Principles of Exercise Physiology: Responses to Acute Exercise and Long-term Adaptations to Training

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Abstract: Physical activity and fitness are associated with a lower prevalence of chronic diseases, such as heart disease, cancer, high blood pressure, and diabetes. This review discusses the body's response to an acute bout of exercise and long-term physiological adaptations to exercise training with an emphasis on endurance exercise. An overview is provided of skeletal muscle actions, muscle fiber types, and the major metabolic pathways involved in energy production. The importance of adequate fluid intake during exercise sessions to prevent impairments induced by dehydration on endurance exercise, muscular power, and strength is discussed. Physiological adaptations that result from regular exercise training such as increases in cardiorespiratory capacity and strength are mentioned. The review emphasizes the cardiovascular and metabolic adaptations that lead to improvements in maximal oxygen capacity.

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INTRODUCTION

For decades, exercise has been used by physiologists as a research tool to understand the workings of several body systems, particularly the skeletal muscle, metabolism, the heart, and the peripheral circulation. More recently, physiologists have focused on understanding exercise itself, because regular physical activity has been shown to be important for disease prevention and health promotion. The purpose of this focused review is to discuss our current understanding of the human body's response to an acute bout of exercise. We will use endurance exercise as an example of this response. For more detailed discussions of other types of exercise, the reader is referred to several alternative sources. In the second part of the review, we also comment on the long-term adaptations induced by endurance exercise in some physiological systems.

TYPES OF SKELETAL MUSCLE ACTIONS

Movement, exercise, and sports require the generation of force by skeletal muscle fibers. Force can be generated while skeletal muscles remain static, become shorter, or increase in length [1]. These actions are the result of biochemical and structural changes that take place within the skeletal muscle fibers after neural activation and that need energy in the form of adenosine triphosphate (ATP). During most types of exercise, muscles alternate between static and dynamic muscle actions.

Static (Isometric) Muscle Actions

Static muscle actions occur when the muscles generate force without changing length, and there is no associated joint movement. In static actions, the myosin and actin myofilaments form cross-bridges and generate force, but the external resistance (weight of the external object) is greater than the force produced by the muscle. Although there is energy expenditure, no work (work = force × distance) is done because there is no displacement. An example of this type of muscle action is the performance of a cross on the rings apparatus by a gymnast (Figure 1).

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Figure 1. A gymnast performing the Iron Cross, which is executed by extending both arms straight out from the sides of the body and holding the isometric muscle action while suspended in the air. Printed with permission.

Dynamic (Isotonic) Muscle Actions

Dynamic muscle actions can be divided into concentric or eccentric muscle actions.

Concentric Actions. During concentric actions, the muscles produce enough force to overcome the external resistance, myosin and actin myofilaments form cross-bridges, the filaments slide pass by each other, muscle shortening occurs, and joints move. Given that there is force production and displacement, energy expenditure results in work (sometimes referred to as positive work). This type of muscle action is used when moving the body during exercise (ie, running) or sports activities (Figure 2) and/or when moving external objects.

Eccentric Actions. During eccentric actions, the muscle lengthens while it generates force. The lengthening occurs because the external resistance moves in the direction opposite to the shortening. Eccentric actions can be voluntary, such as when lowering a barbell after a biceps curl exercise, or involuntary, such as when the person resists dropping a heavy object. Because the displacement is in the direction opposite to the standard concentric action, eccentric muscle actions are sometimes known as producing negative work. These muscle actions provide an important training stimulus because of the high force generated by the contractile elements. Eccentric actions have been associated with muscle damage and soreness, and it is recommended that, at least initially, the eccentric component of exercise training be limited. The use of eccentric actions is of particular clinical value during the rehabilitation of tendon injuries [2].

Figure 2. Concentric muscle actions are used when moving the body during running. Printed with permission.

Table 1. *Characteristics of muscle-fiber type*

Muscle-Fiber Type	Shortening Velocity	Metabolic Profile	Fatigability	Myosin Heavy Chain Isoform Type	Sports Predominance*
I	Slow	Oxidative	Resistant	I	Long duration (marathon runners)
IIa	Fast	Intermediate	Intermediate	IIa	Team sports
IIx	Faster	Glycolytic	Fatigable	IIx	Sprints, weight lifting

*Fiber-type distribution is highly variable in humans; this classification is only intended to illustrate the relationship between the metabolic demands of a particular sport and the predominant fiber-type distribution.

Dynamic (Isokinetic) Muscle Actions

Isokinetic muscle actions are characterized by constant velocity, a condition that exists in the laboratory or clinic but not in nature [3]. Isokinetic actions can be concentric or eccentric, and require special (and usually expensive) computerized equipment to maximize resistance at each angle of the range of motion. These devices can be used for training or for testing purposes. Athletes may use isokinetic devices to perform exercises that simulate the actual speeds of their sport-specific activities.

MUSCLE-FIBER TYPES

Human skeletal muscle is a heterogeneous tissue in the sense that muscle fibers vary in terms of their mechanical, physiological, and biochemical properties (Table 1). Different methods have been used to classify skeletal muscle fibers, including histochemical techniques, such as ATPase and oxidative enzyme stains, measurements of contraction (twitch) or fiber-shortening velocity, and the identification of the myosin heavy chain isoform by using protein electrophoresis. In general, human skeletal muscles may contain 3 types of fibers in varying proportions: fiber types I, IIa, and IIx [4]. Fibers that express type I myosin heavy chain isoform are the slow, oxidative, fatigue-resistant fibers. Type IIx fibers, however, are very fast contracting, glycolytic, and fatigable fibers. Type IIa fibers have intermediate properties, that is, fast contracting but with an oxidative metabolic profile. It is important to note that human muscle fibers can express more than one type of myosin heavy chain isoform simultaneously [4]. These fibers are known as hybrid fibers and various combinations (I/IIa, IIa/IIx, I/IIa/IIx) have been reported. These hybrid fibers may be more prevalent in muscles recovering from injury, aging, and undergoing strength training.

ACUTE METABOLIC RESPONSES DURING EXERCISE

Energy drawn from high-energy phosphate bonds is needed for muscle activity. The cell stores a small amount of ATP near the contractile proteins [3]. The use of this ATP is not dependent on a supply of oxygen, and, therefore, the energy is available as soon as the muscle requires it. For exercise to continue beyond a few seconds, cells must synthesize ATP through 1 of 2 metabolic pathways: anaerobic (glycolytic) or aerobic (oxidative). All energy systems contribute to meet the energy demands of different sporting events but 1 or 2 predominate according to the sports-specific characteristics (predominantly aerobic or anaerobic).

Activities that depend primarily on the ATP-phosphocreatine (PC) system and anaerobic glycolysis are classified as anaerobic activities. Examples of exercises in this category include 100-800-m track races, golf or tennis swings, throwing events in track and field, and other events that require muscle activity for 2-3 minutes [5]. Activities of longer duration (>2-3 minutes) that depend primarily on oxidative metabolism, such as long-distance swimming and running, are classified as aerobic activities. Many sports activities require a blend of both anaerobic and aerobic metabolism (Figure 3). In "stop and go" sports such as basketball and tennis, approximately 60%-70% of the energy comes from ATP-creatine phosphate (CP) stores and anaerobic glycolysis and the remaining 30% from oxidative processes [6].

Figure 3. In a 2-minute round of boxing, anaerobic adenosine triphosphate resynthesis contributes the majority of the total energy required for muscle actions during the first 30 seconds, and aerobic metabolic energy provision predominates in the last part of the round; training programs should include exercises that train both metabolic pathways. Reprinted with permission from Jose Perez PR Best Boxing Promotions.

Figure 4. The energy needed to perform a high jump is derived from the adenosine triphosphate and creatine phosphate that is stored in muscle cells. Printed with permission.

ANAEROBIC METABOLISM

Stored ATP and CP

Energy at the onset of exercise and for muscle actions of very-high intensity (85%-100% of maximal capacity) and, therefore, of short duration (up to 10 seconds) is derived from a small amount of ATP and CP that is stored in muscle cells [5-7]. The total energy available in stored ATP-CP is enough for short-duration exercise, such as a weight lifting, high jump (Figure 4), or a 10-second sprint.

Anaerobic Glycolysis

During high-intensity exercise, the cardiovascular system is unable to supply the cells with oxygen quickly enough. If activity is to continue, once the ATP-CP stores are exhausted, the muscles resort to the rapid breakdown of stored glycogen-glucose for ATP regeneration via the glycolytic pathway [6]. Anaerobic glycolysis can provide energy for events such as the 400-800-m sprints and during the beginning of low-intensity exercise when muscle energy needs are high and the oxygen transport system is not yet fully activated. Unfortunately, this may result in the production and accumulation of lactic acid, which leads to fatigue because muscle acidification impairs enzyme function, decreases the calcium-binding capacity of muscle fibers, and impairs the muscle fiber's ability to generate force. The fuel used in anaerobic glycolysis is carbohydrates. Each mmol of glucose or glycogen provides 3 mmol of ATP. Patients with certain types of metabolic myopathies may have limited capacity to generate ATP and perform exercise due to enzymatic abnormalities in the glycolytic pathway.

AEROBIC METABOLISM

If exercise intensity is low and there is a steady supply of oxygen to the cells, then energy is produced via oxidative phosphorylation [7]. The oxidative system has a high-energy yield and is the most important pathway for energy production during prolonged exercise. This aerobic process takes place in the mitochondria of active muscles and uses the Krebs cycle and the respiratory chain. The energy yield of aerobic metabolism is much higher than that obtained through anaerobic glycolysis: 36-39 mol of ATP can be generated per mmol of glycogen. Fats also enter the Krebs cycle and the respiratory chain after being broken down in a metabolic process known as β-oxidation. Amino acids can be converted to glucose or to various intermediates of oxidative metabolism, but in general, they contribute little to energy production.

Oxygen Transport Chain

Oxidative phosphorylation is dependent on a continuous supply of oxygen. Because the amount of oxygen stored in cells in hemoglobin and myoglobin is small and of short duration, oxygen must be replenished from the environment. A series of mechanisms ensure an adequate supply of oxygen to the site of oxidation in the mitochondria of active tissues: uptake of environmental oxygen through alveolar ventilation, diffusion of oxygen into the blood, flow of blood to the tissues, and, finally, diffusion of oxygen into muscle cells and mitochondria [8]. Different pathologic processes may interfere with one or more of these steps and limit a patient's exercise capacity. However, a strong relationship has been shown between exercise performance in endurance sports and the capacity for oxygen transport to the working muscles [9].

Oxygen Uptake and Exercise Intensity

When a person exercises at progressively higher-power outputs, there is a linear increase in oxygen uptake to match the demand of the active skeletal muscles until the maximal oxygen consumption (VO_2 max) is reached. The VO_2 max is an indicator of the system's ability to deliver oxygen to active muscle as well as a biomarker of health. Individuals may be able to continue exercising for a short period of time after the VO_2 max is reached because energy can be provided through anaerobic processes, for example, glycolysis. The VO_2 max can be twice as high in trained athletes compared with sedentary individuals because of their enhanced stroke volume, improved myocardial function, and higher capacity for oxidative metabolism in active muscles. Patients with lung disease, heart disease, and peripheral vascular disease have a low VO_2 max. Healthy young individuals have an average VO_2 max value of 38 mL/kg per minute (women) and 44 mL/kg per minute (men). It is important to note that in-

creases in aerobic fitness, as measured by VO_2 max, have been related to a reduction in death from all causes. The VO_2 max can increase by approximately 15% with training, although there is significant intersubject variability.

ACUTE CARDIOVASCULAR RESPONSES DURING EXERCISE

The determinants of oxygen consumption are summarized in the Fick equation as follows:

$$VO_2 = CO \times (CaO_2 - CVO_2),$$

where VO_2 is oxygen consumption, CO is cardiac output, and $CaO_2 - CVO_2$ is the O_2 difference between arterial and venous blood, or the a-vO_2 difference [10,11]. Thus, there are 2 major factors that could limit VO_2 max: cardiac output and the capacity of active muscle to extract oxygen from arterial blood.

Cardiac Output

Cardiac output is the product of stroke volume and heart rate. In general, cardiac output increases linearly with exercise intensity, from a resting value of approximately 5 L/min to 20-40 L/min, depending on the level of conditioning. During exercise, there is a redistribution of blood flow so that approximately 95% of the CO is diverted to the heart and active skeletal muscles. In healthy individuals, stroke volume increases with increasing power output up to approximately 40%-60% of the VO_2 max and then levels off [12]. The rest of the increase in CO with increasing exercise intensity is primarily mediated by increasing heart rate. During maximal exercise in the upright position, stroke volume can increase from 50 mL at rest to 120 mL. In the supine position, blood does not pool in the lower extremities and venous return is enhanced. Thus, resting stroke volume values are higher in the supine position, and the increase in stroke volume during exercise, such as in swimming, is only approximately 20%-40% of the resting value.

a-VO_2 Difference (CaO_2 - CVO_2)

The a-vO_2 difference is an indicator of the effectiveness of active muscles in extracting oxygen from arterial blood. At rest, approximately 20%-30% of the blood's original oxygen content (20 mL of oxygen per 100 mL of arterial blood) is extracted at the tissue level. In the absence of lung disease, CaO_2 is constant (at rest and during exercise) and CVO_2 is reduced during exercise, thus the a-vO_2 difference increases progressively with exercise intensity.

Blood Pressure

In healthy individuals, both systolic and mean blood pressure increase with exercise intensity while diastolic blood pressure remains relatively unchanged [10,11,13]. If the exercise is performed with the arms only, then the increase in blood pressure is approximately 10% greater than when exercise is performed with the legs because the smaller muscle mass and vasculature of the arms present greater resistance to blood flow. Thus, arm exercise should be done with caution by individuals with cardiovascular disease. During exercise that involves static muscle actions, there is a moderate increase in cardiac output and a localized vasoconstriction that restricts blood flow. This combination causes a rise in systolic, diastolic, and mean blood pressures that is higher than during dynamic exercise at similar exercise duration and intensity [10]. During maximal static muscle actions of the arms, systolic and diastolic blood pressures can exceed 220 and 150 mm Hg, respectively.

LIMITATIONS TO OXYGEN CONSUMPTION DURING EXERCISE

Chronic inactivity as well as several medical conditions [11,12,14] can impair one or more of the mechanisms involved in either oxygen transport (stroke volume and/or heart rate) or oxygen utilization (CaO_2 or CVO_2), which results in a decrease in VO_2 max and impaired exercise performance. For example, patients with aortic stenosis have a low stroke volume during exercise due to the increased resistance imposed by the stiff aortic valve, which leads to a reduction in maximal cardiac output, muscle blood flow, and oxygen delivery, and to low exercise tolerance. Patients who use β-blockers have a slower heart rate at rest and the increase associated with exercise is less. Conditions that may result in a reduction in arterial oxygen content, for example, asthma, may impair oxygen delivery and exercise performance. Finally, diseases such as muscular dystrophies may impair the capacity of muscles to extract oxygen.

FACTORS THAT AFFECT AEROBIC EXERCISE PERFORMANCE

The capacity for prolonged exercise and sports performance is also dependent on other factors, such as muscle buffering capacity, gender, age, and genetics [15-21].

Acid-Base State of Muscle

As mentioned above, lactic acid, a metabolic byproduct of anaerobic glycolysis, increases the intracellular acidity of muscles and impairs muscle actions. The lactate threshold or the exercise intensity at which lactate begins to accumulate is a good indicator of the individual's performance in endurance events.

Gender

Women have smaller hearts, lower blood volumes, and lower hemoglobin concentrations, which result in a lower stroke

Table 2. *Exercise prescription model*

Fitness Component	Type of Exercise	Frequency, d/wk	Intensity	Duration
Muscle strength and endurance	8-10 exercises: major muscle groups; free weights, pulleys, elastic bands isokinetic dynamometer	3-4	60%-80% 1 RM; 6-10 RM	8-12 reps; 3 sets
Cardiorespiratory endurance	Walking briskly, jogging, swimming, cycling, rowing, dancing, endurance sports, prolonged duration sports	3-5	40%-85% VO_2R; 40%-85% HRR; 65%-95% HRmax	At least 30 min

RM = repetition maximum; reps = repetitions; HRR = heart rate reserve; HRmax = heart rate maximum.; VO_2R = oxygen uptake reserve.

volume and blood oxygen carrying capacity. Women have a VO_2 max that is approximately 75% that of men; this gender-related difference is lower when adjusted for differences in size and body weight.

Age

With increasing age, there is a decline in aerobic capacity partially due to a reduction in habitual physical activity. Aerobic capacity decreases by approximately 10% per decade in men and women [19-21]. In athletes who maintain a high level of endurance training, the decline in VO_2 max is approximately half that of sedentary men (approximately 5% per decade). The primary factor that causes the reduction of VO_2 max with age is a reduction in cardiac output due to increased peripheral resistance and lower stroke volume.

Genetics

Studies on identical and fraternal twins have suggested that genetics account for 20%-30% of VO_2 max values [15,22]. It appears that elite endurance athletes are born with exceptional genetic potential for the development of a very high level of cardiorespiratory fitness.

HYDRATION AND MUSCLE FUNCTION DURING EXERCISE

During exercise, a substantial volume of body water may be lost via sweating to enable evaporative cooling, especially in hot environments [16,23]. Sweating rates can be of 1-2 L per hour and even higher in well-trained and heat-acclimatized athletes [23]. Individuals who exercise for prolonged periods must drink fluid to restore the body's water loss and prevent dehydration [24]. Furthermore, many athletes carry a fluid deficit from their previous workout into the next workout, whereas others purposely dehydrate to "make weight" before sports competition [25].

The negative consequences of dehydration include an increase in cardiovascular strain, hyperthermia, impairment of exercise performance, and an increased risk for heat illness. Dehydration of as little as 2% of initial body weight can impair endurance [23]. In addition, the available evidence suggests that a dehydration of 3%-4% of initial body weight appears to diminish muscle strength by approximately 2%, muscle power by approximately 3%, and high-intensity endurance (activities that last >30 seconds but <2 minutes) by approximately 10% [26]. Exercise-associated muscle cramps [27] appear to be more prevalent during prolonged exercise in hot and humid conditions, especially in fatigued, dehydrated individuals and in those with high sweat sodium losses ("salty sweaters"). As a result of extracellular water loss with dehydration, a mechanical deformation of nerve endings may occur, which causes selected motor nerve terminals to become hyperexcitable and spontaneously discharge.

EXERCISE PRESCRIPTION FOR THE DEVELOPMENT OF PHYSIOLOGICAL CAPACITIES

According to the *2008 Physical Activity Guidelines for Americans* [28], all adults need at least 2 hours and 30 minutes (150 minutes) of moderate-intensity aerobic activity every week in addition to muscle-strengthening activities that exercise all major muscle groups on 2 or more days a week. Regular physical activity and exercise can result in long-term functional and health benefits, such as a reduction in the risk of developing chronic diseases such as heart disease, some types of cancer, and type 2 diabetes [28]. An exercise prescription includes the type of exercises, frequency of the sessions (days per week), intensity, and duration of the sessions (Table 2).

LONG-TERM PHYSIOLOGICAL ADAPTATIONS TO ENDURANCE EXERCISE TRAINING

Exercise training is associated with significant adaptations in many physiological systems that are specific to the type of training. This section will briefly summarize the main adaptations to one type of exercise training that emphasizes endurance. Other sources present a more detailed discussion of these adaptations [6,11,16].

Endurance training elicits many adaptations in skeletal muscles and in the metabolic and cardiorespiratory systems (Table 3). Together, these adaptations improve the ability to

Table 3. *Summary of cardiovascular and metabolic adaptations with endurance training*

Physiological Parameter	Rest	Submaximal Exercise	Maximal Exercise
Stroke volume	↑	↑	↑
Heart rate	↓	↓	↓ or —
Cardiac output	—	—	↑
a-vO_2 difference	—	↑	↑
VO_2	—	—	↑
Systolic blood pressure	↓	↓	—
Diastolic blood pressure	—	↓	↓
Blood volume	↑	↑	↑
Capillary density	↑	↑	↑
Mitochondrial density	↑	↑	↑

↑ = increase; ↓ = decrease; — = no change; a-vO_2 = (CaO_2 – CVO_2); VO_2 = oxygen consumption.

deliver and utilize oxygen for energy production, the capacity for prolonged exercise, sports performance, and the performance of activities of daily living without undue fatigue. It has been estimated that gains in maximal aerobic capacity after endurance training are strongly influenced by genotype [29].

Metabolic Adaptations in Skeletal Muscle

Endurance training causes an increase in the number of capillaries per muscle fiber and in the number and size of mitochondria in skeletal muscles [30-32]. The new capillaries that form in trained muscles result in an increase in blood flow to active muscles and provide a greater surface area for the exchange of gases during exercise. The increase in mitochondrial content and concentration of enzymes involved in carbohydrate and lipid metabolism enhances the muscle's oxidative capacity and ability to extract and utilize oxygen from arterial blood. As a result, glycogen stores are spared and lactate production at a given exercise intensity is less. The increase in mitochondria in the subsarcolemmal region of the muscle fibers shortens the diffusion distance for oxygen.

Cardiovascular Adaptations

Endurance training increases plasma and total blood volume. Of importance is the fact that this effect is noted within the first 7-10 days of training. The increase in plasma volume also results in relative hemodilution and a lower hemoglobin concentration (runner's pseudoanemia). The low blood viscosity enhances the movement of blood through the capillaries and may improve oxygen delivery to the active muscles. At the level of the heart, the increase in plasma volume causes an increase in end-diastolic volume and in the elastic recoil of the left ventricle [33]. Endurance training also leads to an increase in left ventricular muscle mass and dilatation that results in a more forceful contraction. Both of these adaptations enhance the ejection fraction and stroke volume at rest, and during submaximal and maximal exercise.

Resting heart rate decreases after a few weeks of endurance training due to an increase in parasympathetic activity and a reduction in sympathetic activity [34]. A submaximal heart rate at the same relative exercise intensity also decreases, and genetics play a determinant role in this response to training [35]. Maximal heart rate decreases or remains unchanged. A lower maximal heart rate allows for an increase in left ventricular filling time so that maximal stroke volume and cardiac output are optimized. Resting and submaximal cardiac output do not change significantly after endurance training but, because of the increase in maximal stroke volume, maximal cardiac output increases significantly after training. Finally, endurance training causes a reduction in resting and submaximal systolic and diastolic blood pressure in both healthy individuals and in patients who are hypertensive [36]. The cardiovascular mechanism that leads to an increase in VO_2 max is dependent on age, with adaptations in older people more dependent on changes in the a-vO_2 difference and less on cardiac output [37].

SUMMARY

Regular exercise is important to improve physiological function, physical fitness, and health. Physical activity and fitness are associated with a lower prevalence of many chronic diseases such as heart disease, cancer, high blood pressure, and diabetes. Exercise activities can be categorized in terms of the major metabolic pathway involved in energy contribution: predominantly aerobic or predominantly anaerobic. Repeated bouts of exercise result in significant adaptations in many physiological systems of the body. Further, regular aerobic exercise leads to an improvement in VO_2 max that reflects several cardiovascular and metabolic adaptations. Although the VO_2 max has a significant genetic component and it is affected by the aging process, it can improve significantly with training at any age and in both genders. Exercise training should include exercises to increase strength and endurance.

REFERENCES

1. Behm DG. Neuromuscular implications and applications of resistance training. J Strength Cond Res 1995;9:264-274.
2. Witvrouw E, Mahieu N, Roosen P, McNair P. The role of stretching in tendon injuries. Br J Sports Med 2007;41:224-226.
3. MacDougall JD, Wenger HA, Green HJ. Physiological Testing of the High-Performance Athlete. 2nd ed. Champaign, IL: Human Kinetics; 1991.
4. Canepari M, Pellegrino MA, D'Antona G, Bottinelli R. Single muscle fiber properties in aging and disuse. Scand J Med Sci Sports 2010;20: 10-19.
5. Bogdanis GC, Nevill ME, Boobis LH, Lakomy HK. Contribution of phosphocreatine and aerobic metabolism to energy supply during repeated sprint exercise. J Appl Physiol 1996;80:876-884.

6. Kenney WL, Wilmore JH, Costill DL. Physiology of Sport and Exercise. 5th ed. Champaign, IL: Human Kinetics; 2011.
7. Spriet LL, Howlett RA. Metabolic control of energy production during physical activity. In: Lamb DR, Murray R, eds. Perspectives in Exercise Science and Sports Medicine: The Metabolic Basis of Performance and Sport. Vol 12. Carmel, IN: Cooper Publishing; 1999, 1-51.
8. Weibel ER. The Pathway for Oxygen. Cambridge, MA: Harvard University Press; 1984.
9. Jacobs RA, Rasmussen P, Siebenmann C, et al. Determinants of time trial performance and maximal incremental exercise in highly trained endurance athletes. J Appl Physiol 2011;111:1422-1430.
10. Rowell LB. Human Cardiovascular Control. New York, NY: Oxford University Press; 1993.
11. American College of Sports, Medicine. ACSM's Guidelines for Exercise Testing and Prescription. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.
12. Gledhill N, Cox D, Jamnik R. Endurance athletes' stroke volume does not plateau: Major advantage is diastolic function. Med Sci Sports Exerc 1994;26:1116-1121.
13. MacDougall JD. Blood pressure responses to resistive, static, and dynamic exercise. In: Fletcher GF, ed. Cardiovascular Response to Exercise. New York NY: American Heart Association; 1994, 155-173.
14. Sesso HD, Paffenbarger RS Jr, Lee IM. Physical activity and coronary heart disease in men: The Harvard Alumni Health Study. Circulation 2000;102:975-980.
15. Bouchard C, An P, Rice T, et al. Familial aggregation of VO_2max response to exercise training: Results from the HERITAGE Family Study. J Appl Physiol 1999;87:1003-1008.
16. McArdle WD, Katch FI, Katch VL. Essentials of Exercise Physiology. 3rd ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2005.
17. Laughlin MH. Cardiovascular response to exercise. Am J Physiol 1999; 277:S244-259.
18. Rowell LB. Human Circulation. New York, NY: Oxford University Press; 1986, 137-256.
19. Jackson AS, Beard EF, Wier LT, Ross RM, Stuteville JE, Blair SN. Changes in aerobic power of men, ages 25-70 yr. Med Sci Sports Exerc 1995;27:113-120.
20. Jackson AS, Wier LT, Ayers GW, Beard EF, Stuteville JE, Blair SN. Changes in aerobic power of women, ages 20-64 yr. Med Sci Sports Exerc 1996;28:884-891.
21. Trappe SW, Costill DL, Vukovich MD, Jones J, Melham T. Aging among elite distance runners: A 22-yr longitudinal study. J Appl Physiol 1996;80:285-290.
22. Bouchard C, Dionne FT, Simoneau JA, Boulay MR. Genetics of aerobic and anaerobic performances. Exerc Sport Sci Rev 1992;20:27-58.
23. Sawka MN, Burke LM, Eichner ER, Maughan RJ, Montain SJ, Stachenfeld NS. Exercise and fluid replacement. American College of Sports Medicine position stand. Med Sci Sports Exerc 2007;39:377-390.
24. Coyle EF, Hamilton M. Fluid replacement during exercise: Effects on physiological homeostasis and performance. In: Gisolfi CV, Lamb DR, eds. Perspectives in Exercise Science and Sports Medicine: Fluid Homeostasis During Exercise. Vol 3. Carmel, IN: Cooper Publishing; 1990.
25. Rivera-Brown AM, De Felix-Dávila RA. Hydration status in adolescent judo athletes before and after training in the heat. Int J Sports Physiol Perform 2012;7:39-46.
26. Judelson DA, Maresh CM, Anderson JM, et al. Hydration and muscular performance: Does fluid balance affect strength, power and high-intensity endurance? Sports Med 2007;37:907-921.
27. Layzer RB. The origin of muscle fasciculations and cramps. Muscle Nerve 1994;17:1243-1249.
28. US Department of Health and Human Services. 2008 Physical Activity Guidelines for Americans; 2008. Available at http://www.health.gov/paguidelines/guidelines/default.aspx. Accessed October 13, 2012.
29. Timmons JA, Knudsen S, Rankinen T, et al. Using molecular classification to predict gains in maximal aerobic capacity following endurance exercise training in humans. J Appl Physiol 2010;108:1487-1496.
30. Laughlin MH, Roseguini B. Mechanisms for exercise training-induced increases in skeletal muscle blood flow capacity: Differences with interval sprint training versus aerobic endurance training. J Physiol Pharmacol 2008;59(Suppl 7):71-88.
31. Holloszy JO. Regulation by exercise of skeletal muscle content of mitochondria and GLUT4. J Physiol Pharmacol 2008;59(Suppl 7): 5-18.
32. Holloszy JO. Metabolic consequences of endurance exercise training. In: Horton ES, Terjung RJ, eds. Exercise, Nutrition, and Energy Metabolism. New York, NY: Macmillan; 1988.
33. Goodman JM, Liu PP, Green HJ. Left ventricular adaptations following short-term endurance training. J Appl Physiol 2005;98:454-460.
34. Carter JB, Banister EW, Blaber AP. Effect of endurance exercise on autonomic control of heart rate. Sports Med 2003;33:33-46.
35. Rankinen T, Sung YJ, Sarzynski MA, Rice TK, Rao DC, Bouchard C. Heritability of submaximal exercise heart rate response to exercise training is accounted for by nine SNPs. J Appl Physiol 2012;112:892-897.
36. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. Exercise and hypertension. American College of Sports Medicine position stand. Med Sci Sports Exerc 2004;36:533-553.
37. Murias JM, Kowalchuk JM, Paterson DH. Mechanisms for increases in VO_2max with endurance training in older and young women. Med Sci Sports Exerc 2010;42:1891-1898.