

Energy cost of growth during infancy

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Adequate energy and a balance of essential nutrients are dietary requisites if optimal growth and development are to be achieved during infancy. Energy deposition will be determined by the relative balance between the oxidative and synthetic processes within the body. The energy cost of growth may be regarded as two components, the energy deposited in newly synthesized tissues and the energy expended to support the metabolic processes necessary to achieve tissue accretion. Theoretical and experimental derivations of the total cost of growth and its components during infancy are the subject of this paper.

The total energy cost of growth will be referred to as E_{cg} and its parts as $E_{\text{components}}$ and $E_{\text{synthesis}}$. Estimation of $E_{\text{components}}$ depends on the accurate assessment of body composition. Derivation of $E_{\text{synthesis}}$ requires knowledge of the biochemical transformations necessary to maintain and support net tissue accretion. Deposition of dietary fat as fat tissue is the most efficient transformation with a loss of only 0.04 kJ/kJ deposited (Millward *et al.* 1976). The interconversions of carbohydrate into fat, and protein into protein, result in a loss of 0.63 kJ/kJ deposited. Synthesis of fat from protein is the least efficient with a loss of 1.30 kJ/kJ deposited.

Developmental aspects of body composition and whole body metabolism affect the energy cost of growth. Throughout the first year of life, changes occur in the composition of weight gain. Chemical maturation and the differential contribution of various organs to body-weight gain alter not only the maintenance requirement for energy, but also the energy cost of growth. Changes in relative organ size influence both energy and protein metabolism. Protein synthesis proceeds at a high rate in the neonate and declines throughout infancy. High protein turnover contributes to the relatively high energy requirement of the newborn (Reeds *et al.* 1982). Protein synthesis accounts for approximately 23% of the daily energy expenditure in the human neonate (Young, 1981) and 7% in the older infant (Millward *et al.* 1976). Because of these developmental changes, the energy cost of growth is expected to vary throughout infancy.

Theoretical estimates of the energy cost of growth

The energy cost of growth may be estimated from biosynthetic pathways and energy equivalents of the nutrients deposited, if the body composition is known. Based on the weight and chemical composition of various organs, Hommes (1980) calculated the increments in protein, triglycerides, phospholipids, cholesterol, glycogen, DNA, and RNA for a 3-week-old male infant growing at a rate of 6.9 g/kg per d. From the biosynthetic pathways, the energy required to synthesize these components was 1.21 kJ/g gained. Energy deposition in the newly synthesized tissues, the composition of which was 13.7% protein and 10.0% fat, was 6.57 kJ/g. Based on these theoretical considerations, the total energy cost of growth would be 7.78 kJ/g. Because of the developmental

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changes in body composition throughout infancy, however, these computations apply only to the neonate. Nevertheless, this approach could be applied to later stages of infancy if sufficient information on body composition was available.

The energy cost of synthesis, however, may be underestimated by this approach, because all biochemical reactions are assumed to proceed at optimal efficiency without the occurrence of metabolic interconversions. Futile cycling, ion leakage, high rates of protein turnover, and nutrient interconversions do occur, however, and would decrease the efficiency of nutrient utilization. In addition, the extent to which these processes occur varies among individuals. For this reason, direct experiments with infants are necessary to confirm theoretical estimations.

Energy cost of growth derived from body composition studies

If the composition of the tissue deposited is known, an estimate of the energy cost of growth may be calculated. Kielanowski (1965) determined from experiments on baby pigs that 31.4 and 48.5 kJ were required to deposit 1 g protein and fat, respectively. Applying these values to the 'male reference infant' with a weight gain of 32.6 g/d (11.4% protein and 40.8% fat), Fomon *et al.* (1971) derived a value of 23.4 kJ/g for the E_{cg} .

Because the composition of weight gain changes throughout the first year of life, it follows that $E_{components}$ will vary. Body compositional changes during infancy were estimated from measurements of total body water by deuterium dilution, and fat-free body mass (FFBM) by whole body counting of ^{40}K (Fomon *et al.* 1982). Based on metabolizable energy equal to 16.7 kJ/g protein and 37.6 kJ/g fat, $E_{components}$ was computed as a function of age and sex (Table 1). $E_{components}$ increases to approximately 17.6 kJ/g over the first 3 months of life and then declines to approximately 6.7 kJ/g.

Table 1. *Energy cost of growth derived from body composition studies*

	Age (months)	Wt gain (g/d)	Fat gain (g/d)	Protein gain (g/d)	Energy gain (kJ/d)	$E_{components}$ (kJ/g)
Boys	0-1	29.3	6.0	3.7	288	10
	1-2	35.2	14.1	3.5	590	17
	2-3	29.9	12.9	3.0	536	18
	3-4	20.8	8.3	2.3	351	17
	4-5	16.6	5.5	2.0	240	14
	5-6	15.2	4.1	2.0	188	12
	6-9	12.6	1.8	2.0	101	8
	9-12	10.7	1.0	1.8	68	6
Girls	0-1	26.0	5.6	3.3	266	10
	1-2	28.6	12.8	2.8	529	18
	2-3	24.3	10.1	2.6	424	17
	3-4	18.6	7.3	2.1	310	17
	4-5	16.1	5.9	1.9	254	16
	5-6	15.0	4.9	1.9	216	14
	6-9	11.2	1.7	1.8	94	8
	9-12	10.0	1.2	1.7	74	7

$E_{components}$, part of the total energy cost of growth.

*Adapted from Fomon *et al.* (1982).

TDEE of infants has been difficult. Thus, estimates of the TDEE were made by extrapolation from measurements of oxygen consumption and carbon dioxide production monitored for less than 24 h, or by 24-h heart rate monitoring standardized with indirect calorimetry. Application of the doubly-labelled water method enables measurement of the TDEE of infants in a non-invasive manner (Lifson & McClintock, 1966; Roberts *et al.* 1986).

To date, $E_{\text{components}}$ has been calculated by two methods: (1) as the ratio of energy storage (MEI-TDEE):WtG and (2) as the slope of the regression of energy storage on WtG. The ratio method is correct only if energy storage is equal to zero at zero weight gain. Values of $E_{\text{components}}$ for infants recovering from malnutrition were between 13.8 and 25.9 kJ/g (Kerr *et al.* 1973; Spady *et al.* 1976; Jackson *et al.* 1977). Estimates for preterm infants were somewhat less, ranging between 10.9 and 18.0 kJ/g (Brooke *et al.* 1979; Reichman *et al.* 1982; Whyte *et al.* 1982; Sauer *et al.* 1984; Freymond *et al.* 1986). Differences in $E_{\text{components}}$ can be ascribed to differences in the composition of the tissues synthesized. These estimates suggest that preterm infants deposit proportionally less fat than malnourished infants undergoing 'catch-up' growth, but this interpretation requires experimental verification.

Energy cost of tissue synthesis has been computed as (1) the difference between E_{cg} and $E_{\text{components}}$, (2) the slope of the regression of TDEE on WtG and (3) the difference between metabolic rate and heat loss divided by WtG. The second approach assumes that factors affecting TDEE, other than WtG, are constant over the range of growth rates studied. This assumption would not be true, for example, if activity varied systematically with growth rate. The third approach is controversial because of the assumption that part of the energy used for tissue synthesis is not given off as heat and, therefore, the net energy of tissue synthesis may be derived from the difference in TDEE calculated from indirect and direct calorimetry.

Spady *et al.* (1976) calculated $E_{\text{synthesis}}$ by difference and arrived at a value of 4.6 kJ/g for infants recovering from malnutrition. Using the same approach, Brooke *et al.* (1979) reported a value for $E_{\text{synthesis}}$ of 7.1 kJ/g for preterm infants. Regression analyses indicated that $E_{\text{synthesis}}$ ranged between 2.2 and 2.8 kJ/g for preterm infants (Chessex *et al.* 1981; Gudinchet *et al.* 1982; Reichman *et al.* 1982). Sauer *et al.* (1984) reported a value of 1.1 kJ/g for preterm infants. A positive correlation between WtG and metabolic rate, as well as between energy intake and metabolic rate, was noted by Chessex *et al.* (1981) indicating that the augmented metabolic rate with increasing energy intake was associated with growth, and not at the expense of growth. The extra energy expended for tissue synthesis is believed to include the thermic effect of feeding. Brooke & Ashworth (1972) found that the increase in O_2 consumption after a feed was related directly to the rate of WtG and could be regarded as a part of the energy cost of growth.

Energy cost of growth derived from energy balance studies on term infants

There is a paucity of experimental data on the energy cost of growth for term infants. A recent investigation of the energy balance of term infants provides the information necessary to compute this cost (N. F. Butte, W. W. Wong, C. Garza and P. D. Klein, unpublished results). The energy intake, TDEE and growth rate of ten breast-fed and ten formula-fed infants were measured at 1 and 4 months of age (n 40). Human milk intake was determined from a 5 d test-weighing record. The intake of formula and supplemental foods was quantified for 5 d by weighing bottles before and after use. The energy content of 24-h representative human milk samples, formula, and supplemental foods was determined by bomb calorimetry. MEI was assumed to be 92% of gross energy intake (Southgate & Barrett, 1966). TDEE was determined by the doubly-labelled water

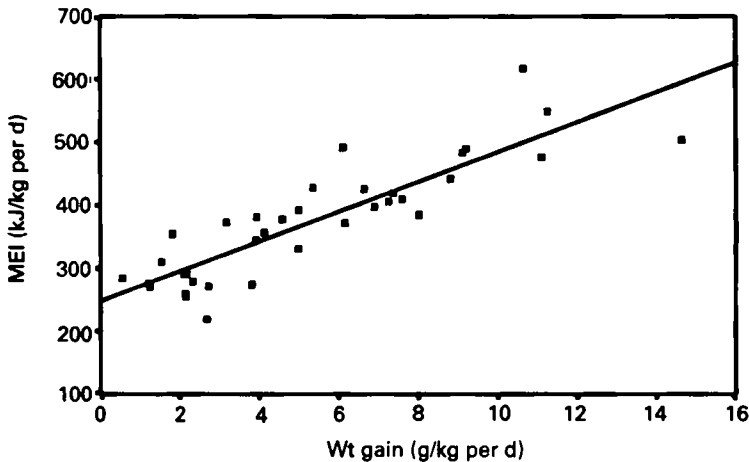


Fig. 1. Relation between metabolizable energy intake (MEI, kJ/kg per d) and weight gain (g/kg per d) for 1- and 4-month-old term infants,

$$Y = 248 + 24 X; r^2 0.76 (P < 0.001).$$

technique (Roberts *et al.* 1986). Growth rate was computed over a 2-week interval.

The mean (SD) gross energy intake of these infants was 473 (79) kJ/kg per d at 1 month and 318 (54) kJ/kg per d at 4 months. Mean (SD) TDEE was 276 (29) kJ/kg per d at 1 month and 289 (38) kJ/kg per d at 4 months. Average growth rate was 8.5 (SD 3.0) and 2.6 (SD 1.3) g/kg per d for the 1- and 4-month-old infants, respectively. These data were utilized to compute E_{cg} , $E_{components}$ and $E_{synthesis}$.

E_{cg} , calculated from the simple regression of MEI on WtG, was 23.8 kJ/g (Table 3, Fig. 1). In the computation of E_{cg} , $E_{components}$ and $E_{synthesis}$, the dependent and independent variables are usually normalized by body-weight. Whyte *et al.* (1982) have suggested that standardization by weight, as was done here, may result in an incorrect slope. Alternatively, a multiple linear regression model may be used to estimate the partial coefficient, b_2 :

$$MEI (kJ/d) = A + b_1 \text{ body-weight (kg)} + b_2 \text{ WtG (g/d)}.$$

This multiple regression analysis was performed including variables of feeding mode, age and sex. E_{cg} was equal to 20.1 kJ/g by this approach. No interactions were detected between the independent variables, indicating that E_{cg} was not a function of body-weight. Partial coefficients were parallel and coincided for breast-fed and formula-fed infants (20.1 v. 16.3 kJ/g respectively), and for 1- and 4-month-old infants (15.9 v. 18.4 kJ/g respectively). Partial coefficients were indistinguishable between the sexes.

Energy storage for these infants averaged 481 (SD 464) kJ/d or 96 (SD 96) kJ/kg per d, which was equivalent to 21.6 (19.3)% of MEI. $E_{components}$ derived from the simple regression of energy storage on WtG was equal to 22.6 kJ/g (Table 4, Fig. 2). $E_{components}$ was 19.2 kJ/g estimated from the multiple regression model:

$$\text{energy storage (kJ/d)} = A + b_1 \text{ body-weight (kg)} + b_2 \text{ WtG (g/d)}.$$

No significant interactions were demonstrated for the independent variables. The partial coefficients for the breast-fed and formula-fed infants (25.1 v. 10.0 kJ/g respectively) were not statistically different, the partial coefficients derived for the 1- and 4-month-old

Table 3. Energy cost of growth derived from simple and multiple linear regression analyses of term infants (n 36)

E_{cg} (kJ/g)	Simple regression MEI (kJ/kg per d) = 248 + 24 WtG (g/kg per d) ($S_b = 2, P < 0.001$)	Multiple regression MEI (kJ/d) = 686 + 143 Wt (kg) + 20.1 WtG (g/d) ($S_b = 2.9, P < 0.001$)
$E_{components}$ (kJ/g)	$E_{storage}$ (kJ/kg per d) = -24 + 22 WtG (g/kg per d) ($S_b = 3, P < 0.001$)	$E_{storage}$ (kJ/d) = 552 - 108 Wt (kg) + 19 WtG (g/d) ($S_b = 4, P < 0.001$)
$E_{synthesis}$ (kJ/g)	TDEE (kJ/kg per d) = 272 + 1 WtG (g/kg per d) ($S_b = 2, NS$)	TDEE (kJ/d) = 136 + 251 Wt (kg) + 0.5 WtG (g/d) ($S_b = 2, NS$)

E_{cg} , total energy cost of growth; MEI, metabolizable energy intake; WtG, weight gain; Wt, weight; $E_{components}$, energy deposition in tissues; $E_{storage}$, energy storage; $E_{synthesis}$, energy cost of synthesis; TDEE, total daily energy expenditure; NS, not significant.

Table 4. Energy cost of growth derived from simple and multiple linear regression analyses of breast-fed (BF) (n 18) and formula-fed (FF) (n 18) infants

E_{cg} (kJ/g)	BF: Simple regression MEI (kJ/kg per d) = 240 + 24 WtG (g/kg per d) ($S_b = 3, P < 0.001$)	Multiple regression MEI (kJ/d) = 736 + 126 Wt (kg) + 20 WtG (g/d) ($S_b = 4, P < 0.025$)
$E_{components}$ (kJ/g)	FF: MEI (kJ/kg per d) = 264 + 22 WtG (g/kg per d) ($S_b = 4, P < 0.001$)	MEI (kJ/d) = 837 + 146 Wt (kg) + 16 WtG (g/d) ($S_b = 6, P < 0.01$)
$E_{synthesis}$ (kJ/g)	BF: $E_{storage}$ (kJ/kg per d) = -35 + 26 WtG (g/kg per d) ($S_b = 3, P < 0.001$)	$E_{storage}$ (kJ/d) = 194 - 68 Wt (kg) + 25 WtG (g/d) ($S_b = 4, P < 0.001$)
	FF: $E_{storage}$ (kJ/kg per d) = -12 + 20 WtG (g/kg per d) ($S_b = 5, P < 0.005$)	$E_{storage}$ (kJ/d) = 1322 - 193 Wt (kg) + 10 WtG (g/d) ($S_b = 8, P < 0.10$)
	BF: TDEE (kJ/kg per d) = 275 - 1 WtG (g/kg per d) ($S_b = 2, NS$)	TDEE (kJ/d) = 540 + 194 Wt (kg) - 5 WtG (g/d) ($S_b = 3, P < 0.10$)
	FF: TDEE (kJ/kg per d) = 275 + 2 WtG (g/kg per d) ($S_b = 2, NS$)	TDEE (kJ/d) = -485 + 339 Wt (kg) + 6 WtG (g/d) ($S_b = 4, P < 0.10$)

E_{cg} , total energy cost of growth; MEI, metabolizable energy intake; WtG, weight gain; Wt, weight; $E_{components}$, energy deposition in tissues; $E_{storage}$, energy storage; $E_{synthesis}$, energy cost of synthesis; TDEE, total daily energy expenditure; NS, not significant.

Table 5. Energy cost of growth derived from simple and multiple linear regression of 1-month-old (n 18) and 4-month-old (n 18) infants

E_{cg} (kJ/g)	Age (months)	Simple regression	Multiple regression
$E_{components}$ (kJ/g)	1	MEI (kJ/kg per d) = 310 + 17 WtG (g/kg per d) (S_{b_2} = 4, $P < 0.005$)	MEI (kJ/d) = -519 + 427 Wt (kg) + 16 WtG (g/d) (S_{b_2} = 5, $P < 0.005$)
	4	MEI (kJ/kg per d) = 246 + 21 WtG (g/kg per d) (S_{b_2} = 8, $P < 0.01$)	MEI (kJ/d) = 996 + 98 Wt (kg) + 18 WtG (g/d) (S_{b_2} = 8, $P < 0.025$)
$E_{synthesis}$ (kJ/g)	1	$E_{storage}$ (kJ/kg per d) = 57 + 14 WtG (g/kg per d) (S_{b_2} = 6, $P < 0.025$)	$E_{storage}$ (kJ/d) = -1247 + 340 Wt (kg) + 12 WtG (g/d) (S_{b_2} = 6, $P < 0.05$)
	4	$E_{storage}$ (kJ/kg per d) = -6 + 10 WtG (g/kg per d) (S_{b_2} = 7, $P < 0.10$)	$E_{storage}$ (kJ/d) = 46 - 14 Wt (kg) + 11 WtG (g/d) (S_{b_2} = 7, $P < 1.0$)
E_{total} (kJ/g)	1	TDEE (kJ/kg per d) = 254 + 3 WtG (g/kg per d) (S_{b_2} = 3, NS)	TDEE (kJ/d) = 728 + 88 Wt (kg) + 4 WtG (g/d) (S_{b_2} = 3, $P < 0.10$)
	4	TDEE (kJ/kg per d) = 252 + 10 WtG (g/kg per d) (S_{b_2} = 6, $P < 0.05$)	TDEE (kJ/d) = 954 + 112 Wt (kg) + 8 WtG (g/d) (S_{b_2} = 6, NS)

E_{cg} , total energy cost of growth; MEI, metabolizable energy intake; WtG, weight gain; Wt, weight; $E_{components}$, energy deposition in tissues; $E_{storage}$, energy storage; $E_{synthesis}$, energy cost of synthesis; TDEE, total daily energy expenditure; NS, not significant.

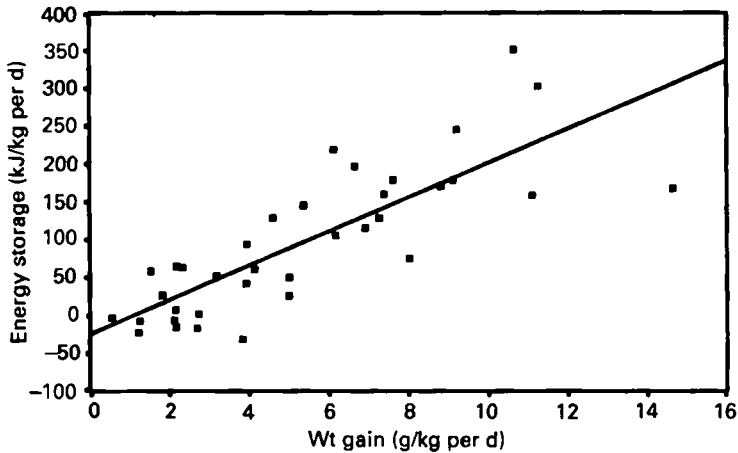


Fig. 2. Relation between energy storage (kJ/kg per d) and weight gain (g/kg per d) for 1- and 4-month-old term infants,

$$Y = -24 + 22 X; r^2 0.66 (P < 0.001).$$

infants (11.7 v. 10.9 kJ/g respectively) did not differ, and the partial coefficients for boys and girls were not different. The ability to detect statistically significant differences by feeding mode, age or sex is limited by individual variation and experimental error.

The gross composition of the WtG may be estimated from $E_{\text{components}}$ (Spady *et al.* 1976). Based on the assumptions that FFBM contains 12.7% protein (Fomon *et al.* 1982) and that metabolizable energy is equal to 16.7 kJ/g protein and 37.6 kJ/g fat, $E_{\text{components}} = (16.7 \times 0.127 \text{ FFBM}) + 37.6 (1 - \text{FFBM})$. $E_{\text{components}}$, 22.6 kJ/g, would be associated with 43% FFBM and 57% fat. The value, 19.2 kJ/g, would correspond to 51% FFBM and 49% fat.

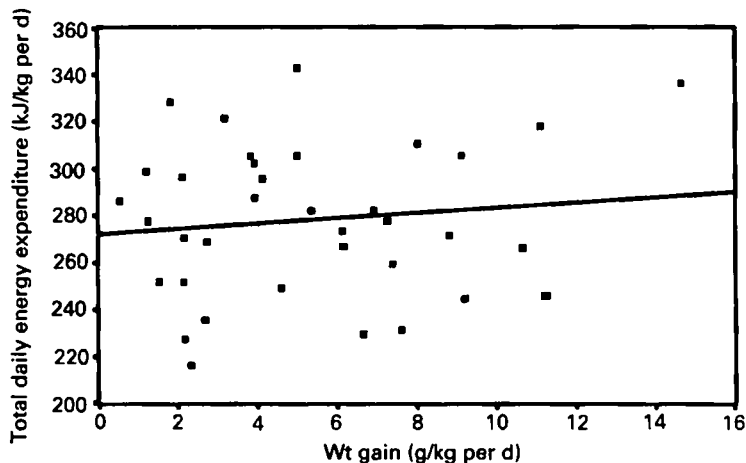


Fig. 3. Relation between total daily energy expenditure (kJ/kg per d) and weight gain (g/kg per d) for 1- and 4-month-old term infants,

$$Y = 272 - 1.13 X; r^2 0.01 (P < 0.49).$$

$E_{\text{synthesis}}$, computed as the slope of the simple regression of TDEE on WtG, was 1.2 kJ/g (Table 5, Fig. 3). It should be noted that the slope was not statistically different from zero. Large variability in the energy balance data may preclude attempts to estimate precisely a relatively small quantity, such as $E_{\text{synthesis}}$. A value of 0.4 kJ/g was predicted by the multiple regression model:

$$\text{TDEE (kJ/d)} = A + b_1 \text{ body-weight (kg)} + b_2 \text{ WtG (g/d)}.$$

The partial coefficient, 0.4 kJ/g, was not statistically significant. These estimates of $E_{\text{synthesis}}$, 1.2 and 0.4 kJ/g, are considerably less than most experimentally determined values for infants (Table 2), and imply partial energy efficiencies in the range of 0.95 to 0.98. The values of $E_{\text{synthesis}}$, however, were similar to theoretical estimates derived from biosynthetic pathways (Hommes, 1980). The values of $E_{\text{components}}$ indicated that approximately 95% of the energy storage was attributable to fat. If dietary fat were the major source for fat deposition, the process might indeed be highly efficient. High rates of energy efficiency in the term infant are speculative, however, because $E_{\text{synthesis}}$ was not resolved with any confidence from the present data set. The large variability in the major components of energy expenditure in the term infant, i.e. maintenance and activity, may preclude attempts to estimate precisely a relatively small quantity, such as $E_{\text{synthesis}}$.

In summary, the energy cost of growth and its components have been calculated from energy balance data on term infants. Values for E_{cg} and $E_{\text{components}}$ were consistent with published values derived from body composition data and values determined from energy balance studies on preterm infants and infants recovering from malnutrition. Values for $E_{\text{synthesis}}$ were less than most experimentally determined values, but in agreement with theoretical estimates based on biosynthetic pathways.

The authors wish to thank the women who participated in the study. We also thank C. Boutte, A. Cavese, L. L. Clark, L. Ferlic, C. Heinz, E. R. Klein, M. E. Lewis, N. Mehta, B. Patterson, C. Rafanan, E. O. Smith and J. Young for technical support of this investigation.

This work is the copyright of the USDA/ARS Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, TX. This project has been funded in part with federal funds from the US Department of Agriculture, Agricultural Research Service under Cooperative Agreement number 58-7MN1-6-100. The contents of this publication do not necessarily reflect the views or policies of the US Department of Agriculture, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.

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