



A PHARMACY CONTINUING EDUCATION PROGRAM

W-F Professional Associates, Inc. 400 Lake Cook Rd., Suite 207 Deerfield, IL 60015 847-945-8050

May 2006 "Obesity & Its Management" 707-000-06-005-H01



THIS MONTH
"Obesity and Its
Management"

FLORIDA PARTICIPANTS—The HIV/AIDS Requirement will be addressed in the June & July lessons.

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HAVE YOU RECENTLY MOVED? PLEASE NOTIFY US.

Again, we have responded to your requests. This lesson is a direct response to feedback from participants. Our overall goal is to discuss therapeutic options. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings.

**The program ID # for this lesson is 707-000-06-005-H01.
Pharmacists completing this lesson by May 31, 2009 may receive full credit.**

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. Describe the prevalence of obesity.
2. List the etiological factors that contribute to obesity.
3. Explain the pathophysiology of obesity.
4. Describe the medical complications that may be encountered in obese persons.
5. Discuss the nonpharmacological & pharmacological methods used in weight management.
6. Describe the efficacy as well as the safety of prescription & OTC drugs used for weight loss.

All opinions expressed by the author/authors are strictly their own and are not necessarily approved or endorsed by W-F Professional Associates, Inc. Consult full prescribing information on any drugs or devices discussed.

INTRODUCTION

Obesity may be defined as a complex medical and social condition characterized by excessive accumulation of body fat stores that may result from an imbalance between calorie intake and calorie expenditure. Even though there is a distinction between the terms obesity and overweight, there is tendency to use them interchangeably. Overweight is defined as excess body being weight relative to height, using body mass index (BMI) as an indicator. The BMI is defined as weight of a person in kilograms divided by height in meters square. Obesity is a term describing the body fat contents as determined by skin fold thickness, body density using underwater body weight, computed tomography and bioelectric impedance. A person is considered obese when body fat contents exceed 30% of total weight in women or 25% in men. A percentage of body fat that exceeds 40% in women or 35% in men is considered severely obese. The aforementioned methods used to measure fat contents are considered expensive, time consuming and impractical for routine clinical purposes. Therefore, the BMI is the most widely and acceptable method of determining the extent of being overweight and/or obese. In 1998 the national Heart, Lung, and Blood Institute of the National Institute of Health announced new BMI values for Overweight and Obesity in a report titled "Clinical Guidelines on the identification, Evaluation, and Treatment of Overweight and Obesity in Adults. The report defines a BMI of < 18.5 as underweight, 18.5-24.9 as normal, 25-29.9 as overweight, 30-34.9 as obesity, and e" 40 as extreme obesity. Obesity is classified as class I (mild obesity) when BMI has a value of 30-34.9, Class II (moderate obesity) has a BMI value of 35-39.9 and class III (severe or morbid obesity) has a BMI of e" 40. Waist circumference, which is considered as a predictor of obesity, and abdominal fat content may both predict increased risk of weight related health risks. Men with a waist circumference of greater than 40 inches and women of 35 inches are at risk to develop Type 2 diabetes, hypertension and cardiovascular disease. Fat tissue deposited in the abdominal area appears to present more health risks than accumulation of fat on the hips or thighs and even in patients with normal or ideal weight.

A large segment of the population attempts to reduce their eating habits and maintain a healthy body weight. Five years ago, it was estimated that approximately 97 million adults in the US were overweight or obese, and about 44% of women and 29% of men felt a need for body weight reduction. It has been estimated that ten years ago, over \$30 billion were spent in the US On ways to lose weight. Additionally, medical costs and loss of income due to obesity reached an estimated \$68 billion. In general, men have lesser tendency than women to lose weight. Up to 66% of adolescent girls and 15% of adult females diet annually in the US. Even though diet programs, work out equipment, and exercise are widely used, obesity and being overweight are public health problems in the US that have reached epidemic proportions. Records of BMI of e" 30 kg/m² had risen in 1960 from 10.4% to 19.9% in men and 15.1% to 24.9% in women. The sharpest rise took place from 1988 to 1994. At the present time about 50% of adults in the USA are considered overweight, i.e, BMI e" 25 kg/ m². More sobering statistics show that from 1990-1994, 11.4% of children aged 6-11 were considered overweight. The alarming increase in obesity incidence has occurred in spite of the fact that so much emphasis has been placed on the importance of being slim and the use of weight loss products, exercise, and availability of books and video tapes about diet. Social pressure to be slim is mounting. Negative attitude toward obese individuals is encountered in the workplace, schools and in searching for jobs.

CE PRN® (ISSN 0199-5006) is owned and published by W-F Professional Associates, Inc.
400 Lake Cook Road, Suite 207, Deerfield, Illinois 60015.

William J. Feinberg, President

CE PRN® is published eleven times per year, monthly, January through November.
Subscription rate is \$99.00 per year. Second-Class Postage paid at Deerfield, Illinois 60015
and at additional mailing offices.

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May 2006

ETIOLOGY

Increased fat tissue deposits occur when calorie intake exceeds energy expenditure. Overeating, in particular carbohydrates and fats, results in excess energy that is usually deposited and stored as fat. Physiologically, the body responds to being underweight with an increased tendency to being hungry and decreased metabolic rate. However, the human body does not respond to combat being overweight.

There are many causes for obesity that include physiologic factors, overeating, genetic predisposition, disturbance of hunger and satiety centers in the brain, social and environmental factors, psychological factors, medical conditions and the intake of certain medications.

PHYSIOLOGIC FACTORS

The extent of being overweight and obesity is determined to a large extent by the degree of energy ingested to energy expended. The metabolic rate of an individual plays a very important role in determining energy expenditure. Resting energy expenditure (REE) is the energy expended by a resting individual. Basal metabolic rate (BMR) is defined as the resting energy expenditure recorded within a short time after awakening in the morning and no less than 12 hours after the last meal. Normally, the BMR of a person rises after a meal, depending on the amount and the make-up of the meal. The metabolic rate peaks about 1 hour after the intake of food and returns to basal level 4 hours after consumption of food. The rise in metabolic rate is referred to as the thermogenic effect of food. The difference in values between BMR and REE is 10%, and consequently the two terms are used interchangeably.

The hypothalamus contains two areas, the satiety center and the appetite center which control eating. When a normal individual eats an adequate meal, neurotransmitters such as serotonin, which normally turns off appetite, signal the satiety centers to reduce the desire to eat. Any abnormality in the satiety centers will lead to overeating and obesity. Hunger may be related to the extent of glucose utilization by glucostat cells. Low level of glucose utilization will result in a reduced inhibitory effect on the appetite centers, thereby increasing the desire for eating. Conversely, high glucose level results in inhibition of the appetite centers and the desire to eat is diminished.

GENETIC FACTORS

The discovery of the obese gene (*ob*), genetic predisposition, enhanced the understanding of the role of genetic factors in causing obesity. A relationship between this gene and the protein leptin produced in the tissues of mice has been established. It has been postulated that leptin signals the satiety centers in the brain to lower appetite. Obese mice of the *ob/ob* strains are devoid of leptin. However, when given leptin, the mice lost their appetite, resulting in weight loss. The occurrence of this phenomenon does not appear to occur in humans. Heredity and family environment studies have shown that there is a relationship between obesity and family members. This relationship exists between parents and children, and between siblings. Genetic factors of monozygotic twins who lived apart appear to contribute to approximately 70% of BMI, while family factors contribute to between 25% to 40%. A strong relationship appears to exist between BMI of adult adoptees and their biologic parents, whereas such observation is absent between adoptees and adoptive parents. Reports have indicated that 80% of children with obese parents are obese, while 40% of children with one obese parent are obese, and 10% of children with normal-weight parents.

ENVIRONMENTAL FACTORS

Environmental risk factors undoubtedly play an important role in developing obesity. Fast food and all-you-can-eat restaurants, advertising for food products, occupational factors, inactivity, life-style, social and economical factors can contribute to obesity. Jobs that require sitting behind a desk, watching television for long hours while having frequent high-calorie snacks and/or alcoholic or non-alcoholic beverages, frequent use of elevators and escalators instead of stairs, and driving even for short distances can contribute to development of obesity. Adolescent children who watch four or more hours of television are more susceptible to obesity than those who watch television for short periods of time.

PSYCHOLOGICAL FACTORS

Psychological disorders can contribute to compulsive overeating. Depression as well as childhood sexual abuse or sexual trauma often spark overeating.

MEDICATIONS AND MEDICAL CONDITIONS

There are a number of medications and medical conditions associated with weight gain. These include corticosteroids, estrogen, progesterone, testosterone, lithium, insulin, sulfonylureas, antipsychotic, and protease inhibitors. Medical conditions such as hypothyroidism, diabetes mellitus, congestive heart failure, depression, schizophrenia and pregnancy could lead to becoming overweight.

MEDICAL COMPLICATIONS OF OBESITY

Obesity may be a complicating factor for a number of conditions. Prevalence of hypertension, hyperlipidemia, insulin resistance, coronary artery disease, stroke, sleep apnea, degenerative joint disease, hirsutism, endometriosis, and cancers of the breast, colon, or prostate in patients with BMI of ≥ 25 are relatively high.

MANAGEMENT OF OBESITY

Losing weight or maintaining a weight loss is a challenge that can be achieved by a combination of diet, exercise, lifestyle change, pharmacologic therapy (if indicated) and, in certain cases, surgery. Obese individuals usually seek weight reduction to decrease risk of medical complications, improve quality of life, reduce the psychological burden which may lead to low self-esteem, enhance social acceptance and /or improve their functional status and appearance. The main objectives of management of obesity are to stop further weight increase, reduce body weight, and maintain the weight loss in the future. Even though weight loss is a lifelong challenge, it can be achieved by following a sustained obesity treatment plan. Taking extreme measures for weight reduction can be hazardous to health. Thus, it is important that the method of therapy and the risks associated with it be discussed with the patient. Some obese persons set aggressive goals to achieve normal weight, others seek a moderate approach that leads to slow and steady weight loss over a reasonably extended period of time. An initial weight reduction target of 10% is recommended. In cases where obesity is causing physical impairment such as osteoarthritis, sleep apnea, and difficult mobility, 10% to 20% should be the initial target. Drastic and quick weight reduction such as "starvation" should be avoided.

DIETARY THERAPY

Since energy stores increase when energy intake exceeds energy expenditure, dietary changes play a central role in any plan for weight loss. A dietary plan that leads to slow and steady weight loss should be selected. Diet programs range from reduction in calorie intake to adjustments in fat, protein, and carbohydrate composition of meals taken by the patient. Even though many of those programs lead to positive results in the short run, all too often, patients regain the weight they lose. The long term efficacy and safety of these programs is not clear. It has been shown that patients regain about two thirds of the lost weight within one year after the end of their plan and practically all of it after five years. Lack of will power and noncompliance often result in abandonment of such programs. Daily caloric allowance depends on gender, age, weight, and physical activity. Daily caloric intake allowance of a young man who is moderately active and weighing about 155 lbs is approximately 3200, while a male 65 years of age will need 2500 Cal. For women 25 and 65 years old weighing 130 lbs, the allowance is 2300 and 1800 Cal respectively. The intake allowance for pregnant and nursing women increases by 300 and 500 Cal respectively. An excess in intake of 3500 Cal over expenditure, assuming a steady state of physical activity, will result in an increased weight of 1 lb. Similarly, an expenditure of 3500 Cal causes a reduction of 1 lb of body fat.

There are two generally accepted restrictive dietary weight loss methods; a low-calorie diet that consists of a daily intake of approximately 800 Cal, and a very low-calorie diet consisting of an intake of from 500-800 Cal daily. Since the energy expenditure is higher than that of intake, these plans result in weight loss. However,

patients' compliance weakens with time, and lost weight is usually regained. There are a myriad of calorie-restricted diet programs. Total or modified fasts in which the patient may lose 3.5 to 5.00 lbs per week are advocated by some investigators. Such programs need to be conducted under medical supervision. A controversial dietary program that consists of high protein, low carbohydrate, and provides 800 to 1000 Cal daily has been suggested. Other low carbohydrate diets advocate eating fatty and protein rich foods as long as there are no carbohydrates included in the meal. A high-fat, low-carbohydrate diet has a short-lived success. It appears that getting the habit of eating a low-calorie or moderate-calorie (2500 to 3000 Cal daily) diet that consists of 15% protein, 30% fat (mostly of plant origin) and 55% of carbohydrate low in sucrase may give good results. Such a diet is a balanced one, and provides the vitamins and minerals needed. It should be kept in mind that patients should be advised to take vitamin and mineral supplements during any of the therapies used in treating obesity.

The use of artificial sweeteners and fat-substitutes for the purpose of reducing calorie intake has found wide acceptance. Sweeteners such as saccharin, aspartame, splenda, fructose, and sorbitol are all popular, and can result in removing a modest number of calories from the diet.

EXERCISE

Increased physical activity whether used alone or in combination with other dietary programs, is essential for the success of obesity/overweight therapy. Sustained and well planned physical activity tends to increase energy expenditure and help maintain the desired weight achieved by reduced caloric intake. The decrease in weight as a result of exercise alone is about 2 to 3% of body weight. Reliance on increased physical activity as the sole method of decreasing body weight is not advisable. It is usually used as an adjunct to dietary programs.

BEHAVIORAL THERAPY AND LIFESTYLE CHANGE

Behavioral modification and lifestyle change are essential in the long-term success of weight reduction. Identification of eating habits and adjustments need to be made. There must be monitoring of physical activity and social support through group or individual sessions.

SURGERY

Surgery should be limited to certain patients with moderate to severe obesity. The objectives of surgery are to reduce the absorptive capacity of the GI tract by reducing its surface area, and to reduce the stomach size. These procedures may result in weight loss equal to one third of the weight prior to surgery. However, surgical procedures may result in complications such as cirrhosis, cholelithiasis, nephrolithiasis, anemia, stomach stenosis and ulceration, and frequent nausea.

PHARMACOLOGICAL THERAPY

Pharmacologic management of obesity is usually reserved for moderately and severely overweight patients. In mild cases, obesity can be controlled by sustained dietary therapy, increased physical activity and behavioral modification. Drugs may be used in patients whose BMI is equal to or greater than 30, and in the absence of other conditions, as well as for patients with a BMI of 27 or greater with concurrent obesity-related disease and who experience a disappointing weight loss following low-caloric diet, exercise and behavioral modifications. It should be kept in mind that drugs should not be used as a substitute for diet and exercise, rather as adjunct therapy. Patients who respond positively to initial treatment with drugs appear to continue in their weight loss with continuation of therapy. However, patients who do not experience a significant initial weight loss, most likely will not respond to further drug use. Drugs used in the management of obesity consist of the following categories; noradrenergic agents, serotonergic agents, noradrenergic/serotonergic agents and gastrointestinal lipase inhibitors.

NORADRENERGIC AGENTS

Amphetamines: The anorexic activity of amphetamines is due to activation of the central noradrenergic receptor systems and enhancing neurotransmitter release in the CNS. These drugs, that include: benzphetamine, diethyl propion, mazindol, methamphetamine, phendimetrazine and phentermine, are not frequently used due to their CNS stimulation and potential for abuse.

Diethylpropion: Diethylpropion enhances the release of norepinephrine from presynaptic granules. This increase in the level of neurotransmitter, results in activation of the hypothalamus centers, thereby suppressing appetite. The drug may be taken in 3 daily doses of 25 mg before meals. To enhance compliance, an extended-release capsule containing 75 mg is taken once a day. Because of its CNS stimulant activity, diethylpropion may cause insomnia. It is less of a stimulant than mazindol, and causes less insomnia than phentermine.

Mazindol: Structurally, mazindol differs from amphetamine and phentermine, but possesses amphetamine-like appetite suppression activity. Mazindol acts as an appetite suppressant. It has been postulated that it acts by stimulating hypothalamic activity and inhibition of norepinephrine reuptake. The usual dose is from 1 to 3 mg once a day prior to breakfast or lunch. Dry mouth and urinary retention may be encountered. However, its CNS stimulation is not as strong as either phentermine or amphetamine. The drug is contraindicated in glaucoma, cardiovascular disease and concurrent intake of MAO inhibitors.

Phenylpropanolamine: Phenylpropanolamine (PPA) has been used in OTC drugs, both as a nasal decongestant and appetite suppressant. About 25 years ago products containing this chemical were recognized by experts as safe and effective. However, in 1991 the FDA established that active ingredients utilized for weight reduction, including PPA were not safe and effective. The FDA and the pharmaceutical industry conducted a study to investigate the risk of hemorrhagic stroke associated with the use of PPA. Results of this Project, titled the Hemorrhagic Stroke Project, were submitted to the FDA in May 2000. In November 2000 the FDA Non-prescription Drug Advisory Committee determined that PPA is not safe, and products containing this drug should be discontinued. The study revealed that a relationship exists between the use of products containing PPA and hemorrhagic stroke in women. The risk occurred in women using the weight control products within 3 days after the initial use. Despite the fact that the risk of hemorrhagic stroke is practically insignificant (1 of every 107,000 to 3,268,000 women) the FDA took this action due to the seriousness of the side effect.

Phentermine: This drug has a structure that resembles that of amphetamine and acts by enhancement of neurotransmission of both norepinephrine and dopamine. It causes less CNS stimulation than amphetamine and possesses lower potential for abuse. Like all amphetamine derivatives, it may cause an increase in blood pressure, palpitations, and arrhythmias. Additionally, it may cause a hypertensive crisis when taken along with MAO inhibitors. Due to the CNS stimulation caused by this drug and other amphetamine and amphetamine-like drugs, it should not be taken at night or before bedtime. Phentermine, for short-term therapy, is useful when administered as an adjunct to diet, exercise, and life-style change.

Ephedrine: Ephedrine is a constituent in the plant ephedra, and is often used in products for the management of obesity. Structurally it is related to PPA, and appears to act by causing the release of presynaptic norepinephrine and the stimulatory effect of the thermogenic β -adrenergic receptors. The anorexic effect of ephedrine may be enhanced by the inclusion of caffeine. The side effects of ephedrine alone or in combination with caffeine include insomnia, agitation, tremor, tachycardia, and palpitation. Due to the seriousness of the adverse effects, ephedrine-containing products have been withdrawn from the market.

SEROTONERGIC AGENTS

Serotonin is a neurotransmitter that effects sleep-wake cycles, blood pressure, emotional status, and appetite. Its main source is the amino acid l-tryptophan, which is mostly provided from food. The hypothalamic effect of serotonin leads to inhibition of appetite, and triggers satiety. Thus, an increase in the level of serotonin in the brain may cause a reduction in food intake. Serotonergic drugs at one time were used in

weight control because they acted by stimulating the release of presynaptic stores, and prevented the reuptake of serotonin, thereby increasing central concentration of this transmitter. However, two examples of the group have been discontinued worldwide due to serious adverse effects.

NORADRENERGIC-SEROTONERGIC AGENTS

Subutramine: Subutramine was approved by the FDA in November 1997 and became available on the market in early 1998. Subutramine and two of its metabolites may increase the concentration of serotonin, norepinephrine, and dopamine by inhibition of reuptake. Weight loss occurs as a result of enhancement of satiety as well as thermogenic effect. There is a tendency for regaining weight after 6 months of use. Adverse effects of subutramine include dry mouth, insomnia, constipation, dizziness, nausea, and increase in blood pressure.

LIPASE INHIBITOR

Orlistat: Orlistat was approved by the FDA in 1999. This drug represents a new approach for weight reduction. Unlike appetite suppressants, orlistat acts by preventing fat absorption from the GI tract. Compared to protein and carbohydrate, fat is a dense source of energy. One gram of fat contributes 9 Cal, whereas protein and carbohydrates are responsible for approximately 4 Cal per gram. Thus, reducing the amount of fat in meals, as well as preventing absorption of fat, can lead to weight loss. Even though the body is capable of synthesizing fat from ingested carbohydrate, diet is the major source of fat. The enzyme lipase plays an important role in the hydrolysis of fat, and the conversion of the long-chain triglycerides into free fatty acids and monoglycerides before it can be absorbed. Orlistat irreversibly inhibits lipase, thereby preventing the absorption of a significant amount of ingested fat. Unhydrolyzed triglycerides are excreted intact from the body. It has been reported that orlistat is capable of preventing the absorption of 30% of fat contents when given at a daily dose of 360 mg. Increase in dose does not result in a decrease in fat absorption. The drug should be given during meals or within one hour after the intake of food, especially one that contains fat.

Adverse effects are mostly not systemic in nature. Up to 80% of patients complained of soft or loose stools, abdominal discomfort, flatulence, and fecal urgency. Such adverse effects are usually mild to moderate, and may be experienced in the first one to two months of therapy. Since orlistat prevents absorption of significant amounts of fat, malabsorption of fat-soluble vitamins may be encountered. Patients should be advised to take vitamin supplements.

HERBAL AND NATURAL PRODUCTS

Even though the FDA does not strictly regulate the production of herbal and natural ingredients intended for weight loss, such products are widely promoted and used by many patients. Many of these lack clinical data to support safety or effectiveness, especially for weight loss. Until recently, **ma huang (ephedra)** was used in many herbal dietary supplements, in particular in combination with caffeine. The main ingredient in ephedra is ephedrine. However, such products result in serious adverse effects such as hypertension, tachycardia, stroke, seizures and death. The FDA has banned the use of such products. **Guarana** has caffeine contents higher than coffee beans. The concurrent use of this natural product with ephedra may result in serious health consequences. **Chromium** picolinate, a mineral, has been included in weight loss products and promoted as a fat metabolism enhancer. Unlike the possibly carcinogenic hexavalent form of chromium, trivalent chromium is an essential nutrient. However, its effectiveness in weight loss is unclear. **St. John's Wort** is a widely used herbal product for a variety of unproven treatments, including weight loss. The constituents of St. John's Wort, hypericin and pseudohypericin, are believed to increase synaptic concentration of serotonin and norepinephrine. However, its safety and effectiveness for weight loss are unclear.

CONCLUSION

Obesity is a public health problem that may result in medical complications such as high blood pressure, diabetes, kidney diseases, degenerative diseases, cardiovascular disease, and various types of cancer. Management of obesity requires a combination of self-discipline, compliance, diet, modification of life style, and medications, when needed.

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LESSON EVALUATION

Please fill-out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

Describe the prevalence of obesity	Yes	No					
List the etiological factors that contribute to obesity	Yes	No					
Explain the pathophysiology of obesity	Yes	No					
Discuss the treatment of obesity	Yes	No					
Describe medical complications associated with obesity	Yes	No					
Describe efficacy of OTC & prescription drugs for obesity	Yes	No					

2. Was the program independent & non-commercial?

	Yes	No				
Poor			Average		Excellent	

3. Relevance of topic to your practice

	1	2	3	4	5	6	7
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4. What did you like most about this lesson? _____

5. What did you like least about this lesson? _____

(WATCH OUR WEBSITE FOR RESULTS OF PARTICIPANT EVALUATIONS)

Quiz—Please Select the Most Correct Answer

1. Obesity is classified as mild when BMI has a value of:
 - A. 35 - 39.9
 - B. 30 - 34.9
 - C. ≥40
 - D. 25 - 29.9
2. The metabolic rate peaks about 4 hours after intake of food.
 - A. True
 - B. False
3. Which statement is correct?
 - A. Leptin causes weight gain in mice
 - B. No relationship between obesity & family members
 - C. Medications play no role in weight increase
 - D. About 80% of children with obese parents are obese
4. Daily caloric allowance for:
 - A. 65 year old male is 3000 Cal
 - B. A woman 25 years of age weighing 130 lbs is 1800 Cal
 - C. A woman 65 years of age weighing 130 lbs is 3000 Cal
 - D. A pregnant woman increases by 300 Cal
5. Noradrenergic agents are not frequently used in the management of obesity due to:
 - A. The risk of causing hyperlipidemia
 - B. Their carcinogenic activity
 - C. CNS stimulation & potential abuse
 - D. The risk of causing hirsutism
6. Patients who follow a restrictive dietary weight loss program should:
 - A. Take minerals & vitamin supplements
 - B. Sleep more than 8 hours at night
 - C. Restrict their fluid intake
 - D. Increase the intake of caffeine containing drinks
7. Phenylpropanolamine was withdrawn from use because:
 - A. It causes cancer
 - B. Causes deformity in unborn fetus
 - C. Increases risk of hemorrhagic stroke
 - D. It is completely ineffective
8. Use of mazindol is contraindicated in:
 - A. Asthma
 - B. Concurrent intake of MAO inhibitors
 - C. Arthritis
 - D. Peptic ulcers
9. The mechanism of action of orlistat:
 - A. It enhances release of serotonin from CNS
 - B. Thermogenic activity
 - C. Higher reuptake of neurotransmitters
 - D. Stops absorption of fat from GI tract
10. Which of these is not an adverse effect of orlistat?
 - A. Soft stool
 - B. Tachycardia
 - C. Flatulence
 - D. Fecal urgency

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Program ID #707-000-06-005-H01.

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