

The Total Energy Expenditure and its Components in Premature Infants Maintained under Different Nursing and Environmental Conditions

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Extract

It seemed desirable and interesting to study the total energy expended during a period of several hours under conditions most commonly encountered under different infant care practices.

The investigations were carried out on a total of 23 premature infants with a birth weight ranging from 1100 to 2120 g and aged from 2 to 31 days. Oxygen consumption was measured by an open circuit method using the Kipp diaferometer. Using three thermal conditions, measurements were started when four hours had elapsed after the last feed. Physical activity was observed and recorded continuously by an arbitrary method. The basal metabolic rate and the metabolic response to cold subtracted from the total metabolism measured under different experimental conditions gave the combined number of calories produced by specific dynamic action and physical activity. The information obtained from a previous study on specific dynamic action made it possible to approximate the calorogenic effect of food in the four series of examinations reported.

Details of the studies carried out on premature infants while receiving human milk and kept in incubators with temperature maintained between 33-36° are shown in table I. In addition to the basal metabolic rate, total heat production observed throughout the observational period, calculated total daily heat production, and the percentage distribution of times spent in sleep and in physical activity with various intensity are also listed. The average total heat production observed exceeds the minimal metabolic rate by 9.8 kcal/kg/24 h per subject. If allowance is made for the specific dynamic action expected from the average daily intake of human milk (1.1 g protein/ml) 3.0 kcal/kg/24 h can be attributed to muscular activity. The magnitude of this component of the total energy expenditure is consistent with the markedly reduced physical activity exhibited by premature infants maintained in a thermally neutral environment.

The results obtained on premature infants receiving an artificial formula containing 3.43 % protein are listed in table II and shown diagrammatically in figure 1. The total daily caloric output averages 55.0 kcal/kg/24 h, a value roughly 39 % above the basal rate, in contrast to the average increase of 25 % observed in breast milk-fed infants. This difference in the combined quota of specific dynamic action and physical activity (8.8 and 15.3 kcal/kg/24 h, respectively) is due partly to the higher protein and caloric intake, and partly to the lesser proportion of time spent in deep sleep.

Table III summarizes the results of studies of the energy exchange of five swaddled premature infants kept at a room temperature of 20-22°. It can be seen that the total daily heat production averages 58.3 kcal/kg/24 h, which is not appreciably greater than that observed in Adapta-fed infants maintained at neutral temperature. The extra calories above the basal amount to 18.6 kcal/kg/24 h,

representing a 47% rise above the minimal rate. This amount of heat includes not only the specific dynamic action and the activity quota, but also thermoregulatory heat production. The metabolic response to cold amounts roughly to 10 kcal/kg/24 h. The remaining extra calories above those required for basal heat production are partitioned between specific dynamic action and physical activity; this distribution is consistent with the proportion of times spent sleeping and with activity of various intensity. It is also consistent with the observation that the calorogenic effect of food manifests itself as an additional amount of heat in a heat-losing environment.

Table IV presents the observations made on six premature infants kept unclothed at 28–29°. The total daily energy expenditure, almost 100% above that of basal heat production, averaged 80 kcal/kg: 41.3 for basal metabolism; 15.3 for chemical heat regulation without gross, visible muscular activity; 7.3 for specific dynamic action; and 16.1 for activity. The relative proportion of these components is shown in figure 3. The magnitude of the activity quota is readily explained by the percentage of time spent awake while displaying periodically increasing struggling and restless crying.

Speculation

The results obtained have much bearing on the feeding of premature infants. It appears important to reevaluate the caloric needs for maintenance at neutral temperatures, since it has become increasingly accepted that the majority of small premature infants should be cared for under neutral thermal conditions. The observations suggest, in addition to the caloric need for maintenance, that the total caloric requirements are considerably lower than the widely employed figures used to approximate the caloric need of premature infants. Hence, the desirability of extending such studies to include the total caloric requirement is quite obvious. It would be most interesting to complete our knowledge concerning the adequacy and physiological basis of the caloric feeding of premature infants cared for under different thermal conditions.

Introduction

Since TALBOT *et al.* [28, 29] and GORDON and LEVINE [9, 10, 13, 14] reported fundamental observations on the energy expenditure of full-term and premature infants, new knowledge has accumulated and has profound bearing on our understanding of basal metabolic rates and the metabolic response to cold. Research on the relation between ambient temperature and thermoregulatory heat production [1, 2, 4, 5, 6, 11, 16, 19, 20, 23] and clinical studies exploring the optimum environmental conditions for the care of the young premature infant [3, 7, 8, 26, 27] strongly suggest not only a marked difference in total daily heat production attributable to age, maturity and temperature of the surrounding radiating surfaces, but also point to the appreciably varying relative importance of the main components involved in total caloric output under different conditions of nursing and environment.

Theoretical considerations, in light of the advances in knowledge of the energy exchange of premature infants, support the assumption that the widely employed figures for caloric requirements of maintenance proposed by GORDON and LEVINE [9, 10, 13, 14] are over-

estimates, and do not reflect the changing partitioning of total metabolism between its main components under different conditions. Hence, it seemed desirable and interesting to study the total energy expended during a period of several hours under conditions most commonly encountered in different infant care practices. The practical importance and desirability of using more physiological approximations in the estimation of the changing caloric needs of maintenance is quite obvious, and the present series of studies were designed to reevaluate the total heat production of premature infants within the first month of life.

Material and Methods

The investigations were carried out on a total of 23 premature infants with a birth weight ranging between 1100 and 2120 g, and aged from 2 to 31 days. The experimental and environmental conditions under which respiratory metabolism was continuously measured were the following:

(a) In experiments performed within the zone of thermoneutrality (33–36°), 13 infants were studied.

They were placed in an incubator under a perspex hood through which room air was drawn at a rate of 4.6 l/min. The lower parts of the trunk and the legs which were outside the hood were loosely covered by a nylon sheet attached around the air inlet of the hood, ensuring that the infant expired only into the air flowing over the face. Relative humidity ranged between 45 and 60 %. The daily feeding schedule of the infants comprised 10 or 7 feedings given at intervals of 2 or 3 hours. Nine infants were fed breast milk, and four received an artificial formula containing 3.43 % protein. This was provided at a caloric concentration of 70 kcal/100 ml.

(b) Five infants, swaddled in soft, down feather quilts, were kept at room temperature (20–22°). The head, the upper part of the trunk, and the upper limbs were under a perspex hood within which the air temperature was 1–2° higher than that of the room. The daily diet of these infants comprised 10 or 7 feedings of human milk.

(c) The respiratory metabolism of five naked infants receiving human milk was followed at an incubator temperature of 28–29°.

Oxygen consumption and CO₂ production were measured using the Kipp diaferometer [3a, 11a]. This apparatus measures heat conductivity in a gas. The changes in heat conductivity of a gas mixture depend upon the concentrations of its components and cause changes in the resistance of a heated platinum wire connected to a Wheatstone bridge. The apparatus is equipped with two Wheatstone bridges and two sensitive galvanometers, one for O₂ and one for CO₂. The composition of expired air, diluted by room air introduced at a constant flow, is compared with that of room air.

The calibration given by the factory was checked frequently using known gas mixtures or by simultaneous determination of the O₂ and CO₂ concentration in air coming from the patient using the diaferometer and Scholander's microanalytical method [25]. These were found to be constant over a long period of time. The reliability of the method was checked by two or more determinations on the same infant in a large number of cases. The instrument functioned with an accuracy of ±3 %.

The observation period in the three groups of infants varied between 4 and 11 hours. Readings of the diaferometer were made every minute except when reference was made to room air and when a feed was offered. The infants had no difficulty in sucking and swallowing in the apparatus. Gavage feeding by an indwelling tube, introduced through the nose and long enough to reach out of the hood, permitted continuous recording of oxygen consumption.

Under all three thermal conditions, measurements

were started when four hours had elapsed after the last feeding. Before the infants were exposed to the respective thermal conditions, minimal oxygen consumption at the neutral temperature had already been measured.

Physical activity was observed and recorded continuously using the following designations:

00: asleep, physically totally quiet.

0: eyes open or closed with occasional jerks or slight movements.

+ : awake, some activity (moving arms and legs now and then).

++ : intensive and more or less continuous activity.

+++ : vigorous activity with crying and restlessness.

The percentage of the total observation period spent in sleep and with different levels of activity was calculated.

Minimal metabolism, metabolic response to cold, and total metabolism were expressed as oxygen consumption in ml/kg/min (STPD) and heat production in kcal/kg/24 h. Although CO₂ production was also recorded, we used the RQ 0.875 for the calculation of heat production, which corresponded roughly to the average RQ observed in the individual experiments. The caloric value for oxygen (4.84/l) was obtained for Michaelis' nomogram assuming that protein metabolism constitutes about 15 % of total metabolism [20]. The choice of an average RQ of 0.875 was based on the following considerations: (1) The lowest and highest RQ's observed in the experiments were 0.78 and 0.94, respectively. In all infants, the resting RQ varied over a smaller range (0.80–0.90), the upper and lower limits of which were never exceeded regardless of experimental conditions. (2) The RQ observed during and following hyperventilation and crying associated with restlessness was probably obscured by changes in CO₂ elimination due to changes in ventilation. Thus, short periods of measurement would not indicate exactly the metabolically produced CO₂. (3) The average RQ in the individual experiments varied closely around a mean of 0.875. (4) For RQ's between 0.78 and 0.94, the calculation of heat production based on the RQ 0.875 may cause errors of –2.4 % up to +1.7 %; for RQ's between 0.80–0.90, the error varies from –2 % to +0.7 %. An error of this size is acceptable in calculations of heat production particularly when a rough estimation is made of the contribution of protein metabolism to the total.

The basal metabolic rate and the metabolic response to cold subtracted from the total metabolism measured under different experimental conditions gave the combined number of calories produced by specific dynamic action and physical activity. The information obtained from a previous study [17, 18] on specific dynamic action of human milk and of an artificial formula containing a 3.43 % protein (Adapta) [30] made it pos-

sible to approximate the calorogenic effect of food in the four series of examinations. The average values of 6% (human milk) and 7.5% (Adapta) of ingested calories were used regardless of the thermal conditions. Thus, the absolute and relative contributions of the basal rate, metabolic response to cold, and specific dynamic action of food and activity under different nursing conditions could be determined. For statistical analysis, the means and standard deviations were calculated; when it seemed necessary, significance was estimated by Student's *t*-test.

Results

Investigations Performed in a Thermoneutral Environment

Infants receiving human milk. Details of examinations carried out on premature infants receiving human milk and kept in incubators, the temperature of which was maintained between 33 to 36°, are shown in table I. In addition to the basal metabolic rate, the total heat production observed throughout the period of observations and the percentage distribution of times spent in sleep and in physical activity with various intensity are also tabulated.

The calculation of basal metabolic rate per kg/24 h is based on an average of minimal oxygen consumption over a 6- to 10-minute period obtained at the beginning of the experiment after a fast of four hours. Thus, the values of minimal oxygen consumption shown in table I represent the true basal metabolic rate and do not include the specific dynamic action of food.

Examination of table I and figure 1 indicates that the average total heat production/kg/24 h computed from the total heat production actually observed exceeds the minimal metabolic rate by 8.8 kcal/kg/24 h. It became apparent from a study on the specific dynamic action under the same environmental conditions that the total calorogenic response to human milk amounted to about 6% of the ingested calories [16]. If allowance is made for the specific dynamic action expected from the average daily intake of human milk (5.8 kcal/kg/24 h), only 3.0 kcal/kg/24 h is attributable to muscular activity. The magnitude of this component in relation to the total expenditure is consistent with the markedly reduced physical activity exhibited by premature infants maintained in the thermoneutral environment. The combined average time during which the infants were asleep, or exhibited occasional jerks or slight movements (00+0), amounted to 85% of the total experimental period.

It has been shown that the basal heat production of premature infants increases with postnatal age [12, 15]. Although the present small series of examinations includes only one infant older than 15 days, the relation

between age and minimal metabolism is quite obvious if the average basal rates of infants younger than 7 days are compared, 31.3 kcal/kg/24 h and 36.6 kcal/kg/24 h, respectively. This difference is also mirrored by the total caloric output, 40 kcal/kg/24 h vs 47.5 kcal/kg/24 h, obtained in these infants.

The combined quota of physical activity and specific dynamic action in the infants older than 7 days is larger by 1.6 kcal/kg/24 h than that calculated for the younger ones. This difference is certainly due to the higher caloric intake and to the somewhat lesser proportion of time spent in deep sleep, 60% vs 70%. These figures vary too much from one individual to another to permit any statistical evaluation; nevertheless, inspection of the individual figures without resorting to statistics confirm this point.

Infants fed an artificial formula (Adapta) containing 3.43% protein. The results obtained in four premature infants maintained at the neutral temperature and fed a formula containing 3.43% protein are listed in table II and shown diagrammatically in figure 1. It can be seen that the mean basal metabolic rate, 39.7 kcal/kg/24 h, is higher than that obtained in the former group of infants, 35.4 kcal/kg/24 h. This difference can be

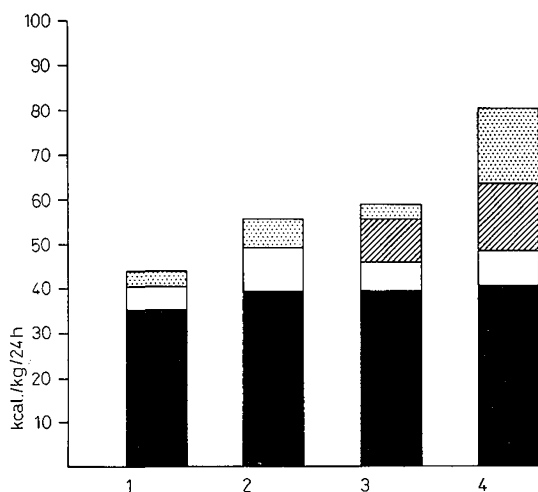


Fig. 1. The partitioning of the total heat production of premature infants into its components. 1: infants maintained at neutral temperatures (33–36°) and fed human milk; 2: infants maintained at neutral temperatures (33–36°) and fed an artificial formula containing 3.4% protein; 3: swaddled infants maintained at 20–22° and receiving the artificial formula; 4: naked infants maintained at 28–29° and receiving the artificial formula. ■ basal metabolism; □ specific dynamic action; ▨ metabolic response to cold; ▤ physical activity.

Table I. Basal metabolic rate, total heat production and activity pattern of nine premature infants maintained at neutral temperatures (33–36°) and fed human milk

Age in days	Birth weight g	Actual body weight g	Daily food intake g	Ambient temperature °C	Body temperature °C	Experimental period in minutes	Minimal energy metabolism		Heat production kcal/kg/exp. period	Heat production kcal/kg/24 h	Relative distribution of sleeping and activity periods				
							O ₂ ml/kg/min	kcal/kg 24 h			00	0	+	++	+++
2	1400	1370	10×10	34.0	36.5	408	3.8	26.5	9.3	33.0	72.1	25.7	2.0	0.2	–
3	1800	1850	10×10	35.0	36.7	636	4.3	30.0	14.8	33.4	70.3	22.9	4.3	1.7	0.8
3	1560	1520	10×20	34.0	36.4	584	4.6	32.0	18.2	45.0	79.9	17.3	–	2.4	0.4
5	1800	1680	7×30	34.0	36.8	473	5.3	37.0	15.8	48.2	58.6	19.5	15.2	4.0	2.8
9	1850	1810	7×60	34.5	36.4	246	5.5	38.2	6.9	40.5	58.1	30.0	9.8	2.0	–
11	1100	1020	10×20	35.0	36.2	670	4.2	29.4	20.0	43.0	76.6	17.0	3.1	1.6	1.6
11	1560	1600	10×30	34.0	36.6	514	6.0	41.7	18.0	50.0	52.1	25.9	15.2	6.2	0.6
15	1750	1760	7×35	35.0	36.7	525	4.8	33.5	19.7	54.0	50.1	21.7	10.5	5.5	12.2
30	1560	1850	7×50	34.0	36.6	422	5.8	40.5	14.8	50.0	60.2	17.1	17.5	4.5	0.7
Mean						497	4.9	35.4	15.3	44.2	64.2	29.0	9.7	3.2	2.7
Standard deviation							±0.76	±5.4		±7.4	±10.0	±4.6	±6.0	±2.0	±4.2

Table II. Basal metabolic rate, total heat production and activity pattern of premature infants maintained at neutral temperatures (33–36°) and fed an artificial formula (Adapta) containing 3.43 % protein

Age in days	Birth weight g	Actual body weight g	Daily food intake g	Ambient temperature °C	Body temperature °C	Experimental period in minutes	Minimal energy metabolism		Heat production kcal/kg/exp. period	Heat production kcal/kg/24 h	Relative distribution of sleeping and activity periods				
							O ₂ ml/kg/min	kcal/kg 24 h			00	0	+	++	+++
6	1360	1300	10×20	34.0	36.0	600	5.3	37.0	21.2	51.0	60.0	34.0	4.2	1.8	–
8	1750	1750	10×30	34.5	36.5	520	5.5	38.2	18.8	52.2	52.4	34.6	8.0	3.8	1.2
14	1750	1800	7×50	34.0	36.3	500	5.8	40.5	19.8	57.2	45.0	34.2	13.3	5.5	2.0
22	1600	1700	7×50	33.0	36.6	420	6.2	43.0	17.3	59.5	50.0	30.2	7.6	9.0	3.2
Mean						510	5.7	39.7	19.3	55.0	51.9	33.3	8.3	5.0	2.1
Standard deviation							±0.37	±2.6	–	±4.0	±6.2	±2.0	±2.6	±3.0	±1.0

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explained by the fact that three of the four infants were older than 7 days. The total daily caloric output averages 55.0 kcal/kg, which is roughly 39 % above the basal rate, in contrast to the average increase of 25 % observed in breast milk-fed infants. This difference in the combined quota of specific dynamic action and physical activity, 8.8 and 15.3 kcal/kg/24 h respectively, is due partly to the higher protein and caloric intake and partly to the lesser proportion of time spent in deep sleep ($p < 0.01$). Taking into consideration that the calorogenic effect of Adapta under different conditions amounts to about 7.5 % of the ingested calories, the partition of the mean increase of 15.3 kcal/kg/24 h above the basal rate into its two components gives 9.3 kcal/kg/24 h for the specific dynamic action and 6.0 kcal/kg/24 h for the activity quota (fig. 2).

Examinations Carried Out in a Heat-Losing Environment

Observations on swaddled infants. Table III summarizes the results of studies on the energy exchange of five swaddled premature infants kept at a temperature of

20 to 22°. In order to estimate the contribution of chemical heat regulation to total heat production, basal metabolic rate had been measured before continuous recording of oxygen consumption at 20 to 22° was started.

One notes from table III and figure 1 that total daily heat production averages 58.3 kcal/kg, which is not appreciably greater than that observed in Adapted infants maintained at neutral temperatures. The extra calories produced amount to 18.6 kcal/kg/24 h, representing a 47 % rise above the normal rate. This amount of heat includes not only the specific dynamic action and the activity quota, but also the thermoregulatory heat production. The distribution of calories between the four components and their relative proportion in the total daily expenditure of energy is graphed in figures 2 and 3. It can be seen that the metabolic response to cold amounts roughly to 10 kcal/kg/24 h, with a range of 4.0 to 15.4, and the partitioning of the remaining extra calories over and above those needed for basal heat production between specific dy-

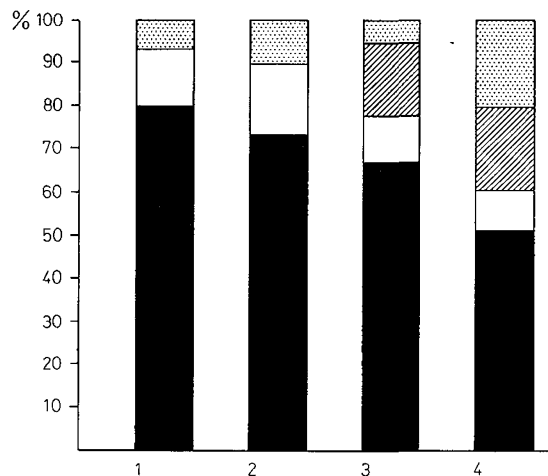


Fig. 2. ■ the relative contribution of the basal metabolism; □ specific dynamic action; ▨ metabolic response to cold; ▩ physical activity to the total heat production of premature infants. 1: infants maintained at neutral temperatures (33–36°) and fed human milk; 2: infants maintained at neutral temperatures (33–36°) and fed an artificial formula; 3: swaddled infants maintained at 20–22° and fed an artificial formula; 4: naked infants maintained at 28–29° and fed an artificial formula.

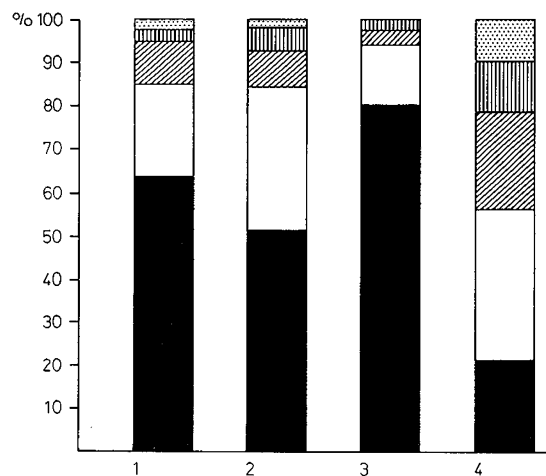


Fig. 3. The relative distribution of sleeping and activity of different intensity displayed by premature infants maintained under different thermal and feeding conditions. 1: infants maintained at neutral temperatures (33–36°) and fed human milk; 2: infants maintained at neutral temperatures (33–36°) and fed an artificial formula; 3: swaddled infants maintained at 20–22° and fed an artificial formula; 4: naked infants maintained at 28–29° and fed an artificial formula. ■: asleep, physically totally quiet; □: eyes open or closed with occasional jerks or slight movements; ▨: awake, some activity moving arms and legs now and then; ▩: intensive and more or less continuous activity; ▩: vigorous activity with crying and restlessness.

Table III. Basal metabolic rate, metabolic response to cold, total heat production, and activity pattern of swaddled, premature infants maintained at temperatures of 20–22° and fed formula with 3.43 % protein

Age in days	Birth weight g	Actual body weight g	Daily food intake g	Ambient temperature °C	Body temperature °C	Experimental period in minutes	Minimal energy metabolism		Energy metabolism at room temp.		Heat production exp. period kcal/kg	Heat production kcal/kg 24 h	Relative distribution of sleeping and activity periods				
							O ₂ ml/kg/min	kcal/kg 24 h	O ₂ ml/kg/min	kcal/kg 24 h			00	0	+	++	+++
6	1820	1760	7×40	20	36.2	243	5.0	34.8	7.0	48.5	9.7	57.5	74.0	25.1	0.8	-	-
11	1350	1430	10×25	22	36.5	238	5.3	36.8	7.5	52.2	10.2	62.0	86.5	9.3	4.3	-	-
15	1720	1840	7×40	22	36.1	256	5.7	39.6	7.0	48.5	11.0	62.0	83.2	9.4	5.1	2.3	-
20	1900	2040	7×50	23	36.4	336	6.4	44.5	7.0	48.5	12.9	55.5	83.3	14.3	2.4	-	-
31	1900	2400	7×60	20	36.8	290	6.2	43.0	7.4	51.5	10.9	54.5	75.5	11.4	10.4	2.8	-
Mean						273	5.7	39.7	7.2	49.8	10.9	58.3	80.5	13.9	4.6	2.5	-
Standard deviation						-	±0.6	±4.0	±0.2	±1.7		±3.5	±5.4	±6.5	±3.6	-	-

Table IV. Basal metabolic rate, metabolic response to cold, total heat production and activity pattern of naked, premature infants maintained at an ambient temperature of 28–29° and fed formula with 3.43 % protein

Age in days	Birth weight g	Actual body weight g	Daily food intake g	Ambient temperature °C	Body temperature °C	Experimental period in minutes	Minimal energy metabolism		Energy metabolism at room temp.		Heat production exp. period kcal/kg	Heat production kcal/kg 24 h	Relative distribution of sleeping and activity periods				
							O ₂ ml/kg/min	kcal/kg 24 h	O ₂ ml/kg/min	kcal/kg 24 h			00	0	+	++	+++
6	1950	1720	7×35	28	37.0	300	5.7	39.6	8.0	55.5	16.8	81.0	20.1	30.0	26.7	11.7	11.7
10	1790	1710	7×40	28	36.8	266	5.7	39.6	7.5	52.2	14.4	78.0	22.6	26.3	28.2	15.0	7.9
11	2120	1890	7×50	29	36.0	260	6.5	45.3	8.7	60.5	15.8	88.0	19.2	46.2	15.4	7.7	11.5
22	1500	1800	7×50	29	36.7	269	6.3	43.7	8.5	59.0	14.5	78.0	17.1	37.2	24.2	14.9	6.7
28	1000	1260	10×25	28	36.2	240	5.5	38.2	8.0	55.0	12.5	75.0	29.2	38.3	16.7	5.4	10.4
Mean						267	5.9	41.3	8.2	56.6	12.5	80.0	21.6	35.6	22.2	10.9	9.6
Standard deviation							±0.43	±3.0	±0.47	±3.3		±4.9	±4.6	±7.7	±5.8	±4.2	±2.2

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dynamic action and physical activity is consistent with the proportion of times spent in sleeping and in activity of various intensity. In addition, the calorogenic effect of food manifests itself as an additional amount of heat in a heat-losing environment [18].

Observations on Naked Premature Infants Maintained at an Ambient Temperature of 28–29°

Table IV presents the details of observations on five premature infants aged from 6 to 28 days. The naked infants were kept in incubators at a temperature of 28–29° while oxygen consumption was continuously measured throughout an average test period of 267 minutes. Minimal metabolism under basal conditions and the resting heat production at 28–29° were also determined.

In table IV and figures 1 and 2 it can be seen that the total daily energy expenditure, which is practically 100 % above the basal heat production, averages 80 kcal/kg: 41.3 for basal metabolism; 15.3 for chemical heat regulation without gross, visible muscular activity; 7.3 for specific dynamic action; and 16.1 for activity. The relative proportion of these components is shown in figure 2. The magnitude of the activity quota is readily explained by the percentage of time spent awake while displaying various degrees of physical activity.

Discussion

Total heat production is the sum of four components: basal metabolic rate; specific dynamic action of food; muscular activity; and chemical heat regulation. Except for the thermoregulatory heat production, all the components involved in the energy metabolism of full-term and premature infants were studied and considered in the classical work of TALBOT *et al.* [27, 28] and later in the investigations of GORDON and LEVINE [9, 10, 13, 14].

The average figure for total daily heat production of premature infants reported by GORDON and LEVINE [9, 10] is still regarded as the most reliable standard for estimating total daily maintenance caloric needs. In light of our present knowledge concerning energy metabolism of premature infants, it can be stated that the value of 70 kcal/kg for daily heat production observed by GORDON and LEVINE (60 for basal metabolism, 10 for physical activity and specific dynamic action) is invalid in many cases. New data indicate that a variety of factors may influence the energy expenditure of premature infants. These factors often require individual assessment if the caloric requirement of a specific infant is to be determined under any specific care regimen. This is particularly true of the energy requirements for temperature regulation. A careful experimental re-

evaluation of the maintenance caloric requirements under various conditions and at different levels of growth at birth and thereafter is needed.

Energy Expenditure in a Thermoneutral Environment

The total heat production of premature infants maintained at neutral temperatures in incubators or in an air-conditioned ward comprises only three components: basal metabolism; specific dynamic action; and physical activity.

The basal metabolic rate of premature infants is lower and increases at a slower rate during the first month of life than does that of full-term infants [11, 12, 26]. Within the first ten days of life, the minimal metabolism of infants with a birth weight less than 1500 g is significantly lower than that of heavier ones [15]. The basal metabolism of prematures weighing between 1000 and 2000 g varies from 30 to 45 kcal/kg/24 h within the first month of extrauterine life when measured on infants maintained at temperatures of 33–36°. Comparing these rates with those reported by GORDON and LEVINE [9, 10], 52.8 to 62 kcal/kg/24 h, it becomes apparent that this large difference is explained largely by the different thermal conditions under which measurements are made.

GORDON's values refer only to premature infants weighing more than 2000 g and, in all probability, also include a certain amount of heat deriving from the metabolic response to cold. It should be noted, however, that the daily basal heat production observed by TALBOT *et al.* in 1923 [29], and particularly that reported by SCHADOW in 1934 [22] agree reasonably well with the values observed under basal conditions reported in recent publications [5, 15, 21, 24]. To perpetuate the values proposed by GORDON and LEVINE seems unsound.

The present series of investigations show that the total daily caloric output at neutral temperatures is considerably lower than that predicted by classical physiology. This is explained mainly by the average basal heat production of 35.4 kcal/kg/24 h and 39.4 kcal/kg/24 h observed in the breast milk-fed and Adapta-fed infants, respectively, and corresponds well with our own observations [15]. The extra calories produced above the basal are the sum of the energy expended for specific dynamic action and physical activity. The combined quota of these two components differs in our two series of observations. When these are considered in addition to the higher basal metabolic rate, they explain the larger total expenditure of energy in the Adapta-fed infants. In figure 3, which shows the relative distribution of the three factors involved in total production, it can be seen that the specific dynamic action of food is the second largest component of heat produced at neutral temperature. This contribution is

subject to wide differences because of variation in the daily protein and caloric intake. The difference observed in the increase of heat production above the basal metabolism between the two groups of infants is in agreement with the results obtained in a study concerning the cumulative specific dynamic action of breast milk and artificial formula [17].

The participation of activity in total heat production that appears to be a function of age under thermoneutral conditions (fig. 3) scarcely exceeds 10 %, which coincides well with the percentage of times spent in sleeping and in physical activity of different intensities. The difference in the activity quota between the breast milk-fed and Adapta-fed infants is also reflected in the distribution pattern of sleeping and muscular activity. From the relatively small fraction of heat produced by movement and restlessness, it follows that basal metabolism and specific dynamic action are the most important components to be considered in estimating the magnitude of energy expended in a neutral thermal environment.

Energy Expenditure in a Heat-Losing Environment

During the last decade, extensive research has identified the metabolic response to cold of premature infants [4, 5, 19, 21, 24, 26]. The findings reported by different authors show conclusively that premature infants with different degrees of immaturity are capable of increasing heat production in a cold environment. Chemical thermoregulation in the naked infant is always accompanied by motor activity, the intensity of which increases with the degree of cold stress. Intermittent struggling, restlessness, and crying (fig. 3) cause a considerable cyclic variation in heat production which, under totally nude conditions, renders difficult the determination of the magnitude of metabolic response to cold, independent of gross muscular activity. The situation regarding motor behavior is quite different if a swaddled or clothed infant is exposed to a temperature of 20–22°. Under these conditions, the infant does not manifest discomfort, yet responds by a small but definite rise in heat production.

In estimating the total heat production of premature infants maintained in a heat-losing environment, thermoregulatory heat production should be carefully considered. The actual magnitude of this component and, hence, the total energy expenditure, as demonstrated in the present study, may vary greatly because of variations in cold stress.

The total amount of heat per kg/24 h produced by naked premature infants kept at 28–29° exceeds that obtained in swaddled infants kept at room temperature by 20 kcal. Partitioning of the total heat production into its components discloses that it is the activity quota associated with chemical heat regulation of the naked

infants which accounts for the difference between the two series of examinations. This fact is also reflected in the percentage distribution of sleeping and different activities observed under the two thermal conditions.

In naked premature infants maintained at a temperature of 28–29°, deep sleep was rarely observed; increasing struggling and restless crying were displayed periodically. The swaddled infants were continuously quiet and even slept significantly more than the naked ones maintained at the neutral temperature ($p < 0.01$). Despite the absence of overt muscular activity, thermoregulatory heat production could be observed, indicating that, from a thermoregulatory point of view, the swaddled infants were not in the thermoneutral state.

Since the oxygen consumption of the naked infants maintained below the critical temperature was also followed during the rarely occurring and short-lasting quiet or sleeping periods, the participation of the metabolic response to cold, unaccompanied by gross muscular activity in total heat production, could also be determined. It can be seen that powerful movements, struggling, and restless crying doubled the quota of thermoregulatory heat production making a total daily metabolism of 80 kcal/kg, which was 100 % above basal.

The proportion of total caloric output in the cold environment due to specific dynamic action has also been calculated. Its consideration as an additive quota of energy seems justified on the basis of observations made on premature infants [18] concerning the relation of the calorogenic effect of food and the metabolic response to cold. It has been shown that the thermogenic effect of food in the cold environment does not significantly differ from that observed at neutral temperatures. Hence, not only within the zone of thermoneutrality but also in a heat-losing environment, allowance should be made for the specific dynamic action as an additional factor in the energy metabolism of maintenance.

The results of these studies give some information of the possible total energy metabolism of premature infants weighing not more than 2000 g, younger than 30 days, and cared for under different thermal conditions. The magnitude of the components and, hence, their contribution to the total may vary considerably according to maturity, postnatal age, and thermal conditions.

The basal metabolism of a premature infant within the first month of life is not a fixed factor; thus, it is not justified to use a uniform basal value for the approximation of energy metabolism for maintenance in premature infants of different gestational and postnatal ages. If we consider, for example, 35 kcal/kg and 40 kcal/kg as an average daily basal rate within the first two weeks of life for infants receiving human milk and weighing between 1000–1500 and 1501–2000 g, respectively,

then the total daily heat production at neutral temperature will not exceed 45 and 50 kcal/kg in the respective group of infants. These values are 20–25 kcal/kg lower than those reported by GORDON and LEVINE (69 kcal/kg) [9]. On the basis of the present observations, it might appear to be a rough overestimation; but considering that the body weight of the infants studied by GORDON and LEVINE ranged between 1.8 to 2.7 kg and that the measurements were probably carried out in a heat-losing environment, the value of 69 kcal/kg/24 h is only 10 kcal/kg higher than what one would expect.

Additional discrepancies between the findings of GORDON and LEVINE and those in the present report arise, however, if one attempts to partition total heat production into its components. The low basal metabolic rate accounts for the surprisingly low total caloric output in a neutral temperature; however, as a proportion of the total metabolism (80 %), it is the largest among the three components to be considered when approximating the maintenance caloric requirement at neutral temperatures. Therefore, the amount and quality of food should be regarded as the second major factor which may significantly alter the total caloric output at neutral temperatures.

In a heat-losing environment, a fourth component of energy comes into play. It is well known that a variety of factors, such as temperature of the surrounding radiating surfaces, humidity, wind, and clothing influence thermoregulatory heat production and therefore alter the contribution of these factors to total caloric output. Attention should be paid to the energy relations in the maintenance metabolism of premature infants cared for unclothed below the critical temperature. Under these conditions, actual heat production due to physical activity increases considerably and, in contrast to the values for infants maintained in a thermal neutral environment or under swaddled conditions at room temperatures, it becomes one of the decisive factors in total energy expenditure.

The results obtained in the present study have an important bearing on the caloric needs of premature infants. It is essential to reevaluate the caloric needs for maintenance at neutral temperatures, since it has become generally accepted that the majority of small premature infants should be maintained under neutral thermal conditions. These observations further suggest that caloric needs for maintenance and total caloric requirements are considerably lower than those usually used. Hence, it is desirable to extend studies to encompass total caloric requirements, including the quota for growth and fecal loss. It is also important that we complete our knowledge concerning the physiological basis of the caloric feeding of premature infants receiving care under different thermal conditions.

Summary

Total heat production and its partitioning into the various components of energy metabolism of premature infants under different environmental and feeding conditions has been investigated. A number of observations have been made:

1. The total daily caloric output at neutral temperature is considerably lower than one would expect on the basis of earlier data. Basal metabolism and specific dynamic action are the most important components to be considered in approximating total heat production under these conditions.

2. The total amount of heat per kg/24 h produced by naked premature infants maintained at a temperature of 28–29° is considerably greater than that observed in swaddled infants maintained at room temperature. In addition to the greater metabolic response to cold of the naked infants, the appreciably increased activity quota accounts for the difference between the values obtained under these environmental conditions.

3. The magnitude of the various components of energy metabolism and their contribution to the total vary according to maturity and postnatal age, as well as to thermal and feeding conditions; hence there is no justification for using a uniform value in approximating the total energy metabolism for maintenance. In light of the advances in knowledge of the energy exchange of premature infants, it seems desirable to reevaluate our viewpoint concerning the caloric needs for maintenance of premature infants.

References and Notes

1. ADAMS, F.H.; FUJIWARA, T.; SPEARS, R. and HODGMAN, F.: Temperature regulation in premature infants. *Pediatrics* 33: 487 (1964).
2. ADAMSONS, K.; GANDY, G.M.; DANIEL, S.S. and JAMES, L.S.: Thermal factors influencing O₂ consumption in the immediate neonatal period. *J. Pediat.* 65: 1076 (1964).
3. AGATE, F.J. and SILVERMAN, W.A.: The control of body temperature in the small newborn infant with low energy infrared radiation. *Pediatrics* 31: 725 (1963).
- 3a. BALOGH, L.: A kísérleti orvostudomány vizsgálati módszerei, vol. III, pp. 147–166 (Akadémiai kiadó, Budapest 1957).
4. BRÜCK, K.; BRÜCK, M. und LEMTIS, H.: Thermoregulatorische Veränderungen des Energiwechsels bei reifen Neugeborenen. *Pflügers Arch. ges. Physiol.* 267: 382 (1958).
5. BRÜCK, K.: Temperature regulation in the newborn infant. *Biol. Neonat.* (Basel) 3: 65 (1961).

6. BRÜCK, K.; PARMELEE, A.H. and BRÜCK, M.: Neutral temperature range and range of 'thermal comfort' in premature infants. *Biol. Neonat. (Basel)* 4: 32 (1962).
7. BUETOW, K. C. and KLEIN, S.W.: Effect of maintenance of 'normal' skin temperature on survival of infants of low birth weight. *Pediatrics* 34: 163 (1964).
8. Day, R. L.; CALIGURI, L.; KAMENSKI, C. and EHR- LICH, F.: Body temperature and survival of prema- ture infants. *Pediatrics* 34: 171 (1964).
9. GORDON, H.H. and LEVINE, S.Z.: Respiratory metabolism in infancy and in childhood. XVIII. The respiratory exchange in premature infants basal metabolism. *Amer. J. Dis. Child.* 52: 810 (1936).
10. GORDON, H. H.; LEVINE, S. Z.; DEAMER, W. C. and McNAMARA, H.: Respiratory metabolism in infancy and in childhood; daily energy requirements of pre- mature infants. *Amer. J. Dis. Child.* 59: 1185 (1940).
11. HILL, J.R. and RAHIMTULLA, K. A.: Heat balance and the metabolic rate of newborn babies in rela- tion to environmental temperature; and the effect of age and weight on basal metabolic rate. *J. Physiol.* 180: 239 (1965).
- 11a. KARLBERG, P.; MOORE, R. E. and OLIVER, T. K., Jr.: Responses of the newborn baby to noradrena- line. *Acta paediat. (Uppsala)* 54: 225-238 (1965).
12. KERPEL-FRONIUS, E.; VARGA, F. and MESTYÁN, J.: Clinical aspects of stability. *Ciba Foundation Sym- posium on Somatic Stability in the Newborn*, ed. WOLSTENHOLME, G.E.W. and O'CONNOR, M., p. 3214 (Churchill, London 1961).
13. LEVINE, S.Z.: Infant metabolism. *Proceedings of the World Health Organization. Seminar held at Leyden and Stockholm, 1950* (Macmillan, New York 1956).
14. LEVINE, S.Z. and ADOLPH, E.F.: Physiology of prematurity. *Transactions of the fourth confer- ence* (J.T. Lanman Josiah Macy Foundation, New York 1959).
15. MESTYÁN, J.; FEKETE, M.; BATA, G. and JÁRAI, I.: The basal metabolic rate of premature infants. *Biol. Neonat. (Basel)* 7: 11 (1964).
16. MESTYÁN, J.; JÁRAI, I.; BATA, G. and FEKETE, M.: Surface temperature versus deep body temperature and the metabolic response to cold of hypothermic premature infants. *Biol. Neonat. (Basel)* 7: 230 (1964).
17. MESTYÁN, J.; JÁRAI, I.; FEKETE, M. and SOLTÉSZ, G.: The specific dynamic action in premature in- fants: The calorogenic response to human milk, arti- ficial formula containing 3.43 % protein and casein in the thermoneutral environment (to be published).
18. MESTYÁN, J.; JÁRAI, I.; FEKETE, M. and SOLTÉSZ, G.: The specific dynamic action in premature in- fants: II. The calorogenic response to an artificial formula containing 3.43 % protein in a heat losing environment (to be published).
19. MESTYÁN, J. and VARGA, F.: Chemical thermo- regulation of full term and premature newborn infants. *J. Pediat.* 56: 623 (1960).
20. MICHAELIS, A.M.: Clinical calorimetry. A graphic method of determining certain numerical factors in metabolism. *J. biol. Chem.* 95: 51 (1924).
21. PRIBYLOVÁ und H. ZNAMENÁČEK, K.: Über die Entwicklung von einigen Indices der chemischen und physikalischen Thermoregulation bei unreifen Kindern. *Ann. paediat.* 201: 305 (1963).
22. SCHADOW, H.: Der Betriebsstoffwechsel und Kalo- rienbedarf frühgeborener Säuglinge. *Jb. Kinder- heilk.* 136: 1 (1932).
23. SCOPES, J.W. and AHMED, I.: Range of critical temperature in sick and premature newborn ba- bies. *Arch. Dis. Childh.* 41: 417 (1966).
24. SCOPES, J.W. and AHMED, I.: Minimal rate of oxy- gen consumption in sick and premature infants. *Arch. Dis. Childh.* 41: 407 (1966).
25. SCHOLANDER, P.F.: Analyzer for accurate estima- tion of respiratory gases in one-half cubic centi- meter samples. *J. biol. Chem.* 167: 235 (1947).
26. SILVERMAN, W.A. and AGATE, F.J., Jr.: Variation in cold resistance among small newborn infants. *Biol. Neonat. (Basel)* 6: 113 (1964).
27. SILVERMAN, W.A.; FERTIG, J.W. and BERGER, A.P.: The influence of the thermal environment upon the survival of newly born premature infants. *Pediatrics* 22: 87 (1958).
28. TALBOT, F.B.: The basal metabolism of prema- turity. *Amer. J. Dis. Child.* 24: 249 (1963).
29. TALBOT, F.B.; SISSON, W.R.; MORIARTY, M.E. and DALRYMPLE, A.I.: The basal metabolism of prematurity. III. Metabolism findings in 21 pre- mature infants. *Amer. J. Dis. Child.* 26: 29 (1923).
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