Total energy expenditure and physical activity in prepubertal children: recent advances based on the application of the doubly labeled water method[1–3]

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ABSTRACT The prevalence of obesity in children has continued to increase despite a general increased awareness of health and fitness. Epidemiologic data show that the prevalence of obesity in children is ≈25%, with a higher prevalence in some subgroups of the population. In addition, the incidence of obesity-related diseases is dramatically increasing in children. For example, the incidence of type 2 diabetes in children and adolescents has increased 10-fold over the past decade, and this increase is more pronounced in obese persons. The etiology of the development of childhood obesity and subsequent disease is poorly understood, but is likely to be explained by alterations in the regulation of energy balance between energy expenditure and energy intake. It is not known whether obesity is caused by an increase in energy intake relative to energy needs, a decrease in energy expenditure relative to energy needs, or the effect of both. This review will focus on recent studies that have attempted to elucidate the etiology of childhood obesity and have increased our understanding of the regulation of energy balance in prepubertal children by using the doubly labeled water method for estimating total energy expenditure and physical activity–related energy expenditure. This review serves as a brief summary and general update of recent reviews of this topic. *Am J Clin Nutr* 1998;68(suppl):944S–9S.

KEY WORDS Energy expenditure, body composition, physical activity, obesity, leptin, metabolism, children

INTRODUCTION

The prevalence of obesity in children has continued to increase despite a general increased public awareness of health and fitness. Epidemiologic data (1) show that the prevalence of obesity in children is ≈25%, with a higher prevalence in some subgroups of the population (2, 3). In addition, the incidence of obesity-related diseases is dramatically increasing in children. For example, the incidence of type 2 diabetes in children and adolescents has increased 10-fold over the past decade, and this increase is more pronounced in obese persons (4). The etiology of the development of childhood obesity and subsequent disease is poorly understood, but is likely to be explained by alterations in the regulation of energy balance between energy expenditure and energy intake. It is not known whether obesity is caused by an increase in energy intake relative to energy needs, a decrease in energy expenditure relative to energy needs, or both. This article will focus on recent studies that have attempted to elucidate the etiology of childhood obesity and have increased our understanding of the regulation of energy balance in prepubertal children by using the doubly labeled water (DLW) method for estimating total energy expenditure (TEE) and physical activity–related energy expenditure (AEE). This review serves as a brief summary and general update of reviews of this topic (5–7).

BIOLOGICAL AND ENVIRONMENTAL DETERMINANTS OF TOTAL ENERGY EXPENDITURE

An important prerequisite for understanding the role of energy expenditure in the etiology of obesity is to understand the determinants of energy expenditure in children. The following section summarizes recent studies in children that have examined the influence of body composition, parental obesity, sex, ethnicity, seasonality, geographic location, growth stunting, and serum leptin on TEE by using the DLW method.

We examined the influence of body composition, physical fitness, ethnic background, sex, physical activity, geographic location, and seasonality on TEE by pooling data from a diverse group of prepubertal children that we have studied over the past 6 y, comprising 232 white American, African American, Guatemalan, and Mohawk Indian children (8). In all children, TEE was most strongly correlated with body weight (r = 0.81), fat-free mass (r = 0.79–0.81, depending on the method), peak $\dot{V}O_2$ in a smaller subset (r = 0.74), and resting energy expenditure (REE; r = 0.74). REE was most strongly correlated with body weight (r = 0.85) and fat-free mass by anthropometry (r = 0.8–0.87, depending on the method). AEE was most strongly correlated with peak $\dot{V}O_2$ in a subset (r = 0.54), fat-free mass by dual energy X-ray absorptiometry (DXA; r = 0.50), and fat mass

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by DXA (r = 0.49). Thus, in summary, body weight is a strong determinant of TEE because of the combined effects of fat-free mass on all components of energy expenditure as well as the effect of fat mass on AEE. Body weight and composition explain more of the variance in TEE than in REE. In addition, peak $\dot{V}O_2$ serves as a good proxy indicator of AEE, although only 25% of the variance is explained.

In 104 white children studied in either Vermont or Alabama, TEE was significantly influenced by season (P = 0.03; ≈0.42 MJ/d higher in spring than in fall), sex (P = 0.04; ≈0.42 MJ/d higher in boys), and geographic location (P = 0.05; ≈0.42 MJ/d higher in Vermont), after adjustment for fat mass and fat-free mass (8). The significant effect of sex on TEE was explained through a sex effect on REE, whereas the influence of season and geographic location on TEE were explained through their effects on AEE (8). In all children, after adjustment for fat mass, fat-free mass, and season, there was no effect of sex, but there was a significant effect of ethnicity (P < 0.01) on TEE (8). The significant effect of ethnicity on TEE was explained by significantly lower adjusted values in Guatemalan children, whereas values for white, Mohawk, and African American children were similar (8). The significant effect of ethnicity on TEE was mediated through an effect on AEE. Because the DLW method only measures AEE, it is unclear whether this ethnic effect is due to less physical activity per se or to a lower cost of specific physical activities. Studies that examined ethnic differences in REE found mixed results. Some investigators reported no ethnic effect on REE in white, Mohawk, Pima, African American, and white children after adjusting for body composition (8–10). In contrast, REE was found to be 14% lower in African American than in white children after adjustment for age, sex, body weight, fat-free mass, and fat mass (11). A 4% lower REE was also found in normal-weight African American girls compared with white girls after adjustment for fat-free mass and bone density (12). These studies indicate that ethnicity may be an important determinant for REE in children; however, the effects of ethnicity remain uncertain.

In many developing countries, ≥30% of children under 5 y of age may be stunted (13). It is often assumed that stunted children have adapted to lower food availability and increased episodes of infection via changes in their body composition and a reduction of energy expenditure and, thus, a lowering of energy needs (14). Despite this general perception, only limited data on body composition and energy expenditure of children of short stature are available. We examined energy expenditure and body composition in 15 short-stature (height-for-age ≤ −1.5 SDs relative to the standards of the National Center for Health Statistics) and 15 normal-stature (height-for-age > −1.5 SDs) Guatemalan children aged 4–6 y (15). Fat mass and total body water were not significantly different in the 2 groups after adjustment for fat-free mass. The REE of the short-stature children was not significantly different from that of the normal-stature children, and the regression between resting metabolic rate and fat-free mass was also not significantly different between the 2 groups. TEE and the regression coefficients between TEE and fat-free mass were also not significantly different between the 2 groups. In a study of 10 Mexican boys, TEE and REE were not significantly different during mild *Giardia intestinalis* infestations and after treatment (16). Thus, after adjustment for fat-free mass, TEE and REE do not seem to be influenced by stunting or infection.

In recent years, the role of leptin in the regulation of energy expenditure has attracted special attention. Leptin is a product of the mouse *ob* gene and is a hormone secreted by adipocytes. In leptin-deficient animals, exogenous administration of leptin has been shown to normalize energy expenditure and food intake relative to that in nonobese animals (17), suggesting a role for leptin in the regulation of energy balance.

Two existing studies that investigated the association between serum leptin concentration and energy expenditure in children 5–10 y old provided contrasting results (18, 19). Salbe et al (19) examined the correlation between serum leptin concentration and components of energy expenditure in 123 5-y-old Pima Indians. They found a positive association between serum leptin concentration and TEE after adjustment for body weight and sex (r = 0.42; P < 0.0001). No significant correlation was found between serum leptin concentration and REE adjusted for fat-free mass, fat mass, and sex (r = 0.21, P = 0.2). Expressed as the ratio of TEE to REE, physical activity level was significantly and positively related to serum leptin concentration (r = 0.26, P = 0.003). In contrast, the study by Nagy et al (18) did not support the role of leptin in energy expenditure. This study was conducted in 47 African American and 29 white children aged 4.7–10.9 y. After adjustment for fat-free mass, fat mass, and sex, the serum leptin concentration was not related to TEE, REE, or AEE.

Despite similar technical procedures, different approaches were used to mathematically estimate AEE and statistically adjustment the findings. In Salbe et al's study (19), physical activity was calculated by the ratio of TEE to REE; different adjustments were used for evaluating energy expenditure components (TEE was adjusted for body weight and sex; REE was adjusted for fat-free mass, fat mass, and sex; and the ratio of TEE to REE was adjusted by percentage fat). In Nagy et al's study (18), AEE was estimated by the difference between TEE and REE after considering a 10% thermic effect of meals; all components of energy expenditure were adjusted for fat mass and fat-free mass, with sex and ethnicity as class variables. Because ethnicity was suggested in a previous study to not be an independent determinant for any measures of energy expenditure (20), it was not entered in the statistical models. In addition, homogeneity may also be a factor when comparing different results because the 2 studies examined different populations. Pima Indian children, subjects in Salbe et al's study, were more homogenous with respect to other variables; Nagy et al's study, however, included both African American and white children of differing ages.

ENERGY EXPENDITURE IN THE ETIOLOGY OF CHILDHOOD OBESITY

Some evidence suggests that reduced energy expenditure may be involved in the etiology of childhood obesity (21, 22). Roberts et al (21) examined the relation between TEE and weight gain in 18 infants born of both lean and obese mothers from birth to 1 y of age. TEE was measured at 3 mo of age by the DLW method for 7 consecutive days, before the infants became overweight; it was then related to weight changes during the first year of life. The infants who became overweight (n = 6) were significantly heavier than other infants at 9 and 12 mo of age, but not at other points of time. TEE was 20.7% lower in infants who later became overweight than in infants of normal weights. This result suggested that lowered TEE contributed to later weight gain in infants who became overweight.

Other cross-sectional studies in prepubertal children do not support the concept that reduced energy expenditure may be related to obesity. DeLany et al (23) did not observe any relations between TEE and body composition (fat mass and fat-free mass) in 46 children across a wide weight range. This group was divided into tertiles according to their weight. Fat mass was significantly different in the upper tertile, but fat-free mass was not significantly different across tertiles. Despite the differences in body weight between the highest and the lowest (14 kg) and intermediate (11 kg) weight tertiles, there were no significant differences in TEE across groups [from lowest to highest: 8.95 ± 0.42, 9.82 ± 0.42, and 9.74 ± 0.42 MJ/d ($\bar{x}$ ± SD)]. There were also no significant differences across tertiles in resting metabolic rate (5.35 ± 0.21, 5.31 ± 0.21, and 5.64 ± 0.21 MJ/d); AEE was also not significantly different across the tertiles (3.18 ± 0.33, 3.97 ± 0.33, and 3.39 ± 0.33 MJ/d). Similarly, Treuth et al (24) examined TEE by the DLW method, 24-h sedentary metabolic rate in a chamber, and resting metabolic rate in obese and nonobese girls. No components of energy expenditure were significantly different after adjustment for body composition (24). Thus, differences in fat mass were not related to variation in energy expenditure components.

Degree of parental obesity was examined as a potential determinant for energy expenditure in 74 prepubertal children (5.0 ± 0.9 y of age) of both lean and obese parents (25). Children were divided into 4 groups according to the status of the parents' obesity: both parents nonobese, obese father and nonobese mother, obese mother and nonobese father, or both parents obese. TEE and AEE were not significantly different among the 4 groups after adjustment for fat-free mass (25). Relative to that in children with 2 nonobese parents, REE adjusted for fat-free mass was ≈0.21 MJ/d lower in children when only the mother was obese or only the father was obese but not when both parents were obese. In addition, there were no significant correlations between components of energy expenditure in children and body fat in mothers or fathers.

Other studies of the role of energy expenditure in the etiology of obesity include studies in subjects with genetic conditions associated with obesity. For example, the DLW method has been used to examine energy expenditure and requirements in children with Down syndrome, who have a high prevalence of obesity (26). In this study, 13 prepubescent children with Down syndrome had lower resting metabolic rates than control subjects (n = 10) of similar body sizes; the resting metabolic rate was expressed as a percentage of the basal metabolic rate [87.8% ± 15.7% in subjects with Down syndrome and 109.8 ± 10.0% in control subjects ($\bar{x}$ ± SD; $P < 0.005$)]. However, no significant differences were found for TEE and non-REE (TEE/REE was 1.85 ± 0.23 in subjects with Down syndrome and 1.62 ± 0.16 in controls).

A major limitation of most studies that examined the role of energy expenditure in the etiology of obesity is their cross-sectional design. Because growth of individual components of body composition is likely to be a continuous process, longitudinal studies are needed to evaluate the rate of body fat change during the growing process. We therefore examined whether childhood energy expenditure and body composition in the previously cited study (25) influenced the rate of change in body fat relative to fat-free mass over a 4-y period (27). We used hierarchical linear modeling to define individual trajectories of change in body fat mass, and adjusted this for change in fat-free mass to account for overall individual growth.

The average rate of change in absolute fat mass was 0.89 ± 1.08 kg/y (range: −0.44 to 5.6). The rate of change in fat mass adjusted for fat-free mass was 0.08 ± 0.64 kg/y (range: −1.45 to 2.22), and was similar among children of 2 nonobese parents and children with 1 nonobese and 1 obese parent, but significantly higher in children with 2 obese parents (0.61 ± 0.87). The major determinants of change in fat mass adjusted for fat-free mass were sex (greater fat gain in girls), initial fatness, and parental fatness; none of the components of energy expenditure were inversely related to change in fat mass adjusted for fat-free mass (27). The major predictors of the individual change in fat mass relative to fat-free mass were sex (higher in girls than boys), initial fatness, and parental fatness (27).

Other preobese models that have been used to study the potential role of energy expenditure on the etiology of obesity include examination of ethnic groups at higher risk of obesity (eg, Mohawk Indians and African Americans). In Mohawk children in upstate New York, the prevalence of obesity has been estimated as 44% (2). We showed previously that TEE was actually 8.5% higher in Mohawk children than in white children living in Vermont because of a 37% higher AEE in the Mohawk children (28). African American children had a 14% lower REE than white children, after adjustment for age, sex, weight, fat-free mass, and fat mass (11). In girls aged 6–16 y, a lower REE was also found in African Americans than in whites, after adjustment for both body weight and lean body mass (29). In Birmingham, AL, the prevalence of obesity in African American children is almost twice that in white children (3). We examined energy expenditure components and body composition in healthy prepubertal white (17 girls and 22 boys) and African American (29 girls and 30 boys) children (20). There were no significant effects of ethnicity on TEE, REE, or AEE after body composition was adjusted for.

Collectively, the findings presented above show that there are discrepant findings regarding the role of energy expenditure in the etiology of obesity in children. This could be explained by several additional factors. For example, differences or changes in energy expenditure, energy intake, or both could occur at distinct critical periods of development (such as in early infancy or adolescence) and may thus result in energy imbalance. In addition, there could be individual differences and susceptibility to the effect of altered energy expenditure on the regulation of energy balance as shown in studies like those of Bouchard et al (30, 31) in which twins were challenged with under- or overfeeding. Thus, the effect of energy expenditure on the etiology of obesity could vary among different subgroups of the population (eg, boys compared with girls or different ethnic groups) and could also have differential effects within individuals at different stages of development. It is conceivable that susceptible individuals fail to compensate for periodic fluctuations in energy expenditure. Also, although a 14-d measure of energy expenditure by using the DLW method is considered a long-term measure, this time period is actually short when compared with the time scale for the development of childhood obesity, which could also be a slow and gradual process. For example, in our previously cited longitudinal study (27) comparing children of 2 obese parents and children of 2 nonobese parents, the difference in the rate of change in fat mass relative to fat-free mass was <1 kg fat/y, or <3 g excess fat gain/d. This is equivalent to a continual daily energy imbalance of 0.11 MJ (≈2% of total daily energy flux). From a methodologic standpoint, even the most sophisticated of current techniques would be unable to identify this energy imbalance as a defect in energy expenditure components (or as an excess in energy intake relative to needs).

ROLE OF AEE IN THE ETIOLOGY OF OBESITY

Because AEE is the most variable component in daily energy expenditure, it plays a key role in the regulation of energy balance (32). However, only a few studies have examined the effect of a physical activity intervention on daily energy expenditure in children. In a group of obese girls (n = 11) participating in a school-based, low-volume strength training program for 5 mo (20-min sessions, 3 times/wk), TEE did not significantly change from before (8.57 ± 1.27 MJ/d) to after (8.32 ± 1.30 MJ/d) training after adjustment for fat-free mass or body weight (33). AEE also remained unchanged with training after similar adjustments (33). Because the physical activity intervention was a low-volume training program, it is possible that a higher-volume, more intense strength training program may alter energy expenditure.

Aside from the role of intensity of physical activity in energy expenditure, data obtained from 101 prepubertal children (34) suggest that the time devoted to physical activity may have a more important influence on energy regulation than the daily energy cost of physical activity. After fat-free mass, sex, and age were adjusted for, body fat mass was significantly and inversely related to physical activity in hours per week derived by questionnaire ($r = -0.3$), but not to AEE over 14 d derived from the DLW method (34). Similarly, in 49 8–11-y-old girls, self-reported number of hours of physical activity at high intensity was significantly related to blood lipid concentrations, whereas AEE measured by the DLW method was not (35). Collectively, these findings support the notion that qualitative aspects of physical activity that are not measured by the DLW method (ie, duration and frequency of physical activity) may be more important than AEE in the regulation of energy balance and health. Thus, thorough characterization of physical activity using a variety of quantitative and qualitative tools is essential.

Whereas many social and behavioral factors determine physical activity habits, some studies have implicated ethnicity as a determinant of exercise patterns, with African American and other ethnic minorities being less active than whites (36). According to the 1990 Youth Risk Behavior Survey (36), female African American students (grades 9–12) were the least likely to be vigorously active ≥3 times/wk. We have shown that the relation between $\dot{V}O_2$max and AEE was significant in white children ($r^2 = 0.18$; $P < 0.05$), but not significant ($r^2 = 0.066$, $P = 0.143$) in African American children. In addition, AEE values were not significantly different in African American and white children, but $\dot{V}O_2$max was lower in African American children (37). These data suggest that white children participated in activities of higher intensities.

USE OF THE DOUBLY LABELED WATER METHOD FOR ASSESSMENT OF PHYSICAL ACTIVITY METHODS IN CHILDREN

Physical activity is a broadly used term, and its heterogenous nature makes it extremely difficult to characterize and quantify. Physical activity can be defined as any physical movement that is a result of skeletal muscle contraction. Physical activity is often measured by energy cost, but this may not be appropriate because the benefits and health effects of physical activities using a high rate of energy expenditure (eg, running at a certain intensity) compared with a low rate of energy expenditure (eg, strength training) may not be related to the energy cost of the physical activity. Thus, because different aspects of physical activity may have different effects on health outcome, the quantification and description of physical activity should probably consider all aspects, including the following: *1*) type and purpose of physical activity (eg, recreational or obligatory, aerobic or anaerobic, or occupational), *2*) intensity (strenuousness), *3*) efficiency, *4*) duration (time), *5*) frequency (ie, times per week), and *6*) specific energy cost of the activity performed.

The combination of the DLW method (to measure TEE) and indirect calorimetry (to measure REE) can be used to estimate AEE by difference. Thus, the major advantage of this approach is the quantification of AEE under free-living conditions over extended time periods. However, the technique does not describe physical activity pattern, nor does it differentiate between different types of physical activity (eg, playing outside at a low intensity for 2 h compared with riding a bike for 30 min).

Several studies have used this approach to measure AEE in children under free-living conditions (25, 38, 39). These studies show that the energy expended in physical activity is ≈1.67 MJ/d in young children but is highly variable. This low level of AEE is consistent with several studies showing that children spend only a small fraction of their active time in high intensity activities (40, 41). Thus, although children often appear to be very active, the combined energy cost of these activities is not that high. In addition, AEE is only weakly related to fat-free mass (r = 0.32) and body weight (r = 0.28–0.29). These observations may seem counterintuitive because the energy cost of physical activity is usually thought to be a function of body weight (at least for weight-bearing exercise). However, the physical activity being measured combines all physical activities throughout the day (including exercise, spontaneous and obligatory physical movement) and is a combination of weight-bearing and non-weight-bearing activities.

Although there are several physical activity questionnaires for children (42, 43), only 1 published study has compared activity data by questionnaire in children with AEE by the DLW method (34). In 101 white children, physical activity in hours per week with use of the Kriska questionnaire (44) was not related to free-living AEE. The reason for this disparity is likely that the 2 instruments being compared actually measure different things. The activity index derived by the questionnaire is simply a reflection of time devoted to recreational activities. It is not dependent on factors such as intensity or efficiency. AEE measured by the DLW method reflects time and intensity of all physical activities and also has a built-in efficiency factor. Thus, physical activity behavior by questionnaire may not be synonymous with AEE. This is because time spent in different physical activities may not be representative of the daily energy expended in physical activity by children. Thus, the future development of physical activity instruments may need to consider quantitative as well as qualitative information on physical activity.

One technique that has been rigorously examined in children is the heart rate method (38). Some of the limitations of this technique are that it is time consuming, it requires close cooperation from the subjects, and there is some concern that heart rate may vary independently of energy expenditure. However, a study by Livingstone et al (38) in children suggests that the heart rate method may yield accurate group assessments of physical activity. Heart rate was measured continuously for 2–3 d in 36 children (7–15 y of age) and compared with TEE measured over 14 d by the DLW method. The heart rate method relies on the individual laboratory calibration of the relation between heart rate and oxygen uptake, as measured during standardized activities in the laboratory. Also a "FLEX" value for heart rate is identified that represents the heart rate unique to each person that distinguishes rest from exercise. When heart rate falls below the "FLEX" value, energy expenditure is assumed to be equivalent to REE. In the entire group, TEE was estimated to within ±20% from heart rate data when compared with the DLW method, and the correlation between the 2 techniques was 0.91 (38).

One of the most basic approaches to measuring physical activity involves direct observation and analysis of motion using motion counters and accelerometers. The basis of the technique is that a transducer records any body acceleration and a charge is produced that is proportional to force of movement. In studies in children there are reasonable correlations ($r \approx 0.7$–0.9) between registered counts and energy expenditure during specific activities performed under laboratory conditions (45, 46). However, no published studies in prepubertal children have compared accelerometry counts with AEE by the DLW method in free-living conditions. One of the major limitations of the older accelerometers is that movement registration is limited to recording of vertical movement only. Thus, three-dimensional accelerometers have been designed to record movement in 3 dimensions (47, 48). These devices compare well with energy expenditure during specified laboratory tests and free-living energy expenditure in adults (47), but have yet to be examined in children.

SUMMARY

Recent advances in measurement of energy expenditure with use of the DLW method have provided much information relating to various aspects of research in energy metabolism in young children. The DLW method has enabled measurement of TEE and AEE in a wide array of different subgroups of the population. The biological determinants of TEE include body composition, and both fat mass and fat-free mass positively influence TEE. Environmental factors such as seasonality and geographic location have also been shown to influence TEE through their effects on AEE, the most variable component of energy flux in children. A few studies have examined the relation between plasma leptin concentrations and energy expenditure in young children. These studies have also found mixed results. Either plasma leptin has different effects on energy expenditure in different subgroups of the population, or inappropriate data normalization has led to spurious conclusions. Cross-sectional and longitudinal data in prepubertal children do not support the concept that energy expenditure is involved in the etiology of obesity—in contrast with other data in infants and Pima Indian adults. It is conceivable that differences in energy expenditure may have different effects on energy balance at different stages of the maturation process. Alternatively, different conclusions can be drawn depending on how data are handled; extreme caution is warranted when energy expenditure data are adjusted to compare subjects of different body sizes because spurious findings are possible (49–51). Further longitudinal studies throughout growth and development in different at-risk subgroups of the population are required. Only a few intervention studies have examined the effects of exercise on energy flux in children, and these have had mixed findings; this is an area requiring further investigation to identify the optimal exercise program for improving energy balance and metabolic health in children. There are some data to suggest that qualitative aspects of physical activity (eg, duration and intensity) may be more important than the absolute cost of AEE in the maintenance of energy balance and metabolic health. Finally, the DLW technique has been used to examine the validity of various methods for assessing physical activity. These studies generally show that existing methods do not accurately reflect individual physical activity levels, and further methodologic development of physical activity tools should be a high priority for research.

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