



Obesity: Understanding and Achieving a Healthy Weight

9

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Keywords

Obesity · Body mass index · Diet · Treatment · Bariatric surgery

Key Points

- Obesity is a chronic, relapsing, stigmatized disease process that is increasing in prevalence, affecting both adults and children.
- A small positive energy imbalance from too much food or too little activity causes the obesity that is influenced by many environmental factors.
- The food we eat is more than “calories.” Focusing on calories alone may not be as productive as focusing on patterns of eating and the role of sugar and fat in the diet.
- Obesity increases the risk of many diseases and shortens life span.
- Weight loss provides benefits in reducing health risks and improving the quality of life.
- Management of obesity must redress the energy imbalance with diet, lifestyle modification, exercise, medications, and, potentially, bariatric surgery.
- Five drugs are approved by the FDA for long-term treatment of obesity, and they can effectively improve health-related risks.
- Bariatric surgery has become a major treatment strategy and can reduce long-term health risks from obesity.

Introduction

Obesity is a chronic, relapsing, stigmatized disease that is increasing in prevalence worldwide and affecting both children and adults [1]. This chapter reviews the key facts around obesity with a primary focus on prevention and treatment. Since the subject is a large one, and we cannot cover all of its details, we have provided additional sources of information.

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Definition

Obesity means having too much body fat, but measuring body fat accurately requires facilities that are not generally available. For this reason, measures of height and weight are usually substituted. Of these, the body mass index (BMI) is the most widely used. The BMI is defined as weight divided by the square of height [weight/height²]. Table 9.1 provides the definitions of BMI used in the United States and some, but not all other countries, the exceptions being largely Asian countries.

Prevalence of Obesity

Using BMI as the criterion, a worldwide epidemic of obesity began in the 1980s and continues today [3]. Table 9.2 provides the most recent information from the Centers for Disease Control using the National Health and Nutrition Examination Survey data.

From the survey in 1999–2000 through the survey in 2017–2018, the prevalence of obesity increased from 30.5% to 42.2% and the prevalence of severe obesity, that is, individuals with a BMI ≥ 40 kg/m², increased from 4.7% to 9.2% indicating that heavier people are getting fat even faster than people with less fat. There are also clear effects of ethnicity and of gender (Table 9.2).

Centrally Located Body Fat

Excess fat located as intra-abdominal fat in deposits such as the liver or visceral adipose tissue is particularly hazardous to health. Measuring centrally located fat can be done accurately with magnetic resonance imaging (MRI) or computed tomographic (CT) scans, but these are costly to use for this purpose. The waist circumference is a practical alternative for use by healthcare professionals to

Table 9.1 Classification of weight status in the United States using the body mass index

BMI range	Weight status
Below 18.5	Underweight
18.5–24.9	Normal or healthy weight
25.0–29.9	Overweight
30.0 and above	Obese
30.0 to 34.9	Class I obesity
35.0 to 39.9	Class II obesity
≥ 40.0	Class III obesity

Data from CDC. Overweight and Obesity. Defining Adult Overweight and Obesity. <https://www.cdc.gov/obesity/adult/defining.html> [2]

Table 9.2 Prevalence of obesity using body mass index in data calculated by measuring a random sample of Americans over Age 20

Prevalence of obesity (BMI ≥ 30 kg/m ²)			
	Total	Male	Female
Non-Hispanic White	42.2%	44.7%	39.8%
Non-Hispanic Black	49.6%	41.1%	56.9%
Hispanic	44.8%	45.7%	43.7%
Non-Hispanic Asian	17.4%	17.5%	17.2%

Data from: Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017–2018. NCHS Data Brief, no. 360. Hyattsville, MD: National Center for Health Statistics [4]

estimate central adiposity. If the BMI is between 20 and 35 kg/m², a waist circumference of >40 in. in American men and > 35 in. in American women provides a high-risk category. Most other areas of the world use lower cut points of 90–94 cm [35.5–37 in.] for men and 80 cm [31.5 in.] for women.

Basic Facts About Obesity

Etiology

At its simplest, obesity results from an imbalance between energy intake and energy expenditure [5, 6]. However, it is the connection between these two components that provides clues about how we should understand, prevent, and manage obesity [7]. Modification of future obesity begins with the pregnant woman and her fetus. This is a time where the healthcare professional can easily intervene – advise a pregnant woman not to smoke, to avoid consumption of sugary beverages, keep her weight gain within prescribed levels, and treat gestational diabetes if it occurs since all of these increase risk to the infant for obesity later in life [7].

Postnatal factors also affect the risk of obesity, but intervention is more challenging. Genes clearly underlie the risk of obesity [8], and “genes can be said to load the gun, while the environment pulls the trigger” [9].

Food patterns including the “Western” high-fat/high-sugar diet and sugary beverages enhance the risk of weight gain [5, 7]. Social settings including watching television and the amount of sleep an individual gets are other factors which an individual can modulate [7]. Portion sizes have increased, providing more energy to people with each portion, and people tend to eat more when larger portions are provided. Medications, toxins, viruses, and the microbiome are additional factors that play a role in the risk of obesity. Obesogens, a group of chemical agents used in many manufacturing processes including plastics, can produce obesity in animals and are of concern for humans. Viruses are known to produce obesity in animals, and their potential role in obesity in humans needs further study.

Some medications are known to cause weight gain, and these are listed in Table 9.3 along with potential alternatives. The health professional can use this knowledge to intervene by replacing the medications which cause weight gain with the ones that do not when this is medically reasonable. Physical activity has gradually declined, meaning we need less food energy for our daily life [7].

Pathology and Pathogenesis of Diseases Associated with Obesity

The pathology of obesity results from enlarged and/or too numerous fat cells. The fat they contain and the adipokines they release have effects on distant tissues that can cause disease. Increasing body fat increases demands from many other organ systems and can be the basis for causing many of the diseases associated with obesity including diabetes mellitus, hypertension, nonalcoholic fatty liver disease, sleep apnea, osteoarthritis, coronavirus (SARS-2-CoV-2) or COVID-19, and cardiovascular disease as described in the paper by Bray et al. [1].

Costs Associated with Obesity

Obesity is an expensive disease process, costing between 3% and 8% of healthcare budgets [10].

Table 9.3 Medications that produce weight gain and possible alternatives

Category	Drugs that may cause weight gain	Possible alternatives
Antipsychotics	Thioridazine; olanzapine; quetiapine; risperidone; haloperidol; perphenazine; clozapine	Molindone Ziprasidone
Antidepressants Tricyclic antidepressants Monoamine oxidase inhibitors Selective serotonin Reuptake inhibitors	Amitriptyline; nortriptyline Imipramine; trimipramine Mirtazapine Paroxetine Doxepin	Protriptyline Bupropion Nefazodone Fluoxetine (short-term) Sertraline (<1 year)
Anticonvulsants	Valproate, Carbamazepine Gabapentin	Topiramate Lamotrigine Zonisamide
Antidiabetic drugs	Insulin Sulfonylureas Glinides Thiazolidinediones	Acarbose Miglitol Metformin Pramlintide Exenatide; liraglutide SGLT-2 inhibitors
Antiserotonin	Pizotifen	
Antihistamines	Cyproheptidine	Inhalers Decongestants
β -Adrenergic blockers α -Adrenergic blockers	Propranolol Terazosin	ACE inhibitors Calcium channel blockers
Steroids for chronic inflammatory disease	Glucocorticoids	Nonsteroidal anti-inflammatory agents and disease-modifying anti-rheumatic drugs
Contraceptives	Progestational steroids	Barrier methods
Endometriosis	Depot leuprolide acetate	Surgical intervention

Treatment

The first step in treating any patient with obesity is to evaluate them and their needs and wishes [11]. Guidelines for the management of the patient with obesity have been published by three organizations [11–13]. The Guidelines for Obesity from the AHA/ACC/TOS provide an algorithm to help in making this assessment [11]. It is a useful framework on which to hang basic clinical information that is collected during the examination. Effective weight loss requires a reduction in energy (calorie) intake relative to energy expenditure that lasts over time [11]. The energy in our diet comes from protein, fat, and carbohydrate. It is the manipulation of the amounts of these macronutrients, and the foods that provide them that is the basis for all dietary approaches to weight loss.

There is high variability of weight loss with all weight loss programs. Some patients will lose a lot of weight, others a modest amount, and some will actually gain weight. In one clinical trial with over 3000 people (Look AHEAD) which used the best available lifestyle intervention, 10% of the individuals lost less than 1 kg after 1 year and 25% lost less than 3 kg, while the average loss was about 7.5 kg, meaning that some patients lost a lot of weight – 25% lost more than 12 kg and 10% lost more than 17 kg [14]. Thus, no matter what program you and your patient/client select, there will be some great successes and other dismal failures. The patient needs to be prepared for this because we have no way of predicting success or failure with any confidence before treatment begins.

The fourth concern for patients and healthcare providers is that with all weight loss programs, initial weight loss slows and then stops at a “plateau” which is often less than the patient’s desired weight loss which is followed in turn by frustration and weight regain. This is one of the most perplexing problems for patients and healthcare providers alike. For many patients, a “dream weight loss” would be the amount of a loss of nearly 30% of their body weight, which is outside the efficacy of any program other than surgery [15]. A loss of less than 17%, which is also greater than can be delivered by most lifestyle programs, was considered by many patients to be a disappointment. It is thus important for the patient and healthcare provider to recognize that an initial weight loss of 10% is a success and is one that will produce measurable health benefits.

A final issue is the “false hope syndrome.” Each year sees the publication of new diet books which promise amazing results. Each year people who have regained weight the year before vow to try again using the next popular diet or weight loss plan, believing they can overcome last year’s failure. They labor under the delusion of the “false hope syndrome,” i.e., that having failed last time, they are sure to succeed this time [16].

Components of a Comprehensive Program

The cornerstone of treatment for obesity is a comprehensive program involving diet, exercise, and behavioral therapy aimed at helping patients lose and maintain weight loss [11]. The elements of such a program are outlined in Table 9.4.

Table 9.4 Key components of comprehensive behavioral weight loss interventions to achieve a 7–10% weight loss [11]

Component	Weight loss	Weight loss maintenance
Frequency and duration of treatment contact	Weekly contact, in person or by telephone, for 20–26 weeks (internet/e-mail contact yields smaller weight loss) Group or individual contact	Every-other-week contact for 52 weeks (or longer) Monthly contact likely adequate Group or individual contact
Dietary prescription	Low-calorie diet (1200–1500 kcal for those <250 lb.; 1500–1800 kcal for those ≥250 lb) Typical macronutrient composition: ≤30% fat (≤7% saturated fat), 15–25% protein, remainder from carbohydrate (diet composition based on individual needs or preferences)	Consumption of a hypocaloric diet to maintain reduced body weight Typical macronutrient composition similar to that for weight loss
Physical activity prescription	180 minutes/week of moderately vigorous aerobic activity (e.g., brisk walking), strength training also desirable	200–300 minutes/week of moderately vigorous aerobic activity (e.g., brisk walking), strength training also desirable
Behavior therapy prescription	Daily monitoring of food intake and physical activity by the use of paper or electronic diaries Weekly monitoring of weight Structured curriculum of behavior change (e.g., diabetes prevention program) Regular feedback from an interventionist	Occasional to daily monitoring of food intake and physical activity by the use of similar diaries Twice weekly to daily monitoring of weight Curriculum of behavior change, including relapse prevention and individualized problem solving Periodic feedback from an interventionist

Adapted from Jensen MD, Ryan DH, Donato KA et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22(S2):S1–S410

Diet

Diet has two meanings. On the one hand, it describes the sum total of foods that we consume to maintain health. On the other hand, diet focuses on specific combinations of foods for specific health purposes. It is this latter meaning that we explore below.

Each year the US News and World Report publishes a list of “healthy” diets for Americans based on the review by a panel of experts [17]. We have included their sub-list that ranks weight loss diets (Table 9.5).

Since the calories (energy) in food comes from proteins, fats, carbohydrates, and alcohol in those foods, it is the reduction of one or more of these components of the diet that is essential if calorie

Table 9.5 Popular weight loss diets based on their ranking of the US News and World Report in 2020. Information from US News and World Report 2020. <https://www.usnews.com/info/blogs/press-room/articles/2020-01-02/us-news-reveals-best-diets-rankings-for-2020> [17]

Diet name	Rank	Score	Type of diet
Weight Watchers diet	1	3.6	Healthy fast weight loss
Vegan diet	2 ^a	3.5	Extremely restrictive diet
Volumetrics diet	2 ^a	3.5	Safe, nutritious diet focusing on low energy dense foods
Flexitarian diet	4 ^a	3.4	Mostly vegetarian, meat occasionally
Jenny Craig diet	4 ^a	3.4	Weight loss diet
Ornish diet	6	3.3	Heart-healthy, low-fat diet
Engine 2 diet	7 ^a	3.2	Restrictive diet
Mayo Clinic diet	7 ^a	3.2	Healthy lifelong eating habit
Raw food diet	7 ^a	3.2	Impossible to follow
DASH diet	10 ^a	3.1	Moderate fat, balanced
HMR program	10 ^a	3.1	Fast weight loss, pricey
Nutrisystem diet	10 ^a	3.1	May have nutrient deficiencies
Slim fast diet	10 ^a	3.1	Less healthy, better for weight loss on short term
Vegetarian diet	10 ^a	3.1	Plant-based diet
Atkins diet	15 ^a	3.0	High-fat, not a good all-purpose diet
Biggest loser diet	15 ^a	3.0	Fast weight loss
Keto diet	15 ^a	3.0	High-fat, low-carb, using fat for energy
Mediterranean diet	15 ^a	3.0	Higher fat, healthy
Nutritarian diet	15 ^a	3.0	Plant-based nutrient density focus
Optavia diet	15	3.0	Low for healthy eating, quick weight loss
South Beach diet	15 ^a	3.0	Restrictive rapid weight loss
Asian diet	22 ^a	2.9	Traditional Asian diet
Nordic diet	22 ^a	2.9	Healthy plant-based diet
Macrobiotic diet	24 ^a	2.8	Strict macrobiotic plan
TLC diet	24 ^a	2.8	Promotes cardiac health
Zone diet	24 ^a	2.8	Tedious with macronutrient targets
MIND diet	27	2.7	Aims to prevent mental decline
The fast diet	28 ^a	2.6	Lack of nutritional guidance
Paleo diet	28 ^a	2.6	Caveman diet
Dukan diet	30 ^a	2.5	Too restrictive, no evidence
Glycemic index diet	30 ^a	2.5	Good carb, bad carb diet
Dr. Weil’s anti-inflammatory diet	32 ^a	2.4	Cardiovascular-focused diet
Fertility diet	32 ^a	2.4	Pregnancy-aimed diet
Whole30 diet	34	2.3	No science; severely restrictive
Alkaline diet	25	2.1	Avoids acidic foods

^aTie; diets were rated by the experts on a scale of 1 to 5 with 5 being best

intake is to be reduced below daily energy expenditure for successful weight loss. Protein usually makes up 12–20% of dietary calories, fat anywhere between 25% and 45%, and carbohydrate the rest. Since carbohydrate and fat are the major sources of calories, they are the central focus for most diets.

Balanced Low-Calorie Diets

Diets in this category reduce the intake of both fat and carbohydrate which may increase the percentage of protein. The underlying hypothesis is that reducing calories is essential for weight loss [11]. Examples would be the DASH diet; a lower calorie diet based on MyPyramid food guide; Weight Watchers diet, a derivative of the Prudent Diet; and the Volumetrics diet. However, most meal plans can be balanced yet provide lower calorie intake if the individual self-monitors their calorie intake.

Low-Carbohydrate/Keto Diets

The low- and very-low-carbohydrate or keto diets reduce the quantity of carbohydrate below 30% and often go as low as 10% or less. They have been popular for more than 100 years, and books touting them occur on a regular basis. The hypothesis behind this diet is the carbohydrate-insulin hypothesis which argues that dietary carbohydrate stimulates insulin which drives fat formation and thus obesity [18], a concept which isn't universally accepted [19]. Two large trials have compared the diet composition and found that very low, moderately low, or normal carbohydrate made no difference in weight loss [20, 21]. In a meta-analysis comparing low-fat and low-carbohydrate diets where the two diets had the same amount of protein, Hall and Guo [22] concluded that there was no clinically significant difference.

Low-Fat Diets

The low-fat diet is premised on the idea that reducing fat will decrease energy intake and thus produce weight loss. These diets like the low-carbohydrate diets have been popular for more than 100 years. Examples of these diets include the Ornish diet, the Pritikin diet, the T-factor diet, and others.

Table 9.6 is a compilation of several of diet types which provide the main elements for many diets. Assessing the value of diets is best done with a meta-analysis of head-to-head comparisons. A recent such meta-analysis examined 121 trials with 21,942 patients comparing 14 named diets and 3 control diets. Compared with the usual diet, diets low in carbohydrate or low in fat had similar effects on weight loss at 6 months (4.63 kg vs 4.37 kg) and reduction in systolic blood pressure and diastolic blood pressure [23]. Moderate-macronutrient diets resulted in slightly less weight loss and blood pressure reductions. Low-carbohydrate diets had less effect than low-fat diets and moderate-macronutrient diets on reduction in LDL cholesterol but an increase in HDL cholesterol, whereas low-fat diets and moderate-macronutrient diets did not. Among popular named diets, those with the largest effect on weight reduction and blood pressure in comparison with a usual diet after 6 months were the Atkins diet, the DASH diet, and the Zone diet. No diets significantly improved levels of HDL cholesterol or C-reactive protein at 6 months. Weight loss diminished at 12 months with all dietary patterns and

Table 9.6 Comparison of diet programs and eating plans to the typical American diet

Type of diet	Example	General dietary characteristics	Comments	AHA/ACC/TOS evaluation
Typical American diet		Carb: 50% Protein: 15% Fat: 35% Average of 2200 kcal/d	Low in fruits and vegetables, dairy, and whole grains High in saturated fat and unrefined carbohydrates	

(continued)

Table 9.6 (continued)

Type of diet	Example	General dietary characteristics	Comments	AHA/ACC/TOS evaluation
Balanced nutrient, moderate-calorie approach	DASH diet or diet based on the MyPyramid food guide; commercial plans such as diet center, Jenny Craig, NutriSystem, Physician's weight loss, Shapedown pediatric program, Weight Watchers, Setpoint diet, Sonoma diet, and Volumetrics	Carb: 55–60% Protein: 15–20% Fat: 20–30% Usually 1200–1800 kcal/d	Based on a set pattern of selections from food lists using regular grocery store foods or prepackaged foods supplemented by fresh food items Low in saturated fat and ample in fruits, vegetables, and fiber Recommended reasonable weight loss goal of 0.5–2.0 lb./week Prepackaged plans may limit food choices Most recommend exercise plan Many encourage dietary record keeping Some offer weight-maintenance plans/support	
Low- and very-low-fat, high-carbohydrate approach	Ornish diet (eat more, weigh less), Pritikin diet, T-factor diet, choose to lose, fit or fat	Carb: 65% Protein: 10–20% Fat: ≤10–19% Limited intake of animal protein, nuts, seeds, and other fats	Long-term compliance with some plans may be difficult because of the low level of fat Can be low in calcium. Some plans restrict healthful foods (seafood, low-fat dairy, poultry) Some encourage exercise and techniques for <i>stress management</i>	The same weight loss at 6 months comparing <30% fat to >40% fat Strength of evidence – Moderate
Low energy density	Volumetrics	Carb: 55% Protein: 10–25% Fat: 20–35% Focus on fruits, vegetables, and soups	Four food categories: Very low energy density – Non-starchy fruits and veggies, nonfat milk, broth-based soups Low energy density – Starchy fruits/veggies, grains, breakfast cereal, low-fat meats, and mixed dishes Medium energy density – Meat, cheese, pizza, fries, dressings, bread, etc. High energy density – Desserts, nuts, and butter, oils Focus on categories 1 and 2, some from 3, minimum from 4	More weight loss at 6 months with low-energy-dense diet: RCT

Table 9.6 (continued)

Type of diet	Example	General dietary characteristics	Comments	AHA/ACC/TOS evaluation
Portion-controlled	The use of meal replacements, both liquid and solid meals			Weight loss at 1 year in the look AHEAD trial related to the frequency of consuming portion-controlled meals
Mediterranean style diets		Carb: 35–40% Protein: 12–20% Fat: 40–50% Approximately 25–30% of energy from monounsaturated fat	Eat primarily plant-based foods (fruits, vegetables, whole grains, legumes, and nuts) Healthy oils (olive) instead of saturated fats Limit red meat to a few times a month Eat fish and poultry at least twice a week Red wine in moderation, if you choose to drink alcohol Be active and enjoy meals with family and friends	Meta-analysis showed more weight loss with Mediterranean diet than low-fat diets (weighted-mean difference = 2.2 kg)
Low-carbohydrate, high-protein, high-fat approach	Atkins new diet revolution, protein power, Stillman diet (<i>the Doctor's quick weight loss diet</i>), <i>the carbohydrate Addict's diet</i> , Scarsdale diet	Carb: ≤20% Protein: 25–40% Fat: ≥55–65% Strictly limits carb to less than 100–125 g/d	Promotes quick weight loss (much is water loss rather than fat) Ketosis causes loss of appetite. Can be too high in saturated fat Low in carbohydrates, vitamins, minerals, and fiber Not practical for long term because of rigid diet or restricted food choices	The same weight loss at 6 months comparing <30 g/d vs 55% carb, 15% protein, or 40% carb and 30% protein: Strength of evidence – Low
Higher-protein, moderate-carbohydrate, moderate-fat approach	The zone diet, sugar busters, south beach diet	Carb: 40–50% Protein: 25–40% Fat: 30–40%	Diet rigid and difficult to maintain Enough carbohydrates to avoid ketosis Low in carb; can be low in vitamins and minerals	The same weight loss at 6 months comparing 25–30% vs 15% protein Strength of evidence – High
Glycemic load (GL)	The glycemic-load diet – Rob Thompson	Carb: 40–>55% Protein: 15–30% Fat: 30%	Focus on low-GL foods	The same weight loss at 6 months comparing high vs low GL Strength of evidence – Low
Low- or no sugar-sweetened beverages (SSBs)	Not really a diet but just a call to reduce SSB intake as a preventive strategy	No recommendations other than to reduce/remove SSBs from the overall diet plan	Meta-analyses show that the consumption of SSBs is related to the risk of obesity, diabetes, and heart disease	In sustained intervention studies, low-energy beverages showed lower energy intake and less weight gain than sugar-containing beverages

(continued)

Table 9.6 (continued)

Type of diet	Example	General dietary characteristics	Comments	AHA/ACC/TOS evaluation
Novelty diets	Immune power diet, rotation diet, cabbage soup diet, Beverly Hills diet, Dr. Phil	Most promote certain foods, or combinations of foods, or nutrients as having allegedly magical qualities	No scientific basis for recommendations	
Very-low-calorie diets	Health management resources (HMR), Optavia, Optifast	Less than 800 kcal/d	Requires medical supervision For clients with BMI ≥ 30 or BMI ≥ 27 with other risk factors; may be difficult to transition to regular meals	
Weight-loss online diets	Cyberdiet, DietWatch, eDiets, Nutrio.com	Meal plans and other tools available online	Recommend reasonable weight loss of 0.5–2.0 lb./week Most encourage exercise Some offer weight maintenance plans/support	

popular named diets. The benefits on cardiovascular disease essentially disappeared at 12 months, except for the Mediterranean diet.

Energy Density

The Volumetrics diet was no. 5 in the US News and World Report list of diets in 2020 [17]. It focuses on energy density as a guide to selecting foods and reducing energy intake. The diet is low in fat and rich in fruits and vegetables which give the diet a high-water content. This diet reduces calorie intake by providing bulkier foods with more water and less fat, thus enhancing satiety.

Portion-Controlled Diets

Portion control is one dietary strategy with promising long-term results. A trial in patients with diabetes using portion-controlled diets as part of the lifestyle intervention in the Look AHEAD Study found that weight loss was increased across each quartile of increased use of portion control foods [24].

Timed-Food Intake: Intermittent Fasting and Timed Meals

Intermittent fasting and time-restricted Feeding are two other strategies that may reduce energy intake and thus produce weight loss. When 11 studies of intermittent fasting or timed-energy restriction were compared to continuous calorie restriction, 9 of the studies showed no difference [25], and the 2 studies which reported benefit from these strategies were modest, at best. One study suggested that early timed-restricted feeding might improve insulin sensitivity in individuals with prediabetes even when there was no weight loss.

Behavior Modification and Lifestyle Interventions

Behavioral modification in lifestyle programs has been an important part of programs for weight loss for more than half a century with weight losses in the 5–10% range [11]. Behavior modification has a

number of components. First, it is a strategy designed to help people understand their eating behavior, from the triggers that start eating to the location, speed, and type of eating, through the consequences of eating and the rewards that can change it. In addition, it consists of strategies to help people develop assertive behavior, learn cognitive techniques for handling their internal discussions, and ways of dealing with stress. The newest innovation in the use of lifestyle intervention is to implement it over the Internet which has shown some promising results [1].

Exercise

Exercise is important for maintaining weight loss, but when used alone it does not generally produce much weight loss. A comparison of people who successfully maintain weight loss and those who do not shows a critical role of exercise. More than 200 min/week provides greater likelihood of maintaining weight loss than lower levels of exercise. Using a pedometer or wrist-activated device allows counting of steps. Working toward 10,000 steps per day is a good goal, and one that the healthcare provider should encourage.

Medications

Five medications are currently approved by the US Food and Drug Administration for long-term management of obesity along with four older drugs approved for short-term use (Table 9.7) [1, 12]. In addition there are several drugs that affect body weight but are not currently approved by the FDA for management of patients with obesity. These include leptin, amylin, oxyntomodulin, and inhibitors of glucose transport in the kidney or intestine (SGLT 1 or 2).

Noradrenergic Drugs (Many Trade Names)

Diethylpropion, phentermine, benzphetamine, and phendimetrazine were approved in the 1950s by the US Food and Drug Administration (FDA) for short-term use, based on data from clinical trials that were usually less than 3 months [1]. These drugs probably work by enhancing the availability of norepinephrine in the interneuronal space either by blocking reuptake of norepinephrine into neurons or enhancing its release. Phentermine is one of the most widely prescribed appetite suppressants [26]. The clinician is advised to use this drug and other similar drugs with care and to inform patients of the potential for abuse and the potential cardiovascular risks.

Drugs That Increase Intestinal VOLUME

Gelesis

Gelesis 100 (Plenity[®]) was approved by the US FDA for the management of obesity in 2019 and is the latest prescription drug to be approved. It is taken with water before lunch and dinner. It is produced by cross-linking cellulose and citric acid to create a three-dimensional hydrogel matrix. The capsules release thousands of non-aggregating particles that rapidly absorb water in the stomach, creating small individual pieces of gel which have the firmness of plant-based foods, such as vegetables, but without providing calories. This product is approved for individuals with a BMI as low as 25 kg/m². There is also no limit on how long Gelesis100 can be used. A clinical trial with Gelesis100 produced a weight loss of 6.4% versus 4.6% for the placebo group after 6 months [27].

Table 9.7 Drugs approved by the US Food and Drug Administration for the management of obesity

Drug and mechanism of action	Trade name(s)	Dosage	Comments
Gastrointestinal fiber			
Gelesis 100 (2019) (not scheduled)	Plenity	3 capsules 20 min before lunch and dinner with 16 oz. of water	No DEA schedule Approved for BMI 25–40 kg/m ² Composed of cellulose and citric acid
Pancreatic lipase inhibitor approved for long-term use orally			
Orlistat (1999) (not scheduled)	Xenical	1120 mg tid before meals OR 660 mg tid before meals (OTC)	GI side effects including steatorrhea, oily spotting, flatulence, fecal urgency, fecal urgency, and/or incontinence
Glucagon-like receptor-1 agonist approved for long-term use by injection			
Liraglutide (2015) (not scheduled)	Saxenda	33.0 mg/d – Dose-escalation over 5 weeks from 0.6 mg/d to 3.0 mg/d	Boxed warning: Thyroid C-cell tumors in mice. Nausea with some vomiting are principal side effects; acute pancreatitis or gall bladder disease can occur; hypoglycemia with some antidiabetic drugs
Combination of two drugs approved for long-term use orally			
Phentermine/topiramate extended release (2012) DEA schedule IV (combination of sympathomimetic and anticonvulsant)	Qsymia	3.75 mg/23 mg, first week; 7.5 mg/46 mg thereafter; can increase to 15 mg/92 mg for inadequate response	Contraindicated in pregnancy; fetal toxicity with monthly pregnancy test suggested; paresthesias and change in taste (dysgeusia); acute myopia (rare) Metabolic acidosis and glaucoma are rare; do not use within 14 days of a MAOI antidepressant
Naltrexone SR/bupropion SR (2014) (not scheduled) Opioid receptor antagonist Dopamine and norepinephrine reuptake inhibitor	Contrave (US) Mysimba (Europe)	32 mg/360 mg tabs; take two twice daily after dose- escalation	Boxed warning: Suicide risk in depression; contraindicated in pregnancy, in seizures, with uncontrolled hypertension and glaucoma. Nausea, constipation, headache Avoid in patients receiving opioids, MAOI, antidepressants, and with history of seizure disorder
Noradrenergic drugs approved for short-term use			
Diethylpropion (1959) DEA schedule IV	Tenuate	25 mg tid	Dizziness, dry mouth, insomnia, constipation, irritability Cardiostimulatory
	Tenuate Dospan	75 mg q AM	
Phentermine (1959) DEA schedule IV	Adipex Fastin	15–37.5 mg/d	Dizziness, dry mouth, insomnia, constipation, irritability Cardiostimulatory
	Oby-cap Iionamin slow release	15–30 mg/d	
Benzphetamine (1960) DEA schedule III	Didrex	25–50 mg tid	Dizziness, dry-mouth, insomnia, constipation, irritability. Cardiostimulatory
Phendimetrazine (1959) DEA schedule IV	Bontril Plegine Prelu-2 X-Troazine	17.5–70 mg tid 105 mg qd	Dizziness, dry mouth, insomnia, constipation, irritability Cardiostimulatory

Drugs That Modify Intestinal Absorption of Fat

Orlistat (Marketed Worldwide as Xenical)

Orlistat (Xenical[®]) is a potent and selective inhibitor of pancreatic lipase and thus reduces intestinal digestion of fat. In a meta-analysis of 31 studies using orlistat, the maximal weight loss using computer modeling was -6.65 kg, and the half-time to the maximal effect occurred by 35.4 weeks [28].

Orlistat is the only FDA-approved medication for weight management in both adolescents and adults with obesity. It is available by prescription at a dose of 120 mg tid before meals and also over-the-counter at a dose of 60 mg under the trade name Alli[®]. Small but significant decreases in fat-soluble vitamin levels may occur, and it is recommended that patients take vitamin supplements. Frequent oily bowel movements and steatorrhea often occur in patients using orlistat. Reducing dietary fat will reduce this unwanted outcome.

Lorcaserin (Withdrawn in February 2020)

Lorcaserin (Belviq[®]) was withdrawn from the market in February 2020 due the report of 7.7% incidence of cancer in the lorcaserin arm compared to 7.1% in the placebo arm.

Glucagon-Like Peptide Receptor-1 Agonists

Drugs with this mechanism of action have been approved for the management of both diabetes and obesity. In some cases the same chemical is used for both conditions, but with different trade names and different dose recommendations. In other cases, a specific drug is only approved for one indication and not the other.

Exenatide

Exenatide (Byetta[®], Bydureon[®]), approved in 1995 by the US FDA for diabetes, is a long-acting analogue of glucagon-like peptide-1. This drug delays gastric emptying and promotes a feeling of fullness after eating. In addition, some patients experience weight loss during treatment, but the drug is not approved for the management of obesity. One disadvantage of this medication is that it must be injected subcutaneously twice daily. In addition, it causes severe nausea in some patients, especially during the initiation of therapy.

Liraglutide (Marketed as Victoza[®] for Diabetes at a Dose of 1.2 or 1.8 mg/d and as Saxenda[®] at a Dose of 3.0 mg/d for the Management of Obesity)

Liraglutide has a 97% homology to GLP-1, which extends the circulating half-life from 1–2 minutes to 13 hours. The use in adult and pediatric patients with diabetes is limited to 1.2 mg/d or 1.8 mg/d. Weight loss is often observed in both adults and children with diabetes who are treated with liraglutide [29].

For the management of obesity, a higher dose of 3.0 mg/d (Saxenda[®]) should be prescribed in combination with a reduced-calorie diet and increased physical activity in adult patients with obesity who have an initial BMI of ≥ 30 kg/m² or in adult patients with a BMI ≥ 27 kg/m² and who have diabetes mellitus, hypertension, or dyslipidemia. Liraglutide has not yet been approved for the management of obesity in children.

In a meta-analysis of three studies using liraglutide, the maximal computer-modeled weight loss was -7.68 kg, and half the maximal effect occurred by 12.7 weeks [28].

This drug is contraindicated in patients with a history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2. Clinicians should not prescribe liraglutide for patients with a history of pancreatitis and should discontinue liraglutide if acute pancreatitis develops. If weight loss doesn't exceed 4% after 16 weeks, liraglutide should be stopped.

There have been two cardiovascular outcome trials with liraglutide (1.8 mg/d). In patients with diabetes mellitus, liraglutide significantly lowered the rate of the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

Combination of Two Drugs for the Management of Obesity

Two different drug combinations are currently approved by the US FDA for the management of obesity.

Combination of Topiramate and Phentermine: Extended Release

The combination of phentermine/topiramate ER (PHEN/TPM ER) (marketed as Qsymia[®]) is approved by the US FDA, but not by the European Medicines Agency. It uses lower doses of phentermine than are usually prescribed when phentermine is used alone. Phentermine acts on norepinephrine reuptake receptors, whereas topiramate may reduce appetite through its effect on GABA receptors.

A meta-analysis of six studies using the combination of phentermine/topiramate found a maximal weight loss of -15.6 kg, and the half-time for the maximal effect was 29.8 weeks using a computer-modelled approach [28]. There were improvements in blood pressure, glycemic measures, HDL cholesterol, and triglycerides with both the middle and the top doses, which were related to the magnitude of weight loss. In patients with obstructive sleep apnea, this combination reduced the severity of these symptoms.

Topiramate, alone, in the first trimester of pregnancy may increase the risk of cleft lip/cleft palate in infants, and this combination is contraindicated in pregnancy. Glaucoma is a rare side effect of topiramate, and the drug is contraindicated in glaucoma as it is in patients with hyperthyroidism and within 14 days of treatment with monoamine oxidase inhibitors. Topiramate is a carbonic anhydrase inhibitor that often produces tingling in the fingers and may affect the taste of carbonated beverages. Other potential issues include a risk for kidney stones (associated with topiramate) and increased heart rate in patients susceptible to phentermine.

Combination of Naltrexone-Bupropion: Sustained Release

Naltrexone/bupropion (Contrave[®] in the United States; Mysimba[®] in Europe) is approved by the US FDA and in Europe. Bupropion, as a single agent, is approved for the treatment of depression and for smoking cessation. It reduces food intake by acting on adrenergic and dopaminergic receptors in the hypothalamus. Bupropion alone has a modest effect on weight loss, but is not approved as a separate medication for management of obesity. Bupropion stimulates the pro-opiomelanocortin (POMC) neurons in the hypothalamus to produce α -melanocyte-stimulating hormone, which reduces food intake, and β -endorphin (which stimulates feeding). Naltrexone blocks the effect of β -endorphin on appetite, thus allowing the inhibitory effects of α -melanocyte stimulating hormone to reduce food intake by acting on the melanocortin-4 receptor system.

In a meta-analysis of six studies using naltrexone/bupropion, the maximal computer-modeled weight loss was -13.2 kg, and the half-time to the maximal effect was 35.2 weeks which was probably related to the titration schedule [28]. Treatment improved fasting glucose, fasting insulin, homeostasis assessment model of insulin resistance (HOMA-IR), and HDL cholesterol, but there was a transient increase in BP.

Best Practices for the Use of Medications Approved for the Management of Obesity

Criteria for using medications approved for long-term management of obesity were agreed upon between the 2013 American Heart Association/American College of Cardiology/The Obesity Society Guideline for the Management of Overweight and Obesity in Adults [11] and the 2015 Endocrine Clinical Practice Guideline on Obesity Pharmacotherapy [12]. Clinicians may consider prescribing medications to reduce body weight in patients who (1) struggle to achieve weight loss goals, (2) meet label indications (BMI >30 kg/m² or >27 kg/m² with comorbidities), and (3) need to lose weight for

health reasons (such as osteoarthritis, prediabetes, fatty liver, or other conditions). Furthermore, the American Association of Clinical Endocrinologists/American College of Endocrinology Comprehensive Clinical Practice Guidelines for Medical Care of Patients with Obesity from 2016 [13] indicate that clinicians may consider pharmacotherapy as a first line for weight management if patients present with one or more severe comorbidities and would benefit from weight loss of 10% or more. Those guidelines do not require that patients fail lifestyle therapy before clinicians prescribe medications.

Dietary Supplements Used to Manage Obesity

In addition to prescription medications, there are a number of agents available in pharmacies and health food stores that are touted by some to be helpful for patients with obesity [30]. Table 9.8 shows a list of some of these complementary and over-the-counter products with comments on their efficacy and safety.

Table 9.8 Complementary and over-the-counter products used by some individuals for the management of obesity

Ingredient	Proposed mechanism of action	Evidence of efficacy	Safety concerns
Chromium	Increases lean muscle mass; promotes fat loss; and reduces food intake, hunger levels, and fat cravings	Several clinical trials of varying methodological quality <i>Research findings:</i> Minimal effect on body weight and body fat	No safety concerns reported at recommended intakes (25–45 mcg/day for adults) <i>Reported adverse effects:</i> Headache, watery stools, constipation, weakness, vertigo, nausea, vomiting, and urticaria (hives)
β -Methyl- β -hydroxybutyrate	Metabolite of leucine produced in 0.3 g/d, but is taken in doses of 30–60 g/d	Used in conditions of muscle wasting and to augment muscle in athletes. A 2015 meta-analysis found HMB supplementation can preserve lean muscle mass in older adults	In humans, no adverse effects in young adults or older adults have been reported when HMB-ca is taken in doses of 3 grams per day for up to a year
Pyruvate	Increases lipolysis and energy expenditure	Few clinical trials of weak methodological quality <i>Research findings:</i> Possible minimal effect on body weight and body fat	Few safety concerns reported <i>Reported adverse effects:</i> Diarrhea, gas, bloating, and (possibly) decreased high-density lipoprotein levels
Conjugated linoleic acid (CLA)	Promotes apoptosis in adipose tissue	Several clinical trials <i>Research findings:</i> Minimal effect on body weight and body fat	Few safety concerns reported <i>Reported adverse effects:</i> Abdominal discomfort and pain, constipation, diarrhea, loose stools, dyspepsia, and (possibly) adverse effects on blood lipid profiles

(continued)

Table 9.8 (continued)

Ingredient	Proposed mechanism of action	Evidence of efficacy	Safety concerns
Calcium	Increases lipolysis and fat accumulation, decreases fat absorption	Several large clinical trials <i>Research findings:</i> No effect on body weight, weight loss, or prevention of weight gain based on clinical trials	No safety concerns reported at recommended intakes (1000–1200 mg/day for adults) <i>Reported adverse effects:</i> Constipation, kidney stones, and interference with zinc and iron absorption at intakes above 2000–2500 mg for adults
Green tea (<i>Camellia sinensis</i>) and green tea extract	Increases energy expenditure and fat oxidation, reduces lipogenesis and fat absorption	Several clinical trials of good methodological quality on green tea catechins with and without caffeine <i>Research findings:</i> Possible modest effect on body weight	No safety concerns reported when used as a beverage, contains caffeine; some safety concerns reported for green tea extract <i>Reported adverse effects (for green tea extract):</i> Constipation, abdominal discomfort, nausea, increased blood pressure, liver damage
Green coffee bean extract (<i>Coffea arabica</i> , <i>Coffea canephora</i> , <i>Coffea robusta</i>)	Inhibits fat accumulation, modulates glucose metabolism	Few clinical trials, all of poor methodological quality <i>Research findings:</i> Possible modest effect on body weight	Few safety concerns reported but not rigorously studied; contains caffeine <i>Reported adverse effects:</i> Headache and urinary tract infections
Caffeine (as added caffeine or from guarana, kola nut, yerba mate, or other herbs)	Stimulates the central nervous system, increases thermogenesis and fat oxidation	Short-term clinical trials of combination products <i>Research findings:</i> Possible modest effect on body weight or decreased weight gain over time	Safety concerns not usually reported at doses less than 400 mg/day for adults, significant safety concerns at higher doses <i>Reported adverse effects:</i> Nervousness, jitteriness, vomiting, and tachycardia
Forskolin <i>Plectranthus barbatus</i>	Activates the enzyme adenylyl cyclase and increases intracellular levels of cAMP	Oral ingestion of forskolin (250 mg of 10% forskolin extract twice a day) for a 12-week period was shown to favorably alter body composition while concurrently increasing bone mass and serum-free testosterone levels in overweight and obese men [31]	Forskolin should be used with caution or avoided altogether in women who are pregnant.
Fucoxanthin	Increases energy expenditure and fatty acid oxidation, suppresses adipocyte differentiation and lipid accumulation	Studied only in combination with pomegranate seed oil in one trial in humans <i>Research findings:</i> Insufficient research to draw firm conclusions	No safety concerns reported but not rigorously studied <i>Reported adverse effects:</i> None known

Table 9.8 (continued)

Ingredient	Proposed mechanism of action	Evidence of efficacy	Safety concerns
<i>Garcinia cambogia</i> (hydroxycitric acid)	Inhibits lipogenesis, suppresses food intake	Several short-term clinical trials of varying methodological quality <i>Research findings:</i> Little to no effect on body weight	Few safety concerns reported <i>Reported adverse effects:</i> Headache, nausea, upper respiratory tract symptoms, and gastrointestinal symptoms
Yohimbe (<i>Pausinystalia yohimbe</i> , yohimbine)	Has hyperadrenergic effects	Very little research on yohimbe for weight loss <i>Research findings:</i> No effect on body weight; insufficient research to draw firm conclusions	Significant safety concerns reported <i>Reported adverse effects:</i> Headache, anxiety, agitation, hypertension, and tachycardia
Hoodia (<i>Hoodia gordonii</i>)	Suppresses appetite, reduces food intake	Very little published research in humans <i>Research findings:</i> No effect on energy intake or body weight based on results from one study	Some safety concerns reported, increases heart rate and blood pressure <i>Reported adverse effects:</i> Headache, dizziness, nausea, and vomiting
Raspberry ketone	Alters lipid metabolism	Studied only in combination with other ingredients <i>Research findings:</i> Insufficient research to draw firm conclusions	No safety concerns reported but not rigorously studied <i>Reported adverse effects:</i> None known
Guar gum	Acts as bulking agent in gut, delays gastric emptying, increases feelings of satiety	Several clinical trials of good methodological quality <i>Research findings:</i> No effect on body weight	Few safety concerns reported with currently available formulations <i>Reported adverse effects:</i> Abdominal pain, flatulence, diarrhea, nausea, and cramps
Bitter orange (synephrine)	Increases energy expenditure and lipolysis, acts as a mild appetite suppressant	Small clinical trials of poor methodological quality <i>Research findings:</i> Possible effect on resting metabolic rate and energy expenditure; inconclusive effects on weight loss	Some safety concerns reported <i>Reported adverse effects:</i> Chest pain, anxiety, and increased blood pressure and heart rate
Chitosan	Binds dietary fat in the digestive tract	Small clinical trials, mostly of poor methodological quality <i>Research findings:</i> Minimal effect on body weight	Few safety concerns reported, could cause allergic reactions <i>Reported adverse effects:</i> Flatulence, bloating, constipation, indigestion, nausea, and heartburn
Glucomannan	Increases feelings of satiety and fullness, prolongs gastric emptying time	Several clinical trials of varying methodological quality, mostly focused on effects on lipid and blood glucose levels <i>Research findings:</i> Little to no effect on body weight	Significant safety concerns reported with tablet forms, which might cause esophageal obstructions, but few safety concerns with other forms <i>Reported adverse effects:</i> Loose stools, flatulence, diarrhea, constipation, and abdominal discomfort

(continued)

Table 9.8 (continued)

Ingredient	Proposed mechanism of action	Evidence of efficacy	Safety concerns
White kidney bean (<i>Phaseolus vulgaris</i>)	Interferes with breakdown and absorption of carbohydrates by acting as a “starch blocker”	Several clinical trials of varying methodological quality <i>Research findings:</i> Possible modest effect on body weight and body fat	Few safety concerns reported <i>Reported adverse effects:</i> Headache, soft stools, flatulence, and constipation

Adapted from National Institutes of Health, Office of Dietary Supplements with additions <https://ods.od.nih.gov/factsheets/WeightLoss-HealthProfessional/> Accessed 2016.09.12 [30]

Table 9.9 Some features of interventional surgery for the treatment of obesity

	Gastric bypass	Adjustable gastric banding	Sleeve gastrectomy
30-day mortality	0.08%	0.11%	0.50%
Complications	21.0%	13%	13%
Reoperations	2.56%	12.23%	9.05%
BMI change from baseline at 1 year	−14.5 kg/m ²	−10.5 kg/m ²	−16.2 kg/m ²
% excess body weight loss	72%	33.4%	69.7%
Diabetes remission	95%	73.9%	83% (obs studies)
Hypertension remission	81%	53.5%	83% (obs studies)
Dyslipidemia remission	80%	39%	–
Sleep apnea remission	95%	94%	–

Adapted from Chang, SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. *JAMA Surg.* 2014;149:275–87 [32]. The data from randomized controlled trials were used when available. Where they were not reported data from observational studies were used

Surgical Procedures for the Management of Obesity

Surgical strategies to treat obesity began more than 50 years ago and have now risen to over 200,000 procedures per year in the United States [1].

Surgical Procedures

There are three principal surgical procedures now widely used. Sleeve gastrectomy (SG) is the most common procedure, and Roux-en-Y gastric bypass (RYGB) is second, with laparoscopic adjustable gastric banding being less commonly used. The technically complicated biliopancreatic diversion is occasionally performed, but there is insufficient controlled data to include it. Data on the response to these three procedures are summarized in Table 9.9 [32].

Criteria for Bariatric Surgery

Criteria established in 1991 considered appropriate candidates as those with a BMI ≥ 35 kg/m² and a related comorbidity or a BMI ≥ 40 kg/m² in the absence of comorbidities as appropriate candidates for bariatric surgery. These criteria have since been modified in a joint statement by international diabetes groups indicating that bariatric or metabolic surgery is a consideration for patients with poorly controlled diabetes mellitus and a BMI of 30–35 kg/m². The Endocrine Society has also released pediatric guidelines for bariatric surgery based on the high rate of reversion of diabetes to normal glucose tolerance.

Outcomes of Bariatric Surgery

There is a low rate of mortality (see Table 9.9) as well as some serious complications that occur in about 4.1% of all patients. The experience of both the surgeon and the surgical center are predictors of surgical outcomes. Longer-term complications can include intestinal obstruction, marginal ulcer, ventral hernia, and gallstones. Additional metabolic complications include nephrolithiasis, osteoporosis, and hypoglycemia. Mineral and vitamin deficiencies and weight regain occur in a variable number of patients. Micronutrient deficiencies following gastric bypass include iron deficiency in 33 to 55%; calcium/vitamin D deficiency in 24 to 60%; vitamin B12 deficiency in 24 to 70%; copper deficiency in 10 to 15%; and thiamine deficiency in <5%. Established guidelines recommend that the healthcare provider routinely give nutrient supplementation that includes multivitamins, vitamin B₁₂, iron, minerals, calcium, and vitamin D.

There are clear benefits of bariatric/metabolic surgery that may outweigh the risks and potential complications. Weight loss is significant with most of it being retained over the long-term. The poorest weight loss following gastric bypass is comparable to the best reported weight loss for nonsurgical interventions. Changes in weight from baseline to 5 years in surgically treated groups were superior to the changes seen with medical therapy. Body weight decreased 23% with gastric bypass and 19% with sleeve gastrectomy, but only 5% with drug therapies. But like other forms of treatment for obesity, there is considerable variability of response. In a large follow-up study of patients undergoing a Roux-en-Y gastric bypass, the trajectories of initial weight loss in the first year tended to be retained for up to 7 years and varied from 12 to 45% of the initial weight. Weight loss following laparoscopic banding is similarly variable, but weight losses are only about half that seen with gastric bypass.

The single best predictors of sustained postoperative weight loss (identified by the LABS Consortium) are postoperative eating and lifestyle behaviors. Specifically, subjects who self-monitor by weighing themselves frequently and who avoid eating when full and avoid snacking between meals appear to experience the best weight loss.

The remarkable remission of T2DM following bariatric/metabolic surgery was originally noted by Pories et al. [33]. The durability of the remission was sustained for up to 7 years in many participants. There may also be a remission of dyslipidemia, sleep apnea, and hypertension following bariatric/metabolic surgery.

In the large, long-term Swedish Obese Subjects study, mortality was significantly reduced by 29% in the operated patients [34, 35] who also showed a reduction in myocardial infarction, stroke, and reduced incidence of diabetes mellitus. Cancer was significantly reduced in women.

Vagal Blockade

In addition to the major gastrointestinal procedures, there are several other surgical strategies. Vagal blockade can be produced by activating electrodes placed around the vagal trunks at the diaphragm in order to produce intermittent vagal blockade. Weight loss occurs by reducing appetite and inducing early satiety. Weight loss is modest, but superior to sham-treated controls yet less successful than conventional surgical procedures described above.

Endoscopically Placed Balloons

In 2015, the US FDA approved two intragastric balloons and a third one in 2016. The Orbera Intragastric Balloon System is filled with 400 to 700 mL of saline. The ReShape Integrated Dual Balloon System contains two connected saline-filled balloons. The Obalon Balloon System expands with air after insertion. Technical improvements to these devices have resulted in a favorable safety profile. The present protocol requires removal of these intragastric balloons after 3–6 months, which is a limitation to the long-term efficacy of this intervention. In August 2017, the US FDA sent a letter to healthcare providers noting seven deaths associated with liquid-filled intragastric balloon systems

used to treat obesity. Four of the reports involved the Orbera Intra-gastric Balloon System and one the ReShape Integrated Dual Balloon System. Two earlier deaths were also noted.

Another intra-gastric device is a specially designed percutaneous gastrostomy tube called the AspireAssist device. It allows patients to directly remove ingested food from the stomach. In a clinical trial lasting 1 year using this device, patients lost 12.1% compared to 3.6% in the control group. This aspiration technique requires available facilities to discard the aspirated food and is not for everyone.

Finally, there are two endoscopic procedures for placing a duodenal-jejunal luminal sleeve to reduce absorption of nutrients and activation of GI hormones and another which involved reducing duodenal absorptive surface by abrasion. The duodenal-jejunal luminal bypass liner shows promise. In a study that examined endoscopic ablation of duodenal mucosa, there was an enhanced glycemic control of T2DM with a reduction of HbA1c that persisted 6 months after ablation.

Liposuction

Liposuction (also known as lipoplasty or suction-assisted lipectomy) is the most common esthetic procedure performed in the United States, with over 400,000 cases performed annually. This is not generally considered a bariatric procedure, but clinicians use it to remove and contour subcutaneous fat following recovery from bariatric surgery when there is excess subcutaneous fat. The procedure involves aspiration of fat and fluid after injecting physiologic saline into fat tissue. As the technique has improved, it is now possible to remove significant amounts of subcutaneous adipose tissue. However, visceral fat and other ectopic fat deposits are unaffected. Whether this procedure improves the metabolic profile has been examined in a study by Klein et al. [36]. They studied seven women with diabetes who were also overweight and eight women with normal glucose tolerance that were overweight both before and after liposuction. The control women lost 9.1 kg of body fat, and the women with diabetes lost 10.5 kg of fat. Despite these significant reductions in body fat, there were no changes in blood pressure, lipids or cytokines, or C-reactive protein. There was also no improvement in insulin sensitivity, suggesting that the removal of subcutaneous adipose tissue without reducing visceral fat has little influence on the risk factors related to being overweight.

Conclusion

The epidemic of obesity over the past 50 years has increased by threefold the number of individuals with obesity. Since no one chooses to be fat, this has led to the search for cures for the patient with obesity. This chapter has outlined obesity as a chronic relapsing disease process for which bariatric surgery is the most effective treatment. However, many people do not want surgery, and for them there are a variety of diets, exercise programs, and behavioral programs which can be supplemented by the use of pharmacological treatment in many cases. The difficulty of reversing obesity is well recognized and poses one of the major challenges for those working on this obstinate problem.

COVID-19 Addendum

Since the time this chapter on understanding and achieving a healthy weight was completed, the world has been through the SARS-2-Cov-2 coronavirus pandemic which has affected individuals with obesity and those with diabetes more than any other group, except the elderly and nursing home residents. The impact of this pandemic on scholarly activity is shown by the fact that in March 2021, there were 337 papers, 91 of which were published in 2021, identified as related to COVID-19 and obesity in PubMed, a large medical indexing system. The impact of COVID-19 has been worldwide. This is nicely shown in the meta-analysis by Popkin et al. [37]. Individuals who were overweight/obese were 46% more likely to test positive for COVID-19, had a 113% higher risk of being hospitalized, a 74%

higher likelihood of entering an intensive care unit (ICU), and a 48% increased risk for mortality. Similar increases in hospitalization, admission to the ICU, use of ventilators, and mortality were reported by Kompaniyets et al. [38] and by Huang et al. [39]. In another meta-analysis using fully adjusted data from six studies, Hoong et al. found that the odds ratio for severe disease and mortality was more than twice that of the normal weight subjects [40]. The magnitude of the obesity also impacted outcomes. Poly et al. [41] reported that individuals with Class I obesity (BMI 30–34.9 kg/m²) had a 27% increase in mortality, those with Class II obesity (BMI 35–39.9 kg/m²) had a 56% increase in mortality, and those in Class III (BMI > 40 kg/m²) had a 92% increase in mortality. The interaction of obesity and age over 65 was particularly apparent in the rate of hospitalization and death with increasing BMI [38].

Obesity affects many systems as noted earlier, and several of these systems may be involved in enhancing the risk of the coronavirus disease [1]. First, the virus enters the respiratory system where patients with obesity may express larger amounts of the angiotensin-converting enzyme-2 (ACE-2) receptors to which the coronavirus locks on in the body [42]. This in turn may activate the complement system with lysis of cytokine-containing cells followed by the often lethal cytokine storm. If there is vitamin D deficiency, this too may augment the risk. Patients with obesity often have reduced pulmonary ventilation, and this may increase their risk of ending up on a ventilator. Thus, COVID-19 in the patient with obesity and especially those who are older is a serious risk to their health.

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