Accuracy of Predictive Equations for Estimating Resting Energy Expenditure in Obese Adolescents

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Objective To compare resting energy expenditure (REE) measured by indirect calorimetry with REE predicted using different equations in obese adolescents.

Study design We recruited 264 obese patients (body mass index ranging from 30.0-70.0 kg/m^2) between 14 and 18 years of age. Data were obtained comparing measured and predicted REE derived from published equations for normal weight and obese adolescents. The average differences between measured and predicted REE, as well as the accuracy at ±10% level, were evaluated.

Results Evaluating the mean REE in 109 males (1938 ± 271 kcal/d) and 155 females (2569 ± 459 kcal/d), we found that the Lazzer equation in males had the smallest difference between measured and predicted REE; in females the Henry-1, Food and Agriculture Organization/World Health Organization/United Nations University, Schmelze, and Lazzer equations were the most accurate. The prediction accuracy was considered adequate within ±10%.

Conclusions REE predictive equations developed in obese patients and for specific age groups are more suitable than those for the general population. Inaccuracy of predicted REE could affect dietary prescription appropriateness and, consequently, dietary compliance in this age group. *(J Pediatr 2015;166:1390-6)*.

During the last 3 decades, the prevalence of overweight and obesity has precipitously increased in European adolescents.[1] An accurate assessment of energy requirements is needed to improve individual clinical evaluation in order to plan an appropriate dietary intervention. Indeed, in obese subjects, an accurate prediction of resting energy expenditure (REE) is of utmost importance for an adequate dietary prescription. It provides the basic background to calculate a desired level of energy restriction. REE is defined as the amount of energy spent at rest in a fasted state at a thermoneutral condition. Life processes such as respiration, circulation, cellular metabolism, and the maintenance of body temperature are sustained by energy expenditure. In sedentary normal weight individuals, REE represents more than 70% of total energy expenditure.

In clinical practice, indirect calorimetry is considered the gold standard method for REE measurement. Although this method has a high clinical usefulness, the equipment costs, the time spent on accomplishing a correct measurement, and the need to hire trained personnel who are able to run the test have prevented the widespread use of indirect calorimetry for individual patients, particularly in critically ill adults.[2,3] Consequently, predictive equations are used in clinical nutrition practice and, also, on very young patients. Previous studies have described the use of predictive equation in obese adolescents in different populations in the US as well as in Asia.[4,5] Some authors have tried to address the problem by developing equations for REE prediction in adolescents on the basis of anthropometric and body composition measures.[6,7] However, some of these equations have been developed in groups of normal-weight[8-13] or overweight subjects[12-19] appearing to be also influenced by ethnicity.[18-22] These may not be accurate when applied to some patient groups (ie, obese youngsters). The aim of our study was to compare REE calculated by different predictive equations (**Table I**; available at www.jpeds.com) with REE measured by indirect calorimetry in obese adolescents.

Methods

Caucasian Southern Italian severely obese patients were recruited for the study: 109 males (age 16.5 ± 1.3; weight 125 ± 26 kg; height 173 ± 6 cm) and 155 females (age 16.2 ± 1.5; weight 102 ± 23 kg; height 162 ± 7 cm) aged 14.0-18.0 years, BMI ranging from 30.0-70.0 kg/m^2. Subjects who had previously participated in weight loss programs, affected by overt metabolic and/or endocrine diseases, and/or regularly taking medications or using any drug known to affect energy metabolism were excluded. All females were in post menarche age. Measurements were performed at stable body weight period starting

BIA	Bioimpedance analysis
BIAS	Mean percentage error between predictive equation and measured value
BMI	Body mass index
REE	Resting energy expenditure
RMSE	Root mean squared error

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6 months before the initiation of any weight reduction program. All measurements were made in the early morning on fasting patients who attended the clinical nutrition laboratory. All data were collected in young patients consecutively undergoing a routine clinical protocol in the outpatient obesity clinic at Federico II University Hospital in Naples from 2004-2010. The study was carried out according to the Declaration of Helsinki, and its protocol was approved by the local ethic committee.

Weight was measured to the nearest 0.1 kg using a platform beam scale and height to the nearest 0.5 cm using a stadiometer (Seca 709; Seca, Hamburg Germany). BMI was calculated as weight (kg) divided by the square of height (m). Bioimpedance analysis (BIA) was performed at 50 kHz (Human Im Plus II, DS Medica) at room temperature of 22°C-25°C. Measurements were carried out on the nondominant side of the body in the postabsorptive state, after being in the supine position for 20 minutes; the subjects voided prior to measurements.[23] The measured BIA variables were resistance and reactance[24]; fat free mass and fat mass were estimated using the prediction equations developed by Kushner.[25]

REE was measured by indirect calorimetry using a canopy system (V max29; Sensormedics, Anaheim, California) at an ambient temperature of 23°C-25°C. The instrument was checked by burning ethanol, and oxygen and carbon dioxide analyzers were calibrated using nitrogen and standardized gases (mixtures of nitrogen, carbon dioxide, and oxygen). Subjects were fasting (12-14 hours) and lying down on a bed in a quiet environment. Females were in the postmenstrual phase. After a 15-minute adaptation period, oxygen consumption and carbon dioxide production were determined for 45 minutes. The inter-day coefficient of variation (as determined in 6 obese individuals on subsequent days) was always less than 3%. Energy expenditure was then calculated employing the abbreviated Weir formula, neglecting protein oxidation.[23]

Equations most used for REE prediction in children and adolescents were selected and divided into samples: predictive equation for normal-weight subjects (Henry-1, Henry-2, Schofield, and Food and Agriculture Organization/World Health Organization/United Nations University), both normal-weight and obese subjects (Molnar and Muller), and for only obese subjects (Tverskaya, Derumeaux-Burel, Schmelze, and Lazzer) (Table I); we used all these equations for all our samples, independent of their weight status.

Statistical Analyses

One-way ANOVA was used to compare data between sexes. Accuracy of the predictive equations at individual and population levels were calculated. The mean percentage difference between the predicted and measured REE, respectively, was considered a measure of accuracy at group levels.[26,27]

The percentage of patients having a predicted REE within ±10% of the measured REE was considered a measure of accuracy at an individual level. A measured REE predicted value within 90% and 110% was considered an accurate prediction, a measured REE value lower than 90% was classified as an under-prediction, and a measured REE value higher than 110% was classified as an over-prediction. The root mean squared error (RMSE) was used to better indicate the prediction obtained with this model in our data set. The statistical analysis for REE comparison of measured and prediction equations was performed taking into account Bland and Altman plots to estimate limits of agreement.

Results

Table II shows anthropometric data, body composition, and REE measurements in the 2 sexes and divided into BMI groups: <45 kg/m^2 and >45 kg/m^2. Weight and height were lower ($P < .001$) in females than in males, and BMI SDS was significantly lower ($P < .001$) in males than in females. Body composition was significantly different between the 2 sexes in all samples, and there were no significant differences between BMI groups. Measured REE was higher ($P < .001$) in males than in females, and this result was confirmed also between BMI groups. Measured REE adjusted for fat free mass was similar in boys and girls.

REE data are reported as mean and SD of predictive REE and difference predicted-measured REE (kcal/d); the percentage of accurate predictions, under-predictions, and over-predictions; and the mean percentage error between predictive equation and measured value (bias) and RMSE (kcal/d; Tables I and III). In males, mean difference between predicted and measured REE varied widely from −528 kcal/d (Muller equation) to +315 kcal/d (Henry-2 equation; Table III). Lazzer and Derumeax equations had the lowest RMSE (280 and 315, respectively kcal/d) and the smallest bias (-0.9% -0.8%; Table III).

The percentage of accurate predictions varied between equations from 64.7% (Lazzer equation) to 22.0% (Muller equation; Table III). The bias for equations varied from −19.9% (Muller equation) to +13.6% (Henry-2 equation), and RMSE varied from 280 kcal/d (Lazzer equation) to 541 kcal/d (Muller equation; Table III).

Mean differences between predicted and measured REE ranged from −301 kcal/d (Muller equation) to −19 kcal/d (FAO/WHO/UNU equation; Table I) for females. The FAO/WHO/UNU equation had the lowest RMSE (207 kcal/d) and the lowest bias (+0.9%; Table I). The percentage of accurate predictions varied between equations from 61.9% (Lazzer equation) to 26.5% (Muller equation; Table I). The bias for equations varied from −12.7% (Muller equation) to +0.9% (FAO/WHO/UNU equation), and the RMSE varied from 207 kcal/d (FAO equation) to 346 kcal/d (Muller equation; Table I).

The number of under-predictions within ±10% range varied from 77.1% (Muller equation) to 4.5% (Schofield equation) in males and from 66.8% (Muller equation) to 20.6% (FAO equation) in females (Tables I and III). The number of over-prediction varied from 53.2% (Henry-2 equation) to 0.0% (Lazzer equation) in males and from 24.8% (Derumeaux equation) to 0% (Lazzer equation) in females (Tables I and III). Moreover, the maximum negative error was −40.0%

Table II. Evaluation of REE with 10 different predictive equations in 109 obese male adolescents based on differences predicted-measured, percentage of accuracy, bias, and RMSE

REE predictive equations	Difference predicted-measured, kcal/d	SD	Accurate prediction*, %	Under-prediction†, %	Over-prediction‡, %	BIAs§, %	Maximum negative error, %	Maximum positive error, %	RMSE, kcal/d
Equation for normal weight subjects									
Henry-1	118	354	51.4	13.8	34.8	6.0	−20.0	42.2	299
Henry-2	315	378	42.2	4.6	53.2	13.6	−14.8	50.4	388
Schofield	301	369	45.0	4.5	50.5	13.1	−14.9	50.8	376
FAO	272	368	46.8	5.0	48.2	12.0	−15.8	49.3	361
Equation for both normal weight and obese subjects									
Molnar	−191	332	45.0	43.1	11.9	−6.1	−28.9	31.1	315
Muller	−528	357	22.0	77.1	0.9	−19.9	−40.0	21.5	541
Equation for obese subjects									
Tverskaya	−180	355	44.0	44.0	12.0	−5.3	−29.5	35.9	325
Lazzer	−62	337	64.7	35.3	0.0	−0.9	−25.0	38.9	280
Derumeaux	−76	376	48.4	39.4	12.2	−0.8	−37.2	44.3	315
Schmelze	−266	350	44.0	47.7	8.3	−8.4	−31.9	36.0	350

Average REE measured with indirect calorimetry = 2569 ± 459 kcal/d.

*The percentage of patients predicted by this predictive equation within 10% of the measured value.

†The percentage of patients predicted by this predictive equation <10% of the measured value.

‡The percentage of patients predicted by this predictive equation >10% of the measured value.

§Mean percentage error between predictive equations and measured value.

(Muller equation) in males and −36.2% (Teverskaya equation) in females, whereas the maximum positive error was 50.8% (Schofield equation) and 67.9% (Derumeaux equation) in males and females, respectively (**Tables I-III**).

In this study group, few equations obtained an accuracy within ±10% range for more than 50% of the Lazzer and Henry-1 equations in males and Lazzer, FAO/WHO/UNU, Schmelze, Henry-1, and Henry 2 equations in females (**Table I**). The prediction of REE according to BMI subclasses showed that the accuracy decreased in adolescents with higher BMI (>45 kg/m^2) except for Schofield equation in females, the Molnar equation in males and females, and the Tverskaya, Lazzer, and Schmelze equations in males.

Bland-Altman plots of predicted-measured REE differences vs mean predicted-measured REE obtained with all equations are reported in **Figures 1** and **2**. There is a good agreement for most of the predictive equation except for the plots of Muller and Derumeaux-Burel equation in females, and Schmelze and Muller equation for males.

Table III. Evaluation of REE with 10 different predictive equations in 155 obese female adolescents based on differences predicted-measured, percentage of accuracy, bias, and RMSE

REE predictive equations	Difference predicted-measured, kcal/d	SD	Accurate prediction*, %	Under-prediction†, %	Over-prediction‡, %	BIAs§, %	Maximum negative error, %	Maximum positive error, %	RMSE, kcal/d
Equation for normal weight subjects									
Henry-1	−71	261	54.8	29.7	15.5	−2.7	−32.5	43.6	214
Henry-2	−150	269	0.0	80.5	19.5	−6.4	−32.8	32.0	250
Schofield	−212	273	34.2	56.8	9.0	−9.8	−35.2	28.0	288
FAO	−19	260	58.1	20.6	21.3	0.9	−24.9	45.6	207
Equation for both normal weight and obese subjects									
Molnar	−241	269	34.8	58.7	6.5	−10.6	−26.2	29.5	298
Muller	−301	294	26.5	65.8	7.7	−12.7	−42.5	50.6	346
Equation for obese subjects									
Tverskaya	−205	284	41.3	51.0	7.7	−8.5	−36.2	47.2	279
Lazzer	−68	264	61.9	38.1	0.0	−1.8	−30.2	40.7	217
Derumeaux	−145	298	43.1	32.1	24.8	−4.7	−33.3	67.9	257
Schmelze	−80	260	55.5	31.0	13.5	−2.2	−31.6	41.3	216

Average REE measured with indirect calorimetry = 2018 ± 385 kcal/d.

*The percentage of patients predicted by this predictive equation within 10% of the measured value.

†The percentage of patients predicted by this predictive equation <10% of the measured value.

‡The percentage of patients predicted by this predictive equation >10% of the measured value.

§Mean percentage error between predictive equations and measured value.

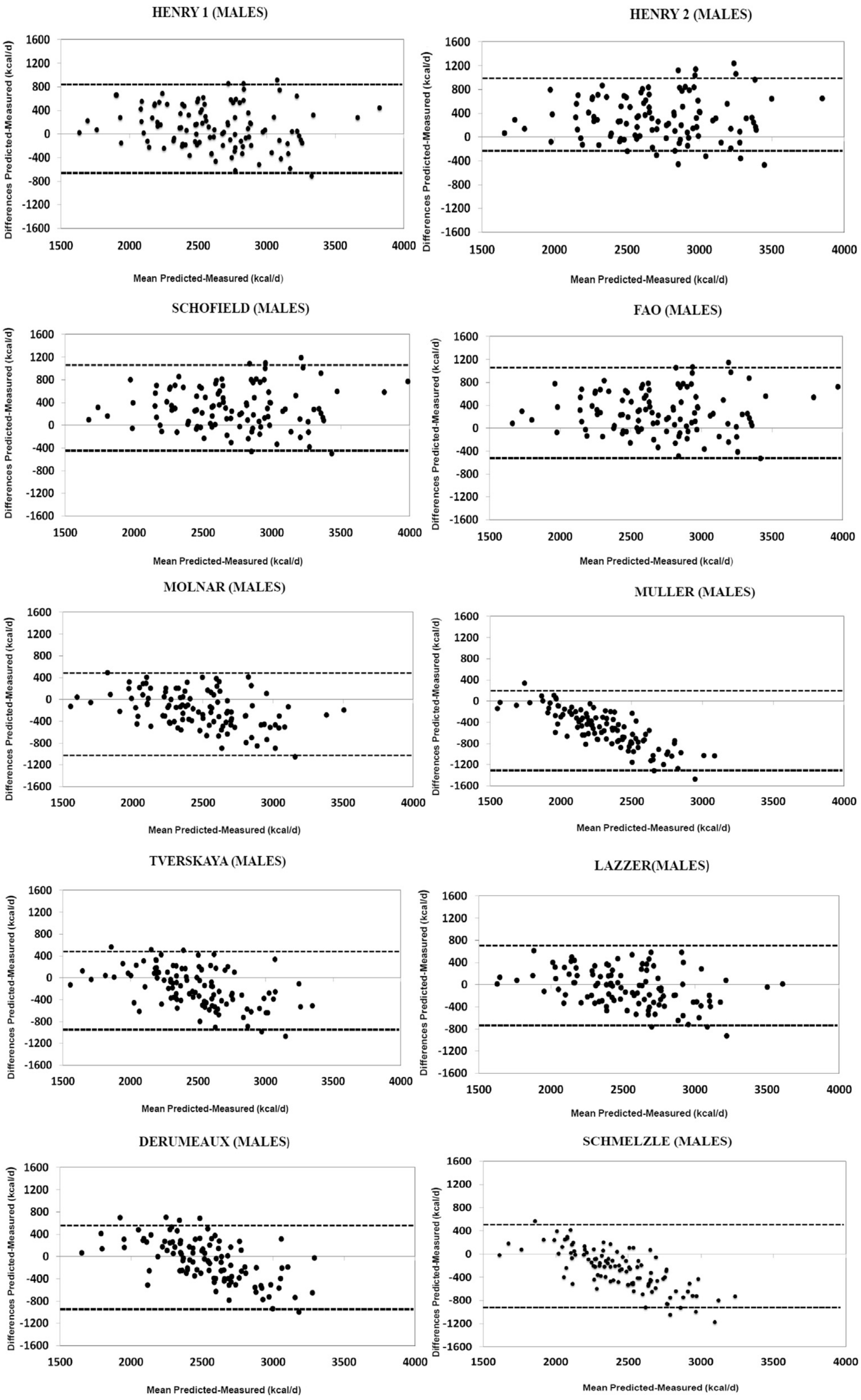

Figure 1. Bland-Altman plot of differences in REE measured using the indirect calorimeter and calculated using 10 different predictive equations in 264 male obese adolescents. The *dotted lines* represent 2 SDs from the mean (limits of agreement).

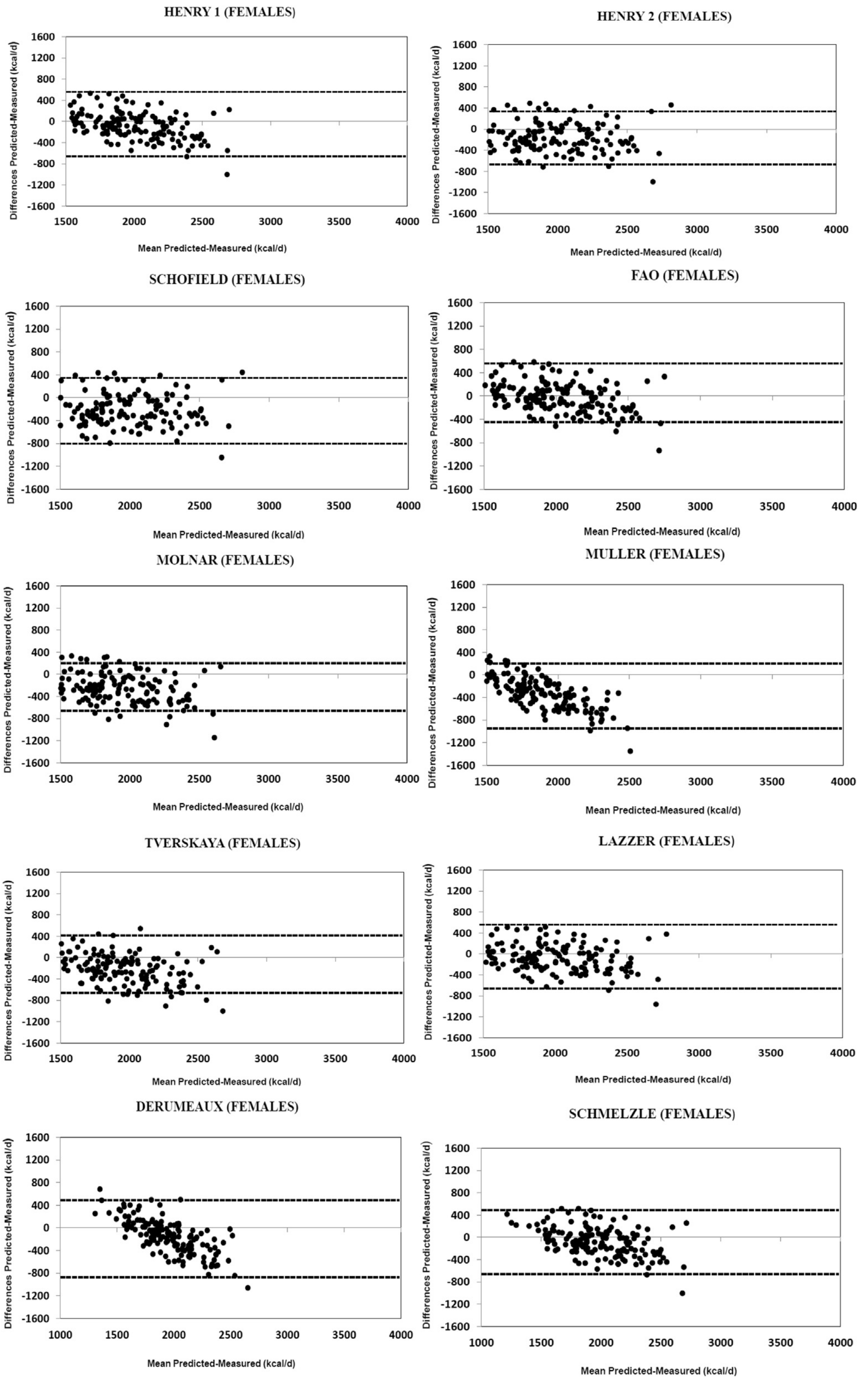

Figure 2. Bland-Altman plot of differences in REE measured using the indirect calorimeter and calculated using 10 different predictive equations in 264 female obese adolescents. The *dotted lines* represent 2 SDs from the mean (limits of agreement).

Discussion

This study shows a wide range of differences between predicted and measured REE in Italian adolescents aged 14.0-18.0 years who are severely obese. Our results suggest that the Lazzer equation both in males and females and the Schmelz and Henry-1 equations in females only are the most suitable equations for REE prediction (ie, the differences between predicted and measured REE was less than 1%) among the published equations taken into consideration in this study, at least in this population of obese individuals. In the individual patient, accuracy (calculated as the number of subjects whose REE was predicted to be within ±10% of measured REE) did not reach 50% considering all predictive equations. In particular, the Lazzer equation reached 43% accuracy in females aged 14.0-18.0 years. In males, the Molnar, Muller, Teverskaya, and Schmelze equations mainly underestimated the REE; whereas Henry-2, FAO/WHO/UNU, and Schofield equations mainly overestimated the REE. In females, the Schofield, Molnar, Muller, and Tverskaya equations mainly underestimated REE. It also appears quite evident that usual predictive equations of REE are not suitable for predicting REE in obese individuals with BMI higher than 45 kg/m^2.[28]

Weijs et al[29] demonstrated in Dutch that in Holland, the Mifflin equation, previously applied to US population, is the most accurate for REE estimation in class I and II overweight and obese adults. Furthermore, this study suggests using FAO equation in overweight adults and Lazzer equation in obese subjects for REE prediction in normal weight adults. Hofsteenge et al[30] suggested that the Molnar equation, developed in Hungarian obese adolescents, was the most accurate REE predictive equation in overweight and obese adolescents.

Our study clearly demonstrates that age-specific equations derived from European populations and, in particular, the Lazzer equation developed in Italian obese adolescents, has the smallest predicted-measured differences for REE in Italian obese adolescents of both sexes. This study suggests that proper equations for young obese subjects are more suitable than those for the general population for REE prediction in clinical practice. On the other hand, the accuracy remains relatively low.

Accordingly, when the most accurate equation derived from a similar age and ethnic population is applied for REE prediction in young obese adolescents, it, nevertheless, has an estimation superior to 10% in more than one-half of the study group. This inaccuracy could contribute to the restricted compliance to dietary prescriptions based on unreliable REE predictive equations. Because the predictive equation for very severe obese patients lack accuracy, the evaluation of body composition should be encouraged in order to better understand the amounts of fat mass. A simple method, such as BIA, could be more frequently adopted because of its safety, and other methods, such as dual energy X-ray absorptiometry and double-labeled water, are not routinely used in clinical practice in adolescents. REE measurement carried out with indirect calorimetry could be useful to obtain more accurate information on energy requirements in the clinical evaluation of obese adolescents. ■

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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Cerebrospinal Fluid Protein Values of Premature Infants

Bauer CH, New MI, Miller JM. J Pediatr 1965;66:1017-22

Fifty years ago in *The Journal*, Bauer et al reported cerebrospinal fluid (CSF) protein levels among 71 preterm infants, 39 “with indications” for lumbar puncture (LP) and 32 control infants “without indications” for LP. Protein content was quantified using a turbidimetric method with sulfosalicylic acid. The authors found that premature infants have elevated protein CSF content compared with full-term infants and adults, with mean protein content of 143 mg/dL and 155 mg/dL for the LP-indicated and control groups, respectively. However, this paper also casts doubt on the diagnostic or prognostic value of elevated CSF protein levels in the premature newborn infant because there was no significant difference between values obtained in the presence and absence of neurologic indications for the LP.

Today, the authors’ conclusions remain relevant and generally accurate. The average CSF protein content for premature infants ranges from 115-162 mg/dL,[1,2] depending on birth weight and chronological age. As Bauer et al demonstrated in subjects with serial LPs, it was recently confirmed that CSF protein levels decrease with advancing postnatal age.[3] Elevated CSF protein is associated with bacterial meningitis, although CSF protein levels are highly variable and have poor positive predictive value, as the authors correctly noted in 1965.

Bauer et al further sought to analyze CSF protein levels in relationship to IQ at age 3 to 4 years. Of 71 initial subjects, 13 were seen for follow-up evaluations. The authors acknowledge that with so few subjects seen at follow-up, meaningful statistical analyses were not possible. The authors also note their study “exemplifies the difficulty of pursuing any follow-up study—difficulty in encouraging patients to return,” which similarly remains a challenge for researchers today.

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Table I. Predictive equations for REE in children and adolescents

Author	N	Sex	Age range	Predictive equation for REE
Equation for normal weight subjects				
Henry-1	195	M	10-15 y	kJ/d: 66.9 Wt + 2876
		F		kJ/d: 47.9 Wt + 3230
Henry-2	10 552	M	10-18 y	kcal/d: 18.4 Wt + 581
		F		kcal/d: 11.1 Wt + 761
Schofield	1309	M	10-18 y	MJ/d: 0.068 Wt + 0.574 Htm + 2.157
		F		MJ/d: 0.035 Wt + 1.948 Htm + 0.837
FAO/WHO/UNU		M		kcal/d: 17.5 Wt + 651
		F		kcal/d: 12.2 Wt + 746
Equation for both normal weight and obese subjects				
Molnar	371	M	10-16 y	kJ/d: 50.9 Wt + 25.3 Htcm − 50.3 Age + 26.9
		F		kJ/d: 51.2 Wt + 24.5 Htcm − 207.5 Age + 1629.8
Muller	243	T	5-17 y	MJ/d: 0.02606 Wt + 0.04129 Htcm + 0.311 Sex − 0.08369 Age − 0.808
Equation for obese subjects				
Tverskaya	110	T	10-18 y	kcal/d: 775 + 28.4 FFM + 3.3 FM − 37 Age + 82 Sex
Derumeaux-Burel	752	M	3-18 y	MJ/d: 0.1096 FFM + 2.8862
		F		MJ/d: 0.1371 FFM − 0.1644 Age + 3.3647
Schmelzle	82	M	4-15 y	kcal/d: 6.6 Wt + 13.1 Htcm − 794
		F		kcal/d: 11.9 Wt + 0.84 Htcm + 579
Lazzer	574	T	7-18 y	kJ/d: 68.39 FFM + 55.19 FM + 909.12 Sex − 107.48 Age + 3631.23

F, female; *FAO/WHO/UNU*, Food and Agriculture Organization/World Health Organization/United Nations University; *FAT*, fat mass; *FFM*, fat free mass; *Htcm*, height in cm; *Htm*, height in m; *M*, male; *N*, number of subjects; *T*, total (male and female); *Wt*, weight.

Sex (M = 1, F = 0).