Morbidity and Treatment of Clinically Important Obesity: An Internal Medicine Perspective

J. David Fachnie
Obesity is defined as an excess storage of energy in the form of fat. Physicians know that additional morbidity and mortality is the consequence of obesity: hypertension, hypercholesterolemia, and diabetes mellitus are more common in obese persons. Less commonly appreciated is the increased risk of cancer in obese compared to nonobese persons: obese men have higher mortality from colon, rectum, and prostate cancer, and obese women have higher mortality from gallbladder, biliary passage, breast (postmenopausal), uterine (both cervix and endometrium), and ovarian cancer (1). Obesity has a complex etiology (somatic, psychologic, and sociocultural), and the numerous therapies are mostly ineffective over the long term. The obese patient continues to present a challenge to the clinician. In this review of the problem of obesity, from an internist's point of view, the following topics will be discussed: clinically important obesity, medical assessment, dietary treatments prescribed by physicians, risks and benefits of weight reduction induced by a very low calorie diet, and pharmacotherapy.

Clinically Important Obesity

Obesity can be described in many different ways. Clinically, the most commonly used term is the Metropolitan Relative Weight (MRW) scale which defines ideal weight at each height in terms of life insurance mortality statistics. The second most common term is the body mass index (BMI) which is defined as body weight in kg/(height in m²). Even modest degrees of obesity (MRW > 110%) should be noted because of the relationship to cardiovascular disease risk (2,3). The National Institutes of Health Consensus Development Conference stated that weight reduction should be recommended for all persons with a MRW > 120% (using the midpoint on 1983 tables for a medium-build person) or a BMI > 27.2 for men and > 26.9 for women (1). Risk factors for cardiovascular disease such as hypertension, personal or family history of noninsulin-dependent diabetes mellitus (NIDDM), or dyslipidemia should prompt intervention at lower levels of adiposity.

Medical Assessment

Two questions must be addressed in the medical evaluation of obese persons: What are the causative factors of the obesity, and what morbidity has the patient suffered because of obesity? The most prevalent causative factors are listed in Table 1. Although there is no doubt that much obesity can be attributed to eating behaviors that are learned, the physician should consider physical disease as a possible cause. A detailed family history will elucidate genetic factors (4). The onset of obesity, either in childhood or adulthood, as well as its exacerbation during periods of physical or psychologic stress may be helpful in understanding the factors that have contributed to the obesity. Hypothyroidism should be considered in all obese persons, but its prevalence is less than 5% of those screened (5). Hypothalamic tumors, especially craniopharyngioma, may affect the appetite center and present with obesity, headaches, and visual disturbance (6). The Cushing syndrome is exceedingly rare and should be excluded when the obesity is adult-onset and especially when hypertension, hyperglycemia, stria, and the like are present. Hypogonadism may be present in obese men, and women with polycystic ovarian disease are often obese. Persons with the Prader Willi syndrome or the Down syndrome or mental subnormality are frequently severely obese (7).
The medical morbidity of obesity is legion (Table 2). A comprehensive history and physical examination should be attempted despite the difficulties attendant to examining some persons who are severely obese. Assess the regularity of menstruation and its appropriateness relative to menopausal status; disorders of androgen metabolism and ovulation are common. Examine breasts, pelvis, rectum, and prostate. Obtain stool for occult blood. Obtain an electrocardiogram. Where indicated, obtain mammogram and proctoscopy. Obtain blood for tests of thyroid, liver function, and fasted blood for measurement of glucose, cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol. Depressed HDL cholesterol (8), fatty metamorphosis of the liver (9), and focal glomerulosclerosis (10) may be seen especially in the severely obese.

The anthropomorphic assessment of obese persons should include measurement of height, weight, waist, and hip and calculation of MRW or BMI and waist/hip ratio. The waist/hip ratio provides supplementary information about the adverse metabolic impact of the person’s obesity: adipocytes that are distributed in the gluteal-femoral region may be relatively metabolically inert, except during the latter part of pregnancy and during lactation; adipocytes that are distributed over the abdomen are more responsive to the lipolytic effects of catecholamines. The central distribution of adiposity brought about by abdominal adipocytes predominating is termed android obesity and is defined as a waist/hip ratio > 1 for men and > 0.8 for women. Android obesity is associated with cardiovascular risk factors (hypertension, dyslipidemia, diabetes mellitus) and is a risk factor for ischemic heart disease, stroke, and death. Android obesity should be treated vigorously. The peripheral distribution of adiposity is seen when the waist/hip ratio is ≤ 1 for men and ≤ 0.8 for women and is called gynoid obesity. Gynoid obesity (gluteal-femoral) may not be as responsive to treatment efforts and may not carry as adverse a prognosis (11).

### Dietary Treatments Prescribed by Physicians

The evident cause for obesity is an imbalance between energy utilization and energy intake leading to excessive fat stores in the adipocytes. According to Jequier (12), who reviewed the question of energy utilization in human obesity, a deficient energy utilization is not universally present in human obesity. That observation, if true, prompts the conclusion that excessive energy intake leads to obesity. Indeed, there may be an uncoupling between energy utilization, stimulated by exercise, and caloric intake in obese but not in lean subjects (13). Environmental (14) and neurochemical factors (15) may influence appetite and perhaps food choice. Most dietary treatments aim to redress the energy imbalance by restricting energy intake (caloric restriction) and increasing energy utilization (increasing physical activity). The present genre of medical treatments emphasize that both dietary and physical exercise modifications must be made to attain short- and long-term success with weight reduction therapy.

While numerous popular and out-of-vogue fad diets exist, physicians have traditionally limited dietary prescriptions to diets that are moderate in caloric restriction yet similar to a standard diet in the amount of carbohydrate, fat, protein, and other nutrients. These are the so-called balanced-deficit diets (BDDs). The BDD is calculated from an estimate of caloric expenditure, eg, 34 to 42 kcal/kg/day in adult men and 29 to 38 kcal/kg/day in adult women (16). By subtracting 500 kcal/day from the estimated caloric expenditure, a weekly caloric deficit leading to 0.50 kg (1.1 lb) weight loss can be expected. A 60 kg (132 lb) woman might be allowed as few as 1,240 kcal/day, and a 70 kg (154 lb) man might be allowed as few as 1,880 kcal/day. Given a protein intake of 20% of total calories, the recommended daily allowance of 0.8 g/kg/day would easily be met. The risk from these diets is minimal for all persons except the insulin-taking diabetic with close to normal blood glucose control; such persons must have downward adjustment of their insulin dose and close monitoring of blood glucose when caloric-restricted dieting begins.

Given a diet prescription, what will be the predicted weight loss in a compliant person? James (17) described equations to estimate the daily energy (E) requirements of very sedentary, mild and moderately obese persons (Table 3). Because of the reduced basal metabolic rate with dieting, the factor 1.4 should be reduced to 1.25 in all equations after one month on the diet. Once E has been calculated, the difference between E and the energy intake (I) in kcal/day will yield the daily energy gap (G). A deficit of 7,200 kcal is associated with a 1 kg (2.2 lb) loss of weight; hence, predicted weight loss can be estimated. Variations in energy expenditure among the obese are not very great (18); therefore, failure to achieve close to the predicted weight loss suggests that dietary indiscretion is at fault.

### Table 1

**Differential Diagnosis of Obesity**

- Familial
- Sociocultural
- Behavioral
- Hypothyroidism
- Mental subnormality
- Hypogonadism in males
- The Cushing syndrome
- Hypothalamic disease
- The Prader Willi syndrome
- Drug-induced

### Table 2

**Medical Morbidity Associated with Obesity**

- Hypertension
- Diabetes mellitus
- Hypercholesterolemia
- Depressed HDL cholesterol
- Obesity hypoventilation syndrome, obstructive sleep apnea syndrome
- Osteoarthritis
- Malignancy in females (breast, ovary, endometrium, cervix, gallbladder, biliary passages)
- Malignancy in males (colon, rectum, prostate)
- Cholelithiasis
- Menstrual disorders
- Hirsutism
- Coronary artery disease
- Fatty metamorphosis of liver
- Focal glomerulosclerosis
The most popular medical therapy for severe obesity is the very low calorie diet (VLCD) which is also called the protein-sparing modified fast. The VLCD is intended to promote rapid weight loss by reducing calories: between 400 and 800 kcal/day are prescribed. The dangerous loss of lean body mass from total weight loss by reducing calories: between 400 and 800 kcal/day is largely the consequence of diuresis, but a negative nitrogen balance has also been frequently observed. Other losses include potassium, sodium, magnesium, phosphate, zinc, copper, calcium, and B vitamins. Balance studies have shown that with supplementation a positive balance in sodium, magnesium, copper, and B vitamins can be obtained (19). Meticulous attention must be paid to vitamin and mineral replacement during very low calorie dieting.

Within days of starting the VLCD, a brisk diuresis and natriuresis ensues. Therefore, diuretic therapy must be used with caution. Orthostatic hypotension may be seen in some persons, especially those who fail to maintain adequate fluid and electrolyte intake. Hyperuricemia and precipitation of acute gouty arthritis may occur, although rarely. Persons on insulin or oral hypoglycemic agents must be monitored carefully with appropriate reduction of medication as indicated by frequent blood glucose measurements. Transient elevation of SGOT or SGPT is usually followed, within months, by normalization of the aberrant values (10). Cholesterol and triglyceride decrease during the VLCD; this reduction supports the impression that the patient is complying with the diet (8). Values for sodium, potassium, creatinine, albumin, calcium, and glucose remain normal in most instances but should be monitored along with liver function tests at least every four

### Table 3

**Predicting Weight Loss From a Diet***

1. **Estimating daily energy (E) requirements (kcal/day):**
   - 18 to 30 years:
     - Men: $E = 1.4(0.063 \times \text{weight} + 2.9) \times 240$
     - Women: $E = 1.4(0.062 \times \text{weight} + 2.0) \times 240$
   - 30 to 60 years:
     - Men: $E = 1.4(0.048 \times \text{weight} + 3.65) \times 240$
     - Women: $E = 1.4(0.034 \times \text{weight} + 3.5) \times 240$

2. **Specify daily dietary intake (I)**
3. **Daily energy gap (G): G = E - I**
4. **Convert kg weight loss: 7.200 kcal deficit leads to 1 kg weight loss**


*kg body weight.

### Table 4

**Indications and Contraindications to the Very Low Calorie Diet**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>&gt; 30% over MRW*</td>
<td>During growth and development*</td>
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<tr>
<td>Morbidity due to obesity</td>
<td>Pregnancy or risk of pregnancy</td>
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<tr>
<td></td>
<td>Age over 65 years*</td>
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<tr>
<td></td>
<td>Recent cardiovascular or cerebrovascular event</td>
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<td>Recent major surgery</td>
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<td></td>
<td>Major organ failure (cardiac, renal, hepatic)</td>
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<td></td>
<td>Unstable angina pectoris</td>
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<td></td>
<td>Active peptic ulcer disease</td>
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<tr>
<td></td>
<td>Untreated psychosis or depressive illness</td>
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<tr>
<td></td>
<td>Active alcoholism</td>
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*Metropolitan Relative Weight. See text for definition.
*Occasionally a very low calorie diet may be justified.

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**Risks and Benefits of Weight Reduction Induced by a VLCD**

In the late 1970s, many deaths were reportedly associated with hypocaloric dieting. In most reported cases, hydrolyzed collagen, a substance with low biologic value, was the main protein source of the diet (20). The cause of death was cardiac: myocardial atrophy was seen pathologically. Curiously, the deaths occurred earlier in the less obese than in the more obese persons, which suggested that persons with more severe obesity were relatively protected from loss of lean body mass when compared to those who were less obese (21). The present generation of VLCDs uses high biologic value protein and has been shown to produce protein sparing by decreasing body protein mobilization and increasing reutilization of body protein. The present genre of VLCDs are relatively safe when compared to the hydrolyzed collagen diets. In a comprehensive review of the VLCD, Fisler and Drenick (19) described variable loss of protein or fat over time with VLCD ingestion: during the first two weeks on a VLCD, the protein loss is 6% to 10% and fat loss is 30% to 50%; by the fourth week a stable pattern emerges with protein loss of 5% to 10% and fat loss of 70%. The early loss of lean body mass is largely the consequence of diuresis, but a negative nitrogen balance has also been frequently observed. Other losses include potassium, sodium, magnesium, phosphate, zinc, copper, calcium, and B vitamins. Balance studies have shown that with supplementation a positive balance in sodium, magnesium, copper, and B vitamins can be obtained (19). Meticulous attention must be paid to vitamin and mineral replacement during very low calorie dieting.
weeks. The dangerous cardiac arrhythmias and myocardial atrophy associated with the hydrolyzed collagen fasts are not seen in the presently used VLCD (22). However, an electrocardiogram should be obtained periodically; pay particular attention to rhythm and the QT interval (23).

Obese women who experience irregular menstrual cycles have elevated levels of blood androgens whether or not hirsutism is present (24). Weight reduction may ameliorate the hyperandrogenic state. One consequence of weight loss is the resumption of ovulatory menstrual cycles; two patients in our clinic conceived unexpectedly while on the VLCD. Because the VLCD may be unsafe for use during pregnancy, we urge the use of effective birth control methods and warn against pregnancy in all reproductive-age women on the VLCD, regardless of the history of fecundity.

The three major morbidities of obesity (hypertension, hypercholesterolemia, and diabetes mellitus) are improved by weight reduction. The relationship of obesity and hypertension is discussed in an excellent review article in this Journal (25). The dyslipidemia of obesity is characterized by elevation of cholesterol and depression of HDL cholesterol. During the period of weight loss induced by a VLCD, the total cholesterol and triacylglycerides fall; after the VLCD is completed, when the person is maintaining a stable, lower weight, the HDL cholesterol is higher and the cholesterol/HDL cholesterol ratio is lower than before the diet—a favorable change from the standpoint of cardiovascular risk (8, 26, 27). Persons who are genetically at risk for NIDDM will carry a greater risk for becoming overtly hyperglycemic if factors that increase the target cell resistance to insulin action are present. Obesity is associated with hyperinsulinemia and resistance to the action of insulin; the binding of insulin to target cells is diminished (28, 29). The VLCD will reduce blood glucose and hyperinsulinemia in obese persons with NIDDM (30, 31). Despite weight reduction, defects in the first phase of insulin release by the pancreas may not reverse (32).

The safety of the VLCD depends on careful prescribing of a high biologic value, nutritionally complete supplement to carefully selected, compliant persons. Few deaths have been attributed to the present genre of VLCDs. The efficacy of the VLCD is excellent in terms of its ability to induce rapid weight loss with safety, typically 1 to 2 kg/week (22). A recent study of weight loss in a combined VLCD and behavior therapy program has reported that poor patient compliance adversely affects long-term maintenance of weight loss (33). Adverse behaviors include 1) premature withdrawal from the VLCD prior to achieving goal weight, and 2) failure to enroll in a weight maintenance program after the VLCD to help sustain weight loss.

Pharmacotherapy

Current therapy for obesity emphasizes behavioral modification to change adverse eating behaviors, reduction of caloric intake, and rarely surgical treatment. Anorexic agents have fallen into disfavor because of side effects, abuse potential, and uncertain long-term efficacy. Douglas and Munro (34) recommend antiobesity drugs if dietary treatment has failed after four to eight weeks. Galloway et al (35) state that weight regain after discontinuation of antiobesity drugs limits their indications to short-term goals such as presurgery weight reduction. Stunkard et al (36) obtained evidence that fenfluramine treatment resulted in more long-term weight regain than behavior therapy alone. The possibility that combinations of available anorexics may achieve similar degrees of weight loss with fewer side effects is promising (37). The declining clinical use of available anorexics will not reverse until their cost/benefit ratio is shown to be more favorable. The atomistic approach to developing new antiobesity drugs is well summarized by Sullivan et al (38).

Final Comment

Each obese person should be counseled about the known medical risks of obesity. This counseling is best done in a supportive and nonjudgmental way. Referral for obesity treatment should be appropriate to the patient's risk from the disorder: for milder obesity, give dietary advice; for severe obesity, refer to a well-run multidisciplinary obesity treatment program. Curative treatments for obesity are not on the horizon. The benefits of treatment cannot be assessed solely by the rate of recidivism after a specified period of time. Periodic weight loss may be beneficial to obese persons even if substantial relapse of obesity subsequently occurs (8). Obese persons who are regaining weight lost must be encouraged to return promptly to the obesity treatment program. Patients who attend maintenance programs that incorporate exercise and diet modification will be more likely to sustain weight loss.

References

13. Pi-Sunyer FX. Exercise effects on calorie intake. Part III. Control of cal-


