MATTERS ARISING

Brown adipose tissue and diet-induced thermogenesis

IT has been proposed[1,2] that 'diet-induced thermogenesis' in brown adipose tissue enables animals to dissipate excessive intake of energy and so avoid obesity. The hypothesis is claimed to justify the view that thermogenesis is more important in regulation of energy balance than control of food intake[3], and the report by Rothwell and Stock[1] has been presented by the media (a BBC Television programme *Horizon*, 10 December 1979) as embodying an important discovery in relation to human obesity. We consider their data and arguments inadequate to support the hypothesis for the following reasons:

(1) The first paper hinges on an experiment in which one group of six rats was induced to overfeed by 'cafeteria feeding' (that is, providing a variety of tasty foods)[4,5] for 3 weeks, with a second group as controls. The amount of energy the cafeteria-fed rats stored as fat was much less than the increase in their intake of energy—this discrepancy supposedly demonstrated thermogenesis. We consider that it is hazardous to infer energy expenditure in this way (see Table 1 of ref. 1), particularly where it is the quantity of primary interest. (The paper includes in Table 2 some sample measurements of oxygen consumption as 'confirmation of lowered efficiency', but energy expenditure is too variable for short measurements to be useful in balance experiments, and the adjustment of the data for body weight complicates interpretation.) Accurate measurements of energy intake, expenditure and storage over a balance period are laborious and technically exacting; any systematic errors, however, cumulate in balance experiments, thus unless all three components of energy balance are measured there is no check on accuracy.

(2) Metabolizable energy intake (that is, the energy in food supplied minus the losses due to scattering and in excreta) cannot be reliably predicted from food composition tables or prior measurements: bomb calorimetry of the actual materials is essential. This must apply particularly to cafeteria feeding, where a variety of proprietary foods of high energy density are offered.

(3) Energy storage was determined by subtracting initial from final carcass energy values, determined by *post mortem* analysis; the method and its precision are not stated. The initial values were obtained from a group of six rats, killed at the start; their body composition was stated to be identical with that of the two groups used in the experiment, on the basis of *in vivo* tritium dilution measurements. We believe that estimation of body fat by *in vivo* body water measurement is inevitably inaccurate, and that this view is confirmed by Rothwell and Stock's data[6] on the tritium method.

(4) Rothwell and Stock[7-9] previously reported that cafeteria-fed rats showed similar resting oxygen consumption to controls and rapid increase of weight; that is, there was no evidence of thermogenesis (though it was reported to occur briefly after cafeteria feeding had ended). There are two possible explanations, other than experimental error, for these contrasting results. Rothwell and Stock[1,10] state that rats obtained from two suppliers, although of the same strain, differed in their capacity for thermogenesis and propensity to obesity. The only difference quoted in absolute terms was that energy expenditures during cafeteria feeding were 390 and 340 kJ per day. This difference, though statistically significant, is not large, and might be within the margin of error. If it is real, the selection of rats from one source rather than the other as the basis for a general theory would seem to require justification.

(5) We believe the age of the rats may provide the explanation. In Rothwell and Stock's earlier work[7-9] female rats weighed ~300 g and males 400 g and controls gained weight at 0.5–1.0 g per day, values typical of adult rats. The rats used in the later experiment[1] were described as 'adult' but their age was not stated; the control group were gaining weight at 5 g per day which is a rate typical of young, actively growing rats. Elsewhere Rothwell and Stock[2,10] describe as 'adult' rats which were 6 weeks, 10 weeks and 75 days old. Growth is costly of energy and its rate is sensitive to the supply of energy; thus it is well known that young, actively growing animals do not acquire fat readily. We believe a discrepancy between increased energy intake and fat storage, seen in young rats but not in adults, is more likely to reflect the young animals' capacity to use energy for growth than to demonstrate a new mechanism for energy dissipation. If the young animals' capacity for growth were to be regarded as a regulatory mechanism for energy balance, it would have to be made clear that it is not one available to adults. In adults, deposition of fat, although a relatively efficient process, entails dissipation as heat of about a third as much energy as is stored[11-13]; any discrepancy found in adults between excess intake and storage would have to be shown to exceed this before any possibility of a new mechanism arose.

(6) Since the work of Dawkins, Hull and others in the 1960s[15,21] it has been accepted that brown fat, controlled by noradrenergic sympathetic nerves, is an important heat-producing organ in the regulation of body temperature in infant animals of many species. Existing evidence indicates that the amount of brown fat in the body, and the heat produced in response to noradrenaline, decline with age[14-17]. The suggestion that, in animals possessing it, brown fat might be activated in response to overfeeding is an interesting one, although in young animals such a response would be expected to be antagonistic to growth. Miller and Payne[18] and Gurr *et al.*[19] have reported that diet-induced thermogenesis is conspicuous in young pigs; the pig is thought to possess no brown fat[20]. In our view, however, better evidence is required that diet-induced thermogenesis exists at all, before the question of its mechanism is worth pursuing. Extension of the suggestion to humans, and to adults, (and so relevance to human obesity) would seem doubly doubtful. The pair of IR thermograms[1] presented are certainly not adequate evidence: the effect seen after administration of ephedrine could as readily be ascribed to circulatory changes (G. A. Brown, RAF Institute of Aviation Medicine, personal communication).

Rothwell and Stock's hypothesis may still prove correct. Our point is that a novel theory which reverses previously accepted views needs substantial supportive evidence that can stand up to critical evaluation. We do not think such evidence has yet been presented.

G. R. HERVEY
G. TOBIN

Department of Physiology,
University of Leeds, Leeds LS2 9JT, UK

1. Rothwell, N. J. & Stock, M. J. *Nature* **281,** 31–35 (1979).
2. Brooks, S. L., Rothwell, N. J., Stock, M. J., Goodbody, A. E. & Trayhurn, P. *Nature* **286,** 274–276 (1980).
3. Perkins, M. N., Rothwell, N. J., Stock, M. J. & Stone, T. W. *J. Physiol.* (in the press).
4. Sclafani, A. & Springer, D. *Physiol. Behav.* **17,** 461–471 (1976).
5. Rolls, B. J. & Rowe, E. A. *J. Physiol.* **272,** 2P (1977).
6. Rothwell, N. J. & Stock, M. J. *Br. J. Nutr.* **41,** 625–628 (1979).
7. Rothwell, N. J. & Stock, M. J. *J. Physiol.* **291,** 59P (1979).
8. Stock, M. J. & Rothwell, N. J. in *Animal Models of Obesity* (ed. Festing, M. F. W.) 141–151 (Macmillan, London, 1979).
9. Rothwell, N. J. & Stock, M. J. *J. comp. physiol. Psychol.* **93,** 1024–1034 (1979).
10. Rothwell, N. J. & Stock, M. J. *Proc. nutr. Soc.* **39,** 20A (1980).
11. Blaxter, K. L. in *Obesity in Perspective* (ed. Bray, G. A.) 127–135 (DHEW Pub. No. (NIH) 75–708, 1975).
12. Pullar, J. D. & Webster, A. J. F. *Br. J. Nutr.* **37,** 355–363 (1977).
13. van Es, A. J. H. *Nutr. Metab.* **21,** 88–104 (1977).
14. Alexander, G. *Int. Rev. Physiol.* **20,** 43–155 (1979).
15. Smith, R. E. & Horwitz, B. A. *Physiol. Rev.* **49,** 330–425 (1969).
16. Heaton, J. M. *J. Anat.* **112,** 35–39 (1972).
17. Himms-Hagen, J. *Pharmac. Rev.* **19,** 367–461 (1967).
18. Miller, D. S. & Payne, P. R. *J. Nutr.* **78,** 255–262 (1962).
19. Gurr, M. I., Mawson, R., Rothwell, N. J. & Stock, M. J. *J. Physiol.* **291,** 60P (1979).
20. LeBlanc, J. & Mount, L. E. *Nature* **217,** 77–78 (1968).
21. Dawes, G. S. *Foetal and Neonatal Physiology* Ch. 15 (Year Book, Chicago, 1968).

ROTHWELL AND STOCK REPLY—We shall deal with points (1), (2) and (3) above together. Estimation of energy expenditure by the carcass balance method (that is, intake minus storage) is an accepted

0028–0836/81/080699—02$01.00