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.

REFERENCES


MECHANISMS CONCERNED WITH APPETITE

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THE TITLE given to this paper is a bit inappropriate for a discussion in physiology, since the word "appetite" has a psychologic rather than physiologic meaning. Both hunger and appetite, as well as satiety, refer to sensations or affective states, and none of the three words has an accurate or precise definition. In the following discussion they are used only for convenience, 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, ventilation of the lungs is said to be regulated through the interaction of respiratory centers, reflexes, stretch receptors and chemoreceptors. Analogous mechanisms doubtless serve to regulate feeding.

Like the regulation of respiration, the control of intake of food is one of the important functions of the central nervous system. The digestive apparatus is concerned only in a limited way and that as a system regulated, rather than as the regulator. Sherrington noted as early as 1900 that feeding persists after operations upon the stomach, including nearly complete removal 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 observations upon patients who have undergone the several types of operation upon nerves supplying the stomach and intestine, including patients subjected to vagotomy. A second type of evidence has come from experimental laboratories, where Bash, using rats, and Ivy and associates, 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.
of food, while administration of amphetamine depressed intake of food just as it does in normal animals. These observations all imply that the site of regulation is outside the gastrointestinal tract.

The role of the central nervous system in regulating intake of food appears to have been suggested first by the discovery that either obesity or emaciation may occur in patients with nervous diseases. There was at first a notion that pituitary disturbances cause obesity, but Hetherington clarified this situation by showing that the hypophysis is in no way directly concerned with the obesity following injury to the base of the brain. He noted that when the pituitary gland is intact, injury to the hypothalamus yields obese rats of adult skeletal size, while the same hypothalamic operation upon hypophysectomized rats produces fat dwarfs. Later studies in other laboratories revealed that in hypothalamic obesity the excess of body fat represents extra food eaten by the animal. There is a good correlation between the amount of extra food eaten and the extra gain of body weight, and it is now generally agreed that in this type of obesity, the primary disturbance is one of regulation of feeding, rather than some difficulty in utilizing fat or carbohydrate, or some other abnormality in the intermediary metabolism. Hypothalamic obesity is believed to be the result of a regulatory deficit which has been called hypothalamic hyperphagia.

From the time of its discovery, this hyperphagia was assumed to be a release phenomenon, brought about through the destruction of an inhibitory mechanism, just as decerebrate rigidity is due to a release of the brainstem from inhibition normally arising in higher centers. If overeating occurs after production of certain lesions, it can only mean that under normal conditions feeding must be controlled by at least two mechanisms—one, the mechanism responsible for the eating and preserved in the hyperphagic animal, the other, a mechanism inhibiting eating and injured by hypothalamic lesions. In 1951, Anand discovered that the former of these, the one maintaining feeding, is also represented within the hypothalamus, lying on both sides of the brain just lateral to the inhibitory mechanism. When Anand destroyed the lateral hypothalamic area bilaterally, eating was completely and permanently abolished. His rats did not seem to be abnormal otherwise, because their body temperature was normal, and they were awake and active. Yet they refused food, and resisted every attempt to feed them by placing food in contact with their lips and teeth. On certain of his animals, Anand performed operations in two or three stages. After a unilateral operation the rats ate normally until the second stage was performed upon the opposite side. Or, if lesions were made in the more medial portion of the hypothalamus, the animal began to overeat and to become obese; later, when lateral lesions were made, eating was abolished and the rat began slowly to starve to death, although food was always present in the cage. The more lateral mechanism has been called a feeding center, or even an appetite center, while the more medial one has been called a satiety center. Joliffe termed the two, together, the "appetstat."

These hypothalamic mechanisms probably do not represent the most basic mechanisms of feeding behavior, since the spinal cord, medulla, and pons are known to contain pathways essential for feeding activity. These lower pathways apparently have the properties of reflex arcs. Induced by an appropriate stimulus to sensory receptors, nerve impulses are carried by afferent neurons to the brain or spinal cord. There, connections are made with internuncial neurons, which, in turn, may activate motor neurons supplying the muscles that accomplish the feeding. Miller and Sherrington described reflexes of this type in decerebrate animals from which the hypothalamus had been completely removed. Although I have not been able to find a similar analysis of the behavior of human infants, I believe that their feeding responses
Facilitation

| Sensory end organ (olfactory epithelium, retina, cochlea, etc.) |
| Contractions of empty stomach |
| Cold environment |
| Lowered supply of glucose |

Feeding Reflexes

| Reflex centers (brain stem) |
| Distension of stomach |
| "Metering" in mouth and pharynx |
| Dehydration |
| Warm environment |
| Exercise |
| Drugs |
| Amphetamines |

Inhibition

| Motor units (muscles of head, neck, mastication, etc.) |

**Fig. 1.** Outline of factors affecting intake of food, with a suggestion as to their capacity to induce either central facilitation or inhibition of feeding reflexes. (From Brobeck, J. R.: In Fulton, J. F.: Textbook of Physiology. Philadelphia, Saunders, 1955.)

are generally assumed to be based upon comparable reflexes, including those which take part in locating the nipple, in grasping it, in sucking and swallowing.

A possible relationship between feeding reflexes and the hypothalamic mechanisms has been outlined in Figure 1. In the center are represented the reflexes, beginning with food and leading to feeding. At the sides of the figure are listed certain factors capable of altering reflex activity through central facilitation or central inhibition. These words, facilitation and inhibition, have technical meanings in neurophysiology, and refer to specific and discrete processes occurring in the neighborhood of neurons; the former, facilitation, increases the tendency of the neuron to produce a nerve impulse; the latter, inhibition, may prevent activity even when the neuron is being subjected to excitatory stimuli from another source. It is not known where in the feeding reflex arcs the facilitation or inhibition is applied; they may conceivably be applied through the internuncial neurons, but they may also act directly upon the motor neurons. To illustrate the operation of these mechanisms, let us examine feeding behavior in a laboratory animal maintained in a cage where food is always present. Under these conditions, feeding will not be continuous, as animals usually eat definite meals even though food is always available. It appears, therefore, that feeding reflexes which might be initiated continually by the sight, odor, or sound of food, or contact with it, can be inhibited somewhere in transit through the nervous system. When the reflexes are not inhibited, feeding occurs. In Figure 1, the conditions listed on the right side under "inhibition" are known to be accompanied by reduced intake of food, while those listed under "facilitation" are associated with an increased consumption of food. Hunger contractions are included in this list as a source of central facilitation, because during hunger the skeletal reflexes (such as the knee jerk) are known to be
hyperexcitable, presumably as a result of central facilitation. From this, it seems reasonable to suggest that other nervous mechanisms, including feeding reflexes, may be correspondingly facilitated.

Another important reaction essential for normal feeding is movement or locomotion, as animals, including infants, are more restless just before they eat. The neurologic basis for locomotion is similar to that of feeding itself, in that the spinal cord and lower brainstem contain centers which, at least in laboratory animals, may induce rhythmic stepping and even progression, while the higher centers include a facilitatory mechanism in the hypothalamus, and an inhibitory one in the basal ganglia. Appetite appears to be a condition of generalized increase in locomotor activity and facilitation of feeding reflexes, which together tend to bring the organism into contact with food and to lead to its ingestion. "Satiety," on the other hand, is regarded as a state in which there is a lack of awareness of food and a reduced activity, possibly even to a point of somnolence.

Infants appear to be the only satisfactory subjects for study of these problems in the human species. In adult subjects the more fundamental reactions become so obscured by training, experience, habit and social factors that trying to clarify them appears to be almost hopeless. An infant, by contrast, although complicated enough, possesses behavior much more susceptible to analysis. If knowledge gained from study of lower animals is to be tested adequately in man, I believe that babies will prove to be by far the best subjects for this purpose.

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A PEDIATRIC-PSYCHIATRIC VIEWPOINT ON OBESITY

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From the viewpoint of the pediatric psychiatrist, the problems of obesity, as seen clinically, can be thought of as having three layers. The first is constitutional, better described as physiologic, which may be broken down into genetic and structural elements. The second is psychologic, consisting of the values that food intake or the obesity itself come to have. The third layer is made of the cultural and social reactions to food and fat. These attitudes encountered inside and outside the home inter-
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