HEALTH PROMOTION AND AGING
"PHYSICAL EXERCISE"

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INTRODUCTION

Disuse invites dysfunction, while use favors function. At the most fundamental level, use connotes viability and activity promotes productivity. Confinement to enforced inactivity and immobility for a prolonged period of time results in numerous undesirable physiologic changes, including a decline in cardiovascular fitness, increase in body fat, decrease in lean body mass, loss of bone density, increase in plasma lipids, decline in glucose tolerance and deterioration in cognitive-motor function, memory and mental acuity. This profile of inactivity is similar to physiologic changes thought to occur with aging.

Aging is associated with a decline in time spent physically active - a behavior "forced" upon many individuals due to their changing lifestyle of increased work stresses, more family obligations and greater fatigue. It follows therefore, that the reverse, a heightened degree of physical activity and fitness, may confer protection or prevent declines in functional capacity. With aging, regular physical activity may make it easier to participate in activities of daily living, thereby prolonging an active, functional independent lifestyle. Thus, for some older individuals the sequellae of physical inactivity may mimic disease. Enforced physical activity may reverse this process; such an outcome would reenforce the causal relationship between reduced physical activity habits and the declines in functional reserve capacity commonly observed with advancing age.

RESEARCH IN GERONTOLOGY

Biological Aging and Declines in Functional Reserve Capacity

The empirical approach to defining the effects of aging in humans has been to focus on time-related declines in organ function. These declines are commonly attributed to a biological aging process; yet, closer inspection of the available information indicates that there is a wide variance in the functional status of individuals and that this diuversity in function increases with advancing age. Unlike diseases which affect certain individuals, the aging process is universal and results in gradual decline in the functional reserve capacity (defined as the difference between basal and maximal function) of the cardiovascular, endocrine, musculoskeletal, and other systems and changes in body composition and may be considered a normal part of the human life experience. While it can be argued that qualitative and quantitative differences in the organ function of older individuals reflect heterogeneity in individual rates of aging *per se*, an alternative hypothesis is that diversity in physiologic function is due to the influence of extrinsic factors and diseases that covary with biological age to affect functional reserve capacity in older humans. To what extent the rate of decline and ability to maintain function into older age is dependent on factors extrinsic to the aging processes is not known. Some of these extrinsic factors may be classified as the purported lifestyle habits of physical activity, dietary control of body weight and saturated fat consumption, and abstinence from cigarettes and alcohol.

The risk for declines in functional capacity of various organs with aging may be exaggerated and the prospects for reversal, delay or prevention of functional loss with aging vastly underestimated. An examination of the effects of treating disease and its consequences, maintaining regular physical activity habits, and controlling body weight by dietary discretion on the functional reserve capacity of the aging human being is necessary in order to understand the health-related consequences of biological aging itself. The impact of diseases and purported age-associated declines in physical activity increases in body weight, indiscretions in diet, stresses of psychosocial or socioeconomic nature and personal habits of alcohol consumption and cigarette smoking, which occur with advancing age on the overall functional performance of the human being is probably underestimated.

Disease and Declines in Functional Reserve Capacity with Aging

Susceptibility to disease increases with advancing age and available evidence suggests that vulnerability to a number of chronic diseases (and subsequent disease-related declines in function) can be attenuated by changing lifestyle habits. For example, reducing body weight lowers risk for non-insulin dependent or type II diabetes; a low fat, low cholesterol diet reduces risk for coronary artery disease; smoking cessation reduces risk for lung cancer and heart attacks; a low salt diet reduces blood pressure and risk for stroke; and avoidance of excess sun lowers the incidence of skin cancer. There is a consistent relationship between physical activity status and the incidence of coronary artery disease that is comparable in magnitude to that related to serum cholesterol, smoking >1 pack/day of cigarettes and systolic hypertension (1). Physical exercise also is associated with a lower risk factor profile (lower lipids, better blood pressure and glucose tolerance, elevated high density lipoprotein cholesterol) for coronary artery disease (2). The interaction among diseases, lifestyle variables, and putative aging makes it difficult to assess the effects of each of these processes on the overall functional capacity of the aging human being unless the influence of all the factors on functional capacity are delineated or controlled while the physiologic effects of one single process are measured. This is not always feasible because change in one usually alters the others, thereby limiting the ability to distinguish the physiological effects of each process independently.

One approach to studying the effects of extrinsic variables on age-related declines in organ function might be to first differentiate the effects of disease from those of biological aging. To identify the effects of one disease is not difficult when clinical signs and symptoms of other diseases are not present; however, the effects of asymptomatic disease can be easily overlooked and may cause substantial functional impairments. Furthermore, the effects of several diseases on functional capacity can be synergistic.

Arteriosclerosis is the main disease process which correlates directly with biological age, and has the greatest impact on cardiovascular function and longterm survival in the elderly (3). Asymptomatic coronary disease was probably responsible for the decline in the peak exercise ejection fraction below resting levels in 72% of apparently healthy volunteers over 60 yrs of age (4). The coexistence of wall motion abnormalities in 50% of individuals older than 70 years of age with an abnormal ejection fraction response to exercise suggests that regional ischemia was indeed present. In contrast, during maximal cycle exercise there was neither a decline in the ejection fraction below resting levels nor were there regional wall motion abnormalities in normotensive older

subjects intensively screened for coronary artery disease by exercise thallium scintigraphy (5). This suggests that biological aging per se does not reduce cardiac function in older individuals who are properly screen for cardiovascular disease. Hypertensive disease also has a substantial effect on cardiac performance by increasing arterial stiffness and pressure, pulse wave velocity and left ventricular wall thickness, decreasing the early diastolic filling rate and prolonging ventricular relaxation (6). There is a 25% increase in left ventricular wall thickness and a 50% reduction in early diastolic filling rate at rest between the third and ninth decades in clinically normotensive individuals (7,8); thus, hypertension might accelerate age-related changes in cardiac function. This would increase afterload in the aging heart, alter the pulsatile component of external cardiac work, reduce arterial distensibility and raise systolic arterial blood pressure, pulse wave velocity and peripheral vascular resistance. Physical conditioning modestly lowers both systolic and diastolic blood pressure, and reduces peripheral vascular resistance in hypertensive middle-aged patients (9), and increases stroke volume, cardiac output and left ventricular wall thickness without changing peripheral vascular resistance in normotensive younger subjects (10). Whether exercise training would increase arterial distensibility and reduce pulse wave velocity and systolic arterial pressure in older subjects is not known; but lower pulse wave velocity and systolic arterial pressure are common in cultures where levels of physical activity are high and the sodium content of diets are low (11).

Rigorous screening for silent ischemia and hypertension at rest and by maximal treadmill exercise testing with electrocardiography and thallium scanning (12) can provide individuals free from coronary artery and other asymptomatic cardiovascular disease in which to study the physiological effects of exercise training, independent of disease, on cardiovascular and endocrine-metabolic functions in aging man. Using these techniques the prevalence of coronary artery disease in subjects over the age of 70 years was estimated to approach the post-mortem finding of greater than 70% narrowing of at least one major coronary artery in 40-60% of unselected hearts (13). Similarly, screening the older individuals for diabetes with the glucose tolerance test by the criteria of the National Diabetes Data Group (14,15) and for hyperlipidemia using criteria from the Lipid Research Clinics Prevalence Study (16,17) allows detection and exclusion of older people with generally accepted abnormalities in glucose and lipoprotein lipid metabolism who may be at high risk for asymptomatic disease or organ dysfunction. While disease causes demonstrable and clearly significant impairments in functional capacity, increased physical activity by raising aerobic capacity, lean body mass and energy level and reducing body fat can have a substantial impact on the functional status of the aging human being.

Physical Activity and Maintenance of Functional Reserve Capacity

An emphasis on maintenance or improvement in functional capacity with advancing age has not been a major focus of gerontologic research. A substantial amount of information regarding the effects of aging on physiologic function is derived from cross-sectional studies which report declines in performance among different age groups. In the analysis of measurements of the various functional status within group data, there is substantial heterogeneity in the physiologic function of individuals within the various age groups. While mean data may show a decline in the functional reserve capacity among the elderly, there are older individuals with either minimal or no loss, and sometimes equal or even better functional capacity than that of the average younger person. This information has come to the forefront in evaluating the physiologic effects of factors extrinsic to

primary biologic aging, such as regular, intense physical activity, on functional reserve capacity. In master athletes, individuals over the age of 50 years who are very physically active, highly conditioned and compete regularly in athletic events, there is minimal loss in cardiovascular function with advancing age, and glucose tolerance, insulin sensitivity, and lipoprotein lipids are comparable to those of younger athletes (18-21). Master athletes, and other older individuals without specific pathologic linked losses in function commonly associated with disease, who have maintained functional reserve capacity comparable to younger counterparts might constitute that category of non-diseased elderly who have aged successfully (22). This suggests there are more important determinants of health than biological (as opposed to functional) age in disease-free older people. The role of these extrinsic factors or lifestyle behaviors, especially physical activity habits, as significant modulators of physiologic function in the elderly requires further evaluation.

A profound effect of physical exercise training on cardiovascular, endocrine-metabolic and musculoskeletal function in younger individuals is now well recognized, and it is likely that many changes in functional reserve capacity that have been previously attributed to an "aging process" are in part due to the sedentary lifestyle and dietary indiscretion that accompanies advancing age. It is not known how much of an improvement in physiological function can be expected in response to varying levels of physical exercise in sedentary elderly subjects, nor is it known to what extent and under what conditions medically unsupervised physical activity can be recommended for healthy or disease-afflicted elderly. Further investigation is needed to understand the mechanisms by which aging affects physiologic responses to acute and long-term physical activity and to define the roles that physical conditioning can play in the promotion and maintenance of health and the prevention of diseases attributed to biological aging.

The perspective gained in this area of gerontologic investigation will be limited if only cross-sectional data are examined, especially when all that is reported are mean data. Only through longitudinal investigations of medically defined, carefully selected cohorts can the impact of physical activity on the functional reserve capacity of aging humans be distinguished from other extrinsic factors, disease and biological aging itself. Several longitudinal studies examining the potential of exercise training to slow age-related declines in cardiovascular, musculoskeletal, bone-mineral, and glucose and lipoprotein lipid metabolism are currently supported by the National Institute on Aging. There are also studies in progress to investigate the mechanisms by which physical exercise may improve the functional reserve capacity and the medical condition of elderly people afflicted with diseases such as coronary artery disease, hypertension, type II diabetes mellitus and osteoporosis. If the results of these studies are to provide insight into the efficacy of aerobic exercise as a therapeutic modality to improve the well-being of the rapidly expanding population of older people, the common experimental problems distinguishing confounding effects of aging, cohort, secular and time effects on the experimental measures must be considered and may require an age-time matrix type of study design (23).

DEFINITION OF THE ISSUES

The specific contributions of physical inactivity and deconditioning to the commonly observed declines in the functional reserve capacity of major organ systems with aging have not been thoroughly delineated. The maintenance of physical activity and conditioning status measured as maximal aerobic capacity

(the ability of the cardiovascular system to deliver blood and oxygen to working muscles and of exercising muscles to utilize the oxygen and energy substrate to perform work in response to a maximal exercise stimulus) (24) into older age may have substantial health and socioeconomic benefits for the elderly. The fact that high levels of maximal aerobic capacity (VO_2max) observed in selected master athletes are associated with improved metabolic function and the maintenance of a high level of functional reserve capacity compared to their sedentary peers suggests that this is the case. Although maximal aerobic capacity is probably the best measure of physical work capacity and fitness in younger individuals, it may not be the only measure of organ performance or necessarily the best measure of functional reserve capacity in the elderly. Energy expenditure, measured as oxygen consumed, or other physiologic responses (hemodynamic, muscular, hormonal, cognitive-motor or otherwise) to submaximal isotonic work on a bicycle or treadmill, to an isometric (weight) stimulus, or to environmental and mental stressors are also important, useful measures of human performance.

The goal of remaining physically active with advancing age is to delay the declines in functional capacity with aging. Not only does regular aerobic exercise maintain muscle strength, coordination, speed, endurance and agility, but it reduces body fat and other risk factors for coronary artery disease, heightens mental acuity, maintains self esteem and enhances quality of lifestyle. The rehabilitative capacity of regularly performed aerobic exercise also is demonstrated in human disease. Physical activity has improved physiological function and overall performance in some patients with ischemic coronary artery disease, hypertension, endstage renal disease, diabetes mellitus, weakness due to muscle wasting and depression. The salutary effects of physical conditioning on behavior include enhanced motivation, increased confidence in the ability to perform daily tasks and activities, successful return to a regular work schedule, and a heightened level of energy for activity; all presumed due to increased aerobic capacity. Such improvements could maintain the functional capacity of older people afflicted with disease, in spite of concomitant physical limitations. This suggests that regular physical activity may be a suitable mode of rehabilitation for older individuals with limited function due to disease and for maintaining the functional reserve capacity of the healthy elderly.

If physical conditioning status is maintained by regular exercise, can age-associated declines in functional capacity be avoided? Can vigorous exercise successfully restore the declines in organ function and vulnerability to diseases and stresses associated with aging? If so, how much exercise is needed? How often and at what intensity? Is there a threshold for activity or set point for VO_2max at which beneficial adaptations will occur or deteriorations ensue? Can the observations in master athletes with high levels of maximal aerobic capacity or in disease-afflicted individuals who regain functional capacity through regular physical activity be solely ascribed to exercise? Many questions need be answered regarding the potential for physical exercise to promote successful, healthy aging and to restore the functional capacity of those afflicted with disease. Substantial research is needed to understand the relationship of regular physical exercise and the maintenance of heightened aerobic capacity to the functional status of the aging human being.

Major Areas Which Require Investigation

Evaluation of the potential role for regularly performed physical exercise in the prevention and/or reduction in the extent of age-related diseases and disorders in humans, and the determination of the exercise

prescription (type, frequency, intensity and duration) and magnitude of the increase in aerobic capacity required to produce these effects.

Assessment as to whether or not there is a threshold for the increase in maximal aerobic exercise capacity required to achieve a specific functional reserve capacity. Are there different benefits for different degrees of exercise intensity?

Investigation of the mechanisms by which regularly performed exercise increases cardiovascular, endocrine-metabolic, cerebral, and other organ function, maximal aerobic capacity, and the ability to work and function independently, and reduces risk factors for disease in the elderly.

Measurement of the biological adaptations to increased exercise/physical activity in man in vivo at functional levels ranging from the whole body to the specific organ systems, tissues and to the cellular and molecular level, and the determination of the influences of advancing age on these processes.

Evaluation of whether or not maximal aerobic capacity (VO_2max) is the best measure of physical conditioning status, cardiovascular function and overall functional reserve capacity in the elderly.

Determination whether functional declines with short- and long-term deconditioning are more rapid and of greater magnitude in older active individuals than in comparably conditioned younger individuals, and an assessment as to whether or not deconditioned older individuals are capable of rehabilitation to previous levels of performance after deconditioning.

Assessment whether the recommendation for increased physical activity in older individuals is medically safe for healthy as well as disease-afflicted elderly. If affirmative, then studies are needed to develop guidelines for baseline medical evaluations and appropriate prescriptions (type, frequency, duration and intensity of activity) for exercise training older people that maximize the benefits of exercise while preventing injury.

THE ELDERLY BE PHYSICALLY CONDITIONED?

: of the longitudinal studies documenting improvements in functional reserve ıcity with aerobic conditioning are in younger and middle-aged individuals; ;s-sectional comparisons in epidemiologic studies provide most of the ɔrmation on the potential of physical exercise training to increase aerobic ıcity and improve functional reserve capacity in the elderly (2, 25-27). In few longitudinal studies examining the effects of exercise training on ɛntary people over the age of 60 years, the training stimulus was of short ıtion and low intensity, and sample sizes were small. As a result, a ;tantial change in maximal aerobic capacity was documented in some (28-30), not in other studies (31-33). These inconsistencies have limited the ability ·each a conclusion about the trainability of older individuals (34). However, physiological results of longitudinal studies in which high intensity ·cise was used to condition older individuals (30,35), the benefits achieved middle-aged and older patients with coronary artery disease (36), type II ɔetes (37,38) and chronic renal disease (39) with participation in vigorous

aerobic exercise programs, and the observations in master athletes (18-21) support the view that exercise has the potential to improve functional capacity and prevent disease in the elderly.

Several studies have attempted to determine the training intensity required to raise VO_2max substantially in older individuals. In an early study (28), 60% of people aged 60-79 yrs increased their aerobic capacity an average of 7% after participation in a 6 week walking and jogging program at an intensity of 40-50% of heart rate reserve. In another study, there were comparable increases in the peak VO_2max of 60-70 year olds after 9 weeks of exercise at an intensity of either 57 or 70% of VO_2max (29). The most comprehensive study to date involved, a 6 month program of walking at 40% of heart rate reserve which increased VO_2max by 12% in 11 healthy subjects ages 65$\pm$3 years (30,35); however, in spite of the rise in VO_2max during the lower intensity exercise, glucose and lipoprotein lipid metabolism did not improve. Subsequently, higher intensity exercise at 80-85% heart rate reserve for 6 months raised VO_2max an additional 18% and substantially improved hemodynamic, metabolic and pulmonary responses (30,35,40,41). It is not clear whether it was the duration or the intensity of the training stimulus which limited the improvement in the functional reserve capacity of these older subjects. Although the older individuals increased their VO_2max an additional 18% in response to the vigorous aerobic exercise program, the lower intensity training stimulus was sufficient to improve cardiac performance, but not the metabolic function of these individuals. While VO_2max increased in older subjects at these lower intensities, higher intensity training programs and a more significant rise in maximal aerobic capacity over a longer time period might be required for older subjects to achieve the metabolic improvements observed in younger and middle-aged subjects after endurance training (42-45). The high VO_2max and associated cardiovascular and metabolic benefits achieved by master athletes who have trained intensely for a long period of time lends credence to this hypothesis (18-21,46,47).

In some older subjects, the cardiovascular and metabolic adaptations to exercise programs may be significantly less than in younger individuals. This may reflect the presence of asymptomatic disease or irreversible changes in cardiac, respiratory and/or skeletal muscle structure and function in older subjects which limits the ability of the exercise stimulus to produce physiologic adaptations in the function of various organs comparable to those observed in healthy younger subjects (48,49). The suggestion that enhanced muscular adaptations, rather than increased cardiac output may be responsible for the greater oxygen extraction at maximal exercise in master athletes suggests that peripheral, not central adaptations are primarily responsible for their elevated VO_2max (49). These changes in skeletal muscle structure and function may take longer to occur in older individuals. Whether or not endurance exercise can induce these peripheral adaptations in sedentary older individuals and raise their VO_2max to levels comparable to those found in younger individuals may require longterm longitudinal studies.

The ability of master athletes to maintain high levels of VO_2max and have glucose tolerance, insulin sensitivity, and plasma lipoprotein lipid levels comparable to those found in younger active individuals (18-21) suggests that maintenance of a high level of physical activity into older age can slow the decline in the functional reserve capacity of the cardiovascular and endocrine-metabolic systems previously attributed to biological aging (48). Preliminary results in several highly conditioned master athletes who began intensive physical exercise training in their 6th decade of life and in one who deconditioned for 10 weeks (VO_2max

declined from 53 to 39 ml/kg·min) suggest that these cardiovascular and metabolic adaptations are probably not inherited (50).

In studies examining the effect of regular chronic wheel exercise on cardiac function in sedentary adult rats there was a mild augmentation in cardiac oxidative enzyme capacity and an attenuation of the age-related decline in myocardial calcium activated actomyosin ATPase activity. This indicates that exercise conditioning can partially reverse the decline in cardiac muscle oxidative capacity observed in aging sedentary rats (51), suggesting that the relative efficacy of chronic exercise to modulate myocardial performance is possible into older age, and apparent age-related declines in myocardial function, at least in rodents, can be reversed by physical conditioning.

It is possible that the vigorous high intensity training program required to test the hypothesis that physical exercise will improve functional reserve capacity in the elderly may not be possible in all older individuals. The ability to condition some older individuals may be limited by obesity or coexistent disease or other medical conditions. Obesity, defined as a body mass index >30 Kg/m^2 (52) is associated with hypertension, diabetes, hyperlipidemia and arteriosclerosis (53), and an increased mortality from coronary heart disease (54). Thus, overweight individuals are at increased risk for complications during exercise training and require careful screening for overt and asymptomatic disease prior to onset of exercise training. Furthermore, oxygen consumption and cardiac work are increased in overweight individuals during exercise (55), increasing risk for cardiovascular complications. Weight reduction prior to participation in a physical exercise program may reduce risk for complications during training and enhance the ability of overweight individuals to raise their maximal aerobic capacity. Simultaneous programs of weight reduction by hypocaloric feeding and behavior modification combined with physical exercise may be even more beneficial, since increased energy expenditure during exercise will enhance the caloric deficit produced by hypocaloric feeding (55,56). Preliminary results in healthy overweight, middle-aged and older men screened for occult coronary disease by maximal treadmill stress testing suggests that such a combined intervention promotes a greater reduction in adipose tissue mass than achieved either by hypocaloric feeding or exercise alone (57). Such an approach seems attractive if confounding extrinsic factors such as disease do not limit the exercise capacity of these sedentary, overweight individuals or place them at risk for injury. Thus, prior screening for disease, especially symptomatic and asymptomatic coronary artery disease by careful medical exam and exercise stress testing with electrocardiography and thallium scans would provide a healthy population of older individuals at low risk for exercise-induced complications in which to test whether prolonged, intensive physical exercise in elderly individuals will cause cardiovascular, metabolic and other physiologic adaptations comparable to those seen in younger individuals.

ARE AGE-RELATED DECLINES IN CARDIOVASCULAR FUNCTION MODIFIABLE BY PHYSICAL EXERCISE

The most effective test to evaluate the maximal functional capacity of the cardiovascular system is to measure maximal oxygen uptake during strenuous exercise. This test determines the capacity of the cardiovascular system to deliver oxygen to working muscles and for exercising muscles to utilize the oxygen to perform the work (24). Most of the studies examining the effects of aging on VO_2max are cross-sectional comparisons of the changes in physiologic responses to maximal exercise stress with age in active, but non-athletic men. They report a rather uniform average 10% per decade or 0.45 ml/kg·min per year

mean decline in VO_2max from age 25-80 years (25,58). However, in highly trained master athletes there was a decline in VO_2max of only 5% per decade (18). The rate of decline in VO_2max with advancing age in longitudinal studies is heterogeneous, and dependent on the physical activity status of the population studied. In subjects aged 40-72 years divided into active and inactive categories, the VO_2max of active men who jogged an average of 3 miles/week declined by much less rapidly than that of sedentary men (59). In men aged 40-60 yrs old who ran an average of 25 km/week, there was no decline in VO_2max over a 10 year period of follow-up (60). In a recent longitudinal study there was a decline in VO_2max of less than 2% per decade in highly conditioned master athletes aged 50-82 yrs who remained competitive and a significant 12% decline per decade in the VO_2max of those who ceased competition but remained highly active during the 10 year period (19). In that study, maximal heart rate and fat free mass decreased and percent body fat increased comparable amounts in both groups, suggesting that the competitive group either increased arteriovenous oxygen difference (i.e., muscular adaptations occurred) or raised stroke volume (i.e., cardiac adaptations occurred since maximal heart rate decreased) during the 10 year period of intensive training. Thus, while maximal heart rate declines with advancing age, it appears that highly conditioned elderly subjects without evidence cardiovascular disease can maintain their aerobic capacity by increasing muscle oxidative capacity (arteriovenous oxygen difference) and by increasing stroke volume and diastolic filling (Frank Starling mechanism) to compensate for the progressive decline in maximal heart rate with advancing age (46-49). In addition to the physiologic adaptations observed with regular high intensity endurance exercise in healthy conditioned older athletes, long term, high intensity aerobic training produces both cardiac and peripheral adaptations in middle-aged patients with ischemic heart disease (36,61,62). In these patients the peripheral adaptations also may be of greater significance then central (cardiac) ones, since left ventricular wall thickness, contractility and function during systole did not change (46).

Thus, while maximal aerobic capacity declines with advancing age, this decline can be attenuated by central and peripheral circulatory adaptations. In highly conditioned master athletes there is a decline in VO_2max with advancing age that can be attributed to a decline in maximal cardiac output caused by the well-documented age-related decline in maximal heart rate (46-48). However, this can be attenuated by continued high intensity aerobic training (19). Thus, because of variability in lifestyle habits there may be diversity in VO_2max and cardiac hemodynamics in elderly individuals such that some older individuals have a VO_2max' comparable to that of younger individuals.

In addition to differences in the disease status, physical activity habits and body composition of older subjects, studies in disease-free older subjects indicate that there are at least three significant age-associated alterations in cardiac structure and function. These are a mild increase in left ventricular wall thickness (8,48), slowed and delayed ventricular relaxation (6,8), and diminished contractile performance during physical exercise (46,48). The first two age-related changes probably reflect a compensatory response to the increased workload imposed by vascular changes (increased peripheral vascular resistance), which increase pulse wave velocity and afterload. This increases the pulsatile component of external cardiac work and raises systolic arterial pressure (11). These changes are magnified in individuals with hypertension (6) and are an independent risk factor for cardiovascular mortality (63). The clinical relevance of the left ventricular hypertrophy observed with advancing age is not clear, but under conditions of acute volume overload or exercise stress may raise

ventricular and pulmonary pressures and increase shortness of breath. Physical conditioning profoundly affects the circulatory system in younger individuals by increasing stroke volume, decreasing peripheral vascular resistance, and increasing left ventricular mass (10,48); in older subjects it might also increase arterial distensibility, reduce pulse wave velocity and lower systolic blood pressure. The effects of physical conditioning on these processes are not known in older people.

The third age-related change in cardiovascular function, a decline in maximal aerobic capacity, defined by the Fick equation as the product of cardiac output and arteriovenous oxygen difference during maximal exercise stress is dependent on the population studied, and age-related changes in the peripheral and central circulation (46-48). In disease-free individuals cardiac output, measured at peak oxygen consumption using the gated blood pool scan technique during cycle exercise to exhaustion, was maintained with advancing age (5,12). However, neither arteriovenous oxygen difference nor cardiac output or their determinants have been measured at VO_2max; and in preliminary studies evaluating the mechanisms regulating aerobic capacity in master athletes and sedentary older subjects, peripheral and not central adaptations seem responsible for the higher levels of VO_2max in highly conditioned master athletes (49). Other possible reasons for differences in VO_2max among older individuals may be the inappropriate normalization of oxygen consumption during maximal exercise stress to total body mass rather than to lean body mass since muscle mass decreases with advancing age (64,65) and the additive effects of the age-associated decline in blood flow to muscle during maximal exercise in elderly subjects (66). While there is a progressive decline in pulmonary function with advancing age that may be caused by effects of biological aging or environmental exposures and lifestyle (67,68), they do not seem to limit exercise capacity in individuals without evidence of pulmonary disease because maximal ventilatory capacity is rarely achieved at VO_2max. Hence, the pulmonary system is usually not rate-limiting in exercise performance, although oxygen exchange in the lung may hinder performance during prolonged exercise.

Thus, the health status and lifestyle habits of the individuals studied seem to have the most profound affect on cardiovascular performance during maximal exercise stress testing. Coronary artery disease, whether overt or asymptomatic has the most significant impact on cardiac function and screening out individuals with cardiovascular disease especially in older populations, dramatically alters cardiac performance (5,12,48). In healthy older individuals, screened for coronary artery disease, differences in cardiac function may be primarily due to physical conditioning status. In the only study addressing this issue, both cardiac output and end diastolic volume were higher at the same level of exercise intensity after a 12 week aerobic training program, but end systolic volume did not change (69). The extent to which the peripheral (muscle mass, blood flow and oxygen extraction) and central (ventricular function, cardiac output, and oxygen exchange) factors determining maximal aerobic capacity (Fick Equation) differ among healthy elderly subjects with varied physical activity habits, and the effects of physical conditioning on these parameters is not known.

ARE GLUCOSE AND LIPID METABOLISM MODIFIABLE BY PHYSICAL EXERCISE IN THE ELDERLY?

Some of the alterations in glucose and lipoprotein metabolism which occur with advancing age predispose older people to diabetes mellitus and hyperlipidemia (15,16), major risk factors for coronary artery disease, the leading cause of death in older Americans (3). If physical inactivity and a reduced aerobic

capacity are major determinants of the decline in metabolic function and increase in adiposity which predispose older individuals to develop atherosclerosis, then interventions which improve physical conditioning status and VO_2max should improve metabolism, reduce risk factors for atherosclerosis and decrease cardiovascular complications during stress. A better understanding of the effects of change in lifestyle habits on glucose and lipid metabolism with advancing age might have important health implications for reducing the prevalence of coronary artery disease and prolonging the survival of older individuals.

A beneficial effect of physical conditioning on glucose and lipoprotein metabolism and body composition is recognized in younger and middle-aged individuals (2,26,27,42-45) and several studies indicate that similar changes occur in older subjects (28-30). The longitudinal studies in older individuals are few in number and most are descriptive, not mechanistic. Furthermore, changes in body fat and diet during training, the duration and intensity of the exercise, and the timing of the last exercise session relative to the performance of the research tests affect glucose and lipoprotein metabolism and may limit the ability to distinguish effects of physical conditioning per se from those of other extrinsic factors affecting metabolism.

Declines in metabolic function with advancing age are highly variable, and in a substantial percentage of older subjects measures of lipoprotein lipids, glucose metabolism and body composition are comparable to those in younger subjects. The reduction in overall muscle mass and blood flow to muscle in elderly individuals contributes to the decline in metabolic function by decreasing muscle structure and function and reducing the peripheral utilization of substrates. Thus, while glucose utilization and lipoprotein turnover traditionally have been normalized to body weight or the pool size of a substrate, it may be appropriate to normalize these parameters for lean body mass and organ function in older individuals.

Glucose Metabolism with Advancing Age

The 5 mg/dl deterioration in glucose tolerance per decade observed with advancing age is primarily caused by peripheral tissue resistance to the action of insulin (14,15). Studies using the glucose clamp technique indicate that at submaximal insulin concentrations both glucose disposal and the suppressibility of hepatic glucose production by insulin on the average are reduced in older subjects despite normal insulin receptor binding (70-72). This raises plasma insulin levels and reduces glucose tolerance, both of which increase risk for accelerated atherosclerosis (73). Tissue responsiveness to insulin, defined as the glucose disposal rate at maximal insulin concentration, is normal in some and reduced in other elderly subjects depending on their degree of hyperinsulinemia and glucose intolerance. This suggests that in some older people there may be a post-insulin receptor defect in insulin action, yet this has not been examined directly at the cellular level. Other mechanisms, such as reduced insulin secretion (74) and increased levels of norepinephrine resulting in impaired insulin secretion and action (75), also may worsen glucose metabolism in older individuals.

Cross-sectional data in master athletes (20) and sedentary younger and older individuals (38,42,43) suggest that the maintenance of high levels of physical activity into older age protects against the age-related deterioration in glucose tolerance and insulin sensitivity. In only one study examining the effects of

aging on glucose metabolism was VO_2max and percent body fat of the subjects measured directly (21); and there are no longitudinal studies of the effects of change in physical conditioning status and body fat on the mechanisms regulating glucose metabolism in older individuals. Thus, the relationship of physical conditioning status to glucose metabolism in older individuals, independent from hereditary factors and other extrinsic variables, is not known.

Lipoprotein Lipid Metabolism with Advancing Age

The finding of elevated levels of high density lipoprotein cholesterol (HDL-C) and lower triglyceride and low density lipoprotein cholesterol (LDL-C) levels in master athletes that are comparable to those in athletic younger individuals suggests that physical conditioning may improve lipoprotein lipid metabolism and reduce risk for coronary artery disease in older individuals. There is little known about the regulation of lipoprotein metabolism in elderly subjects, but the impact of extrinsic factors, genetics and disease on metabolic function is substantial (76). For example, obesity and diets high in cholesterol and saturated fat lower HDL-C, raise LDL-C and increase plasma triglyceride levels (77,78). Alcohol intake (79), medications (80) and chronic diseases also have substantial effects on lipoprotein lipids, most of them undesirable. Chronic diseases, such as diabetes, renal and liver disease, common in elderly populations lower HDL-C and raise plasma LDL-C and triglyceride levels. These abnormalities in lipoproteins are associated with increased risk for atherosclerosis and coronary artery disease (16,76). If the presence of these conditions is undetected, lipoprotein lipid profiles will be altered independent of biological aging.

Thus, the accurate study of the effects of physical activity on lipoprotein metabolism in older individuals requires rigorous screening to select healthy people of comparable body weight and diet without evidence of disease or genetic factors which affect lipoprotein metabolism. Such a design would distinguish the metabolic effects of exercise capacity from those erroneously attributed to biological aging per se. Studies of this type have not been performed in the elderly and might provide insight into the role of physical exercise programs in reducing risk for coronary artery disease in seniors.

CAN AGE-RELATED LOSS OF BONE DENSITY BE PREVENTED BY PHYSICAL EXERCISE?

There is a progressive decline in bone density in both males and females with advancing age. These losses may be so severe in elderly females to result in fractures causing progressive disability, limited activity and substantial declines in functional capacity (81). Although biological aging is considered a major factor in the loss of skeletal bone, the effects of estrogen and vitamin D deficiency, physical inactivity, cigarette smoking and excessive alcohol also contribute to the development of osteoporosis in the elderly (81-84). In postmenopausal females the rate of loss in skeletal mass and bone density is greatly accelerated due to estrogen deficiency; however, this decline can be accelerated by the present of the aforementioned additional extrinsic risk factors which enhance osteopenia.

Physical inactivity is one potentially modifiable factor contributing to the loss of skeletal integrity and bone density. A number of cross-sectional studies suggest that bone loss can be attenuated by physical exercise (84-86); thereby slowing the emergence of osteoporosis and reducing the heightened risk of bone fracture in the elderly. If estrogen is replaced in the postmenopausal female,

bone resorption will decrease; simultaneous weight bearing exercise may further augment bone accretion and increase bone mass (87). Estrogen administration (in the postmenopausal female), cessation of cigarette smoking, reduction in alcohol intake, dietary supplementation with vitamin D (and perhaps calcium) and other extrinsic factors may be additive with the effects of exercise to reduce the progression of osteopenia in the elderly. Although supplemental calcium administration alone or with estrogen does not increase bone density (88), its effects when administered during exercise are not known.

The increase in muscle mass and strength, and enhancement of agility associated with physical exercise may substantially reduce the vulnerability of older individuals, especially postmenopausal women, to risks of bone fracture. While the 1984 Consensus Conference on Osteoporosis (89) recommended modest weight bearing exercise for the possible prevention of bone loss, closer inspection of the literature indicates that more information is needed (90). If it is decided which older individuals might benefit from physical activity, it will be necessary to determine the type, intensity and duration of the exercise program best suited to increase bone density; assess whether there are additional requirements for supplemental hormones, vitamins and minerals to maximize the effects of exercise; and develop measures of bone density and aerobic capacity to accurately evaluate the effects of exercise on bone-mineral metabolism. Many factors can affect the progression/remission of osteoporosis; hence the selection of subjects, size of the sample studied and method of randomization to treatment will be critical.

ARE ADAPTATIONS TO ENVIRONMENTAL STRESS IMPROVED BY PHYSICAL EXERCISE?

The ability to adapt to changes or stresses in the environment declines with advancing age. Older individuals are on the average less tolerant to extremes of temperature (91,92), more prone to orthostatic hypotension after rapid positional change (93) and more often remain tachycardic, hypertensive and fatigued after physical exertion than younger people (94). Tolerance to temperature and recovery from exhaustive exercise are improved in younger and middle-aged individuals after physical conditioning (95-97), but the results of exercise training on these responses are not known in the elderly. Paradoxically, exercise training worsens orthostatic tolerance in younger subjects (98,99), but the effects in older sedentary individuals with impaired baseline orthostatic tolerance are not known. Blood volume, blood flow and thermoregulation (sweating and shivering) affect responses to these environmental conditions; these parameters have neither been measured in healthy older individuals nor related to maximal aerobic capacity, body composition or diet. One would suspect that more physically active older individuals would be more tolerant to these stresses, but this requires investigation.

SUMMARY AND FUTURE PROSPECTS

There is evidence that regularly performed exercise may improve the quality of life and protect against the development of disease in elderly subjects. Several studies have shown that the functional reserve capacity of the cardiovascular, endocrine-metabolic and musculoskeletal systems can be maintained and/or improved by regular exercise in healthy, elderly subjects. Controlled longitudinal studies have shown that regularly performed exercise is associated with fewer risk factors for arteriosclerosis and coronary artery disease in middle-aged men and women and a few studies have documented similar effects in older subjects. Results in master athletes and in patients with disease support the hypothesis

that physical activity will improve the functional capacity of older people. More information is needed to determine the extent to which physical conditioning will benefit the elderly and type and quantity of regular exercise which should be prescribed for older populations. This can be achieved both by large scale longitudinal studies as well as by small short and long term evaluations in healthy and disease afflicted older subjects of the mechanisms by which exercise training improves functional capacity, reduces risk factors for arteriosclerosis and improves the quality of life. If it can be documented that exercise training slows or prevents the age-related deterioration in functional capacity and makes it easier for the elderly to complete activities of daily living with more energy and less fatigue, then regular exercise could be incorporated into programs of public health and preventive medicine as a means by which the productivity, independence, and active lifestyle of the aging population can be prolonged.

In studying the effects of exercise on the functional reserve capacity of the elderly it will be important to determine the age, gender and clinical characteristics of the older subjects most likely to benefit. Guidelines for medical screening and baseline evaluations of functional reserve capacity will be needed to determine the exercise prescription most likely to achieve the desired physiologic result without risking injury to the older participant. This will require determination of the type, intensity, duration and frequency of exercise for each functional decline and risk factor which develops with advancing age. Standardized methods will be required to monitor physiologic responses to exercise, determine the rate of progression to higher levels of exercise and document the physiologic effects of the exercise program. Safeguards will be needed to maintain diet, drugs and other lifestyle habits constant to permit accurate assessment of the physiological effects of physical exercise.

Progress in this area of investigation will require support for centers of excellence to perform large scale exercise studies to document the physiological effects of physical exercise, and its role in the prevention of disease, reduction in the utilization of health resources and improvement in the mental health and the quality of life of elderly populations (100). Longitudinal studies of this type would ultimately have sufficient data to determine the impact of exercise training on morbidity and mortality in the elderly and establish the relationship of physical activity to survival in healthy and disease-affected older individuals.

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