

## Eating and obesity

- Eating and body weight control are not due to the simple homeostasis of blood glucose levels.
- Lesions to the VENTRO-MEDIAL NUCLEUS of the hypothalamus produce overeating, massive obesity and increased metabolic efficiency, whereas lesions to the LATERAL HYPOTHALAMIC AREA produce APHAGIA.
- Eating may well be controlled by monitoring the relative levels of anabolism and catabolism by measuring either portal blood glucose or blood glucagon levels.
- Mild obesity may be due to a failure to interpret INTEROCEPTIVE STIMULI, and hence a need to use EXTERNAL CUES for initiating eating.
- Behavioural treatments of obesity, using CONDITIONED AVERSION, COVERT OPERANT CONTROL, SELF-CONTROL OR GROUP TREATMENTS are more effective than drug therapies, and maintain weight loss longer after treatment has ended.
- Specific food dislikes and CANCER ANOREXIA are both due to food becoming associated with illness by one-trial learning. They can be treated with SYSTEMATIC DESENSITIZATION.

Eating is essential for life but it can be impaired in illness, or even produce illness when improperly controlled.

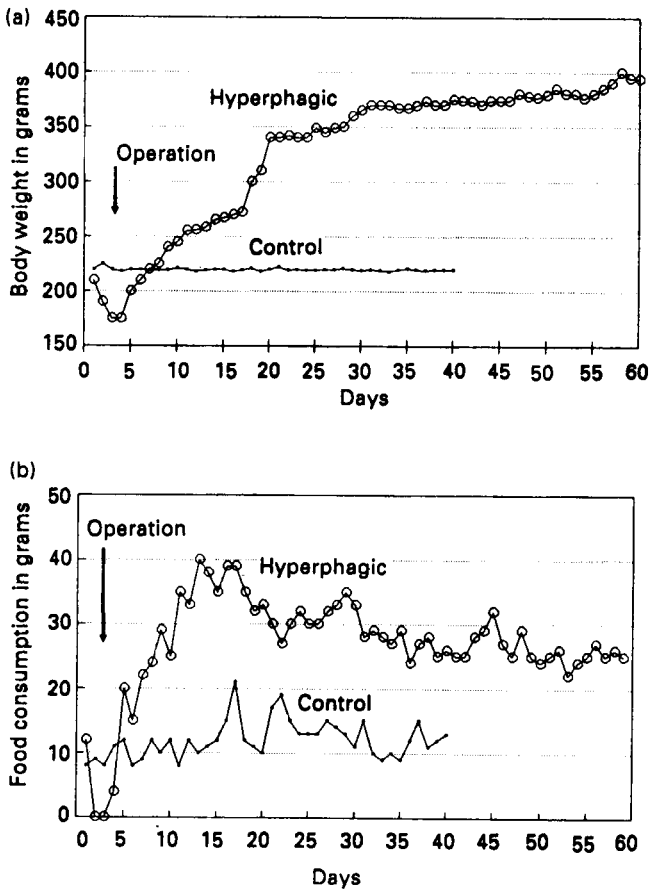
Theories of eating control divide into PERIPHERAL and CENTRAL, each of which is 'thermostatic' in type, with NEGATIVE FEEDBACK as the means of regulation (as when room temperature is controlled by a thermostat connected to a heater). Monitoring is by the mouth, stomach or bowels in peripheral theories, and directly by the brain in central theories. The oldest peripheral theories, such as of Erasmus Darwin (1731–1802), said hunger was caused by the rugae of the empty stomach rubbing together. Gastric activity is indeed greater in hunger than in satiation but such activity cannot explain eating control, since gastrectomy or vagotomy do not produce chronic hunger or obesity (and vagotomy is sometimes used to treat gross obesity). Similarly, taste is unimportant in weight control since rats not only learn to push a lever to inject bland liquid food into the stomach but also maintain accurate weight control if the food is diluted or the schedule of injections is altered, confirming it is the nutrient effect controlling intake.

HUMORAL THEORIES propose that eating maintains a constant level of some substance in the blood. The oldest theory, and the one with the most lay (and often medical) support, is that falling blood glucose causes eating, which increases blood glucose and food intake ceases. The theory fails for several reasons. Undoubtedly intravenous glucose injection causes cessation of eating, and insulin-induced hypoglycaemia causes both hunger and eating. However, continuous glucose monitoring shows blood levels do not fall before meals (which is hardly surprising given the elaborate control mechanisms involving insulin, glucagon, cortisol and growth hormone, whose function is precisely to maintain a constant glucose level); and to encourage eating by removing the brain's principal nutrient is a dubious survival strategy. The non-specific role of glucose is shown by hypoglycaemic eating also being inhibited by non-carbohydrate nutrients such as amino acids. Also problematic is that maturity onset diabetics show chronic *hyperglycaemia* (raised blood glucose) and yet also over-eat and are obese. The final nail in the coffin of simple glucose homeostasis is that after a meal, hunger and eating cease long before blood glucose levels have risen significantly.

Clinical cases have long suggested that hypothalamic lesions, as in FROHLICH'S SYNDROME, could cause gross obesity (and also hypogonadism). In 1939, Hetherington and Ranson showed that bilateral ventromedial nucleus (VMN) lesions in the rat hypothalamus produced massive obesity, animals weighing two or three times their normal body weight. Immediately after operation (Fig. 26.1) the animals become *HYPERPHAGIC* (eating more), and rapidly gain weight (the *DYNAMIC PHASE*) after which food intake decreases, but still remains above normal, and a new steady weight is attained (the *STATIC PHASE*). What is wrong with VMN animals? Certainly they eat more food, which partly explains the obesity. However when pair-fed with a normal rat, so that the VMN rat eats identical amounts to the normal rat, the VMN rat *still* gains more weight than the control rat, implying a more efficient metabolism (Fig. 26.2); this hypothesis is confirmed by the increased lipogenesis found *in vitro* in liver removed 48 hours after VMN lesioning in rats, before weight gain has occurred, confirming that metabolic change is not a *consequence* of weight gain.

If a VMN animal eats more then is it hungrier? Surprisingly the answer is, no. A hungrier animal should be more willing to eat quinine-adulterated food which tastes bitter; VMN rats actually eat *less* adulterated food than normals. Hungrier rats should also work harder to get food; but VMN rats work *less* hard than normal rats. Counter-intuitively, we must conclude that the VMN rat is actually less hungry than a normal rat.

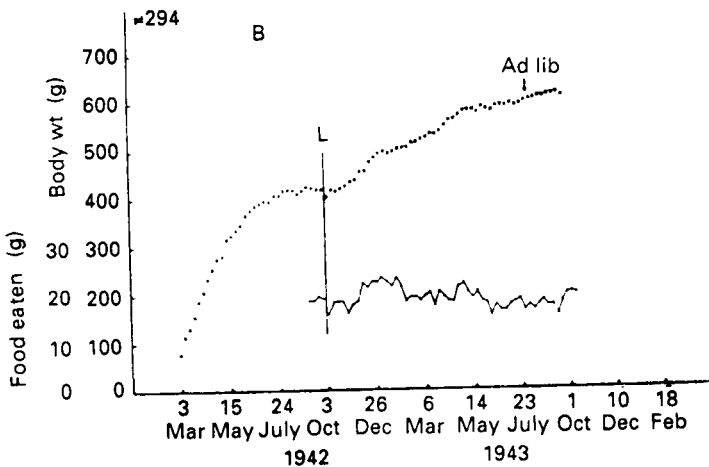
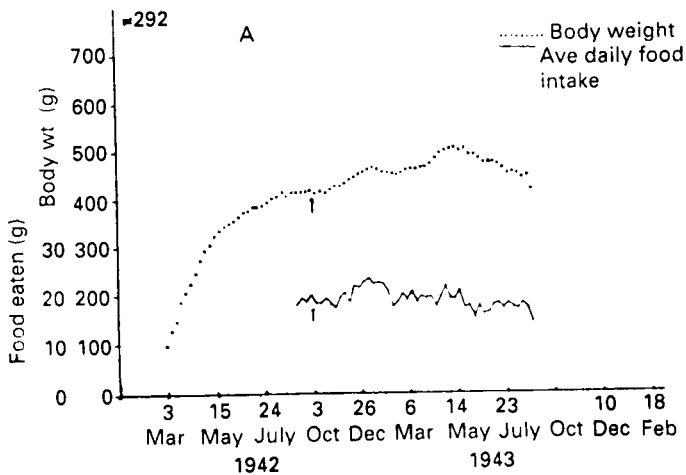
One theory of the VMN rat which failed was that the VMN contained gluco-receptors which the lesion destroyed, resulting in an absence of control, causing weight to rise inexorably because satiation could



**Fig. 26.1** The dynamic (early) and static (late) phases of the development of obesity in a rat following bilateral lesions of the ventro-medial nucleus of the hypothalamus, showing both increased food intake (bottom) and increased body weight (top), compared with a control animal. The dynamic phase lasts until about day 20. Adapted from Teitelbaum P (1961), in Jones M R, Ed, *Nebraska symposium on motivation*, Lincoln, University of Nebraska Press.

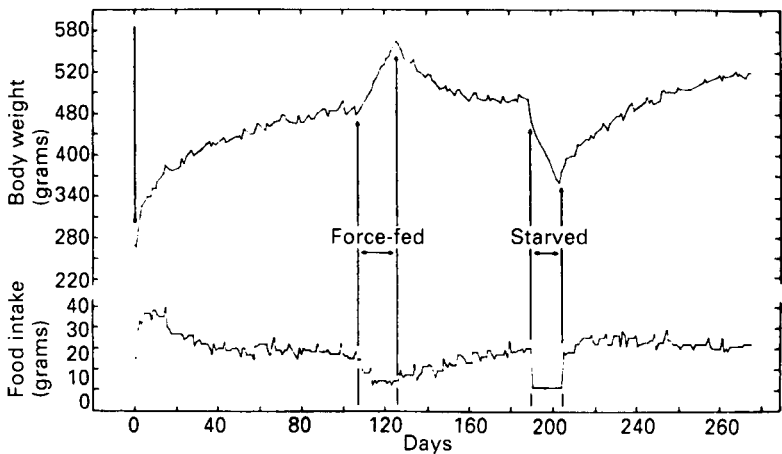
never occur. However if VMN-lesioned rats are force-fed to become even fatter (Fig. 26.3) they then decrease intake and return to their new 'ideal' weight (albeit three times normal) which is 'defended'; the control mechanism is still present, but reset to a higher value than normal.

Bilateral LATERAL HYPOTHALAMIC AREA (LH) lesions have opposite effects to VMN lesions, producing APHAGIA (absence of eating) and ADIPSIA (absence of drinking). Death rapidly ensues due to dehydration, but if tube-fed then eventually there is a very brittle 'recovery' with spontaneous eating. A second, more extensive, lesion causes further



**Fig. 26.2** A yoked experiment in which rat B received a VMN lesion at time L, while rat A, a litter-mate of B, acted as a control. Rat A was allowed to eat freely, *ad libitum*, and rat B was given food exactly in the same amounts as eaten by rat A. Reproduced with permission from Brooks C M and Lambert E F (1946). A study of the effect of limitation of food intake and the method of feeding on the rate of weight gain during hypothalamic obesity in the albino rat. *Am J Physiol.* **147**, 695-707.

aphagia and adipisia, confirming that previous 'recovery' was due to an incomplete first lesion. Chemical stimulation of the LH with adrenaline produces eating whereas acetylcholine produces drinking, implying separate control mechanisms at the same site.



**Fig. 26.3** Figure showing that even in VMN rats who are forcibly overfed or are starved, there is still a particular weight which is 'defended'. The upper line shows body weight and lower shows food intake. The animals were lesioned on day 0. Between days 108 and 126 the animals were force-fed, increasing their weight yet further; immediately after this their weight returned to its previous level. Reproduced with permission from Hoebel R G and Teitelbaum P (1966), Weight regulation in normal and hypothalamic hyperphagic rats, *Journal of Comparative and Physiological Psychology*, **61**, 189-93.

Modern theories of eating in animals are less dogmatically 'peripheral' or 'central'. Although the hypothalamus is important in eating control, the idea of 'eating centres' or 'satiety centres' is unsatisfactory, partly because many and varied lesions can affect eating, and partly because lesions may destroy fibres of passage rather than specific centres. The brain must monitor something which tells it about food balance, and a popular recent suggestion is that hepatic anabolism/catabolism is monitored, since the liver is the focus of energy balance. Monitoring is either by sensory nerves in the vagus, measuring portal glucose levels, or by measuring glucagon levels in blood (and eating is inhibited by glucagon injection and stimulated by glucagon antibodies).

Eating is induced by many environmental manipulations, such as lowering ambient temperature, which requires higher calorific intake. Mild stress, produced by gently pinching a rat's tail, also induces overeating; in man, life-stress, assessed by the Holmes-Rahe scale, correlates with food consumption by the obese (but not by normals). Tail-pinch induced eating is probably mediated via opioid peptides, and opiates in general induce eating (particularly of high-calorie food stuffs) whereas naloxone inhibits eating; opiates apparently act not by initiating more bouts of eating, but by delaying satiation, probably by making food more rewarding. Intriguingly, some food stuffs contain opiate-like substances (EXORPHINS) which, it is postulated, may

themselves induce further eating by stimulating opiate receptors, perhaps causing some types of extreme obesity. Many drugs or physiologically active substances stimulate eating (e.g. barbiturates, benzodiazepines, phenothiazines, lithium, and amitriptyline, all of which are sometimes used in patients *complaining* of obesity), and others inhibit eating (e.g. amphetamine, cocaine, prostaglandins, calcitonin, and thyrotrophin and corticotrophin releasing factors). Currently, no theoretical integration of these disparate effects is available, although a massive research effort continues.

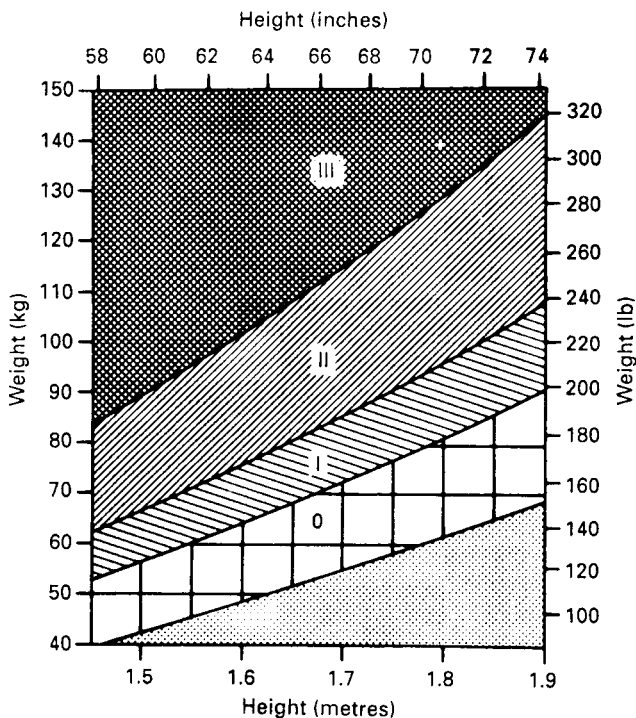
Initiation and termination of eating (SATIATION) are carried out by separate processes, since the effects of food are not physiologically apparent until some time after adequate quantities of food are ingested. The principal cue for cessation of eating is distention of the stomach, although gastrin release may also help in stopping eating.

After considering control of eating in normal individuals we must consider problems of eating control, of which the commonest is OBESITY; we can only really discuss human obesity since spontaneous 'natural' obesity in animals is rare, although genetic mutations such as the *ob/ob* and *fa/fa* genotypes in mice and rats do cause obesity.

Obesity is usually defined relative to height, either as PERCENTAGE OF IDEAL BODY WEIGHT OR DESIRABLE WEIGHT, which has been assessed by life insurance companies, or as indices such as the PONDERAL INDEX, BODY MASS INDEX OR QUETELET'S INDEX defined as  $\text{weight}/(\text{height})^2$ . If weight is measured in kilograms, and height in metres, then ponderal indices greater than 25 are regarded as obese (Fig. 26.4): grade I obesity is clinically minor but causes psychological morbidity; grade II is clinically important, with a doubled mortality; and grade III is almost incompatible with a normal life-style.

Obesity is associated with increased mortality and morbidity from many conditions, particularly in association with smoking and hypertension. There is also substantial psychological morbidity, due to negative social attitudes to the obese; thus 6-year-old children describe the obese as 'cheats, forgets, lazy, sloppy, naughty, dirty, stupid' and even educated adults found them 'unattractive, weak, unsuccessful, not like a wife, old, not like a sister, a follower and uninfluential'. Actual discrimination is suggested from evidence that the obese are downwardly socially mobile, and less likely to enter university, even after taking differences in IQ, attainment and school record into account. Not surprisingly the obese have a NEGATIVE SELF-IMAGE and suffer much anxiety about their problem.

Obesity is common. In the UK 27%, 51% and 71% of 15-29, 30-49, and 50-65 year olds weighed more than 20% of ideal body weight, obesity being slightly more common in females than males. Some evidence suggests there may be two separate types of human obesity, mild and severe, the border-line between the two being at about 150% of ideal body weight.



**Fig. 26.4** Relationship of weight to height, defining the desirable range (0), and grades I, II and III obesity. Reproduced with permission from Garrow J S (1981), *Treat obesity seriously: a clinical manual*, Edinburgh, Churchill Livingstone.

The obese do not generally eat more food than normals, but do eat more quickly, prefer sweet foods, eat larger meals, and eat *less* meals (due to DIETARY RESTRAINT, which often takes the form of missing one meal, usually breakfast). They are, however, more likely to snack frequently between meals, and to ignore or repress this fact when recalling their daily consumption. As in VMN rats, the obese may be metabolically more efficient, although they have a higher basal metabolic rate than normals, and after correction for total body size (or when measured in obese individuals who have dieted to normal weight), it is *lower* than normals. An obese person who has slimmed to normal weight requires *less* food to maintain that weight than a normal person (and hence, in part, the problem of *staying* slim once dieted). In animals, increased metabolic efficiency, the so-called THRIFTY GENOTYPE, is genetically transmitted, and even in non-obese heterozygotes produces increased resistance to starvation, and hence a HETEROZYGOTE ADVANTAGE which maintains the gene in the gene-pool. Human obesity undoubtedly runs in families, and adoption studies strongly suggest that there is a genetic component.

Metabolic problems and hypothalamic damage account for a minority of the grossly obese and do not account for the mildly obese at all. In America, young adults have increased in body weight by about fourteen pounds in the past two decades, a change that is not due to genetic or neurological problems. The most influential psychological explanation for mild obesity is by the American psychologist Stanley Schacter, who is concerned with how individuals infer hunger from sensory data. Sensory inputs are either INTEROCEPTIVE (monitoring the state of the viscera) or EXTEROCEPTIVE (monitoring the outside world by touch, sight, smell and hearing). Schacter suggests the mildly obese cannot interpret internal signals and instead therefore use exteroceptive stimuli to control eating. Following a suggestion by the psychoanalyst Hilde Bruch that parents of obese children fundamentally reject their children and then compensate for a lack of love by over-feeding the child, Schacter argued that such infants had not had appropriate opportunities for understanding their interoceptions. Infants cry not only for hunger, but also if they are thirsty, cold, in pain, needing winding, requiring a nappy change, etc. If parents respond to all these forms of crying with feeding then the child cannot learn to discriminate those bodily states that mean hunger, but will learn to associate eating with any relief of distress. Schacter suggests that the obese depend upon EXTERNAL CUES to signal hunger, rather than internal cues related to metabolic needs. To encapsulate Schacter's theory, normal subjects eat at 6.00 pm because they *are* hungry, but the obese eat at 6.00 pm because it is 6.00 pm and they *should* be hungry. A range of ingenious experiments support this theory. In one experiment subjects reported when they had hunger pangs, while gastric contractions were monitored; in normal subjects the hunger pangs correlated with stomach contractions, but the obese showed no relation, because they were not monitoring their internal state. In another experiment while subjects carried out a range of cognitive tests (the apparent purpose of the study) they were allowed to eat freely from biscuits left on a table. The only furniture in the bare room was a clock which could be speeded up or slowed down by the experimenter. Obese subjects ate more food when they thought it was late (the clock was fast) than when they thought it was early (the clock was slow); normal subjects showed no such relationship.

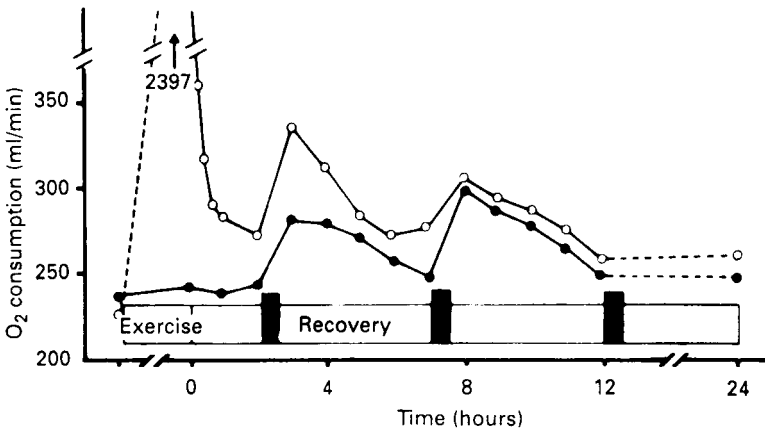
Schacter's theory also predicts the obese will find fasting *easier* if there are no external cues to eating, and more difficult if there are many external cues; normals should show no such differences. Schacter studied New York Jews fasting for Yom Kippur. Obese Jews attending synagogue all day found fasting easy (there being no food-related cues) while those staying at home found fasting difficult (being surrounded by the food-associated cues of everyday life); normal weight Jews found fasting equally difficult at home or at synagogue.

Many treatments are available for obesity. Some, such as intestinal



bypass surgery for the massively obese, are of little psychological interest. Psychological treatments generally try to reduce cues which might suggest eating, to neutralize cues which do occur, to provide strategies for coping with them, and to negate the positive consequences of overeating and reduce food consumption. Three main strategies are used. **CONDITIONED FOOD AVERSION** produces bad associations by presenting food (real or photographs) with aversive stimuli such as electric shocks, foul smells, cigarette smoke, pictures of the obese subject themselves in swimming costume or underwear, or induced nausea or vomiting. Future presentations of food (the conditioned stimulus) produce revulsion (the conditioned response), and food is avoided. In controlled trials weight loss is significantly better than with a placebo condition. **COVERT OPERANT CONTROL TECHNIQUES** use the principle that cognitive behaviours (i.e. thoughts) are reinforced just as actual behaviours. The patient is encouraged to think about the unpleasant consequences of being fat, or the advantages of being slim, before common, everyday, rewarding activity, such as reading the newspaper or watching television, so that each occurrence of the activity results in secondary reinforcement of the thought, and encouragement of weight control behaviour. Once again controlled trials show an advantage over placebo treatments. **SELF-CONTROL PACKAGES** modify deleterious behaviours associated with eating, patients learning to eat at particular times, to pause between bites, to chew food well, to avoid temptation with high calorie foods, to eat moderately in company, and to monitor food intake. Again results are better than placebo treatments. **SOCIAL OR GROUP TREATMENTS** such as **SELF-HELP GROUPS** use social pressure as their main weapon. Patients meet weekly (as in *Weight Watchers* or similar groups), are weighed publicly, and mutual encouragement and support provided by discussion of problems and difficulties. The groups produce very good results. **EXERCISE** is also used, either alone or with other treatments, since the obese are certainly less active than normals, and although a slow treatment, it not only produces a well-maintained weight loss but also has other health advantages as well as enhancing well-being. Exercise is effective only if aerobic for half an hour or more per day, and works not only because of calorie consumption during exercise but also due to an increased metabolic rate lasting 24 hours or more (Fig. 26.5), resulting from enzymatic **FUTILE CYCLING**. **ANORECTIC DRUGS**, usually amphetamine derivatives such as fenfluramine, do produce weight loss, but it is typically small (often because patients believe that with the tablets they can eat *anything*), ceases when treatment ends, and there is a serious risk of dependence or abuse.

**RECIDIVISM**, the tendency to regress when treatment finishes, is a problem with treatment for all behavioural disorders, such as obesity, smoking, alcoholism and drug addiction (see Fig. 24.3 in Chapter 24). Although a particular problem with drug treatments, behaviour

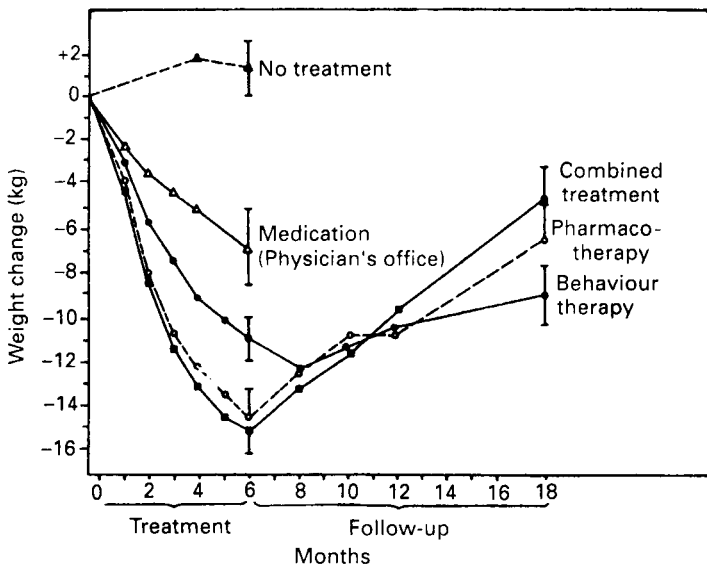


**Fig. 26.5** Oxygen consumption over a 24-hour period with (open circles) and without (closed circles) exercise. The shaded areas indicate meals. Reproduced with permission from Newsholme E A (1983). Exercise and obesity, in *Exercise, health and medicine*, London, The Sports Council, 41–2.

therapies maintain results even after specific treatment has finished (Fig. 26.6), suggesting long-term behavioural change has resulted; consequently behaviour therapy is now the treatment of choice for mild to moderate obesity. Recidivism is a particular problem in treating grade III obesity by JAW WIRING, where weight is rapidly regained despite losing 35 kg from an initial average weight of 111 kg (Fig. 26.7). The simple device of an unstretchable welded nylon cord around the waist provides immediate, unpleasant feedback as weight increases unduly and prevents weight regain.

Although overeating is the commonest eating problem other disorders have undereating as the major problem.

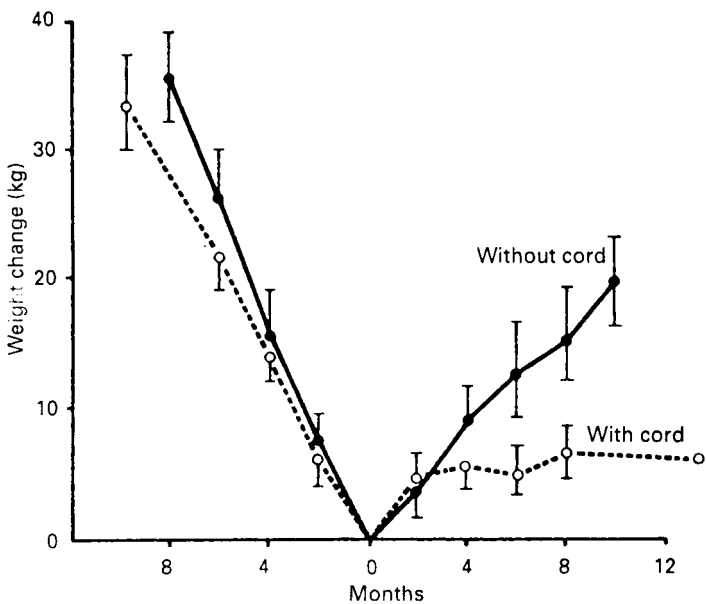
SPECIFIC FOOD DISLIKES are produced by classical conditioning when food ingestion is associated with illness (see Chapter 3). It is well-recognized in wild rats that do not eat poisoned bait after previously nibbling a tiny quantity resulting in illness. In laboratory rats, a novel food (the conditioned stimulus) is given with a lithium chloride injection (the unconditioned stimulus) which induces gastro-intestinal distress and nausea (the conditioned response); future food presentations produce nausea and food avoidance. The procedure works even if illness occurs 24 hours after food ingestion. Undoubtedly, many human dislikes of specific foods are due to similar mechanisms; the psychologist Seligman described cooking a *sauce béarnaise*, developing 'flu 24 hours later, and subsequently disliking the sauce, even though in no sense did the food *cause* the illness. The same mechanism causes CANCER ANOREXIA in which patients on treatment for malignancies develop a lack of interest in food, it should not be confused with CACHEXIA, the massive weight loss caused by the malignancy. Radi-



**Fig. 26.6** Treatment of 145 obese individuals (over 160% of ideal body weight). Patients were randomized to three main treatments: behaviour therapy carried out in groups; pharmacotherapy (fenfluramine) also carried out in groups; and both behaviour and pharmacotherapy. The two control groups received either no treatment or just medication ('doctor's office') where fenfluramine and dietary advice were dispensed from the doctor's office (to control for the group meetings in the main treatment conditions). Active treatment ceased after 6 months and patients were followed for a further 12 months. Reproduced with permission from Craighead L W, Stunkard A J and O'Brien R (1981), Behaviour therapy and pharmacotherapy for obesity, *Arch Gen Psychiat*, **38**, 763-8; copyright 1981, American Medical Association.

otherapy and antineoplastic drugs used in cancer therapy produce nausea and vomiting as side-effects; any food ingested in the previous 24 hours therefore becomes associated with illness and becomes disliked. Conditioned food aversion is readily treated by SYSTEMATIC DESENSITIZATION, the relaxed patient gradually being exposed to more potent food stimuli.

ANOREXIA NERVOSA is a psychiatric condition, particularly common in adolescent women (about one in every hundred), in which a morbid fear of becoming excessively fat results in persistent food refusal, and a very low body weight; menstruation ceases, and infectious disease becomes a serious risk. Some patients also show BINGE-EATING, disposing of excess food by self-induced vomiting and purging, BULIMIA NERVOSA. Anorectics have a DISTORTED BODY-IMAGE, measured by asking the patient to adjust the proportions of a computer-generated photograph until it accurately reflects true bodily proportions, seeing themselves as fatter than they really are, so their own excessive slimness is perceived



**Fig. 26.7** Weight change after jaw wiring in massively obese women. Jaw wires were removed at time 0. Half the women had a nylon cord placed around the waist when the desired result had been achieved. Reproduced with permission from Garrow J S and Gardiner G T (1981), Maintenance of weight loss in obese patients after jaw wiring. *Br Med J*, **282**, 858-60.

as normal. The cause of anorexia is not clear. Social pressure is important, the incidence of disease rising as slimness is emphasized more in sexual attractiveness. However, an unconscious rejection of femininity, and an attempt to suppress menstruation and cause breast atrophy, are also important. Pituitary axis abnormalities occur, although they might be primary or secondary. Treatment of anorexia nervosa is by a combination of psychotherapy, behaviour therapy and drugs such as tricyclic antidepressants.