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Management of obesity

Weight management needs to be commenced early to be successful, with a strong focus on avoiding weight gain as well as trying to achieve weight loss.

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Levels of overweight and obesity in Australia, as well as overseas, are escalating. Unfortunately, awareness of this problem does not always equate to action, as many patients 'slip through the loop' and do not have their weight issues addressed. Barriers to good management strategies are numerous because often medical issues such as diabetes, hyperlipidaemia and hypertension take precedence.

Many GPs and specialists focus solely on the management of the HbA_{1c} or low density lipoprotein cholesterol levels in their patients rather than weight loss attempts. In an obesity practice, it is not unusual to have a patient with diabetes with tightly controlled blood sugar readings whose weight has escalated over the years due to the use of insulin therapy or the introduction of a glitazone. Patients such as this face an enormous task to lose the weight gained, particularly because the need for excellent diabetic control has been so deeply instilled. Many of these patients eat to avoid having episodes of hypoglycaemia, which could be avoided by lowering the insulin dose. There are also many patients in whom the initiation of medication for other illnesses, such as depression, psychosis or asthma, may result in an increase in weight, which again is very difficult to reverse.

Causes of obesity

Both twin and adoption studies have shown that up to 70% of the BMI in adults and children may be explained by genetics. Single gene defects associated with obesity such as Prader-Willi syndrome or Bardet-Biedl syndrome are rare. The more common defects (although still uncommon) involve the hypothalamic leptin–melanocortin pathways. It is thought that 1.8% of obese adults and up to 6% of children with severe, early-onset obesity have monogenic obesity due to gene mutations in the melanocortin-4 receptor. These genes are known to cause abnormal eating behaviours; however, it is thought that the more 'common' type of obesity is

IN SUMMARY

- **Weight loss will occur if an energy deficit is sustained. There are many ways to achieve this and so individual counselling as well as trial and error is necessary.**
- **Weight management should be divided into the initial weight-loss phase followed by long-term weight maintenance. Strategies for both phases need to be developed with acknowledgement of the very easy weight regain seen in patients who are unable to maintain an energy deficit.**
- **Expected weight gain after changes in medication or lifestyle can sometimes be avoided if both the patient and doctor are proactive rather than reactive.**
- **Treatments currently available, either licensed or used off-label, are not usually sufficient to achieve and maintain the ideal bodyweight and so goals such as risk-factor modification and reduction in medications that cause weight gain become more important.**

caused by a combination of abnormal eating as well as altered energy utilisation, which as yet has not been fully elucidated.

In clinical practice, it is clear that some people inherit an ability to gain weight more readily than others, rather than having a well-defined set weight. Although eye colour, initial hair colour and height are relatively immune to environmental changes, bodyweight has been shown to have a strong association with the environment. A larger bodyweight is associated with a stronger genetic component. This means that an individual with a strong genetic tendency to gain weight can only avoid being overweight if a small-portion, low-fat diet is maintained at the same time as undertaking high levels of activity. Any interruption to this energy balance, such as an injury or the development of osteoarthritis, can result in seemingly effortless weight gain (Figure 1).

There are many times during a person's life in which obesity may develop even with a constant dietary intake or a preserved level of exercise (Table 1). It is usually possible to see a change in the energy balance equation due to alteration in incidental activity, although the patient often finds this difficult to recognise. Many patients present with unexplained weight gain after lifestyle changes, such as a new job that may be far more sedentary that the previous one, even though the exercise pattern has remained unaltered and food intake has not changed. An example of this is men in sedentary executive positions who gain weight gradually over time until they reach a weight that becomes more and more problematic. Most patients in this situation believe that the weight gain is inexplicable and that they should be the weight they were at the most active stage of their lives.

As patients tip into the morbid obesity category their ability to be active is markedly limited. Many younger patients with obesity can maintain their exercise but are then less active for the rest of the day, thereby reducing their incidental activity. These patients commonly acknowledge that they need a day or more to recover after any physical exertion and require rests during the day to recuperate. This in turn limits their overall energy expenditure and makes weight loss more difficult. Other patients develop obstructive sleep apnoea (seen in up to 50% of all patients with morbid obesity) and the ability to be active is further compromised. The cycle continues and can be further

accelerated by the introduction of medications that may increase appetite or decrease energy expenditure by causing sedation. Often this occurs as patients become progressively more frustrated by their circumstances and by their increasing inability to lose weight. Clinical depression is common; however, it is often an overwhelming sense of despair that demotivates the patient.

Treatment of obesity

The treatment of obesity should be divided into the initial weight-loss phase followed by the long-term maintenance phase. Many patients who attempt to lose weight relapse because too much attention is focused on the initial weight loss. Patients remain highly motivated as long as results are seen but struggle to maintain momentum after the weight loss slows down. If the goal weight is set at an unachievable level then patients will feel they have failed and stop further attempts at weight loss. Many different treatment options are available for weight loss, as outlined in the box on page 56.

Initial weight loss

For patients to succeed at initial weight loss they need to use techniques that create an energy deficit in which more energy is used than is consumed. This can be achieved in a variety of ways as outlined below.

Reduction in food portion size

A reduction in food-portion size will reduce total energy intake, although it can be problematic

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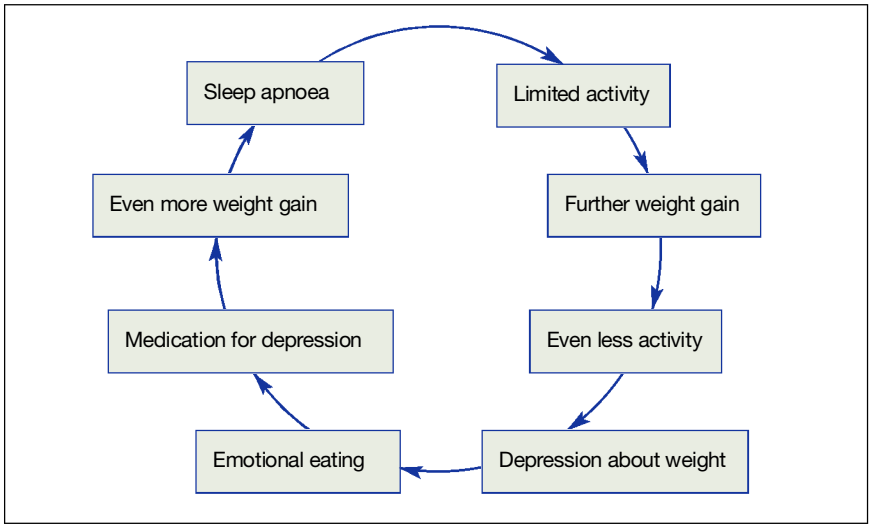

Figure 1. Weight-gain cycle observed in very overweight patients (BMI 40 to 50).

because a patient's appetite is not necessarily reduced and so snacking can occur. Many of the foods consumed between main meals are energy dense and so the attempt at reducing overall energy intake fails. This scenario is relatively common in women who avoid breakfast and lunch but are then starving in the evening. Replenishment occurs but the total calorie intake is consumed in the evening only. It may be valuable to show patients portion sizes using life-size photographs or use known common measures such as cupfuls, hand sizes or even measurements. Many patients benefit from knowing that a main meal could be enough to fill three cups or that a piece of meat should be no larger than their hand size. Some patients are able to control appetite and so can benefit from decreased portion sizes.

Table 1. Changes in lifestyle that may result in weight gain

Change in life pattern	Result
Starting at primary school	Easier access to food
Leaving home	More take away foods
Getting married	More time spent eating and entertaining
Ceasing smoking	Reduction in energy expenditure
Reaching the menopause	Reduction in basal metabolic rate
After having surgery or sustaining an injury	Reduction in activity levels
Developing depression	Emotional eating and inactivity
Developing diabetes	Medications can increase appetite
Developing asthma	Use of corticosteroids and limited activity
Changing job	Reduction in incidental activity
Developing sleep apnoea	Reduction in incidental activity
Developing osteoarthritis	Limited activity
Being promoted or expectation of same	Less time for activity
During pregnancy	Altered food intake – i.e. cravings Change in energy expenditure
Having children	Less time for exercise

Change in energy density of food

A change in the energy density of food allows a reasonable food volume to be consumed while maintaining a lower calorie intake. This is best achieved by reducing fats in the diet and avoiding takeaways and preprepared foods. Foods that increase satiety such as raw fruits, fish and lean meats play a very important role and help patients to avoid snacking between meals. Meals such as porridge for breakfast, one sandwich for lunch, and meat with three handfuls of steamed vegetables for dinner may be sufficient for some patients and help to induce satiety.

Increase in energy expenditure

An increase in energy expenditure can be achieved by either increasing incidental activity such as walking or increasing exercise such as going to the gym. Unfortunately increased physical activity alone with no change in food intake is associated with only moderate weight reduction. A study in which patients ran an average of 32.2 km per week showed an average weight loss of only 2.9 kg in eight months. Many patients simply compensate for increased activity by increasing their food intake, perhaps unknowingly. They become fitter and more toned but do not necessarily achieve the desired effect of weight loss. Increased activity does, however, play a critical role in weight-loss maintenance.

Many varied commercial weight-loss programs are available aimed at achieving one or more of the objectives described above. For many patients it is a matter of finding a regimen that fits their lifestyle,

Weight-loss options

For most patients weight loss can be achieved using diet and exercise modifications, particularly if started when weight gain first occurs. More interventions should be considered as weight gain progresses, with patients in the morbid obese category often needing either long-term, very-low-calorie diets or surgery to enable initial weight reduction.

The following is a list of weight-loss options available in Australia.

- Low-energy diets often described in magazines or books
- Exercise programs set up by the gym or a personal trainer
- Commercial weight-loss programs – e.g. Weight Watchers or Lite and Easy
- Modification of medications – e.g. changing therapies for type 2 diabetes
- Meal-replacement programs (chemist supervised)
- Very-low-calorie diets (medically supervised)
- Medications for obesity – e.g. orlistat or sibutramine
- Medications for mood stability – e.g. sertraline or reboxetine
- Nonsurgical intervention – e.g. intragastric balloons
- Surgical intervention – e.g. laparoscopic gastric banding, sleeve gastrectomy or by-pass procedures

uses familiar foods and is not seen to be too depriving or too time consuming.

Studies of various commercial weight-loss programs have failed to document significant differences in long-term outcomes. Although one method may result in significant weight reduction for one individual, in another patient, feelings of deprivation and the need to increase food intake can be overwhelming. Some patients can be guided through various programs and, as long as there is a sustained overall reduction in calorie intake, manage to be very successful with weight loss. Others seemed to be unable to maintain an energy deficit for any length of time with episodes of binge eating and energy restoration occurring after any diet. For these individuals, medical intervention using either pharmaceutical products or very-low-calorie diets may be appropriate. Ongoing support with frequent visits to a dietician, GP or clinical psychologist may be helpful as long as the healthcare provider is motivated and interested in weight management.

Table 2. Areas of research on obesity drugs

- Beta-3 adrenergic receptor modulators
- Cannabinoid receptor modulators
- Digestive inhibitors/lipid metabolism modulators
- Histaminergic system modulators
- Hormone analogues
- Monoamine reuptake inhibitors/ 5-hydroxytryptamine receptor modulators
- Neuropeptide receptor modulators
- Combination therapies

Pharmaceutical treatments

One of the greatest frustrations in the area of weight management is the lack of effective treatments. For the past decade, many new therapies have shown promise but have been limited by side effects related to their actions. It has become increasingly difficult for a product to be accepted as a weight-loss medication unless there are no or few side effects. Cannabinoid receptor agonists such as rimonabant have been extensively studied and were considered to be safe and effective only to be recently withdrawn due to the potential for depression. New compounds still under investigation include combined therapies as well as various receptor modulators (Table 2).

In Australia only two medications are currently licensed for long-term obesity management (sibutramine and orlistat) and one medication for short-term obesity management (phentermine). The current accepted criteria for pharmacological treatment are a BMI of over 27 and comorbidities such as diabetes, hypertension or hyperlipidaemia, or a BMI of over 30.

The relative lack of medications specific for obesity management has hampered the overall prospect for treatment; however, it has precipitated more of a focus on treatable or improvable comorbidities. For example, depression, obstructive sleep apnoea and type 2 diabetes, if treated appropriately can aid the weight-loss attempt. An example in patients with type 2 diabetes is the use of metformin as initial therapy with the initiation of sitagliptin as second-line treatment. Sitagliptin is a dipeptidyl peptidase-4 inhibitor that increases levels of incretin hormone, reduces gastric emptying and helps weight loss. Other possibilities include the use of exenatide, which works as an incretin mimetic and increases glucose-dependent insulin secretion. If exenatide is used instead of insulin in obese patients with type 2 diabetes who have poor control despite oral therapies, it may prevent the weight gain that is frequently seen. Newer long-acting basal insulins such as glargine and detemir are associated with less weight gain than some of the older insulins.

Drugs approved for obesity

Sibutramine

Sibutramine is a noradrenaline and serotonin reuptake inhibitor that acts centrally to increase satiety while also increasing energy expenditure. It can be valuable as a means of decreasing energy intake while helping to avoid the reduction in energy expenditure that occurs when less food

is eaten. It is available in either a 10 mg or 15 mg dose and it has few side effects.

Sibutramine can occasionally cause insomnia, agitation and constipation as well as a slight increase in blood pressure and pulse rate. These increases are usually not significant clinically and are mitigated if weight loss occurs. Patients who are already taking antihypertensive medication are relatively protected from increases in blood pressure and pulse rate, although they should still have their blood pressure monitored during subutramine treatment. Some patients use sibutramine for initial weight loss, although recently it has been used to prevent weight regain. It is licensed for on-going use in patients with obesity and. A mortality study in patients over 55 years is nearing publication.

Orlistat

Orlistat is a lipase inhibitor acting in the intestine to decrease the absorption of fat by approximately 30%. It can be used by patients to assess the initial content of fat in the diet and can help them pick up 'hidden fats'. Side effects of oil incontinence, flatulence, bloating or other gastrointestinal effects are a result of too much fat in the diet, and can be avoided by eating less energy dense foods. Orlistat can be used to help patients lose weight initially; however, longer-term studies have also shown benefit with reduction in comorbidities as well as weight maintenance. The incidence of type 2 diabetes has also been shown to be reduced by the use of orlistat plus lifestyle changes in a four-year trial.[1]

Phentermine

Phentermine is an adrenergic stimulant that reduces food intake. It is available in Australia although licensed only for the short-term management of obesity. The benefit of this drug is often limited by side effects such as insomnia and agitation, and there are very little data available on safety and efficacy. Phentermine is rarely used as part of a long-term, weight-management strategy.

Off-label drugs for obesity

Sertraline and fluoxetine

Sertraline and fluoxetine are not licensed for the management of obesity; however, for many patients they can limit the sense of deprivation associated with dieting and they have been used as 'enabling agents'. Patients taking these medications often report an increased level of satiety, which enables them to restrict food intake more readily.

Sertraline and fluoxetine can be of particular benefit in patients with mild depression (with or without mood swings) who may become more motivated to lose weight while taking these drugs. Doses of 50 to 100 mg sertraline or 20 mg fluoxetine seem to be associated with increased satiety, whereas higher doses of 150 to 200 mg sertraline or 40 to 60 mg fluoxetine are beneficial in patients with obsessive thoughts regarding food intake. There are only early reports of studies using fluoxetine in patients with obesity and no recent data on either drug in terms of weight management.

Reboxetine

Reboxetine is an antidepressant that acts as a noradrenaline reuptake inhibitor. Although it is of most benefit in depression, it can also be helpful in patients who experience overwhelming tiredness associated with their obesity. Often this lack of energy is attributed to mild depression; however, it may also be part of obstructive sleep apnoea, which is especially prevalent in morbid obese patients. Reboxetine at low doses (2 to 4 mg in the morning) can effectively motivate a patient while also having an effect to decrease appetite. Higher doses of the medication such as 4 mg twice daily may be able to be used, although side effects such as dry mouth, constipation and insomnia may impact negatively on weight loss. Again, there are no controlled studies of reboxetine in obesity and the use of this medication is really only of value if the patient is depressed and demotivated.

Topiramate

Topiramate is a third-line antiepileptic medication that has been shown also to reduce appetite and food cravings. It has recently been licensed for the prophylaxis of migraine but is not licensed for obesity management. Its side effects such as depression occurring in patients without epilepsy meant that studies for obesity management were abandoned. However, in individual patients who are overweight or obese, particularly those with epilepsy or migraine, topiramate can be of benefit because it can help reduce thoughts of food. Doses of 25 to 100 mg have shown some benefit in patients with Prader-Willi syndrome, unlike other medications that have been unable to limit food-seeking behaviour.

Nonpharmaceutical interventions

Although patients with simple obesity (defined as having a BMI of between 30 and 40) can lose weight using many different techniques, those with morbid obesity (defined as having a BMI of more than 40) have a more daunting challenge. These latter patients need to create an energy deficit even though increased physical activity may not be possible. Many are severely limited in terms of their mobility and have difficulty achieving even a small increment in activity. Patients with extreme morbid obesity (defined as having a BMI of more than 50) have great difficulty walking more than 2000 steps a day (on average people in Australia walk 3000 to 4000 steps per day) or even leaving the comfort of their own home. These individuals need to consume fewer calories to achieve an energy deficit. Three nonpharmaceutical methods currently used are detailed below.

Very-low-calorie diets

Optifast is a method by which appetite can be controlled using a ketogenic regimen while maintaining appropriate intake of protein, vitamins and minerals. Patients who use Optifast as a three-meal per day

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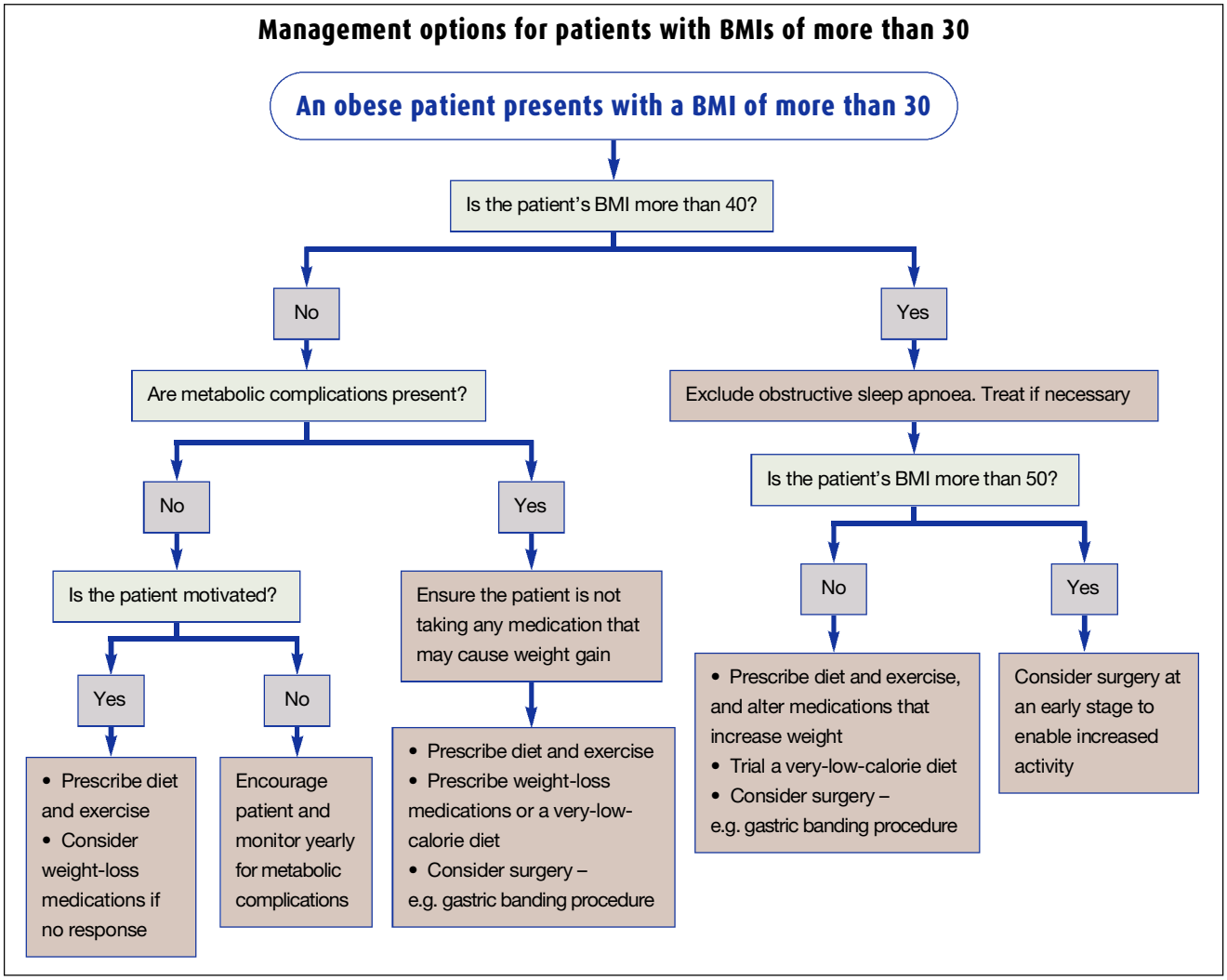

replacement take in fewer than 800 calories per day yet do not feel hunger because they produce ketones. The weight loss achieved is initially rapid but can then continue at the rate of up to 1 to 2 kg per week. It is not unusual for patients to lose 10 to 20 kg in the first three months on this program.

Ongoing weight loss, as well as weight maintenance, can follow if the patient is able (and willing) to reuse the program either as a three-meal per day replacement or a one- to two-meal per day replacement. Optifast is also used in Australia to reduce liver size prior to a laparoscopic gastric banding procedure.

Intragastric balloons

Intragastric balloons are silicon balloons inflated with either air or water. They have been used to treat obesity for the past eight years and are placed via an endoscope under light sedation. Internationally, intragastric balloons have been used to achieve initial weight loss in patients who are about to undergo bariatric surgery, whereas in Australia they have been used for patients unable or unwilling to have surgery even though they are considered ineffective for long-term weight maintenance.

Intragastric balloons can be beneficial in obese patients with lower BMIs (i.e. 30 to 35) who do not fit the criteria for a laparoscopic gastric banding procedure or even in patients with a BMI of 27 to 30 with associated comorbidities. Although there is a strong potential for weight regain after balloon extraction, many patients have been able to sustain weight loss either by increasing energy expenditure or by changing (or ceasing) medications that contributed to the weight gain initially. For example, patients with type 2 diabetes may be able to sustain a lower bodyweight if diabetic control can be achieved by weight reduction (with or without metformin) rather than with insulin.

Table 3. National Weight Control Registry techniques for long-term weight maintenance

- Undertake high level of physical activity (approximately one hour per day)
- Eat breakfast regularly
- Eat a low-calorie, low-fat diet
- Self-monitor weight on a daily basis
- Keep food intake consistent over the week
- Treat sleep apnoea
- Treat depression
- Avoid weight-inducing medications
- Continue adherence to diet and exercise strategies

Bariatric surgery

Surgical options can be either restrictive, malabsorptive or both and can include gastric banding and by-pass procedures. It is appropriate for patients with morbid obesity (BMI of more than 40) or those with a BMI of more than 35 with complications such as type 2 diabetes, hypertension, ischaemic heart disease or sleep apnoea to be considered for surgery, particularly if long-term weight maintenance is difficult (see the flowchart on page 58).

In the past 10 years, laparoscopic adjustable gastric banding has become increasingly popular because patients can achieve significant weight reduction as well as long-term weight maintenance. Weight losses of up to 50% of initial excess weight after two years from surgery are not unusual and metabolic complications of obesity can improve dramatically. Many patients are able to stop insulin therapy for type 2 diabetes, as well as reduce other medications for hypertension, hyperlipidaemia and even continuous positive airflow pressure therapy for obstructive sleep apnoea. However, surgery is not successful in all patients and the postoperative follow up seems to be vital to help patients deal with the long-term restriction in food intake. Patients who are emotional eaters or those with underlying depression or eating disorders may be able to maintain their usual food intake by eating smaller portions more often or by increasing the intake of energy dense fluids. Some of these patients may be more suited to by-pass procedures although these procedures are considered to be more interventional and require life-long monitoring of nutritional needs.

Useful websites on obesity

The NSW Childhood Obesity Summit
www.health.nsw.gov.au/publichealth/healthpromotion/obesity/

The Australian and New Zealand Obesity Society
www.asso.org.au/home

Obesity Surgery Society of Australia and New Zealand
www.ossanz.com.au

Long-term weight-loss maintenance

Avoiding weight regain is usually a challenge because physiological mechanisms, some poorly understood, promote weight regain. There is a general perception that no one succeeds in long-term weight maintenance even though studies have shown that approximately 20% of overweight individuals are successful. One definition of success is losing greater than 10% of initial bodyweight and maintaining the loss for at least one year. In the USA, the National Weight Control Registry (NWCR) is helping to define the techniques that are needed for successful weight-loss maintenance. Members of the NWCR have lost an average of 33 kg and have maintained the loss for more than five years. Techniques that contribute to better weight maintenance as reported by the NWCR are listed in Table 3. They include exclusion and treatment of comorbidities as well as continuing with a far more active lifestyle than prior to the weight loss.

A new concept of weight maintenance is the idea of a 'trigger weight', whereby patients first lose weight by reducing their calorie intake or increasing energy expenditure and then if their weight increases again above the trigger point, they recognise that they may need to return to the successful weight-loss strategy. Many patients can keep their weight under control using this technique but do need to maintain a constant check on their weight and food intake. This awareness of potential weight gain means patients can learn when to return to previous successful methods. For example, if there is an inability to exercise for a period of time, patients can compensate by reducing calorie intake accordingly. Patients also need to be particularly proactive after a time where weight gain is predicted such as during the Christmas period. Although the idea of a trigger weight is aimed at patients coming to terms with their ongoing need to monitor their weight, it is actually the way many slim people maintain a constant bodyweight.

Conclusion

Weight management needs to be commenced early to be successful, with a strong focus on avoiding weight gain rather than only trying to achieve weight loss. Useful websites on obesity are listed in the box on this page. For many patients the onus lies with GPs to detect and perhaps prevent weight gain associated with a change in medication. For example, patients whose medications are changed from oral hypoglycaemics to insulin need regular monitoring and a d equate advice to avoid dose increases being made as a result of increased food intake. If patients are not weighed regularly, the weight gain may go unnoticed until other complications present.

Current therapies specific for obesity are inadequate and it appears that many patients require a fairly aggressive initial approach using a very-low-calorie diet,

medication and/or surgery to achieve a sustainable bodyweight. Ideal bodyweight for many patients is unsustainable because of an inability to alter lifestyle and to be more active. For these individuals, a bodyweight that limits metabolic complications may be the best outcome even if it is above the ideal weight for the patient.

New therapies are eagerly awaited; however, the lessons from the past suggest that a single pharmaceutical intervention may at best reduce bodyweight by approximately 5% more than would placebo. Novel approaches to weight maintenance as well as weight loss are needed and all healthcare givers need to be vigilant to avoid iatrogenic weight gain in their patients. MT

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