Accurate Estimation of Energy Requirements of Young Patients

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ABSTRACT

The provision of optimal nutritional care is based on accurate estimations of patients' resting energy expenditure. The latter can be calculated with the use of predictive equations or measured with indirect calorimetry (IC). Owing to their ease of use, mathematical equations have largely replaced IC in clinical practice. This article examines the limitations and predictive inaccuracy of commonly used equations in pediatrics, which may contribute to the provision of poor nutritional care and directly affect patient outcomes. In addition, the role of IC is discussed and the physiology of nutrient metabolism, in terms of energy expenditure, is reviewed.

Key Words: energy requirements, FAO/WHO/UNU, indirect calorimetry, Oxford, predictive equations, Schofield

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In 1985, the Food and Agriculture Organization/World Health Organization/United Nations University (FAO/WHO/UNU) document ''Energy and Protein Requirements'' recommended that estimates of daily caloric requirements are based on measures of energy expenditure (1). The energy expended at rest, while lying awake at a thermoneutral environment after an overnight fast, is called basal metabolic rate (BMR). Indirect calorimetry (IC) is a clinical tool that measures resting energy expenditure (REE), which even though not identical, approximates BMR. The REE can then be used in the estimation of total energy expenditure when an individual's level of physical activity is known. The ability to measure REE is hence important in assessing an individual's caloric needs.

IC is not widely available in the clinical setting. It is costly, and its use requires training and expertise. For that reason, although it is believed to be the most accurate clinically available tool for the measurement of REE, its use has been largely replaced by predictive equations that estimate one's energy expenditure at rest. The first equations developed were based on IC-derived measurements that had been collected from a small number of primarily white subjects. During the 20th century, the predictive inaccuracy of these equations, particularly when applied to subjects with different characteristics (eg, lean vs overweight, healthy vs ill, those living in tropical vs cool climates), became apparent (2). To address this matter, newer equations (FAO/WHO/UNU (1), Schofield (3), and Oxford (2)) were developed.

For the purposes of the 1985 FAO/WHO/UNU report on energy and protein requirements, Schofield reviewed previously published studies reporting on the BMR of healthy children and adults. He synthesized the results of 114 different studies, including the study that had introduced the Harris-Benedict equation at the beginning of the 20th century (1,3). Schofield data included a total of 7173 BMR measurements. These data were subsequently used for the development of the FAO/WHO/UNU equations, as well as the Schofield equations (called Schofield [weight] and Schofield [weight and height]). The generalizability of these equations has since been found to be limited (4–6), particularly because the studies used in their development did not represent all ethnicities (Europeans and North Americans formed the majority, whereas the representation of individuals from the tropics was poor). In addition, 47% of the measurements were made in Italians, who were subsequently found to have a higher BMR per kilogram of body weight than average, leading to overestimations of BMR when the equations were applied to non-Italian individuals (7). In an effort to address some of these limitations, Henry (2) created the Oxford equations in 2005. These equations were based on 10,552 measurements and excluded the Italian cohort used by Schofield. In addition, measurements from 4018 individuals living in the tropics were included. Presently, clinicians primarily use the FAO/WHO/UNU, Schofield, and Oxford equations in their practice. These equations are summarized in Table 1 (1–3).

Considering their aforementioned limitations, as well as the fact that equations are designed to predict the mean REE of a population, rather than that of individuals, we aimed at reviewing the literature addressing the predictive accuracy of these and other disease-specific equations in the pediatric setting. Specifically, the goals of this article were to discuss the performance of predictive equations in various clinical settings, draw attention to the areas of pediatric clinical care wherein the predictive accuracy of these equations has not been elucidated, and review the pathophysiology of energy metabolism as it relates to energy expenditure. Finally, the role of IC in the nutritional monitoring of children with different health issues is discussed.

IC VERSUS PREDICTIVE EQUATIONS TO ESTIMATE REE OF HEALTHY SUBJECTS

The accuracy and generalizability of the FAO/WHO/UNU and Schofield equations have been studied in healthy children of various ages and physical activity levels. Among other equations, Thomson et al (8) studied the predictive accuracy of the FAO/WHO/UNU and Schofield (weight, weight and height) and Harris-Benedict equations in 36 infants. The FAO/WHO/UNU was the most accurate equation studied; however, all of the equations overestimated the REE in this setting: FAO/WHO/UNU overestimated by 104% ± 14%; Schofield [weight] and Schofield [weight and height] overestimated by 107.5% ± 14% and 106% ± 11%, respectively, and

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TABLE 1. Summary of commonly used predictive equations

Name	Equation	
FAO/WHO/UNU (1)	BMR = 7.4 [wt (kg)] + 482 [ht(cm)] + 217	
	BMR = 12.1 [wt (kg)] + 499	
Schofield (weight and height) (3)	BMR = 8.4 [wt (kg)] + 4.7 [ht (cm)] + 200	
Schofield (weight) (3)	BMR = 13.4 [wt (kg)] + 693	
Oxford (2)	BMR = 0.255wt − 0.141	Males, 0–3 years
	BMR = 0.0937wt + 2.15	Males, 3–10 years
	BMR = 0.0769wt + 2.43	Males, 10–18 years
	BMR = 0.246wt − 0.0965	Females, 0–3 years
	BMR = 0.0842wt + 2.12	Females, 3–10 years
	BMR = 0.0465wt + 3.18	Females, 10–18 years

BMR = basal metabolic rate; ht = height; wt = weight; FAO/WHO/UNU = Food and Agriculture Organization/World Health Organization/United Nations University.

Harris-Benedict overestimated by 182% ± 63%. Finan et al (9) performed a similar study in a cohort of 113 prepubertal children. In this study, although the FAO/WHO/UNU equations performed better than the rest, with 99% of the estimates being within 200 kcal/day, none of the equations assessed accurately predicted energy requirements (9). The validity of predictive equations in moderately active adolescents was assessed by De Lorenzo et al (10). In this study the authors concluded that despite significant variability in the results, the Schofield equations could be used in clinical practice for moderately active 16- to 18-year-olds, because the mean estimated REE was within 1% of that measured. The FAO/WHO/UNU equations were not studied by De Lorenzo et al. Finally, Rodriguez et al (11) assessed the agreement between predictive equations and IC in a cohort of 59 normal weight children, ages 7.8 to 16.6 years. The Schofield [weight] equation performed best in that group, providing results within 300 kcal/day of that measured using IC. Further dividing the cohort based on sex revealed that the Schofield [weight and height] equation was better for boys and the FAO/WHO/UNU for girls. To summarize, the FAO/WHO/UNU equations appear to perform better than others in healthy children; however, they are not consistently accurate across all ages, sexes, and physical activity levels. The Oxford equations remain to be validated in healthy children.

FAILURE TO THRIVE AND EATING DISORDERS

Failure to thrive (FTT) indicates poor physical growth and primarily affects children <3 years of age (12,13). FTT may be secondary to suboptimal energy intake, insufficient nutrient absorption, or increased energy expenditure. Regardless of the cause, children with FTT usually have decreased muscle mass, which is associated with a decrease in BMR. The variability in the etiology of FTT may render predictive equations for BMR inaccurate, as discussed below.

Two studies have compared calculated and measured REE in the setting of FTT with similar results. Sentongo et al (14) assessed 45 children ages 0 to 3 years and Kaplan et al (15) studied 77 children ages 0.2 to 20.5 years. Sentongo et al showed that the FAO/WHO/UNU and Schofield equations estimated REE within 10% accuracy in less than half of the subjects studied and overall tended to underestimate the REE. Kaplan et al found that among the FAO/WHO/UNU, Schofield, and Harris-Benedict equations, the Schofield [weight and height] had the best predictive ability, which was, however, suboptimal because it estimated the REE to be within 20% of that measured. Underestimating the energy requirements of patients with FTT can have significant nutritional implications, such as failure to catch up weight gain, suboptimal linear growth, and potential negative future neurodevelopmental outcomes. The use of IC should be considered in the management of these children, particularly when established nutritional plans do not have the expected outcome in terms of weight gain.

Apart from FTT, Cuerda et al have assessed the accuracy of various equations in predicting the caloric requirements of patients with eating disorders in 2 similar studies (16,17). The intraclass correlation between equations studied (including FAO/WHO/UNU and Schofield [weight and height]) and IC results was poor (0.09–0.20), suggesting that the caloric needs of young, hospitalized girls with eating disorders cannot be accurately predicted. The authors concluded that IC is an important clinical tool to assist in the nutritional management of patients with eating disorders.

OBESITY

Childhood obesity is a growing epidemic. In 1981, 14% of children ages 15 to 19 years were overweight or obese (18); however, by 2009 to 2011 that number more than doubled, with 32% of Canadian children ages 5 to 17 being overweight or obese (*http://www.statcan.gc.ca/pub/82–625-x/2012001/article/11712-eng.pdf*). Children who are overweight or obese have different body composition compared with their healthy-weight peers. Apart from the excess adipose tissue, these patients also have increased muscle mass, which increases their REE. For that reason, predictive equations specific for overweight and obese subjects have been developed; their accuracy does not appear to be consistent, however, as discussed below and summarized in Table 2 (15,19–23).

McDuffie et al (19) examined the predictive ability of equations developed for healthy subjects (including FAO/WHO/UNU, Schofield [weight, weight and height]), as well as other equations developed specifically for obese individuals (Molnar-1 and Molnar-2, Tverskaya, and Maffers). In this study, which included 502 subjects between the ages of 6 and 11 years, not a single equation was found to accurately predict the BMR of most individuals. In response to these results, McDuffie et al (19) generated 4 new sex- and ethnicity-specific pediatric equations, which allowed for more accurate predictions. In a similar study of 102 subjects 3 to 18 years old, Tverskaya et al (20) showed that, of the equations assessed, the FAO/WHO/UNU was the most accurate predictor of energy requirements, especially in adolescents. Given the inaccuracies of the existing equations, Tverskaya et al (20) created a new equation to include weight, fat-free mass, fat mass, age, and height. It was found to predict requirements within 4% of that measured with IC. The equations derived by McDuffie et al (19) and Tverskaya et al (20) have not yet been validated in subsequent studies.

These results, along with the other studies summarized in Table 2, argue the need for pediatric-specific equations that take variables such as sex, ethnicity, puberty, and body composition into consideration. Until such equations are developed and/or validated, IC will remain the most accurate indicator of REE in these subjects.

END-STAGE LIVER DISEASE

Metabolism, energy expenditure, and body composition are altered in patients with end-stage liver disease (ESLD) (24). This is secondary to hepatocellular dysfunction, disease-related complications, and/or malnutrition with associated sarcopenia (25). Shepherd (26) studied 18 infants (mean age 0.44 ± 0.29 years) listed for transplant for ESLD secondary to biliary atresia and showed that the FAO/WHO/UNU and Schofield equations underestimated the BMR by a staggering 30%. Considering the significant prevalence of malnutrition in ESLD (25) and the effects of nutritional status on long-term outcomes (27), IC should be used when available to assist in the nutritional care of these fragile patients. Many studies report

TABLE 2. Summary of predictive equations in obesity

Study	n; setting	Age, y	Predictive equations studied	Results
McDuffie et al (19)	502; boys (n = 191) and girls (n = 311)	6–11	FAO/WHO/UNU	Systematic bias and/or magnitude bias in all equations in obese males and/or females
	Black and white		Schofield	
	37.6% normal weight		Harris-Benedict	
	10.9% overweight		Molnar-1	
	51.4% obese		Molnar-2	
			Tverskaya	
			Maffers	
Tverskaya et al (20)	110; healthy obese males (n = 50) and females (n = 60)	3–18	FAO/WHO/UNU	FAO/WHO/UNU was the best predictor of REE (2%)
			Harris-Benedict	Harris-Benedict underestimated in males by 9%–11%
			Ravussin	Remaining underestimated by 17%–22%
			Cunningham	
Klein et al (21)	58; Hispanic children with obesity	7–15	Schofield	Schofield underestimated the REE by 24%
			Harris-Benedict	Harris-Benedict underestimated by 51%;
			IOM-HW*	Remaining equations underestimated by 22%–23%
			IOM-OS**	
Kaplan et al (15)	102; 55% female, 19% obese	0.2–20.5	FAO/WHO/UNU	FAO/WHO/UNU was ± 10% of measured in 42% of subjects
			Schofield (weight)	Schofield [weight] was ± 10% of measured in 37% of subjects
			Schofield (weight/height)	Schofield (weight/height) was best predictor of REE (95% ± 17%)
			Harris-Benedict	Harris-Benedict was least accurate, overestimating REE in >40% of subjects
Maffeis et al (22)	130; prepubertal, healthy white children, divided as obese and nonobese	6–10	FAO/WHO/UNU	FAO/WHO/UNU overestimated the REE by ~13%
			Robertson and Reid	Robertson and Reid overestimated by ~1%
			Talbot method	Remaining equations overestimated by ~4%–12%
			Fleish	
			Mayo Clinic	
Henes et al (23)	80 obese subjects	7–8	FAO/WHO/UNU	Proportion of subjects in whom the equations predict the REE within ± 10% accuracy:
			Schofield-HW	FAO/WHO/UNU 40%
			Harris-Benedict	Schofield [weight and height] 51%
			IOM-OY (pEE)***	Harris-Benedict 65%
			IOM-OY	Remaining: 47%–61%
			IOM	
			Molnar	
			Mifflin	
			Lazzer	

FAO/WHO/UNU = Food and Agriculture Organization/World Health Organization/United Nations University; REE = resting energy expenditure.
*Institute of Medicine for Healthy-Weight Children.
**Institute of Medicine for Overweight and Obese Children.
***Institute of Medicine for Obese Youth.

improved outcomes after liver transplantation, when an optimal nutritional status is maintained before undergoing surgery (28,29). When taking care of patients in ESLD, clinicians should take into consideration complications such as maldigestion because of cholestasis, when estimating their patients' total caloric requirements.

INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease (IBD) is characterized by intestinal inflammation that waxes and wanes (30). Inflammation and associated fevers increase energy expenditure (31); conversely, malabsorption and anorexia contribute to loss of muscle mass, decreasing energy expenditure. Hill et al (32) studied the accuracy of the FAO/WHO/UNU and Oxford equations in 63 children with IBD at a mean age of 14 years. Neither equation performed well across all subjects because they all underestimated the patients' REE by 5% to 8%. Cormier et al (33) also assessed the FAO/WHO/UNU equation for children of similar age, who were receiving parenteral nutrition. In this setting the FAO/WHO/UNU equations performed well, with a correlation between measured and calculated energy expenditure of $r^2 = 0.73$. Finally, a study of 23 patients with inactive IBD (median age

14 years) demonstrated the inadequacy of the Schofield equation in predicting REE—the results of IC were 79% to 136% of what was calculated with the equations. Despite differences in the cohorts studied (hospitalized vs outpatients, in remission vs flaring), no equation was found to accurately predict energy requirements in all patients. Considering that IBD predominantly affects young teenagers and that energy requirements vary significantly depending on the severity of the clinical phenotype and the patients' body composition, IC is a useful tool to help guide the provision of calories for growth. Similarly to patients with ESLD, it is important to note that when estimating the TEE of patients with IBD, intestinal losses associated with malabsorption need to be taken into account because they lead to increased caloric demand.

CYSTIC FIBROSIS

Apart from muscle mass, the primary determinant of energy requirements in patients with cystic fibrosis (CF) is the severity of lung disease (34). A few studies have compared the results of IC with that of predictive equations in this setting, in a wide spectrum of ages and severity of pulmonary involvement (8,35,36). The results of these studies are similar. Thomson et al (8) showed that in infants with CF (0.4 ± 0.3 years) the FAO/WHO/UNU and Schofield equations underestimate energy requirements by 12% to 16%. In young children (ages 3.25–12.75 years) with CF and stable lung disease the Harris-Benedict and Cystic Fibrosis Consensus Committee equations are also inaccurate, because they underestimate energy expenditure by 13% and 8%, respectively (35). The same is true in teenagers and young girls with CF and pancreatic insufficiency (36). In summary, presently available predictive equations are not reliable in the setting of CF and tend to underestimate the energy needs of this population.

CEREBRAL PALSY

Children with cerebral palsy (CP) are generally at risk for malnutrition (37). The most common finding is decreased muscle mass (sarcopenia), the degree of which depends on the type of neurological injury (spastic vs hypotonic). Considering the direct effect of muscle mass on REE one would expect significant variations in the energy requirements of these patients. Bandini et al (38) assessed 13 children with CP and found that the FAO/WHO/UNU equation estimated the REE within 10% of that measured and was hence useful in determining daily energy needs for this population. In contrast, Dickerson et al (39) found that the mean REE of nonambulatory, neurologically impaired, tube-fed dependent patients was up to 26% lower than the estimate of the FAO/WHO/UNU equations. On the basis of these results, a new equation was developed; its accuracy in predicting REE remains to be validated. Overall there is a risk of overestimating the energy needs of patients with CP when using standard predictive equations. IC may assist in the nutritional management of these challenging patients until equations that include a measure of muscle mass are developed.

INTENSIVE CARE UNIT

Patients admitted to the pediatric intensive care unit are not homogeneous in terms of their underlying illness, medical history, and body composition. In addition, treatments provided in the intensive care unit can vary and have the potential to affect resting energy requirements (eg, paralytic agents). The equations studied in this setting are summarized in Table 3 (40–47). In general, predictive equations are often inaccurate owing to the wide variation in energy expenditure of patients in this setting. The American Society of Enteral and Parenteral Nutrition recommends the use of IC in the intensive care unit in a number of clinical settings (48). It is useful for patients with a body mass index <5th or >85th percentile, weight loss in excess of 10% while in the intensive care unit, in those with central nervous system trauma with dysautonomia or oncologic diagnoses, patients taking muscle relaxants or on ventilatory support for >7 days, and those who have been in the intensive care unit for >4 weeks (49). IC is also recommended for those "at risk for hypo- or hypermetabolism" and in cases of consistent failure to meet caloric goals (49).

NEONATAL INTENSIVE CARE/NEONATES

Guidelines of the Committee on Nutrition of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition suggest that, in addition to adequate protein intakes, healthy premature infants require between 110 and 135 $kcal \cdot kg^{-1} \cdot day^{-1}$ to grow (50). Preterm infants, however, often have a number of other comorbidities, which can directly affect their ability to feed and grow. Preterm infants, particularly very-low-birth-weight infants, are more likely to have an energy deficit as a result of one or more of the following: suboptimal calorie intake, low energy reserves, and/or increased energy requirements. Cai et al (51) compared the measured REE of 154 healthy newborns with weights between 2500 and 4000 g with that calculated using various equations, including the FAO/WHO/UNU, Schofield [weight], and Schofield [weight and height]. The predictive equations overestimated measured REE by approximately 12%. Apart from body composition, the REE of neonates may be affected by their environment, disease activity, and treatment (51), which can render predictive equations inaccurate and lead to suboptimal energy provision. Further research is needed to assess the predictive performance of equations in this setting.

CONGENITAL HEART DISEASE

Congenital heart disease may be associated with premature birth, increased cardiac function and/or work of breathing, as well as other congenital anomalies. These factors may increase the REE of infants, whose outcome is in part dependent on their nutritional status. The energy expenditure of 26 infants with single-ventricle physiology post-Fontan was measured and subsequently compared with the FAO/WHO/UNU equation results in a study by Mehta et al (40). Equations overestimated the REE of 53% of patients by 20% or more and hence, the correlation between the results of the FAO/WHO/UNU equation and that of IC was poor. Similar findings were reported by another study of 38 young patients with congenital heart disease, who had IC performed immediately pre- and 1-week postsurgical repair (52). The Schofield and Altman & Dittmer equations were used to predict REE in this study. In contrast, Avitzur et al (53) showed that the Schofield equation was accurate in predicting energy requirements in young children (<3 years of age) before and 5 days after the repair of their congenital heart disease (predicted REE only 3% lower than measured). The FAO/WHO/UNU equation performed poorly in this setting; the predicted REE was 16% to 20% lower than the measured. The differences in the results of the aforementioned studies may be secondary to variations in body composition, severity of heart disease, as well as other comorbidities of the patients investigated. Further research is needed to clarify the role of predictive equations in children with congenital heart disease.

DISCUSSION

Of all predictive equations reviewed, none provides consistently accurate results in any population. Despite pooling patients into disease-specific conditions, divided further by age, sex, and, in

TABLE 3. Predictive equations in the intensive care unit

Study	n; setting	Age	Predictive equations studied	Results
Hardy et al (41)	52; PICU Respiratory Surgery Trauma Cardiac Other	Median 4.5 y (range 0–22 y)	FAO/WHO/UNU Schofield equations Harris-Benedict Recommended dietary allowance	Poor predictive ability for all equations; proportion of subjects in whom the equations predict the REE within ± 10% accuracy: FAO/WHO/UNU 31% Schofield 36% Harris-Benedict 27%–36% Recommended dietary allowance 4%
Oosterveld et al (42)	46, PICU Sepsis Postoperative Trauma	0–18 y	Schofield equations	Performed accurately (within 1% of measured REE)
White et al (43)	100, PICU Trauma Infection Other	54 mo (SD 53 mo)	FAO/WHO/UNU Schofield equations Harris-Benedict Talbot method White equations	Apart from the Talbot and White equations, all others underestimated the REE by 61–86 kcal/day White equations performed better in infants >2 mo
Framson et al (44)	46, PICU Acute illness Trauma Elective	2 wk–17 y	Schofield equations White equations	Poor predictive ability of all equations Proportion of subjects in whom the equations predict the REE within ± 10% accuracy: Schofield 45% White 30%
De Wit et al (45)	21, CICU Postcardiac operation	Neonate–3 y	FAO/WHO/UNU Schofield equations White equations	Poor performance of all equations The difference between measured and calculated REE was 23% with the FAO/WHO/UNU equations 21% with the Schofield equations 36% with the White equations
Coss-Bu et al (46)	55, PICU Infection ARDS Postoperative	Mean 5.7 y (SD 5.9)	Harris-Benedict Talbot method	Poor predictive ability of both equations Applying a stress factor of 1.5 to these equations revealed a difference between measured and predicted REE of 24–48 kcal/day, respectively
Vasquez-Martinez et al (47)	43, PICU Trauma	Mean 4.2 y (SD 3.7)	FAO/WHO/UNU Schofield equations Harris-Benedict Maffeis Fleisch Kleiber Hunter Caldwell-Kennedy	No equation accurately predicts REE Caldwell-Kennedy equation was the most accurate, demonstrating a bias of 38 kcal/day and precision of ±179 kcal/day
Mehta et al (40)	14, PICU Cardiac	11.2 y (1.6 mo–32 y)	FAO/WHO/UNU Schofield equations Harris-Benedict	Risk of under- or overfeeding with all predictive equations studied

ARDS = acute respiratory distress syndrome; CICU = cardiac intensive care unit; FAO/WHO/UNU = Food and Agriculture Organization/World Health Organization/United Nations University; PICU = pediatric intensive care unit; REE = resting energy expenditure.

some instances, race, generalizations are difficult to make. The common denominator that limits the predictive ability of all equations is the lack of measures of body composition in the calculation. Weight and height are often included; however, neither of those measures reflects body composition. A clinically available tool that allows the determination of muscle mass is the mid-arm muscle circumference. It would be of value to assess the predictive ability of equations that include measures of muscle mass.

In children and adults the major determinant of REE is muscle mass (Fig. 1) (54–56). Conditions associated with changes in muscle mass have been shown to affect REE. An example of such conditions is anorexia nervosa. The REE of children with this eating disorder is significantly decreased and correlates with the degree of sarcopenia (30). Apart from changes in body composition, however, there are other factors associated with chronic illness that have an impact on a patient's REE. Such factors include inflammation, malignancies, neurological impairment, and medications.

Inflammation has been shown to increase the REE via increased expression of cytokines (57). Inflammation is believed to be the reason why patients with Crohn disease have a ''normal''

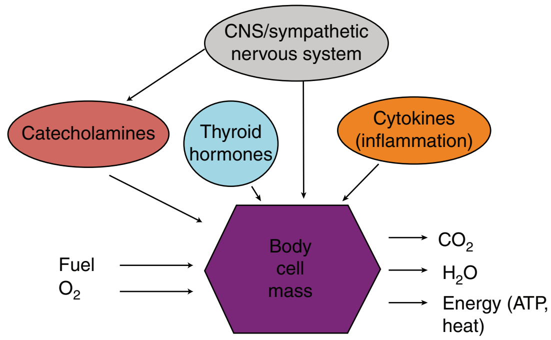

FIGURE 1. Determinants of resting energy expenditure. ATP = adenosine triphosphate.

measured REE, despite measurable decreases in muscle mass (58). Also, inflammation plays a role in patients with CF, whose energy expenditure is higher than what would be considered normal, despite a poor nutritional status (59). The fact that the REE is higher in these patients than in those with Crohn disease suggests that either the inflammatory response is more pronounced in CF or the energy cost of breathing contributes to this increase (60). The latter has been shown in patients with CF, who on average have an increased oxygen uptake per kilogram of lean body mass compared with healthy controls (61). Certain malignancies are also associated with changes in REE. Children with acute lymphoblastic leukemia have an increased REE, which correlates closely with the degree of tumor burden and promptly returns to normal with treatment (62). In contrast, patients with CP have a disproportionately low REE for their degree of sarcopenia (63). It has been postulated that central nervous system impairment may be contributing to this phenomenon (63). Sympathetic nerve activity has been shown to correlate with energy expenditure, and apart from its role in patients with neurological impairment it is also believed to contribute to ethnic variations in REE (63). Finally, medications can have a direct effect on energy expenditure, as shown with nifedipine, which increases the REE and paralytic agents, which are associated with decreases in REE (64,65).

To summarize, REE is reflective of muscle mass but, in the clinical setting, is also determined by disease states and medical interventions. General predictive equations (eg, the FAO/WHO/UNU and Harris equations) are inefficient in predicting REE in most cases because they are not disease specific and they are based on the assumption that weight is reflective of body composition, which does not always hold true.

Of the available equations, the Oxford equations may prove to be the most accurate and generalizable considering the number of BMR measurements used to design them and the wide spectrum of populations and geographical origins they represent. Their validity has not yet been assessed in different settings, and hence their accuracy remains to be determined. Other disease-specific equations will also need to be validated further to determine their predictive ability. Presently, the FAO/WHO/UNU equations perform better than the rest; however, they should be interpreted with caution in certain patient populations. IC should be used, when available, to determine the energy needs of populations at risk (especially those who are extremely young, frail, already malnourished and critically ill).

REFERENCES

1. Energy and protein requirements. Report of a joint FAO/WHO/UNU Expert Consultation. *World Health Organ Tech Rep Ser* 1985;724:1–206.
2. Henry CJ. Basal metabolic rate studies in humans: measurement and development of new equations. *Public Health Nutr* 2005;8 (7A):1133–52.
3. Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr* 1985;39 (suppl 1):5–41.
4. de Boer JO, van Es AJ, Voorrips LE, et al. Energy metabolism and requirements in different ethnic groups. *Eur J Clin Nutr* 1988; 42:983–97.
5. Hayter JE, Henry CJ. A re-examination of basal metabolic rate predictive equations: the importance of geographic origin of subjects in sample selection. *Eur J Clin Nutr* 1994;48:702–7.
6. Wong WW, Butte NF, Hergenroeder AC, et al. Are basal metabolic rate prediction equations appropriate for female children and adolescents? *J Appl Physiol 1985* 1996;81:2407–14.
7. Schofield C. An annotated bibliography of source material for basal metabolic rate data. *Hum Nutr Clin Nutr* 1985;39 (suppl 1): 42–91.
8. Thomson MA, Bucolo S, Quirk P, et al. Measured versus predicted resting energy expenditure in infants: a need for reappraisal. *J Pediatr* 1995;126:21–7.
9. Finan K, Larson DE, Goran MI. Cross-validation of prediction equations for resting energy expenditure in young, healthy children. *J Am Diet Assoc* 1997;97:140–5.
10. De Lorenzo A, Bertini I, Puijia A, et al. Comparison between measured and predicted resting metabolic rate in moderately active adolescents. *Acta Diabetol* 1999;36:141–5.
11. Rodriguez G, Moreno LA, Sarría A, et al. Resting energy expenditure in children and adolescents: agreement between calorimetry and prediction equations. *Clin Nutr* 2002;21:255–60.
12. Nangia S, Tiwari S. Failure to thrive. *Indian J Pediatr* 2013;80:585–9.
13. Cole SZ, Lanham JS. Failure to thrive: an update. *Am Fam Physician* 2011;83:829–34.
14. Sentongo TA, Tershakovec AM, Mascarenhas MR, et al. Resting energy expenditure and prediction equations in young children with failure to thrive. *J Pediatr* 2000;136:345–50.
15. Kaplan AS, Zemel BS, Neiswender KM, et al. Resting energy expenditure in clinical pediatrics: measured versus prediction equations. *J Pediatr* 1995;127:200–5.
16. Cuerda C, Ruiz A, Velasco C, et al. How accurate are predictive formulas calculating energy expenditure in adolescent patients with anorexia nervosa? *Clin Nutr* 2007;26:100–6.
17. Cuerda Compes MC, Ruiz Sancho A, Moreno Rengel C, et al. Study of energy expenditure in anorexia nervosa: agreement between indirect calorimatry and several equations. *Nutr Hosp* 2005;20:371–7.
18. Tremblay MS, Shields M, Laviolette M, et al. Fitness of Canadian children and youth: results from the 2007-2009 Canadian Health Measures Survey. *Health Rep* 2010;21:7–20.
19. McDuffie JR, Adler-Wailes DC, Elberg J, et al. Prediction equations for resting energy expenditure in overweight and normal-weight black and white children. *Am J Clin Nutr* 2004;80:365–73.
20. Tverskaya R, Rising R, Brown D, et al. Comparison of several equations and derivation of a new equation for calculating basal metabolic rate in obese children. *J Am Coll Nutr* 1998;17:333–6.
21. Klein CJ, Villavicencio SA, Schweitzer A, et al. Energy prediction equations are inadequate for obese Hispanic youth. *J Am Diet Assoc* 2011;111:1204–10.
22. Maffeis C, Schutz Y, Micciolo R, et al. Resting metabolic rate in six- to ten-year-old obese and nonobese children. *J Pediatr* 1993;122:556–62.
23. Henes ST, Cummings DM, Hickner RC, et al. Comparison of predictive equations and measured resting energy expenditure among obese youth attending a pediatric healthy weight clinic: one size does not fit all. *Nutr Clin Pract* 2013;28:617–24.
24. Greer R, Lehnert M, Lewindon P, et al. Body composition and components of energy expenditure in children with end-stage liver disease. *J Pediatr Gastroenterol Nutr* 2003;36:358–63.
25. Saunders J. Malnutrition and nutrition support in patients with liver disease. *Front Gastroenterol* 2010;1:105–11.
26. Shepherd R. Energy expenditure in infants in health and disease. *Can J Gastroenterol* 1997;11:101–4.
27. O'Brien A, Williams R. Nutrition in end-stage liver disease: principles and practice. *Gastroenterology* 2008;134:1729–40.

28. Chin SE, Shepherd RW, Cleghorn GJ, et al. Pre-operative nutritional support in children with end-stage liver disease accepted for liver transplantation: an approach to management. *J Gastroenterol Hepatol* 1990;5:566–72.
29. DeRusso PA, Ye W, Shepherd R, et al. Growth failure and outcomes in infants with biliary atresia: a report from the Biliary Atresia Research Consortium. *Hepatology* 2007;46:1632–8.
30. Vaisman N, Rossi MF, Goldberg E, et al. Energy expenditure and body composition in patients with anorexia nervosa. *J Pediatr* 1988;113: 919–24.
31. Puigserver P, Rhee J, Lin J, et al. Cytokine stimulation of energy expenditure through p38 MAP kinase activation of PPARgamma coactivator-1. *Mol Cell* 2001;8:971–82.
32. Hill RJ, Lewindon PJ, Withers GD, et al. Ability of commonly used prediction equations to predict resting energy expenditure in children with inflammatory bowel disease. *Inflamm Bowel Dis* 2011;17: 1587–93.
33. Cormier K, Mager D, Bannister L, et al. Resting energy expenditure in the parenterally fed pediatric population with Crohn's disease. *JPEN J Parenter Enteral Nutr* 2005;29:102–7.
34. Dorlochter L, Røksund O, Helgheim V, et al. Resting energy expenditure and lung disease in cystic fibrosis. *J Cyst Fibros* 2002;1:131–6.
35. Murphy MD, Ireton-Jones CS, Hilman BC, et al. Resting energy expenditures measured by indirect calorimetry are higher in preadolescent children with cystic fibrosis than expenditures calculated from prediction equations. *J Am Diet Assoc* 1995;95:30–3.
36. Stallings VA, Tomezsko JL, Schall JI, et al. Adolescent development and energy expenditure in females with cystic fibrosis. *Clin Nutr* 2005;24:737–45.
37. Stallings VA, Cronk CE, Zemel BS, et al. Body composition in children with spastic quadriplegic cerebral palsy. *J Pediatr* 1995;126 (5 pt 1): 833–9.
38. Bandini LG, Schoeller DA, Fukagawa NK, et al. Body composition and energy expenditure in adolescents with cerebral palsy or myelodysplasia. *Pediatr Res* 1991;29:70–7.
39. Dickerson RN, Brown RO, Gervasio JG, et al. Measured energy expenditure of tube-fed patients with severe neurodevelopmental disabilities. *J Am Coll Nutr* 1999;18:61–8.
40. Mehta NM, Costello JM, Bechard LJ, et al. Resting energy expenditure after Fontan surgery in children with single-ventricle heart defects. *JPEN J Parenter Enteral Nutr* 2012;36:685–92.
41. Hardy CM, Dwyer J, Snelling LK, et al. Pitfalls in predicting resting energy requirements in critically ill children: a comparison of predictive methods to indirect calorimetry. *Nutr Clin Pract* 2002;17:182–9.
42. Oosterveld MJ, Van Der Kuip M, De Meer K, et al. Energy expenditure and balance following pediatric intensive care unit admission: a longitudinal study of critically ill children. *Pediatr Crit Care Med* 2006;7:147–53.
43. White MS, Shepherd RW, McEniery JA. Energy expenditure in 100 ventilated, critically ill children: improving the accuracy of predictive equations. *Crit Care Med* 2000;28:2307–12.
44. Framson CM, LeLeiko NS, Dallal GE, et al. Energy expenditure in critically ill children. *Pediatr Crit Care Med* 2007;8:264–7.
45. De Wit B, Meyer R, Desai A, et al. Challenge of predicting resting energy expenditure in children undergoing surgery for congenital heart disease. *Pediatr Crit Care Med* 2010;11:496–501.
46. Coss-Bu JA, Jefferson LS, Walding D, et al. Resting energy expenditure in children in a pediatric intensive care unit: comparison of Harris-Benedict and Talbot predictions with indirect calorimetry values. *Am J Clin Nutr* 1998;67:74–80.
47. Vazquez Martinez JL, Martinez-Romillo PD, Diez Sebastian J, et al. Predicted versus measured energy expenditure by continuous, online indirect calorimetry in ventilated, critically ill children during the early postinjury period. *Pediatr Crit Care Med* 2004;5:19–27.
48. Energy and Protein Requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. WHO Technical Report Series No. 724. Geneva: Food and Agriculture Organization/World Health Organization/United Nations University; 1985.
49. Mehta NM, Compher C. A.S.P.E.N. Clinical Guidelines: nutrition support of the critically ill child. *JPEN J Parenter Enteral Nutr* 2009;33:260–76.
50. Agostoni C, Buonocore G, Carnielli VP, et al. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2010;50:85–91.
51. Cai W, Yu L, Lu C, et al. Normal value of resting energy expenditure in healthy neonates. *Nutrition* 2003;19:133–6.
52. Nydegger A, Walsh A, Penny DJ, et al. Changes in resting energy expenditure in children with congenital heart disease. *Eur J Clin Nutr* 2009;63:392–7.
53. Avitzur Y, Singer P, Dagan O, et al. Resting energy expenditure in children with cyanotic and noncyanotic congenital heart disease before and after open heart surgery. *JPEN J Parenter Enteral Nutr* 2003; 27:47–51.
54. Bosy-Westphal A, Eichhorn C, Kutzner D, et al. The age-related decline in resting energy expenditure in humans is due to the loss of fat-free mass and to alterations in its metabolically active components. *J Nutr* 2003;133:2356–62.
55. Oshima S, Miyauchi S, Kawano H, et al. Fat-free mass can be utilized to assess resting energy expenditure for male athletes of different body size. *J Nutr Sci Vitaminol (Tokyo)* 2011;57:394–400.
56. Hronek M, Klemera P, Tosner J, et al. Anthropometric measured fat-free mass as essential determinant of resting energy expenditure for pregnant and non-pregnant women. *Nutrition* 2011;27:885–90.
57. Tang T, Zhang J, Yin J, et al. Uncoupling of inflammation and insulin resistance by NF-kappaB in transgenic mice through elevated energy expenditure. *J Biol Chem* 2010;285:4637–44.
58. Azcue M, Rashid M, Griffiths A, et al. Energy expenditure and body composition in children with Crohn's disease: effect of enteral nutrition and treatment with prednisolone. *Gut* 1997;41:203–8.
59. Vaisman N, Pencharz PB, Corey M, et al. Energy expenditure of patients with cystic fibrosis. *J Pediatr* 1987;111:496–500.
60. Fried MD, Durie PR, Tsui LC, et al. The cystic fibrosis gene and resting energy expenditure. *J Pediatr* 1991;119:913–6.
61. Bell SC, Saunders MJ, Elborn JS, et al. Resting energy expenditure and oxygen cost of breathing in patients with cystic fibrosis. *Thorax* 1996;51:126–31.
62. Stallings VA, Vaisman N, Chan HS, et al. Energy metabolism in children with newly diagnosed acute lymphoblastic leukemia. *Pediatr Res* 1989;26:154–7.
63. Azcue MP, Zello GA, Levy LD, et al. Energy expenditure and body composition in children with spastic quadriplegic cerebral palsy. *J Pediatr* 1996;129:870–6.
64. Barton RG, Craft WB, Mone MC, et al. Chemical paralysis reduces energy expenditure in patients with burns and severe respiratory failure treated with mechanical ventilation. *J Burn Care Rehabil* 1997;18: 461–8.
65. Tian Z, Miyata K, Tabata M, et al. Nifedipine increases energy expenditure by increasing PGC-1alpha expression in skeletal muscle. *Hypertens Res* 2011;34:1221–7.