TABLE III.—*Relative Incidence of Blood Groups A and O in Patients with Acute Hepatitis by Geographical Region*

Region	No. in Disease Series	Relative Incidence A : O	χ^2
1	200	1.151	0.841
2	124	1.324	2.137
3	54	2.322	6.975
Total	378		9.953
χ^2	Difference from unity D. of F. = 1 Heterogeneity D. of F. = 2		6.019 $P < 0.014$ 3.934 ($P > 0.1$)

Discussion

Buchanan and Higley (1921) examined the blood-group distribution of 2,446 patients suffering from a variety of diseases, classified in 17 groups, admitted to the Mayo Clinic from January, 1917, to May, 1921. They concluded that there was no relation between blood groups and disease, but later examination of their figures (Roberts, 1957) showed that in 173 cases of "jaundice, all causes," there was an excess of group A. In the original paper, neoplasms, cholelithiasis, acute and chronic gall-bladder disease, splenic anaemia, secondary anaemia, and pernicious anaemia were excluded from "jaundice, all causes," but we do not know how many of the 173 cases were due to infectious hepatitis. Billington (1956) also found an excess of group A in 111 patients with cirrhosis of the liver, most of whom had bleeding oesophageal varices. Our observations provide further evidence for an association of group A with a disease of the liver, more certainly infective in origin.

A similar group A excess was noted in our earlier study for illnesses due to adenovirus, which, like the agent of infectious hepatitis, appears able to infect man by both respiratory and alimentary routes. The virus responsible for human hepatitis has not yet been identified but is almost certainly unrelated antigenically to the adenovirus group. There is evidence that infectious canine hepatitis is due to an adenovirus (Kapsenberg, 1959) and that adenovirus type 5 may cause pathological changes in the liver tissue of hamsters (Pereira, Allison, and Niven, 1962), but there is no indication of any association between adenovirus infection and hepatitis in man. These points tend to suggest that the mechanism underlying the relation

between blood groups and infection, whether immunological or epithelial, is not highly specific.

The excess of group O in Asian influenza was observed in a population meeting the A2 virus for the first time. The group A excess in both adenovirus infection and infectious hepatitis, on the other hand, was found in adults already exposed to both diseases for many years. Our findings in hepatitis and adenovirus infection could therefore be explained in at least two different ways. It might be due to a natural resistance to these infections associated with group O; alternatively, persons of group A may possess more than average resistance to virus infection and so find themselves relatively unprotected in adult life by naturally acquired active immunity.

Summary

The ABO and Rh blood-group distribution of 378 cases of acute hepatitis in the R.A.F. was compared with that for a sample of 47,108 recruits, making due allowance for region of birth. The patients with hepatitis showed an excess of group A and a corresponding deficiency of group O ($P < 0.014$). This and findings previously reported in adenovirus and influenza virus infections suggest that any differences in susceptibility to virus disease associated with blood group are not highly specific.

We are indebted to a number of persons for their contribution to this study—Dr. A. C. Kopeć for allowing us to use for control purposes figures from an analysis of blood groups in R.A.F. recruits; to Dr. J. A. Fraser Roberts for his advice; to Mrs. Judith Munk for statistical assistance; and to the staff of the Medical Records Section of the Air Ministry for their help. We thank the Director-General of Medical Services, Royal Air Force, for granting facilities for this study and for permission to publish the results.

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TRIAL OF A POWDERED FORMULA DIET IN TREATMENT OF OBESITY

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In recent years a new method for restricting the calorie intake of the obese has evolved—namely, the use of the low-calorie concentrated "formula" diet. This diet is of known calorie value and chemical composition, and supplies all the nutritional needs of an individual except energy. The formula diet is usually marketed as a powder or liquid concentrate to which water is added to make a drink. This is taken at meal times in place of ordinary food. Variety is achieved by alternating flavours, by chilling or warming the drink, and by permitting the use of low-calorie foods such as green vegetables. Among the public these formula diets have recently enjoyed a consider-

able wave of popularity (*Time*, 1961), and large quantities have been consumed in Britain and elsewhere, usually without medical supervision. Medical opinion upon the desirability of this method of weight reduction appears to be divided. The Food and Nutrition Council of the American Medical Association (1961) considered the use of formula diets as undesirable, largely on the grounds that they encourage spasmodic self-medication and do nothing to remove the underlying cause of obesity. Other authors (Cass, 1961; Tullis and Allen, 1961; Roberts, 1962) report satisfactory weight loss by selected groups of obese patients treated with such diets.

We now report a study designed to assess whether the obese patient would adhere to his regime and lose weight

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better on a formula diet than on a "routine" 825-calorie reducing diet. Sixty-two obese patients have alternated between these two regimes, and the weight loss on each regime was compared.

Method

Two groups of out-patients were asked to participate in the trial. (1) A group of 17 recalcitrant obese diabetics who had already failed to lose weight over recent months on a routine low-calorie diet, and whose diabetes mellitus was controlled to a glycosuria-free state without the addition of insulin or tablets to the regime. This group was to test whether the formula diet helped with such problem cases. (2) A group of 45 new obese patients without other significant disease referred for diet supervision (including some staff volunteers). These patients were mostly keen to lose weight, and were willing to comply with the supervision and the plan of the regime. By observation of them, therefore, we might compare the advantages and disadvantages of the regimes, and their weight loss should measure each diet's efficiency in a willing subject.

Regimes Compared.—Table I compares the prescribed daily intake on each regime, one being the routine 825-calorie reducing diet used in this hospital along with vitamin supplements, the other being a formula diet. Each day the powder from a tin was mixed with 2 pints (1,140 ml.) of water. This was divided into four drinks, one being taken at each meal-time in place of normal food. In addition the patients were allowed unlimited amounts of low-calorie foods such as green vegetables, black coffee, black tea, and condiments.

TABLE I.—*Approximate Composition of the Two Reducing Diets*

	Formula Diet	Routine Diet
Calories	900	825
Protein (g.) .. .	70	55
Fat (g.) .. .	20	41
Carbohydrate (g.) .. .	110	60
Sodium (mEq)* .. .	39	290

* Excluding salt added at table. Figure for routine diet was mean value obtained by analysis of two specimen day menus. Both these menus included bacon or ham, "marmite" or "bovril," and cheese, so the figure given may be higher than the usual sodium intake on this diet.

Plan of Trial.—The patients were seen individually, weekly or fortnightly, by one of us (R. H.) and by a physician when necessary. They were weighed on the same set of scales at each visit throughout the trial, and were asked for their views upon palatability, satisfaction, and side-effects. Patients entering the trial were started on the routine diet or the formula diet in approximately equal numbers, and were encouraged to follow each regime for similar periods of time. These periods varied widely from two to more than 10 weeks according to individual preference. As the trial was voluntary more patients followed the routine diet for longer periods than the formula diet, and some variations in schedule were found to be necessary throughout the trial. At holiday periods such as Christmas, Easter, and summer vacation all subjects asked to come off the formula diet and go on the routine diet.

Results

Weight Loss by Recalcitrant Obese Diabetic Subjects

Table II summarizes the results observed in this group—clearly little weight was lost with either diet: despite the more careful supervision their weight reduction remained a problem. As with our next group, it proved difficult to persuade these patients to continue with the formula diet, a mean of only two weeks' trial being attained.

TABLE II.—*Weight Loss by 17 Recalcitrant Obese Diabetic Subjects*

	Formula Diet	Routine Diet
Group studied:		
No. of patients (mean age 62 years)	9*	17
Mean time on diet (weeks)	2	4.6
Weight loss:		
Mean weekly weight loss (lb.)	0.47	0.56
No. of patients with weight loss > 2 lb./week	2	3
No. of patients with overall weight gain	3	5

* Eight patients did not take the formula diet for at least one week—three failed to attend, four refused to try the formula diet, and one could not complete one week of the formula diet.

Weight Loss by Willing Obese Subjects

Table III shows that over the whole period all patients lost an average of approximately 1 lb. (450 g.) a week, slightly more being lost while on the formula diet.

TABLE III.—*Weight Loss by 45 Willing Obese Subjects*

	Formula Diet	Routine Diet
Group studied:		
No. of patients (mean age 42 years)	42*	43†
Mean commencing weight (lb.)	197	196
„ time on diet (weeks) ..	7.7	10.1
Weight loss:		
Mean weekly weight loss (lb.) ..	1.34	0.98
No. of patients with weight loss > 2 lb./week (excluding first week)	11	4

* Three patients failed to complete two weeks on the formula diet.

† Two patients failed to complete two weeks on the routine diet.

Close comparison of the two regimes is possible by grouping these patients as shown in Table IV. As would be expected, on starting either reducing diet in place of a normal diet, the first week's weight loss is the greatest, and in this respect the formula diet is better than the routine diet—5.02 lb. (2.28 kg.) as against 2.37 lb. (1.08 kg.)—even moving from a routine diet to a formula diet causes a greater weight loss in the first week than vice versa—1.90 lb. (0.86 kg.) as against 1.11 lb. (0.5 kg.).

However, even in subsequent weeks the formula diet may have a slight advantage over the routine diet. The

TABLE IV.—*Weight Loss in Willing Obese Subjects in Various Subgroupings*

	No. in Group	Weight Loss (lb./Week)	
		Formula Diet	Routine Diet
In first week after any change in diet:			
Normal → Formula	21*	5.02†	2.37†
„ → Routine	27*		
Routine → Formula	43*	1.90†	1.11†
Formula → Routine	35*		
In 2nd, 3rd, and 4th weeks in a trial of 4 consecutive weeks on each regime:			
Formula diet first	13	2.17‡	1.35
Routine „ „	7	1.31‡	1.24
In patients on each regime for equal periods of time 	35 (mean 4.7 weeks)	1.24§	1.05§

* Number of changes. Any patient may be included more than once.

† Each of these rates of weight loss is significantly higher than the one following it (0.06 > P > 0.001).

‡ This weight loss is significantly greater than any other in this subsection (0.05 > P > 0.01).

§ Not significantly different.

|| This subgroup was selected retrospectively. All patients in this group completing three or more weeks (not necessarily consecutive) on both regimes were included. Equal periods on each regime were included; the first week after any change in dietary regime has always been excluded. Where one regime has been followed longer than the other, weeks were selected from the early part of the trial for comparison.

weight loss during the second to fourth weeks of consecutive four-week periods on each regime is slightly greater when on the formula diet, though only when this was the regime started first (2.17 lb. (0.98 kg.) as against 1.24–1.35 lb. (0.56–0.61 kg.) a week). Alternatively, if we compare all the subjects who had followed each regime for an equal period there is a hint that more loss tends to occur on the formula diet (1.24 lb. (0.56 kg.) as against 1.05 lb. (0.48 kg.) a week) than on the routine diet, though this difference is not significant for the numbers observed. Total weight losses achieved by patients in this section are grouped in Table V.

TABLE V.—Total Weight Lost by Obese Patients

	Total No.	Gained Weight	Lost < 10 lb.	Lost 10–20 lb.	Lost > 20 lb.
Formula diet ..	42	2 (5%)	19 (45%)	15 (36%)	6 (14%)
Routine diet ..	43	8 (19%)	20 (46%)	9 (21%)	6 (14%)

Patients' Observations of the Formula Diet

The formula diet was found monotonous and difficult to maintain beyond three to four weeks. Eight patients stopped the diet before completing the first week, nine adhered to it for one to two weeks, 26 for three to four weeks, 11 for five to eight weeks, and only eight persisted with it for more than eight consecutive weeks. The following minor side-effects were attributed by some of the patients to the formula diet: nausea in five cases, vomiting in two, indigestion and flatulence in two, constipation in five, diarrhoea in two, ulcers in mouth in three, and depression in two. Most of these led the patients concerned to change back to the routine diet, and many refused to try the formula diet again. Most of the patients found the formula diet palatable and very convenient, and on the whole they were more satisfied and less hungry on this regime. One patient with peptic oesophagitis and one with duodenal ulcer reported much less indigestion when taking the formula than when taking the routine diet. The fact that patients always asked to be allowed to come off the formula diet at holiday occasions illustrates and emphasizes its lack of social attribute, and also that it is less easy for a patient to transgress on a formula diet.

Discussion

This trial appears to have clearly established four major conclusions. (1) For recalcitrant patients the formula diet appears to have no advantage over a routine diet with more persuasive urging than usual. (2) For the keen "dieter" the formula diet can achieve a slightly faster weight loss than the routine diet, particularly during the first week, and possibly also during subsequent weeks. (3) Even these willing dieters found it difficult to persist with the formula diet beyond four weeks. (4) A prescribed dietary regime for out-patients rarely achieves full adherence, for only about one in four of the willing dieters lost at the rate of 2 lb. (0.9 kg.) a week on either diet (Table III), while in a metabolic ward such patients would lose about 3 lb. (1.36 kg.) a week (Pilkington *et al.*, 1960).

The fourth conclusion clearly emphasizes the problem of the obese out-patient as one of how to avoid transgressing a prescribed dietary regime. The slight advantage shown for the formula diet in this trial may suggest that such a regime does help in this respect, but it is necessary to consider whether any other feature of the composition of the formula diet might give it an advantage. The proportions of carbohydrate, fat, and protein in the two diets are slightly different, but this factor cannot be of importance as the higher carbohydrate content of the formula

diet would tend to give a smaller rate of weight loss during the first week with this diet (Pilkington *et al.*, 1960; Russell, 1962), whereas a greater weight loss was actually observed. Possibly the only important difference in the composition of the two diets is the lower sodium content of the formula diet. This may explain some of the greater weight loss in the initial week on the formula diet. However, as equilibration to a change in sodium or water intake is usually established within seven days (Ross and Winternitz, 1961), the comparisons after the first week should be independent of this factor; and there has been shown a slight advantage for the formula diet (Table IV).

It is apparent that reduced sodium intake is probably not the only factor responsible for the good weight loss observed during the first week on either diet; for even when the patient changed from the formula diet to the routine diet the same weight loss was observed during the first week, when the sodium intake was increased considerably, as during subsequent weeks, when the sodium intake was relatively constant (Table IV). This suggests that any diet is generally adhered to more strictly at first and transgressions become more frequent as time passes; and that some advantage may be gained by alternation of dietary regimes at intervals of, say, two to four weeks, although this point was not specifically assessed in this trial.

The advantage shown for the formula diet probably depends upon its novelty, convenience, simplicity, and inflexibility. Self-deception in the estimation of the size of food portions does not arise; thus is eliminated a source of temptation which may prove irresistible to many patients. A counterbalancing practical disadvantage of formula diets, not assessed in this trial, would be the cost. A routine reducing diet should cost no more than about 5s. 6d. a day, whereas one day's supply of the formula diet as used in this trial costs 8s. 6d., exclusive of supplementary foods and drinks allowed. Another disadvantage is that such a diet, when used exclusively, does not help to correct the basic faulty dietary habits, a factor already emphasized by the Council on Foods and Nutrition of the American Medical Association Council (1961).

Summary

A trial of two dietary regimes was carried out by observing the rate of weight loss among obese out-patients while they alternated between the two regimes. With 17 recalcitrant obese diabetic subjects both regimes were equally ineffective. In a group of 45 new and willing dieters with simple obesity the "formula" diet showed a slight advantage, particularly during the first week on this regime, but also slightly during subsequent weeks. It is suggested that the use of a formula diet for short intervals, alternating with a routine reducing diet with regular professional supervision, may have some advantages over the continuous use of either reducing diet alone.

We are grateful to Mead Johnson and Company for supplies of "metercal," the formula diet we used, and to Dr. S. Wright for help in preparing the statistical data. We also wish to record our thanks to Professor Russell Fraser for his advice and encouragement throughout the trial, and for help in preparing the manuscript.

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