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R. D. Montgomery

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Research Article

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CHANGES IN THE BASAL METABOLIC RATE OF THE MALNOURISHED INFANT AND THEIR RELATION TO BODY COMPOSITION

By R. D. MONTGOMERY *

(From the Medical Research Council Tropical Metabolism Research Unit, University College of the West Indies, Jamaica)

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The measurement of basal metabolic rate in infants by indirect calorimetry was first performed by Rubner and Heubner in an open-circuit apparatus in 1898 (1). A closed-circuit technique was devised by Benedict and Talbot (2) and has since been applied many times (3–5). The normal pattern of changes in basal metabolic rate (BMR) during growth has thus been clearly established.

The effect of malnutrition on this pattern is much less clearly understood. Seven series of studies on marasmic infants have been reported in the past 40 years (6–12). The results indicate that in relation to the subject's actual weight the BMR in marasmus tends to be raised above the normal range, whereas in terms of the expected weight (for age) it tends to be low. The variations in the individual results, however, were very wide. Whereas the normal range for infants weighing up to 13 kg may be expressed as 45 to 60 calories per kg per 24 hours (13), the reported values in marasmus have ranged from 48 to 100.

Almost without exception, these figures were based on single observations, or on the mean of closely repeated observations, on each child at an unstated time during his hospital admission. No series has defined the changes during recovery and re-establishment of growth. The diagnosis of marasmus included a variety of predisposing and complicating conditions, and there have been no comparable measurements in kwashiorkor.

Previous results in infants have run entirely contrary to experience in adult undernutrition, in which a fall in BMR has usually been reported both in terms of surface area and to a lesser extent in terms of body weight (14). It should be noted, however, that Talbot, Dalrymple and Hendry (15) observed a fall in BMR per kilogram in infants after several days' fasting, and Varga (16) found a similar depression in cases of congenital pyloric stenosis, with a brisk rise during recovery.

In the present study, serial observations were made on Jamaican infants suffering from severe protein malnutrition (17). The purpose of the work was threefold: *1*) The oxygen uptake must depend, among other things, on the active tissue mass; its measurement might therefore help in assessing the degree of protein depletion of the body. *2*) Protein malnutrition still carries a heavy mortality in hospital, and death is often unexplained. If this were preceded by an irreversible failure of a vital stage in cellular metabolism, it might be reflected in the BMR. *3*) Little is known of the factors controlling the rate and pattern of growth-recovery after prolonged deprivation; nor indeed is there any clear understanding of the oxygen demands of an excessive anabolic state, of which these infants in recovery are a unique example.

The protein-depleted infant has an abnormally high content of body water, regardless of the degree of clinical edema, and most if not all of this excess is believed to be in the extracellular phase (18–20). As a basis of reference, therefore, the body solid mass, although it includes fat and minerals, may be preferable to the body weight. For this reason, concomitant studies were made of total body water, and the metabolic rate was considered in terms of body solid mass.

CLINICAL SUBJECTS

Thirty-six malnourished infants were studied. Their ages on admission ranged from 4 to 30 months, and the body weight, after loss of clinical edema, ranged from 30 to 72 per cent of the normal weight for their age by American standards (21). The clinical picture ranged from frank marasmus, in which the baby might be mentally alert and hungry but showed extreme loss of fat and muscle and stunting of growth, to the full picture of kwashiorkor, with profound weakness, mental apathy, irritability and anorexia, gross edema, enlarged fatty liver, mucocutaneous ulceration, and the characteristic pigmentary changes of skin and hair (22). The majority fell

* Present address: Department of Experimental Medicine, University of Cambridge, England.

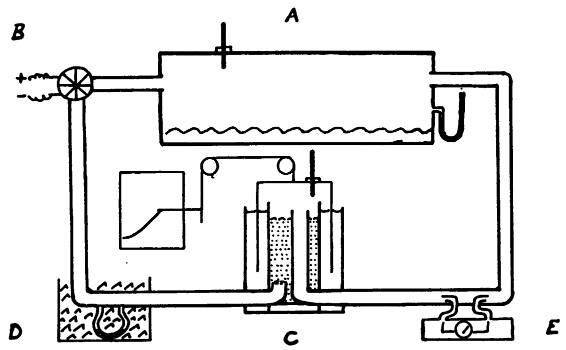

FIG. 1. DIAGRAM OF BMR APPARATUS IN THE PRESENT STUDY. A = respiration chamber. B = fan-type air pump. C = Kendrick respirometer and 60-minute recording drum. D = ice bath. E = CO_2 Katharometer.

into an intermediate category of marasmic kwashiorkor (23, 24), with severe wasting accompanied by apathy, mild or moderate edema, hepatomegaly, and variable skin and hair changes. The history of malnutrition appeared to date from the cessation of breast feeding, development usually being normal during the first few months of life.

In all cases protein malnutrition appeared to be the primary condition, other features such as gastroenteritis or sepsis being of less importance. None of the infants was pyrexial at the time of study. Two of the infants died within 5 days of admission.

METHODS

Oxygen consumption. Indirect calorimetry was performed in a closed circuit consisting of a metal respiration chamber connected by 1-inch Perspex tubing to a fan-type air pump and a modified British Benedict (Kendrick) respirometer (Figure 1). The respiration chamber, of 52-L volume, had a reinforced Perspex lid sealed by a vaseline-coated rubber ring and quick-release clamps. The pump was a Hoover "Dustette" type fitted to a variable resistance and totally enclosed in a copper cylinder with 1-inch outlets.[1] At the start of a test, some 5 L of oxygen was run into the system. Absorption of carbon dioxide was by "Calsoda" (Kendrick), and oxygen uptake was measured volumetrically by the respirometer, which was fitted to a 60-minute recording drum. Cooling was maintained by passing the tubing through a bath of chipped ice, condensed water being collected in a rubber U-tube. An air sample was continuously monitored for carbon dioxide content by passage through a Cambridge Katharometer.

The infant was lightly sedated with oral paraldehyde in the postabsorptive state (3 to 6 hours after feeding) and placed in the chamber on foam rubber and diapers. Soon after admission, ill babies did not require sedation but remained asleep or apathetically awake throughout the test. The others all fell asleep before or soon after the start of the test and seldom awoke before the end. Restless periods rarely occurred during the test and were apparent on the tracing of the recording drum. The experiment was run for 45 to 50 minutes, and readings were based on the record of the last 20 minutes. Control tests of the apparatus without an infant were made every few days to record the baseline, which was always horizontal after 30 minutes' running. Duplicate tests on successive days were made in the case of 5 infants, and the results showed a variation in oxygen uptake of 0 to 4 per cent.

Excess air space in the chamber was filled to maintain the circulating air volume at 44 to 46 L. The temperature rise during the test period ranged from 0 to 0.8° C. An appropriate correction was made for the change in air volume. Throughout the 18 months of these experiments the room temperature ranged only from 26.5° to 30° C (80° to 86° F) and the atmospheric pressure from 745 to 749 mm Hg. A constant factor was therefore used for correction of volumes to 0° C and 760 mm Hg.

The temperature in the chamber during the test period averaged 30° C (86° F), which may be considered to be in the zone of thermal neutrality for the infant. Rectal temperatures in 6 cases were found to be normal before and after the test.

The figures for oxygen consumption were conventionally converted to terms of caloric output by assuming a respiratory quotient of 0.86 and a calorific value for oxygen of 4.825 calories per L (2, 5). Except where otherwise defined, the term BMR in this text refers to the value of calories per kg per 24 hours.

BMR was also considered in terms of weight-in-kilograms$^{\frac{3}{4}}$ as an approximate index of surface area, and in terms of Karlberg's "capacitance" surface area (5) calculated from his height-weight nomogram, which has proved to be a more precise basis for expressing the normal BMR per square meter.

Controls. Seven Jamaican infants were tested as controls. Four of these had been patients with malnutrition at least 4 months previously. At the time of testing they were all growing satisfactorily on an adequate home diet and were representative of healthy Jamaican infants of poor parentage. They all had an appreciable weight deficit by North American standards (Table I), but it has been suggested that such "normal" standards are set some 15 per cent too high for breast-fed infants in underdeveloped countries (25).

Body water. Total body water was estimated by the method of Bradley, Davidsson, MacIntyre and Rapoport (26) as modified by Smith (20). Tritiated water was given by intramuscular injection, and the radioactivity in successive urine samples was measured in a stream of helium in a sensitive gas-flow counter.

Eighteen estimations were made on nine infants whose BMR was studied during the same period, estimations being made at the time when body weight was minimal and again during the stage of recovery.

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[1] I am grateful for the invaluable aid of Dr. B. M. Wright and the technical staff of the National Institute for Medical Research, Mill Hill, London, England, in the construction of the apparatus.

TABLE I

Summarized data of basal oxygen uptake in 20 malnourished Jamaican infants and 7 Jamaican controls

State on admission						Basal metabolism						
Case	Clinical type	Age	Wt*	Ht	Weight, per cent of normal for age†	Oxygen uptake on admission	Oxygen uptake at BMR peak		Oxygen uptake on discharge		BMR on admission	Peak BMR
		mos	*kg*	*cm*	%	*ml/min*	*ml/min*	*days‡*	*ml/min*	*days*	*cal/kg/ 24 hrs*	*cal/kg/ 24 hrs*
OD	Marasmus	13	3.35	60.5	31	28.9	62.3	42	61.9	83	60	93
JM	Marasmus	8	2.94	58	32	24.9	57.0	49	42.5	93	59	108
ER	Marasmus	19	3.75	62	33	40.0	71.2	27	76.2	63	74	112
LS	Marasmus	11	4.04	62	38	29.3	81.2	48	80.1	73	55	101
FA	Marasmus	4	2.14	51	39	22.1	37.8	32	39.2	45	70	112
ED	Marasmus	16	4.45	62	40	40.6	74.4	22	75.8	60	59	99
OM	Marasmic kwashiorkor	9	3.70	63.5	40	19.2	57.3	39	61.8	65	36	74
ID	Marasmic kwashiorkor	22	5.50	70.5	43	38.5	75.8	23	80.1	53	52	72
WH	Marasmus	7	3.60	60	45	25.5	59.1	31	51.3	70	49	97
HE	Marasmic kwashiorkor	30	5.92	67	47	44.1	74.8	32	76.9	74	52	75
MR	Marasmic kwashiorkor	8	4.45	67	52	28.5	54.8	34	62.7	74	45	72
JG	Marasmic kwashiorkor	7	4.50	62	52	39.5	died				61	
DD	Marasmus	7	4.60	64	54	34.2	59.5	17	54.8	81	52	80
DF	Marasmic kwashiorkor	8	4.62§	57	56	22.1	died				34§	
MB	Marasmic kwashiorkor	17	6.20	72	56	49.0	71.9	24	78.5	40	55	71
BL	Marasmic kwashiorkor	12	5.85	66	57	41.7	71.6	41	72.3	59	50	69
LW	Marasmic kwashiorkor	10	5.66	66	59	34.5	56.3	32	55.2	75	42	69
WM	Kwashiorkor	12	6.00	68.5	60	36.7	58.7	28	61.2	40	42	60
GR	Kwashiorkor	14	7.55	72.5	72	59.1	82.6	29	92.6	54	54	74
MW	Kwashiorkor	13	7.20	68	72	57.0	69.1	15	60.9	39	55	65
MA	Control	7	5.66	63.5	70	50.0					61	
EG	Control	15	7.32	69	67	57.3					55	
LL	Control	15	7.80	68	70	66.8					61	
WH	Control	21	7.45	69.5	64	61.3					57	
TS	Control	24	8.80	74.5	69	75.8					61	
ID	Control	28	11.22	79.5	84	94.3					58	
AT	Control	32	9.75	80.5	72	72.3					52	

* Body weight after loss of edema, if any.
† Normal values taken from Nelson's standard tables (21).
‡ Days after admission.
§ Died without loss of edema.

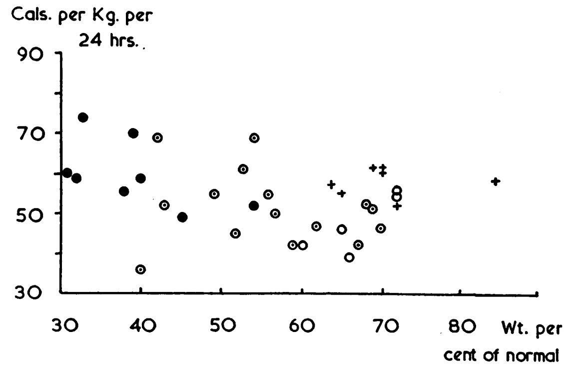

FIG. 2. INITIAL BMR IN 28 MALNOURISHED JAMAICAN INFANTS AND IN 7 JAMAICAN CONTROLS. The abscissa represents the body weight as a percentage of the normal weight for age (21). In edematous cases the initial weight was taken to be the minimum weight after loss of edema. ● = marasmus; ○ = kwashiorkor; ⊙ = marasmic kwashiorkor; + = controls.

RESULTS

BMR in controls. The figures of oxygen consumption in Jamaican controls are given at the bottom of Table I. The BMR range of 52 to 61 calories per kg per 24 hours is similar to that of Talbot (27) but slightly higher than that of Karlberg (5). Possible factors tending to increase the BMR of these subjects are discussed below.

Initial BMR in malnutrition. Initial BMR figures in the three clinical groups are shown in Figure 2 and Table I and are summarized as percentages of normal in Table II. In terms of edema-free body weight, the BMR was variable about a normal mean, being higher in the marasmic group and lower in frank kwashiorkor. In terms of "capacitance" surface area, metabolism was subnormal in 22 of 28 cases, when related to Karlberg's 95 per cent confidence intervals, but the variation was equally great, high figures being found in several marasmic cases. Expression of metabolism in terms of weight$^{2/3}$ gave results closely comparable to those in terms of capacitance surface area.

BMR changes in recovery. In each case, whatever the initial value, the BMR invariably rose during recovery, and this rise sometimes preceded the weight gain. Peak values ranging from 60 to 112 calories per kg per 24 hours were reached in 2 to 6 weeks (Figure 3), after which the levels declined toward the normal. This remarkable change of respiratory behavior in the individual in the course of a few weeks helps to explain wide variations between the isolated observations of earlier workers.

TABLE II

*Initial BMR in malnutrition, in terms of body weight and "capacitance" surface area, expressed as percentages of normal **

Clinical group	Weight, per cent of theoretical weight for age	BMR (per kg), per cent of normal	BMR (per m^2), per cent of normal
	%	%	%
Marasmus (11 cases)	40 (31–54)	113 (92–140)	97 (75–138)
Marasmic kwashiorkor (20 cases)	54 (40–70)	96 (64–130)	85 (56–113)
Kwashiorkor (5 cases)	67 (60–72)	89 (74–104)	83 (76–103)

* In edematous cases initial weight is taken as the minimum after loss of edema. Normal BMR is taken as 53 cals/kg/24 hours (13). The figures in terms of capacitance surface area and their relation to normal are taken from Karlberg's height-weight nomogram (5). Theoretical weights for age are taken from American standard tables (21).

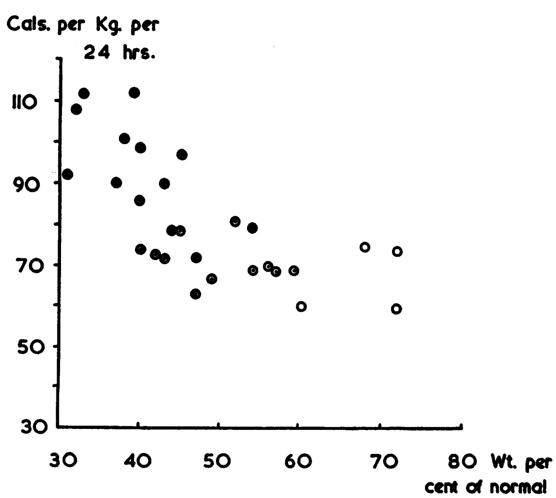

FIG. 3. OBSERVED PEAK BMR DURING REHABILITATION. Abscissa and symbols as in Figure 2.

Relation of BMR to body weight. Marasmic infants not only had higher initial levels of BMR than cases of kwashiorkor, but they showed a more dramatic rise to peak levels during recovery (Figures 3–5). The marasmic group were the most wasted in relation to the normal for age, and it can be seen from Figure 3 that the more emaciated the child, the higher was the BMR peak during recovery. This correlation was more apparent with respect to the weight deficit in relation to age than with the deficit in relation to height.

Plateau of oxygen uptake in recovery. The changes in total basal oxygen uptake in recovery are summarized in Table I. The peak level of BMR represents the beginning of a plateau level of oxygen consumption which is maintained regardless of the further acute changes in the child's body size (Figure 6). Once this plateau is reached the BMR per kilogram falls as weight gain proceeds. Over a period of many months, the plateau shows a gradual rise with increasing age (Figure 7).

Oxygen uptake at the plateau is of the same order as that of Jamaican controls of the same age.

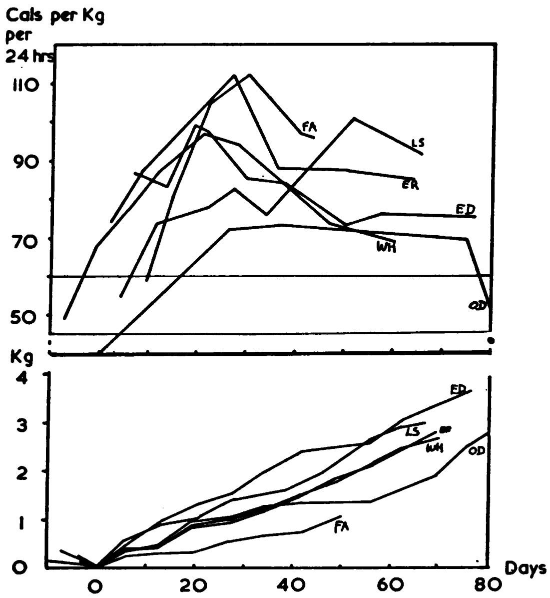

FIG. 4. CHANGES IN BMR DURING RECOVERY IN 6 MARASMIC CASES. The changes in body weight are shown in the lower panel. Day 0 = day of minimum weight.

It is constantly between 68 and 98 per cent of the uptake of a normal American child of the same age, based on a normal BMR of 53 calories per kg per 24 hours (13). As can be seen from Table III, there is no such correlation with the oxygen uptake of normal children of the same height or the same surface area.

Relation of oxygen uptake to the caloric value of the diet. In the treatment of marasmic infants a very high caloric intake may be required to achieve weight gain. The present data (Table IV) indicate that the more emaciated the child, the greater this minimal intake tends to be, and

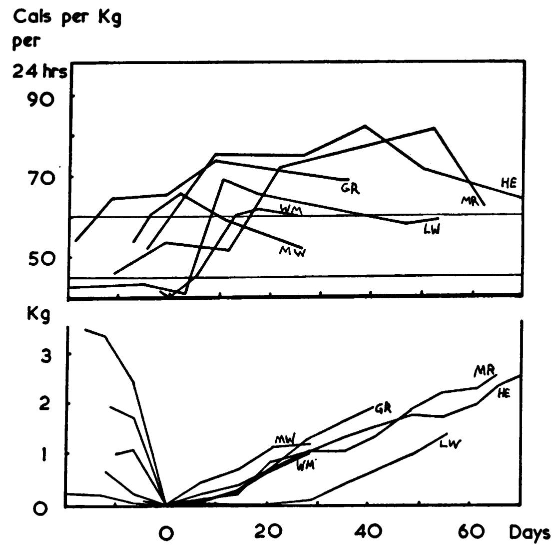

FIG. 5. CHANGES IN BMR DURING RECOVERY IN 6 CASES OF KWASHIORKOR. The changes in body weight are shown in the lower panel. Day 0 = day of minimum weight.

suggest that this depends on the changes in BMR. Thus the primary effect of increased caloric intake is a rise in BMR, but it is only when the caloric intake exceeds the basal caloric consumption by 60 to 85 calories per kg that growth results.

In some cases a high calorie intake was rapidly achieved (FA, OM, ID, BW, RB; Table IV) and weight gain commenced before the BMR had

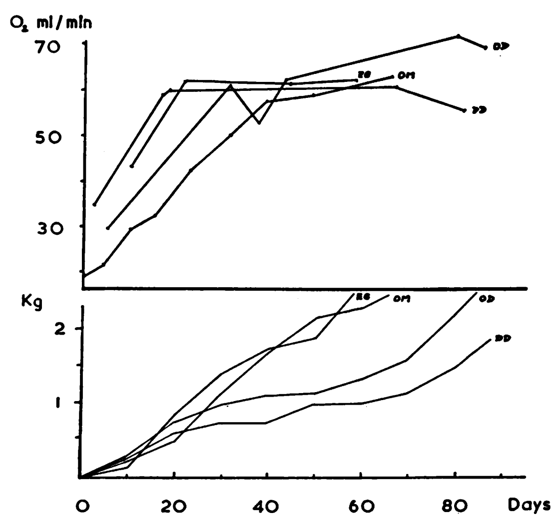

FIG. 6. CHANGES IN TOTAL BASAL OXYGEN CONSUMPTION IN 4 TYPICAL CASES IN RECOVERY, SHOWING THE "PLATEAU" LEVEL. The changes in body weight are shown in the lower panel.

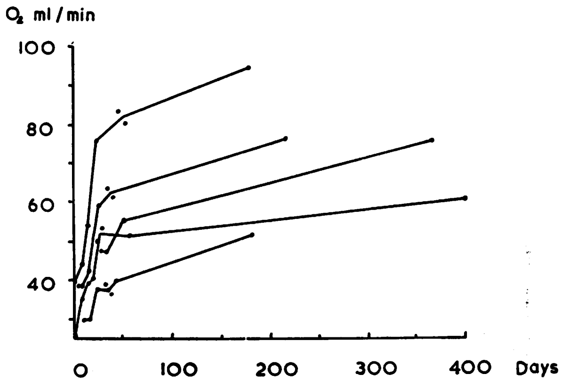

FIG. 7. LONG-TERM STUDIES OF BASAL OXYGEN CONSUMPTION IN RECOVERY IN 5 FURTHER CASES, SHOWING A SLOW RISE IN THE PLATEAU LEVEL.

reached its peak. More often the intake could only slowly be built up, and as the BMR rose a correspondingly higher intake was needed for growth. In cases FA and RB, the BMR "overtook" the intake, and weight gain temporarily ceased.

These interpretations presuppose that on a milk diet calories rather than protein tend to be the limiting factor in growth (28).

TABLE III

"Plateau" level of oxygen uptake in recovery: percentage of normal on the basis of weight, height, capacitance surface area, and age *

Case	Uptake as a percentage of the normal in a child of:			
	Same weight	Same height	Same capacitance surface area	Same age
	%	%	%	%
FA	211	157	157	81
ER	211	141	182	77
JM	203	141	167	79
LS	190	133	182	98
ED	186	148	171	86
WH	182	128	157	88
OD	173	132	154	71
LC	170	103	160	73
EG	161	132	150	75
DS	150	109	133	88
DG	148	110	135	88
RB	141	79	130	75
OM	139	102	126	79
CR	137	105	128	79
MR	135	88	115	94
ID	133	109	124	79
MB	132	102	120	90
BL	132	105	128	86
LW	130	89	119	73
GF	130	85	130	70
GR	120	94	111	94
BW	118	107	118	68
DB	115	84	105	85
MW	113	102	109	85
WM	113	94	11	80
Range	113–211	79–157	105–182	68–98

* Normal values are based on standard tables (21) and a BMR value of 53 calories per kg per 24 hours (13).

Relation of oxygen uptake to dietary protein. At the time when a plateau of oxygen uptake was reached, the infants were usually receiving a full-strength milk mixture fortified by peanut oil, giving a protein intake of the order of 4 g per kg per day. In some cases supplements of cereals, vegetables, and bread had already begun.

Tests were made of the effect on oxygen uptake of altering the diet to: *a*) a low-calorie protein-free diet of 5 per cent dextrose in 0.333 N saline, or *b*) an isocaloric low protein diet in which starch was substituted for skim milk. Four infants were tested on *a* and seven on *b*. The change was made at

TABLE IV

Correlation between the observed minimal caloric requirement for growth and the BMR at the same time

Case	Initial weight, per cent of normal for age	Caloric intake	BMR	Intake −BMR
	%	*cals/kg/day*	*cals/kg/day*	*cals/kg/day*
ER	33	170	100	70
		160	90	70
TS	37	170	90	80
FA	39	170	85*	85
		190	105	85
OM	40	135	55*	80
ID	43	135	50*	95
LC	43	150	75	75
DG	44	145	80	65
WH	45	150	85	65
BW	47	125	55*	70
RB	47	110	50*	60
		130	65	65
LW	59	135	60	75
WS	67	125	55	70
MW	72	130	65	65

* Weight gain commenced before the BMR peak (see text).

a time when the child was gaining weight steadily and had reached a steady plateau level of oxygen uptake. The starch diet was known from previous experience to be inadequate for growth, although the child often maintained weight, as was the case in this series.

In all cases on dextrose-saline, the oxygen uptake fell abruptly and severely, but only after a latent interval of 48 hours. On the starch diet, the same latent interval was observed, followed in three cases by a more gradual fall; in the remainder, no significant fall occurred during test periods of up to 11 days. The mean daily protein intake on the starch diet was 0.87 g per kg in the

TABLE V

Total body water and the metabolic activity of body solids in malnourished infants

Case	Clinical diagnosis	Total body water, per cent of body weight (normal 55–65)	Weight, per cent of theoretical weight (for age)	Body solid mass, per cent of theoretical solid mass (for age)	BMR within a week of admission	
		%	%	%	*cals/kg body wt/ 24 hrs* (Normal 45–60)	*cals/kg body solids/ 24 hrs* (Normal 100–170)
JM	Marasmus	75	32	20	59	236
WH	Marasmus	71	45	33	49	163
MR	Marasmic kwashiorkor	80	52	26	45	225
WS	Marasmic kwashiorkor	75	67	42	42	168
LW	Marasmic kwashiorkor	73	59	40	42	155
GF	Marasmic kwashiorkor	63	54	50	69	186
OM	Marasmic kwashiorkor	73	40	27	36	133
GR	Kwashiorkor	61	72	71	54	139
MW	Kwashiorkor	60	72	72	55	138

cases in which the oxygen consumption fell, and 1.10 g per kg in the remainder. These findings suggest that a protein intake of about 1 g per kg is critical in maintaining the oxygen plateau during recovery.

Relation of oxygen uptake to body solids. The tendency to a high body water content in protein malnutrition was confirmed (Table V). In three grave cases, the body solid mass including fat was initially less than 30 per cent of the normal for age, whereas the body weight was 32 to 52 per cent of normal.

If the body solid content of normal infants is taken as 35 to 45 per cent (19, 29), the normal BMR range of 45 to 60 calories per kg body weight per day represents 100 to 170 calories per kg body solids. The range in nine malnourished infants studied soon after admission was 134 to 236 calories per kg body solids per day (mean 171) (Table V).

The deficit of body solids correlated with the degree of their respiratory hyperactivity at the peak of recovery (Figure 8), in the same way as did the deficit in body weight with BMR (Figure 3).

DISCUSSION

In the untreated case the oxygen consumption, expressed either in terms of body weight or of body solid mass, tends to be depressed in frank kwashiorkor but not in marasmus.

These parameters however are fallacious for two reasons: *1*) a reduction in the proportion of fat in the body solid mass will cause apparent increase in the metabolic activity of the remainder; and *2*) the body solid mass is not only reduced in *amount* compared with a normal child of the same age (Table V); it is also altered as regards the proportions contributed by different organs and tissues.

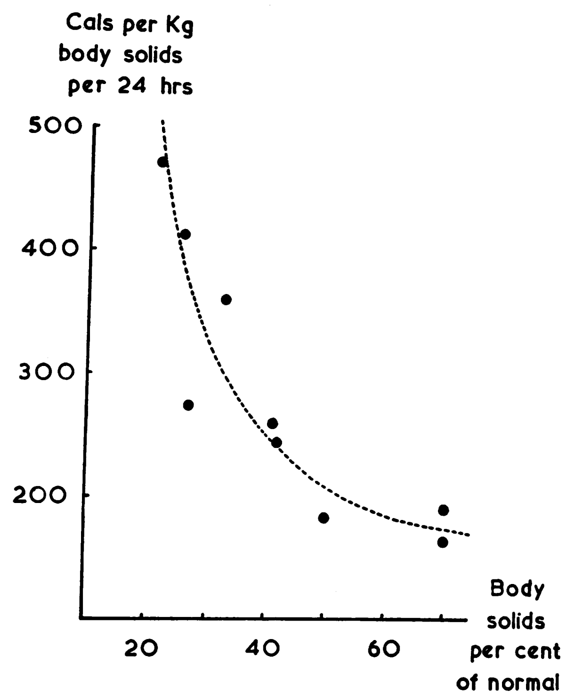

FIG. 8. THE RELATION OF BODY SOLID RESPIRATORY ACTIVITY AT THE PEAK OF RECOVERY TO THE DEFICIT IN BODY SOLID MASS. Body solids are expressed as a percentage of the normal for age. The highest activity occurs in the most depleted cases.

Fat content of body solids. In the normal man or animal, an approximate calculation of body fat can be made from the body weight and the body solid mass by assuming a constant figure of 28 per cent for the proportion of lean body solid mass (LBS) to lean body weight (30–32). The figures for body water show that this relation ceases to be valid in malnutrition. Nor is a normal ratio maintained of LBS to *total* body weight (about 22 per cent), for the body solids may be 20 per cent or less of the body weight in edema-free cases (20), in some of whom significant amounts of fat are known to be present.

Although we have no true measure of the fat content of the body solids, clinical observation agrees with the trends of the data in Table V. The lowest figures for respiratory activity of body solids were found in cases in whom body fat was most apparent, and the highest figures were in marasmic infants whose fat content was minimal. The latter figures fall within or below the normal range in terms of LBS (205 to 275 calories per kg LBS per 24 hours).

In short, whereas the oxygen uptake in terms of body solid mass varies widely about a high normal mean, the uptake of the lean solids appears to be more constant in or below the normal range. This is in keeping with the finding of lowered metabolism in terms of surface area, since surface area is roughly proportional to LBS (33).

Pattern of body solids. In the malnourished growing animal, the "body pattern" is altered at several different levels: *1*) The growth of different *organs* is retarded to different degrees—brain, heart, and kidney being less retarded or depleted than liver, pancreas, and muscle (34–37). *2*) A rough division may be made into proteins that are relatively fixed, mainly extracellular, such as collagen, and those that are more mobile, such as the cytoplasmic proteins of parenchymatous cells (38). There is evidence that some of the fixed protein is much less reduced in amount than are the mobile proteins (36, 39). *3*) At cellular level, the composition of the cell is altered by shrinkage of the cytoplasm in relation to the nucleus (40, 41).

To consider the way in which these alterations in pattern may affect the oxygen uptake, the brain may be taken as a striking example for two reasons: *1*) It is probable that only minor changes in its metabolic rate are compatible with conscious life; and *2*) of all organs, the absolute weight of the brain is least affected by malnutrition.

In the normal infant at 1 year, the brain weight is some 9 per cent of body weight, that is, a brain of 900 g may be found in a 10 kg child. In a series of malnourished infants, the brain has been found to weigh up to 18 per cent of body weight at 1 year, e.g., 700 g in a 4 kg child (42).

No figures are available for the oxygen uptake of the brain in young infants, but for the purposes of calculation two figures may be used: *1*) the rate in normal adults (33 ml per kg per minute = approximately 200 calories per kg per day); and *2*) the rate found in adults in coma, which may be considered to approach the lower limit compatible with life (20 ml per kg per minute = approximately 150 calories per kg per day) (43). These figures may exaggerate the true values in adults by at least 30 per cent owing to systematic errors (44). On the other hand, a brain oxygen uptake as high as 50

TABLE VI

Derived metabolic data from observed brain weight in malnutrition, suggesting that there is over-all depression of metabolism of the lean body mass (LBM)

	A Body wt	B Assumed fat content of body	C LBM	D BMR*	E Total metabolism of body (D×A)	F Brain wt	G Metabolic† rate of brain	H Total metabolism of brain (G×F)	I Total metabolism of rest of LBM (E−H)	J Wt of rest of LBM (C−F)	K Metabolic rate of LBM other than brain (I/J
	kg	*%*	*kg*	*cals/kg/day*	*cals/day*	*kg*	*cals/kg/day*	*cals/day*	*cals/day*	*kg*	*cals/kg/day*
Normal	10	20	8	50	500	0.9	200	180	320	7.1	45
Malnutrition, initial	4	5	3.8	50	200	0.7	150	105	95	3.1	31
Malnutrition at oxygen plateau	5	8	4.6	80	400	0.7	200	140	260	3.9	67

* See Table I.
† For assumptions see text.

ml per kg per minute has been reported in normal 5 year old children (45).

Table VI has been constructed with the adult figures. It leads to a conclusion that at first sight seems paradoxical—that although the over-all metabolic rate may be normal, the metabolism of the individual organs is depressed. The reason for this, of course, is the high proportion of the malnourished body taken up by organs that normally have a high rate of activity. Although in the lean body mass other than brain there is probably an increased proportion of inactive protein such as collagen, it is difficult to believe that this alone could account for the depression of metabolic rate suggested by the calculation, which had already presupposed a depression of brain metabolism. The depression could, however, be partly accounted for by the excess of water.

BMR in marasmus. It has been noted that *some* cases of marasmus showed a high initial BMR both in terms of body weight and surface area. These cases were the most wasted of the whole series and presumably, therefore, had the highest proportion of relatively active brain. It has also been shown that a diet inadequate in calories but "marginal" in protein may result in a sustained increase in BMR without detectable weight gain. That this might have been the initial state of these few infants is suggested by the fact that they were mentally alert and physically active, in contrast to the profoundly mentally apathetic and irritable majority.

Oxygen plateau in recovery. The higher proportion of brain in the body of the Jamaican controls as compared with their heavier American counterparts may account for the fact that their BMR lies in the upper range of "normal." Similarly, the mere restoration of normal activity to the most active organs in the malnourished infant may partly explain the great rise in oxygen uptake during recovery. In addition, there is the high oxygen demand of accelerated anabolism in muscle and in the other tissues which have been the most seriously depleted.

What factors determine the peak level of metabolism? Although it might be anticipated that this acceleration of growth calls for balanced hyperactivity of the endocrine system, radioiodine studies suggest that the thyroid gland plays no significant part in initiating the oxygen changes (42).

The close relation of the level of the oxygen plateau to age is surprising. One possible explanation has already been offered: the recovery of normal activity in those organs whose mass has fallen off least in relation to the normal for age. Another factor arises from consideration of metabolism at cellular level. Respiration in the cell is primarily a function of the mitochondria (46), and it may well be that in an adult cell made smaller by protein depletion the *potential* respiratory activity of the mitochondria is relatively less affected. Thus when optimal conditions are restored, the "metabolic potential" of a body of recovering cells may be related to the cell number rather than to the total cell mass.

In this context, Gray and Deluca (47) found that the respiratory activity of the isolated diaphragm in malnourished rats was increased in terms of tissue mass but was normal in terms of desoxyribonucleic acid, i.e., per "cell unit."

In the child, the picture is complicated by cell growth. There is evidence that in the young rat liver, with complete interruption of body growth by undernutrition, the liver size and total protein content remain constant, but the number of nuclei increases slowly (39). A roughly similar relationship has been found between the mass and sarcolemmal nuclear count of sartorius muscle in malnourished infants (42). Thus in long-standing malnutrition, the increased number of cells per unit of tissue mass may influence the limit of increased oxygen uptake during recovery.

SUMMARY

1. The basal metabolic rate (BMR) was studied by a closed-circuit system in 36 infants suffering from and recovering from severe protein malnutrition. In nine cases, concomitant studies were made of total body water by tritium dilution.

2. In most cases, the initial oxygen consumption tended to be subnormal in relation to calculated surface area, but was approximately normal in terms of body weight and of body solid mass. However, owing to an abnormal preponderance of the most metabolically active organs, notably the brain, this finding suggests a true depression of respiratory activity in the individual organs. In

a few marasmic cases, the BMR was initially increased both in terms of body weight and surface area.

3. Serial tests showed a dramatic rise in total oxygen consumption, often more than twofold, during the early weeks of recovery. This rise was followed by a plateau level which was maintained regardless of variable gains in weight. Total oxygen consumption at this plateau level approached the normal for a healthy child of the same age.

4. Body weight did not increase unless the caloric intake consistently exceeded the BMR by 60 to 85 calories per kg per day. The greater the weight deficit, the higher was the BMR during recovery and the higher the caloric requirement for weight gain.

5. It is suggested that the limit of oxygen uptake in recovery may be determined partly through the restoration of normal activity in the organs which are least reduced in relation to age and partly through the factor of the mean "metabolic potential" of the individual cell. Cell number per unit of tissue mass is increased in the active tissues of the malnourished growing animal. The mean respiratory activity per cell is therefore much reduced initially, but may approach the normal during recovery.

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