A STUDY OF OBESITY IN GENERAL PRACTICE

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MUCH has been written on the subject of obesity, so much that it is impossible to review the literature here. Yet, after all the investigations on the subject, the cause of overweight still evades us, except in a few conditions (e.g., myxœdema), where it occurs as a secondary manifestation of underlying disorder. Basically, of course, if energy input is greater than output, there is increase in weight, but this brings us no nearer the solution to the problem. Why can some eat to their hearts' content and yet retain a slim silhouette, whilst others, who do equally as much exercise, become obese on the same diet? Have the slim some inborn metabolic defect which leads to extravagance in their use of food, or are they incapable of laying down a store? Conversely, have the obese, by some peculiar process of metabolism, the power to extract from their food more value than the "normal" person?

What is the ideal weight? There are two distinct factors which decide this—the æsthetic and the medical. The first, and probably the dominant factor, varies from time to time and from place to place. Beauties of yesterday would not be considered as serious contestants in a present-day contest—nor would the possessor of that Central African hallmark of femininity, steatopygia. From the medical standpoint, the height and weight tables have developed only over the past century, and have been drawn up by the assurance companies, as the result of their experience of the effect of weight on the expectation of life. These tables, it should be realised, are based on commercial considerations, not medical ones, but they do show that the elimination of obesity is desirable. Considered as a disease, obesity has its complications—dyspnœa, "chestiness," strain on the cardio-vascular system (especially in the elderly), leading in extreme cases to frank failure, mild diabetes of maturity-onset type. In the young, displaced epiphyses are commoner in the obese. The psychological effects, too, can be severe, no less on adults than on the young, who suffer the taunts of their school-fellows. Therefore, it would seem to me that obesity is a problem worthy of a serious approach by the general practitioner.

In spite of the absence of a strict definition of obesity, the overweight patient is not difficult to detect, and the question which arises is what shall be done about it? Put simply, the answer should be "Eat less and do more," but in my experience, so many people who carry excess weight have normal behaviour patterns in respect of exercise that I have come to believe that the amount of exertion undertaken by the patient is of only secondary importance, and it would be pointless to recommend extra exercise as a method of losing weight. Indeed, it would appear that this course would defeat its object, because appetite is likely to increase as a physiological response to the increased demand for energy. In any case, the grossly obese have reached the stage where the effort involved in taking exercise is so great that they are incapable of it. The more satisfactory method of attacking this problem is reduction of food intake. Since the quantity

of food eaten is largely a matter of habit, and since habits are notoriously difficult to break, the advisability of using appetite suppressant drugs immediately comes up for consideration. Much has been written on their side effects, and especially on the catastrophe of addiction, particularly with regard to d-amphetamine. Indeed, doubt has been expressed as to whether they have any effect at all on appetite.

A clinical trial was undertaken with the object of solving this problem. The specific questions which it was designed to answer were:—

1. Are the marketed appetite suppressants really effective?
2. How long do they act?
3. Which is best?
4. What is the incidence and nature of side effects?

Method.

About two-thirds of the patients who were admitted to the trial were overweight and themselves desired to lose weight, usually on æsthetic grounds or economic grounds (e.g., their clothes no longer fitted), and about one-third were overweight and required to reduce on medical grounds (e.g., increasing dyspnœa, hypertension). Care was taken that no person who showed any psychiatric instability was admitted on the grounds that they may become habituated or addicted to the agents used. The materials used were dexamphetamine sulphate, a placebo, benzphetamine (Didrex) phenmetrazine (Preludin), and diethylpropion (Tenuate). These were all supplied identical in appearance and labelled respectively 4-M, 5-M, 6-M, 7-M, and 18-K.

Each bottle contained fifty tablets, enough to last sixteen days. Since one of the signs of habituation or addiction is increased tolerance of the particular material, and consequent increase of dosage, any patient who returned before the expiration of two weeks saying that his tablet supply was exhausted would be immediately suspect. There was also a supply of the placebo tablets which were known to me as such and which were used either on patients when they had lost the requisite amount of weight, or to be given should any patient show signs of habituation or addiction, to see whether this subterfuge would relieve the situation. After an initial weighing and examination successive patients received the tablets in a predetermined order and were instructed to take them at a dose of 1 tablet three times daily, taken one hour before mealtime, but not later than 4.30 p.m.

They were reweighed at two-week intervals and enquiry made as to side effects and particularly to detect any suspicion of habituation. When the patient ceased to lose weight or, as in many cases, gained weight, he was transferred to the next agent in the same order as before. Initially no instruction was given as to diet, but it very soon became apparent that this was necessary and, subsequently, all patients were given a standard weight-restricting diet. There was a short period towards the end of the trial when benzphetamine or known placebo was given to all patients still taking part in the study. The measurements taken under these circumstances were included in the results. The trial was, therefore, con-

ducted under double-blind conditions with the exception of this short terminal period. That is at this later stage a known active drug was issued to those patients whose weight loss was inadequate or a placebo if the weight loss was satisfactory.

Results.

Of those patients under treatment for more than six weeks, seven entered the trial on dexamphetamine, five on phenmetrazine, six on benzphetamine, and eight entered on diethylpropion, and eight on placebo. Thirty-four patients took these various agents for a total of 271 weeks before they ceased to lose weight, a mean of 7.97 weeks each. The total weight loss was 265 lb., a mean of 7.79 lb. per patient at a mean of 0.95 lb. per week each. When these results are broken down into two groups, the active agents on the one hand and placebo on the other, there is a very obvious difference: the placebo effect lasts 4.13 weeks against 9.15 weeks for the active agents; the patients taking active tablets lost an overall total of 10.19 lb. (1.11 lb. each per week), whereas among those taking placebo tablets the weight loss was exactly countered by the weight gain. With the numbers at my disposal one cannot compare the various agents with statistical validity, but some idea of their effectiveness can be gained from Table 1.

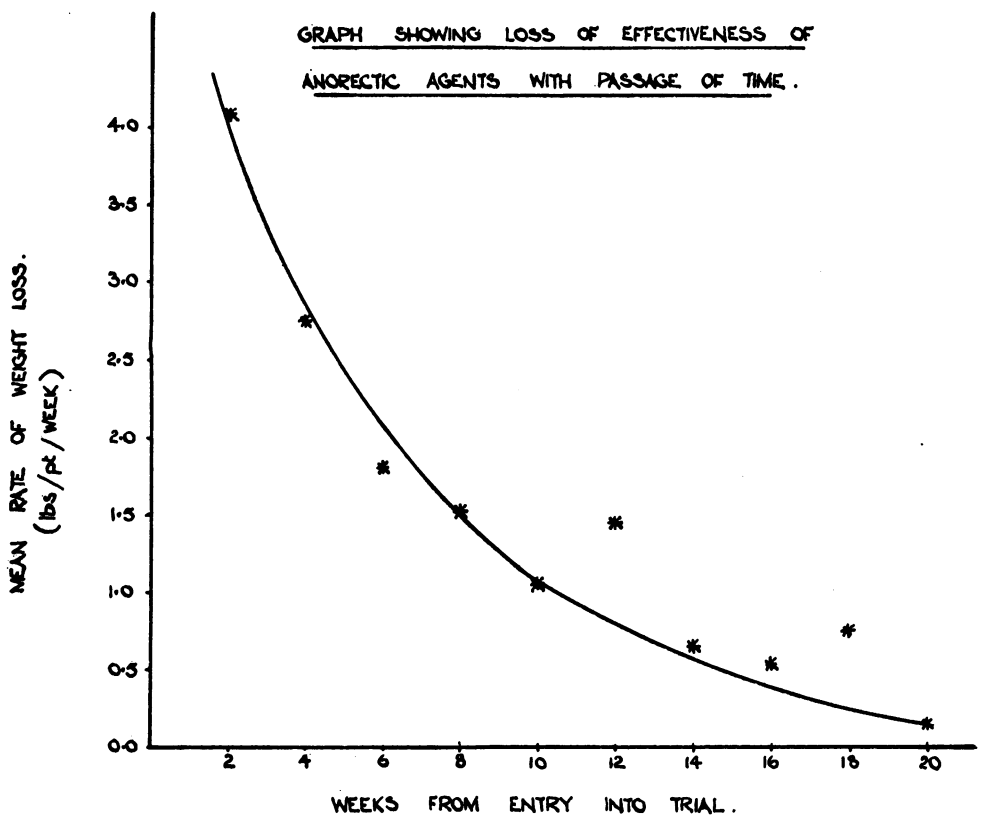

TABLE 1.

	Number of Patients	Duration of Treatment (weeks)	Total Weight Loss (lbs.)	Average Duration Treatment (weeks)	Mean Rate of Weight Loss (lbs./weeks)	Mean Wt. Loss per Pat. (lbs.)
	A	B	C	B/A	C/B	C/A
4 M d-amphetamine:						
Primary course	7	73	74	10.43	1.01	10.57
Subsequent course	9	47	11	5.22	0.23	1.22
5 M placebo:						
Primary course	8	33	0	4.13	0	0
Subsequent course	9	44	−2 (gain)	4.89	−0.05 (gain)	−0.22 (gain)
Known placebo as:						
Course	—	—	—	—	—	—
Subsequent course	10	52	3	5.20	0.06	0.30
Combined known and unknown placebo:						
Primary course	8	33	0	4.13	0	0
Subsequent course	19	96	1	5.05	0.01	0.05
6 M benzphetamine:						
Primary course	6	43	63	7.17	1.47	10.50
Subsequent course	13	59	50	4.54	0.85	3.85
Prescribed benzphetamine as:						
Course	—	—	—	—	—	—
Subsequent course	10	34	16	3.40	0.47	1.60
Combined known+ unknown benzphetamine:						
Primary course	6	43	63	7.17	1.47	10.50
Subsequent course	23	93	66	4.04	0.71	2.87
7 M phenmetrazine:						
Primary course	5	53	60	10.6	1.13	12.0
Subsequent course	8	48	48	6.00	1.00	6.00
18 K diethylpropion:						
Primary course	8	69	68	8.63	0.99	8.50
Subsequent course	12	39	11	3.25	0.28	1.09
Total including placebo:						
Primary course	34	271	265	7.97	0.95	7.79
Subsequent course	71	323	137	4.57	0.42	1.93
Total excluding placebo:						
Primary course	26	238	265	9.15	1.11	10.19
Subsequent course	52	227	136	4.38	0.59	2.62

After weight loss had ceased, the patients were transferred to the next drug (this procedure was repeated with some patients several times) and the same difference was observable between the placebo tablets and the active. It is worthy of note that the known placebo tablets produced quantitatively similar results to the blind-label placebo tablets and the same occurred with the benzphetamine either issued under blind-label or precribed on E.C. 10. The graph shows the rate of weight loss against the time from entry into the trial and demonstrates a progressive loss of effect as time goes by. Whether this is due to a loss of true pharmacological effectiveness or to progressive failure of determination on the part of the patient it is not possible to state.

TABLE 2.

Side Effect	D-amphetamine Sulphate	Benzphetamine	Diethylpropion	Phenmetrazine	Placebo	Total without Placebo	Total with Placebo
Depression	- 1	–	1	1	–	3	3
Tension	- –	2	–	–	2	2	4
Insomnia	- –	1	–	–	–	1	1
Drowsiness	- 1	–	–	–	–	1	1
Sweating	- –	–	1	1	–	2	2
Increase of appetite	- –	1	–	1	1	2	3
Total	- 2	4	2	3	3	11	14
Number of patients taking drug	- 16	29	20	13	27	78	105
Proportion with side effects	- 1 : 8.0	1 : 7.25	1 : 10.0	1 : 4.33	1 : 9.00	1 : 7.09	1 : 7.50

Side effects were reported on fourteen occasions and are listed in Table 2. Certainly the frequency and severity of these were the same whether patients were currently taking the placebo or the active tablets. It is doubtful whether the nature is very different. All were highly subjective (including two who complained of excessive sweating) and none were serious. Whilst insomnia and tension could be anticipated when using this type of material, drowsiness and depression were most unexpected, particularly in the case of dexamphetamine, a drug widely used to combat these very states. Most of the side effects occurred at times when patients were losing weight most rapidly, and it is not improbable that they were due to hunger, or were, indeed "withdrawal" phenomena vis-a-vis food. There was only one patient in whom there developed signs suggesting early habituation. He was at the time taking dexamphetamine sulphate and known placebo tablets were substituted. The incident passed off without trouble. I feel that this particular difficulty is well within the competence of the average general practitioner who, knowing his patients as he does, is capable of detecting with fair accuracy the patient who may become habituated or addicted and with-

holding from him this class of medication. Further, he should (and can) distinguish between those patients desiring these substances for genuine help in reducing weight and those who want them "for kicks."

Conclusion.

To lose weight demands considerable effort on the part of the patient, an effort which must be sustained. A number of patients who entered the trial were unable to maintain this effort for more than six weeks. Certainly, patients require assistance in achieving reduction of weight and this trial shows that there is real benefit to be gained from the various anorectic agents and that this is greater than can be obtained using a placebo. This effect diminishes with time and is virtually nil after some two to three months. During this period the patient can expect to lose 10 lb. It appears that there is little or nothing to be gained by transfer to another agent when weight loss has ceased since only another 2½ lb. are likely to be lost over the next month, but there is great individual variation in these figures.

Side effects occurred with a frequency which was not vastly different in the case of active agent or placebo tablets, and they appear to be more related to the current rate of weight loss than to the drug concerned.

Summary.

A trial is described, using various anorectic agents and placebo tablets on a double-blind basis. It was shown that the active agents were more effective in all respects than placebo tablets. Side effects were not of moment and were not significantly more frequent in any one group. Their possible cause is discussed. No conclusion was possible as to the superiority of any of the active materials used.

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