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REFERENCES

- Barnes, D. J. & Munk, B. (1940). *Proc. Soc. exp. Biol., N. Y.*, **44**, 327.
King, E. J. (1946). *Micro-Analysis in Medical Biochemistry*. London: Churchill.
Klasmer, R. (1944). *Amer. J. Dis. Child.* **67**, 348.
Stearns, G. & Warweg, E. (1933). *J. biol. Chem.* **102**, 749.

The Estimation of the Metabolic Rate in the Starvation State

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In the classical studies of undernutrition in man, reviewed by Lusk (1921), the basal metabolism was found to be reduced whether it was expressed in terms of heat production/sq.m. of body surface or of heat production/kg. body-weight. The percentage fall in basal metabolism was, however, greater when it was calculated with reference to the surface area than when calculated in terms of heat production/kg. body-weight. This discrepancy was not discussed by Lusk who was concerned mainly with drawing attention to the fact that energy production in the starvation state is reduced below normal.

EXPERIMENTAL

Selection of subjects

Studies of energy metabolism in severely undernourished persons in Holland in 1945 and in Germany in 1946 revealed great discrepancies between the levels of basal metabolism when these were expressed in terms of heat production/sq.m. of body surface and of heat production/kg. body-weight. It appeared that the discrepancies increased with increased weight loss. We were unable at the end of our first study in 1945 to decide which method of expressing the basal metabolism was the better index of the rate of tissue oxidation. In Germany we were able to study a group of young adults who, with one exception, were between the ages of 21 and 31 years. During a preliminary period of observation lasting 4 weeks, forty men between 20 and 40 years of age were studied while living on a diet containing not more than 1750 Cal./day and identical with that consumed during the preceding 3 months. By gradual elimination of subjects who had some clinical evidence of organic disease or a recent history of tuberculosis,

a group of men was selected for metabolic studies. Those who gave, over the last 2 weeks of the preliminary period, basal oxygen consumptions which did not vary by more than 5% from day to day, formed the experimental group of eleven individuals. All these men had served in one or other branch of the German armed forces and consequently their normal body-weights were adequately documented. They had all been detained in a civil prison since July 1945 and the fall in body-weight during the period July 1945–July 1946 could be followed as monthly weighings were carried out on all inmates.

Methods

It was assumed that, in their normal state, the heat production/sq.m. of body surface was that appropriate to their age as expressed in the standard tables of Boothby & Sandiford (1929). As these men had been trained during the preliminary period in the use of the spirometer it was necessary to make a deduction of 5% from the Boothby & Sandiford standards to make a fair comparison between the calculated normal and the observed values. The surface areas of the body were calculated from the Du Bois & Du Bois (1916) formula using the recorded normal body-weights and heights for the normal state and the observed weights and heights, at the end of the preliminary period of observation, as those for the starvation state. These data are contained in Table 1. The 'normal' body-weight was the mean of all recorded weights during the period January–June 1945 where known, or, alternatively, the recorded body-weight when admitted to the penal institution (June or July 1945). The weight for the starvation state was that recorded on the morning of the first oxygen-consumption test day after the end of the preliminary period.

Table 1. *Changes in height, weight and surface area of eleven subjects*

Subject	Normal state			Starvation state		
	Height (cm.)	Weight (kg.)	Surface area (sq.m.)	Height (cm.)	Weight (kg.)	Surface area (sq.m.)
Ks.	182	71	1.90	181.5	55.5	1.71
Lv.	184	73	1.94	184	55.7	1.72
Kl.	168	65	1.73	168	53.2	1.59
Wz.	169	71.5	1.84	169	53.8	1.60
Sc.	166	69	1.92	166	55.7	1.60
Gm.	165	70.5	1.77	165	50.1	1.53
Gt.	170	69	1.83	170	48.8	1.55
Rs.	171	67	1.78	171	55.3	1.64
Gd.	170	69	1.79	170	45.5	1.51
Bm.	167	65	1.72	167	47.9	1.52
Ru.	170	70	1.80	170	53.6	1.61

Heat production was calculated from the oxygen consumption by assuming an R.Q. of 0.82 giving a calorific value for oxygen of 4.825 Cal./l. Details of the method used to find basal oxygen consumption have been described in another paper (Beattie & Herbert, 1947). The heat production/sq.m. of body surface/hr. has been compared in Table 2 with the corrected standard value. The body-weight/sq.m. of surface has been calculated for both normal and starvation states.

Table 2. *Changes in basal heat production/sq.m./hr. and in body-weight/sq.m. of eleven subjects*

Subject	Heat production (Cal./sq.m./hr.)			Body-weight (kg./sq.m.)		
	Normal (corrected), calculated	Starvation state, observed	Change from normal (%)	Normal, calculated	Starvation state, observed	Change from normal (%)
	Ks.	38.9	35.5	- 9	37.3	32.4
Lv.	38.3	34.2	- 11	37.6	32.4	- 14
Kl.	38.9	28.3	-27	37.6	33.4	- 11
Wz.	38.3	35.8	- 6	38.9	33.8	- 13
Sc.	38.3	32.2	-16	35.9	34.8	- 3
Gm.	38.9	30.6	-21	39.8	32.8	- 18
Gt.	38.9	27.5	-29	39.9	31.5	-21
Rs.	38.9	36.4	- 6	37.6	33.7	- 10
Gd.	37.8	28.1	-26	38.5	30.1	-22
Bm.	38.3	30.8	-20	37.8	31.5	- 17
Ru.	35.3	33.5	- 5	38.9	33.3	- 14
		Average	- 16			- 14.2

Table 3 contains a comparison of heat production/kg. body-weight in the two states.

Table 3. *Changes in basal heat production and in basal heat production/kg. body-weight/day of eleven subjects*

Subject	Basal heat production (Cal./day)		Basal heat production (Cal./kg.)		
	Normal, calculated	Starvation state, observed	Normal, calculated (A)	Starvation state, observed (B)	Difference from normal (A)-(B)
Lv.	1781	1412	24.4	25.3	- 0.9
Kl.	1617	1080	24.9	20.2	+ 4.7
Wz.	1690	1375	23.6	25.5	- 1.9
Sc.	1764	1236	25.6	22.2	+ 3.4
Gm.	1655	1124	23.5	22.4	+ 1.1
Gt.	1711	1023	23.4	20.9	+ 2.5
Rs.	1664	1433	24.8	25.9	- 1.1
Gd.	1625	1018	23.6	22.4	+ 1.2
Bm.	1581	1124	24.3	23.5	+ 0.8
Ru.	1527	1294	21.8	24.1	- 2.3
		Average	24.1	23.5	+ 0.6

RESULTS

Heat production/sq.m.

The Rubner (1883, 1894) concept that in animals, including man, there is a relative constancy in heat production/unit surface area implies that, as the surface area/unit body-weight increases, the heat production/unit body-weight must increase proportionately. Thus, when an individual declines in weight, his surface area/unit body-weight increases (Table 2), and, consequently, if heat production/unit surface is to remain constant, the heat production/unit body-weight must increase. For example, subject Gd. had a calculated normal surface area of 1.79 sq.m. with a normal body-weight of 69 kg. The body-weight/sq.m. was, therefore, 38.5 kg. In the starvation state his weight had declined to 45.5 kg. and his surface area to 1.5 sq.m. Body-

weight/sq.m. was thus 30.1 kg. If heat production/sq.m. was to remain constant, then 30.1 kg. would have to produce the same amount of heat/unit time in the starvation state as 38.5 kg. produce under normal conditions. Heat production/kg. would thus have to rise to $(38.5/30.1) \times 100 = 128\%$ of the normal value. If, however, heat production/kg. body-weight remained unchanged, the heat production/sq.m. would fall to $(30.1/38.5) \times 100 = 79\%$ of the normal level, i.e. a fall of 21%. The observed fall in heat production/sq.m. in this individual was 26%.

It is thus possible that the change in the ratio of body-weight to unit surface might be responsible for the change in the rate of heat production/sq.m. of surface. The average fall in heat production/sq.m. in Table 2 is 16.0%. The average fall in body-weight/sq.m. is 14.2%. If it were true that the fall in heat production/sq.m. is due to the fall in body-weight/sq.m. then the average percentage falls should be identical apart from error variation. There is, however, a difference of 1.8% (16.0 - 14.2) which may or may not be significant. The eleven values may be subjected to an analysis of variance which will contain two items, the first representing the departure of this mean difference from zero and the second representing the variation of the eleven values around the mean. By the customary methods this analysis appears as follows:

Item	Sum of squares	Degrees of freedom (n)	Mean square
(1) Difference	36.36	1	36.36
(2) Error	657.63	10	65.76
Total	693.99	11	—

Further testing is unnecessary as it is obvious from inspection that the departure of the mean difference from zero is insignificant. So far as this test goes the fall in heat production/sq.m. would appear to be a mere reflexion of the fall in body-weight/sq.m.

Heat production/kg. body-weight

Benedict (1938) has advocated this method of expressing basal metabolism as the simplest, even if not necessarily the most accurate. We calculated the normal rate and the rate in the starvation state and have expressed the differences as percentages of the normal rates (Table 3). The average heat production/kg. body-weight in the normal state was 24.1 Cal., and in the starvation state 23.5 Cal.—a difference of 0.6 Cal. If heat production/kg. remained unchanged in the starvation state from that in the normal state, a zero difference might be expected. Testing the significance of this observed departure from an expected zero difference by an analysis of the variance of the eleven individual differences, we found:

Item	Sum of squares	Degrees of freedom (n)	Mean square
(1) Difference	3.49	1	3.49
(2) Error	52.31	10	5.23
Total	55.80	11	—

It is obvious that the departure of the mean difference from zero is not significant. We are thus justified in concluding that in the starvation state the heat production/kg. body-weight is not significantly different from that in the normal state.

Heat production/kg. active material

When body-weight declines owing to inadequate food intake the active material in the body may not diminish proportionately. In another paper (Beattie, Bell & Herbert, unpublished) we show that the total volume of the extra-cellular fluid (thiocyanate-space volume) in the body shows no significant change in absolute amount from that calculated for the normal body-weight. All the subjects in the present study had such 'normal' thiocyanate-space volumes. On the other hand, their body fat, which can be regarded as inert matter during the period of the oxygen-consumption test, was markedly diminished. It is conceivable, therefore, that, as body-weight falls, the absolute loss of body fat may be compensated for by the constancy of the extra-cellular fluid and hence, for a time at least, the ratio of active to inert material in the body may show no significant change.

Henschell, Mickelsen, Taylor & Keys (1947), as the result of a study of normal adult males subjected to severe food deprivation, came to the conclusion that the thiocyanate-space fluid formed on the average 23.5% of the normal body-weight and that this fluid volume remained constant after 24 weeks of semi-starvation. Keys (1947) also showed by-specific gravity measurements that the body fat fell from 10% of the normal body-weight to 3% of the observed body-weight at the end of the period of semi-starvation. He was unable to demonstrate any loss in bone density (observed radiographically) after semi-starvation. Using these data for these three inert constituents of the body-weight, and assuming that the other inert materials in the body either form an insignificant part of the body-weight or decline in weight proportionately with the fall in the body-weight, we calculated that 62.5% of the body-weight is metabolically active. The active material in the body-weight in the starvation state was calculated by assuming that the extra-vascular-fluid weight remained constant at the normal value, that the body fat formed 3% of the observed body-weight and that the bone salts formed 4% of the normal body-weight.

We calculated heat production/kg. active material for the normal and starvation states (Table 4) and expressed the differences between the normal and starvation values as percentages of the normal. As we have pointed out already that heat production in the starvation state, expressed/kg. body-weight, did not differ significantly from that in the normal state, it was to be expected that no significant difference would be found between heat productions/kg. active material in the two states. The average heat production/kg. active material was 38.5 Cal. in the normal state and 38.6 in the starvation state. This difference is obviously not significant but for the sake of completeness we have analysed the variance of the eleven individual differences by the method employed above:

Item	Sum of squares	Degrees of freedom (<i>n</i>)	Mean square
(1) Difference	0.06	1	0.06
(2) Error	151.04	10	15.10
Total	151.10	11	—

Table 4. *Changes in estimated active material content and in heat production/kg. active material of eleven subjects*

Subject	Active material content as percentage of body-weight			Heat production Cal./kg. active material		
	Normal	Starvation state	Change from normal (%)	Normal (A)	Starvation state (B)	Difference from normal (A)-(B)
Ks.	62.5	62.7	0	40.0	41.9	-1.9
Lv.		61.2	-2	39.0	41.3	-2.3
Kl.		64.0	+2	39.8	31.6	+8.2
Wz.		61.1	-2	37.8	41.7	-3.9
Sc.		63.5	+2	41.0	35.0	+6.0
Gm.		59.0	-6	37.6	38.0	-0.4
Gt.		56.8	-9	37.4	36.8	+0.6
Rs.		64.3	+3	39.7	40.3	-0.6
Gd.		56.0	-11	37.8	40.0	-2.2
Bm.		60.4	-3	38.9	38.9	0
Ru.		61.7	-1	34.9	39.1	-4.2
		Average		38.5	38.6	-0.1

DISCUSSION

It would be tempting to conclude that heat production/kg. active material is an even better index of the metabolic level than heat production/kg. body-weight. The results would agree with such a conclusion but they do not demonstrate its validity unambiguously, for we have pointed out above that on the basis of heat production/kg. body-weight there is no significant difference between the basal metabolism of the two states.

Table 5. *Comparison of percentage change in body-weight and percentage change in active material/kg. body-weight of eleven subjects*

Subject	Percentage change in body-weight (starvation state)	Percentage change in active material (starvation state)
Rs.	-17	+3
Kl.	-18	+2
Sc.	-19	+2
Ks.	-22	0
Ru.	-23	-1
Lv.	-25	-2
Wz.	-25	-2
Bm.	-26	-3
Gm.	-29	-6
Gt.	-33	-9
Gd.	-34	-11

The probable reason for our inability to select heat production/kg. active material as a better index of basal metabolism than heat production/kg. body-weight lies in the fact that the percentage of active material in the body shows little change until the weight loss exceeds 26% (Table 5). Only three subjects out of eleven showed weight losses exceeding 26% and these had changes in the active material percentage of -6, -9 and -11%. We have pointed out above how the loss of body fat is compensated for by the constancy of the extra-cellular-fluid volume. Apparently this compensation

ceases to be effective in maintaining an almost constant ratio of active to inactive material in the body-weight under starvation conditions only when the loss in body-weight exceeds about 26% of the normal body-weight.

SUMMARY

1. The heat production/sq.m. of body surface/kg. body-weight and the heat production/kg. active tissue have been calculated for a series of eleven individuals who had suffered considerable weight loss as the result of long-continued undernourishment.

2. The normal heat production of these individuals was calculated from normal standards with a deduction of 5% for the effect of training in the use of the spirometer.

3. The fall in heat production/sq.m. body surface in the starvation state proved to be related to a fall in the ratio of body-weight to body surface. For this reason this method of expressing basal metabolic rate gives no index of the rate of heat production (oxygen utilization) in the tissues.

4. The rate of heat production/kg. body-weight was not significantly different in the starvation state from the calculated normal rate so expressed.

5. An attempt was made to compare heat production/kg. active tissue in the two states. There was a suggestion that this method of expressing metabolic rate may be better than that based on gross body-weight but the data do not demonstrate unambiguously the validity of such a suggestion.

6. The change in the ratio of active material to the body-weight was greater than 5% only when the loss of body-weight exceeded 26% of normal weight.

7. The data obtained from the eleven subjects indicate that, under the observed conditions, the metabolic activity in the tissues did not deviate significantly from the normal.

We wish to thank Dr K. Mather for advising on the statistical analysis of our data. We are grateful to Dr Ancel Keys for permitting us to compare our data on thiocyanate volumes with those of his group prior to publication of his material, and for allowing us to make use of the unpublished work of his group of workers in our calculations of active material in the body-weight.

REFERENCES

- Beattie, J. & Herbert, P. H. (1947). *Brit. J. Nutrit.* **1**, 192.
 Benedict, F. G. (1938). *Publ. Carneg. Instn.* no. 503.
 Boothby, W. M. & Sandiford, I. (1929). *Amer. J. Physiol.* **80**, 290.
 Du Bois, D. & Du Bois, E. F. (1916). *Arch. intern. Med.* **17**, 863.
 Henschell, A., Mickelsen, O., Taylor, H. L. & Keys, A. (1947). *Amer. J. Physiol.* **150**, 170.
 Keys, A. (1947). Personal communication.
 Lusk, G. (1921). *Physiol. Rev.* **1**, 523.
 Rubner, M. (1883). *Z. Biol.* **19**, 535.
 Rubner, M. (1894). *Z. Biol.* **30**, 73.