Evidence of the Role of Physical Activity and Cardiorespiratory Fitness in the Prevention of Coronary Heart Disease

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Epidemiologic evidence is presented on the now well-accepted contributions of physical inactivity and reduced cardiorespiratory fitness to risk of coronary heart disease (CHD), the principal cause of death and disability in the United States and other Western industrialized nations. The types and dose of physical activity to reduce risk of CHD and plausible biologic mechanisms for the partial protective effect are also reviewed.

Despite a progressive decline in the death rate from coronary heart disease (CHD) since 1968, CHD remains the leading cause of death in the United States and is a major contributor to disability, lost productivity, and medical costs (American Heart Association, 1993). The underlying basis of CHD is atherosclerosis involving the intimal linings of major coronary arteries. The pathogenesis of coronary atherosclerosis involves dysfunction and injury to endothelial cells; lipid (primarily low density lipoprotein or LDL) insudation, alterations, and deposition; macrophage and smooth muscle cell infiltration; fibrosis; and calcium deposition (Leon, 1995). This disease process begins in childhood and progresses in severity over decades. The resulting raised atherosclerotic plaques protrude into the artery lumen, progressively reducing coronary blood flow. Rheologic damage to the plaques and endothelium result in platelet adherence and aggregation, which in the presence of excess plasma fibrinogen, reduced fibrinologic activity, and other hemostatic dysfunctions can lead to thrombotic occlusion of an involved coronary artery. The resulting myocardial ischemia can induce a fatal ventricular arrhythmia or cause myocardial necrosis (i.e., myocardial infarction or heart attack).

As is true with most chronic diseases processes, CHD has a multifactorial etiology (Leon, 1987, 1995; Pooling Project Research Group, 1978; Smith & Leon, 1992). Risk factors include elevated levels of blood total and LDL cholesterol, reduced levels of high density lipoprotein (HDL) cholesterol, elevated levels of...
systolic and diastolic blood pressure, diabetes mellitus, and obesity (particularly the phenotype with a central or abdominal predominance of fat) (Bjorntorp, 1991). The severity of atherosclerosis and risk of CHD progresses with age at a faster rate in men than women until after menopause; however, by age 65 years women have a higher rate of CHD than men (Becker & Corrao, 1992).

Low levels of physical activity (PA) and a reduction in cardiorespiratory fitness or aerobic capacity, associated with the modern mode of living, are now generally recognized as other important contributing factors to the etiology of CHD and the emergence of CHD as a major public health problem. The evidence for this statement is summarized below.

Physical inactivity is a prevalent risk factor in the United States. For example, a recent survey by the Centers for Disease Control and Prevention revealed that 60% of American adults perform little or no recreational PA (Siegel, Brackbill, & Frazier, 1991). The evidence supporting the contribution of PA and fitness to risk of CHD, as well as premature death from all causes, is based primarily on observational epidemiological studies, predominantly involving middle-aged or older men. There is a paucity of research on this topic in women, and the results of existing studies are mixed. Additional supporting evidence for the contribution of physical inactivity to CHD are provided by postmortem studies; pooled data from secondary CHD prevention trials; and experimental evidence from short-term animal and human exercise training studies, which have identified possible protective mechanisms associated with exercise.

Extensive reviews and critiques have been published of the more than 100 observational epidemiological studies appearing in the literature since the 1950s (Berlin & Colditz, 1990; Leaf, 1991; Leon & Blackburn, 1977; Powell, Thompson, Caspersen, & Kendrick, 1987). The initial pioneering epidemiologic studies published in the 1950s and 1960s primarily consisted of retrospective comparisons of occupational PA levels based on job descriptions with CHD events determined from death certificates or medical records (Brunner & Manelis, 1960; Kahn, 1963; Morris, Heady, Raffe, Roberts, & Parks, 1953; Taylor et al., 1962; Zukel et al., 1959). Although these first-generation epidemiologic studies contained many methodological shortcomings, their demonstration of an apparent inverse association between occupational PA and risk of CHD served as the impetus for more sophisticated investigations, an example of which was a landmark 22-year cohort study involving San Francisco Bay longshoremen by Paffenbarger and colleagues (Paffenbarger, Gima, Laughlin, Mary, & Black, 1971; Paffenbarger & Hale, 1975 ). In this study, a threefold increase in death from CHD was associated with low energy expenditure on the job as compared to high energy workout, which persisted after statistical adjustment for age and several other risk factors for CHD in addition to reclassification for job changes.

Most recent epidemiologic studies have been prospective and have emphasized leisure time PA, since few occupations require significant amounts of PA any longer. Of particular interest are major large-scale longitudinal studies, using validated measures of leisure time PA and CHD endpoints and statistical adjustments for many possible confounding variables. These latest generation of prospective epidemiologic studies include a 10-year follow-up of up to 18,000 British male executive clerks and civil service employees (Morris et al., 1973; Morris, Clayton, Everitt, Semmence, & Burgess, 1990), a more than 20 year follow-up of about 17,000 male college alumni (Paffenbarger, Hyde, Wing, & Hsieh, 1986; Paffenbarger et al., 1993; Paffenbarger, Wing, & Hyde, 1978; Paffenbarger, Wing, & Steinmetz, 1984) a 7- and 10.5-year
follow-up of middle-aged men at high risk for CHD, participating in the Multiple Risk Factor Intervention Trial (MRFIT) (Leon & Connett, 1991; Leon, Connett, Jacobs, & Rauramaa, 1987), and a 9.5-year follow-up of almost 8,000 middle-aged men participating in the British Regional Heart Study (Sharper & Wannamethee, 1991).

The results of all of these studies unanimously support the postulated inverse relationship of PA with risk of CHD, as well as with all-cause mortality. In addition, a limited number of studies in the United States and Europe correlated cardiorespiratory fitness, or so-called aerobic power determined by exercise testing, with risk of CHD (Blair et al., 1989; Bruce, Hossack, DeRouen, & Hofer, 1983; Ekeland et al., 1988; Erickssen, 1986; Peters, Cady, Bischoff, Bernstein, & Pike, 1983; Sandvik et al., 1993; Slattery & Jacobs, 1988; Sobolaski et al., 1987; Wilhelmsen et al., 1981). All of these studies observed a strong inverse, generally graded association between fitness and risk of CHD. This includes an 8-year prospective study by Blair et al. (1989) that involved over 10,000 initially healthy men and over 3,000 women, who received maximal treadmill exercise tests at The Cooper Institute for Aerobics Research in Dallas.

Pooled data and meta-analysis of the epidemiologic studies of "better" methodological quality have noted a consistent inverse association of both PA and of aerobic power with risk of CHD. The risk of death from CHD increased about twofold in those individuals who were physically inactive as compared to more active individuals (Berlin & Colditz, 1990; Powell et al., 1987) and increased over fivefold in the least fit as compared to the most fit (Blair, 1993). Adjustment for other risk factors only slightly weakened these associations, suggesting independent relationships. The largest reduction in relative risk of CHD appears to occur with going from a sedentary to moderately-active lifestyle and from below average to average fitness for one's age. In terms of energy expenditure the mass of observational data suggests that physical exertion of even moderate intensity (<6 METs), if performed on the average for 30 minutes or more a day at a total energy cost of 1,050 to 2,000 kcal a week for an average-sized person, is associated with a reduced risk of death from CHD (Haskell, 1985, 1994; Leon et al., 1987; Paffenbarger, Wing, & Hyde, 1978). This can include short bouts of lifestyle-type of PA, such as walking for transportation, stair climbing, and working around the house and yard. Additional protective effects would be expected to accrue from regular higher intensity PA of sufficient volume to improve maximal oxygen uptake, such as recommended by American College of Sports Medicine guidelines (1991), based on available epidemiologic studies and experimental data from training studies.

Additional supporting evidence for the apparent inverse relationship of PA to risk of CHD comes from a limited number of major postmortem studies previously reviewed (Leon, 1983; Leon & Blackburn, 1977). In these studies, the extent of coronary atherosclerosis and of myocardial damage observed in men at autopsy was correlated with antemortem, generally work-related PA habits. The following general conclusions can be derived from these postmortem studies:

1. Death from CHD is twice as common and at an earlier age in men performing light occupational tasks as compared to those performing heavy work.
2. The prevalence of severe coronary atherosclerosis is either unrelated to PA or less severe in physically active men.
3. Physically active men have significantly larger coronary artery luminal areas and less frequent complete or nearly complete coronary occlusions than less
active workers.
4. Physically active workers generally have less evidence of ischemic myocardial damage than less active workers.

Definitive experimental proof of the PA–CHD hypothesis by a large-scale, randomized, controlled, primary prevention trial has been judged to be not feasible due to the large sample size required and the problems of crossovers, adherence and control of other risk factors, and prohibitive costs (Leon & Blackburn, 1977). As an alternative, meta-analysis of pooled data from over 20 secondary prevention trials in the United States and Europe, which included an exercise training component or exercise advice, indicate a reduction of 20 to 25% in 1- to 3-year rates of mortality from cardiovascular disease and from all causes in the treatment group, as compared to control patients (O’Connor et al., 1989). However, the rate for nonfatal CHD events was similar for the intervention and control patients, and the design of these studies does not allow for the assessment of the independent contribution of the exercise component. A recent encouraging finding is the demonstration of the independent contribution of 1,600 kcal per week or more of PA in stopping the progression or even partially reversing the severity of coronary atherosclerosis demonstrated by serial angiograms in patients with known CHD (Hambrecht et al., 1993).

Multiple plausible biological mechanisms have been identified from animal research; small scale, short-term human experimental studies; and cross-sectional comparisons of physically active versus sedentary people to help explain how PA and cardiorespiratory fitness reduce the risk of initial CHD events, and improve survival after a myocardial infarction. These mechanisms consist of anatomic, physiologic, and metabolic adaptations to PA and depend on the type, intensity, frequency, duration, and length of the participation. These adaptations have recently been extensively reviewed, along with the supporting evidence (Blair, Kohl, & Gordon, 1992; Leon, 1990, 1991), and are as follows:

1. Reduction in severity of coronary atherosclerosis both directly and through favorable effects on other major coronary risk factors (i.e., loss of excess weight/body fat, reduction in blood pressure, increase in HDL cholesterol levels, improved insulin sensitivity, and increased glucose tolerance).
2. A reduction in myocardial oxygen demands at rest and during submaximal physical effort by a decrease in heart rate and systolic blood pressure.
3. An increased myocardial oxygen supply through lengthening of diastole by heart rate slowing, as well as perhaps by increasing vascularity.
4. A reduction in risk of coronary thrombosis by decreased platelet adhesiveness and aggregability and promotion of fibrinolysis.
5. Reduced myocardial vulnerability to lethal ventricular arrhythmias in the presence of advanced coronary atherosclerosis, even during heavy physical exertion (Mittleman et al., 1993; Willich et al., 1993).

Some of these benefits may be due to the overlapping of effects of acute bouts of exercise and others require chronic physical activity or exercise training.

The available epidemiologic and experimental data indicate that regular moderate intensity PA acts primarily to reduce susceptibility of people with existing coronary atherosclerosis to fatal CHD by reducing vulnerability to ventricular ar-
rhythmias and perhaps coronary thrombosis. A formal endurance exercise program, sufficient to enhance cardiorespiratory endurance appears to be required to provide the additional protective effects elucidated above. The ideal program, in order to provide the full gamut of protective effects of PA against CHD, would be a combination of lifestyle or recreational PA on a nearly daily basis plus a formal endurance exercise program several times a week to increase aerobic power.

Based on this impressive body of scientific evidence summarized above, many expert groups worldwide have embraced the role of PA and fitness promotion as important public health and medical practice objectives to reduce not only the burden of CHD but also the occurrence of a number of other common medical conditions reviewed by others in this issue of Quest. These organizations include the American Heart Association (Fletcher et al., 1992), the U.S. Department of Health and Human Services (1991) in their Healthy People 2000 health-promotion/disease prevention initiative, the U.S. Centers for Disease Control and Prevention and American College of Sports Medicine (Pate et al., 1995), the U.S. Preventive Task Force (Harris, Caspersen, DeFreise, & Estes, 1989), and the World Health Organization (International Society and Federation of Cardiology, 1992).

**Summary and Conclusions**

Strong, consistent epidemiological evidence exists of an independent association between (a) low levels of both habitual PA and cardiorespiratory endurance and (b) risk of fatal and CHD clinical events in middle-aged or older men with limited supporting evidence also in women. Inactivity at work and during leisure time essentially doubles one’s risk of a fatal and nonfatal myocardial infarction, independent of other risk factors. Low aerobic capacity has an even greater impact on risk of CHD events than a sedentary lifestyle. Additional research has identified multiple anatomic, physiologic, and metabolic adaptations to PA that provide plausible biologic mechanisms involved for the apparent partial protective effect of PA and fitness against CHD.

The dose–response relationship between PA and risk of CHD and the various protective mechanisms are also becoming better defined. Daily moderate intensity lifestyle, recreational physical activities, and formal aerobic exercise programs contribute to protective benefits. To maximize protection against CHD, attention must be paid to all major risk factors, along with performance of 30 minutes or more of almost daily moderate routine and recreational PA plus a formal aerobic exercise program, at least several times per week to promote cardiorespiratory fitness, for a total weekly energy expenditure of 1,050 to 2,000 kcal for an average sized person.

The Activity Pyramid in Figure 1 has been developed by one of us (Norstrom) as a model to graphically display this activity message for the purpose of public education. The Activity Pyramid presents an ideal, stepwise, daily and weekly activity scheme for promoting PA for the purpose of prevention of CHD and other prevalent health problems related to physical inactivity. For an inactive individual, the first step would be to increase nonstructured “everyday” activities at the base of the Pyramid. The next step would be to incorporate more active recreational pursuits and exercise into the weekly routine at least several times per week (middle areas of the Pyramid). This step would provide the stimulus for improving one’s cardiorespiratory fitness. Ideally, this would include resistance exercises to improve strength, as well as flexibility-promoting activities. For those who are presently
only seasonably or sporadically active, the goal would be to become more consistently active by incorporating year-round activities, represented in the middle areas of the Activity Pyramid. For a person already leading an active life, the goal would be to emphasize a life-long maintenance program, including periodically exploring new activities. The overall emphasis can be summed up as progressively adding more physical activities and sitting less (peak of the Pyramid).

References


