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Physical Activity and Health: Atherosclerotic, Metabolic, and Hypertensive Diseases

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A sedentary lifestyle is a risk factor for a number of diseases that become more prevalent with age in both genders. In contrast, regular physical activity performed in a variety of circumstances is proving to be a health-related behavior with favorable consequences on commonly recognized health outcomes. This paper presents an overview of the evidence for the negative effects of sedentarism and the positive influences of a physically active lifestyle on atherosclerotic, metabolic, and hypertensive diseases.

As the body of data on this topic has grown considerably over the last decade, it will not be possible to review all aspects of the relationships between physical activity or inactivity and the relevant health outcomes. Only the main dimensions of the problems will be emphasized in this short document. These topics were reviewed in considerably more detail in the proceedings of the 1992 Toronto International Consensus Symposium on Physical Activity, Fitness, and Health (Bouchard, Shephard, & Stephens, 1994) to which the interested reader is referred for a more comprehensive exposé.

Overweight and Obesity

Variations in body energy content over time can provide indication about whether a person has been or is currently in positive or negative energy balance. The determinants of energy balance can be grouped into three categories: energy intake, energy expenditure, and biological factors modulating nutrient partitioning. All three classes of affectors are very difficult to measure with precision in free-living individuals. Typically, the standard deviation of repeated measurements of these determinants reaches about 10% of the mean value. In addition, energy intake and energy expenditure fluctuate naturally from day to day. For instance, the standard deviation of energy intake assessed over a large number of days for a given person reaches about 1,000 kJ per day. Because physical activity accounts, on average, for only about 20% of the daily energy expended in sedentary individuals, a slight increase in habitual physical activity is unlikely to have a substantial impact on total daily energy expenditure and thus on energy balance. Moreover, the increase in level of activity may be accompanied by a corresponding decrease in spontaneous activity or by an increase in energy intake. Both factors are likely to obscure the effects of a slight increase in regular physical activity on energy balance and body energy content. Little attention has been given to these two compensatory phenomena, which should receive more attention. Indeed, the minimal exercise prescription that would increase daily energy expenditure and generate a sufficient negative energy deficit in both men and women remains to be determined. The spontaneous adjustment of energy intake to increases in energy expenditure produced by increased physical activity clearly warrants further study.

With a more substantial energy expenditure resulting from a higher level of habitual physical activity, greater influences are likely to be seen on energy balance and body energy content (Bouchard, Després, & Tremblay, 1993; Thompson, Jarvie, Lahey, & Cureton, 1982; Tremblay, Després, & Bouchard, 1985). From a practical point of view, daily physical activity leading to an extra energy expenditure of approximately 800 to 1,000 kJ or about 5.5 to 7.0 MJ per week should be sufficient to generate a significant energy deficit. There is clear experimental evidence that a negative energy balance of that magnitude sustained for several months causes a substantial loss of body energy content (Bouchard, Tremblay, et al., 1990, 1994). Interestingly, when such a substantial negative energy balance is generated by regular physical activity instead of by reduced caloric intake, the weight loss is mostly accounted for by a loss of body fat (Bouchard, Tremblay, et al., 1990, 1994). In contrast, when the negative energy balance is caused by lowering energy intake, one loses a significant amount of lean tissues, which may attain under some

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circumstances as much as 50% of the total weight loss (Tremblay et al., 1985).

It seems that a sustained negative energy balance state as a result of a higher level of habitual physical activity is more easily achieved in men than in women (Després et al., 1984; Krotkiewski, 1983, 1985; Tremblay, Després, Leblanc, & Bouchard, 1984). The most important reason for such a gender difference appears to be the acute increase in energy intake in response to exercise in women, a phenomenon which has not been noted in men (Tremblay, Després, & Bouchard, 1988). Another potential gender difference in response to regular physical activity associated with a sustained negative energy balance state concerns the site of fat mobilization. Thus, lipid stores from upper body and abdominal adipose depots are apparently mobilized to a greater extent in men than in women (Després, Tremblay, & Bouchard, 1989). This is not a trivial issue given the metabolic impact of abdominal and upper body fat (Bouchard, Bray, & Hubbard, 1990; Després et al., 1990) and the fact that the loss of abdominal and upper body fat is well correlated with the improvement in glucose and lipid metabolism observed with regular aerobic exercise (Després et al., 1988, 1991).

A common finding of the studies designed to investigate the role of regular physical activity in the treatment of obesity is that it is likely to produce better results in overweight or moderately obese cases (Hill, Drougas, & Peters, 1994) than in severely obese patients (Atkinson & Walberg-Rankin, 1994). Moreover, regular physical activity is becoming one of the most useful behaviors to emphasize in the maintenance of a reduced body weight as suggested by several recent intervention studies (Hill et al., 1994).

Hypertension

Hypertension is a major public health problem. Elevated diastolic or systolic blood pressure is associated with a greater risk of developing congestive heart failure, coronary heart disease, stroke, kidney failure, and intermittent peripheral claudication in men and women. There is a onefold increase in the risk of developing these diseases when blood pressure is greater than 140/90 mmHg. Furthermore, the risk increases by at least threefold when blood pressure values of 160/95 mmHg and higher are reached. The prevalence of hypertension is higher in men prior to age 65, but is greater in women 65 years and older (National Heart, Lung, and Blood Institute Report, 1991).

Hypertension is a heterogeneous condition, and individuals with high blood pressure also show highly variable responses to preventive and therapeutic measures. Obesity, and its related hyperinsulinemic state, particularly in android obesity, are important risk factors for hypertension. High alcohol and salt intake may cause hypertension in a large segment of the population. Losing weight and reducing alcohol and salt intake may reduce elevated blood pressure in many cases. Essential hypertension is a result of functional disturbances in blood volume, cardiac output, total peripheral resistance, and regulation of kidney functions. Some of these alterations are highly prevalent among sedentary and overweight individuals. Any perturbation in the regulatory mechanisms of these functions and systems may chronically elevate blood pressure.

Many epidemiological studies have reported an inverse relationship between level of habitual physical activity and resting blood pressure (Hagberg, 1989, 1990; Paffenbarger, Jung, Leung, & Hyde, 1991). Intervention studies have shown that regular physical activity in essential hypertensives can reduce systolic and diastolic blood pressures by approximately 10 mmHg (Hagberg, 1990), a reduction which is, in several instances, of clinical significance. This favorable effect has not been noted in all cases, and increased physical activity alone may not always be sufficient to normalize blood pressure. The current available data suggest that regular endurance exercise at an intensity of 40 to 60% of maximal oxygen uptake (VO_2max) is sufficient to induce these effects (Hagberg, 1990).

The same beneficial influences of regular physical activity on blood pressure are also observed in older people (Hagberg, 1989). On the other hand, regular physical activity is not likely to have a major impact on the blood pressure of normotensive individuals (Fagard & Tipton, 1994). However, as suggested by prospective studies, a reasonable level of habitual physical activity or fitness may be protective against the increase in blood pressure commonly seen with age in Western societies (Blair, Goodyear, Gibbons, & Cooper, 1984; Paffenbarger, Wing, Hyde, & Jung, 1983).

Blood Lipids, Lipoproteins, and Dyslipoproteinemias

The influences of regular physical activity or a sedentary lifestyle on blood lipids and lipoproteins have been the object of several investigations over the last decade. The surge in scientific and clinical research was motivated by the observation that some plasma lipids and lipoproteins are strong predictors of coronary heart disease and other atherosclerotic diseases. It is now generally recognized that regular physical activity has favorable effects on several aspects of lipid metabolism (Després & Lamarche, 1994; Wood & Stefanick, 1990) and may also be helpful in the nonpharmacological treatment of some dyslipoproteinemias (Hanefeld, 1991).

Cross-sectional comparisons of athletes or very active individuals with age- and gender-matched sedentary persons have consistently found substantial differences in plasma lipids and lipoprotein profiles favoring the active people. Although exercise intervention studies have been supportive of these findings, the magnitude of the changes in blood and lipoproteins with regular physical activity is generally smaller than suggested by cross-sectional comparisons.

Briefly, regular physical activity lowers plasma triglycerides in individuals with initially high levels but has little impact on those with normal concentrations. On the average, regular physical activity increases high-density lipoprotein cholesterol (HDL-C), particularly the cholesterol content of the HDL_2 subfraction, and may also increase apolipoprotein A-I, the main apolipoprotein of HDL. Occasionally, especially among individuals with elevated cholesterol levels, regular physical activity is associated with decreases in total cholesterol and low-density lipoprotein cholesterol (LDL-C). However, regular physical activity may also reduce the LDL particle number without a concomitant decrease in LDL-C levels. This notion has important implications as elevated cholesterol and LDL-C levels are not the most prevalent dyslipidemias in coronary heart disease patients. Indeed, hypertriglyceridemia, elevated apolipoprotein B concentrations, and low HDL-C levels are quite common in coronary heart disease patients, and these variables have been shown to be favorably modified when the exercise prescription was adequate (Després & Lamarche, 1994; Wood & Stefanick, 1990). Several ratios of plasma lipids and lipoproteins are commonly used to assess the overall risk of coronary heart disease, and they are also generally influenced favorably by regular physical activity. Thus, the ratio of total cholesterol to HDL-C, the ratio of HDL_2-C to HDL_3-C, and the ratio of apolipoprotein A-I to apolipoprotein B are higher in highly active individuals as compared to sedentary individuals and are often increased by regular exercise interventions (Després & Lamarche, 1994).

In other words, low plasma triglyceride, total cholesterol, and LDL-C levels, as well as elevated HDL-C levels, are generally recognized as being associated with a low coronary heart disease risk. Regular physical activity is thought to alter lipid transport in the direction of this favorable profile (Haskell, 1986; Wood & Stefanick, 1990). Moreover, the lipid profile may be favorably altered with exercise at a lower intensity than has generally been thought to be required (Hardman, Hudson, Jones, & Norgan, 1989; Leon, Conrad, Hunninghake, & Serfass, 1979; Sopko et al., 1983; Tucker & Friedman, 1990) as long as the increase in energy expenditure generated by exercise is sufficient to induce a substantial negative energy balance (Després & Lamarche, 1994).

The mechanisms by which changes in plasma lipoprotein levels and metabolism occur with regular physical activity are only partially understood (Stefanick & Wood, 1994). Three key enzymes of lipoprotein metabolism appear to be favorably influenced by regular physical activity: Lipoprotein lipase activity is increased, hepatic lipase activity is decreased, and cholesteryl-ester transfer protein activity is reduced (Després et al., 1991; Haskell, 1986; Seip et al., 1993; Wood & Stefanick, 1990). The increase in lipoprotein lipase activity, the key enzyme in the conversion of very low-density lipoprotein to HDL, associated with regular exercise may contribute to the augmentation of the HDL-C level, particularly the HDL_2 subfraction. On the other hand, hepatic lipase is thought to impact on many aspects of lipoprotein metabolism, one of which is involved either in the hepatic degradation of HDL_2 or in the conversion of HDL_2 to HDL_3. The reduction in hepatic lipase activity observed with regular exercise may be one of the mechanisms favoring the high levels of HDL_2-C observed in active individuals. Another mechanism that should be considered is the role of regular physical activity on in vivo insulin action, as activity intends to increase insulin sensitivity and reduce plasma insulin levels, a phenomenon that may also favorably alter plasma lipoprotein-lipid levels.

The above summary undoubtedly presents an optimistic picture of the net effects of regular physical activity on blood lipids and lipoproteins. Several confounders must be considered before the specific influences of regular physical activity can be fully appreciated. For instance, some of the changes observed in lipoprotein metabolism in exercise intervention studies may be largely mediated by changes in body mass and body composition (Wood & Stefanick, 1990). Cross-sectional comparisons of active versus inactive individuals may likewise be affected by group differences in body composition. Other confounding factors that may contribute in cross-sectional or longitudinal study designs include the amount of upper body fat, the amount of abdominal visceral adipose tissue, smoking, dietary cholesterol, dietary fat, and alcohol consumption. Finally, as we have shown that some genotypes are more susceptible to dyslipoproteinemia in the presence of excess abdominal fat (Després et al., 1990), it is likely that some individuals are genetically more susceptible or resistant to improvements of the lipoprotein profile in response to increased physical activity (Després et al., 1988).

Glucose Intolerance, Insulin Resistance, and Diabetes Mellitus

The impairment of the in vivo glucose disposal rate in the presence of insulin is the consequence of an insulin-resistant state in peripheral tissues, particularly the

skeletal muscle. A diminished insulin-mediated inhibition of hepatic glucose output also occurs when the liver becomes resistant to the action of insulin. Both phenomena are associated with various degrees to the development of an abnormal glucose intolerance and to hyperinsulinemia resulting from insulin resistance. These are some of the characteristic features involved in the etiology of non-insulin-dependent diabetes mellitus, which develops primarily in adult men and women who are overweight (about 85% of non-insulin-dependent diabetes mellitus cases) and who have excess abdominal fat accumulation. The vascular complications of diabetes are numerous and include not only coronary heart disease, which is the most frequent cause of death in diabetic patients, but also peripheral vascular disease, nephropathy, retinopathy, and other conditions.

It is thought that regular physical activity has beneficial effects on plasma glucose and insulin homeostasis in nondiabetic and non-insulin-dependent diabetes mellitus individuals. One apparent consequence of regular exercise is an improvement in the sensitivity of liver, skeletal muscle, and adipose tissues to insulin action (Rodnick, Haskell, Swislocki, Foley, & Reaven, 1987). Among the manifestations of the phenomenon, there is a decrease in the basal level of plasma glucose in hyperglycemic individuals, a decrease in fasting insulin levels, a reduction in the insulin response to a glucose load, and an increase in the glucose disposal rate assessed under various conditions during euglycemic-hyperinsulinemic clamp procedures (Exercise and Noninsulin Dependent Diabetes Mellitus, 1990; Vranic & Wasserman, 1990). Regular physical activity may also play a significant role in maintaining normoglycemia and insulin sensitivity in nondiabetic people as suggested by several epidemiological studies.

Glycemic control is improved by regular physical activity, with the response to training generally being better in those with an initially impaired glucose tolerance (Exercise and Noninsulin Dependent Diabetes Mellitus, 1990). Plasma insulin levels decrease with regular exercise (Leon et al., 1979; Tremblay et al., 1990), with hyperinsulinemic patients showing the largest reduction in insulin levels in response to training (Exercise and Noninsulin Dependent Diabetes Mellitus, 1990). Such changes are observed with programs of walking (Leon et al., 1979) and low-intensity, long-duration exercise sessions that do not necessarily cause an increase in maximal oxygen intake (Oshida, Yamanouchi, Hazamizu, & Sato, 1989; Tremblay et al., 1990). It is not fully established whether the insulin-lowering effect of regular physical activity and the apparent improvement of an insulin-resistant state result from an acute or a persistent increase in the insulin sensitivity of skeletal muscle and other peripheral tissues, a reduction in insulin secretion, an increased rate of hepatic removal of insulin, or a combination of these mechanisms. It is also difficult to dissociate these factors, as a diminished insulin secretion following training will, per se, be associated with a greater proportion of insulin extracted by the liver (Bjorntorp, 1981).

The specific contribution of increased physical activity versus concomitant dietary changes and the weight loss often noted when individuals exercise regularly have not been clearly delineated (Exercise and Noninsulin Dependent Diabetes Mellitus, 1990). An important issue is whether the improvements generally seen in glucose and insulin metabolism are lasting effects of the previous exercise episode or result from long-term adaptations and fitness increments. Despite these limitations in current knowledge, it is well recognized that regular physical activity is beneficial to non-insulin-dependent diabetes mellitus patients who are prone to atherosclerotic diseases (Exercise and Noninsulin Dependent Diabetes Mellitus, 1990; Vranic & Wasserman, 1990) by normalizing triglyceride and lipoprotein levels (Gudat, Berger, & Lefèbvre, 1994; Lampman & Schteingart, 1991).

However, the most compelling evidence for a useful role of regular physical activity has to do with the prevention of non-insulin-dependent diabetes mellitus. Three large prospective studies have recently been reported concerning the relations between regular physical activity and the incidence of non-insulin-dependent diabetes mellitus in adult men or women (Helmrich, Ragland, Leung, & Paffenbarger, 1991; Manson et al., 1992; Manson et al., 1991). These three studies unanimously concluded that active people were less likely to become diabetics with age, with the reduction in risk reaching about 20% and, at times, even more. The protective effects of regular exercise were strongest in the obese individuals and in other individuals who were at greater risk for the development of non-insulin-dependent diabetes mellitus. It is therefore believed that regular physical activity may play a greater role in the prevention rather than in the treatment of non-insulin-dependent diabetes mellitus (Gudat et al., 1994). Mechanisms involved for this protective effect have been examined but will require further study.

Vascular Diseases

There is some evidence indicating that regular physical activity may be beneficial in the prevention and treatment of three main types of vascular diseases, namely peripheral vascular disease, coronary heart disease, and stroke. Progressive atherogenic obstruction of peripheral blood vessels is not a rare phenomenon, as about 10% of the adult population suffers from peripheral claudication. Regular physical activity may indeed

be a method of choice in the prevention of the clinical symptoms associated with claudication and also in the treatment of the early stages of the diseases (Ernst, 1987). The mechanisms by which these benefits are brought about with regular physical activity are still a matter of debate (Barnard, 1994).

In the case of stroke, the evidence is somewhat tenuous (Kohl & McKenzie, 1994), but it is growing (Shinton & Sagar, 1993). There is some epidemiological evidence suggesting that the risk of cerebrovascular accidents is reduced in active individuals (Kohl & McKenzie, 1994). It is not clear, however, if the diminished risk can be accounted for by conventional risk factors, such as high blood pressure or obesity. One cannot rule out the possibility that regular exercise may have a favorable influence on cerebral blood vessels and blood flow, thrombotic factors and fibrinolytic activity (Bourey & Santoro, 1988), and other important aspects of the brain's circulation. It has been suggested that vigorous physical activity during early adulthood may confer some protection from stroke in later life (Shinton & Sagar, 1993). Interestingly, physical activity may reduce the risk of thromboembolic stroke only in nonsmokers (Abbott, Rodriguez, Burchfeil, & Curb, 1994).

Several epidemiological studies, dating back to the study by Morris, Heady, Raffle, Roberts, and Parks (1953), have shown that high levels of energy expenditure at work were related to a lower rate of coronary episodes and to less severe and less often fatal heart attacks (Paffenbarger, Hyde, & Wing, 1990). Similar trends have been reported for leisure-time physical activity. Those active in sports or other physical activities during their leisure time have a lower rate of ischemic heart disease and fatal heart attacks. The effect appears to be graded as the risk decreases progressively with the increase in the level of habitual physical activity. The volume of activity necessary to induce some of these apparent benefits is not overwhelmingly high. However, the risk diminishes almost linearly with weekly energy expenditure due to physical activity, ranging from about 500 to 3,000 kcal (Paffenbarger et al., 1990). In other words, a low level of habitual physical activity will have only a small effect, but higher levels will further reduce the risk. If 2,000 kcal per week is taken as the threshold between low and high levels of activity, the more active participants of the 16,936 members of the Harvard Alumni Study had a 28% lower risk of death from any cause during a 16-year follow-up period (Paffenbarger et al., 1990).

There is also some evidence that the level of cardiopulmonary fitness, as assessed variously from cycle ergometer or treadmill tests, is also negatively related with all-cause mortality rate and death rate from coronary heart disease. These relationships have been observed in men and women (Blair et al., 1989). For both level of habitual physical activity and level of fitness, the effects on mortality are significant and graded even after adjustment for a variety of common risk factors, such as body mass index, blood pressure, smoking, blood cholesterol, parental history, and other risk factors (Blair, 1994; Blair et al., 1989; Lakka et al., 1994).

An extensive review of 43 studies that provided sufficient data to calculate a relative risk for the occurrence of coronary heart disease at different levels of physical activity was published by Powell, Thompson, Caspersen, and Kendrick (1987). They concluded that an inverse association between physical activity and incidence of coronary heart disease was consistently observed, particularly in the better designed studies. They also reported that the association was appropriately sequenced, biologically graded, and coherent with existing knowledge. Since then several other investigators have confirmed this inverse relationship in various populations. A recent meta-analysis of studies dealing with physical activity in the prevention of coronary heart disease concluded that the overall relative risk was increased by about 90% in sedentary people compared to active people (Berlin & Colditz, 1990). There is also suggestive evidence to the effect that regular physical activity may be helpful in preventing new infarctions in postmyocardial patients (O'Connor et al., 1989; Oldridge, Guyatt, Fischer, & Rimm, 1988).

Some of the mechanisms that may account for the potential influences of regular physical activity on the proneness to ischemic heart disease have been reviewed by Leon (1991) and by Morris and Froelicher (1991). These mechanisms include attenuation of other risk factors, antithrombotic effects, increased myocardial vascularity and function, and better cardiac electrical stability. One important issue is the intensity and volume of physical activity that is needed to bring about these beneficial effects. Many have reported that a moderate volume of physical activity was sufficient to generate most of the benefits (Blair et al., 1989; Leon, 1991; Shaper & Wannamethee, 1991), whereas others found that the effect was graded from low-to-high volumes of activity or energy expenditure (Paffenbarger et al., 1990). This is an area deserving of further research because of its potentially enormous impact on the health of the citizenry, as coronary heart disease is still the number one cause of mortality in North America. Finally, as it is quite difficult and costly to measure a comprehensive set of metabolic variables in large cohorts used in epidemiological studies, we do not know whether there would be a significant relation of physical activity to the incidence of ischemic heart disease after adjustment for metabolic variables, such as plasma lipoproteins, glucose tolerance, and plasma insulin, as well as for thrombotic factors. It is therefore relevant to consider entering the area of metabolic epidemiology in order to address this issue.

If physical inactivity is an important risk factor for

ischemic heart disease, it is interesting then to compare it to other known risk factors in terms of relative and population attributable risk. In a major United States study, it has been estimated that the association between physical inactivity and coronary heart disease was similar to that for hypercholesterolemia, hypertension, and cigarette smoking (The Pooling Project Research Group, 1978). Hypertension and high cholesterol levels were seen in about 10% of the United States adult population. Twenty percent of these adults were smokers, but almost 60% were classified as physically inactive. Hence the population-based attributable risk analysis would indicate that because physical inactivity is so prevalent, it constitutes a more important risk factor than the other three combined (U.S. Department of Health and Human Services, 1987).

Conclusions

Regular physical activity has much to offer from a population point of view in terms of risk reduction for overweight and obesity (particularly abdominal obesity), glucose intolerance and non-insulin-dependent diabetes mellitus, blood lipid and lipoprotein abnormalities, hypertension, peripheral vascular disease, cerebrovascular accidents, and coronary heart disease. Not everyone who is physically active on a regular basis will remain free from these vascular and metabolic diseases, but the protective effects and the reduction in risk levels are substantial enough to justify the promotion of a physically active lifestyle in all segments of the population.

The recognition by major health agencies (e.g., the World Health Organization, International Society and Federation of Cardiology Fédération Internationale de Medécine du Sport, Centers for Disease Control, American College of Sports Medicine, American Diabetes Association, and American Heart Association) that a sustained sedentary inactive lifestyle is a risk factor for several health outcomes has considerable public health implications (Bijnen, Caspersen, & Mosterd, 1994; Fletcher et al., 1992; Pate et al., 1995; WHO/FIMS Committee on Physical Activity for Health, 1995). Regular physical activity may well represent the most cost-effective and important preventive medicine measure that could be promoted by developed and developing countries, particularly in light of the escalating health care budgets around the world.

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