FAMILIAL ASPECTS OF OBESITY

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No scientific investigation is needed to detect the familial nature of obesity, but the extent of the contribution of constitutional, cultural and other environmental components is not at all clear. That it is especially important, however, to understand these etiologic factors is suggested by the failures experienced by those who have undertaken to treat long standing obesity. A firm grasp of the nature of the causes of the condition is the key to prevention, and the time to prevent is childhood.

Before going on to a discussion of heredity in obesity it might be well to state what is possible in genetic studies on human populations. Genetics is the study of heritable variation, and it attempts to describe the degree to which familial likenesses and dissimilarities result from the action of genes in particular environments. In general, we suppose that gene action is biochemical, and that it is expressed in the control of metabolic reactions in the cells, whether by conferring specificity upon enzymes or by other means.

Several methods for such investigation are available. First we may study discontinuous variation in which differences between individuals are clearly measurable, and a population may be divided into two or several types without misclassification. Such differences are often found to be associated with differences in molecular specificity or quantitative differences in enzyme activity. If these differences are genetic in origin, they are usually found to be due to one or at most a small number of genes, and the intrafamily distribution of the characteristics will follow some mendelian pattern.

A second method involves the analysis of continuous variation. By this is meant differences between individuals which are so small as to make actual measurement of such differences impossible, and covering a wide range or spectrum, so as to form a continuum. Here one can show that differences between families are greater than those within, and there is a strong positive correlation in the measurement of the characteristic under study between parents and children, and between sibs. Such intrafamily similarities are thought to be due to large numbers of genes acting additively or interacting in some fashion, but one of the deficiencies of the method is that nothing can be said concerning the action of such genes, nor whether the characteristic under study is genetically, etiologically and pathogenetically homogeneous. Nor can one neglect the fact that strong positive intrafamily correlations may be due to sharing a common environment.

A third method consists of making observations on similarities and differences between single-ovum and double-ovum twins. Since single-ovum twins are genetically alike, differences between them should be due to environment, whereas differences between double-ovum twins are more likely to be due to genotypic as well as environmental differences. This method has its uses, but has also a number of defects, among them its lack of information concerning the mode of action of genes involved.

The problem of genetic study of human obesity is made difficult by the fact that body weight is a continuous variable, and obesity is defined in terms of this parameter, that is, a person is considered to be obese when he weighs 20% or more above

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an "ideal" weight. It is also made difficult by the obviously profound influence of the individual's personality characteristics; traits in which the development may have very little hereditary component, but which are more likely culturally imposed patterns of behavior. Finally it is made difficult because of the lack of obvious metabolic or clinical differences between most of the cases, a deficiency which may be masking considerable etiologic heterogeneity in any one group of cases.

The studies which have been made have consisted of observations on twins, or else estimates of the familial incidence of obesity. For example Newman and others found a correlation coefficient for weight for single-ovum twins of 0.973. Correlations for fraternal twins and for sib pairs were lower. Other workers found similar correlations, but those for single-ovum twins, reared apart were significantly lower than those for such twins sharing a similar environment. These results suggested an hereditary factor but tell us neither whether or not all the cases of obesity were etiologically the same, nor the extent of the environmental component. Other investigators have used different methods. Bauer, in a series of over 1,000 obese persons, found that 73% had one or both obese parents. Rony in a smaller series found 69% with one or both obese parents. Angel, on the other hand, considered obesity among the offspring of obese parents. He found that half the children of one obese and one average weight parent were obese, while two-thirds of the children were obese if both parents were fat. In a similar study, Gurney found that 73% of the children were obese when both parents were overweight, 41% when only one parent was obese, and 10% when both parents were of average weight. A more recent investigation shows a better correlation between the weights of mothers and obese children than with the weights of their fathers, and in this investigation, though it was a small one, the total incidence of obesity among parents of obese children was considerably smaller than that found by Bauer and Rony. While none of these investigations show family distributions of the characteristic which suggest single gene etiology of obesity, they are of interest and value because they demonstrate objectively the familial nature of the condition. Unfortunately, however, they do not help to say what it is, nor the extent to which it is inherited. Even so, they are of great importance to the pediatrician who may wish to prevent obesity, in suggesting what may lie in the future for the infants of obese parents.

What is needed to make genetic studies more meaningful is the discovery of the metabolic basis of obesity in some cases. Doubtless some persons become obese because of overeating and inactivity, but it is reasonable to suppose that others may be obese because of metabolic differences. Certainly, for example, the distribution of fat over the body is not always the same in all persons, and occasionally one sees similar unusual distributions in parent and child.

Several different kinds of genetic obesity are known in animals in which single gene substitutions produce obesity, each type differing from the others in several characteristics. In one type of mouse, metabolic observations have suggested that oxidation of C-14 radioactive acetate is markedly impaired, so that the radioacetate is more readily incorporated into the fat of the obese. In the same type of animal it has been demonstrated that during prolonged fasting, fat is much less readily mobilized in the obese animals than in their nonobese litter mates. While we have no such well characterized forms of obesity among human beings, current knowledge of the intermediary metabolism of food, and the enzymatic, hormonal and nervous control of such metabolism suggests that such characterization may ultimately be possible. When we have this information, constitutional propensities will be resolved into single gene entities.
that time, prognosis as well as therapeutic and preventive methods may be based upon the particular type of obesity and the particular family pattern at hand.

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MECHANISMS CONCERNED WITH APPETITE

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The title given to this paper is a bit in-
appropriate for a discussion in physi-
ology, since the word “appetite” has a psy-
chologic rather than physiologic meaning. Both hunger and appetite, as well as sa-
tiety, refer to sensations or affective states, and none of the three words has an accu-
rate or precise definition. In the following discussion they are used only for conveni-
ence, and with only their common English meanings. They cannot be studied directly in human infants nor in laboratory animals, but only indirectly by simple observation as to whether food is or is not accepted, or by noting the amount of food eaten or the rate of eating. Perhaps a better title is “Mechanisms that regulate intake of food,” using the word, “regulate,” as it is used in the case of respiration. For example, ven-
tilation of the lungs is said to be regulated through the interaction of respiratory cen-
ters, reflexes, stretch receptors and che-
moceptors. Analogous mechanisms doubtless serve to regulate feeding.

Like the regulation of respiration, the control of intake of food is one of the im-
portant functions of the central nervous system. The digestive apparatus is con-
cerned only in a limited way and that as a system regulated, rather than as the regu-
lator. Sherrington1 noted as early as 1900 that feeding persists after operations upon the stomach, including nearly complete re-
moval of the organ. If such an operation leaves the tract adequate for digestion, it does not lead to any primary, quantitative disturbance of feeding behavior. Similar conclusions may be drawn from observa-
tions upon patients who have undergone the several types of operation upon nerves supplying the stomach and intestine, in-
cluding patients subjected to vagotomy. A second type of evidence has come from ex-
perimental laboratories, where Bash,2,3 using rats, and Ivy and associates,4,5 using dogs, found that even a complete extrinsic denervation of the gastrointestinal tract did not change the quantity of food eaten daily. Moreover, the administration of insulin to the dogs brought about an increase in intake

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