

Concepts in Comprehensive Weight Management
Continuing Education Monograph

Managing Obesity as a Chronic Disease



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Program Preview

The incidence of obesity in the United States has increased tremendously in recent years, with more than one half of adults considered to be overweight. Once thought to be simply a result of poor willpower and overeating, obesity is now recognized as a disease resulting from a complex interaction of genetic, physiologic, and environmental factors. It is also clear that the consequences of obesity reach far beyond the usual negative social stigma and prejudice associated with being extremely overweight. Obesity is associated with a number of significant medical, psychological, and social sequelae.

Obesity, like hypertension and diabetes mellitus, is a serious, chronic medical condition that requires life-long intervention. However, even modest reductions in body weight can result in recognizable health benefits. Dietary modification and increased physical activity are the foundations for any successful weight loss program. In many patients, the addition of pharmacotherapy can increase the chances for long-term success. Ongoing contact with empathetic, concerned health care professionals, including pharmacists, encourages patients in their efforts and facilitates compliance with weight loss interventions.

This monograph describes what is currently known about the causes of obesity, the medical consequences associated with being obese, and various behavioral and medical strategies to achieve weight loss. A special emphasis on the pharmacist's role in identifying patients at risk for obesity-related complications and encouraging patients to seek and adhere to treatment is included.

Learning Objectives

After reading this article, the pharmacist should be able to:

- Explain what is known about the genetic and environmental causes of obesity and the nature of obesity as a chronic disease.
- Describe the different techniques for classifying obesity and discuss their relative merits.
- Describe the effects of obesity on patient morbidity and mortality and list at least six potential health consequences.
- Compare the mechanism of action, efficacy, safety, and usefulness of various prescription and nonprescription weight loss medications.
- Counsel patients regarding the importance of lifestyle modifications to achieve and maintain a healthier weight.

Introduction

Obesity has reached epidemic proportions in the United States, affecting an estimated 97 million adults.¹ While most people would choose to avoid substantial weight gain simply because of the negative social stigma, not everyone realizes the medical consequences that can result from becoming significantly overweight. Obesity is associated with a number of serious health risks including cardiovascular disease (CVD), hypertension, stroke, dyslipidemia, diabetes, gallbladder disease, osteoarthritis, gout, sleep apnea, and certain cancers.^{2,3} In addition, obese individuals may suffer from low self-esteem, feelings of unattractiveness, social prejudices, interference with life activities, and the financial burdens that result from obesity-related health expenses. Subsequently, obesity is increasingly being recognized as a chronic medical condition at the individual level and a serious public health problem on a societal level.⁴

It is estimated that approximately 50% of women and 25% of men in the United States are trying to lose weight at any one time, corresponding to an annual expenditure of \$30 billion on related products and services.⁵ However, despite the apparent public fascination with weight loss diets, workout equipment, dietary supplements, and other weight loss measures, all indexes show that the overall population is becoming more overweight. To illustrate this point, data from several National Health and Nutrition Examination Surveys conducted over the past 40 years are shown in Figure 1. From 1960 to 1994, the prevalence of obesity, defined as a body mass index (BMI) ≥ 30 kg/m², increased from 10.4% to 19.9% in men and from 15.1% to 24.9% in women. Combined, the overall obesity rate in men and women increased from 12.8% to 22.5%. Even more alarming, most of the increase has occurred just within the past decade.³ More than one half of adults in the United States are currently considered overweight, defined as a BMI ≥ 25 kg/m².⁶ Obesity rates in children are also on the rise. Data from the National Center for Health Statistics indicate that 6.5% of children between the ages of 6 and 11 were considered overweight from 1976 to 1980; from 1990 to 1994, 11.4% of children in the same age category were found to be overweight.⁷

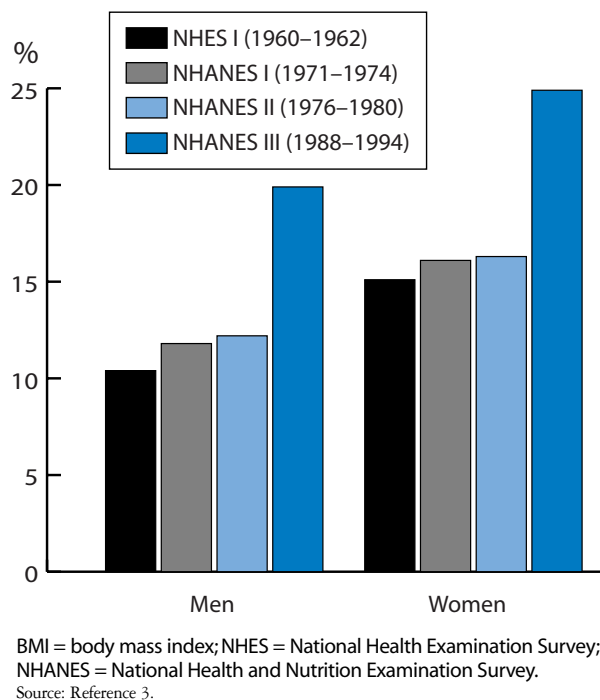
The consequences of obesity extend far beyond the physical and medical complications. Negative attitudes toward obese individuals are widespread in our society, even among health care professionals. Sadly, such prejudice is evident during childhood. Children as young as 6 years old, when shown a silhouette of an obese child, use descriptions such as “lazy,” “dirty,” “stupid,” and “ugly.”⁸ Prejudice toward obesity eventually leads to discrimination, possibly interfering with the obese person’s ability to undertake activities such as gaining acceptance into a college, renting an apartment, finding a job, or getting married.^{3,4,8} In a study of

employer attitudes, 16% of those interviewed said they would not hire an obese woman in any situation, and another 44% indicated they would hire an obese woman only under special circumstances.⁸ Certain employers, including the armed forces, police and fire departments, and airlines, have strict weight regulations governing personnel. Even more distressing is that about three quarters of morbidly obese patients surveyed described feeling as if they “usually” or “always” had been treated disrespectfully by the medical profession because of their weight.⁸

In general, the majority of obese people rate themselves as being physically unattractive and report having perceived negative attitudes from coworkers.⁸ Interestingly, studies suggest that white and black women may display different perceptions of body image and attitudes toward weight. For example, black girls and women generally report less social pressure to be thin, less discrimination related to weight, and a greater acceptance of being overweight compared with white counterparts. Black women may even ascribe positive qualities to being heavy, such as having stamina and strength. It is possible, therefore, that weight management strategies may produce different reactions among white and black women. Body image perception among obese people in other ethnic groups has not yet been well studied.³

Obesity imposes tremendous financial burdens both on patients and society at large. The treatment of obesity and its complications is responsible for 5% to 7% of the annual national health care expenditure in this country.¹ In 1995,

Figure 1. Age-adjusted prevalence of obesity (BMI ≥ 30) in the United States during various time periods.



these direct costs amounted to \$51.6 billion and included hospital care, the services of physicians and other health care professionals, and drugs, all of which could be allocated for other uses.⁹ Indirect costs, such as decreased job productivity and disability claims, were estimated at \$47.6 billion, a figure comparable to the economic losses associated with cigarette smoking.³ Successful treatment can have a substantial impact on obesity-related expenses. In a group of obese patients treated with various weight loss medications, a body weight decrease of 6% to 10% translated into average monthly pharmacy cost savings of \$122.64 for insulin-treated diabetes, \$42.92 for sulfonylurea-treated diabetes, and \$61.07 for hyperlipidemia medications.¹⁰

Pathophysiology

Obesity is a complex and chronic medical condition that develops out of an interaction between genotype and the individual's environment. The pathophysiology of obesity also includes the integration of cultural, physiologic, metabolic, socioeconomic, and psychological factors.^{3,6}

The fundamental basis of obesity is an imbalance between energy intake (calories) and energy expenditure; when energy intake exceeds output, weight gain results.^{2,6,11} The body's regulation of calorie intake, storage, and expenditure is governed by various chemical, hormonal, and neurologic signals.¹¹ Unfortunately, the exact cause(s) for the energy imbalance in any particular person is extremely difficult to elucidate because of the large number of possible contributing factors.

Genetic and Physiological Factors

Genetic predisposition to obesity has been long suspected and was recently confirmed by the breakthrough discovery of the obese (*ob*) gene in 1994.¹² The *ob/ob* strain of mice carries a mutation of the *ob* gene, which results in physical inactivity, overeating, and eventually, morbid obesity. A human *ob* gene has been identified and linked to the protein leptin, which is produced in adipose tissue.⁶ Although the relationship to human obesity is not fully understood, leptin is being carefully studied in the search for genetic clues to obesity. Circulating leptin is thought to act on the brain as a satiety signal to decrease appetite. Obese mice of the *ob/ob* strain produce no leptin and tend to overeat; when given leptin, the mice stop eating and lose weight.¹²

Unfortunately, experiments have failed to duplicate these findings in humans. In fact, not only are serum leptin concentrations generally elevated in obese humans, there is a strong positive correlation between serum leptin levels and the percentage of body fat and BMI.¹² The vast majority of obese individuals appear to have normal genetic sequences for leptin and its receptor, although humans with a known

genetic leptin deficiency do exhibit extreme obesity.^{13,14} In obese humans, therefore, the problem may be a decreased sensitivity, or resistance, to leptin. Additional research is necessary to clarify the role of leptin and other genetic or hormonal influences on the development of obesity.

Regardless of the exact genetic mechanism, heredity clearly plays a role in obesity susceptibility. Heritability studies indicate that genetic factors may account for up to 70% of the variability in human body weight.¹³ First-degree relatives of moderately obese persons have a three- to fourfold risk of obesity relative to the general population; for first-degree relatives of severely obese persons, the relative risk is about 5.³ Other studies have proven that some individuals are more susceptible than others to weight gain or weight loss. Health care professionals need to realize that weight loss is physiologically more difficult for some patients and that failure to lose weight is not entirely related to noncompliance or lack of motivation.³

Environmental Factors

Environmental influences are undoubtedly a significant factor in the development of obesity, as altered genetics alone cannot account for the recent dramatic increases in obesity prevalence.⁶ Environmental situations and pressures exert their primary influence through poor eating habits and decreased physical activity. In the United States, there is ready access to appetizing, inexpensive, and convenient foods, much of which is very high in fat and energy dense. Food products and services are also marketed aggressively to the public, and meals provided outside the home often consist of very generous portions. Emotional stress caused by work or relationships can lead to overeating as a coping mechanism.⁶ Poor dietary habits may also be a result of low income or lack of nutrition education.¹¹

A sedentary, physically inactive lifestyle facilitates the development of obesity. Our society is constantly seeking ways to minimize physical exertion, and many jobs require employees to sit at a desk or the controls of mechanized equipment for an extended time. Elevators and escalators have made stairs almost obsolete in public buildings. Television is a major culprit, not only for the inactivity associated with it, but also because watching television encourages the consumption of high-calorie foods. The amount of time adolescents spend watching television is significantly correlated with body fat content.⁶ It is likely that other sedentary activities, such as Internet use and playing video games and hand-held electronic toys, are also having a negative impact on the physical activity levels of young people.

Pharmacists and physicians should also be vigilant regarding medications that can precipitate weight gain and avoid their

Table 1. Medications Known to Cause Weight Gain**Psychotropic agents**

Tricyclic antidepressants
 Monoamine oxidase inhibitors
 Antipsychotic agents
 Lithium

Anticonvulsant agents

Valproic acid (Depakene—Abbott)
 Carbamazepine (Tegretol—Novartis)

Steroid hormones

Corticosteroids
 Estrogen
 Progesterone
 Testosterone

Source: Reference 15.

use, if possible, in people already struggling with obesity. Table 1 lists a number of medications known to be associated with weight gain.

Assessment and Classification

Appropriate management of the obese patient begins with an assessment of the degree of obesity and classification of risk status. There are several techniques for assessing obesity, including BMI, waist circumference, and waist-to-hip ratio (WHR).

Body Mass Index

BMI, which describes relative weight according to height, is the most commonly used clinical tool for determining obesity.³ BMI is significantly correlated with total body fat content and has been found to correlate with morbidity and mortality.^{3,6} BMI is calculated as weight divided by height squared (kg/m^2). If using conventional units, BMI can be cal-

culated as $(\text{lb}/\text{inches}^2) \times 703$. A BMI between 25.0 and 29.9 is considered overweight, while BMIs between 30 and 34.9 and between 35 and 39.9 are classified as obesity class I and obesity class II, respectively. A BMI >40 is considered extreme obesity. BMI can be easily and inexpensively determined using only a scale to measure weight, a method for determining height, and a calculator or BMI chart (see Table 2).

Waist Circumference

Fat tissue located in the abdominal area presents a greater health risk than peripheral fat stores.³ Therefore, waist (abdominal) circumference can be an independent predictor of weight-related health risks, especially in patients who are considered normal or overweight on the BMI scale. When BMI reaches 35 and over, waist circumference has little added predictive power and is not worth measuring for risk assessment purposes.³ In patients with a BMI between 25 and 34.9, a high waist circumference is associated with an increased risk for type 2 diabetes, dyslipidemia, hypertension, and coronary disease. Waist circumference may actually be a better predictor of risk than BMI in some populations, such as Asian Americans and elderly patients.³

In male patients, a high-risk waist circumference is >40 inches, while in female patients, it is >35 inches. To determine the waist circumference, a measuring tape should be placed around the abdomen at the level of the iliac crest, parallel to the floor. For an accurate reading, the tape measure should be snug, but not so tight that the skin is compressed. The measurement should be read following a normal expiration.⁵

Waist-to-Hip Ratio

Many epidemiologic studies have reported weight-related risks based on the WHR, which is determined by dividing

Table 3. Classification of Overweight and Obesity by BMI, Including Disease Risk According to Waist Circumference

	BMI (kg/m^2)	Obesity Class	Disease Risk ^a Relative to Normal Waist Circumference	
			Men ≤ 40 inches Women ≤ 35 inches	Men >40 inches Women >35 inches
Underweight	<18.5	—	—	—
Normal ^b	18.5–24.9	—	—	—
Overweight	25.0–29.9	—	Increased	High
Obesity	30.0–34.9	I	High	Very high
	35.0–39.9	II	Very high	Very high
Extreme obesity	≥ 40	III	Extremely high	Extremely high

^a Disease risk for type 2 diabetes, hypertension, and cardiovascular disease.

^b Increased waist circumference can be a marker for increased risk even in people of normal weight. BMI = body mass index.

Source: Reference 3.

Table 2. Body Mass Index Chart

Height (ft)	Weight (lb)																		
	125	130	135	140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	
5'0"	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	
5'1"	24	26	26	27	27	28	29	30	31	32	33	34	35	36	37	38	39	40	
5'2"	23	24	25	26	27	27	28	29	30	31	32	33	34	35	36	37	38	38	
5'3"	22	23	24	25	26	27	27	28	29	30	31	32	33	34	35	35	37	37	
5'4"	21	22	23	24	25	26	27	27	28	29	30	31	32	33	33	34	36	36	
5'5"	21	22	22	23	24	25	26	27	27	28	29	30	31	32	32	33	35	35	
5'6"	20	21	22	23	23	24	25	26	27	27	28	29	30	31	31	32	34	34	
5'7"	20	20	21	22	23	23	24	25	26	27	27	28	29	30	31	31	33	33	
5'8"	19	20	21	21	22	23	24	24	25	26	27	27	28	29	30	30	32	32	
5'9"	18	19	20	21	21	22	23	24	24	25	26	27	27	28	29	30	31	31	
5'10"	18	19	19	20	21	22	22	23	24	24	25	26	27	27	28	29	30	30	
5'11"	17	18	19	20	20	21	22	22	23	24	24	25	26	26	27	28	29	29	
6'0"	17	18	18	19	20	20	21	22	22	23	24	24	25	26	26	27	29	28	
6'1"	16	17	18	18	19	20	20	21	22	22	23	24	24	25	26	26	28	28	
6'2"	16	17	17	18	19	19	20	21	21	22	22	23	24	24	25	26	27	27	
6'3"	16	16	17	17	18	19	19	20	21	21	22	22	23	24	24	25	26	26	
6'4"	15	16	16	17	18	18	19	19	20	21	21	22	23	23	24	24	25	26	

Height (ft)	Weight (lb)																		
	215	220	225	230	235	240	245	250	255	260	265	270	275	280	285	290	295	300	
5'0"	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	
5'1"	41	42	43	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	
5'2"	39	40	41	42	43	44	45	46	47	48	48	49	50	51	52	53	54	55	
5'3"	38	39	40	41	42	43	43	44	45	46	47	48	49	50	50	51	52	53	
5'4"	37	38	39	39	40	41	42	43	44	45	45	46	47	48	49	50	51	51	
5'5"	36	37	37	38	39	40	41	42	42	43	44	45	46	47	47	48	49	50	
5'6"	35	36	36	37	38	39	40	40	41	42	43	44	44	45	46	47	48	48	
5'7"	34	34	35	36	37	38	38	39	40	41	42	42	43	44	45	45	46	47	
5'8"	33	33	34	35	36	36	37	38	39	40	40	41	42	43	43	44	45	46	
5'9"	32	32	33	34	35	35	36	37	38	38	39	40	41	41	42	43	44	44	
5'10"	31	32	32	33	34	34	35	36	37	37	38	39	39	40	41	42	42	43	
5'11"	30	31	31	32	33	33	34	35	36	36	37	38	38	39	40	40	41	42	
6'0"	29	30	31	31	32	33	33	34	35	35	36	37	37	38	39	39	40	41	
6'1"	28	29	30	30	31	32	32	33	34	34	35	36	36	37	38	38	39	40	
6'2"	28	28	29	30	30	31	31	32	33	33	34	35	35	36	37	37	38	39	
6'3"	27	27	28	29	29	30	31	31	32	32	33	34	34	35	36	36	37	37	
6'4"	26	27	27	28	29	29	30	30	31	32	32	33	33	34	35	35	36	37	

Underweight
 Normal
 Overweight
 Obesity Class I
 Obesity Class II
 Obesity Class III
 Source: Reference 15.

the waist circumference by the circumference of the hips at the largest point. A WHR >1.0 in men and >0.8 in women has been considered clinical obesity.⁶ However, waist circumference seems to be a better prognostic indicator, and the National Heart, Lung and Blood Institute guidelines currently recommend using waist circumference, not WHR, as a measure of abdominal fat content in clinical practice.³

Risk Status

Waist circumference can be used in conjunction with BMI to determine relative disease risk in overweight patients (see Table 3). These categories of disease risk are meant to denote *relative* risks only (relative to the risks in persons of normal weight). A determination of relative risk assists in making decisions about the urgency of weight management. Any one patient's *absolute* risk needs to take into

account as many individual risk factors as possible. Patients at high absolute risk generally require additional clinical interventions to minimize the specific risks.³

Obese patients are considered at high absolute risk if they have any of the following conditions: established coronary heart disease (CHD), other atherosclerotic disease, type 2 diabetes, or sleep apnea. Patients can also be considered at high absolute risk if they have at least three of the following cardiovascular risk factors: cigarette smoking, hypertension (systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg or the patient is taking antihypertensive agents), low-density lipoprotein cholesterol ≥160 mg/dL, high-density lipoprotein (HDL) cholesterol ≤35 mg/dL, impaired fasting glucose, family history of premature CHD (heart attack or sudden death at or before 55 years of age in father or other male first-degree relative, or at

or before 65 years of age in mother or other female first-degree relative), and age (men ≥ 45 years; women ≥ 55 years or postmenopausal). Other miscellaneous risk factors that heighten the urgency for weight reduction include physical inactivity and serum triglyceride concentrations ≥ 200 mg/dL.³

Health Risks of Obesity

Obesity is associated with a myriad of medical complications. Obese patients are at an increased risk for developing insulin resistance and type 2 diabetes mellitus, gallbladder disease, hypertension, CVD, stroke, dyslipidemia, osteoarthritis, and sleep apnea and other respiratory problems, including asthma.^{3,16,17} The morbidity and/or mortality from endometrial, breast, prostate, gallbladder, and colon cancers are increased in obese individuals.^{4,17} Obesity-related morbidities in women also encompass pregnancy complications, menstrual irregularities, hirsutism, and stress incontinence.³ The prevalence of comorbidities generally increases directly with increasing degrees of obesity (Table 4).

High blood pressure and elevated cholesterol are the most common complications of obesity in men and women.¹⁸ Animal and human experiments have demonstrated that a rise in blood pressure accompanies weight gain.¹⁹ The cardiovascular complications of obesity alone account for more than half of the total costs related to obesity.³ Fortunately, weight loss can bring about an improvement in cardiovascular status. Studies suggest that even modest weight losses of 10% or less can reduce blood pressure and cholesterol levels and improve glycemic control.^{19,20}

Most epidemiologic studies suggest that mortality begins to rise as BMI increases above 25. However, the most dramatic increase in mortality is seen when BMI reaches 30 or higher, at which point mortality from all causes, especially CVD, increases by 50% to 100% relative to that observed in people with BMIs between 20 to 25.^{3,21} While increasing BMI is generally associated with greater levels of risk, it should be noted that black men and women appear to have lower risks of death compared with white counterparts of the same BMI.²¹

Managing Obesity

It has been said that obesity is among the easiest-to-recognize and the most difficult-to-treat medical conditions.⁴ However, there is convincing evidence that even modest weight reduction in obese and overweight individuals can reduce the risk factors for diabetes and CVD in addition to other health benefits, including increased longevity.^{3,20}

Certain patients are not appropriate candidates for weight loss treatment, including most pregnant or nursing women, patients with unstable psychiatric illness, and patients with any other serious illness in which caloric restriction might exacerbate the condition.³

Patient Motivation

Patient motivation is crucial for the success of any weight loss endeavor. Obese patients may have cycled unsuccessfully through various weight reduction programs and may be pessimistic about additional intervention. It may be helpful to discuss with the patient his or her previous weight loss

Table 4. Prevalence of Common Comorbidities of Obesity According to Weight Category

Health Condition		Prevalence by Weight Status Category (%)				
		Normal	Overweight	Obesity Class I	Obesity Class II	Obesity Class III
Men	Type 2 diabetes mellitus	2.03	4.93	10.10	12.30	10.65
	Gallbladder disease	1.93	3.39	5.38	5.80	10.17
	Coronary heart disease	8.84	9.60	16.01	10.21	13.97
	High blood cholesterol level	26.63	35.68	39.17	34.01	35.63
	High blood pressure	23.47	34.16	48.95	65.48	64.53
	Osteoarthritis	2.59	4.55	4.66	5.46	10.04
Women	Type 2 diabetes mellitus	2.38	7.12	7.24	13.16	19.89
	Gallbladder disease	6.29	11.84	15.99	19.15	23.45
	Coronary heart disease	6.87	11.13	12.56	12.31	19.22
	High blood cholesterol level	26.89	45.59	40.37	40.96	36.39
	High blood pressure	23.26	38.77	47.95	54.51	63.16
	Osteoarthritis	5.22	8.51	9.94	10.39	17.19

Source: Reference 18.

attempts and explain the differences of the new plan. A patient who feels supported and respected by his or her health care professional is more likely to generate the motivation required to stick with a treatment regimen.³ It is also helpful if the patient's motivation to lose weight is based on improving overall health, not just achieving a particular weight or body shape; purely aesthetic goals usually result in patient frustration.²²

Goals of Weight Loss and Management

The general goals of a weight loss strategy are to prevent further weight gain, reduce current body weight, and maintain a lower body weight in the future. A realistic initial target for weight loss is about a 10% decrease in body weight.^{3,23} However, health care professionals should expect that obese patients may not be very enthusiastic about a target weight reduction of only 10%. In a study of 60 obese women attending a university clinic-based weight loss program, the average weight loss goal expressed by the patients was a 32% reduction in body weight. Furthermore, when the women were asked to define a potential weight loss outcome that would be considered "not successful in any way," the mean response was 17 kg (38 lb), which in this sample of women corresponded to a 17% reduction in body weight.²⁴

A slow and steady reduction in weight should be the overall goal. If weight reduction occurs too rapidly, subsequent weight regain is almost inevitable. Furthermore, very rapid weight loss is associated with an increased rate of gallstone formation and electrolyte imbalance. A reasonable time frame for achieving a 10% reduction in weight is about 6 months. This level and rate of weight loss is realistic and can be maintained over time. Maintaining a modest weight reduction over a period of time is actually preferable to experiencing a setback after a more dramatic weight loss. If the initial goal is achieved and sustained for at least 6 months, additional weight loss goals can be considered.³ Patients need to understand that permanent changes in lifestyle are necessary to maintain weight loss. Continually cycling on and off diets will not produce long-lasting results.

Nonpharmacologic Options

Most successful weight management programs are multifaceted and combine a variety of approaches to achieve weight reduction. The most commonly employed strategies are dietary therapy and physical activity. In addition, a number of behavior modification strategies are being used to help patients identify and alter any habits that may be contributing to their weight problem.

Dietary Therapy

Modification of a patient's diet is one of the most common weight-loss tactics. In fact, for most overweight and obese patients, dietary adjustments will be necessary, regardless of other treatments they may be using. The key to dietary success is to strive for a slow but steady loss of weight through a moderate reduction in daily caloric intake. A calorie deficit of 500 to 1,000 kcal/day should lead to a weight loss of 1 to 2 lb per week, which is ideal. Theoretically, this rate of weight reduction should produce a total loss of 26 to 52 lb over a 6-month period, although actual amounts of weight lost over this period usually average 20 to 25 lb. Most patients on dietary regimens reach a weight loss plateau after about 6 months. Reasons for this include slowed metabolic rates secondary to calorie restriction and difficulty in sticking to the prescribed diet.³

The classic dietary weight loss strategy for overweight patients is a low-calorie diet (LCD), characterized by a diet providing 800 to 1,500 kcal/day with $\leq 30\%$ of calories derived from fat sources (Table 5). Typical LCDs include 1,000 to 1,200 kcal/day for women and 1,200 to 1,500 kcal/day for men. It is important to note that reducing dietary fat content alone without reducing total calories will not be sufficient to achieve weight loss.³

The LCD should not be confused with the very low-calorie diet (VLCD), which provides only 250 to 850 kcal/day. Although concern exists that VLCDs may reduce resting metabolic rates, the metabolic rate rebounds within 8 to 12 weeks.²⁵ The VLCD generally does not produce results superior to the LCD and is not usually recommended for routine weight loss programs. In fact, studies have shown that the weight loss achieved over a 1-year period is similar between patients using an LCD or a VLCD.³ The risk of gallstone formation is also higher in patients using VLCDs.³ With proper compliance, LCDs appear to be the safest dietary strategies, although VLCDs may be useful in certain situations, for example, to quickly reduce the risk of comorbid conditions in severely obese individuals or to provide an initial weight-loss momentum to encourage the patient.^{6,26}

Unfortunately, success rates with dietary modification alone are disappointing. Only about one half of patients manage to maintain their weight loss after 1 year, and only 1 in 10 patients sustains the loss over 5 years.⁶ A permanent change in food choices and activity level is required in order to maintain weight loss.

Physical Activity

Exercise is an important contributor to weight loss, whether used alone or in combination with dieting. It is an excellent way to boost energy expenditure and help achieve and sus-

Table 5. Low-Calorie Diet—General Guidelines

Nutrient	Recommended Intake
Calories	~500 to 1,000 kcal/day reduction from usual intake
Total fat	≤30% of total calories
Saturated fatty acids	8% to 10% of total calories
Monounsaturated fatty acids	≤15% of total calories
Polyunsaturated fatty acids	≤10% of total calories
Cholesterol	<300 mg/day
Protein ^a	~15% of total calories
Carbohydrate	≥55% of total calories
Sodium chloride	≤100 mmol/day (~2.4 grams of sodium or ~6 grams of sodium chloride)
Calcium	1,000 to 1,500 mg
Fiber	20 to 30 grams

^aProtein should be derived from plant sources and lean sources of animal protein.

Source: Reference 3.

tain weight loss. While exercise can produce a calorie deficit and lead to weight loss if used alone, the average weight decrease is usually only 2% to 3% of body weight or BMI. Physical exercise is best implemented as an adjunct to dietary therapy.³ In addition to supporting weight loss, increased physical activity enhances cardiorespiratory fitness in obese patients, which secondarily improves mood, self-esteem, physical function, and ultimately, quality of life.³ The most prominent benefits of exercise are related to overall health improvement and the maintenance of weight loss. A number of studies have documented that people who maintain weight loss over time continue to exercise regularly, while those who regain weight do not exercise.²⁷

Physical activity should generally be introduced slowly in obese patients, and the intensity gradually increased. The patient should always consult a physician before starting any exercise program. Because of its safety and accessibility, walking is one of the most suitable choices for an initial exercise activity. The patient can begin by walking at a slow pace for 10 minutes a day, 3 days a week and work up to 30 or 45 minutes of more intense walking at least 3 days a week. At this level, the patient can expend an additional 100 to 200 calories per day. As fitness increases and the patient begins to lose weight, more strenuous activities may be substituted including cycling, cross-country skiing, aero-

bic dancing, or rope jumping.³ Eventually, patients should strive for 60 to 80 minutes of at least moderately intense activity every day in order to achieve and maintain weight loss. This may sound overwhelming, but activities can be accumulated throughout the day to reach the total goal.²⁸ In fact, several shorter bouts of activity may foster better compliance than a single, long exercise period each day.²⁷

Obese patients generally have very poor adherence rates to formal exercise programs. Obese individuals may be intimidated at public gyms where they have to work out in the presence of other people. Planning activities that the patient can incorporate into the home or work environment may be more successful, especially in patients psychologically resistant to exercise.²⁸ For example, patients should be encouraged to consider changing elements of their everyday routine in order to increase physical activity, such as exiting public transportation one stop earlier than usual, parking farther from the door at work or shopping centers, standing or pacing while on the telephone, and taking the stairs instead of an elevator or escalator.²⁷ New hobbies involving physical activity, such as gardening or walking a dog every day, might be encouraged. Patients using lifestyle activity modification may demonstrate similar degrees of weight loss compared with those involved in traditional exercise programs.²⁷ Whatever the chosen activities, patients should be encouraged to make exercise a priority, dedicate time for exercising in their daily schedule, and keep a diary documenting the duration and intensity of all activities.³

Behavioral Therapy

Behavioral therapy is crucial, since long-term weight reduction is highly unlikely unless a patient can develop permanent new attitudes, eating patterns, and activity habits. Behavioral strategies are used to reinforce changes in diet and physical activity and teach methods for overcoming related barriers.³

Early behavioral interventions for obesity were very simplistic, focusing almost entirely on modifying eating habits. Obesity is now recognized as a complex disease, and behavioral strategies have accordingly become more comprehensive.²³ During the past 15 years, behavioral strategies have begun to incorporate cognitive approaches, which acknowledge the significance of a patient's thinking patterns. In other words, the way someone thinks about a situation will determine his or her feelings and, probably, actions in the particular situation. An understanding of the patient's thought processes may help identify techniques for modifying behavior.

There are a number of specific types of behavioral therapy, any of which can be used alone or in combination with other types. No single technique or combination of methods has

been shown to be dramatically more effective than others. The individual patient's needs should be considered when selecting the appropriate behavior modification techniques. Behavioral therapy can be conducted on an individual basis or in a group setting.³ Most programs are designed in a group format and consist of weekly, hour-long sessions.²⁹ The duration of behavioral programs averages about 18 weeks. Behavior modification, when used along with diet and exercise, produces an average weight loss of about 1 lb per week, and, in one study, 66% of patients maintained their new weight after 52 weeks of follow-up without continued treatment.²² Some common behavioral therapy methods are self-monitoring, stimulus control, cognitive restructuring, stress management, and social support.

Self-monitoring is considered the cornerstone of behavioral therapy.^{22,27} The patient is encouraged to continually assess eating and exercise behaviors and record the details of these activities. One study found that patients who self-monitored caloric intake and expenditure lost more weight than patients who did not use self-monitoring.³⁰

Stimulus control involves modifying the patient's environment to protect them from the cues and situations that would encourage inappropriate eating. Some examples of stimulus control include learning to purchase healthful foods and keeping high-calorie items out of the house, limiting the times and places for eating, and purposely avoiding situations which would predispose the patient to overeating.³

Cognitive restructuring is aimed at addressing patients' unrealistic goals and irrational attitudes regarding weight loss and body image. Feelings of self-rejection and defeat can be huge obstacles to any weight loss program, and patients should be encouraged to develop an outlook based on self-acceptance.²² Patients can be taught to deal positively with day-to-day setbacks and recognize a setback for what it is—a temporary slip from which it is possible to recover.²⁷ Cognitive restructuring is also useful in helping patients accept weight losses that are smaller than desired. Many behavioral programs include education about the limitations of weight loss and promote the skills needed to counter unrealistic expectations such as "I won't be happy until I can wear a size 6 dress."²⁷

Stress may contribute to weight gain in some patients by triggering dysfunctional eating as a response or coping mechanism. Stress management techniques may ward off situations which could otherwise lead to overeating. Specific stress reduction strategies that have been proven effective include the use of coping strategies, meditation, and relaxation techniques.³

A dependable system of social support from relatives, friends, or colleagues can facilitate weight reduction. Support and encouragement from other individuals can help motivate

the patient. Organized weight loss support groups are another option that may benefit certain patients, particularly if other forms of social support are lacking. In families with more than one overweight individual, a family weight control strategy might be considered.³

Pharmacotherapy

For mildly overweight patients, dietary changes and behavioral strategies are generally sufficient for weight reduction. However, drug treatment may be considered in patients with a BMI ≥ 27 who have failed to lose at least 1 lb per week during a 6-month period of therapy with an LCD, exercise, and behavior modification. Patients and health care providers need to keep in mind that the primary purpose of drug treatment is to augment diet and exercise strategies, not replace them.³ Patients need to understand that weight loss medications are not "magic bullets" that will melt away pounds without the need for lifestyle modification.

Most weight loss medications should be used only in patients considered to be at serious medical risk because of their weight. This would include patients with a BMI ≥ 27 with an established risk factor such as hypertension, dyslipidemia, CHD, type 2 diabetes, or sleep apnea. Patients with a BMI ≥ 30 are considered at high risk, regardless of other known risk factors, and are appropriate drug therapy candidates.^{2,3} Because obesity is a chronic disease, short-term drug administration is not beneficial. Drug treatment should be planned within the context of a long-term treatment strategy.³

Pharmacotherapy for obesity is certainly not a panacea and not every patient will respond. Studies suggest that an initial weight loss response indicates that a continued response is likely. Conversely, patients who fail to respond initially (i.e., do not lose between 4 and 5 lb during the first 4 weeks) are less likely to ever respond, even with dosage adjustment. Drug treatment should be discontinued if the patient fails to respond or if serious adverse effects occur.³

Drug treatment of weight loss has received ample media attention over the past several years as a number of popular products have been withdrawn from the market for safety reasons. Fenfluramine and dexfenfluramine are serotonergic agents that demonstrated good weight loss efficacy in clinical studies. Both products were voluntarily withdrawn from the U.S. market in September 1997 due to reports of serious heart valve disease related to their use.^{6,31} These products were also associated with a risk of primary pulmonary hypertension. The number of cases that progressed to a state of clinically significant valve dysfunction was quite small, even though mild valvular irregularities occurred in almost a third of patients who took fenfluramine or dexfenfluramine.

Another recent recall involved the drug phenylpropanolamine (PPA), a popular appetite suppressant found in many over-the-counter (OTC) weight loss preparations and products for treating the common cold. Beginning in 1979, published case reports began to surface which described intracranial hemorrhage following PPA ingestion. These reports prompted a formal epidemiologic study by scientists at Yale University School of Medicine.^{32,33} This study found that, for women using PPA in appetite suppressant products, the adjusted odds ratio for risk of hemorrhagic stroke (relative to matched controls) was 16.58 ($P=.011$). With regard to first-dose use of PPA, reported only in cough-cold product users, the adjusted odds ratio was 3.13 ($P=.042$).³² These results prompted the Food and Drug Administration (FDA) to announce a recall of all products containing PPA in November 2000.³¹

Most drug therapies currently used for the treatment of obesity are noradrenergic agents which act as appetite suppressants (Table 6). A newer noradrenergic/serotonergic agent, sibutramine, decreases food intake by enhancing satiety and may also have thermogenic effects. Serotonergic agents (i.e., fluoxetine, sertraline) have been studied for weight loss, but are neither FDA approved nor recommended for treating obesity. Orlistat is a lipase inhibitor that interferes with the digestion of dietary fat. Although herbal therapies are also promoted for weight loss, they are not recommended for weight loss, because their active ingredient composition and potential side effect profiles are unpredictable.³ Currently, only sibutramine and orlistat are recommended for long-term administration.

Noradrenergic Agents

Noradrenergic drugs act by enhancing catecholamine transmission in the central nervous system, increasing sympathetic activity, and reducing appetite. This class of drugs includes benzphetamine, diethylpropion, mazindol, methamphetamine, phendimetrazine, and phentermine. With the exception of phentermine, noradrenergic agents are rarely used in clinical practice. Most of these agents have a substantial abuse potential, most likely related to their dopaminergic effects.²

Phentermine

Phentermine (Ionamin—Celltech; Adipex-P—Gate; Fastin—GlaxoSmithKline) decreases appetite through the same sympathetic mechanisms as other noradrenergic agents but lacks dopaminergic activity, reducing the risk of addiction. As monotherapy, the usefulness of phentermine is limited by patient intolerance to its stimulatory activity. Common side effects include headache, insomnia, nervousness, dizziness, dry mouth, and irritability. Palpitations,

tachycardia, and blood pressure elevations are also possible.^{2,6} Phentermine was most useful in combination with fenfluramine (the widely popular “phen-fen” combination) because the stimulant effects of phentermine were somewhat counteracted by the lethargy and drowsiness related to fenfluramine.² As discussed previously, fenfluramine is no longer available, thus the combination is no longer a treatment option. Phentermine alone does not appear to cause the heart valve problems associated with the “phen-fen” combination.

Phentermine is generally given as a single 15 mg to 37.5 mg dose in the morning or at least 10 to 14 hours before bedtime. Alternatively, it can be given in divided doses of 8 mg three times a day one-half hour before each meal.⁶ Late day administration should be avoided because of the potential for insomnia. Phentermine is labeled only for short-term use (i.e., a few weeks) as an adjunct to other weight loss measures. Phentermine should not be used in patients with hyperthyroidism, glaucoma, advanced arteriosclerosis, CVD, hypertension, agitated states, or in patients with a history of drug abuse. Phentermine should not be given concomitantly with or within 14 days following monoamine oxidase inhibitor (MAOI) administration.³⁶

Orlistat

Orlistat (Xenical—Roche), approved by FDA in early 1999, is one of the most recent and novel drugs to become available for the treatment of obesity. Orlistat exerts its weight loss effects by preventing the absorption of fat. Dietary fat (in the

Table 6. Prescription Drugs Used in the Treatment of Obesity

Generic Name	Trade Name(s) & Manufacturer(s)
<i>Noradrenergic Agents</i>	
Benzphetamine	Didrex—Pharmacia & Upjohn
Diethylpropion	Tenuate—Aventis Tepanil—3M Pharmaceuticals
Mazindol	Mazanor—Wyeth-Ayerst Sanorex—Novartis
Methamphetamine	Desoxyn—Abbott
Phendimetrazine	Bontril—Amarin Metra—Forest
Phentermine	Adipex-P—Teva Fastin—GlaxoSmithKline Ionamin—Celltech
<i>Noradrenergic and Serotonergic Agent</i>	
Sibutramine	Meridia—Abbott
<i>Lipase Inhibitor</i>	
Orlistat	Xenical—Roche
<i>Serotonergic Agents</i>	
Fluoxetine ^a	Prozac—Lilly
Sertraline ^a	Zoloft—Pfizer

^aNot FDA approved for the treatment of obesity.

Sources: References 34 and 35.

form of triglycerides) must be hydrolyzed by gastrointestinal (GI) lipases into free fatty acids and monoglycerols before it can be absorbed. Orlistat specifically and irreversibly inhibits pancreatic and gastric lipases, preventing about 30% of ingested fat content from being absorbed, and undigested triglycerides are excreted in the feces.^{37,38} Other pancreatic enzymes are apparently not inhibited, including phospholipase A₂, amylase, and trypsin.³⁷

The recommended dosage of orlistat is 120 mg three times daily with each meal that contains fat. The dose may be taken during the meal or up to 1 hour afterward. If a meal is occasionally missed or contains no fat, the orlistat dose can be skipped. Doses higher than 120 mg three times daily have not been shown to produce any further benefits.³⁹

A number of relatively short-term trials (1 year or less in duration) of orlistat in obese adults have shown it to be safe and more effective than diet alone.⁴⁰⁻⁴³ Orlistat consistently produced significantly greater weight loss compared with placebo; statistically significant decreases in serum lipids were also observed. In a meta-analysis of 1-year studies, subjects receiving orlistat 120 mg three times daily in conjunction with a hypocaloric diet experienced a 9.2% weight loss, compared with a 5.8% weight loss in the placebo group ($P < .001$).⁴²

Orlistat has also been studied in longer-term trials ranging from 57 weeks to 2 years.⁴⁴⁻⁴⁷ Figure 2 illustrates the percentage of patients in these studies who achieved at least a 5% or 10% decrease in body weight after 1 year of treat-

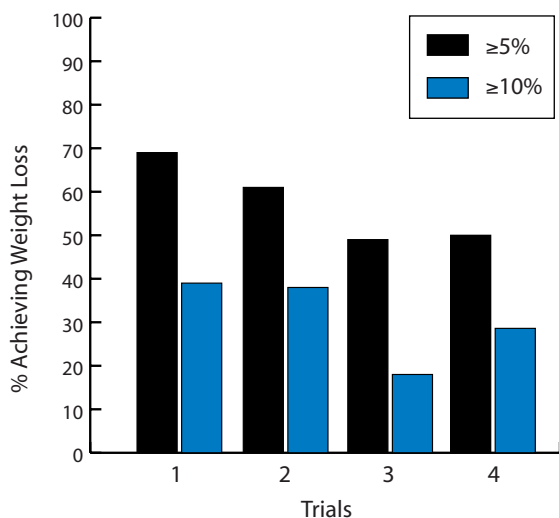
ment with orlistat plus a LCD. The percentage of patients losing $\geq 10\%$ of body weight ranged from 18% to 39%. Dietary management clearly had an influence in these studies, as patients receiving placebo achieved average weight loss reductions ranging from 4.3% to 6.6%. However, orlistat consistently produced significantly greater weight loss compared with placebo ($P < .001$ during year 1).

The use of orlistat beyond 1 year has produced good results with regard to weight maintenance. In a trial reported by Sjostrom et al., patients were initially randomized to receive either orlistat 120 mg three times daily or placebo in conjunction with a calorie-restricted diet. After 1 year of treatment, the treatments were reassigned. During the second year of treatment, patients who continued to receive orlistat regained only half as much weight, on average, as patients switched from orlistat to placebo ($P < .001$). Placebo patients switched to orlistat during year 2 lost an additional 0.9 kg (2 lb), while patients continued on placebo regained an average of 2.5 kg (5.5 lb).⁴⁴ Hauptman et al. reported that after 2 years, orlistat continued to be superior to placebo with regard to percentage of patients achieving $\geq 5\%$ weight loss (34.3% versus 24.1%; $P < .001$) or $\geq 10\%$ weight loss (18.6% versus 6.6%; $P = .001$).⁴⁷

Orlistat has also been shown to be effective in patients with type 2 diabetes taking sulfonylureas, in whom achieving and sustaining a $\geq 5\%$ weight loss is particularly difficult.³⁸ In these patients, orlistat use resulted in mean weight loss of 6.2% over 1 year. Moreover, significant improvements in glycemic control were observed, including decreases in HbA_{1c} ($P < .001$) and fasting plasma glucose ($P < .001$), and even dosage reductions in sulfonylurea medications ($P < .01$).⁴⁶

Since orlistat is not absorbed to any great extent, there are few systemic adverse effects.⁴⁸ In addition, orlistat has no known effects on the cardiovascular system, making it particularly suitable for treating obese patients with preexisting CVD.³⁸ However, local GI adverse effects are common. The incidence of GI-related adverse effects seems to be proportional to dietary fat content, and this may act as an additional incentive for patients to restrict fat in their diet.³⁸ GI complications tend to occur early in orlistat treatment. During the first year of clinical trials, more than 20% of patients receiving orlistat experienced oily fecal spotting, flatus with discharge, fecal urgency, and fatty or oily stools; these events were reported in $\leq 3\%$ of placebo patients, except for fecal urgency, which was reported in 7% of placebo patients. These effects tended to abate over time when orlistat was used with a low-fat diet. During the second year of clinical trial treatment, none of the GI side effects occurred at a frequency greater than 6% in the orlistat group. Fewer than 4% of subjects discontinued orlistat studies because of adverse events.⁴⁸

Figure 2. Percentage of patients losing $\geq 5\%$ and $\geq 10\%$ of body weight while receiving orlistat.



Trial 1 Sjöström L et al. *Lancet*. 1998;352:167.

Trial 2 Rössner S et al. *Obes Res*. 2000;8:49.

Trial 3 Hollander PA et al. *Diabetes Care*. 1998;21:1288.

Trial 4 Hauptman J et al. *Arch Fam Med*. 2000;9:160-7.

Source: References 44-47.

Finally, due to the minimal absorption of orlistat, the potential for drug interactions appears to be low. The absorption of a number of fat-soluble vitamins is mediated by pancreatic carboxylester lipase in the presence of dietary fat. Therefore, it stands to reason that plasma levels of vitamins A, D, E, and β -carotene may be reduced in patients receiving orlistat. In general, levels remain within acceptable ranges, but use of a multivitamin supplement is recommended to ensure adequate nutrition.³⁸ It is recommended that the vitamin supplement be taken at least 2 hours before or after the administration of orlistat, such as at bedtime.³⁹

Sibutramine

Sibutramine (Meridia—Abbott), approved by FDA in November 1997, is another recent breakthrough in obesity management. The weight loss effect of sibutramine may result from a combined effect of decreased food intake (enhancement of satiety) and increased energy expenditure (thermogenic mechanism).⁴⁹ Sibutramine and its two active metabolites are potent reuptake inhibitors of both norepinephrine and serotonin and, to a lesser extent, dopamine. As a result, sibutramine enhances feelings of satiety, leading to reduced food intake.⁵⁰ Animal research suggests that sibutramine may also have a thermogenic effect, further contributing to weight loss.

Sibutramine is indicated for the management of obesity, including both weight loss and maintenance, in patients with a BMI ≥ 30 or in patients with a BMI ≥ 27 who have other risk factors such as hypertension, diabetes, or dyslipidemia. Sibutramine should be used in conjunction with a reduced calorie diet.⁵¹

Initial clinical research with sibutramine indicated a clear dose-response effect in producing weight loss. In 683 obese patients who completed a 24-week study, the percent weight loss from baseline in various sibutramine treatment groups was as follows: 1 mg, 2.7%; 5 mg, 3.9%; 10 mg, 6.1%; 15 mg, 7.4%; 20 mg, 8.8%. With the exception of the 1 mg dose, the weight loss in each sibutramine group was statistically significantly different compared with placebo at all time points during the study ($P < .05$).⁵² Patients receiving sibutramine 5 mg reached a weight loss plateau around 12 weeks, but patients in the 10 mg to 30 mg treatment groups continued to lose weight from 12 weeks through 24 weeks.⁴⁹

A large 52-week trial studied the efficacy and tolerability of sibutramine 10 mg once daily following 4 weeks of a VLCD.³³ Patients who lost at least 6 kg (13.2 lb) in the dietary phase were randomized to receive either sibutramine 10 mg or placebo once daily in the morning. The VLCD was stopped at the point of randomization, although patients were counseled to decrease their caloric intake by 20% to

30% relative to their pre-VLCD eating habits. The mean weight decrease in the sibutramine patients at the end of 52 weeks was 5.2 kg (11.4 lb), compared with a mean gain of 0.5 kg (1.1 lb) in the placebo group ($P = .004$). At the end of 1 year, 86% of patients in the sibutramine group had lost at least 5% of their prestudy weight, compared with 55% of patients in the placebo group ($P < .001$). In addition, 75% of patients receiving sibutramine maintained 100% of the weight loss achieved by the VLCD at the beginning of the study. Figure 3 summarizes the weight loss results of this and two other sibutramine studies. All three studies showed statistically significant results with more patients achieving $\geq 5\%$ or $\geq 10\%$ weight loss with sibutramine compared with placebo ($P < .05$).⁵²⁻⁵⁴

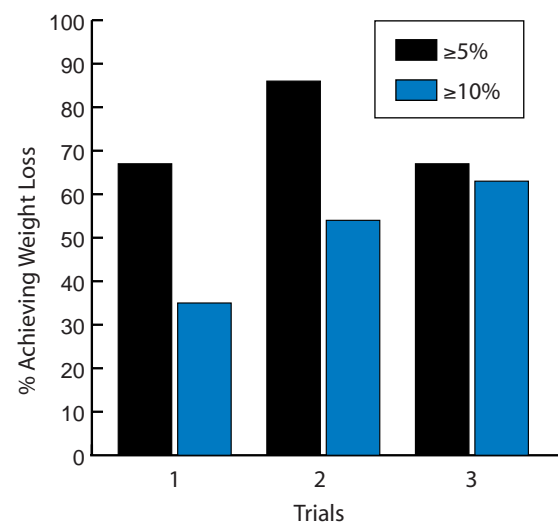
The Sibutramine Trial in Obesity Reduction and Maintenance was a 2-year, randomized, double-blind trial designed to evaluate the long-term effectiveness of sibutramine in maintaining weight loss.^{54,55} During the first 6 months of this study, 605 obese patients were treated with sibutramine 10 mg daily in addition to a weight loss program of diet and exercise. Mean weight loss during the initial 6-month period was 22 lb, corresponding to a 9.8% decrease from prestudy weight. After 6 months, patients who achieved a decrease in weight of at least 5% ($n = 467$; 77%) were randomized to receive sibutramine 10 mg/day

Figure 3. Percentage of patients losing $\geq 5\%$ and $\geq 10\%$ of body weight in three clinical trials of sibutramine.

Trial 1: sibutramine 15 mg QD X 6 months.

Trial 2: sibutramine 10 mg QD X 1 year, following 4 weeks of VLCD.

Trial 3: sibutramine 10-20 mg QD X 2 years.



$P \leq .001$ versus placebo

Trial 1 Brey GA et al. *Obes Res.* 1999;7:189.

Trial 2 Apfelbaum M et al. *Am J Med.* 1999;106:179.

Trial 3 James P et al. *Obes Res.* 1999;7(suppl 1):505.

Source: References 52-54.

(n=352) or placebo (n=115) for an additional 18 months. At the end of the trial, 43% of sibutramine-treated patients maintained at least 80% of the weight loss achieved during the initial 6 months of the study, while only 16% of patients in the placebo group achieved this degree of weight loss maintenance ($P < .001$). Furthermore, 27% of sibutramine-treated patients maintained their full initial weight loss at the end of the additional 18 months of treatment. Substantial decreases from baseline were also noted in serum concentrations of triglycerides, very-low-density lipoprotein (VLDL) cholesterol, insulin C peptide, and uric acid. In patients receiving placebo, concentrations of triglycerides and VLDL cholesterol returned toward baseline levels. In addition, serum concentrations of HDL were significantly increased after 2 years in patients receiving sibutramine. Sibutramine was safe and well tolerated in this 2-year study.

Sibutramine has also been shown to be effective in obese patients with type 2 diabetes in whom weight management is particularly difficult. In one study of patients with type 2 diabetes, the proportion of patients who lost $\geq 5\%$ of their baseline weight after 12 weeks was 19% in patients receiving sibutramine 15 mg daily compared with 0% in patients receiving placebo ($P < .001$). Fasting blood glucose levels decreased by a mean of 0.3 mmol/L in the sibutramine patients but increased by 1.4 mmol/L in the placebo group.⁵⁶ Fujioka et al. reported similar findings in a 24-week trial in obese patients with type 2 diabetes mellitus. Compared with placebo, sibutramine treatment was associated with greater absolute (4.3 kg versus 0.4 kg) and percentage (4.5% versus 0.5%) reductions in weight (both comparisons, $P < .001$). Sibutramine-treated patients also demonstrated improvements in glycemic control, fasting insulin, triglycerides, HDL cholesterol, and quality-of-life assessments.⁵⁷

The recommended starting dose of sibutramine is 10 mg once daily, preferably in the morning. If weight loss results are inadequate after 4 weeks, the dose may be increased to 15 mg once daily. A daily dose of 5 mg can be used in patients who cannot tolerate the 10 mg dose. Doses higher than 15 mg are not recommended. Sibutramine is contraindicated in patients with anorexia nervosa and should not be used in combination with other centrally acting appetite suppressant drugs or MAOIs.⁵¹

Sibutramine is generally well tolerated. The most common adverse events reported in placebo-controlled studies were headache, dry mouth, anorexia, constipation, and insomnia.⁵¹ Sibutramine treatment has been associated with small increases in SBP and DBP in normotensive patients; however, in a controlled trial of sibutramine in obese patients with hypertension, clinically significant increases in blood pressure (SBP or DBP > 10 mm Hg) were rare and comparable

to those seen in patients receiving placebo.⁵⁸ Blood pressure and pulse rate should be monitored prior to therapy and at regular intervals during treatment.⁵¹ Sibutramine does not appear to cause cardiac valve dysfunction.⁵⁹

Because sibutramine inhibits serotonin reuptake, it should not be used concomitantly with MAOIs. Caution is suggested with the use of sibutramine plus other centrally active drugs and drugs that may raise blood pressure and/or heart rate. There should be at least a 2-week interval between stopping MAOIs and starting sibutramine.⁵¹

Serotonergic Agents

Serotonergic agents, such as fluoxetine (Prozac—Eli Lilly) and sertraline (Zoloft—Pfizer), work by inhibiting the reuptake of serotonin and increasing serotonin concentrations in the hypothalamus, leading to an increase in satiety.^{6,15} Although these products are not FDA approved for obesity management, they have been associated with weight loss in some patients.⁶ To date, clinical studies with fluoxetine or sertraline have not demonstrated consistent weight loss, and in some cases, weight changes were not significantly different from placebo.^{15,60,61} Weight loss, if it occurs, becomes evident during the first several weeks or months of treatment, but patients tend to regain the weight even if maintained on therapy for 1 year or more.⁶⁰ A further issue confounding the effectiveness of fluoxetine and other selective serotonin reuptake inhibitors is that weight gain can be a side effect in certain patients.⁶⁰

Natural Products

A large number of natural ingredients are promoted for weight loss (Table 7). Use of nonprescription, natural products may seem like a safe, attractive treatment option for the overweight patient who feels ashamed or uncomfortable seeking professional help. Many marketed products contain multiple ingredients, most of which have few scientific data upon which to base their long-term efficacy or safety.⁴⁸

Ma huang (ephedra) is one of the most common ingredients in many herbal dietary supplements. The primary active ingredient in ma huang is ephedrine, a central nervous system stimulant. Ephedrine and xanthines, such as caffeine, act to increase the metabolic rate. Combinations of these ingredients have been shown to promote weight loss in short-term trials, but serious cardiac complications are possible, including hypertension, increased heart rate, stroke, heart attack, seizures, and death. FDA is considering restricting the sale of products containing combinations of ephedrine and caffeine or other stimulants.⁶⁵ Ma huang is often combined with St. John's wort and promoted as "herbal phen-fen." FDA warns that this combination has not been well studied and can be harmful.⁶

Table 7. Natural Products Promoted for the Treatment of Obesity

Product	Other Names	Mechanism	Side Effects/Comments
Ma huang	Ephedra, desert herb, ephedrine, sinica, ephedronin, <i>Sida cordifolia</i>	Stimulant; naturally occurring ephedrine	Same as ephedrine (tremor, agitation, insomnia, usually transient); linked to 17 cardiac deaths
Guarana	Paullinia cupana, Brazilian cocoa, guarana bread	Stimulant; naturally occurring caffeine	Same as caffeine
Ephedrine + caffeine OR Ma huang + caffeine		Decreased appetite; increased metabolic rate	Transient (8 weeks) mild tremor, agitation, insomnia
Ma huang + St. John's wort	Herbal phen-fen	Same as ma huang; St. John's wort meant to replace fenfluramine component of Rx phen-fen regimen	Same as ephedrine
Garcinia	Hydroxycitric acid, <i>Garcinia hanburyi</i> , Camboge, Gutta Combodia, Tom Rong, Cambodia	Said to prevent body from storing fat	Strong laxative effect, possible abdominal pain and vomiting at large doses; appears no more effective than placebo
Guggul gum	Guggal resin, didin, didthin, gugalipid	Said to release endogenous thyroid hormone	None reported; no studies to support weight loss claims
Chitin	Chitosan, Fat-Absorb, Fat-Blocker	Fat-binding polymer	Allergic reactions in persons allergic to shellfish
Chromium	Chromium picolinate	Said to facilitate fat metabolism and proper function of insulin receptors	No data to support use in obesity
Cholecystokinin	CCK, Satiatrol	Hormone which signals satiety	None reported; no long-term studies
L-carnitine		Said to aid in fatty acid oxidation	No data to support use in obesity
Tiratricol	TRIAC	Thyroid hormone; touted as a "fat burner"	Signs of excess thyroid hormone: insomnia, nervousness, sweating, diarrhea; stroke/heart attack risk at high doses

Sources: References 6, 62–64.

Guarana, derived from the crushed seed of a South American shrub, is used in Brazil to produce a stimulating beverage similar to coffee or tea. It has a very high caffeine content, ranging from 3% to 5%; in comparison, coffee beans contain from 1% to 2% caffeine. Guarana is promoted as a metabolism booster and "fat burner." When used in combination with ephedra, the toxic potential is increased and may include high blood pressure, stroke, or death.^{62,66}

Chitin is one of the newest herbal weight loss products being promoted to consumers. Chitin is a positively charged polysaccharide derived from the shells of crustaceans such as shrimp, crab, and lobster, and also from the exoskeletons of marine zooplankton. Negatively charged molecules, such as bile acids and free fatty acids, are attracted to the positive

charge of chitin and become ionically bound. Hence, chitin binds and prevents the absorption of dietary fat.⁶ However, in a randomized clinical trial comparing chitin with orlistat, chitin had no effect on fat absorption, while orlistat inhibited fat absorption by about 40%.⁶⁷

Garcinia, or hydroxycitric acid, has been shown to inhibit enzymes that convert citrate into coenzyme A, thereby preventing the body from storing excess energy as fat. It may also inhibit appetite, a phenomenon observed in rat studies. Garcinia has not been shown to be any more effective than placebo for weight loss.⁶²

Chromium picolinate is a mineral that is touted as a facilitator of fat metabolism. Chromium picolinate is also thought to be essential for the proper functioning of cellular

insulin receptors and regulating blood sugar. L-carnitine is another common ingredient claimed to aid in fatty acid oxidation. There appear to be no data supporting the effectiveness of these agents in facilitating weight loss.⁶

Combining Therapies

In general, the more interventions that are included in the overall weight management program, the better the outcome. Almost all recognized guidelines for obesity management encourage the use of multifaceted treatment. Figure 4 illustrates the findings of a study that compared the weight loss outcomes in patients managed with pharmacotherapy alone (sibutramine), pharmacotherapy plus behavior and lifestyle interventions, or a combination of pharmacotherapy, behavioral interventions, and dietary changes.⁶⁸ The results demonstrated that the combined use of drug therapy plus behavioral interventions produced a significantly greater weight loss compared with drug treatment alone ($P < .05$). In fact, each additional intervention was associated with an extra 5 kg (11 lb) to 6 kg (13 lb) loss over a 6-month period.

Surgery

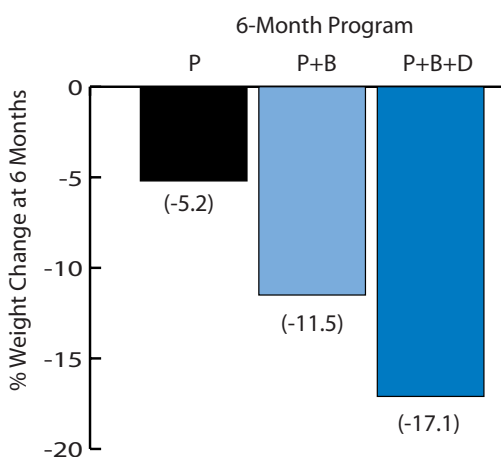
Bariatric surgery is an extreme weight control treatment which should be reserved for patients with a BMI ≥ 40 who have failed to respond to medical and lifestyle weight control measures. Less severely obese individuals (BMI between 35 and 40) may also be candidates if they have significant morbidities such as disabling joint disease, pulmonary insufficiency, hypertension, diabetes mellitus, or if weight-induced physical problems interfere with the performance of daily activities.^{3,29} There are two basic types of bariatric surgery in current use: gastric resection and gastric bypass.

The premise of gastric resection, also known as gastropasty, is to reduce the size of the functional stomach to a point that a patient can eat only a small amount of food (e.g., $\frac{1}{2}$ to 1 cup) at a time without feeling uncomfortable or nauseous. In the upper portion of the stomach, a small pouch is formed by surgical stapling (hence the common reference to “gastric stapling”). This small pouch empties into the rest of the stomach through a small channel, or stoma.⁶⁹ Gastric resection works best if patients maintain a bulky diet; high-calorie liquids (e.g., ice cream, milkshakes) can slide right through the pouch, defeating the purpose of the procedure.

In gastric bypass procedures, not only is food intake restricted, but segments of the intestine are also removed. The stomach and the entire duodenum are bypassed, reducing absorption of calories. In the common Roux-en-Y procedure, a small pouch (approximately 10 mL) in the upper portion of the stomach is anastomosed to a segment of proximal jejunum. Gastric bypass prohibits the patient from eating large quantities of food and also induces a “dumping syndrome” (i.e., abdominal cramping, diarrhea, sweating, chills, flushing) if the patient ingests a high-sugar liquid meal.^{29,69} Gastric bypass has generally been found to be more effective than gastric resection techniques.⁷⁰ Common complications include vitamin B₁₂ deficiency, incisional hernia, depression, staple-line failure, gastritis, and cholecystitis.³

In relation to all other treatment options for obesity, surgery produces the greatest and most sustained weight loss, although patients still need to be realistic in their expectations. During the first 12 to 24 postoperative months, patients experience an average 50% to 60% drop in excess body weight (weight above ideal body weight) and a 10 kg/m² decrease in BMI. For example, a person weighing 300 lb prior to surgery might achieve an ultimate weight of 200 to 220 lb, not 120 to 150 lb. Eventual weight regain may occur in some patients; however, long-term weight maintenance results are generally substantial. Weight-related morbidity is also substantially decreased postoperatively. Type 2 diabetes mellitus resolves in approximately 90% of patients, and high blood pressure normalizes in about two thirds. Improvements can also be seen in serum lipid levels, cardiac and pulmonary functions, and musculoskeletal disabilities. Psychologically, the patient’s mood, self-esteem, self-confidence, and body image are almost always improved.⁶⁹

Figure 4. Comparative weight loss in patients receiving pharmacotherapy alone (P), pharmacotherapy plus behavior or lifestyle changes (P+B), and pharmacotherapy plus behavior or lifestyle changes plus dietary changes (P+B+D).



Source: Reference 68.

Maintaining Weight Loss

Obesity truly is a chronic disease with no simple cure, much like hypertension or diabetes. Therefore, treating obesity should be approached with the knowledge that it will require life-long follow-up.⁷¹ For example, most obese patients who achieve some degree of weight reduction through changes in diet will regain most or all of the weight after dietary restric-

tions are lifted. While this leads some to conclude that “diets don’t work,” these findings are not at all surprising when obesity is correctly viewed as a chronic disorder.

In patients undergoing weight loss programs, the rate of continued weight loss generally plateaus after about 6 months of treatment. At this point, weight maintenance becomes the critical issue. Successful weight maintenance is defined as a weight regain of no more than 3 kg (6.6 lb) over a 2-year period, along with a sustained decrease in waist circumference of at least 4 cm (~1.5 inches).³

Two pharmaceutical companies have developed formal programs for motivating patients and encouraging long-term weight loss success. The Point of Change weight management program, run by Abbott Laboratories, manufacturer of sibutramine, provides incentive and follow-up at no cost to physicians or patients. Anyone wishing to lose weight can voluntarily enroll in the program, which involves individualized support, patient questionnaires, periodic newsletters, and weight loss information.

The Xenicare patient support program, developed by Roche Pharmaceuticals, manufacturer of orlistat, is a Web-based program designed to give users tools and encouragement to help them manage their weight. Xenicare provides registered users with a personalized Web site that is refreshed on a regular basis, as well as regular updates on the health benefits of weight management, tips for achieving goals, and a variety of other useful materials.

Role of the Pharmacist

Obese individuals, probably even more than individuals afflicted with other chronic conditions, need ongoing reinforcement and support from health care providers because treatment failure is so common. The National Heart, Lung and Blood Institute guidelines for obesity management underscore the importance of frequent contact between patients and health care practitioners because such contact can increase the likelihood of successful weight loss. These guidelines also state that weight loss maintenance programs can be conducted by practitioners without specialization in weight management, as long as the person gains adequate knowledge.³

As the most accessible health care professionals, pharmacists are in a good position to become involved in obesity counseling and management. Due to the chronic nature of obesity, pharmacists are likely to interact with these individuals on a regular basis. Pharmacists should be able to visually recognize individuals with excess body weight. Furthermore, by using patient medication profiles, it is possible to identify individuals who are already being treated for obesity-related complications. In fact, interactions regarding health prob-

lems such as CVD or diabetes can serve as a catalyst for weight management discussions. Pharmacists communicate regularly with physicians and sometimes other health care professionals, including dietitians. Pharmacists with a weight management focus can obtain assistance from these individuals and, when warranted, refer patients to them. A patient profile review can detect if patients are being prescribed any medications that could be adding to their weight problem. The pharmacist can discuss possible changes to therapy with the patient and the physician.

Targeted counseling to obese individuals can dramatically help them in their efforts to lose weight. In an empathetic, professional manner, the pharmacist can seek to determine the person’s awareness of the need to treat obesity. The pharmacist can assist patients in assessing their health risk by calculating BMI and measuring waist circumference. In discussions with patients, it is more dignifying to focus on the health benefits of losing weight, versus the aesthetic component. Patients and their families should understand that obesity is a chronic disease and that weight management requires dedication and perseverance.¹¹ Patients need continual reinforcement regarding the importance of diet and lifestyle changes and that medication use is intended to supplement these interventions, not replace them. Patients should be counseled to avoid using OTC weight loss products, especially those that contain sympathomimetics, ephedra alkaloids, or thyroid extracts. The use of fad diets and “hyped up” nutritional supplements (e.g., fat burners) should also be discouraged.¹¹ Within the pharmacy, appropriate messages regarding healthful lifestyles can be promoted through posters or pamphlets. Pharmacists can also help patients locate other resources about obesity that are available (see Resources).

Finally, structured weight management programs can be developed directly in the pharmacy setting. There is little formal training available, but motivated pharmacists can easily educate themselves on the strategies and specifics of obesity management. The Healthy Outcomes Nutrition & Weight Loss program is a successful pharmacy-based obesity management program.⁵ The format of a typical 45-minute weekly session involving up to six patients is as follows:

- Weigh each participant in private and graph weight changes from previous visit.
- Measure blood pressure in hypertensive patients.
- Begin the session with an icebreaker, such as sharing a recipe, viewing a portion of a videotape, etc.
- Ask for participant feedback regarding written materials or sections of the program manual they have read.
- Answer any questions.

- Develop strategies to prevent overeating, maintain a diary, drink water, and exercise.
- Review patient diaries.
- Encourage participants that they can overcome lapses and relapses that occur.

Patients are provided with pocket-sized calorie and fat food guides as well as diaries to track diet and exercise behaviors.⁵ The Healthy Outcomes Nutrition & Weight Loss program offers training and support in marketing a weight loss program (800-876-1307). Pharmacists can also play a key role in the Point of Change and XeniCare programs, described earlier. The pharmacist can encourage patients to enroll in the programs and can reinforce the treatment recommendations outlined by their physician.

Summary

Obesity is now recognized as a chronic disease resulting from a combination of genetic and environmental factors. Obesity is a significant health problem in the United States that deserves the same attention and long-term intervention as other serious, chronic health conditions. Effective treatment produces substantial health benefits in the form of reduced blood pressure and cholesterol levels and improved glycemic control. Unfortunately, many health care professionals do not aggressively address the issue of obesity with their patients.

BMI and waist circumference determinations can be performed easily and aid in assessing a patient's risk for developing obesity-related complications and the urgency of achieving weight loss. A successful weight loss program is based primarily on proper dietary guidelines, increased physical activity, and other behavioral strategies. Drug therapy, as an adjunct to these measures, can provide effective long-term weight loss and weight maintenance. Two currently available agents, orlistat and sibutramine, have been shown to be safe and effective when used over periods of up to 2 years. Other FDA-approved agents for weight loss are not as frequently used because of stimulant side effects and abuse potential. Serotonin reuptake inhibitors have not demonstrated consistent efficacy in obesity treatment and may, in fact, cause weight gain in some patients. Patients should be discouraged from using OTC and herbal products promoted for weight loss. For extreme cases of obesity, surgical treatments may produce dramatic weight loss.

Pharmacists can play an important role in identifying patients who would benefit from weight loss and by encouraging patients to seek and continue with treatment.⁷² Frequent contact with a health care professional has been recommended as a way of greatly increasing the chances for weight loss success. Pharmacists can encourage patients and help monitor weight loss on an ongoing basis as an adjunct to physician visits. Formal weight loss programs can be

established within the pharmacy. Obesity is a lifelong problem with serious consequences, but there are successful management techniques available. The dedicated concern and intervention of pharmacists and other health care professionals can help reduce the incidence, morbidity, and mortality of this chronic disease.

Resources

The following resources provide additional information on obesity, related conditions, and dietary information as well as patient support.

- **American Dietetic Association**
216 West Jackson Boulevard
Chicago, IL 60606-6995
800-877-1600
<http://www.eatright.org>
- **American Obesity Association**
1250 24th Street, NW, Suite 300
Washington, DC 20037
800-986-2373
<http://www.obesity.org>
- **Association for Morbid Obesity Support**
<http://www.obesityhelp.com/morbidobesity>
- **National Institute of Diabetes and Digestive and Kidney Diseases**
31 Center Drive, MSC-2560
Building 31, Room 9A-04
Bethesda, MD 20892-2560
301-496-3583
<http://www.niddk.nih.gov>
- **National Institutes of Health/National Heart, Lung and Blood Institute**
Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults. Available at:
http://www.nhlbi.nih.gov/guidelines/obesity/ob_home.htm
- **North American Association for the Study of Obesity**
8630 Fenton Street, Suite 412
Silver Spring, MD 20910
301-563-6526
<http://www.naaso.org>
- **Point of Change Weight Management Program**
<http://www.4meridia.com/poc/Logon.jsp>
- **The Weight-Control Information Network/National Institute of Diabetes and Digestive and Kidney Diseases**
1 WIN WAY
Bethesda, MD 20892-3665
301-570-2177
800-WIN-8098
- **Weight-Control Network of the National Institute of Diabetes and Digestive and Kidney Diseases**
<http://www.niddk.nih.gov/health/nutrit/nutrit.htm>
- **XeniCare Patient Support Program**
<http://www.xenicare.com>

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C.E. Assessment Questions

Instructions: For each question, circle the letter corresponding to the correct answer on the answer sheet provided. Please review all of your answers to be sure you have circled the proper letter. There is only one correct answer to each question.

- Obesity is defined as a body mass index (BMI) of:**
 - ≥ 25 kg/m².
 - ≥ 27 kg/m².
 - ≥ 30 kg/m².
 - ≥ 35 kg/m².
 - ≥ 40 kg/m².
- Which of the following can be a consequence of obesity?**
 - Increased risk for developing insulin resistance and type 2 diabetes.
 - High blood pressure and hyperlipidemia.
 - Increased morbidity and mortality from endometrial, breast, prostate, gallbladder, and colon cancers.
 - Difficulty finding a job.
 - All of the above answers are correct.
- The most dramatic increase in obesity-related mortality is seen when BMI reaches:**
 - ≥ 25 kg/m².
 - ≥ 27 kg/m².
 - ≥ 30 kg/m².
 - ≥ 35 kg/m².
 - ≥ 40 kg/m².
- Which of the following statements regarding leptin is false?**
 - In obese mice of the *ob/ob* strain, leptin administration produces anorexia and weight loss.
 - Humans with a known genetic leptin deficiency exhibit extreme obesity.
 - Most obese humans have normal genetic sequences for leptin and its receptor.
 - In humans, obesity may be related to a decreased sensitivity or resistance to leptin.
 - Initial research with leptin administration in obese patients demonstrated significant weight loss in the vast majority of treated subjects.
- Which of the following are considered the most useful tools for assessing obesity?**
 - BMI, waist circumference, waist-to-hip ratio (WHR), and IBW (ideal body weight).
 - BMI and WHR.
 - BMI and waist circumference.
 - BMI and IBW.
 - Waist circumference and IBW.
- A high-risk waist circumference in male and female patients, respectively, is considered to be:**
 - >40 inches; >35 inches.
 - >42 inches; >35 inches.
 - >40 inches; >38 inches.
 - >45 inches; >35 inches.
 - >45 inches; >38 inches.
- Why is a 10% loss of body weight over 6 months suggested as an initial goal?**
 - Too rapid a reduction in weight is often associated with rapid weight regain.
 - There is an increased rate of gallstone formation and possibly electrolyte abnormalities with very rapid weight reduction.
 - This level and rate of weight loss is realistic and can be maintained over time.
 - Health benefits are apparent even with this modest level of weight reduction.
 - All of the above answers are correct.
- A calorie deficit of 500 to 1,000 kcal/day should produce an ideal weight loss rate of:**
 - 0.25 lb per week.
 - 0.5 lb per week.
 - 1 to 2 lb per week.
 - 3 to 4 lb per week.
 - None of the above answers is correct.
- Most patients on dietary regimens reach a weight loss plateau after about:**
 - 3 months.
 - 6 months.
 - 9 months.
 - 12 months.
 - 2 years.
- Which of the following statements regarding exercise is false?**
 - Walking is one of the most suitable choices for an initial exercise program in obese patients.
 - It is recommended that daily exercise be conducted in a single session for optimal benefits.
 - Patients using lifestyle modifications may demonstrate similar degrees of weight loss compared with those involved in traditional exercise programs.
 - Physical exercise is best implemented as an adjunct to dietary intervention.
 - In addition to weight loss, increased physical activity has secondary benefits such as improved mood, self-esteem, and increased cardiorespiratory fitness.
- Which of the following is considered the cornerstone of behavioral therapy?**
 - Self-monitoring.
 - Stimulus control.
 - Cognitive restructuring.
 - Stress management.
 - Social support.
- Drug treatment of obesity may be considered in patients having which of the following characteristics?**
 - BMI ≥ 27 kg/m² regardless of the presence of any risk factors.
 - BMI ≥ 27 kg/m² with established risk factors such as hypertension, dyslipidemia, coronary heart disease, type 2 diabetes, or sleep apnea, or any patient with a BMI ≥ 30 kg/m².
 - BMI ≥ 30 kg/m² and only in the presence of established risk factors.
 - Patients unwilling to attempt weight loss through diet and exercise strategies.
 - None of the above answers is correct.

13. *Which of the following statements best describes the recommended role of herbal weight loss products in obesity management?*
- Herbal weight loss products should be tried after diet and therapy have failed and before using prescription drugs.
 - Herbal weight loss products containing a single ingredient are safe and effective when used as recommended.
 - The combination of ma huang and St. John's wort is a practical herbal alternative to the banned prescription "phen-fen" combination.
 - Herbal products can be safely and effectively used to augment prescription drug therapy.
 - Herbal medications are not recommended for weight loss, because their active ingredient composition and potential side effect profiles are unpredictable.
14. *Which of the following best summarizes the weight loss results generally observed with fluoxetine?*
- Studies with fluoxetine have demonstrated consistent weight loss that is significantly greater than that seen with placebo.
 - Weight loss with fluoxetine is generally not seen until several weeks or months into therapy and peaks at about 12 months.
 - Weight loss may be seen during the first several weeks or months of therapy but weight regain is common, even with continued treatment.
 - Weight loss may be seen during the first several weeks or months of therapy and persists as long as treatment is continued.
 - None of the above answers is correct.
15. *Which of the following parameters are improved in obese patients with type 2 diabetes treated with sibutramine?*
- Glycemic control.
 - Fasting insulin.
 - High-density lipoprotein cholesterol.
 - Quality of life.
 - All of the above answers are correct.
16. *The weight loss effects of sibutramine are a result of:*
- Increased satiety.
 - Thermogenic effects.
 - Inhibition of norepinephrine uptake.
 - Inhibition of serotonin uptake.
 - All of the above answers are correct.
17. *Which anti-obesity drugs have been studied for long-term periods of up to 2 years?*
- Phendimetrazine, phentermine, mazindol, sibutramine, orlistat.
 - Phentermine, mazindol, sibutramine, orlistat.
 - Mazindol, sibutramine, orlistat.
 - Sibutramine, orlistat.
 - None of the above answers is correct.
18. *Which of the following statements is false regarding orlistat administration?*
- The recommended dosage is 120 mg three times daily with each meal that contains fat.
 - Each dose may be taken during the meal or up to 1 hour afterward.
 - If a meal is occasionally missed, the orlistat dose can be skipped.
 - If a meal contains no fat, the orlistat dose can be skipped.
 - Increasing the dosage to 240 mg with each meal that contains fat further inhibits fat absorption.
19. *Which of the following statements regarding bariatric surgery is false?*
- Appropriate candidates have a BMI >40 kg/m² and have failed to respond to other weight control measures.
 - Patients with a BMI between 35 kg/m² and 40 kg/m² are candidates if they have significant obesity-related morbidity.
 - In gastric resection procedures, a small pouch is formed which empties into the rest of the stomach through a small stoma.
 - Gastric resection works best if patients maintain a low-bulk, high-calorie liquid diet.
 - In the Roux-en-Y gastric bypass procedure, a section of jejunum is anastomosed to a small pouch at the entrance of the stomach.
20. *Overall, which treatment strategy would be expected to produce the most significant long-term weight reduction?*
- Dietary restrictions plus exercise.
 - Drug therapy with dietary restrictions.
 - Drug therapy plus exercise.
 - Drug therapy plus dietary restriction and exercise.
 - Drug therapy plus dietary restriction and exercise with continued follow-up by a concerned health care professional.

C.E. Credit:

To obtain 2 hours of continuing education credit (0.2 CEU) for "Managing Obesity as a Chronic Disease," complete the assessment exercise, fill out the "C.E. Credit" page at the end of this publication, and return the page to APhA. A statement of credit will be awarded for a passing grade of 70% or better. Pharmacists who complete this exercise successfully before August 15, 2004, can receive credit.



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Please circle your answers (one answer per question).

- | | |
|---------------|---------------|
| 1. a b c d e | 11. a b c d e |
| 2. a b c d e | 12. a b c d e |
| 3. a b c d e | 13. a b c d e |
| 4. a b c d e | 14. a b c d e |
| 5. a b c d e | 15. a b c d e |
| 6. a b c d e | 16. a b c d e |
| 7. a b c d e | 17. a b c d e |
| 8. a b c d e | 18. a b c d e |
| 9. a b c d e | 19. a b c d e |
| 10. a b c d e | 20. a b c d e |

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