Severe undernutrition in growing and adult animals

5.* Metabolic rate and body temperature in the pig

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An association between undernutrition and cold must have existed in men's minds for centuries (Petronius, *c.* A.D. 60). Keys, Brožek, Henschel, Mickelsen & Taylor (1950) mentioned this association in one of their subjects and gave a short list of famine observers by whom cold skins and subnormal body temperatures had been recorded, but there are many more. Clinical records, for example, go back to that of Guislain (1836) and Lebrun (1865). Subnormal body temperatures were observed during the potato famine in Belgium and recorded by Mareska (1849–50), as part of his impressive description of its effects on the population. The association was frequently detected in Austria, Germany and Poland during the First World War (Budzynski & Chelchowski, 1916; Schiff, 1917; Jansen, 1918; Schittenhelm & Schlecht, 1919; and see Keys *et al.* 1950), and again in the closed communities and concentration camps of the Second World War (Gounelle, Bachet, Sassier & Marche, 1941; Giraud, Bert & Desmonts, 1942; Nicaud, Rouault & Fuchs, 1942; Beaussart, Feuillet & Secques, 1943; Martin & Demole, 1943; Schwarz, 1945; Cardozo & Eggink, 1946; Justin-Besançon, 1946; Leyton, 1946). Trowell & Muwazi (1945) reported it in the disease called kwashiorkor as seen by them in Uganda.

There is little experimental work to set off against this rich background of observation. Morgulis, Diakow & Zuntz (1913) and Morgulis (1923*a*, *b*) recorded work of their own on dogs in which a profound loss of weight and subnormal body temperatures were produced and then maintained for weeks by prolonged undernutrition. They showed, moreover, that this situation could be reversed by restoring the animals to a normal diet. Lasarew (1897) studied the effect of starvation on some sixty guinea-pigs and showed that the body temperature was well maintained until the animals had lost 18–23 % of their original weight. By the time the loss of weight had reached 30 % body temperatures of 34° were usual, and a further rapid fall took place to 25° or even less on the last day of life. The classical and in many ways still the most stimulating work on this subject was that of Chossat (1843), who worked mostly on pigeons and doves, but also on some rabbits and guinea-pigs. He made, among others, two

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observations which are fundamental to the current issue: (1) Body temperatures began to fall towards the end and the fall became more and more rapid as death approached. (2) The birds could be revived from their coma and restored to activity by warming them. If they did not at this time have convulsions and were allowed to eat their fill they often survived and became normal. In the light of the work on human undernutrition in adults and newborn infants which has been done since 1942 (Gounelle, Marche, Bachet & Digo, 1942; Lhermitte & Sigwald, 1942; Bellier, 1943; Rosencher, 1946; Lohr, 1947; Mann & Elliot, 1957) and on newborn animals (Goodwin, 1957; McCance, 1959*a*, *b*) these convulsions were probably due to hypoglycaemia. A close connexion between the state of nutrition, food supply and body temperature of small passerine birds has often been demonstrated (Kendeigh, 1945), and McCance & Widdowson (1959) showed that hypoglycaemia, depletion of glycogen stores and progressive hypothermia could all be brought on more quickly in starving newborn piglets by exposing them to a low ambient temperature and so raising their metabolic rate. Some important observations bearing upon these problems have been made in Yugoslavia. Giaja & Gelineo (1931), for example, showed that lowering the ambient temperature of rats raised their metabolic rate, but that the maximum production of heat (and therefore the greatest effort to preserve the body temperatures) only became apparent after the body temperature had itself begun to fall. Barić (1953), moreover, showed that over a limited range of external temperature the young rat aged 2–4 days behaved like a homoeotherm when it had been well fed but like a poikilotherm when it had been starved.

Since the experiments on themselves by Zuntz & Loewy (1918), carried out over a large number of years, and the work of others in the First World War, undernutrition has repeatedly been shown to lower the basal metabolic rate in man (Keys *et al.* 1950), but there are few simultaneous records of the body temperature, and it may be assumed that most of the observations were made when the subjects were comfortably warm in bed.

In an attempt to examine the relation between these variables the present investigation was designed to study the metabolic rates and body temperatures of small very undernourished pigs and their response to change in the ambient temperature.

METHODS

Eleven undernourished pigs from two litters, A and B, have been used, and their ages and weights at the time of test are given in Table 1. Some of them subsequently died, some were killed, and some were rehabilitated and allowed to grow.

The test animals were reared as described by McCance (1960) and their weight curves were similar to those given in Fig. 1 of the paper by Widdowson, Dickerson & McCance (1960). The food was adjusted to maintain the weights of the piglets as constant as possible, but they generally increased slowly as the months passed. The heavier animals to be tested, therefore, were those that had been undernourished for the longest periods, but even they weighed little more than 6 kg, whereas a pig normally fed would have weighed about 120 kg by the time it was a year old. On the morning of the experimental day they were given their morning and midday rations of food together, and they were then taken in a warmed box in a warm vehicle to the laboratory and brought back to their warmed cage at about 5 p.m.

Table 1. *Ages and weights of the eleven undernourished pigs used in these experiments*

Litter	Pig no.	Age (days)	Weight (kg)
A	1	42	4·30
		103	4·47
		222	5·77
	2	42	4·40
		103	4·83
	3	49	4·60
		104	5·30
		222	5·52
	4	49	3·33
		104	4·12
	5	42	4·15
		105	4·98
	6	49	4·00
		105	4·71
		223	5·78
B	1	369	5·87
	2	362	6·15
	3	272	5·90
	4	285	5·35
		334	5·82
		370	6·26
	5	291	5·55

The controls were animals of approximately the same weight. One group was reared on the sow in an open unheated pigsty with an infrared lamp in one corner. Another group was weaned at the age of about 1 week and reared on a mash made from Amvilac no. 1 (Glaxo Laboratories Ltd) in a thermostatically controlled cage similar in location, size and temperature setting to the one housing the undernourished animals. The oxygen consumption and body temperatures of the control pigs were measured at ages ranging from 11 to 36 days (see Table 2).

On arrival at the laboratory each animal was weighed and introduced into the metabolic chamber after its body temperature had been recorded. The chamber of this metabolism apparatus was large enough to allow the pig to turn round and adopt any position without restraint; no food or water was placed in it. The measurements of oxygen consumption were carried out mainly at two ambient temperatures, one near 30° and the other near 11°, but some tests have been made at intermediate temperatures. Measurements were not made until equilibrium had been attained. The total length of time for which the pig was in the metabolism chamber at any given temperature was at least 1 h, of which the last 30 min were used for the measurements. The oxygen consumption was calculated as ml of dry gas at s.t.p. per kg min.

Rectal and skin temperatures were measured by copper–constantan thermocouples; for rectal temperature the thermojunction was introduced 3·5–5 cm inside the rectum, and for skin temperatures thermojunctions were stuck on to the skin by rubber solution under a patch of thin rubber dam about 1 cm square. Records were always made from three sites—the back of the head and the upper and ventral surfaces of the body. The figures given in Table 5 are the means of a number of observations from all three of them. Oxygen consumption was measured from a spirometer in a closed-circuit system, similar to that used by Mount (1959) for newborn pigs.

RESULTS

Little trouble was experienced in getting records of oxygen consumption of piglets in a resting state, for once the metabolic chamber had been made dark by putting on the cover the animals sat or lay perfectly quiet.

Table 2 gives the mean weights and oxygen consumption of the undernourished and control animals at ambient temperatures close to 11° and 30°. For this purpose

Table 2. *Mean values and ranges of body-weight and oxygen consumption at ambient temperatures close to 11° and 30°, of undernourished and normal piglets of the same weight*

Type of animal	Body-weight (kg)		No. of obser-vations	Ambient temperature (° C)		Oxygen consumption (ml/kg min)	
	Mean	Range		Mean	Range	Mean	Range
Sow-reared controls	4·78	3·24–6·15	11	11·8	10·8–14·4	20·1	15·7–28·3
			18	30·2	30·0–31·5	12·0	9·0–16·2
Weaned controls	5·09	3·53–6·27	16	12·1	10·4–15·8	15·5	11·8–20·1
			16	30·4	30·0–31·0	10·9	8·9–14·4
Undernourished, 1 month	4·13	3·33–4·60	6	11·8	10·6–12·7	14·6	11·4–17·8
			6	30·1	30·0–30·2	5·8	5·1–7·2
Undernourished, 3 months	4·74	4·12–5·30	6	11·6	11·0–12·1	13·7	10·8–17·5
			6	30·1	29·9–30·3	6·8	4·6–8·7
Undernourished, 7 months	5·69	5·52–5·78	3	10·6	10·2–10·9	13·8	11·4–15·3
			3	30·2	30·0–30·4	7·4	5·3–9·1
Undernourished, 12 months	5·84	5·35–6·26	4	11·1	9·5–12·8	11·0	5·4–13·4
			7	30·2	29·9–30·9	9·3	9·1–15·1

The undernourished animals are grouped according to their approximate ages; the ages of the control animals were between 11 and 36 days.

the undernourished animals were grouped according to their age, and therefore the duration of their undernutrition. The two lots of normal animals can be seen to have had similar oxygen consumptions at ambient temperatures near 30°, however they had been reared, but round about 11° the weaned controls reared on Amvilac at 24° had oxygen consumptions around 16 ml/kg min and these values were significantly lower than those of the other controls ($P = 0{\cdot}0025$). It was probably due to the warm and stable environmental temperature at which the piglets had been reared, for the piglets with the sow in the open sty had been exposed to fluctuations of temperature which enhance the response of many animals to a fall of ambient temperature (Hart, 1958). Since, therefore, all the undernourished animals were reared at 24°, the normal animals so reared have been taken to be the best controls. At the lower ambient temperatures the oxygen consumptions of the undernourished animals were lower, but not much lower, than those of these controls. A normal pig of the same age as the older undernourished ones, i.e. 9–12 months old, would have had an oxygen uptake of about 3·5 ml/kg min at these environmental temperatures (Brody, 1945) so that the undernourished animals, in spite of their undernutrition, had oxygen uptakes in keeping with their size rather than their age.

Table 3. *Mean oxygen uptakes with their standard errors of undernourished and normal piglets adjusted to a body-weight of 5 kg and ambient temperatures of 11° and 30°*

(The number of observations is given in parentheses)

Type of animal	Oxygen consumption (ml/kg min) at ambient temperature: 11°	30°
Sow-reared controls	20·72 ± 1·41 (11)	11·85 ± 0·35 (18)
Weaned controls	15·91 ± 0·58 (16)	11·47 ± 0·35 (16)
Undernourished, 1 month	14·33 ± 1·14 (6)	5·47 ± 0·23 (6)
Undernourished, 3 months	13·70 ± 0·84 (6)	6·65 ± 0·58 (6)
Undernourished, 7 months	14·17 ± 1·39 (3)	7·67 ± 1·17 (3)
Undernourished, 12 months	11·93 ± 1·38 (4)	10·24 ± 1·19 (7)

Table 3 shows the oxygen consumptions given in Table 2 after adjustment to a body-weight of 5 kg and ambient temperatures of 11° and 30° to facilitate direct comparisons of normal and undernourished animals. These adjustments were made as follows. (*a*) The rate of oxygen consumption for these pigs was assumed to be proportional to $(\text{body-weight})^{0\cdot7}$. The value of 0·7 for the exponent was chosen as being an approximately central value derived from the figures of Brody (1945), Kleiber (1947) and Mount & Rowell (1960). (*b*) The critical temperature for normal pigs in the weight range 4–6 kg has been found to be 27° (Mount, 1960). (The critical temperature is the lower limit of the range of thermal neutrality, where this extends over several degrees; thermal neutrality is the ambient temperature at which the animal's heat production is at its lowest.) On the assumption that the critical temperature would be the same for an undernourished pig of the same weight, the results for all the pigs at the lower temperature were adjusted to 11°, a negative linear relationship between metabolic rate and ambient temperature being assumed. Even if the critical temperature were as high as 30° in the undernourished animals, as suggested later, any change so produced in the coefficient would not affect the validity of the results or the conclusions based on them. The values observed near 30° were assumed to be close enough to those obtainable within the zone of thermal neutrality to require no adjustment.

At 30° the oxygen consumptions of the animals undernourished for 1 month were significantly lower than those of the weaned controls ($P < 0\cdot001$) or than those of the undernourished animals at 11° ($P < 0\cdot001$). The results indicate that undernutrition led to an early and considerable fall in the metabolic rate at 30°, but that as the months went by it was succeeded by a gradual rise. At 11° ambient temperature the oxygen consumptions of the animals in the early stages of undernutrition were nearly the same as those of the controls, but they became steadily lower and after 12 months of age were significantly lower than those of the controls ($P = 0{\cdot}01$) and not any longer were they significantly higher than those of the undernourished animals at 30° ($P > 0{\cdot}15$). These observations clearly corroborate and extend the findings of low basal metabolic rates in man made at less well-defined ambient temperatures.

Table 4. *Mean rectal temperatures with their standard errors of undernourished and normal piglets at the beginning and the changes in them during the measurements of oxygen consumption at 11°*

(The number of observations is given in parentheses)

Type of animal	Initial rectal temperature (° C)	Change in rectal temperature during approximately 1 h (° C)
Sow-reared controls	39·67 ± 0·09 (21)	−0·36 ± 0·13 (21)
Weaned controls	39·49 ± 0·11 (18)	−0·26 ± 0·08 (18)
Undernourished, 1 month	36·32 ± 0·71 (6)	+0·82 ± 0·55 (6)
Undernourished, 3 months	34·42 ± 0·75 (6)	+0·22 ± 0·68 (6)
Undernourished, 7 months	34·63 ± 0·86 (3)	−1·83 ± 1·08 (3)
Undernourished, 12 months	35·03 ± 0·43 (6)	−1·03 ± 0·54 (6)

Table 5. *Relation between rectal temperature and skin temperature of undernourished and normal piglets*

(Time of day 11 a.m.; weight of pigs 5·90–7·08 kg; ambient temperature 24°)

Type of animal	Rectal temperature (° C)	Skin temperature (° C)	Difference (° C)	'Thermal insulation'* Rectum–skin	Skin–air	Rectum–air
Undernourished						
1	35·3	33·0	2·3	—	—	—
2	37·0	33·8	3·2	—	—	—
3	36·1	33·6	2·5	—	—	—
Mean	36·1	33·5	2·6	0·06	0·21	0·27
Normal						
1	39·5	35·7	3·8	—	—	—
2	38·3	33·6	4·7	—	—	—
Mean	38·9	34·6	4·3	0·06	0·16	0·22

* Estimated mean oxygen consumption of the undernourished pigs was 53 ml/min, and of the normal pigs 80 ml/min. 'Thermal insulation' was calculated by dividing the appropriate temperature gradient in ° C by 85 % of the estimated oxygen consumption in ml/min at 24° ambient temperature (see page 515).

Table 4 gives the initial rectal temperatures and their changes during the measurement of oxygen consumption at 11°. The outstanding feature was the temperature of the undernourished animals. The differences between each group and the weaned controls were all highly significant ($P < 0{\cdot}001$), in complete agreement with the findings recorded in the literature. There was no significant difference between the two lots of normal animals ($P = 0\cdot1$), and the duration of undernutrition seemed to make little difference to the resting body temperature. Exposure for these limited periods to 11° led to a small rise in the rectal temperature of animals undernourished for only 1 month. The change was significantly different from the small fall found in the weaned controls ($P = 0\cdot05$) and also from the fall in body temperature recorded after 12 months' undernutrition.

Table 5 gives the relation between the rectal and skin temperatures of some of the piglets undernourished for 7 months. The 'controls' had been reared at the same ambient temperature but their reactions and temperatures differed little from those of other normal animals reared in rather different surroundings. The skin temperatures of the undernourished animals were nearer those of the controls than the rectal temperatures were. It was not easy to get good records of the oxygen consumptions while the skin temperatures were being taken because the pigs were a little disturbed by the wires required for taking them. An estimate of their mean oxygen uptakes, therefore, was made by a procedure similar to that used in the calculation of values in

Table 6. *Concentrations (mg/100 ml) of glucose in the serum of undernourished and normal piglets 2 and 9 h after food*

(Ambient temperature 24°)

Type of animal	2 h after food	9 h after food
Undernourished		
1	81	61
2	82	69
3	86	51
Mean	83	60
Normal		
1	115	106
2	109	81
Mean	112	93

Table 3, and thermal-insulation indices were calculated. The insulation between the rectum and the skin was defined as the rectal temperature minus the skin temperature divided by the oxygen consumption in ml/min after thermal equilibrium had been attained minus the evaporative heat loss. The insulation between the rectum and the air and the skin and the air was also calculated from the rectum–air and skin–air temperature differences. In making these calculations the evaporative heat loss was taken to be 15% of the whole. The chief feature is the similarity of the two groups of animals with, however, a rather higher resistance to the passage of heat from the skin to the air in the undernourished pigs, which may be explained by the fact that they had more hair. The insulations between rectum and skin and between skin and air behave as resistances in series, and when added give the rectum–air insulation.

Table 6 shows the concentration of glucose found in the serum of the undernourished and normal animals whose skin and rectal temperatures are shown in Table 5. The undernourished animals always had slightly lower concentrations of reducing substances but they were never dangerously low, as they have been reported to be clinically in man and as they might have been in these animals at lower ambient temperatures or in newborn piglets (Goodwin, 1957; McCance & Widdowson, 1959) after 9 h without food.

DISCUSSION

There are certain features about these experiments which can be discussed without reference to much other work. The undernourished pigs, whatever their age, lived in thermal equilibrium at 24°. At an ambient temperature of 11° they had a metabolic rate in rough correspondence to their size, not to their age, and not very different from the rate of the controls of the same size, although it showed signs of falling as the months of undernutrition passed. In the earlier stages of undernutrition, and while the animals were still not much older than the controls, they had lower metabolic rates at 30° and their response to a fall in the ambient temperature was greater. These findings recall those of Graham, Wainman, Blaxter & Armstrong (1958–9), who found that a low plane of nutrition lowered the minimal oxygen consumption and raised the critical temperature of adult clipped sheep.

Another matter to which attention must be drawn is the subnormal deep body temperature of the undernourished animals. A normal pig weighing 6 kg with a central temperature of 35° and at an ambient temperature of 24° would have been shivering violently and would have had such an intense production of heat that his core temperature would have risen until it reached a normal level. Evidently the undernourished animals did not respond with normal intensity to the stimuli reaching their peripheral sense organs and to their low central temperatures. It was only when the skin temperature had fallen below the normal level, and the central temperature also, that the heat production of the animals was sufficient to maintain them in thermal equilibrium at 24°, and to provide nearly as much heat as the controls for at least 30 min at 11° ambient temperature. Judging by the body temperatures and metabolic rates recorded in human undernutrition, there is probably an equally weak response in this species to the normally, and usually, adequate external and internal thermogenic stimuli.

If these facts are now thought of in connexion with the wider problems of thermal control at younger ages and various planes of nutrition, it is evident that the undernourished animals behaved like newborn animals in many ways—although not necessarily for the same reasons. The findings in newborn animals have been reviewed by McCance (1959*a*, *b*) and may be summarized in the following way. In the first place the newborn animal, whether it be pig or lamb or man, does not attain thermal balance till its heat production has been stimulated by a fall in skin temperature and core temperature below that of the adult. They are therefore relatively unresponsive to the stimuli to which more mature animals of the same size would respond. The same is true of their response to other stimuli, a change in their serum sodium for example, or pH, and this lack of response is often referred to as their superior tolerance of such a change. Secondly, the response of the newborn animal to a fall in its ambient temperature is very much a matter of its nutritional state. Barić (1953), for example, showed that the young rat made virtually no response to a fall in the ambient temperature unless it had been well fed for the previous 24 h. Our piglets made a very poor and certainly quite inadequate response when they were a year old, and at all stages of undernutrition the response would certainly have fallen off if the exposure had been prolonged. Newborn pigs and babies behave like that and die in a state of hypothermia and hypoglycaemia (Goodwin, 1957; Mann & Elliott, 1957; Bower, Jones & Weeks, 1960), while there is still some glycogen left in the muscles and livers. The undernourished piglets had not reached this stage after 9 h at an ambient temperature of 24° without food, but they probably would have done at one of 11° (McCance & Widdowson, 1959). In order to link up these observations it would be very desirable to know why the response of a newborn animal and an undernourished animal to ambient temperatures below the critical range is so poor and only becomes sufficient to maintain thermal balance when it has been raised to the required level by a fall in the skin and deep body temperatures.

SUMMARY

1. Young pigs were kept at weights of about 6 kg for 12 months by undernutrition from early in lactation.

2. They maintained thermal equilibrium at an ambient temperature of 24°. They produced less heat in this environment and their deep body temperatures and skin temperatures were lower than those of normal animals of the same size. Their thermal insulation was about the same.

3. In the earlier stages of undernutrition they produced much less heat than normal animals at 30°, but increased their production of heat considerably with a fall in the ambient temperature to 11°.

4. After a year their heat production was nearer that of the controls at 30°, and their response to a fall in the ambient temperature was weak.

5. Their blood-sugar concentrations were lower than those of the normal animals.

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REFERENCES

Barić, I. (1953). *Bull. Acad. serbe Sci. math. nat.* **12**, 77.
Beaussart, P., Feuillet, C. & Secques, J. (1943). *Pr. méd.* **51**, 110.
Bellier, L. (1943). Les hypoglycémies de famine. Thesis, Faculty of Medicine and Pharmacology, University of Lyons.
Blaxter, K. L., Graham, N. McC., Wainman, F. W. & Armstrong, D. G. (1958–9). *J. agric. Sci.* **52**, 25.
Bower, B. D., Jones, L. F. & Weeks, M. M. (1960). *Brit. med. J.* i, 303.
Brody, S. (1945). *Bioenergetics and Growth*, p. 456. New York: Reinhold Publishing Corp.
Budzynski, B. & Chelchowski, K. (1916). *J. trop. Med. (Hyg.)*, **19**, 141.
Cardozo, E. L. & Eggink, P. (1946). *Canad. med. Ass. J.* **54**, 145.
Chossat, C. (1843). *Mém. prés. Acad. Sci., Paris (Sci. Math. et Phys.)*, **8**, 438.
Giaja, J. & Gelineo, S. (1931). *Ann. Physiol. Physicochim. biol.* **7**, 152.
Giraud, G., Bert, J. M. & Desmonts, T. (1942). *Montpellier méd.* ser. 3, **21–22**, 278.
Goodwin, R. F. W. (1957). *J. Physiol.* **136**, 208.
Gounelle, H., Bachet, M., Sassier, R. & Marche, J. (1941). *Bull. Soc. méd. Hôp. Paris.* ser 3, **57**, 635.
Gounelle, H., Marche, J., Bachet, M. & Digo, R. (1942). *Bull. Acad. Méd., Paris*, ser. 3, **126**, 459.

Graham, N. McC., Wainman, F. W., Blaxter, K. L. & Armstrong, D. G. (1958–9). *J. agric. Sci.* **52**, 13.
Guislain, J. (1836). *Gaz. Méd.* **4**, 33.
Hart, J. S. (1958). *Fed. Proc.* **17**, 1045.
Jansen, W. H. (1918). *Münch. med. Wschr.* **65**, 10.
Justin-Besançon, L. (1946). *Précis de Pathologie Médicale*, vol. 6, p. 845. Paris: Masson et Cie.
Kendeigh, S. C. (1945). *J. Wildlife Mgmt*, **9**, 217.
Keys, A., Brožek, J., Henschel, A., Mickelsen, O. & Taylor, H. L. (1950). *The Biology of Human Starvation.* Minneapolis: University of Minnesota Press.
Kleiber, M. (1947). *Physiol. Rev.* **27**, 511.
Lasarew, N. (1897). *Russk. Arkh. Pat.* **3**, 399.
Lebrun, A. F. (1865). Quelques considérations sur la misère dans ses rapports avec la médecine. Thesis. Paris: Lesueur, Baillehache et Cie.
Leyton, G. B. (1946). *Lancet*, **251**, 73.
Lhermitte, J. & Sigwald, J. (1942). *Bull. Acad. Méd., Paris*, ser. 3, **126**, 384.
Lohr, H. (1947). *Brit. med. J.* i, 540.
McCance, R. A. (1959*a*). *Arch. Dis. Childh.* **34**, 361.
McCance, R. A. (1959*b*). *Arch. Dis. Childh.* **34**, 459.
McCance, R. A. (1960). *Brit. J. Nutr.* **14**, 59.
McCance, R. A. & Widdowson, E. M. (1959). *J. Physiol.* **147**, 124.
Mann, T. P. & Elliott, R. I. K. (1957). *Lancet*, **272**, 229.
Martin, E. & Demole, M. (1943). *Gastroenterologia, Basel*, **68**, 169.
Mareska, J. (1849–50). *Bull. Acad. Méd. Belg.* ser. 1, **9**, 513.
Morgulis, S. (1923*a*). *Fasting and Undernutrition.* New York: Dutton and Co.
Morgulis, S. (1923*b*). *Hunger und Unterernährung: eine Biologische und Soziologische Studie.* Berlin: J. Springer.
Morgulis, S., Diakow, M. & Zuntz, N. (1913). *Biochem. Z.* **55**, 341.
Mount, L. E. (1959). *J. Physiol.* **147**, 333.
Mount, L. E. (1960). *J. agric. Sci.* **55**, 101.
Mount, L. E. & Rowell, J. G. (1960). *Nature, Lond.*, **186**, 1054.
Nicaud, P., Rouault, M. & Fuchs, H. (1942). *Bull. Soc. méd. Hôp. Paris*, **58**, 307.
Petronius, G. (*c.* A.D. 60). *Satyricon*, sect. 41, Loeb text and translation (1922). London: Heinemann.
Rosencher, H. (1946). *Brit. med. J.* ii, 953.
Schiff, A. (1917). *Wien. med. Wschr.* **67**, 2133.
Schittenhelm, A. & Schlecht, H. (1919). *Z. ges. exp. Med.* **9**, 1.
Schwarz, O. (1945). *Schweiz. med. Wschr.* **75**, 1136.
Trowell, H. C. & Muwazi, E. M. K. (1945). *Trans. R. Soc. trop. Med. Hyg.* **39**, 229.
Widdowson, E. M., Dickerson, J. W. T. & McCance, R. A. (1960). *Brit. J. Nutr.* **14**, 457.
Zuntz, N. & Loewy, A. (1918). *Biochem. Z.* **90**, 244.

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