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Energy Balance, Physical Activity, and Thermogenic Effect of Feeding in Premature Infants

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ABSTRACT. In order to assess the contribution of the thermogenic effect of feeding and muscular activity to total energy expenditure, nine premature infants were studied for 2 consecutive days during which time repeated measurements of energy expenditure by indirect calorimetry were performed throughout the day, combined with a visual activity score based on body movement. The infants were growing at 16.6 ± 4.0 g/kg/day (mean ± SD) and received 110 ± 8 kcal/kg/day metabolizable energy (milk formula) and 522 ± 40 mg N/kg/day. Their total energy expenditure was 68 ± 4 kcal/kg/day indicating that 41 ± 7 kcal/kg/day was retained for growth. Based on the combination of energy + N balances it was estimated that 80% of the weight gain was fat-free tissue and 20% was fat tissue. The rate of energy expenditure measured minute-by-minute was significantly and linearly correlated with the activity score in both the premeal ($r = 0.75$; $p < 0.001$) and the postmeal periods ($r = 0.74$; $p < 0.001$) with no difference in the regression slope, but with a significant difference in intercept. In preset feeding schedules the latter allowed an estimation of the thermogenic effect without the confounding effect of activity. This was found to be 3.1 ± 1.8% when expressed as a percentage of metabolizable energy intake. However when the "classical" approach was used as a comparison (integretation of extra energy expenditure induced by the meal), the thermogenic effect was found to be greater, *i.e.* 9.5 ± 3.8% of the meal's metabolizable energy, due to the superimposed effect of physical activity in the postprandial state. The study suggests that the intradaily variation in energy expenditure in premature infants nursed according to present day techniques is almost equally due to the thermogenic effect of feeding (3.2 kcal/kg/day), and to variations in muscular activity (3.6 kcal/kg/day) both representing a small fraction of the total energy expenditure in premature infants (*i.e.* 4.7 and 5.3%, respectively). (*Pediatr Res* 20: 638–645, 1986)

Abbreviations

CHO, carbohydrate
REM, rapid eye movement
R.Q., respiratory quotient

Since the development of open system indirect calorimeters (1–6) allowing measurements under ordinary conditions of nursing and feeding, the study of energy metabolism in preterm infants has progressed at a rapid pace. However, measurements of energy expenditure in premature babies have been generally of short duration (5, 7–9), *i.e.* approximately 1–3 h. Therefore the extent to which these limited periods of measurement can be extrapolated to 24 h is still uncertain. When energy expenditure of preterm infants is continuously monitored over 24 h (6), the variability of measurements generally observed is mainly due to two factors: variations in physical activity (*i.e.* whole body movements, crying), and the thermogenic response to feeding.

Although several methods have been developed to score changes in spontaneous physical activity of infants (7, 9–16), it is not known to what extent these scores are related to the rate of energy expenditure. Because the thermogenic response itself can be influenced by several factors such as duration of measurement, feeding frequency, size and type of test meal, the published measurements give variable results (9, 12, 17–20). The aims of the present study was to measure the energy metabolism of premature babies of less than 34 gestational wk, to assess the magnitude of intradaily variations in energy expenditure and to partition the latter between muscular activity and thermogenic response to feeding.

PATIENTS AND METHOD

Infants. Nine premature babies were studied for 2 consecutive days. All were all appropriate for gestational age (mean 33 ± 1.2 wk; 1740 ± 180 g birth weight; 43 ± 1.5 cm length; 29.7 ± 0.9 cm head circumference, age at study 21 ± 5 days). None had major medical problems, none had neurologic problems, and ultrasound evaluations showed that none had undergone major intraventricular hemorrage or significant periventricular leucomalacia.

The purpose and the procedures of the study were carefully explained to the parents and their agreement was obtained. Most parents were at the bedside while the measurements were done. The investigation has been approved by the Ethical Committee of the Medical Faculty, University of Lausanne.

Diet. All infants were fed through a nasogastric tube (Argyle). The volume of every meal was precisely measured with a 10-ml syringe. Seven infants had their diet distributed in eight meals/day, the remaining two in 10 and 12 meals/day, respectively. Their supply in calories, protein (expressed as N), lipid, and CHO is shown in Table 1. They were all fed a formula adapted for preterm infants (Alprem, Nestlé). Three infants received part of their daily feeding as their own mother's milk. The diet administrated during the studies had been initiated at least 2 days before the study onset. An aliquot of milk formula and breast milk was immediately sampled and frozen. According to the volume of diet actually ingested by the infant, a pool of formula

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Table 1. *Balances of energy and nutrients*

Infant	Gross energy intake	Metabolizable energy intake	Energy expenditure	Energy gain	Gross N* intake	N digested	Urinary N	N gain
		(kcal/kg/day)				(mg/kg/day)		
PG	128.6	106.4	64.4	42.0	541	429	89	340
AL	124.7	115.5	71.2	44.3	542	506	254	252
SB	117.3	107.6	66.0	41.6	492	428	141	287
ED	120.0	115.0	73.3	41.7	522	505	160	345
DP	139.7	126.9	74.0	52.9	608	575	232	343
SF	129.6	104.2	70.0	34.2	500	417	174	243
MS	121.0	107.7	66.3	41.4	527	461	120	341
LJ	114.4	105.6†	60.6	45.5	498	470†	95	375
JK	107.7	99.0	69.9	29.1	469	463	94	369
Mean	122.6	109.8	68.4	41.4	522	473	151	322
± SD	9.4	8.2	4.4	6.7	40	50	60	49

Infant	Gross lipid intake	Lipid digested	Lipid oxid.‡	Lipid gain‡	Gross CHO intake	CHO digested	CHO oxid.‡	CHO gain‡
		(g/kg/day)				(g/kg/day)		
PG	5.7	3.9	0.6	3.3	14.9	14.7	13.3	+1.4
AL	5.9	5.1	0.2	4.9	13.9	13.9	14.7	−0.8
SB	5.8	5.1	0.9	4.2	12.5	12.5	12.8	−0.3
ED	5.7	5.4	1.1	4.3	13.3	13.2	13.9	−0.7
DP	6.6	5.4	−0.2	5.7	15.3	15.3	16.6	−1.3
SF	5.5	3.9	0.3	3.6	16.0	14.2	14.9	−0.7
MS	5.7	4.5	0.5	4.0	13.4	13.4	13.9	−0.5
LJ	5.4	4.6†	0.7	3.9	12.7	12.7†	12.2	+0.5
JK	5.1	4.4	1.8	2.5	12.0	11.6	12.1	−0.5
Mean	5.7	4.7	0.7	3.9	13.8	13.5	13.8	−0.3
± SD	0.4	0.6	0.6	1.0	1.4	1.2	1.4	0.8

* N × 6.38 = protein.

† Assuming: energy digest. = 92.8%; N digest. = 94.2%; lipid digest. = 85.7% assumed values = mean of corresponding values in our completely formula fed infants (PG, AL, ED, MS, JK).

‡ Assessed by the R.Q. method (see text).

(and of breast milk) constituted the diet composition of the 2 days together.

Gross intake, net intake (apparent digestible energy), apparent digestibility, and metabolizable energy. Gross energy was determined by bomb calorimetry (Parr Instrument, Chicago, IL); gross protein intake via total nitrogen (Kjeldahl) and gross lipid intake was derived from the measurement of esterified glycerol (Boehringer, Mannheim, Germany). The energy provided by gross CHO intake was obtained from equations 1 and 2 (Appendix). The gross supply of CHO (in g/kg/day) was computed using the energy equivalent of lactose, 3.95 kcal/g for mothers' milk, and an energy equivalent of 3.86 kcal/g for formula (the milk formula contained one-third of its CHO as glucose and two-thirds as lactose). Apparent digestible energy was calculated by subtracting the energy content of feces (bomb calorimetry) from the gross energy intake (equation 3).

The stools were collected separately from urine during an average period of 42 ± 9 h, and analyzed according to a previously described method (21). Equations 4–8 define the apparent digestibility of N, lipid, CHO, and the metabolizable energy. Urine was continuously collected during an average period of 45 ± 4 h an adhesive plastic bag connected via a plastic tube to a 50-ml glass cylinder. It contained 0.1 ml HCl 6 N and was surrounded by melting ice. The cylinders were changed before each meal and were kept at 0°C until analysis. The 24-h volume was pooled. Urea (urease method), creatinine (Jaffé reaction), and total N were measured in the 24-h urine pools of the study. Glucosuria was absent in all infants as assessed by clinitest sticks (Boehringer).

Energy expenditure and activity scores. A previously described, open circuit indirect calorimeter was used to measure energy expenditure (5). Briefly the calorimeter consists of an airtight perspex box, containing the whole infant, placed inside the incubator. The infant's $\dot{V}O_2$ and $\dot{V}CO_2$ is obtained by the difference of O_2 and CO_2 fractions measured at the inlet and the outlet. From these data and total urinary N, energy expenditure is computed on the basis of oxygen volumes required to oxidize CHO, lipid, and protein (equations 9–12). During calorimetry the activity state of each infant was monitored minute by minute using the scale developed by Brück *et al.* (10) and simultaneously by a simplified activity scale (Table 2). The assessments were performed by the same investigator. Since the rate of activity may change within a single minute, the highest score of activity observed over the minute considered was recorded. the assessment of activity was synchronized to the measurement of energy expenditure by moving the calorimetric values back by 2 min. This time lag was assessed for our calorimeter (5) and includes a 50% exponential mixing time.

Energy retention, assessment of growth, and composition of weight gain. The retained energy was calculated from the difference between metabolizable energy and energy expenditure (equation 13). Body weight was measured every day to the nearest 10 g. The rate of weight gain was calculated over the week which bracketed the study period. In order to minimize the influence of day to day variations the gain was calculated using the least square regression line of daily weight *versus* time. However, the energy results were referred to the actual infant's body weight on the day of the measurement. The composition of the infant's weight gain was estimated by two different methods. The first method was based on the measurements of the energy gain in

Table 2. *Activity scales*

Brück's activity scale (10)		
+5	Crying	
+4	Eyes open	Total body movement
+3	Eyes open	Arm and/or leg movement
+2	Eyes open	Facial movement
+1	Eyes open	No movement
0	Eyes opening and closing	No movement
−1	Eyes closed	Total body movement
−2	Eyes closed	Arm and/or leg movement
−3	Eyes closed	Facial movement
−4	Eyes closed	No movement
Simplified activity scale		
0	No body, arm, or leg movement; facial movements present or not	Eyes closed or open
1	Arm or leg movement	Eyes closed or open
2	Total body movement	Eyes closed or open
3	Crying	

conjunction with the Nitrogen balance (equations 13–16). The second method (R.Q. method) was based on the nutrient balance obtained by subtracting the nutrients oxidized from the nutrient intake (equations 17 and 18). The fat free mass was calculated by difference between the weight gain and the lipid gain (equation 19). The weight gain not due to protein, fat, and CHO retentions was assumed to represent noncaloric compounds such as water, bone minerals, and electrolytes.

Analysis of data. Since discontinuous calorimetric measurements were performed at various times throughout the study (Fig. 1), three distinct periods were defined: 1) the premeal period consisting of 30 min of continuous measurement immediately before the meal; 2) the postmeal period measured over 180 min after the meal, and 3) the peak thermogenic response to feeding measured during 30 min (30–60 min postmeal). The energy expenditure during each of these periods was calculated by simple arithmetic average. The so-called overall daily energy expenditure was obtained by a weightened average procedure taking into account the number of meals fed per day, *i.e.* by calculating the contribution of each period to the total energy expenditure. In order to estimate the energetic cost of physical activity, the minute by minute energy expenditure was related to the corresponding physical activity estimated simultaneously by Brück's scale (10) and the simplified activity scale (see Table 1), both in the premeal and postmeal periods. A similar approach has been used previously with adults (22).

The thermogenic response to feeding was estimated by two methods: the "classic" one obtained by comparison between premeal and postmeal measurements (equations 20 and 21). The premeal baseline was the energy expenditure measured over a 3- to 5-min period of inactivity (zero activity on the simplified scale) during the 30-min premeal period. The postmeal excess of energy expenditure above the baseline was measured over a 180-min period. This value was taken as the thermogenic effect of feeding provided the infant keeps quiet during the postmeal calorimetry. This shortcoming can be obviated by the second or "regression" method. Two regression lines of energy expenditure *versus* activity are drawn: the first corresponds to the minute by minute synchronized measurements of energy expenditure and activity (0–3 scale) during the premeal period; the second corresponds to the same measurements, but done during the postmeal period. The difference between the premeal and the postmeal regression line gave an estimate of the thermogenic effect of food intake without the confounding effect of physical activity.

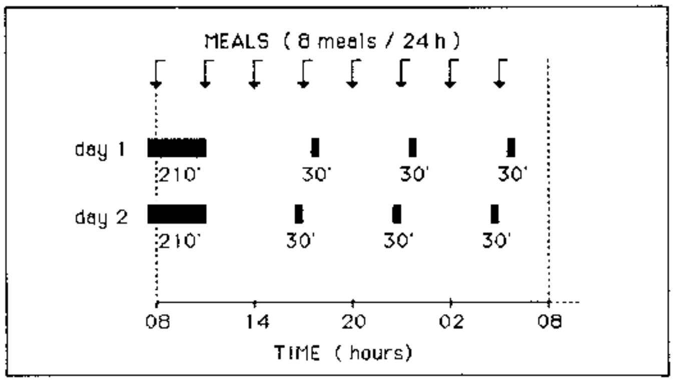

Fig. 1. Experimental design. Each day, 4 to 5 h of discontinued calorimetric measurements were performed (*black bars*): one "long" measurement of 210 min aimed to obtain the complete thermogenic response to a meal and three "short" measurements. On day 1, the "short" runs of 30 min were performed 30–60 min after the beginning of the meal, aimed to scan the peak thermogenic effect. The whole procedure was repeated on day 2, except that the "short" runs had a different timing in order to investigate the premeal period (30–0 min before meal).

RESULTS

Energy and nutrient balances. Table 1 shows the individual values for energy, protein lipid, and CHO. The energy digestibility was 90.1 ± 5.4% (mean ± SD). The nitrogen, lipid, and CHO digestibilities averaged respectively 90.1 ± 6.8, 81.9 ± 9.1, and 97.9 ± 3.9%.

There was a significant correlation between energy digestibility and lipid digestibility ($r = 0.963$, $n = 8$, $p < 0.001$). The metabolizable energy intake was 109.8 ± 8.2 kcal/kg/day, a value 10% lower than the gross energy intake. The overall daily energy expenditure averaged 68.4 ± 4.4 kcal/kg/day. The N gain was + 0.322 ± 0.049 g N/kg/day or 2.0 ± 0.3 g retained protein/kg/day. The lipid balance was largely positive (3.9 ± 1.0 g/kg/day), whereas the CHO gain was close to zero (−0.3 ± 0.8 g/kg/day).

Weight gain and composition of weight gain (Table 3). The mean rate of weight gain of the studied infants was 16.6 ± 4 g/kg/day, representing an energy gain 41.4 ± 6.7 kcal/kg/day, *i.e.* 38% of metabolizable intake, 87% of this energy was due to fat, the remaining part to protein retention. Estimates of the composition of weight gain by either described method gave similar results (compare Tables 1 and 3): CHO retention was negligible; 80% of weight gain was fat free mass whose average protein content was 16 ± 4% and 20% of weight gain was fat.

Energy expenditure and physical activity. Table 4 shows the individual values for the rate of energy expenditure, the degree of physical activity using Brück's scale and the simplified activity scale, and the respiratory quotient. Comparison of morning *versus* afternoon measurements showed no significant daytime variation for energy expenditure or activity. Furthermore no difference was found between days 1 and 2. There was a curvilinear relationship (3rd degree regression curve, $r = 0.752$) between Brück's activity score and energy expenditure (Fig. 2).

Figure 3 *upper diagram* shows the individual values of energy expenditure at each level of the simplified activity scale. Figure 3 *lower diagram* shows the linear relationship between energy expenditure and activity. The two regression lines correspond to the premeal period and to the peak thermogenic period following the meal. The mean activity in the premeal period was significantly greater than after the meal (0.93 respectively 0.66 units

Table 3. *Composition of wt gain estimated from energy and nitrogen balance*

Infant	Wt gain (g/kg/day)	Protein gain (g/kg/day)	Energy stored in protein* (kcal/kg/day)	Energy stored in lipid* (kcal/kg/day)	Lipid gain* (g/kg/day)	Fat-free mass (g/kg/day)	Fat-free mass (%)	Protein fat-free mass (%)
PG	24.8	2.1	11.9	30.1	3.2	21.6	87	10
AL	13.9	1.6	8.9	35.5	3.8	10.1	73	16
SB	14.3	1.8	10.0	31.6	3.4	10.9	76	16
ED	18.2	2.2	12.1	29.6	3.3	14.9	82	14
DP	16.6	2.1	12.0	40.9	4.4	12.2	74	18
SF	13.1	1.5	8.5	25.7	2.8	10.3	79	15
MS	11.5	2.1	11.9	29.5	3.2	8.3	72	26
LJ	18.6	2.3	13.1	31.9	3.4	15.2	82	15
JK	18.2	2.3	12.9	16.2	1.7	16.5	91	14
Mean	16.6	2.0	11.3	30.1	3.2	13.3	84	16
± SD	4.0	0.3	1.7	6.7	0.7	4.1	6	4

* Energy stored in protein = protein gain × 5.6 (kcal/kg/day) energy stored in lipid = energy gain–energy stored in protein lipid gain = energy stored in lipid/9.3 (kcal/g).

Table 4. *Energy expenditure, physical activity, and R.Q.*

	30–60 min before meal				30–60 min after meal			
		Activity				Activity		
Infant	Energy expenditure (kcal/kg/day)	0–3 scale	Brück's scale	R.Q.	Energy expenditure (kcal/kg/day)	0–3 scale	Brück's scale	R.Q.
PG	65.1	0.93	−1.8	0.96	67.9	0.73	−2.6	0.97
AL	71.5	1.30	+1.0	0.94	69.4	0.43	−2.0	1.02
SB	65.4	0.90	−0.9	0.95	67.2	0.55	−1.6	0.97
ED	73.7	0.93	−1.1	0.94	69.7	0.75	−2.2	0.94
DP	73.3	1.06	−0.2	1.04	74.0	0.78	−1.6	0.99
SF	70.2	0.86	−0.8	0.97	70.8	0.60	−2.0	0.99
MS*	65.2	0.67	−1.1	0.97	69.1	0.66	−2.3	0.96
LJ**	57.8	0.70	−1.5	0.96	63.4	0.60	−1.8	0.99
JK	67.0	0.99	−1.0	0.95	72.2	0.87	−1.3	0.94
Mean	66.6	0.93	−0.82	0.96	69.3	0.66	−1.9	0.97
± SD	6.2	0.19	0.82	0.03	3.0	0.13	0.4	0.03
	Average over 24 h							
PG	64.4	0.72	−2.5	0.96				
AL	71.2	0.92	−0.4	0.97				
SB	66.0	0.82	−1.4	0.95				
ED	73.3	0.87	−1.6	0.94				
DP	74.0	0.91	−1.1	0.99				
SF	70.0	0.75	−1.5	0.94				
MS*	66.3	0.66	−2.0	0.97				
LJ†	60.6	0.67	−1.6	0.96				
JK	69.9	0.92	−1.5	0.92				
Mean	68.4	0.80	−1.5	0.96				
± SD	4.4	0.11	0.6	0.02				

* Twelve meals/day.

† Ten meals/day.

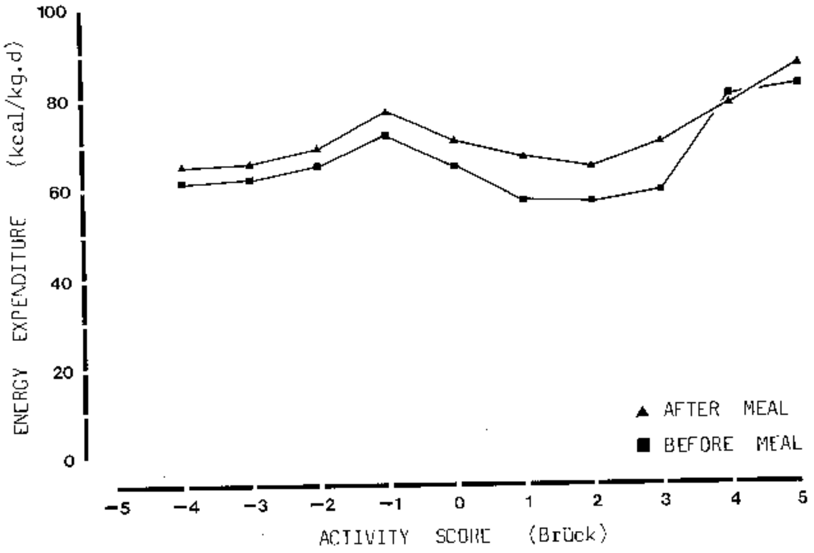

Fig. 2. Relationship between energy expenditure and Brück's (10) activity scale: The premeal values ■ were obtained during the 30-min period before the test meal. The values measured 30–60 min after the meal ▲ corresponds tothe meal's peak thermogenic effect. There is a lack of linearity between energy expenditure and activity when activity is scored primarily on inspection of the eyes.

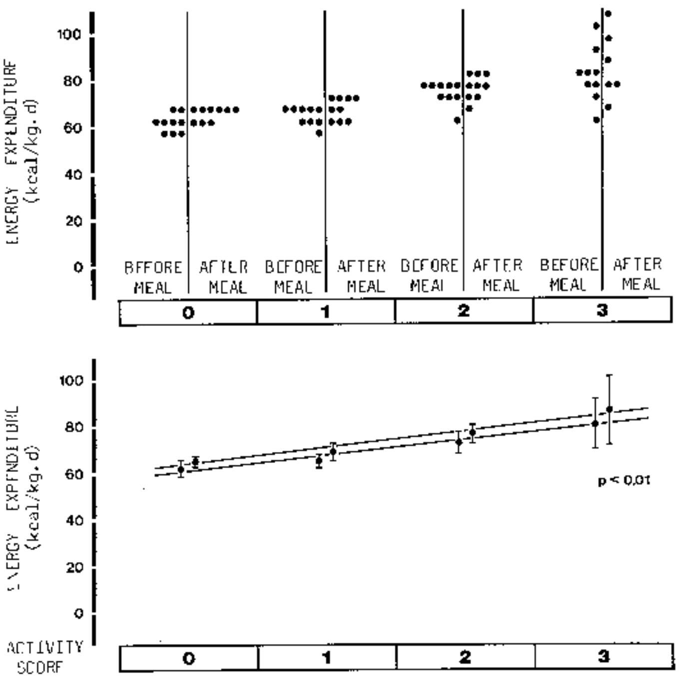

Fig. 3. Relationship between energy expenditure and activity (simplified activity sacle). *Upper diagram*, each *point* represent the mean values of energy expenditure at activity score 0–3. The measurements were done 30–0 min before and 30–60 min after the meal. Three infants of nine did not cry (score 3) after the meal. *Lower diagram*, linear relationship obtained between energy expenditure and activity derived from the values of Figure 3 *upper diagram*. The *lower line* shows the premeal regression ($y = 60.6 + 6.67\times$; $r = 0.752$; $p < 0.001$), the *upper line* the postmeal regression ($y = 61.1 + 6.87\times$; $r = 0.739$; $p < 0.001$). At each level of activity there was a significant pre- to postmeal difference in energy expenditure. The mean premeal activity is higher than after the meal (0.93 ± 0.19 *versus* 0.66 ± 0.13; $p < 0.05$).

on the activity scale, $p < 0.05$). However, at each level of activity, the premeal to postmeal differences in energy expenditure were comparable.

Table 5. *Thermogenic effect of test meals estimated by the "classic" and by the "regression" method (mean ± SD)*

	13.1 ± 2.1	
Test meals ME* (kcal/kg/3 h)	"Classic"	"Regression"
Premeal EE (kcal/kg/day)	58.2 ± 6.0	61.6 ± 3.4
Postmeal EE (kcal/kg/day)	69.1 ± 5.0	64.8 ± 3.5
Difference in EE (kcal/kg/3 h)	1.3 ± 0.6	0.4 ± 0.3
Thermogenic response to test meal		
% of ME in test meal	9.5 ± 3.8	3.1 ± 1.8
% of premeal baseline EE	19.2 ± 8.4	5.9 ± 3.2

* Metabolizable energy.
† Energy expenditure.

Thermogenic response to feeding (Table 5). If one considers only the mean energy expenditure, there was no significant premeal to postmeal difference, even during the peak thermogenic period (66.6 ± 6.2 versus 69.3 ± 3.0 kcal/kg/day). But, as mentioned previously, the corresponding levels of physical activity were not the same. According to the "classic" estimate, the increase above the premeal baseline energy expenditure was 19.2 ± 8.4 or 9.5 ± 3.8% of the meal's metabolizable energy. However this method compares a zero activity premeal energy expenditure to a postmeal energy expenditure measured at activity levels different from zero (0.83 ± 0.17). The "regression" method, which compares premeal to postmeal energy expenditure at zero activity levels, gives lower values −5.9 ± 3.2% increase in energy expenditure above baseline and 3.1 ± 1.8% of the meal's metabolizable energy.

DISCUSSION

Nutrient balance and composition of weight gain. The average values for apparent energy, protein (expressed as N), lipid, and carbohydrate digestibility were very close to our previous study (21). They compare with the higher range of reported values (20, 23–28). The composition of weight gain in premature babies is the object of daily clinical concerns in the neonatal units. A number of practical considerations preclude the utilization of methods like body density or K–40 measurements to get this information. Therefore bedside, noninvasive methods have to be used and a limited number of investigations have been performed

(6, 21, 23, 29, 30). The measured protein gain as well as the rate of weight gain are comparable to the studies using different milk formulas and different levels of energy intakes (6, 23, 29, 30). By contrast there are differences in fat gain between this and the above mentioned studies which seem closely linked to the difference in metabolizable energy. The comparatively lower metabolizable energy intake in our study resulted in a reduced fat gain despite a similar protein gain.

The composition of weight gain estimated by the two methods (energy and N balance *versus* R.Q. method) were similar. The smaller fat retention found with the balance method represents only 5% of the body weight gain. This is probably the precision within which fat retention can be estimated in premature babies. The comparison between the studied premature babies and fetuses of the same age is interesting, even if there is little rationale to do so. Their growth, in terms of weight gain and protein gain is comparable, whereas their fat gain differs (23, 29, 30). The premature infants' fat accumulation is higher than intrauterine values at the comparable postconceptional age and lower than that of term babies at a comparable postnatal age. Presently there is a lack of information about "physiologic" ranges of fat gain in premature infants.

Energy cost of activity. A number of authors have developed activity scales based primarily on visual observation of the infant's body movements (7, 9–16). Their aim were either to investigate the rate of physical activity as an index of the infant's brain function (13, 14, 16), or to assess criteria for physical rest in metabolic studies (7, 9, 11, 12, 15, 16, 31–36). In a few studies (7, 9, 31–34) an attempt was made to determine the energy expenditure at given levels of activity, but no attempt was made to correlate the grade of activity to the rate of energy expenditure. The results obtained by the Brück's scale (10) suggest that, as far as energy expenditure is concerned, some activity levels are not different from each other (−3, 0, +1, +2 *versus* −4). These states correspond to very low levels, *i.e.* no body movements, facial movements present or not, with eyes open or not. The scoring of activity levels, based primarily on the discrimination between open and closed eyes cannot be used to predict energy expenditure. This can be explained for the following reasons: 1) REM-sleep can occur on Brück's scale levels ranging from −4 to +3. 2) The clinical diagnosis of REM-sleep is unreliable in 19% of the cases (16) and finally, 3) $\dot{V}O_2$ differences between REM and non-REM sleep are controversial (7, 33, 34).

The simplified activity scale developed in the present study shows a highly significant linear correlation between its four activity levels and their corresponding energy expenditure values (Fig. 3); the slope of the regression line (6.7 kcal/kg/day/unit) represents the energy expended for one unit change in physical activity. Furthermore, the slopes of the regression lines obtained in the premeal and postmeal periods were similar, indicating no difference in the net cost of physical activity between both conditions. The overall energy cost of activity visualized in Figure 4 is close to the reported value of 3–5 kcal/kg/day (37); the higher values reported by Brooke *et al.* (9) (23 kcal/kg/day) were obtained at higher activity levels.

Thermogenic response to feeding. There is a conceptual problem that stems from the fact that the thermogenic response to a meal has been investigated in adult human physiology where premeal values were considered to reflect a fasting state. In premature infants this is never the case and the "real" thermogenic effect cannot be measured. Our results, obtained by the "classical" method (see Table 5), are comparable to the published values, 1.1 kcal/kd/4 h (9) and 1.7 kcak/kg/4 h (17). The latter range from 4 to 9% when expressed as percent of the test meal's metabolizable energy and from 17 to 26% when expressed as percent increase over the premeal baseline.

With present day's nursing routines eight to 12 meals/day) the premeal baseline cannot be regarded as a basal postabsorbtive value. Prematures are constantly under food stimulation and part of their thermogenic responses are still present in the following premeal energy expenditure. Therefore, the greater the number of meals per day, the smaller the expected postprandial response. Indeed our values obtained with eight meals/day are lower than those reported for a six meals/day study (17). The baseline energy expenditure of the "classic" method must be measured during a motionless premeal period. Since the infants do not stay quiet over the 180-min postmeal period, the effect of physical activity on energy expenditure is superimposed on the thermogenic effect of the meal. This results in an overestimation of the latter. We attempted to circumvent the difficulty by using the "regression" method to obtain the thermogenic effect of the meals in our nursing conditions. As expected, the obtained thermogenic response was smaller. Finally the results show that the variations of energy expenditure during the course of 24 h are equally due to physical activity and to the thermogenic effect of feeding (Fig. 4).

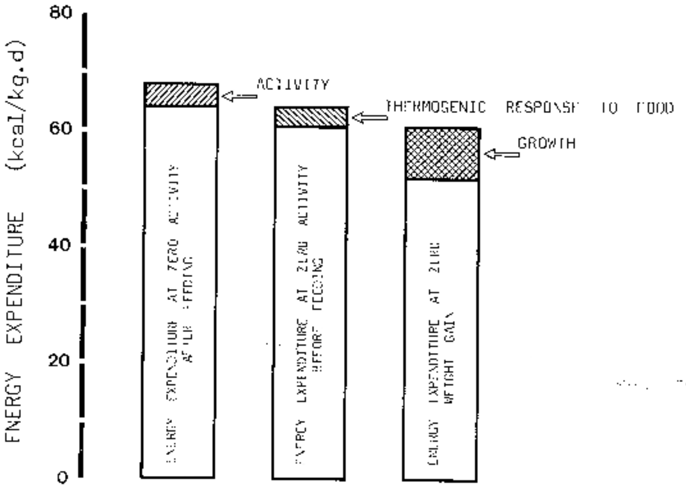

Fig. 4. Partition of energy expenditure between activity and thermogenic response to food. The *left column* represents the average energy expenditure over 24 h (68.4 ± 4.4 kcal/kg/day). Using the "regression" method it is possible to assess the postmeal resting energy expenditure (64.8 ± 3.5 kcal/kg/day). The difference between these two values represents the energetic cost of activity. The *second column* allows the comparison between pre- (61.6 ± 3.4 kcal/kg/day) and postmeal energy expenditure at the zero activity level: the difference in energy expenditure represents the thermogenic effect of food; the *third column* represents our previous results (5) done with the same method on a comparable sample of premature babies. It shows that the energy expenditure related to physical activity and thermogenic effect of feeding is relatively small compared to the metabolic cost of growth.

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APPENDIX

Gross energy and nutrient intakes apparent digestibility and metabolizable energy.

Energy equivalent of CHO intake (E CHO) in kcal/g:

$$\text{E CHO} = \text{GE} - (\text{g N} \times 6.38 \times 5.6) - (\text{g lipid} \times 9.25) \qquad \text{Eq 1}$$

GE	gross energy of milk (kcal/kg/day)
6.38	g of milk protein per g Nitrogen
5.6	gross energy equivalent of protein (kcal/kg/day)
9.25	gross energy equivalent of lipid (kcal/kg/day)

CHO intake (I CHO) in g/kg/day:

$$\text{I CHO} = \text{E CHO}/3.95 \qquad \text{Eq 2}$$

3.95	gross energy equivalent of lactose (kcal/kg/day)

Apparent digestible energy (DE) in kcal/kg/day:

$$\text{DE} = \text{GE} - \text{E feces}$$

$$\text{DE (\%)} = (\text{GE} - \text{E feces}) \times 100/\text{GE} \qquad \text{Eq 3}$$

Apparent N digestibility (DN) in mg/kg/day:

$$\text{DN} = \text{N intake} - \text{N feces}$$

$$\text{DN (\%)} = \frac{(\text{N intake} - \text{N feces}) \times 100}{\text{N intake}} \qquad \text{Eq 4}$$

Apparent lipid digestibility (DL) in g/kg/day

$$\text{DL} = \text{lip. intake-fecal lip.}$$

$$\text{DL (\%)} = \frac{(\text{lip. intake} - \text{fecal lip.}) \times 100}{\text{lipid intake}} \qquad \text{Eq 5}$$

Apparent CHO digestibility (D CHO) in g/kg/day:

$$\text{D CHO} = \text{CHO intake} - \text{CHO feces} \qquad \text{Eq 6}$$

$$\text{D CHO (\%)} = \frac{\text{CHO intake} - \text{CHO feces} \times 100}{\text{CHO intake}}$$

$$\text{CHO feces} = [\text{E feces} - (\text{fecal lipid E} + \text{fecal protein E})]/3.75 \qquad \text{Eq 7}$$

The gross energy equivalent of fecal protein, lipid and CHO are respectively 5.6, 9.3 and 3.75 kcal/g

CHO in feces are assumed to be monosaccharide

Metabolizable energy intake (ME) in kcal/kg/day:

$$\text{ME} = \text{GE} - (\text{E feces} - \text{E urine}) = \text{DE} - \text{E urine} \qquad \text{Eq 8}$$

Energy expenditure (EE) measured by indirect calorimetry in kcal/kg/day.

$$\text{EE} = 4.686 + \frac{(\text{NPRQ} - 0.707) \times 0.361\ \text{NP}\dot{\text{V}}\text{O}_2 + 4.46\ \text{P}\dot{\text{V}}\text{O}_2}{0.293} \qquad \text{Eq 9}$$

$P\dot{V}O_2$	oxygen consumed by protein oxidation in 1/kg/day
$NP\dot{V}O_2$	nonprotein oxygen consumption in 1/kg/day
NPRQ	nonprotein respiratory quotient
0.707	NPRQ for total fat oxidation
0.293	difference in NPRQ between that of fat oxidation and CHO oxidation (1 − 0.707)
4.686	caloric equivalent (kcal/liter O_2) of 1 liter oxygen at NPRQ = 0.707
0.361	difference between the caloric equivalents of one liter oxygen at a NPRQ of 1 and 0.707
4.64	caloric equivalent (kcal/kg/day) of one liter oxygen when protein is oxidized

Oxidation rates in protein, lipid and CHO (P ox, L ox, CHO ox) in g/kg/day.

$$\text{P ox} = \text{N} \times 6.25 \times 0.966 \qquad \text{Eq 10}$$

$$\text{L ox} = \text{NP}\dot{\text{V}}\text{O}_2 \times \frac{(1 - \text{NPRQ})}{0.293 \times 2.019} \qquad \text{Eq 11}$$

$$\text{CHO ox} = \text{NP}\dot{\text{V}}\text{O}_2 \times \frac{(\text{NPRQ} - 0707)}{0.293 \times 0.829} \qquad \text{Eq 12}$$

N	total Nitrogen excretion in g/kg/day
6.25	protein equivalent of N
0.966	volume of oxygen required to oxidize one g of protein
2.019	volume of oxygen required to oxidize one g of lipid
0.829	volume of oxygen required to oxidize one g of CHO expressed as starch

Energy gain in kcal/kg/day, protein gain, CHO gain, and lipid gain in g/kg/day.

a. Energy and N balance method:

$$\text{E gain} = \text{ME} - \text{EE} \qquad \text{Eq 13}$$

$$\text{N gain} = \text{gross N intake} - (\text{fecal} + \text{urinary N}) \qquad \text{Eq 14}$$

$$\text{P gain} = \text{N gain} \times 6.25 \qquad \text{Eq 15}$$

CHO gain is assumed to be negligible

$$\text{L gain} = \text{E stored in lipid}/9.25 = \text{E gain} - (\text{P gain} \times 5.6)/9.25 \qquad \text{Eq 16}$$

b. R.Q. method:

N gain = gross N intake − (fecal + urinary N)

P gain = N gain × 6.25

$$\text{CHO gain} = \text{MCHO} - \text{CHO ox} \qquad \text{Eq 17}$$

$$\text{L gain} = \text{ML} - \text{L ox} \qquad \text{Eq 18}$$

ME	metabolizable energy intake (kcal/kg/day)
ML	metabolizable lipid intake (g/kg/day)
MCHO	metabolizable CHO intake (g/kg/day)

Fat free mass gain (FFM) in g/kg/day:

$$\text{FFM gain} = \text{weight gain} - \text{lipid gain} \qquad \text{Eq 19}$$

The thermogenic effect of feeding (TEF) was estimated by two methods.

a. The "classic" method:

TEF (%) over premeal baseline EE

$$= \frac{(\text{postmeal EE} - \text{premeal baseline EE}) \times 100}{\text{premeal baseline EE}} \qquad \text{Eq 20}$$

TEF (%) of testmeal ME

$$= \frac{(\text{postmeal EE} - \text{premeal baseline EE}) \times 100}{\text{ME content of test meal}} \qquad \text{Eq 21}$$

premeal baseline EE is the EE measured over a 3- to 5-min period of inactivity (0 activity on the simplified scale) during the 30-min premeal period

postmeal EE is the EE measured over 180 min after the testmeal.

b. The "regression" method:

TEF (%) over premeal EE

$$= \frac{(\text{postmeal EE} - \text{premeal EE}) \times 100}{\text{premeal EE}} \qquad \text{Eq 22}$$

TEF (%) of testmeal ME

$$= \frac{(\text{postmeal EE} - \text{premeal EE}) \times 100}{\text{ME content of test meal}} \qquad \text{Eq 23}$$

premeal EE is the value of the premeal regression line (EE *versus* 0–3 activity score) at the zero activity intercept.

the premeal regression line is obtained by plotting the minute by minute EE measurements versus activity during the 30-min premeal period.

postmeal EE is the value of the postmeal regression line (EE *versus* 0–3 activity score) at the zero activity intercept.

the postmeal regression line is obtained by plotting the minute by minute EE measurements versus activity during the 180-min postmeal period.