The treatment of obesity

Dear Sir:

Two original communications appeared in the February 1973 issue of this journal. One deals with the problem of so-called "luxus consumption" and is entitled "Response of Body Weight to a Low Carbohydrate, High Fat Diet in Normal and Obese Subjects" by Kasper et al.; the other, on the use of human chorionic gonadotrophin for the treatment of obesity, is entitled "Effect of Human Chorionic Gonadotrophin on Weight Loss, Hunger, and Feeling of Well-being" by Asher and Harper. It may not have been the intent of either set of authors, but these communications will be quoted for some time to come as adequate rationale for treating the obese with ketogenic or other unusual diets and also for the use of injections of human chorionic gonadotrophin to help in weight reduction. It is therefore particularly important to review these articles in sufficient critical detail to determine just what it is that has been established by these publications and to what extent the findings are relevant for the treatment of obesity.

The work of Asher and Harper on human chorionic gonadotrophin concludes that a group of obese patients who received this hormone or a mixture of hormones lost more weight than the placebo group and, furthermore, experienced less hunger and generally better feeling. Fortunately, data on starting weight and weight loss are supplied in a table and constituted the basis for our re-analysis of the results. On first view it looks good, percent body weight loss of the treated group exceeded that of the placebo group at highly significant values. (Our analysis of the data with the t test gave a t value of 4.67, which, with 38 degrees of freedom, suggests that such weight loss would occur on random grounds less than one time out of a thousand.) A more detailed examination, however, reveals that in the placebo group, many patients received fewer than the 36 injections which constituted the original experimental plan. In fact, there is quite a scatter of the number of injections received. (By our calculations, the standard deviation of the number of injections received by the experimental group was 3.8, but in the placebo group it was 10.3. A t test of the differences in the number of injections received, 33.85 for the experimental group vs. 29.05 for the placebo, shows a barely significant t value of 1.95 at 38 degrees of freedom.)

It is most informative to look at the question as to whether the number of injections received even in the placebo group (who received no chorionic gonadotrophin) bore any relationship to the results. In point of fact, this is precisely the case. A correlation coefficient relating number of injections received to percent weight loss shows a correlation of 0.683. Such a correlation, occurring with a t value of 3.97 and 18 degrees of freedom, is a highly significant observation. In fact, one can say that within the placebo group, nearly one-half of the variance observed is the result of the number of injections. Clearly then, the number of injections is important. Keeping this in mind, if one then goes back to the original data and deletes both from the chorionic gonadotrophin and the placebo group, those who received fewer than 36 injections, one finds that there is still a slight increase in the weight loss of the treated group as compared with the placebo group, but the significance of this difference declines sharply and the probability that this is occurring on random grounds drops from less than 1 in 1,000; actually, it is close to 2 in 100.

One must ask why the placebo group received fewer injections on the average than those in the treated group. Was this a random occurrence? Did the patients or someone know just who was who? The authors note that the patients were told that "the slightest deviation from any of the details will result in utter disaster." Given this dire statement, it is hardly surprising that individuals who missed injections for whatever reason might feel they were on the brink of disaster. Thus, Table 3, which gives data relating to the feeling of the patients...
and their hunger, appears to show not unexpectedly some difference in the treated and untreated groups. It should be pointed out that in Table 3 the data obtained are nonparametric, that is, patients were not asked to give any known numerical estimates of hunger or feeling, but simply to ascertain whether they felt “none,” “little,” “some,” or “much” hunger, or whether their general feeling, was “poor,” “fair,” “good,” or “excellent.” Such nonparametric data require a special type of statistical analysis. There is no evidence given in the article that this was done. What was done, however, was that some groups were lumped together. Hunger of degrees “none” and “little” were put together as were hunger of degrees “some” and “much.” A similar maneuver was used with the four categories of feeling. This is an arbitrary and totally unwarranted procedure from a statistical viewpoint. It would be most revealing to know exactly which patients showed what in terms of numbers of injections received relative to ratings of hunger and feeling.

We think it is fair to conclude from this communication of Asher and Harper that individuals who received more injections may adhere better to a low calorie diet than those who do not, and it makes little difference what the injection is. Only with a much more carefully executed study could one determine whether or not human chorionic gonadotrophin had any effect. Judging from the data at hand, it seems most unlikely. Furthermore, one can conclude that the data given in the article permit no analysis whatsoever as to hunger or feelings of well-being as a function of receiving this mixture of hormones or of the placebo. Presumably, the authors have the data at hand and perhaps some further analysis of this point could be done. This publication is of some interest in the sense that it indicates that medical attention in the form of injections, particularly in a population threatened by “utter disaster” should there be any deviation from details, will provoke a little better adherence to a diet when injections are numerous than when they are less frequent. We leave it to the reader of this letter to make his own decision as to whether or not this piece deserved publication, but we would vigorously dispute the concept that this publication lends any credence to the notion that human chorionic gonadotrophin has a place in the treatment of human obesity, but would agree with the last statement of the authors that “additional investigation of the influence of HCG on weight loss, hunger, and well-being seems indicated.” We would add the hope that better experimental design and analysis of data be incorporated into any further studies of this matter.

In our opinion, the other article also has little relevance to the treatment of obesity. Kasper and his associates did a twofold study. In the first part, individuals of normal body weight, varying between roughly 80 and 95 kg, were given formula diets containing 168 g carbohydrate, 64 g protein, and 39 g fat. To this basic diet, either corn oil or olive oil was added in increasing amounts to make a total of 6,878 kcal/day. It is claimed that two of the individuals receiving olive oil gained weight, but those receiving a high fat diet rich in linoleic acid, so abundantly present in corn oil, did not gain as much weight. It is stated that “a distinct discrepancy between the caloric intake and the response of the body weight was detectable.” There appeared to be a marked tendency toward sweating and a marked sensation of heat over the entire body when fat was administered. However, no measurements of heat loss or energy outgo are included in this paper.

The data are given in the form of three figures. Figure 2 shows an increase in body weight as one subject ingested more and more olive oil and, if one assumes that this subject needed somewhere in the neighborhood of 2,800 or 3,000 kcal for energy needs, the additional calories given over the period of time stated explain quite well the weight gain on the basis of each 7 kcal excess leading to 1 g of weight gain. Figure 1 showing all subjects receiving high corn oil and high olive oil has an unusually compressed ordinate; thus, the weight scale is exceedingly difficult to decipher. One notes immediately, however, that three of the subjects were studied for only approximately 10 to 12 days, so of the seven subjects studied, three can immediately be discarded, because within a period of 10 to 12 days, such electrolyte and fluid shifts would occur as to invalidate the findings. We are left, then, with four individuals. Two of these individuals, subjects 6 and 7, as labeled in the figure, received olive oil, so these two can be “discarded” from a consideration of “luxus consumption,” as olive oil is claimed to have no
such effect. Now we are left with only subjects 1 and 2. A careful perusal of subject 2 shows that his curve of weight gain is much like that of subjects 6 and 7, so presumably one of the two individuals who received corn oil for a time longer than 10 to 12 days did in fact gain weight. At first, there was a drop in weight with subject 2, as one might expect with fluid and electrolyte shifts on a relatively ketogenic diet and afterward, there was weight gain. Subject 1 who was studied for approximately 35 days appears to be the exception. This subject lost some weight initially and then had a small weight gain up to 35 days, even though calorie intake was increased. We assume that the detailed figure shown in Fig. 3 is of this same unusual subject, labeled in Fig. 1. We note in this subject that over a 10-day period, there was weight loss as fat calories were increased, something to be expected on a relatively ketogenic diet, with early acidosis, dehydration, et cetera, and then in spite of increments in fat every 5 days, there was only a slight weight gain, perhaps a kilogram over a period of 25 days. The authors note that “the objection that the weight loss obtained under the low carbohydrate, high fat diet was due only to increased dehydration can be disregarded in view of the prolonged experimental period of up to 45 days.” Perhaps this refers to the second part of the study, yet to be discussed, as it surely does not refer to subject 1 shown in Fig. 3, who was studied for a shorter period of time than 45 days. The lack of weight gain is indeed somewhat puzzling, but it occurred in only one subject, insofar as one can reasonably tell from these rather poorly prepared figures. What does this mean? Were all calories ingested? What was the state of fluid balance and total body water before and after the experiment? Should one entertain this one clinical anecdote as being hard evidence for “luxus consumption?”

If one were to accept the authors’ contention that “... under a relatively low carbohydrate and protein intake, increasing amounts of fat produce an increase in the metabolic rate that becomes particularly marked if fats high in linoleic acid are given,” then the reader appears to be drawn into the following chain of calculations. A young man requires approximately 3,000 kcal/day, assuming a modest activity level. Approximately one-half of this amount is needed to support his basal metabolism (BMR). If, by consuming large quantities of corn oil, he then increases heat production sufficient to dispose of 2,900 (5,900 minus 3,000) additional calories, this “luxus consumption” would seem to require an elevation of the subject’s BMR by nearly 200% (on the average). Because patients with severe hyperthyroidism exhibit a BMR somewhat in excess of +50%, the data of Kasper et al. would call for this normal young subject to manifest a degree of hypermetabolism (24 hr/day) three- to fourfold greater than that associated with the most toxic form of Graves’ disease. It is perhaps not out of place to mention also that, for every degree (Fahrenheit) of temperature rise above normal, there is supposed to be an associated 8% increase in metabolic rate. In view of this fact, it seems inconceivable that the sensation of “heat over the entire body” reported by the subjects on a high corn oil intake could account for the almost 200% increase in BMR implied by the observations of Kasper et al.

The second part of this study shows that in brief intervals, nearly 10 days at a time, varying calorie and fat and carbohydrate ratios causes variations in the rate of weight loss in obese individuals. Four individuals received a fairly high carbohydrate diet. All appear to have been somewhat restricted in total calorie intake. In those receiving the high carbohydrate diet for from 6 to 14 days, weight loss was quite poor. The well-known effects of a high carbohydrate diet, even during calorie restriction, in promoting fluid retention, is so well-known to the readership of this journal as to deserve no further comment.

As with the previous article, one must leave it to the reader’s judgment as to whether or not our knowledge of clinical nutrition has been advanced by finding these two papers in The American Journal of Clinical Nutrition. As to whether these two communications have any bearing on the treatment of human obesity, a different judgment is in order. There is none.

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