CALORIE INTAKE IN RELATION TO BODY-WEIGHT CHANGES IN THE OBESE

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MANY different types of diet have been successfully used to reduce weight in those considered obese. The principle on which most of them are constructed is to effect a reduction of calorie intake below the theoretical calorie needs of the body. Experience with these patients has suggested, however, that this conception may be too rigid. Many of them state that a very slight departure from the strict diet which can hardly affect calorie intake, results in them failing to lose weight for a time. Though it is realised that evidence from such patients is notoriously inaccurate owing to their approach to this particular condition, it is too constant a belief among them to be entirely discarded.

Furthermore, most of the diets in common use not only restrict the intake of calories but also radically alter the proportions provided by protein, fat, and carbohydrate. In this country a healthy sedentary person may be supposed to consume some 2200 calories daily, made up of about 70 g. of protein, 60 g. of fat, and 350 g. of carbohydrate: protein supplies 12% of the calories, fat 24%, and carbohydrate 64%. On most reducing diets, however, the carbohydrate and fat will be restricted while the protein remains about the same; and in a diet yielding 1000 calories protein may provide 30%, fat 37%, and carbohydrate 33%.

Finally, Lyon and Dunlop (1932) observed that patients on isocaloric reducing diets lost weight more rapidly when the largest proportion of the calories was supplied by fat than when it was supplied by carbohydrate. Anderson (1944) attributed these findings to the different amounts of salt (causing water retention) in the diets used by these workers. More recently, Pennington (1951, 1954) has recommended high-fat diets in the treatment of obesity. It therefore seemed important to establish which factor has the greater effect—restriction of calories, or alteration in the proportions of protein, fat, and carbohydrate in the diet.

Materials and Methods

The subjects selected for our study were definitely obese. It has been debated whether an increase of weight above that laid down in normal height-weight charts is a satisfactory criterion of obesity, and other definitions have been suggested; but all the persons chosen for the present investigation were manifestly obese, and this description could not have been questioned either by skilled or by lay observers. All had weights more than 35% above the standard weight for height according to the tables compiled by the Metropolitan Life Insurance Company (1942, 1943).

All were admitted to hospital and allowed a moderate amount of exercise in the ward. During the first few days after admission they lost weight even when given free choice of food (fig. 1). This observation has been made before (Newburgh 1942), and therefore a period of stabilisation was arranged to precede our studies. After that period their daily weight became relatively stable, and at this point all were placed on one or other of three series of diets prepared by Miss Wilkinson Hughes, chief dietitian to the Middlesex Hospital. These diets were drawn up from the tables of McCance and Widdowson (1946), and in every case aliquot samples of all the diets were turmixed and analysed. The results agreed within 10% with those in the tables.

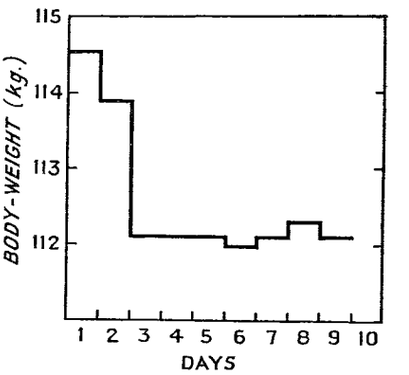


Fig. 1—Loss of weight on full diet soon after admission to hospital.

Diets of Series 1

In the first series the proportions of protein, carbohydrate, and fat were kept constant and the intake of calories was varied. In all of them protein supplied about 20%, fat 33%, and carbohydrate 47% of the calories. The water in the diet was determined and a supplement of water given to each patient to make 3000 ml. per day. The same procedure was adopted with sodium chloride, which totalled 10 g. per day. For periods of 7–9 days the patients were kept on either 2000 calories, 1500 calories, 1000 calories, or 500 calories per day (fig. 2). Six patients were studied in this way, each patient having each diet for 7–9 days, and a definite relation was found to exist between the deficiency of calories and the amount of weight lost.

Diets of Series 2

The final proof that the amount of weight lost depends directly on the deficiency of calories should be adduced by observing a constant loss of weight in each patient whose calorie intake is constant regardless of the type of food making up the diet.

Fourteen patients were put on diets in which the calorie intake was kept constant at 1000 a day and 90% of it was provided in turn by carbohydrate, fat, or protein. Measured amounts of water and of sodium chloride were again added to each diet to make up an intake of 3000 ml. of water and 10 g. of sodium chloride per day (fig. 2). So different were the rates of weight-loss on these isocaloric diets that the composition of the diet

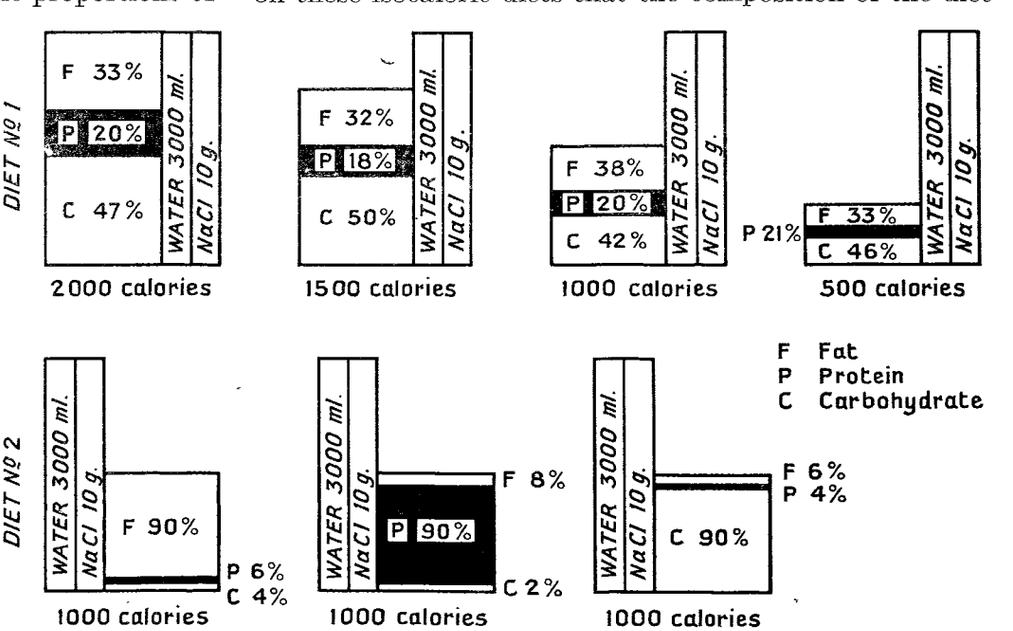


Fig. 2—Composition of diets of series 1 and 2.

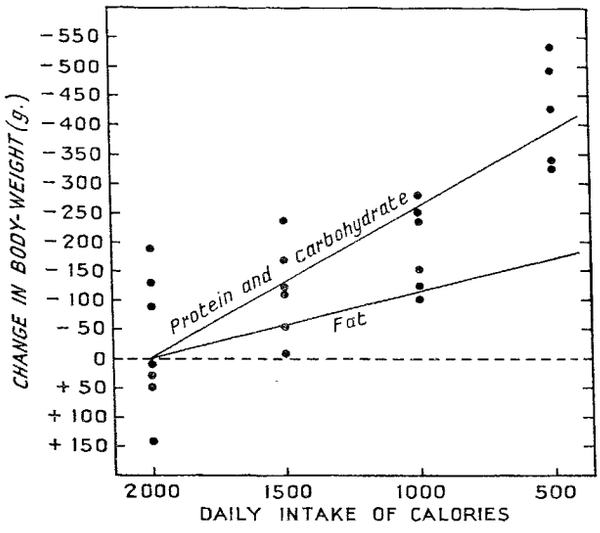


Fig. 3—Daily changes of weight in 6 patients (means of 7-9 days on each diet).

appeared to outweigh in importance the intake of calories.

Diets of Series 3

In order to confirm this point a third series of patients was studied who were put on to 2000-calorie diets of normal proportions to show that their weight could be maintained while in hospital at this level and then placed on high-fat, high-protein diets providing 2600 calories per day. It was demonstrated that these patients on the whole could maintain or gain weight on 2000 calories but except in one instance, lost weight consistently on a 2600 daily calorie intake.

During these periods the patients were weighed daily and in some of them balance studies were carried out in respect of water, nitrogen, fat, sodium, chloride, and potassium. Total body-water and the basal metabolic rate (B.M.R.) were estimated weekly or at the end of the period on each diet. The methods employed for these estimations have already been listed (Kekwick and Pawan 1953).

In such a study the difficulties are formidable. The first and main hazard was that many of these patients had inadequate personalities. At worst they would cheat and lie, obtaining food from visitors, from trolleys touring the wards, and from neighbouring patients. (Some required almost complete isolation.) At best they coöperated fully but a few found the diet so trying that they could not eat the whole of their meals. When this happened the rejected part was weighed, and the equivalent calories and foodstuffs were added to a meal later in the day. The results we report are selected, a considerable number of known failures in discipline being discarded.

Another factor of importance which could not be eliminated was that many patients were women, in whom the retention and the losses of water associated with the menstrual cycle affected the daily weight and the estimation of total body-water. We were surprised to find how great such factors could be, amounting in one woman to the retention of more than 3 litres of water.

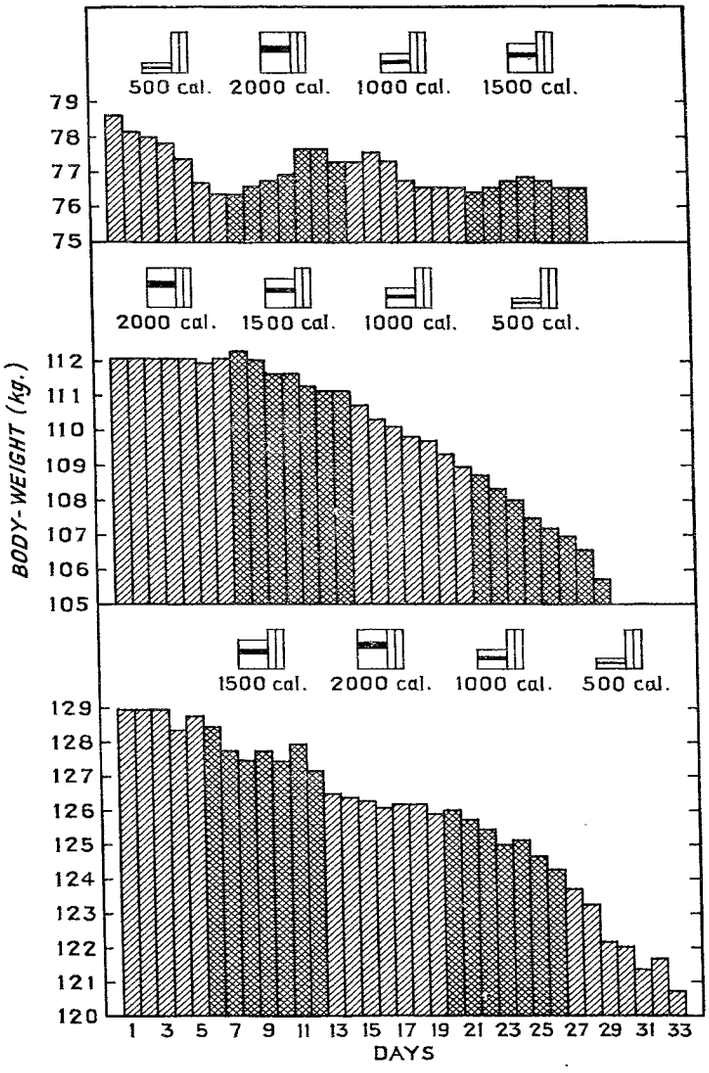


Fig. 4—Loss of weight in 3 patients on diets of series I given in different order.

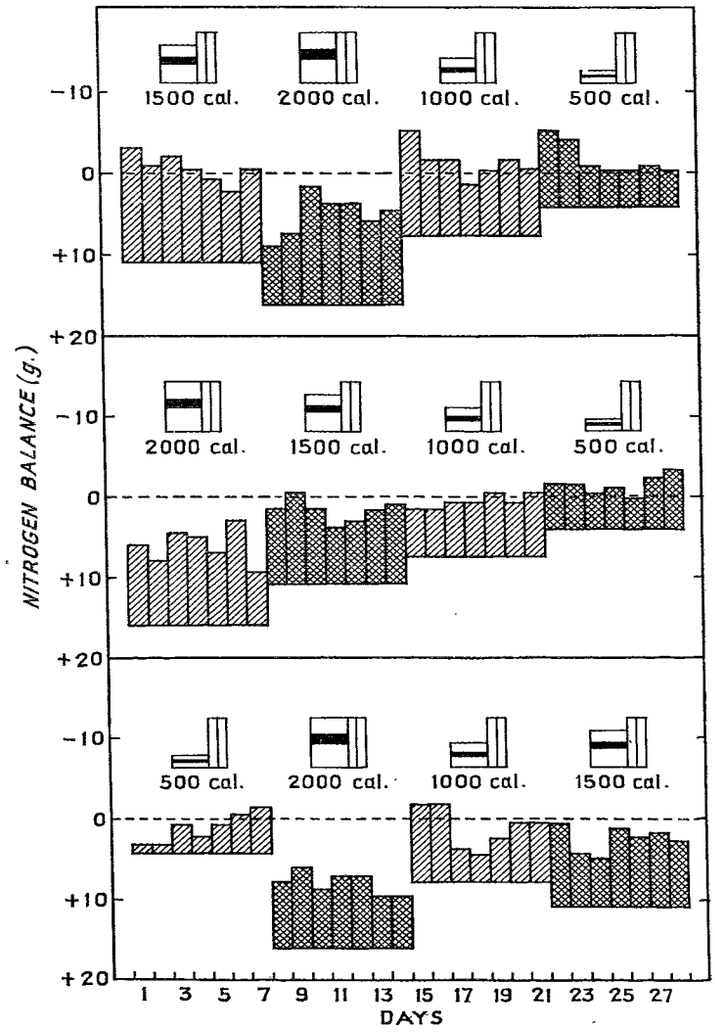


Fig. 5—Nitrogen-balances of 3 patients on diets of series I.

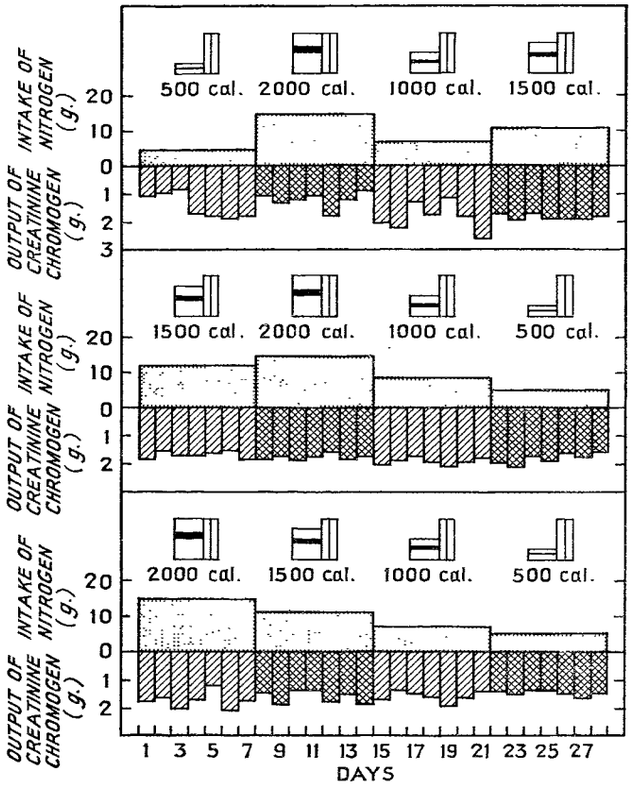


Fig. 6—Intake of nitrogen and urinary output of " creatinine chromogen " of 3 patients on diets of series 1.

Results

Diets of Series 1

If weight-loss in the obese is merely the result of a deficiency in calorie intake below a constant requirement, the effect of these diets should be that, when the loss of weight is plotted against the intake of calories, the resulting graph is a straight line unless obscured by changes in total body-water (Newburgh 1942). If 2000 calories are expended and only 1500 calories are consumed, there is a daily deficiency of 500 calories; and this deficiency represents 125 g. of carbohydrate or protein or about 55 g. of fat. If only 1000 calories are consumed, there is a daily deficiency of 1000 calories—250 g. of protein or carbohydrate or 110 g. of fat. Fig. 3 illustrates two theoretical lines showing this relationship if the loss is in terms of carbohydrate and protein on the one hand or fat on the other. The plotted points are the actual losses seen in these patients. Fig. 4 shows that, in three patients, this loss of weight was independent of the order in which the diets were given. The type of diet during any period is represented at the top of each figure as a miniature of the diagram in fig. 2.

Protein is not, however, lost during these dietary periods. Fig. 5 shows the nitrogen balances carried out on three patients during these periods. It is clear that nitrogen output closely follows intake; the patients remaining in approximate nitrogenous equilibrium. Fig. 6 shows that the urinary excretion of " creatinine chromogen " remained approximately constant regardless of the intake of nitrogen—which suggests that there was no significant alteration in the breakdown of endogenous protein on the different diets. Any minor deviations from equilibrium were quite insufficient to account, in terms of protein, for the weight lost.

TABLE I—CHANGES IN BODY-WEIGHT AND TOTAL BODY-WATER IN 5 PATIENTS ON DIETS OF SERIES 1

Initial body-weight (kg.)	Initial body-water (litres)	Initial body-water as % of body-weight	Period of study (days)	Final body-weight (kg.)	Final body-water (litres)	Final body-water as % of body-weight
78·6	40·4	51	29	76·9	38·6	51
116·3	59·4	51	28	112·6	58·3	52
127·7	63·5	50	28	119·7	61·5	51·5
110·6	56·7	51	21	105·7	54·8	52
117·7	61·8	52·5	21	113·2	57·0	50
Total 550·9	281·8	..	..	527·2	270·2	..

Alternatively it is unlikely that the patients became depleted of carbohydrate reserves. These reserves are small and could not account for the amount of weight lost (Soskin and Levine 1950).

Loss of weight may be the result of losing " available " body-water. This term means total body-water, which was measured by the urea-dilution method of McCance and Widdowson (1951) with the precautions previously described by Pawan (1954) and is probably a measure of intracellular fluid, extracellular fluid, and circulatory fluid. Table I shows for these patients the initial body-weights and the measurements of the total available body-water. It will be noted (column 3) that in all the patients the available water initially represented 50–52·5% of the body-weight. By the end of about four weeks on the diets the proportion of body-water to weight remained the same (50–52%) (column 7). During the intervening periods the five patients had lost 23·7 kg. of body-weight (column 1–column 5) and apparently 11·6 litres of available body-water. During these periods of weight reduction the total available body-water was apparently kept in constant relationship with body-weight. On these diets only about half the weight lost could be accounted for in terms of body-water.

Four patients were studied at the beginning and end of the week when the loss of weight was greatest—i.e., on 500 calories per day. Table II shows that the scatter is much greater, but this is because in one patient (marked with an asterisk in the table) the period on 500 calories coincided with the retention of body-water associated with the menstrual cycle. In the four as a whole, however, the total loss was 12 kg. in body-weight and 4 litres of available body-water—a proportion very similar to that given above. The assumption therefore is that, over the period of observation, 33–50% of the weight-loss of these patients on these diets was loss of available body-water and the remaining 50–67% was probably loss of fat.

TABLE II—LOSS OF BODY-WEIGHT AND TOTAL BODY-WATER IN 4 PATIENTS ON 500-CALORIE DIET FOR 7 DAYS

Loss of weight (kg.)	Loss of body-water (litres)	% loss of weight as body-water
3·9	1·4	36
2·3	0·8	35
2·3	1·3	56
3·5	0·5	14 *

* See text.

Diets of Series 2

It has been argued above that, if deficiency of calories alone accounts for loss of weight in the obese, diets of equal calorie value should produce the same loss of weight in the same patient, no matter what the composition of the diet. Manifestly they do not, as can be seen in the patients on diets of series 2. Fourteen patients were each given diets all containing 1000 calories per day, but during one period 90% of the calories was given as carbohydrate, during another as fat, during another as protein, while during a fourth a diet of normal proportions was given. Fig. 7 shows the daily losses of weight during these periods. It will be seen that weight was lost rapidly when 90% of the calories was given as fat or as protein, but that weight could be maintained during these brief periods when 90% of the calories was given as carbohydrate. Fig. 8 shows the detailed weight changes in three patients to illustrate that the order in which the diets were given did not matter.

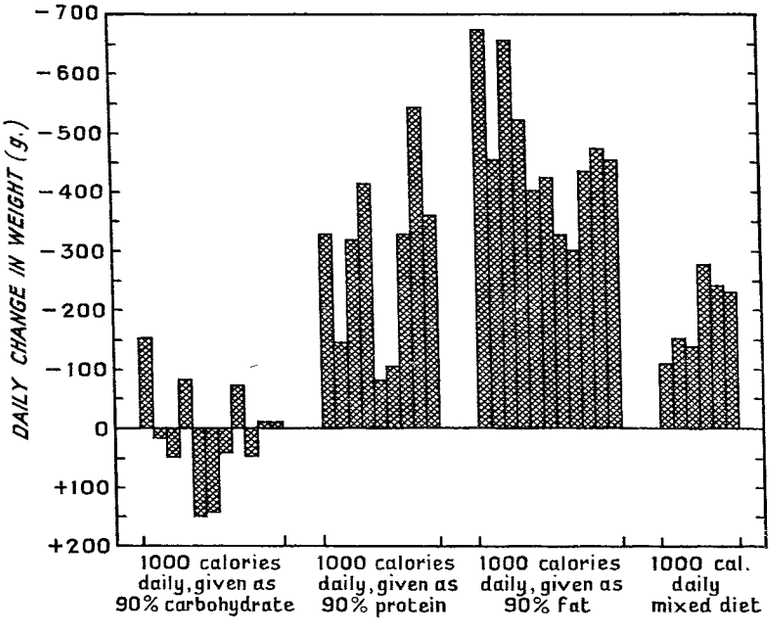


Fig. 7—Daily changes of weight of patients on 1000-calorie diets of different composition (mean of 5-9 days on each diet).

The first and obvious explanation is that the patients failed to absorb either the protein or the fat in the diets. Fig. 9 shows the nitrogen balance in three patients and demonstrates that approximate nitrogenous equilibrium is maintained. There was retention of nitrogen during the periods of large intake of nitrogen. Fig. 10 shows that the urinary excretion of "creatinine chromogen" was independent of the intake of nitrogen. It therefore seems that there was no lack of absorption of the dietary nitrogen, nor any large change in the breakdown of endogenous protein.

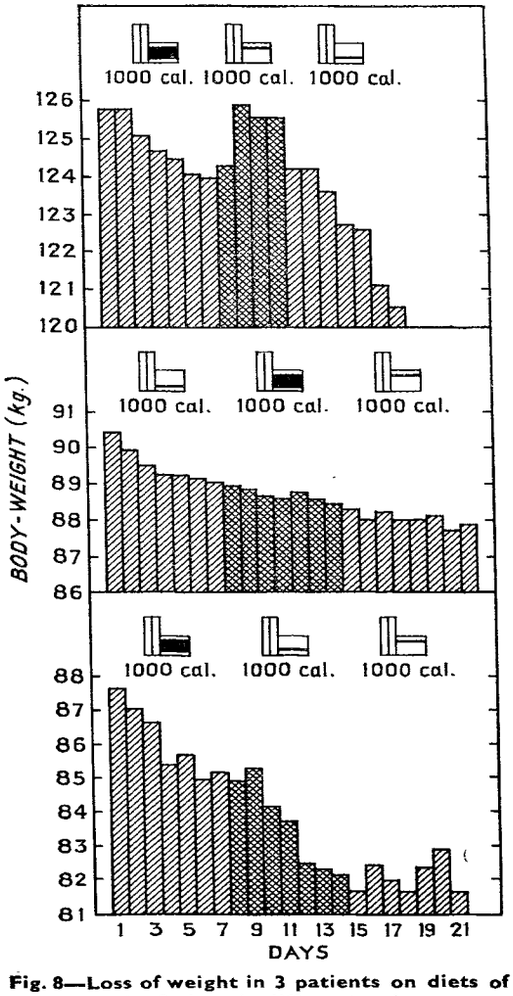


Fig. 8—Loss of weight in 3 patients on diets of series 2 given in different order.

Table III shows the fat-balances in eight patients during the periods on the high-fat diets. In view of the large percentage of fat absorbed (column 3) there is no reason to suppose that the loss of weight in these patients was due to inadequate absorption.

Measurement of available body-water displays the same phenomenon as in the first series of patients (table IV). The range of proportions of total body-weight and total body-water was of the same order but somewhat wider (column 3). It can be seen that in any individual patient the proportion of body-water to body-weight remained surprisingly constant throughout the period of study. The twelve patients in whom these measurements were made lost 51·3 kg. of body-weight and 18 litres of available body-water (35%). Table V shows the losses of body-weight and body-water in patients on the high-fat and the high-protein diets. The high-carbohydrate diets are excluded because changes in body-weight and body-water were negligible during this period. Once again it appears that, of the total weight lost, 41–52% was in the form of available body-water and the remaining 48–59% probably in the form of body-fat.

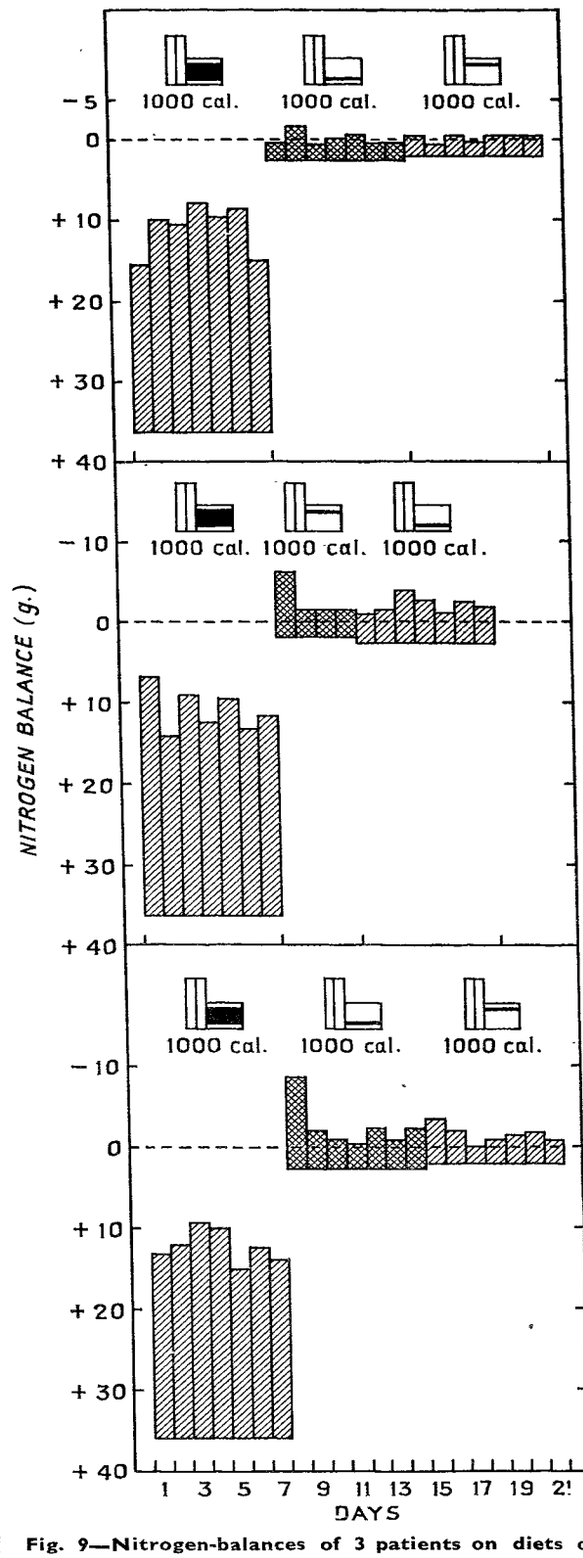


Fig. 9—Nitrogen-balances of 3 patients on diets of series 2.

Diets of Series 3

It seems that the qualitative composition of the diet has a profound effect on weight-loss in the obese when the intake of calories is already deficient. The extent of these changes suggests that this may be an important factor in the dietetic therapy of obese patients. It was decided to test this idea in another way. Five obese patients were put on a 2000-calorie diet containing a normal proportion of protein, fat, and carbohydrate. During a period of 7 days it was shown that they either maintained their weight or gained a little. The number of

TABLE III—FAT-BALANCE IN 8 PATIENTS ON HIGH-FAT DIETS OF SERIES 2

Total intake of fat (g.)	Fæcal fat (g.)	Fat absorbed (%)
686	23·0	97
686	26·1	96
686	23·6	97
882	24·0	97
686	32·0	95
686	26·0	96
686	22·0	97
598	18·0	97

calories was then increased in the same patients to 2600 per day, but the proportions of the diets were altered by increasing the amount of fat and protein and reducing that of carbohydrate. Table VI shows that four of the five patients lost weight although the calories were much increased. Table VII shows the measurements of available body-water during these periods, and the same phenomenon appears as described above: 30–50% of the weight lost was shed as available body-water.

Discussion

If these observations are correct, there seems to be only one reasonable explanation—namely, that the composition of the diet can alter the expenditure of calories in obese persons, increasing it when fat and protein are given, and decreasing it when carbohydrate is given. This is not surprising as regards protein, whose specific dynamic action has long been recognised. It is, however, surprising as regards fat, whose action in this respect seems to be even greater than that of protein.

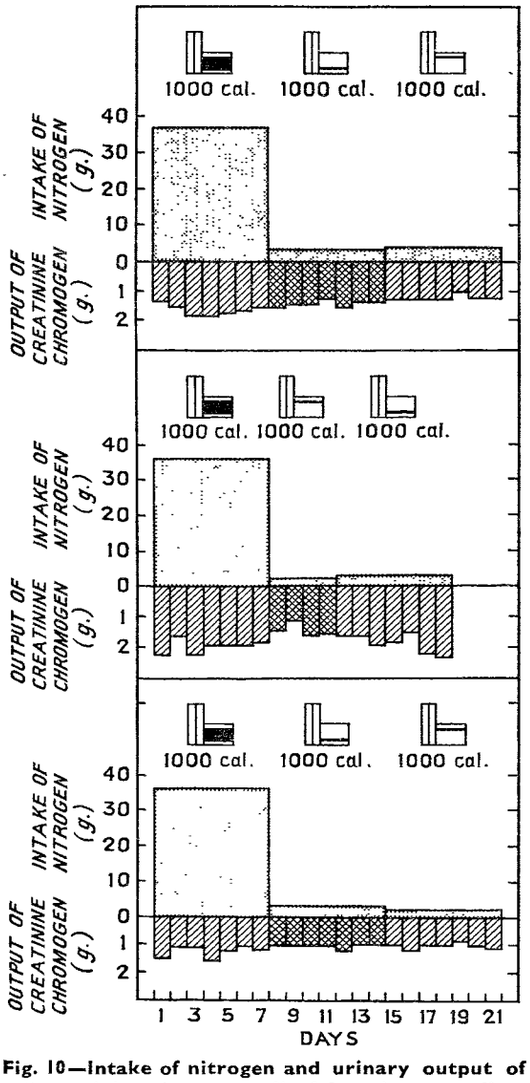


Fig. 10—Intake of nitrogen and urinary output of "creatinine chromogen" of 3 patients on diets of series 2.

Direct confirmation of such altered metabolism is hard to obtain. The B.M.R., for example, is measured at a time of day and under other conditions specifically designed to eliminate the effect of diet or reduce it to a minimum. In some patients the B.M.R. was measured at the beginning and at the end of each dietary period. Table VIII shows that neither variation in calories nor variation of the composition of the diet with a constant intake of calories significantly changed the B.M.R. during these short dietary periods.

TABLE IV—CHANGES IN BODY-WEIGHT AND BODY-WATER IN 12 PATIENTS ON DIETS OF SERIES 2

Initial body-weight (kg.)	Initial body-water (litres)	Initial body-water as % of body-weight	Period of study (days)	Final body-weight (kg.)	Final body-water (litres)	Final body-water as % of body-weight
79·6	44·4	56	20	72·8	44·1	61
87·7	51·8	59	21	81·7	49·0	60
127·7	59·2	47	18	120·9	57·7	48
121·3	62·6	52	14	117·1	60·8	52
116·4	64·4	55	16	114·6	65·2	57
68·2	51·7	75	23	64·0	49·4	77
94·1	51·6	55	21	90·5	52·1	58
89·7	49·0	55	21	86·7	47·4	55
100·2	50·1	50	13	96·6	47·6	50
93·1	49·6	53	16	89·6	47·9	53
100·5	43·7	43	15	96·8	40·6	43
100·9	39·5	39	12	96·8	37·8	39
Total 1179·4	617·6	..	..	1128·1	599·6	..

As the insensible loss of water from the skin and respiration in some of these patients was being measured in an attempt to determine water-balances accurately, it was considered that this might provide some indirect index of general metabolic rate, as suggested by Benedict and Root (1926) and Johnston and Newburgh (1930).

TABLE V—LOSS OF BODY-WEIGHT AND TOTAL BODY-WATER IN 14 PATIENTS ON HIGH-FAT DIET OF SERIES 2; 7 ON HIGH-PROTEIN DIET OF SERIES 2 FOR 5–9 DAYS

On high-fat diet		On high-protein diet	
Loss of body-weight (kg.)	Loss of body-water (litres)	Loss of body-weight (kg.)	Loss of body-water (Litres)
3·2	0·5	2·5	0·6
0·6	0·1	3·8	1·2
3·0	2·1	0·3	0·2
3·2	0·6	1·6	1·5
2·2	0·2	0·4	0·2
1·6	0·9	2·0	1·7
2·3	1·4	1·3	0·8
1·5	0·4		
2·9	1·5	Total 11·9	6·2
2·8	1·6		
2·0	1·3		
2·4	1·3		
2·4	1·1		
2·6	0·6		
Total 32·7	13·6		

Measurements were made by weighing the patient at intervals of one hour on scales specially constructed for this purpose by Messrs. W. & T. Avery Ltd. which are sensitive to 2 g. over the range of weights concerned. During these hours no food was taken and neither urine nor fæces voided, and errors due to temperature, activity,

TABLE VI—WEIGHT CHANGES IN 5 PATIENTS DURING PERIODS ON NORMAL 2000-CALORIE DIET AND ON HIGH-FAT 2600-CALORIE DIETS OF SERIES 3

Case no.	Daily calories	Initial body-weight (kg.)	Final body-weight (kg.)	Period of obs. (days)	Change in body-weight (kg.)
1	2600	94·3	93·0	6	−1·3
	2000	93·0	93·7	5	+0·7
	2600	93·7	91·8	9	−1·9
2	2000	81·9	82·4	7	+0·5
	2600	82·4	80·9	8	−1·5
	2000	80·9	81·1	8	+0·2
3	2600	111·9	109·3	14	−2·6
	2000	109·3	109·3	8	±0
	2600	109·3	107·7	8	−1·6
4	2000	111·6	111·2	8	−0·4
	2600	111·2	111·3	4	+0·1
5 *	2600	93·5	92·5	10	−1·0
	2000	88·5	90·3	7	+1·8

* Intermediate period between 2 observations put on 2000-calorie high-fat diet on which weight dropped from 92·5 to 88·5 kg.

TABLE VII—CHANGES IN BODY-WEIGHT AND IN BODY-WATER IN 5 PATIENTS ON NORMAL 2000-CALORIE DIET AND HIGH-FAT 2600-CALORIE DIETS OF SERIES 3

Normal 2000-calorie diet		High-fat 2600-calorie diet	
Change of body-weight (kg.)	Change of body-water (litres)	Change of body-weight (kg.)	Change of body-water (litres)
−0·7	−0·2	−1·3	−0·6
−0·5	+0·1	−1·9	−0·6
−0·2	−0·1	−1·5	−1·2
±0	−0·1	−2·6	−1·3
−0·4	−0·5	+0·1	±0
−1·8	+0·2	−1·0	+0·7
Total −2·8	±0·0	−8·2	−3·0

and air draughts were avoided as far as possible. Fig. 11 shows that insensible loss varies in a single patient during the day but it remains fairly constant from day to day. Fig. 12 shows the effect of isocaloric diets on the hourly insensible loss in one patient, and fig. 13 the mean figures in three patients. All three patients showed the same tendency to increase insensible loss on increased intake of protein and fat. The rate of insensible loss appears to be much affected by the type of food, provided that the water and sodium intakes are kept constant throughout the period of observation; whether this increased rate of insensible loss is a measure of bodily metabolic activity must remain in question. Even if metabolic activity cannot be measured directly, the difference in weight responses seen with these diets does not seem to be completely due either to an altered state of hydration or to a simple deficiency of calories. We suggest that the rate of katabolism of body-fat may alter in response to changes in the composition of the diet.

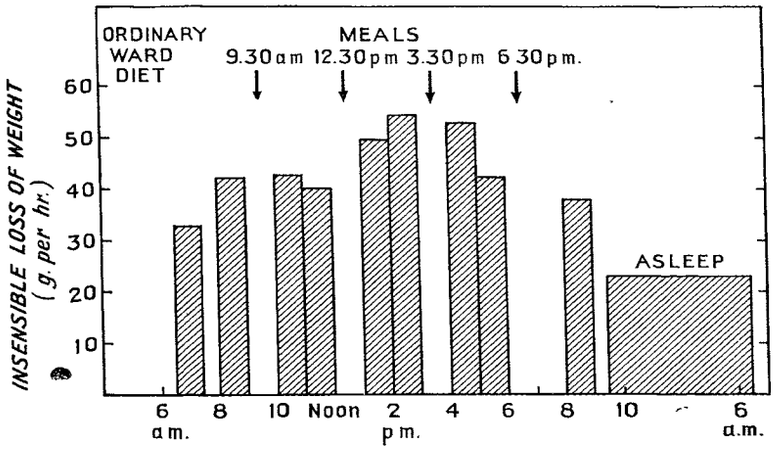


Fig. 11—Relation of insensible loss of weight to time of day (mean of 2 days).

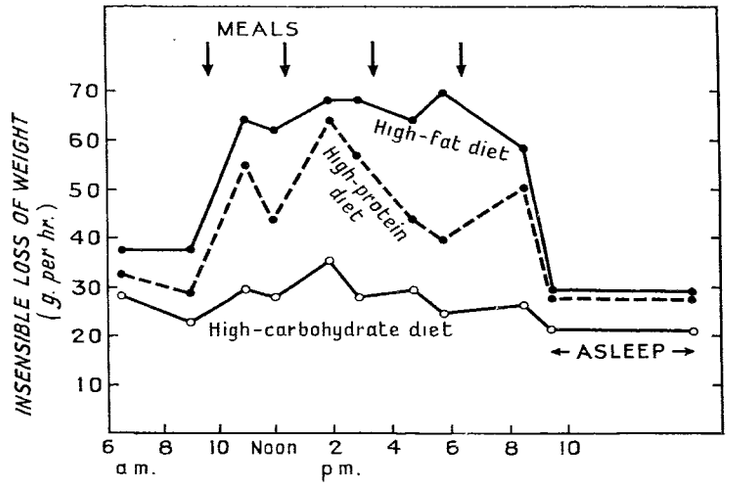


Fig. 12—Relation of insensible loss of weight to dietary intake.

Summary

1. Loss of weight can be successfully achieved in obese patients by numerous diets, most of which restrict calorie intake. At the same time almost all such diets alter the proportion of protein, carbohydrate, and fat as compared with the normal, restricting carbohydrate and fat in particular. It seemed desirable to investigate which factor was of the greatest importance in weight reduction—calorie restriction or alteration in the composition of the diet.

2. The rate of weight-loss has been shown to be proportional to the deficiency in calorie intake when the proportions of fat, carbohydrate, and protein in the diet are kept constant at each level of calorie restriction.

3. When calorie intake was constant at 1000 per day, however, the rate of weight-loss varied greatly on diets of different composition. It was most rapid with high-fat diets; it was less rapid with high-protein diets; and weight could be maintained for short periods on diets of 1000-calorie value given chiefly in the form of carbohydrate.

4. At a level of intake of 2000 calories per day, weight was maintained or increased in four out of five obese

TABLE VIII—CHANGES IN B.M.R. (ROBERTSON-REID STANDARDS) IN PATIENTS ON DIETS OF SERIES 1 AND 2

	Diets of series 1			
	2000 calories	1500 calories	1000 calories	500 calories
Change in B.M.R.	+6 +9 −4 −3 −4 +8 +2 +2	0 +5 0 −4 +2 +3	+4 −1 +6 −8 +9 +7 −14 +11 −3	+2 0 +3 +5 −3 +7 +1

	Diets of series 2 (1000 calories)		
	High-fat	High-protein	High-carbohydrate
Change in B.M.R.	0 −3 −3 +4 −11 +1 −2 −2 +2 +5	−2 +3 +4 −1 +2 −11 −9 +6	+3 0 +2 0 +5 +5 +15 −1 −5 +2

Each figure represents the difference between the two B.M.R. readings; one at the beginning and the other at the end of the dietary period.

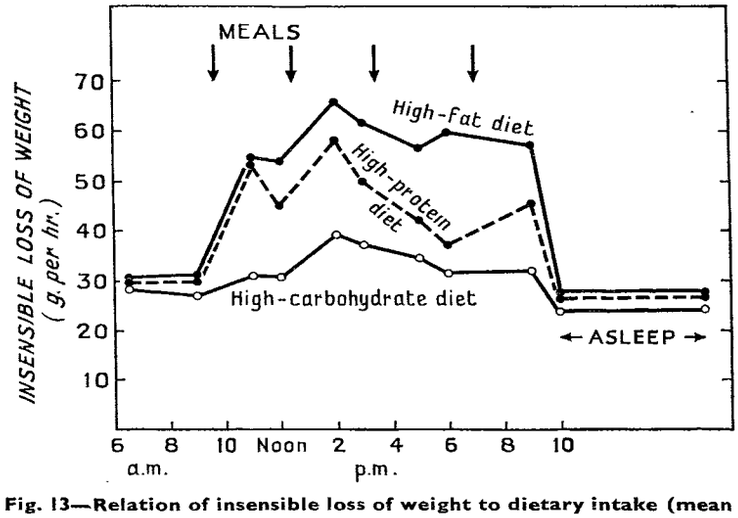


Fig. 13—Relation of insensible loss of weight to dietary intake (mean of 6 measurements made on 3 patients, 2 measurements being made on each patient on separate days in each dietary period).

patients. In these same subjects significant weight-loss occurred when calorie intake was raised to 2600 per day, provided this intake was given mainly in the form of fat and protein.

5. No defect in absorption of these experimental diets occurred to account for the weight-loss. There was neither loss of body-protein stores nor of carbohydrate stores to a degree which significantly contributed to the reduction in weight.

6. The weight lost on these diets appeared to be partly derived from the total body-water (30–50%) and the remainder from body-fat (50–70%).

7. As the rate of weight-loss varied so markedly with the composition of the diets on a constant calorie intake, it is suggested that obese patients must alter their metabolism in response to the contents of the diet. The rate of insensible loss of water has been shown to rise with high-fat and high-protein diets and to fall with high-carbohydrate diets. This supports the suggestion that an alteration in metabolism takes place.

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VENO-OCCLUSIVE DISEASE OF THE LIVER

ESSENTIAL PATHOLOGY

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SEVERAL diseases of the liver, though of different pathogenesis, possibly have a common factor—e.g., undernutrition. Such are kwashiorkor and marasmus, veno-occlusive disease, and vomiting sickness (acute toxic hypoglycæmia).

Our observations on Jamaican children for more than six years confirm early reports (McFarlane and Branday 1945, Royes 1948) that infantile fibrosis and cirrhosis of the liver are common in Jamaica.

Liver-biopsy studies on infants and children—occasionally with multiple follow-ups in the same patient—have enabled us to trace the morphogenesis of what appears to be the commonest type of fibrosis and cirrhosis (Bras et al. 1954) and led us to suggest the name veno-occlusive disease. Since then 23 of these patients have come to necropsy, and we feel that a recapitulation of the essential pathological findings is indicated.

Clinical Picture

As reported earlier, the children appear to be somewhat stunted, and the major signs are ascites and hepatomegaly. These characteristics are at present under intensive study by the pædiatric department of the University College Hospital. Veno-occlusive disease of the liver has been subdivided into three clinical stages : the acute stage, largely characterised by acute ascites and hepatomegaly ; the subacute stage ; and the chronic stage, characterised by cirrhosis of the liver (Hill et al. 1953, Jelliffe et al. 1954).

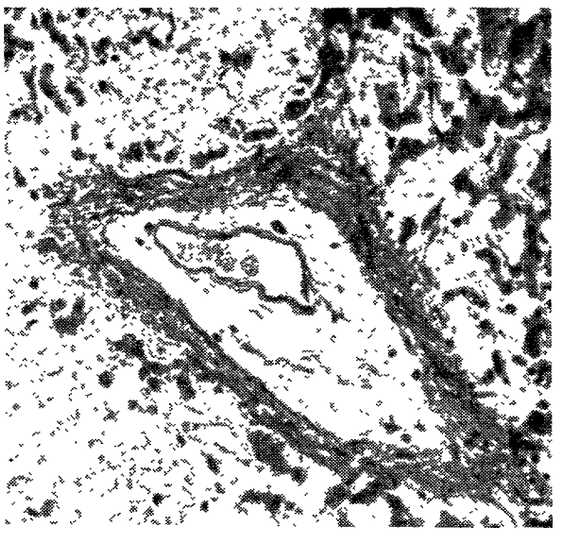


Fig. 1—Acute subendothelial swelling in branch of hepatic vein. (Periodic-acid Schiff stain. × 146.)

Veno-occlusive disease of the liver has been predominantly seen in children, usually aged 2–5 years. The youngest child observed so far was aged 7 months. Adults, however, have also presented with the same picture (Stuart and Bras 1955). In the Caribbean area veno-occlusive disease of the liver has been observed in Jamaica and in Barbados (Stuart and Bras 1956).

Morbid Anatomy

Liver

In the *acute stage* the essential findings are blockage of the small hepatic veins, the medium-sized veins being somewhat affected and the larger veins being essentially free from lesions. The blockage is a result of a subendothelial swelling of the intimal tissues, at first apparently mainly consisting of œdema (fig. 1) but becoming organised later (fig. 2). It has been suggested that this swelling may represent either acute exudation of œdematous fluid in the subendothelial tissues or (less likely in our opinion) a deposition of blood (plasma) constituents which has become overdrawn by endothelium—i.e., a " Duguid lesion " (Bras et al. 1954, Bras and Watler 1955). The block is followed by massive centrolobular congestion, and the macroscopic appearance in this stage is like that of a " nutmeg " liver (figs. 3

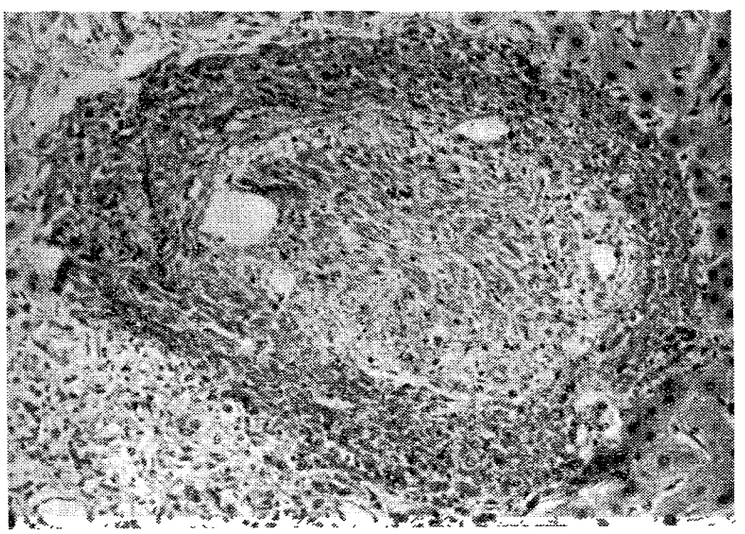


Fig. 2—Chronic phase of veno-occlusion, with collagenous connective tissue occluding lumen of branch of hepatic vein. (Mallory trichrome stain. × 146.)