BIOCHEMICAL CHANGES RESULTING FROM DRASTIC WEIGHT LOSS IN OBESITY

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INTRODUCTION

Numerous reports on the treatment of obesity have been published during the past few years, but the aetiology of this condition still remains a subject of controversy. The combination of diet and appetite-reducing drugs has given good results in the hands of many investigators, but on cessation of treatment and resumption of normal diets, patients so treated soon return to their original weight and in many cases even exceed it.

This paper is a report on 20 obese patients who achieved very drastic weight loss within a comparatively short period of time. Certain clinical and biochemical studies were carried out before and after treatment, and the

patients were followed-up to ascertain whether they had remained at their new 'low' weight.

SUBJECTS AND METHODS

Biochemical investigations were originally carried out on 23 obese patients, all of whom were required to lose at least 80 pounds in weight. Three of these did not complete the treatment. Sixteen of the 20 on whom this study is based were females and 4 were males, their ages varying from 15 to 54 years (average age 34 years). Seven (all females) were in sedentary occupations, 8 (5 females and 3 males) were in semi-sedentary occupations and 5 (4 females and 1 male) were engaged in active occupations. Before commencing treatment each patient had a complete physical examination, including an electrocardiogram.

Patients then attended the South African Institute for Medical Research where their weights were recorded. Specimens of blood were drawn early in the morning, before breakfast and after a 12 hours' overnight fast. Serum was separated within 2 hours of the collection of the specimen.

The following biochemical investigations were carried out:

1. Serum protein-bound-iodine level.[1,2]
2. Blood-urea level (by the Technicon auto-analyser).[3,4]
3. Serum-creatinine level.[5,6]
4. Serum-uric-acid level.[7,8]
5. A 3-hour glucose-tolerance test was carried out after administration of 100 G. of glucose.[9]
6. Serum-protein electrophoretic analyses were determined using a Spinco analytrol model A, procedure A.
7. Serum-lipid studies, including total lipids, cholesterol, phospholipids, total fatty acids, triglycerides, beta-lipoproteins and beta-cholesterol.[10]
8. Basal metabolic rate (Benedict-Roth apparatus using Boothby and Sandiford tables.[11] Two 6-minute tracings were taken).
9. Urinary 17-ketosteroids.[12-14]
10. Urinary 17-hydroxycorticosteroids.[15,16]
11. Urinary total 17-hydroxycorticosteroids.[17]

On completion of these investigations the following scheme of treatment was initiated: For 30 days 10 mg. of long-acting dextro-amphetamine combined with barbiturate ('barbidex'), and 60 mg. of potassium chloride were given daily. 500 and 250 mg. of chlorothiazide were administered to the female and male subjects respectively for 5 consecutive days at a time, followed by an interval of 2 days, for the entire period of 30 days. Subsequently the dose of dextro-amphetamine was increased to 15 mg. per day, the dose of chlorothiazide and potassium chloride remaining constant. This regime was followed throughout the period of treatment.

During this period patients were told to drink a minimum of 4 pints of water a day, but there were no dietary restrictions; indeed, diet was not mentioned at all. The importance of weight loss and the hazards of obesity were repeatedly impressed upon the patient.

After 2 months on the above treatment, daily intramuscular injections of chorionic gonadotrophin (125 units) were given,[18] and the patients were started on a daily diet of approximately 500 calories. This diet consisted of 140 G. (uncooked weight) of lean animal protein, 2 heaped tablespoonsful of low-calorie vegetables, 2 items of fruit (orange or apple), and 3 slices of melba toast or 3 rusks, divided into 2 meals. The juice of one lemon was allowed, and unrestricted amounts of salt, pepper and vinegar. Patients were encouraged to drink at least 4 pints of water daily.

After 20 days of the above regime the chorionic gonadotrophin injections were discontinued and the patients were put on to an 'adaptation' diet of approximately 900 calories per day for 6 weeks. This diet was substantially the same as the previous one, increased quantities being allowed with a choice of lean meat, fish, eggs or cheese, and a wider choice of fruit.

Any patient who at the end of the 6-week period was still 40 lb. or more overweight, received a second course of intramuscular chorionic gonadotrophin injections and reverted back to the 500 calorie per day diet. Those who still had to lose 40 lb. or less continued on the adaptation diet until their 'normal' weight was achieved. For the purpose of this study 'normal' weight for these patients is considered to be 15 lb. above that shown on the chart of the Metropolitan Life Insurance Co. (1937).

Patients on reaching this 'normal' weight weighed themselves daily and were allowed to increase their food intake gradually to the point at which their weight remained constant. The doses of dextro-amphetamine, chlorothiazide and potassium chloride were gradually reduced, until by the end of 3 months they were completely withdrawn.

Intramuscular multivitamin injections were given during the last 4 months of treatment.

On cessation of treatment all biochemical determinations were repeated and the patients were again subjected to a complete physical examination.

RESULTS

Twenty patients achieved the required weight loss: Average pre-treatment weight 241½ lb. (range 207 - 288 lb.); average post-treatment weight 151 lb. (range 124 - 190 lb.). The average weight loss during the entire period of treatment (7 months) was 90½ lb.

Blood-pressure levels (in mm.Hg) before treatment ranged from 120/90 to 260/165 (mean 164/99), and on completion of the course from 110/68 to 145/100 (mean 124/76), resulting in a significant decrease both in the systolic and diastolic pressures. Patients who had tachycardia before treatment subsequently had a normal pulse rate.

Biochemical Results

The results of the biochemical investigations carried out before and after cessation of treatment are shown in Table I.

Serum protein-bound-iodine levels, blood-urea levels, serum-creatinine levels, serum-uric-acid levels, protein electrophoretic analysis, basal metabolic rate, and urinary

TABLE I. BIOCHEMICAL ANALYSES

Test	Pre-treatment Range	Pre-treatment Mean	Post-treatment Range	Post-treatment Mean
Blood:				
Serum PBI (μg./100 ml.)	4·3–7·8	5·8	4·0–8·8	5·9
Blood urea (mg./100 ml.)	16–38	26	13–58	24
Serum creatinine (mg./100 ml.)	0·4–1·9	1·3	0·4–1·8	1·2
Serum uric acid (mg./100 ml.)	2·5–6·9	4·7	2·5–7·2	4·9
Glucose tolerance:				
Fasting blood sugar (mg./100 ml.)	79–131	94	50–100	80
½ hour blood sugar (mg./100 ml.)	110–185	153	64–158	118
1 hour blood sugar (mg./100 ml.)	122–227	164	60–184	123
1½ hours' blood sugar (mg./100 ml.)	108–280	154	42–167	118
2 hours' blood sugar (mg./100 ml.)	90–294	150	49–155	111
3 hours' blood sugar (mg./100 ml.)	67–222	114	44–147	97
Total protein (G./100 ml.)	6·3–7·8	7·2	6·4–7·5	7·8
Albumin %	42·5–59·0	48·6	41·1–56·5	46·8
Albumin G./100 ml.	2·93–4·13	3·53	2·85–3·68	3·3
Alpha-1-globulin %	3·3–6·9	5·2	3·6–7·9	5·9
Alpha-1-globulin G./100 ml.	0·22–0·47	0·38	0·26–0·54	0·41
Alpha-2-globulin %	7·8–12·6	9·5	7·8–12·8	9·9
Alpha-2-globulin G./100 ml.	0·53–0·93	0·69	0·51–0·94	0·68
Beta-globulin %	11·5–19·3	15·4	12·5–19·9	15·8
Beta-globulin G./100 ml.	0·78–1·39	1·12	0·86–1·41	1·10
Gamma-globulin %	15·5–24·8	21·2	17·1–26·0	21·7
Gamma-globulin G./100 ml.	1·18–1·89	1·54	1·11–1·82	1·46
Beta-lipoprotein cholesterol (%)	64–85	73·2	61·82	72·7
	70–91	82·3	66–91	79·1
Total lipids (mg./100 ml.)	540–858	715	549–947	637
Phospholipids (mg./100 ml.)	174–322	245	182–306	222
Total cholesterol (mg./100 ml.)	180–273	229	148–302	214
Free cholesterol (mg./100 ml.)	50–85	66	47–97	65
Cholesterol esters (mg./100 ml.)	124–196	163	101–210	149
Esterified cholesterol (%)	65–78	71	68–75	69
Cholesterol: phospholipid ratio	0·83–1·09	0·94	0·82–1·17	0·96
Total fatty acids (mg./100 ml.)	242–504	394	235–402	349
Triglycerides (mg./100 ml.)	14–213	127	32–189	98
Basal metabolic rate (%)	(–26) to (+36)	+1	(–20) to (+15)	±1
Urine:				
17-Ketosteroids (mg./24 hrs.)	8·4–27·3	15·1	7·4–65	15·3
17-Hydroxycorticosteroids (mg./24 hrs.)	7·8–18·3	10·9	3·9–18·2	9·9
Total 17-hydroxycorticosteroids (mg./24 hrs.)	12·0–25·3	19·5	12·2–30·3	18·7

TABLE II. RESULTS OF ABNORMAL GLUCOSE-TOLERANCE TESTS IN 6 PATIENTS—PRE- AND POST-TREATMENT (IN MG./100 ML.)

Time period	Pre-treatment Patients 1	2	3	4	5	6	Mean	Post-treatment Patients 1	2	3	4	5	6	Mean
Fasting blood sugar	99	105	131	106	103	117	110	69	87	64	86	68	84	76
Blood sugar ½ hour after 100 G. of glucose	141	185	178	157	135	166	160	88	130	70	158	108	116	112
Blood sugar 1 hour after 100 G. of glucose	160	207	227	170	156	180	183	67	152	65	184	110	167	124
Blood sugar 1½ hours after 100 G. of glucose	184	195	280	206	160	175	200	78	152	70	152	94	167	119
Blood sugar 2 hours after 100 G. of glucose	153	175	268	217	294	170	213	75	148	82	152	68	143	111
Blood sugar 3 hours after 100 G. of glucose	112	101	222	170	99	122	137	44	125	65	140	88	121	97

17-ketosteroids, 17-hydroxycorticosteroids, and total 17-hydroxycorticosteroids showed no significant differences in their levels before and after treatment. Although there was a slight decrease after treatment in the total lipids, total cholesterol, total fatty acids and triglycerides, none of these differences were statistically significant.

There were significant decreases in the mean blood-sugar levels after treatment. Six patients who could be regarded as diabetics from their glucose-tolerance tests, showed no sign of hyperglycaemia after gross weight loss (Table II).

Follow-up

A follow-up study 12 months after cessation of treatment showed that only 2 of the 20 patients had gained weight (55 lb. and 40 lb. respectively). The weight in all the other patients remained stable.

DISCUSSION

In the White South African obesity is a common condition and most forms of treatment have proved unsatisfactory. It is not very difficult for individuals to lose weight, but it is extremely difficult to maintain the reduction for long periods. H. J. Roberts summarized the position as follows: 'The effective management of obesity continues to pose one of the greatest and most frequent challenges to practising physicians'.[19]

This investigation was an attempt to find out what changes, if any, took place in certain biochemical results after gross and relatively rapid weight loss, and also to ascertain to what extent the new low weight could remain constant.

In 6 subjects the fasting blood sugar exceeded 100 mg. per 100 ml. After 100 G. of glucose the peak was reached in 2 subjects after 1 hour, in 2 after 1½ hours, and in 2 after 2 hours. Only 2 glucose-tolerance curves returned to the base line within 3 hours. Thus, all 6 showed hyperglycaemic glucose-tolerance curves as occur in diabetes mellitus (consistent with the diagnosis of diabetes mellitus). (These 6 individuals can be considered as true diabetics.) There was no other hormonal imbalance, i.e. the serum protein-bound-iodine, and the 17-ketosteroid, and 17-hydroxycorticosteroid values were within the normal range.

Loss of excessive weight restored the abnormal glucose-tolerance curve to a normal one in all 6 cases. The mechanism by which the glucose-tolerance curve is lowered from an abnormal to a normal one is not known. Several investigators have described an association between obesity and diabetes mellitus,[20-22] and it would appear from our investigation that diabetes mellitus in obesity is reversible, i.e. once excess weight is lost the diabetes disappears.

Despite the fact that our subjects were grossly overweight, the mean serum-lipid levels (including total lipids, cholesterol, beta-cholesterol and triglycerides) fell within the range of normality. This would confirm previous observations that the simple state of obesity, like the state of leanness, in humans appears to be associated with no abnormal concentrations or patterns of serum lipids, and this lack of connection between adiposity and serum lipids is further shown by the fact that weight changes in the obese are not accompanied by parallel changes in the concentration of serum lipids.[23,24]

Keys and Anderson[25] also posed the question whether obesity *per se* is associated with an elevated level of serum cholesterol and stated that the distribution of high and low values for serum cholesterol is much the same in groups of fat men as in groups of thin men of the same age, though there may be a more significant relationship between cholesterol levels and overweight in the *active* state of developing obesity. Keys[26] also expressed the opinion that, though extreme obesity is a health hazard in general and perhaps for heart disease in particular, the relationship between obesity and coronary artery disease is far from convincing, and that it seems impossible to assign to obesity, as far as coronary heart disease is concerned, more than some aggravating or accelerating influence to a process, i.e. to atherosclerosis, that is primarily conditioned by other factors. Our observations on the lipid levels in the subjects studied before and after treatment, lend support to this view.

There was a marked fall in blood pressure (systolic and diastolic) in those patients who suffered from hypertension, and the electrocardiograms which had in some instances shown abnormalities, became normal.

The general health of the subjects studied remained good throughout the treatment and all patients stated that they felt better, more alert and energetic. Those patients who had complained of dyspnoea reported improvement after treatment. It is apparent that gross and rapid weight loss may have no deleterious effects on the general health provided the restricted diet is complete in essential nutrients.

Follow-up studies after 12 months showed that, with the exception of only 2 patients, all had been able to maintain their new low weights, provided that at the first sign of weight increase they temporarily restricted their food intake.

SUMMARY

1. Biochemical estimations were carried out on 20 markedly obese subjects, to ascertain what changes, if any, occurred after drastic weight reduction.

2. The average weight lost was 90 lb. over a period of 7 months.

3. The glucose-tolerance test, which was abnormal in 6 patients before treatment, became normal after weight reduction.

4. There did not appear to be a correlation between the state of obesity and serum-lipid levels.

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