Metabolic Cost of Growth in Very Low-Birth-Weight Infants

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Summary

Forty-eight measurements of energy expenditure were performed in 15 very low-birth-weight infants during the first 6 wk of life. Their mean birth weight and gestation age was 1223 g and 31 wk respectively. Their mean weight gain was 11.2 g/kg·d (range: -6.6 to +15.9 g/kg·d.). The mean energy expenditure increased from 170 kJ/kg·d (wk 1) to 252 kJ/kg·d (wk 6). There was a significant relationship between weight gain and energy expenditure ($r = 0.58$, $P < 0.001$) and also between the net increase in body weight gain and the net increase in energy expenditure ($r = 0.80$, $P < 0.001$). From the slopes of these regression lines, the metabolic cost of growth was found to be approximately 2.3 kJ/g of weight gain. Carbohydrate oxidation represented 80% of energy expenditure at the second wk and decreased to 65% the 6th wk, whereas lipid oxidation during the same period increased from 14 to 30% and the relative protein oxidation remained unchanged, covering 5-6% of the energy expended.

Speculation

There is need for information on the metabolic cost of growth in very low-birth-weight infants because a significant proportion of energy expenditure is associated with the metabolic cost of growth due to tissue synthesis. An attempt has been made to investigate the relationship between weight gain and energy expenditure in very low-birth-weight infants. In addition, substrate oxidation was determined during the first wk of life in order to elucidate which fuel was oxidized during this period of rapid growth.

Although many authors have studied the energy expenditure of very low-birth-weight infants (4, 7, 11, 12, 16, 23, 26, 27, 29, 31) the energetics of growth has received little attention, particularly the partition of energy expenditure between growth and non-growth functions (30). In healthy immature infants, high rates of weight gain are achieved and the metabolic cost of growth may represent a substantial part of the total daily energy expenditure. Such a situation is also found in children recovering from protein-energy malnutrition (3, 34) and from burn injury (18).

Recently, several energy balance studies have been performed in very low-birth-weight infants (4, 29), but there is little information on repetitive long term measurements of energy expenditure and on the metabolic cost of growth. The total energy requirement of a growing infant can be separated into two components (25): one is the energy content of tissues deposited (stored energy), the other is the extra energy expended to synthesise and deposit new tissues (metabolic cost of growth). This study is concerned with the latter and with the fuels oxidized by very low-birth-weight infants during the first 6 wk of life.

MATERIALS AND METHODS

Infants. Fifteen very low-birth-weight infants admitted to the neonatal intensive care unit of the University hospital were stud-

ied. The characteristics of each child are given in Table 1. None of these infants had major medical problems at the time of the study. All were admitted to our unit within the first 3 h of life. Their mean birth weight ranged between 760-1640 g. Their gestation age ranged between 27-35 wk, confirmed by the Dubowitz score (9). All but two infants were adequate for gestational age, the remaining two being small for gestational age. The experimental protocol was approved by the ethical committee of the University hospital. Informed parental consent was obtained for each infant and the parents were frequently present during the measurements.

Feeding. The infants were perfused with glucose from admission until feeding was adequate. Feeding was started within the first 6 h of life and gradually increased. The mean energy intake during the first wk was 299 kJ/kg·d (S.D. ± 91). The full diet of 544 kJ/kg (S.D. ± 83) was reached between the 5th and the 8th day. Six infants were partially fed with their mother's milk (identified in Table 1) and ten with a formula (Alprem MCT, Nestlé Ltd., Vevey, Switzerland) prepared from whole milk, whey, medium chain triglycerides, lactalbumin and vegetable oils (36). Both milk formula and mother's milk were given by nasogastric tube, and the ingested volume was measured with a 10-ml syringe. The gross energy content of the powder determined by bomb calorimetry (Parr Instruments Co., Moline, IL, USA) was 21.67 kJ/g powder (S.D. ± 0.03). The number of the meals ranged between 10-12 per day, according to the weight of the infants.

Measurement of energy expenditure. Total daily energy expenditure was measured by open circuit indirect calorimetry, each infant being repeatedly studied during the first weeks of life. The measurements were made with a new type of calorimeter: it consists of a tight perspex box containing the whole infant, large enough to allow for free movement, which is placed inside an incubator. The air within the box is continuously renewed with fresh air from a cylinder at a rate measured by a pneumotachograph connected to a differential manometer (Hewlett-Packard 47305, Loveland, CO, USA). The air flow was set to maintain a CO₂ concentration in the calorimeter of approximately 0.5%. The outflowing air was continuously sampled and its O₂ and CO₂ concentrations were measured using a Perkin-Elmer MGA 1100 mass spectrometer (Perkin-Elmer Corp., Norwalk, CT, USA). The O₂ consumption ($\dot{V}O_2$) and the CO₂ production ($\dot{V}CO_2$) was then calculated using Haldane's correction for $\dot{V}O_2$ (15, 22). Urine was collected over 24 h and analysed for total nitrogen excretion according to Kjeldahl. The equations to compute $\dot{V}O_2$, $\dot{V}CO_2$, and the metabolic rate (MR) are given in the "Appendix." After the calculation of the protein oxidation rate from the total nitrogen excretion, the nonprotein respiratory quotient, fat and carbohydrate oxidation were calculated as described by Consolazio *et al.* (8). The response time of the chamber to a step change in $\dot{V}O_2$ or $\dot{V}CO_2$ was found to be approximately 1.5 min under usual conditions of measurements. The analyser was calibrated using pure O₂, CO₂, N₂ gases, and gas mixtures prepared with a proportional mixing pump (Wohstoff, Bochum, Germany). In order to avoid the influence of changes in water vapor on the measurements, a

steady and very low level of water vapor was obtained by equilibrating the gas samples and the calibrating gases at 0°C. The accuracy of the measurements of O₂ consumption and CO₂ production was controlled by using a small butane burner inside the calorimeter; the measured values were within $\pm 2\%$ of the calculated ones obtained from the weight change of the butane.

All infants were nursed in incubators, and Hey's charts (10) were used to set the ambient temperature. During energy expenditure determinations, the infants' thermoneutrality was continuously monitored via a thermistance placed on the abdominal skin (Yellow Springs no 421, Instruments Co., Yellow Springs, OH, USA). The mean abdominal temperature throughout the study was 36.6°C (range 36.2–37.3°C). Activity was checked every minute using Brück's activity scale (6, 7). The latter varies from a –4 level (eyes closed, no movement) to a +5 level (crying, eyes opened or closed). All the infants were tube fed at the time of the study, so the energy cost of bottle feeding did not need to be taken into account.

Table 1. Clinical characteristics of 15 very low-birth-weight infants

Infant	Sex	Birth weight (g)	Birth length (cm)	Gestational age (wk)
1 L.D.	M	760	32	27
2 P.S. ¹	M	770	38	27
3 C.S. ¹	M	800	37.5	27
4 S.M. ¹	F	1270	39.5	30
5 C.B.	F	1260	39	30
6 C.Ba. ¹	F	1310	41	31
7 B.B.	M	1460	41	31
8 S.V.	M	1290	38	31
9 P.A. ¹	M	1640	41	32
10 S.St.	F	1630	42.5	32
11 C.H.	F	1390	41	32
12 E.W. ¹	M	1380	41	32
13 C.C.	F	1280	39	33
14 M.M.	F	930	37	34
15 S.C.	M	1170	39	35
Mean		1223	39	31
$\pm$ S.D.		287	3	2

¹ Infants partially fed with human milk.

Measurements of metabolic rate were repeatedly carried out in the morning in five infants and in the afternoon in 10 infants, immediately after the completion of the meal. The duration of the measurements ranged from 90 min to 3 h. In order to test the variability of energy expenditure during the day and night, and the validity of extrapolating measurements of several hours over the whole day, we made repeated measurements of energy expenditure in three infants over a 24-h period on two consecutive days. The coefficients of variation of $\dot{V}O_2$ were 3.5%, 6.6% and 6.5% for the three infants respectively. $\dot{V}O_2$, $\dot{V}CO_2$, respiratory quotient (RQ), metabolic rate and substrate oxidation were calculated every 5 min and averaged over the period of measurement.

Assessment of growth. The following measurements were made during the course of the study: weight was measured daily on a Sauter balance (August Sauter, K.G., Ebingen, Germany) to the nearest 5 g. The mean weight at each week of life was obtained by averaging individual weight over the considered week. The weekly weight gain was calculated from the regression line of daily weight over time. This procedure was used to avoid imprecision in weight gain estimated due to fluctuations in body weight. Head circumference was measured weekly using a cloth tape. Crown-heel length was checked weekly using a neonatal stadiometer.

Determination of the metabolic cost of growth. The energy expended for growth was obtained from the relationship between the weight gain and the energy expenditure. Because an increase in body size will increase energy expenditure, the weight gain was normalized for body mass (g/kg·day). The latter was taken as the independent variable and the energy expenditure per kg body weight as the dependent variable. If both variables are significantly correlated, the slope of the regression line, *i.e.*, the extra energy expended per g of weight gain, gives an index of the energy cost of growth.

RESULTS

Growth rates. Table 2 shows the individual mean weight and weight gain during the first 6 wk of life. During the first wk, the mean weight was 1153 g (S.D. $\pm$ 278) and increased to 1793 g (S.D. $\pm$ 400) by the sixth wk. The mean weight gain was negative during the first wk: –6.6 g/kg·d (S.D. $\pm$ 10.0), reached 15.9 g/kg·d (S.D. $\pm$ 5.7) at the third wk and 14.9 g/kg·d (S.D. $\pm$ 5.0) at the sixth wk (Table 2). There was a significant increase in weight gain per kg between the first and 2nd wk of life ($P < 0.001$) but not subsequently.

Table 2. Mean weight and weight gain during the first 6 wk of life

Infant	Mean weight (g)						Weight gain (g/kg·day)					
	1 ¹	2	3	4	5	6	1 ¹	2	3	4	5	6
1 L.D.	723	706	824	934	1060	1106	–19.3	16.2	23.8	16.8	7.4	15.2
2 P.S.	718	744	860	982	1080	1189	–2.7	22.1	18.3	11.0	13.6	13.8
3 C.S.	761	717	869	963	1036	1151	–18.5	29.4	16.0	21.1	15.5	9.6
4 S.M.	1176	1204	1314	1469	1644	1907	–7.3	2.7	24.7	16.1	17.8	26.0
5 C.B.	1207	1230	1354	1547	1722	1996	–8.0	12.8	15.0	16.7	23.2	19.0
6 C.Ba.	1281	1297	1463	1631	1844	2093	–5.9	5.5	16.4	14.7	18.2	20.0
7 B.B.	1410	1510	1727	1924	2117		–6.6	18.7	18.4	16.5	8.8	
8 S.V.	1216	1236	1364	1529	1640	1794	–4.7	12.4	13.1	13.1	14.4	7.8
9 P.A.	1459	1473	1643	1876	2104	2413	–22.3	11.2	12.2	18.9	20.5	16.4
10 S.St.	1616	1630	1793	1891	2004	2229	–4.4	13.8	5.6	6.6	10.0	17.0
11 C.H.		1359	1411	1489	1591	1747		–1.3	12.7	5.5	13.5	11.0
12 E.W.	1319	1327	1459	1563	1717	1856	–1.9	11.6	17.9	16.7	10.0	10.4
13 C.C.	1130	1194	1291	1430	1600	1834	–10.8	9.9	8.0	16.5	15.6	18.3
14 M.M.	930	1003	1174	1384	1554	1690	3.1	15.0	24.7	23.0	11.7	9.7
15 S.C.	1199	1341	1469	1627	1881	2097	17.6	18.1	11.4	17.6	15.2	14.7
Mean	1153	1198	1334	1483	1640	1793	–6.6	13.2	15.9	15.4	14.4	14.9
S.D.	278	287	298	317	350	400	10.0	7.6	5.7	4.8	4.4	5.0

¹ Weeks of life.

² $P < 0.001$ versus week 1.

Energy expenditure. The individual and mean weekly values of 48 measurements of energy expenditure made in 15 infants are given in Table 3. The mean energy expenditure during the first wk was 188 kJ/d (S.D. ± 71) and increased to 434 kJ/d (S.D. ± 80) at the sixth wk. The energy expenditure expressed per kg body weight was 170 kJ/kg·d (S.D. ± 11) during the first wk and increased significantly during the 2nd and 3rd wk to reach 214 kJ/kg·d (S.D. ± 41 , $P < 0.05$) and 269 kJ/kg·d (S.D. ± 21 , $P < 0.005$) respectively. There was no more change subsequently (Table 3).

Relationship between weight gain and energy expenditure. Figure 1 shows the relationship between weight gain and energy expenditure for the 48 measurements and the regression equation. The relationship is positive and statistically significant ($r = 0.58$, $P < 0.001$). From the slope of the regression one can see that each g of

weight gain was associated with an extra energy expenditure of 2.26 kJ. At zero weight gain, the energy expenditure calculated from the regression equation was 214 kJ/kg·d.

The net increase in energy expenditure (Δ energy expenditure) was also plotted against the net increase in body weight gain (Δ weight gain) using the largest observed time span between two measurements of energy expenditure (Fig. 2). The relationship between Δ weight gain expressed per kg body weight and the Δ energy expenditure per kg body weight was highly significant ($r = 0.80$, $P < 0.001$). The slope of the regression line was similar to that found with the pooled regression, *i.e.*, 2.33 kJ/g. The Y intercept of the line at 0 weight gain was not significantly different from zero.

RQ and substrate oxidation. Individual and mean weekly value of RQ are given in Table 4. There was a progressive decrease in

Table 3. Energy expenditure expressed in kJ/day and kJ/kg·day during the first 6 wk of life

Infant	Energy expenditure (kJ/day)						Energy expenditure (kJ/kg·day) ²					
	1 ¹	2	3	4	5	6	1 ¹	2	3	4	5	6
1 L.D.		182	230		264	277		246	287		249	254
2 P.S.	118			235			162			247		
3 C.S.	121	177		245			163	224		258		
4 S.M.		223		359		432		181		239		244
5 C.B.		277		422	435	462		233		281	265	232
6 C.Ba.	233	222			371		185	175			204	
7 B.B.			405	510	546				238	267	254	
8 S.V.			352	454	439	488			271	291	261	271
9 P.A.	282	400	477				179	276	298			
10 S.St.		255		384				151		197		
11 C.H.			348	354	380	440			240	236	226	242
12 E.W.			429	383	507	530			269	250	298	276
13 C.C.	186	233					162	195				
14 M.M.			347		424	412			275		279	245
15 S.C.		326	391	397	492			245	277	248	267	
Mean	188	255	372	374	429	434	170	214 ³	269 ⁴	251	256	252
S.D.	71	71	73	85	84	80	11	41	21	26	28	16

¹ Weeks of life.

² Body weight measured on the test day.

³ $P < 0.05$ vs week 1.

⁴ $P < 0.005$ vs week 2.

Fig. 1. Relationship between weight gain and energy expenditure during the study period.

Fig. 2. Relationship between the net increase in body weight gain and the net increase in energy expenditure during the study period.

Table 4. Mean respiratory quotient during the first 6 wk of life

Infant	Weeks of life					
	1	2	3	4	5	6
1 L.D.		0.90	0.97		0.98	0.98
2 P.S.	1.02			0.90		
3 C.S.	1.01	1.05		0.94		
4 S.M.		0.96		0.93		0.91
5 C.B.		0.98		0.94	1.00	0.93
6 C.Ba.	1.04	0.99			0.90	
7 B.B.			0.89	0.90	0.86	
8 S.V.			0.99	0.97	0.89	0.90
9 P.A.	0.84	0.94	0.92			
10 S.St.		0.85		0.94		
11 C.H.			0.83	0.85	0.87	0.87
12 E.W.			0.88	0.89	0.89	0.88
13 C.C.	0.93	0.93				
14 M.M.			0.88		0.82	0.84
15 S.C.		0.92	0.92	0.86	0.86	
Mean	0.97	0.95	0.91	0.91	0.90	0.90
S.D.	0.08	0.06	0.05	0.04	0.06	0.05

mean RQ from 0.97 at the first wk to 0.90 at the 5th and 6th wk. In occasional cases, RQs greater than 1 were observed. Figure 3 shows the average amount of carbohydrates (CHO), lipids and protein oxidized from wk 1–6, expressed in g/kg·d. Oxidation of CHO was 8.4 g/kg·d (S.D. $\pm$ 2.5) during the first wk, 10.6 g/kg·d (S.D. $\pm$ 2.8) at the third wk and 9.5 g/kg·d (S.D. $\pm$ 2.1) at the sixth wk. If these results are converted into % of energy expended during the first 2 wk, CHO oxidation represented 80% of the energy expended, whereas lipid and protein oxidation contributed 14% and 6% of the energy expenditure respectively; at the 6th wk, CHO oxidation decreased to 65% and lipid oxidation increased to 30% of the energy expended whereas protein oxidation remained constant.

DISCUSSION

Growth rates. It is generally admitted (33, 35) that immature infants show an early weight loss of 5–10% of body weight mainly due to a negative water balance. In this study, the weight loss was

Fig. 3. Proportion of substrates oxidized during the first weeks of life. Carbohydrate (□); lipid (▨); protein (■).

probably not due to a decrease in body energy stores, because the mean energy expenditure during the first wk was 170 kJ/kg·d, whereas the mean energy intake was 299 kJ/kg·d. An energy deficit is therefore unlikely. Most infants recovered their birth-weight between the first and the second wk. Their rate of weight gain was similar to that observed by Largo *et al.* (20) and Brandt (2) for the same postconceptional age. After the first wk, weight gain was assumed to be a good assessment of tissue growth.

RQ and substrate oxidation. In term infants, Brück (6, 7) showed that after the first few days of life, the RQ rises from 0.7 to approximately 0.85, a value observed in adult ingesting a mixed diet. In the very low-birth-weight infants studied, RQ was 0.97 during the first wk of life, which indicates preferential utilisation of CHO (80% of the energy expenditure). This value was certainly influenced by the glucose infusion. In contrast to the results in term infants, the time course of RQ in very low-birth-weight infants was marked by a progressive decrease from 0.95 at the second wk to 0.90 at the 6th wk, which corresponds to a decrease in CHO oxidation with a rise in lipid utilisation. This pattern of glucose utilisation differs from the study of Rubecz and Mestyán (27), in which a shift in CHO utilisation from 66% to 80% was observed between the nongrowing and growing period, whereas there was a decrease in fat and protein metabolism. The discrepancy of fuels oxidized during the nongrowing period may result from different diets, glucose administration being given earlier and in larger amounts in our study than in that of Rubecz and Mestyán. In contrast, the rate of protein oxidation found in our study was very close to that found by Rubecz and Mestyán (27) during the growing period (6% of energy expenditure). The latter corresponds to the proportion reported for full size and preterm infants (21, 27).

Energy expenditure. Basal metabolic rate cannot be defined easily in very low-birth-weight infants because they can never be kept in the basal fasting conditions. In this study, the overall energy expenditure measured included basal metabolic rate, dietary induced thermogenesis, a minimum amount of activity and the metabolic cost of growth. It was also difficult to partition the postprandial increase in metabolic rate between dietary-induced thermogenesis and activity, because of the low activity score values observed. Furthermore, there was no significant change in activity according to Brück's scale from wk 3 to wk 6. The observation that the mean energy expenditure per kg did not increase from the third to the sixth wk of life corresponds well with the observation of a constant low activity level.

The estimation of 24 h energy expenditure from measurements made during 1.30–3 h is validated because the coefficient of variations for measurements performed over 24 h are low. The stable pattern of oxygen consumption throughout the day confirms earlier observations in very low-birth-weight infants (28).

The metabolic rate of very low-birth-weight infants has been measured by many authors (4, 7, 11, 12, 16, 23, 26, 27, 29, 31). Their data show that the oxygen consumption is the lowest in the first few days after birth and increases during the first and the second wk (11, 12, 23, 31). Findings about resting metabolic rate after the second week are controversial (11, 12, 17). In our study, the greatest stimulation in metabolic rate took place between the first (170 kJ/kg·d) (S.D. $\pm$ 11) and the third (269 kJ/kg·d) (S.D. $\pm$ 21) wk of life, a period characterised by a significant increase in weight gain.

Many authors did not have the opportunity to measure the maintenance energy expenditure directly. The latter includes basal metabolic rate, dietary-induced thermogenesis and the energy expended for a minimum amount of physical activity, but it does not include the requirement for growth. Assuming that the weight loss observed at the first wk was merely due to a negative water balance and not to a loss of tissue, our mean value for energy expenditure at the same week (170 kJ/kg·d) (S.D. $\pm$ 11) represents an estimate of maintenance energy expenditure (Table 3).

Relationship between weight gain and energy expenditure. Various

indirect approaches have been used to estimate the metabolic cost of growth (4, 13, 14, 29, 34). A statistically significant correlation ($r = 0.58$, $P < 0.001$) between weight gain and energy expenditure was obtained in this study, which allowed to estimate the metabolic cost of growth to 2.26 kJ/g of weight gain. The relationship between incremental values (Δ weight gain and Δ energy expenditure) gave a higher coefficient of correlation between the two variables ($r = 0.80$, $P < 0.001$) with a similar estimate of the metabolic cost of growth, *i.e.*, 2.33 kJ/g of weight gain. Other authors (4, 34) failed to show such relationships, probably because of smaller range in weight gain achieved and the lack of repetitive measurements throughout the first weeks of life. Although Rubecz and Mestyán (27) showed a significant relationship between weight change and energy expenditure per kg body weight, they did not stress the importance of growth as a major factor influencing metabolic rate. In addition, Brück in his review of the factors able to modify Kleiber's prediction equation for metabolic rate from body size (5, 19) considered sex, body shape, body composition and age, but did not mention the influence of growth rate. Our findings suggest that the extra energy expenditure from 170 kJ/kg·d the first wk to 269 kJ/kg·d the third one is mainly due to the energy cost of growth resulting from synthetic processes. During the first 6 wk of life for a mean weight gain of 11.2 g/kg·d, the figure one shows an extra energy expenditure of 11.8% over the zero growth energy expenditure (214 kJ/kg·d).

Comparison of our results with that of Brooke and Ashworth (3) is of interest because these authors have studied the energy expenditure of children during the catch-up growth process in relationship with the rate of weight gain. Although these authors have studied a different sample of children in terms of age, weight and nutritional status, we have attempted to compare both studies. Calculated for the same rate of growth, their average increase in energy expenditure was similar (*i.e.*, 11.4%) as in our study. Thus the increment in energy expenditure due to rapid weight gain in very low-birth-weight infants does not substantially differ from that found in children recovering from protein-energy deprivation. By contrast, when Ashworth (1) investigated the energy expenditure at rest 4 h after the last meal, there was no longer an increment of energy expenditure per kg body weight in relationship with growth rates; therefore, part of the process of dietary induced (or postprandial) thermogenesis in growing infants may include the metabolic cost of growth (1).

The metabolic cost of growth represents the energy expended for the synthetic processes associated with weight gain, but it does not include the energy of the substrates which form the components of the new tissue. It is difficult to assess the energy content of new tissues, because they can contain as little as 5 to as much as 30 kJ/g according to their protein, fat, and water content (25). It is obvious that the requirements for growth have to take into account both the energy content of the new tissues and the energy expended for the synthetic processes.

In a recent study, Brooke *et al.* (4) found a very high value (*i.e.*, 7.2 kJ/g of weight gain) for the metabolic cost of growth in very low-birth-weight infants. Their measurements of energy expenditure were, however, performed only during short periods (5–10 min) and the values obtained were much larger than that reported in this study and by others (11, 12, 23, 24, 26). An overestimate of the energy expended during 24 h may explain this high value of metabolic cost of growth.

It is concluded that by repetitive measurements of energy expenditure in very low-birth-weight infants during the first weeks of life, a relationship has been shown between the rate of weight gain and the energy expended. The metabolic cost of weight gain was found to be approximately 2.3 kJ/g, which represents a significant part (*i.e.*, 12–13%) of the overall energy expenditure. By contrast with term newborns who have low RQs (5, 6, 16, 32), very low-birth-weight infants during the first two weeks of life exhibited RQs near unity indicating preferential carbohydrate utilisation, with an economy of lipid.

APPENDIX

The equations to compute $\dot{V}O_2$, $\dot{V}CO_2$ and the metabolic rate (MR) with the open circuit indirect calorimeter has been described by Jéquier (15):

$$\dot{V}O_2 = \frac{1}{1 - F_{in}O_2} \left[\dot{V}_{out}(\Delta F_{O_2} - \Delta F_{CO_2} F_{in}O_2) + V \left(\frac{dF_{out}O_2}{dt} - \frac{dF_{out}CO_2 F_{in}O_2}{dt} \right) \right] \quad 1$$

$$\dot{V}CO_2 = \dot{V}_{out}\Delta F_{CO_2} + V \frac{dF_{out}CO_2}{dt} \quad 2$$

where $F_{in}O_2$ = fraction of O_2 at the inlet; $F_{out}O_2$ = fraction of O_2 at the outlet; $F_{in}CO_2$ = fraction of CO_2 at the inlet; $F_{out}CO_2$ = fraction of CO_2 at the outlet; $\Delta F_{O_2} = F_{in}O_2 - F_{out}O_2$; $\Delta F_{CO_2} = F_{out}CO_2 - F_{in}CO_2$; $\dot{V}_{out}$ = rate of air flow at the outlet; V = volume of the chamber.

The following equation, in which all volumes are converted to STPD conditions, was used to compute the metabolic rate:

$$MR = [19.5 + 5.0 (NPRQ - 0.707)] \dot{V}_{O_2 NP} + 18.7 \dot{V}_{O_2 P} \quad 3$$

where MR = metabolic rate in kJ/min; NPRQ = "non protein" respiratory quotient = $\dot{V}_{CO_2 NP} / \dot{V}_{O_2 NP}$; $\dot{V}_{O_2 NP}$ = O_2 consumption (l/min), due to carbohydrate and lipid oxidation; and $\dot{V}_{O_2 P}$ = O_2 consumption (l/min), due to protein oxidation.

Note: A NPRQ above 1.0 reflects net lipogenesis i.e., net conversion of carbohydrate into lipid. Under these conditions the above equations remain valid (15).

REFERENCES AND NOTES

- Ashworth, A.: Metabolic rates during recovery from protein-calorie malnutrition: the need for a new concept of specific dynamic action. *Nature*, 223: 407 (1969).
- Brandt, I.: Growth dynamics of low-birth-weight infants with emphasis on the perinatal period. In: Faulkner, F. and Tanner J.M.: *Human growth 2 Postnatal growth* p. 565 (Plenum press, New York, 1978).
- Brooke, O. G. and Ashworth, A.: The influence of malnutrition on the postprandial metabolic rate and respiratory quotient. *Brit. J. Nutr.*, 27: 407 (1972).
- Brooke, O. G., Alvear, J., and Arnold, M.: Energy retention, energy expenditure and growth in healthy immature infants. *Pediatr. Res.*, 13: 215 (1979).
- Brück, K.: Heat production and temperature regulation. In: U. Stave: *Perinatal physiology* 2nd edition, p. 455 (Plenum medical book company New York, 1978).
- Brück, K.: Temperature regulation in the newborn infant. *Biol. Neonate*, 3: 65 (1961).
- Brück, K., Parmelee, A. H., Brück, M.: Neutral temperature range and range of thermal comfort in premature infants. *Biol. Neonate*, 4: 32 (1962).
- Consolazio, C. F., Johnson, R. E., and Pecora, L. J. In: *Physiological measurement of metabolic functions in man*, p. 316 (McGraw-Hill, New York 1963).
- Dubowitz, L. M. S., Dubowitz, V., and Goldberg, C.: Clinical assessment of gestational age in the newborn infant. *J. Pediatr.*, 77: 1 (1970).
- Hey, E. N.: The care of babies in incubators. In: *Recent advances in pediatrics*, 4th edition, p. 171 (Churchill, London, 1971).
- Hill, J. R. and Robinson, D. C.: Oxygen consumption in normally grown, small-for-dates and large for dates newborns infants. *J. Physiol. (London)*, 199: 685 (1968).
- Hill, J. R. and Rahimtulla, K. A.: Heat balance and the metabolic rate of newborn babies in relation to environmental temperature, and the effect of age and weight on basal metabolic rate. *J. Physiol. (London)*, 180: 239 (1965).
- Hommes, F. A., Drost, Y. M., Geraets, W. X. M., and Reijenga, M. A. A.: The energy requirement for growth: an application of Atkinson's metabolic price system. *Pediatr. Res.*, 9: 51 (1975).
- Hommes, F. A.: The energy requirement for growth, a reevaluation. *Nutr. Metab.*, 24: 110 (1980).
- Jéquier, E.: Long term measurement of energy expenditure in man: direct or indirect calorimetry? In: *Recent advances in obesity research III. Proceedings of the 2nd international congress on obesity*. G. Bray Ed. (Newman Publishing, London, 1981).
- Jonxis, J. H. P., Van der Vlugt, J. J., deGroot, C. J., Boersma, E. R., and Meijers, E. D. K.: The metabolic rate in premature, dysmature and sick infants in relation to environmental temperature. In: *Nutricia Symposium*, H.E. Stenfort Kroese, p. 201-209 (Leiden, Holland, 1968).
- Karlberg, P.: Determination of standard energy metabolism (basal metabolism) in normal infants. *Acta Paediatrica Scandinavica* 41 suppl., 89: 67 (1952).
- Kien, C. L., Rohrbaugh, D. K., Burke, J. F., and Young, V. R.: Whole body protein synthesis in relation to basal energy expenditure in healthy children and in children recovering from burn injury. *Pediatr. Res.*, 12: 211 (1978).
- Kleiber, M.: *The fire of life: an introduction to animal energetics*. (John Wiley and sons, New York, 1961).
- Largo, R. H., Wälli, R., Duc, G., Fanconi, A., and Prader, A.: Evaluation of perinatal growth. *Helv. Paediatr. Acta*, 35: 419 (1980).
- McCance, R. A., Strangeways, W. M. B.: Protein catabolism and oxygen consumption during starvation in infants, young adults and old men. *Brit. J. Nutr.*, 8: 21 (1954).
- McLean, J. A. and Watts, P. R.: Analytical refinements in animal calorimetry. *J. Appl. Physiol.*, 40: 827 (1976).
- Mestyán, J., Jarai, I., Bata, G., and Fekete, M.: The basal metabolic rate of premature infants. *Biol. Neonate*, 7: 11 (1964).
- Mestyán, J.: Energy metabolism and substrate utilisation in the newborn. In: Sinclair, J. C.: *Temperature regulation and energy metabolism in the newborn*. Grune and Stratton, New York (1979).
- Millward, D. J. and Garlick, P. J.: The energy cost of growth. *Proc. Nutr. Soc.*, 35: 339 (1976).
- Rubecz, I. and Mestyán, J.: Energy metabolism and intravenous nutrition of premature infants I: the responses of oxygen consumption, respiratory quotient and substrate utilisation to infusion of Aminosol glucose. *Biol. Neonate*, 23: 45 (1973).
- Rubecz, I. and Mestyán, J.: The partition of maintenance energy expenditure and the pattern of substrate utilisation in intrauterine malnourished newborn infants before and during recovery. *Acta Paediatrica Academiae scientiarum hungaricae*, 16 (3-4): 335 (1975).
- Rutter, N., Brown, S. M., and Hull, D.: Variations in the resting oxygen consumption of small babies. *Arch. Dis. Child.*, 53: 850 (1978).
- Sauer, P. J. J., Pearce, R. G., Dane, H. J., and Visser, H. K. A.: The energy cost of growth estimated from simultaneous direct and indirect calorimetry in infants of less than 2500 g. In: Visser HKA (Ed) *Nutrition and metabolism of the fetus and infant 93-107* (Martinus Nijhoff publishers b.v., The Hague, 1979).
- Schutz, Y.: Estimates of the energy cost of growth in young children. *International Journal for vitamin and nutrition research* (suppl.), 20: 113 (1979).
- Scopes, J. W. and Ahmed, I.: Minimal rates of oxygen consumption in sick and premature newborn infants. *Arch. Dis. Child.*, 41: 407 (1966).
- Senterre, J. and Karlberg, P.: Respiratory quotient and metabolic rate in normal full term and small-for-date newborn infants. *Acta Paediatr. Scand.*, 59: 653 (1970).
- Silver, H. K.: Growth and development. In: Kempe, H.C., Silver, H.K., O'Brien, D., *Current pediatric diagnosis and treatment* 5th edition, p. 13. (Lange medical publications, Los Altos, 1978).
- Spady, D. W., Payne, P. R., Picou, D., and Waterlow, J. C.: Energy balance during recovery from malnutrition. *Am. J. Clin. Nutr.*, 29: 1073 (1976).
- Sweet, A. Y.: Classification of the low-birth-weight infant. In: Klaus, M. H., Fanaroff, A. A. *Care of the high risk neonate* 2nd edition p. 82 (W.B. Saunders Company, Philadelphia, 1979).
- Voyer, M., Nobre, R., Antener, L., Colin, J., Charles, J., and Satge, P.: Alimentation des prématurés avec un lait industriel contenant des triglycérides à chaînes moyennes. *Annales de Pédiatrie* 26, 6: 417 (1979).
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