Annotations

Thoughts on obesity

It is difficult to write a readable statement on 'simple' obesity without making assertions for which there is little scientific evidence. Indeed reviews on the subject should probably carry a warning to this effect. This annotation is no exception.

From the clinical point of view the only thing that is simple about obesity is the diagnosis; when it matters you can tell at a glance. However, the aetiology in any one individual is likely to be complex, and the management difficult and often unsuccessful.¹ From much of what is written it would appear to be a preventable disorder and as paediatricians are particularly concerned with preventive measures they must respond to any suggestions which propose ways by which obesity might be avoided.

When the 'fat cell number and size' hypothesis was launched over 10 years ago, it presented an immediate challenge, for not only did it offer an explanation for obesity, it also suggested a way of preventing it. It had been found that when very young rats were overfed at a time when their adipose tissue was growing, an increased number of fat cells appeared, whereas underfeeding at this time led to decreased adipocyte multiplication and fewer cells. After a certain age overfeeding and underfeeding affected cell size only.² These rats with excess adipocytes became obese adults. One attractive explanation for these observations is the 'fat cell number and size' hypothesis which states that overfeeding when adipocytes are forming leads to hyperplasia and an increase in the overall number of adipocytes, and that individuals with increased cell numbers are more subject to obesity.

The search was then on to explore the situation in man. Observations in children relating early onset obesity with detectable fat cell numbers were consistent with the hypothesis,^{3–4} so the idea found favour in the eyes of paediatricians and nutritionists. Ten years later, after many animal and clinical studies, the weight of evidence is against the 'fat cell number and size' hypothesis.⁵ For example, the number of adipocytes correlates with the degree of obesity but not independently with the age of onset.^{6–8} Many of the earlier observations can be explained on the basis of empty cells filling or the adipose organ developing more rapidly at higher

planes of nutrition. Much of the human adipose organ develops before birth and thus it would be reasonable to expect that infants of diabetic mothers would have a marked propensity to obesity, and that toddlers who were obese were at grave risk of remaining so into adult life. Neither appears to be the case.^{9–10} Adipocyte transplantation studies would suggest that it is the internal environment which determines the size of the adipose organ.^{11–12} In a recent annotation, Brook concluded that 'overfeeding' causes cell hypertrophy which is probably the trigger for cell fat replication at any time of life.¹³ Others have suggested that the number of adipocytes may already be fixed by the time of birth.⁵

Like the mark of a severe winter in the rings of a tree, or tetracycline in the bones of a growing child, the 'fat cell number and size' hypothesis remains in the minds of 'health professionals', induced as it was by popular scientific television and reinforced by health education programmes—for example, the excellent Open University teaching programmes on parenthood. The message was clear, if you overfed toddlers you increased their fat cell numbers and thus their chances of becoming and remaining fat. Memorable but probably not true. I say probably, because the original ideas were generated by techniques and findings which are open to different interpretations, and to establish that overfeeding in early life does not have any special effect on subsequent adipocyte function from the methods and clinical information available is equally not possible. The 'fat cell number and size' hypothesis does have the virtue that it gives some comfort to the sufferer for it transfers some of the responsibility for his embarrassing shape to his well-meaning, loving parents.

In the light of this recent experience paediatricians might be excused for viewing with suspicion a new hypothesis to explain obesity. However a new one has arisen and it is difficult to resist, for it is equally attractive. It offers an explanation for a well known and socially unfair phenomenon, that some individuals can eat a lot and not get fat, whereas others eat little and grow round. We tend to belittle these variations in our clinical approach to patients, taking the only 'realistic' view that

obesity is due to eating too much, and that the remedy is to eat less. The unhappy implication is that within every fat child hides a little glutton. I have often felt guilty when recommending dietary restriction that this is what is inferred. In some instances at least, the implication is both unkind and untrue.

The new idea, which I shall call the 'burn it off' hypothesis, proposes that thin individuals, when overfed, burn off the excess; the fat ones, being deficient in this capacity, have no choice but to store the excess nutrient and put on weight. Adiposity then moves from being a limitation in the adipocyte or the adipose organ, to being a disorder in the capacity to 'burn it off'. It has also been proposed that the tissue responsible for burning off the excess is brown adipose tissue.

Brown adipose tissue has been shown to have a remarkable capacity to oxidise fat to release heat, and this function is important in thermoregulation in mammals which cold-adapt or hibernate, and in the newborn of many species including man.¹⁴⁻¹⁵ Adult man is not thought to respond to cold exposure with 'nonshivering thermogenesis' to any significant degree. There is considerable evidence from animal studies that thermogenesis in brown adipose tissue falls after birth as the capacity for shivering thermogenesis increases. The reasons for this decline are not known. Histologically the brown adipocyte changes to resemble more the white adipocyte. At the beginning of the century classical histologists fiercely debated whether or not brown adipocytes were a precursor of white adipocytes, or whether they were and remained distinct tissues.¹⁶ It would appear in mammals that certain adipocytes can revert to a thermogenic activity. Although multilocular cells resembling brown adipocytes have often been reported in human adults there is no evidence to indicate that they have thermogenic activity.

The 'burn it off' hypothesis arose out of two series of studies, one on animals, again that long-suffering experimental animal, the rat, and the other on man. Normally rats will only eat that amount of food required to meet their energy requirements and maintain body weight. However, Rothwell and Stock¹⁷ succeeded in tempting rats with certain delicacies so that they ate nearly twice their food energy requirements and it was found that although the rats put on a little excess weight, they did not become as fat as might have been expected. With the increase in food intake there was an increase in metabolic rate, and this higher metabolic rate was maintained even when the dietary luxuries were withdrawn and until the body weights of the rats had reverted to that of the controls. In other words, they burnt off the excess. The study was made on

adolescent rats, both control and study animals were still growing.

They went on to show that overfeeding led to hypertrophy of brown adipose tissue, and that dietary-induced thermogenesis, like cold-induced thermogenesis in the newborn, could be provoked by noradrenaline and blocked by propranolol. There appears to be no doubt that dietary-induced thermogenesis in brown adipose tissue occurred in overfed laboratory rats and that as a consequence the rats 'burnt off' energy.

The second series of experiments was on man. There have been many studies over the years comparing metabolic rates of obese and nonobese individuals—it seems as though the investigators felt there was a hidden secret to be discovered. In 1979 Jung *et al.*¹⁸ found that obese individuals and others who had been obese but had managed to reduce their weight, had a smaller increase in their metabolic rates in response to noradrenaline infusion when compared with the habitually thin. This fits in nicely with the 'burn it off' hypothesis.

No wonder journalists found the idea irresistible. On television one woman was shown expressing her delight that a chemical explanation for her obesity had been discovered. If the 'chemistry' is wrong then there is a hope that doctors will find a way to put it right and the endless struggle with the appetite would be at an end. The hypothesis has immediate appeal to scientists and doctors, and to overweight patients.

However, the clinician must remain cautious. The 'fat cell number and size' hypothesis did at least strengthen the resolve of those who encouraged mothers not to overfeed their toddlers. If we accept that there is a fault in the capacity of an individual to burn it off, we might feel less able to urge our obese patients to eat less.

Before the 'burn it off' hypothesis becomes part of our thinking in the management of obese patients, it would be comforting to have more evidence that diet-induced thermogenesis occurs in man; that diet-induced thermogenesis acts to control body weight—that is, it is not merely secondary to high plane nutrition; that obese patients have defective diet-induced thermogenesis and that is why they are obese; and also some indication of the controlling mechanisms and how they, or the end organ, are defective in the obese subject.

If this evidence is forthcoming, then the second series of questions may be even more exciting. What is the natural history of the 'defect'? Can it be identified early and preventive measures introduced? Is the function open to therapeutic induction? Could it be that simple obesity is a glandular disorder after all?

References

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