Energy intake and energy expenditure in prepubertal males with asthma


ABSTRACT: This study aimed to measure energy intake (EI) and total energy expenditure (TEE) of asthmatic males and to validate diet history as a method of estimating their energy requirements.

EI was assessed by dietary history and TEE by the heart-rate monitoring method in a group of asthmatic and nonasthmatic males. Resting energy expenditure (REE) adjusted for fat-free mass was higher in asthmatic than in nonasthmatic males (5.037 vs. 4.839 MJ·day⁻¹, p<0.05). TEE (9.3±1.8 versus 8.4±1.4 MJ·day⁻¹, respectively; p=NS) and EI (9.2±1.5 versus 8.8±1.5 MJ·day⁻¹, respectively, p=NS) were not statistically different in asthmatic and nonasthmatic males. EI was not statistically different from TEE in both groups of males. Asthmatic males showed an acceptable agreement between TEE and EI at the individual level (range of agreement: -3.2 to 2.9 MJ·day⁻¹), and a good agreement at the group level (95% confidence interval for the bias, - 1.1 to 0.8 MJ·day⁻¹).

Males with mild-to-moderate asthma have a higher metabolic activity per unit fat-free mass than nonasthmatic males. This increased requirement is apparently well compensated by an adequate energy intake. Diet history is a suitable method for estimating energy requirements in males with mild-to-moderate asthma.


Material and methods

Study subjects

Forth nine prepubertal males participated in the study. Twenty three males had asthma as defined by the American Thoracic Society, and a positive response to a standard questionnaire [12, 13]. Twenty six healthy males were enrolled as controls. The control children were recruited from the nonobese children who voluntarily enrolled in a study designed to assess the relationship between energy expenditure, physical activity and adiposity, which was in progress at the same time in the Department of Paediatrics of the University of Verona [14]. Obesity was defined as weight >20% in excess of ideal body weight for height, age and sex. Medical history, a physical examination, and a negative response to a standard questionnaire allowed us...
to reasonably exclude health problems in the subjects. Asthmatic children were recruited from the paediatric outpatient clinic of the Department of Paediatrics of the University Hospital in Verona, Italy. Following a preliminary study, the subjects were followed on an ambulatory basis for 3 days. Medical history and a physical examination did not reveal any health problems other than asthma. They had mild-to-moderate asthma as established by the current National Heart, Lung and Blood Institute guidelines for severity [13] and by the regular treatment necessary to obtain good asthma control [9]. No child with concomitant eczema was admitted to the study. All the asthmatic patients were on their prophylactic medication with cromoglycate and/or inhaled steroids. Pubertal stage was assessed according to TANNER [15] by evaluating pubic hair and genitalia development. All subjects were graded at Tanner score 1 for sexual maturity. Informed consent was obtained from the subjects and their parents. The protocol was approved by the Ethics Committee of the University Hospital of Verona, Italy.

Physical characteristics

Anthropometric measurements (weight, height and skinfold thickness) were taken by the same investigator (M. Zaffanello). Height was measured to the nearest 0.5 cm on a standardized, wall-mounted height board. Weight was determined to the nearest 0.1 kg on a standard physician's beam scale with the child dressed only in light underwear and without shoes. The body mass index was calculated by dividing weight (kg) by height squared (m²).

A Harpenden skinfold calliper (CMS Weighing Equipment Ltd, London, UK) was used to measure skinfolds at the biceps, triceps, supra iliac and sub-scapular sites. Body fat as a percentage of body weight was calculated from the sum of the four skinfolds [16]. Fat-free mass (FFM) was obtained as the difference between body weight and fat mass.

Study design

The asthmatic children were seen in the outpatient clinic 1 week before energy intake and energy expenditure measurements. Pulmonary function studies were performed by means of a Compact Vitalograph Spirometer (Vitalograph Ltd, Buckingham, UK), and bronchial hyperresponsiveness was evaluated by methacholine challenge [17]. Their current treatment with cromolyn or inhaled steroid was kept unchanged. However, β2-adrenergic agonists were not allowed during the 24 h preceding the resting energy expenditure (REE) measurement and the treadmill test performed for the assessment of the relationship between HR and oxygen consumption V'O₂. During the days preceding the REE measurement and the treadmill test, the subjects were put on an unrestricted diet; the day before they were requested to avoid any intense physical activity. The subjects arrived by car at the Department of Paediatrics at 07:30 h after a 12 h fast. After 30 min of rest, during which the subjects were lying down on a hospital bed in a comfortable, temperature-controlled environment (22–24°C), continuous respiratory exchange measurements were taken by indirect calorimeter to measure REE, as previously described [18]. Then, a light breakfast was served, and approximately 2.5 h later, a treadmill test (intermittent incremental) was performed to evaluate energy expenditure [19]. Peak expiratory flow rate (PEFR) was measured before, during and after the exercise test in order to check for any bronchial obstruction.

Energy intake

Typical weekly meal and snack intakes were obtained from an interview with the mothers and subjects [20]. Information regarding portion size, food preparation and place of consumption was also recorded. A dietician (M. Golinelli) consulted with the family to obtain a careful record of foods and portions consumed that had not been mentioned. As an aid to determining the amount of food consumed, pictures of different food items were presented, and cups, glasses, spoons and food shapes of different portion sizes were used. Food intake at school was assessed by reviewing a typical week's menu with the children and asking them to indicate which and how much of these meals that they usually ate. Meals, snacks, portion sizes and frequency of eating were recorded on a standard form. All interviews were conducted by the same dietician. Food energy values were calculated from tables of food composition set by the Italian Institute of Nutrition [21] using a computerized database and analysis programme (Contrali, Dietsystem, Milan, Italy).

Energy expenditure calculation from heart rate

The relationship between HR and V'O₂ was established for each subject following the treadmill test. To determine the individual HR-V'O₂ regression line, a physical exercise test was performed, during which V'O₂ and HR were simultaneously measured under standardized conditions, as previously described [19]. Briefly, V'O₂ and carbon dioxide production (V'CO₂) were measured with a standard open circuit method. Sedentary values of V'O₂ and HR were obtained while the subject was in a lying, sitting, and standing position. The sedentary energy expenditure was defined as the mean of the energy expenditure value for the three resting activities, as calculated from V'O₂ values. Five calibration points for the nonresting activities were made during walking and running on the treadmill (PV Rolling belt, Beta, Milan, Italy) at a speed of 2, 3, 5, 6, 7 km·h⁻¹ respectively. Measurements of V'O₂ and HR were made during the last 3 min of each walking or running period, thus in a steady-state condition. The energy expenditure was calculated from V'O₂ by means of the simplified Weir formula, which assigns 20.5 kJ·L⁻¹ of O₂ consumed [22].

A critical heart rate, the FLEX HR, was determined for each child as previously described [19]. FLEX HR is an individually predetermined HR cut-off point that can be used to discriminate between resting and exercise HR in free-living conditions. It was calculated as the arithmetic mean between the highest HR obtained for the resting activities (lying, sitting and standing positions) and the lowest HR obtained during the lightest imposed exercise. Above the FLEX value, the calibration curve used to estimate energy expenditure corresponded to that of the active period, and below the FLEX, the sedentary energy
The energy expenditure value was used to determine the energy expenditure during inactivity. The TEE was calculated by summing the sleeping energy expenditure (SEE), sedentary energy expenditure and activity energy expenditure. Sleeping energy expenditure was assessed by multiplying the sleeping time (min) by REE (kJ·min⁻¹). Sedentary energy expenditure was calculated by multiplying the nonsleeping time (daily time under FLEX HR) by SEE. Nonsedentary energy expenditure was calculated by determining $V'O_2$ for each HR greater than the FLEX HR from each individual calibration line.

Heart rate monitoring

HR was recorded continuously for 3–4 days (usually including two weekdays and one weekend day) during normal daily activities under free-living conditions, as previously described [19]. Briefly, the HR transmitter was attached to the chest with an elastic band. Parents were instructed to attach the band with the electrodes and the HR transmitter to the chest and to turn the recorder on the wrist on and off. The pulse was recorded at 1 min intervals continuously up to 16 h. Information was retrieved daily at the subject’s home by the same operator (M. Zaffanello) via an interface unit and a personal computer. HR monitoring started in the morning immediately after waking and continued until bedtime. The sleeping time was assessed by recording the time between going to bed and waking up, recorded by the subjects and/or their parents in a notebook. Whenever the HR daily recording was incomplete (in $\leq$15% of cases), the subjects were asked to repeat the monitoring for an additional day. At the end of the study, complete 3-day HR measurements were obtained from each child.

TEE measurement was performed in 16 asthmatic males. However, only data for 15 subjects are reported because one subject developed eczema on the skin under the HR transmitter and so had to interrupt the HR recording and was eliminated from the study.

Analysis

The results are expressed as means and standard deviation. The Mann-Whitney test was used to compare anthropometric characteristics, REE, TEE, and EI in asthmatic and nonasthmatic males. ANCOVA, using FFM as the covariate, was used to calculate REE adjusted for FFM [19]. Friedman’s test was performed to compare reported EI and TEE calculated from HR monitoring. The agreement between estimates of TEE and EI was assessed using the method of BLAND and ALTMAN [23]. Correlations between REE and respiratory function variables were determined using Pearson’s product-moment correlation.

Results

Physical and respiratory characteristics

Physical characteristics of asthmatic and nonasthmatic children are shown in table 1. The anthropometric values were not significantly different between the two groups of subjects. The data on pulmonary function and results of methacholine challenge in asthmatic subjects are shown in table 2. Only four patients in our study population required occasional treatment with $\beta_2$-agonists more than once a week.

Energy intake

Mean energy intake assessed by diet history was not statistically different between the asthmatic and nonasthmatic subjects (9.17±1.54 versus 8.83±1.50 MJ·day⁻¹ (p=NS)). In both groups, EI was not statistically different to TEE (fig. 1). In the asthmatic subjects, the level of agreement between the two measurements was acceptable at the individual level: mean difference -0.1 MJ·day⁻¹ (range of agreement (mean difference±1.96 $\sigma$) -3.2 to 2.9 MJ·day⁻¹) (fig. 2), and good agreement at the group level (95% confidence interval of agreement = -1.05 to 0.85 MJ·day⁻¹) (fig. 3).

Table 1. – Physical characteristics of asthmatic and non-asthmatic subjects

<table>
<thead>
<tr>
<th></th>
<th>Asthmatic (n=23)</th>
<th>Nonasthmatic (n=26)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs</td>
<td>9.2±0.9</td>
<td>9.2±1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Weight kg</td>
<td>32.6±5.4</td>
<td>33.7±6.6</td>
<td>NS</td>
</tr>
<tr>
<td>Height cm</td>
<td>136±6</td>
<td>135±6</td>
<td>NS</td>
</tr>
<tr>
<td>BMI kg·m⁻²</td>
<td>17.7±3.6</td>
<td>18.7±3.4</td>
<td>NS</td>
</tr>
<tr>
<td>FM %</td>
<td>18.2±4.6</td>
<td>20.6±8.7</td>
<td>NS</td>
</tr>
<tr>
<td>FM kg</td>
<td>6.1±2.3</td>
<td>7.4±4.4</td>
<td>NS</td>
</tr>
<tr>
<td>FFM kg</td>
<td>20.5±3.4</td>
<td>26.3±3.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are shown as mean±SD. BMI: body mass index; FM: fat mass. FFM: fat-free mass. NS: nonsignificant.

Table 2. – Pulmonary function parameters of asthmatic subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Asthmatic (%)</th>
<th>Nonasthmatic (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 % pred</td>
<td>86±7</td>
<td>83±18</td>
<td>NS</td>
</tr>
<tr>
<td>FEV1/VC</td>
<td>0.79±0.08</td>
<td>0.76±0.07</td>
<td>NS</td>
</tr>
<tr>
<td>PEF % pred</td>
<td>69±15</td>
<td>69±15</td>
<td>NS</td>
</tr>
<tr>
<td>PEF25–75% % pred</td>
<td>1.6±1.3</td>
<td>1.6±1.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are shown as mean±SD and expressed as a percentage of the value predicted for patient height and age, and the provocative dose of methacholine causing a 20% fall in forced expiratory volume in one second (FEV1; PC20; FEF25–75%: forced mid-expiratory flow. PEF: peak expiratory flow. VC: vital capacity.

![Fig. 1. – Energy intake (○) assessed by diet history and total energy expenditure (■) measured by heart rate monitoring in asthmatic and nonasthmatic children. Data are shown as mean±SE.](image-url)
In the asthmatic group, the relationship between REE adjusted for FFM and forced expiratory volume in one second (FEV1) (% predicted), FEV1/vital capacity (VC), peak expiratory flow (PEF; % pred), and forced mid-expiratory flow (FEF25–75%; % pred) was not significant (table 4). The provocative concentration causing a 20% fall in FEV1 (PC20) showed a negative, significant correlation with REE adjusted for FFM (r=-0.32; p<0.05).

**Total daily energy expenditure.** Resting HR, FLEX HR, daytime HR and peak V'O2 were not significantly different between the two groups (table 5). HR at 50% peak V'O2 was significantly lower (p<0.001) in the group of subjects with asthma than in the control group, whereas HR at 70% peak V'O2 was not statistically different in the two groups. The time spent on moderate or vigorous activity, (for example the time spent with an HR ranging from 50–70% of peak V'O2 and an HR>70% peak V'O2, respectively), was higher (p<0.02) in males with asthma than in the control group.

TEE expressed as an absolute value was not significantly different between subjects with or without asthma (9.3±1.8 MJ·day⁻¹ versus 8.4±1.4 MJ·day⁻¹, p=NS). When expressed per kg of FFM (352±43 versus 320±39 kJ·kg⁻¹·day⁻¹, p<0.01) or per kg of body weight (286±41 versus 250±33 kJ·kg⁻¹·kg⁻¹·day⁻¹, p<0.01), TEE was significantly higher in subjects with asthma than in nonasthmatic subjects.

The energy expenditure during physical activity (including thermogenesis), for example TEE-REE, expressed as an absolute value, was higher in the asthmatic than in the nonasthmatic group (4.5±1.6 versus 3.0±1.1 MJ·day⁻¹, p<0.05). Expressed per kg of FFM (165±46 versus 144±39 kJ·kg⁻¹·FMM·day⁻¹, p=NS) or per kg of body weight (138±38 versus 115±30 kJ·kg⁻¹·kg⁻¹·day⁻¹, p=NS), it was not statistically different between the asthmatic or nonasthmatic subjects.

The activity index, TEE/REE ratio, was not statistically different between the two groups (asthmatic versus nonasthmatic: 1.89±0.28 versus 1.78±0.22, p=NS).

The subjects with asthma spent significantly more time sleeping than the nonasthmatic subjects did (fig. 3); therefore, the energy expenditure for sleeping was significantly higher in the former (fig. 4). The time devoted to sedentary activities (time spent with HR below FLEX HR) and to nonsedentary activities (time spent with HR above FLEX HR) was not statistically different in the two groups of children. The energy expenditure for resting and nonresting activities was not statistically different between the two groups.

### Table 4. – Relationship between resting energy expenditure (REE) adjusted for fat-free mass and respiratory variables in asthmatic subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Asthmatic</th>
<th>Nonasthmatic</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEFbasal</td>
<td>50.3±7.6</td>
<td>50.3±7.6</td>
<td></td>
</tr>
<tr>
<td>FEF25–75%</td>
<td>0.05</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>PEFbasal methacholine</td>
<td>-0.32</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

**Energy expenditure**

**Postabsorptive resting energy expenditure.** Expressed as an absolute value, REE was not statistically different between the two groups of subjects (table 3). REE adjusted for FFM, *i.e.* the metabolic active tissue, using FFM as the covariate, was higher in the asthmatic than in the nonasthmatic children (p<0.05).

In the asthmatic group, the relationship between REE adjusted for FFM and forced expiratory volume in one second (FEV1) (% predicted), FEV1/vital capacity (VC), peak expiratory flow (PEF; % pred), and forced mid-expiratory flow (FEF25–75%; % pred) was not significant (table 4). The provocative concentration causing a 20% fall in FEV1 (PC20) showed a negative, significant correlation with REE adjusted for FFM (r=-0.32; p<0.05).

### Table 3. – Postabsorptive resting energy expenditure (REE) in asthmatic and nonasthmatic subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Asthmatic</th>
<th>Nonasthmatic</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>REE kJ·day⁻¹</td>
<td>5037</td>
<td>4839</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>REE adjusted for FFM</td>
<td>5045±447</td>
<td>4832±381</td>
<td>ns</td>
</tr>
<tr>
<td>RQ</td>
<td>0.88±0.04</td>
<td>0.88±0.03</td>
<td>ns</td>
</tr>
</tbody>
</table>

Values are shown as mean±SD and are expressed as an absolute value (µg·day⁻¹) and adjusted for fat-free mass (FFM) by ANCOVA, using FFM as a covariate and respiratory quotient (RQ).
ties (above FLEX heart rate)) in children with and without asthma.

Fig. 3. – Time spent on different activities ( : sleeping; : sedentary activities (below FLEX heart rate); : nonsedentary activities (above FLEX heart rate)) in children with and without asthma.

Fig. 4. – Energy spent during different activities ( : sleeping; : sedentary activities (below FLEX heart rate); : nonsedentary activities (above FLEX heart rate)) in children with and without asthma.

Dietary recommendations are based on energy requirements, i.e. TEE [1]. Subjects suffering from chronic diseases such as obesity, cystic fibrosis, chronic obstructive pulmonary disease, cerebral palsy, heart diseases, etc. may have different energy requirements than those of the age- and sex-matched healthy population [3–7]. Asthma is the most common respiratory disease in children, with a mean prevalence of ~10% in Italy [24]. This is the first study to investigate TEE in asthmatic children. The results show that the TEE of males suffering from mild-to-moderate asthma are not significantly different from those of nonasthmatic males. However, males with mild-to-moderate asthma, receiving conventional inhaled treatment, spend more energy per unit FFM than nonasthmatic males. This is mainly due to REE, the main component of TEE, since more energy per unit FFM than nonasthmatic males. This is mainly due to REE, the main component of TEE, since energy expenditure during activity (+ thermogenesis), i.e. TEE - REE, expressed per kg of FFM, is not significantly different in the two groups of subjects. The mean value of REE adjusted for FFM was significantly higher in the asthmatic subjects, and is in agreement with the data reported by ZEITLIN et al. [2].

Several factors might contribute to explaining the higher metabolic activity of FFM in males with asthma. Drugs, in particular β-adrenergic agonists, affect energy expenditure by means of their multisystemic actions. They may potentially play a role in increasing REE in asthmatic children who use these medications, although a short-duration (60–90 min after administration) thermogenic effect of these drugs has been demonstrated [25]. To avoid this effect, β-adrenergic agonists were not allowed during the 24 h preceding the measurement of the postabsorptive metabolic rate and the treadmill test for the assessment of the HR/V̇O₂ relationship. Another contributing factor could be the inflammatory response associated with asthma. The evidence of bronchial hyperresponsiveness in our children, as shown by the positive response to the methacholine challenge, indicates bronchial inflammation. In fact, we found a negative correlation between methacholine PC20 and REE adjusted for FFM. In this sample of subjects, the inflammatory level in the airways was not specifically investigated with bronchial washing, biopsy or evaluation of cells in induced sputum. Eczema, which is another inflammatory process that potentially may contribute to increasing energy expenditure [2], was not found in any subject. Finally, the energy cost of breathing might potentially affect REE in asthmatic children, as suggested by the inverse relationship between PC20 and V̇O₂ (V̇O₂ in asthmatic subjects, and is in agreement with the data reported by ZEITLIN et al. [2].

Several factors might contribute to explaining the higher metabolic activity of FFM in males with asthma. Drugs, in particular β-adrenergic agonists, affect energy expenditure by means of their multisystemic actions. They may potentially play a role in increasing REE in asthmatic children who use these medications, although a short-duration (60–90 min after administration) thermogenic effect of these drugs has been demonstrated [25]. To avoid this effect, β-adrenergic agonists were not allowed during the 24 h preceding the measurement of the postabsorptive metabolic rate and the treadmill test for the assessment of the HR/V̇O₂ relationship. Another contributing factor could be the inflammatory response associated with asthma. The evidence of bronchial hyperresponsiveness in our children, as shown by the positive response to the methacholine challenge, indicates bronchial inflammation. In fact, we found a negative correlation between methacholine PC20 and REE adjusted for FFM. In this sample of subjects, the inflammatory level in the airways was not specifically investigated with bronchial washing, biopsy or evaluation of cells in induced sputum. Eczema, which is another inflammatory process that potentially may contribute to increasing energy expenditure [2], was not found in any subject. Finally, the energy cost of breathing might potentially affect REE in asthmatic children, as suggested by the inverse relationship between PC20 and V̇O₂ (V̇O₂ in asthmatic subjects, and is in agreement with the data reported by ZEITLIN et al. [2].


discussion

Dietary recommendations are based on energy requirements, i.e. TEE [1]. Subjects suffering from chronic diseases such as obesity, cystic fibrosis, chronic obstructive pulmonary disease, cerebral palsy, heart diseases, etc. may have different energy requirements than those of the age-
modest in children with mild or moderate asthma [26]. No direct measurements of the oxygen cost of breathing were taken in this study to verify this hypothesis.

The subjects with asthma showed patterns of activity and a mean level of activity that were not significantly different from those of the control group. In fact, the energy spent above the postabsorptive metabolic rate (TEE - REE), including the energy expenditure devoted to physical activity, postprandial thermogenesis and the metabolic cost of growth (assumed to be negligible and within our error of measurement in 9 yr old children), was not statistically different between the two groups, when it was expressed per unit of FFM or body weight. In addition, the time and energy expenditure devoted to sedentary and nonsedentary activities were not significantly different in the two groups of subjects. These data are confirmed by the TEE/REE ratio, a gross index of activity, which was not significantly different in the two groups.

Some of the results of this study (HR at 50% peak VO₂, sleeping time, time spent in moderate and vigorous activity) suggest that asthmatic subjects may be more physically fit than nonasthmatic subjects. This could be the result of the encouragement to perform physical activity given to the asthmatic children who are in a good respiratory condition. In fact, asthmatic subjects seem to be slightly (although not significantly) more physically active than nonasthmatic subjects. This result is supported by the finding that EI assessed on the basis of the diet history method was not significantly different from TEE and from the Recommended Dietary Allowances for age [27] in both groups. In other words, the food intake of the asthmatic subjects appeared to be adequate for their mean daily energy requirements, as suggested by the results of the Bandini LG, Schoeller DA, Cyr HN, Dietz WH. Validity of reported energy intake in obese and non-obese adolescents. Am J Clin Nutr 1990; 52: 421–425.


17. Peroni DG, Boner AL, Vallone G, Antolini I, Warner JO. Effective allergen avoidance at high altitude reduces

In conclusion, males with mild-to-moderate asthma have a higher metabolic activity per unit fat-free mass than nonasthmatic males. This increased requirement is apparently well compensated for by an adequate energy intake. No evidence of a negative energy balance in children with mild-to-moderate asthma was found. Diet history may be used to estimate energy requirements in children with mild-to-moderate asthma.

References


17. Peroni DG, Boner AL, Vallone G, Antolini I, Warner JO. Effective allergen avoidance at high altitude reduces


