THE CLINICAL SPECTRUM OF OBESITY*

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My contribution to this discussion is an attempt to survey the clinical field of obesity in the light of recent knowledge. The underlying point of view is that appetite plays the fundamental part and that, although endocrine factors are capable of causing changes in weight based on internal rearrangements of protein and fat, the usual reason for gain of weight is an excess of calorie intake over expenditure.

Experimental Obesity

Probably the most important recent contribution has been the direct production of experimental obesity by damage to certain nuclei in the medial hypothalamus, which has been shown by several workers and confirmed for several species of animals (Hetherington and Ranson, 1939; Brobeck, 1946). The essential feature of this obesity is that it is based on an enormous increase in appetite, and the close dependence of appetite on hypothalamic function has been further demonstrated by the discovery of lateral nuclei, destruction of which leads to total loss of appetite. In fact, it is possible to make an animal obese by first destroying the medial hypothalamic nuclei, and then to convert this into a fatal anorexia by subsequent destruction of the lateral nuclei (Anand and Brobeck, 1951a, 1951b). Clinically, this is reminiscent of the fat girl who subsequently develops anorexia nervosa, which, unless treated, may prove fatal.

The course of the increased appetite and consequent obesity in animals with hypothalamic damage is of great interest. Immediately after operation the appetite is voracious and indiscriminate, so that a rat may double or even treble its previous intake, and the gain of weight is very rapid. Both the appetite and the rate of gain then gradually decrease until a plateau is reached, on which extra weight can be maintained on a diet not significantly greater than normal. If these animals are starved and their weight is reduced they immediately return to their previous high level when allowed to refeed. In such animals fat may account for as much as 70% of their total weight, and water retention plays no part. Their appetite is now more capricious, and in this they appear to resemble both older rats and those that are naturally fat (Kennedy, 1950).

Maternal Obesity

These experimental findings may well have a direct application to some forms of human obesity, and indeed clinical study of maternal obesity shows so close a parallel to the experimental condition that there must be factors in common. The agreement covers the initial stage of voracious appetite, the plateau stage, and the amount of final gain achieved.

As clinicians we have undoubtedly been too ready to accept fat people as they are without a close inquiry into the rate of onset of the condition. The case literature is in fact extremely meagre on this point. It is, of course, difficult to obtain accurate information concerning weights in relation to time in the past, but individual accuracy can to some extent be replaced by multiple case histories, and in 80 cases of maternal obesity I have been able to collect 19 records of weight gain over different but definite periods (see Chart). It is remarkable how the rates of gain of these different women appear to be following a common path. They were all women whose gain of weight began after the birth of a baby, and the available information consisted of

a weight record taken during the puerperium and a subsequent record at a known but haphazard interval of time, which of course varied from patient to patient. It will be obvious that the general picture bears a close resemblance to that which has just been described in rats after hypothalamic damage; the gain of weight may begin with the same dramatic rapidity and then gradually tail off until a more or less steady state is reached, which in the case of these patients appeared to take about a year. Subsequent gain, if present at all, is extremely slow.

Records of weight gain (pounds per week) in cases of maternal obesity.

Thus, a woman had her baby in January, 1940, and weighed 133 lb. (60.3 kg.); in April, 1940, she weighed 168 lb. (76.2 kg.)—a gain of 35 lb. (15.9 kg.) in approximately 16 weeks, or a little more than 2 lb. (about 1 kg.) a week. She then refused to face the scales until April, 1944, when she weighed 218 lb. (98.9 kg.) so that in the interval she had gained 50 lb. (22.7 kg.) in some 208 weeks—less than $\frac{1}{4}$ lb. (0.11 kg.) a week. Over the whole period, however, she had gained 85 lb. (38.6 kg.) in 224 weeks, approximately 0.4 lb. (0.17 kg.) a week.

Development of Obesity

When one discovers that other individuals, who knew their weights only at the beginning and the end of a similar period of years, had not only experienced the same average rate of gain but also said that they remembered having put on weight very rapidly to begin with, one cannot help surmising that they may have followed a similar course. There is no doubt that some fat people have gained their weight slowly and steadily, but there are others who do so with a great initial rapidity which tends subsequently to be forgotten, and I would plead for more extensive studies of the actual rate of development of obesity. Not only does the rate of increase in these cases of maternal obesity parallel the experimental one, but in the very few cases that I have been able to see I have satisfied myself that the period of rapid gain was accompanied by an excess appetite.

Thus one woman who was gaining at a rate of slightly more than 3 lb. (1.36 kg.) a week not only ate her full ordinary meals with second helpings but also consumed sweets and raided the larder during the intervals. This is common enough, but when in addition it was found that after partaking of a special supper immediately before retiring she also took food to bed with her, knowing that she would wake up ravenous in the night, and then required her husband to bring up bread and cheese with the morning cup of tea, one is justified in ascribing the gain of weight to a voracious appetite. It is of interest that she herself refused with some anger any suggestion that she was overeating, as she never had "more than her fill," and in response to later questioning would undoubtedly have denied any excess intake—for the patient is apt to deal with questions on this point as if they implied an accusation of greed.

When the rate of gain is at its steepest hunger seems to arise immediately after a meal and there is no feeling of satiety, however much has been eaten. As the rate slows off the intervals before hunger reappears seem to lengthen, the progression being from "I'm never satisfied" to "I get hungry again an hour after a good meal," and so on. It is as if a satiety mechanism which is nil at the start gradually increases as the weight approaches a target already set.

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Calorie Intake

When the woman has reached a plateau in which either the added weight is steady or is subject at the most to a very slow increase, clinical observation shows quite clearly that many of them are not taking an excessive diet (Sheldon, 1949) and that, in their own words, they "do not deserve to be fat"—which agrees with the experimental findings (Kennedy, 1950). Their eating habits are often unusual; they may cut out some meals altogether—usually breakfast—and depend on one or two very large meals, and many of them admit to an almost irresistible appetite in the presence of articles of food for which they have a partiality. In their study of actual diets consumed Widdowson and McCance (1936) found no significant correlation between body weight and calorie intake, and we should remember that fat individuals may very well not deserve to be fat in the light of their present intake, but they have undoubtedly at some time in the past deserved to become fat, and may since have been able to maintain their added weight on a reasonable intake. Since their basal metabolism is normal, and this is calculated on a bigger surface area, the only way they can achieve this result is by a diminution in activity. This has been shown to occur in the experimental animal (Brobeck, 1946), and, although it is virtually impossible to demonstrate clinically, yet I think that general observation suggests it may be true.

Since the final gain achieved may be as much as 150% of the original weight, simple calculation shows that some 60% of the total weight would be due to fat, and this again is in keeping with the experimental findings.

Hypothalamic Regulation

The general concordance between experimental obesity produced by hypothalamic damage and the clinical findings in maternal obesity is so close that one must assume a hypothalamic mechanism to be concerned in the latter, and, if so, its possible role in other types of human obesity has to be considered. The cases in which obesity develops after inflammation of or injury to the lower brain, as an occasional complication to encephalitis or chorea and to a fractured base or subarachnoid haemorrhage, would seem to be the direct human equivalent of the experimental damage. The interesting syndrome of periodic somnolence and morbid hunger (Kleine-Levin) is also a close analogue and serves as a link with those instances which are to be associated with alterations in hypothalamic function rather than with actual structural damage. In view of their close functional relations, one naturally looks to the cortex as one possible source of such alterations in hypothalamic function, and clinical experience does indeed reveal several types of obesity in which a cortical factor must be assumed. The obesity which sometimes follows frontal leucotomy undoubtedly belongs to this group, as also does the increased appetite which is well known to occur in some people in response to emotional states (Shorvon and Richardson, 1949). One wonders also whether the well-known gain of weight that follows abstinence from tobacco may not have a similar origin.

It is an interesting commentary on the difficulties of clinical medicine that an obesity of apparent emotional origin may often arise in the midst of a disturbed endocrine background. Bruch (1940) has shown that fat children are apt to have an emotional tension which is eased by the taking of food, and at the same time their bone growth is in advance of their age—which may, nevertheless, be a derivative from rather than antecedent to the increased intake. Maternal obesity begins immediately after the birth of the baby, when there is a considerable endocrine stress associated with the establishment of lactation. When such obesity occurs in the first and only pregnancy or in the last pregnancy, boy babies are no fewer than four times as common as girl babies, and one cannot avoid the speculation that it is the appearance of the male infant which has released an emotional state in the mother, leading in turn to the increase of appetite.

Other Types of Obesity

The types of obesity already mentioned are, of course, only a part of the whole clinical spectrum, and an application of the same point of view to other forms is not immediately obvious. They are characterized essentially by the fact that the obesity presents itself to the clinician in company with other features which imply an abnormal endocrine state, and in the latter it is natural to seek for an explanation of the former. This may be hazardous, for we have as yet no full understanding of the many factors involved in the established state of overnutrition. It is, of course, well known that insulin is involved and that obesity leads to hypertrophy of the islet tissue, but the endocrine adaptations are certainly complex, and probably involve both the anterior pituitary and the adrenal cortex in addition. When clinical evidence of ostensible endocrine derangements therefore are found to accompany obesity, it is well to remember that they may derive from rather than be causative of the obesity. Neglect of this aspect led to the mistaken view, held for many years in many quarters, that patients with anorexia nervosa were suffering from an organic hypopituitarism—a warning that should make one cautious.

Nevertheless, it is true in general to say that obesity tends to arise at three periods—growth and puberty, maternity, and the menopause—all of which have in common an endocrine departure from a relatively static state. It would be interesting to know more about the menopausal middle-age spread than we do. Accurate information is curiously at a minimum, and there is certainly here an untapped field of clinical observation. One's general impression is that the gain is a slow one, which suggests that it may be due to a continuance of previous dietary habits at a time when energy expenditure has become somewhat less.

Relation to Growth Factor

The obesity which is so common an accompaniment of late adolescence in association with growth and puberty has been more closely studied, although the occasional excesses have proved more congenial than the normal development of "puppy fat," which never gets to the doctor at all. The work of Young (1951) on the relation of obesity to growth factor of the anterior pituitary may well be relevant here. In dogs the hormone causes a deposition of protein accompanied by an increased catabolism of fat. If the diet be controlled the animal can gain weight on a diet that previously only kept the weight static, owing to the different calorie values of protein and fat. The normal animal, however, does not keep his intake steady, but responds by a great increase of appetite, and this may be so big that the excess fat laid down more than compensates for the energy lost to the body by growth. The appetite response is, in fact, a coarse one and leads to the taking in at this time of life of an unnecessarily large calorie total—an experimental observation which would appear to be in harmony with both the insatiable appetite and the "puppy fat," which are so common in adolescence.

The effect of growth hormone has also been invoked as an explanation of maternal obesity. It is a well-established observation that women who develop diabetes in middle life are apt to have given birth to larger babies than non-diabetic women, and these women are also often obese; it has been suggested that overproduction of growth hormone has led to the large baby and, in the course of time, to the appearance of diabetes.

Nevertheless a general clinical review of these two types of obesity suggests that even at these epochs it is unlikely to be the only factor, for if growth factor were the sole agent one would justifiably expect the extreme cases to show clinical appearances tending towards gigantism or acromegaly. It is a remarkable fact that, on the contrary, these are conspicuous by their absence, and where there is evidence of endocrine excess in the obesities of growth or maternity the clinical appearances are those associated with abnormal function of the adrenal cortex. Thus striae distensae are very common, and I am in complete agreement with Simp-

son (1950, 1951) in the stress he lays on their importance. Although they can appear in diverse clinical states, the available evidence suggests that they derive from an altered or excessive adrenal steroid metabolism, and they can certainly occur in the course of treatment with A.C.T.H. Simpson (1951) has described some of these cases of pubertal obesity under the names of adipose gynism and adipose gynandrium, and there is no doubt that they constitute a definite clinical picture which we have all seen, although Le Marquand (1951) may well be right in regarding them as extremes of the continuous spectrum of childhood obesity rather than as isolated entities. However this may be, it would appear to be impossible to understand them without regard to the adrenal cortex, and the same applies to maternal obesity, for when endocrine abnormalities occur in these women their trend is always in the direction of a Cushing syndrome and never in that of acromegaly. Indeed, pregnancy is a well-recognized precursor of the Cushing syndrome.

Our present knowledge, however, does not enable us to go much farther than the general statement that the adrenal cortex is undoubtedly concerned in the mechanism of obesity. Apart from the possibility that it may affect the site of the deposition of fat, and that Kendall's compound A (11-hydroxycorticosterone) and compound B (corticosterone) may cause a decrease in weight accompanied by an increase in the percentage of fat, there is some clinical evidence that the gland may have a direct effect on appetite, and, if so, this may provide a link with what has already been said concerning the hypothalamus. It is well known that the use of both cortisone and A.C.T.H. may occasionally be accompanied by a marked increase of appetite and gain of weight; in my experience this is particularly true of A.C.T.H., and I well remember one child, given it for nephrosis, who immediately developed an appetite so insatiable that it was like that described for rats after hypothalamic damage; for if food were not at hand she would consume her chalks, and so long as food was available she would go on eating. Simpson (1952) has described the case of a child with a tumour of the adrenal cortex who developed a similar appetite with resultant obesity. The link between the adrenal cortex and such appetite is still a mystery.

We have no understanding of how the hypothalamic regulation of appetite is itself controlled, but Kennedy (1953) has suggested that hypothalamic damage leads to an increased appetite by interference with the satiety mechanism, which may normally be actuated by a sensitivity in the appropriate hypothalamic cells to metabolites in the blood stream. No single metabolite has been proved to be capable of exerting this control, though glucose has been suggested. One cannot avoid the speculation that adrenal steroids may influence appetite by a direct effect on the hypothalamic cells concerned, and that an excess of certain steroids may provide the hypothalamus with entirely false information, causing it to legislate for a state of need in the presence of a state of plenty. For this is essentially what happens when the hypothalamus is injured or a child with an adrenal cortical tumour develops an insatiable appetite.

Speculation is hazardous; nevertheless it seems fitting to end on such a note, for the problem of obesity has not yet disclosed all its secrets.

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ASSESSMENT AND RESULTS OF
OBESITY*

BY

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For my purpose I shall define obesity as the condition in which the amount of body fat is greater than normal; the tiresome question of normality I have discussed at length elsewhere (Sinclair, 1948). The term "overweight" merely means that the body weight is greater than normal, having regard to such factors as race, sex, somatotype, height, and age.

Assessment of Obesity

A common but highly erroneous method is to obtain the weight and height of a person and compare the former with so-called standards of weight for given sex, age (if not adult), and height. The basis of the standards is seldom considered. When nutritional surveys were conducted in Germany for the Control Commission immediately after the war considerable attention was paid to body weight, and especially to longitudinal studies of body weight in individuals. Some 100,000 persons in a wide variety of categories were weighed monthly, and these weights were compared by the Hollerith method with the previous weights; unfortunately the Control Commission had these monumental results pulped in a moment of lightheartedness. Such longitudinal studies on single individuals are very valuable, although it must be remembered that undernourished persons may adapt by doing less work, thereby conserving their body weight, and that extracellular fluid may increase and mask a decrease in the weight of the fat and tissues. But a single estimate of body weight in cross-sectional studies did not give much information.

The standard tables available were those of Hassing-Schall; it was very difficult to discover their origin, which in fact proved to be unimpressive. Since the standards were much higher than those in the use of the U.S. Army, it was not surprising that Germans appeared in many cases to have lost a considerable amount of weight, and the possibility that Hassing's subjects were obese had not been considered. Further, his male figures (Brugsch, 1922) contained the common error of being the average or arithmetic mean of a large number of observations (his female figures were obtained by subtracting an arbitrary 0.89 from the male figures): since body weights are not normally distributed about the mean but are skewed to the right, the average weight of a group of persons is more than the centre of the distribution (or mode).

A very important variable in considering the assessment of obesity from overweight is the somatotype. As W. H. Sheldon (1940) has shown, every person has a greater or less degree of endomorphy, mesomorphy, and ectomorphy. Those persons in whom one or other of the first two predominates will tend to be overweight, and the ectomorph will tend to be underweight. The endomorph has excessive fat, and his overweight indicates obesity; but the mesomorph has large muscles and bones, though he may not be tall, and the amount of fat is not necessarily excessive. Indeed, a mesomorph

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