

Energy expenditure of malnourished children during catch-up growth*

By C. R. FJELD†, *Instituto de Investigación Nutricional, Apartado 18-0191, Lima 18, Peru* and D. A. SCHOELLER, *Clinical Nutrition Research Center, University of Chicago, Chicago, IL 60637, USA* and K. H. BROWN, *Division of Human Nutrition, Johns Hopkins University, Baltimore, MD, USA*

Refeeding strategies require knowledge of energy partitioning. By principles of energy balance, energy intake (E_i) is partitioned between maintenance (E_m), activity (E_a), growth (E_g) and faecal and urinary losses (E_w). Energy requirements can thus be calculated as the sum of the components of the energy-balance equation (equation 1). Under anabolic conditions, E_i is equal to dietary E_i requirements.

$$E_i = E_m + E_a + E_g + E_w. \quad (1)$$

E_g is partitioned between energy expended for tissue biosynthesis (E_{syn}) and energy stored as new tissue (E_{st}). Both values vary according to the composition of weight gained. Since E_m and E_a cannot be easily separated, the sum E_{m+a} is estimated.

From estimates of normal growth in the reference infant, less than 15% of dietary E_i is partitioned to E_g , whereas during rapid catch-up growth, E_g may be 50% or more of E_i . Reasonable estimates of E_{m+a} and of E_g would enable prediction of energy requirements for refeeding during accelerated weight gain.

Energy expenditure for maintenance and activity, E_{m+a}

Based on the fact that all metabolizable energy is either expended or stored, one approach to estimating E_{m+a} is regression of metabolizable energy intake (MEI; Y) on rate of weight gain (X). This assumes (1) no net deposition of tissue at zero weight gain and thus no energy partitioned to E_g , (2) all energy expended at zero weight gain is for maintenance and activity which is estimated by the Y -intercept. The advantages of this approach are that estimates can be made independently of actual measurements of energy expenditure or of energy storage, particularly during recovery from malnutrition because of accelerated rates of weight gain. The accuracy of the estimates is limited, however, by the accuracy of dietary intake and faecal excretion values.

A widely-cited estimate of E_{m+a} , 343 kJ (82 kcal)/kg per d published by Spady *et al.* (1976), was actually the unweighted mean of three independent estimates of E_{m+a} . The first was estimated as 358 kJ (85.5 kcal)/kg from the Y -intercept of the regression of MEI *v.* rate of weight gain of sixteen subjects in the rapid-weight-gain phase of recovery from malnutrition. The second was 341 kJ (81.5 kcal)/kg, the Y -intercept of MEI on weight gain or loss of four subjects in the acute phase of malnutrition and in negative energy balance. The third estimate was based on an assumed basal metabolic rate of 222 kJ (53 kcal)/kg, approximated in an independent study of other malnourished children (Ashworth, 1969*a*) and the assumption that E_{m+a} is equal to 1.5 times basal metabolic rate. The latter approach estimated 335 kJ (80 kcal)/kg as E_{m+a} . We have made similar estimates (Table 1) from published values of dietary intake (Waterlow, 1961; Ashworth *et al.* 1968; Ashworth, 1969*a,b*; Krieger & Chen, 1969; Kerr *et al.* 1973). Where authors

*Supported by The Thrasher Research Foundation, and National Institutes of Health grants DK 26678 and DK 30031.

†Present address: Washington University School of Medicine, Metabolism Division, Box 8127, 660 S. Euclid Avenue, St Louis, MO 63110, USA.

Table 1. *Estimates of energy costs of maintenance, activity and growth*

Study	n	Period of study (d)		Y-intercept‡	Slope§
		Wt*	Balance‡		
Kerr <i>et al.</i> (1973)	10	14	14	92	5.3
Spady <i>et al.</i> (1976)	15	14	3	85.5	4.4
Ashworth <i>et al.</i> (1968)	47	20	20	89.2	6.2
Waterlow (1961)	50	12	?	97.2	5.9
Ashworth (1969a,b)¶	6	20	2	95.7	5.7
Krieger & Chen (1969)	29	27	-	81.3	4.3

*Period (d) during which mean weight gain (g/kg per d) was calculated.

‡Period (d) during which food intake was measured.

§Y-intercept of regression of metabolic energy intake (Y) v. weight gain X, where Y-intercept is energy costs of maintenance and activity.

¶Slope = energy cost of growth.

||Metabolic energy intake recalculated as 90% gross intake.

¶Metabolic energy intake recalculated as 80% gross intake, observed in subsample of subjects.

provided only gross intake values, we subtracted 10% from gross intake to approximately adjust for the energy content of the excreta (Rose & Mayer, 1968; Kerr *et al.* 1973; Spady *et al.* 1976; Kerner & Sunshine, 1979). Studies were 12–27 d in duration. The Y-intercepts of regressions of MEI v. weight gain ranged from 339 to 406 kJ (81 to 97 kcal)/kg.

These estimates are all based on estimates of MEI, which in turn rely on accurate estimates of dietary E_i and of faecal output values. Estimates of MEI may be inappropriate for the estimation of E_{m+a} for three reasons. First, errors of the metabolic collection method tend to compound to overestimate MEI. Second, if subjects are kept in metabolic beds, activity may be unrepresentative and thus the estimate of E_{m+a} inaccurate. Third, estimates from other subjects used in lieu of metabolic collections may be unreliable.

A method for estimating E_{m+a} which avoids these errors is based on measured energy expenditure and weight gain. This approach assumes (1) the Y-intercept of energy expenditure (kJ (kcal)/kg) on weight gain (g/kg) estimates energy expenditure at zero weight gain and (2) that this estimate is E_{m+a} . Advantages of this approach are that it obviates errors from uncertainties over actual dietary E_i and energy losses via the excreta. The doubly-labelled-water method for measuring energy expenditure is accurate in studies of 5–10 d in children (Schoeller *et al.* 1985; Roberts *et al.* 1986; Jones *et al.* 1987) and has the advantage of being safe, unencumbering, and appropriate to field settings. Developed for use in small animals (Lifson & McClintock, 1966), the method is based on differences in rates of elimination from the body of two tracers. One, $^{18}\text{O}_2$, is eliminated from the body as water and as CO_2 , whereas the other, ^2H , is eliminated as water. The difference in the elimination rates is a function of the rate of CO_2 production. A key advantage of the method is that it can be applied in natural settings without interrupting normal activity patterns. The limitations of the method are that it requires accurate measurement of isotopic enrichments using mass spectrometry and relies on appropriate factors for converting isotopic elimination rates of CO_2 to energy expenditure.

We used the doubly-labelled-water method to measure energy metabolism over 5–10 d in twenty-two malnourished children. Mean height was 0.70 (SD 0.05) m, height-age was

7.9 (SD 3.3) months, weight was 7.84 (SD 1.32) kg, and chronological age was 15 (SD 6.1) months. Rates of weight gain were 1.7–16g/kg per d (mean 6.8 (SD 3.6) g/kg per d). E_{m+a} , estimated from the intercept of energy expended (kJ (kcal)/kg per d) on weight gain (g/kg per d) was 323 (SE 45.6) kJ (77.2 (SE 10.9) kcal)/kg.

Our estimate of E_{m+a} differs from that of Spady *et al.* (1976) by 6%. This 6% difference is small, but it may reflect real differences in E_{m+a} between the two groups studied. E_a has been estimated as 79.5 kJ (19 kcal)/kg per d (calculated from Rose & Mayer, 1968; Kerner & Sunshine, 1979). The 20.9 kJ (5 kcal)/kg difference between our estimate of E_{m+a} and that of Spady *et al.* (1976) is within the range of biological variation on expenditure for activity in children.

Alternatively, differences in body composition could explain apparent differences in expenditure per kg body-weight because energy expenditure is a function of active tissue mass. We therefore estimated E_{m+a} per kg fat-free mass (FFM) from body water (our best estimate of active tissue mass) in our subjects (mean 58.4 (SE 13.4) %), assuming FFM is 77% water (recalculated from Fomon *et al.* 1982). In our subjects, body-weight was 76% FFM. However, in reference boys 12 months of age, FFM accounts for 77.5% body-weight. We recalculated energy expenditure per kg FFM for each subject based on height-age and the estimated hydration coefficient for that age (calculated from Fomon *et al.* 1982). The Y-intercept of the regression of energy expenditure *v.* weight gain was 441 (SE 20.9) kJ (105.5 (SE 5.0) kcal) E_{m+a} /kg FFM. Using this and FFM as percentage body-weight, E_{m+a} /kg body-weight in 1-year-old children with reference to body composition would be estimated as 342 kJ (81.8 kcal)/kg body-weight.

We estimate that E_{m+a} is approximately 343 kJ (82 kcal)/kg body-weight in young children with reference to body composition. However, the estimated E_{m+a} of 441 kJ (105.5 kcal)/kg FFM and an estimate of FFM as percentage body-weight should improve the predictability of E_{m+a} /kg body-weight.

Values for E_g and E_w need to be added to E_{m+a} (kJ (kcal)/kg body-weight) to estimate requirements for E_i .

Energy cost of growth, tissue synthesis, and storage (E_g , E_{syn} , E_{st})

E_g is partitioned to energy expended for tissue biosynthesis (E_{syn}) and stored as new tissue (E_{st}), both of which vary according to the composition of weight gained. E_{st} amounts to the combustible fuel value of body tissue, estimated as 23.6 kJ (5.65 kcal)/g protein and 39.6 kJ (9.46 kcal)/g fat (Lusk, 1976). Estimates of E_{syn} are more variable, and are based on theoretical metabolic costs and on a few experimental observations.

Spady *et al.* (1976) estimated E_{syn} as the arithmetic difference between E_g and E_{st} , where E_g was estimated from the slope of MEI *v.* rate of weight gain and E_{st} was calculated as the arithmetic difference between MEI and energy expenditure. Subjects were infants recovering from malnutrition whose weight gain was approximately 30% fat. The resulting estimate of E_{syn} was 4.6 kJ (1.1 kcal)/g gain. The accuracy of E_{syn} calculated in this way relies on measurements of MEI and energy expenditure.

Using the doubly-labelled-water method, we have measured E_{syn} as the slope of the regression of energy expenditure *v.* weight gain. The regression was based on twenty-two patients. The slope was 4.6 (SE 2.8) kJ (1.1 (SE 0.66) kcal)/g gain. We estimated the composition of the weight gained using an energy-mass balance approach. Briefly, total energy stored was estimated as the difference between metabolizable and expended energy; energy stored as protein was calculated from nitrogen retention ($N \times 6.25 \times 23.6$ kJ (5.65 kcal)/d) and fat gain was estimated from the difference (total energy stored – energy stored as protein) 39.6 kJ (9.46 kcal)/g. Approximately 50% of the weight gained was fat. In the present study, E_{st} was estimated as 22.6 (SD 9.6) kJ (5.4 (SD

2.3) kcal)/g gain based on the difference between MEI and average daily energy expenditure. Other studies (Garrow *et al.* 1965; Kerr *et al.* 1973), where 50% of the weight gained was fat, estimated E_{st} as 21.8 kJ (5.2 kcal)/g gain. In the study by Spady *et al.* (1976), 30% of the weight gain was fat.

There is no gold standard against which these estimates can be compared. However, based on a theoretical expenditure of 0.628 kJ (0.15 kcal) expended per kJ (kcal) deposited as protein, the theoretical cost of protein synthesis is 3.56 kJ (0.85 kcal)/g protein synthesized (Millward *et al.* 1976). In young force-fed rats, 1.34 kJ (0.32 kcal) were expended per kJ (kcal) deposited as protein (McCracken & Weatherup, 1973). Thus, in force-fed rats, the experimentally-determined cost of protein synthesis was 7.57 kJ (1.81 kcal)/g protein synthesized.

Fat synthesis has a theoretical cost of 0.4184 kJ (0.1 kcal)/g fat synthesized. This estimate was based on an estimated requirement of 6 ATP/mol triglyceride (Millward *et al.* 1976).

Using either theoretical or experimental E_g values and 0.4184 kJ (0.1 kcal)/g fat, and estimates of weight gain of 50% fat, the estimated E_g would be 21.8 kJ (5.2 kcal) and E_{syn} would be 0.8 kJ (0.2 kcal)/g gain. The difference between a theoretical cost of E_{syn} and the value we determined experimentally could be due to the metabolic costs of absorption, transport and activation of substrates. These metabolic costs would be included in E_{syn} calculated from regression of either MEI or energy expenditure *v.* weight gain, but would be excluded from theoretical costs which are based on the energetics of bond formation alone. Flatt (1978) estimated that the specific dynamic action (SDA), or the metabolic costs of nutrient transport and activation, range from 4% of the combustible energy value of the substrate of fat to 25% of the combustible energy value of protein. The SDA includes the cost of bond formation, which is the only cost included in the theoretical estimate of E_{syn} . From Flatt's (1978) values and our diets of 230 kJ (55 kcal)/kg per d carbohydrate, 268 kJ (64 kcal)/kg per d fat and 59 kJ (14 kcal)/kg per d protein, and an average weight gain of 6 g/kg per d, we calculate energy cost of absorption and storage of 29 kJ (7 kcal)/g per d or 4.184 kJ (1 kcal)/g. In addition there is the potential for non-obligatory post-prandial thermogenesis, a cost not included in Flatt's (1978) theoretical estimate of SDA. Although the theoretical cost of E_{syn} varies with the composition of weight gained, the present values, particularly when compared with the results of the study by Spady *et al.* (1976), suggest that variation in the costs of nutrient transport, or other metabolic costs not specific to bond formation, overshadow the theoretical differences in costs of bond formation in protein and fat synthesis.

In summary the doubly-labelled-water method was used to evaluate energy requirements in children recovering from malnutrition. The energy costs of maintenance and activity/kg can be estimated from 444 kJ (106 kcal)/kg FFM, and the percentage body-weight which is the FFM. The energy cost of tissue biosynthesis is apparently 4.6 kJ (1.1 kcal)/g gain when 50% of the weight gain is fat. These estimates should be relevant to children between 3 and 15 months of age.

REFERENCES

- Ashworth, A. (1969a). *Nature* **223**, 407-409.
 Ashworth, A. (1969b). *British Journal of Nutrition* **23**, 835-845.
 Ashworth, A., Bell, R., James, W. P. T. & Waterlow, J. C. (1968). *Lancet* **ii**, 600-603.
 Flatt, J. P. (1978). *Recent Advances in Obesity Research* **2**, 211-228.
 Fomon, S. J., Haschke, F., Zielger, E. E. & Nelson, S. E. (1982). *American Journal of Clinical Nutrition* **35**, 1169-1175.

- Garrow, J. S., Fletcher, K. & Halliday, D. (1965). *Journal of Clinical Investigation* **44**, 417–425.
- Jones, P. J. H., Winthrop, A. L., Schoeller, D. A., Swyer, P. R., Smith, J., Filler, R. M. & Heim, T. (1987). *Pediatric Research* **21**, 242–246.
- Kerner, J. A. & Sunshine, P. (1979). *Seminars in Perinatology* **3**, 417–434.
- Kerr, D., Ashworth, A., Picou, D., Poulter, N., Seakins, A., Spady, D. & Wheeler, E. (1973). In *Endocrine Aspects of Malnutrition*, pp. 467–486 [L. I. Gardner and P. Amacher, editors]. Santa Ynez, California: The Kroc Foundation.
- Krieger, I. & Chen, Y. C. (1969). *Pediatrics* **44**, 647–654.
- Lifson, N. & McClintock, R. (1966). *Journal of Theoretical Biology* **12**, 46–74.
- Lusk, G. (1976). *The Elements of the Science of Nutrition*, 4th ed. New York: Academic Press.
- McCracken, K. J. & Weatherup, S. T. C. (1973). *Proceedings of the Nutrition Society* **32**, 66A.
- Millward, D. J., Garlick, P. J. & Reeds, P. J. (1976). *Proceedings of the Nutrition Society* **35**, 339–349.
- Roberts, S. B., Coward, W. A., Schlingenseipen, K. H., Nohria, V. & Lucas, A. (1986). *American Journal of Clinical Nutrition* **44**, 315–322.
- Rose, H. E. & Mayer, J. (1968). *Pediatrics* **41**, 18–29.
- Schoeller, D. A., Fjeld, C. R. & Brown, K. H. (1985). In *Synthesis and Applications of Isotopically Labelled Compounds*, Proceedings of the Second International Symposium, pp. 325–330. Amsterdam: Elsevier.
- Spady, D. W., Payne, P. R., Picou, D. & Waterlow, J. C. (1976). *American Journal of Clinical Nutrition* **29**, 1073–1078.
- Waterlow, J. C. (1961). *Journal of Tropical Paediatrics and African Child Health* **7**, 16–22.