SYMPOSIUM ON OBESITY

A REORIENTATION ON OBESITY

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DURING the past half-century, investigation of the problem of obesity has followed two distinct lines: that of the intermediary metabolism and that of the energy exchange. It would be natural to expect that the two types should merge and support each other in a unified concept of obesity, for, if a defect in the intermediary metabolism causes ingested food to be diverted to storage as excess fat, the total energy exchange should reflect this abnormality. Actually, however, two schools of thought have arisen and contended through the years, and it has only recently become possible to reconcile them. It is interesting that both types of approach to the problem originated with von Noorden, who first suggested a defect in carbohydrate metabolism and later abandoned this as he focused attention on the energy exchange as a means of explaining the phenomena of obesity.

INTERMEDIARY METABOLISM

Von Noorden first suggested a prediabetic state as a cause of obesity and amplified this as follows: “Obese individuals of this type have already an altered metabolism for sugar, but instead of excreting the sugar in the urine, they transfer it to the fat-producing parts of the body, whose tissues are still well prepared to receive it.” It immediately became apparent that, if obesity could arise in this way, the adipose tissues, instead of readily releasing for energy the fat that had been formed from carbohydrate, must hold on to it with unusual tenacity; in 1908 von Bergmann announced the “lipophilia” concept, which attracted many investigators.

Those who sought the answer to the problem of obesity in studies of the intermediary metabolism found a number of clues that led them to the view that some defect of carbohydrate metabolism was involved and that the rate of fat storage exceeded that of its mobilization and destruction. An endocrine influence was also thought to exist, as expressed by Falta: “For fattening is necessary a functionally intact pancreas.”

In connection with carbohydrate metabolism Lichtwitz, and then Kugelman, found that the blood lactic acid level of the obese after light muscle exercise was much higher than that in normal persons. Proger and Dennig confirmed these results in experiments that took into account the greater energy expenditure of the obese in performing a given task, and they ruled out all possible causes of the increased lactic acid except “definite chemical disturbances in the muscle.”

Studies of the intermediary metabolism of fat were all but impossible until the introduction of isotopes and their use in tagging molecules for physiologic experiments. Details of the metabolism of fat and of carbohydrate as well, previously shrouded in mystery, then became clarified, and old experimental findings yielded to new interpretations. It seems, now, to have become clear that the increase in the blood level of lactic acid observed by Proger and Dennig cannot be due, as they thought, to an inability of the muscle tissues to resynthesize glycogen, for glycogen is not normally resynthesized here. An interpretation more in accord with a modern understanding of carbohydrate metabolism is that the tissues of the obese are more limited than normal in their capacity for oxidizing pyruvic acid — the blood levels of lactic and pyruvic acid both reflect the degree to which the tissues fail to oxidize the pyruvic acid formed in them from the glycolytic phase of carbohydrate breakdown. This interpretation, along with Wertheimer’s recent finding that pyruvic acid inhibits the oxidation of fatty acids, suggests that obesity may be caused by a defective capacity of the cells for breaking down carbohydrate beyond the stage of pyruvic acid and that the presence of increased amounts of this substance, by inhibit-
ing the utilization of fat, causes fat storage to gain the ascendancy over fat mobilization and destruction. This process, which would result in an increased size of the adipose deposits, would require the presence of a functionally intact pancreas. Thus, the concept of obesity as a defect of intermediary metabolism appears to find some modern support.

Energy Exchange

Von Noorden soon abandoned his earlier theory and became preoccupied with studies of the energy exchange in obesity. In 1907 he made the famous classification of "exogenous" and "endogenous" obesity. The latter was to be distinguished by a diminished energy expenditure dependent upon a "slowing of metabolism." For many years the thyroid gland was suspected as being at fault in common obesity; metabolism tests, calculated from a surface-area formula based on body weight alone, gave abnormally low readings in obesity as well as in hypothyroidism. The hypothyroid as well as the entire hypometabolic concept of obesity was largely abandoned, however, when the introduction of Du Bois' more accurate surface-area formula, based on height as well as weight, gave more normal metabolic readings in uncomplicated obesity. In 1930 Newburgh and Johnston announced that endogenous obesity was a misconception. It seemed reasonable that, if a defect of metabolism could account for obesity, the defect would be reflected in the energy exchange, and, since this appeared to be normal, it was concluded that any explanation of obesity other than that of a primarily disturbed appetite must violate the law of conservation of energy.

It is well known that the basal metabolic rate of the obese is normal by the standard test. This means that obese people oxidize as much food per square meter of skin surface as those of normal weight. The use of the surface area as the measuring rod for metabolism tests has been upheld on the ground that, throughout the animal kingdom, there is a constant mathematical relation between the caloric output and the surface area of the body. It has been found, however, that throughout the animal kingdom an equally close mathematical relation exists between the caloric output and the weight of the body and that the only exceptions to this rule are in people of abnormal build. The metabolic rate in obese human beings, when a weight formula is used, is lower than that in human beings of normal build. Therefore, the basal metabolic rate of the obese is normal when the surface area is used as the criterion and subnormal when the weight is the criterion; this is the only essential difference in the choice of the two methods, which apply with fairly equal universality except in the obese. It has been claimed that the surface-area rule is superior to the weight rule because it causes the metabolic rate of the obese to appear normal, a circumstance that gives it greater universality. It must not be forgotten, however, that the purpose of metabolism tests is to find out if the metabolism is normal. The whole question depends on whether the surface-area rule or the weight rule is the correct one to use, and the decision cannot be made on the basis of which one makes the obese come out normal, for that would indicate an a priori assumption that the obese are actually normal, and the assumption would be used to prove itself.

The current metabolic standards were derived from measurements of a supposedly normal group, which included the obese as well as the lean. One of the supposedly normal group, Mrs. McK., was 4 feet, 11 inches, tall and weighed 204 pounds. The metabolic formula arrived at and adopted as a criterion of normality, therefore, assumes that the obese are metabolically normal. Consequently, they must, by mathematical necessity, come out normal when the formula is used. Justification for the selection of the surface area in metabolic calculations originated in the belief that the surface area of the body caused the rate of metabolism to be what it is, but when it was found that the surface area was not causally related to the metabolism no scientific basis for its use remained. The surface-area formula has been useful, empirically, in the clinical diagnosis of thyroid disease. When applied to obesity, however, it merely compares the metabolism with the average in other obese people and does not show the metabolic status of obesity itself. It seems, therefore, that valuable though the surface-area formula may be in clinical diagnosis, its application must be restricted to determining departures from the average in any weight-and-height group of people, and that it should not be used in scientific investigations of the metabolic status of obesity. The question whether the metabolism of the obese is normal or not, therefore, remains at least an open one.

Dynamic and Static Phases of Obesity

In 1940 Rony observed that many people gain weight over an interval and then maintain constant though excessive weight for long periods or indefinitely. To this observation he applied Cannon's concept of homeostasis, through which the remarkable ability of the human organism to maintain constant weight is negotiated. He described obesity as an alteration in the homeostatic forces that regulate the voluntary intake of food to the energy output. In the weight-gaining stage of obesity, which he called the "dynamic" or "progressive" phase, the homeostatic equilibrium was disturbed, disposing to an energy intake greater than the energy expenditure, but in the static phase the two were again equalized. He observed that
positive caloric balance in the dynamic phase did not necessarily cause that phase:

Positive caloric balance may be regarded as the cause of fatness when fatness is artificially produced in a normal person by forced excessive feeding or forced rest or both. But obesity ordinarily develops spontaneously; some intrinsic abnormality seems to induce the body to establish positive caloric balance leading to fat accumulation. Positive caloric balance would be, then, a result, rather than a cause of the condition.19

Rony suggested that the dynamic phase of obesity would be more likely to reveal abnormalities of metabolism than studies of the static phase. Since it would be impossible to know if a person who had been gaining weight was still in the dynamic phase or had already reached the static phase, he suggested that, for study, the dynamic phase be induced by the application of low-calorie diets. The obese person would then lose weight to a level below that at which his weight had become stabilized, and any abnormal metabolic processes of the dynamic phase would be exposed.

**Dynamic Phase**

Strang and Evans21 studied the energy exchange of obese persons before and after they lost weight on low-calorie diets. They reported, "When obese patients are reduced by dietary measures alone, the energy exchange diminishes proportionally much more than the weight or surface area." A lowered metabolism in the dynamic phase of obesity seemed, therefore, striking and obvious. In interpreting their careful and painstaking experiments, however, they assumed, as many did at the time, that adipose tissue is metabolically inert. This led them to the view that the weight of the fatty deposits should not be counted when metabolic calculations are made, and they devised a method of calculating metabolic rates, based on the height and the ideal, rather than the actual, weight. In this way the significance of the decline in metabolism became minimized, for, with the actual weight replaced by a constant figure for any given height, the only variable remaining in the metabolic standard was the height. The formula, therefore, was based on height alone, and it gave abnormally high readings for the metabolism of the obese.22 More recent investigations indicate that adipose tissue, far from being inert, is metabolically very active.23, 24 The assumption on which the formula of Strang and Evans was based, therefore, can no longer be held valid. It seems more justifiable to interpret the results of their experiments in a simple and direct manner and to conclude that, in the dynamic phase of obesity induced by low-calorie diets, the basal metabolism is abnormally low.

**Reconciliation of energy exchange and intermediary metabolism.** The finding of an abnormally low energy exchange in the dynamic phase of obesity appears to demand a correlative disturbance in the intermediary metabolism, for it indicates that the large fat stores are not being mobilized and oxidized rapidly enough to maintain a caloric production equal to that which would normally be expected. The problem of obesity, therefore, appears to resolve itself into that of finding an explanation for the decreased rate of mobilization and destruction of fat. In the rare cases of hypothalamic obesity in human beings it has been suggested that the neural mechanism regulating fat storage may be impaired.24 In other cases of obesity, it seems reasonable to consider the evidence for a defect in the ability of the tissues to oxidize pyruvic acid and the inhibiting effect of this substance on the oxidation of fatty acids.26 Under these circumstances, much of the fat that is regularly formed from carbohydrate in the body would accumulate in the adipose deposits; the tissues would suffer a relative deprivation of nutriment, and if the deficit were not supplied by an increased intake of food a decline in metabolic rate must ensue. Under conditions in which the voluntary intake of food was allowed free play, the homeostatic mechanisms that regulate appetite to energy needs would dictate an increased food consumption, and thus the subject of the study would become obese.

**Confirmatory studies on animals.** Rony's concept of the dynamic and static phases of obesity has been found to apply in the genetic obesity of mice28 and also in the hypothalamic obesity induced by operation on laboratory animals.29 In both, after a period of weight gain, it has been noted that the weight curve strikes a plateau. Restriction of food intake then causes weight loss, but the lost weight is quickly regained when food restrictions are removed. Many experimenters were first inclined to consider the weight gain in these animals as due to a primary disorder of appetite. It has been found, however, in genetically obese mice and also, recently, in experimental hypothalamic obesity, that there is a retardation in the rate at which fat is mobilized from the adipose deposits.27, 28 In the dynamic phase of hypothalamic obesity a decline in metabolic rate occurs if the food intake is not increased; on equal amounts of food, animals operated on gain more weight than those not operated on,29 and also show an increased rate of conversion of carbohydrate into fat.30

As an explanation for the static phase of obesity in laboratory animals it has been suggested that "as fat stores become enormous, even the possibly impaired mechanisms for breaking down fat might be sufficient to supply all the fat that the cells can use and thus gradually impair the urge for new fat formation."30

**Static Phase**

The static phase in the rare cases of hypothalamic obesity in human beings may well be explained by the same process as that suggested for hypothalamic obesity in laboratory animals. In cases of obesity
that arise from a disturbance in the intermediary metabolism of carbohydrate, it may be assumed that the neural and hormonal mechanisms regulating the mobilization of fat continue to operate, though hindered by the forces that inhibit fat oxidation. A lowered rate of mobilization of fat per unit of adipose tissue might then be completely compensated for by the greater total mass of adipose tissue, after the subject had reached a certain degree of obesity. More fat would be mobilized, but the inhibition on its use by the general tissues would cause the blood level of fatty acids to increase. Supporting this concept is the finding that in the majority of cases of obesity the fatty acid blood level is elevated. The increased blood level of fatty acids would induce a more rapid oxidation of fatty acids by the tissues. As a result, the tissues would be more adequately supplied from the adipose deposits, and the homeostatic mechanisms that relate the appetite to energy needs would dictate only the amount of food required to maintain the body weight at a constant, though excessive, level. Thus, obesity might be considered as a compensatory hypertrophy of the adipose tissues, providing for an increased use of fat by an organism that suffers an impairment in its ability to oxidize carbohydrate.

**Implications in Treatment**

Low-calorie diets, although they reduce the weight of the obese may, it seems, merely disturb the balance of forces that exists in the static phase and re-establish the dynamic phase of obesity, in which the forces tending to cause weight gain are re-activated. This would mean that treatment had been directed only toward the outward and most obvious symptom of a profound metabolic disturbance, which would continue to promote excessive fat storage unless counteracted by continued caloric restriction. The tendency of people to regain weight lost through dieting is notable. Brown and Ohlson reported cases in which, after reduction of weight, constant weight was maintained on remarkably low food intakes. It seems that the obese person who is treated by the low-calorie method must remain on a subnutrition diet the rest of his life if he wishes to prevent weight gain. If the formerly obese person, with his subnormal caloric expenditure, ate as everyone else does and still did not regain weight the law of conservation of energy would be violated.

Low-calorie diets, it seems, operate not so much by causing the body to “draw on” its fat reserves as by limiting the formation of new fat by withholding the necessary materials. At the same time, these nutrient materials are being withheld from the tissues that require them for energy. It seems desirable, in the treatment of obesity, to direct efforts toward an increased utilization of fat. If this could be accomplished with sufficient effectiveness, no caloric restriction would be necessary, for a large part of the energy needs would be supplied by the body stores, and the homeostatic mechanisms that relate the appetite to the energy output would dictate an intake of food requisite to make up the remainder. Weight would be lost, but a normal caloric production would be maintained. The final result would be what, to extend Rony’s terminology, might be called a “negative dynamic” or “retrogressive” phase of obesity, in which the tendency to gain weight on an unrestricted caloric intake would be reversed. There are indications that such a treatment of obesity is quite possible.

**Physiologic Determinants in Weight Reduction**

The over-all determinant in weight reduction is the degree to which the caloric expenditure exceeds the intake, but a number of physiologic factors determine both these variable quantities. Since much of the carbohydrate as well as the fat ingested is regularly stored as fat before it is utilized, and since fat cannot be reconverted to carbohydrate in any significant amount, the oxidation of fat for energy plays an important part in the continuing metabolism. The significance of the role of fat has only recently been recognized. It is used readily by the general tissues as fatty acids and as the ketones that are formed in the liver, without the necessity of the simultaneous oxidation of carbohydrate. After the usual overnight fast 60 per cent of the energy needs of the body are met by fat, and after two days of fasting this figure is increased to 90 per cent. It appears that the mechanism by which increased amounts of fat are made available for fuel is by means of the ketosis that develops when carbohydrate is in short supply.

The ketosis is followed by mobilization of fatty acids from the adipose deposits. Then, with the blood levels of ketones and fatty acids increased, the tissues oxidize both substances at a faster rate. Ketosis is, essentially, a benign process that spares protein, its effect in stimulating the metabolism offsets, to some extent, the specific decline in metabolism attendant on starvation. The low-calorie diets employed by Strang and Evans were ketogenic and this circumstance, it seems, made possible a somewhat favorable contrast between their use in the obese and the use of nonketogenic diets in the nonobese. Unless low-calorie diets are ketogenic, it seems, they cannot operate by increasing the use of fat by the organism but only by decreasing the formation of new fat.

An increased use of fat by the organism can apparently be induced by two methods, which have special applicability to the obese. Restriction of carbohydrate, productive of ketosis in the lean, would be even more effective in the obese if, as there seems ground for believing, the obese on a highly carbohydrate type of diet form an excess of pyruvic acid, for the removal of this excess would
eliminate the inhibition on the oxidation of fatty acids. The ingestion of fat, on the other hand, which ordinarily causes ketosis by stimulating the pituitary gland to produce a ketogenic principle, has three times as great an effect in the majority of the obese as in the lean. In the obese the blood level of ketones induced by fat feeding reaches about 12 mg. per 100 cc. Although this is higher than the level in the lean, it is less than half the moderate level of ketosis found after two days of fasting and only a thirtieth of the level reached in severe diabetes. Reference to ketosis, it seems, should always indicate the actual level of ketones in the blood; otherwise, the benign and even beneficial levels of ketonemia are confused with those associated with severe illness.

The type of treatment of obesity to which these considerations logically lead is that of a diet in which carbohydrate, alone, is restricted and protein and fat are allowed ad libitum. Such a diet was studied thoroughly at the Russell Sage Institute in 1928, though not with the problem of obesity in mind. Subject V. S. of that study, who was a few pounds overweight, lost his excess weight in the first few weeks of an exclusive diet of lean and fat meat. His basal expenditure rose from 60.96 calories to 66.38 calories per hour during the period of weight loss, indicating an increase of 8.9 per cent. He continued on the diet a full year, with no apparent ill effects. His blood cholesterol level at the end of the year, while he was still on the diet, was 51 mg. lower than it had been at the start. It rose a little after he resumed an ordinary, mixed diet. After losing his excess weight he maintained constant weight the rest of the year, though food was taken in as desired. His total intake ranged from 2000 to 3100 calories a day. He derived, by choice, about 80 per cent of his energy needs from fat and 20 per cent from protein. These proportions are close to those derived by a person from his own tissues during prolonged fasting. The instinctive choice of about 80 per cent of the calories from fat seems to be based on selection by the metabolic processes of the organism. It has been found that when carbohydrate is restricted in the diet, the appetite for fat greatly increases. The organism adapts itself to a greater use of fat for energy when this substance is increased in the diet.

The proportion of 80 per cent of the calories from fat and 20 per cent from protein would be represented by one part of fat to three parts of lean meat, by weight. Carbohydrate, as the glycogen contained in the meat, would be present to the extent of 1 or 2 per cent of the calories. In round figures the amounts of food consumed would be from 6 to 9 ounces of lean meat and 2 to 3 ounces of fat, cooked weight, at each of the three meals of the day. The precise amounts ingested were, of course, regulated entirely by the appetite, and they varied from day to day, paralleling the daily variations in energy needs.

This type of diet has been applied clinically in the treatment of obesity and has worked out very well. In most cases the addition of carbohydrate, not exceeding 60 gm. a day, has been found compatible with effective weight loss. Much more than this, it seems, would be likely to check ketogenesis and thus make weight loss impossible on an ad-libitum intake of protein and fat. Carbohydrate foods used were potato, rice, grapefruit, grapes, banana, melon, blueberries and raspberries in amounts yielding an average of not more than 20 gm. of carbohydrate at each meal. In a few cases even this much carbohydrate prevented weight loss, though an ad-libitum intake of protein and fat, more exclusively, was successful. In rare cases, suspected of being cases of hypothalamic obesity, it has been ineffective.

Adjunctive measures have been restriction of salt, for the purpose of increasing the metabolic rate, and liberal amounts of water, for the same reason. A cup of black coffee or tea has been allowed with each meal. A most helpful adjunct, and one that has appeared to be beneficial in many ways in addition to weight reduction, has been the prescription of a half-hour walk before breakfast each morning. This accentuates the fasting state and throws the metabolism over to an increased use of fat for energy. In addition, it appears to drain the liver and gall bladder and to facilitate greatly the handling of fat by the digestive tract.

A remarkable finding in the use of this type of treatment has been the large total caloric intake, which appears to be compatible with a weight loss of 7 to 12 pounds a month. This is not surprising, however, when it is realized that the obese have large requirements for maintaining a constant, though excessive, weight level, and that with this type of treatment there is an increase in the caloric expenditure, rather than a decrease, as in treatment by caloric restriction.

If this concept of obesity and its treatment is accepted, credit must be given to Dr. Vilhjalmur Stefansson, anthropologist and Arctic explorer, who observed that Eskimos were never obese when following their accustomed diet of lean and fat meat but that obesity appeared among them with great rapidity when concentrated carbohydrate foods were introduced, and to Dr. Blake F. Donaldson, who, for two decades when little was known about the intermediary metabolism, applied this type of treatment in his practice and reported on it in conferences at the New York City Hospital.

**Summary**

It appears possible to reconcile studies of the intermediary metabolism and of the energy exchange in obesity by the concept that this condition arises from a defective capacity of the tissues for oxidizing