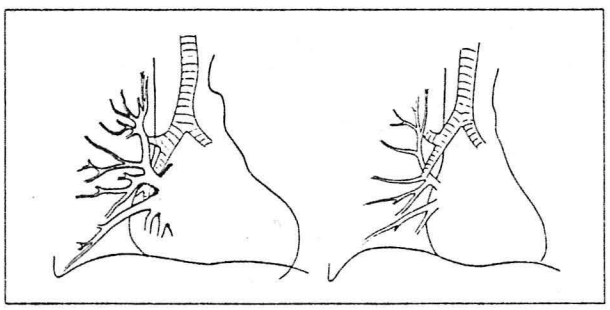
MEDICAL GRAND ROUNDS

NOVEMBER 8, 1979



ATHLETE'S HEART

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Athlete's heart or the athletic heart syndrome are vague empirical terms which denote a condition of considerable physiological and clinical interest. The syndrome is important to the physiologist because it represents a successful adaptation to extreme physiological demands and to the clinician because the adaptive changes may at times simulate heart disease.

The 19th century definition of athlete's heart was heart disease with cardiomegaly and chronic failure, caused solely by an excessive amount of physical activity. This concept was widely accepted well into the 1940's but reports introducing the current view that the enlarged heart of the athlete is an appropriate physiological adaptation had actually appeared at the turn of the century. The first paper clearly associating the cardiomegaly in athletes with superior function was published by Henschen in 1899. He examined (by percussion) the participants in a 60-mile cross-country ski race and noted that the most successful skiers also had the largest hearts. Radiological examination of the participants in the 1928 Olympic games (Herxheimer, 1929) confirmed and extended Henschen's findings. Large-scale British studies during the 1930's (reviewed by Jokl and Jokl, 1977) demonstrated that heart disease attributable exclusively to athletic training and participation was extremely rare if it existed at all.

More recent British epidemiological studies (Morris et al., 1953) on the relationship between physical activity and coronary disease provided a stimulus that completely reversed the original concept of athlete's heart and eventually produced a fringe movement (Bassler, 1977) that claims that marathon running confers absolute immunity against lethal coronary disease.

The adaptation to habitually high levels of physical acitvity involves multiple organ and organ systems. The effects on the heart must be considered in the context of the changes that are induced in the peripheral vasculature, skeletal muscle, in autonomic and hormonal regulatory processes and in metabolic activity. Aspects of the extra-cardiac consequences of physical activity will therefore be included in this presentation.

Human performance capacity has multiple determinants. The ability to perform any physical task is a function of (a) the capacity of the various aerobic and anaerobic mechanism for transformation of chemical energy to mechanical work, and, (b) the ability to activate and control these mechanism. Performance capacity has a significant (Figure 1) genetic component (Klissouras, 1971; Komi et al., 1977). Age and habitual level of physical activity are the most important of many physiological modifiers.

Clinical exercise physiology for the internist and cardiologist primarily deals with aerobic exercise and the mechanisms that are involved in oxygen

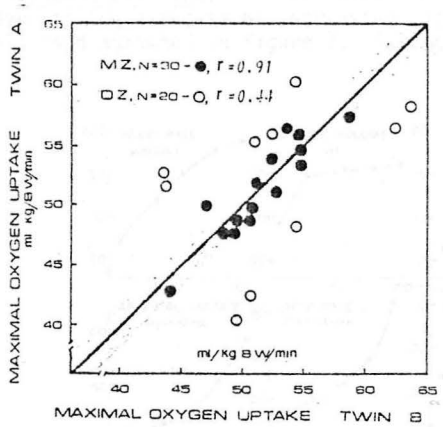


Figure 1. Genetic contribution to performance capacity. Maximal oxygen uptake in pairs of monozygotic (MZ) and dizygotic (DZ) twins. The shaded area represents the magnitude of the error of measurement. Measurement of maximal heart rate produced similar MZ and DZ distributions with linear correlation coefficients of 0.90 and 0.48. (Klissouras, 1971).

transport and utilization. Dynamic or isotonic exercise is defined as activity associated with changes in muscle length with little change in tension. The energy requirements of dynamic exercise that lasts for at least a few minutes and activates large muscle groups, e.g. various forms of locomotion, can only be covered by aerobic metabolism. This mode of exercise has the potential of imposing a greater load on the cardiovascular system than any other stimulus associated with normal daily life activities and is particularly likely to precipitate symptoms in patients with heart disease. It is also the mode upon which most clinical exercise tests and therapeutic training programs are based.

Isometric or static exercise during which there is tension development with little change in muscle length, is also included in many physical tasks. Muscle blood flow is compromised even at relatively low intensities of isometric work and anaerobic glycolysis is the primary source of energy.

ACUTE HEMODYNAMIC AND METABOLIC RESPONSES TO EXERCISE

The acute hemodynamic and metabolic responses to common forms of dynamic and static exercise (Mitchell and Blomqvist, 1979) are distinctly different. Large muscle dynamic exercise of increasing intensity produces a marked increase in cardiac output and a fall in peripheral resistance. Most of the energy is derived from aerobic metabolisms. Isometric exercise is associated with a pressor response with elevation of systolic, diastolic, and mean arterial pressure. The blood pressure elevation is more clearly related to the intensity of the effort than to the magnitude of the active muscle mass. The pressor response is normally produced by modest increase in cardiac output with little or no change in peripheral resistance.

Dynamic exercise. The principal features of the normal human response to dynamic leg exercise of increasing intensity up to and including maximal levels is diagrammed in Figure 2. (Blomqvist, 1978).

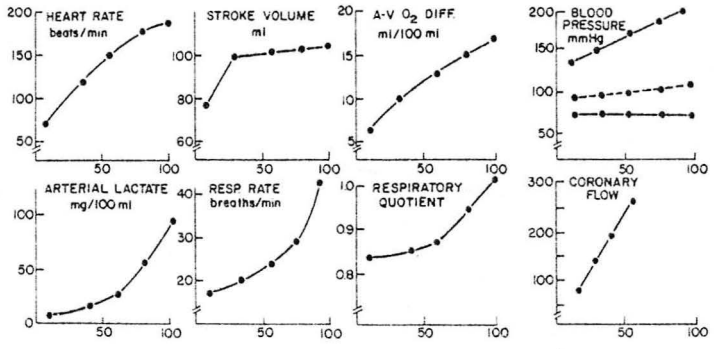


Figure 2. Principal features of cardiovascular, respiratory, and metabolic responses to dynamic leg exercise in the upright. Data points represent sitting rest, three levels of submaximal exercise, and maximal exercise. Values are plotted against relative load, i.e., actual oxygen uptake as percentage of maximal oxygen uptake. Blood pressure data represent systolic, mean, and diastolic brachial artery pressures. Coronary flow measurements are given as milliliters per minute per 100 g cardiac muscle. (Based on data of Saltin et al., 1968; Holmberg et al., 1971; and Nelson et al., 1974).

Transition from sitting rest to maximal exercise in young normal subjects causes a 10-fold increase in metabolic rate i.e., an increase in oxygen uptake from 0.3 to 3 liters/min. The increased peripheral oxygen demand is partially met by a progressive increase in heart rate from 70 to about 190 beats/min. and in stroke volume from 75 to about 105 ml, a 4-fold increase in cardiac output to about 20 liters/min. The remainder of the oxygen demand is met by redistribution of blood flow and increased extraction by active tissues, primarily skeletal muscle. As a result, the total body A-V O_2 difference increases by a factor of about 2.5. Systolic arterial pressure increase linearly and steeply whereas there is little change in diastolic pressure and only a small increase in mean arterial pressure. Pulmonary arterial pressures show a proportionately larger increase during exercise than the systemic pressures which means that there is a less prominent reduction in pulmonary than in systemic vascular resistance (Ekelund and Holmgren, 1967). Coronary flow also tends to increase linearly during exercise and approximates (measured in ml/100g myocardium) the product of heart rate and systolic blood pressure X 10^{-2} (Holmberg et al, 1971; Nelson et al., 1974).

The mechanisms responsible for the maintenance and increase in stroke volume during exercise, particularly the role of the Frank-Starling mechanism in normal man, has been a matter of controversy. Hemodynamic studies have shown that left-sided filling pressures (Fig. 3) increase to about twice the resting level (Ekelund and Holmgren, 1967; Thadani and Parker, 1978). However, right ventricular filling pressure remain constant or fall slightly during exercise in young subjects and increase only in older men (Granath et al., 1964). These data probably underestimate the changes in effective right and left end-diastolic pressures which are likely to increase significantly. Mean pleural and intrathoracic pressure falls during exercise and is likely to equal -10 mm/Hg at maximal levels (unpublished data, Johnson, R.L., Jr.). This gradient should be added to the conventional measurements (where atmospheric pressure is taken as 0) to obtain the physiologically relevant filling pressure.

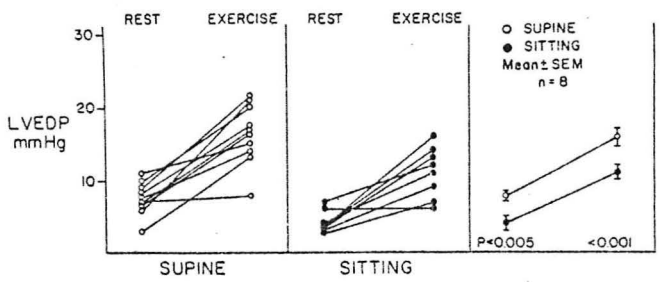


FIGURE 3. Individual and group mean values of left ventricular end-diastolic pressure (LVEDP) in the supine and sitting positions at rest and during exercise. Left ventricular end-diastolic pressure in the sitting position was recorded in only eight subjects. (Thadani and Parker, 1978)

The combined results of recent studies based on echocardiographic and radionuclear imaging techniques (Stein et al., 1978; Crawford et al, 1979, Weiss et al, 1979; Rerych, 1979) have finally resolved the Starling question and indicate that an adequate stroke volume during exercise is achieved by a combination of an increase in preload end-diastolic volume and an increased contractile state with a more complete emptying, i.e. an increased ejection fraction and decreased end-systolic volume. Salient data from a recent study performed at this institution (Poliner et al., 1979) are presented in Fig. 4 There is no doubt that dynamic exercise presents a volume load to the left ventricle.

Respiratory rate and tidal volume increase during exercise to provide a ventilatory volume of about 120 liters/min. at the maximal level.

The metabolic adjustments during dynamic exercise are reflected by changes in RQ., i.e. the respiratory quotient or the volume ratio excreted CO_2/ consumed O_2. The quotient is primarily determined by substrate utilization. At rest and during exercise at low intensities approximately equal energy amounts are released from carbohydrates and fats and R.Q. approximates 0.8. The balance is shifted toward carbohydrates with increasing exercise intensities. The R.Q. is 1.0 during maximal exercise and reflects exclusive use of carbohydrates at this level.

There is a progressive rise in arterial lactate levels. Lactate is produced at submaximal exercise levels by the anaerobic metabolism that is required to cover the oxygen deficit that is incurred at the onset of exercise but there is also preferential anaerobic glycolysis in certain muscle fibers (Hermansen, 1976). Arterial pH is maintained at normal resting levels until a maximal or near-maximal work load level is reached. The large oxygen debt with high lactate levels that athletes can accumulate can cause pH-levels below 7.oo. Potassium is released from working muscle and arterial levels may exceed 6.o mEq/l (Saltin et al., 1968). Mechanisms involved in the potassium release and their physiological implications have recently been reviewed by Knochel (1979).

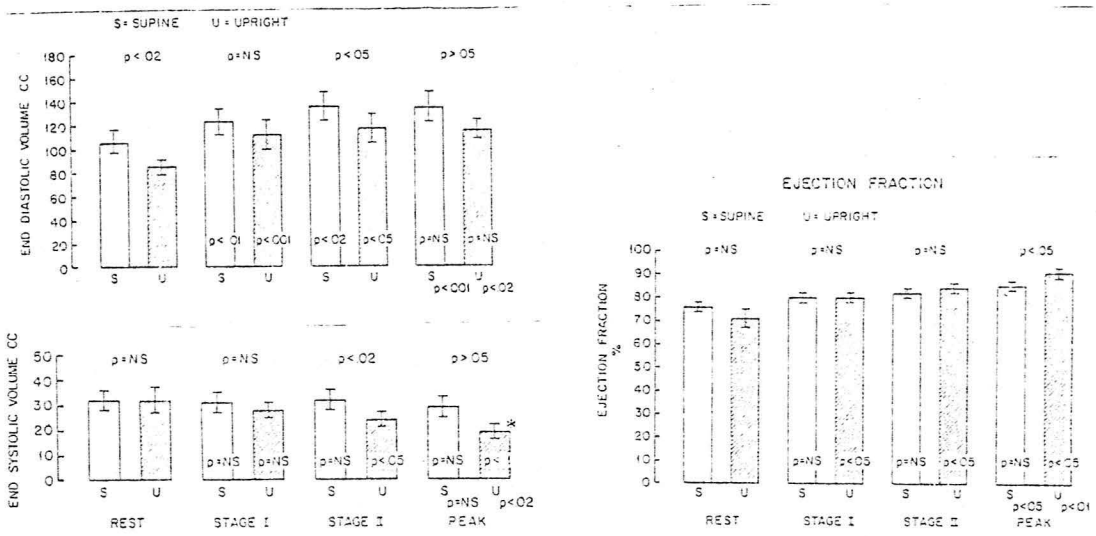


Figure 4. Left ventricular performance during upright and supine bicycle exercise in 7 young normal subjects studied by equilibrium radionuclide ventriculography. (Poliner et al., 1979).

Static exercise. The typical hemodynamic response to static exercise is illustrated in Fig. 5 and Table 1. The pressor response is associated with a small increase in left ventricular end-diastolic pressure and an enhanced contractile state. Table 1 also included data obtained during dynamic exercise with small muscle groups. Under these conditions, static and dynamic exercise produce similar hemodynamic effects. These results challenge the traditional concept that the mode of exercise, i.e. static vs. dynamic, is the primary determinant of the hemodynamic response but derive support from neurophysiological studies. Stimulation of receptors which have the capacity to sense motion - muscle spindles, receptors in joints, tendons, and ligaments - has little or no effect on the cardiovascular system. (Mitchell et al., 1977).

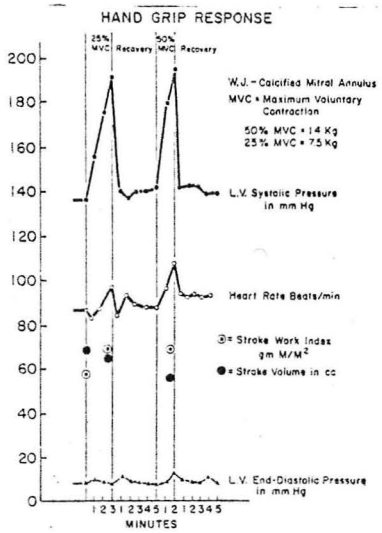


Figure 5. Hemodynamic response to static exercise (hand grip) in a subject with normal ventricular function. Loads correspond to 25 and 50% of a maximal voluntary contraction (MVC). From Mullins and Blomqvist, 1973.

Table 1. Cardiovascular Response to Isometric and Small-Muscle Dynamic Exercise

	$\dot{V}O_2$ (L/MIN)	$\dot{Q}$ (L/MIN)	HR (BEATS/MIN)	SBP MM	DBP Hg
REST	0.25 ± .02	5.6 ± .3	70 ± 5	112 ± 3	74 ± 2
1 HG, 25% MVC	0.34 ± .01	6.3 ± .5	79 ± 4	144 ± 3	100 ± 2
1 ARM CURL, 75%	0.44 ± .05	7.0 ± .7	82 ± 6	138 ± 5	100 ± 4
1 HG, 50% MVC	0.42 ± .05	7.2 ± .6	90 ± 4	154 ± 4	114 ± 4
1 ARM CURL, 100%	0.61 ± .05	7.9 ± .6	91 ± 4	154 ± 4	104 ± 4

HG = Handgrip MVC = Maximal Voluntary Contraction
n = 6 (Lewis et al., unpublished data).

FACTORS LIMITING PERFORMANCE CAPACITY

Oxygen transport and utilization. The principal links of the chain of mechanisms transferring oxygen from ambient air to the tissues are listed in Table 2 (Johnson, 1976). There is solid evidence from numerous longitudinal and cross-sectional studies that (except at high altitude) the lungs do not

Table 2. Principal steps in the Oxygen Transport Chain (Johnson 1976)

1. Ventilatory transport
2. Diffusion into blood
3. Chemical reaction with hemoglobin
4. Aortic transport (cardiac output x arterial O_2 capacity)
5. Distribution of cardiac output and diffusion to sites of tissue utilization.

Table 3 (Johnson, 1976).

Average Functional Capacities of the Heart and Lungs at Peak Exercise: Comparison of Normal College Students and Athletes of Similar Age and Height

	5 Male College Students			
	Control	After 3 Weeks Bed Rest	After 8 Weeks Training	6 Olympic Athletes
Max. voluntary ventilation (MVV) liters/min	191	201	197	219
Transfer coefficient for oxygen (D_{L-O_2}) (ml/min)/(mm Hg)	96	83	86	95
Lung capillary blood volume ($\dot{V}_c$) ml	140	141	206	241
Maximal cardiac output (Q_{max}) liters/min	20.0	14.8*	22.8*	30.4†
Stroke volume (SV) ml	104	74*	120*	167†
Lung capillary transit time (Δt) sec	0.42	0.57	0.54	0.48
Arteriovenous 0_2 difference (AV $\Delta 0_2$) vol%	16.2	16.5	17.1*	18.0
Blood 0_2 capacity (0_2cap) vol%	21.9	20.5	20.8	22.4
Ventilation at max. exercise ($\dot{V}_{Emax}$) liters/min	129	99*	156*	193†
Maximal oxygen uptake ($\dot{V}_{O_2max}$) liters/min	3.30	2.43*	3.91*	5.38†

*Significantly different from control $P < .05$.
†Significantly different from college students after training $P < .05$.

limit oxygen transport in normal subjects or in patients with cardiovascular disease. The tissue diffusing capacity which - according to Krogh's concept is a function of capillary density, metabolic rate, and the capillary-tissue O_2 pressure gradient - may be altered by training and age. However, it is doubtful that the classical model is applicable to skeletal muscle (Saltin et al., 1977) and variations are in any case not likely to be of sufficient magnitude to explain the large interindividual differences in maximal oxygen uptake that can be demonstrated in groups of normal subjects. Therefore, the mechanism limiting aeorbic work capacity is either cardiovascular oxygen transport or the capacity of the tissues, particularly skeletal muscle, to utilize oxygen. This concept is supported by the experimental data presented in Table 3. Various measurements that relate to the first 3 steps in the oxygen transport chain (Table 2) show no differences between athletes and non-athletic normal subjects. Large difference with respect to maximal oxygen uptake are paralleled by differences in cardiac output. However, it may be argued that cardiac output determined by the load of oxygen utilization rather than the reverse.

Physiology of skeletal muscle. The functional and metabolic characteristics of skeletal muscle have been studied extensively during the past decade. Links have been established between chemical and histochemical characteristics and physical performance capacity. Important changes relating to changing activity patterns have been described in detail (Burke et al., 1975; Holloszy and Booth, 1976; Saltin et al., 1977; Gollnick and Sembrowich, 1977).

Table 4. Characteristics of Skeletal Muscle in Sedentary Man

	Slow-Twitch(Red) ST	Fast-Twitch(White) FT_a	FT_b
Contractile Properties			
Myosin ATPase	+	+++	+++
Metabolic Potential			
Glycolysis	++	+++	++++
Oxidation	+++	++	+
Substrate Utilization			
Glycogen	++	++	++
Triglycerides	+++	+	+
Capillary Supply	+++	++	+
Fiber Size	++	+++	+

(Modified from Saltin, 1977)

Human skeletal muscle contains two basic fiber types that differ with respect to metabolism and contractility (Table 4). Slow-twitch (ST) or red fibers are rich in myoglobin and mitochondria and have high oxidative capacity. Their contractile response is slow, and they have low myofibrillar myosin ATPase activity. Fast-twitch (FT) or white fibers have a lower myoglobin content and fewer mitochondria. The contractile response is fast, and FT fibers have high myosin ATPase activity. There are - at least in sedentary man - two distinct subgroups of FT fibers that differ with respect to their metabolic properties (Table 4). The fiber types are distributed in a mosaic pattern (Figure 6).

The ratio of red fibers to white fibers in humans varies greatly from individual to individual. As would be expected because of the basic fiber

characteristics, the best athletes in endurance sports have a very high proportion of red fibers, whereas many athletes successful in sports requiring great speed and high-intensity work of short duration have mainly white fibers.

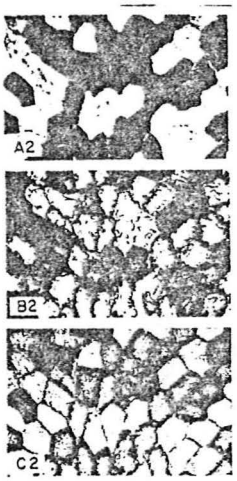


Figure 6. Serial cross sections of biopsy samples from the vastus lateralis muscle of man strained for myofibrillar ATPase (series A) to show ST (light) and FT (dark) fibers. Series B is stained for NADH-diaphorase activity to show oxidative enzymes, series C is an alpha-glycerophosphate stain for anaerobic activity.

(From Gollnick and Sembrowich, 1977).

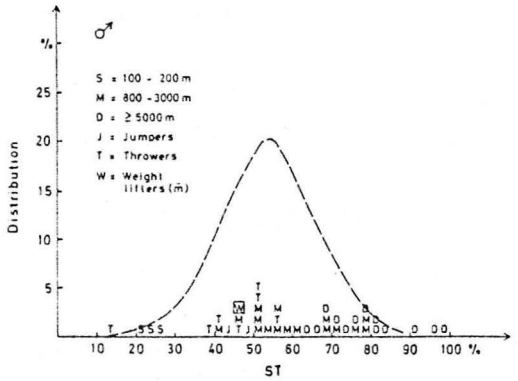
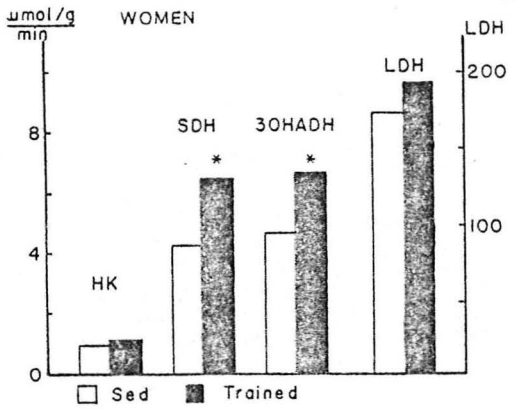


Figure 7. Percent slow-twitch(ST) fibers in a group of sedentary men (dashed curve) and in individual biopsies from successful athletes. From Saltin et al., 1977.

The differences between sprinters and long distance runners are particularly impressive (Fig. 7) whereas jumpers and throwers have a more balanced fiber composition. It is possible that in these events muscle mass and the ability to recruit instantaneously a majority of the fibers are more important factors than the fiber type. The distribution is genetically determined (Komi et al., 1977). The oxidative capacity of both red and white fibers can be greatly increased by physical training, but glycolytic capacity and contractile properties are not modified. Mitochondrial volume increases significantly (Fig. 8 and 9, from Gollnick and Sembrowich, 1977).

There are important differences between red and white fibers with respect to innervation. The two fiber types are recruited selectively during exercise. Red fibers are supplied by small neurons with a low threshold of activiation and are used preferentially during exercise of low intensity. White fibers are innervated by larger neurons with a high threshold, and they resist activation until exercise reaches high intensities. Both fiber types are active during very high intensities of exercise.



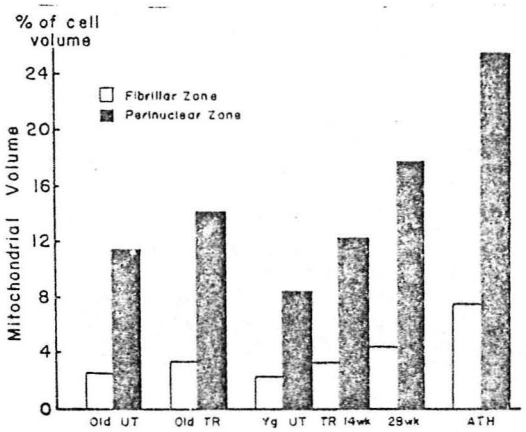


Figure 8. Hexokinase (HK), succinate dehydrogenase (SDH), beta hydroxy-acyl-CoA dehydrogenase (3OHADH) and lactate dehydrogenase (LDH) activities in the vastus lateralis muscle of a group of untrained and endurance trained women. Unpublished observations from Petersen, Rassmusen, Sembrowich and Gollnick, March 1976.

Figure 9. Mitochondrial volumes in the fibrillar and perinuclear zones of untrained and trained old men, young (yg) men before and after 14 and 28 weeks of training and top class athletes (Ath).

(From Gollnick and Sembrowich, 1977)

The presence of prominent adaptive changes in skeletal muscle has lent support to the hypotheses that (1) the peripheral training effects are primary and any changes affecting the central circulation are secondary, and, (2) the peripheral oxidative capacity is the main determinant of aerobic capacity (Kaiser, 1970). There is no doubt that local adaptations have significant effects on the systemic response to exercise. However, several lines of evidence support the traditional view that the cardiovascular oxygen transport capacity is the limiting mechanism during exercise with large muscle groups.

Quantitative estimates of the activities of various oxidative enzymes indicate that the potential of the total skeletal muscle mass to utilize oxygen exceeds the cardiovascular transport capacity (Gollnick and Sembrowich, 1977). Studies in middle-aged men have demonstrated that training may cause significant muscular enzymatic changes in the absence of any effects on maximal oxygen uptake (Orlander et al., 1977). Furthermore, an increased oxygen content of the ambient air produces - in the absence of significant changes in density and viscosity of the inhaled gas mixture - an oxygen uptake that is significantly higher than the maximum measured at sea level partial pressures (Fagreus et al., 1973). Maximal oxygen uptake may therefore in normal subjects and patients with cardiovascular disease be viewed as an index of cardiovascular functional capacity.

EFFECT OF PHYSICAL TRAINING

Maximal Oxygen Uptake. There is ample evidence (reviewed by Clausen 1975 and 1977 and by Scheuer and Tipton 1977) that dynamic exercise training programs of a duration of at least 4-6 weeks and based on exercise with large muscle groups will produce a significant increase in maximal oxygen uptake. The magnitude of improvement in normal subjects (Saltin, 1971) tends to be inversely proportional to capacity before training and to age (Figure 10). An inverse relationship between the degree of improvement and pre-training capacity has been established also for patients with coronary disease with and without angina pectoris (Detry et al., 1971 and 1973).

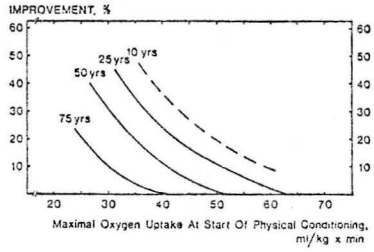


Figure 10. Relation between initial state of fitness and the magnitude of improvement in maximal oxygen uptake after training in different age groups. Data from 16 different studies, compiled by Grimby and Saltin. From Saltin, (1971).

Internationally successful athletes participating in endurance events generally have a maximal oxygen uptake exceeding 80 ml $\cdot$ Kg$^{-1}\cdot$min^{-1} compared to the 35 to 40 (with a standard deviation of about 5) found in young normal subjects. The development of a champion athlete clearly requires a combination of exceptional inborn characteristics and hard physical training.

Other determinants of the magnitude of the response to training than the pre-training functional state include the intensity, frequency, duration of the training sessions and the total duration of the program. Attempts have been made to define the relative importance of these characteristics but a consistent pattern has yet to emerge (Shephard, 1968; Pollock, 1973; Nordesjo, 1974). Intensity may be the most important single determinant (Kilbom, 1971; Nordesjo, 1974). The minimal amount of physical activity that may produce a training effect has also been investigated. Heart rates during training of 130 beats/min and a relative load (defined as actual oxygen uptake as a percentage of individual maximum) of 40% have sufficed in some series (Karvonen et al., 1957; Roskamm, 1967; Kilbom, 1971 a and b; Pollock, 1973; Nordesjo, 1974). As little as 30 minutes of relatively high-intensity exercise accomplished during 2-3 weekly sessions produced significant effects in one series of very sedentary middle-aged men but a single weekly 12-minute session failed to maintain the improvement (Siegel et al., 1970).

More data are needed on the time at which the various training-induced adaptations occur. A phase-shift between the metabolic adaptations of skeletal muscle and the changes in maximal oxygen uptake has been observed in man (Saltin, 1977). Animal experiments suggest that changes in coronary flow patterns precede other circulatory adaptations to training (Stone, 1977).

The general relationship between the amount of training (intensity, frequency, duration of sessions and total duration of the program) and the degree of the improvement seems to be defined by a sigmoid stimulus-response curve (Siegel et al., 1970). There is an apparent threshold level - which probably is a function of peak habitual levels of activity before training - and returns rapidly diminish once a certain stimulus level has been reached.

Specific Circulatory Effects of Training. The over-all functional cardiovascular effects of training may be viewed in terms of a rearranged Fick equation where Oxygen Uptake = Stroke Volume x Heart Rate x A-V O_2 difference. Cross-sectional comparisons of individuals with markedly different maximal oxygen uptake indicate that the variations can largely be accounted for by

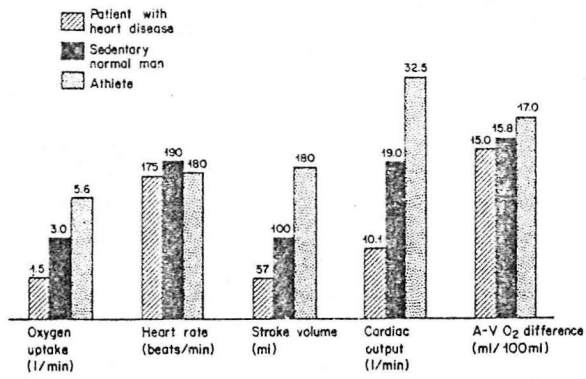


Fig. 9. Typical values at maximal oxygen uptake for a patient with heart disease, a sedentary normal man, and an endurance athlete.

(From Mitchell and Blomqvist, 1979).

differences in maximal stroke volume and cardiac output. Variations in total A-V O_2 difference and maximal heart rate are quantitatively far less important as illustrated in Figure 11. (Saltin, 1971; Rowell, 1974; Clausen, 1975 and 1977; Johnson, 1977; Scheuer and Tipton, 1977).

Any training-induced increase in maximal oxygen uptake in normal subjects is likely to be associated with an increase in maximal stroke volume and cardiac output. Maximal heart rate is either unchanged or only slightly lower after training but a decreased heart rate at any given submaximal level of oxygen uptake is the most consistent of all training effects. (Figure 12) A few investigators have reported decreased submaximal cardiac output after training (Andrew et al., 1966; Hanson et al., 1968; Ekblom, 1969) but most series have shown no change in the relation between submaximal oxygen uptake and cardiac output (Rowell, 1962; Saltin et al., 1968; Saltin, 1971; Clausen, 1975 and 1977; Scheuer and Tipton, 1977). The maximal A-V O_2 difference is in subjects with normal arterial O_2 content a function of the capacity to extract oxygen and to redistribute cardiac output by reflex vasoconstriction in inactive tissues and metabolically induced vasodilation in muscle. The A-V O_2 difference is wider after training in normal young men (Saltin et al., 1968) but does not change in women (Kilbom, 1971a) or middle-aged men (Hartley et al., 1969). The reasons for this discrepancy are not apparent. Data relating to oxidative capacity, blood flow, and vascularity of skeletal muscle provide no clues.

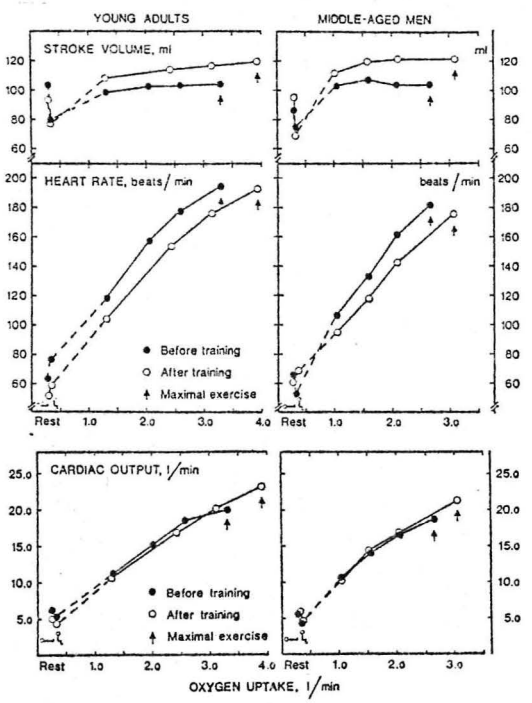


Figure 12. Stroke volume, heart rate, and cardiac output before and after training in young and middle-aged men. From Saltin 1971.

Training can induce an increase in the in-vitro activity of oxidative enzymes in most subjects irrespective of age and sex (Gollnick and Sembrowich, 1977) but absolute levels tend to be lower in women than in men (Saltin et al., 1977). The number of capillaries per muscle fiber also increases with training and increasing maximal oxygen uptake and decreases with age. However the capillary/fiber ratio is similar at comparable levels of maximal oxygen uptake in men and women (Saltin et al., 1971). Furthermore, there is no evidence for any age- or sex-related impairment of vasoconstriction in inactive tissues during exercise (Rowell, 1974).

The principal features of the cardiovascular response to training and inactivity in normal subjects were well documented by the mid-1960's (Rowell, 1962; Andrew et al., 1966; Saltin et al., 1968; Hanson et al., 1968; Ekblom et al., 1969). More recent studies have demonstrated that the gross cardiovascular changes are produced by a complex set of interacting central and peripheral mechanisms operating at multiple levels, e.g. structural, metabolic, and regulatory.

Cardiac Dimensions. There is a large older, mainly German and Scandinavian literature on the relationship between heart size and physical performance in athletes and normal subjects. In general, total heart size as estimated from bi-plane radiographs has in cross-sectional studies been found to correlate closely with maximal oxygen uptake, cardiac output, and stroke volume (Holmgren and Strandell, 1959; Musshoff et al., 1959; Pyörälä et al., 1967; Saltin and Grimby, 1968; Åstrand and Rodahl, 1977). The results from longitudinal series are less consistent and range from a close correlation between changes in maximal oxygen uptake and stroke volume and total heart size in young normal subjects (Saltin et al., 1968) to no correlation in middle-aged men (Saltin et al., 1968; Ehsani et al., 1978). On the other hand, former endurance athletes, including young women, who have trained intensely over several years and later adopted a level of relative inactivity, maintain a large heart size (Holmgren and Strandell, 1959; Pyörälä et al., 1967; Saltin and Grimby, 1968; Erikson et al., 1975).

TABLE 5. *Echocardiographic Measurements of Athletes and Controls*

	Athletes (N = 10)	Control subjects (N = 10)	*P* values
Age (yr)	25.4 ± 1.1*	26.5 ± 1.1	NS
Height (in)	76.4 ± 1.4	76.7 ± 0.8	NS
Weight (lb)	192.1 ± 7.3	192.5 ± 2.5	NS
BSA (m^2)	2.19 ± 0.06	2.20 ± 0.02	NS
HR (beats/min)	53.4 ± 2.0	65.9 ± 2.6	0.001
RVEDD (mm)	20.8 ± 1.1	12.9 ± 2.2	0.004
Septal thickness (mm)	13.7 ± 0.5	12.8 ± 0.6	NS
Septal/posterior wall	1.2 ± 0.1	1.3 ± 0.1	NS
LVEDD (mm)	53.7 ± 1.3	49.9 ± 0.7	0.02
LVESD (mm)	31.9 ± 1.5	31.1 ± 0.8	NS
LVPW thickness (mm)	11.1 ± 0.6	9.8 ± 0.3	0.05
LVEDV (ml)	157 ± 11	126 ± 5	0.02
SV	123 ± 8	95 ± 4	0.007
EF (%)	79 ± 2	76 ± 1	NS
Mean Vcf (circ/sec)	1.13 ± 0.04	1.18 ± 0.05	NS

*All data are reported as mean ± SE.
Abbreviations: BSA = body surface area; HR = heart rate; RVEDD = right ventricular end-diastolic dimension; LVEDD = left ventricular end-diastolic dimension; LVESD = left ventricular end-systolic dimension; LVPW = left ventricular posterior wall; LVEDV = left ventricular end-diastolic volume; SV = stroke volume; EF = ejection fraction; Vcf = rate of circumferential fiber shortening; NS = not significant.

From Roeske et al., 1975. The study group consisted of professional basketball players.

Studies based on echocardiographic (Gilbert et al., 1975; Morganroth et al., 1975; Roeske et al., 1975; Underwood and Schwade, 1977; Zoneraich et al., 1977; DeMaria et al., 1978; Ehsani et al., 1978; Longhurst et al., 1979) and radionuclear techniques (Rerych et al., 1979) have generated specific and detailed dimensional data. It has been suggested that endurance training, i.e. a chronic volume load, causes an increase in left ventricular end-diastolic volume without major changes in wall thickness, whereas isometric exercise, a pressure load, produces an increased wall thickness without any change in left ventricular volume (Morganroth et al., 1975).

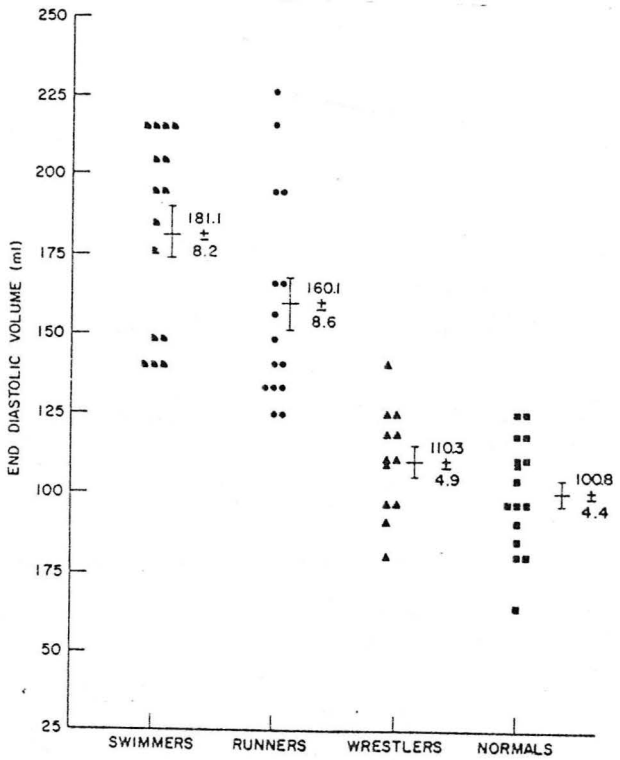


FIGURE 13. Echocardiographically measured left ventricular end diastolic volume in college athletes. Numbers represent mean values ±standard errors (SE). Data on swimmers and runners are statistically different from those of wrestlers and normal subjects ($p < 0.001$). (From Morganroth et al., 1975 and 1977).

The exercise-induced cardiac hypertrophy appears to be global. (Table 5) Left atrial and right ventricular demensions are consistently increased in subjects with left ventricular hypertrophy (Roeske et al., 1976; Zoneraich et al., 1977; Underwood and Schwade, 1977; Muntz, 1979).

Several groups (Roeske et al., 1976; Underwood and Schwade, 1977; Laurenceau et al., 1977) have reported abnormal wall thickness ratios, i.e. septal/left ventricular posterior wall thickness ratio $\geq$ 1.3, in up to 10 percent of the athletes studied. The abnormal wall thickness ratio was once considered strong evidence for idiopathic hypertrophic subaortic stenosis, IHSS or ASH, asymmetrical septal hypertrophy (Henry et al., 1973). However, in no case has the abnormal wall thickness ratio been associated with the abnormal systolic anterior motion of the mitral valve that is characteristic of obstructive cardiomyopathy. It is possible that the disproportionate increase in septal thickness is an artifact due to the anatomical characteristics of the chest and an oblique direction of the beam traversing the septum (Roeske et al., 1976).

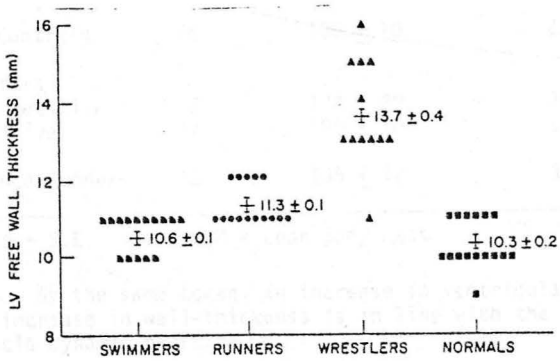


FIGURE 14. Echocadiographically measured left ventricular (LV) free wall thickness in college athletes. Numbers represent mean values ±SE. Data on wrestlers are statistically different from those of swimmers, runners, and normal subjects ($p < 0.001$).

(From Morganroth et al., 1975 and 1977).

Two recent studies at this institution, an echocardiographic human study by Longhurst et al., (1979) and a morphological experimental study on weight-lifting cats (Muntz, 1979) have provided interesting new information. Longhurst et al. compared several groups of endurance athletes and weight-lifters with appropriate sedentary control groups.The results confirmed that both dynamic and isometric training cause an increase in absolute left ventricular mass but also demonstrated that only endurance training increases mass normalized with respect to lean body mass. (Table 6). The left ventricular mass/volume ratio was increased only in competitive weight lifters.

Characteristically, the normal heart muscle grows to match the work level imposed on the ventricle, maintaining a constant relationship between systolic pressure and the ratio of wall thickness to ventricular radius, irrespective of

ventricular size (Ford, 1976). This means that normally wall tension is kept constant according to the law of Laplace. The weight lifters' increased mass/volume ratio is inappropriate relative to their blood pressure at rest. But the increased wall-thickness is most likely appropriate to the hemodynamic conditions during isometric exercise and strength training which induce a marked

Table 6. Effect of Physical Training on Left Ventricular Mass
Echocardiographic Data from Longhurst et al., 1979

	N	Absolute Mass (Grams)	Relative Mass (Grams/KG LBM)
Sedentary Controls	24	136 ± 10	2.3 ± .2
Weight Lifters			
Non-Competitive	7	174 ± 20	2.5 ± .2
Competitive	17	190 ± 10	2.6 ± .1
Long-Distance Runners	12	195 ± 12	3.2 ± .2

Mean Values ± S.E. LBM = Lean Body Mass

pressor response. By the same token, an increase in ventricular volume with a secondary small increase in wall-thickness is in line with the volume load during large-muscle dynamic exercise.

The quantitative relationship between the amount of training and hypertrophy has not been established. A threshold level may be present, above which there is a positive correlation between the degree of hypertrophy and the intensity and duration of training (Muntz, 1979). Some experimental studies on endurance training have failed to produce hypertrophy (Scheuer and Tipton, 1977; Muntz, 1979), whereas only a few minutes daily weight-lifting exercises produced a marked cardiac and skeletal muscle hypertrophy in the cats studied by Muntz 1979.

The physiological hypertrophy due to dynamic or isometric exercise training can be clearly separated from the changes induced by severe chronic volume and/or pressure overloads by morphological criteria. Physiological hypertrophy causes only a moderate increase in heart size. Weights higher than 500 grams are rarely seen in athletes (Linzbach, 1960) whereas valvular and myocardial disease may produce weights well above 1,000 grams. The primary mechanism in both the abnormal and physiological situation is hypertrophy of the individual muscle fiber. No convincing signs of hyperplasia have been described. The ratio myocardium/interstitial tissue remains normal in physiological hypertrophy but is increased in failure (Fuster et al., 1977; Muntz, 1979).

There is experimental evidence for a training-induced increase in the size of the coronary vascular bed (Scheuer and Tipton, 1977; Wyatt and Mitchell, 1978; Muntz, 1979). The extent to which the increase exceeds the increase in mass in the normal heart remains to be determined but it is unlikely that myocardial perfusion is a primary limiting factor in normal subjects. Direct measurements in man have demonstrated that a linear relationship between coronary flow and myocardial work is maintained also during maximal and near-maximal total body work loads (Holmberg et al., 1971; Jorgensen et al., 1977). The exercise ECG is usually normal in physiological hypertrophy (Raskoff et al., 1976) but often abnormal in left ventricular hypertrophy due to hypertension or valvular disease also in the absence of coronary artery disease.

Ventricular Function. It seems likely that an increase in left ventricular dimensions contributes significantly to the improved pump performance after training. Further studies are necessary to define the importance of changes in ventricular mass compared to other determinants of cardiac performance, e.g. intrinsic contractile state, autonomic cardiac activity, and changes in preload and afterload.

Experimental studies have demonstrated cardiac biochemical adaptations to training which generally are less prominent than the changes in skeletal muscle and affect the utilization rather than the formation of high-energy phosphate bonds (Scheuer and Tipton, 1977). Studies based on isolated perfused and

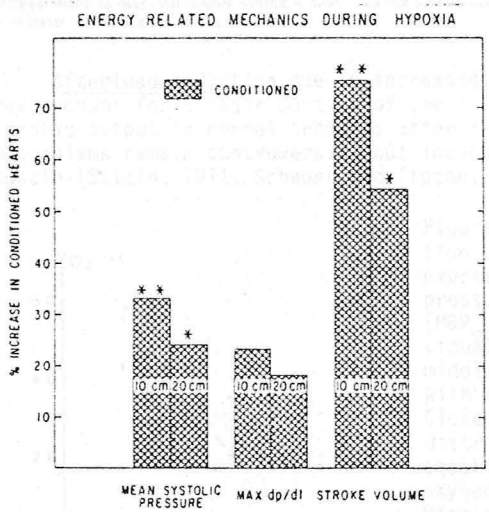


Figure 15. Percent increase for conditioned hearts over sedentary hearts in energy-related functions. Max dp/dt = maximal rate of pressure rise. Measurements at two different preload levels, i.e. end-diastolic pressures of 10 and 20 cm H_2O. From Scheuer 1977.

working heart preparations suggest improved mechanical myocardial performance and relative resistance to ischemia after training (Scheuer, 1977, Figure 15)

but results from papillary muscle preparations are highly variable and inconclusive (Table 7 from Nutter and Fuller, 1977). Human data are difficult to evaluate due to training-induced changes in heart rate, afterload and preload. Longitudinal and cross-sectional echocardiographic studies (Morganroth et al., 1975; Roeske et al., 1975; Ehsani et al., 1978; DeMaria et al., 1978; Longhurst et al., 1979) have provided no convincing evidence for physiologically significant changes in intrinsic contractile properties. However, training may improve myocardial performance by enhancing the contractile response to β-adrenergic stimulation. Support for this mechanism can be derived from experimental studies (Stone, 1977; Mole, 1978; Wyatt et al., 1978). Corresponding human data is not available.

Table 7. Training Effect on Isolated Cardiac Muscle (Nutter and Fuller 1977)

Source	Animal	Training	Cardiac Hypertrophy	Myocardial Mechanics Active	Passive
Molé (11)	Rat	Swimming	Yes	↑ isometric isotonic	n.c.
Steil (15)	Rat	Swimming	Yes	n.c. or ↑ isometric	n.c.
Amsterdam (1)	Rat	Swimming	Yes	n.c. isometric	n.c.
Grimm (5)	Rat	Running	Yes	n.c. or ↓ isometric	n.c.
Williams (16)	Cat	Running	No	n.c. isometric isotonic	n.c.
Nutter (12)	Rat	Running	Yes	↓ isometric	n.c.

Myocardial mechanics results that compare isometric or isotonic data from papillary muscles or left ventricular trabeculae of trained hearts with data from sedentary controls. nc = no change in mechanics with training.

Afterload reduction due to increased conductance of working skeletal muscle may account for a major portion of the increase in maximal stroke volume and cardiac output in normal subjects after training (Clausen, 1975). The exact mechanisms remain controversial but include an increased vascularity of skeletal muscle (Saltin, 1971; Scheuer and Tipton, 1977; Saltin et al., 1977). A large

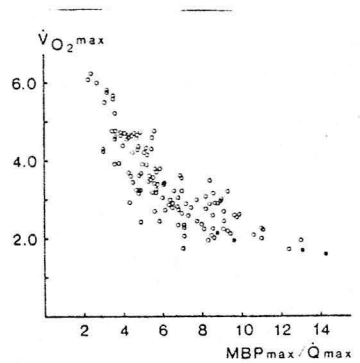


Figure 16. Maximal oxygen uptake as a function of total systemic peripheral resistance, expressed as the ratio Mean arterial blood pressure/Cardiac output during maximal work (MBP_{max}/Q_{max}). Open circles represent individual measurements in normal young and middle-aged men and women and in patients with coronary heart disease or hypertension. Closed circles denote group mean values. The distribution is defined by the regression equation: $y = 11.8/x^{0.72}$ where y is maximal oxygen uptake in liters/min. and x the ratio Mean arterial blood pressure (mmHg)/Cardiac output (liters/min.) The correlation coefficient is 0.87. From Clausen 1975.

amount of data from cross-sectional and longitudinal studies have demonstrated a strong correlation (Figure 16) between total systemic conductance and maximal oxygen uptake. Cardiac output may reach 40 liters/min. in a champion endurance-athlete who is likely to have a lower mean arterial pressure during maximal work than a sedentary middle-aged individual with a maximal cardiac output of 10 liters/min., i.e. data representing a better than four-fold difference with respect to maximal conductance. Physical training generally produces a lower arterial pressure at rest but blood pressures during exercise in young normal subjects do not change significantly (Saltin et al., 1968; Clausen, 1975; Scheuer and Tipton, 1977). Older and unfit subjects are more likely to show a blood pressure reduction as are patients with hypertension or coronary disease.

There are only limited data on the effect of training on venous return and preload. A reduction in systemic vascular resistance would by itself have a favorable effect on venous return according to Guyton's model (Green, 1979). Acute blood volume expansion has little or no effect on maximal performance (Robinson et al., 1966) unless the oxygen carrying capacity of arterial blood is increased (Ekblom et al., 1976). However, there is some evidence to suggest an increased preload during exercise after training. Changes in physical activity and maximal oxygen uptake are paralleled by small but significant changes in total blood volume (Saltin et al., 1968), usually without major changes in hemoglobin concentration or hematocrit. Well-trained athletes have higher pulmonary arterial wedge pressures during supine exercise than sedentary normal subjects (Bevegard et al., 1963). Both right and left ventricular filling pressures during exercise increase with age and very high wedge pressures have been recorded in elderly men with high maximal oxygen uptake and cardiac output (Strandell, 1964). The improved pump performance after training in patients with coronary disease also appears to be associated with higher left ventricular filling pressures and larger left ventricular end-diastolic volumes (Frick et al., 1971; Wallace et al., 1978).

Regulatory and Peripheral Training Effects. Several features of the response to progressively heavier exercise are normally more closely related to relative than to absolute work load (Rowell, 1974; Astrand and Rodahl, 1977). Substrate utilization (fat versus carbohydrates), pattern of recruitment of specific fiber types, heart rate, respiratory rate, total A-V O_2 difference and the degree of vasoconstriction in the renal and hepato-splanchnic circulations can all be related to relative load. An increased maximal oxygen uptake therefore means that work at any given absolute submaximal level can be performed more economically. The cost of oxygen transport is reduced, i.e. myocardial and respiratory work is lower, and the hemodynamic and metabolic reserve capacity is enhanced (Figure 17). The exact mechanisms that link responses to relative load have not been clearly defined. The response to exercise is affected by multiple reflex mechanisms with receptors in skeletal muscle and in the central circulation. There are also links between the motor cortex and regulatory cardiovascular centers providing a matrix for "central command" and "cortical radiation" (Mitchell et al., 1977; Longhurst and Mitchell, 1979). Chemoreceptors sensing the condition of mixed venous blood

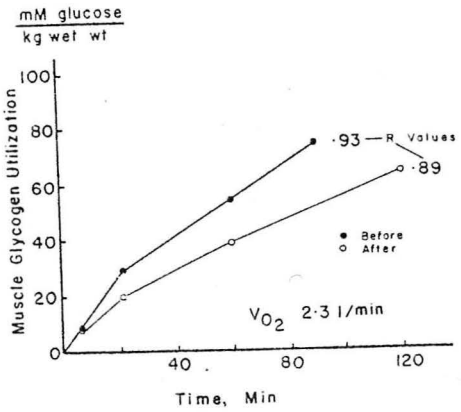


Figure 17. Rate of glycogen utilization at a given submaximal work load before and after training. The decreased rate after training reflects an increased utilization of fat and an increased metabolic reserve capacity.
From Gollnick and Sembrowich, 1977.

would provide a means of monitoring relative load but attempts to isolate such receptors have failed. Studies of dynamic and isometric exercise, including training studies and the use of arm exercise and one-legged exercise, have documented that local adaptations significantly alter the systemic hemodynamic response (Clausen, 1975 and 1977; Saltin, 1977). The metabolic state of the muscle - which is closely linked to relative load - probably determines impulse traffic in the muscle afferents. Stimulation of muscle receptors is a major determinant of the cardiovascular response to isometric exercise (Mitchell et al., 1977; Longhurst and Mitchell, 1979) and there are also data supporting an important role in dynamic exercise (Bonde-Petersen et al., 1978). The separation and identification of training effects on central command or cortical radiation muscle reflexes, and reflexes originating in the carotid and intrathroacic baro- and chemoreceptors remains a key area of investigation in exercise physiology.

The complexity of the regulatory changes that are induced by training is well illustrated by the effects on heart rate. The normal heart rate response to exercise is mediated by a combination of vagal withdrawal and β-adrenergic stimulation. The esentially linear relationship between heart rate during exercise and relative load is not altered by training or deconditioning (Saltin et al., 1968) but sinus bradycardia at rest and decreased heart rate at any absolute level of submaximal oxygen uptake is the hallmark of a cardiovascular training effect. The bradycardia is usually associated with an increase in stroke volume but the relationship is not obligatory or casual. Training-induced bradycardia often occurs in patients with coronary disease in the absence of any stroke volume changes (Detry, 1973; Clausen, 1975: Scheuer and Tipton, 1977).

The combined results from normal and abnormal human subjects and various experimental preparations (Scheuer and Tipton, 1977; Tipton, 1977) have provided indirect evidence for decreased adrenergic activity after training.

Plasma levels of epinephrine during exercise are lower both in normal subjects and in patients with coronary disease (Cooksey et al., 1978). There is little or no change in norepinephrine levels. Data on myocardial levels of catecholamines are conflicting (Tipton et al., 1977). Responses to beta-adrenergic stimulation and blockade in various models have also been inconsistent. Less epinephrine may be present at cardiac receptor sites after training but the sensitivity of the β_1 receptors may be increased (Tipton et al., 1977). There is more agreement on the training effects on the parasympathetic system with considerable evidence relating the bradycardia to increased availability of acetylcholine at the cardiac receptor level, perhaps due to an increased synthesis (Ekstrom, 1974).

Several studies have also demonstrated a significant non-autonomic component of the training-induced bradycardia, i.e. a decrease in intrinsic sinus node rate as measured after combined vagal and beta-adrenergic blockade (Lewis, 1977). The exact mechanisms are not known. However, all cardiac pacemakers respond to stretch with an increased rate of discharge (Jensen, 1971) and it is tempting to speculate that the hemodynamic volume load associated with training may produce a stress relaxation phenomenon in the sinus node.

The exercise-induced reduction of blood flow to tissues that are metabolically less active than skeletal muscle, i.e. the kidneys, the liver, and the splanchnic organs, is strongly related to relative load (Rowell, 1974; Clausen, 1975 and 1977) and to the level of adrenergic stimulation. The training effects on blood flow patterns parallel the effects on heart rate, i.e. the inverse relationship between relative load and flow remains essentially the same after training but perfusion is improved at any absolute submaximal level of oxygen uptake.

Thus, autonomic function is a major determinant of the acute response to exercise and training induces major adaptive changes. Nevertheless, there is strong evidence that training effects can be produced also in the absence of an intact autonomic nervous system. Significant changes in maximal oxygen uptake and hemodynamic responses have been observed in patients with coronary disease (Vetrovec and Abel, 1977; Welton et al., 1979) and normal subjects (Lester and Wallace, 1978) who during endurance training were treated with moderately high doses of beta-blocking agents. Training effects have also been induced in a variety of experimental animal models (Scheuer and Tipton, 1977; Tipton et al., 1977) with significantly altered autonomic and metabolic regulation (unilateral vagotomy, immunological sympathectomy, diencephalic lesions, thyroidectomy, adrenalectomy, hypophysectomy, genetic hypertension). This is an area that needs further exploration to provide more insight into basic mechanisms and to identify harmful and beneficial inter-actions between training and autonomic agonists and antagonists. For example, there is evidence for differential inotropic and chronotropic responses to acute stimulation of cardiac β_1 receptors (Tuttle and Mills, 1975). Available data suggest decreased

chronotropic and increased inotropic sensitivity after training (Tipton et al., 1977; Scheuer and Tipton, 1977; Stone, 1977; Mole, 1978; Wyatt et al., 1978) but the effects on different subsets of receptors has not been systemically studied. The role of α-adrenergic mechanisms as determinants of the acute response to exercise is poorly understood and even less is known about training effects (Siltovouri, 1977). It would also be important to establish the extent to which the autonomic and metabolic conditions that characterize large muscle exercise at moderate and high intensities are essential to the achievement of classical circulatory training effects. Preliminary data suggest that peripheral training effects, including enzymatic adaptation in skeletal muscle, can be achieved at very low levels of myocardial and total body work by sequential high-intensity dynamic exercise training of small muscle groups (Gaffney, Grimby et al., personal communication).

Knochel (1979) has recently demonstrated that training causes an increase in total body potassium, decreased plasma and increased intracellular levels, and a hyperpolarization of the skeletal muscle membranes. The altered potassium distribution may have important effects at multiple levels, including reflex and hormonal regulation.

CLINICAL FEATURES OF ATHLETE'S HEART

Physical examinations are often required for participants in organized sports and are at times supplemented by electrocardiograms and chest X-rays. Many athletes, particularly those taking part in endurance events, will have findings that may be taken as evidence for heart disease, e.g. cardiomegaly, murmurs, gallop sounds, and a variety of ECG abnormalities. A majority of these findings can clearly be attributed to physiological adaptations when viewed in the context of a history of athletic training and participation. A standard clinical exercise test and echocardiography often provides valuable support for a diagnosis of physiological hypertrophy by demonstrating normal or superior exercise capacity and the absence of any valvar or myocardial disease or dysfunction.

PHYSICAL EXAMINATION AND PHONOCARDIOGRAPHY

The physical demands of various sports are reflected by characteristic somato-types. Most champion long-distance runners are of average height or less, show little skeletal muscle hypertrophy and have very low levels of body fat and a low total body weight (Pollock et al., 1977; Wilmore et al., 1977). Average weight in elite distance runners is about 62-63 kg with a relative fat content of 4-5% compared to 75 kg and 13% in average young men.

Cardiac findings. Physical signs of definite right or left ventricular hypertrophy are absent. The heart rate is slow (see the ECG section below). Third and fourth heart sounds are common (Gott et al., 1968). Roeske et al., (1976) noted third sounds in 24/25 professional athletes and 14 or 56% had fourth heart sounds. The audible third sound has no clinical significance below age 35-40 and is a function of a prominent rapid filling phase during early diastole. The mechanisms responsible for the fourth sound are uncertain. The abnormal fourth sound - which is loud and relatively high-pitched - is usually associated with a reduced left ventricular distensibility due to increased

wall thickness and/or increased end-diastolic pressures. Filling pressures at rest are normal in athletes. A combination of a long P-R and a thin chest wall may make a normally inaudible (but easily recorded) fourth sound audible (Blomqvist, 1979).

Systolic murmurs are present in as many as 40% of athletes participating in endurance events (Gott et al., 1968). The murmurs are of the ejection-type and often intermittent. The mechanism is presumably non-laminar flow across normal pulmonic and/or aortic valves due to a large stroke volume. The same basic mechanism can occasionally produce an apical S 3 - rumble complex (Gott et al., 1968). Both the systolic and diastolic murmurs disappear or become less prominent with decreased ventricular filling and stroke volume in the upright position.

CHEST X-RAY

As previously discussed, there is a strong correlation between radiological heart size, stroke volume, and maximal oxygen uptake. A routine chest X-ray of an endurance athlete often shows a globular heart without specific chamber enlargement (Beckner and Winsor, 1954) (Figure 18) with a cardio-thoracic ratio at or slightly above the upper normal limit of 0.50. Raskoff et al., 1976 reported a mean value of 0.42 in a series of runners and 4 of 23 had ratios > 0.50.

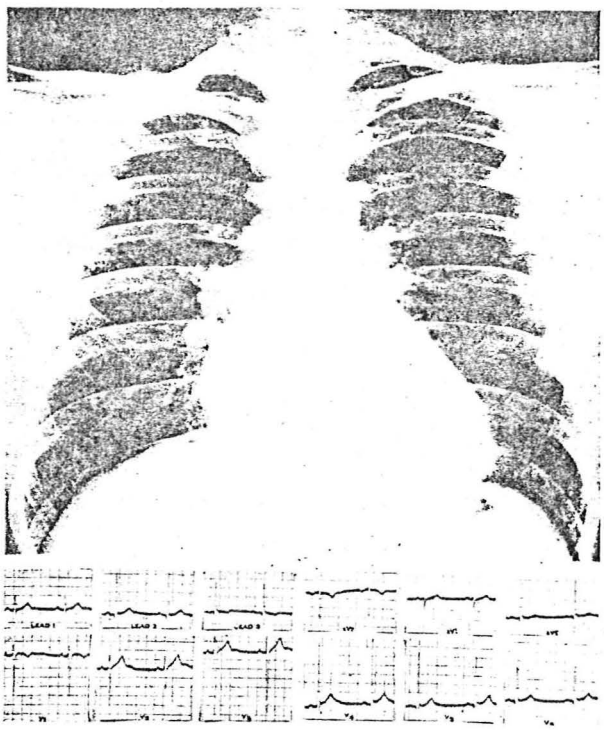


FIG. 20. Teleoroentgenogram and electrocardiogram of a 45 year old runner who has trained for 20 years. The cardiac area, as well as the long, transverse and broad diameters exceed normal values for his height and weight. High voltage of QRS complexes is a prominent feature of the electrocardiogram. The S waves in V_1 are deep. (From Beckner and Winsor, 1954).

ELECTROCARDIOGRAM

A wide spectrum of ECG abnormalities has been described. Two major categories are recognizable: (1) Abnormalities with respect to rhythm, A-V conduction and repolarization (ST-T), related to increased parasympathetic and decreased β-adrenergic drive, diminished or abolished by vagal block and/or exercise, (2) P and QRS abnormalities attributable to cardiomegaly and increased myocardial mass.

The ECG patterns in athletes have been studied extensively. Several major reviews of large series, each with numerous references, are available (Klemola, 1951; Beckner and Winsor, 1954; Arstila and Koivikko, 1966, VanGanse et al., 1970; Lichtman et al., 1973).

Rate and Rhythm. Heart rate at rest tends to vary inversely with maximal oxygen uptake. Sinus bradycardia at rates below 40 may be seen in highly trained long-distance runners (Smith et al., 1964; Schamroth and Jokl, 1969). The sinus bradycardia is usually associated with marked sinus arrhythmia. Coronary sinus rhythm and wondering atrial pacemaker are also common (Lichtman et al., 1973). Junctional escape rhythms are seen is about 1% (Klemola, 1951). The junctional pacemaker (Figure 19) may also show vagal effects with a relative bradycardia and rates below 45/min. (Schamroth and Jokl, 1969). Ventricular escape beats are common and may take the form of bigeminy (Lichtman et al., 1973).

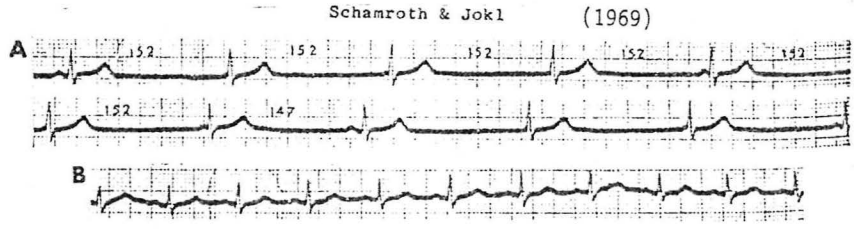


Fig. 1.—Electrocardiogram (Standard lead I) recorded from a 20 year old long distance runner. A: at rest. After winning a cross country race over 2.82 miles. B.

First degree A-V block is common with a prevalence of 5 to 30% in different series (Lichtman et al., 1973) compared to the 0.7% reported in a large normal population (Hiss and Lamb, 1962). Second-degree A-V block i.e. Wenckebach or Mobitz Type I block is extremely rare in the general population but several cases have been reported in endurance athletes. Exercise virtually always restores sinus rhythm with normal A-V conduction but the abnormal rhythms reappear post-exercise.

P Waves. P wave changes consistent with right (amplitude > 2.5 mm leads II, III, or AVF) and left (duration ≥ 0.12 seconds) atrial overload have been reported with prevalence figures as high as 50% (Lichtman et al., 1973).

QRS Complex. The classical QRS changes are well illustrated in Figure 20, i.e. large amplitudes but a duration within normal limits. It is difficult due to variations with respect to criteria and characteristics of the study group to arrive at any reliable estimates of the prevalence of left (LVH) and right (RVH) ventricular hypertrophy. Most investigators have given prevalence figures between 20 and 50 percent for LVH. The rate of RVH is usually somewhat lower (Lichtman et al., 1973). Arstilla and Koivikko (1964), who combined vector- and electrocardiographic techniques, reported a predominance of RVH in young and of LVH in old endurance athletes.

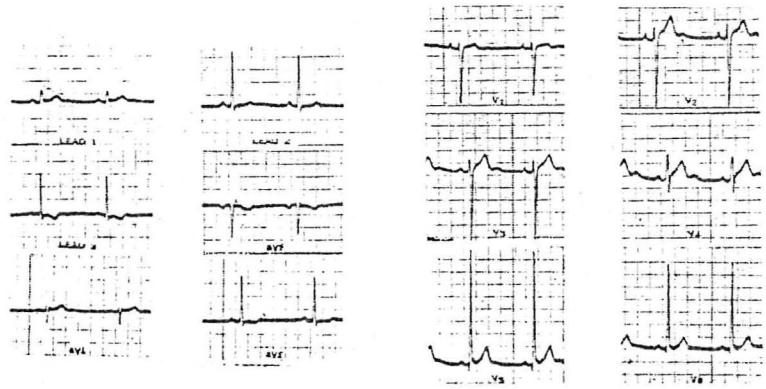


FIG. 20. Electrocardiogram of a marathon runner rest recorded after five years of running in national mile races. The slow cardiac rate, high voltage of QRS complexes in the precordial leads and shift the transitional zone to the left are prominent features of this tracing. (Beckner & Winsor).

The correlation between the ECG findings and anatomical data derived from chest X-rays and echocardiograms is poor (Arstilla and Koivikko, 1964; Raskoff et al., 1976). This is perhaps to be expected. The magnitude of the body surface potentials is a fraction of cardiac size and muscle mass but heavily influenced by the geometric relationships between the heart and the torso. The combination of a large heart, thin chest wall, and relatively small total body size explains the very large potentials in runners. The increased total cardiac muscle mass in weight-lifters with a large total body mass produces no ECG signs of hypertrophy (Longhurst et al., 1979). Furthermore, the cardiac hypertrophy in athletes is global and the ECG recognition of balanced or biventricular hypertrophy is notoriously poor.

The location of the QRS transition zone is variable. Q-QS waves in V_{1-3} simulating old anteroseptal myocardial infarction have been described (Figure 21) but this finding is much less common than the RVH pattern with tall R waves in the medial chest leads (Figure 22).

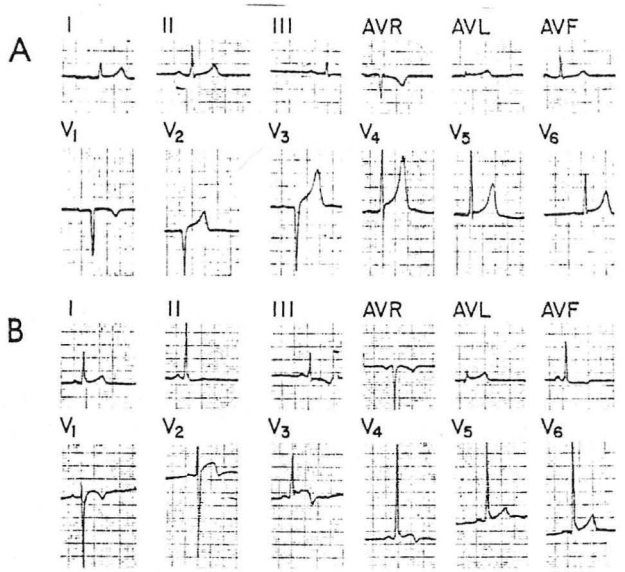


Fig 21.–A, Sinus bradycardia and prominent Q waves in leads V_1 to V_3 accompanied by tall, peaked T waves in mid and lateral precordial leads. B, Increased voltage and ST-segment elevation in precordial leads. There is also terminal P-wave inversion in leads V_1 to V_4.

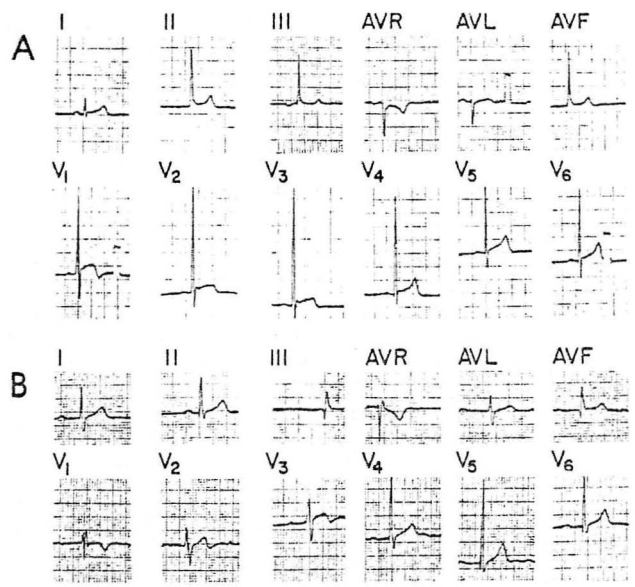


Fig 22.–A, Tall R waves in right precordial leads along with evidence of generalized ST-segment elevation. B, First-degree AV block, a right ventricular conduction abnormality and prominent lateral precordial voltage. Not illustrated are sinus bradycardia and intermittent 4:2 2° Wenckebach AV block that were also recorded in this patient.

(From Lichtman et al., 1973).

Minor conduction defects, particularly in complete right bundle branch block (Figure 22) are common and have been reported in up to 50% of the athletes in some series (Lichtman et al., 1973). The QRS abnormalities, including the incomplete RBBB, often resolve after cessation of training (Roskamm et al., 1966).

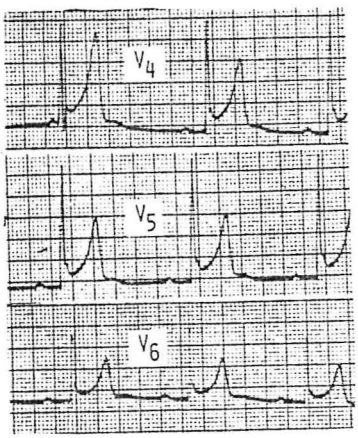


Figure 23. Marked ST elevation and T wave changes typical of early repolarization in a long-distance runner. The ST elevation is most prominent in the leads with the tallest T waves. Note also the slurring of the terminal QRS. From Gibbons et al., (1977).

ST-T Segment. The typical secondary ST-T wave abnormalities of LVH are absent in physiological hypertrophy. "Early repolarization" denotes normal variant ST elevation, usually combined with a notch or slur on the down-stroke of the R wave and absence of the normal S wave, a gradual transition between QRS and ST, and tall T waves. The pattern is probably more common in black than in white sedentary normal subjects but the prevalence difference is minor. There are also contrary to common belief only minor age differences (Parisi et al., 1971; Kambara and Phillips, 1976). Vagal tone is a major determinant of the ST-T amplitudes which are normally inversely proportional to heart rate. The early repolarization pattern is usually completely abolished by exercise-induced tachycardia. The heart rate dependence and the association with a typical terminal QRS pattern serves to differentiate the variant ST elevation from a current of injury to pericarditis or infarction.

A "juvenile" T wave pattern with negative or biphasic T amplitudes in leads V_{1-4} is common (10-15%) and T wave changes are occasionally seen in leads V_{5-6} (2-3%). The lateral T wave changes tend to be labile and often disappear after atropine administration or exercise (Lichtman et al., 1973).

SUDDEN CARDIAC DEATH IN ATHLETES

Cardiovascular deaths in young athletes during taining or competition are relatively rare. Such deaths account for less than 0.1% of the 3,000 cases that are investigated annually by the Medical Examiner's Office in Dallas County (Petty - personal communication). Approximately 1/2 of the deaths in ages below 20 occur without any demonstrable pathology and are presumably due to primary arrhythmias, i.e. "instantaneous physiological deaths". Coronary heart disease is the dominant cause in ages above 20 (Scnwartz, 1974).

The rarity of fatal events when the base population is limited to participants in organized athletics makes it difficult to exclude bias in published data. Most series consist of cases drawn from poorly defined source populations. Some trends are nevertheless apparent. Rose (1969) collected information on 44 cardiac deaths in organized sports occurring in the U.S.A. during the period 1961-67. Thirty-eight or 88% were in ages between 14 and 19. More than half the deaths occurred during pre-season football practice. Deaths due to heat stroke (Knochel, 1977) were eliminated. Six subjects had congenital heart disease, 2 myocarditis and 2 (age 19 and 22) coronary disease, 2 chest trauma with myocardial contusion, and 1 rheumatic heart disease. The presumptive diagnosis in the remaining group of 31 or 70% was primary arrhythmias, i.e. findings in agreement with the experience at the Dallas Medical Examiner's Office.

Deaths due to arrhythmia without anatomical cardiac disease are rare in ages over 20 and occurred in only one of 24 cases in a series recently studied at the National Institute of Health (Table 8, Maron et al., 1978).

Table 8. Etiology of Sudden Deaths in Athletes (Maron et al., 1978)

Age 14-30, N = 21

Diagnosis	n
Hypertrophic cardiomyopathy	7
Idiopathic concentric left ventricular hypertrophy	5
Anomalous coronary artery origin	3
Coronary artery disease	2
Marfan's syndrome, ruptured aorta	2
Coronary artery hypoplasia	1
No cause identified	1

The high risk of effort-induced sudden death in coronary disease and in IHSS and other forms of cardiomyopathy is well established. Congenital and functional abnormalities of the coronary circulation are less widely recognized as a cause of sudden death.

Congenital abnormalities of the coronary arteries accounted for 4 deaths 19% of the NIH series. Levin et al., (1978) lists 4 major types: (1) Coronary fistulae (2) Origin of the left coronary artery from the pulmonary artery (3) Congenital stenosis or atresia (4) Origin of the left coronary artery from the right sinus of Valsalva with subsequent passage of the vessel between the aorta and right ventricular infundibulum. They described 34 angiographic cases, 21 of type (1), 12 of type (2), and 1 of type (3), but the distribution appears to be different in series of sudden death.

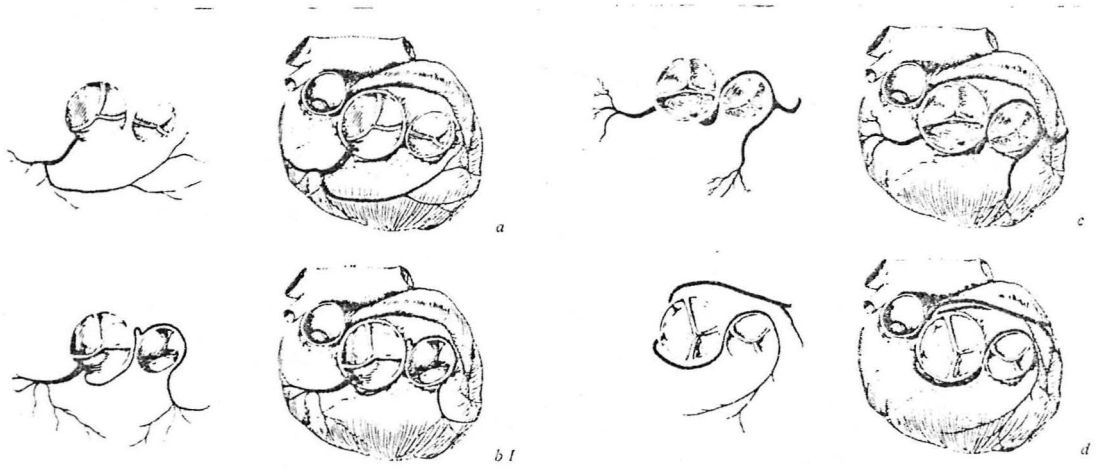


Fig. 24. Anomalies of coronary arteries in 4 additional cases. *a:* Left coronary artery absent, *b I:* both coronary arteries originating from common funnel in right aortic sinus, *c:* both coronary arteries originating separately from right aortic sinus, *d:* both coronary arteries originating from displaced right aortic cusp. (Jokl & McClellan, 1971)

Jokl and McClellan (1971) reported 7 cases of sudden death during sports events due to congenital coronary abnormalities. None of the subjects had been symptomatic. One subject had generally hypoplastic arteries and in two the left main artery originated from the pulmonary artery. In the remaining 4, both right and left coronary arteries originated (either separately or as a single main trunk) from the right sinus of Valsalva. In 3 of the 4 cases in this subgroup the left main coronary artery followed a course between the aorta and the pulmonary artery (Figure 24). A review by Cheilin et al. (1974) provides further support for the view that anomalous origin of the left coronary artery is an important cause of effort-related sudden death.

Myocardial bridging or intramural course of a major coronary artery (usually the left anterior descending) is another congenital abnormality that recently also has received attention (Noble et al., 1976; Faruqui et al., 1978). It is a relatively rare abnormality with a prevalence of 0.5% according to angiography. Physiological studies suggest that significant effort-induced ischemia may be present at least in some cases (Noble et al., 1976).

Exercise-induced myocardial infarction with normal coronary arteries has been documented in young subjects by Kimbiris et al.(1972). Detailed data on a fatal myocardial infarction in a 44-year old participant in the Boston Marathon with essentially normal coronary arteries have also been published by Green et al. (1976).

Thus, the combined data indicate that cardiac sudden death occurs in young athletes in the absence of any demonstrable lesions. Subtle changes, (evident only after the application of demanding and time-consuming techniques) and congenital functional abnormalities, e.g. the long QT syndrome, may account for some of these deaths (James et al., 1967). The concentration of "physiological" deaths in the younger age groups suggest that dysfunction of the autonomic nervous system is a primary mechanism. Exercise-induced hyperkalemia and acidosis may be important contributing factors.

The overwhelming majority of the deaths in athletes above age 20 can clearly be attributed to disease or congenital abnormalities. Primary arrhythmic deaths are rare but do occur also in this age group.

The much publicized concept that marathon running guarantees absolute immunity against deaths due to coronary atherosclerosis (Bassler, 1977) deserves a footnote. The concept has now conclusively been proven false. Noakes et al. (1979) have recently described 2 autopsy verified coronary deaths in established marathon runners.

LONG-TERM PROGNOSIS

Leon and Blackburn (1977) have recently summarized several studies on longevity and incidence of cardiovascular disease in former athletes (Table 9). The data are not relevant in terms of the general relationship between physical activity and mortality and morbidity since the selection processes involved in athletic participation makes it virtually impossible to assemble valid control groups. The combined data nevertheless rule out any major deleterious effects and suggest that at least athletes who participated in endurance events have a significantly better long-term survival than the general population (Figure 25).

Table 9.
Leon & Blackburn: Physical Activity and Heart Disease (1977)

RETROSPECTIVE AND CROSS-SECTIONAL (PREVALENCE) STUDIES

Primary Investigator	Type of Athlete	Reduced Cardiovascular Disease	Increased Longevity
Comparisons of cause of death and differences in life expectancy among former athletes and nonathletes using questionnaires, letters to relatives, college records and death certificates			
Morgan [42]	College oarmen	—	Positive
Dublin [44]	College	Negative	Negative
Rook [45]	College	Positive	Negative
Montoye [46]	College	Negative	Negative
Karvonen [47]	Finnish skiers	—	Positive
Pomeroy [48]	College football	Positive	—
Paffenbarger [49]	College	Positive	—
Polednak [50,51]	"Major" college sports "Minor" college sports	Negative	Negative
Schnohr [52]	Danish champions	Negative	Positive
Prout [53]	College oarmen	Negative	Positive
Bassler [54,55]	Marathon runner	—	Positive
Metropolitan Life [56]	Ex-Major League Baseball Players	Positive —	— Positive

Detailed studies of former athletes (Holmgren and Strandell, 1959; Roskamm et al., 1964; Pyörälä et al., 1967; Erikson et al., 1967; Grimby and Saltin, 1965; Saltin and Grimby, 1968) including functional evaluation, have demonstrated that former athletes retain a higher maximal oxygen uptake than their age-matched controls. The heart size and QRS amplitudes also remain larger than in sedentary subjects. The prevalence of clinical coronary disease and of ECG manifestations consistent with ischemia is not substantially different from the prevalence in control groups.

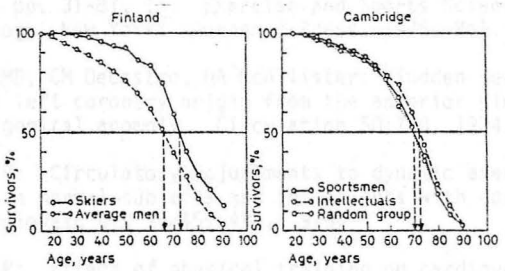


Fig. 15. Graphic summary of results of 2 studies of longevity of athletes conducted by ROOK [1954] of Cambridge University, England and by KARVONEN and BARRY [1967] of Helsinki, Finland.

(From Jokl and Jokl, 1975).

REFERENCES

Andrew CM, CA Guzman, MR Becklake: Effect of athletic training on exercise cardiac output. J Appl Physiol 21:603-608, 1966.

Arstila M, L Koivikko: Electrocardiographic and vectorcardiographic signs of left and right ventricular hypertrophy in endurance athletes. J Sports Med Phys Fitness 4:166-175, 1964.

Åstrand PO, K Rodahl: Textbook of Work Physiology (2nd ed.), New York: McGraw-Hill, 1977.

Bassler TJ: Marathon running and immunity to atherosclerosis. Ann NY Acad Sci 301:579-592, 1977.

Beckner GL, T Winsor: Cardiovascular adaptations to prolonged physical effort. Circulation 9:835-846, 1954.

Bevegård S, A Holmgren, B Jonsson: Circulatory studies in well trained athletes at rest and during heavy exercise with special reference to stroke volume and the influence of body position. Acta Physiol Scand 57:26-50, 1963.

Bonde-Petersen F, LB Rowell, RG Murray, CG Blomqvist, R White, E Karlsson, W Campbell, JH Mitchell: Role of cardiac output in the pressor responses to graded muscle ischemia in man. J Appl Physiol 45:574-580, 1978.

Blomqvist CG: Clinical exercise physiology, pp. 133-148, In: Rehabilitation of the Coronary Patient, ed by NK Wenger. New York: John Wiley and Sons, 1978.

Blomqvist CG: Significance of third and fourth heart sounds in patients with coronary disease. Practical Cardiol 5:89-98, 1979.

Burke RE, VR Edgerton: Motor unit properties and selective involvement in movement, pp. 31-81, In: Exercise and Sports Sciences Review, ed by JH Wilmore and JF Keogh. New York: Academic Press, 1975, Vol. 3.

Cheitlin MD, CM DeCastro, HA McAllister: Sudden death as a complication of anomalous left coronary origin from the anterior sinus of valsalva. A not-so-minor congenital anomoly. Circulation 50:780, 1974.

Clausen JP: Circulatory adjustments to dynamic exercise and effect of physical training in normal subjects and in patients with coronary artery disease. Progr Cardiovasc Dis 18:459-495, 1975.

Clausen JP: Effect of physical training on cardiovascular adjustments to exercise in man. Physiol Rev 57:779-816, 1977.

Cooksey JD, P Reilly, S Brown, H Bomze, PE Cryer: Exercise training and plasma catecholamines in patients with ischemic heart disease. Am J Cardiol 42:372-376, 1978.

Crawford MH, DH White, KW Amon: Echocardiographic evaluation of left ventricular size and performance during handgrip and supine and upright bicycle exercise. Circulation 59:1188, 1979.

DeMaria AN, A Neuman, G Lee, W Fowler, DT Mason: Alterations in ventricular mass and performance induced by exercise training in man evaluated by echocardiography. Circulation 57:237-244, 1978.

Detry JMR, M Rousseau, G Vandenbroucke, F Kusumi, LA Brasseur, RA Bruce: Increased arteriovenous oxygen difference after physical training in coronary disease. Circulation 44:109-118, 1971.

Detry JMR: Exercise testing and training in coronary heart disease. Baltimore: Williams and Wilkins, 1973.

Ehsani AA, JM Hagberg, RC Hickson: Rapid changes in left ventricular dimensions and mass in response to physical conditioning and deconditioning. Am J Cardiol 42:52-56, 1978.

Ekblom B: Effect of physical training on oxygen transport system in man. Acta Physiol Scand Suppl 328:5-45, 1969.

Ekblom B, G Wilson PO Åstrand: Central circulation during exercise after venesection and reinfusion of red blood cells. J Appl Physiol 40:379-383, 1976.

Ekelund LG, A Holmgren: Central hemodynamics during exercise. Circ Res 20-21(1): 1-33, 1967.

Ekstrom J: Choline acetyltrainsferase in the heart and salivary glands of rats after physical training. Quart J Exp Physiol 59:73-80, 1974.

Erikson BO, A Lundin, B Saltin: Cardiopulmonary function in former girl swimmers and the effects of physical trianing. Scand J Clin Lab Invest 35:135-150, 1975.

Fagreus L, J Karlson, D Linnarson, B Saltin: Oxygen uptake during maximal work at lowered and raised ambient air pressures. Acta Physiol Scand 87:411-421, 1973.

Faruqui AMA, WC Maloy, JM Felner, RC Schlant, WD Logan, P Symbas: Symptomatic myocardial bridging of coronary artery. Am J Cardiol 41:1305-1310, 1978.

Ford LE: Heart size. Circ Res 39:297-303, 1976.

Frick MH, M Katila, AL Sjögren: Cardiac function and physical training after myocardial infarction, pp. 431-451, In: Coronary Heart Disease and Physical Fitness, ed by OA Larsen, RO Malmborg. Copenhagen: Munksgaard, 1971.

Fuster V, MA Danielson, RA Robb, JC Broadbent, AL Brown Jr, LR Elveback: Quantitation of left ventricular myocardial fiber hypertrophy and interstitial tissue in human hearts with chronically increased volume and pressure overload. Circulation 55:504-508, 1977.

Gilbert C, S Nutter, S Heymsfield, J Perkins, R Schlant: The endurance athlete. Cardiac structure and function. Circulation, Suppl 2:115, 1975.

Glanz M: The heart in athletes. Ann Intern Med 83:574, 1975.

Gollnick PD, WL Sembrowich: Adaptations in human skeletal muscle as a result of training, pp 70-94, In: Exercise in Cardiovascular Health and Disease. ed by EA Amsterdam, JH Wilmore, AN DeMaria. New York: Yorke Medical Books, 1977.

Gott PH, HA Roselle, RS Crampton: The athletic heart syndrome. Arch Intern Med 122:340-344, 1968.

Granath A, B Johnson, T Strandell: Circulation in healthy old men studied by right heart catheterization at rest and during exericse in the supine and sitting position. Acta Med Scand 176:425, 1964.

Green JF: Determinants of systemic flow, pp 33-65, In: International Review of Physiology, Vol. 18. Cardiovascular Physiology III, ed by AC Guyton and DB Young. Baltimore: University Park Press, 1979.

Green LH, SI Cohen, CT Kurland: Fatal myocardial infarction in marathon racing. Ann Int Med 84:704-706, 1976.

Grimby G, B Saltin: Physiological analysis of physically well-trained middle aged and old athletes. Acta Med Scand 179:513, 1966.

Hanson JS, BS Tabakin, AM Levy, W Nedde: Long-term physical training and cardiovascular dynamics in middle-aged men. Circulation 38:783-799, 1968.

Hartley LH, G Grimby, Å Kilbom, WJ Nilson, I Åstrand, J Bjure, B Ekblom, B Saltin: Physical training in sedentary middle-aged and older men. Scand J Clin Lab Invest 24:335-344, 1969.

Henry WL, CE Clark, SE Epstein: Asymptomatic septal hypertrophy: Echocardiographic identification of the pathognomonic anatomic abnormality of IHSS. Circulation 47:225, 1973.

Henschen SE: Eine medizinische Sportstudie. Skilauf and Skiwettlauf. Mitteilungen aus der Medizinischen Klinik zu Uppsala. Jena: Fischer, 1899.

Hermansen L, PD Gollnick: Biochemical adaptations to exercise: Anaerobic metabolism, pp 1-43, In: Exercise and Sport Sciences Reviews, Vol. 1, by JH Wilmore. New York: Academic Press, 1973.

Herxheimer H: Die Herzgrosse der Amsterdamer Olympia Teilnehmer. Klin Wochenschr 8:402-404, 1929.

Hiss RG, LE Lamb: Electrocardiographic findings in 122,043 individuals. Circulation 25:947-961, 1962.

Holloszy JO, FW Booth: Biochemical adaptations to endurance training in muscle. Ann Rev Physiol 38:273-291, 1976.

Holmberg S, W Serzysko, E Varnauskas: Coronary circulation during heavy exercise in control subjects and patients with coronary heart disease. Acta Med Scand 190:465-480, 1971.

Holmgren A, T Strandell: The relationship between heart volume, total hemoglobin and physical working capacity in former athletes. Acta Med Scand 163:149-160, 1959.

Jensen D: Intrinsic Cardiac Rate Regulation. New York: Meridith Corp., 1971.

James TN, P Froggart, TK Marshall: Sudden death in young athletes. Ann Intern Med 67:1013-1021, 1967.

Johnson RL Jr: Oxygen transport, pp 74-84, In: Clinical Cardiology, ed by JT Willerson, CA Sanders. New York: Grune and Stratton, 1977.

Jokl E, P Jokl: Heart and sport, pp 36-67, In: Medicine and Sport, ed by E Jokl. Basel: S Karger, 1977.

Jokl E, JT McClellan (eds): Exercise and cardiac death, vol. 5, In: Medicine and Sport. Baltimore: University Park Press, 1971.

Jorgensen CR, FL Gobel, HL Taylor, Y Wang: Myocardial blood flow and oxygen consumption during exercise. Ann NY Acad Sci 301:213-223, 1977.

Kaiser L: Limiting factors for aerobic muscle performance. Acta Physiol Scand Suppl. 346:1-96, 1970.

Kambara H, J Phillips: Long-term evaluation of early repolarization syndrome (Normal variant RS-T segment elevation). Am J Cardiol 38:157-161, 1976.

Karvonen MJ, E Kentala, O Mustala: The effects of training on heart rate. A longitudinal study. Ann Med Exp Fenn 35:307-315, 1957.

Kilbom Å: Physical training in women. Scand J Clin Lab Invest Suppl 119:1-34, 1971a.

Kilbom Å: Effect on women of physical training with low intensities. Scand J Clin Lab Invest 28:345-352, 1971b.

Klemola E: Electrocardiographic observations on 650 Finnish athletes. Ann Med Fenn 40:121-132, 1951.

Klissouras V: Heritability of adaptive variation. J Appl Physiol 31:338-344, 1971.

Knochel JP: Potassium deficiency during training in the heat. Ann NY Acad Sci 301:175-182, 1977.

Knochel JP: The factors regulating serum potassium and their disorders. Medical Grand Rounds, Southwestern Medical School, Nov. 1, 1979.

Komi PV, JHT Viitasalo, M Havu, H Thorstenson, B Sjödin: Skeletal muscle fibres and muscle enzyme activities in monozygous and dizygous twins of both sexes. Acta Physiol Scand 100:385-392, 1977.

Laurenceau FL, J Turcot, F Dumesnil: Echocardiographic findings in olympic athletes (abst.) Circulation Suppl. III-25, vols. 55,56, 1977.

Leon AS, HW Blackburn: The relationship of physical activity to coronary heart disease and life expectancy. Ann NY Acad Sci 301:561-578, 1977.

Lester RM, AG Wallace: Cardiovascular adaptations to beta-adrenergic blockade during physical training (abst.). Circulation 57,58, Suppl. II:140, 1978.

Levin DC, KE Fellows, HL Abrams: Hemodynamically significant primary abnormalities of the coronary arteries. Angiographic aspects. Circulation 58:25-34, 1978.

Lewis SF: Central versus peripheral cardiovascular effects of endurance training with special reference to the mechanisms of bradycardia. PhD Thesis, Stanford: Stanford University, 1977.

Lichtman J, RA O'Rourke, A Klein, JS Karliner: Electrocardiogram of the athlete. Arch Int Med 132:763-770, 1973.

Linzbach AJ: Heart failure from the point of view of quantitative anatomy. Am J Cardiol 5:370-381, 1960.

Longhurst JC, JH Mitchell: Reflex control of the circulation by afferents from skeletal muscle, pp 126-148, In: Cardiovascular Physiology III, Vol. 18, ed by AC Guyton, DB Young. Baltimore: University Park Press, 1979.

Longhurst JC, AR Kelly, WJ Gonyea, JH Mitchell: Left ventricular mass in athletes. J Appl Physiol. In print.

Maron BJ, WC Roberts, HA McAllister, DR Rosing, SE Epstein: Etiology of sudden death in athletes. Circulation Suppl II, Vols 57-58:II-236, 1978.

Mitchell JH, CG Blomqvist: Response of patients with heart disease to dynamic and static exercise, pp 86-95, In: Heart Disease and Rehabilitation, ed by ML Pollock, DH Schmidt. Boston: Houghton-Mifflin, 1979.

Mitchell JH, WC Reardon, DI McCloskey, K Wildenthal: Possible role of muscle receptors on the cardiovascular response to exercise. Ann NY Acad Sci 301:232-242, 1977.

Mole PA: Increased contractile potential of papillary muscles from exercise-trained rat hearts. Am J Physiol 234:H421-H425, 1978.

Morganroth J, BJ Baron, WL Henry, SE Epstein: Comparative left ventricular dimensions in trained athletes. Ann Intern Med 82:521-524, 1975.

Morganroth J, BJ Maron: The athlete's heart syndrome: A new perspective. Ann NY Acad Sci 301:931-941, 1977.

Morris JN, JA Heady, PAB Raffle, CG Roberts, JW Parks: Coronary heart disease and physical activity of work. Lancet 265:1053-1057, 1953.

Mullins CB, CG Blomqvist: Isometric exercise and the cardiac patient. Texas Med 69:53-58, 1973.

Muntz KH: Morphological adaptation of the heart to a long term isometric training program in the cat. PhD Thesis (Physiology), UTHSCD, Dallas, 1979.

Musshoff K, H Reindell, H Klepzig: Stroke volume, arteriovenous differences, cardiac output and physical working capacity and their relationship to heart volume. Acta Cardiol 14:427-452, 1959.

Nelson RR, FL Gobel, CR Jorgensen, Y Wang, HL Taylor: Hemodynamic predictors of myocardial oxygen consumption during static and dynamic exercise. Circulation 50: 1179-1180, 1974.

Noakes TD, LH Opie, AG Rose, PHT Kleynhans: Autopsy-proved atherosclerosis in marathon runners. New Engl J Med 301:86-89, 1979.

Nordesjö LO: The effect of quantitated training on the capacity for short and prolonged work. Acta Physiol Scand Suppl 405:1-54, 1974.

Nutter DO, EO Fuller: The role of isolated cardiac muscle preparation in the study of training effects on the heart. Med Sci Sports 9:239-245, 1977.

Örlander J, KH Kiessling, J Karlson, B Ekblom: Low intensity training, inactivity, and resumed activity in sedentary men. Acta Physiol Scand 101:351-362, 1977.

Parisi AF, CH Beckman, MC Lancaster: The spectrum of ST segment elevation in the electrocardiograms of healthy adult men. J Electrocardiol 4:137-144, 1971.

Poliner LR, GJ Dehmer, SE Lewis, RW Parkey, CG Blomqvist, JT Willerson: Comparison of supine and upright left ventricular performance during rest and exercise on normal subjects. Circulation. Submitted, 1979.

Pollock ML: The quantification of endurance training programs, pp 155-188, In: Exercise and Sports Sciences Reviews, ed by JH Wilmore. New York: Academic Press, 1973.

Pollock ML, LR Gettman, A Jackson, J Ayres, A Ward, AC Linnerud: Body composition of elite class distance runners. Ann NY Acad Sci 301:361-370, 1977.

Pyörälä K, MJ Karvonen, P Taskinen, J Takkunen, H Kyrönseppä, P Peltokallio: Cardiovascular studies on former endurance athletes. Am J Cardiol 20:191-205, 1967.

Raskoff WJ, S Goldman, K Cohn: The "athletic heart". J Amer Med Assoc 236:158-162, 1976.

Rerych SK, PM Scholz, DC Sabiston, RH Jones: Effects of training on left ventricular function in normal subjects: A longitudinal study (abstr.). Am J Cardiol 43: 1067, 1979.

Robinson FB, SE Epstein, RL Kahler, E Braunwald: Circulatory effects of acute expansion of blood volume. Studies during maximal exercise and at rest. Circ Res 19:26-32, 1966.

Rose KD: The potential for cardiovascular accidents in athletes with a heart problem. Med Sci Sports 1:144-151, 1969.

Roskamm H, H Reindell, H Weinleder, G Kessler, K Aletser: Zur frage der spätschaden nach intensivem Hochleistungssport. Med Welt 2170, 1964.

Roskamm H, J Weidenbach, H Reindell: Nachuntersuchungen von 18 Sportlern die vor wenigstens 10 Jahren einen unvollständigen bzw. Einen physiologischen Rechtsschenkelblock in EKG gehabt hatten. Z Kreislaufforsch. 55:783-794, 1966.

Roskamm H: Optimum patterns of exercise for healthy adults. Canad Med Assn J 96:895-900, 1967.

Rowell LB: Factors affecting the prediction of the maximal oxygen intake from measurements made during submaximal work with observations related to factors which may limit maximal oxygen intake. PhD Thesis, Univ. of Minnesota, 1962.

Rowell LB: Human cardiovascular adjustments to exercise and thermal stress. Physiol Rev 54:75-159, 1974.

Saltin B, G Grimby: Physiological analyses of middle-aged and old former athletes. Comparison with still active athletes of the same ages. Circulation 38:1104-1115, 1968.

Saltin B, CG Blomqvist, JH Mitchell, RL Johnson Jr, K Wildenthal, CG Chapman: Response to exercise after bed rest and after training. Circulation Suppl. 7 38:1-78, 1968.

Saltin B: Central circulation after physical conditioning in young and middle-aged men, pp 21-26, In: Coronary Heart Disease and Physical Fitness, ed by OA Larsen, EO Malmborg. Copenhagen: Munkogaard, 1971.

Saltin B, J Henrikson, E Nygaard, P Andersen: Fiber types and metabolic potentials of skeletal muscles in sedentary man and endurance runners. Ann NY Acad Sci 301: 3-29, 1977.

Saltin B: The interplay between peripheral and central factors in the adaptive response to exercise and training. Ann NY Acad Sci 301:224-242, 1977.

Schamroth L, E Jokl: Marked sinus and A-V nodal bradycardia with interference-dissociation in an athlete. J Sports Med Phys Fitness 9:128, 1969.

Scheuer J: The advantages and disadvantages of the isolated perfused working rat heart (Symposium on experimental preparations to study the effect of training on the cardiovascular system). Med Sci Sports 9:231-238, 1977.

Scheuer J, CM Tipton: Cardiovascular adaptations to physical training. Ann Rev Physiol 39:221-251, 1977.

Schwartz RR: Presentation reviewed in the Medical News Section. JAMA 227:1361-1362, 1974.

Shephard RJ: Intensity, duration, and frequency of exercise as determinants of the response to a training regime. Int Z Angew Physiol 26:272-278, 1968.

Siegel W, CG Blomqvist, JH Mitchell: Effects of a quantitated physical training program on middle-aged sedentary men. Circulation 41:19-29, 1970.

Siltovouri A, R Tirri, MNE Harri: Alpha-receptor subsensitivity of isolated atria from rats following physical training or repeated ACTH injections. Acta Physiol Scand 99:457-461, 1977.

Smith WG, KJ Cullen, ID Thorburn: Electrocardiograms of marathon runners in 1962 Commonwealth Games. Brit Heart J 26:469-476, 1964.

Stein RA, D Michielli, EL Fox, N Krasnow: Continuous ventricular dimensions in man during supine exercise and recovery. An echocardiographic study. Am J Cardiol 41:655, 1978.

Stone HL: The unanesthetized instrumented animal preparation (Symposium on experimental preparations to study the effect of training on the cardiovascular system). Med Sci Sports 9:253-261, 1977.

Strandell T: Circulatory studies on healthy old men. Acta Med Scand Suppl 414, 1964.

Thadani U, JO Parker: Hemodynamics at rest and during supine and sitting bicycle exercise in normal subjects. Am J Cardiol 41:52, 1978.

Tipton CM, RD Matthes, TK Tcheng, RT Dowell, AC Vailas: The use of the Langerdorff preparation to study the bradycardia of training. Med Sci Sports 9:220-230, 1977.

Tuttle RR, J Mills: Dobutamide: Development of a new catecholamine to selectively increase cardiac contractility. Circ Res 36:185-196, 1975.

Underwood Rh, JL Schwade: Noninvasive analysis of cardiac function of elite distance runners: Echocardiography, vectorcardiography, and cardiac intervals. Ann NY Acad Sci 301:297-309, 1977.

Vanganse W, L Versee, W Eylenbosch, K Vuylsteek: The electrocardiogram of athletes. Brit Heart J 32:160-164, 1970.

Vetrovec GW, PM Abel: Results of exercise conditioning in propranolol and nonpropranolol treated patients trained at low heart rates (abstr.). Circulation 55,56, Suppl. III:197, 1977.

Wallace AG, SK Rerych, RH Jones, JK Goodrich: Effects of exercise training on ventricular function in coronary disease (abstr.). Circulation 57,58, Suppl II-97, 1978.

Weiss JL, ML Weisfeldt, SG Mason, JB Garrison, SV Livengood, NJ Fortuin: Evidence of Frank-Starling effect in man during severe semi supine exercise. Circulation 59:655-661, 1979.

Welton DE, WG Squires, GH Hartung, RR Miller: Effects of chronic beta-adrenergic blockade therapy on exercise training in patients with coronary heart disease (abstr.). Am J Cardiol 43:399, 1979.

Wilmore JH, CH Brown, JA Davis: Body physique and composition of the female distance runner. Ann NY Acad Sci 301:764-776, 1977.

Wyatt HL, JH Mitchell: Influences of physical conditioning and deconditioning on coronary vasculature of dogs. J Appl Physiol 45:619-625, 1978.

Wyatt HL, L Chuck, B Rabinowitz, JV Tyberg, WW Parmley: Enhanced cardiac response to catecholamines in physically trained cats. Am J Physiol 234:H608-H613, 1978.

Zoneraich S, JJ Rhee, O Zoneraich, D Jordan, J Appel: Assessment of cardiac function in marathon runners by graphic non-invasive techniques. Ann NY Acad Sci 301:900-917, 1977.