# **EXERCISE PRESCRIPTION**

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#### INTRODUCTION

Individualized prescriptive physical activity is central to the rehabilitation concept. (1-5) The prescriptive components of exercise include its "dosage" – comprised of the frequency, duration, and intensity of exercise: and the specific type of exercise. (6)

Once the patient has recovered adequately from an acute myocardial infarction and has often reached a level of endurance sufficient to return to work (not uncommonly in the 4-to 8-week period postinfarction), more intensive exercise training can be undertaken with the goal of enhancing cardiovascular function. Prior multilevel exercise stress testing is required both for the accuracy and for the safety of exercise prescription. When patients are tested to a sign-or symptom-limited endpoint, the heart rate prior to this endpoint is characterized as the highest heart rate safely achieved at exercise stress testing. Age-predicted target heart rates cannot be used for exercise prescription for patients with symptomatic coronary disease; coronary disease per se may attenuate the heart rate response to exercise, as may disease of the sinus or AV nodes or therapy with beta adrenergic blocking agents.

Comment is also appropriate about cardiac medications and exercise stress testing for exercise prescription. Patients should be tested on their optimal medication regimen, indeed on the regimen on which they are to be trained. (7) This includes beta adrenergic blocking agents, digitalis, diuretics, antihypertensive agents, etc. This ensures that their exercise prescription will be appropriate. Indeed, should there be a major change in the medication regimen, repeated exercise testing is warranted for revision of the exercise prescription.

#### COMPONENTS OF THE EXERCISE PRESCRIPTION

The minimum "dosage" recommended to achieve a training effect requires that the patient exercise at least 2 or 3 times per week, preferably on nonsuccessive days. More than four exercise sessions weekly does not appear to effect a significant additional increase in maximal oxygen uptake; conversely, unfit individuals or sedentary elderly patients may improve their physical work capacity with one or two exercise sessions per week, although further increase in MVO<sub>2</sub> can be attained with more frequent training. Exercise sessions should be 30 to 45 minutes in duration, including warm-up and cool-down periods; this time frame is adequate to stimulate aerobic metabolism at the exercise intensity recommended below. The exercise prescription identifies that, during exercise sessions, the recommended intensity (the component requiring prior exercise stress testing) is that patients attain a heart rate between 70 and 85 percent of the highest level safely achieved at exercise stress testing. In general, the lower target heart rate range, 70 to 75 percent, is recommended for patients who exercise individually in an unsupervised exercise setting, and the higher target heart rate range, 80 to 85 percent, for patients who exercise in supervised hospital or gymnasium group programs. The 70- to 85-percent heart rate range corresponds to approximately 60 to 78 percent of the peak oxygen uptake, an effective yet safe range within which to stimulate aerobic metabolism (8), the range within which the "training effect," to be discussed subsequently, has been shown to occur. Although it appears that an increased duration and/or frequency of exercise can compensate for a decreased exercise intensity, the use of this approach (increasing the duration and frequency of exercise) tends to engender an excess of orthopedic complications and poorer adherence to the exercise program (9).

Interestingly, in the National Exercise and Heart Disease Project, low-level training (under 70 percent heart rate) of postinfarction patients effected a decrease in heart rate and blood pressure, particularly in unfit individuals (10).

#### THE TYPE OF EXERCISE

#### DYNAMIC VS ISOMETRIC ACTIVITY

The type of exercise prescribed is dynamic (isotonic or aerobic), i.e., activities involving rhythmic repetitive movements of large muscle groups. The physiologic response to dynamic activity is an increase in heart rate that parallels the intensity of the imposed activity and an increase in stroke volume; there is a gradual, progressive increase in systolic blood pressure with maintenance of or slight decrease in the diastolic blood pressure, widening the pulse pressure. Redistribution of blood flow shunts blood away from the viscera to working muscle, where increased oxygen extraction widens the systemic arteriovenous oxygen difference. Dynamic exercise thus imposes primarily a volume load on the heart, the basis for its "cardiac conditioning" effect.

By contrast, with isometric or static exercise, activities involving less than 20 percent of the maximum voluntary contraction of the involved muscle group evoke only a trivial alteration of the systolic and diastolic blood pressures and the heart rate. Isometric exercises are characterized by the development of tension without a change in length of the involved muscle group or joint motion, ie., a sustained contraction against a fixed resistance. With greater than 20 percent of the maximum voluntary contraction of the particular muscle group, the increase in heart rate is modest, bearing no linear relationship to the intensity of the imposed stress, but there occurs a sudden and precipitous increase in systolic blood pressure. This increase in afterload may be poorly tolerated by a potentially ischemic left ventricle and may precipitate angina pectoris, left ventricular dysfunction (11), and/ or ventricular arrhythmia (12). This is the basis for recommending avoidance or limitation of isometric activity in the patient with recent myocardial infarction. Imposition of a pressure load effects no significant improvement in cardiovascular function.

Dynamic exercise training increases both left ventricular mass and end diastolic volume; with static training, left ventricular mass increases, but end diastolic volume remains unchanged or may even decrease (13-15). This refers to the major characteristic of the exercise training, as most forms of exercise entail both dynamic and static components.

#### ARM VS LEG WORK AND TRAINING

For any given level of oxygen uptake, arm work evokes a higher heart rate and systolic blood pressure response than does leg work, probably due to the combination of dynamic and isometric activity characteristic of arm work. The clinical relevance is that most occupational and recreational activities require either exclusive or predominant arm work. In this context, the lack of interchangeability of arm and leg training effects also deserves emphasis as a basis for the design of a physical activity program, mandating specific arm muscle training for improved performance. With leg training, there is diminution in the heart rate and blood pressure response to leg work, but not to arm work. Conversely, with arm training, it is only arm work for which the double product is lessened; the double product remains unchanged, after arm training, in response to leg work (16). This emphasizes the substantial component of the conditioning or training response related to peripheral adaptation, i.e., the improved oxygen extraction by trained muscle (17).

# **RECOMMENDED ACTIVITIES**

Recommended activities include walking, running, swimming, bicycling, selected calisthenics, ropejumping, etc. Although in many formal exercise programs selected games tend to make the exercise session more enjoyable and thus lead to improved adherence, early in the course of exercise training competition and excitement should be limited because of the unpredictable increase in heart rate response engendered by these components.

#### DESIGN OF AN EXERCISE TRAINING PROGRAM FOR PATIENTS WITH SYMPTOMATIC CORONARY DISEASE (18)

Individualized exercise prescription varies considerably with the needs and goals of the patient, the initial level of fitness, the level of physical performance, the planned occupational and recreational activities, and the patient's skills, likes and dislikes. Accessibility of facilities and equipment must also be considered. However, basic concepts of program design will help ensure a safe and effective program. Ideally, patients should be encouraged, at least initially, to participate in medically supervised programs. In addition to enabling proper guidance regarding exercise, medical supervision often provides increased motivation and reassurance, as well as insuring appropriate emergency care for cardiovascular emergencies occurring during training (19). The signing of an informed consent document prior to entry into an exercise training program, in addition to its medicolegal implications, affords the physician an additional opportunity to inform the patient about the purposes, design, safety

features and potential problems (as well as ways to help avert them) of the cardiac rehabilitative physical activities.

The exercise training, however, must be considered in the context of being part of a comprehensive program involving education regarding diet, weight control, smoking cessation, appropriate medicationtaking, etc., and typically in the setting of return to gainful employment and re-establishment of a normal social life pattern, and recreational and/or retirement activities.

#### WARM-UP

The initial 5-10 minute warm-up period entails primarily stretching and range of motion exercises to enable muscle and joint adaptation and readiness for exercise. A gradual circulatory adaptation also occurs.

# TRAINING OR ENDURANCE COMPONENT

The 15-20 minute aerobic training or endurance component, designed to stimulate the oxygen transport system, the time during which the target heart rate is to be achieved, typically initially involves either walkrun sequences or exercises on a stationary bicycle or treadmill, activities where skill is a minimal component of the intensity of work demand. However, since these activities primarily train the legs, they should be supplemented with arm training exercise: selected calisthenics, use of shoulder wheels, rowing machines, etc. Activities are initially of low-level intensity and rhythmic in character. The choice of activities in a program will vary with the space and equipment available; the presence or absence of routine, continuous ECG monitoring; and the number of patients involved. Dr. Karl Stoedefalke has defined the ideal program characteristics as: individual, supervised, therapeutic, dynamic, aerobic, viable intensity, educational, recreational, non-competitive, relaxing and enjoyable (20). Individual exercise recommendations for unsupervised home programs can vary considerably; determining features, in addition to those obtained from functional evaluation at exercise stress testing, relate to the patient's general health status, age, musculoskeletal competence, job requirements, recreational preferences, motivation, etc. It is preferable that instructions for home exercise, in a detailed, specific and quantitative fashion, be provided in written form: type of exercise; intensity, duration, frequency; target heart rate range and method of checking; recommended clothing; signs and symptoms which serve as indications of excessive exertion: cautions regarding exercise relationship to meals. weather conditions, etc. In addition to walk-run-jog sequences, effective endurance activities include rope-jumping, bicycling, skating, swimming, rowing, aerobic dancing, etc.

Most cardiac patients initially expend about 50 Kcal per exercise session, gradually building up to a 200-300 Kcal expenditure per exercise session (300 Kcalories per session is a typical activity expenditure recommended for previously sedentary normal individuals).

During the exercise session, patients in programs without continuous electrocardiographic monitoring

should intermittently measure their heart rate response to insure that it remains in the desired range. Counting of the radial (carotid or temporal) pulse is recommended for 10 or 15 seconds, multiplying to get the heart rate per minute. Counting the pulse rate for a full minute will result in an inappropriately low heart rate, because of its gradual postexercise decline during the period of counting. At no time should a patient exercise at a level higher than that documented to maintain an appropriate cardiovascular response during prior exercise testing. When pulse rhythm irregularities, e.g., suggesting premature beats, are detected during pulse counting, patients should have an ECG rhythm strip recorded; in many programs this is readily accomplished by using the defibrillator paddles as ECG leads.

Although continuous training is more effective in increasing endurance, interval training is more appropriate for the cardiac patient to avoid the imposition of an excessive oxygen debt. Interval training may involve alternating periods of activity and rest, or, more typically, alternating periods of high- and lowintensity activity. Often program design alternates activities which primarily effect leg training with those which selectively involve arm muscles. An additional advantage of interval training for the cardiac patient is that it permits a greater total workload to be imposed per exercise session before the appearance of activitylimiting symptoms, particularly angina pectoris.

Aerobic games, as an optional recreational component – volleyball, basketball, tennis, handball, etc. – add variety and interest to an exercise program and encourage adherence. They offer the added advantage of providing upper body (arm and torso) exercise. However, variations in skill and in the degree of excitement and competitiveness can significantly vary the oxygen cost of these activities.

# PATIENT EDUCATION

Patients must be taught to identify an inappropriate symptomatic response to exercise - chest pain, palpitations, undue breathlessness or fatigue, etc. - and to report these to the exercise supervisor. They should also have been carefully instructed why they should not exercise during an intercurrent illness, when unusually fatigued or under excessive stress, etc. Patients returning to an exercise regimen after a hiatus of several days to weeks (because of illness or other reasons) should be cautioned to begin activity at a lesser intensity and gradually progress to higher levels of exercise. The over-competitive individual should be repeatedly cautioned to avoid excessive physical activity levels; and increased or more prolonged supervision and guidance may be needed for these patients.

# COOL-DOWN

The cool-down final 5-10 minutes is a gradual decrease in exercise intensity. It allows the heart rate to subside slowly and averts the post-exercise hypotension attendant upon sudden cessation of activity when maximum peripheral vasodilatation is still present, with resultant pooling of blood in the legs. The exercise heat load can be gradually dissipated.

Post-exercise showering should be with lukewarm water, avoiding the extremes of temperature which may produce undue peripheral vasoconstriction or vasodilation.

# SAFETY FEATURES

Recommendations for exercise programs for cardiac patients define the need for trained personnel and appropriate equipment for emergency cardiac care, including cardiopulmonary resuscitation (21). Not uncommonly, electrical "death" (i.e., ventricular fibrillation) can be reversed without the occurrence of myocardial infarction.

In a 1978 survey of cardiovascular complications of medically supervised exercise training programs for cardiac patients, encompassing about 1.6 million exercise hours, there was one cardiac arrest per 33,000 patient hours and one myocardial infarction per 233,000 patients hours. The fatal complication rate was one death per 116,000 patient hours of participation in the early years and one death per 212,000 patient hours in recent years. Although complication rates were lower in exercise programs with continuous ECG monitoring, it is not known whether the monitoring per se or the closer medical supervision was the determinant (22). Continuous ECG monitoring is not feasible on a long-term basis and may engender undue dependence of the patient on this type of supervision for activity.

# LONG-TERM PHYSICAL ACTIVITY

Since fitness is not "stored", continued regular physical activity is necessary to maintain it. But for physical activity to become a lifetime pattern, it must be enjoyable to the patient. Therefore, patients leaving a more formal supervised exercise program require counsetling about long-term activities, particularly patients with a prior sedentary lifestyle who have never explored their activity likes and dislikes. This may, in part, explain the improved adherence among patients with a prior history of habitual exercise. For example, the initial walk-run-jog sequences can be replaced by bicycle riding, swimming, aerobic dancing, and a number of other endurance sport activities of comparable metabolic cost.

Both for patients continuing in supervised group exercise programs and for those exercising individually, serial assessment is needed at 3- to 6-month intervals. Coronary patients in an exercise training program require this serial exercise stress testing to see whether, indeed, the desired training effect has been achieved in that they can perform more work before the onset of signs or symptoms of myocardial ischemia. The exercise testing can document performance changes and permit the revision of the exercise prescription to increase the target heart rate and incorporate training activities of greater intensity. Serial testing may also help define the need for revision of presciption of antianginal, antiarrhythmic, or antihypertensive medications.

With adequate adherence to an appropriately designed exercise regimen, if a training effect is not documented and patients do not improve their functional status, careful reevaluation of the patient is required to assess the need for additional diagnostic procedures which would lead to additional subsequent medical or surgical therapy or both. This is because not all patients can improve their cardiac function, even when their selection for exercise training appears appropriate and when they have been enrolled in and have adhered to a suitably designed exercise training regimen. Lack of functional improvement may relate to the development of left ventricular dysfunction or even overt cardiac failure with higher levels of exercise; alternatively, during a more prolonged period of training, there may be progression of the underlying coronary atherosclerotic heart disease (23).

Interestingly, the desire for health maintenance and the fear of incapacitation seem equal as motivating factors for adherence to an exercise regimen. A positive attitude of the spouse and family toward exercise favorably affects adherence, as do increased severity of the illness, evidence of prior adequate coping capacity with illness and stress, and higher educational and social class levels. Feedback to the patient regarding progress, i.e., functional improvement, via serial reports also helps sustain the patient's motivation. The improvement in function and maintenance of that improvement, documented by serial exercise testing, is an important motivational force in continued adherence to exercise regimens. The ultimate goal of long-term physical activity should emphasize reasonable independence of the patient in exercising - thus mandating a weaning initially from the monitored setting and subsequently from the ritualization of the more formal exercise training programs, and progressive involvement in an exercise setting that is social, pleasurable, convenient, and appropriate.

# THE "TRAINING EFFECT"

Exercise training in coronary patients, with and without angina pectoris, and after myocardial infarction can increase the maximal oxygen uptake as much as 20 percent. In one study, the improvement in exercise capacity of patients with angina pectoris was comparable to that obtained by giving untrained patients with angina sublingual nitroglycerin prior to exercise (24).

The goal of prescriptive physical activity is an improvement in cardiovascular function, designated the "training effect." (25-29) Current data suggest primarily a peripheral mechanism, related to a decrease in the heart rate and systolic blood pressure response to any given level of submaximal work. The "training effect" to be anticipated from cardiac conditioning exercises includes a decrease in the resting heart rate and systolic blood pressure, and a lesser increase in heart rate and systolic blood pressure for any level of submaximal work. Because these two components, the heart rate and the systolic blood pressure, the so-called "rate-pressure product" or "double product," are major determinants of myocardial oxygen demand, it is not unexpected that the trained individual will experience less or no angina pectoris and demonstrate less or no ischemic electrocardiographic changes at any level of submaximal

work. Training thus reduces the myocardial oxygen demand for any given body oxygen demand. However, as the patient continues to exercise at progressive work increments and finally achieves the "double product" at which chest pain and ischemic ECG changes previously occurred, they will again appear; but they now occur only at a greater work intensity. Thus, in the performance of usual daily activities, the trained individual manifests a lower heart rate and blood pressure response for any submaximal workload, and both functions farther from the ischemic threshold and perceives a lesser intensity of exertion for a given task because of its lesser percent of the now increased physical work capacity, described as increased "stamina" or "endurance."

Peripheral oxygen extraction by working muscle is improved as a result of training, in addition to the improved redistribution of cardiac output with exercise, further decreasing the demand for oxygen transport. This increase in oxygen extraction by skeletal muscle, coupled with increased vagal tone, lessened catecholamine release, and a number of other factors may decrease the double product and other determinants of myocardial oxygen demand by as much as 18 percent (30). There is currently little evidence that exercise training improves intrinsic myocardial performance, especially in the older individual with significant coronary disease, although this aspect remains controversial (31). Exercise training of some patients with symptomatic coronary disease has been shown to increase the resting and exercise end diastolic volume and stroke volume; at maximum levels of exercise, despite the increase in heart rate, blood pressure, and end diastolic volume (increased myocardial oxygen demand), the ejection fraction did not fall. The mechanism remains unclear in that no appreciable changes were evident at coronary angiography in major coronary vessels or collateral vessels (32). It has also been suggested that long-term, high-intensity training may effect an improvement in myocardial contractility, in contrast to the short-term occurrence of peripheral changes (33). Long-term high-intensity training, feasible only in a select subset of patients with symptomatic coronary disease, may be needed to assess whether training improves maximum cardiac output and myocardial oxygenation. The reported occurrence of angina only at a higher double product or triple product than prior to training (26, 34) is not well understood but may reflect an improvement in myocardial oxygen supply or utilization, or changes in myocardial oxygen demand not accounted for by the rate-pressure product.

Training can be accomplished in the patient receiving concomitant drug therapy, (7, 35, 36) and thus therapy can often improve the ability to exercise. Nitroglycerin and longer-acting nitrate drugs, for example, can improve coronary blood flow, alter venous return, improve wall function and thereby increase the ejection fraction. An increase in exercise capacity of about one met is not unusual after the administration of nitrate drugs. As training progresses, the need for nitrate drugs may be decreased. Despite the decrease in heart rate and blood pressure occasioned by the beta adrenergic blocking drugs, exercise training of patients receiving these agents has been demonstrated to increase physical work capacity.

#### APPROPRIATE AND INAPPROPRIATE EXPECTATIONS FROM CARDIAC CONDITIONING EXERCISES

The major beneficial effect of exercise training is the improvement in functional capacity. This occurs in patients with angina pectoris, after myocardial infarction, and after coronary bypass surgery. The hemodynamic determinants include an increase in the maximal cardiac output and oxygen consumption, a decrease in the resting heart rate and a lesser increase in heart rate and systolic blood pressure for any level of submaximal work, and the more rapid return to normal of the exercise heart rate. Thus, for any given level of exercise in the trained individual, myocardial oxygen requirements are less, enabling an improved intensity and duration of work capacity and a reduction in chest pain by increasing the exercise threshold for angina (37).

There is currently no evidence that exercise training alters the coronary artery lesions as assessed by angiography or increases the coronary collateral circulation in man (38), at least not a collateral circulation of a magnitude sufficient to be detected anglographically (39-41). When a change in the collateral circulation is documented at angiography subsequent to training, it appears only when there is progression of the underlying coronary atherosclerotic heart disease. Initially, the concern was appropriately raised that angiography documents only coronary anatomy and would not reflect an increase in flow through existing collateral vessels. However, radionuclide studies confirm the absence of increased myocardial perfusion related to exercise training (42). Left ventricular performance, as assessed by ventriculography and hemodynamic response to exercise, also appears unchanged (41).

Thus the improvement in functional capacity after exercise training is apparently primarily a peripheral effect; the decrease in the heart rate and blood pressure response, and thus in myocardial oxygen demand, previously described for any given level of submaximal work. As previously noted, whether improvement occurs in myocardial performance remains controversial (43), particularly in the patient with significant coronary arterial obstruction; as does the question of whether exercise training alters the electrical stability of the heart and thus the incidence of life-threatening abnormalities of cardiac rhythm. Catecholamine release, in addition to augmenting myocardial oxygen demand, may produce electrical instability in ischemic myocardium (44). In normal individuals, the plasma catecholamine response to exercise decreases with training (45). However, with continued training, the exercise heart rate continues to decrease even after the catecholamine response has plateaued, suggesting an additional component responsible for the reduced exercise heart rate (46). To what extent this occurs in patients with symptomatic coronary disease and whether it alters ventricular

ectopy or more serious ventricular dysrhythmias remains to be determined.

Most important, there are no data as to whether exercise training alters the natural history of coronary atherosclerotic heart disease - either longevity or the occurrence or recurrence of myocardial infarction and the incidence of coronary death. The results of a number of randomized clinical trials, attempting to define this feature, have been inconclusive, primarily related to the high incidence of drop-outs among the patients randomized to exercise therapy, and, more recently, to the high incidence of "drop-ins," i.e., patients in the control group exercising regularly although not in a formal exercise training program (47-51). An additional problem is that patients involved in postinfarction exercise trials, individuals who are candidates for physical activity training, constitute a pre-selected subgroup with an improved functional status and probably less extensive coronary disease and/or myocardial dysfunction. Current studies have not defined whether exercise training alters myocardial ischemia or myocardial function; the use of newer radionuclide techniques may permit this type of evaluation. Animal studies, particularly exercise training studies in young or immature animals, suggest that long-term physical activity may favorably affect myocardial mitochondrial function and myocardial metabolism, increase coronary vascularity even disproportionate to the the myocardial hypertrophy and thus improve myocardial perfusion and function; whether this occurs in man, and particularly in older individuals with significant coronary atherosclerosis, remains speculative. However, a recent multifactorial intervention trial after myocardial infarction showed a reduction, particularly in sudden death and during the initial six months after infarction, in association with an exercise program, guality medical care, and intensive patient education (52).

With exercise training, serum triglyceride levels decrease (53), but the effect on total serum cholesterol is unpredictable. A modest decrease in total cholesterol level usually accompanies weight loss. The highdensity lipoprotein cholesterol component appears increased in physically active individuals (54-59). Whether exercise training predictably alters the ratio of high- to low-density lipoproteins remains unknown (60-62). The increase in lipoprotein lipase with activity may be the mechanism effecting the lowering of triglyceride levels and the increase in HDL (63). The effect of exercise training on fibrinolysis is uncertain; augmentation of fibrinolysis in response to venous occlusion has been shown to occur with moderate physical activity (64). Catecholamine levels appear to decrease.

Exercise training may affect coronary disease by modification of other and more powerful coronary risk factors (65, 66); patients who exercise often decrease or discontinue cigarette smoking, weight reduction or weight control is improved, there is an increased health consciousness which may alter diet and encourage blood pressure control, when appropriate, etc.

Additional beneficial effects of physical activity

are psychosocial. Patients who exercise tend to feel better; have an improvement in self-confidence and self-esteem; show less anxiety, depression, denial, and dependency on standard psychometric tests; and appear better able to tolerate life crises. They tend to participate increasingly in leisure activities and, in some studies, have better work attendance. Emphasis on the importance of psychosocial features derives from the finding that more patients after myocardial infarction, as well as after coronary bypass surgery, are disabled by psychological than by the physiologic features.

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# REFERENCES

- 1. Frick MH, and Katila M: Hemodynamic consequences of physical training after myocardial infarction. Circulation 37: 192, 1968.
- 2. Clausen JP, Larsen OH, and Trap-Jensen J: Physical training in the management of coronary artery disease. Circulation 40: 143, 1969.
- Committee on Exercise, American Heart Association: Exercise Testing and Training of Individuals with Heart Disease or at High Risk for Its Development: A Handbook for Physicians. American Heart Association, New York, 70-008-B, 1975.
- 4. American College of Sports Medicine. Guidelines for Graded Exercise Testing and Exercise Prescription, Lea and Febiger, Philadelphia, 1975.
- 5. Mitchell JH: Exercise training in the treatment of coronary heart disease. Adv Intern Med 20: 249, 1975.
- Fox SM III, Naughton JP, and Gorman PA: Physical activity and cardiovascular health: I. Potential for prevention of coronary heart disease and possible mechanisms; II. The exercise prescription: Intensity and duration; III. The exercise prescription: Frequency and type of activity. Mod Concepts Cardiovasc Dis 41: 17, 1972.
- Jorgensen CR, Wang K, Wang Y, Gobel FL, Nelson RR, and Taylor H: Effects of propranolol on myocardial oxygen consumption and its hemodynamic correlates during upright exercise. Circulation 48: 1173, 1973.
- 8. Hellerstein HK, Hirsch EZ, Ader R, Grenblott N, and Siegel M: Principles of exercise prescription for normal and cardiac subjects. In Naughton JP, Hellerstein HK, and Mohler IC (eds): Exercise Testing and Exercise Training in Coronary Heart Disease, Academic Press, New York, 1973, p. 129.
- 9. Pollock M, Gettman L, Milesis C, Bah MD, Durstine L, and Johnson RB: Effects of frequency and duration of training on attrition and incidence of injury. Med Sci Sports 9: 31, 1977.
- Naughton J: Exercise and myocardial infarction: The national exercise and heart disease project: An overview. Proceedings of the Workshop or Physical Conditioning and Rehabilitation, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, In Press.
- Flessas AP, Connelly GP, Handa S, Tilney CR, Kloster CK, Rimmer RH Jr, Keefe JF, Klein MD, and Ryan TJ: Effects of isometric exercise on the end-diastolic pressure, volumes and function of the left ventricle in man. Circulation 53: 839, 1976.
- 12. Atkins JM, Matthews OA, Blomqvist CG and Mullins CB:

Incidence of arrhythmias induced by isometric and dynamic exercise. Br Heart J 38: 465, 1976.

- Morganroth J, Baron BJ, Henry WL, and Epstein SE: Comparative left ventricular dimension in trained athletes. Ann Intern Med 82: 521, 1975.
- 14. Ehsani AA, Hagberg JM, and Hickson RC: Rapid changes in left ventricular dimensions and mass in response to physical conditioning and deconditioning. Am J Cardiol 42: 52, 1978.
- DeMaria AN, Neumann A, Lee G, Fowler W, and Mason DT: Alterations in ventricular mass and performance induced by exercise training in men evaluated by echocardiography. Circulation 57: 237, 1978.
- 16. Clausen JP, Klausen K, Rasmussen B, and Trap Jensen J: Central and peripheral circulatory changes after training of the arms or legs. Am J Physiol 225: 675, 1973.
- 17. Schwade J, Blomqvist CG, and Shapiro W: A comparison of the response to arm and leg work in patients with ischemic heart disease. Am Heart J 94: 203, 1977.
- Haskell WL: Design and implementation of cardiac conditioning programs. In Wenger NK, and Hellerstein (eds): Rehabilitation of the Coronary Patient, John Wiley & Sons, New York, 1978.
- Bruce EH, Frederick R, Bruce RA and Fisher FD: Comparison of active participants and dropouts in CAPRI cardiopulmonary rehabilitation programs. Am J Cardiol 37: 53, 1976.
- Stoedefalke KG: The principles of conducting exercise programs. In Naughton JP, Hellerstein HK, and Mohler IC (eds): Exercise Testing and Exercise Training in Coronary Heart Disease, Academic Press, New York, 1973, p. 299.
- 21. The Exercise Standards Book, American Heart Association, 70-041-A, Dallas, Texas, 1979.
- Haskell WL: Cardiovascular complications during exercise training of cardiac patients. Circulation 57: 920, 1978.
- Bruce RA, Kusumi F, and Frederick R: Differences in cardiac function with prolonged physical training for cardiac rehabilitation. Am J Cardiol 40: 597, 1977.
- 24. Clausen JP, and Trap-Jensen J: Heart rate and arterial blood pressure during exercise in patients with angina . pectoris. Circulation 53: 436, 1976.
- Detry J-M R, Rousseau M, Vandenbroucke G, Kusumi F, Increased arteriovenous oxygen difference after physical training in coronary heart disease. Circulation 44: 109, 1971.
- Redwood DR, Rosing DR, and Epstein SE: Circulatory and symptomatic effects of physical training in patients with coronary artery disease and angina pectoris. N Engl J Med 286: 459, 1972.
- 27. Kentala E: Physical fitness and feasibility of physical rehabilitation after myocardial infarction in men of working age. Ann Clin Res (Suppl 91), 1972, p. 1.
- Rousseau MF, Brasseur LA, and Detry J-M: Hemodynamic determinants of maximal oxygen intake in patients with healed myocardial infarction. Influence of physical training: Circulation 48: 943, 1973.
- Detry J-M R, Rousseau M, and Brasseur LA: Early hemodynamic adaptations to physical training in patients with healed myocardial infarction. Eur J Cardiol 2/3: 307, 1975.
- Clausen JP: Circulatory adjustments to dynamic exercise and effect of physical training in normal subjects and in patients with coronary artery disease. Prog Cardiovasc Dis 18: 459, 1976.
- Saltin B: The interplay between peripheral and central factors in the adaptive response to exercise and training. Ann NY Acad Sci 301: 224, 1977.

- Wallace A, Reryeh S, Jones R, and Goodrich J: Effects of exercise training on ventricular function in coronary disease. Circulation 57: 197 (Suppl II), 1978.
- Paterson DH, Shephard RJ, Cunningham D, Jones NL, and Andrew G: Effects of physical training on cardiovascular function following myocardial infarction. J Appl Physiol 47: 482, 1979.
- Sim DN, and Neill WA: Investigation of the physiological basis for increased exercise threshold for angina pectoris after physical conditioning. J Clin Inves 54: 763, 1974.
- 35. Lester RM, and Wallace AG: Cardiovascular adaptations to beta-adrenergic blockade during physical training (abstract). Circulation 57-58 (suppl II): 140, 1978.
- 36. Welton DE, Squires WG, Hartung GH, and Miller RR: Effects of chronic beta adrenergic blockade therapy on exercise training in patients with coronary heart disease (abstract). Am J Cardiol 43: 399, 1979.
- 37. Ferguson RJ, Cote P, Gauthier P, and Bourassa MG: Changes in exercise coronary sinus blood flow with training in patients with angina pectoris. Circulation 58: 41, 1978.
- Cohen, MV, Yipintsoi, T, Malhotra, A, and Scheuer J: Effects of exercise on coronary collateral function. Am J Cardiol 39: 362, 1977.
- 39. Ferguson RJ, Petitclerc R, Choquette G, Chaniotis L, Gauthier P: Effect of physical training on treadmill exercise capacity, collateral circulation, and progression of coronary disease. Am J Cardiol 34: 764, 1974.
- 40. Conner JF: Effects of exercise on coronary collateralization and angiographic studies of six patients in a supervised exercise program. Med Sci Sports 8: 145, 1976.
- Kennedy CC, Spiekerman RE, Linsay MI Jr, Mankin HT, Frye RL: One-year graduated exercise program for men with angina pectoris. Mayo Clin Proc 51: 231, 1976.
- Nolewajka AJ, Kostuk WJ, Rechnitzer, PA, and Cunningham DA: Exercise and human collaterization: An angiographic and scintigraphic assessment. Circulation 60: 114, 1979.
- Letac B, Cribier A, and Desplanches JF: A study of left ventricular function in coronary patients before and after physical training. Circulation 56: 375, 1977.
- Wit AL, and Bigger JT Jr: Possible electrophysiological mechanisms for lethal arrhythmias accompanying myocardial ischemia and infarction. Circulation 52 (suppl III): 96, 1975.
- Hartley HL, Mason JW, Hogan RP, Kotchen TA, Mougey EH: Multiple hormonal responses to graded exercise in relation to physical training. J Appl Physiol 33: 602, 1972.
- 46. Winder WW, Hagberg JM, Hickson RC, and McLane JA: Time course of sympathoadrenal adaptation to endurance exercise training in man. J Appl Physiol 45: 370, 1978.
- 47. Kentala E: Physical fitness and feaibility of physical rehabilitation after myocardial infarction in men of working age. Ann Clin Res (Suppl 91), 1972, p. 1.
- Rechnitzer PA, Picaird HA, Paivio AV, Yuhasz MS, and Cunningham D: Long term follow-up study of survival and recurrence rates following myocardial infarction in exercising and control subjects. Circulation 45: 853, 1972.
- 49. Wilhelmsen L, Sanne H, Elmfeldt D, Tibbins G, and Wedel H: A controlled trial of physical training after myocardial infarction: Effects on risk factors, nonfatal reinfarction, and death. Prev Med 4: 491, 1975.
- 50. Palatsi I: Feasibility of physical training after myocardial infarction and its effect on return to work, morbidity, and mortality. Acta Med Scand Suppl. 599-602, 1976, p. 1.
- 51. Selvester R,Camp J, and Sanmarco M: Effects of exercise training on progression of documented coronary

atherosclerosis. In Mulvey P (ed): The Marathon: Physiological, Medicał, Epidemiological, and Psychological Studies, New York Academy of Sciences, 1977, p. 495.

- 52. Kallio V, Hamalainen H, Hakkila J, and Luurila O: Reduction in sudden deaths by a multifactoral intervention programme after acute myocardial infarction. Lancet 2: 1091, 1979.
- 53. Oscai LB, Patterson JA, Bogard KL, Beck RJ, and Rothermel BL: Normalization of serum triglycerides and lipoprotein electrophoretic patterns by exercise. Am J Cardiol 30: 775, 1972.
- 54. Enger SC, Herbjornsen K, Erikkssen J, and Fretland A: High density lipoproteins (HDL) and physical activity: The influence of physical exercise, age and smoking on HDL-cholesterol and the HDL-total cholesterol ratio. Scand J Clin Lab Invest 37: 251, 1977.
- 55. Lampman RM, Santinga JT, Hodge MF, Block WD, Flora JD, and Bassett DR: Comparative effects of physical training and diet in normalizing serum lipids in men with type IV hyperlipoproteinemia. Circulation 55: 4, 1977.
- Lehtonen A, and Viikari J: The effect of vigorous physical activity at work on serum lipids with special reference to serum high-density lipoprotein cholesterol. Acta Physiol Scand 104: 117, 1978.
- 57. Williams P, Robinson D, and Bailey A: High-density lipoprotein and coronary risk factors in normal men. Lancet 1: 72, 1979.
- 58. Wood PD, Haskell WL, Stern MP, Lewis S, and Perry C:

Plasma lipoprotein distribution in male and female runners. Ann NY Acad Sci 301: 748, 1977.

- 59. Wood PD, and Haskell WL: The effect of exercise on plasma high-density lipoprotein. Lipids 14: 417, 1979.
- 60. Lopez SA, Vial R, Balart L, and Arroyave G: Effect of exercise and physical fitness on serum lipids and lipoproteins. Atherosclerosis 20: 1, 1974.
- 61. Ratliff R, Elliott C, and Rubenstein C: Plasma lipid and lipoprotein changes with chronic training. Med Sci Sports 10: 55, 1978.
- 62. Melish J, Bronstein D, Cross R, Dann D, White J, Hunt H, and Brown V: Effect of exercise training on type II hyperlipoproteinemia. Circulation (abstract) 58: 38, 1978.
- Nikkila EA, Taskinen M-R, Rehunen S, and Harkonen M: Lipoprotein lipase activity in adipose tissue and skeletal muscle of runners: Relation to serum lipoproteins. Metabolism 27: 1661, 1978.
- 64. Williams RS, Logue EE, Lewis JL, Barton T, Stead NW, Wallace AG, and Pizzo SV: Physical conditioning augments the fibrinolytic response to venous occlusion in healthy adults. N Engl J Med 302: 987, 1980.
- 65. Mann GV, Garrett HL, Farhi A, Murray H, and Billings FT: Exercise to prevent coronary heart disease. An experimental study of the effects of training on risk factors for coronary disease in men. Am J Med 46: 12, 1969.
- 66. Bonanno JA, and Lies JA: Effects of physical training on coronary risk factors. Am J Cardiol 33: 760, 1974.