1. General effects of physical activity

Authors

Jan Henriksson, MD, PhD, Professor, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

Carl Johan Sundberg, MD, PhD, Associate Professor, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

Introduction

All of the body's tissues and our genetic material generally look like they did in our ancestors 10,000 years ago. The human body is built for movement. Body and mind benefit from physical activity. Most organs and tissues are affected by physical activity and adapt to regular exercise. Regular physical activity significantly reduces the risk of premature death.

This chapter focuses on the immediate effects of physical exertion and the long-term effects of regular physical activity/fitness training (aerobic training). Physical activity refers to all bodily movement that results from the contraction of the skeletal muscles and results in increased energy expenditure (1). For greater detail and references, we refer to textbooks and overview articles in the exercise physiology literature (2–6) or the more focused references provided in each section. Aspects of strength training are discussed in a separate chapter.

Physical activity can be carried out at different levels of intensity. The more intense, the greater the immediate impact on various bodily functions. Oxygen consumption, which is directly linked to energy expenditure, increases from 0.25 litres per minute at rest to slightly more than 1 litre per minute during a relaxed walk. During maximum exertion, it increases to 2–7 litres per minute, i.e. up to 10–25 times the resting rate.

During physical exertion, the pulse rises and cardiac output increases. Ventilation multiplies, blood pressure increases, body temperature rises, perfusion in the heart and muscles increases, more lactic acid is formed and the secretion of hormones such as adrenaline, growth hormone and cortisol increases.

Maximum oxygen uptake capacity depends on body size, gender, age, fitness level, genetics and more. The factors that limit performance capacity in full-body exertion differ depending on the length of the session. The durations stated in the following text shall only be viewed as approximate for an "average", middle-aged person – major differences

exist. In maximal exertion that lasts 5–15 minutes, central circulation (the heart) is generally considered to comprise the most important limitation of the performance capacity (by limiting the maximum oxygen uptake capacity). The longer the exertion continues, the more performance capacity is limited by properties of the engaged skeletal muscles (mitochondria, capillaries, some transport molecules, buffer capacity, etc.), which affect the so-called anaerobic threshold (see below for definition). In terms of long-term endurance (more than 30–60 minutes), the muscles' carbohydrate deposits (glycogen) also comprise a limitation.

What determines the response to exercise training?

Several factors determine how much a person improves if the degree of physical activity increases. One important factor is the fitness/performance level when the period of exercise training begins. A person who is inactive and in poor shape improves more in relative terms than a person who is well trained. The effects of exercise are specific to the organs and tissues that are exercised – only the muscles that are used adapt and only the parts of the skeleton that are loaded are strengthened. The length of the period of exercise training also plays a major role. Although some effects from exercise can be seen after a surprisingly short time of one to a few weeks, the effects are considerably greater if training continues for several months to years. Of course, the effect of exercise gradually "levels off" and eventually a considerable amount of training is required just to maintain the prevailing level of fitness.

Three other important factors are frequency (how often the person exercises), duration (how long a session is) and intensity (how hard/intense the session is). These three factors determine the combined "exercise dose". In other words, the higher the dose, the greater the effect. It should be pointed out that low doses also have an effect, although to a more limited extent.

Frequency

For physical activity to have the maximum performance and health effects, it must be pursued often and regularly. The effect that an exercise session has can affect the body for several days, and then subside. Consequently, for low-intensity physical activity, a daily "dose" is recommended.

Duration

As a rule, the longer the activity continues, the greater the effect it has. In many cases, the daily activity session can be divided up into several separate 10–15 minute periods, as long as the total time is sufficient. One common recommendation with regard to time is 30 minutes of physical activity per day.

Intensity

The harder an exercise session is, the greater its performance and health effects usually are, although excessively intense exercise can lead to deteriorations. Good health-related effects

often seem to be achieved at a lower intensity, although a higher intensity is important to be able to improve fitness and to maintain an improvement in condition.

Moreover, there are of course a large number of factors that affect the outcome of the exercise training. For example, exercise can be conducted with relatively constant or with varying intensity (interval training) and with varying size of the engaged muscle mass (arm, abdomen and leg muscles compared with just leg muscles, for example). Genetics also seem to play a relatively large role in how large the response to exercise training is, perhaps accounting for around a third to one half of the variation between people. There is some evidence in the literature that individuals who increase their performance capacity at a certain exercise dose more than others appear to activate key genes in a stronger way (7, 8). It has not been established whether differences in exercise response are only due to genetic mechanisms (9). Age can be of significance, although older persons do not generally appear to have a worse ability to increase their relative performance. The composition of the diet may also play a role; a deficient diet lessens the response to exercise training. Dietary supplements provide no proven effect, however.

Effects of acute exertion and regular exercise

When discussing the effects of physical activity on the bodily organs and organ systems, it is necessary to differentiate 1) what happens in the body during (and after) a session of physical activity compared with the situation at rest, and 2) what differences are achieved (at rest or under exertion) after a certain period of exercise training compared with an untrained condition. In this text, the former is referred to as "Effects of acute exertion" and the latter as "Effects of exercise training". The effects of acute exertion are due to a number of factors and differ between different tissues. The time for achieving different effects from exercise training varies from function to function, some processes start immediately in connection with the first exercise session, others take weeks to months before they are noticeable.

From a physiological perspective, a physical activity is called either aerobic or anaerobic, depending on which form of metabolism is dominant. One rule of thumb is that physical activity is aerobic (dependent on oxygen) if the maximum time one can perform the activity exceeds two minutes (3). Then the muscles mainly obtain their energy from the oxygen-dependent degradation of carbohydrates or fat. If one has the energy to carry out the activity for two minutes, but no longer, the metabolism is probably approximately 50 per cent aerobic and 50 per cent anaerobic (not oxygen-dependent). In short-term, intense physical activity, the muscles work without a sufficient oxygen supply (anaerobic metabolism) and the dominant energy-providing process is the splitting of glycogen and glucose into the degradation product lactic acid. Consequently, it is natural that aerobic exercise and anaerobic exercise provide different effects of exercise training. Aerobic exercise performed for a sufficient period of time stimulates the adaptation of the heart and the aerobic systems of the skeletal muscles, which is why regular exercise leads to the heart increasing its capacity accompanied by an increased mitochondrial volume in the

engaged skeletal muscle cells. The exercise time in pure anaerobic exercise (such as sprint training) is too short to provide these exercise responses in the heart and muscles. Such anaerobic training instead leads to improved conditions for greater lactic acid production and lactic acid tolerance.

Daily physical activity often has elements of both aerobic and anaerobic activities, such as walking in hilly terrain. Strength training, especially with heavy weights, is an extreme form of anaerobic exercise. In interval training (such as interspersed 10–15 second periods of hard exertion and equally long periods of rest), aerobic and normally anaerobic exercises are combined so that the total period of exercise at heavy loads can be kept sufficiently long to provide an exercise effect on both the heart and the muscles' aerobic systems (81).

Measurement of exercise dose and exercise effects

Measurement of heart rate or perceived exertion (10) are methods to adjust the exercise dose to the person's own capacity. This is discussed in depth in a separate chapter. Pedometers, or step counters, that measure vertical movements, are good aids for measuring the total number of steps when walking and running, but are relatively insensitive to many other movements. To obtain objective measurements of an individual's physical activity during a certain period of time, tri-axis accelerometers are used instead, measuring frequency, intensity and duration of movements on horizontal, sagittal and vertical planes (11).

Training effects in aerobic exercise are often measured as the change in the maximum oxygen uptake capacity. This is the highest oxygen consumption a person can achieve and is measured when the individual works with a maximum pulse during e.g. running. In short-term exercise (5–15 minutes), the maximum performance capacity is largely dependent on the maximum oxygen uptake capacity (12). This can be improved by 20–50 per cent in 2–6 months if exercise is of sufficient intensity. However, there are very large individual differences in the response to exercise. From the maximum oxygen uptake capacity, the individual's maximum energy expenditure can be calculated, since every litre of consumed oxygen corresponds to an amount of energy of approximately 20 kJ (5 kCal). Since direct measurement of the maximum oxygen uptake capacity is relatively difficult, and requires both special equipment and nearly maximum exertion by the individual, an indirect approach is often used where the maximum oxygen uptake capacity is calculated based on heart rate measurements at lower levels of exertion (3). The reliability of the indirect methods is limited, however.

Determination of the anaerobic threshold (lactic acid threshold test) can be achieved in a reliable manner from blood lactic acid samples taken during non-maximum exertion (13). The anaerobic threshold is defined as "the highest sustained exertion intensity at which lactic acid appearance in the blood will be equal to the rate of its disappearance". In terms of percentages, it increases more than the maximum oxygen uptake capacity after a period of endurance training. The economy of motion can also be improved with exercise. Accordingly, less energy is consumed for the same amount of work performed (measured as lower oxygen consumption), efficiency is improved. This may be very noticeable for many activities such as running while for others, such as cycling, efficiency is gener-

ally identical for all individuals. Besides the aforementioned effects of exercise training, which are significant to performance capacity, important exercise effects can be measured that are primarily of significance to one's metabolism (and risk of disease). Among these are glycosylated hemoglobin (HbA1C) – an integrated measure of blood sugar increases over an extended period; glucose tolerance – a measure of plasma glucose two hours after the consumption of 75 grams of glucose, inverse measure of insulin sensitivity and blood glucose control; and fat tolerance (14) – a measure of blood lipids in the hours after a fat-rich meal, inversely related to insulin sensitivity. Other methods to measure the effects of regular exercise include underwater weighing, skin-fold, DXA, BOD POD (15) – methods to measure the body's fat content; and immunoglobulin A in saliva (16) – method of measuring immunity in connection with physical activity.

Heart

Acute exertion

During exercise, which involves large muscle groups, there is a high demand on the heart and blood circulation. The skeletal muscles' requirement of a supply of oxygen and nutrients and the need for greater removal of carbon dioxide and other waste products as well as the need for temperature and acid-base balance demands greater blood circulation. With help from the autonomic nervous system, this increased need can be felt, which leads to an increase in pulse and the contractile force of the heart. An increase from a resting heart rate, usually 60–80 beats per minute, up to a pulse of around 120 beats per minute is accompanied by an increase in the heart's stroke volume, meaning the amount of blood pumped out with each heartbeat. Under exertion, heart frequency increases from a resting heart rate of approximately 60–80 beats per minute to the maximum pulse, which can be 150–230 beats per minute depending mainly on age, but also on individual factors. The greater contractile force of the heart increases pressure in both chambers of the heart. Pulse rate and contractile force increase in proportion to the work load and the amount of blood the heart pumps out increases from 4–5 litres per minute at rest to 20–40 litres per minute at maximum exertion intensity. The greater cardiac exertion increases demand on the heart's own circulation (coronary circulation), which increases 5–8 fold.

Effects of exercise training

The effects of exercise training on the heart, like the majority of organs and tissues, depends on the frequency, intensity and duration of the exercise sessions. After a few months of sufficiently intensive exercise, it is typical for the resting heart rate and the pulse during submaximum exertion to be 5–20 beats per minute lower, for the stroke volume to increase by 20 per cent or more, and for the heart's contractility to improve, which is reflected in a greater ejection fraction (the percentage of the heart's blood volume that is pumped out in one heartbeat) at maximum exertion intensity. The maximum heart rate is unaffected or only slightly decreased. Structurally, the heart's internal volume increases significantly and its wall thickness increases somewhat, which altogether means greater cardiac muscle

mass, primarily due to the individual cardiac muscle cells increasing in size. In addition, the number of capillaries and mitochondria increases. The expansion capacity of the coronary vessels is improved with exercise training (17). The extent to which the occurrence of and sensitivity of receptors to signal substances and hormones in the cardiac muscles change with regular exercise is not fully established (18).

Skeletal muscles

Acute exertion

Acute muscle exertion demands greater activation of individual motor units and the recruitment of more motor units. In low intensity exertion, mainly motor units with slow-twitch muscle fibres (type I) are recruited and in more intense exertion, fibres in fast-twitch motor units (type IIa and IIx) are also recruited.

Muscle exertion demands a great deal of energy in the form of adenosine triphosphate (ATP). The primary sources of energy for ATP production are carbohydrates and fatty acids. Carbohydrates are stored in the form of glycogen in the liver and skeletal muscles. These stores are limited and must be refilled daily. Fatty acids are mostly stored in adipose tissue in virtually unlimited amounts.

Several factors affect the choice of energy sources during exertion, such as:

Exertion intensity

Energy expenditure is proportional to the exercise intensity. At rest, 60 per cent of the energy needed is provided by fats and, in low-intensity exertion, roughly the same proportion of the energy is extracted from fat as from carbohydrates. In more intense exertion, relatively more carbohydrates are used. This is due to several factors, including the fact that the fast, less oxidative and more glycolytic muscle fibres are involved to a greater extent and that the muscle cells' access to oxygen (oxygen pressure) gradually decreases. With higher work loads, the need for carbohydrates per unit of time increases sharply and can reach above 200 grams per hour. In maximum aerobic exertion, virtually only carbohydrates are considered to be burned and in even more strenuous, so-called supra-maximum exertion, large additional amounts of carbohydrates are split to lactic acid. The higher the load, the more lactic acid is formed, which makes both muscle tissue and blood more acidic (lower pH). However, the fatty acid need levels out with increasing work load and rarely exceeds 20–30 grams per hour. If exertion continues for several hours, 50 grams per hour may be burned.

The highest level of fat burning in skeletal muscles (grams per minute) is achieved at exercise intensities approximately corresponding to 50 per cent of the maximum oxygen-uptake capacity in the general population and to slightly more than 60 per cent of the maximum oxygen-uptake capacity in very fit individuals (19). However, it should be added that the total fat expenditure (during and after the exertion) is primarily dependent on the total energy expenditure, which is why the fat expenditure in high-intensity exertion is greater overall than in low-intensity exertion lasting the same amount of time. However,

the duration of high-intensity exercise is often very short and, consequently, fat expenditure is limited.

Fitness level
A well-trained person uses more fat for energy extraction and thereby saves carbohydrates with each work load, which means that it is possible to maintain a higher intensity of exertion for a longer period of time.

Duration of exercise
The longer a session of exercise of sub-maximal intensity lasts, the greater is the proportion of fat used. This is partially related to the gradual emptying of the body's carbohydrate deposits.

Diet
The composition of the diet also affects which energy sources are used. When fasting or on a fat-rich/carbohydrate-poor diet, fatty acids are used to a greater extent. After so-called carbohydrate loading, carbohydrates are used to a greater extent during exercise, but in spite of this glycogen (the storage form of carbohydrates) also lasts longer.

Body temperature
In strong hypothermia or heat loading, relatively more carbohydrates are used.

Oxygen supply
When oxygen availability is limited, such as at high altitudes, and when the blood flow to the working arm or leg is restricted, carbohydrates are used to a greater extent. An example of the latter situation is exercise with the arms when held above the heart. In acute exercise, the blood flow increases sharply (by 50–100 times) in the working muscles. This improves the oxygen supply and is mainly due to the vasodilatation (expanding of the vessels) brought about by various factors in the muscles.

Muscle fatigue
Fatigue upon exertion can be due to many different factors in multiple tissues. The local fatigue in the muscles can, for example, be caused by the accumulation of products from ATP decomposition or a lack of glycogen. Dehydration affects the circulating blood volume and can cause fatigue.

Effects of exercise training

The skeletal muscles comprise a very adaptable tissue. Endurance training affects its structure and function significantly. In terms of the muscles' contractile function, some studies have found increased activation and increased recruitment of motor units after a longer period of exercise training (20). Local fatigue in the working muscles decreases after a period of exercise training.

Structure

The size of the muscle fibres changes only slightly in endurance training, while it can of course increase sharply if the endurance training has elements of strength training. The slow-twitch fibres (type I) can become somewhat larger. In terms of the distribution between fibre types within the type II group (fast-twitch fibres), the proportion of type IIx decreases after around one week at the same time that the proportion of type IIa increases. The transition from type II to type I (slow-twitch) fibres is very limited in the short term, although the proportion of slow protein increases in many fibres.

The amount of mitochondria increases markedly (see below). The small capillaries also increase in number. This improves the blood flow and extends the perfusion time of the tissue, which facilitates the exchange of oxygen and nutrients. However, in contrast to some animals, it appears to be difficult to affect myoglobin content with exercise in humans.

Transport capacity

The occurrence of so-called glucose transporters (GLUT-4) in the skeletal muscle cell membrane increases immediately in connection with an exercise session and even more after a longer period of exercise training. This increases sensitivity to insulin and tolerance to sugar (glucose). The occurrence of fatty acid-binding proteins increases on the capillary wall and in the muscle cell. Exercise training also improves the occurrence of special transport molecules for fatty acids into the muscle cell and its mitochondria, and transport molecules for lactic acid out of the muscle cell. This raises the transport capacity considerably. Furthermore, as early as within a few days, the ATPase activity of the sodium-potassium pumps (enzyme rate) increases, which probably improves the ability to restore the ion balance (contractility) after the end of muscle exertion (21).

Nutrient deposits

The amount of deposited carbohydrates (in the form of glycogen) and fatty acids (in the form of triglycerides) in skeletal muscle cells can be more than doubled (glycogen is tripled or quadrupled) with exercise training.

Fat and carbohydrate use

The amount of enzymes that break down fatty acids increases very rapidly after exercise training, which facilitates fatty acid use. The mitochondrial density, and consequently the muscle's fat and carbohydrate burning capacity, increases relatively quickly with exercise training. Within just 4–6 weeks, a 30–40 per cent increase can be noted. The very well-trained have 3–4 times higher mitochondrial densities in trained muscles than those that do not exercise.

After just a few weeks' training, a higher "metabolic fitness" is achieved, meaning that carbohydrates are "saved" and fat is used to a greater extent for energy extraction under exertion at a given, sub-maximal load level. These tangible differences in substrate selection are due in part to higher mitochondrial density and a greater transport capacity for fatty acids. The production and concentration of lactic acid is lower at a given load. The

buffer capacity for lactic acid is also improved (22). At maximum exertion (higher exertion intensity possible after exercise training), the lactic acid concentration is significantly higher.

Mechanisms

During acute exertion, the external and internal environments of the skeletal muscle cells change. Hormones and growth factors surround and are bound to the cells to a greater extent. One example is Vascular Endothelial Growth Factor (VEGF), which affects the new formation of blood vessels (23). Inside the cells, the temperature, calcium content and occurrence of the ATP molecule's decomposition products increase. At the same time, pH and oxygen pressure decrease. These and other factors directly and/or indirectly affect a number of proteins in the skeletal muscles. For example, the degree of phosphorylation of so-called mitogen-activated protein kinases (24) and mitochondrial factors (25, 82) is affected, which in turn affects processes that control the adjustment to exercise training, such as the activity degree of some genes. It should also be noted that only the muscles used/exercised adapt, hence, the exercise is specific, which is of crucial significance.

Blood

Acute exertion

Upon exertion, the working muscles swell up somewhat, which is due to all of the metabolites formed in the muscle cells osmotically "extracting" fluid from the blood. This fluid withdrawal to the working muscles directly decreases blood volume somewhat, which means that the concentration of hemoglobin (blood value) increases by 5–15 per cent. After the exertion, this increase subsides.

The occurrence of leukocytes also rises sharply under exertion, largely because leukocytes are released from lymphatic tissue, such as lymph nodes and the spleen.

Effects of exercise training

Regular endurance training entails a significant increase in both plasma and blood cells, which together increase blood volume by 10–15 per cent or more (26). The plasma expansion begins as early as the first week after the first exercise session. A change in the number of red blood cells, which is relatively less, can first be observed after a few weeks. Because the plasma volume expands more, the percentage of the blood comprised by red blood cells will drop due to dilution. This is why, paradoxically, a person often has a lower Hb value (blood count) after a period of exercise training despite a higher total amount of red blood cells. The increased blood volume increases the venous return of blood to the heart and consequently the end-systolic volume of the heart, which contributes to increasing the stroke volume and lowering the heart rate at rest and in sub-maximal exertion.

Mechanisms

The increased plasma volume is probably due to hormonal factors that increase fluid retention and to an increased synthesis of albumin that binds more fluid in the plasma. The increased formation of red blood cells is probably due to an increase in the erythropoietin (EPO) concentration.

Lipoproteins

Acute exertion

Significant changes in blood lipid levels (lipoproteins) are seen after individual exercise sessions, with higher levels of HDL cholesterol (4–43%), especially subfractions 2 and 3, associated with a reduction of the levels of triglycerides and very low density lipoproteins (VLDL). These changes can last 24 hours after the end of exertion (27). A work load corresponding to five kilometres of running at an intensity corresponding to the anaerobic threshold has also been given as a threshold value for achieving these changes (28).

An exercise session, such as a one-hour long brisk walk, done within 24 hours before a fat-rich meal means that the increase in lipoproteins in connection with the meal will be significantly lower than if no exercise session had been done (29). This can probably in part be explained by the enzyme lipoprotein lipase in the skeletal muscles' capillaries being activated by the exertion and increasing its decomposition of the fat molecules (triglycerides) that flow through the capillaries, and in part by a decreased secretion of triglycerides from the liver. Both of these effects are probably connected to the lack of energy (reduced levels of energy substrate) that occurs in the skeletal muscles and liver after an exercise session of a sufficient length (30).

Effects of exercise training

Changes in the composition of lipoproteins with exercise are among the changes that are thought to underlie the reduced risk of cardiopulmonary diseases among fit individuals. Physically fit individuals normally have higher levels of HDL cholesterol (high-density lipoproteins) and lower levels of triglycerides than untrained individuals. The increase in HDL cholesterol is considered to be especially important due to its role in the process (reverse cholesterol transport) whereby the body extracts cholesterol from peripheral tissues for transport to the liver and excretion.

Other changes in prolonged training, although not as constantly occurring, include lower overall cholesterol and LDL cholesterol (low-density lipoproteins) (83) as well as lower concentrations of Apolipoprotein B. The approximate exercise volumes required to obtain these positive effects from exercise have been given as the equivalent of 25–30 km jogging or fast walking per week, or in other words an exercise-related energy expenditure of 1,200–2,200 kcal per week. Higher exercise volumes entail additional positive effects. With this level of exercise, people of both genders can expect the HDL cholesterol level to rise by 10–20 per cent and the triglyceride level to decrease by 10 to 30 per cent (31).

The significance of relatively extensive physical exercise to influence the composition and concentrations of lipoproteins is clearly exemplified by a large U.S. study (32) in which overweight men and women were divided into four groups, one control group and three exercise groups, that were monitored for eight months. Group A exercised (ergometer cycling, jogging) with an energy expenditure that corresponded to 32 km jogging per week and with a strenuous load (65–80% of maximum oxygen uptake capacity), group B exercised at the same intensity, but with a shorter distance (corresponding to an energy expenditure of 19 km jogging per week), while group C underwent the same amount of exercise as group B, but at a lower intensity (corresponding to 40–55% of the maximum oxygen uptake capacity). After eight months of exercise, the concentration of HDL cholesterol had only increased in group A (+ 9%), together with several other beneficial lipoprotein changes (such as lower LDL concentrations with an increase in the LDL particles' size). Some changes were also noted in groups B and C (primarily an increase in the size of the LDL and VLDL particles), but to a much lower extent (32).

Blood coagulation factors and platelet characteristics

Acute exertion

An exercise session leads to a significant increase in the number of platelets in the blood. This cannot be explained by the decrease in the plasma volume that occurs in acute exertion (see above), but rather is probably due to a release of blood platelets from various organs, such as the spleen, bone marrow and from pulmonary circulation. An activation of blood platelets has also been observed during acute exercise sessions, primarily among untrained individuals. Such an activation is reflected in an increased occurrence of the protein, P-selectin, on the platelets' surface, with greater aggregation tendency of platelets and greater formation of thrombin and fibrin leading to a shortened coagulation time. It is mainly higher intensity exertion that provides these potentially negative effects of physical exercise. Studies of individuals with coronary disease provide clear support for the theory that platelet aggregation and activation increase through physical activity. Interestingly, this increase does not appear to be inhibited by acetylsalicylic acid, which is normally an effective treatment for conditions of increased blood clot tendency (33).

These results can be compared with what is known about the risk of being afflicted by a cardiac infarction in connection with physical exertion. It should be noted that it is relatively uncommon for a heart attack to be triggered by physical exertion; only around 5 per cent of cardiac infarctions occur during or within one hour of physical exertion. Of these cases, 70 per cent can be related to coronary occlusion by a platelet-rich blood clot. The definition of physical exertion that is commonly used in these contexts is an energy expenditure that is six times higher than the energy expenditure at sitting rest (six metabolic equivalents or 6 MET), which can normally be said to correspond to light jogging or shovelling snow, for example.

In various studies, the risk of being struck by a heart attack during a randomly selected hour was compared with the same risk during and within one hour after physical exertion.

In several studies, large increases in risk were reported in connection with physical exertion (34, 35). However, the results only apply to untrained men who rarely (less than once a week) subjected themselves to this degree of exertion. Regular exercise constitutes strong protection against the increased risk of cardiac infarction in connection with physical exertion, and the risk has been estimated to only be 2.5 times (34) and 1.3 times (35) greater, respectively, than at rest for men who exercise regularly (>6 MET at least 4–5 days per week). For women, the risk of being struck by a heart attack during and in connection with physical exertion is very small (compared with the risk during a randomly selected hour without physical exertion), and the small risk that has been reported appears to vanish with regular exercise. For both men and women who exercise regularly, the risk of having a heart attack at all (that is at any hour of the day) is less than half of that among untrained individuals (36).

Effects of exercise training

The sharply reduced risk of sudden death or acute cardiac infarction during an exercise session among people who exercise regularly indicates that prolonged exercise gives rise to changes that counteract the increased aggregation tendency of platelets under exertion. This has also been shown (37). Another important explanation is that the mechanism for the dissolution of blood clots, fibrinolysis, is enhanced among individuals who exercise regularly (38). Other important explanations of the reduced tendency for blood clots among fit individuals may be that regular exercise leads to higher levels of prostaglandin, in part as a result of higher levels of HDL cholesterol, and a higher nitrogen oxide content, both of which inhibit blood clot formation.

Vessels, blood pressure and blood flow distribution

Acute exertion

Arterial blood pressure depends on the cardiac output (volume of blood per minute) and the peripheral resistance in the vessel tree. During a session of acute exercise, the cardiac output increases significantly at the same time that peripheral resistance decreases sharply, although not to the same extent that the cardiac output increases. This means that the mean blood pressure increases, almost entirely dependent on a systolic blood pressure increase in proportion to the exertion intensity. At maximum intensity, the blood pressure, measured over the brachial artery, is 180–240 mm Hg. The change in resistance is not uniform in the various tissues of the body.

In the vessels of the working muscles and the heart, a marked vasodilation occurs with a resulting decrease in resistance. This results in the skeletal muscles' share of the blood flow at rest increasing from approximately one fifth (of 4–5 litres per minute) to approximately four fifths (of 20–30 litres per minute) under exertion. In other groups of vessels, such as in the digestive tract, kidneys and resting skeletal muscles, there is a constriction of the resistance vessels, which decreases the relative perfusion in these areas. Under strenuous exertion, particularly if the exertion is prolonged and occurs in a high ambient

temperature, the skin receives a relatively larger share of the blood flow. In the hours after a session of acute exertion, blood pressure drops by 5–20 mm Hg below the normal resting blood pressure.

Effects of exercise training

Up to just two decades ago, researchers believed that the vessels, except the capillaries, were relatively passive tubes that could not change with exercise. However, it turns out that regular exercise improves the function and structure of vessels that supply the engaged skeletal muscles and those in the heart muscle.

The dilation capacity of arterioles is improved and the inner volume of large arteries increases. Thanks to this and the increased capillarisation, an even larger proportion of the blood flow (84) can be guided to the working skeletal muscles. These and other mechanisms, such as increased parasympathetic activity and decreased release of adrenaline and noradrenaline (see the section on the hormone system), contributes somewhat to lowering resting blood pressure among those with normal blood pressure despite an increased blood volume.

Mechanisms

Through the "friction" exerted by the flow of blood against the vessel wall (shear stress), nitric oxide synthase, the enzyme that catalyses the formation of nitric oxide (NO), is induced. NO makes the smooth muscles relax and the vessels open. Capillary formation is probably induced through the formation of so-called angiogenic factors, of which vascular endothelial growth factor (VEGF) is the most studied. Together with anti-inflammatory mechanisms and better antioxidant activity, the increased NO formation contributes to counteracting arteriosclerosis/atherogenesis (hardening of the arteries/plaque formation).

Immune system

Acute exertion

The prevalent view is that regular physical activity of moderate to average intensity improves the function of the immune system and can reduce sensitivity to infections. However, hard or prolonged exercise in endurance sports can lead to immunosuppression and greater infection sensitivity (85).

During sessions of acute exertion, there is an increase in the majority of leukocyte populations in the blood, primarily neutrophil granulocytes and natural killer (NK) cells, and there is also a marked lymphocyte mobilisation to the blood. These changes have been related to the immune-stimulating function of moderate to intense physical exertion (39). However, in the process after a session of intense exertion, there is often a period of weakened immune function with reduced NK-cell activity and reduced lymphocyte proliferation (39). This immunosuppression is also clear in several organs, such as the skin, mucous membranes of the upper respiratory passages, lungs, blood and muscles, and appears to comprise an "open window" of diminished immunity through which viruses and bacteria

can enter and gain a foothold in the body. This immunosuppression can last from 3 to 72 hours after an intense exercise session, depending on which immunological markers are measured (40). Among athletes, the risk of developing a clinical infection in this situation can be particularly large upon exposure to new pathogenic flora when travelling, and to a lack of sleep, mental stress, poor food, etc. It has been shown that the concentrations of immunoglobulin A (IgA) and M (IgM) in saliva decrease immediately after an intense exercise session, after which they return to normal levels within 24 hours (41). Prolonged intense exercise can, however, result in a chronic reduction of these levels. This increases the risk of respiratory infections and it has been proposed that measurements of IgA and IgM in saliva during periods of intense training may be a way of keeping the risk of infection somewhat under control.

Macrophages are important cells in the immune system for phagocytosis, the elimination of microorganisms and tumour cells, and for T-lymphocyte-mediated immunity. There are preliminary indications that physical exertion can stimulate the macrophages' function in the former two areas, and possibly reduce T-lymphocyte-mediated immunity. Hard exercise has also been shown to give rise to raised levels of several both pro-inflammatory and anti-inflammatory cytokines, cytokine inhibitors and chemokines. The increase in the IL-6 cytokine after an exercise session is particularly sharp, but the significance of this increase is still unknown. It is well-known that physical activity leads to an activation of endogenic opioid peptides (86), which probably also plays a role in the immune system (42).

Effects of exercise training

Research regarding the relationship between the degree of physical exercise, the immune system and sensitivity to infections and other diseases is still in an early phase, and it is often difficult to draw definite conclusions from the results available in the literature. At rest, trained and untrained individuals appear to show relatively small differences in their immune system, with the exception of the activity of NK cells, which are usually higher among well-trained individuals. Besides these changes, reduced function of neutrophil granulocytes and reduced concentrations of NK cells have also been observed among over-trained individuals as a result of prolonged intense exercise (40).

Skeleton

Maximum bone mass is reached at the age of 20–30 years for both men and women, and then slowly decreases with rising age. Besides women having relatively greater bone-mass loss with age, there is also a sharp drop in connection with menopause. This means that post-menopausal women have significantly less bone mass than men (43). In the majority of studies of the significance of physical activity, bone mass refers to the bone's mineral density or mineral content. Mineral density can be measured through quantitative computed tomography, ultrasound densitometry or dual-energy x-ray absorptiometry (DXA) on selected parts of the skeleton or the entire body. It is also known that the bone's

size (volume), structure and protein content are affected by mechanical loading (44, 45), and it has been observed that these variables can often be more informative, since bone density measurements can underestimate the strengthening of the bone structure as a result of exercise (46).

Bone tissue is continuously reformed through resorption and synthesis, whereby the balance between these two processes determines if a net formation or decomposition occurs. How large the bone mass ultimately becomes is also dependent on the initial conditions and time. The common perception is that the balance is determined by the mechanical load the bone cells are subjected to (micro-strain), and that deficient loading leads to decreased bone mass and excess loading to increased bone mass. Important factors include how often the load is repeated and the direction, duration, speed, etc. of the load. For example, dynamic loading with higher speed is more significant than static loading or loads with a low speed. There is also data that indicates that varying types of loading can be more effective than repeating the same loading (47, 48). What in a given situation constitutes the threshold load for bone synthesis to exceed resorption depends on multiple factors, such as the levels of calcium, vitamin D and hormones. When mechanical loading is combined with an increase in oestrogen or androgen levels, the effect on new bone formation is greater than if each factor is allowed to act separately (49). For women, normal ovarian function is therefore very important to the development of bone.

In light of this, it can be expected that it is the intensity of exercise rather than its duration that is important to achieving greater bone density, and that types of exercise with high, temporary loading of the bone (high impact) are particularly effective. The greatest mineral density among athletically active men and women is also found in sports that involve impact loading, such as weightlifting, aerobics, squash, volleyball and football. The difference in bone density among trained and untrained persons, or between the hitting arm and the non-hitting arm among tennis and squash players, is usually on the magnitude of 10–20 per cent, while changes in bone tissue volume and strength may be larger (44).

It is known that intense physical exercise in adolescence, meaning mechanical loading on the skeleton, results in larger, stronger and more mineral-dense bones and that this effect is more pronounced if the exercise is begun early (50). If the exercise starts at an adult age, only small improvements in bone density are achieved. In spite of this, it has been clearly shown that the risk of a hip fracture is lower among trained individuals, while the proof that exercise at an adult age would reduce other types of fractures related to osteoporosis is not currently as strong (51). On the other hand, monotonous repetitions of the same load over time can cause microscopic damage that weakens the bone and eventually gives rise to so-called stress fractures (52). An interesting finding is that veteran cyclists, with many years of training behind them, have significantly lower bone density than control persons of the same age and, although very physically fit, they therefore have a higher risk of being affected by brittle bones with increasing age (53). Among women, intense exercise training such as long-distance running can also lead to diminished bone density, probably due to hormonal changes, possibly in combination with low energy consumption (49). The state of proof is relatively weak with regard to training with low to moderate intensity exercise also providing a positive effect on the skeleton. In

terms of non-weight-bearing activity, such as swimming, such activities do not normally lead to greater bone density.

In light of the fact that half of all women and one third of all men will be affected by a brittle bone fracture in their lifetime (51), it is of great interest to know if it is possible to build up a strong skeleton during adolescence that can protect against fractures later in life. However, available data does not conclusively indicate the existence of any such lasting protective effect (51) and it has been reported that the risk of fractures among former athletes is not lower than among those previously not athletically active (51). On the other hand, in recent years, studies have been published that support the hypothesis that physical activity in the teenage years and as young adults really is linked to higher bone density late in life, such as for lumbar vertebra (54) and proximal femurs after menopause among women (54, 55), as well as for lumbar vertebra and femurs among older men (56), which in turn could reduce the risk for a fracture in a long-term perspective.

Cartilage

Isolated cartilage cells respond to mechanical loading and an increased strain of a cyclically varying type leads to greater net synthesis of extracellular matrix in cartilage in organ baths. However, static loading commonly leads to decreased matrix production. In animal experiments, both intense physical activity on one hand and total immobilisation on the other have proven to lead to osteoarthritis-like changes. Intense and prolonged physical activity in human beings is also probably associated with osteoarthritis in hips and knees (57). The function of cartilage tissue is linked to the interaction between tissue matrix and the extra-cellular fluid that is bound to proteoglycan molecules in the cartilage tissue. Loading leads to deformation of the cartilage with fluid outflow from the tissue matrix to the surroundings, which normalises in the hours after the exertion. After 100 knee bends in people, this normalisation is reported to take more than 90 minutes (58). Consequently, it can be assumed that the balance between deformation and restitution is an important factor, and if this is kept at an appropriate level, damage to the cartilage in connection with physical activity may be avoided (87). What constitutes an appropriate level can probably vary significantly depending on different joint anatomy, joint mobility, etc. (59). There are research results that indicate that kinesiotherapy and passive motion training have positive effects on cartilage tissue by speeding the restitution phase (57).

Connective tissue

Connective tissue responds to strain with increased collagen synthesis, while immobilisation has the opposite effect. It is believed that a session of physical activity may in fact lead to increased decomposition of connective tissue as a result of the activation of protease enzymes. Analogous to what was reported above for cartilage, it therefore appears as if the actual exercise session leads to a degradation, meaning a reduction of the

synthesis rate, while synthesis markedly increases in the restitution phase in the ensuing days. Consequently, it is the balance between the effect on synthesis and decomposition that determines if a certain training programme leads to improved ligament strength or to a degradation with ruptures or damage as a result (60). It has also been shown that several hormonal growth factors and inflammatory mediators play a role in this balance. An interesting observation is that a considerable net synthesis of new connective tissue often requires several weeks or months of exercise, because the enhanced decomposition is most pronounced at the beginning of a period of exercise and can counteract the increased new formation of connective tissue (60). The strong ligaments that characterise well-trained individuals provide greater sustainability because the load per cross-sectional area decreases.

Lungs and gas exchange

Acute exertion

In low-intensity exertion, it is mainly the size of each breath (tidal volume) that increases. In more high-intensity exertion, the respiratory rate increasingly rises. Altogether, this means that the pulmonary ventilation increases from 6–8 litres per minute at rest to up to 150 litres per minute among the untrained and up to 200 litres per minute among well-trained persons under maximum exertion.

Under exertion, large amounts of oxygen is consumed and roughly the same amount of carbon dioxide is formed. Despite the sharply increased carbon dioxide formation, the content in arterial blood and exhalation air decreases at maximum exertion. This is due to the pulmonary ventilation increasing by 15–30 times at the same time that carbon dioxide formation increases by only 10–15 times. The extraction of oxygen from arterial blood increases from around 25 per cent at rest to more than 75 per cent under strenuous exertion.

Effects of exercise training

The pulmonary ventilation under maximum exertion increases. Under sub-maximum exertion, the respiratory rate, tidal volume and consequently pulmonary ventilation is significantly lower after exercise training. Exercise training improves the endurance of the respiratory muscles. This occurs by adaptations in the same way as in other skeletal muscles that are regularly exercised (see above). The lungs' blood flow distribution changes and there is a lesser degree of mismatch between perfusion and air ventilation; the upper parts of the lungs in particular receive a greater blood flow. The lungs' gas diffusion improves.

Mechanisms

The probable underlying causes behind the training-induced changes in the respiratory muscles are the same as for other muscles (see above). In terms of the improved blood flow distribution in the lungs, it may be due to the increased blood volume combined with changes in the vessels of the lungs.

Body composition and adipose tissue

The sharp increase in overweight and obesity that has occurred in the Western World in the past 15–20 years has been associated with growing inactivity, although the relative significance of decreased physical activity compared with altered caloric intake and mealtime patterns is unknown (61).

The energy expenditure when running on level ground is on a magnitude of 1 kcal per kg of body weight and kilometre, while the corresponding value for walking is 20–25 per cent lower. Accordingly, one hour of walking corresponds to 1/10 of the energy expenditure per day of a standard man (2,800 kcal per day) or woman (2,100 kcal per day). It being difficult and nearly impossible to predict on an individual level how more physical activity will affect body weight and body composition is illustrated by the fact that three glasses (of 2dl each) of a soft drink that may be consumed in connection with training also corresponds to 10 per cent of the daily energy needs. It has been said that the increase in the average weight of 20–40 year-olds in the U.S. in the 1990s (approximately 7–8 kg in eight years) could have been avoided if 100 kcal more of energy on average had been expended (or 100 kcal less food consumed) per day. This corresponds to just 15–20 minutes of walking or one glass of a soft drink (62).

The appetite can also be affected by physical activity in various ways. Low energy levels and low levels of insulin in plasma, which is often observed after an exercise session, stimulates the appetite through neuropeptide Y-releasing neurons in the central nervous system. On the other hand, intense exertion can lower the appetite through the release of corticotropin-releasing hormone (CRH) from the hypothalamus with an anorectic effect. At the population level, knowledge about how regular physical activity affects body composition is more certain, and several major studies with observation times of approximately 3–4 months show that various exercise programmes can be expected to provide a decrease in fat weight of an average of 0.1 kg per week. As a rule, the decrease in fat weight is always larger than the decrease in body weight, and body weight often does not change at all due to increased muscle mass (63). The decrease in fat weight is seen in both genders. Although a tendency of larger decreases are seen in men, it cannot be said for certain that any gender difference exists.

There is support from studies of rats that exercise training-induced changes occur in adipose tissue similar to those seen in skeletal muscles, with increases in both mitochondrial enzyme activity and in the level of glucose transport protein (GLUT-4). One difference from the skeletal muscles (where exercise training provides a decrease) is that there is an increase in adipose tissue of the hormone-sensitive lipase enzyme (HSL) with training, that is to say the enzyme responsible for the release of fatty acids (lipolysis) into the blood. This agrees with studies in organ baths of fat cells from humans and rats, where it could be shown that adrenaline (which stimulates HSL) gives rise to significantly greater release of fatty acids in fat cells that were taken from trained individuals than in fat cells from untrained individuals. It is known that being overweight leads to lower HSL concentrations in the adipose tissues, but that the concentration increases in connection with periods of fasting. The increased adrenaline effect on the release of fatty acids among trained individ-

uals can, however, also be due to a higher level of the adenylate cyclase enzyme in the fat cells. Adenylate cyclase conveys the effects of adrenaline by giving rise to the messenger molecule cyclic adenosine monophosphate, cAMP. The number of receptors for adrenaline on the surface of the fat cells is probably not affected by exercise, however. To some extent, the increased fat degradation activity in adipose tissue from trained individuals can be seen as a compensation for a lower overall adipose tissue mass in a trained individual (64).

In the past decade, it has been discovered that adipose tissue is significantly more metabolically active that was previously known. Today, it is known that several potent peptides are released from adipose tissue and have important effects on other organs in the body. Two such peptides are leptin, which has an anorectic effect on the energy balance and also affects sugar metabolism, and adiponectin, which stimulates fat burning. Adipose tissue also releases pro-inflammatory proteins such as tumour-necrosis factor alpha (TNF-α) and other cytokines and acute phase proteins. Angiotensinogen (AGT) formed in adipose tissue affects blood pressure, and can play a role in the blood pressure increase seen in overweight individuals. It has not been established how physical activity and exercise training affect these factors, but the decreased fat mass seen with exercise training can be expected to decrease the significance of these factors (88). Leptin has been examined in several studies, but there does not appear to be any unambiguous effect of exertion or exercise training on leptin levels. However, lower plasma levels of TNF-α have been observed among well-trained people, which is of interest because TNF-α formed by adipose tissue is considered to result in diminished tissue sensitivity to insulin, primarily in skeletal muscles. A decreased level of TNF-α could therefore contribute to the greater insulin sensitivity that exercise training entails (65).

Nervous system

Much of the knowledge that applies to the effects of acute exertion and exercise training on the nervous system is gathered from studies of animals, but growing numbers of human studies of cognition and learning are being published.

Acute exertion

During exertion, the brain has a total metabolism and total blood flow that do not significantly differ from that at bodily rest. However, during exertion, the activity, metabolism and blood flow in the areas that take care of motor activity increase measurably. The glucose concentration increases interstitially in the central nervous system (CNS) regardless of the blood sugar concentration. Besides glucose, the brain uses lactic acid as an energy substrate under intense exertion. The release of neurotransmitters (signal substances) such as dopamine, serotonin and glutamate in various parts of the brain are also affected during physical exertion.

Effects of exercise training

Regular physical activity affects several different functions in the human nervous system (89). Functions connected more directly to physical activity improve, such as coordination,

balance and reaction ability. This increases the functional ability, which can contribute to the increased well-being which is tied to regular physical activity. Moreover, cognitive ability (especially planning and coordination of tasks) is retained better, sleep quality is improved, depression symptoms decrease and self-esteem improves. Experiments in animals have shown that growth factors significant to cells in the central nervous system are affected by physical activity (66). In the hippocampus (important to memory formation), the gene expression of a large number of factors increases. For example, the occurrence of IGF-1, a very important growth factor, increases. The occurrence of noradrenaline increases in the brain. There are also studies that indicate that the new formation of brain cells increases in animals that are allowed to run (67). These animals also show better learning ability. Other studies have shown that the new formation of vessels increases in the cerebral cortex after exercise training, which can be of significance to the supply of nutrients. In cells in the peripheral nervous system, studies in animals have shown that markers for oxidative capacity/aerobic capacity increase. In addition, there are findings that indicate that cell size can increase with regular physical activity.

Mechanisms

The increased metabolism associated with more activity in parts of the cells of the brain, spinal cord and peripheral nervous system entails an effect on gene activity, in part caused by increased production of growth factors such as brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF) and galanin (68). Local hypoxia may potentially drive the formation of new blood vessels around the brain cells.

Skin

Acute exertion

Under acute exertion, especially prolonged exertion in heat, perfusion of the skin increases sharply and the degree of sweating can be multiplied many times over. A well-trained person can excrete 2–3 litres of sweat per hour under extreme conditions. Various hormones affect the sweat glands so that salt is largely saved.

Effects of exercise training

Exercise improves sweating function and thereby heat-regulation capacity. Therefore, a well-trained person has better heat tolerance at rest and under exertion. Among other factors, this is due to altered perfusion and changed gene expression in the cells of the sweat glands. Regular physical activity reduces the amount of subcutaneous fat.

Gastrointestinal tract and liver

Acute exertion

The gastrointestinal tract is affected in many ways during and after acute exertion (69). Under strenuous exertion, symptoms occur such as stomach aches, diarrhoea, etc. It is not easy to determine the degree to which such symptoms are related to stress, dietary and fluid intake, or the physical exertion. The frequency at which the stomach empties decreases, at most during strenuous exertion. Besides motility, digestion and absorption, the gastrointestinal tract's blood flow, its secretion of hormones and other factors are affected. The stomach's lymphoid tissue and the mucous membranes' immunological functions, such as IgA, are also affected. Under exertion, the liver increases its glycogenolysis, which contributes to maintaining blood sugar (see below under "Hormone system").

Effects of exercise training

A well-trained person has a higher gastric emptying rate. The risk of the formation of gall stones is also reduced.

Hormone system

Acute exertion

Several hormone systems are activated under exertion, and physical activity entails increased plasma concentrations of multiple hormones, such as adrenaline/noradrenaline, adrenocorticotrophic hormone (ACTH), cortisol, beta endorphin, growth hormone, renin, testosterone, thyroid hormone and several gastrointestinal hormones. The levels of glucagon in arterial blood is only affected to a small degree by physical exertion, while the concentration of insulin decreases (70). The decrease in the insulin level in plasma during exertion, which can be very sharp (a drop to half or less of the resting level), is probably mediated by the increased activity in sympathetic nerves and by small reductions in the blood glucose level during the exertion. The latter explains why the insulin decrease under exertion is counteracted or even converted to an insulin increase upon sugar intake during the exercise session. Because glucagon, like insulin, exerts a significant part of its effect on the liver, one is at risk of underestimating the significance of glucagon under exertion when measuring arterial concentrations since the concentration in the portal vein, which is the concentration "seen" by the liver, is significantly higher and probably significantly raised under exertion (71).

The catecholamines adrenaline and noradrenaline increase sharply and exponentially with increasing work load. The source of the circulating adrenaline is the adrenal medulla and the increase in plasma adrenaline in physical exertion is due to increased sympathetic nerve activation of this organ. Although the blood's noradrenaline also comes in part from the adrenal medulla, the most important cause of the sharp rise in the plasma content of noradrenaline under exertion is a "flood" of noradrenaline from the sympathetic nerves. The most important sympathetic nerves in this respect are those stimulating a higher heart

rate and cardiac contractile force during exertion, as well as those which innervate the liver and adipose tissue. It is believed that a lower glucose concentration in the portal vein is an important cause of the strong activation of the sympathetic nervous system under exertion. The increase in noradrenaline starts at a lower work load than the increase in adrenaline, and noradrenaline also increases more sharply when exertion intensity increases. These hormones can increase 10–20 fold in strenuous or prolonged exertion. The noradrenaline content of the blood is often raised for several hours after the end of exertion, while the adrenaline concentration goes back to resting values within a few minutes (72).

The liver's greater release of glucose is one of the most important metabolic changes under exertion and compensates for the muscles' increased glucose uptake without the blood glucose level dropping too much. It is practically entirely caused by the changes in insulin and glucagon (73). The reduction of the plasma insulin level that takes place with exertion is believed to make the liver more sensitive to the glycogen-degrading effect of glucagon. The increased activation of the sympathetic nervous system during physical exertion appears to lack any direct significance to the liver's increased glucose release. However, under prolonged exertion, when the adrenaline levels are at their highest, adrenaline can have some stimulatory effect on the liver's glucose release in addition to glucagon. Adrenaline and noradrenaline are mainly of significance to the carbohydrate metabolism at the muscle level by making the muscle's glycogen degradation process sensitive to the stimulatory effect that the contraction process (actually the calcium ions that are released) has. However, if prolonged exercise leads one to "hit the wall" due to a blood glucose reduction, a crisis reaction is triggered, whereby adrenaline is released, which leads to an increase in the liver's glucose release. The liver's limited glycogen deposits mean that new synthesis of glycogen in the liver (so-called gluconeogenesis) becomes important in prolonged exertion (in addition to the sugar consumed by drinking). Here, the hormone cortisol plays an indirect role by increasing the capacity of the enzymatic machinery that takes care of this process.

Another crucial enzymatic process during physical exertion is the release of free fatty acids from the body's fat deposits, since free fatty acids are the body's other important nutrient during exertion. Here, noradrenaline, released by the sympathetic nerves that innervate adipose tissue, plays the most important role. Insulin has an inhibitory effect on the release of fatty acids, although this effect is diminished by its plasma concentration dropping sharply during exertion.

Increased levels of beta endorphines during prolonged exercise can be of significance to well-being and blood pressure reduction in connection with an exercise session (74).

Effects of exercise training

Naturally, lower hormone responses at a given work load are observed among well-trained than among untrained individuals. This applies to the increases in noradrenaline, adrenaline, growth hormone, ACTH and glucagon as well as the reduction in insulin. The reduced hormonal activation during exertion among well-trained persons is particularly notable with regard to the sympathetic nervous system, where the change occurs rapidly, normally during the first two weeks of exercise (75). The physiological mechanism behind

this rapid change is unknown, but the activation of stress hormones that occurs with other stress stimuli is not reduced among fit individuals. It is also well-known that the adrenal medulla's capacity to excrete adrenaline is greater among well-trained individuals (sports adrenal medulla).

The so-called hypothalamus-pituitary-adrenal (HPA) axis is a messenger for the body's responses to various states of stress. The resting state of the HPA system is affected by regular endurance training so that the daily rhythm is shifted (the morning peak comes earlier) and the release of the pituitary gland's control hormone ACTH is increased. Although this can be interpreted as a hormonal stress state in the trained body, the effector hormone of the HPA axis, cortisol, does not change its resting level as a result of regular exercise, however. This apparent paradox seems to be explained by the fact that cortisol provides less effective feedback inhibition of the pituitary and possibly of the hypothalamus in well-trained individuals, which leads to an increased level of ACTH (76, 77). This is suspected to be one of several different explanations of the menstruation disruptions that occur in female athletes. Disturbances of the reproductive system in male athletes are rarely discussed, but may also exist (90).

Well-trained individuals have lowered insulin concentrations in plasma, both basally and after sugar intake, due to both a reduced release of insulin from the islets of Langerhans (78) and an increased tissue sensitivity to insulin (79). The increased insulin sensitivity is strongly linked to the reduced risk of having cardiovascular disease that is characteristic of physically trained individuals. As described above in the section on adipose tissues, regular exercise leads to an increased capacity for lipolysis in the adipose tissue. This contributes to a well-trained person being able to maintain a sufficient fat release during physical exertion even though the activation of the sympathetic nervous system, which controls lipolysis, is sharply reduced. Regular exercise has a carbohydrate-saving effect by a large part of the energy need being met with the burning of fat. This is registered by the liver and, after just 10 days of exercise, the liver's glucose release during a two-hour exercise bout can be reduced by 25 per cent (80). In spite of this, regular physical exercise leads to a greater capacity for gluconeogenesis in the liver.

Table 1. The effect of endurance training on a few physiological reactions during sub-maximum and maximum exertion. The direction of the arrows or ± 0 indicate the change compared with an untrained state.

	Submax.	**Max.**
VO_2*	±0	↑
Blood pressure	↓	±0
Heart rate	↓	±0
Pulmonary ventilation	↓	
Muscle metabolism		
Glycogen metabolism	↓	only glycogen
Fatty acid metabolism	↑	none
Lactic acid formation	↓	
Sweating	↑	↑
Body temperature	↓	±0
Adrenaline concentration in blood	↓	↑

* VO_2 = oxygen uptake capacity.

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