The chemical composition of the tissue lost by obese patients on a reducing regimen

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The excess weight of obese people is not all attributable to fat. Adipose tissue contains cells with their nuclei, blood vessels and nerves in addition to fat. In most obese people there may be hypertrophy of skeletal and cardiac muscle, and perhaps of other organs, which have to support and move the increased mass of fat.

Keys & Brožek (1953) introduced the term 'obesity tissue' to describe the material laid down in response to an excessive calorie intake. Obesity tissue is composed of fat, protein and other cell solids and water. It is described in chemical terms and so distinguished from adipose tissue, which is an anatomical term.

In this paper we present an analysis of the composition of obesity tissue lost by the seven patients on the reducing regimen described in the preceding paper (Strong, Passmore & Ritchie, 1958).

EXPERIMENTAL

The changes in body protein were calculated by multiplying the measured nitrogen balance by 6·25. The calories derived from this loss were obtained by multiplying by 4·1.*

The energy intake in the diet and the energy output in the daily activities were both measured (see below), the difference between the two giving the energy balance. On any reducing regimen energy output exceeds input and the deficit has to be made good by calories derived from fat and protein from the tissues. The calories derived from tissue protein having been determined from the N balance, the calories derived from tissue fat may be calculated by subtracting the tissue-protein calories from the total calorie deficit. The value, divided by 9·3,† gives the weight of fat lost. It can be assumed that the loss of carbohydrate is negligible.‡ The loss of body water can then be obtained by subtracting the loss of tissue protein and tissue fat from the total loss of body-weight.

* For the weeks when the N balance was positive, the calorie value of the protein laid down was obtained by multiplying by the heat of combustion for protein, i.e. 5·3 Cal./g.

† The heat of combustion of fat is used and not the Atwater factor of 9·0 which includes a correction for incomplete absorption from the intestine.

‡ Total body carbohydrate is normally about 500 g and is kept remarkably constant even in starvation. A loss could never exceed 200 g and is probably much less. This would give a maximum average daily loss of 5 g for our patients, at most equivalent to 20 Cal./day. The body store of carbohydrate is therefore negligible as a source of calories, except for very short periods.

Diet. For the most part the diet contained about 400 Cal./day provided by about 25 g protein, 40 g carbohydrate and 15 g fat, as already described (Strong *et al.* 1958). McCance & Widdowson's (1946) tables were used to calculate the caloric value of the diets and the protein intake. The use of tables for this purpose rather than chemical analysis of duplicate samples of the diet inevitably introduces errors: but on the reducing regimen the diet supplied less than 20 % of the energy output, the remainder coming from the patient's own tissues. Even if the tables introduced an error of 15 % (certainly a maximum figure), it would only amount to 60 Cal./day, which is smaller than the error involved in calculating the total energy derived from the breakdown of the tissues each day. Passmore, Meiklejohn, Dewar & Thow (1955*b*) found no significant difference between the figures for the N content of diets when calculated from tables and when determined by chemical analysis.

Recording of physical activities. Each patient kept a diary in which activities over the whole of the 24 h of each day were noted, as described by Garry, Passmore, Warnock & Durnin (1955). Activities were divided into four groups and the time spent on each recorded. These activities were (1) lying in bed, (2) sitting, (3) walking, (4) 'up and about'. Walking included only regular exercise. 'Up and about' included time spent in washing and dressing and in carrying out light tasks to help other patients in the wards.

Measurements of metabolic rates. Rates of energy expenditure during each of these four forms of activity were determined by indirect calorimetry at regular intervals throughout each patient's stay in hospital. The Kofranyi–Michaelis respirometer (Müller & Franz, 1952; Orsini & Passmore, 1951), was used for measuring ventilation rates and collecting samples of expired air. Expired air was analysed in the Haldane apparatus, duplicate analyses being carried out on each sample. For each patient some thirty to fifty measurements of metabolic rates were made covering all four types of activity during the whole period in hospital.

Calculations of daily rates of energy expenditure. The energy spent each day in each activity was calculated by multiplying the time spent by the metabolic cost of that activity. The total energy expenditure was then determined by adding up the energy spent in each activity. Table 1, which gives the results for one subject for 3 weeks, illustrates the method. Previous studies using this method (Passmore *et al.* 1955*a*; Garry *et al.* 1955) have shown that reliable results can be obtained. Past experience suggests that under the circumstances of the present observations, the errors in estimating daily energy expenditure would be not more than 10 % and possibly much less.

Errors arise from two sources. First, there may be inaccurate diary keeping by the patients. Each diary was examined by one of us several times each week and difficulties were discussed with the patients. In the first few days appreciable errors may have been present, but all patients soon settled down to the routine. We are satisfied that the diaries were accurately kept and no substantial error arose from this source. Secondly, an activity as performed during a metabolic measurement may not be a true sample of how that activity was carried out at other periods of the day. It was not possible, for instance, to see that the patients walked at a standard rate during their periods of exercise. However, the number of measurements made on each subject when walking was large and enabled some estimate to be made of the range of variation. Patients were frequently observed when measurements were not being made and there was no reason to suppose that any systematic sampling error was present. No measurements of metabolic rates were made during the night; for the period 'in bed', the metabolic rate was taken to be 90 % of the metabolic rate determined when lying down during the day. The maximum error, so introduced, probably does not exceed 50 Cal./day (Passmore & Durnin, 1955).

Table 1. *Mean daily energy expenditure of subject, Miss McN., for 3 weeks*

Activity	Week 1	Week 2	Week 3
	Time spent (min)		
Lying	603	598	632
Sitting	554	528	475
Up and about	114	113	102
Walking	169	201	231
	Calories expended (Cal./min)		
Lying	1·50	1·45	1·40
Sitting	1·80	1·65	1·55
Up and about	3·5	3·3	3·1
Walking	6·2	6·0	5·8
	Calories expended (Cal./day)		
Lying	905	867	885
Sitting	997	871	736
Up and about	399	373	316
Walking	1048	1206	1340
Total	3349	3317	3277

Urine. Samples were collected for 24 h periods and the N content was determined in duplicate by the micro-Kjeldahl method.

Faeces. These, as soon as passed, were put in a refrigerator and weighed within 24 h. Samples were pooled over a 5–7-day period. A portion was dried and then its N content determined.

RESULTS

Table 2 shows the calculated composition of the obesity tissue lost by the seven patients over the whole period on the regimen. Fat varied from 73 to 83 %, protein from 4 to 7 % and water from 10 to 23 % of the total weight loss in the different patients. The caloric value of the tissue lost lay between 7000 and 8100 Cal./kg.

This analysis covering a period of 6 weeks may give, however, a false picture of what is happening at any one time. The results for all the patients were calculated over 5- or 7-day periods. In individual periods for each patient, the nature of the tissue lost showed marked variation from the overall picture given in Table 2. All the basic values from which these variations were calculated are given in Table 3.

Losses and gains in body water. Table 3 also gives the calculated changes in body water. Whereas all the patients lost large quantities of water during the first 5–7 days, these losses were not maintained. Indeed for some periods each patient was actually retaining rather than losing water. Water retention was found in twenty out of the forty-seven periods for which the values were calculated, although body-weight fell in each. Fig. 1 shows diagrammatically the results for Mrs R. and Miss B. It will be seen that during the 1st week more than half the weight lost by both patients was water. Subsequently, Mrs R. retained water during the 2nd week, remained in virtual equilibrium during the 3rd and 4th weeks and again retained water in the 5th week. In the last week she lost water, but only sufficient to restore the balance to the level reached at the end of the 1st week. Miss B. retained water during weeks 2–5, and at the end of week 6 the total water lost was less than at the end of week 1.

Table 2. *Percentage composition of obesity tissue lost by seven patients during 40–45 days on the regimen*

	Mr I.	Mrs R.	Mrs L.	Miss McN.	Miss B.	Miss M.	Mr W.
Total weight loss (kg)	13·4	16·3	16·0	15·0	13·0	17·3	16·0
Consisting of:							
Fat (%)	80	79	73	81	83	76	75
Protein (%)	6	6	4	5	7	4	6
Water (%)	14	15	23	14	10	20	19
Calorie value (Cal./kg) of 'obesity tissue' lost	7700	7600	7000	7700	8100	7200	7200

Losses of fat. Fig. 1 shows that these were regular and remarkably constant. For instance the fat loss of Miss McN. varied only between an average of 250–305 g/day during the different weeks. This constancy is a reflection of the regularity with which the schedule of walking was maintained, as shown in Table 1.

Losses of protein. It is known that the protein content of the body is not fixed, and that a labile store of protein exists (Whipple, 1956; Holmes, Jones & Stanier, 1954). The size of this store depends partly on the protein content of the diet. To what extent, if at all, it is altered in obesity is unknown. In some obese persons, especially those who are physically active, there appears to be muscular hypertrophy arising out of the need to move the excess body-weight (McCance & Widdowson, 1951). Thus, when people gain or lose fat, some corresponding change in the protein content of the body is to be expected. How much protein it is desirable or permissible for any one obese person to lose is a question which cannot be answered easily.

For the most part the diet contained about 4 g N/day (equivalent to about 25 g protein). In the 1st week the loss of N was usually large and balances varied from −4 to −9 g N/day, indicating daily losses of from 25 to 60 g protein. The loss of weight in this week was always high and associated with large losses of water. However, in the different subjects, there was no relation between the weight loss and the size of the negative N balance.

In subsequent weeks the net N losses were reduced, but there was no indication that any of the subjects would reach equilibrium on a dietary intake of 4 g/day. Fig. 2

Table 3. *Mean daily measurements of changes in body-weight, energy balance and nitrogen balance, and the estimated changes in body water of seven patients on the regimen*

Subject	Period (days)	Weight change (g)	Energy exchange: Expenditure (Cal.)	Energy exchange: Intake (Cal.)	Nitrogen: In diet (g)	Nitrogen: Urinary (g)	Nitrogen: Faecal (g)	Calculated change in body water (g)
Mr I.	7	−400	3250	440	4·1	8·4	1·1	−79
	14	−371	3260	450	4·3	8·1	1·1	−51
	21	−230	2920	780	16·4*	15·8	0·7	+1
	28	−200	2920	780	17·1*	18·0	1·0	+37
	35	−357	2800	410	4·2	7·7	1·0	−84
	42	−357	2800	440	4·5	6·5	0·9	−93
Mrs R.	7	−700	3200	410	4·2	9·6	1·0	−377
	14	−271	3900	410	4·3	7·3	1·2	+119
	21	−357	3600	410	4·1	7·6	0·8	+2
	28	−329	3340	480	8·4†	9·3	1·0	−4
	35	−43	3290	470	8·3†	8·6	0·7	+264
	42	−629	2890	380	4·1	6·5	0·4	−349
Mrs L.	7	−779	3350	370	3·9	8·5	0·9	−440
	14	−569	3360	400	3·9	7·2	0·8	−236
	21	−163	3200	480	8·5†	8·4	0·5	+131
	28	−161	2630	490	8·8†	8·3	0·3	+68
	35	−203	3120	380	4·0	6·2	0·4	+102
	42	−407	2680	340	3·7	5·5	0·3	−148
Miss McN.	7	−648	3350	410	4·1	10·4	1·7	−305
	14	−348	3320	360	3·8	8·1	0·5	−13
	21	−308	3280	380	4·0	6·1	0·8	+14
	28	−366	3210	380	3·8	5·5	0·7	−53
	35	−300	3010	390	3·9	5·3	0·7	−11
	42	−179	3051	810	12·7‡	9·3	0·6	+53
Miss B.	7	−600	2200	390	3·9	8·9	0·8	−386
	14	−240	2810	370	3·8	7·8	0·7	+38
	21	−243	2960	350	3·5	6·7	0·3	+50
	28	−276	2950	380	3·8	6·2	0·3	+10
	35	−203	3250	400	3·8	5·3	0·4	+110
	42	−300	2940	370	3·8	5·9	0·4	−14
Miss M.	1–5	−931	3530	360	4·1	9·5	0·4	−569
	6–10	−499	3330	360	4·0	8·6	0·6	−162
	11–15	−272	3400	360	4·0	7·4	0·3	+68
	16–20	−79	3270	410	4·0	5·8	0·9	+238
	21–25	−341	3350	410	3·8	5·1	0·8	−17
	26–30	−454	3360	430	10·9§	9·9	0·8	−140
	31–35	−148	3140	440	4·3	4·6	0·9	+147
	36–40	−128	3070	950‖	3·9	3·0	1·0	+101
	41–45	−613	2880	410	3·9	4·2	1·1	−343
Mr W.	1–5	−976	3940	400	4·0	12·1	1·3	−583
	6–10	−182	3970	400	3·8	10·3	0·4	+204
	11–15	−440	3770	420	3·9	6·5	1·0	−88
	16–20	−79	3470	1030‖	3·8	5·1	0·1	+177
	21–25	−522	3440	410	3·9	5·7	0·7	−209
	26–30	−454	3500	420	10·9§	11·9	0·3	−135
	31–35	−238	3290	400	10·9§	10·5	0·4	+60
	36–40	−306	3350	420	4·0	10·0¶	0·3	−3

* Diet supplied about: protein 100, carbohydrate 27, fat 30 g/day.
† Diet supplied about: protein 50, carbohydrate 35, fat 15 g/day.
‡ Diet supplied about: protein 80, carbohydrate, 50, fat 30 g/day.
§ 15 g urea given daily.
‖ Diet supplied about: protein 25, carbohydrate 200, fat 10 g/day.
¶ In this patient the loss in body water for the last three periods was calculated on the assumption that the rate of tissue-protein loss was uniform.

The results of giving urea or a high-carbohydrate diet to two patients are recorded here, but will be discussed in another paper.

shows the N balances for three of the subjects. Miss McN. was in positive balance when N intake was raised to over 12 g/day. Mrs L. was only in slightly negative balance when N intake was raised to 8–9 g/day. Miss B. remained in negative balance to the extent of about 2 g/day on an intake of 4 g. The indications are that all of the subjects would have required at least 6–7 g N/day for equilibrium, with a total caloric intake of approximately 400 Cal./day.

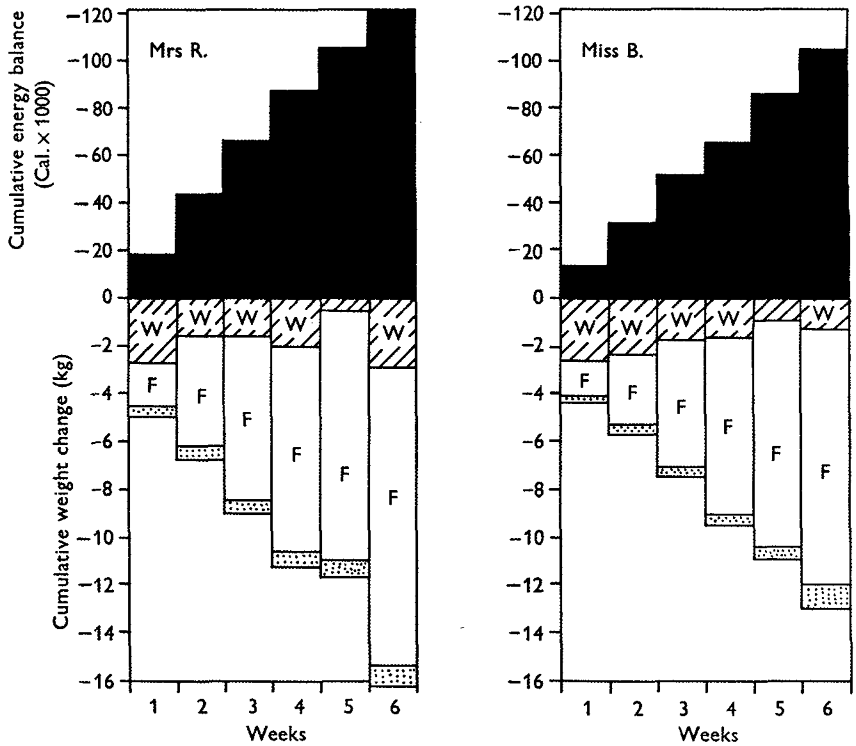

Fig. 1. Energy balance and weight loss of Mrs R. and Miss B. for 6 weeks. The cumulative energy deficit is shown above the zero line. The cumulative weight loss and the relative amounts of water, fat and protein are shown below the zero line for the corresponding periods. The blocks represent cumulative changes—the upper solid blocks, the increasing calorie deficit, and the lower blocks the increasing loss of weight. The weight loss is divided into water, fat and protein losses. W, water; F, fat; stipple, protein.

Table 4 shows the estimated total loss of tissue protein by each subject and also the total intake of protein in the diet. In view of the uncertainty about the extent of the protein stores in obese patients, it might be thought that the larger losses may have led to undue depletion and a consequent fall of serum-albumin levels and retention of water. This point was not investigated, except in Miss B. At the end of the 6 weeks, when her estimated loss of tissue protein was 920 g, her serum-protein concentration was within the normal range (total proteins 7·3 g, albumin 4·8 g/100 ml.) and the electrophoretic pattern was normal.

In other obese patients, not fully reported here, there were marked differences in N excretion. Thus, Mrs D., aged 50, had been almost immobilized for many years by osteo-arthritis and obesity. At a time when she weighed 120 kg, she was given a diet of 400 Cal./day containing 5 g N. For several weeks she lived on this diet and excreted only 5–6 g N daily. On the other hand, T., an active man aged 24, weighing 147 kg, excreted when on a similar diet 12–16 g N daily in the urine for the first 3 weeks. At the end of 5 weeks his daily urinary output of N was still between 8 and 12 g. During this time he took long walks and lost 15·9 kg weight, of which at least 1·5 kg was protein.

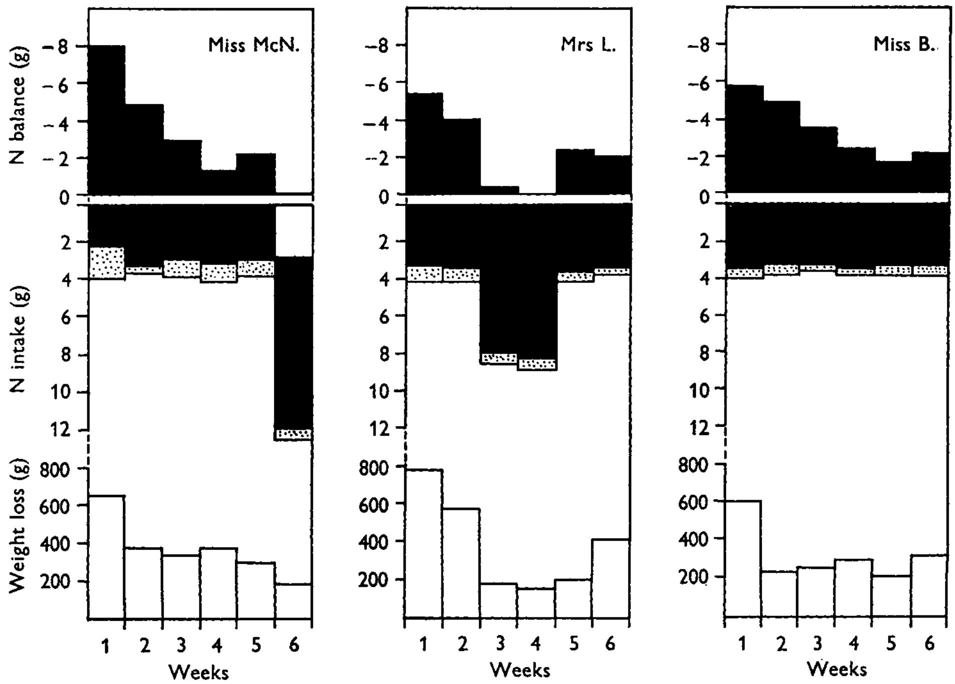

Fig. 2. Mean daily nitrogen balance and weight loss for each week of three subjects. Intake is read from the zero line downwards. Excess of output over intake is shown as the blocked area above the zero. Solid blocks, urinary nitrogen; stippled blocks, faecal nitrogen.

Table 4. *Total dietary protein and estimated loss of tissue protein of seven patients for the 40–45 days of the observation period*

	Dietary protein (g)	Loss of tissue protein (g)
Mr I.	2210	860
Mrs R.	1460	900
Mrs L.	1440	640
Miss McN.	1410	760
Miss B.	990	920
Miss M.	1120	700
Mr W.	980	990

Obese patients vary greatly in their need for dietary protein to maintain N equilibrium and also in the size of the labile protein store. To estimate these factors requires several weeks of detailed study for each patient.

The N balances take no account of two possible sources of error. First, some N will have been lost in the sweat and in the shedding of cutaneous epithelium and the growth of hair. Holmes *et al.* (1954) discuss these losses and point out the impossibility of measuring them accurately. They probably amount to between 1 and 2 g/day. Their omission makes the negative N balance shown in Fig. 2 and the protein losses recorded in Table 3 slight understatements. Secondly, no allowances have been made for a possible fall in the non-protein N in the body fluids. Such a fall would reduce the estimates of body protein lost, but spread over 40 days this error, if indeed it exists, must be very small.

Caloric value of obesity tissue. The variations in water loss alter this value greatly. The overall figure of 7000–8000 Cal./kg of obesity tissue, which was found for all the patients, masks the weekly changes. During the 1st week, when water losses were high, the values were less than 5000 Cal./kg. In subsequent weeks, they were much greater and, when water was being retained, over 10,000 Cal./kg. Keys & Brožek (1953) calculated the change in body composition in a group of mental patients, whose metabolism appeared to be normal during a period of overfeeding. They calculated that the mean calorie value of the obesity tissue gained was 6700 Cal./kg. Subsequently, in a study of young men on a restricted ration, Brožek, Grande, Taylor, Anderson, Buskirk & Keys (1957) reported values for the tissue lost varying between 2600 and 8700 Cal./kg.

Obesity tissue obviously varies in composition in different circumstances. In response to a period of caloric imbalance, the human body does not gain or lose weight by laying down or discarding tissue of fixed chemical composition. The nature of the obesity tissue lost or gained depends upon the previous state of nutrition and perhaps on the amount of physical exercise taken. It will also vary in different subjects. The concept of obesity tissue is useful, and further investigations of the variations in its chemical composition would be valuable.

DISCUSSION

Two main conclusions can probably be drawn from the results. First, at the beginning of treatment, the patients had a labile portion of water (about 2–4 l.) which was readily lost during the first few days on the reducing regimen (initial dehydration). Secondly, after this early loss, subsequent water losses were small and all patients gained water for some period (secondary water retention). This retention of water took place at times when fat and protein continued to be lost.

The initial dehydration may well be due to the change from a mixed diet with a metabolic mixture predominantly derived from carbohydrate to semi-starvation with a metabolic mixture mostly from endogenous fat. It is well known to paediatricians (Holt, 1957) that when infants are transferred from a high-carbohydrate to a high-fat diet they lose weight and this weight is at once regained when the transfer is reversed. These changes are attributable to changes in body-water content. Similar changes may occur in adults. Thus Benedict & Milner (1907) studied one subject doing hard muscular work, whilst living in a calorimeter chamber. For 3 days on a high-carbohydrate diet, with a net caloric value of 4276 Cal./day, the subject gained 184 g in weight, and the measured gain in body water was 496 g. For the next 3 days he continued the same regimen with a high-fat diet (4407 Cal./day). On these 3 days he lost 2741 g in weight, of which 2718 g were shown to be water. Perhaps the adult body may require 2–4 l. more body water whilst metabolizing carbohydrate rather than fat. This hypothesis is consistent with the observations of the great losses of body-weight at the beginning of a period of total starvation (Johansson, Landergren, Sondén & Tigerstedt, 1897; Cathcart, 1907) and the initial loss of weight of the arctic explorer Stefansson and his colleague when they adopted an exclusively meat diet (McClellan & Du Bois, 1930). Kekwick & Pawan (1956) also showed that over periods of 5–7 days obese persons lost most weight on a high-fat diet, but little on an isocaloric high-carbohydrate diet.

Severe starvation does not appear to be necessary for this initial dehydration to occur. An obese patient (not otherwise reported here) Mrs G., aged 50, weight 120 kg, was admitted to hospital and put on a diet providing 1980 Cal./day. For a week she seldom left the ward and spent most of her time in bed: yet she lost 1·69 kg weight, of which 1·05 kg was estimated to be water. Shorvon & Richardson (1949) have studied patients with obesity associated with severe psychological disturbances. They found that after psychotherapy there might be a sudden loss of weight (5–10 kg) without any dietary treatment, and suggested that the 'tension' associated with psychological strains may have led to the accumulation of excess quantities of water, which were rapidly eliminated when the 'tension' was relieved by treatment. It is possible that loss of water is a frequent reaction of the body to any sudden change in either physical environment or psychological state. Differences between the temperature in the hospital ward and in the patients' homes cannot be excluded as a factor which might have contributed to the initial dehydration. But we have no reason to suppose that these differences were either large or important.

Secondary water retention occurring in obese patients on a reducing regimen might be of similar origin to the water retention that occurs in normal people during chronic semi-starvation giving rise to famine oedema. Famine oedema has a large literature, which has been reviewed by McCance (1951). The oedema is due to accumulation of extracellular fluid, the cause of which is not known. McCance concludes that there is no evidence that the oedema arises as a result of renal failure or hormonal disturbance. A low level of serum albumin can be at most a contributory factor. Youmans, Wells, Donley & Miller (1934) first suggested that when there is tissue wasting, after a time the elasticity of the skin is not sufficient to maintain the tissue tension. The body may become 'too small for the skin' and water may be retained to keep up the normal tension. Unfortunately, experimental support for this hypothesis is hard to obtain owing to the difficulties of getting true readings for tissue tensions. It might well be that the laxity of the skin after an initial loss of weight in the obese leads to a fall in tissue tension and subsequent retention of water.

The changes in total body water are brought about by variations in fluid intake and in fluid excretion both by the kidneys and in the evaporative water loss. We have measured the total intake of water and the output through the various channels in five of the patients. The results, together with the sodium and potassium exchanges will be presented in a subsequent paper.

SUMMARY

1. The chemical composition of the tissue lost by seven obese patients on a reducing regimen has been calculated.

2. Over a period of 6 weeks fat formed 73–83 % of the weight lost, protein 4–7 % and water 10–23 %.

3. In the first few days on the regimen each patient lost large amounts of body water, up to 2–4 l. (initial dehydration). Subsequently, water losses were much reduced and each patient was found to be retaining water for periods lasting several days (secondary water retention).

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