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REVIEW ARTICLE

The effects of exercise on primary and secondary coronary heart disease

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SUMMARY. This review focuses on the ways in which exercise interacts with coronary heart disease. There is compelling epidemiological evidence to suggest that regular exercise plays a substantial part in the prevention of coronary heart disease. Whether in an industrial or leisure setting, the daily energy expenditure plays an important part in decreasing mortality from coronary heart disease. 'How much?' and 'how often?' are the questions that are difficult to answer. Is fitness or activity the prerequisite for protection? The intensity of exercise becomes important when one considers sudden death – a potential consequence of exercise – and the primary and secondary ways in which we can prevent it. The functional exercise test to facilitate safe prescription of activity for the rehabilitation of the post-cardiac patient completes a unique cycle of interaction.

INTRODUCTION

Despite the intense effort to enlighten the public about the risk factors associated with coronary heart disease (CHD), it remains society's most significant 'killer. One of the major reasons for this is the clear inertia against the changing of sedentary lifestyle patterns.

This review will examine the intricate way in which exercise interacts with CHD across the total continuum from health through to disease. There is evidence to associate exercise with sudden death, and with prevention of CHD and to suggest its use as a powerful diagnostic indicator. In addition, it has become a major feature in the rehabilitation of the postcardiac patient. On the basis of this, many of the vast number of investigations undertaken within each of these specific areas will not be discussed. It is the author's intention to make the reader aware of the unique way in which exercise plays an important role in the prevention and clinical treatment of CHD. Whenever possible, direction will be given towards the more comprehensive reviews of specific areas.

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SUDDEN DEATH

Unfortunately, a sudden death within a cohort of exercising individuals brings with it concern, confusion and a prospective consideration of their future activity patterns. The uncertainty is brought about by the paradox of death during exercise of apparently healthy and fit individuals. When these individuals are carrying the torch of activity with the charisma and enthusiasm of Jim Fixx (Higdon H 1984), it represents an even greater catastrophe for the battle against sloth and casts doubt in the minds of even the most enthusiastic elite of athletes. The source of this confusion is the failure to identify the difference between health and fitness. Noakes and Rose (1984) describe a 42-year-old runner who completed a 3-h, 6-min marathon three weeks before an autopsy showed that he had complete occlusion of a major coronary artery and 75% narrowing of the other two. In addition, there was evidence of hypertrophic cardiomyopathy. This individual was clearly an extremely fit but very unhealthy individual.

Sudden death in fit, active, older (>35 years) individuals is predominantly the result of underlying coronary artery disease. In the younger athlete (<35 years), such a death is normally related to congenital structural cardiac abnormalities (Maron et al 1980). In a recent review, Shephard (1996) questions the diagnostic frequency of death due to hypertrophic cardiomyopathy in young athletes. He comments on

the data of Maron and several other investigators who he feels have used extremely loose criteria for clinical classification. He cites the study of Chillag et al (1980) who, following a computerized literature search covering a 50-year period, identified a total of four likely cases of hypertrophic cardiomyopathy in athletes who were under the age of 40 years.

There is a need to recognize that it is not clinically clear why young athletes die during exercise. In addition, there is a need to be aware that these unfortunate incidents do occur, albeit very infrequently. Unquestionably, both the young and the older individuals who die are fit, but it is probable that they were the victims of abnormalities of the heart and circulation. It is also very likely that the physical fitness that they have acquired could mask the prodromal symptoms, which would probably be recognized in a more inactive population. This proposition is enhanced by the lack of evidence supporting the hypothesis that trained athletes are more capable of assessing their rating of perceived exertion (RPE) (Borg 1973).

The younger, more elite athletes predispose themselves to the acute threat of the disease by their participation in high-intensity activities, often under competitive conditions. Many choose to ignore the classical prodromal symptoms associated with the malfunctioning heart, which they associate with the pain commensurate with attaining success. The author has experienced this in an elite athlete who developed chest pain and dyspnoea during training, which was consistently ignored for several months. Following exercise electrocardiography and echocardiography, a life-threatening cardiomyopathy was diagnosed.

It is encouraging to note that, for those who become involved in increasing levels of habitual high-intensity exercise, there is a reduction in the transient increase in risk of a primary cardiac arrest during activity. Among apparently healthy men with low levels of habitual activity, the risk was increased 56 fold, compared to 5 fold in those who were regularly active (Siscovick et al 1984).

There are several investigations that suggest that individuals who are involved in extreme forms of endurance exercise have a greater probability of developing clinical problems. Rowe (1993) reports that runners who have been involved in multiple marathons are highly susceptible to coronary vasospasm in the absence of atherosclerosis at autopsy and Douglas et al (1990) observed echocardiographic changes in myocardial performance that are suggestive of myocardial fatigue during the Hawaii Ironman Triathlon. Several investigations have suggested damage to the endothelium and thrombus formation conducive to myocardial necrosis followed by fibrosis (Factor & Sonnenblick 1985), which may occur in regions of focal coronary narrowing (Gertz et al 1981). Lewis (1992) reports on the 13 runners who completed one of the world's most gruelling races across the USA – a distance of 4700 km. The winner accomplished the feat in 64 days. Is it possible that this form of extreme exercise could bring about coronary injury via increased catecholamines (Chilian et al 1986) and myocardial necrosis (Rona 1985), particularly in runners with a significant number of coronary risk factors?

Carrier (1984) makes an interesting comment with reference to specific populations such as the bushmen of the Kalahari Desert, the Tarahumara Indians of the mountains of Northern Mexico, the Navajo of the US southwest and the Aborigines of Australia. It would seem that these groups have the capability of chasing their prey for up to two days until the animal drops from exhaustion. He suggests that the urban endurance runner has not had sufficient time to learn teleologically what humans have had to learn over 3 million years. Perhaps this is one of the reasons why extreme endurance running has been reported to be associated with permanent injury to a normal heart, as manifested by Sy Man, the World record-holder for completing the most marathon runs (Rowe 1991). It has been suggested that the heart became vulnerable to coronary vasospasm in the absence of coronary atherosclerosis at necropsy. When considering fatalities associated with exercise, there is a need for uniformity in assessing the type and intensity of exertion, as well as careful definition of the temporal sequence between the exertion, collapse and death. Attention to such issues will allow improved understanding of the rates and risks of exertion related to sudden cardiac death. This topic has been discussed by Kohl et al (1994).

The sinister growth of the drug culture within active populations, in particular elite activity groups, poses an additional hazard. There is documented evidence that cocaine is strongly associated with life-threatening cardiac events (Isner et al 1986). The recreational use of cocaine has increased significantly in Western societies and educational and counselling programmes should be implemented to emphasize clearly the dangerous interactions of this and other drugs with activity.

Sickle-cell trait (SCT) is found in approximately 8% of African Americans, most of whom are unaware of their status (Eichner 1993). SCT is generally considered benign with the absence of symptoms, but there have been several reports relating SCT to sudden death. This has occurred even in well-conditioned subjects who have previously tolerated similar exercise challenges. The pathophysiological processes involved could be either hyperlactataemia or hypoxaemia during exercise (Le Gallais et al 1996). The association between exertional rhabdomyolysis and possibly sudden death appears to be multifactoral. This would explain why many individuals with SCT have no problems when exposed to the same physical environmental stress (Francis 1981). At present,

reassurance cannot be given to haemoglobin S patients. However, the risk of sudden death, if any, is low (Williams 1991) and unrestricted athletic competition is therefore allowed.

Irrespective of the underlying disease, the most frequent cause of sudden death is a malignant ventricular arrhythmia – in most cases, ventricular fibrillation – resulting from myocardial ischaemia (Cobb et al 1975) and this makes it very responsive to immediate secondary prevention.

Many of the sudden deaths associated with exercise could be prevented if primary measures such as clinical screening could be introduced in conjunction with secondary measures such as cardiopulmonary resuscitation (CPR) and education programmes.

This would facilitate a more objective prescription of exercise and an identification of the high-risk individuals. In addition, it would ensure and increase the probability of more effective resuscitation procedures being undertaken in the event of a collapse during exercise.

Considering the present documented knowledge relating cardiomyopathy and sudden death (Maron et al 1980; Maron et al 1996) and the questions being asked (Shephard 1996), it would still seem prudent to recommend that all young elite athletes who have the potential to represent their country should undergo a functional diagnostic exercise test (FGXT) in conjunction with echocardiography, prior to undertaking the intense training regimens that are a feature of elite athletes' preparation. These are exceptional individuals, and if the objectives were to assess health and baseline fitness, valuable feedback could be given to the athete. In addition, the occasional clinical threat would be identified, and the athlete counselled accordingly.

With older athletes and recreationalists, it would not be economically sound to recommend similar screening procedures. Nevertheless, some of the more recent research indicates that alternative methods are available, which could result in identifying the older individuals who are at risk of developing cardiac complications as a result of participation in exercise regimens. The probability of underlying coronary artery disease is significantly correlated with the number of coronary risk factors identified in an individual (Keys 1975). Therefore, a two-stage screening process would facilitate the identification of a high-risk cohort in whom the prevalence of disease would, in all probability, be high. Functional diagnostic exercise testing in this cohort would therefore have a high sensitivity and predictive value.

The first stage in this process would be an assessment of documented CHD risk factors such as sex, age, smoking, obesity and family history (Levy et al 1990). Individuals with two or more of these risk factors would be recommended to attend their family practitioner for a brief clinical examination that would include assessment of their blood pressure and blood lipids. A high overall cardiac risk score at stage two would result in the individual undertaking a FGXT. Using these stratified screening procedures, the post-exercise test information would certainly facilitate a more objective exercise prescription. The alternative would be to prescribe an exercise programme with only resting data, which, on some occasions, would include a high-risk individual with no information on his physiological responses to exercise.

EXERCISE PRIOR TO EXERCISE?

It seems paradoxical that, in order to try to prevent what is an extremely low probability of sudden death during exercise, we use a modified form of exercise. This is undertaken in a laboratory with all the safety precautions for such a procedure prevailing. A controlled, graded exercise test with the cardiovascular responses to the effort closely monitored provides key information with which to judge an individual's capacity to undertake exercise (Ellestad 1980).

Since Master et al (1942) first used the simple step test to ascertain a patient's cardiovascular response to a standard workload, exercise has become an important diagnostic aid in the field of cardiology. FGXT has been accepted clinically in the assessment of symptomatic post-myocardial infarction (MI), angioplasty, bypass, valve and transplant patients. The controversy surrounds the use of exercise tests in the assessment of asymptomatic individuals and the problems with false positive results (Froelicher et al 1976). Like all other diagnostic tests, exercise electrocardiography (ECG) conforms to the statistical theorem of Bayes (Jones 1979). It can be demonstrated that the sensitivity of a test is directly related to the prevalence of CHD in the population that is being assessed (Jones 1979). Therefore, undertaking exercise tests to identify CHD in a group of 20-year-olds, where the prevalence of CHD is very low, would be ill-advised. However, one could argue for recommending exercise testing in males above 40 years of age, where the prevalence of the disease is increased significantly and a resulting positive test would therefore be more meaningful, particularly if these individuals were anticipating becoming, or were presently involved in intensive activity. In addition to this, statistical analyses of epidemiological data have revealed that abnormal ECG responses to exercise stress-testing in asymptomatic patients are associated with a significant increase in the probability of such persons developing clinically evident CHD compared with those recording a normal test (Council on Scientific Affairs 1981).

Abnormal exercise ECG in high-risk individuals can identify those who are likely to have a 15–25 times greater risk of future CHD events, including sudden death (Ellestad & Halliday 1977). Following such testing, a small number of individuals will have their

exercise programmes attenuated or will be prohibited from exercise until further investigations have been undertaken (Davies et al 1996). In the majority of cases, the tests will provide sufficient information to objectively, and confidently, prescribe a programme of exercise that can be undertaken with safety. Bruce & Fisher (1987) and Davies et al (1996) have found these procedures very effective. Indeed, in 5000 asymptomatic patients, the latter investigators identified 26 people with multi-vessel disease who underwent coronary bypass surgery and seven who were referred for coronary angioplasty. Several of these individuals were very fit – some running 50 miles per week – had completed several marathons and intended to run in future high-profile marathons.

PRIMARY RISK-FACTOR CONTROL

An emphasis on educational programmes that bring about a reduction in the risk factors associated with CHD should, by implication, reduce the incidence of sudden death. It is documented that these risk factors are strongly associated with CHD morbidity and mortality (Keys 1975). In the Yugoslavia Cardiovascular Disease Study, Demirovic et al (1985) reported that the highest proportion of sudden deaths was among men aged 45–54 years, with the most significant and independent risk factors associated with sudden cardiac death being age, blood pressure and cigarette-smoking. Scandinavian studies have shown that a simple waist-to-hip ratio gives a powerful indication of abdominal fat and individuals with a high risk of coronary disease (Larsson et al 1984) and Hjermann (1990) has reported that controlling selected CHD risk factors such as blood pressure, serum lipids, body weight and physical activity substantially reduces the incidence of CHD. These measures, in conjunction with other risk-factor assessments, will go a long way towards increasing the primary prevention of sudden death during exercise. In addition, the secondary prevention of sudden death must be considered. It is essential to remove the aura of immortality presented by many fitness advocates to the exercising population. It must be appreciated that, despite the most conscientious efforts, very occasionally a crisis will occur.

SECONDARY PREVENTION

There is a need to significantly increase the number of individuals who are competent in cardiopulmonary resuscitation (CPR) procedures. Hossack and Hartwig (1982) clearly demonstrated the value of effective CPR procedures in patients participating in a cardiac rehabilitation programme. Of the 25 cardiac arrests occurring over 16 years, all were treated within 30 s and, remarkably, all survived. This confirms how successful immediate CPR can be and emphasizes the need for prompt treatment in the field. Young et al (1984) successfully resuscitated all 32 individuals in their study. There were no deaths, myocardial infarctions (MIs), strokes or any lasting morbid events. It is important to remember that patients who have survived an episode of failed sudden cardiac death are a high-risk group because 30–40% have an annual recurrence (Cobb et al 1975). In addition, a substantial number of these individuals have severely depressed ventricular function (Gabry et al 1987).

The review by Cummins and Eisenberg (1985) endorses the effectiveness of lay bystander-initiated resuscitation introduced in Seattle, WA, USA. Non-physicians were trained in the principals of CPR in order that they could provide a very rapid initial CPR response that was then supported by more skilled paramedical personnel. As a result of the introduction of this system, 25–35% of patients in Seattle are expected to survive cardiac arrests. Lay bystander-initiated CPR is very often immediate and this is of critical importance in long-term survival. A more recent study by Spaite et al (1990) suggested that, even when the arrival of the hospital emergency team was extremely efficient, with short response times, lay bystander-initiated CPR prior to their arrival improved long-term outcome. There are some investigators who are of the opinon that lay bystander-initiated CPR in patients experiencing ventricular fibrillation, ventricular tachycardia or asystole do not improve ultimate survival (Stueven et al 1986). Hoekstra (1990) suggests that most studies on the subject do support the theory that the early initiation of lay bystander-initiated CPR improves the outcome. Therefore, we should encourage those professionals who are administering events involving moderate and intense activity to ensure that personnel skilled in CPR are available in cases of emergency. If possible, the necessary screening procedures should be in place to prevent high-risk individuals from participation in high-risk events. An introduction of the primary and secondary screening procedures outlined would certainly bring about a further reduction in what is presently a very small probability of serious events.

There is general agreement that vigorous exercise does increase the probability of sudden death (Shephard 1984). It would seem that, to gain the protection that has been clearly documented from long-term activity patterns, sedentary individuals have to go through a period of risk in order to obtain the benefits from exercise. This risk would depend on the type and quantity of exercise and would generally be greater in individuals above 40 years old and would increase in direct proportion to the number of risk factors identified in healthy individuals and in post-MI patients. It is also important to emphasize that, with prudence, an exercise catastrophe is an extremely unusual event. The Rhode Island study between 1975

and 1980 documented 12 deaths whilst jogging, 11 from heart attacks; five of the men studied were known to have had heart disease prior to their deaths. The incidence of death was 1 per 396 000 h of jogging (Thompson et al 1982). Since the inception of the London marathon, the records to date show 1 death per 2.5 million hours of jogging (D. Tunstall-Pedoe personal communication 1996). On the basis of the benefits for the exercising individuals and considering that there is a documented risk associated with exercise, should we be encouraging the population to increase their activity patterns? To facilitate this decision, the investigations relating activity patterns with CHD should be examined.

CORONARY HEART DISEASE AND ACTIVITY

The majority of the research that has examined the hypothesis that regular exercise prevents the development of CHD has shown a clear advantage in favour of active as opposed to sedentary lifestyles. Many of the studies have come under criticism due to inherent problems that have been difficult to account for in the experimental design. When data are collected on active and sedentary groups, one must consider the possibility that people with the first signs of disease feel they cannot cope with activity and move to an inactive group. This type of pre-morbid movement between groups, plus socioeconomic status, and the problems of defining and quantifying inactive as opposed to active groups, can seriously contaminate statistical conclusions. The perfectly designed investigation that will produce the unequivocal proof that exercise prevents heart disease would be far too costly to be undertaken. Therefore, we have to arrive at conclusions based on the numerous epidemiological studies undertaken over the last 30–40 years, making allowances for important confounding variables.

An obvious source of data that allow us to investigate retrospectively the relationship between exercise and CHD is examination of the life-expectancy of aerobic athletes. Karvonen (1977), Yamaji and Shephard (1977), and Sarna et al (1993) have suggested an increase in life-expectancy in these groups. Beaglehole and Stewart (1983) found the life-expectancy curves of New Zealand rugby players similar to that of the normal population and Sarna et al (1993) arrived at similar conclusions on examining the life-expectancy of wrestlers and weight-lifters. These data would suggest that aerobic activities, as opposed to activities featuring strength and anaerobic demands, favour an increase in life-expectancy. There is certainly a need for more research in this area, particularly amongst women who are participating in sporting activities and within the groups of individuals who are participating regularly in the extreme endurance events.

ACTIVITY PATTERNS DURING WORK

Many of the observational studies have examined retrospectively the frequency of fatal heart attacks in selected industrial occupations of varying energy demands. This provided an opportunity to classify people using activity as an independent variable. One of the earliest studies using this methodology (Hedley 1939) analysed 5116 deaths from acute coronary occlusion in Philadelphia, PA, USA and concluded that the incidence of death from this cause was greater among men in sedentary occupations than among those who had more active jobs. This type of study has been repeated on numerous occasions within many countries using bus drivers and bus conductors (Morris et al 1953), longshoremen (Paffenbarger et al 1970), railroad workers (Taylor et al 1962), Post Office workers (Kahn 1963), Kibbutz workers (Brunner et al 1974), farmers (Zukel et al 1959) and, most recently, in black South African workers (Sparling et al 1994). Almost without exception, these and many other investigations have clearly identified a decrease in the frequency of CHD in the more active occupations when compared to the sedentary occupations. From the evidence available, it is difficult to ascertain the amount of protection that exercise will give an individual. Most of the studies to date have reported a two-to-four-times greater frequency of death from CHD in sedentary groups. Following an eight-year follow-up in 24 UK towns, Shaper and Wannamethee (1991) concluded that the overall level of physical activity is an independent protection factor against heart attacks.

With the development of automation across most sections of modern civilization, the energy gradients between occupations have been significantly reduced. A modern miner, for instance, no longer hews and loads the coal with a pick and shovel. Modern automated machines cut, load and transport the coal to the surface. Many of the high-energy occupations have been converted to passive sedentary occupations. This has been a feature within and between most of the heavy industrial environments. The occupations of bus conductors and drivers who provided much of the early data for Morris et al (1953) have virtually disappeared with the introduction of the one-man bus system, and the energy gradients in longshoremen (Paffenbarger et al 1970) have been significantly reduced. If these protective energy gradients are no longer a feature of the working man's life, then energy used in non-working time must be increased to provide an equal protection. There has been a shift in thought to account for this and many of the more recent investigations relating activity patterns to the frequency of CHD mortality have quantified leisure time as the major variable in energy expenditure.

ACTIVITY PATTERN DURING LEISURE

An extensive and significant epidemiological study of physical activity and the incidence of CHD among male alumni of Harvard University was reported by Paffenbarger et al (1978). The investigators examined the relationship between adult physical activity and heart attacks in 16 936 past students aged 35–74 representing 117 680 person-years of follow-up. A questionnaire was used to indicate the daily activity such as numbers of stairs climbed, distance walked and sports played regularly. A physical activity index (blocks walked, stairs climbed, sports played) was devised to provide a composite estimate of the energy expenditure related to activity in kcals/week. They concluded that alumni with low physical activity indices had a 64% greater risk of heart attack than did their more energetic classmates. Age-adjusted reduction in both fatal and non-fatal heart attacks was sharp for physical activity indices from 500 through 2500 kcals/week. Beyond this range, further reductions in heart attack trends were not significant. For the break point of 2000 kcals/week the heart attack rates were 1.24 and 1.37 for non-fatal and fatal heart attacks respectively. For all heart attacks the rates for physical activity indices below 500 kcals/week as compared with 2000 kcals/week were increased 176%, 32%, 147% and 131% for the respective age groups of 25–44, 45–54, 55–64 and 65–74 years. Even when accounting for other CHD risk factors within the group, the relative risk based on physical activity showed lower heart attack rates with higher levels of energy expenditure. A particularly important observation, because of its practical implications, was that the inverse relationship between activity and heart rate was only associated with those who maintained an active lifestyle from their university days. Being an outstanding athlete was only a protection if you maintained your activity pattern throughout life. In other words, you cannot store physical fitness.

Morris et al (1973) monitored the weekend leisure patterns of 16 882 executive-grade civil servants across England. The men recorded on Monday morning their leisure-time activities during the previous Friday and Saturday. A vigourous activity was defined as one that is likely to reach energy peaks of at least 7.5 kcals/min, which corresponds to heavy industrial work. For men recording vigorous physical energy, the relative risk of developing CHD was about a third of that of comparable sedentary men. They concluded that habitual vigorous exercise during leisure time reduces the incidence of CHD in middle-aged males. A further analysis of the above study following eight-and-a-half years was reported (Morris et al 1980). Once again, the results indicated a positive relationship between activity and CHD. They concluded that vigorous exercise resulted in a 40% decrease in fatal heart attacks and 50% decrease in non-fatal attacks when compared to individuals who did not report vigorous weekend leisure-time activity. It was suggested that vigorous exercise is a natural defence of the body with a protective effect on the ageing heart against ischaemia and its consequences.

Further analyses of these data into the 1980s (Morris et al 1990) continued to support the hypothesis concerning the advantages of adequate physical activity and positive lifestyle and a decrease in the frequency of CHD.

In the most recent analysis of the Harvard Alumni Study, Paffenbarger and Kampert (1994) reported on 165 402 man-years of follow-up. They concluded that adapting a physically active lifestyle, stopping cigarette-smoking and remaining normotensive independently delay all-cause mortality and extend longevity. Using a physical activity index of ≥ 1500 kcal.wk^{-1}, the 15% of men who dropped below that level increased their risk of death by 13% and the 21% who increased their activity to that level, or above, decreased their risk by 28%. Decreasing walking to less than 15 km/week was accompanied by a 21% higher risk of mortality. Encouragingly, men who were inactive and smoked until their ages ranged between 65 and 84 and then became active could expect to live two to three years longer. This would suggest that it is never too late to increase activity patterns.

There is compelling evidence, gathered over the last 40 years, that moderately active people have a significantly lower chance of developing CHD as compared to sedentary individuals. Unfortunately, the activity has been loosely assessed in many of the studies. Indeed, something other than sedentary was in many cases considered active. This has presented difficulties when the evidence for activity has been accepted and the questions are asked 'how much?', 'what type?' and 'for how long?'. Initially, Morris et al (1973) stated that men reporting vigorous exercise experienced the lowest rate of CHD. Later analysis (Morris et al 1990), suggested vigorous aerobic exercise such as swimming, badminton, tennis, brisk walking, cycling, or jogging would be required. In addition, it was suggested that age could influence the response to activity patterns, with older people gaining similar benefits with lower quantities of the same activities. This was probably the result of the relationship between exercise intensity relative to the maximal aerobic capacity. Aerobic capacity is a fundamental measure of cardiovascular fitness. It is strongly influenced by training and high levels of activity patterns (Pollock & Wilmore 1990). Increasing age significantly decreases this value: at the age of 60 years, it approximates 70% of the value observed at 25 years of age (Buskirk et al 1987; Bruce 1984). It was also noted that some of the less strenuous activities such as golf, ballroom dancing and table tennis showed no evidence of benefit.

Paffenbarger et al's (1978) study on Harvard alumni found a significant protective factor in those

who were involved in walking, stair-climbing and leisure-time sports activities equating to > 2000 kcals/week of energy expenditure. The relative risk being about 40% below that for the less active men. In the multiple risk factor intervention trial, Leon et al (1987) demonstrated that the treadmill time and percentage of subjects who achieve their target heart-rate were significantly higher among subjects with increased leisure-time activities. The lower resting heart rates in these individuals suggest an improvement in cardiovascular fitness, which could be an important CHD risk factor facilitated by activity.

FITNESS OR ACTIVITY?

Several investigations – Lie et al (1985); Slattery et al (1989); Ekelund et al (1988) and Blair et al (1989) – have looked at physical fitness as a CHD risk factor. All of these studies suggest a clear inverse relationship between physical fitness and the frequency of CHD. Ekelund et al's (1988) study used the heart rate achieved at stage 2 of the Bruce protocol (Bruce & McDonough 1969) and related this to CHD mortality over an eight-and-a-half year follow-up. The cumulative CHD mortality among men in the least fit quartile was 6.5 times that of the most fit quartile. Blair et al (1992) used maximal treadmill time as a measure of physical fitness among middle-aged executives. During an eight-year follow-up, the mortality rate from CHD in the highly fit group was significantly lower than for the least fit group. In both of the above studies, adjustment for cigarette-smoking, blood pressure level and blood lipoprotein did not alter the relative risks significantly.

Lakka et al (1994) investigated the associations between the type, duration, and intensity of leisure-time physical activity assessed by a questionnaire and directly measured maximal oxygen uptake with the risk of acute MI in Finnish men. They concluded that conditioning physical activity and maximal oxygen uptake were inversely associated with the risk of acute MI. Neither non-conditioning physical activity, nor walking or bicycling to work was associated with coronary risk. The risk of acute MI was decreased by 60% in the active group, compared to the inactive, with just two hours of conditioning physical activity a week. They suggest that an oxygen capacity of 6 METs (the oxygen consumption per kg of body weight per minute in supine rest) may be required to decrease the risk of acute MI.

The relationship among daily physical activity, physical fitness and the risk factors for CHD were studied in a comparison of 477 pre-menopausal women and 178 naturally post-menopausal women (Yanagibori et al 1993). The investigators concluded that there was no relationship between physical fitness and daily activity level in either group. In pre-menopausal women, daily activity was associated with blood pressure, triglycerides and blood sugar only in the low-fitness group. There was no relationship between CHD risk factors and daily activity in the high-fitness group. In both groups, the total cholesterol to high-density-lipoprotein ratio (TC/HDL) was lower in the high-fitness group. This suggests that serum lipids have a closer relationship to fitness than to daily activity. They also conclude that daily activity is one of the most important factors to reduced CHD risk factors in unfit or post-menopausal women.

Berthouze et al (1995) used a physical activity questionnaire that they had designed and used in conjunction with laboratory measured maximal aerobic capacity ($\dot{V}O_2$ max). They were examining the factors influencing the relationship between mean habitual daily energy expenditure and $\dot{V}O_2$ max. Using this method, they concluded that the mean habitual daily energy expenditure was an accurate indication of physical fitness and the most important factor of $\dot{V}O_2$ max variation. Long-term studies using more objective methods to quantify the independent variable would certainly provide a more meaningful analysis of the relationship among physical activity, physical fitness and the frequency of CHD.

Halle et al (1996) examined the influence of physical fitness and body mass index (BMI kg/m^2) on metabolic coronary risk factors in 160 healthy men. Those with the lowest fitness ($\dot{V}O_2$ max < 40 ml/kg/min) and a BMI > 25 had a reduced HDL_2 cholesterol and an increased number of small dense low-density lipoprotein (LDL) particles when compared to those with a fitness level > 40 ml/×kg×min^{-1}. They also noted no further improvement of the risk profile for those exceeding 50 ml/×kg×min^{-1}. They concluded that a $\dot{V}O_2$ max < 38 ml and a BMI > 27 ×kg×min^{-1} have a negative prognostic value, due to an unfavourable metabolic risk profile but also emphasize that even moderate physical fitness may be sufficient for a risk-reduction. It is interesting to note that many investigators (Depres et al 1992) are considering the distribution of fat as opposed to a relatively crude index such as BMI. The author and his colleagues are presently assessing upper abdominal fat as a more meaningful measure of the adipose tissue that is associated with CHD.

The evidence to date would suggest that physical fitness has a greater influence on CHD mortality than activity patterns. The death rates from CHD in the fit-versus-unfit groups range from five to eight times higher in the latter (Lie et al 1985; Blair et al 1989). The more physically active groups, when compared to sedentary groups, have an approximately three-fold reduction in mortality in favour of the active groups. The difference between using physical fitness compared with physical activity as an indicator from sedentary living may well provide a more accurate and precise assessment of the independent variable. Physical fitness can be measured with precision and accuracy and is therefore more likely to assess the true

value of an active versus a sedentary lifestyle. It should be noted that non-exercise test prediction models fail to meet the accuracy necessary for estimating cardiorespiratory fitness in large epidemiological studies where the intended purpose is to assess health risks (Whaley & Kaminsky 1995).

The early work of Bouchard et al (1984) and Bouchard et al (1986) would suggest that activity patterns and fitness are significantly influenced by genetics. The aerobic capacity, the propensity to want to improve it, and the sensitivity to react to changing activity patterns are all genetically predetermined. Early predictions have tended to wilt with time. Howald (1976) reported no significant genetic contribution in maximal aerobic power, which strongly contradicts Klissouras (1971), who is of the opinion that 93% of this phenotype variation is determined by the genotype. Later comments by Bouchard et al (1992) seemed to modify earlier opinions; they suggested that the genetic influence on aerobic power and capacity reaches not more than 40–60% of the variation and is probably nearer 25% or less of the maximum aerobic capacity. It would seem that environmental factors, such as habitual level of physical activity, have a significant influence on physical fitness despite the genetic influences (Perusse et al 1987). However, the desire to exercise and the rewards from such exercise are still very much influenced by genetics (Bouchard et al 1988) and remain an extremely important influence on activity patterns within societies.

EXERCISE PRESCRIPTION – HOW MUCH?

There are extremely complex interactions among physical fitness, genetics, activity and lifestyle. Therefore, it is not surprising that controversy and inconsistency exist when we consider the prescription of activity for the prevention of CHD. Data on the type, duration and frequency of exercise that is required for protection are limited and inconsistent. The position statement by the American College of Sports Medicine (ACSM 1991) clearly defines the exercise required to improve aerobic capacity in apparently healthy individuals. In addition, investigators have demonstrated a clear association among physical activity, aerobic capacity and health (Berlin & Colditz 1990; Ekelund et al 1988; Sandvik et al 1993; Lakka et al 1994; Andersen & Haraldsdottir 1995). Many of the investigations mentioned in this review have identified a lack of activity as an independent risk factor for CHD, at a level comparable to that of other established risk factors such as hypertension and hypercholesterolaemia.

Activity that conforms to the ACSM's (1991) guidelines in frequency and intensity will bring about a predicted improvement in aerobic capacity and the preventive benefits associated with such gains. But these guidelines do not identify the optimal exercise regimen that would result in maximum health benefits for the least time invested. Many individuals are not particularly keen to acquire a high level of physical fitness but would certainly be prepared to increase their activity if the minimum level required for the prevention of CHD was clearly established.

The ACSM's (1991) guidelines of 60–90% maximum heart rate for 20–60 min three times per week will bring about significant changes in aerobic capacity and it has been suggested that there is a minimal threshold intensity below which a training effect will not occur (Shephard 1968). But is this a prerequisite for improvements in health?

Blair et al (1992) have suggested that the most sedentary section of the population would receive clinically significant health benefits from 30 min of walking per day. In a recent study, Lakka et al (1994) demonstrated that conditioning activity and maximal oxygen uptake were inversely associated with the risk of acute MI. Neither non-conditioning physical activity nor walking or bicycling to work was associated with coronary risk. Two hours of conditioning physical activity a week decreased the risk of acute MI. Slattery et al (1989), examining data in the US Railroad Study, also showed a decreased mortality from CHD with low-to-moderate leisure-time physical activity. Morris (1994) has suggested the following grades of exercise intensity for a 70-kg male:

1. *Light: <3 METs, e.g. strolling < 3 m.p.h.*
2. *Moderate: 3–6 METs, e.g. walking 3–4 m.p.h.*
3. *Vigorous: 6 + METs, e.g. walking > 4 m.p.h.*

1 MET is equivalent to an oxygen uptake of 3.5 ml/kg^{-1}/min^{-1}

Morris has commented on the possible health advantages in progressing from the light activity (< 3 METs) to the moderate activity (3–6 METs). Lakka et al (1994) indicated that a mean intensity of 6 METs may be required to decrease the risk of CHD. They suggest that the inconsistency among previous studies may be due to the differences in the classification of physical activity. If future studies consistently quantify the activity precisely and accurately using METs or an equivalent energy marker, then the comparison between studies would be more meaningful. Duncan et al (1991) demonstrated that increases in aerobic capacity were related to the intensity of a 24-week programme in pre-menopausal women. However, increases in high-density lipoprotein (HDL) cholesterol were similar across the three intensities of walking, with a constant volume suggesting that volume rather than intensity may be more influential in changing some CHD risk factors. It would certainly be difficult to confidently prescribe the intensity of an exercise programme from the results of the latter studies. The evidence is beginning to suggest that improving health via exercise may be a different proposition to improving aerobic capacity.

Rather than a set duration of exercise being a key feature, it has been proposed that all of the small

daily units of energy expenditure can be summed to produce a total daily energy expenditure (ACSM 1990). Debusk et al (1990) have shown that 3 x 10-min bouts of exercise per day of walking or jogging at 65–75% of maximum heart rate five times per week for eight weeks significantly improved aerobic capacity. The improvement was approximately 6% below the group who spent the same time training at 30 min per day continuously. It would seem reasonable to assume without any present evidence that 30 min of short-duration (1–3 minutes of moderate-intensity) activity could bring about a health-and-fitness benefit.

Berthouze et al (1995) concluded from their recent study that the individual differences in $\dot{V}O_2$ max were accounted for almost entirely by a combination of differences in quantity of energy expenditure. The maximal habitual daily energy expenditure was found to be the most important factor of variation of VO_2 max. It is probable that a volume of exercise that positively alters some of the CHD risk factors may not be of sufficient intensity to improve the aerobic fitness. It would seem that, by chance, many of the activity programmes undertaken are of sufficient volume and intensity to bring about an improvement in both the fitness and health of the participants. Although it must be noted that, in some of the studies that have examined the relationship between health and activity (Morris et al 1990) or fitness (Ekelund et al 1988), it has been found to exist across the full continuum of activity and fitness, with the most fit and active having the least frequency of CHD mortality rates. In addition, the greatest benefits from health are gained by the least active who become moderately active (Haskell 1994).

When considering the health of populations, it is possible that cardiovascular fitness may not be the necessary prerequisite to attain in order to gain protection from CHD. In 1995, a group of scientists representing the Centres for Disease Control and Prevention and the American College of Sports Medicine recommended that 'Every US adult should accumulate 30 minutes or more of moderate intensity physical activity on most, preferably all, days of the week' (Pate et al 1995). This advocates a shift along the exercise continuum from vigorous to moderate activity that is well below the earlier recommendation of the American College of Sports Medicine 1990. It is interesting that, following the National Fitness Survey in the UK, which demonstrated very low levels of physical fitness (one third of middle-aged men are unable to continuously walk at a normal pace of 3 m.p.h.), similar recommendations were presented as a means of improving the Nation's health (Allied Dunbar National Fitness Survey 1992).

There is obviously a great deal of controversy with reference to physical activity, physical fitness and their relationship to CHD prevention. There are some investigators who claim that the CHD risk-rating can be improved with 30–60 min of brisk walking each day (Blair & Kohl 1992) and others who have found VO_2 max to be the most powerful influence (Andersen & Haraldsdottir 1995). Andersen and Haraldsdottir (1995) have made some interesting comments about the relationship between physical activity and physical fitness, which they indicate is not linear but S-shaped. This curve will be influenced by age, sex, genetics and the intensity of activity. Therefore, when an individual attains a certain level on the curve there is a need for a substantial increase in physical activity for further improvements in fitness. Sedentary populations by comparison will show significant gains in fitness with low levels of physical activity. They also point out that the relationship between the fitness level and CHD risk is exponential, with small gains in fitness bringing about large improvements in the risk factor profile in a sedentary group when compared to a highly trained group. If this supposition is true, the basic fitness level, and the training intensity at the commencement of an investigation would have a significant influence on the conclusions made with reference to fitness and CHD risk factors. It also explains why walking may be a very effective prophylactic in sedentary populations. The evidence collated to date clearly identifies activity and/or fitness as important components of an individual's health profile, in particular when it relates to CHD. In the author's opinion, the wise individual should be participating in activities which equate to 300–400 kcals of energy per day, in one exercise bout, or several smaller sessions. It is not the intention of this review to give a comprehensive analysis of the research that examines the interaction of exercise with other accepted CHD risk factors. However, it is certainly of value to consider some of the literature which presents possible reasons relating to the protective characteristics of exercise.

EXERCISE AND CORONARY HEART DISEASE RISK FACTORS

It is generally accepted that several of the CHD risk factors such as hypertension, diabetes and obesity are chronic diseases independently capable of bringing about functional decline. Of all the CHD risk factors, the blood lipids seem to be eminently modifiable via diet and exercise, and powerfully linked to the development of atherogenesis (Ross 1986). It is of particular interest to consider a selected group of investigations that have considered exercise and its influence on the blood lipids. With the development of more sophisticated analytical procedures, the diagnosis of dyslipoproteinaemias has become a dynamic, rapidly changing challenge, requiring constant updating and interpretation. More recent investigations have identified the particle size, and the small dense LDL particles as disease progressors with the HDL_2 particles playing a disease-inhibiting role (Austin et al 1988; Blankenhorn et al 1990).

EXERCISE AND HIGH DENSITY LIPOPROTEINS

Many investigations have indicated a powerful relationship between the ratio of total cholesterol (TC) to HDL and CHD. Lifestyle manoeuvres that will bring about an increase in HDLs, thereby reducing the TC:HDL ratio and a decrease in small dense LDL particles would be highly protective (Williams et al 1986). Regular endurance exercise, such as that associated with long-distance runners and skiers, has consistently demonstrated a significant increase in the plasma HDL-C concentrations (Wood & Haskell 1976; Carlson & Mossfeldt 1964). A meta-analysis of 66 training studies including both genders and a separate analysis of 27 training studies on women found lower levels of both cholesterol and triglyceride after training with no change in HDL-C (Lokey & Tran 1989; Tran et al 1983). Kiens and Lithell (1989) reported that physical activity alone appears to induce a reduction in triglyceride levels and changes in lipoprotein levels, particularly increases in HDL levels. There is evidence to suggest a dose–response relationship between increases in HDL cholesterol levels and the amount of exercise performed (Wood et al 1983).

These investigators found that the HDL cholesterol level was significantly correlated with the number of miles run over a one-year training programme. Several investigations have found the volume of activity to be associated with increased HDLs (Marti et al 1990; Stein et al 1990). Whilst other studies have failed to find significant associations (Oscai et al 1972; Brownell et al 1982), it would seem that the variability in the conclusions of the training studies could be the result of many confounding factors (Macauley et al 1996). However, the more consistent findings in the athletes would suggest that body-weight, training regimens and long-term lifestyle will have considerable influence on the interpretation of training studies.

To date, the evidence would suggest volume, i.e. frequency and duration, has a greater influence on HDL levels that the intensity of exercise. Wood et al (1988), Durstine et al (1994) and Haskell (1994) have shown that changes in body-weight are responsible for many of the effects of exercise on HDL levels. This has been confirmed by Tran and Weltman (1983) using meta-analysis.

Most of the studies investigating the influence of exercise on blood lipids have concentrated on HDL-C. Cross-sectional studies have shown that serum levels of LDL and its major apoprotein, apo B, are lower in trained individuals (Lakka & Salonen 1992; Williams et al 1986). Exercise-induced reductions in LDL levels are greatest when concomitant weight-loss is observed (Tran & Weltman 1983). It has been shown that people exercising regularly have a reduction of LDL levels (Tran & Weltman 1983). The relationship between exercise and LDL cholesterol once again suffers from confounding variables. In the tightly designed studies involving control groups, and accounting for body-weight, plasma-volume, body-composition and diet, there have been no changes reported (Durstine et al 1994).

LOW-DENSITY LIPOPROTEIN PARTICLE SIZE

There is increasing evidence that a denser LDL subfraction profile is associated with increased risk of CHD (Austin 1992). In an analysis of 109 patients with MI, Austin and Breslow et al (1988) showed that subfraction pattern B (diameter of LDL particles < 25 nm) was associated with a three-fold increase of MI, independent of sex, age and weight. Krauss (1991) endorsed these findings. Rajman et al (1994), discussing particle-size and atherogenicity, state that clinical studies have indicated that a small LDL subfraction profile is associated with an increased risk of heart disease even when total cholesterol is only slightly raised. Although LDL particle-size is genetically determined, its phenotypic expression may also be affected by environmental factors such as drugs, diet, obesity, disease and exercise. They comment that factors that shift the LDL subfraction profile towards larger particles may reduce the risk of heart disease. Several investigators have considered exercise and its influence on metabolism and the LDL subfractions. There is evidence that exercise specifically influences the level of certain LDL subfractions (Lamon-Fava et al 1989).

Although plasma LDL concentrations remained unaltered following 14 weeks of endurance training in 13 men, increase in LDL molecular weight and particle-diameter were associated with a reduction in fat mass, plasma triglyceride concentration and physical activity. The LDL lipid-to-protein ratio also increased with training by 7% primarily because of an increase in LDL-free cholesterol content. The investigators (Houmard et al 1994) suggest that it is the formation of LDL particles that are more cholesterol-enriched and protein-poor with exercise training that provides additional evidence for the cardioprotective effect of long-term physical activity. In trained males who were hypercholesterolaemic, the levels of small dense LDL particles were normal, when compared to increased levels in untrained hypercholesterolaemic individuals (Baumstark et al 1991). Following an endurance triathlon, 7 of 40 individuals showed an increase in LDL particle size. The increase in LDL particle size coincided with those individuals recording large reduction in triglycerides (Lamon-Fava et al 1989). It is encouraging to find that the research to date indicates a favourable influence on LDL particles, which will bring about an anti-atherogenic action.

SHORT-TERM EFFECTS OF EXERCISE

Considering the short-term effects of exercise Pronk (1993) has suggested that 48 hours' abstinence from exercise be allowed before baseline blood lipid measurements are taken. This should certainly be considered prior to ascertaining changes in blood lipids following exercise. Berg et al (1983) reported on the short-term changes in HDL subfractions following a single bout of exercise. Significant increases in HDL were noted and attributed to the concomitant significant increase and decrease of HDL_2 and HDL_3 respectively. In addition, triglycerides decreased significantly. It was concluded that physical exertion increases HDL level mainly through formation of the less dense HDL_2 particle. Given the suggested antiatherogenic properties of a lipid profile with elevated HDL and HDL_2 (Manninen et al 1988), it seems that prolonged exercise allows a transient beneficial shift in the lipid profile of men, quantified by increases in HDL and HDL_2 and decreases in triglycerides.

Baumstark et al (1996) examined the influence of regular in addition to acute exercise on the activity of cholesterol ester transfer protein (CETP). They found a significantly lower CETP activity in triathletes compared to the students. The lower CETP activity indicates that less cholesterol ester is transferred from HDL to LDL particles. Therefore HDL cholesterol increases and LDL cholesterol decreases. This is a mechanism by which physical activity positively influences lipoprotein mechanism. Seip et al (1996) also concluded that the decrease in CETP due in part to plasma expansion is also a characteristic biochemical adaptation to exercise. Following average energy expenditure of 450 kcal for ten to thirteen days, CETP decreased by 16.6% in men with a mean age of 60. Younger men who expended 600–800 kcal/day for five days decreased plasma CETP by 18.1%.

Clasing et al (1996) were attempting to ascertain the optimal load to influence fat metabolism and by implication prevention of CHD. They exercised 23 trained men using three continuous treadmill protocols, walking 6 km/h, jogging 8.5 km/h and running 12 km/h, whilst measuring on-line oxygen consumption. The measured energy required for walking, jogging and running was 5.0 kcal/kg, 9.4 kcal/kg and 12.8 kcal/kg respectively. The response of the respiratory exchange ratio (RER) and free fatty acids (FFAs) in the blood indicated that only after 20 min of exercise does the mobilization of FFAs from the fat depots equal the energy needs taking place. The highest absolute fat consumption occurred at 60–65% VO_2 max. The investigators recommended that, because of the lag in fat-mobilization, an exercise time of greater than 20 min should be recommended for preventative training.

In addition to the atherogenic characteristics of an abnormal lipid profile, the clotting mechanisms of blood can also be negatively influenced. The balance between coagulation and fibrinolysis can be disturbed with hypertriglyceridaemia (Nordoy et al 1990) with the overall balance between fibrinolytic inhibitors and activators shifting towards inhibition. Therefore, it is highly probable that activity, in addition to influencing the blood lipids, could also bring about a favourable response in the ability of the blood to combat unnecessary clotting.

The majority of the investigations to date have demonstrated a close link between the lipoprotein profile and CHD morbidity and mortality. It would seem that a lipid profile containing an elevated serum cholesterol, triglyceride, small LDL particles and a reduced HDL_2 subfraction is the one to avoid (Austin et al 1990). In addition, there is powerful evidence that physical exercise can result in a moderate improvement of the lipid profile and consequently bring about a decreased risk of CHD. In individuals who have extremely high-risk lipid profiles in conjunction with other CHD risk factors, it is likely that exercise in conjunction with pharmacological intervention would be more effective.

It is beyond the scope of this review to discuss the vast amount of research that has been undertaken into investigating the relationship between lipid profiles and CHD. There is much to discover, in particular with reference to particle size and dose response, and exercise continues to provide a positive stimulus as a preventative measure via its influence on the lipid profile.

To date, the importance of exercise in beneficially changing the lipid profile has been discussed. This was very much a brief overview of an extensive area of investigation. Rather than repeat a similar exercise discussing many of the CHD risk factors that have also been extensively reviewed and investigated, it is the author's intention to comment briefly on selected risk factors and to discuss further the interaction of exercise with a collection of risk factors that are associated with the insulin-resistance syndrome.

FIBRINOGEN

Following a number of investigations, fibrinogen has become recognized as a major independent risk factor for CHD, stroke and peripheral disease (Meade et al 1980; Kannell et al 1987; Meade et al 1986; Yarnell et al 1991). Fibrinogen within the usual range for presumably healthy persons (150–350 mg/dl) was also found to be a major independent risk factor of CHD, cardiovascular disease (CVD) and all-cause mortality. This excess mortality persists following adjustment for the standard CHD risk factors (Kannell et al 1987). Increased levels of fibrinogen and clotting activity are associated with accelerated atherosclerosis in the arterial intima, both fibrinolytic activity and plasminogen concentration are decreased in CVD. Enhanced blood-coagulation frequently coexists with

hyperlipidaemia and, together, these may have a synergistic effect on atherogenesis (Smith 1986). Thus, it seemed reasonable to gain insight into the effects of exercise on fibrinogen. El-Sayed (1996) has recently reviewed the problems of measurement and interpretation during acute and chronic exercise. During acute exercise, fibrinogen has been reported as increasing but, following correction for haemoconcentration, no real increase was found (El-Sayed & Davies 1995; Watts 1991). In addition, a decrease has been recorded (Bartsch et al 1990; Martin et al 1985) with Collen et al (1977) recording no changes. The differences between these investigations is probably due to variations in exercise protocols and the problems of standardizing the measurement of fibrinogen. Fifty one per cent of the variance of the plasma fibrinogen is accounted for by genetic heritability, whereas the cultural heritability was negligible. The combined effect of obesity and smoking was found to explain only 3% of the variation, which demonstrates a significant genetic control and powerful support for plasma fibrinogen being a primary risk factor for CHD (Hamsten et al 1987).

Morris et al (1990) and Rosengren et al (1990) reported an inverse relationship between long-term physical activity and fibrinogen. Connelly et al (1992) supported these data when recording activity patterns in men aged 45–69 years but Watts (1991) found no difference in highly trained men who ran 62.4 km/week when compared to a control group who were classified as sedentary. When looking at training programmes of three months' duration (Ernst et al 1985) and six months' (Stratton et al 1991), significant decreases in fibrinogen were recorded in both groups. In the latter study, young men and old men were compared. Despite similar training responses, the younger group's decrease in fibrinogen (–4%) did not reach significance.

Rankinen et al (1994) looked at the effects of six months' training and El-Sayed and Davies (1995) three months' training on fibrinogen levels. There were no significant differences between control and exercise groups in fibrinogen levels, before or after training. It would seem that fibrinogen responses to training are at the present moment equivocal, once again suffering from the interaction of confounding variables. Considering the influences that plasma fibrinogen has on the development of CHD, it is extremely important that its relationship with activity be unequivocally defined in the near future.

INSULIN-RESISTANCE SYNDROME

This is characterized by a constellation of CHD risk factors, which include obesity, hypertension, hypertriglyceridaemia, decreased HDL cholesterol and glucose-intolerance or hyperinsulinaemia (Reaven 1988). Landin et al (1990) have also reported elevated fibrinogen and tissue plasminogen activator inhibitor with this syndrome and it should also include raised small dense LDL particles (Barakat et al 1990; Reaven et al 1993). It is obvious from the preceding discussions that many of the characteristics associated with this syndrome are powerful risk factors for CHD in their own right. Therefore, an aggregation of these will significantly increase the probability of developing CHD. It would seem that the frequency of occurrence of this syndrome is estimated to be about 25–35% of Western populations (Rupp 1992).

Barnard and Wen (1994) have commented extensively on the probable causes of this syndrome, suggesting that the combination of physical inactivity in conjunction with a high-fat, refined-sugar diet, plays a significant role in genetically susceptible individuals. They are of the opinion that individuals with a genetic predisposition for central obesity also have a genetic predisposition for other characteristics of the insulin-resistance syndrome. They site the work of Odea (1992) who reported a high incidence of insulin-resistance and characteristics of the insulin-resistance syndrome in Australian Aborigines who have adopted a Western lifestyle. The fact that some of the characteristics are absent in this group is further evidence of a genetic involvement.

As previously discussed, the problems of inactivity and high-fat diets are a feature of Western society. Improvements in activity patterns and fitness levels have been shown to influence the majority of risk factors associated with this syndrome, and it would seem logical that exercise should have a positive influence on this syndrome in total. Barnard and Wen (1994) reported that the bulk of evidence indicates that insulin-resistance and hyperinsulinaemia are the factors responsible for the other characteristics of the insulin-resistance syndrome, including hypertriglyceridaemia, hypertension, obesity, small dense lipoproteins and enhanced clotting. Therefore, in order that we can treat the cause of the syndrome, ways should be sought which can normalize the CHD risk factors via the manipulation of insulin-resistance.

A single bout of exercise dramatically increases skeletal muscle glucose transport, which is a similar action to that of insulin (Ivy 1987). This effect lasts for several hours and is observed when the serum insulin is decreased as a result of exercise-induced activation of the sympathetic nervous system. Following the initial response, there is another response that involves increased insulin-sensitivity and may last up to 24 h after the completion of exercise (Barnard & Youngren 1994).

When investigators have examined the effects of chronic exercise on insulin-sensitivity responses comparable to the acute reactions have been reported (Mikines 1992). Exercise has improved the diabetic state in young non-insulin dependent diabetes mellitus (NIDDM) patients, but is less effective in older patients (Wallberg-Henricksson 1992). This is probably

due to the frequency and intensity of training. It is interesting that Depres et al (1992) reported that insulin-sensitivity, as well as plasma lipids, can be modified by exercise that does not bring about an increase in cardiorespiratory fitness as assessed by VO_2 max. This seems to link up with the low-intensity walking recommended by Blair et al (1992) and indeed by Depres et al (1992), who suggest that brisk walking on a regular basis represents the best exercise for the metabolic complication of abdominal obesity. There is sound evidence indicating that aerobic exercise can have a positive effect on insulin-resistance and most of the other characteristics associated with the insulin-resistance syndrome, in particular when it is combined with a low-fat, high-complex carbohydrate diet. The syndrome has been found in a high percentage of obese young adults aged 18–26 years (Srinivasan et al 1993) so an intense effort in this population to develop behaviour patterns consisting of wise eating and regular activity should have a significant effect on the prevention of CHD.

Atherosclerotic coronary artery disease (CAD) is the most common cause of death in the Western world and there is a high probability that many millions of people have asymptomatic CHD. Without question, the behavioural changes brought about in the last three decades have significantly reduced the number of individuals succumbing to cardiac disease. Nevertheless, in the next decade, many people will experience MIs, angioplasty, bypass surgery and heart transplants. These people will need to be re-educated so that they can achieve a lifestyle that is commensurate with halting the advancement of the disease and acquiring a quality of life which enables them to continue as key members of society. Cardiac rehabiliation has emerged as an integral part of cardiovascular care with exercise providing a key element in the treatment of the post-cardiac patient.

POST-CARDIAC REHABILITATION

Whilst primary prevention is by far the most effective way of combating CHD, secondary prevention presents a greater challenge to the scientific and medical personnel because the margins of error are smaller and the manifestation of mistakes significantly greater.

It has been known for a long time that heart patients have a 10–20 times greater chance of another heart attack than that of the general population, and that during exercise the risk of ventricular fibrillation can increase from 3 to 60 (Shephard 1977). The risk of problems is obviously influenced by the cardiac injury, emotional state and the intensity and duration of the exercise undertaken. It is, therefore, essential to get the correct balance between exercise-intensity and the cardiac risk to the patient. The problems of an increase in ventricular dysrhythmia in exercising cardiac patients has been documented by Goldschlager et al (1973) and in high-risk patients (Lillis & Hanson 1989), who also show an additional increase in ventricular ectopic activity during daily living. Fardy et al (1982) reported on ten out of seventy patients who displayed contraindications to exercise in the form of potentially life-threatening cardiac abnormalities. Yet none of these patients was able to perceive the contraindications recorded.

So, the challenge for the exercising cardiac patient in terms of volume and intensity is very similar to those of healthy runners. But, the question of the minimum amount for the maximum gain in functional capacity is absolutely critical because minimum effort is generally associated with a lower risk to the patient. Folta and Metzger (1989) summarized the effects of exercise on functional capacity in patients having mild, moderate, severe and very severe left ventricular damage after MI. They found that patients who were involved in low-energy activities of daily living programmes did not improve functional capacity assessed on a pre-discharge treadmill test. In contrast, moderate-energy outpatient exercise programmes improve functional capacity through an increase in arteriovenous oxygen difference. These changes were found in a large majority of patients with mild and moderate ventricular damage and in a few with severe ventricular damage.

Jette et al (1991) examined the effects of a short-term exercise programme on patients with moderate-to-severe left ventricular dysfunction after a recent large anterior infarction. The ejection fractions ranged from less than 30% to 50%. The patients were evaluated for filling pressures, heart volume and work capacity. The mean work capacity and peak oxygen consumption improved significantly in the group with ejection fractions less than 30% but was accompanied by an increase in mean pulmonary wedge pressure. Resting ejection fractions improved markedly in both control and training groups but were not associated with work capacity. Exercise had little or no effect on haemodynamic measurements and the investigators concluded that the training effects achieved in patients with left ventricular dysfunction are most likely due to a corrected impaired vasodilation. The wide inter-individual variations in training responses were emphasized.

Goble et al (1991) reported that light exercise training as opposed to aerobic training in post-MI patients produces the same improvements in cardiac performance measures such as maximum heart rate, rate pressure product and maximum systolic blood pressure.

The findings of these studies emphasize the challenge to prescribe the correct training programme and suggest a possible explanation as to why exercise capacity increases to a variable degree in coronary patients during rehabilitation. It also highlights the problems of exercise prescription to maximize performance in the cardiac patient.

Opinions are divided as to whether patients should attend an organized medically supervised programme, or supervise their own rehabilitation in a home-based programme. If we accept that the frequency of ventricular dysrhythmias rises with increased heart rate (McHenry et al 1976; Lillis & Hanson 1989), and the comments on resuscitation proceedings made by Hossak and Hartwig (1982) outlined earlier, there must be a powerful argument for the cardiac patients exercising in close proximity to a trained resuscitation team, for at least the first 6–12 months post MI.

However, Squires et al (1991) have reported on a home-based programme using trans-telephonic ECG monitoring on 67 cardiac patients during 1865 exercise sessions. These patients began exercising between 14 and 25 weeks after hospital dismissal. The patients represented a broad spectrum of patients with CHD and performed their exercise on a variety of ergometers for 30–50 min for 1–3 weeks. The investigators concluded that, using this equipment, cardiac patients can exercise safely at home, or in remote hospitals.

So it would seem that supervised and unsupervised programmes can be undertaken with success. In contrast to these studies, Kugler et al (1990) suggested that a combination of both unsupervised home and supervised exercise could be effective. They compared a supervised versus a home exercise cardiac rehabilitation programme in 52 patients using an eight-week duration. Their results indicate that the degree of supervision and the type of prescribed home exercise are key features in success. It was found that the completely unsupervised home programme was the least successful in improving aerobic fitness, suggesting that patients need to be directed in order to maximize the effectiveness of an exercise programme. From the author's experience of 20 years, a prescribed supervised exercise programme following a functional exercise test proved to be highly effective in terms of compliance, safety, improvements of cardiovascular fitness and return to work (Davies 1993). In addition, if enzyme markers of myocardial ischaemia are used in conjunction with the exercise test, a more sensitive clinical and functional assessment of the post-MI patient can be made (Davies et al 1983).

The success of this programme format for the rehabilitation of post-cardiac patients must be credited to the early work of Hellerstein (1968). His conclusions with reference to the physiological benefits and safety of the programme have been confirmed by many investigators (Foster et al 1984; Hartung & Rangel 1981). It is generally accepted that, in conjunction with behaviour changes to improve other CHD risk factors, exercise is highly effective in improving the quality of life (Franklin & Rubenfire 1980).

The standard format for post-cardiac rehabilitation begins about three to four days post MI, with bedside sitting, shaving and commode. This progresses to standing and short walking spells, with a functional graded exercise test prior to discharge from hospital approximately seven to ten days post MI or bypass surgery. Prescribed progressive exercise at home is followed by enrolment in a community-based, supervised programme for a minimum of six months, at which time the patients progress to a home-based maintenance programme. They undergo a functional exercise test at hospital discharge and three, six, nine and twelve months. The data obtained from these tests are used to safely increase the volume and intensity of the exercise regimen.

During the functional exercise test, should the patient be allowed to attain 85% of age predicted maximum heart rate (APHR) or 100% APHR? This is still open for debate. Shaw (1981) reported that a significantly small group (15%) reached 100% asymptomatic APHR compared to the 54% who were able to attain 85% asymptomatic APHR. The number of symptom-limited patients increased from 34% to 68% at 100% APHR, with 10% experiencing sub-endocardial ischaemia compared to 7% at 85% APHR. It was concluded that the maximum test was as safe as the 85% APHR with a significantly greater yield of abnormal responses. The mortality rate for those failing to attain greater than 85% APHR was 8% compared to 4.2% if 100% APHR was reached. The three-year mortality rates for patients registering a physical work capacity of 6 METs or lower was 13% compared to 2.9% for those with an aerobic capacity greater than 7 METs. Patients whose response was limited to a systolic blood pressure less than 140 mmHg had a mortality rate of 13%, compared with 4% for those who exceeded this. In addition, the patients who recorded sub-endocardial ischaemia had a mortality of 11.7%, compared with 4.8% for those who did not. So it can be seen that the information from a well-designed maximal functional test is extremely valuable when one is prescribing exercise and attempting to anticipate possible responses to a long-term training regimen. If the test is reproducible, then repeated tests at selected intervals provide valuable clinical and functional data relating to training response.

It has been shown that exercise conducted at least three times per week, requiring an energy utilization of 200–300 calories per session, improves aerobic capacity (Shaw 1981), has a favourable influence on lipid profiles (Hartung & Rangel 1981) and decreases mortality and morbidity (O'Connor et al 1989). If exercise is undertaken in conjunction with behavioural changes in lifestyle, the changes in the coronary risk profiles of individuals are significantly improved. It is interesting to note that Rechnitzer et al (1983) recorded a 7.9% increase in mortality in a group who were exercising at a higher intensity (above their prescribed heart rate) compared to those who were working at a lower intensity. Once again, caution is

indicated; more may not necessarily be better for the majority of patients.

In addition to the development of cardiovascular efficiency, a restoration and maintenance of muscular strength would be an obvious asset for quality of life. Following many years of apprehension, it is now confirmed that appropriately prescribed resistance exercises can improve strength and can be safely undertaken by cardiac patients. This topic has been comprehensively reviewed by Verrill and Ribisl (1996). It is recommended that future programmes should attempt to effectively combine the cardiovascular and strength components to maximize the development of both.

If the programmes are well planned, then post-MI patients can undergo exercise safely. The estimated fatality is one per 784 000 patient-hours, one cardiac arrest per 112 000 patient-hours and one infarction per 294 000 patient-hours. This represents a very low level of risk for the exercising cardiac patients (Van Camp & Peterson 1986). A comprehensive rehabilitation programme can benefit patients with significant cardiac disease. This includes patients with heart failure and who have undergone transplant surgery. It can provide a significant contribution to the enhanced quality of life. Quite recently, Ornish et al (1993) have demonstrated that the severity of lesions within human coronary arteries could be reduced using an aggressive lifestyle modification of which exercise was a key feature.

For the past four decades, the human intellect has continued to produce a preponderance of food and develop sophisticated forms of automation with a corresponding decrease in the daily demand for human energy. Sloth has become a feature of Western society, with sedentary leisure activities such as fishing, golf and television predominating the modern lifestyle. Humans have evolved as hunter–gatherers, designed to expend energy, and there is a need to use our leisure activity to significantly increase our daily energy expenditures. Nevertheless, we must recognize that there are risks, which will vary between and within a specific group. To enable us to maximize the overall potential benefits that exercise has for society, we must ensure that the risks are kept to a minimum. The profound effects that exercise has on the human body are equal to that of many drugs. Therefore, it should be treated with respect, and always prescribed on an individual basis.

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