OBESITY,AN OVERVIEW

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INTRODUCTION

The prevalence of obesity is steadily increasing in the developed world and is rapidly approaching epidemic proportions in many countries. Over half the adult population of Europe is now classified as overweight, while 16-17% of English adults are clinically obese.

Obesity has marked adverse influences on both morbidity and mortality. It is associated with a wide variety of diseases, including coronary heart disease (the major killer in the Developed World), hypertension, type 2 diabetes and certain cancers.

In this article we review the impact of obesity on health, its possible causes and current treatment options in obesity.

DEFINITIONS

Several different measurements have been used to quantify the degree of obesity, including: weight, waist-to-hip ratio, skin-fold thickness and various estimates of total body fat. Perhaps the most established and widely-used measure is the body mass index (BMI), calculated as weight (in kilograms) divided by the square of the height (in metres) (see Table 1).

TABLE 1
Established values for body mass index.[*]

Body Mass Index	Classification
<18.5	Underweight
18.5-24.9	Healthy
25-29.9	Overweight
>30	Obese

[*]BMI = Weight (kg) / Height^2 (m)

There are certain recognised limitations to the usefulness of BMI, such as with body-builders who have a spuriously high BMI despite having a low total body fat. In general though, it is a quick and readily calculated measure of obesity and has a good correlation with various indices of body fat content, e.g.:

%body fat=1.2 (BMI) + 0.23 (age) - 10.8 (gender) -5.4

(With gender being male = 1 and female = 0).[1] This formula also underlines the fact that body fat mass is also age- and sex- related.

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The BMI does not provide any indication of the distribution of fat in the body. This is important, because adipose tissue in a truncal ('android') distribution (around and in the abdomen) has a particularly strong relationship with the adverse metabolic and vascular effects of obesity. By contrast, fat deposited in the 'gynoid' distribution (around the hips) carries a much lower burden of disease.

The distribution of fat can be assessed simply and usefully in the clinic by measuring the waist:hip ratio (WHR) or the waist circumference. Waist circumference correlates with cardiovascular risk.[2,3] Certain cut-off values are recognised as 'alerting levels' and 'action levels' and these correlate with threshold values of BMI and WHR (see Table 2). A large waist circumference is associated with an excess of burden of ill health.[4]

TABLE 2
Classification of obesity by waist circumference and the proposed cut-off points at which the patient is recommended to avoid further weight gain or make a concerted effort to lose weight.[2,3]

LEVEL 1
'ALERTING ZONE'
[*]avoid further gain

	Waist circumference	BMI (kg/m2)	Waist: hip ratio
MEN	≥94 cm (~37 inches)	≥25	≥0.95
WOMEN	≥80cm (~32 inches)	≥25	≥0.80

LEVEL 2
'ACTION LEVEL'
[*]lose 10 kg and seek professional help

	Waist circumference	BMI (kg/m2)	Waist: hip ratio
MEN	≥102 cm (~40 inches)	≥30	0.95-1.13
WOMEN	≥88 cm (~35 inches)	≥30	0.8-1.20

EPIDEMIOLOGY OF OBESITY

The average BMI in the United Kingdom has been increasing steadily since the turn of this century.[5] This is by no means a unique phenomenon, as over half the adult population (aged 35-65 years) of Europe are now overweight and 10–20% of men and 15–25% of women are obese.[6] In the United States, the prevalence of clinical obesity is over 50% in certain subgroups of the population (Hispanics and

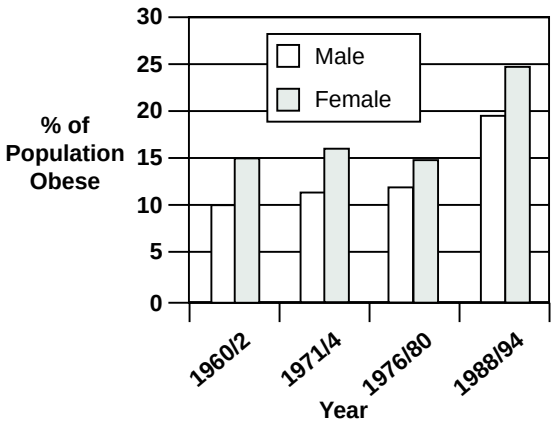

FIGURE 1
Prevalence of obesity (BMI > 30kg/m^2) in USA

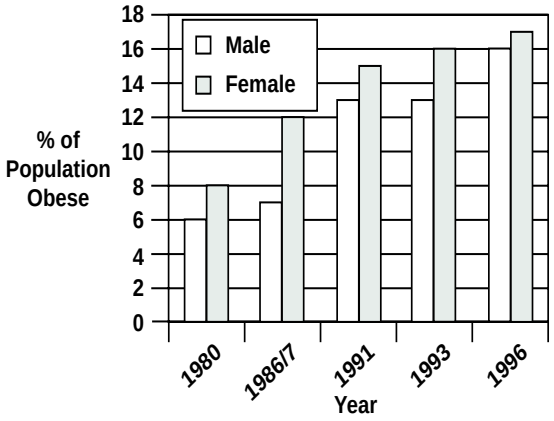

FIGURE 2
Prevalence of obesity (BMI >30kg/m^2) in UK

Blacks).[5] This steady trend towards ever-increasing weight is illustrated by the aeroplane manufacturers Boeing, who have had to increase the assumed weight of each passenger by over 20 pounds since they first began to produce planes;[5] in addition, the impression of those who visit the USA at intervals is that the diameter of the standard American restaurant plate has steadily expanded. Figures 1 and 2 show the rising prevalence of obesity in both the United Kingdom and the United States.[7,8]

HEALTH COSTS OF OBESITY

Health care professionals have no difficulty in accepting that obesity is an expensive disease, even though governments and health-care providers may be less easily convinced. There are several problems in estimating the total health care costs arising from obesity, including uncertainty about which cut-off value for BMI to use and how to calculate the proportion of the costs of obesity-associated disorders which is attributable to obesity, and the general paucity of data.

Colditz has made estimations of the total cost of obesity[9] by identifying the co-morbidities associated with obesity (such as hypertension, type 2 diabetes, coronary heart disease, etc.) and then calculating the percentage of the cost of these diseases attributable to obesity (by multiplying the proportion of patients with the disease who are obese by the proportion of obese patients who have the disease). Colditz and Wolfe used this method to calculate that the total cost of treating obesity in the USA in 1990 was $45.8 million, approximately 6% of the country's total expenditure on health care.[10] Using similar methods, West calculated that the total costs of obesity in the UK were around 15% (£29 million) of the total health care expenditure (£195 million).[11] The mathematical precision of these estimates is still vigorously debated, but it is generally accepted that obesity absorbs 5-10% of the health budget in western countries. Less tangible effects of obesity - depression, limited mobility, poor performance in certain jobs, limited employment prospects - are even harder to quantitate but are also likely to be very costly.

AETIOLOGY OF OBESITY

In simple terms, obesity results from a mismatch of energy intake and energy expenditure and is ultimately related to over-eating relative to the level of physical activity. In the vast majority of cases, obesity is due to multiple influences, including genetic, environmental and behavioural factors.

ENERGY BALANCE IN OBESITY

Total energy expenditure is a combination of basal expenditure (the energy burned off by simply staying alive), thermogenesis (extra heat generated in response to eating, cold exposure and other factors) and physical activity. Energy expenditure rises as body weight rises, because energy expenditure is a function of lean body mass, which also increases in parallel with body fat. Therefore, obese people have higher energy expenditure than lean people; a person with a BMI of 35 kg/m^2 expends approximately 30% more energy than one whose BMI is < 25 kg/m^2.[12,13] Therefore, from the first law of thermodynamics, an obese person must eat more than a lean person to maintain steady weight at a higher level.

Practical implications of this are:

- Obese people do not have a ' sluggish metabolism' (in contrast to certain animal models of obesity, such as the fatty Zucker rat, which do have a low resting metabolic rate).
- Obese people consume more energy than lean people, not less.
- Dietary records in obese people are unreliable. The obese consistently underestimate energy intake (typically by about 30%); the heavier the person, the more they underestimate.[14] Also the obese tend to overestimate the level of exercise they do, again by about 30%.
- As weight falls, so does energy expenditure. It follows that, to maintain a total energy deficit (e.g.-600 kcal day) to induce weight lose, energy intake must be reduced even further as weight decreases to overcome the damping effect of reduced energy expenditure.
- The obese patient's claim to be eating virtually nothing must therefore be disregarded.

GENETIC FACTORS

Only in a few cases is obesity contributable solely to genetic factors, such as the single-gene defect of the Prader-Willi syndrome and the recently described mutations in leptin and the leptin receptor (see below). Genetic influences are generally polygenic, with the overall familial correlation in BMI being: parent to child 0.2 and sibling to sibling

0.25;[15,16] in some families obesity is transmitted as an autosomal dominant. Twin studies have attributed 50-70% of the difference in BMI in later life to genetic factors.[17,18] There is also a strong relationship between BMI of adoptees with their biological parents, but no relationship with their adoptive parents.[19,20] Possible genetic mechanisms include variations in taste preference, sensitivity of the gastrointestinal tract to neuropeptides controlling appetite and satiety, or patterns of physical activity. Certain individuals may be metabolically more efficient or 'thrifty' (i.e. tend to store rather than consume energy) than others;[21] this could exacerbate weight gain during the dynamic phase of developing obesity but there are no exceptions to the rule that obesity, once established, is a state of increased energy input and output.

In certain ethnic groups (e.g. the Pima Indians of Arizona) the prevalence of obesity is 50%. This ethnic predisposition may in part be due to their gene pool (that favours energy storage in fat) being essentially stable and not able to adapt rapidly enough to the changing environmental demands of Westernisation, with its readily available energy dense food and physical inactivity. In previous earlier times, a 'thrifty genotype' would have helped these races to survive in times of famine, but this ability to conserve energy predisposes to obesity when food is plentiful.

It should be emphasised that the rapid increase in the prevalence of obesity in recent years (doubling since 1980 in the UK) is too fast for genes to be primarily responsible. Rather, this must result from the interaction between genes and environment, with lifestyle-related factors having greater impact in individuals with a genetic predisposition to obesity.

LEPTIN

Leptin is the 14-kDa hormone that is expressed in fat (and also in the placenta). It acts on leptin OB receptors which are found in many tissues, and is believed to be one mechanism whereby adipocytes communicate with the brain. Leptin has been suggested as a potential regulator of body mass, as mutations that inactivate leptin itself (*ob* in the mouse) or the leptin receptor (*db* in the mouse, *fa* in the rat) lead to obesity.[22,23] The role of leptin in human obesity is uncertain. Mutations analogous to *ob* and *db* of *fa* are vanishingly rare in man; these patients develop early-onset morbid obesity, although weight gain may be less marked than in other syndromes (e.g Prader-Willi) in which defects in leptin are not implicated.

In man, as in other species, plasma leptin levels rise in parallel with fat mass. In the vast majority of cases, human obesity is not a state of leptin deficiency or of extreme leptin insensitivity. As leptin levels increase in obese people, and as any anti-obesity activities of the hormone are evidently not fully manifested, it has been suggested that there may be partial 'resistance' to leptin action, or that its transport from blood into the CSF (from where it can reach the brain) is impaired. In general, leptin levels increase in proportion to body fat mass and it apparently acts as a feedback messenger on the brain (Figure 3, below).

There has been much interest in the possible use of leptin to treat human obesity (see below). In the rat at least, leptin acts on the brain to reduce feeding and increase thermogenesis and recombinant leptin injections lead to a fall in body weight, percentage body fat, serum glucose and insulin levels.[24] Preliminary studies suggest that leptin may act in part by inhibiting hypothalamic neurones expressing neuropeptideY (NPY),[25] a peptide that induces

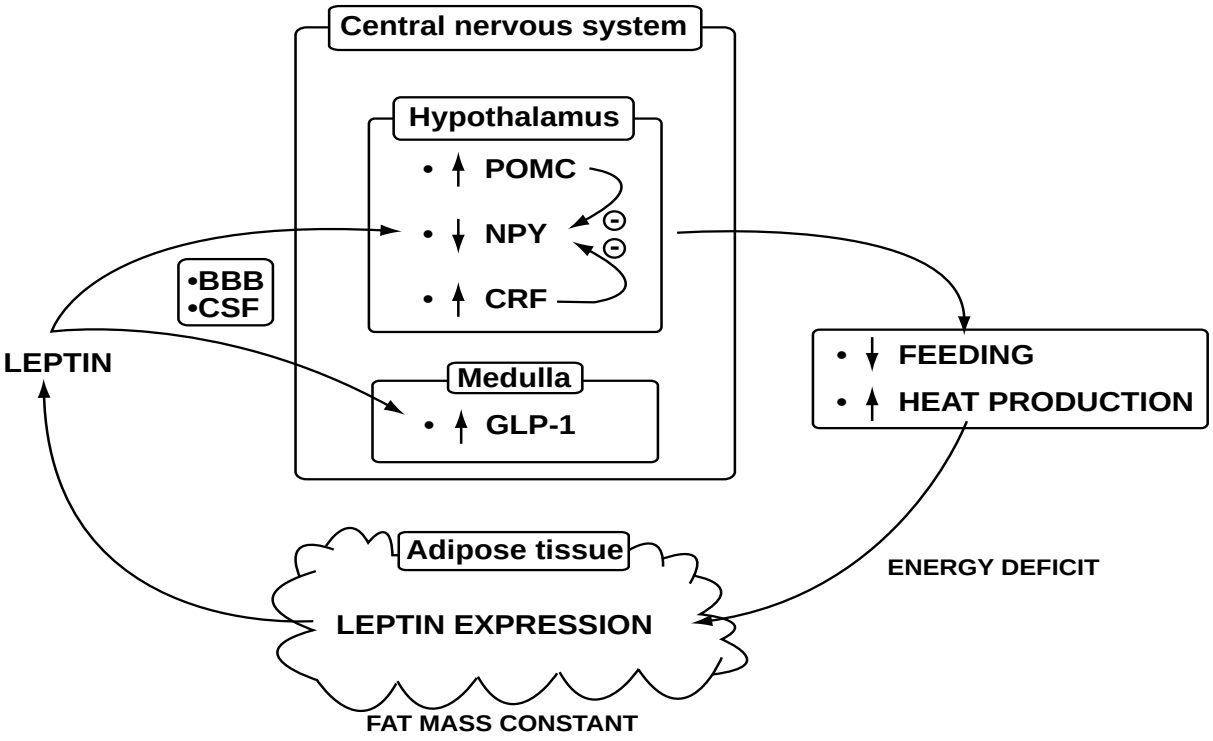

FIGURE 3
The suggested role of leptin as a regulator of body fat mass.
BBB = blood brain barrier; CSF = cerebrospinal fluid; POMC = pro-opiomelanocortin; NPY = neuropeptide-Y; CRF = corticotrophin-releasing factor; GLP-1 = glucagon-like peptide-1

hyperphagia, reduces thermogenesis, and leads to obesity.[26]

ENVIRONMENTAL FACTORS

BMI tends to increase with increasing age, at least up to the age of 50-60 years, and women have generally higher BMI than men. In the developed world at least, there is an inverse relationship between BMI and educational status. Socio-economic status is also related to obesity; in the United Kingdom 10.7% of socio-economic class I are obese, whereas 25% of socio-economic class V are.[27] Both marital status and parity are related to obesity, with BMI in women rising after marriage and with parity; generally, weight gain is <1 kg per pregnancy.

Modifiable risk factors are largely related to lifestyle. Diet plays a major role in the aetiology of obesity: only a small energy excess (100-150 kcal/day) can lead cumulatively to a weight gain of 10 kg over ten years (for the purpose of these calculations, 1 kg of human adipose tissue contains about 7,000 kcal).

The type of food consumed also influences obesity, with protein-rich foods being most satiating and high-carbohydrate foods being efficient inhibitors of subsequent food consumption. By contrast the highly palatable high-fat foods typical of the western diet are only weakly satiating. Moreover, fat has more than double the energy content of protein and carbohydrates (9 kcal/g versus 4 kcal/g).[28] The modern Westernised diet - high in fat and low in fibre - therefore predisposes to obesity. Moderate alcohol consumption may also be associated with increasing BMI.

Smoking is associated with a lower BMI, mainly because nicotine reduces the preference for sweet foods (it may also have a mild thermogenic effect). Conversely stopping smoking causes weight to increase, by an average of 2.8 kg in men and 3.8 kg in women.[29] Patients are often in a dilemma as to whether continuing to smoke or the weight gain associated with stopping smoking is the more detrimental to health. Obesity is dangerous, but smoking is even more so: it is estimated that a gain of 11-13 kg would be required to negate the benefits on mortality of stopping smoking.[30]

Physical activity is the other major modifiable risk factor. The increasing prevalence of obesity has been linked to a reduction in physical exercise. Our jobs are becoming less physical and the increasing use of televisions, videos and computers is turning us into a nation of 'couch potatoes'. Watching television for more than five hours per day leads to a 5.3-fold increase of risk of obesity compared with watching for less than two hours per day.[31] Everyday factors such as the increasing use of motorised transport and relying on lifts instead of stairs is exacerbating the problem.

SECONDARY OBESITY

Various medical causes of obesity must always be considered. Most fall into the realm of endocrinology: hypothyroidism, Cushing's syndrome, hypogonadism in the male, polycystic ovary syndrome (PCOS) in the female, growth hormone deficiency, as well as the well-known but rare tumours and other lesions involving the hypothalamic appetite-controlling areas. Numerous medications can cause or exacerbate obesity, such as excessive doses of insulin or sulphonylureas in diabetic patients, glucocorticoids and certain anti-epileptic drugs (e.g. sodium valporate and vigabatrin).

THE HARMFUL EFFECTS OF OBESITY

Obesity has widespread impacts on both physical and mental wellbeing, with a variety of symptoms and signs leading to obese patients consulting their doctors. Obesity is associated with many diseases including vascular disease, type 2 diabetes, dyslipidaemia and hypertension (see Table 3) as well as premature death. It is an independent risk factor for arterial disease and a central feature of Syndrome X. A J-shaped mortality curve previously described with obesity shows an excess of mortality at the lower end of BMI (<20 kg/m^2), but this is apparently due to an excess of smokers and people with pre-existing wasting diseases (see Table 4).[32,33] Obesity is particularly strongly associated with type 2 diabetes, as shown in Table 5.[34,35]

Not only are mortality and disease-related mortality increased, but also the quality of life is seriously affected by obesity, with obese subjects being subjected to bullying, prejudice and social isolation, as well as reduced opportunities in employment, marriage and education.[5]

TABLE 3
Diseases and morbidity attributable to obesity.

Cardiovascular disease	Hypertension Coronary heart disease Stroke Deep venous thrombosis
Metabolic	Type 2 Diabetes mellitus Dyslipidaemia (↓ HDL, ↑TG, ↑LDL-3) Insulin resistance Polycystic ovary syndrome (PCOS)
Gastrointestinal	Hiatus hernia Gall-stones Colorectal cancer Non alcoholic hepatic steatosis (fatty liver)
Respiratory	Breathlessness Obstructive sleep apnoea Hypoventilation (Pickwickian syndrome)
Neurological	Nerve entrapment Sciatica
Breast	Breast cancer Gynaecomastia
Genitourinary	Stress incontinence Reduced fertility (including PCOS) Pregnancy complications
Orthopaedic	Osteoarthritis of weight-bearing joints
Psychological	Poor self-esteem Depression Anxiety

TABLE 4
Multivariate relative risk of death from all causes among women aged 30 to 55 years (who never smoked and had recently stable weight).[33]

Body mass index	Multivariate RR
≤ 19.0	1.0
19.0-21.9	1.2
22.0-24.9	1.2
25.0-26.9	1.3
27.0-28.9	1.6
29.0-31.9	2.1
≥ 32.0	2.2

TABLE 5
Relative risk of diabetes in relation to BMI (compared to BMI 22-23).[34,35]

Women		Men	
Body mass index	**Increased risk of diabetes**	**Body mass index**	**Increased risk of diabetes**
25	5	25-26.9	2.2
30	28	29-30.9	6.7
35	93	>35	42

MANAGEMENT OF OBESITY

There is no 'quick fix' in the management of obesity, gradual and sustained weight loss should be encouraged from the outset. Overall management of obesity should include: prevention of weight gain as well as weight loss, maintenance of weight loss and modification of concurrent risk factors for mortality and morbidity such as smoking, diabetes, hypertension and hyperlipidaemia.

Most of the data on the outcome of treatment of obesity come from specialist centres, where many patients are referred after failure (or perceived failure) of suboptimal management in primary care. This has unfortunately biased these data and lend support to Stunkard's adage that 'most obese people will not enter treatment, most who do will not lose weight and most who lose weight regain it'.

On the other hand, those managing obesity in hospital have no reason for complacency, as the record of hospital-based management leaves much to be desired. The situation may be improving, as some community-based audits are more favourable.[5] Weight-loss programmes should have two distinct aims: firstly to lose weight and secondly, to maintain weight loss. Maintaining lower weight is essential for reducing cardiovascular and all-cause mortality,[36] as repeated cycles of weight loss and regain (the 'yo-yo' effect) have been associated in some studies[37] with increased coronary-heart disease mortality.

TREATMENT TARGETS

The treatment goal for most obese patients should not be their 'ideal' weight, as this is unrealistic and demoralising when the patient fails to reach that level. Instead, the patient should be informed of the benefits of a 10% reduction in weight (see Table 6)[38] and encouraged to use this figure as their target.

TABLE 6
Some suggested cardiovascular benefits of 10 kg weight loss.

Mortality	>20% fall in total mortality >30% fall in diabetes-related deaths >40% fall in obesity-related deaths
Blood pressure	Fall of 10 mmHg systolic Fall of 20 mmHg diastolic
Newly-diagnosed type 2 diabetes	Fall of 50% in fasting glucose
Lipids	Fall of 10% in total cholesterol Fall of 15% in LDL Fall of 30% in triglycerides Increase of 8% in HDL

Weight loss should not be at a dramatic rate: 0.5-1 lb per week (i.e. 10 kg weight loss over 20-40 weeks) is optimal because at faster rates the patient will lose not only fat, but also muscle, liver glycogen and water. One kg of fat contains 7,000 kcal; the desirable rate of weight loss therefore equates to an energy deficit of 500-600 kcal/day. The patient must understand that weight loss may take a long time and should be encouraged and reinforced throughout.

DIET AND LIFESTYLE

The cornerstone of any treatment programme for obesity must be lifestyle modification, ideally on both an individual level and on a public-health level. It is now clear that simple overeating cannot explain the epidemic of obesity in the UK, as the nation's diet has shown a steady reduction in energy intake from the 1960s, with the consumption of sugar, fat and eggs declining (in the affluent at least) and that of fresh fruit increasing.[39,40] Rather, the problem is our inability to reduce energy intake to match the declining levels of physical activity.

Behavioural therapy to encourage patients to become aware of their eating and activity patterns and to try to change these may help to prevent and treat obesity, as well as maintaining weight loss.

Initially obese patients should be encouraged to stop smoking and increase exercise, advised to reduce the amount of saturated (animal) fat in their diets and increase their consumption of fish (to three portions per week) and fresh fruit and vegetables (ideally five portions per day).

Unfortunately, certain powerful groups have a vested interest in factors that promote obesity, such as car manufacturers, television giants and the food industry. It has been estimated that 70% of the population of England are insufficiently active.[41] Exercise should be encouraged in the individual and even simple health promotion measures have been shown to increase exercise, such as placing a sign

next to elevators saying 'Stay Healthy, Save Time, Use the Stairs'.[42] Patients should be encouraged to increase their exercise to 30 minutes of brisk walking per day. Physical activity alone may produce modest weight loss of the order of 2-4 kg over 12 months and should be used in combination with diet to produce and maintain weight loss.[43]

DIETARY STRATEGIES

There are a number of different dietary strategies, ranging from a very low calorie diet (VLCD) to ad-lib advice. VLCDs (<800 kcal/day) can achieve mean weight loss of 1.5-2.5 kg/week[44] but should only be used when supervised by a physician, as they are associated with certain hazards: up to 10% of patients experience cholelithiasis [44] as well as possible problems with muscle loss and exacerbation of ischaemic heart disease. Moreover, most patients are unable to comply with a VLCD for longer than a few weeks and tend to revert to their usual lifestyle. Less extreme diets (<1,200 kcal/day, which may represent an energy deficit of 2,000 kcal/day) have been reported to achieve a mean weight loss of 0.5-0.6 kg/week (basic energy-balance calculations suggest that this must indicate poor compliance as a 2,000 kcal/day deficit should cause a weight loss of 2 kg/week).[36] Overall, an ad-lib, low-fat, high-carbohydrate diet may be the most successful for long term weight loss and maintence.[45]

DRUG TREATMENT

Drug therapy has not always been regarded in a favourable light for a number of reasons:

- There is a potential for abuse by subjects with a body image problem or eating disorders.
- Some of the early amphetamine-based agents were addictive, though this does not apply to any of the drugs currently available.
- The costs of life-long maintenance therapy need to be reconciled with the cost savings resulting from improved long-term health in people who lose weight.
- No drug is free from side-effects, as recently highlighted by the withdrawal of dexfenfluramine and fenfluramine because of their association with carcinoid-like heart valve lesions and primary pulmonary hypertension.[46-48]

Fortunately, there are a number of drugs in various stages of development, which offer some hope for the future treatment of obesity.

CENTRALLY-ACTING ANTI-OBESITY AGENTS

Amphetamines, which enhance central noradrenergic activity, were early centrally-acting anti-obesity drugs. They are effective but are contraindicated because of their potential for abuse. Serotonin (5-HT) suppresses food intake when injected centrally in rodents, and fenfluramine (now withdrawn) seem to act by blocking the reuptake and stimulating the release of serotonin.

A new class of anti-depressant drugs, the Selective Serotonin Reuptake Inhibitors (SSRIs), such as fluoxetine, also enhance serotonin action. However, they do not have clinically useful effects in general obesity, although they may be useful in reducing feeding binges in certain eating disorders.

More promising are the Monoamine Reuptake Inhibitors, which act by increasing levels of both 5-HT and noradrenaline in specific brain regions. Sibutramine, the first of this new class of drugs, has been shown to induce weight loss in a dose-related fashion[49,50] and has recently been granted a licence in the United States. Sibutramine induces a mean weight loss of about 8 kg, which is maintained for at least 12 months in patients who respond to it i.e. those who lose 2 kg during the first month of treatment.[51] Sibutramine will soon become available in the UK. Like all anti-obesity drugs, it is only indicated for clinically significant obesity and used only as part of a comprehensive weight-management programme. It should only be used in conjunction with lifestyle management measures and under physician supervision, in patients with a BMI >30 kg/m^2 or >28 kg/m^2 in the presence of obesity related co-morbid factors such as type 2 diabetes, hypertension or dyslipidaemia.

DRUGS BLOCKING FAT DIGESTION AND ABSORPTION

Orlistat (tetrahydrolipostatin) acts by inhibiting pancreatic lipase, the key enzyme that hydrolyses triglyceride, thus reducing fat absorption in the small intestine. It has the predictable side-effects of fat malabsorption including loose or liquid stools and steatorrhoea, particularly after a meal rich in fat; interestingly, these side-effects may actually help to modify eating behaviour to favour a low-fat diet. Orlistat has been hailed as 'a watershed for the treatment of obesity',[52] although its weight reducing effect is comparable with fenfluramine: it causes greater weight loss (4 kg over 12 months) than placebo and this weight loss is sustainable for up two years.[53] Orlistat should only be used under a doctor's supervision, in patients with a BMI >30 kg/m^2 or >28 kg/m^2 in the presence of obesity-related co-morbid factors. Patients must be advised to follow a low-fat diet (providing <30% of total energy intake). The EU criteria, which apply in the UK, require 2.5 kg weight loss on diet alone before starting orlistat, and then a loss of 5% body weight after three months on treatment. About 30% of patients fulfilling these criteria will go on to lose an average of 16% of body weight and keep that weight off for two years.

THERMOGENIC AGENTS

These agents act directly on the thermogenic tissues to produce more heat and thus lead to increased energy expenditure. Noradrenaline released by sympathetic terminals and acting on the β_3 adrenoreceptors is believed to be the physiological activator of thermogenic tissues in both rat and man. However, it is now clear that the human receptor has quite different pharmacological properties from the rodent and this has greatly complicated the design and discovery of thermogenic drugs. To date, there are no reliable agents in this category.

LEPTIN

Leptin has been suggested as a potential regulator of body mass (see earlier). Recombinant leptin injections in obese rodents lead to marked falls in body weight and fat.[24] Clinical trials in human obesity are ongoing; preliminary data suggest that it may cause greater weight lose than placebo in some patients and in one leptin-deficient patient.[54]

SURGICAL TREATMENT

The most significant reductions in body weight have been achieved with surgery. Various methods have been tried,

including gastric bypass and gastroplasty.

Vertical banded gastroplasty is the currently accepted method. This reduces the effective volume of the stomach, leaving a small gastric pouch of approximately 30 ml, which causes the patient to feel full rapidly and thus greatly limiting their intake of solid foods. This has been shown to induce weight loss of approximately 20-25 kg during the first three months and weight tends to level out after 12-18 months when the patient may have lost 60-75% of their initial excess weight.[55,56] Surgery is limited to patients with BMI >40 kg/m^2 or >35 kg/m^2 with serious secondary problems, and should only be considered where a multidisciplinary team is available for long term management.

Jaw wiring can reduce weight but is readily bypassed by determined patients with ingenuity. We feel, like many in the field, that this method achieves little in the long term and is dangerous and obsolete.

CONCLUSIONS

Obesity is associated with many adverse effects on both physical and mental well-being. Its incidence and prevalence are increasing exponentially and have already reached epidemic proportions. Because of the multifactorial nature of this disease and the difficulty in convincing patients to modify their lifestyle, it is an extremely difficult condition to manage. Many of the above studies indicate encouraging improvements in end-points such as weight loss, reduction in blood pressure and incidence of diabetes. However, it must be conceded that we do not yet have compelling evidence from interventional studies that weight reduction with the means currently at our disposal will decrease premature mortality - arguably the hardest end-point of all.

There are a number of exciting new developments which should hopefully lead to a much brighter future for the management of this common, important and neglected disease. A change in attitude of doctors is required to recognise the major medical benefits from a relatively modest (10%) weight loss, which is maintained in the long term, and the importance of prevention where possible.

REFERENCES

1. Deurenberg P, Weststrate JA, Seidell JC. Body mass index as a measure of body fatness: age-and-sex-specific prediction formulas. *Br J Nutr* 1991; **65:**105-14.
2. Han TS, Van Leer EM, Seidell JC, Lean MEJ. Waist circumference action levels in the identification of cardiovascular risk factors: prevalence study in a random sample. *BMJ* 1995; **311:**1401-5.
3. Lean MEJ, Han TS, Morrison CE. Waist circumference indicates the need for weight measurements. *BMJ* 1995; **311:**158-61.
4. Lean MEJ, Han TS, Seidell JC. Impairment of health and quality of life in people with large waist circumference. *Lancet* 1998; **351:**853-6.
5. Prentice AM. Obesity-the inevitable penalty of civilisation? *Brit Med Bull* 1997; **53:**229-37.
6. WHO MONICA Project. Risk factors. *Int J Epidemiol* 1989; **18**(Suppl. 1):546-55.
7. Seidell JC, Flegal KM. Assessing obesity: classification and epidemiology. *Brit Med Bull* 1997; **53:**238-52.
8. Prescott-Clarke P, Primatesta P. Health survey for England 1996; a survey carried out on behalf of the Department of Health. London: Stationary Office 1998 (Series HS; no 6).
9. Colditz G. Economic costs of obesity. *Am J Clin Nutr* 1992; **55:**5035-75.
10. Wolf A, Colditz G. The cost of obesity: the US perspective. *Pharmaco Economics* 1995; **5**(Suppl. 1):34-7.
11. West R. *Obesity* Office of Health Economics Monographs on Current Health Issues, no. 112. London: Office of Health Economics, 1994.
12. Prentice AM, Black AE, Coward WA *et al*. High levels of energy expenditure in obese women. *BMJ* 1986; **292:**983-7.
13. Prentice AM, Black AE, Coward WA, Cole TJ. Energy expenditure in affluent societies: an analysis of 319 doubly labelled water measurements. *Eur J Clin Nutr* 1996; **50:**93-7.
14. Black A, Prentice A, Goldberg G *et al*. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 1993; **93:**572-9.
15. Bouchard C, Perusse L, Leblanc C *et al*. Inheritance of the amount and distribution of human body fat. *Int J Obes* 1988; **12:**205-15.
16. Friedlander Y, Kark J, Kaufmann N *et al*. Familial aggregation of body mass index in ethnically diverse families in Jerusalem: The Jerusalem Lipid Research Clinic. *Int J Obes* 1988; **12:**234-47.
17. Allison D, Kaprio J, Korkeila M *et al*. The heritability of body mass index among an international sample of monozygotic twins reared apart. *Int J Obes* 1996; **20:**501-6.
18. Stunkard A, Harris J, Pedersen N, McClearn G. The body mass index of twins who have been reared apart. *N Engl J Med* 1990; **322:**1483-7.
19. Vogler G, Sorensen T, Stunkard A *et al*. Influences of genes and shared family environment on adult body mass index assessed in an adoption study by a comprehensive path model. *Int J Obes* 1995; **19:**40-5.
20. Stunkard A, Sorensen T, Hanis C *et al*. An adoption study of human obesity. *N Engl J Med* 1986; **314:**193-8.
21. Thurby P, Trayhurn P. The role of thermoregulatory thermogenesis in the development of obesity in genetically obese *(ob/ob)* mice pair-fed with lean siblings. *Br J Nutr* 1979; **42:**377-85.
22. Caro J, Kollaczynnski J, Nyce M *et al*. Decreased cerebrospinal fluid/ serum leptin ratio in obesity: a possible mechanism for leptin resistance. *Lancet* 1996; **348:**159-61.
23. Zhang Y, Proenca R, Maffei M *et al*. Positional cloning of the mouse gene and its human homologue. *Nature* 1994; **372:**425-32.
24. Pellymounter M, Cullen M, Baxter M *et al*. Effects of the obese gene product on body weight regulation in *ob/ob* mice. *Science* 1995; **269:**540-2.
25. Stephens T, Basinki M, Bristow P *et al*. The role of Neuropeptide Y in the anti-obesity action of the obese gene product. *Nature* 1995; **377:**530-2.
26. Stanley BG, Kyrkoyli SE, Lampert S, Leibowitz SF. Neuropeptide Y chronically injected into the hypothalamus: a powerful neurochemical inducer of hyperphagia and obesity. *Peptides* 1986; **7:**1189-92.
27. Bennett N, Dodd T, Flatley J *et al*. *Health survey for England 1993* London: HMSO, 1995.
28. Jebb SA. Aetiology of obesity. *Brit Med Bull* 1997; **53:**264-85.
29. Williamson DF, Madans J, Andra RF *et al*. Smoking cessation and severity of weight gain in a national cohort. *N Engl J Med* 1991; **324:**739-45.
30. Jung RT. Obesity as a disease. *Brit Med Bull* 1997; **53:**307-21.
31. Gortmaker S, Must A, Sobel A *et al*. Television viewing as a cause of increasing obesity among children in the United States. *Arch Pediatr Adolesc Med* 1996; **150:**356-62.
32. Royal College of Physicians. Obesity. *J R Coll Physicians Lond* 1983; **17:**3-58.
33. Manson J, Willet W, Stampfer M *et al*. Body weight and mortality among women. *N Engl J Med* 1995; **333:**677-85.
34. Colditz G, Willet W, Rotnitzky A, Mason J. Weight gain as a risk factor for clinical diabetes in women. *Am J Intern Med* 1995; **122:**481-6.
35. Chan J, Stampfer M, Rimm E *et al*. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men.

Diabetes Care 1994; **17:**961-9.
36 Lee IM, Paffenbarger RS. Change in body weight and longevity. *JAMA* 1992; **268:**2045-9.
37 Muls E, Kempen K, Vansant G, Saris W. Is weight cycling detrimental to health? A review of the literature in humans. *Int J Obes* 1995; **19**(Suppl. 3):S46-S50.
38 SIGN (Scottish Intercollegiate Guidelines Network). *Obesity in Scotland. Integrating prevention with weight management* Edinburgh: HMSO, 1996.
39 Kelly S, Dunnell K, Fox J. Health trends over the last 50 years. *Health Trends* 1998; **30:**10-15.
40 Charlton J, Quaife K. Trends in diet 1841-1994. In: Charlton J, Murphy M (eds). *The health of adult Britain 1984-1994* London Stationary Office, 1997; 93-113 (Vol 1; Decennial Supplement no. 12).
41 Allied Dunbar National Fitness Survey. Main findings. London: Sports Council and Health Education Authority, 1992: 46.
42 Blamey A, Mutrie N, Aitchison T. Health promotion by encouraged use of stairs. *BMJ* 1995; **311:**289-90.
43 Wood PD, Stenfanick ML, Dreon DM *et al*. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N Engl J Med* 1988; **319:**1173-9.
44 National Task Force on the Prevention and Treatment of Obesity. Very low calorie diets. *JAMA* 1993; **270**: 967-74.
45 Toubro S, Astrup A. Randomised comparison of diets for maintaining obese subjects' weight after major weight loss: ad lid, low fat, high carbohydrate diet v fixed energy intake. *BMJ* 1997; **314:**29-34.
46 Brenot F, Hervé P, Petitpretz P *et al*. Primary pulmonary hypertension and fenfluramine use. *Br Heart J* 1993: **70**: 537-41.
47 Abbenhaim L, Moride Y, Brenot L. Appetite-suppressant drugs and the risk of primary pulmonary hypertension. *N Engl J Med* 1996; **335:**609-16.
48 Connolly HM, Caary JL, McGoon MD *et al*. Valvular heart disease associated with Fenfluramine-Phentermine. *N Engl J Med* 1997; **337:**581-8. [Erratum, *N Engl J Med* 1997; **337:**1783].
49 Jones SP, Newman BM, Romanec FM. Sibutramine hydrochloride: Weight loss in overweight subjects. *Int J Obes* 1994; **18**(Suppl. 2):61.
50 Drouin P, Hanotin C, Courcier S, Leutenegger E. A dose ranging study: efficacy and tolerability of sibutramine in weight loss. *Int J Obes* 1994; **18**(Suppl. 2):60.
51 Lean MEJ. Sibutramine - a review of clinical efficacy. *Int J Obes* 1997; **21**(Suppl. 1):S30-S36.
52 Bray GA. Obesity: a time bomb to be defused. *Lancet* 1998; **352:**160-1.
53 European Multicentre Orlistat Study Group. Randomised placebo-controlled trial of orilstat for weight loss and prevention of weight regain in obese patients. *Lancet* 1998; **352:**167-72.
54 Jebb SA. Personal communication.
55 Mason EE, Doherty C. Surgery. In: Stunkard AJ, Wadden TA (eds). *Obesity, theory and therapy 2nd edition* New York: Raven, 1993; 313-25.
56 Kolanowski J. Gastroplasty for morbid obesity: the internist's view. *Int J Obes* 1995; **19**(Suppl. 3):S61-S65.