REVIEW ARTICLE

Sports Med 2000 Dec; 30 (6): 405-422
0112-1642/00/0012-0405/$20.00/0

Metabolic and Hormonal Responses to Exercise in Children and Adolescents

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Abstract

Ethical and methodological factors limit the availability of data on metabolic and hormonal responses to exercise in children and adolescents. Despite this, it has been reported that young individuals show age-dependent responses to short and long term exercise when compared with adults.

Adenosine triphosphate (ATP) and phosphocreatine stores are not age-dependent in children and adolescents. However, phosphorus-31 nuclear magnetic resonance spectroscopy (^{31}PNMR) studies showed smaller reductions in intramuscular pH in children and adolescents during high intensity exercise than adults. Muscle glycogen levels at rest are less important in children, but during adolescence these reach levels observed in adults.

Immaturity of anaerobic metabolism in children is a major consideration, and there are several possible reasons for this reduced glycolytic activity. There appear to be higher proportions of slow twitch (type I) fibres in the vastus lateralis part of the quadriceps in children than in untrained adults, and anaerobic glycolytic ATP rephosphorylation may be reduced in young individuals during high intensity exercise. Reduced activity of phosphofructokinase-1 and lactate dehydrogenase enzymes in prepubertal children could also explain the lower glycolytic capacity and the limited production of muscle lactate relative to adults. These observations may be related to reduced sympathetic responses to exhaustive resistance exercise in young people.

In contrast, children and adolescents are well adapted to prolonged exercise of moderate intensity. Growth and maturation induce increases in muscle mass, with proliferation of mitochondria and contractile proteins. However, substrate utilisation during exercise differs between children and adults, with metabolic and hormonal adaptations being suggested. Lower respiratory exchange ratio values are often observed in young individuals during prolonged moderate exercise. Data indicate that children rely more on fat oxidation than do adults, and increased free fatty acid mobilisation, glycerol release and growth hormone increases in preadolescent children support this hypothesis.

Plasma glucose responses during prolonged exercise are generally comparable in children and adults. When glucose is ingested at the beginning of moderate exercise, plasma glucose levels are higher in children than in adults, but this may be caused by decreased insulin sensitivity during the peripubertal period (as shown by glucose **:** insulin ratios).

Conclusions: Children are better adapted to aerobic exercise because their energy expenditure appears to rely more on oxidative metabolism than is the case in adults. Glycolytic activity is age-dependent, and the relative proportion of fat utilisation during prolonged exercise appears higher in children than in adults.

Children and adolescents are not adults in miniature. They grow up and mature at their own rate and as such, metabolic and hormonal responses to exercise vary accordingly as they progress through childhood and adolescence. Rates of cellular growth and proliferation depend on the actions of specific hormones such as growth hormone (GH), insulin-like growth factors (IGFs) and steroid sex hormones (SSHs). These hormones also directly regulate metabolic processes during rest and exercise. Other hormones such as insulin are indirectly involved in the control of growth. At puberty, accelerated development and intense endocrine activity (GH and SSH) may affect the metabolic regulation of exercise. Unfortunately, most of those mechanisms have not yet been explored in humans. Methodological and ethical considerations probably explain why little research on exercise in young individuals has been carried out. The aim of this review is to report the evidence for specific metabolic and hormonal responses in children and adolescents during short and long term exercise. Specific maturity-related differences in substrate utilisation could influence exercise performance. This review will summarise the limited data available from the literature and will also try to establish recommendations for children and adolescents undertaking physical activity.

1. Summary of Morphological, Functional and Metabolic Changes Through Childhood

The pubertal growth spurt relies on the release of important hormones (GH, IGFs, SSHs) that induce increases in growth velocity, bone and muscle maturation, functional ability and metabolic adaptation. These changes may influence the development of physical capacity and performance during childhood and adolescence.

Adrenarche (as defined by synthesis and secretion of androgens when the adrenal zona reticularis matures) takes place between 6 and 8 years of age in girls and 8 to 10 years of age in boys in Caucasian populations.[1] In both genders, there is a progressive increase in the secretion of adrenal hormones (androgens and estrogens).[1,2] The gonadarche (as defined by activation of the testes and ovaries at puberty) follows 2 to 3 years after this first stage and is under the control of GH, IGF-1 and SSHs. The release of these hormones is controlled by the pulsatile stimulation of a hypothalamic factor, gonadotrophin-releasing hormone (GnRH). The GnRH that is subject to both positive and negative feedback control by circulating SSHs (testosterone in boys, and estradiol and progesterone in girls) also stimulates secretion of follicle stimulating hormone (FSH) and luteinising hormone (LH). SSHs from the adrenal glands and gonads mediate the later pubertal changes.[3] Increased plasma levels of GH, testosterone, estradiol and progesterone have an anabolic effect on structural protein production (including various enzyme pathways). The synergistic action of GH and gonadal steroids promotes the pubertal growth spurt, mainly in bones and muscles, that may contribute to aspects specific to children and adolescents' metabolic and hormonal regulation during exercise.

2. Methodological and Ethical Aspects During Exercise in Young Individuals

2.1 General Information

The lack of information on metabolic and hormonal responses during exercise in young individuals is mainly attributable to ethical concerns and methodological constraints. Paediatric exercise scientists perform biopsies, use radioactive materials or insert arterial catheters in young individuals only very rarely. With healthy children, measurements have to be indirect and relatively noninvasive,[4,5] and must carry little or no risk to health.[6]

2.2 Plasma or Blood Concentrations

The most common (but invasive) indirect technique used to assess metabolic and hormonal responses is based on plasma or blood measurements. These metabolic or hormonal levels may indirectly reflect a balance between production and utilisation during exercise. However, it is difficult to assess the precise effect of a hormone upon a metabolic pathway. For example, an increase in plasma levels of a hormone or substrate does not necessarily reflect an increase in secretion, but may be caused by a decrease in metabolic clearance rate (MCR).[7] It may be due also to a decrease in plasma volume which leads to haemoconcentration.[8] Other factors such changes in posture, timing, site of blood sampling and method of measurement can influence results. Furthermore, hormonal activities depend not only on plasma or blood levels, but also on receptor availability and sensitivity.

For these reasons, it is important to understand the limitations of the measurement of plasma or blood metabolic and hormonal activities during exercise in children when compared with adults, where other techniques (e.g. radioactive materials, venous and arterial catheters, biopsies) are frequently used.

2.3 Respiratory Exchange Ratio

The measurement of respiratory exchange ratio (RER), expressed by $\dot{V}CO_2/\dot{V}O_2$ as measured in the mouth, is usually used as an indicator of the respiratory quotient (RQ), which represents the same ratio at a cellular level. RER provides information on substrate utilisation only at steady state and with exercise intensities below the respiratory anaerobic threshold (to prevent the influence of CO_2 from buffering of lactate). The ratio is equal to 1.00 when carbohydrates are used exclusively, and is 0.70 for fats and 0.82 for proteins. However, RER can be calculated as a nonprotein RQ, since protein oxidation is limited. Nevertheless, the RER can be corrected for the oxidation of proteins as computed from nitrogen excretion in urine and sweat.[9] Thus, RER appears to be a good indirect and noninvasive method for the assessment of the relative contributions as metabolic substrates of carbohydrates and fats.[10]

2.4 Phosphorus-31 Nuclear Magnetic Resonance Spectroscopy

Phosphorus-31 nuclear magnetic resonance (NMR) spectroscopy (^{31}PNMR) is a noninvasive method for the study of muscle bioenergetics during exercise.[11] As such, this technique has been used with young individuals.[12-15] Advances in ^{31}PNMR could help to clarify the development of specific metabolic responses in exercising children and adolescents. However, this method is limited to the measurement of the types of exercise possible in an NMR tube. Furthermore, the cost of this technique restricts its utilisation and limits sample sizes.

The ^{31}P spectrum is used to evaluate changes in phosphocreatine (PCr) and inorganic phosphate (Pi) and to calculate the Pi/PCr ratio.[12] As the rate of adenosine triphosphate (ATP) hydrolysis approaches the maximal rate of tissue oxidative phosphorylation, glycolysis, which is activated by adenosine diphosphate (ADP) and Pi, contributes to a progressively greater extent to energy production. In healthy adults, the relationship between Pi/PCr and work rate is represented by an initial linear portion. The slope of Pi/PCr to work rate is directly proportional to the rate of mitochondrial oxidative metabolism. A second steeper slope then appears that indicates the activation of glycolysis[16] as shown by lactate production and release of hydrogen ions (H^+). ^{31}PNMR may therefore also be used as an indirect method for the measurement of intracellular pH.

3. Metabolic and Hormonal Responses During Exercise in Children and Adolescents

3.1 Anaerobic Metabolism

3.1.1 Anaerobic Metabolism and Performance

Indoor and outdoor sprint tests reveal better performance during the growth spurt period.[17] For example, under field conditions, Falize[18] reported a steady mean velocity increase from 3.64 m/sec (6 years) to 5.94 m/sec (12 years) and 7.76 m/sec (20 years) in males. A force-velocity test performed indoors showed increasing power output (mean maximum output, P_{max}) from 6 W/kg (7 to 8 years) to 8.6 W/kg (11 to 12 years) and 10.2 W/kg (14 to 15 years) in boys.[19,20] More specifically, Duché et al.[20] pointed out that increased anaerobic power is related mainly to the development of muscle mass. Accordingly, Mercier et al.[21] correlated P_{max} with the increase of lean body mass (LBM) in children. However, these authors suggested that increased P_{max} cannot be linked to muscle mass alone because the P_{max}/LBM ratio shows a steady increase between 11 and 15 years of age. Others factors could also be involved in the increase in anaerobic performance seen during childhood and adolescence: these include neuromuscular activation, changes in enzyme activities or improvements in motor control.[21]

3.1.2 Muscle Fibre Characteristics

Maturation of skeletal muscle fibre patterns might account for growth-related changes in the metabolic response to high intensity exercise. Few investigations on muscle fibre characteristics in children and adolescents have been published. This is attributable to difficulty in subjecting children to muscle biopsy.

Postnatal muscle growth is considered to be primarily caused by muscle hypertrophy, in contrast to prenatal muscle growth which is characterised as the period of muscle fibre hyperplasia.[22] Histological studies by Colling-Saltin[23] and Elder and Kakukas[24] have clearly demonstrated that embryological development of muscle fibre in humans is linked to the differentiation of immature fibres (IIc) from the third month of gestation onwards. The development of fast twitch fibres (type IIb) increases progressively during pregnancy. At the same time, type IIa and slow twitch (type I) fibres appear. This development and differentiation continues during the first few years of life and is largely complete by the age of 2 to 3 years.[25] The study of Elder and Kakukas,[24] performed on brachial biceps and triceps, has shown that <10% of fibres remain immature in the prepubertal period.

Histochemical investigations on muscle biopsies from children and adolescents have found no differences from adults in muscle fibre components.[26-28] However, few studies have reported age-related differences in the proportional distribution of muscle fibres; thus, children show a higher proportion of slow twitch (type I) fibres in the vastus lateralis muscle as compared with untrained adults.[26,29,30] This difference disappears during late adolescence.[27,31,32] Differences in percentages of fibre types in children and adolescents as compared with untrained adults may indirectly account for lower glycolytic potential. The extension of magnetic resonance imaging (MRI) techniques, already used in adults to determine muscle fibre distributions,[33-35] should help to resolve some of the key issues of debate with respect to the maturation of muscle in children and adolescents.

3.1.3 Adenosine Triphosphate (ATP), Phosphocreatine and Glycogen Stores

Colling-Saltin[23,36] has reported changes in muscle metabolic properties that follow the development from fetus to adult. Muscle ATP levels appear very low in the fetus (approximately 0.5 mmol/kg of wet muscle). This muscle content increases rapidly after birth and reaches 5 mmol/kg (wet muscle), a similar figure to that in adult skeletal muscle. According to Colling-Saltin,[36] PCr follows the same progressive increase during the first year of life.

ATP and PCr muscle stores do not differ between children/adolescents and adults.[12,29,37] Indeed, after taking muscle biopsies from the vastus lateralis of the quadriceps femoris, Eriksson et al.[37] reported that resting ATP and PCr levels are similar in healthy 13-year-old boys and adult males (ATP ≈5 mmol/kg of wet muscle and PCr ≈17 mmol/kg of wet muscle). In a follow-up study, Eriksson and Saltin[29] extended this study for different age-groups (boys of mean age 11.6, 12.6, 13.5 or 15.5 years) and showed that ATP and PCr concentrations at rest were comparable to values found in adults.

In contrast, liver and muscle glycogen stores, expressed in g/kg, are lower in children than in adults.[38,39] Bougnères et al.[38] and Schiffrin and Colle[39] reported that liver glycogen was restricted to 15g for a baby weighing 10kg. Moreover, there are age-dependent variations in liver glycogen production and glucose uptake by the CNS under resting conditions. A child produces about 6 mg/kg/min of liver glycogen, with glucose uptake by the CNS reaching 4 mg/kg/min. In contrast, an adult liver (with a total glycogen store of about 100g) produces nearly 1.7 mg/kg/min of glycogen while the glucose uptake by the CNS is restricted to 0.86 mg/kg/min of glucose. This could lead to greater glycogen store depletion in children than in adults.[38,39] Different studies have shown the glycogen content of muscle in children to be 50 to 60% of that of adults,[37,40] but this low amount increases with maturation.[29] Thus, in Eriksson and Saltin's study[29] muscle glycogen levels at rest were 54 mmol/kg of wet muscle, glucose units for the 11.6-year-old boys, and increased to 70, 69 and 87 mmol/kg of wet muscle for the 12.6, 13.5 and 15.5-year-old boys, respectively. The values in the oldest boys were similar to those observed in sedentary adults.[29]

3.1.4 ATP Rephosphorylation, Glycolysis Capacity and Enzyme Activities

Using ^{31}PNMR, Petersen et al.[15] suggested that glycolytic metabolism in physically active children is not maturity-dependent. Indeed, no significant differences in the mean values for intracellular pH or the Pi:PCr ratio were observed in prepubertal (10 to 11 years) and pubertal (15 to 16 years) girls during exercise. However, using the same technique, Zanconato et al.[12] and Kuno et al.[14] have shown that preadolescent children (7 to 10 years) and adolescents (12 to 15 years), both trained and untrained, are less able than adults to achieve ATP rephosphorylation by anaerobic metabolic pathways during high intensity exercise. This observation could result either from changes in the mechanism of glycolysis in muscles or from a different pattern of fibre type recruitment.

Limited studies have suggested that children have a lower anaerobic or glycolytic capacity for supplying ATP during high intensity exercise.[37,40] It would be reasonable to assume that lower glycolytic capacity in children is not related to fibre distribution (see section 3.1.2), but to a difference in muscle metabolism as compared with adults. The limited data available on paediatric glycolytic capacity are characterised by small sample sizes and must therefore be interpreted with caution. This immaturity of glycolytic ability may be explained by lower activities of anaerobic enzymes such as lactate dehydrogenase (LDH) and phosphofructokinase-1 (PFK),[40,41] and by glycogen content.[29,37] Accordingly, Eriksson et al.[40] showed that boys aged 11 to 13 years had a 50% lower PFK activity than adults. However, anaerobic enzyme activity evolves with pubertal maturation.[41-43] Thus, in studies using more 'mature' individuals, other reports have failed to detect adolescent-adult differences in various glycolytic enzymes including LDH and PFK.[41,44] Furthermore, some studies did report higher levels of oxidative enzymes such as succinate dehydrogenase (SDH) and isocitrate dehydrogenase (ICDH) in children than in adults.[27,40,41] Differences in the ratio of PFK to ICDH between children (0.884) and adults (1.633) indicate greater pyruvate oxidation in young individuals,[41] which suggests that children are more able than adults to use aerobic pathways.

3.1.5 Lactate Production, Intramuscular pH and Buffering System

No difference is found at rest in muscle pH between children and adults.[12] The compromised ability to generate energy from glycolysis during exercise induces lower maximal muscle lactate levels in young individuals.[29,37,45] Accordingly, ^{31}PNMR shows less reduction in intramuscular pH in children[12] and adolescents[14] than in adults during intense exercise.

Short term exercise elicits a gradual increase in maximal levels of muscle and plasma lactate which is related to pubertal maturation.[29,37,45] When comparing preadolescent individuals and adults during a graded exercise test, Rostein et al.[46] reported lower blood lactate levels in the younger individuals. During an exercise test on a cycle ergometer (pedal rate of 60 rpm) performed by 4 groups of children (mean ages 11.6, 12.6, 13.5 and 14.5 years), Eriksson and Saltin[29] reported that muscle lactate production increased with age. Maximal blood lactate levels appear to be directly related to increased testicular volume[37] and testosterone levels in saliva.[47]

Crielaard et al.[48] showed a positive correlation between plasma (or blood) lactate and anaerobic performance. Additionally, Zanconatto et al.[12] and Kuno et al.[14] reported a relationship between anaerobic performance and the production of H^+ in children aged 7 to 10 years and adolescents aged 12 to 15 years.

The pubertal growth spurt involves increases in bone mass that contribute to enhancement of bicarbonate storage capacity. This increased buffering capacity explains the ability of adolescents to sustain lower pH values in muscle and blood during strenuous exercise.[49,50] According to Matejkova et al.,[50] the ability to buffer excess H^+ increases at a rate of between 0.001 and 0.002 pH units per year from the age of 8 up to the age of 18 years. Along the same lines, plasma buffer excess decreases from 1.0 to 1.5 meq/L/year.

3.1.6 Catecholamine Responses

During high intensity exercise, the sympathoadrenal system and catecholamines (adrenaline and noradrenaline) affect substrate mobilisation.[51] In addition, adrenaline has been shown to be a potent stimulator of muscle glycolysis.[52,53] In intense anaerobic exercise, increases in catecholamine levels are higher than in prolonged aerobic exercise in both adults[54] and children.[55,56] Pullinen et al.[56] showed that young male athletes aged 15 ± 1 years (mean ± standard deviation) experienced reduced sympathetic nervous activity during 4 different half-squatting exercises when compared with adult male athletes aged 25 ± 6 years. The authors suggested that exhausting resistance exercise may induce a lower sympathetic response in younger individuals than in adults, with no differences in adrenal medulla activity.

3.1.7 Effects of Training on Anaerobic Metabolism

There are few publications dealing with the effects of training on anaerobic metabolism in children and adolescents. Different studies have reported that a training session may increase ATP, PCr and glycogen muscle stores in adults[57,58] and children.[43] Eriksson[59] suggested that training also increases substrate utilisation in young individuals, because of an increase in activities of muscle enzymes. Thorstensson et al.[60] supported this hypothesis by reporting increases in activity (of 20 to 35%) of adenylate kinase and phosphocreatine kinase. In addition, these increases were related to raised muscle and blood lactate levels during maximal exercise. These data suggest that strength training enhances glycolytic activity, although these adaptations return to basal levels if training ceases.[27]

3.1.8 Conclusions and Practical Considerations

Because muscle ATP and PCr levels at rest are similar in children/adolescents and adults, it appears, from a practical viewpoint, that the capacity for physical activity of young individuals is not impaired as long as the duration of exercise does not exceed 10 to 15 seconds. Thus, sports such as short distance running and swimming, jumping, shooting, etc., are easily undertaken by young athletes.

Conversely, it seems that preadolescents may have some difficulty in maintaining high intensity activities of durations ranging from 15 seconds to 1 to 2 minutes. Indeed, energy delivery from anaerobic metabolism appears to be limited because of immature glycolytic capacity and, possibly, by reduced sympathetic nervous activity. For these reasons, physical activities such as middle distance running or swimming must be carefully and progressively introduced in young athletes to allow for adaptation.

During recovery from intense exercise, however, it appears that children and adolescents exhibit lower blood lactate and H^+ levels than adults.[61,62] Consequently, young athletes may need shorter rest periods than those commonly required by adults undertaking high-intensity interval training.

3.2 Aerobic Metabolism

3.2.1 Glycogen Content and Glycogen Depletion

It is well known that activity lasting more than 1 hour and with an intensity equating to around 70% of maximal oxygen uptake ($\dot{V}O_{2max}$) or more is limited by carbohydrate stores (i.e. muscle glycogen content).[63] Because muscle glycogen levels in children may be lower than in adults,[37,40] children may deplete these glycogen stores more rapidly than adults.

Very few data on glycogen depletion rates during exercise in children and adolescents are available. This lack of information is attributable to ethical concerns over the taking of muscle biopsies from young people. In the study of Eriksson et al.,[40] 8 healthy 11- to 13-year-old boys performed a maximal ergocycle test. Muscle biopsies were obtained from the vastus lateralis of the quadriceps femoris at each workload and at peak exercise. Muscle glycogen content decreased from 54 mmol/kg (at rest) wet weight to 34 mmol/kg of wet muscle glucose units at exhaustion. According to these authors, glycogen depletion rates in children did not differ from those in adults. However, in a later review, Eriksson[59] speculated that the breakdown of glycogen may be lower in children than in preadolescents. This hypothesis is supported by muscle lactate data obtained under conditions of submaximal and maximal exercise that show increases in levels with age. It is difficult to conclude at this time that glycogen depletion rates are age-dependent.

3.2.2 Mitochondrial to Myofibrillar Volume Ratio

Bell et al.[26] reported similar mitochondrial to myofibrillar volume ratios in prepubertal and adult muscle tissue. This suggests that the large increases in total contractile proteins that accompany growth and maturation are paralleled by increases in number and size of mitochondria. Thus, the metabolic potential of children and adolescents is not limited by mitochondrial volume during growth.

3.2.3 Respiratory Exchange Ratio Changes

Evaluation of substrate utilisation by RER measurements requires steady-state exercise (in ventilation and acid-base balance) which is not always easy to obtain. Thus, only few data are available concerning RER changes in children and adolescents as compared with adults during prolonged exercise.

Martinez and Haymes[64] reported that active or very active prepubertal girls (8 to 10 years) had lower RER values than active or very active women (20 to 32 years) during a 30-minute run at 70% $\dot{V}O_{2max}$ after a 12-hour fast. These authors concluded that there are differences in substrate utilisation between girls and women during treadmill exercise of moderate intensity. Because RER values were smaller in children, Martinez and Haymes[64] suggested that girls rely more than women on fat utilisation during this type of exercise. In contrast, when exercise was sustained at the same absolute intensity, no significant differences in RER were observed. Other studies have reported significantly lower RER values in boys than in adolescents and adult males during submaximal exercise at the same relative[65,66] and absolute intensities.[67-70]

However, contradictory results have been reported. Rowland and Rimany[71] and Macek et al.[72] did not show lower RER in young individuals than in adults. Thus, Rowland and Rimany[71] reported no RER differences during sustained steady cycling (40 minutes) at 63% $\dot{V}O_{2max}$ between girls aged 9 to 13 years and women aged 20 to 31 years. Similarly, Macek et al.,[72] obtained similar RER values in prepubertal boys and in men cycling at 60% $\dot{V}O_{2max}$ for 60 minutes.

RER is usually used to determine substrate utilisation during exercise.[10] Lower RER values indicate greater fat than carbohydrate utilisation during exercise. Thus, results recorded in young individuals suggest greater fat oxidation than in adults. However, data are both conflicting and sparse, and further research is required to clarify this issue fully.

3.2.4 Blood Measurements

Plasma Volume Changes

Increases or decreases in plasma volume during exercise modify metabolic and hormonal activities in blood. Thus, in the assessment of differences between young individuals and adults in blood levels of various metabolites, it is important to measure plasma volume changes during exercise. Usually, plasma volume changes are determined from changes in blood haematocrit and haemoglobin levels.[73,74]

At rest and following maximal exercise, Fahey et al.[75] reported that 27 males ranging in age from 5 to 18 years showed similar haemoglobin and haematocrit levels. Thus, haematological changes induced by exercise were not affected by stage of puberty.

As in adults,[76-78] Delamarche et al.[79] found that a 60-minute cycle exercise at 60% $\dot{V}O_{2max}$ induced moderate haemoconcentration in boys aged 8.5 to 11 years. However, results have not been consistent. Indeed, haemodilution has been observed in young prepubertal boys during treadmill or cycle exercise at 40% $\dot{V}O_{2max}$, while a 6% haemoconcentration was reported at 60% $\dot{V}O_{2max}$.[72] Reduced sweat loss[80,81] and movement of water or osmolar particles between extra- and intravascular beds may account for this particular adjustment in children.[79] These results indicate that plasma volume changes must be measured to correct differences in plasma levels between young individuals and adults. Indeed, failure to consider plasma volume changes may lead to erroneous conclusions with respect to age-related differences. For example, in the study of Martinez and Haymes,[64] blood glucose levels were determined at rest and after a 30-minute run in prepubertal girls and young adult women. This study showed that, if plasma volume changes were not taken into consideration, blood glucose levels appeared higher in women than in girls.

Metabolic Responses to Long Term Exercise

Blood lactate. It is recognised that children produce less lactate than adults during similar relative exercise (section 3.1.4).

Exercise intensity eliciting a blood lactate level of 4 mmol/L during a steady-state incremental exercise protocol has been described by Sjodin et al.,[82] and this concept has been referred to as ‘onset of blood lactate accumulation’ (OBLA). In adults, OBLA has been shown to correlate well with endurance performance[83] and to be sensitive to training-induced improvement in endurance capacity.[84] OBLA in prepubertal and teenage boys corresponds to a percentage of $\dot{V}O_{2max}$ higher than that in adults.[85-88] Thus, the blood lactate level of 4 mmol/L determined in 11-year-old boys during an incremental exercise test was obtained with exercise intensity of approximately 80% of $\dot{V}O_{2max}$[86] compared with the usual 70% $\dot{V}O_{2max}$ reported in adults.[89] For this reason, it may be difficult to use OBLA in young individuals to monitor and predict exercise endurance.[85-87]

Plasma glucose. Several studies emphasised that glucose tolerance is reduced under resting conditions during puberty in healthy children.[90,91] Indeed, a decrease in insulin sensitivity at rest has been demonstrated from the onset of the peripubertal period.[92] Exercise is associated with an increase in glucose uptake by the working muscle. Thus, there may be age-related differences in plasma glucose levels during prolonged exercise. Plasma glucose level during exercise represents the balance between muscle glucose uptake and hepatic glucose production through glycogenolysis and gluconeogenesis. Thus, differences in plasma glucose levels during exercise in children as compared with adults may be associated with muscle glucose uptake or liver production pathways. However, no clear picture of the plasma glucose response to exercise in children can be drawn on the basis of current data.

Studies suggest that children, adolescents and adults have similar plasma glucose levels during prolonged exercise of moderate intensity.[64,93-95] Oseid and Hermansen[93] carried out a 2-year longitudinal study in 23 prepubertal boys of mean age 10.5 years. These children underwent an 1-hour treadmill test performed at 70% $\dot{V}O_{2max}$ 1.5 hours after a light breakfast of 2 small sandwiches and a glass of milk. In the first year, no change in plasma glucose levels before and after work was noted (resting level 4.87 mmol/L was compared with 5.08 mmol/L 5 minutes after end of exercise). A year later, a slight but significant increase of 12% in glycaemia (from 4.7 to 5.4 mmol/L) was observed between rest and the end of the exercise test. These results were similar to those typically reported in adults under the same conditions.

Wirth et al.[95] reported an investigation carried out in 41 swimmers of both genders (aged 8 to 18 years) who were divided into 3 groups according to maturity. After an overnight fast, the participants exercised for 15 minutes at 70% $\dot{V}O_{2max}$ on a cycle ergometer. Mean plasma glucose levels at rest were 4.79, 4.56 and 4.60 mmol/L in prepubertal, pubertal and postpubertal children, respectively. Levels reached 5.22, 4.83 and 4.72 mmol/L, respectively, by the end of exercise. Prepubertal children had a slight increase in glycaemia induced by exercise ($p < 0.05$), but no significant changes were observed in pubertal and postpubertal individuals.

Eriksson et al.[94] examined 4 healthy men aged 23 to 34 years and 4 healthy boys aged 12 to 13 years after a standardised breakfast of 100 kcal. Exercise consisted of 1 hour's work on a bicycle ergometer at a mean load of 63% (range 55 to 73%) of their $\dot{V}O_{2max}$. Plasma glucose levels tended to decrease in both groups. No age-related glycaemic difference was observed during exercise.

Lastly, Martinez and Haymes[64] reported no differences in plasma glucose levels between prepubertal girls aged 8 to 10 years and women aged 20 to 32 years during 30 minutes' treadmill running at 70% $\dot{V}O_{2max}$ after a 12-hour fast.

From these results, no clear age-dependent plasma glucose differences are apparent during exercise. Nevertheless, the limited information and protocol variations (e.g. age, gender and number of participants, intensity and duration of exercise, training level) do not permit any conclusions on this topic. Furthermore, few studies indicated that children might experience difficulty in maintaining a constant blood glucose level at the onset of moderate exercise.[79,94,96]

Delamarche et al.[79,96] reported a significant decrease in plasma glucose levels in 10 boys and 7 girls aged 8.5 to 11 years after 15 minutes of a 60-minute cycling session at about 60% $\dot{V}O_{2max}$ after a standardised breakfast (50 kcal/kg, carbohydrates 50%, lipids 35%, proteins 15%). These changes differed from adult male responses. Indeed, Hoelzer et al.[97] reported that blood glucose levels in men remained constant during the first 15 minutes of exercise at 60% $\dot{V}O_{2max}$. According to Delamarche et al.,[79] children cannot maintain steady blood glucose levels because of immaturity of the glucoregulatory system. This lack of regulation induces a transient and slight hypoglycaemia which is compensated for after several minutes of exercise. Similar results were described by Eriksson et al.,[94] who showed a downward trend in blood glucose levels in prepubertal boys at the onset of similar levels of exercise (60% $\dot{V}O_{2max}$).

Thus, despite a transient decrease in the plasma glucose level which sometimes occurs in young individuals at the beginning of moderate exercise, data indicate that children, like adolescents, are well adapted to regulate glycaemia during prolonged exercise of moderate intensity.

In a further study, Boisseau et al.[98] investigated the effects of a glucose load in boys aged 8 to 11 years and men aged 21 to 23 years during a 30-minute ergocycle test performed at 60% $\dot{V}O_{2max}$. Their results showed that oral glucose ingestion (0.5 g/kg) at the beginning of the third minute of exercise induced higher plasma glucose levels in boys. Similar results were reported in prepubertal girls as compared with women subjected to the same protocol.[99] It may be speculated that plasma glucose uptake after a glucose load is altered in children during exercise. This phenomenon could be explained partly by reduced insulin sensitivity at rest during the peripubertal period.[92] This hypothesis is supported by data obtained during exercise that show higher glucose : insulin ratios in children than in adults.[98,99]

Plasma free fatty acids and glycerol. Increases in free fatty acids (FFA) and glycerol in blood are indicators of fat mobilisation from peripheral stores. An increase in lipolysis and FFA oxidation may be induced by GH secretion during the peripubertal period in exercising children and adolescents.[100]

Martinez and Haymes[64] reported that FFA and glycerol concentrations increased significantly during treadmill exercise at 70% $\dot{V}O_{2max}$ in prepubertal girls and women. These increases were not age-dependent. Several studies have shown similar exercise-induced responses in blood FFA and glycerol levels in children and adults.[94,95,101] For example, Eriksson et al.[94] indicated similar plasma FFA and glycerol levels in four 12- to 13-year-old boys and four 23-year-old men during cycling at 55 to 73% $\dot{V}O_{2max}$. Moreover, Lehmann et al.[101] reported no plasma FFA and glycerol differences in 8 boys aged 12.8 ± 0.8 years and 7 adults aged 27.8 ± 2.9 years during a graded treadmill exercise test. Wirth et al.[95] reported similar results when comparing 41 swimmers of both genders aged 8 to 18 years during 15 minutes of bicycle ergometer exercise performed at 70% $\dot{V}O_{2max}$.

However, other studies showed greater fat utilisation in children than in adults during long term moderate exercise. Delamarche et al.[79] measured plasma FFA and glycerol levels in prepubertal boys during 1-hour exercise on a cycle ergometer at 60% $\dot{V}O_{2max}$. They estimated the FFA turnover (FFAt) using the equation proposed by Costill[102] (FFAt = 3 Δ glycerol – FFA). FFA turnover per minute and per litre of $\dot{V}O_2$ was greater in boys than in adults during exercise of similar duration and relative intensity.[97] According to Delamarche et al.,[79] prepubertal boys rely on fat more than adults for energy supplies during exercise. Using a similar protocol in 17 prepubertal children of both genders, Delamarche et al.[96] showed similar results with no gender differences. Berg et al.[103] established the relationship between postexercise serum FFA and glycerol levels in male as compared with children and adolescents after intensive endurance exertion. They reported reduced FFA : glycerol ratios during exercise in children, which implies improved FFA utilisation relative to male adults. These authors assumed greater FFA oxidation in children than in adults, since the enzymatic capacity of muscle tissue is a precondition for the enhanced breakdown of compounds based on acetylcoenzyme A.[104]

In contrast, Martinez and Haymes[64] showed similar FFA : glycerol ratios in girls and women during exercise. Despite this result, these authors concluded on the basis of RER findings that girls rely more on fat utilisation and less on carbohydrate metabolism than do women during exercise of moderately heavy intensity. After a glucose load given at the beginning of a moderate prolonged exercise, Boisseau et al.[99] reported greater plasma FFA levels in girls with a mean age of 9.7 years than in women with a mean age of 21.5 years. The authors speculated that children are more able than adults to use fats during exercise. As insulin inhibits fat utilisation, enhanced lipolysis may be associated with reduced insulin sensitivity observed in children and adolescents as compared with adults at rest[92] and during exercise.[98,99]

From the available data, it may be postulated that children rely more on fatty acids for energy provision during exercise than do adults. This greater fat utilisation may compensate for reduced glycolytic capacity and may allow children to maintain appropriate plasma glucose levels during exercise.

Hormonal Responses to Long Term Exercise

During the peripubertal period, alterations in hormone levels may influence the control of metabolism both at the level of regulation of endocrine function and at the level of hormone receptors.

Insulin. During exercise, insulin and muscular activity act synergistically to increase glucose uptake over and above the rates produced by each factor independently.[105] Indeed, contractile activity and insulin both induce the translocation of specific glucose transporters (GLUT4) into the plasma membrane.[106,107] Long term activity induces greater insulin sensitivity.[108]

In adults, plasma insulin levels decrease during prolonged moderate exercise (75% $\dot{V}O_{2max}$).[109] In light of decreased insulin sensitivity in the peripubertal period[92] and enhanced glucose-induced insulin secretion during puberty,[110] specific responses would not be surprising in children and adolescents during physical activity.

Despite this observation, lack of data makes the characterisation of age-related changes in plasma insulin levels during exercise impossible.[94,93,96,98,99] Only one study (Wirth et al.[95]) indicates a pattern related to maturity.

Eriksson et al.[94] investigated men aged 23 to 34 years and boys aged 12 to 13 years who underwent 1-hour ergocycle exercise at ≈63% $\dot{V}O_{2max}$. Plasma insulin levels decreased during exercise but there was no significant difference between the 2 groups.

Oseid and Hermansen[93] reported plasma insulin levels in 23 prepubertal boys during a treadmill test performed at approximately 70% $\dot{V}O_{2max}$. A decrease in plasma insulin levels was shown in 17 of the boys. The greatest reduction was observed during the first 20 minutes of exercise, which accounted for approximately 70% of the total. Plasma insulin levels did not differ from those frequently reported in adults, however.

Similarly, Delamarche et al.[96] described a continuous decrease in plasma insulin levels in 10 boys and 7 girls (pubertal stage 1) during a 60-minute period of cycle exercise at 60% $\dot{V}O_{2max}$.

After an oral glucose load taken in the first few minutes of a prolonged period of moderate exercise (30 minutes, 60% $\dot{V}O_{2max}$), Boisseau et al.[98,99] indicated stable plasma insulin levels in prepubertal children of both genders aged 8 to 11 years. The same result was reported in men and women aged 21 to 23 years. There was no age effect.

However, Wirth et al.[95] reported maturity-related differences in pre-, circum- and postpubertal boys and girls. Blood insulin levels were determined during 15 minutes' exercise at 70% $\dot{V}O_{2max}$ on a cycle ergometer. Insulin levels increased during exercise in the prepubertal children, remained constant in pubertal individuals and decreased in the postpubertal group, with blood glucose levels being similar in the 3 groups. These results suggest reduced insulin sensitivity during the peripubertal period, which is usually compensated for by greater insulin secretion.[110] Nevertheless, Wirth et al.[95] speculated that these specific insulin responses are caused by age-related differences in catecholamine levels and/or receptor sensitivities.

Catecholamines. Glycogenolysis and lipolysis are inhibited by insulin. In contrast, these processes are stimulated by catecholamines that oppose the action of insulin.[111] The well known wide inter-individual variability of plasma catecholamine levels makes the comparison of children, adolescents and adults difficult. Few data are available on this topic and results are predominantly inconsistent.

Maturity-related differences in sympathoadrenergic activity are sometimes observed, but these findings remain difficult to interpret. No clear answers to questions surrounding age-related catecholamine responses can be formulated, and more research must be carried out to shed light on this topic.

Delamarche et al.[79] investigated plasma adrenaline and noradrenaline levels in 10 prepubertal boys aged 8.5 to 11 years during 1 hour's cycling at 60% $\dot{V}O_{2max}$. Relative to resting values, there was a 2.4-fold increase in noradrenaline levels during the first 15 minutes of exercise. A rapid decrease to basal levels was observed during recovery. In contrast, a progressive and linear increase in levels of adrenaline was recorded throughout exercise. The maximal peak (1.6 times the sitting value at rest) was recorded at the 60th minute of exercise. During a similar investigation in adults, Hoelzer et al.[97] showed maximal peaks for adrenaline and noradrena line of 2.7 and 3 times resting values, respectively. Thus, adrenaline peaks appear higher in adults, whereas noradrenaline peaks appear not to be affected by age.

Lehmann et al.[101] investigated 11 endurance-trained boys aged 12.8 ± 1.2 years and 12 adolescents aged 17.7 ± 0.5 years during a 10 000m race. Pre-exercise sympathoadrenergic activity expressed as free adrenaline and noradrenaline excretion in urine were similar for the 2 groups. The mean average excretion rate during the 10 000m race increased 4- to 5-fold and did not show any bodyweight-related differences between young boys and adolescents. However, Lehmann et al.[112] reported that sympathetic neurological activity at maximal exercise may be lower in children than in adults. These authors found 30% lower peak noradrenaline levels during progressive treadmill runs in 12-year-old boys than in young male adults.[112] These results are comparable to those reported in adults by Fleg et al.[113] and Lehmann and Keul[114] who observed a close relationship between plasma noradrenaline levels at $\dot{V}O_{2max}$ and the age of the individual.

However, maturity-related differences in catecholamine responses during maximal or submaximal exercise are not universally recognised.[115] Rowland et al.[115] measured plasma noradrenaline at rest, during 2 submaximal cycle exercise sessions (different intensities) and during maximal exercise in 11 boys aged 10 to 12 years and 11 men aged 24 to 35 years. No statistical differences were reported for plasma noradrenaline levels at rest or during the exercise tests. These findings argue in favour of the absence of differences in sympathic drive between children and adults. Nevertheless, noradrenaline levels during maximal exercise reported in boys and men by Rowland et al.[115] were still about 10% lower in children, and statistical significance may not have achieved because of the extremely wide variation between individuals in this study. When this point is considered, the data do not differ markedly from the results of Lehmann et al.[112]

GH and endorphins. In adults, GH levels are known to increase during exercise, but the physiological action of this hormone is not completely understood. GH may play a central role in the regulation of the utilisation and storage of energy, and appears to influence in particular fat mobilisation from adipose tissue.[111] GH secretion is pulsatile in nature, and peak values are difficult to interpret during exercise events.[93]

At a certain time in a child's life, there is an increase in the amplitude of GnRH pulses, which triggers a cascade of events including increases in the amplitude of FSH and LH pulses, followed by marked increases in gonadal sex steroid output, which in turn increases secretion of GH and IGF-1. For this reason, growing individuals might exhibit characteristic or excessive GH response patterns during exercise. Surprisingly few studies have reported plasma GH levels in children and adolescents during exercise.

Eriksson et al.[94] showed the effects of repeated prolonged exercise on plasma GH levels in 13-year-old boys and in adults aged 23 to 24 years. Two identical exercise bouts were performed successively, 3 hours apart. The exercise consisted of 1 hour on a cycle ergometer at a mean 63% $\dot{V}O_{2max}$ (range 55 to 73%). No typical pattern was found for GH increase during exercise, and peak levels were observed differing intervals from the beginning of exercise in each individual. However, responses to the first exercise session were significantly greater than those noted in the second. No differences were found between adults and boys. Marin et al.[116] reported that the peak GH response to exercise increased significantly with pubertal stage ($r = 0.57$, $p < 0.0001$), however. Exercise consisted of 15 minutes on a treadmill at a speed corresponding to a heart rate of between 170 and 190 beats/min.

Wirth et al.[95] found that plasma GH responses during exercise differ with respect to level of maturity in both genders. In their study, 41 swimmers (girls and boys aged 8 to 18 years) were investigated during a submaximal bicycle ergometer exercise at 70% $\dot{V}O_{2max}$. At the end of the exercise, the plasma GH level was almost 3 times higher in postpubertal than in prepubertal individuals. Plasma GH levels were also higher in pubertal than in prepubertal swimmers. No gender differences were observed.

The same result was reported by Bouix et al.[117] during a 15-minute session on a cycloergometer, with heart rate maintained at 90% of the theoretical maximal value. These authors reported that exercise-induced plasma GH levels were higher in pubertal than in prepubertal boys and girls. Plasma β-endorphin values were also determined during this study. The findings indicated comparable exercise-induced increases in plasma β-endorphin levels in pubertal and prepubertal children. The similarity of the β-endorphin responses to exercise between prepubertal and pubertal children does not therefore support the controversial hypothesis that plasma β-endorphin modulates the GH response to exercise.[117]

Wirth et al.[95] postulated that age-related differences in plasma GH responses during exercise could be explained by differences in sex hormone levels. This hypothesis has been supported in part by Marin et al.,[116] who reported that estrogen administration in 84 healthy children (41 girls and 43 boys) significantly increased the peak GH response to exercise.

Sex hormones. Few investigations have been performed on sex hormone levels in active children and adolescents. Currently, most of the data on the influence of physical activity on the reproductive system in peripubertal children are extrapolated from information reported in studies in adults and animals. These extrapolations have to be interpreted with caution because the function of the reproductive system differs between peripubertal individuals and adults. Indeed, the transition from the childhood to adult state of the reproductive system is spread over a period of several years.[118] Consequently, during exercise, specific sex hormone responses should be observed in young individuals as compared with adults.

Some studies have provided information on sex hormone responses to exercise with respect to sexual maturation. During an ergocycle test of 20 minutes' duration at 60% $\dot{V}O_{2max}$, the dependence of exercise-induced hormone responses on sexual maturation was tested over a 3-year period in 34 girls aged 11 to 12 years at the start of the study.[119] After exercise, β-estradiol responses were highest in stage V. A significant increase in progesterone and testosterone responses appeared in stages IV and V, respectively.

The same longitudinal protocol was applied in boys.[120] Seventeen healthy boys aged 10 years and over were investigated. A significant increase in testosterone response appeared after reaching stage III. Thus, these authors postulated that, in girls and boys, advanced sexual maturation is associated with enhanced sex hormone responses.

Fahey et al.[75] compared 27 males in different stages of pubertal development at rest and following maximal exercise. Resting levels of serum testosterone increased with pubertal stage, but no differences were observed at the end of maximal exercise. These results do not support the hypothesis of a critical pubertal stage which could induce a higher serum testosterone response to exercise. However, taking into account an important interindividual variability of serum testosterone levels during childhood and adolescence, the longitudinal approach seems more appropriate for the establishment of specific sex hormone responses at different stages of puberty.

It was observed that training in young individuals may modify sex hormone responses at rest and during exercise. Cacciari et al.[121] reported the plasma levels of several hormones [notably cortisol, dehydroepiandrosterone sulphate (DHEA-S), testosterone and GH] in 175 boys aged 10 to 16 years (trained and untrained) and classified as prepubertal and pubertal individuals (aged 10 to 11 years, 12 to 13 years and 14 to 16 years both chronologically and by bone age groups). Their results show that the plasma level of DHEA-S was significantly higher in trained children. This enhanced plasma DHEA-S concentration was related to higher levels of testosterone, GH and cortisol. These authors concluded that adrenal hyperactivity may be chiefly responsible for the earlier onset of pubertal growth and maturity in exercising males.

Mero et al.[122] described serum testosterone levels under conditions of rest before, during and after a year of long distance running, sprint running, weightlifting and tennis training in boys aged 10 to 12 years. Compared with untrained boys, the initial plasma testosterone concentration was almost 3 times higher in these individuals. Furthermore, the mean testosterone level was approximately doubled after a year of training. These results suggest that endurance training may alter gonadal hormone production in young athletes. Accordingly, Rowland et al.[123] reported serum levels of total and free testosterone in 15 adolescent male cross-country runners (mean age 16.1 years) during the course of a competitive season. No significant changes were observed in either total or free testosterone levels during the 8-week period of training. In this study, the age of the athletes may have accounted for the absence of enhanced testosterone levels.

3.2.5 Conclusions and Practical Considerations

The available data on metabolic and hormone responses to exercise in children and adolescents are sometimes conflicting and limited by the age, gender and training status of the individuals. Despite the lack of precise information relevant to age, children and adolescents are well adapted for long term physical activity. The major differences when comparing young individuals and adults who perform prolonged exercise are restricted to 2 observations:

(i) lower muscle glycogen stores in children, which leads to an earlier depletion than is seen in adults

(ii) a potentially greater utilisation of fat stores in young individuals.

The latter hypothesis is supported by indirect evidence such as lower RER, enhanced plasma FFA mobilisation, greater increases in plasma glycerol levels, decreased insulin sensitivity during the peripubertal period and increased GH secretion at rest and during exercise.

Regular endurance exercise is beneficial as it prevents obesity, reduces the risk of cardiovascular disease and offers enhanced wellbeing during childhood. For these reasons, children and adolescents must be encouraged to practice regular endurance exercise adapted to their age, their level of sexual maturation and their emotional wishes.

4. Conclusion

Humans are born to be physically active, both as children and adults, although children are generally keener than adults to engage in physical activity. Ethical and methodological considerations limit invasive research in children (section 2). Nevertheless, the limited data available reveal that several activities (such as jumping, sprinting, cross-country running, long-distance skating, etc.) may induce specific metabolic and hormonal responses that are age-dependent. As compared with adults, these differences could be related to 2 main factors. First, lower muscle strength, related to fibre growth, confers lower anaerobic capacity in children (section 3.1). Second, specific metabolic and hormone adaptations favour the utilisation of fat during prolonged exercise (section 3.2). In addition, multiple factors such as sexual maturation, gender, training level, type, duration and intensity of exercise also play a part. Despite these observations, it is not possible to give a clear picture of the specific mechanisms involved when comparing young individuals and adults. However, it appears that children and adolescents are well adapted to prolonged exercise and that they need specific programmes to improve their performance.

References

1. Lac G, Duché P, Falgairette G, et al. Adrenal androgen profiles in saliva throughout puberty in both sexes. In: Coudert J, Van Praagh E, editors. Pediatric work physiology. XVI. Children and exercise. Paris: Masson, 1992: 221-3
2. Sizonenko PC, Paunier L. Hormonal changes in puberty III: correlation of plasma dehydroepiandrosterone, testosterone, FSH and LH with stages of puberty and bone age in normal boys and girls and in patients with Addison's disease or hypogonadism or with premature or late adrenarche. J Clin Endocrinol Metab 1975; 41 (5): 894-904
3. Martha PM, Gorman KM, Blizzard RM, et al. Endogenous growth hormone secretion and clearance rates in normal boys, as determined by deconvolution analysis: relationship to age pubertal status and body mass. J Clin Endocrinol Metab 1992; 74: 336-44
4. Bar-Or O. Pediatric sports medicine for the practitioner. New York: Springer Verlag, 1983
5. Rowland TW. Developmental aspects of physiological function relating to aerobic exercise in children. Sports Med 1990; 10 (4): 255-66
6. Armstrong N, Welsman JR. Developmental aspects of aerobic fitness in children and adolescents. In: Holloszy JO, editor. Exercise and sport sciences reviews. Baltimore (MD): Williams & Wilkins, 1994: 435-76
7. Keizer H, Poortman J, Bunnik GS. Influence of physical exercise on sex-hormone metabolism. J Appl Physiol 1980; 48 (5): 765-9
8. Wilkerson JE, Horvath SM, Gutin B. Plasma testosterone during treadmill running. J Appl Physiol 1980; 49 (2): 249-53
9. Lemon PWR, Nagle FJ. Effect of exercise on protein and amino acid metabolism. Med Sci Sports Exerc 1981; 13: 141-9
10. Wilmore JH, Costill DL. Physiology of sport and exercise. 2nd ed. Champaign (IL): Human Kinetics, 1999
11. Sapega AA, Sokolow DP, Graham TJ, et al. Phosphorus nuclear magnetic resonance: a non-invasive technique for the study of muscle bioenergetics during exercise. Med Sci Sports Exerc 1987; 19 (4): 410-20
12. Zanconato S, Buchthal S, Barstow TJ, et al. ^{31}P-magnetic resonance spectroscopy of leg muscle metabolism during exercise in children and adults. J Appl Physiol 1993 May; 74 (5): 2214-8
13. Kuno S, Miyamaru M, Itai J. Muscle energetics during exercise of elite sprinter in children by ^{31}PNMR. Med Sci Sports Exerc 1993; 25 Suppl. 5: S175
14. Kuno S, Takahashi H, Fujimoto K, et al. Muscle metabolism during exercise using phosphorus-31 nuclear magnetic resonance spectroscopy in adolescents. Eur J Appl Physiol Occup Physiol 1995; 70 (4): 301-4
15. Petersen SR, Gaul CA, Stanton NM, et al. Skeletal muscle metabolism during short-term, high-intensity exercise in prepubertal and pubertal girls. J Appl Physiol 1999, 87 (6) : 2151-6
16. Cooper DM. Development of the oxygen transport system in normal children. In: Bar-Or O, editor. Advances in pediatric sport sciences: biological issues. 3. Champaign (IL): Human Kinetics, 1989: 67-100
17. Williams CA. Children's and adolescents' anaerobic performance during cycle ergometry. Sports Med 1997; 24: 227-40
18. Falize J. Le développement moteur de l'enfant: perspectives d'application. In: De Potter JC, Levarlet H, editors. Développement moteur et éducation. Brussels: Presses Universitaires de Bruxelles, 1984: 47-66
19. Falgairette G, Bedu M, Fellmann N, et al. Bioenergetic profile in 144 boys age from 6 to 15 years with special reference to sexual maturation. Eur J Appl Physiol Occup Physiol 1991; 62 (3): 151-6
20. Duché P, Falgairette G, Bedu M, et al. Longitudinal approach of bioenergetic profile in boys before and during puberty. In: Coudert J, Van Praagh E, editors. Pediatric work physiology. XVI. Children and exercise. Paris: Masson, 1992: 43-5
21. Mercier B, Mercier J, Granier P, et al. Maximal anaerobic power: relationship to anthropometric characteristics during growth. Int J Sports Med 1992; 13: 21-6
22. Allen RE, Merkel RA, Young RB. Cellular aspects of muscle growth: myogenic cell proliferation. J Anim Sci 1979; 49 (1): 115-27
23. Colling-Saltin AS. Enzyme histochemistry on skeletal muscle of the human foetus. J Neurol Sci 1978; 39: 169-85
24. Elder GCB, Kakukas BA. Histochemical and contractile property changes during human muscle development. Muscle Nerve 1993; 16 (11): 1246-53
25. Vogler C, Bove KE. Morphology of skeletal muscle in children. Arch Pathol Lab Med 1985; 109: 238-42
26. Bell RD, MacDougall JD, Billeter R, et al. Muscle fibres types and morphometric analysis of skeletal muscle in six years old children. Med Sci Sports Exerc 1980; 12 (1): 28-31
27. Fournier M, Ricci J, Taylor AW, et al. Skeletal muscle adaptation in adolescent boys: sprint and endurance training and detraining. Med Sci Sports Exerc 1982; 14 (6): 453-6
28. Mero A, Jaakkola L, Komi PV. Relationships between muscle characteristics and physical performance capacity in trained athletic boys. J Sports Sci 1991; 9: 161-71
29. Eriksson O, Saltin B. Muscle metabolism during exercise in boys aged 11 to 16 years compared to adults. Acta Paediatr Belg 1974; 28 Suppl.: 257-65
30. Gollnick PD, Armstrong RB, Saubert CW, et al. Enzyme activity and fiber composition in skeletal muscle of untrained and trained men. J Appl Physiol 1972; 33 (3): 312-9
31. Hedberg G, Jansson E. Skeletal muscle fibre distribution, capacity and interest in different physical activities among students in high school [Swedish]. Pedagogiska Rapporter 1976: 54
32. du Plessis M, Smit P, du Plessis L, et al. The composition of muscle fibers in a group of adolescents. In: Binkhorst RA, Kemper HCG, Saris WHH, editors. Children and exercise. XI. Champaign (IL): Human Kinetics, 1985: 323-8
33. Houmard JA, Smith R, Jendrasiak GL. Relationship between MRI relaxation time and muscle fibre composition. J Appl Physiol 1995; 78: 807-9
34. Parkkola R, Alanen A, Klimo H, et al. MR relaxation times and fiber type predominance of the psoas and multifidus muscle. Acta Radiol 1993; 34: 16-9
35. Kuno S, Katsuta S, Inouye T, et al. Relationship between MR relaxation time and muscle fiber composition. Radiology 1988; 169: 657-68
36. Colling-Saltin AS. Some quantitative biochemical evaluation of developing skeletal muscle in the human foetus. J Neurol Sci 1978; 39: 187-98

37. Eriksson BO, Karlsson J, Saltin B. Muscle metabolites during exercise in pubertal boys. Acta Paediatr Scand 1971; 217 Suppl.: 154-7
38. Bougnères PF. Rôle des substrats lipidiques dans l'adaptation au jeune du nouveau-né et de l'enfant. J Annu Diabetol Hotel Dieu 1988: 303-14
39. Schiffrin A, Colle E. Hypoglycemia. In: Collin R, Ducharme JR, editors. Pediatric endocrinology. New-York: Raven Press, 1989: 649-73
40. Eriksson BO, Gollnick PD, Saltin B. Muscle metabolism and enzyme activities after training in boys 11-13 years old. Acta Physiol Scand 1973; 87: 485-97
41. Haralambie G. Enzyme activities in skeletal muscle of 13-15 years old adolescents. Bull Eur Physiopathol Respir 1982; 18 (1): 65-74
42. Mero A. Measurement of aerobic and anaerobic performance capacity in young boys. In: Coudert J, Van Praagh E, editors. Pediatric work physiology. XVI. Children and exercise. Paris: Masson, 1992: 19-21
43. Eriksson BO. Physical training, oxygen supply and muscle metabolism in 11-13 year old boys. Acta Physiol Scand 1972; 384 Suppl.: 1-48
44. Berg A, Kim SS, Keul J. Skeletal muscle enzyme activities in healthy young subjects. Int J Sports Med 1986; 4: 236-9
45. Falgairette G, Bedu M, Fellmann N, et al. Modifications of aerobic and anaerobic metabolism in active boys during puberty. In: Beunen G, Ghesquiere J, Reybrouk T, et al., editors. Children and exercise. IV. Stuttgart: Ferdinand Enke Verlag, 1990: 42-9
46. Rostein A, Dofan R, Bar-Or O, et al. Effect of training on anaerobic threshold, maximal aerobic power and anaerobic performance of preadolescent boys. Int J Sports Med 1986; 7 (5): 281-6
47. Rilling JK, Worthman CM, Campell BC, et al. Ratios of plasma and salivary testosterone throughout puberty: production versus bioavailability. Steroids 1996; 61 (6): 374-8
48. Crielaard JM, Pirnay F, Franchimont P. Croissance et exercice anaérobie lactique. In: Benezis C, Simeray J, Simon L, editors. L'enfant, l'adolescent et le sport, actualités en médecine du sport. Paris: Masson, 1986: 33-51
49. Von Diter H, Nowacki P, Simai E, et al. Das Verhalten des Säure-Basen-Haushalts nach erschöpfender Belastung bei untrainierten und tranierten Jungen und Mädchenim Vergleich zu Leistungssportlern. Sportarzt Sportmed 1977; 28: 45-8
50. Matejkova J, Kroprikova Z, Placheta Z. Changes in acid-base balance after maximal exercise. In: Placheta Z, editor. Youth and physical activity. Purkyne (Czechoslovakia): JE University, 1980: 191-9
51. Galbo H. Autonomic neuroendocrine responses to exercise. Scand J Sports Sci 1986; 8 (1): 3-17
52. Richter EA, Ruderman NB, Galbo H. Alpha and beta adrenergic effects on metabolism in contracting perfused muscle. Acta Physiol Scand 1982; 116: 215-22
53. Spriet L, Ren JM, Hultman E. Epinephrine infusion enhances muscle glycogenolysis during prolonged electrical stimulation. J Appl Physiol 1988; 64: 1439-44
54. Kindermann W, Schnabel A, Schmitt WM, et al. Catecholamines, growth hormone, cortisol, insulin and sex hormone in anaerobic and aerobic exercise. Eur J Appl Physiol 1982; 49: 389-99
55. Lehmann M, Keul J, Da Prada M, et al. Plasmakatecholamine, glucose, lactat und sauerstoffaufnahmefähikeit von kindern bei aeroben und anaeroben bealastungen. Dtsch Z fur Sportmed 1980; 8: 230-6
56. Pullinen T, Mero A, Mac Donald E, et al. Plasma catecholamine and serum testosterone responses to four units of resistance exercise in young and adult male athletes. Eur J Appl Physiol 1998; 77: 413-20
57. Boobis LH, Williams C, Wooton SA. Influence of sprint training on muscle metabolism during brief maximal exercise in man [abstract]. J Physiol (Lond) 1983; 342: 36-7
58. Nevill ME, Boobis LH, Brooks S, et al. Effect of training on muscle metabolism during treadmill sprinting. J Appl Physiol 1989; 67: 2376-82
59. Eriksson BO. Muscle metabolism in children: a review. Acta Paediatr Scand 1980; 283 Suppl.: 20-8
60. Thorstensson A, Sjodin B, Karlsson J. Enzyme activities and muscle strength after sprint training in man. Acta Physiol Scand 1975; 94: 313-8
61. Hebestreit H, Mimura k, Bar-Or O. Recovery of anaerobic muscle power following 30s supramaximal exercise: comparison between boys and men. J Appl Physiol 1993; 74: 2875-80
62. Hebestreit H, Meyer F, Htay-Htay G, et al. Plasma electrolyte and hydrogen ion levels following a 30s high intensity task: boys *vs* men [abstract no. 1183]. Med Sci Sports Exerc 1994; 26 Suppl.: S210
63. Astrand PO, Rodhal K. Textbook of work physiology. New York: McGraw-Hill, 1986
64. Martinez LR, Haymes EM. Substrate utilization during treadmill running in prepubertal girls and women. Med Sci Sports Exerc 1992; 24 (9): 975-83
65. Asano K, Hirakoba K. Respiratory and circulatory adaptation during prolonged exercise in 10- to 12-year-old children and in adults. In: Imaarinen J, Vaalimaki I, editors. Children and sport. Berlin: Springer-Verlag, 1984: 119-28
66. Eynde BV, Van Gerven D, Vienne D, et al. Endurance fitness and peak height velocity in Belgian boys. In: Oseid S, Caarlsen K, editors. Children and exercise. XIII. Champaign (IL): Human Kinetics, 1989: 19-27
67. Robinson S. Experimental studies of physical fitness in relation to age. Int Z Angew Physiol Einschl Arbeitphysiol 1938; 10: 251-323
68. Morse M, Schltz FW, Cassels E. Relation of age to physiological responses of the older boys (10-17 years) to exercise. J Appl Physiol 1949; 1: 638-709
69. Montoye H. Age and oxygen utilization during submaximal treadmill exercise in males. J Gerontol 1982; 37: 396-402
70. Rowland TW, Auchinachie JA, Keenan TJ, et al. Physiological responses to treadmill running in adult and prepubertal males. Int J Sports Med 1987; 8: 292-7
71. Rowland TW, Rimany TA. Physiological responses to prolonged exercise in premenarcheal and adult females. Pediatr Exerc Sci 1995; 7: 183-91
72. Macek M, Vavra J, Novosadova J. Prolonged exercise in prepubertal boys II. Changes in plasma volume and in some blood constituents. Eur J Appl Physiol 1976; 35: 299-303
73. Van Beaumont W. Evaluation of hemoconcentration from hematocrit measurements. J Appl Physiol 1972; 32: 712-3
74. Hill DB, Costill DL. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. J Appl Physiol 1974; 37: 299-303
75. Fahey TD, Del Valle-Zuris, Oehlsen G, et al. Pubertal stage differences in hormonal and hematological responses to maximal exercise in males. J Appl Physiol 1979; 46 (4): 823-7

76. Astrand PO, Saltin B. Plasma and red cell volume after prolonged severe exercise. J Appl Physiol 1964; 19: 829-32
77. Flandrois R. Conséquences de l'exercice de longue durée sur l'hydratation de l'organisme: réactions hormonales. In: Lacour JR, editor. Comptes-rendus du colloque de Saint-Etienne. Facteurs limitant l'endurance humaine. Paris: Masson, 1977: 38-42
78. Melin B, Eclache JP, Geelen G, et al. Plasma AVP, neurophysin, renin activity and aldosterone during submaximal exercise performed until exhaustion in trained and untrained men. Eur J Appl 1980; 44: 141-51
79. Delamarche P, Monnier M, Gratas-Delamarche A, et al. Glucose and free fatty acid utilization during prolonged exercise in prepubertal boys in relation to catecholamine responses. Eur J Appl Physiol 1992; 65: 66-72
80. Davies CTM. Thermal responses to exercise in children. Ergonomics 1981; 48: 55-61
81. Delamarche P, Bittel J, Lacour JR, et al. Thermoregulation at rest and during exercise in prepubertal boys. Eur J Appl Physiol 1990; 60: 436-40
82. Sjodin B, Schele R, Karlsson J, et al. The physiological background of onset blood lactate accumulation. International series on sports sciences. Vol. 12. Exercise and sport biology. Champaign (IL): Human Kinetics, 1982
83. Sjodin B, Jacobs I. Onset of blood lactate accumulation and marathon running performance. Int J Sport Med 1981; 2: 23-6
84. Sjodin B, Jacobs I, Svedenhag J. Changes in onset blood lactate accumulation and muscle enzymes after training at OBLA. Eur J Appl Physiol 1982; 49: 45-57
85. Mocellin R, Heusgen M, Korsten-Reck U. Maximal steady state blood lactate levels in 11-year-old boys. Eur J Pediatr 1990; 149: 771-3
86. Mocellin R, Heusgen M, Gildein HP. Anaerobic threshold and maximal steady-state blood lactate in prepubertal boys. Eur J Appl Physiol 1991; 62: 56-60
87. Williams JR, Armstrong N, Kirby BJ. The 4mM blood lactate level as an index of exercise performance in 11-13 year old children. J Sports Sci 1990; 8: 139-47
88. Tolfrey K, Armstrong N. Child-adult differences in whole blood lactate responses to incremental treadmill exercise. Br J Sports Med 1995; 29 (3): 196-9
89. Farrel PA, Wilmore JH, Coyle EF, et al. Plasma lactate accumulation and distance running performance. Med Sci Sports Exerc 1979; 11: 338-44
90. Amiel S, Sherwin R, Simonson D, et al. Impaired insulin action in puberty a contributing factor to poor glycemic control in adolescents with diabetes. N Engl J Med 1986; 315: 215-9
91. Bloch C, Clemons P, Sperling M. Puberty decreases insulin sensitivity. J Pediatr 1987; 110: 481-7
92. Cook J, Hoffman R, Stene M,et al. Effects of maturational stage on insulin sensitivity during puberty. J Clin Endocrinol Metab 1993; 77: 725-30
93. Oseid S, Hermansen L. Hormonal and metabolic changes during and after prolonged muscular work in prepubertal boys. Acta Paediatr Scand 1971; 217 Suppl.: 147-53
94. Eriksson BO, Persson B, Thorell JI. The effects of repeated prolonged exercise on plasma growth hormone, insulin, glucose, free fatty acids, glycerol, lactate and β-hydroxybutyric acid in 13-year old boys and in adults. Acta Paediatr Scand 1971; 217 Suppl.: 142-6
95. Wirth A, Trager E, Scheele K, et al. Cardiopulmonary adjustment and metabolic response to maximal and submaximal physical exercise of boys and girls at different stages of maturity. Eur J Appl Physiol 1978; 39: 229-40
96. Delamarche P, Gratas-Delamarche A, Monnier M, et al. Glucoregulation and hormonal changes during prolonged exercise in boys and girls. Eur J Appl Physiol 1994; 68: 3-8
97. Hoelzer DR, Dalsky GP, Clutter WE, et al. Glucoregulation during exercise: hypoglycaemia is prevented by redundant glucoregulatory systems, sympathochromaffin activation and changes in islet hormone secretion. J Clin Invest 1986; 77: 212-21
98. Boisseau N, Rannou F, Delamarche P, et al. Peripubertal period decreases insulin sensitivity and glucose utilisation during exercise. In: N Armstrong, J Welsman, editors. Children and exercise. XIX. London: E & FN Spon, 1997: 413-7
99. Boisseau N, Rannou F, Gratas-Delamarche A, et al. La tolérance au glucose à l'exercice prolongé chez la petite fille prépubère. Sci Sports 1999; 14: 173-9
100. Arslanian SA, Kalhan SC. Correlations between fatty acid and glucose metabolism. Potential explanation of insulin resistance of puberty. Diabetes 1994; 43: 908-14
101. Lehmann M, Keul J, Hesse A. Zur aeroben und anaeroben kapazität sowie catecholamine exkretion von kindern und jugendlichen während langdauernder submaximaler Körperarbeit. Eur J Appl Physiol 1982; 8: 135-45
102. Costill DL, Fink WJ, Getchell LH, et al. Lipid metabolism in skeletal muscle of endurance-trained males and females. J Appl Physiol 1979; 61: 1796-801
103. Berg A, Keul J, Huber G. Biochemische akutveranderunggen bei ausdauerbelastungen im kindes- und jugendalter. Monatsschr Kinderheilkd 1980; 128: 490-5
104. Haralambie G. Skeletal muscle enzymee activities in female subjects of various ages. Bull Eur Physiopathol Respir 1979; 15: 259-67
105. Nesher R, Karl IE, Kipnis DM. Dissociation of effects of insulin and contraction on glucose transport in rat epitrochlearis muscle. Am J Physiol 1985; 249 (3 Pt 1): C226-32
106. Holloszy JO, Hansen PA. Regulation of glucose transport into skeletal muscle. Rev Physiol Biochem Pharmacol 1996; 128: 99-193
107. Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. Annu Rev Med 1998; 49: 235-61
108. Wallberg-Henriksson H. Exercise and diabetes mellitus. Exerc Sports Sci Rev 1992; 20: 339-68
109. Richter EA, Galbo H, Sonne B, et al. Adrenal medullary control of muscular and hepatic glycogenolysis and of pancreatic hormonal secretion in exercising rats. Acta Physiol Scand 1980; 108: 235-42
110. Caprio S, Plewe G, Diamond M, et al. Increased insulin secretion in puberty: a compensatory response to reductions in insulin sensitivity. J Pediatr 1989; 114: 963-7
111. Galbo H. Endocrine factors in endurance. In: Shepard RJ, Astrand PO, editors. Endurance in sport. Oxford: Blackwell scientific publications, 1992
112. Lehmann M, Keul J, Korsten-Reck V. Einfluβ einer stufenweisen laufbanderergometrie bei kinder und erwachsenen auf die plasmacatecholamine, die aerobe und anaerobe kapazität. Eur J Appl Physiol Occup Physiol 1981; 47 (3): 301-11
113. Fleg JL, Tzankoff SP, Lakatta EG. Age related augmentation of plasma catecholamines during dynamic exercise in healthy males. J Appl Physiol 1985; 59 : 1033-9
114. Lehmann M, Keul J. Age-associated changes of exercise-induced plasma catecholamines responses. Eur J Appl Physiol Occup Physiol 1986; 55 (3): 302-6

115. Rowland TW, Maresh CM, Charkoudian N, et al. Plasma norepinephrine responses to cycle exercise in boys and men. Int J Sports Med 1996; 17 (1): 22-6
116. Marin G, Domené HM, Barnes KM, et al. The effects of estrogen priming and puberty on the growth hormone response to standardized treadmill exercise and arginine-insulin in normal girls and boys. J Clin Endocrinol Metab 1994; 79 (2): 537-41
117. Bouix O, Brun JF, Fedou C, et al. Plasma beta-endorphin, corticotrophin and growth hormone to exercise in pubertal and prepubertal children. Horm Metab Res 1994; 26 (4): 195-9
118. Treolar AE, Boynton RE, Behn BG, et al. Variation of human menstrual cycle through reproductive life. Int J Fertil 1967; 12: 77-126
119. Viru A, Laaneots L, Karelson K, et al. Exercise-induced hormone responses in girls at different stages of sexual maturation. Eur J Appl Physiol Occup Physiol 1998; 77 (5): 401-8
120. Viru A, Viru M, Kuusler K , et al. Exercise-induced hormonal responses in boys in relation to sexual maturation [poster-abstract]. In: XXth international symposium of the European group of Pediatric Work Physiology; 1999 Sep 15-19; Sabaudia, 135
121. Cacciari E, Mazzanti L, Tassinari D, et al. Effects of sport (football) on growth: auxological, anthropometric and hormonal aspects. Eur J Appl Physiol Occup Physiol 1990; 61 (1-2): 149-58
122. Mero A, Jaakkola L, Komi PV. Serum hormones and physical performance capacity in young boys athletes during a 1-year training period. Eur J Appl Physiol Occup Physiol 1990; 60 (1): 32-7
123. Rowland TW, Morris AH, Kelleher JF, et al. Serum testosterone response to training in adolescent runners. Am J Dis Child 1987; 141: 881-3

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