It has been found quite recently that other fluoride salts are much more effective afterwards. A lot of work has been done on stannous fluoride, which is much more readily absorbed by the enamel of teeth and is much more effective than the forms of fluorine you can put in water or rinse your mouth with. It has been put in tooth-paste commercially. There is some evidence that it is taken up by teeth, and there is work going on with chewing gum, but I do not think there is much evidence that drinking water has an effect topically on erupted teeth.

Question: One thing we general practitioners can do is to apply to our water undertakings, to find out what the local fluoride level is and publish this in our surgeries. I have done this. Our own water has a fluoride content of 0.8 ppm., which is a reasonable level and not one that would need augmenting.

OBESITY

I

The Physiological Approach

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There is a school of thought, mainly in America, which holds that one cannot get fat without over-eating, or in other words that obesity and gluttony are the same thing. The evidence for this is said to be that one cannot cheat the laws of thermodynamics. Of course one cannot, and I do not think anyone wants to, but energy requirements vary enormously from one person to another, and what is gluttony in one person or at one time of life can be perfectly normal at another. You all know that a young woman who has found that the price of having babies has been to turn her into a shapeless lump of fat is not interested in the first law of thermodynamics, the law of conservation of energy. She knows that before she was married she could eat pretty well anything that she wanted, and that she cannot do this any more. To tell her that she is fat because she eats more than she needs, although it is perfectly true, is about as useful as telling an alcoholic that he drinks too much. What matters to the patient is why she used to be able to regulate her appetite to fit her energy expenditure whereas now

she cannot. We do not know the entire answer to this question of regulating energy balance, but we do know part of it, mostly based on experiments on laboratory animals, and I think what we do know may help towards a more rational approach to human obesity than in the past.

Catch phrases about thermodynamics can of course be very misleading. As its name suggests, thermodynamics was invented to help engineers to understand the workings of heat engines or steam engines; it works quite well within its limits and will tell one, for example, how much useful energy a locomotive of a particular specification can extract from a ton of coal. But rigorous thermodynamic treatment of this sort has never been achieved for metabolic processes. Some text-books, it is true, give the impression that if one has data such as height, weight, age, and occupation, the specification of a man so to speak, one can predict his energy utilization. This is not true, for the text-book figures are averages. In these days of statistics there is an awful tendency to equate the average with the normal, but there are many perfectly " normal " people who would rapidly get fat if they ate the same amount as the hypothetical average person of the text-books. So let us get rid of the idea that one will learn anything much from the clinical ritual of listing what a patient eats on a typical day. Even if one had exact details of his work, one would still have missing from the energy equation his mechanical efficiency. It would not be practical politics to try to measure mechanical efficiency in clinical practice, but enough normal people have been examined to know that it is an extremely variable quantity.

Yet somehow the ordinary man or the ordinary animal does equate intake and output in energy and one of the most profitable starting points for a consideration of the physiology of obesity is to consider how energy balance is regulated. I say energy balance advisedly, and not appetite. For convenience, of course, one starts with appetite, but I hope to convince you that appetite regulation is not the whole story. The idea that the hypothalamus somehow regulates body weight goes back a century or more to 1840, when a German physician, Mohr, described the first case of hypothalamic tumour causing obesity. It was almost a century (1939) before Hetherington and Ransom in Chicago showed that they could cause obesity experimentally in a laboratory rat. They used thin electrodes to produce small areas of damage near the ventro-medial nucleus of the hypothalamus. The same effect of gross obesity follows similar lesions in the same position in all other species so far examined. Lesions somewhat more lateral lead to the opposite effect of total cessation of eating and drinking, and seem to act on

some basic feeding and drinking centre.

The lesions that Hetherington and Ranson used in their early experiments were large by modern standards, and produced many effects such as sham rage which had nothing to do with obesity. Also the gonads of all the animals atrophied, reminding one of the adiposogenital syndrome which Froehlich described half a century earlier. Another of the apparent side-effects that was regularly found was greatly reduced general locomotor activity. As the technique of making lesions in animals has improved, and smaller lesions have been used, most of the side-effects have been separated and physiologists have become convinced that even inactivity is not really essential to obesity, which is mainly due to overeating and increased appetite. I think that is probably a misunderstanding, due to the unnatural way the experiments are carried out. It is always a problem to know how best to apply laboratory findings to real life, even the normal life of the animal one has studied. Anybody who has seen a conventional set-up in a laboratory animal house knows the cosy, rather small cages with five or six white rats huddled in a corner. These rats have precious little scope for taking any exercise. The marvel is that they do not, in general, become fat, but in fact they eat very little.

For our experiments we generally use a different sort of cage, copied from the little treadmill devices that small boys use for keeping white mice, the front half consisting of small living compartments, just big enough for the rat to eat and sit comfortably but no more than that, and the back half containing a freely rotating drum in which they can take exercise. As far as we can see, the animals approve of the arrangement, because recorders attached to the drum show that they run on an average 10 to 15 miles in 24 hours. Of course, all this exercise has to be paid for, and an animal in this type of cage eats approximately twice as much as if it had been kept in the conventional type of cage. When we make hypothalamic lesions in rats housed under these conditions, and then allow them to eat only the same amount as they had eaten freely before, they become just as fat as if they were allowed to eat all the food they wanted. Of course, they become fat more slowly than if they were given unlimited food, but the final state is exactly the same. If in the ordinary way one had done the experiment in a conventional animal cage, the restriction even before operation would have been so severe that making an animal completely inactive by hypothalamic puncture would have had relatively little further effect.

These anatomical centres are certainly present in the human brain, and pathological lesions have the same effect as they have in animals, but what about the ordinary functional disorder of clinical

obesity one sees in practice? Two groups of workers, headed by Stunkard, a psychiatrist in Philadelphia, and Mayer, a nutritional professor in Boston, have both studied large numbers of patients, and have shown that inactivity may be, and often is, as important a cause of obesity in the human as overeating. Somehow at one time a myth got around that one had to take fantastic amounts of exercise to have any worthwhile effect on body weight, that it was necessary to work like a lumberjack to burn up a pound of fat, and that in doing this work the subject would get an appetite that would put two pounds back. This seems incorrect. Even sustained mild exercise involves a considerable energy cost in itself, but it is much more useful to energy regulation than that, because it appears to help the appetite-regulating centres to function properly. With hypothalamic lesions one cannot really separate appetite from activity and in the intact normal animal the same thing seems to be true. An animal unable to take exercise is apparently unable to judge properly its energy requirements, and it gets fat. This is one of the oldest tricks in animal husbandry; it is the way one fattens up any stock animal. But throughout the physiological range of exercise the normal animal can adjust its food intake so as to keep its weight steady. Eventually at very high forced activity levels the animal fails to get enough food to make up for the energy it is using and it becomes thin, so that physiologically at least there is every reason to encourage patients to take exercise within their capability, even if it is believed that the real cause of obesity is overeating.

It sometimes helps in understanding a physiological regulation or mechanism to see how it develops in the growing animal. It is especially worth looking at in this context because deciding how to treat obesity in the growing child is sometimes a troublesome problem. In animals at least, there seems to be little hypothalamic restraint on appetite during rapid growth. Growth itself makes considerable demands for food, and food intake is extremely high in infant animals. In fact, in a rat the intake in terms of body weight is twice as high just after weaning as it is in the adult, and it falls steadily as growth slows down. By producing lesions in the hypothalamus at different ages, we have been able to show that in infant rats the lesion does not raise food intake any higher. This is not surprising, because intake in terms of body weight is already as high as it is in the hypothalamic adult. However, rats with lesions inflicted when they are three weeks old, instead of cutting down their intake when growth stops, go on eating large amounts of food, so eventually they become extremely fat. It looks as though the hypothalamus has a special function during development to cut back food intake and incidentally to increase activity as the

energy demands of growth become less, and so to prevent obesity, Occasionally a hypothalamic lesion in an infant rat seems to block the release of pituitary growth hormone or to interfere with growth some other way, and when this happens all the excess food immediately goes into making depot fat, and the rat very rapidly becomes obese. This actually was the only type of growth abnormality we ever found in rats with lesions and they never became really fat in infancy unless something had interfered with their growth.

This ties up reasonably well with what I understand to be true in obese children. Wolf showed a few years ago that fat children from working-class families in the Midlands grew faster and developed more rapidly than their thin playmates from the same social group, but they did not grow faster than normal youngsters from more well-to-do families. In the present so-called affluent society, the average child grows faster than was usual a few decades ago, and it is probable that the fat child, like our fat rats, simply grows at an optimal rate. So long as there is no actual malnutrition or disease interfering with growth, I should have thought that obesity would be unlikely to become a major problem in the rapidly growing child, and it would seem perhaps more sensible to put up with some fatness than to risk interfering with growth by strict dieting. Perhaps something can be hoped for from increasing the amount of exercise taken by fat children and of course this would carry no risk of inhibiting growth. Whether it is a practical proposition is for you to decide. If after adolescence obesity persists, this is another matter and stricter dieting may be necessary.

I have been talking so far as though all obesity was due to hypothalamic dysfunction. Endocrine obesity is a diagnosis that seems out of favour at the moment, largely because the obesity of Froehlich's disease was shown experimentally and pathologically to be hypothalamic and not pituitary, but that does not prove that all obesity is hypothalamic. What about Cushing's syndrome, particularly the juvenile type of Cushing with enormous obesity? Moreover it is quite simple to produce endocrine obesity in the laboratory. A normal rat given a daily injection of zinc protamine insulin will grow very fat in spite of having a normal hypothalamus. As soon as injections stop, the hypothalamus will take over again and the rat will stop eating for a time or reduce its intake until it gets thin again. To me the most interesting form of endocrine obesity, because I suspect it is probably the commonest, is the type found in young women after pregnancy. J. H. Sheldon described this condition under the name of maternal obesity, and recently we found it possible to reproduce it experimentally in the laboratory rat, not by going to the trouble of studying a series of pregnancies

but by using a closely allied endocrine condition of pseudo-pregnancy, which is easily induced and lasts 2 to 3 weeks. A series of these stimuli will produce obesity just as great as hypothalamic obesity. I mention the condition simply to counteract the idea that there is only one form of experimental obesity, or, for that matter, of clinical obesity.

Having said that, I have to confess that I think that the nervous system is probably at fault in most overweight people. There seems in the literature to be general agreement about the association of clinical obesity with emotional disturbance, so let me try to sketch briefly a possible physiological basis for psychogenic obesity. The hypothalamus does not work in isolation. It has important connections both in the cortex and in the brain stem; at the cortical end, it is connected with the phylogenetically ancient part of the cortex, the rhinencephalon or smell brain. Like most physiologists, I am fairly sceptical about the findings of some of our psychiatric colleagues, but I find it interesting that the earliest correct suggestions about the function of this smell-brain in higher animals were made by Sigmund Freud purely speculatively. He wondered what happened when man became upright and the importance of the sense of smell became obviously less, and he worked out fairly accurately the sort of picture modern physiologists have of the emotional functions which these rhinencephalic structures have taken over. Since then, a lot of direct experiment has been done and many observations have been made during neurosurgical operations, and it does appear that the rhinencephalon acts as a visceral brain, carrying on not only the obvious visceral and autonomic functions, but what one might call visceral emotions. If you think for a moment what a basic part the snout of the carnivore plays in self-preservation and in the preservation of the species, it is not surprising that the corresponding part of the brain should have an important emotional role. With the development of the erect posture in primates, the hand was released to take over many of the mechanical functions of the snout but apparently the emotional centres stayed put in the rhinencephalon.

The brain-stem connections of the hypothalamus are almost equally interesting, because they are entirely with the so-called reticular activating substance of the brain stem. The main function of the brain stem is to transmit arousal or waking stimuli to the cerebral cortex, and it is not only concerned in the actual rhythm of sleep and waking, but in the degree of arousal and the amount of spontaneous activity of the individual. These three regions—rhinencephalon, hypothalamus, and central reticular substance—act together to govern not only appetite in its various senses, but also sleep and consciousness, activity, some forms of emotional

response to environmental stress, and the pituitary and through it the endocrine system—a very imposing list. A great deal of the detail remains to be worked out, but I hope I have given enough background to make it plain that there is plenty of physiological basis for the idea that obesity, like the related anorexia nervosa, may be a psychosomatic disorder. It certainly needs a great deal more clinical study than it has had up to date or is implied in the catch-phrase that " all obesity is due to overeating ".

II

The Approach to the Patient

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Obesity is one of the four major addictions—machines, food, tobacco, and alcohol—which affect morbidity and mortality in this and similar countries, and are replacing the former scourges more than adequately. These addictions are, of course, perfectly well known to you. Few, I think, would suggest that tobacco consumption is not a form of addiction or would deny that the record of Medicine by way of personal example in giving up smoking and so preventing a large number of unnecessary deaths from lung carcinoma has been lamentable. We have known for a significant number of years that carcinoma of the lung is in some curious and close way related to the consumption of tobacco, but it required a courageous president of the Royal College of Physicians to let a formidable report go forward in order to start a substantial effort in preventive medicine which will require continuous support from each one of us. We all tend to go to cocktail parties, and to set an example to our lay friends by giving them hospitality from time to time, and we all know that alcoholism is increasing fairly rapidly in this country. These are unfortunate demonstrations that an affluent society is not necessarily in every way the better off for being affluent, and not the least is this true in respect of its alcohol consumption. Both tobacco and alcohol are very significant addictions in that they are interrelated so closely, and we will accept without more discussion that these are two addictions very relevant to the theme of the