an excess risk of primary cardiac arrest during and shortly after strenuous exercise in all subjects regardless of their level of habitual physical activity.[12] But these investigators also found a much lower overall risk of sudden coronary death in subjects who were habitually active. Thus, in a public health sense, they suggested that the reduced risk of sudden death due to regular physical activity was greater than the excess risk of sudden death during vigorous activity. This is small comfort to the families of those stricken while running. It seems likely, however, that brisk walking is the more reasonable prescription for sedentary and middle-aged people who have not maintained their fitness from their youth.

Given the uncertainty, from lack of "proof," about the protective effect of physical activity against CHD, studies of its effects on risk factors and mechanisms provide a sound basis for rational prevention. The Stanford trial is an important step toward understanding the role of physical activity and diet in weight loss. The correction of obesity in an affluent, sedentary society, however, should not focus on decreased energy intake. Rather, it should emphasize greater energy expenditure, with a disproportionately lower intake during the period of active weight loss. One would thereby achieve better nutrition, reduce obesity, and bring about more favorable plasma lipoprotein levels and metabolism. The increased energy requirements of greater activity are best met by eating cereals, legumes, vegetables, and fruits.

Lifelong regular physical activity and the existence of a vigorous populace have other obvious benefits, including just the ability to move about and keep up with children and grandchildren. We are left, then, with a powerful lesson: that humankind departs from evolutionary adaptations to habitual diet and physical activity at its own risk.

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REFERENCES

1. Wood PD, Stefanick ML, Dreon DM, et al. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. N Engl J Med 1988; 319:1173-9.
2. Curfman GD, Thomas GS, Paffenbarger RS Jr. Physical activity and primary prevention of cardiovascular disease. Cardiol Clin 1985; 3:203-22.
3. Leon AS. Physical activity levels and coronary heart disease: analysis of epidemiologic and supporting studies. Med Clin North Am 1985; 69:3-20.
4. Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction: combined experience of randomized clinical trials. JAMA 1988; 260:945-50.
5. Powell KE, Thompson PD, Caspersen CJ, Kendrick JS. Physical activity and the incidence of coronary heart disease. Annu Rev Public Health 1987; 8:253-87.
6. Leon AS, Connett J, Jacobs DR Jr, Rauramaa R. Leisure-time physical activity levels and risk of coronary heart disease and death: the Multiple Risk Factor Intervention Trial. JAMA 1987; 258:2388-95.
7. Slattery ML, Jacobs DR Jr, Nichaman MZ. Leisure time physical activity and coronary heart disease death: the U.S. Railroad Study. Circulation (in press).
8. Slattery ML, Jacobs DR Jr. Physical fitness and cardiovascular disease mortality: the US Railroad Study. Am J Epidemiol 1988; 127:571-80.
9. Peters RK, Cady LD Jr, Bischoff DP, Bernstein L, Pike MC. Physical fitness and subsequent myocardial infarction in healthy workers. JAMA 1983; 249:3052-6.
10. Keys AB. Seven countries: a multivariate analysis of death and coronary heart disease. Cambridge, Mass.: Harvard University Press, 1980.
11. Paffenbarger RS Jr, Hyde RT, Wing AL, Steinmetz CH. A natural history of athleticism and cardiovascular health. JAMA 1984; 252:491-5.
12. Siscovick DS, Weiss NS, Fletcher RH, Lasky T. The incidence of primary cardiac arrest during vigorous exercise. N Engl J Med 1984; 311:874-7.