Clinical Endocrinology

Obesity

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Obesity is best defined as an excessive accumulation of triglyceride fat in the adipose tissue depots of the body. Adipose tissue is not present simply to provide insulation against the cold or produce pleasing cosmetic effects in the female—nor is it an inert mass. Fat is in a dynamic metabolic state, storing excess calories not metabolized immediately after ingestion in the form of triglyceride, and releasing free fatty acids when these are required for energy.

Pathogenesis

The seeds of obesity are all too often sown in childhood by well-meaning but misguided parents and other relatives, and nurtured in adolescence by incorrect and ill-advised feeding habits, fertilized in some cases by seductive advertisements which sometimes make it appear vaguely sexual (and therefore desirable) to give or receive luxury carbohydrate foods. The harvest of obesity is reaped in adult life in a crop of major and minor mental and physical disabilities, culminating in a shortened life span.

Apart from the well-recognized association with diabetes, in which it has been suggested (contrary to the usual belief) that obesity may be the result of the primary metabolic abnormality rather than the cause,¹ the disease as defined above is seldom, if ever, a direct result of endocrine disease. "Endocrine" features such as delayed puberty, menstrual irregularities, abdominal striae, raised urinary 17-oxosteroid and 17-hydroxycorticosteroid excretion, insulin resistance, and a blunted growth hormone release in response to hypoglycaemia are commonly present, but are promptly corrected when weight loss is achieved and maintained. There is no evidence of any inborn error of fat metabolism in obesity which might result in impaired mobilization of fatty acids—in fact the fatty-acid turnover rate is increased in obesity.² All available evidence suggests that excessive accumulation of body fat arises because the intake of calories over a period of time has exceeded the output. There is no way by which an excess of calories may be excreted, nor is an increased intake of energy automatically followed by an increased output—rather the reverse. The excess is therefore laid down as fat. Several factors, acting separately or together, may be responsible for this imbalance between intake and output.

ENERGY BALANCE

Fluctuations in energy balance may be expressed in terms of calories, and may be positive or negative. This concept of balance

between the intake and output of energy is important, though comparatively few individuals are in day-to-day energy balance³ and many will only reach balance in cycles of a week or more. Nevertheless, sustained positive balance, leading to obesity, may obviously arise either because of an increase in the gain of calories to the body (food intake) or because of a reduction in the output of calories from the body (basal and activity metabolism), and, in the initial stages of obesity, both probably play a part, though either can predominate. Thus in childhood obesity overeating is usually the dominant factor, whereas in adult life a reduction in physical activity while intake is maintained at a constant level is a significant cause of "middle-aged spread". The balance may be altered further by the apparently trivial variations in the absorption of calories from ingested food which may occur between different individuals. Such differences in the digestion and absorption of apparently isocaloric diets have been shown to account for net amounts of calories that would supply 80-140 kcal more to one type of individual than to another.⁴

Changes in the level of energy balance occur as obesity becomes established. As the weight rises, so the energy used by the individual, both in basal metabolism and on activity, increases⁵ (see Table). This might serve as a compensating mechanism which could retard weight gain by stabilizing calorie

Energy expenditure (kcal/hr) Measured in Two Obese Patients under Various Conditions and Expected Energy Expenditure in Normal-weight Individuals of Comparable age⁶

	A (Man, 32 yr)	B (Girl, 16 yr)	"Normal Man"	"Normal Woman"
Weight (kg)	158	142	70	60
Basal	118	113	68	59
Sitting at rest	137	124	81	74
Walking $\frac{1}{4}$ mile (400 m) (on the level)	299	380	190	185

balance once more, though at a higher level, were it not for the fact that as weight rises the less active the individual tends to become. Many studies have confirmed that the level of daily activity of the obese patient is considerably lower than that of the lean.^{6, 7} Nevertheless, despite low activity levels the daily energy requirements of the obese tend to exceed those of lean individuals of the same age and sex, often by a considerable degree, because even such simple processes as breathing demand more physical work.

The degree of positive balance which leads to obesity may be very small, provided it is continued over a sufficiently long period of time—obese patients are not always gluttons. Continued positive balance to the extent of 100 kcal per day (a 3% error in the balance of a fairly active man) will result in a weight gain of 10 lb (4.5 kg) per year. One hundred kcal are contained in two thin slices of white bread, $\frac{3}{4}$ oz (19 g) of milk chocolate, a medium sized boiled potato, or one large apple.

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Control of Feeding and Energy Metabolism

The factors that control these functions are complex and not fully understood. Hunger contractions of the stomach in animals may increase food drive, but in civilized man are only a crude and urgent mechanism that sets a lower limit to food intake. Animals studies have shown the presence of hypothalamic appetite and satiety centres, and the supposition in man is that these may be influenced by nervous or humoral pathways from the stomach and duodenum. They may also be affected by the rate of metabolism of glucose.⁸ Fluctuations in body temperature or of blood lipids and other humoral factors have also been postulated as modifying the actions of the hypothalamic centres.⁴⁻⁹ Nevertheless, in civilized man the automatic control which might be exercised by hypothalamic centres may be dominated by cortical factors and conditioned reflexes, even in what appears to be automatic feeding. In civilized communities (except in situations of extreme poverty) food is readily available and man eats by the clock rather than by the hypothalamus. This seems to apply particularly to the appetite centre, though the satiety centre still seems to be important in calling a stop to eating. It is therefore of interest that the sensation of satiety is absent or much diminished in many obese patients.¹⁰

Several extrinsic factors may modify feeding patterns, presumably by an effect on the higher centres. Genetic factors are of little importance in regulating appetite, and environmental and individual factors are all important. Obesity is a disease of civilization—both of affluence and, paradoxically, of relative indigence. Palatability, habit, socioeconomic, cultural, and familial influences play a large part in determining the feeding pattern of an individual. Carbohydrate foods, the main caloric variable in the diet of civilized man, and particularly those containing a high proportion of refined sugar, are readily available, palatable, and comparatively cheap. In times of financial depression carbohydrate foods may be consumed in large quantities for these reasons. Thus habits and tastes may be instilled in the child which may last a lifetime. At the other end of the social scale, 500 kcal or more may be consumed effortlessly at a moderately lavish cocktail party. Eating patterns are also important. Many obese patients fall into the group described as “nibblers,” while others are “binge eaters,” in that they consume the great majority of their daily calories in one meal, usually in the evening. Both patterns tend to produce excessive caloric intake and hence lead to obesity.

Psychological factors should not be underemphasized. Obesity in childhood often follows an emotional crisis such as the death of a parent and in adult life it may be associated with a latent depression, the patient eating for solace or out of boredom. Depression may become overt if strict dieting is enforced.

In general it can be said that eating is pleasant, helps to pass the time, and can cost little. It can be indulged in at will and does not interfere with the lives of others. Excessive eating—unlike drug taking, overindulgence in alcohol, or even heavy smoking—is a vice which is socially acceptable and sometimes unavoidable in a civilized community.

Prevalence

Obesity is today the commonest form of malnutrition in civilized communities. As many as 30% of young men and 20% of young women are significantly overweight, the prevalence rising to over 50% in both sexes from the age of 40 upwards.¹¹ Such figures, when derived from actuarial and insurance statistics, probably underestimate the size of the problem, since the grossly obese tend to be excluded from them.

Diagnosis

The diagnosis of obesity is not difficult in most patients, but a simple and reliable method of assessing body fat content is

badly needed in less obvious cases. Several complex laboratory methods for the estimation of total body fat are available, but these are of no value in routine use, and all are liable to error and misinterpretation. Most doctors rely on comparing the body weight of an individual with standard tables of ideal (“best”) weight for height and sex derived from actuarial statistics, accepting significant obesity as being present when body weight exceeds the ideal by 10% or more. However, total body weight may not reflect fat mass accurately, and usually when such tables are used the doctor is forced to decide whether his patient is of “small”, “medium”, or “large” frame—an entirely subjective assessment and a potentially misleading one since (for example) the weight range (small to large frame) for a male patient of 5 ft 8 in (1.7 m) is from 132 lb to 166 lb (60 to 75 kg).¹² Diagnostically it is probably more helpful to base an assessment on *average* rather than ideal weights, while accepting that average weight is significantly heavier than ideal weight. It does, however, have the advantage of giving a single figure for each sex and height.

Nevertheless, there are simple techniques using skin fold thickness (measured by spring-loaded calipers of the Harpenden type which exert a constant pressure at all ranges of thickness over a standard area) which are sufficiently reliable, with practised use, to enable them to be used as reasonably accurate ways of measuring total body fat.¹³⁻¹⁴ Results obtained in this way show that as an approximate value with a considerable range, the average fat content of the bodies of young men is 15% of body weight and of young women 25%¹³⁻¹⁵ Older patients have higher proportions of body fat, reflecting the high incidence of obesity in this group. Significant obesity in the adult may be said to be present when body fat content exceeds 20% in men and 30% in women.

Diabetes must always be excluded in obese patients.

Treatment

The theory is simple, the practice difficult, and the long-term results, in general, disappointing. The principles of treatment are identical both in the child with obesity and in the adult, and the best results are obtained when: (1) the patient has a genuine desire to lose weight; (2) an explanation of how the condition has arisen and how it is to be treated is given to the patient; (3) stress is laid on dietary re-education rather than restriction; (4) there is frequent contact between the patient and the physician and, if possible, the dietitian.

The will to lose weight must be present and the outlook is not good unless the patient seeks advice of his own volition. The prognosis is poor in the middle-aged woman, who commonly has a mild depression which is aggravated by dieting. Appeals to vanity in the young and threats of future morbidity and mortality are not usually heeded, and though many patients do well if they have a definite goal in view such as weight reduction in anticipation of a surgical operation or in the treatment of diabetes this is not always the case. The patient must never be allowed to get the impression that obesity is due to “the glands” (an excuse for failing to diet) and the doctor should be firm but sympathetic. Accusations of gluttony at the first consultation will damage future relationships with the patient. The patient must be discouraged from daily weighing—once a week or once a fortnight is quite sufficient and is psychologically preferable. It is advisable not to set a final goal (“ideal weight”) when the patient is first seen—this will usually seem so far off that the patient rapidly becomes disillusioned and it is much better to set repeated targets which the patient should aim for at his successive visits.

DIET

In the long term the only factor that causes reduction in weight is a reduction in the intake of calories to a level below that of energy loss. This therapeutic negative calorie balance may only

be small yet still produce satisfactory weight reduction. A negative balance of 200 kcal per day will, if maintained, reduce weight by about 20 lb (9 kg) in a year, and such a regimen has been recommended in the treatment of obesity.⁴ The aim must be to re-educate the patient in correct habits of eating, and any abnormal eating patterns such as nibbling must be corrected. The best diet is one which provides variety, is low in total calories (1,000-1,500 daily), is attractive, simple for the patient to follow, and well balanced as regards all essential nutrients. It should not disorganize the eating habits of the family—though it is often a good thing if the whole family as well as the patient participate in the re-education process.

The more restrictive a diet in calories, the less likely is the patient to follow it unless motivation is strong, and very low calorie diets (400-600 daily) also often induce a feeling of light-headedness which is distressing to the patient. The diet devised by Marriott¹⁶ is useful for initial use. It is simple to understand, reduces measurement to a minimum, and allows a wide range of foods which may be eaten in *normal* amounts. However, the choice of diet is probably less important than the fact that, whichever diet is prescribed, a full and detailed explanation of it *must* be given. The services of a dietitian are invaluable if they can be obtained. The expense of a weight reducing diet is commonly put forward by patients as an excuse for not following it, but if care in the selection of foods is exercised (the patient should not feel that he must buy and consume expensive protein foods in abundance) the cost of a 1,000 kcal diet need not exceed that of a free diet.

Proprietary "slimming" foods must be discouraged. Not only are they expensive, and in the case of diabetic foods high in calories in the form of sorbitol, but they may mislead the patient into supposing that he may consume them in addition to his diet and still lose weight. Some physicians recommend high-protein or high-fat diets low in carbohydrate. The former are satisfying and may increase energy loss due to specific dynamic action, but are very expensive. The latter seem mainly to be effective because they are unpalatable, though there may be some theoretical basis for their use.¹⁷ Nevertheless, Kinsell *et al.*¹⁸ have shown that in the long term qualitative modification of the diet makes little or no difference to the rate of the loss of weight, which is determined almost entirely by the caloric content of the diet regardless of the relative proportions of its constituent nutrients. Fasting must never be carried out except during hospital admission and then only for relatively short periods (up to 14 days) and in carefully selected patients. Repeated short periods of fasting are theoretically an ideal way of treating patients,^{10 19} but few hospitals have the beds available to afford this luxurious form of treatment.

APPETITE SUPPRESSANTS

Appetite suppressants have a small role in the treatment of obesity. Those containing amphetamines or close amphetamine derivatives must never be given. Both fenfluramine and diethylpropion have been shown in controlled clinical trials^{20 21} to have significant anorectic effect and appear to be well tolerated and safe, though habituation with each is a risk. Unfortunately in obesity real life is so very different from the clinical trial that in routine use both tend to be rather disappointing. Fenfluramine has been reported to have interesting metabolic as well as anorectic effects²² but while these are of theoretical benefit to the obese patient it is difficult to see how the metabolic effects reported can induce weight loss *per se*, distinct from the anorectic action of the drug, and a comparative trial of fenfluramine and diethylpropion has failed to show that the former possesses any obvious advantages over the latter.²³ Appetite suppressants should not be given without an explanation of the aims behind their use; otherwise the patient places more emphasis on taking the tablets than on following his diet, in the forlorn hope that his fat will magically melt away. Motivation regarding diet is greatest at the start of treatment and for these

reasons I never use anorectics in initial treatment. They may, however, sometimes be useful at a later stage when a patient has shown that he can lose weight on a diet but is beginning to make heavy weather of it, and has insight into his problem. If after two months the drug chosen has been seen to be ineffective, its use should be discontinued.

Bulk Preparations

Bulk preparations of methyl cellulose are sometimes recommended in the hope that they will produce a feeling of satiety. They appear to have little effect, and there is no physiological basis for their use. Dietary dilution studies in rats have shown that these animals, at least, eat for calories (energy) rather than bulk²⁴ and, according to Sebrell,²⁵ so too does man. In any case many obese patients do not appear to experience the sensation of satiety.¹⁰

Biguanides

Both phenformin and metformin have been reported to induce weight loss in some obese non-diabetic patients^{26 27} and do not appreciably reduce blood glucose levels in these individuals. Part of this weight loss seems to be due to a purely anorectic effect, but biguanides also cause a slight reduction in the gastrointestinal absorption of carbohydrate²⁸ and markedly reduce the fasting and post-glucose hyperinsulinism²⁹ which so often accompanies obesity³⁰ and which will tend to potentiate and aggravate the obese state unless caloric intake is strictly curbed. Results using these drugs are not consistently good, but a trial of one or the other is recommended, particularly in those who are diabetic or who have a family history of diabetes.²⁷ Metformin is usefully given in the form of Glucophage, 850 mg twice daily, and phenformin as the Dibotin sustained-release capsule, 50 mg twice daily. In each case the drugs should be given with or after meals to minimize gastric irritation.

OTHER AIDS TO WEIGHT REDUCTION

Group therapy should not be derided and is probably one of the main reasons for the apparent success of "Weight-Watchers" clubs. Many general practitioners have started group obesity clinics with results at least as good, though the financial considerations involved in "Weight-Watchers" clubs are undoubtedly additional incentives which are shown to greatest effect in "health farms." There is no doubt that an enthusiastic general practitioner, with help from health visitors and perhaps a dietitian, can achieve worthwhile and lasting results by starting an obesity clinic, though much enthusiasm and patience are necessary and a degree of frustration is to be expected.

Prevention

Obesity is preventable and, as with other diseases, prevention is infinitely better than cure, though this does not imply that all of us should become obsessed with dieting and daily weighing. Rather does it mean that children should be educated at an early stage of life into correct eating habits, which in turn means education of their parents. This concentration on the next generation is starting, but much more can and must be done, whether by schools, general practitioners, health visitors, welfare clinics—or even the mass media. Above all else, it must be remembered that children are in their moral development influenced most by their environment and by those with whom they are in closest contact. The same is true of feeding habits, and schools, parents, and relatives must bear this in mind.

References

- ¹ Vallance-Owen, J., *Diabetes*, 1964, 13, 241.
- ² Issekutz, B. Jr., Bortz, W., Miller, H. I., and Paul, P., *Metabolism*, 1967, 16, 1001.
- ³ Edholm, O. G., et al., *British Journal of Nutrition*, 1970, 24, 1091.
- ⁴ Durnin, J. V. G. A., *British Journal of Hospital Medicine*, 1971, 5, 649.
- ⁵ Anderson, J., unpublished data.
- ⁶ Mayer, J., *Annals of the New York Academy of Sciences*, 1965, 131, 502.
- ⁷ Bloom, W. L., and Eidex, M. F., *Metabolism*, 1967, 16, 679.
- ⁸ Mayer, J., *New England Journal of Medicine*, 1953, 249, 13.
- ⁹ Morgane, P. J., and Jacobs, H. L., *World Review of Nutrition and Dietetics*, 1969, 10, 100.
- ¹⁰ Hollifield, G., Owen, J. A., jun., Lindsay, R. W., and Parson, W., *Southern Medical Journal*, 1964, 57, 1012.
- ¹¹ Montegriffo, V. M. E., *Annals of Human Genetics*, 1968, 31, 389.
- ¹² *Statistical Bulletin of the Metropolitan Life Insurance Company*, 1959, 40, cited in *Documenta Geigy Scientific Tables*, Seventh edition, p. 712, Basle, J. R. Geigy, 1970.
- ¹³ Pascale, L. R., Grossman, M. I., Sloane, H. S., and Frankel, T., *Human Biology*, 1956, 28, 165.
- ¹⁴ Durnin, J. V. G. A., and Rahaman, M. M., *British Journal of Nutrition*, 1967, 21, 681.
- ¹⁵ Durnin, J. V. G. A., and Passmore, R., in *Les Maigreurs*, ed. H. P. Klotz and J. Trémolières. Paris, Expansion Scientifique Française, 1965.
- ¹⁶ Marriott, H. L., *British Medical Journal*, 1949, 2, 18.
- ¹⁷ Kekwick, A., and Pawan, G. L. S., *Metabolism*, 1957, 6, 447.
- ¹⁸ Kinsell, L. W., et al., *Metabolism*, 1964, 13, 195.
- ¹⁹ Duncan, G. G., Jenson, W. K., Cristofori, F. C., and Schless, G. L., *American Journal of Medical Sciences*, 1963, 245, 515.
- ²⁰ Cunningham, G. L. W., *Journal of the Royal College of General Practitioners*, 1963, 6, 347.
- ²¹ Munro, J. F., Seaton, D. A., and Duncan, L. J. P., *British Medical Journal*, 1966, 2, 624.
- ²² Butterfield, W. J. H., and Whichelow, M. J., *Lancet*, 1968, 2, 109.
- ²³ Silverstone, J. T., Cooper, R. M., and Begg, R. R., *British Journal of Clinical Practice*, 1970, 24, 423.
- ²⁴ Teitelbaum, P., and Epstein, A. N., *Psychological Review*, 1962, 69, 74.
- ²⁵ Sebrrell, W. H., *Federation Proceedings*, 1961, 20, 393.
- ²⁶ Pedersen, J., Olesen, E. S., *Acta Endocrinologica*, 1968, 57, 683.
- ²⁷ Roginsky, M. S., and Sandler, J., *Annals of the New York Academy of Sciences*, 1968, 148, 892.
- ²⁸ Czyzyk, A., *Acta Diabetologica Latina*, 1969, 6, Suppl. 1, 636.
- ²⁹ Boshell, B. R., Roddam, R. F., and McAdams, G. L., *Annals of the New York Academy of Sciences*, 1968, 148, 756.
- ³⁰ Karam, J. H., Grodsky, G. M., and Forsham, P. H., *Diabetes*, 1963, 12, 197.

Any Questions?

We publish below a selection of questions and answers of general interest

Werdnig-Hoffmann Disease

What is known about the aetiology of spinal muscular atrophy (Werdnig-Hoffmann disease), and what are the chances of a couple who have two affected babies having a normal child?

Spinal muscular atrophy (Werdnig-Hoffmann disease) is the result of an autosomal recessive gene and therefore arises when two heterozygous carriers of the gene have offspring. In accordance with the usual pattern of autosomal recessive inheritance, the risk that the union of two such carriers will produce an affected child is 1 in 4 for every child being born. The family described is unfortunate but by no means unique in that two successive children have been affected, but the risk remains 1 in 4 for any subsequent pregnancy and most parents faced with such odds decide against having further children.

No method is at present known of detecting the heterozygous carriers of the gene responsible for this disease.

Notes and Comments

Cervical Spondylosis.—Mr. R. M. KALBAG (Regional Neurological Centre, Newcastle upon Tyne General Hospital) writes: "Any Questions?" is a deservedly popular and widely-read feature of the *B.M.J.*, which is all the more reason to deplore the pessimism of your Expert's views in the answer to this question ("Any Questions?" 2 October, p. 44). The anterior surgical approach^{1 2} affords dramatic relief in the pain from radiculopathy in about 90% of patients who have not responded to the simpler conservative measures. The results are particularly gratifying where the distribution of the pain is such as to make recognition of the nerve root involved possible on the history alone.

The situation with regard to spondylotic myelopathy is not quite as clear cut. Symon and Lavender,³ by adopting criteria for pre- and postoperative assessment similar to those of Lees and Turner,⁴ showed significantly better results after laminectomy than with immobilization in a collar. On the

other hand, Northfield and Osmond-Clarke,⁵ reviewing 10 published series, could not make any convincing case for laminectomy. In myelopathy, though radiologically there is mechanical compression, the clinical picture and pathological studies point to an ischaemic process. The work of Shimomura *et al.*⁶ suggests that the radicular arteries do not play as important a part in the production of myelopathy as often believed.^{7 8 9} They conclude that the principal factor is obstruction of the blood vessels on the surface of the spinal cord, including the anterior and dorsolateral spinal arteries, the medullary parts of the radicular arteries, and the pial plexus. The obstruction is intermittent and related to mechanical compression with each neck extension. It seems reasonable to expect surgical treatment to be more effective where the history and therefore the period of intermittent ischaemia is relatively short.

The Cloward operation, in theory at least, deals at one and the same time with all the mechanical factors. It is possible to remove the posterior osteophyte and decompress the intervertebral foramen. The subsequent interbody fixation then eliminates the posterior indentation by limiting movement at the affected levels. The operation of course is not feasible where the degenerative changes involve more than three levels. Perhaps what is required is a comparative study with serial timed performance tests, as is being attempted in Newcastle in collaboration with my neurological colleagues, who can be presumed to introduce an objectivity that apparently eludes surgeons. In such a trial one hopes to compare the progress of four groups viz., laminectomy, the Cloward procedure, collar, and placebo.

- ¹ Cloward, R. B., *Journal of Neurosurgery*, 1958, 15, 602.
- ² Robinson, R. A., and Smith, G. W., *Bulletin of the Johns Hopkins Hospital*, 1955, 96, 223.
- ³ Symon, L., and Lavender, P., *Neurology (Minneapolis)*, 1967, 17, 117.
- ⁴ Lees, F., and Turner, J. W. A., *British Medical Journal*, 1963, 2, 1607.
- ⁵ Northfield, D. W., and Osmond-Clarke, H., *Cervical Spondylosis and Allied Disorders*, ed. W. R. Brain and M. Wilkinson. London, Heinemann, 1967.
- ⁶ Shimomura, Y., Hukuda, S., and Mizuno, S., *Journal of Neurosurgery*, 1968, 28, 565.
- ⁷ Chakravorty, B. G., *Annals of the Royal College of Surgeons of England*, 1969, 45, 232.
- ⁸ Taylor, A. R., *Neurology (Minneapolis)*, 1964, 14, 62.
- ⁹ Woollam, D. H. M., and Millen, J. W., *Journal of Neurology, Neurosurgery and Psychiatry*, 1955, 18, 97.