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Energy Provision, Tissue Utilization, and Weight Loss in Prolonged Starvation

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Summary

Daily weight loss measurements in 76 fasting, obese patients (58 females, 18 males) have shown a characteristic pattern of rapid loss initially (up to day 14) followed by a slower but uniform reduction in weight. There were significant sex differences. Measurements of tissue breakdown showed that the initial rapid weight loss was due to the continuing utilization by the nervous system of glucose derived from lean tissue. This requirement fell noticeably from the second week of starvation. Irreversible fluid elimination also contributed to the initial phase of rapid weight loss. Fat remained the primary source of energy throughout starvation and in established fasting (more than 14 days) contributed 96% of that requirement.

Introduction

Many obese patients can undergo prolonged starvation and lose large amounts of weight (Drenick *et al.*, 1964; Thomson *et al.*, 1966; Runcie and Thomson, 1970). Under these conditions the rate of weight loss is greatest initially and thereafter falls off (Rapoport *et al.*, 1965). It has been suggested that weight loss in starvation results from the breakdown of lean rather than adipose tissue (Benoit *et al.*, 1965). We have reviewed the weight loss responses in 76 fasting, obese patients (58 females and 18 males) throughout extended starvation to define the normal response. Since there are no large carbohydrate

reserves in the body metabolic energy needs can be met only by the catabolism of fat in adipose tissue or protein in lean body mass or of some combination of these two—the metabolic “fuel mix.” In this study breakdown of lean tissue was measured continuously throughout fasting in a number of patients as either total protein degradation (urinary nitrogen excretion) or urinary potassium loss to provide a continuous measure of the varying proportions of lean tissue and fat metabolized. These values were also used to calculate the mean energy production of fasting, obese subjects.

Patients and Methods

The patients' obesity was either massive or refractory to treatment or they suffered from serious intercurrent disease aggravated by obesity. Before fasting all patients received a normal ward diet. The therapeutic regimen consisted simply of no food. Water-soluble vitamins (Multivite tablets) were the only supplements allowed. Water was not restricted. Patients adopted their own level of physical activity. No attempt was made to measure energy utilization direct, primarily because of the long starvation periods employed. Patients were weighed daily after rising and emptying the bladder. The urine of 35 patients was collected continuously throughout fasting and an aliquot of each 24-hour specimen was analysed for its potassium content by a standard flame photometer technique. In 28 patients (18 females and 10 males) urinary nitrogen excretion was measured by a macroKjeldahl method incorporating a multidistillation apparatus.

In seven females changes in whole-body potassium throughout starvation were measured by a scanning type of whole-body monitor. The machine is housed in a custom-built steel room. It consists of a ring of six sodium iodide detectors, three above and three below the patient. Each detector is 15 cm in diameter and 10 cm in depth. An estimation takes 44 minutes. Calibration data, principally to take account of the differences in absorption of radiation by subjects of varying size and body thickness, were obtained by extensive studies with ⁴⁰K-filled phantoms. Water-filled bags were used to simulate varying thicknesses of adipose tissue. The results were similar to the calibration data of Cohn and Dombrowski (1970) for a monitor of comparable detector geometry and are shown in fig. 1. The standard deviation for each estimate of total body potassium, including statistical and calibration errors, was 4%.

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FIG. 1—Whole-body potassium calibration data derived from studies with ^{40}K -filled phantoms. Varying thicknesses of adipose tissue were simulated by means of water-filled bags.

Results

WEIGHT LOSS

To facilitate presentation and analysis of data and comparison of results weight loss up to day 30 of starvation is considered. This period divided into two phases, 1 to 14 days and 15 to 30 days, to separate the initial phase of rapid weight loss and the later, slower weight loss of established starvation. The choice of day 14 to divide these phases is slightly arbitrary in that the transition commonly occurs between days 4 and 8 of starvation but in some patients occurs later than day 8 and in a few occurs before day 4. In all cases the transition had taken place by day 14. Males and females were analysed separately (table I).

During days 1 to 14 the mean weight loss (± 2 S.E.) was significantly greater in males (10.2 ± 0.9 kg) than in females (7.7 ± 0.5 kg) ($P < 0.001$). This was largely attributable to the greater initial weight of males. But when this effect was removed by considering percentage weight losses this difference ($8.3 \pm 0.5\%$ for males; $7.4 \pm 0.4\%$ for females) remained significant ($P < 0.01$). In established starvation (more than 14 days) the mean weight losses between days 15 and 22 and 23 and 30 were similar for males and females, showing that the normal response was one of a linear loss of weight in this period. There were, however, wide individual variations on this pattern. This was most apparent in females, some of whom showed a stepwise weight loss. These differences are thought to be due to variable but reversible water retention by the kidneys. In the extreme form this may be manifested as periodic oedema.

Weight loss data can alternatively be expressed by plotting the mean daily weights, as shown in fig. 2. Each value is expressed

FIG. 2—Mean daily weight of patients during starvation exposed as percentage of weight before fasting.

as a percentage of the mean weight for the group before fasting. The best-fit curve to the data is in each case linear after 14 days ($r = 0.965$ for males and 0.96 for females), with a slope (± 2 S.E.) of $0.3 \pm 0.046\%$ /day for males and $0.26 \pm 0.025\%$ /day for females. The difference in percentage weight loss in established starvation between the sexes is not significant ($P > 0.10$). When the absolute mean weight loss in this period (0.37 ± 0.046 kg/day for males; 0.27 ± 0.03 kg/day for females) is considered the difference between the sexes is significant ($P < 0.001$).

TABLE I—Pattern of Weight Loss in 76 Fasting Subjects

Case No.	Age (Years)	Prefast Wt. (kg)	Weight Loss					
			1-14 Days		15-22 Days		23-30 Days	
			kg	%	kg	%	kg	%
Female Patients								
1	18	105.2	7.26	6.90	3.41	3.24	2.61	2.48
2	53	112.7	8.17	7.24	2.56	2.27	1.59	1.41
3	59	109.4	9.03	8.25	2.84	2.59	2.61	2.38
4	34	98.3	6.58	6.69	2.50	2.54	1.50	1.52
5	58	109.2	8.85	8.10	2.72	2.49		
6	30	134.3	9.67	7.20	2.36	1.76	2.72	2.02
7	45	95.0	8.63	9.08	2.27	2.39	2.41	2.54
8	40	117.2	6.13	5.23				
9	17	90.3	7.46	8.26				
10	42	101.1	9.90	9.79	2.92	2.88	1.88	1.86
11	47	89.6	6.56	7.32	1.96	2.19	2.27	2.53
12	19	107.6	8.77	8.15	2.27	2.11	1.73	1.61
13	16	94.7	8.74	9.23	1.25	1.32	2.95	3.11
14	14	82.7	7.95	9.61	3.06	3.70	2.61	3.15
15	46	119.9	8.63	7.20	3.09	2.58	2.41	2.01
16	29	98.9	5.17	5.23	1.90	1.92	2.22	2.24
17	39	90.7	7.97	8.79	3.04	3.35	2.75	3.03
18	30	111.7	8.09	7.24	2.92	2.61	0.68	0.61
19	33	86.3	4.65	5.39	2.61	3.02		
20	34	100.4	6.36	6.33	3.92	3.90	2.90	2.89
21	45	102.8	8.34	8.11	1.08	1.05	1.82	1.77
22	28	93.5	5.99	6.41	2.56	2.74		
23	34	114.4	8.71	7.61				
24	41	82.5	7.83	9.49	2.38	2.88	2.61	3.16
25	29	127.6	8.65	6.78	2.33	1.83	2.07	1.62
26	34	122.1	2.84	2.32	1.79	1.47	1.50	1.23
27	16	92.7	8.09	8.73	1.09	2.04		
28	17	99.3	8.51	8.57	0.99	1.00	3.12	3.14
29	40	119.0	8.37	7.03	3.12	2.62	3.12	2.62
30	52	94.9	8.29	8.73	0.45	0.47	1.48	1.56
31	42	129.5	9.37	7.23	3.35	2.59	2.98	2.30
32	49	95.1	6.47	6.80	1.82	1.91	1.19	1.25
33	31	93.1	5.45	5.85	1.73	1.86	1.68	1.80
34	36	136.3	9.99	7.33	0.74	0.54	1.48	1.08
35	35	99.7	8.40	8.42	1.90	1.90	5.17	5.18
36	37	117.8	9.19	7.80	1.36	1.15	2.04	1.73
37	47	153.2	8.85	5.78	5.45	3.56	4.09	2.67
38	34	142.1	10.44	7.35	2.84	2.00	1.59	1.12
39	22	105.1	7.72	7.34	0.82	0.78	1.39	1.32
40	44	138.9	7.44	5.36	2.30	1.65	1.90	1.37
41	29	78.5	8.06	10.27	2.16	2.75		
42	40	105.6	7.26	6.78	1.93	1.83	2.07	1.96
43	61	86.7	6.13	7.07	1.93	2.23	1.11	1.28
44	57	80.8	8.06	9.97	2.04	2.52		
45	54	124.7	7.38	5.92	2.16	1.73	2.72	2.18
46	57	93.8	3.74	3.99	0.29	0.31	2.22	2.37
47	52	93.5	9.08	9.71	2.04	2.18	2.95	3.15
48	61	101.6	4.85	4.77	1.36	1.34	2.47	2.43
49	58	107.7	10.10	9.38				
50	52	83.1	5.39	6.49				
51	51	117.4	11.01	9.38	2.95	2.51	2.78	2.36
52	55	118.9	8.51	7.16	0.20	0.17	1.19	1.00
53	71	74.9	4.09	5.46	1.82	2.43	1.59	2.12
54	56	89.4	8.00	8.95	2.33	2.61	2.33	2.31
55	62	86.8	4.85	5.59	1.14	1.31	1.14	1.31
56	55	81.9	7.49	9.14	1.45	1.77	1.93	2.36
57	25	127.3	9.76	7.67	1.82	1.43	2.50	1.96
58	55	106.2	8.23	7.75	3.18	2.99	0.57	0.54
Mean		104.7	7.68	7.41	2.17	2.09	2.18	2.08
S.D.		17.63	1.74	1.61	0.94	0.85	0.84	0.83
Male Patients								
59	22	113.7	9.71	8.54	3.29	2.89	3.29	2.89
60	26	126.2	9.85	7.80	3.58	2.84	2.80	2.22
61	55	132.2	12.95	9.79				
62	49	75.8	6.92	9.13	1.90	2.51	1.16	1.53
63	53	105.8	8.74	8.26				
64	44	108.3	7.89	7.28	2.78	2.57	3.12	2.88
65	46	112.6	8.17	7.25	3.50	3.11	2.40	2.13
66	29	117.1	9.40	8.03	3.18	2.71	3.24	2.77
67	31	144.0	12.00	8.33	3.20	2.22	3.40	2.36
68	39	111.5	11.90	10.67	3.17	2.84	2.30	2.06
69	30	86.3	8.17	9.47	3.63	4.21	3.18	3.68
70	25	122.4	10.40	8.50	3.90	3.19	3.50	2.86
71	26	129.3	10.65	8.24	2.45	1.89	3.60	2.78
72	46	123.9	10.00	8.07				
73	66	114.5	9.20	8.03	1.95	1.70	2.80	2.44
74	48	184.3	12.90	7.00	3.63	1.97	3.40	1.84
75	51	199.3	12.70	6.37	1.36	0.68	1.70	0.85
76	56	115.0	11.45	9.96	3.76	3.27	2.80	2.43
Mean		123.4	10.17	8.30	3.02	2.57	2.84	2.38
S.D.		29.44	1.84	1.10	0.77	0.82	0.70	0.67

PROTEIN DEGRADATION

Protein degradation was measured direct in 28 subjects (18 females and 10 males) as daily urinary nitrogen excretion (fig. 3). The mean daily nitrogen output (± 2 S.E.) in females and males on day 1 was 9.45 ± 0.8 and 11.7 ± 1.2 g respectively. On day 30 the respective values were 4.2 ± 0.8 and 3.6 ± 0.6 g.

FIG. 3—Mean daily nitrogen excretion during starvation in 18 female and 10 male patients.

Urinary Potassium Excretion

Urinary potassium excretion was measured in 35 subjects (25 females and 10 males) (fig. 4). The mean daily loss (± 2 S.E.) for females and males on day 1 was 35.3 ± 3.2 and 37.2 ± 5.0 mEq respectively. The respective values on day 30 were 14.5 ± 3.2 and 16.5 ± 3.2 mEq. The mean (± 2 S.E.) cumulative potassium loss in females over this period was 635 ± 102 mEq.

FIG. 4—Mean daily potassium excretion during starvation in 25 female and 10 male patients.

WHOLE-BODY POTASSIUM CHANGES

Whole-body potassium changes were measured in seven females over days 1 to 30 (table II). When recorded as a percentage of the prefast value (fig. 5) the best-fit curve to the data yields a value for the mean (± 2 S.E.) cumulative potassium loss in

females of 502 ± 100 mEq over days 1 to 30. This does not differ significantly from the value of 635 ± 102 mEq found by direct measurement of urinary potassium loss ($P > 0.05$).

FIG. 5—Mean daily whole-body potassium content during starvation expressed as percentage of value before fasting.

TABLE II—Changes in Whole-body Potassium (mEq) in 7 Women during Starvation

Day of Fast	Case 1 105.2 kg 162.0 cm 18 yr	Case 2 112.7 kg 152.3 cm 53 yr	Case 3 109.4 kg 147.0 cm 59 yr	Case 4 98.3 kg 157.2 cm 34 yr	Case 5 109.2 kg 156.3 cm 58 yr	Case 6 134.3 kg 160.5 cm 30 yr	Case 7 95.0 kg 153.0 cm 45 yr
0	2,610	2,916	2,519	2,749	2,672	2,724	2,557
1					2,641	2,736	2,480
2					2,378		2,531
3	2,634		2,560		2,416		
4				2,634			2,519
5		2,762					
6	2,289		2,200	2,480		2,657	
7							2,480
8						2,634	2,416
9	2,210	2,634		2,506			2,173
10						2,462	
11	2,166	2,570		2,301		2,442	
12		2,583					
13							
14							
15							
16	2,072						
17							
18	2,059	2,608			2,110		
19	2,033						
20			2,100	2,122			
21							
22					2,301		
23						2,442	
24				2,212			
25		2,429					
26							
27						2,401	2,097
28							
29							
30						2,071	

Analysis

LEAN TISSUE DEGRADATION

Measurements of urinary nitrogen loss can be readily converted to the amount of lean tissue degradation. Lean tissue was strictly defined as a fat-free, non-bony tissue containing 25% protein and 75% water (Kinney *et al.*, 1970). It is basically protein with its water of hydration. Degradation of 1 kg of lean tissue will yield 40 g of urinary nitrogen (since 1 g of urinary nitrogen is equivalent to 6.25 g of protein degraded) and is assumed to result in a weight loss of 1 kg. To obtain the mean lean tissue breakdown (kg/day) daily urinary nitrogen excretion (g/day) is divided by 40. This value is recorded for females and males over days 1 to 30 in fig. 6 and shows that lean tissue breakdown for females on day 1 of starvation was 0.24 kg and on day 30 0.1 kg. The comparable values for males were 0.29 and 0.09 kg. Comparable values for lean tissue degradation can

be indirectly calculated from urinary potassium excretion. For this purpose the potassium content of lean tissue, as defined here, is taken to be 130 mEq/kg, based on published data on the concentration of potassium in muscle cells (Graham, 1970). From the values of lean tissue breakdown shown in fig. 6 the potassium yield would be 34 mEq on day 1, if the data for both sexes are combined, and on day 30 the value would be 13 mEq. These agree closely with the observed values of 36 and 15 mEq in this study.

FIG. 6—Mean daily breakdown of lean tissue and fat in prolonged starvation.

FAT BREAKDOWN

The magnitude of fat breakdown can be calculated as the difference between total weight loss (fig. 2) and the amount of lean tissue breakdown, provided that no irreversible fluid shifts have occurred and that fat oxidation is complete. When applied to weight loss in established starvation acceptable values of fat breakdown are obtained. For example, on day 30 the mean fat breakdown for females was 0.17 kg and for males 0.28 kg. Since lean tissue contains 25% protein and terminal combustion of protein yields 4 kcal/g the energy yield of lean tissue is 1 kcal/g. The corresponding value for fat is 9.3 kcal/g. Hence on day 30 estimated energy production from tissue catabolism is 1,680 kcal for females and 2,690 kcal for males.

When this calculation is applied to the phase of rapid weight loss (days 1 to 14) the values obtained for the magnitude of fat breakdown are clearly erroneous unless there is a reduction of some 50% in the efficiency of fat oxidation in this period. This would be an unreasonable assumption. If it can be assumed that energy requirements are relatively constant throughout starvation, and this has been shown in established starvation, a simple relation can be used to measure fat breakdown in that at any point (t) in starvation $9,300 W_f(t) + 1,000 W_l(t) = 2,690$ kcal for males or 1,680 kcal for females where W_f and W_l are the weights of fat and lean tissue catabolized on any day t.

Substitution of the appropriate values of $W_l(t)$ allows $W_f(t)$ to be calculated. In fig. 6 the mean measured values of lean tissue breakdown in starvation and the derived values for fat breakdown are plotted for males and females. These results show the primacy of fat as the energy source throughout fasting. On day 1 fat provided 88% of the energy requirements and on day 30 95%.

Integration of the data in fig. 6 shows that the contribution of lean tissue and fat breakdown to total weight loss during days

1 to 14 was 6.8 ± 0.8 kg in males and 4.7 ± 0.6 kg in females. The observed weight losses, however, were 10.2 ± 0.9 and 7.7 ± 0.5 kg respectively. The excess losses of 3.4 ± 1.2 kg in males and 3.0 ± 0.8 kg in females can be accounted for only by irreversible fluid loss in this period.

Discussion

Though there are wide variations among obese patients in the amount of weight lost over a period of starvation this study shows that weight loss usually conforms to a typical and highly reproducible pattern (fig. 2). The biphasic nature of weight loss was not apparent in early studies because the fasting periods never exceeded 14 days (Bloom, 1959; Duncan *et al.*, 1962). At the outset weight loss is a complex effect resulting from breakdown of lean tissue (hydrated protein), utilization of body fat, and elimination of some 3 to 5 l. of body fluid. In established starvation (more than 14 days) the rate of weight loss is less but virtually constant and is due solely to the catabolism of lean tissue and fat.

The results (fig. 6) show that protein is never a significant source of energy at any point in starvation. Its comparatively large-scale catabolism in the initial period of fasting is due to a continuing dependence of the central nervous system on protein-derived glucose as a metabolic substrate (Cahill *et al.*, 1966). The subsequent switch of nervous tissue to direct utilization of the products of fat breakdown reduces body demand for glucose. The metabolic needs of those tissues, such as the red cell and the adrenal medulla, which remain obligatorily glycolytic can be met largely by glucose synthesis *de novo* from carbon fragments by the liver and kidney (Felig *et al.*, 1969). Though it has been shown that the enzymes necessary for ketone body dissimulation are present widely and in high concentration throughout the brain (Page and Williamson, 1971) the factors which promote this change are not known. A better understanding of this mechanism raises the intriguing possibility that the prognosis in brain-damaged subjects might be improved if this change in cerebral substrate utilization could be effected.

Obesity is a heterogeneous disease complex showing social bias in women and a correlation with alcoholism in men (Goldblatt *et al.*, 1965). Further evidence of this heterogeneity can be inferred from table I. There were significant sex differences in weight loss but, in addition, in males the response was more uniform, as shown by their smaller standard deviations. During days 1 to 14 eight females (14%) lost less than 5.5% of their prefast weight. By contrast the least weight lost by males in this period was 6.3%, and this was in the heaviest subject. This difference was maintained in established starvation. Energy is required for basal metabolism, a relatively constant requirement, and physical activity. Since all patients adopted their own level of physical activity this finding suggests that obesity in some females, more so than in males, may be due to an abnormally low level of spontaneous activity. This variant of obesity would require a different therapeutic approach. In grossly obese patients (over 100 kg) a related phenomenon may be observed. In many, after marked but variable weight loss is achieved the rate of weight loss increases, suggesting that a real increase in spontaneous activity has occurred. Such a response would explain, at least in part, the refractory nature of gross obesity and underlines the need to promote meaningful weight loss in such subjects.

In clinical practice the characteristic weight loss responses in fasting obese patients has two important advantages. In established starvation failure to maintain a uniform weight loss has proved a sensitive indicator of surreptitious eating. When it occurs this results in an obvious pattern of randomly interspersed weight gains when individual weight losses are charted. Secondly, this effect can be used to predict weight loss at any point in established starvation, a factor which is often helpful in maintaining morale.

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Long-term Follow-up of Therapeutic Starvation

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Summary

A total of 75 grossly obese patients were admitted to hospital for 80 episodes of prolonged starvation. Five took their own discharge within two weeks of admission and 12 defaulted from follow-up within 12 months of discharge. The others were all followed up for periods of 12 to 64 months. Altogether 39 episodes in 34 patients were classified as failures, eight as modified successes, and 16 as successes, though five of the latter patients subsequently defaulted. Success was associated with regular follow-up attendance but could not be otherwise predicted. A number of patients obtained tangible benefit from starvation despite a subsequent gain in weight.

Introduction

Starvation is an effective method of weight reduction but entails lengthy periods of stay in hospital and is not without risk. It can be justified only if there is a pressing need for temporary weight loss or if the long-term results are superior to those obtained with conventional treatment. Previous experience had suggested that prolonged inpatient starvation might be of permanent value if patients were reduced to within 25% in excess of their ideal weight (Munro *et al.*, 1970). We describe here the further follow-up of 75 patients with refractory obesity after fasting.

Patients and Methods

All the patients had failed to make satisfactory progress while attending an obesity clinic, had expressed the desire to be

admitted to hospital for starvation, and were willing to remain in hospital until reduced to within 25% in excess of their ideal weight. Altogether 27 were male patients with an average age of 30 years (range 14 to 53 years) and 48 were female patients with an average of 29 years (range 15 to 57 years). They were admitted to a hospital with good rehabilitative facilities and began the starvation regimen after a short assessment period. The emphasis throughout was on trust rather than supervision and many admitted to periodic cheating. Initially a low-energy, carbohydrate-restricted meal was provided if specifically requested and many took one such meal a week. This offer was subsequently withheld but in other respects the regimen as previously described was followed (Munro *et al.*, 1970).

Five patients (three women and two men) discharged themselves within a week or so and are excluded from further analysis. The mean admission weight of the remaining 45 women was 75.3% (range 41 to 141%) in excess of their ideal weight and that of the 25 men 77.5% (range 45 to 123%) in excess of their ideal weight.

At the completion of fasting patients were re-fed in hospital for four to seven days and offered further dietary advice. During follow-up the policy was to see them at intervals of four weeks or less. They were given every encouragement to lose weight and they and their close relatives had the opportunity of attending a monthly "group" session held during and after starvation. Many were treated with anorectic drugs, four were readmitted for starvation, and 11 underwent further short periods of outpatient fasting. The patients were subdivided according to sex, percentage in excess of their ideal weight at the time of admission, and whether or not they reduced to within 25% in excess of their ideal weight at the completion of fasting. The following criteria were applied to evaluate the outcome of treatment: *default*, default from the clinic within 12 months of discharge and without subsequent reattendance; *failure*, a gain of 15 kg or of 50% of the total weight lost during starvation; *modified success*, a gain of 10 to 15 kg or of 33 to 50% of the total weight lost during starvation; *success*, a gain of less than 10 kg and less than 33% of the weight lost. Patients followed for at least 12 months but who then failed to attend were classified as "successes," "modified successes," or "failures," with subsequent default.

Results

During a mean fast of 14 weeks the mean weight loss was 29.6 kg, but only 39 patients, including four of the 12 most

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