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# Energy Metabolism in Children and Adolescents

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## 1. Introduction

Energy metabolism is the most integral body function, and, as any functional activity, it has an effect on energy expenditure. Body energy expenditures are composed of three unequal parts: basal metabolism, energy supply of functional activity and energy expenditure on growth, development and the adaptive processes. The proportion of these expenditures is determined by the stage of individual development and specific life conditions.

Basal metabolism (the minimum level of energy production in conditions of complete rest), in its turn, is composed of three primary energy expenditure types: minimum level of vital physiological functions; intracellular futile cycles of biochemical processes; and reparative processes, including growth and development expenditure.

With age, basal metabolism expenditure and growth and development expenditure is considerably reduced, while functional expenditure can increase (for instance, muscle energy expenditure of an adult can be sometimes more than that of a child), but in any case they undergo important qualitative changes.

## 2. Age changes of basal metabolism

Methodological requirements for basal metabolism measuring are hard to be implemented outside a clinic, therefore metabolism in a state of rest is most commonly measured (lying down, comfortable temperature, 2-4 hours after food intake, without any stress factors), which is approximately 10-20% more than the level of basal metabolism. Present-day children have resting metabolism values even lower than standard norms of basal metabolism (Kornienko, 1979), proposed by Harris and Benedict (1919), which might be the result of acceleration of growth and development, observed up to the 1980s (Godina, 2009). With age the rate of resting metabolism (per body mass unit) is reduced – from infancy to the adulthood– by 1.5 – 2 times. The reasons for this reduction have been discussed for the last 150 years.

Since Max Rubner's time (1883) it has been known that as mammals gain body mass, heat production per mass unit is reduced, while the metabolism rate, relative to the surface space, is practically constant ("the rule of surface"). These metabolism changes were primarily explained by thermoregulation expenditure, but it turned out that in a thermoneutral conditions, without any extra heat production, this alignment persists. Moreover, this relation between metabolism rate and body size is observed in invertebrates (Schmidt – Nielsen, 1987; Ivanov, 1990).

For a long time the increased metabolic rate in infants has been attributed to metabolic expenditure on growth (Karlberg, 1952). But this hypothesis was not corroborated by facts. An infant's growth is most intense in the first 6 months after birth. The growth coefficient during this period is 4.0 (Schmal'hausen, 1935). At one year after birth, the coefficient is sharply reduced, by more than 10 times - to 0.3. Basal metabolism rate is at its peak at the age of one. Special calculations (Kornienko & Gohblit, 1983) proved that true expenditure on synthesis, associated with growth processes, even in the first 3 postnatal months, when the infant's growth velocity is at its peak, is no more than 20 kcal /day, which is 7–8% of the total expenditure. According to King et al. (1994), total energy expenditure of a woman body during pregnancy is on the average 325 MJ (77621 kcal). It is approximately a 20% increase in metabolism rate, compared to basal energy expenditure of a female. Evidently most of this energy expenditure is the expenditure on extra functions of maternal body systems, including the ones associated with the required adaptation to the increased physical load: during the second half of the pregnancy period the condition of the mother is bearing an extra load weighing from 2-3 kg to 10-12 kg (that includes the weight of the foetus, placenta, amniotic fluid, grown uterus, etc.). In fact, the growth processes takes a small part of the volume of energy expenditure. The energy expenditure on proliferative processes of kids older than one year is even less (under 1%), when the growth velocity becomes 12-15 times slower compared to intrauterine period.

Empiric formulae are used to express the relation between body size and metabolic rate. Kleiber (Kleiber, 1961) proposed the following formula for mammals, including humans:

$$M = 67.7 \cdot P^{0.75} \text{ kcal / day} \quad (1)$$

Where M is the heat production of the whole body, and P is body mass.

But age changes in basal metabolism cannot be calculated using this equation. During the first year after birth, heat production is not reduced as required by the Kleiber equation, but stays on the same level or even increases, while the body mass during this period is tripled. Only one year after birth is the metabolism rate of 55 kcal/kg per day reached, "proposed" by the Kleiber equation for the body with the mass of 10 kg.

Only after 3 years does the basal metabolic rate starts to gradually reduce, and reaches the level of an adult person (25 kcal/kg per day) only during puberty.

Increase in the basal metabolic rate within the first year of an infant's life is correlated by some authors with a decrease in volume of intracellular space in most tissues. According to Brück (1970), if the oxygen consumption rate per mass unit of newborn infants in rest is 5.0 ml O<sub>2</sub>/kg/min, and in one-year infants – 8.2 ml O<sub>2</sub>/kg/min, then recalculated per an active cellular mass unit, it turns out that a newborn consumes 9.0 ml O<sub>2</sub>/kg/min, and a one year-old child – 10.9 ml O<sub>2</sub>/kg/min.

Rate of basal metabolism starts reducing from the age of three (Fig. 1). The first place among the probable reasons for this phenomenon is change in body composition correlated with age - increase in relative mass of tissue with a small rest metabolism rate (bone tissue, fat tissue, skeletal muscles, etc.). M. Holliday (1971) has already proven that a gradual decrease in the metabolism rate of children can be easily explained by the uneven growth of organs, presuming that the metabolic rate of tissue growth in the process of postnatal development is constant. For instance, it is known that mass of the brain (which greatly contributes to the level of basal metabolism) for newborns is 12% of their body mass, while in adults it's only 2%. Internal organs (liver, kidneys, etc.) also grow unevenly, and have a high level of energy

metabolism even during rest – 300 kcal/kg/day. At the same time, the muscle tissue whose relative quantity is almost doubled in the period of postnatal development, is characterized by a very slow resting metabolism rate – 18 kcal/kg/day.

It should be noted, that the dynamics of age changes in resting metabolism is not just a simple decrease in metabolism rate. As it is given in Fig. 1, periods characterized by a rapid decrease in metabolism rate, are replaced by age intervals where resting metabolism values are stabilized (Kornienko, 1979; Kornienko & Gohblit 1983; Kornienko et al, 2000). Taking this into consideration, a close correlation of changes in metabolic rate and growth velocity is found. Columns in Fig. 1 show relative annual increase in body mass. Turns out that, excluding the first year after birth, the higher the relative growth velocity, the higher the rate of resting metabolism lowering during this period. Inhibition of growth processes at the age of 1.5-2 coincides with the highest values of resting metabolism, and the increase in growth velocity by ages 6 through 7 is accompanied by a considerable decrease in metabolism. After this there is the next inhibition of growth, during which the level of metabolism is stabilized, and the next value decrease coincides with a new acceleration of growth processes. The last peak of resting metabolism is observed at about the age of 14 years, before the puberty growth spurt, and soon after that the energy metabolism rate is stabilized on the level typical for adults. According to longitudinal observations, all these changes are typical both for boys and girls, but in girls they are usually observed 0.5-1 years earlier (Kornienko & Gohblit, 1983).

Rate value of basal metabolism is especially important for diagnosing and treating several endocrinological diseases, as well as obesity. Because of that there are ongoing discussions in scientific literature about methods of calculating basal metabolism values using various formulae – Harris & Benedict (1919), the WHO committee and others (White & Seymour, 2005; Frankenfield et al., 2005; Garrel et al., 1996; Hayter & Henry, 1994; Tverskaya et al., 1998, etc.). Most contemporary authors consider the volume of cellular mass or the value of lean body mass the most important factor, as well as age, sex, constitution, race and ethnicity (Bosy-Westphal et al., 2009; McDuffie et al., 2004; St-Onge & Gallagher, 2010; Vermorel et al., 2005).

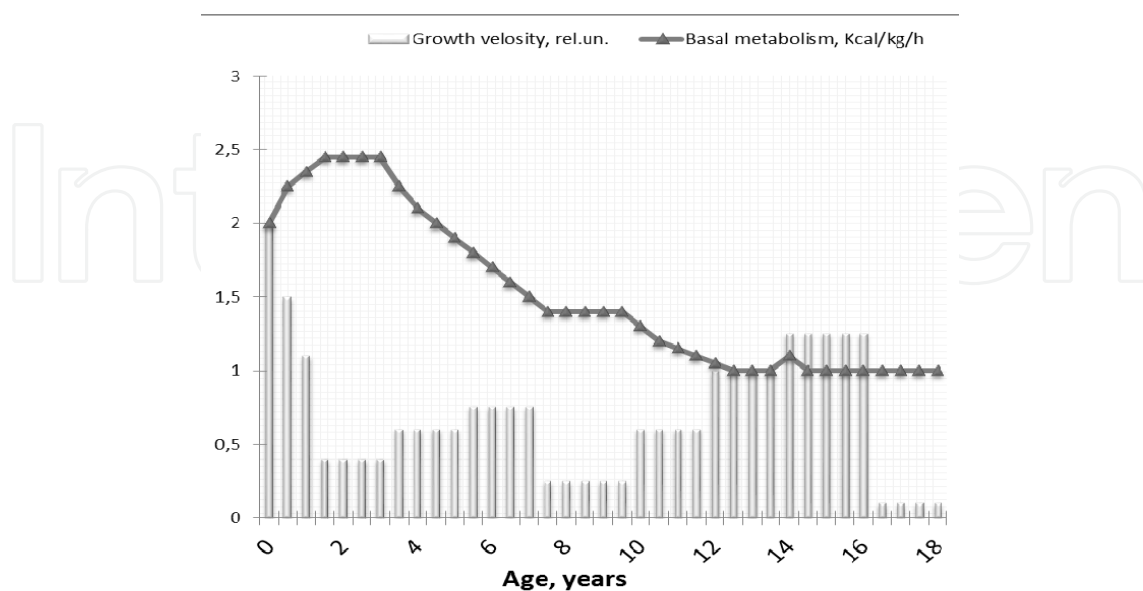


Fig. 1. Dynamics of growth velocity and basal metabolic rate in children from birth to maturity (after: Kornienko, 1979; modified)

Another factor might play an important role – the change in metabolic activity of tissues in a growing organism, that occurs with age (Conrad & Miller, 1956; Nagorny et al., 1963). To test this assumption, our laboratory researched age changes in the mitochondrial apparatus of various tissues (Demin, 1983; Kornienko, 1979). Using Chance's differential spectrophotometer we measured cytochrome a concentration, which is a terminal ferment of the oxidative chain of mitochondria, in tissue homogenates of Wistar rats during ontogeny (Fig.2). The higher cytochrome a concentration, the higher oxidation activity is developed by a given tissue under the influence of an appropriate stimulus, provided it is adequately supplied with substrates and oxygen. This data allows to compare not just the potential metabolic activity of various tissues, but also to observe its changes, including changes occurring with age.

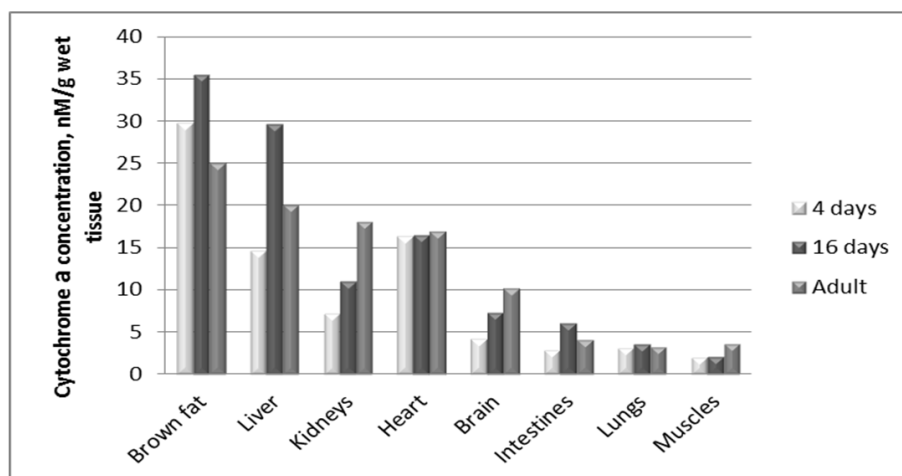


Fig. 2. Cytochrome a concentration in tissue homogenates of Wistar rat during ontogeny (after: Kornienko, 1979; modified).

Brown adipose tissue has the highest potential metabolic activity, both in young and adult rats; the liver is second in potential. Both tissues are characterized by the fast rise of cytochrome a concentration at the age of 16-20 days, which can be explained by the fact that at that time young rats leave their nest and start their separate life, which requires the activation of thermoregulatory processes. The food type changes at the same age, which has an effect on cytochrome a concentration in the intestine tissue. When adulthood is reached, cytochrome content in all these tissues is considerably reduced.

Content of oxidation ferments in cardiac and lung tissues is the most stable – it stays almost unchanged with age. But oxidation ferments in tissues of rat kidneys and brain increase approximately by a factor of 2.5 by adulthood. If the increase in tissue mass is considered, it turns out that the metabolic potential of brown adipose tissue during postnatal ontogenesis grows 10 times, the brain's - 11.4 times, the liver's -38.5 times, the kidney's -57 times, the skeletal muscles' -87 times. That directly affects the level and structure of energy metabolism.

It has been proven using this method (based on post-mortem materials from a trauma clinic) that cytochrome concentration is increased considerably in some grey matter areas in the brain cortex (4, 6, 10th and 17th fields according to Broadman), in the subcortical structures, and in the homogenates of children's whole brain at the age of 1–1.5, compared to the first months of life (Kornienko, 1979). Since at this age the human brain accounts for at least 50% of basal metabolism, it can be assumed that a more active oxidation processes of this tissue

will have an effect basal metabolism of the whole body. Important qualitative changes in nervous and mental activity occur in children age 1-2, due to differentiation processes in neural tissue (Farber & Machinskaya, 2009; Tsekhmistrenko et al., 2009). Meanwhile it has been proven 40 years ago that tissue differentiation in ontogenesis always starts with mitochondria development and a more active oxidation metabolism (Macler et al., 1971; Makhin'ko & Nikitin 1975).

Calculations by Kornienko (1979) have demonstrated that for humans the contribution of various organs to the basal metabolism is changes with age. The adult human brain accounts for 24% of basal metabolism, the liver for 20%, the heart for 10.2% and the skeletal muscles for 28%. A one-year old child's brain accounts for 53% of basal metabolism, while the skeletal muscles account only for 8%. The liver's contribution is about 18% (Fig.3).

### 3. Energy supply for functions during ontogenesis

#### 3.1 Daily energy expenditure structure

Unlike basal metabolism, which is the minimum level of body energy expenditure, average daily metabolism includes the sum of all expenditures associated with the realization of various body functions. Food processing and digestion, thermoregulation and muscle activity are the most power-consuming functions. Unfortunately, there is almost no data in literature on the energy value of mental activity (not taking into consideration the indirect calculations by Holliday, 1971).

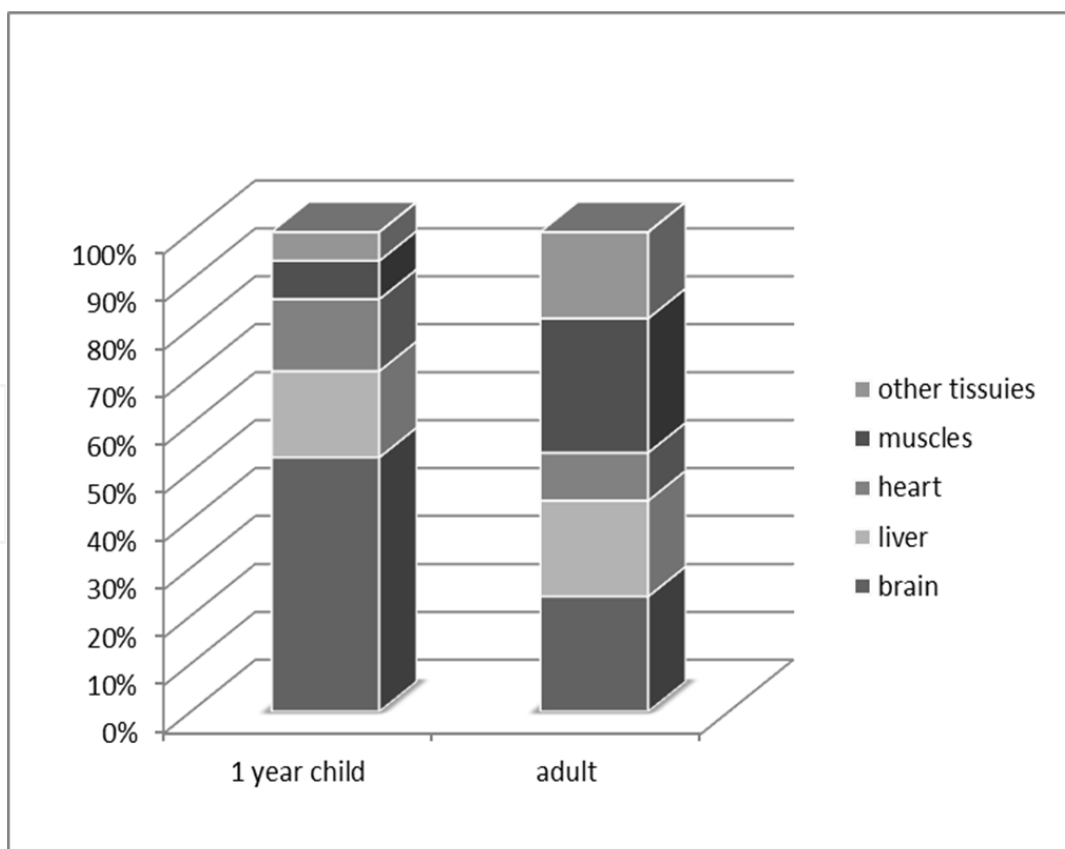


Fig. 3. Age changes in contribution of various organs and tissues into the structure of human basal metabolism (After: Holliday, 1971; Kornienko, 1979; modified)



### 3.2 Functional range

Various body tissues can change their metabolic activity to a different degree, ranging from rest to maximum functional activity. It depends on the organization of metabolic paths in cells that form the corresponding tissue. Based on content and activity data of vital energy ferments in body tissues, Demin (1983) calculated the hypothetical values of minimum and maximum metabolic activity for the liver, brain and muscles of a young man (Fig. 4). Characteristics of the functional range in skeletal muscles obtained using this method are close to the actual measured maximum energy expenditure (Son'kin, 1990; Kornienko, et al, 2000). As seen in fig. 3, muscles have both the highest potential for metabolic activity and the widest functional range. It should be noted that the maximum level of functional activity is carried out through the anaerobic metabolic processes, not limited by the possibilities of mitochondrial oxidation. The functional range value of various tissues can be affected differently depending on age. According to Demin (1983), this value for the brain is at its peak in childhood; for the liver it stays more or less the same at all periods of postnatal ontogenesis; for skeletal muscles it considerably increases from birth to the end of puberty.

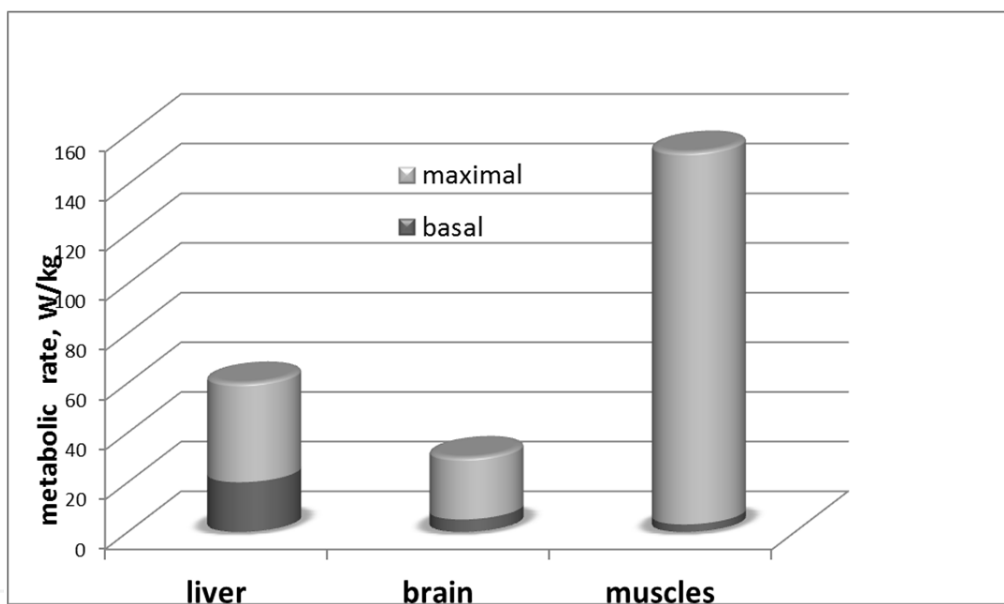


Fig. 4. Comparative characteristic of functional range in various tissues of human body (calculation for a young man) (After: Demin, 1985; modified)

The intensity of body functions in a child is much higher than of an adult. The rate of children's basal metabolism is 1.5-2 times higher, but the maximum activity level is considerably lower than that of an adult. This results in a smaller functional range, and that makes the child body's existence more stressful.

The high intensity of energy metabolism in children becomes particularly obvious when you look at the fact that the child's body reacts with higher intensity to an impact equal in power, demonstrating a higher lability of autonomic systems and metabolic processes. These differences are well known, when talking about muscle activity (Åstrand, 1952; Kornienko et al, 2000). The fact that similar differences are evident in metabolic reactions to other functional loads, in particular food load, is less known.

### 3.3 Specific – Dynamic (thermogenic) effect of food

The rate of heat production is considerably increased after food consumption, despite of lack of muscle activity, and it remains elevated for 2-3 hours (depending on the structure of food and other factors). Though the thermogenic effect of food is a known phenomenon and has been studied since the end of the 19th century, there is still no single opinion about its reasons and occurrence mechanisms. The simplest explanation, which states that extra energy production is required to activate a motor function of the gastrointestinal tract, has not been borne out by experiments: the thermogenic effect of glucose cannot be recovered in patients with diabetes and lab animals, even though carbohydrate is absorbed to the bloodstream and is extracted with urine (Lusk, 1919).

Today the most probable reason considered for the thermogenic effect of food is the effect of enterohormones produced by the duodenum epithelium. For example, it has been proven that the lack of these hormones in blood results in a lower body temperature, meaning heat production (Ugolev et al, 1976). But even in this case it is unclear which particular tissue accounts for extra heat production. Recently brown adipose tissue has been considered as the reason (Himms-Hagen, 1989; Nedergaard & Cannon, 2010), which, according to recent data, is preserved in adults (Nedergaard et al., 2007) and maintains substrate homeostasis (Son'kin et al., 2010).

A unique systematic research of age changes in the thermogenic effect of food substance (glucose) in school children was made in the laboratory of I.A.Kornienko (Kornienko et al, 1984). A standard test was used to evaluate glucose tolerance during this study: glucose was taken orally on an empty stomach in quantity proportional to mass (1g/kg). Content of glucose in blood in such a probe is usually increased during 30 minutes after intake and gradually normalizes within 2-3 hours. As glucose increases, with some delay (about 0.5 hours) oxidation processes start in the body, and in 3 hours the oxygen consumption levels return to the primary level. Total intensification of energy production with age for children of 7-8 up to 15-17 years is considerably reduced, especially for boys (Table 1).

The given data proves that reactivity of oxygen metabolism decreases with age, meaning efficiency of mechanisms providing homeostasis increases. The difference in age dynamics of thermogenic glucose effect for boys and girls is the most interesting phenomenon. It is known that adult women, on average, have a better tolerance to glucose than men (Korkushko & Orlov, 1974). Possibly, the given data reflects the formation of such sex differences.

Age, years	Boys	Girls
7 - 8	2.125 ± 0.16 (n=18)	1.825 ± 0.14 (n=23)
11 - 12	1.255 ± 0.10 (n=22)	1.365 ± 0.11 (n=21)
15 - 17	0.585 ± 0.06 (n=16)	1.060 ± 0.08 (n=14)

Table 1. Total thermogenic effect of glucose (per oral 1 g/kg) for school children for 3 hours of observation (kcal/kg, M±m) (After: Kornienko et al., 1984)

In the same research (Son'kin et al., 1975) it was proved that glucose put into the body depends considerably on their body constitution: children of 11-12 years with a low fat content in the body of no less 1/3 introduced glucose is oxidized in process of a thermogenic response to its putting into the body, while children with a high fat content a thermogenic response to input of glucose is considerably less. Similar results for adult persons are described in press of the last years (Nedergaard & Cannon, 2010).



Results obtained in such studies as well as other data about thermogenic effect of food cast doubt on the validity of widely used calculations of caloric food value. All such calculations do not take into account energy expenditure on digestion of food substances which are known to take from 1/5 up to 1/3 caloric value of the taken food substance. The problem is complicated by the fact that fats and proteins have a greater thermogenic effect than carbohydrates (Kassirsky, 1934), while mixed products have a smaller thermogenic effect than the total thermogenic effects of food substances they contain (Forbes & Swift, 1944). It is proven that liquid food, with similar calorie value has a less specifically dynamic effect than solids (Habas & Macdonald, 1998). We think that mechanical calculations of food calorificity based on the caloric equivalent of proteins, fats and carbohydrates in it which is widely used in clinic and health-improving systems, including paediatric practice (Morgan, 1980; Young et al. 1991; Schmelzle et al., 2004) need to be corrected.

### 3.4 Thermoregulation development in ontogenesis

Thermoregulation, support of constant temperature in the body core is determined by two basic processes: heat production and heat dissipation. Heat production (thermogenesis) depends primarily on the rate of metabolic processes, while heat dissipation is defined by heat insulation provided by cutaneous coverings, vascular reactions, active outer respiration and perspiration. Because of this, thermogenesis is considered a mechanism of chemical thermoregulation, and heat dissipation regulation – a mechanism of physical thermoregulation. Both these processes change with age, as well as their role in providing a constant body temperature.

As a result of laws of physics, increase in mass and body absolute dimensions reduces the contribution of chemical thermoregulation. Thus, the value of thermoregulation heat production for newborn children makes about  $0.5 \text{ kcal/kg} \cdot \text{hour} \cdot ^\circ\text{C}$ , and for adults –  $0.15 \text{ kcal/kg} \cdot \text{hour} \cdot ^\circ\text{C}$ .

A newborn child, if temperature of the environment lowers, can enlarge heat production to adult levels – to  $4 \text{ kcal/kg} \cdot \text{hour}$ . But because of lower heat insulation ( $0.15 \text{ } ^\circ\text{C} \cdot \text{m}^2 \cdot \text{hour/kcal}$ ) the chemical thermoregulation range of a newborn is small – no more than  $5^\circ$ .

At that it should be accounted that the critical temperature level ( $T_h$ ), switching thermogenesis for a healthy newborn is  $33^\circ\text{C}$ , by the adult period it falls down to  $27-23^\circ\text{C}$ . But in clothes with heat insulation usually making 2.5 CLO, or  $0.45 \text{ } ^\circ\text{C} \cdot \text{m}^2 \cdot \text{hour/kcal}$ ,  $T_h$  value falls down to  $20^\circ\text{C}$ , therefore a child in his usual clothes at room temperature is in a thermoneutral environment, meaning that in these conditions a child requires no extra expenditure to support body temperature.

If the temperature falls down below threshold values (for instance, during the change of a child's clothes), mechanisms of extra heat production switch on. For a child they are mainly, "nonshivering thermogenesis", localized in metabolically active tissues – liver and brown adipose tissue (Brück, 1970; Kornienko, 1979). Researches of the latest years have revealed that an acute short-term cooling of adults also results in activation of nonshivering thermogenesis in brown adipose tissue (Nedergaard et al., 2007; Son'kin et al., 2010), which is proved to be preserved for most adults residing in a moderate climatic zone (Nedergaard & Cannon, 2010). Another mechanism of thermogenesis is a cold-induced muscle tremor which is usually observed in adults when the cooling effect is strengthened or prolonged. For children this physiological mechanism turns out inefficient due to particular features of

the child's body constitution, therefore it is activated in the last turn, if temperature of the body core falls down despite the processes (Kornienko, 1979).

High activity of special mechanisms of thermogenesis in infants is connected not only with small size and large relative surface increasing heat insulation, not only with low heat insulation of cutaneous coverings, but with a relatively low level of basal metabolism, which has been noted before in this paper. Within the first year of life all these parameters are changing and the chemical thermoregulation activity is reduced. For a child of 5–6 months the importance of physical thermoregulation is considerably increased; it makes the temperature threshold and latent period of an interscapular brown adipose tissue activation almost double compared with the same parameters for infants 1-2 months old (Gohblit et al, 1975; Kornienko, 1979).

Under usual conditions the child older than 3 years old has a high value of heat flow in relation to the body surface unit, and heat insulation of cutaneous coverings is low, therefore children's skin is practically always warm. Even at the age of 4.5–5 years for girls and 5.5–6 years for boys the body heat insulation is very low:  $0.226 \pm 0.003 \text{ } ^\circ\text{C} \cdot \text{m}^2 \cdot \text{hour/kcal}$ , not changed a lot compared to infants. Their mechanisms of physical thermoregulation are poorly developed. Therefore, if such a child is in conditions of room temperature (+ 20°C) in underwear and T-shirt, in 80 cases of 100 his thermoregulatory heat production is activated (Kornienko, 1979).

Intensification of growth processes at the age of 5-7 years results in accelerating the length and surface area of extremities, providing a regulated heat exchange of the body with the environment. It is, in turn, results in the fact that from the age of 5.5–6 years (it is especially visible for girls) the thermoregulation function is considerably changed. The body heat insulation is increased, and the chemical thermoregulation activity is substantially reduced. This method of body temperature regulation is more efficient and it becomes predominant in further development with age. In girls this transformation of thermoregulation happens, on average, one year earlier than boys.

At the age of 10 years for girls and 11 years for boys quicker growth processes and considerably lower rate of basal metabolism which are typical for them are observed again. According to thermoregulation conditions, this age can be marked out as a crucial period: physical thermoregulation is activated again, with chemical thermoregulation becoming less important. For boys these changes are distinctly expressed at the age of 12 years.

The next stage of thermoregulation development is during pubescence, becoming apparent in the frustration of the forming functional system. For 11–12-year old girls and 13-year old boys, despite the continuous decrease in the resting metabolism rate, there is no corresponding adjustment of vascular regulation. Worse heat insulation facilities of covering tissues result in the fact that, notwithstanding the age tendency, the critical temperature shifts to higher values with the temporarily growing role of chemical thermoregulation – most teenagers (up to 80%) enlarge their heat production even under slight cooling conditions effects.

Distinct sex differences in dynamics of thermoregulation development are seen during pubescence (Kornienko & Gohblit, 1988). Parallel to decrease in basal metabolism, for girls after the second stage of pubescence (according to Tanner), heat insulation properties are rapidly increased, and the function of physical regulation is restored in full. By the age of 16 this process is usually over, and all thermoregulation parameters reach the values typical for adults. The same tendencies exist in boys, but by the age of 16 years, processes forming

mechanisms of physical thermoregulation are incomplete. Only in youths after pubescence do thermoregulation facilities reach their final level. Increase in tissue heat insulation to the level of 1.1 CLO allows to function without activating the chemical thermoregulation (meaning extra heat production) even when the environment temperature falls down by 10-15 degrees below thermoneutral. Such body reaction is naturally more economical and efficient.

The given data prove that in the process of postnatal ontogenesis the primary line of the system development providing temperature homeostasis is indirect (Falk, 1998). At each stage of individual organism development there is a complex dependence of thermoregulation active mechanisms on growth and development, the rate of metabolic processes and conditions of some autonomic functions. It is this dependence that determines a primary activity of physical or chemical thermoregulation mechanisms, providing temperature homeostasis at the corresponding stage of development.

#### **4. Muscle function energy supply development**

Muscle activity is the most energy-intensive function: even for a person engaged in mental work about half of daily energy expenditure is used to provide a contracting activity of somatic muscles. One of the first works researching ontogenesis of the muscle function energy supply was made by Robinson (1938), who discovered age changes in maximum oxygen consumption in children, teenagers and adults. The research of P.-O. Astrand (1952), still a classic, presents data of maximal aerobic capacity of people from 6 up to 60 years old.

As compared with other tissues, skeletal muscles have the greatest functional range (Fig.4) – metabolic process can change its velocity in muscles by a factor of dozens. Such amplitude of metabolic activity change is impossible to be explained through the work of mitochondrial apparatus; therefore muscles can get the energy required for contraction even from the glycolysis process in cytoplasm and macroergs reserves accumulated in cells in the form of ATP and creatine phosphate. It forms a specific character of muscle tissue energetics. These specifics were expressed by Margaria (1963) in his conception of three energy sources for the muscle activity: aerobic (oxidative, mitochondrial); anaerobic glycolytic (lactacide); anaerobic phosphagenic (alactacide). In combination with the anaerobic threshold conception (Mader & Heck, 1986; Skinner, 1993), these presentations are now the theoretic base of muscle bioenergetics (Volkov, 2010).

Ample data prove an uneven development of aerobic and both anaerobic sources with age, like, for example, heterochrony determines a qualitative peculiarity of skeletal muscles energetics at separate stages of ontogenesis (Guminskiy et al., 1985; Demin, 1983; Kornienko, 1979; Kornienko et al., 2000, 2005; Son'kin, 1988; 2007; Tambovtseva, 2003; Van Praagh, Dore, 2002).

##### **4.1 Aerobic (oxidative) source**

Facilities of aerobic energy supply in skeletal muscles are considerably changed in the course of individual development. It is provided by both the change in content of most important oxidizing ferments in the somatic muscle tissue (Kornienko, 1979), and structural change in the oxidative chain of mitochondria (Demin, 1983, 1985; Demin et al., 1987; Son'kin & Tambovtseva, 2011). Naturally, the most important factor is absolute and relative age increase in mass of somatic muscles. Generally, the maximum oxygen consumption

(MOC) rises proportionally to the muscle mass growth (Kornienko et al., 2000), but it lacks information about qualitative changes in muscle energy supply of children and teenagers (Son'kin & Tambovtseva, 2011).

Age, years	Cytochrome <u>a</u> concentration, nM/g raw mass of muscle tissue	Muscle mass, kg (after: Holliday, 1971)	MOC, l/min (after: Åstrand, 1952)	MOC, ml/kg muscle mass
Newborn	0,9	0,6	-	-
5 - 7	4,6	6,7	1,01	151
9	5,2	10,5	1,8	171
11	6,6	11,6	2,1	181
14	4,8	21,2	3,5	165
20	4,5	25,0	4,1	164
36-40	3,7	28,3	3,9	138

Table 2. Age changes in cytochrome a content in thigh muscle and human aerobic capacity (After: Kornienko, 1979)

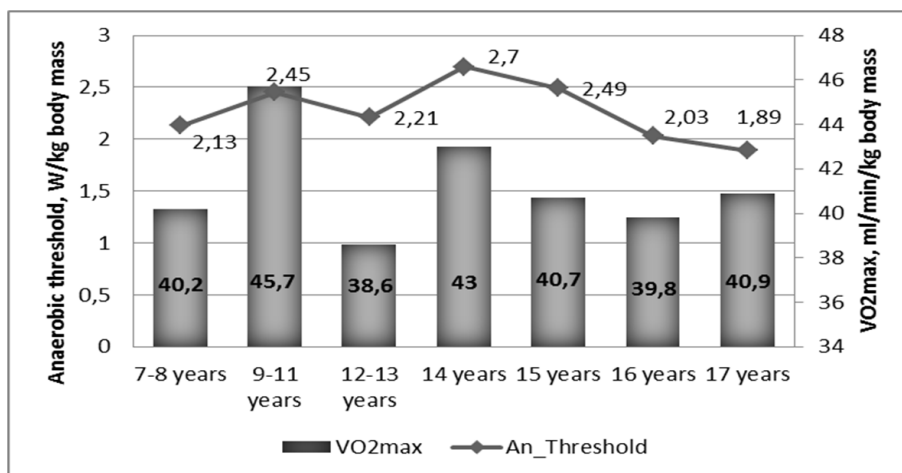


Fig. 5. Dynamics of aerobic capacity indices in schoolboys

Age dynamics of cytochrome a content – a terminal site of the oxidative chain – in human skeletal muscles (Kornienko, 1979; Demin et al., 1987) is given in Table 2. Calculations of the estimated value for specific MOC (per 1 kg of somatic muscle mass) are shown. As obvious from the given data, the highest cytochrome a concentration is registered in skeletal muscles for boys 9-11 years old. It is also proved by data of electron microscopic researches (Kornienko, 1979; Kornienko et al, 1987): the number of mitochondria in relation to the area of myofibrils for 11-year old boy is considerably more than in an adult man (Table 3). It is remarkable, that, according to data of morphologists, a capillary network in the muscles of extremities turns out to be more developed in children of 9-11 years (Topol'sky, 1951), which is the age when there is the highest content of oxidizing ferments in the muscle tissue. Thus, an age development of the energy production aerobic source in skeletal muscles does not happen monotonously, but gets the expressed maximum during prepubescence (Fig.5). These conditions have a considerable effect on the functioning of the muscle energy supply system.



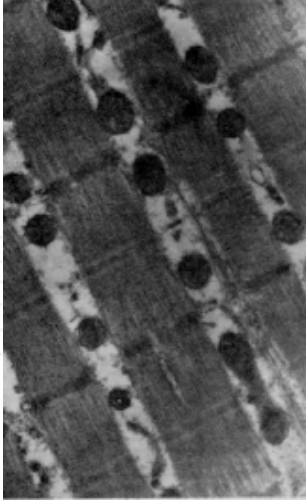
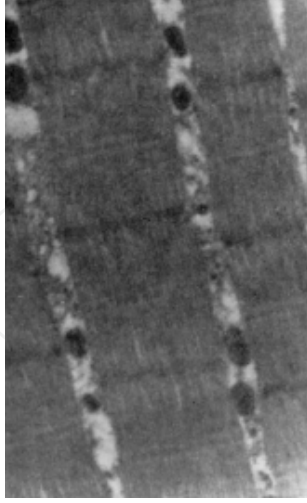
Index	11-year old boy	35-year old man	Difference, %
Electron micro photos of somatic muscle lengthwise cuts (m. Quadriceps Femori)			
Mean diameter of mitochondria, micron	236	175	-35
Mean thickness of myofibrils, micron	505	590	+14
Ratio of mitochondria area to myofibril area	0,034	0,016	-113
Ratio of mitochondria total area to myofibril total area	0,153	0,097	-58

Table 3. Morphometric indices of skeletal muscles mitochondria in 11-year boy and adult man according to electron microscopy (After Kornienko, 1979; modified)

Such special energetic structure of skeletal muscles for children in prepubescence, as we see it, is caused by the fact that this ontogenesis period is the preparation for the radical reconstructing structural and functional characteristics of somatic muscles, occurring during pubescence under the influence of sex hormones. We used special histochemical tests to prove this (Tambovtseva, 2003).

#### 4.2 Morpho-functional changes of skeletal muscles during postnatal ontogenesis

Fiber structure of mixed skeletal muscles is usually considered to be determined genetically and not dependent on age and training (Van Praagh & Dore, 2002; Yazvikov et al., 1978). But according to results of histochemical investigations, the ratio of various fiber types in the structure of skeletal muscles is not constant in ontogenesis (Kornienko et al., 2005; Son'kin & Tambovtseva, 2011; Tambovtseva & Kornienko, 1986a,b, 1987).

Research primarily made on laboratory animals – Wistar rats and Guinea pigs – made possible a conclusion that at an early age the most part of mammals is non-differentiated fibers which further acquires features of red oxidative fibers. The share of quick fibers is rapidly increased during pubescence, which become predominant after pubescence (Tambovtseva & Kornienko, 1986a; 1987).

These studies continued on post mortem material of males within the age bracket from birth to adulthood (Tambovtseva & Kornienko, 1986b). On Fig. 6 there are results characterizing

the structure of large skeletal muscles in human extremities, achieved by the method of histochemical revelation of ATP myosin activity.

It turns out that all large human skeletal muscles are characterized by the same age tendency: undifferentiated embryo fibers are changed by fibers with a slow actomyosin ATP-ase, by 4-7 years an "aerobic profile" of mixed muscles is formed, which prevails up to 11-12 years. Then, with start of pubescence there is a two-phase transformation of the muscle structural-functional composition, which results in considerable reduction in a share of red oxidizing fibers (I type), some increase in a share of intermediate fibers (IIA type), and a considerable increase in presented glycolytic fibers (IIB type).

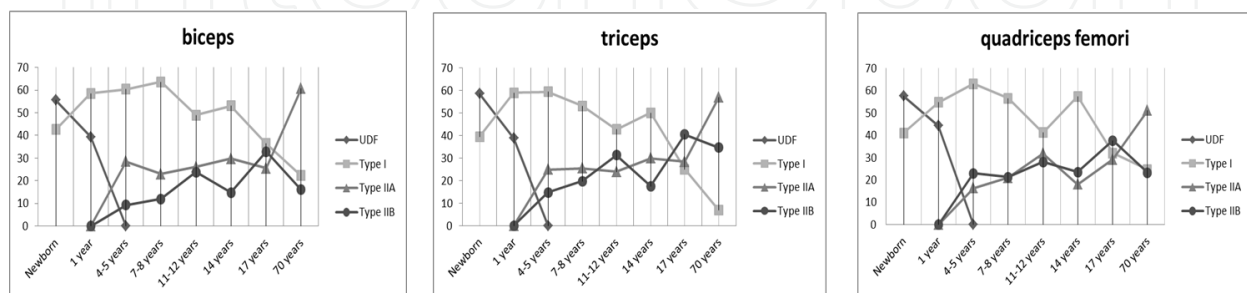


Fig. 6. Age changes of muscle fiber composition in men (% of each fiber type). By X-line – age from 4 months intrauterine development up to 70 years. By Y-line – fiber share (%): MB undifferentiated, MB I type, MB IIA type, MB IIB type. UDF – undifferentiated fibers.

Only by 17-18 years is a definite picture formed, which is characterized by predominance of anaerobic – glycolytic fibers in all large muscles. Such muscle structure is likely to be preserved up to the start of involutive processes at the old age, which might be connected with decreased activity of genital glands.

It should be noted that in the world literature there is no definite view on the age development of somatic muscle structural components. The relatively scarce researches of age features in human skeletal muscles provide conflicting results (Blimkie & Sale, 1998; Van Praagh, 2000). According to some authors, there is a relatively large share of undifferentiated fibers at birth (10-20%). Amount of I-type fibers grows rapidly after birth, and II-type fibers reduces. By the age of one year the structure which is similar to adults is formed (Bell et al., 1980; Colling-Saltin, 1980; Elder & Kakulas, 1993). The ratio of IIA-type and IIB-type fibers is also disputable (Colling-Saltin, 1980; du Plessis et al., 1985; Jansson, 1996). But, according to other authors, children until pubescence are more characterized by I type than adults (Eriksson & Saltin, 1974; Lexell et al., 1992; Lundberg et al., 1979). According to Jansson (1996), development of muscles from birth up to 35 years old for men corresponds to  $\Omega$ -model: from birth up to 9 years old a substantial increase in percent of I-type fibers is observed, at the age of about 9 there is a maximum, whereupon their share is reduced considerably by 19 years old. It is evident that this model is very close to results produced by the I.A.Kornienko laboratory.

#### 4.3 Age changes of anaerobic metabolism ferments activity in muscles

In 1971 Swedish scientists demonstrated, by means of needle biopsy, that untrained boys at the age of 12 have a sharp (twofold) increase in the activity of phosphofructokinase (Eriksson et al., 1971). That was the first work where age changes in possible human



anaerobic – glycolytic source at the tissue level were discovered. Next by means of biochemical (Eriksson, 1980; Ferretti et al., 1994; Kornienko et al, 1980; Ratel et al, 2002), histochemical (Tambovtseva, 2003; Kornienko et al, 2000) and physiological (Kornienko et al, 2000; Pyarnat & Viru, 1975; Son'kin, 1988;) methods numerous confirmations of an abrupt activation of anaerobic – glycolytic energy production in the process of pubescence reconstructions were obtained, especially for boys (Boisseau & Delamarche, 2000; Van Praagh & Dore, 2002).

In ontogenesis of rats an activity of glycolysis key ferment – lactate dehydrogenase (LDG) was traced in detail (Musaeva, 1986; Demin et al., 1987). LDG molecule consists of 4 monomers and each of them can have one of two following isoforms: "H" – subunits which are typical for LDG from a cardiac muscle, "M" – subunits which are mainly in skeletal muscles of adult mammals (Lehninger, 1965). These isoferment forms differently participate in a cycle of glycolysis reactions, therefore the ratio of "H" and "M" activities – LDG subunits can be used as a sufficiently informative activity ratio index for aerobic and anaerobic – glycolytic sources.

In these studies it was proven that an age increase in “aerobic” ferment activity in muscles of male rates occurs generally parallel to increasing facilities of the oxidizing source and is complete by the start of pubescence, while total LDG activity rapidly grows in pubescence and even after it. Therefore, in process of pubescence qualitatively reconstructed is organization of energy metabolism in somatic muscle cells: an abrupt extension of facilities for anaerobic – glycolytic energy production in terms of stabilization and even some decrease in a relative capacity of aerobic energy production.

The given facts have proposed an important role of sex hormones in regulation of muscle energetics. Direct evidence of this hypothesis was obtained by Musaeva (1986) in tests on male rates with orchotomy at the age of 3 weeks or artificial androgenization: androgenization accelerates and orchotomy inhibits the formation of ferment systems, which are responsible for anaerobic mechanisms producing energy in somatic muscles, and practically does not have an effect on conditions of mitochondria (aerobic) energy production. Under the influence of exogenous testosterone, the fraction of muscle fibers with a high activity of ATP-ase in the structure of extremities considerably increased, meaning those, which are mainly characterized by anaerobic energy supply. Orchotomy has the opposite results (Musaeva, 1986; Son'kin & Tambovtseva, 2011).

Probably, male sex hormones play a role that is not less significant in formation of a morphological-functional status of human skeletal muscles (Boisseau & Delamarche, 2000; Ferretti et al., 1994; Jansson, 1996; Round et al., 1999; Tambovtseva & Kornienko, 1986; Van Praagh & Dore, 2002). It is remarkable that for girls the same effects of pubescence processes on the structure and function of their skeletal muscles are not revealed (Petersen et al., 1999; Tambovtseva, 2003; Treuth et al., 2001), which can be explained by various structural – metabolic consequences of androgen and estrogen effects. For boys testosterone content is increased 4 times at primary stages of pubescence and more than 20 times – at its last stages. For girls the testosterone is only 4 times increased from the primary to the last stages of pubescence (Blimkie & Sale, 1998).

In literature there are no data on creatine phosphokinase (CrK) activity in human muscles with age. In recent years, with development of magnetic resonance research methods (Ross et al., 1992), data on creatine phosphate (CrP) content in muscles in rest as well as under physical load and recreation have been obtained (Zanconato et al., 1993; Ferretti et al., 1994;

Boisseau & Delamarche, 2000; Van Praagh & Dore, 2002). Data available in press are contradictory.

At that same time, dynamics of these indices for various tissues in ontogenesis of rats was studied by Demin in detail (1983, 1985). According to these results, CrK activity in muscles of animal hind extremities in a nest life period makes 2.5 – 2.7  $\mu\text{mol}/\text{min}/\text{g}$  and it is practically unchanged in the first 2 weeks of life. At the same age CrK activity in cardiac tissue is somehow less than in leg muscles while in neck muscles, which perform the most thermoregulation function – it is 2 times more, than in leg muscles. With start of an active independent motion activity for young rats (3 weeks), CrK in leg muscles grows intensely reaching by pubescence (60 days) the level of 39  $\mu\text{mol}/\text{min}/\text{g}$ . This is 4.5 times more than in neck and cardiac muscles, 12 times more than in brain tissue and 50 times more than in the liver.

For this period CrP content in muscles is approximately increased by 3 times - from 5.4 up to 15.9  $\mu\text{mol}/\text{g}$  (in a 60-day rat's heart CrP content – 7.1  $\mu\text{mol}/\text{g}$ ; in brain – 5.7  $\mu\text{mol}/\text{g}$ ; in liver – 2.43  $\mu\text{mol}/\text{g}$ ).

CrP content and CrK activity are increased in skeletal muscles asynchronously with age and it provides age changes in potential duration of CrP expenditure at maximum activity. The most substantial increase in CrK activity is observed at the last stages of pubescence, which provides a considerable acceleration of ATP forming velocity in a creatine kinase reaction, meaning the capacity of an alactacide energy system. As a result, according to Demin (1985), ATP formation velocity in process of a creatine kinase reaction in muscles of rat extremities is increased from 20  $\mu\text{mol}/\text{g}/\text{min}$  at the age of 12 days up to 80  $\mu\text{mol}/\text{g}/\text{min}$  at the age of 40-45 days (an active phase of pubescence), and by the end of pubescence changes it grows up to 160  $\mu\text{mol}/\text{g}/\text{min}$ .

The given facts prove that the pubescence period is a “divide” between two qualitative conditions in energetics of somatic muscles. Prior to pubescence changes in muscles, like in other mammal tissues, the predominant role in energy supply is played by mitochondria oxidation. After pubescence changes, muscles acquire that colossal functional range and those specific features of organizing energy metabolism, which differentiates them from other tissues of an adult body, and the role of anaerobic energy sources is rapidly increased (Kornienko et al., 2000). Such reconstruction of energetics in skeletal muscles allows after some time the increase of the realized capacity of outer mechanical production, considerably extending the functional range, as well as promoting repeated growth of efficiency and reliable body function under strenuous muscle activity (Kornienko & Son'kin 1999). However, it should be noted, that the data of Demin, like most other similar results, were obtained for male rats. Sex differences in dynamics of energy facilities for skeletal muscles are studied insufficiently. According to the results of research made by means of up-to-date methods (Boisseau & Delamarche, 2000; Petersen et al., 1999; Treuth et al., 2001; Van Praagh, Dore, 2002), for girls at pre- and post-pubescent age such considerable differences in energy metabolism structure under muscular load were not revealed.

## 5. Conclusion

Energy metabolism, presenting the most integral body function, demonstrates logical age changes reflecting qualitative and quantitative redevelopments of a child's organism. The principle of functional economy is likely to be the most vivid of these changes with age development. This principle is implemented in age-related reduction of basal metabolism, in

slower rate of thermoregulatory reactions, decrease of food thermogenic effect with age, in change of daily energy expenditure structure with age. This is the structure of daily expenditure, where there are most vivid qualitative changes reflecting heterochronic development of most energy-intensive functions. If at an early age the energy metabolism priority is the brain and neural processes associated with it, with growth of the muscular system and formation of its functional facilities energy expenditure on kinesis starts taking a greater share in the daily energy balance.

This, together with the general tendency to fall in relative heat production, corresponding to the views of progressive functional economy in rising ontogenesis, with growth and development of skeletal muscles the maximum energy production is considerably increased, which is provided by activation of the least economic anaerobic – glycolytic source of energy production. In other words, by the example of age changes in energy metabolism the most important principle of development can be distinctly demonstrated – a principle of biological suitability, which is sometimes implemented due to the breach of other principles with lower value, to implement biosocial objectives of the corresponding ontogenesis stage.

For many decades the researchers of age changes in energy metabolism have been paying attention to reduction in the rate of exchange processes in rest with age. It was attempted to be explained by smaller relative surface of the body (Rubner, 1883), growth of relative muscular mass value (Arshavskii, 1967), lower relative mass of internal organs with a high rate of oxidizing metabolism (Holliday, 1971; Javed et al., 2010; Kornienko, 1979; Wang et al., 2010). But now we think that the most important age redevelopment is the combined reduction of basal and increased maximum energy expenditure (including expenditure pursuant to anaerobic ways to transform energy with realization of the intense muscle activity), which results in the considerable development of a functional range. That is the biological development objectives of energy production mechanisms, as a vast functional range provides implementation of a wide spectrum of social and biological problems facing the adult organism (Son'kin & Tambovtseva, 2011).

Theoretical views of the laws valid for age changes in energy metabolism can considerably effect the formation and implementation of practical methods and means, firstly in such directions as conditioning to the cold, organization of proper nutrition and rational physical activity of children and teenagers.

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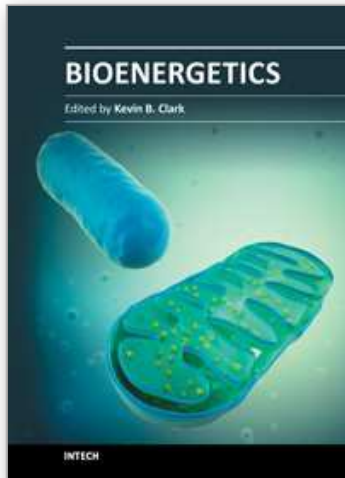
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