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Famine and Refeeding: Adaptations in Energy Metabolism

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I. INTRODUCTION

Throughout history, man has been subjected to food shortages, hungry seasons, and famine, whether imposed by nature, misadventure, or fellow

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man. Under such circumstances, natural selection is a powerful force. It favors those who can survive high mortality famines, or those who can continue to reproduce under less severe conditions of chronic undernutrition.

One trait that aids survival is man's capacity to store a prodigious amount of energy as subcutaneous fat, and to accrue this store very rapidly when food is available. A sexual dimorphism in humans results in these fat stores being twice as large in women as in men when expressed as a percentage of body weight. It is these fat stores that are the target of anorexic patients' distorted body image and that provide the first link among anorexia, famine, and our evolutionary past.

A second survival trait is the ability to invoke metabolic, physiologic, and behavioral energy-sparing mechanisms that can prolong survival by reducing energy and substrate consumption. Undoubtedly, humans are capable of a variety of adaptations that significantly prolong survival when food intake is reduced or ceases completely.

The purpose of this chapter is to explore the similarities and differences between the adaptations in energy metabolism during famine and refeeding, and those in anorexia nervosa and bulimia. We shall attempt to define whether the changes occurring in patients with eating disorders are a simple recapitulation of survival mechanisms or whether they are associated with a distinct pathophysiology. Evidence will be drawn from our own studies of seasonal food shortages in Africa, from man-made famines during the two World Wars, and from experimental studies of semistarvation.

II. SEASONAL FOOD SHORTAGES

A. Background

For the past 15 years, our laboratory has been conducting nutritional studies among subsistence farming communities in a group of rural villages in The Gambia, West Africa. Owing to the poor rainfall in this sub-Sahelian region, the villagers can rarely grow sufficient staple foods to last a year. Each year, they suffer a "hungry" period when the previous year's stocks run low prior to the annual harvest (Prentice *et al.*, 1981), and they often have to rely on assistance from international food aid organizations. The effects of the food shortages on energy balance are exacerbated by the fact that they coincide with the period when adults have to increase their energy expenditure in agricultural tasks.

Figure 1 illustrates the consequences of this annual energy deficit on the body weight of women. At the height of the Sahelian drought in the late 1970s, body weight fluctuated by about 6 kg in an average woman. Serial

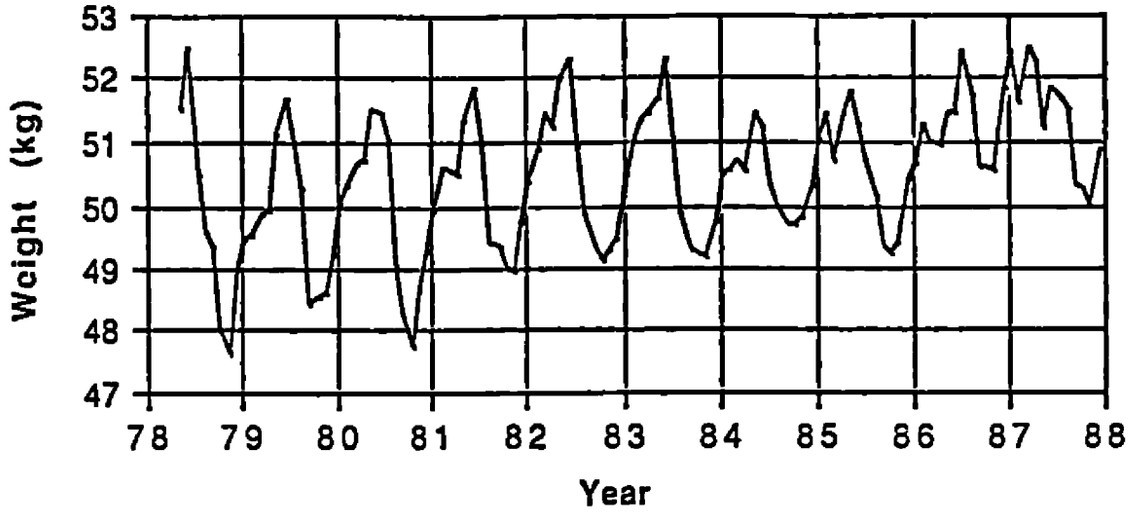

Fig. 1. Seasonal fluctuations in body weight in child-bearing Gambian women. Plot derived from over 20,000 measurements in pregnant, lactating, and nonpregnant, nonlactating women, and corrected for the effects of pregnancy and lactation by multiple regression analysis.

measurements of body composition using deuterium dilution revealed that lean body mass (LBM) shows no significant fluctuation (Lawrence *et al.*, 1987). Therefore, the weight changes are largely fat and represent a swing of over 50% of adipose stores in an average woman.

B. Alterations in Basal Metabolism

Detailed longitudinal studies of basal metabolic rate (BMR) in 50 pregnant and lactating women from these villages were performed by Lawrence *et al.* (1986) and subjected to within-subject multiple regression analysis to determine the effect of season on maintenance energy requirements. As anticipated, the hungry season was associated with a significant reduction in absolute BMR ($p < .01$) and in BMR per kilogram ($p < .05$), but the effect was modest with a peak-to-trough difference of only 260 kJ/day. Other studies of seasonal food shortages support this conclusion that any energy-sparing adaptations that do occur are rather small (Ferro-Luzzi *et al.*, 1988).

C. Alterations in Voluntary Physical Activity

As mentioned above, the changes in physical activity in rural Gambia are dominated by the farming calendar, and total energy expenditure is substantially increased during the period when food is short. This activity pattern acts antagonistically to the changes in BMR and almost certainly runs counter to the natural physiologic urge to be less active in times of hunger (see Section III.C). The levels of activity at this time are remarkably

high by any standards, averaging about 10.5 MJ/day, or 2 x BMR (Singh *et al.*, 1989). Clearly, the imperative of having to work hard to provide food for the future overrides immediate protective adaptations.

In theory, the Gambian villagers provide an attractive model to investigate parallels between natural hunger and anorexia nervosa because energy expenditure is raised at the time of food restriction (as often occurs in anorexics), and because we have data on women, whereas most of the subsequent data in this paper pertain to men. However, although these seasonal food shortages provide a classic example of famine and refeeding, and although they may have played an important role in shaping womens' physiologic defense mechanisms, the degree of weight loss does not approach that seen in anorexia, and in practice, few parallels can be drawn between the two conditions.

III. FAMINES

A. Background

In reviewing the literature on starvation, Keys *et al.* (1950) provided a chronology of over 450 major famines recorded in world literature and historical records. They warned that their list was far from complete since most documentation is confined to the British Isles, Northwestern Europe, and the Mediterranean basin, and regional famines continue to this day as a result of crop failures and international conflict. At first sight, this terrible abundance of famines might be thought to provide a substantial data base with which to contrast the effects of anorexia and bulimia. The reality is less helpful for a number of reasons. The most important reason is that it would be quite unethical to study the physiologic effects of starvation when the same effort and resources could be diverted toward the relief of that hunger. Thus, almost all metabolic measurements have been performed by physicians who were themselves caught up in famine during the World Wars, or by relief teams who studied the process of rehabilitation.

B. Alterations in Basal Metabolism

Table I summarizes much of the reliable published information on the changes in basal metabolism during wartime famine. Most of the studies compared the metabolic rate of their subjects against the Harris–Benedict standards (Harris and Benedict, 1919). This approach is satisfactory when the technical competence of the investigators is not in question, but a number of data sets have had to be rejected because they give patently im-

TABLE I

Published Data on Basal Metabolic Rate (BMR)

Circumstance	Source	BMR (% of predicted)
World War I diet	Jansen (1917)	77–83
World War I diet	Loewy and Zuntz (1916)	90
World War I diet	Zuntz and Loewy (1916)	84
World War II famine	Covaerts (1947)	77
WW II Warsaw famine	Fliederbaum *et al.* (1946)	60–70

plausible figures compared with those of Harris–Benedict (Keys *et al.*, 1950). A second problem with the data is that as a consequence of the circumstances under which it was collected, most of the studies have poor information regarding the degree or the composition of weight loss. With these shortcomings in mind, it is prudent to limit our conclusions to the following statements: Adaptations in BMR do occur; they appear to be largely coincident with changes in body weight; and they range from -10% to a minimum of about -40%.

C. Alterations in Physical Activity

Descriptions of famine are abundant in the literature. The following two quotations are fairly typical of the general impression given with regard to changes in physical activity. In an account of the London famine of 1837–1838 Howard (cited by Keys, *et al.*, 1950) stated, "The first indications of a deficiency of food are languor, exhaustion, and general debility." Charles M. Doughty used similar descriptors in his Travels in Arabia Desert (cited by Keys *et al.*, 1950): "I suffered their summer famine with the nomads. . . . languor of hunger, the desert disease, was in all the tents. The days passed by days in this weakness of famine." From both historical and contemporary accounts such as these, we can safely conclude that the natural tendency is to conserve energy during starvation by cutting down on all but a minimal level of essential activity.

IV. EXPERIMENTAL SEMISTARVATION

A. Background

The adaptive responses to starvation have fascinated physiologists for well over a century, and there is a surprisingly voluminous literature on the subject (Keys *et al.*, 1950). This ranges from studies of professional

fasters who denied themselves food for 30 days or more, to highly controlled interventions in groups of volunteer subjects. Of the latter, the best known are the Carnegie Nutrition Laboratory experiment of Benedict *et al.* (1919) and the Minnesota experiment of Keys *et al.* (1950). The target weight losses in these studies were 10% and 25%, respectively. In our Cambridge laboratory, we recently performed an underfeeding experiment that involved a modest level of restriction; average weight loss was 9% (Diaz *et al.*, 1991b). This study adds to the classic investigations by virtue of having serial whole-body calorimeter and doubly labeled water measurements of energy expenditure that allowed all components of the energy balance equation (basal metabolism, thermogenesis, and activity) to be measured. Information in this section is drawn primarily from the Keys and Diaz studies, for which brief methodological summaries follow.

The Keys semistarvation study enrolled 32 young male conscientious objectors into a protocol involving baseline assessments, 24 weeks of restricted food intake (1570 kcal/day), and 12 weeks of controlled rehabilitation. The subjects were divided into four subgroups, given different levels of intake prior to a final release onto an *ad libitum* diet of their own choosing. The subjects were investigated with a battery of physiologic and psychological tests throughout the protocol.

The underfeeding data from the Diaz study are from the second phase of a protocol that investigated adaptive responses to both positive and negative perturbations of energy balance (Diaz *et al.*, 1991a&b). Six lean and three obese men were studied using a 7-month protocol involving 3 weeks baseline; 6 weeks overfeeding at baseline plus 50%; 6–8 weeks free diet; 6 weeks underfeeding when subjects received an energy intake equivalent to BMR; and 6–8 weeks free diet. Regular measurements of body composition (by deuterium dilution, densitometry, and skinfolds) and of the components of daily energy expenditure (by whole-body calorimetry) were made throughout the protocol. Total free-living energy expenditure was assessed by the doubly labeled water method over the last 2 weeks of each phase of the study.

B. Alterations in Basal Metabolism and Thermogenesis

1. *The Minnesota Experiment*

Figure 2 illustrates the changes in body weight and composition measured at weeks 12 and 24 of semistarvation and expressed relative to baseline. The initial target of a 25% weight loss was achieved by the end of the restriction period. At this stage, muscle mass had declined by 40% and fat mass by 70%. As described in Section VI, the Minnesota experiment subjects' final body composition was very similar to that of anorexic males.

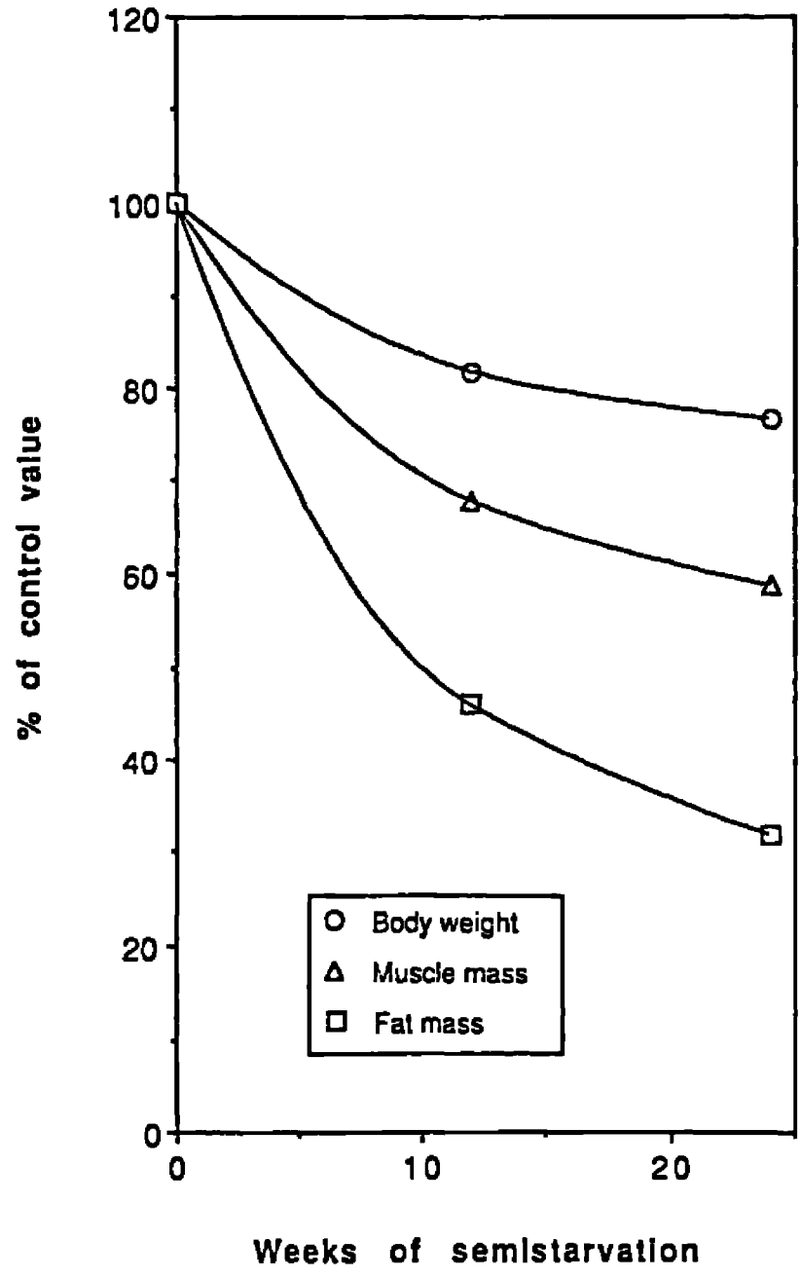

Fig. 2. Alterations in body composition during 24 weeks of semistarvation in the Minnesota experiment. (Adapted from Keys *et al.*, 1950.)

Figure 3 shows the changes in BMR. When expressed per man, BMR declined by 39.8% compared with baseline, and even when expressed per kilogram of body weight, there was a highly significant suppression. The data also indicate a significant (17%) suppression of BMR per kilogram of active tissue mass (not illustrated). These findings are compatible with numerous others in the literature, which show that metabolic rate is universally depressed in all but the mildest energy restriction, and that there are two components to the suppression: a loss of metabolically active tissue, and a decrease in the metabolic rate of the remaining active tissue.

An important issue with regard to anorexia is the question of how rapidly and how completely BMR can be expected to return to normal with the successful nutritional rehabilitation of a patient. Figure 4 illus-

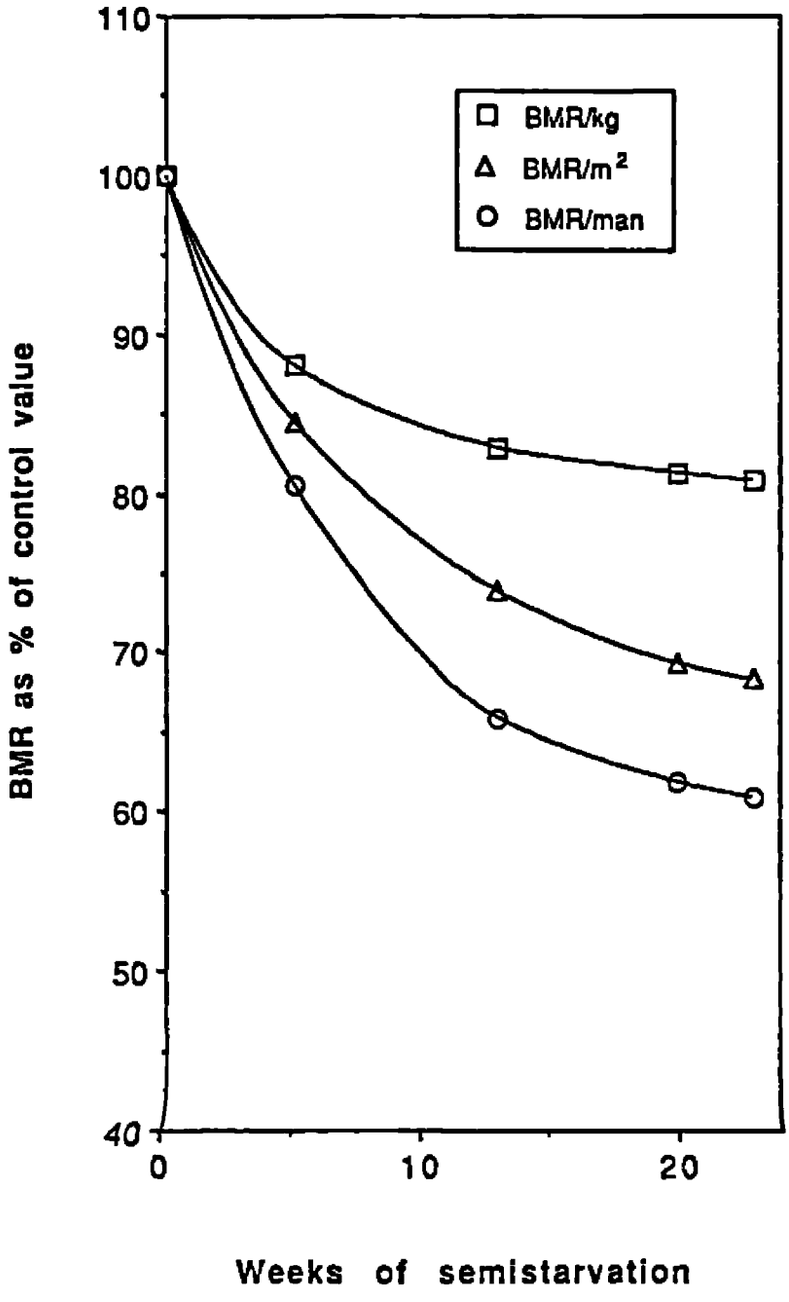

Fig. 3. Alterations in basal metabolic rate (BMR) during 24 weeks of semistarvation in the Minnesota experiment. (Adapted from Keys *et al.*, 1950.)

trates the recovery of BMR in the Minnesota experiment. It illustrates that BMR closely tracked body weight and, by the time of the final measurement, was very close to the original baseline in the fast rehabilitation group, and was slightly above baseline but returning toward it in the slow rehabilitation group. This apparent overshoot is probably an artifact caused by the very high food intakes of the subjects at the beginning of the *ad libitum* eating period. Under conditions of excessive intake, the classic definition of BMR as being measured 12 hr postabsorption may not leave an adequate interval for the complete disappearance of diet-induced thermogenesis. The Keys data therefore suggest that BMR will re-

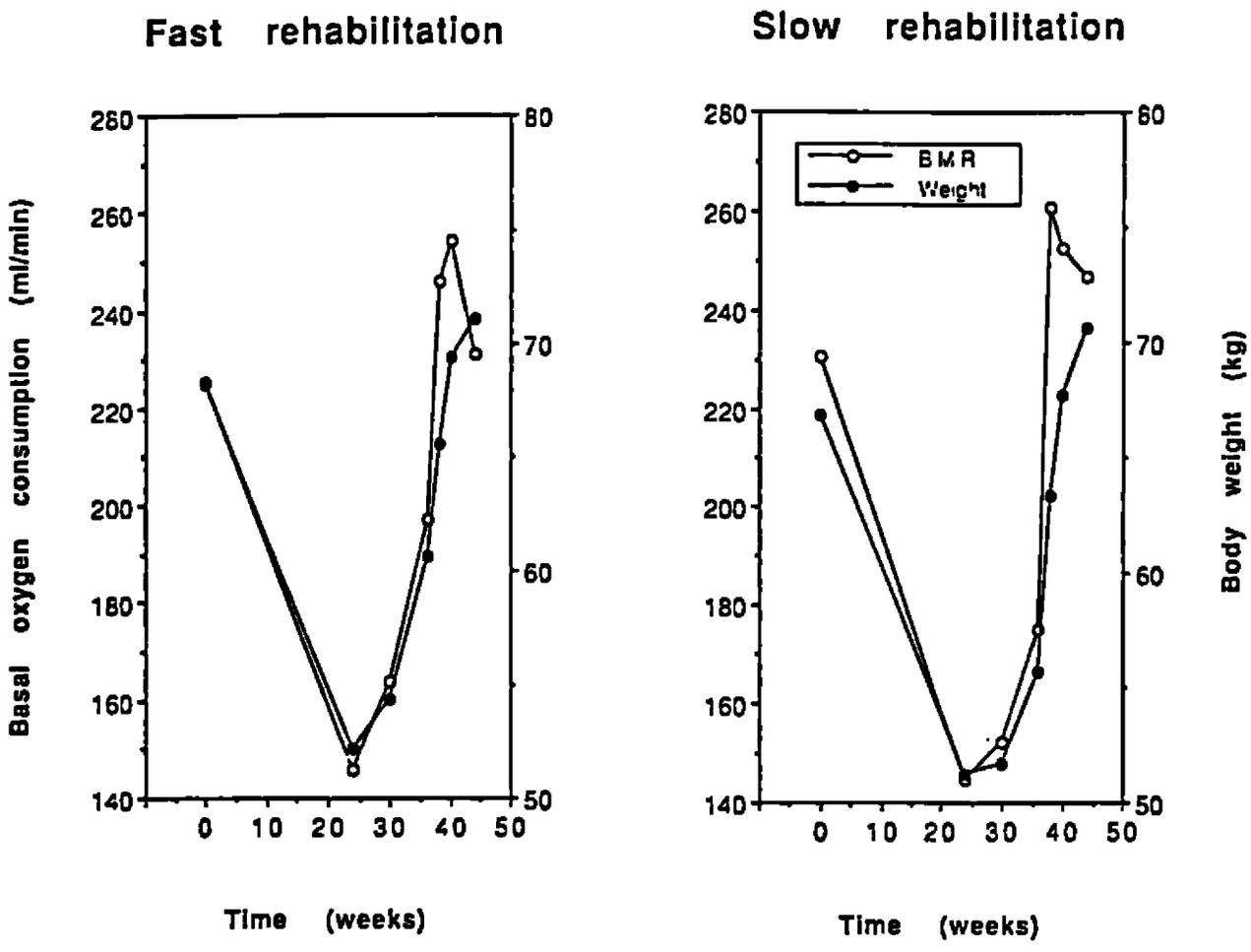

Fig. 4. Recovery of basal metabolic rate (BMR) during fast and slow rehabilitation from semistarvation in the Minnesota experiment. (Adapted from tabulated data in Keys *et al.*, 1950.) (The impression given that the relative changes in body weight and BMR are identical is an artifact produced by the choice of scales.)

turn essentially to normal once body weight and composition have been normalized.

2. *The Cambridge Study*

The Cambridge study of experimental underfeeding is modest by the standards of the Minnesota experiment, but has the advantage that very detailed measurements of energy expenditure were performed. The average energy deficit of 240 MJ (5.7 MJ/day for 42 days) caused a very uniform weight loss averaging 5.6 kg (range 4.8–6.1 kg). By the end of the underfeeding, BMR had decreased by 0.6 MJ/day (8%, $p < .001$). When expressed per kilogram of fat-free mass (FFM), BMR decreased by 5% ($p < .01$). Twenty-four–hour energy expenditure on the fixed protocol in the whole-body calorimeter decreased by 1.0 MJ/day (9%, $p < .001$). By subtracting the decrease in BMR from the decrease in 24-hr expenditure in the calorimeter, we can make a good estimate of the extent to which diet-in-

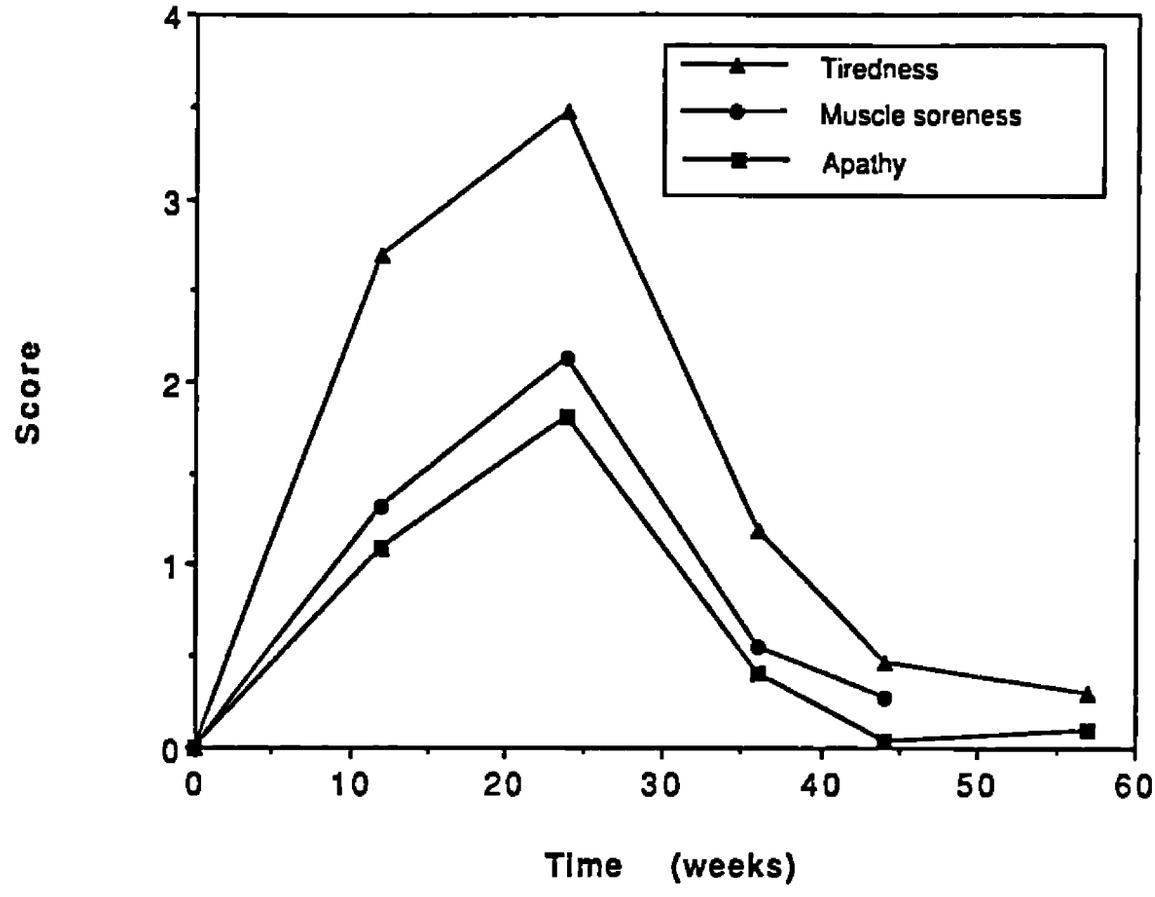

Fig. 5. Alterations in subjective ratings of tiredness, muscle soreness, and apathy in the Minnesota experiment. (Adapted from Keys *et al.*, 1950.)

duced thermogenesis was reduced because physical activity was kept constant. This calculation suggests that thermogenesis was suppressed by about 0.4 MJ/day (12%, $p < .01$). These results confirm and extend earlier starvation experiments.

C. Alterations in Physical Activity

1. *The Minnesota Experiment*

There were no formal measurements of physical activity in the Minnesota study, but a number of pieces of indirect evidence all indicate that the subjects became much less physically active as appears to occur in natural famine. Figure 5 illustrates the subjects' ratings of tiredness, muscle soreness, and apathy, all of which are likely to correlate inversely with activity. Each of these subjective ratings showed a very marked increase by the end of the 24 weeks of semistarvation and returned toward normal during rehabilitation. The subjects' diaries also indicated a pronounced lethargy.

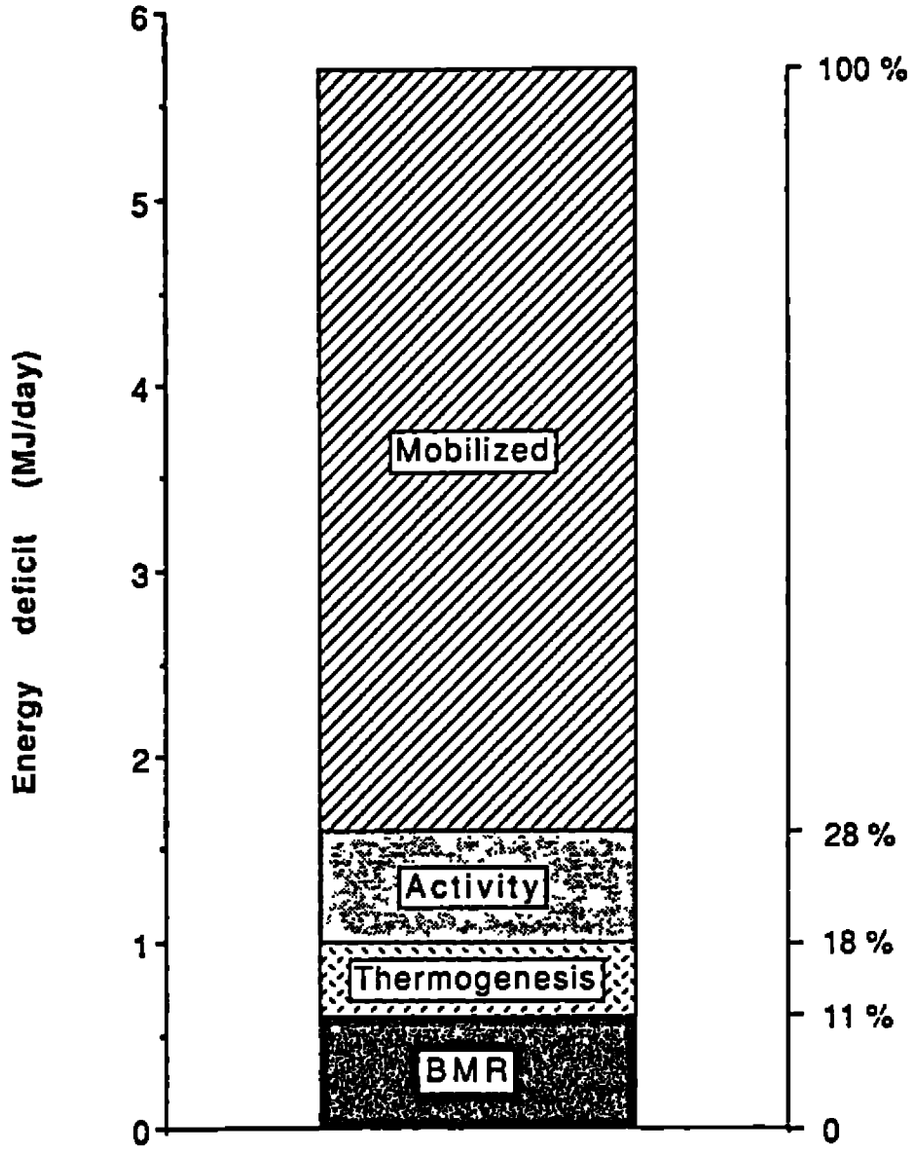

Fig. 6. The limited impact of energy-sparing adaptations in balancing an energy deficit. Data from the Cambridge 6-week underfeeding experiment (Diaz *et al.*, 1991b).

2. *The Cambridge Study*

In the Cambridge study, gross physical activity was intentionally held constant during the whole-body calorimeter measurements. However, the doubly labeled water measurements of free-living energy expenditure indicated that outside the confines of the calorimeter, there was a behavioral component of energy conservation, with the subjects decreasing their voluntary activity by about 0.6 MJ/day. This is again consistent with anecdotal reports from natural famines.

One feature of the Cambridge data is that it allows us to create an energy balance sheet, and to identify exactly how the subjects coped with the energy deficit. This is summarized in Figure 6, which makes the important point that although a number of energy-sparing mechanisms are

TABLE II

Published Data on Basal Metabolic Rate (BMR) in Anorexic Patients

Circumstance	Sample Size	BMR (% of predicted)
Moller (1924)	4	68–82
Labbe and Stevenin (1925)	8	61–90
Mason *et al.* (1927)	5	79–85
Berkman (1930)	117	58–100
Stordy *et al.* (1977)	15	mean = 75
Forbes *et al.* (1984)	12	61–81
Vaisman *et al.* (1988)	25	69±10
Melchior *et al.* (1989)	11	mean = 70

invoked by semistarvation, they have only a limited capacity to make up for the shortfall. In the Cambridge study, this amounted to a saving of 28%; the remaining 72% had to be mobilized from body energy reserves.

V. ANOREXIA NERVOSA AND BULIMIA NERVOSA

A. Alterations in Basal Metabolism and Thermogenesis

Table II provides a broad summary of the published changes in BMR observed in anorexic patients. As with the wartime data, there is quite a wide range in the results, with average values at about 20–30% below predicted BMR and minimum values at about 40% below predicted BMR. Note that the 40% depression of BMR in the Minnesota subjects was on a whole-body basis. The anorexia nervosa values already include a correction for weight change, since the predicted values themselves are calculated on the basis of the subjects' body weights. The true level of suppression therefore appears to be more pronounced in anorexia.

Most of the studies cited in Table II do not provide data on the body composition of the anorexic patients in whom metabolic rate was assessed. It is therefore difficult to make any definitive statements about whether metabolism is suppressed per unit of active tissue. This problem is compounded by the difficulty of establishing the most appropriate denominator for expression of mass-specific BMR. Luke and Schoeller (1991) presented an analysis that fits BMR to FFM in the manner suggested by Ravussin and Bogardus (1989), using collated data from control

subjects. For those studies of anorexics for whom FFM was available, and with the addition of a limited amount of new data, Luke and Schoeller concluded that BMR was significantly lower than would be expected at any given FFM. This is consistent with expectations based on experimental underfeeding studies.

Altemus *et al.* (Chapter 8., this volume) and Fernstrom and Weltzin (chap. 13) present data on BMR in bulimic patients. Altemus *et al.* report that resting energy expenditure (REE) is slightly depressed in normal weight bulimics compared with controls (909 vs. 1021 kcal/day, $p = .14$) when they are studied during a controlled nonbinging phase. When measured during an active binging phase, REE was significantly greater than in the abstinent phase (1137 vs. 909 kcal/day, $p < .02$) and was no longer lower than in the control group. Altemus *et al.* suggest that this may represent a biological explanation for binging insofar as it may offset a naturally low BMR in bulimic patients, and therefore confer an advantage in terms of weight control. Fernstrom and Weltzin (Chapter 13) report that RMR is suppressed in normal weight bulimic patients, confirming a recent report by Devlin *et al.* (1990) and a number of studies published in abstract form and cited by Sedlet and Ireton-Jones (1989).

Fernstrom and Weltzin (Chapter 13) also report that diet-induced thermogenesis (DIT) in response to a standard meal is significantly lower in bulimics than in controls. In contrast, Stordy *et al.* (1977) reported that thermogenesis in response to an oral glucose load was more than double in anorexics in the course of treatment when compared with controls. These results are very difficult to interpret for a number of reasons. Stordy *et al.* pointed out that a large increase in DIT in anorexic patients who are gaining weight would be consistent with Ashworth's observations in infants recovering from malnutrition (Ashworth, 1969; Brooke and Ashworth, 1972). However, they also acknowledged that the very high level of DIT observed in their anorexics may have been partly explained by anxiety arising from the forced ingestion of a large quantity of carbohydrate. The virtual absence of any DIT in bulimic patients reported by Fernstrom seems incompatible with the fact that there are inevitable biochemical costs involved with digesting, absorbing, transporting, storing, and metabolizing ingested food. Finally, Leblanc (Chapter 3, this volume) demonstrated significant cephalic effects on DIT, which are likely to further confuse the interpretation of DIT results in anorexic and bulimic patients since their cephalic responses are likely to be very different from those of normal controls. Although understanding the nature of alterations in DIT may be useful in elucidating the exact nature of perturbations in energy metabolism in patients with eating disorders, it is of relatively little quantitative importance in terms of the overall energy balance equation.

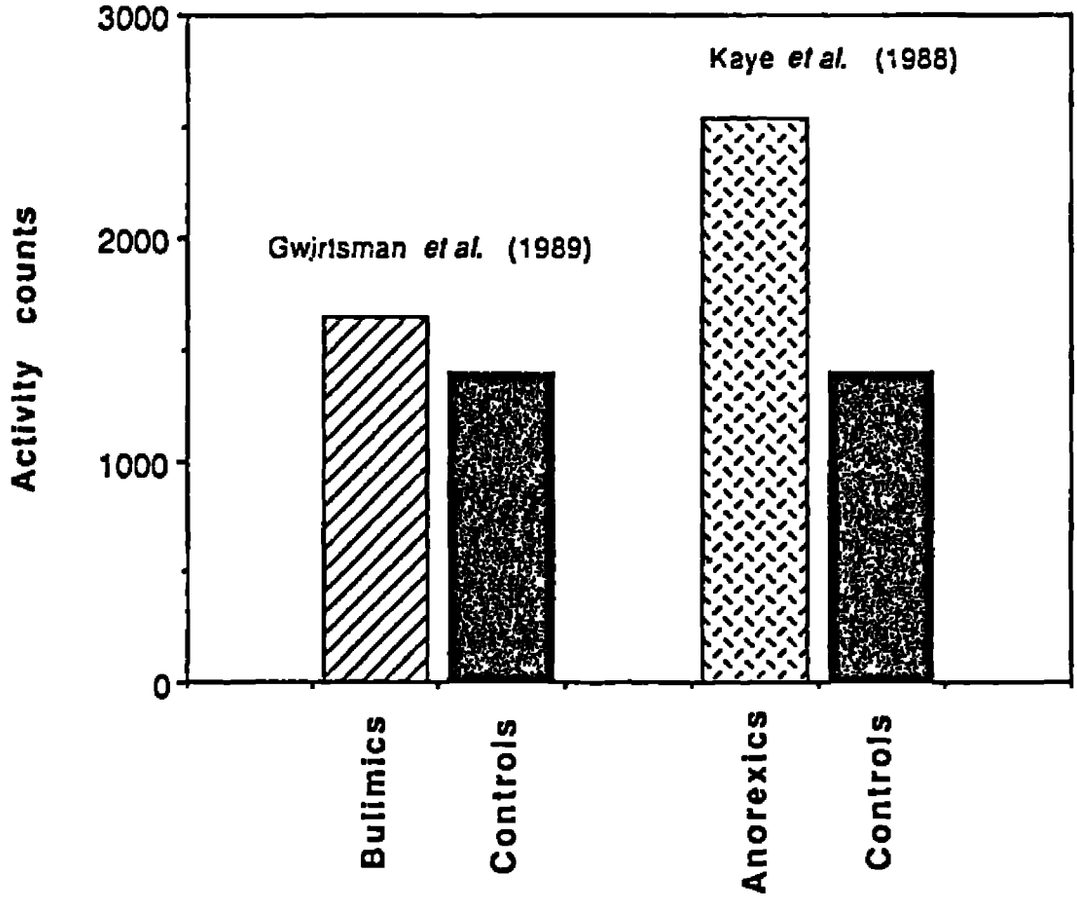

Fig. 7. Actometer measurements of physical activity in bulimic (n = 17), anorexic (n = 11), and control (n = 10) subjects. Note that the same control data were used in each study.

B. Alterations in Physical Activity

It has long been observed that anorexic patients are frequently hyperactive. Keys *et al.* (1950) commented, "Although some anorexic patients are reticent, apathetic and depressed like famine victims, a considerable number show a feverish press of activity, at times manic in character, extending even into the most severe cachectic phase. A similar state of excitement in famine victims is very rare and short-lived in any case."

Kaye's group has published a number of studies using actometers to obtain quantitative information on physical activity, although the cost in energetic terms is not assessed. Some of their results are summarized in Figure 7, which indicates that bulimic patients may be slightly more active than controls, and that anorexic patients are substantially more active (Kaye *et al.*, 1986; Gwirtsman *et al.*, 1989a). They also reported that activity counts were lower in short- and long-term weight-restored patients (Kaye *et al.*, 1986), but this is contradicted by findings reported by Falk *et al.* (1985), who found no decrease in activity during treatment.

Casper *et al.* (1991) reported the first doubly labeled water measurements in anorexic patients. The average daily energy expenditure of the

six anorexic patients was 1960 ± 670 kcal/day. When expressed as absolute values, the expenditure was similar to that of a group of age- and height-matched control women (1970 ± 370 kcal/day), but it was significantly greater when expressed as a multiple of BMR (1.97 vs. 1.49 x BMR). The energy expended on physical activity by the anorexics and controls, respectively, was estimated to be 880 ± 460 versus 580 ± 280 kcal/day, or 20 ± 7 versus 10 ± 5 kcal/kg/day. This confirms both the subjective ratings of activity in anorexia and the previous studies with actometers. The hyperactivity associated with anorexia nervosa stands out as the greatest difference between any of the eating disorders and famine or experimental underfeeding.

VI. BODY COMPOSITION CHANGES IN ANOREXIA NERVOSA

In view of the fact that energy metabolism is heavily influenced by body composition and particularly by lean body mass, we briefly consider the effects of starvation and anorexia nervosa. A theoretical analysis suggests a variety of opposing influences on protein mass. Those tending to deplete include the starvation itself, which drains protein in order to provide glutamine and glucogenic substrates. In natural famine conditions, this effect may be somewhat ameliorated by the fact that a deterioration in diet quality, with a consequent increase in the carbohydrate ratio, is a common feature of food shortages. This certainly occurs during the hungry season in The Gambia. In anorexia nervosa, there does not appear to be any radical change in the proportion of dietary energy derived from the different macronutrients (i.e., anorexics do not appear to selectively avoid carbohydrate), but the total intake of carbohydrate is nonetheless severely reduced by the overall decrease in food intake (Gwirtsman *et al.*, 1989b), and this may be low enough to create a demand for protein-depleting gluconeogenesis. A further factor that may tend to deplete protein mass is that there appears to be an unexpected increase in carbohydrate oxidation during semistarvation and anorexia, as evidenced by a raised respiratory quotient (RQ) during calorimetric measurements. In the Minnesota study, the RQ measured when the subjects performed a standard light exercise was higher during starvation than during the baseline period (0.933 ± 0.006 vs. 0.878 ± 0.005, respectively, $p < .001$). Vaisman *et al.* (1988) observed a similar trend during resting metabolic rate (RMR) measurements in anorexic patients (0.892 ± 0.011 vs. 0.844 ± 0.005, $p < .02$). The reason for these raised RQs is not at all clear under conditions when fat mobilization and ketone body oxidation would be anticipated, but the effect is likely to be an increased catabolism of protein. Wu and Marliss (Chapter 14, this volume) consider some additional factors that may tend to deplete protein.

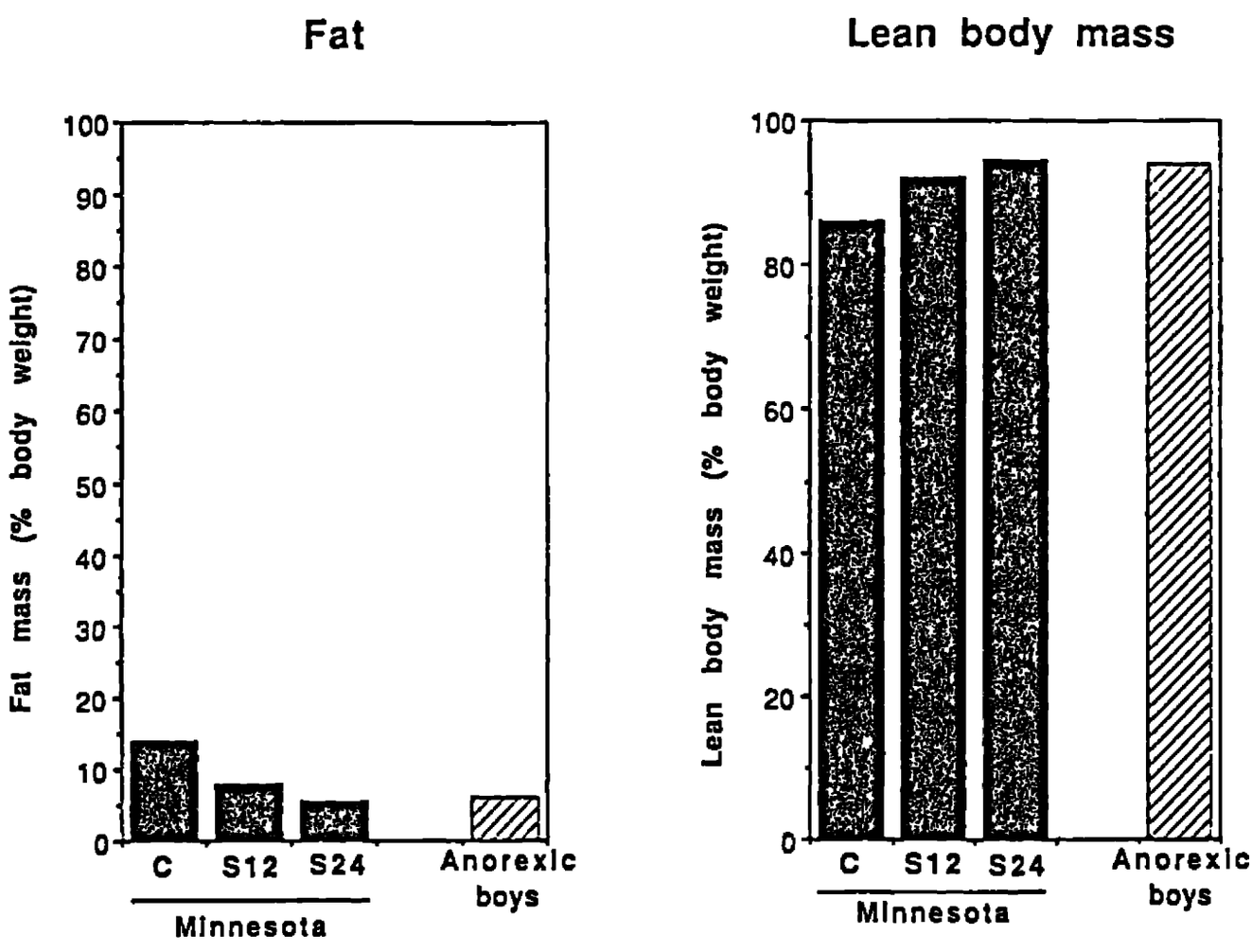

Fig. 8. Body composition of the Minnesota experiment subjects during control period and after 12 and 24 weeks of semistarvation (C, S12, and S24) compared with anorexic adolescent boys ($n = 5$) studied by Davies *et al.* (1978).

The factors tending to protect lean mass include the high levels of exercise undertaken by anorexics and the reduction in T3 levels. Abundant evidence from studies of obese people on slimming regimes indicates that both of these act to protect body protein (Prentice *et al.*, 1991), and it seems likely that the same effect would occur over a wide range of weight loss.

Figure 8 compares the body composition of the Minnesota subjects after 24 weeks of semistarvation with data on 5 anorexic boys published by Davies *et al.* (1978). The composition of the two groups is extremely similar.

Figures 9 and 10 show the body composition of adult anorexic women (mean age 25 years) compared with healthy controls and our Gambian subjects. It can be seen that although the Gambian women are small (52 kg) and thin (20% fat) compared with the Caucasian control women (63 kg and 30% fat), they are considerably less wasted than any of the anorexic groups. This is the basis for our conclusion in Section II.C that we can make only limited extrapolation of the Gambian data to the situation in eating disorders. The reduction in body fat in the anorexic patients is of

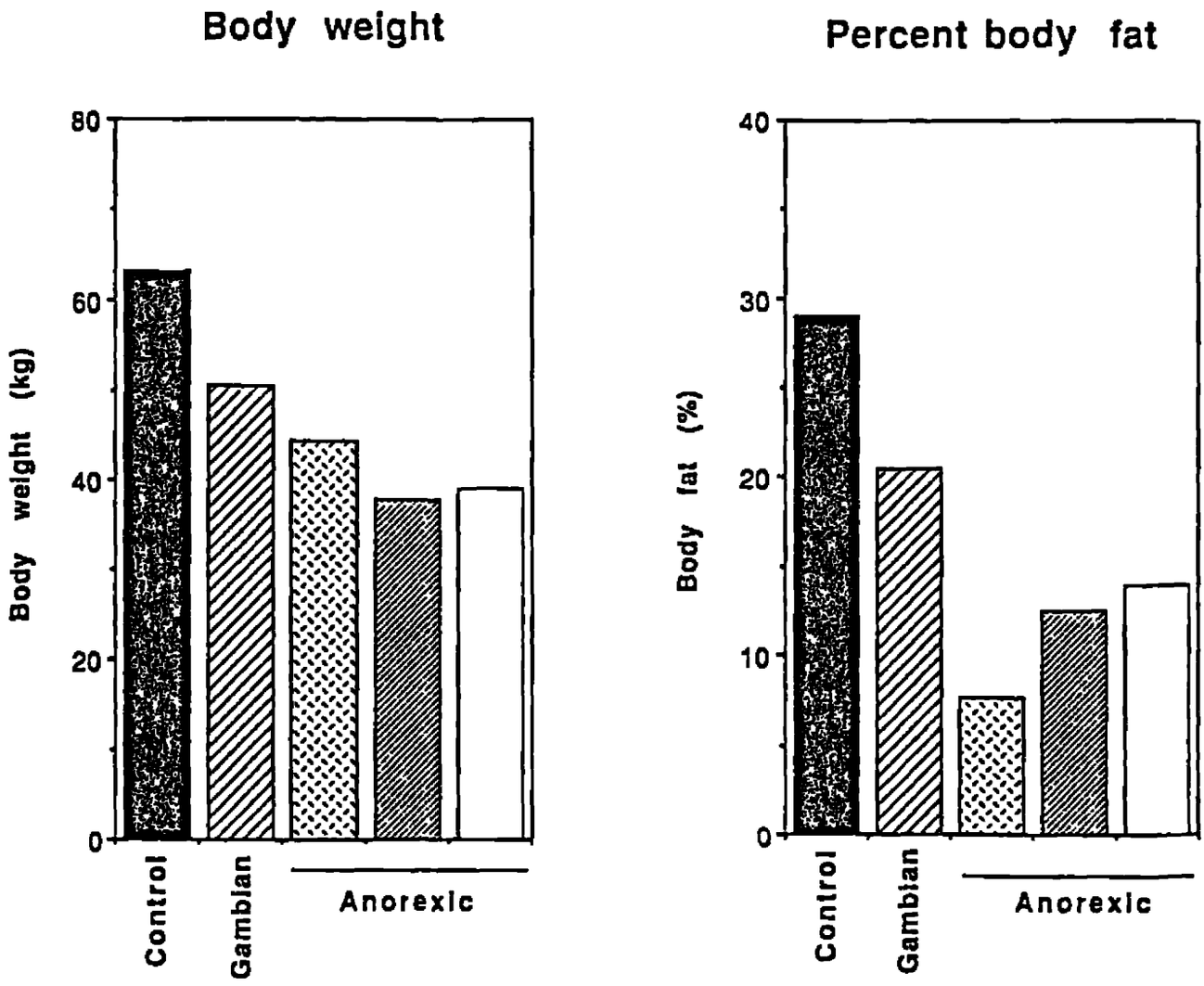

Fig. 9. Body weight and body fat in well-nourished caucasian women, in chronically undernourished Gambian women, and in three groups of anorexic women. All groups had a mean age of 25 years. (Data from Durnin and Womersley, 1974; Russel *et al.*, 1983; Dempsey *et al.*, 1984; Lawrence *et al.*, 1987; Mazess *et al.*, 1990).

the order of 60–70%. Figure 10 shows that the percentage of reduction in lean body mass is much lower, at about 10–25%. As a consequence, lean body mass, when expressed as a percentage of total body weight, rises to over 85%.

Figures 11 and 12 show similar data for groups of adolescent anorexics compared with adolescent controls. The changes are very similar to those seen in the older women.

A recent report of body fat distribution assessed by computerized tomography (CT) scanning of the abdomen (approximately umbilical level) in anorexic patients suggests some profound alterations in body fat distribution, as well as in absolute amount (Mayo-Smith *et al.*, 1989). Fifteen anorexic women (age 15–33 yr) were compared with 39 control women (18–35 yr). Intra-abdominal fat differed by only a factor of 2 between patients (12 ± 2 cm^2) and controls (26 ± 2 cm^2, $p < .001$), but subcutaneous fat differed by a factor of 5 (30 ± 6 vs. 166 ± 11, $p < .001$, respectively).

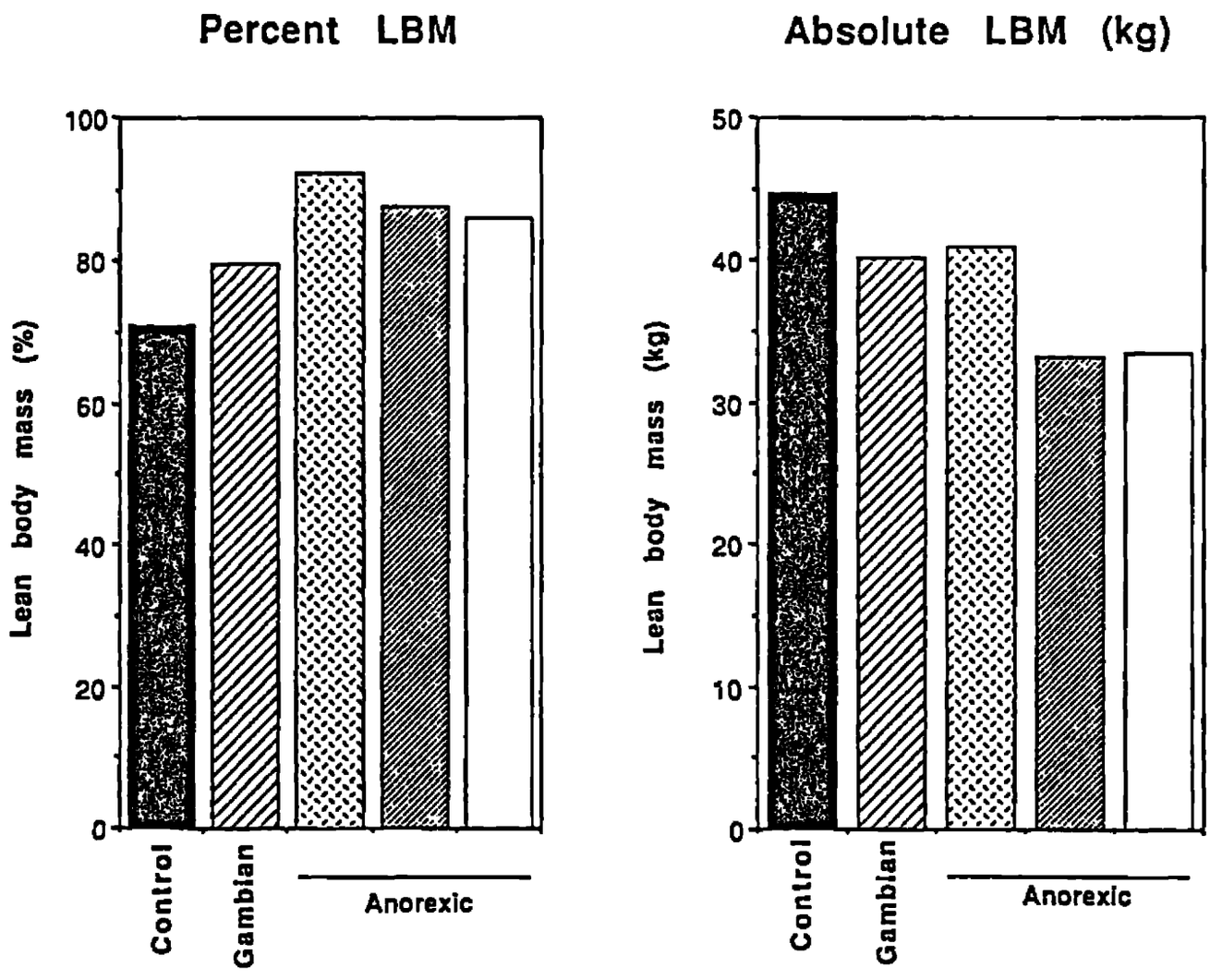

Fig. 10. Absolute and percentage lean body mass (LBM) in the same subjects illustrated in Figure 9.

There are many difficulties in interpreting the LBM data and in determining whether LBM is preferentially protected. Among these are the fact that the measurements may be interfered with by the processes of starvation (e.g., by redistribution of intra- and extracellular water, which will affect methods based on body water determination and loss of bone mineral, which may in turn affect densitometry). These issues are discussed by Pencharz and Azcue (Chapter 21, this volume).

Another problem relates to the lack of a substantial body of CT or magnetic resonance imaging data that could quantify muscle versus organ loss. The only data of which we are aware is summarized in Table III. It was derived from three anorexic patients and eight normal subjects, all of whom were studied to provide comparative data for a study of cancer cachexia (Heymsfield and McManus, 1985). If expressed as a percentage of body weight, muscle and spleen weights are lower in anorexics and kidney weight is slightly higher. However, when expressed relative to the total FFM, all organ weights except kidney seem to be low. This was in

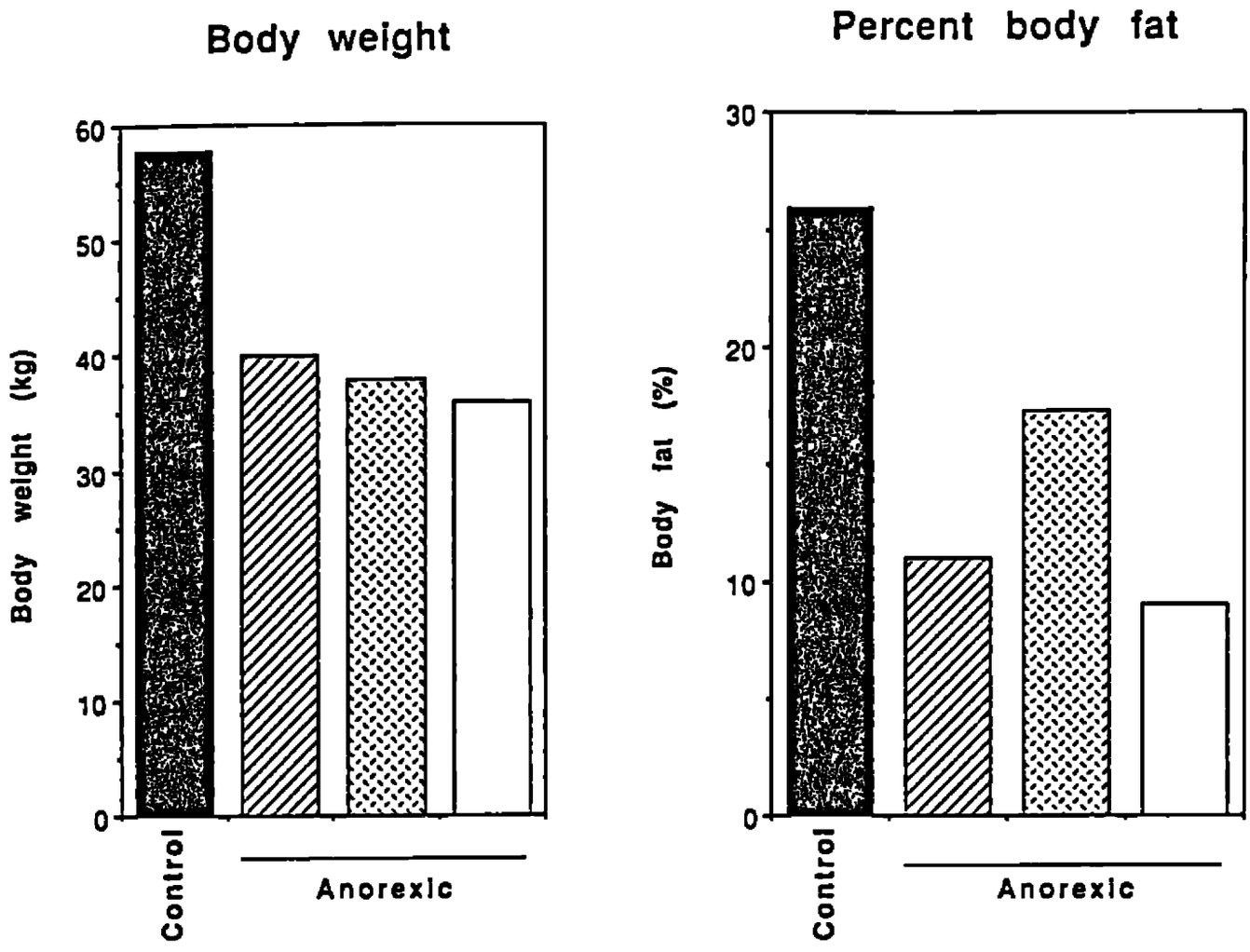

Fig. 11. Body weight and percentage body fat in well-nourished and anorexic adolescent girls (mean ages 16–17 years). (Date from Durnin and Womersley, 1974; Davies *et al.*, 1978; Forbes *et al.*, 1984; Vaisman *et al.*, 1988).

marked contrast to the data from depleted cancer patients (not tabulated) in whom visceral organ weights appeared to be much closer to normal. This type of data will become increasingly available as new technologies become more widely used, and will provide much more meaningful insights into the metabolic and physiologic alterations that accompany anorexia nervosa. However, in view of the fact that the present data derives from only three patients and from a control group with a much wider age range, we should presently view it as indicative rather than conclusive.

The final problem relates to the definition of normal. Forbes (1987) described a generalized relationship between body fat and lean mass at different levels of adiposity. This can be used to assess whether a given lean tissue loss is greater than expected when body weight changes. However, anorexic patients lie at the extreme end of the generalized prediction, and this region of the predictive curve was itself generated from data in anorexics. Thus, any attempted comparison would be compounded by a problem of circular logic.

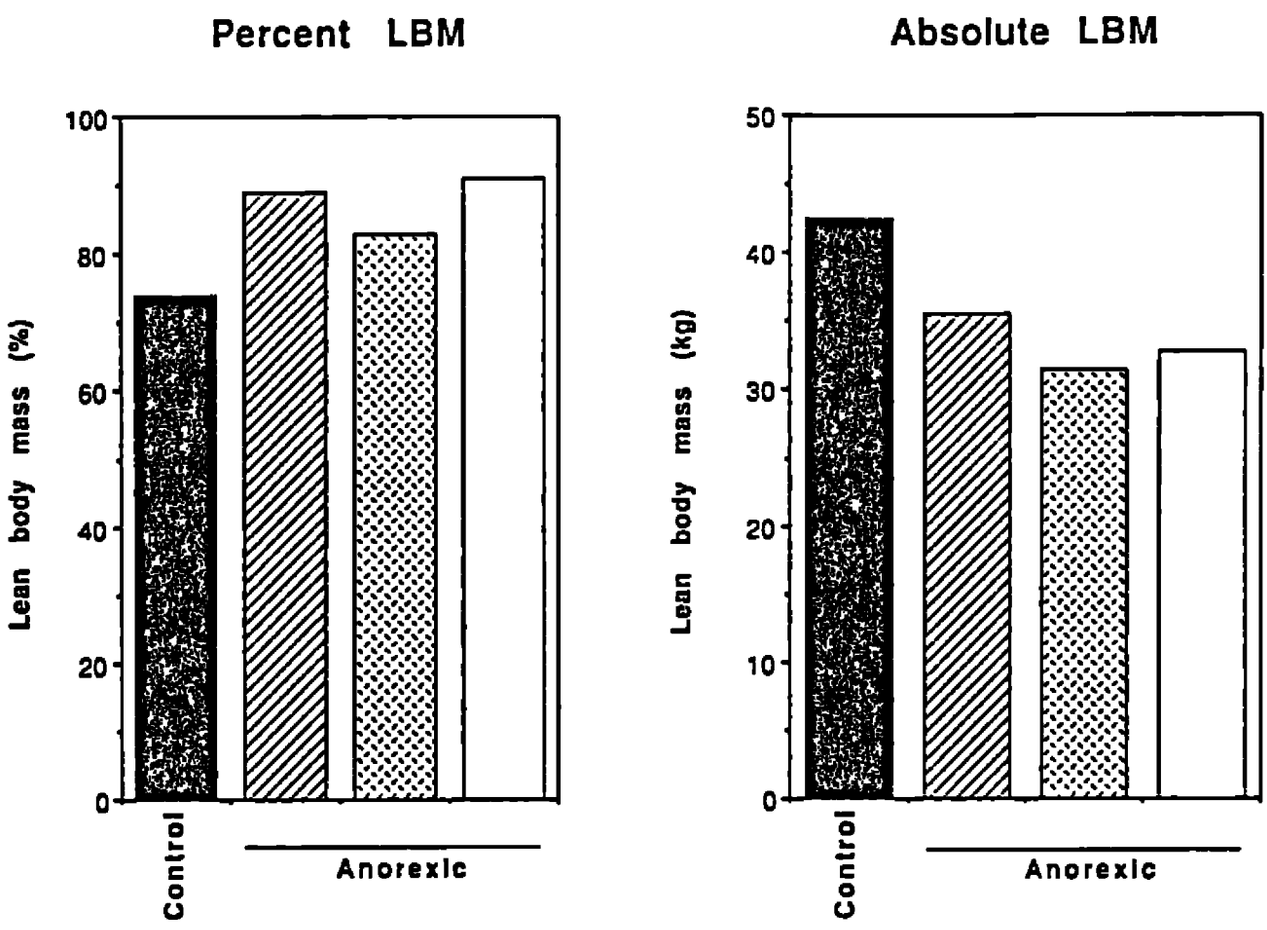

Fig. 12. Absolute and percentage lean body mass (LBM) in the same subjects illustrated in Fig. 11.

TABLE III

Data on Organ Weights in Anorexic and Control Women

	Control (n = 8)	Anorexia nervosa (n = 3)
Expressed as percentage of body weight		
Fat	23	11
Fat-free mass	77	89
Muscle	33	26
Liver	2.4	2.3
Kidney	0.42	0.51
Spleen	0.30	0.18
Heart	1.2	1.0
Expressed as percentage of fat-free mass		
Muscle	43	30
Liver	3.2	2.6
Kidney	0.55	0.58
Spleen	0.39	0.21
Heart	1.5	1.1

Data from Heymsfield and McManus, 1985.

In summary, therefore, we can do little better than describe the changes and point out that the loss of lean tissue is considerably less severe than the loss of fat.

VII. CONCLUSIONS

We conclude that the changes in energy metabolism in anorexia nervosa are very similar to the changes observed in natural starvation, and that they are probably a secondary feature of the disease. There is some evidence that a low metabolic rate may be a primary feature of bulimia nervosa, but it is far from conclusive.

The one feature that stands out as being quite different is the hyperactivity of anorexic patients. An improved understanding of the changes in total energy expenditure will be important, both for improving clinical management of eating disorders and in furthering our knowledge of the disease process itself. The doubly labeled water method is ideally suited for such research, and it seems likely that new data will be forthcoming in the near future.

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