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CARDIOVASCULAR RESPONSE TO EXERCISE

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This article is intended for instructors who teach cardiovascular physiology. In our physiology course exercise physiology is used as a tool to review and integrate cardiovascular and respiratory physiology. It is assumed that the students already have mastered the fundamentals of cardiovascular and respiratory physiology. Because this paper is part of a cardiovascular refresher course, I have deleted much of the respiratory physiology. The objectives of this presentation are for the student to *1*) understand the relationship between maximal oxygen consumption and endurance during sustained exercise and be able to define ''maximal oxygen consumption''; *2*) understand the determinants of maximal oxygen consumption; *3*) understand the effects of dynamic exercise on the cardiovascular system and mechanisms for these effects; *4*) understand the relationships between exercise intensity and major cardiorespiratory parameters, including heart rate, cardiac output, blood flow distribution, left ventricular stroke volume, arterial pressures, total peripheral resistance, and arterial and venous blood oxygen content; *5*) be able to compare and contrast the cardiovascular effects of dynamic and isometric exercise in man and the mechanisms responsible for the major differences; and *6*) be able to apply knowledge of the cardiovascular effects of exercise to understanding causes of cardiovascular symptoms in disease and in diagnosis of disease states. This material contains many areas that stimulate discussion with students and allow exploration of concepts that are challenging for the student. This give and take between teachers and student is difficult to summarize in an article of this sort. Therefore, subjects that in my experience often stimulate questions and discussion with the students are indicated in the text.

Dynamic exercise produces the most striking burden on the cardiorespiratory systems of any of the various stresses encountered in normal life. The study of exercise physiology provides an excellent method to improve understanding of how the circulatory and respiratory systems respond and interact. Exercise stress is also used clinically to evaluate and quantify the severity of cardiovascular and/or respiratory disease.

Most of the cardiorespiratory effects of exercise are related to supplying adequate oxygen and nutrients to the working muscles. This task becomes more difficult when the exercise is performed in a hot environment. In this lecture we will only consider exercise in a thermal-neutral environment. There are many forms of physical activity that can be considered as exercise. These can be grouped into two general types of exercise: dynamic exercise (walking, running, cycling, and swimming) and isometric exercise. We will consider the cardiovascular effects of these two general types of exercise separately. In dynamic exercise there is a linear relationship between oxygen consumption and exercise intensity up to the maximal amount of oxygen a subject can consume.

DETERMINANTS OF MAXIMAL OXYGEN CONSUMPTION IN DYNAMIC EXERCISE

Figure 1*A* illustrates the time course of changes in oxygen consumption from initiation of exercise. At the onset of dynamic exercise, oxygen consumption begins to increase, continues to increase over the first minute of sustained exercise, and then plateaus as the oxygen uptake and transport are increased sufficiently so that oxygen consumption becomes matched to demand of the tissues. At the end of the exercise bout there is a gradual decrease in oxygen consumption during recovery. The excess postexercise oxygen consumption, above resting baseline oxygen consumption, observed during recovery has been referred to as ''oxygen debt.'' In Fig. 1*B*, *left*, the time course of changes in oxygen consumption from initiation of exercise is illustrated for six different workloads. In Fig. 1*B*, *right*, the relationship between steady-state oxygen uptake and exercise intensity obtained from these data is shown. Note that as exercise intensity increases, oxygen consumption (measured at the plateau) increases until maximal oxygen consumption is reached. Maximal oxygen consumption is reflected as the point at which there is no further increase in oxygen uptake despite further increases in workload. When workload exceeds intensity that produces the subject's maximum oxygen consumption, the increased workload is possible because energy is provided by nonaerobic processes, which results in a rapid buildup of lactic acid and a prolonged increase in oxygen consumption during recovery (Fig. 1*C*).

Figure 2 presents data for oxygen consumption plotted as a function of exercise workload for normal subjects and for subjects who were sedentary, conditioned, or highly trained athletes. Note that the level of physical conditioning influences the magnitude of maximal oxygen consumption; sedentary humans have the lowest maximal oxygen uptake, and endurance athletes have the greatest (Fig. 2). What are the factors in the cardiovascular system that contribute to the differences in maximal oxygen consumption seen in various human subjects?

Determinants of maximal oxygen consumption.
There are several important determinants of maximal oxygen consumption that can limit exercise perfor-

mance in health and disease. In this lecture we will focus on cardiovascular determinants of maximal oxygen consumption. The oxygen Fick equation is one useful way to summarize these determinants: $\dot{V}_{O_2} = CO(Ca_{O_2} - Cv_{O_2})$, where $\dot{V}_{O_2}$ is oxygen consumption (l/min), CO is cardiac output (l/min), Ca_{O_2} is arterial blood oxygen content, and Cv_{O_2} is mixed venous blood oxygen content. Let us consider the effects of exercise on each of these determinants of oxygen consumption.

The relationship between cardiac output and exercise intensity is similar to that shown for oxygen consumption as illustrated in Fig. 2, reflecting the dominant role of cardiac output as a determinant of maximal oxygen consumption. Cardiac output is determined by heart rate and stroke volume. As is true for oxygen consumption and cardiac output, there is a linear relationship between heart rate and exercise intensity up to maximal heart rates. [At this point I encourage the students to plot cardiac output and heart rate as functions of exercise intensity on Fig. 2. It is important that they appreciate the tight coupling between these parameters and exercise intensity.]

The other major determinant of cardiac output, stroke volume, is determined by the difference between end-diastolic and end-systolic volumes. [It is often necessary to review the determinants of end-diastolic and end-systolic volumes at this point in the lecture: heart rate, contractility, preload, afterload, ejection time, etc. You can tell from the reaction of the students if they understand the determinants of ventricular stroke volume.] The major causes of increased stroke volume during exercise in humans are increased myocardial contractility and increased venous return to the heart. Contractility increases with increasing heart rate. This allows greater ejection of blood at the end of systole and shortens systole, allowing more time for diastolic filling of the ventricles.

The relationships between exercise intensity and *1*) stroke volume, *2*) end-systolic volume, and *3*) end-diastolic volume are different when exercise is performed in the supine posture versus exercise in the upright posture, as illustrated in Fig. 3. These differences are largely the result of the effects of the force of gravity on venous return. During dynamic exercise, venous return is increased in proportion with in-

creased cardiac output. The increased venous return is aided by a redistribution of blood flow and venous volumes from viscera to active skeletal muscle and by the effects of the muscle pump and the respiratory pump on venous return.

Another major determinant of oxygen consumption is the difference between the arterial and venous oxygen contents ($Ca_{O_2} - Cv_{O_2}$) (i.e., the amount of oxygen from each ml of blood transported to and consumed by the tissue). Arterial oxygen content is
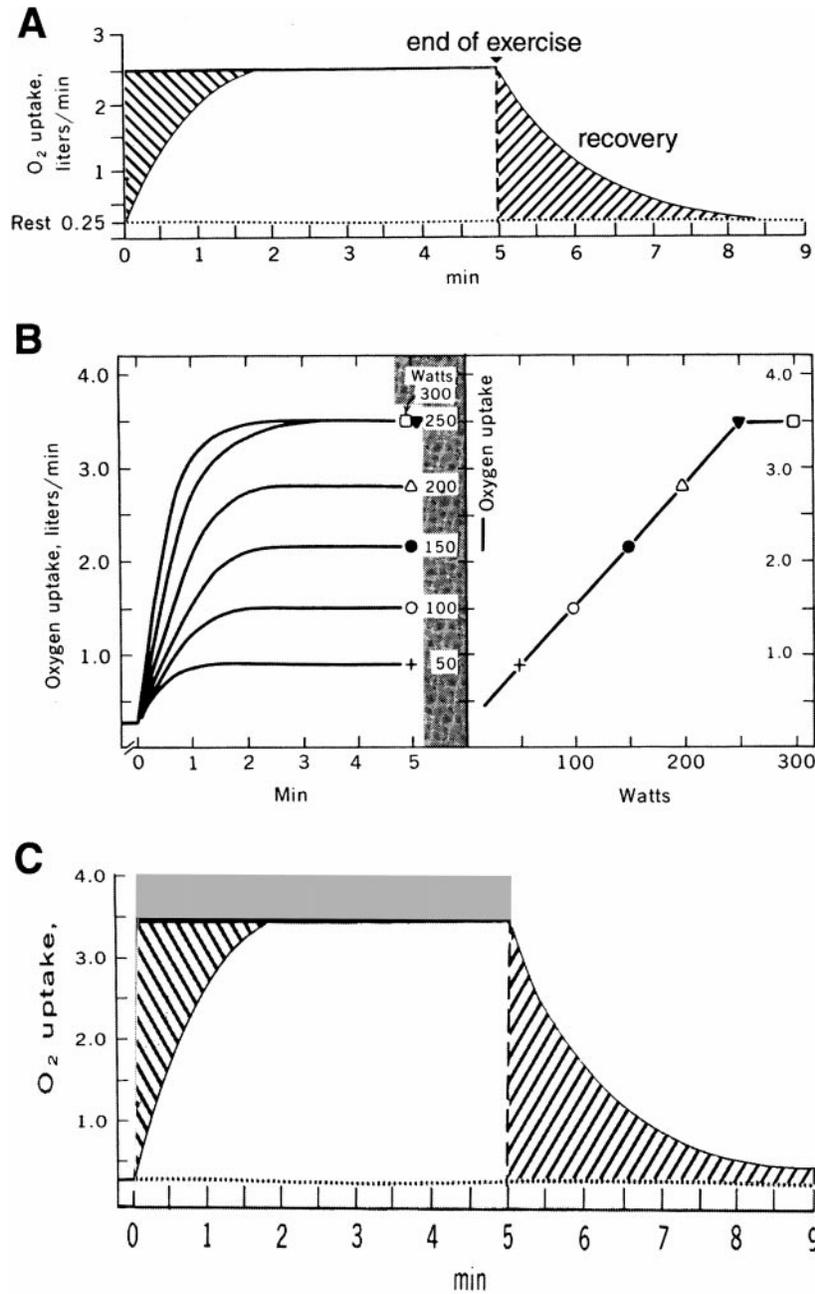

FIG 1.

determined by arterial oxygen carrying capacity (hematocrit) and by the ability of the respiratory system to load oxygen in the pulmonary capillaries. As illustrated in Fig. 4, arterial oxygen carrying capacity and content increase slightly with increasing exercise intensity in humans. Arterial oxygen carrying capacity is increased because of increased arterial hematocrit resulting from splenic constriction. The increase in hematocrit produced by this mechanism is much greater in other, more athletic animals such as horses and dogs, in which hematocrit can reach 60% (resting hematocrits are similar to those for humans) during intense exercise. [I believe it is beneficial to present data for arterial oxygen content of the horse during exercise and review the importance of hematocrit and hemoglobin content in determination of oxygen carrying capacity of blood. It is also beneficial to ask the students to consider what effect anemia will have on exercise capacity.]

The huge increase in ($Ca_{O_2} - Cv_{O_2}$) observed during intense exercise is primarily the result of decreased mixed venous oxygen content. Mixed venous oxygen
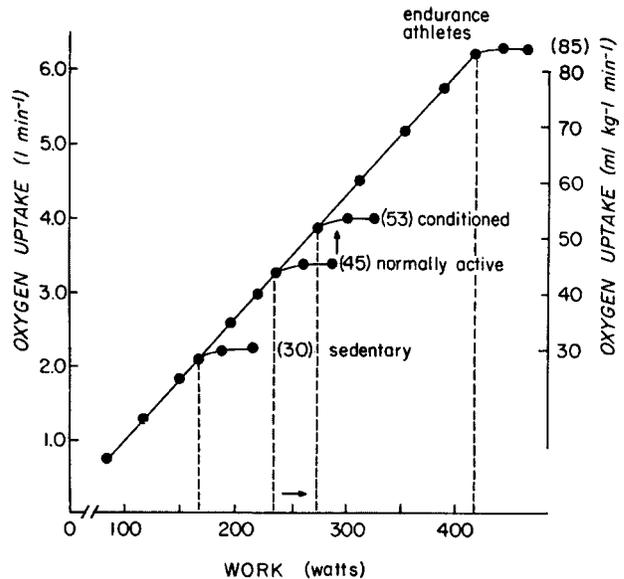

FIG. 2.
The relationship between exercise intensity and oxygen uptake is similar in human subjects with different levels of physical conditioning, but their maximal oxygen uptakes are quite different. Values for oxygen consumption are expressed in l/min (*left*) and ml·min⁻¹·kg⁻¹ (*right*). [Reprinted from Rowell (7) with permission.]

FIG. 1.
Oxygen consumption (O_2 uptake) as a function of time during and after steady-state, dynamic exercise. *A*: With initiation of steady-state exercise (*time 0*), oxygen uptake increases over the first 1–2 minutes and levels off at a steady-state value. During the 1st minute of exercise, oxygen uptake does not match oxygen demand, resulting in an oxygen deficit (crosshatched area, *upper left*). During the plateau, oxygen demand of the exercise is matched to oxygen supply. During recovery, there is a gradual decrease in the oxygen uptake down to resting levels. The excess oxygen consumed during recovery (crosshatched area, *lower right*), above resting values, has been called the oxygen debt. *B*: increases in exercise intensity modify the time course of changes in oxygen uptake and the steady-state amount of oxygen uptake (*left*). Oxygen uptake at 5 minutes of exercise is plotted as a function of exercise intensity in watts (*right*). Note that when exercise intensity was increased from 250 to 300 W, oxygen uptake did not increase. The increased workload was fueled by anaerobic processes (*C*). *C*: When exercise intensity produces an oxygen demand that exceeds the subject's maximal oxygen consumption (in this case, when exercise intensity was 300 W), anaerobic processes provide the needed energy. The portion of the exercise oxygen requirement that cannot be supplied by aerobic metabolism is illustrated above the maximal oxygen consumption ($\dot{V}o_{2max}$; shaded area). Note that recovery oxygen consumption is elevated above resting for a longer period of time. [Modified from Astrand and Rodahl (1) with permission.]

content decreases with increasing exercise intensity (Fig. 4). The decrease in mixed venous oxygen content during exercise is primarily the result of redistribution of cardiac output from tissues that extract small amounts of oxygen, such as the liver and kidney, to tissues that extract large amounts of oxygen, such as cardiac and active skeletal muscle. The data in Fig. 5 illustrate this effect. At rest, 20–30% of cardiac output is distributed to cardiac and skeletal muscle. The oxygen content of blood in the coronary veins and veins draining active skeletal muscle is very low (2–4 vol%). During maximal exercise, ~95% of total cardiac output is going to the heart and active skeletal muscle (Fig. 5), and as a result, 95% of venous return comes from muscle tissue where venous oxygen content is very low. Thus, with increasing exercise intensity, the relative amount of venous blood returning to the heart from active striated muscle increases so that mixed venous oxygen content decreases as shown in Fig. 4. With this review of the determinants of maximal oxygen consumption as background, let us consider the cardiovascular effects of dynamic exercise in more detail.
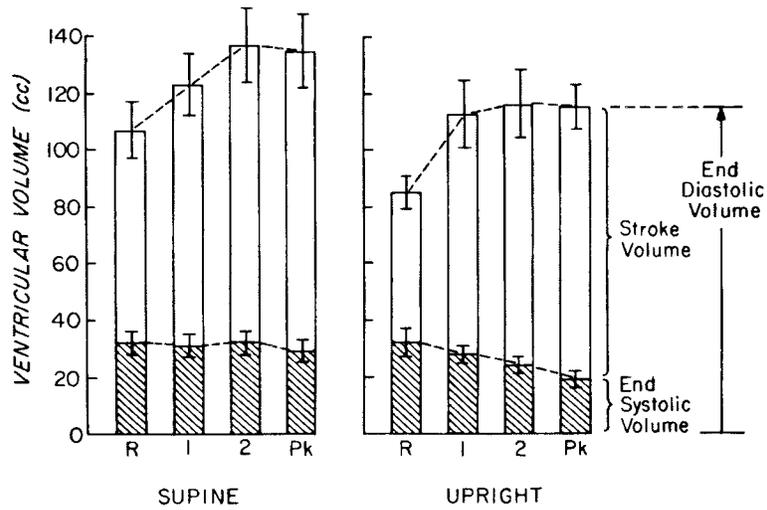
FIG. 3.

Ventricular volumes at rest and as a function of exercise intensity in supine and upright postures. Note that end-diastolic volume increases during exercise. Also, in the upright posture, end-systolic volume decreases with increasing exercise intensity. *R*, rest; exercise intensities were mild (1), moderate (2), and peak (Pk). Values are means ± SE. [Reprinted from Rowell (7) with permission.]
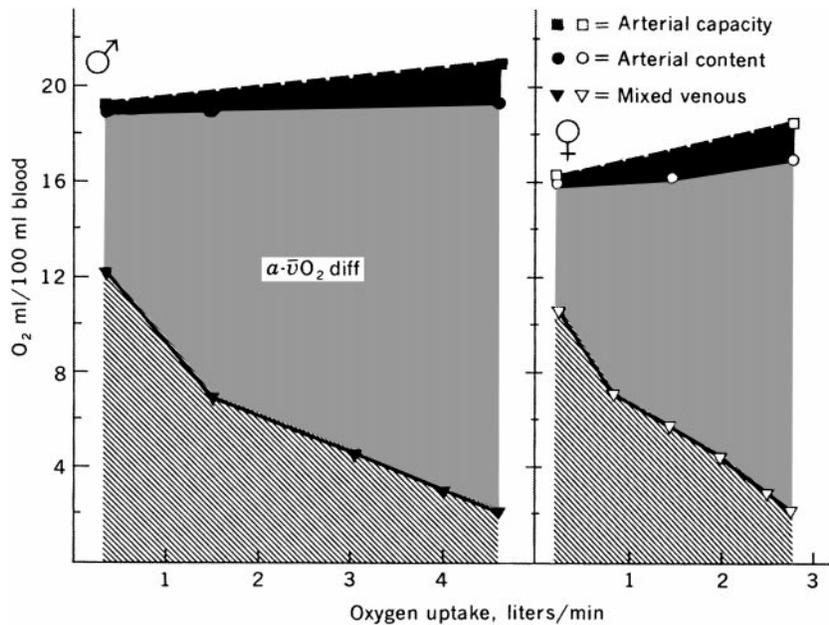

FIG. 4.

Arterial and venous oxygen contents and arterial oxygen carrying capacity plotted as a function of exercise intensity, reflected in measurements of oxygen uptake. Mean values for 5 male (*left*) and 5 female (*right*) subjects are presented. [Reprinted from Astrand and Rodahl (1) with permission.]
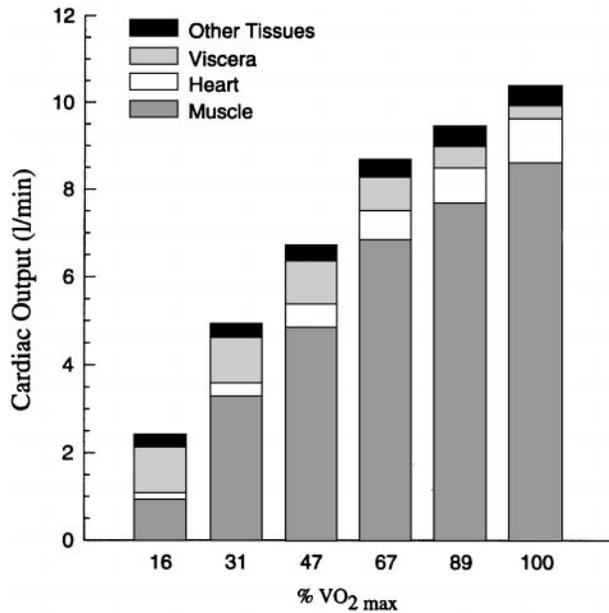
FIG. 5.
Cardiac output and distribution of cardiac output to skeletal muscle (muscle), heart, visceral tissues, and other tissues of miniature swine as a function of exercise intensity, reflected in measurements of oxygen consumption. Note that with increasing intensity of exercise the portion of cardiac output distributed to skeletal muscle increases, whereas the amount of cardiac output distributed to viscera decreases. [Reprinted from Laughlin et al. (4).]

CARDIOVASCULAR EFFECTS OF DYNAMIC EXERCISE

As described above, heart rate, cardiac output and oxygen consumption all increase linearly with exercise intensity up to maximal levels. Dynamic exercise also alters other key cardiovascular parameters. Dynamic exercise has modest effects on arterial blood pressures. As illustrated in Fig. 6, mean and systolic blood pressures increase with increasing exercise intensity. When dynamic exercise is performed with the arms, the magnitude of increases in arterial pressure are ~10% greater than those seen with the leg exercise shown in Fig. 6.

In contrast to most other conditions under which arterial blood pressure is increased, the increase in blood pressure observed during dynamic exercise is not the result of increased total peripheral resistance. Indeed, during dynamic exercise at maximal levels, total peripheral resistance is less than one-half its
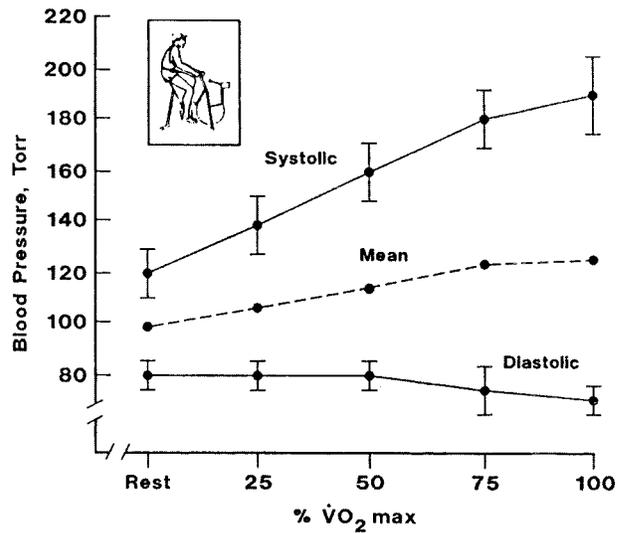

FIG. 6.
Systolic, mean, and diastolic arterial pressures of human subjects graphed as a function of exercise intensity (bicycle exercise), reflected in measurements of oxygen consumption. $\dot{V}o_{2max}$, maximal oxygen consumption. Note that with increasing intensity of exercise, systolic and mean arterial pressures increase. Values are means ± SE for systolic and diastolic pressures. [Reprinted from MacDougall (5) with permission of Futura.]

value at rest. [At this point I encourage the students to plot total peripheral resistance as a function of oxygen consumption on Fig. 2. It is common for them to associate vasoconstriction in the viscera with increases in arterial pressure and be confused.] The decrease in total peripheral resistance is the result of decreased vascular resistance in skeletal muscle vascular beds, leading to increased blood flow. The increase in blood flow to cardiac and skeletal muscle produced by exercise is called exercise hyperemia. Providing adequate cardiac output to support exercise hyperemia is the primary driving force for most of the cardiovascular effects of dynamic exercise. There are five important features of skeletal muscle exercise hyperemia.

Important features of exercise hyperemia. The first major determinant is the magnitude of the response. As illustrated in Fig. 5, there is simply a huge amount of blood flowing through skeletal muscle during high-intensity exercise. Note that cardiac output increases nearly sixfold and that all of this increased cardiac output is going to skeletal muscle.

Indeed, blood flow is also redistributed away from visceral tissues to active skeletal muscle (1, 6, 7). Similar changes in muscle blood flow, cardiac output, and its distribution occur in most mammals (4). Blood flow is not uniformly distributed within the skeletal muscles during locomotory exercise; rather, the pattern of blood flow, as a function of exercise intensity, is not the same for different muscle tissue. Blood flow decreases in white skeletal muscle whereas it increases in red muscle of animals during exercise at low intensity. In contrast, during sprinting, blood flow increases even in the white skeletal muscle. However, during sprinting, the magnitude of the increase in blood flow is much greater in red muscle than in white. It seems likely that similar patterns of blood flow distribution within and among muscles are present in humans during locomotory exercise.

How do these dramatic changes in muscle blood flow occur during exercise? To answer that question, we need to consider the primary forces that cause the movement of fluid through tubes. The force that causes fluid to move through a tube, pipe, or blood vessel is a pressure gradient. In the vascular system the pressure gradient is most often in the form of the difference between arterial pressure and venous pressure. The second major determinant of blood flow is vascular resistance to flow through the vascular tree (tubes). The primary cause of increased blood flow to the active muscle is a decrease in vascular resistance. Vascular resistance is determined primarily by the caliber (radius) of resistance arteries and arterioles, which is controlled by the contraction of vascular smooth muscle in the walls of these arteries. Thus the third feature of exercise hyperemia is that it occurs because of dramatic increases in vascular conductance (decreased vascular
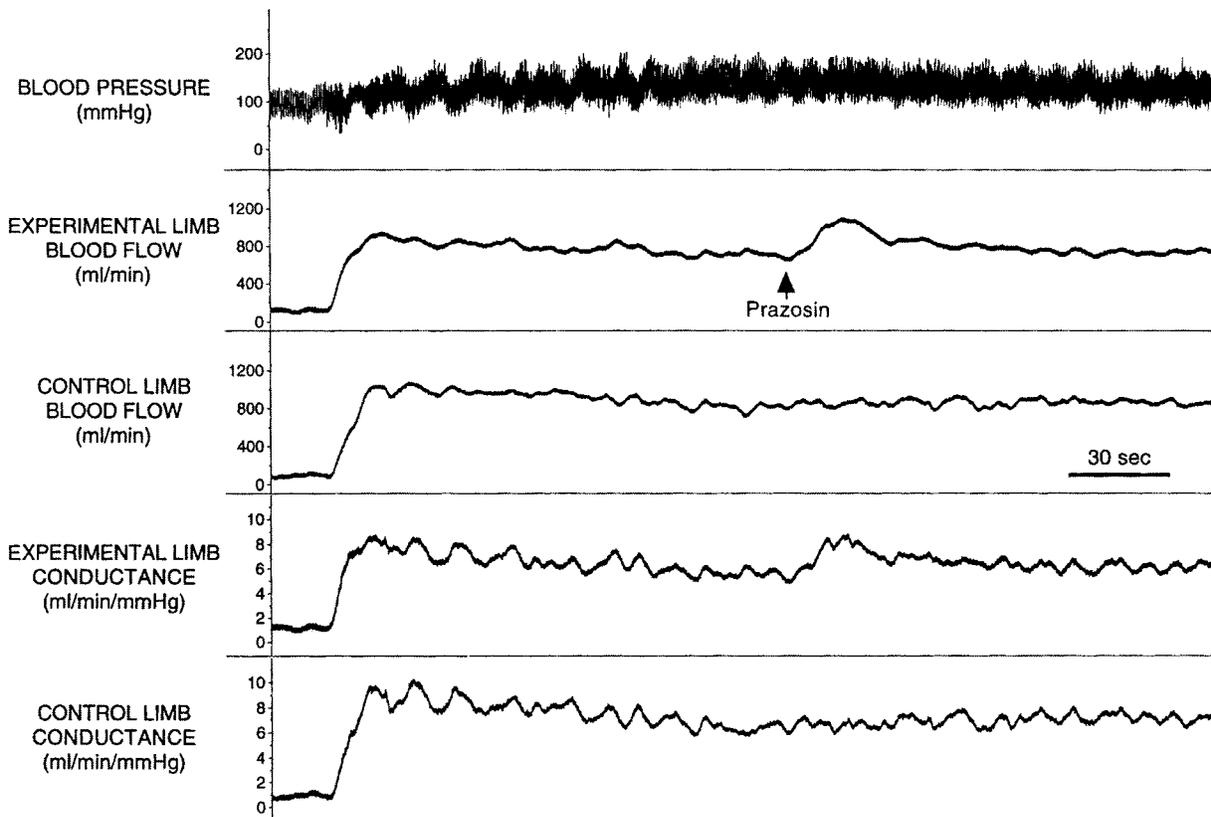

FIG. 7.

Recordings of blood pressure, limb blood flow, and conductance as a function of time for a dog at rest and during dynamic exercise. Note that limb blood flow and conductance increased at the initiation of exercise at 6 miles/h. Note the rapid increase in blood flow that occurs at the initiation of exercise. As shown, prazosin (0.1 mg; arrow) was administered (intra-arterially unilaterally to the experimental limb) at 2 minutes of exercise to block α_1-adrenergic receptors, providing evidence of α_1-adrenergic vasoconstriction during exercise. [Reprinted from Buckwalter et al. (2) with permission.]
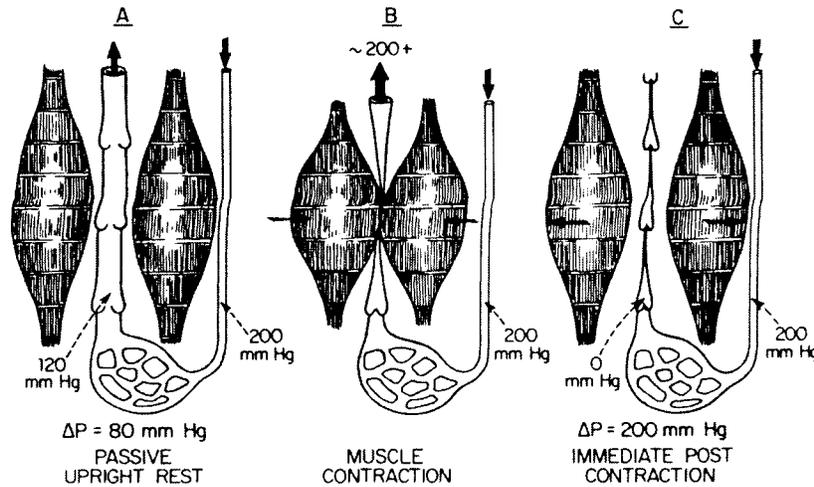
FIG. 8.

Illustration of muscle pump effect on venous return and muscle blood flow to active muscle tissue. *A*: hemodynamic conditions for a skeletal muscle of lower limb of a subject in upright posture, at rest. ΔP, change in pressure. *B*: effects of muscle contraction on vasculature. Muscle contraction forces blood out of venous segments, increasing venous driving pressure toward the heart, and blocks arterial inflow. *C*: conditions believed to exist immediately after muscle contraction. Note that pressures in small veins fall to zero and that, because of venous valves, refilling must occur from the arterial system through the capillary bed. The net effect of the muscle pump is to increase driving pressure for blood flow through muscle and to enhance venous return to the heart. [Reprinted from Rowell (6) with permission.]

resistance) mediated by relaxation of vascular smooth muscle in the resistance arteries and arterioles feeding the active skeletal muscle.

The fourth important feature of exercise hyperemia is the fact that blood flow to active striated muscle increases in a linear fashion with increasing oxygen consumption. Although the relationship is not as tight at very low oxygen consumption levels, in the skeletal muscles of conscious animals performing exercise it appears that blood flow is linearly related to oxygen consumption. This relationship is part of a host of evidence that metabolic rate of muscle plays a key role in control of muscle blood flow during exercise (4).

The fifth and final feature of exercise hyperemia in conscious subjects is the rapid onset of the increases in blood flow associated with the initiation of exercise. For example, Buckwalter et al. (2) measured blood flow and conductance in the iliac arteries of dogs during the transition from rest to exercise. Figure 7 presents data which illustrate the rapid increase in blood flow that occurs at the time the dogs begin to

exercise. Blood flow increases with the first step and reaches a plateau within 3–5 seconds (Fig. 7).

Mechanisms for exercise hyperemia. It is generally believed that exercise hyperemia is a local phenomenon. Perhaps the strongest evidence in support of this notion is the fact that isolated, perfused skeletal muscle preparations exhibit exercise hyperemia. In an intact subject, central control systems are superimposed on the local vascular control processes discussed below. Thus exercise hyperemia appears to be primarily a local event that is modulated by central cardiovascular control processes.

Blood flow to skeletal muscle is determined by the interactions among perfusion pressure, extravascular mechanical effects of muscle contraction, and the caliber of resistance vessels. Thus, during high intensities of exercise, the increase in mean arterial pressure contributes to the increase in skeletal muscle blood flow.

During contraction of both cardiac and skeletal muscle, extravascular mechanical effects of contraction in-
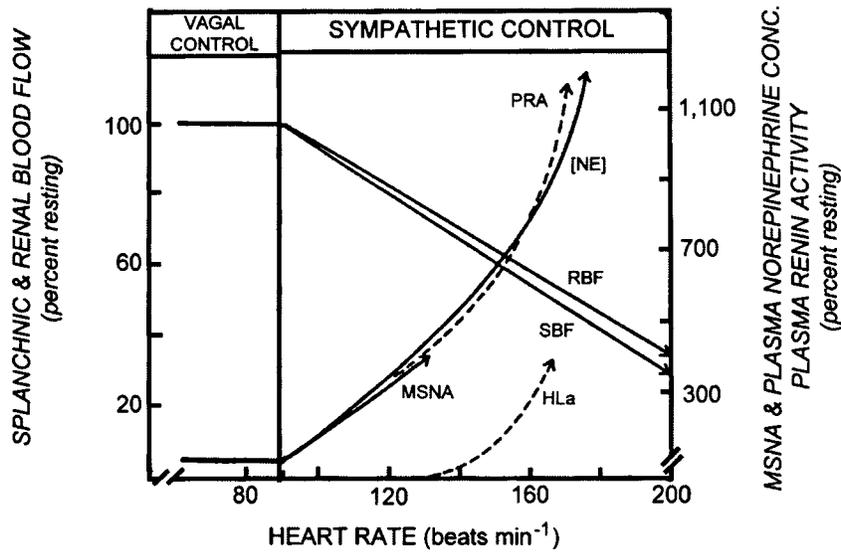
FIG. 9.

Illustration of effects of increasing exercise intensity on sympathetic control of blood flow and vascular conductance in humans, reflected in measurements of heart rate. Note that at rest, when heart rate is low, the heart is under vagal (parasympathetic) control. Sympathetic nervous system activity increases as vagal control is withdrawn. Sympathetic nervous activity increases with increasing exercise intensity as reflected in decreases in splanchnic (SBF) and renal blood flow (RBF) to vascular beds, increased plasma norepinephrine concentrations ([NE]), increased plasma renin activity (PRA), and increased muscle sympathetic nerve activity (MSNA). Blood lactate concentration (HLa) does not increase until exercise intensity is 50–60% of maximal (heart rates of 130–140 beats/min). [Reprinted from Laughlin et al. (4) as adapted from Rowell (6, 7).]

crease resistance to blood flow so that blood flow ceases during contraction. However, with the rhythmic contractions of skeletal muscle associated with dynamic exercise, the "muscle pump effect" appears to increase blood flow during dynamic exercise (3, 4, 6, 7). As illustrated in Fig. 8, the interactions of compression of the small veins produced by muscle contraction and the venous valves facilitate venous return of blood to the heart and perfusion of the muscle tissue (3, 6).

Another important cause of increased blood flow in skeletal muscle is the fact that vascular conductance is tightly coupled to metabolic rate so that conductance increases with increased muscle activity. The caliber of resistance arteries is regulated by local control factors, including metabolic, myogenic, and endothelial components (4). Metabolic control appears to play a central role in exercise hyperemia in both cardiac and skeletal muscle tissue as evidenced by the tight

relationship between blood flow and metabolism. Relaxation of vascular smooth muscle in arteries and arterioles produced by increased metabolism increases blood flow and recruits more perfused capillaries in the muscle tissue.

The mechanisms responsible for arteriolar vascular smooth muscle relaxation in arterioles appear to be similar in cardiac and skeletal muscle during exercise, but the relative importance of these mechanisms is different in cardiac and skeletal muscle and among types of skeletal muscle (4). The metabolites responsible for metabolic vascular control have not been clearly established. Recent research indicates that endothelium-mediated vascular control also plays an important role in exercise hyperemia of cardiac and skeletal muscle through flow-induced dilation and/or propagated vasodilation (4). At this time it appears that exercise hyperemia in skeletal muscle is mediated by a combination of metabolic vasodilation, endothe-
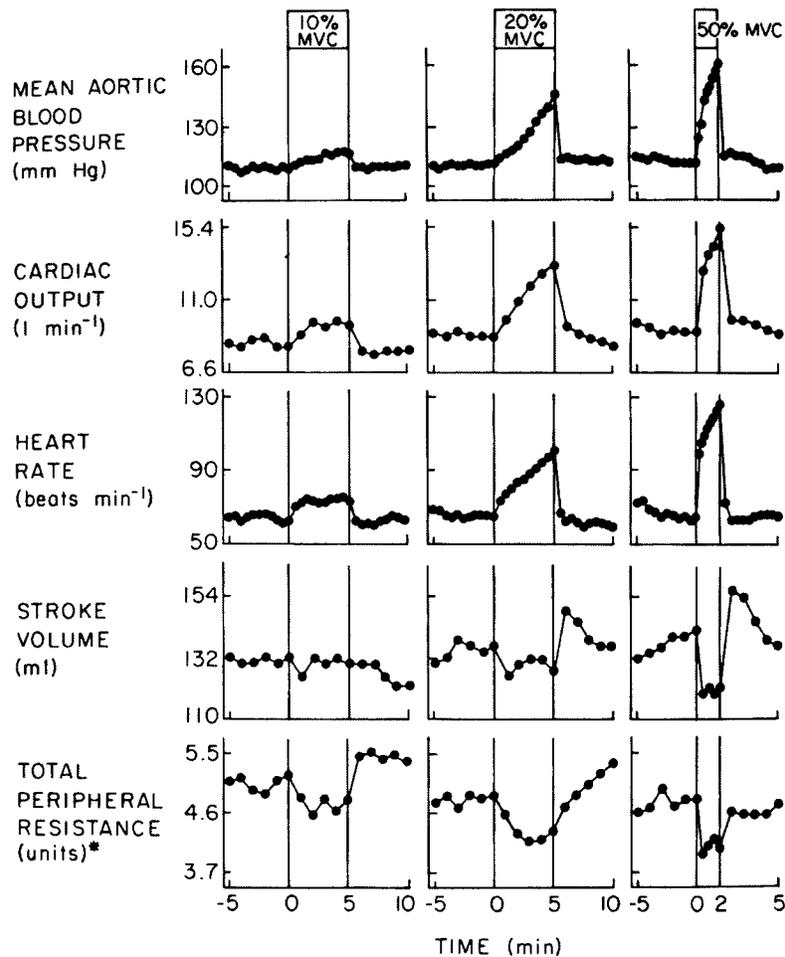
FIG. 10.

Hemodynamic effects of isometric contraction of forearm muscle (isometric handgrip) at 10, 20, and 50% maximal voluntary contraction (MVC) for 1 subject. Peripheral resistance units (PRU) are expressed as $dyn \cdot s^{-1} \cdot cm^{-5} \times 10^3$. Note that with increasing intensity of exercise, systolic and mean arterial pressures increase and the magnitude of increase is greater than that observed in subjects during dynamic exercise (see Fig. 6). Values are means ± SE for systolic and diastolic pressures. [Reprinted from Rowell (7) with permission.]

lial vasodilator mechanisms, and the muscle pump mechanism. As illustrated in Fig. 9, there is also evidence that sympathetic nervous activity to skeletal muscle increases with increasing exercise intensity. The effects of the increased sympathetic stimulation appear to be blunted by the aforementioned vasodilator signals leading to the integrated response. The enormous decrease in vascular resistance in skeletal muscle vascular beds during dynamic exercise causes total systemic vascular resistance to decrease. Mean

arterial pressure is increased despite the decrease in resistance because cardiac output is increased more than vascular resistance is decreased.

As shown in Fig. 5, at the same time that vascular resistance in skeletal muscle vascular beds and the coronary circulation is decreasing, vascular resistance is increasing in visceral tissues, causing blood flow to these tissues to decrease. The increase in vascular resistance in the visceral tissues (renal and splanchnic
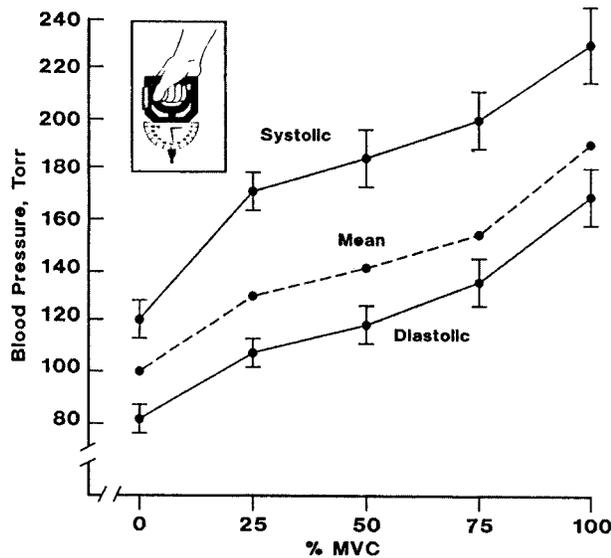
FIG. 11.

Systolic, mean, and diastolic arterial pressures of human subjects graphed as a function of exercise intensity (isometric handgrip) expressed as %MVC. Note that with increasing intensity of exercise, systolic and mean arterial pressures increase and that the magnitude of increase is greater than that observed in subjects during dynamic exercise (see Fig. 6). Values are means ± SE for systolic and diastolic pressures. [Reprinted from MacDougall (5) with permission of Futura.]

FIG. 12.

Mean arterial pressures of human subjects graphed as a function of duration of contraction (isometric exercise). Note that pressure is highest during dead lift exercise and lowest during handgrip exercise and that pressure increases with time of contraction for all 3 types of exercise. Values are means ± SE for systolic and diastolic pressures. [Reprinted from MacDougall (5) with permission of Futura.]

tissues) is the result of a progressive increase in sympathetic stimulation to these vascular beds. As illustrated in Fig. 9, as exercise intensity increases, producing heart rates >100 beats/min, sympathetic constriction of resistance arteries in renal and splanchnic vascular beds increases as evidenced by increasing plasma norepinephrine levels. Also, plasma renin activity increases with increasing exercise intensity, contributing to the increased vascular resistance and decreased blood flow to the viscera. Figure 9 also illustrates the fact that muscle sympathetic nerve activity (MSNA) increases with increasing exercise intensity. However, in the active skeletal muscle, increased metabolism and other mechanisms discussed above result in a net decrease in vascular resistance and increase in blood flow to skeletal muscle (Fig. 5).

CARDIOVASCULAR EFFECTS OF ISOMETRIC EXERCISE

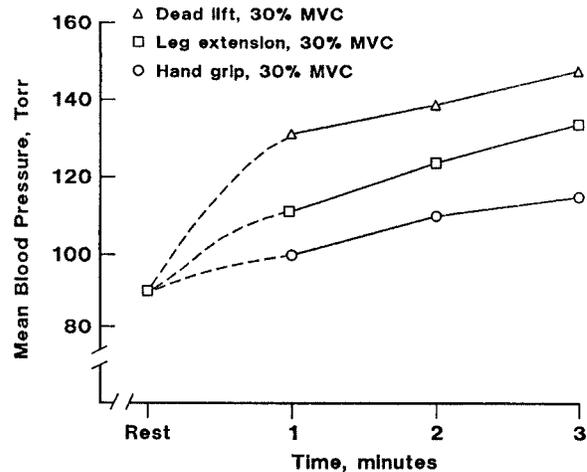The effects of sustained isometric muscle contraction are much different than those seen in dynamic exercise. The effects of isometric arm exercise on the cardiovascular system can be appreciated from the data presented in Fig. 10. Note that mean arterial pressure, cardiac output, and heart rate all increase with increases in isometric contractile force. The increase in blood pressure produced by isometric voluntary muscle contraction is far greater than the metabolic cost of the exercise. Indeed, in general, the heart rate and blood pressure increases produced by isometric exercise exceed those of dynamic exercise when duration, intensity, and active muscle mass are similar. For example, note in Fig. 11 that systolic pressures are in excess of 220 mmHg and mean pressures in excess of 180 mmHg during maximal isometric contraction of the arm. Figure 12 illustrates the fact that the magnitude of increase in arterial pressures is proportional to the size of the muscle mass activated and the duration of sustained contraction. Another important difference between dynamic exercise and isometric muscle contraction is that cardiovascular adjustments to isometric contraction do not reach a steady state. As shown in Figs. 10 and 12, even after several minutes of exercise, blood pressures and heart rates are continuing to increase.

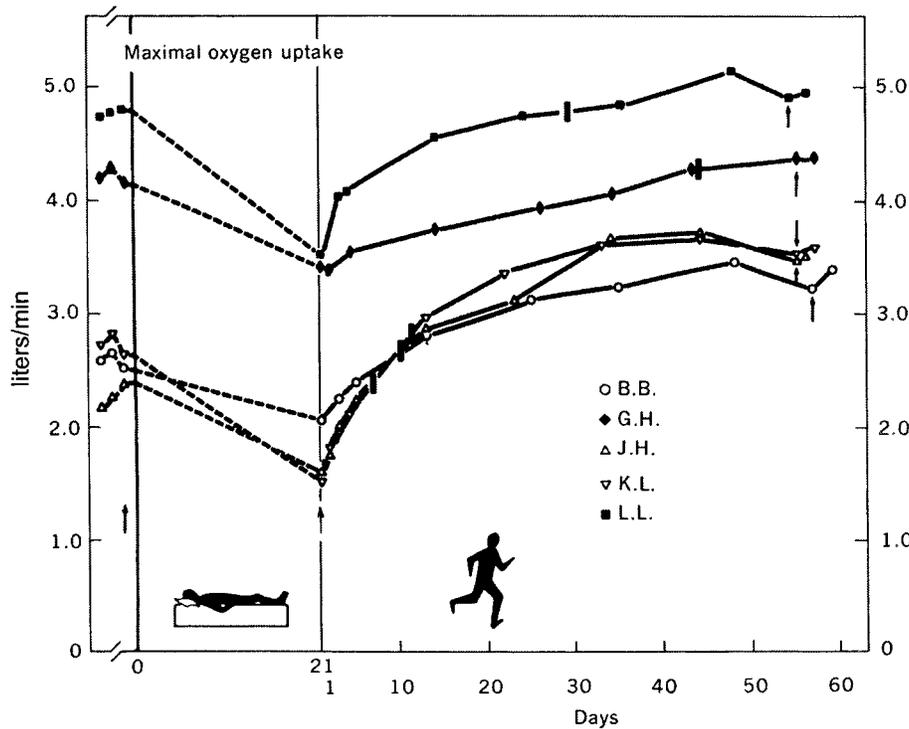Blood flow to muscles contracting isometrically increases if the contractions develop <30% maximal

FIG. 13.

Effects of 21 days of bed rest and subsequent exercise training on maximal oxygen uptake measured during treadmill exercise in 5 human subjects. Circulatory studies summarized in Figs. 14 and 15 were performed at times indicated by arrows. Symbols represent subjects' initials. [Reprinted from Astrand and Rodahl (1) using data of Saltin et al. (8) with permission.]

voluntary contraction (MVC). When contraction develops >40–60% MVC, blood flow is decreased or ceases during contraction and increases with muscle relaxation. The large increases in blood pressure seen during intense isometric contractions appear to be partially the result of the muscle chemoreflex. These effects of isometric arm exercise have important consequences in cardiovascular disease such as coronary heart disease. For example, shoveling snow is a common cause of angina and heart attack in patients with coronary heart disease. This appears to be the result of the excessive increases in heart rate and blood pressure produced by isometric arm exercise.

CHRONIC INACTIVITY AND TRAINING ALTER CARDIOVASCULAR RESPONSE TO EXERCISE

When normal humans become restricted to bed rest or prolonged exposure to weightlessness, their exercise tolerance is dramatically decreased. This is associated with a decrease in maximal oxygen consumption. This is illustrated in Fig. 13 from the classic study by Saltin et al. (8). Note that after 21 days of bed rest, all 5 subjects had decreased maximal oxygen uptake. Equally important, when the subjects began exercise training, their maximal oxygen consumption began to recover within days and by 50 days was even greater than values before bed rest. Figure 14 summarizes data collected from these subjects and allows analysis of the determinants of maximal oxygen uptake responsible for changes related to bed rest and exercise training. First, note that the subjects exhibited linear relationships between cardiac output and oxygen uptake that were similar except that the maximal cardiac output was least after 21 days bed rest and greatest after training. $(Ca_{O_2} - Cv_{O_2})$ was similar in controls and after bed rest but was increased slightly after exercise training. Stroke volume was significantly decreased at rest and at all intensities of
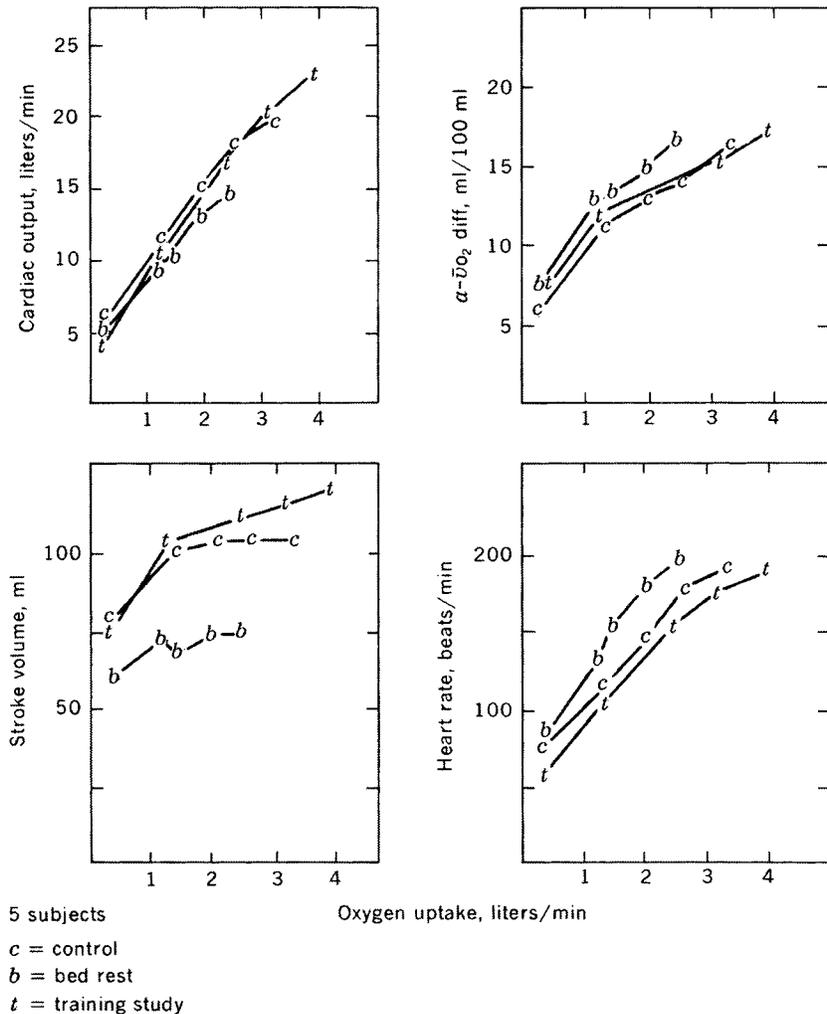
FIG. 14.
Cardiac output, arteriovenous oxygen content difference, stroke volume, and heart rate as functions of exercise intensity, reflected as oxygen uptake for the subjects illustrated in Fig. 13. *c*, control values before intervention; *b*, after a 20-day period of bed rest; *t*, after 50 days of exercise training. [Reprinted from Astrand and Rodahl (1) using data of Saltin et al. (8) with permission.]

5 subjects
c = control
b = bed rest
t = training study

exercise in the bed rest subjects. Resting stroke volume was similar in control conditions and after training. However, with exercise, stroke volume increased more after exercise training. Finally, resting heart rate was decreased after training and was slightly higher than control after bed rest. Heart rate increased with increases in exercise intensity under all three conditions, and the maximal heart rate was similar. However, the heart rate tended to be less at each given level of oxygen uptake after exercise training.

Figure 15 summarizes what these data indicate were the changes that produced decreases in maximal oxygen consumption when these subjects underwent 21 days of bed rest. Maximal cardiac output was decreased because of decreased stroke volume. The decreased stoke volume appears to be primarily caused by decreased venous return. With exercise training, these subjects exhibited increased stroke volume compared with controls and an increased (Ca_{O_2} − Cv_{O_2}) at maximal exercise. This appears to result from
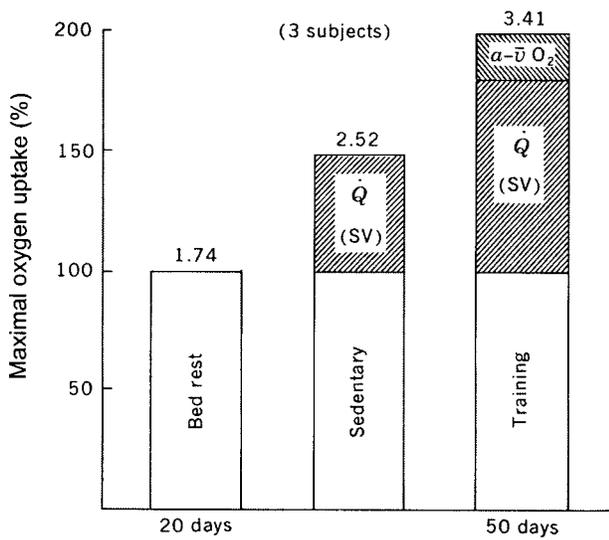
FIG. 15.

Illustration of mechanisms for changes in maximal oxygen uptake produced by altered physical activity. Data are for 3 subjects after 20 days of bed rest where maximal oxygen uptake was 1.74 l/min. In these subjects before bed rest, oxygen uptake was greater than bed rest values because of increased maximal stroke volume (SV) and cardiac output. Increases in maximal oxygen uptake ($\dot{Q}$) produced by exercise training were results of further increases in stroke volume and cardiac output and increases in arteriovenous oxygen content difference. [Reprinted from Astrand and Rodahl (1) using data of Saltin et al. (8) with permission.]

the increased muscle blood flow available in the subjects after training. The increased stroke volume appears to result from increased venous return during exercise and improved cardiac performance. These results reflect how these hemodynamic parameters influence maximal oxygen consumption and the mechanisms involved in changes in oxygen transport

FIG. 16.

Illustration of cardiovascular responses to dynamic exercise of increasing intensity, reflected in measurements of oxygen uptake. Results are presented for normal subjects (NA), highly trained athletes (ATH), and subjects with mitral stenosis (MS). Vertical dashed lines represent maximal oxygen uptake for each group. Note that the splanchnic and renal blood flows begin to decrease and plasma [NE] (NE conc.) begin to increase when heart rates are equal to ~100 beats/min, as shown in Fig. 9. These data illustrate that, in all 3 groups of subjects, sympathetic vasoconstriction in visceral vascular beds increases in proportion to relative exercise intensity. [Adapted from Rowell (6) with permission.]

capacity produced by chronic changes in a person's level of physical activity.

Examination of cardiorespiratory responses to exercise can also be used in diagnosis of cardiorespiratory disease. In general, if a patient has limited exercise tolerance, he or she has disease or pathology at some point in the pathway for oxygen leading to decreased maximal oxygen uptake. If the problem is respiratory,
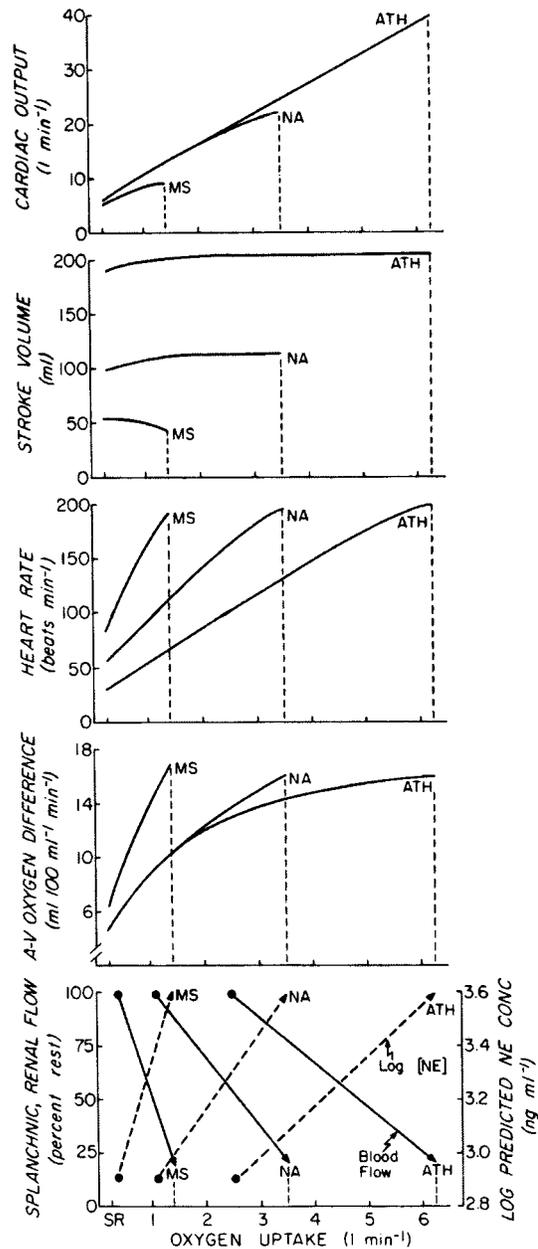
then hemodynamic parameters will be normal and the patient will have systemic hypoxia (Ca_{O_2} will be decreased). If the patient has cardiovascular disease, then Ca_{O_2} will usually be normal but blood flow delivery to skeletal muscle will be limited because of limited cardiac output and/or peripheral vascular disease. For example, let us compare and contrast results from normal subjects, trained athletes, and patients with decreased cardiac function caused by mitral stenosis. Mitral stenosis serves here only as an example. Any condition that limits cardiac function and cardiac output will have similar effects.

EFFECTS OF MITRAL STENOSIS ON CARDIOVASCULAR EFFECTS OF EXERCISE

Mitral stenosis will limit the flow of blood into the left ventricle and, as a result, limit cardiac output. Figure 16 summarizes the expected effects of mitral stenosis on the cardiovascular response to exercise and allows comparison with responses in normal adults and athletes. Note that the major problem is limited maximal cardiac output (Fig. 16, *top*). This limitation is caused by low stroke volume, because maximal heart rate is similar across the three subjects. Maximal ($Ca_{O_2} - Cv_{O_2}$) is also similar across subjects. The mitral stenosis subjects compensate for the low stroke volume at rest by having increased heart rate and ($Ca_{O_2} - Cv_{O_2}$). The results presented in Fig. 17 illustrate the regional distribution of cardiac output in these subjects. Note that at rest, blood flows are similar in the mitral stenosis, normal, and trained (athletes) subjects. When the subjects exercise at their maximal level, blood flow to all tissues except muscle are similar across the subjects but muscle blood flow is very limited in the mitral stenosis subjects. The major difference is that the mitral stenosis subjects have much less cardiac output left to distribute to skeletal muscle.

An important feature of the relationship between exercise intensity and sympathetic stimulation to the viscera is revealed in the results presented in Fig. 16, *bottom*, where visceral blood flows are decreased maximally and sympathetic stimulation is near maximal in the mitral stenosis subjects at an oxygen consumption of only 1.5 l/min. At this same level of oxygen consumption there is only a modest decrease in blood flow in normal subjects and no change from resting in the athletes. However, if the *x*-axis is
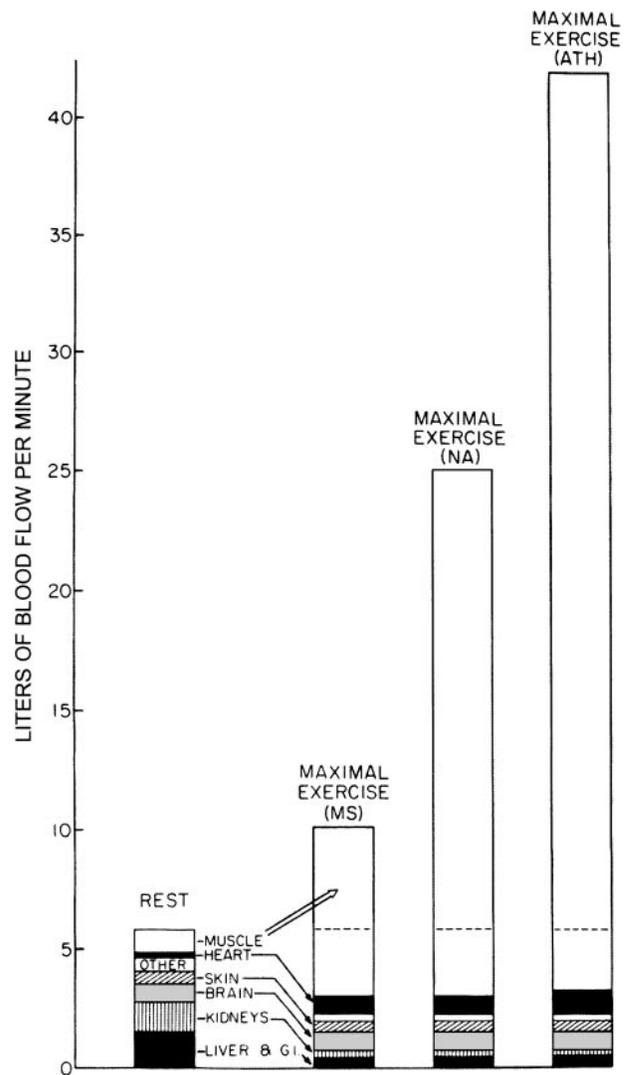

FIG. 17.
Cardiac output and distribution of cardiac output to tissues at rest and during exercise at intensities producing maximal oxygen uptake (maximal exercise). Results are presented similarly to data in Fig. 16. At rest, cardiac output and blood flow distributions are similar in all 3 groups. Also, blood flows to nonmuscular regions are similar in all 3 groups during maximal exercise. However, blood flow to active skeletal muscle and total cardiac output is much different among the 3 groups. GI, gastrointestinal. [Adapted from Rowell (7) with permission.]

changed to percent maximal oxygen consumption, then the three curves superimpose. [At this point I encourage the students to regraph these data by changing the *x*-axis to %maximal oxygen consump-

tion. As a result, the data for all 3 groups of subjects become superimposable.]. Thus these results indicate that the sympathetic nervous system response is linked to ''relative'' exercise intensity. Because the mitral stenosis subject is exercising at a maximal oxygen consumption of 1.5 l/min, sympathetic constrictor tone is maximal to the renal and splanchnic vascular beds.

In summary, the cardiovascular effects of dynamic exercise are driven by the demands of active skeletal muscle for oxygen. During dynamic exercise, cardiac output increases five- to sixfold. The dramatic increases in cardiac output result from increased pump function of the heart and increased venous return to the heart. All of this increased blood flow is distributed to skeletal muscle. In addition, sympathetic vasoconstrictor tone is increased in visceral vascular beds diverting blood flow to active skeletal muscle. Sustained isometric muscle contractions produce exaggerated increases in heart rate and arterial pressures. Anything that decreases the ability of the cardiovascular system to deliver oxygenated blood to active muscle will limit exercise performance. Such changes can be produced in normal subjects. For example, during heat stress, skin blood flow increases to control core body temperature. As much as 7.0 l/min of cardiac output can be distributed to skin in severe heat stress. As a result, exercise capacity is limited in hot, humid environments because less cardiac output can be delivered to active muscle. Also, exercise stress can be used in diagnosis of cardiorespiratory disease because of the tight relationship between exercise intensity, heart rate, cardiac output, and cardiovascular function.

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References

1. **Astrand, P., and K. Rodahl.** *Textbook of Work Physiology.* New York: McGraw-Hill, chapt. 6, 9, and 12, 1970, p. 117–183, 279–318, and 375–430.
2. **Buckwalter, J. B., P. J. Mueller, and P. S. Clifford.** Sympathetic vasoconstriction in active skeletal muscles during dynamic exercise. *J. Appl. Physiol.* 83: 1575–1580, 1997.
3. **Laughlin, M. H.** Skeletal muscle blood flow capacity: the role of the muscle pump in exercise hyperemia. *Am. J. Physiol.* 253 (*Heart Circ. Physiol.* 22): H993–H1004, 1987.
4. **Laughlin, M. H., R. J. Korthuis, D. J. Duncker, and R. J. Bache.** Control of blood flow to cardiac and skeletal muscle during exercise. *Handbook of Physiology. Exercise: Regulation and Integration of Multiple Systems.* Bethesda, MD: Am. Physiol. Soc., 1996, sect. 12, chapt. 16, p. 705–769.
5. **MacDougall, J. D.** Blood pressure responses to resistive, static, and dynamic exercise. In: *Cardiovascular Response to Exercise.* Mount Kisco, NY: Am. Heart. Assoc., 1994, chapt. 9, p. 155–173.
6. **Rowell, L. B.** *Human Circulation.* New York: Oxford Univ. Press, 1986, chapt. 7–9, p. 137–256.
7. **Rowell, L. B.** *Human Cardiovascular Control.* New York: Oxford Univ. Press, 1993, chapt. 5–8, p. 162–325.
8. **Saltin, B., B. Blomqvist, J. H. Mitchell, R. L. Johnson, Jr., K. Wildenthal, and C. B. Chapman.** Response to submaximal and maximal exercise after bed rest and training. *Circulation* 38, *Suppl.* 7: 1–78, 1968.