

## Current Views on Obesity

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**Although the disorders associated with obesity have been extensively studied, little attention has been paid to the fact that obesity is itself a chronic disease. This misunderstanding of the nature of obesity has contributed to the stigmatization of obese persons and to the use of inappropriate or inadequate treatment regimens. Although the etiology of obesity is still unclear, genetic, metabolic, and social factors are all believed to play a role in its development and progression. Behavioral therapy, exercise, very-low-calorie diets, drug therapy, and surgery affect the treatment of obesity of differing levels of severity. The regaining of weight following treatments other than surgery is very frequent, in part because periods of weight loss are rarely followed by maintenance programs. An increasing awareness of the chronic, multifactorial nature of obesity will ideally lead to the development of new long-term treatment programs that are safe and effective. Such programs are urgently needed in light of new data that show that the prevalence of obesity is increasing in the United States, as much as 30% in the last decade.**

The medical hazards of obesity and the chronic diseases in which it plays a causal role have been extensively documented,<sup>1-5</sup> and it has recently been estimated that 280,000 deaths a year are attributable to "overnutrition," making it second only to smoking as a cause of death.<sup>6</sup> Below are some of the disorders through which obesity exerts its effect.

Obese persons are at considerably higher risk than lean ones for developing hypertension, dyslipidemia, insulin resistance, and hyperinsulinemia.<sup>1-3</sup> In addition to being responsible for these coronary risk factors, obesity is also an independent risk factor, although compared to other risk factors, it is not a particularly strong one.<sup>1,7</sup> Upper-body obesity, however, strongly predisposes to coronary heart disease, independent of the overall level of obesity.<sup>2,5</sup> Noninsulin-dependent diabetes mellitus is strongly associated with obesity;

80% of all type II diabetics are obese and the prevalence of diabetes increases with increasing age and increasing body weight.<sup>2</sup> Gallstones appear in 30% of obese persons compared to 10% in nonobese ones.

Obesity is also associated with abnormal pulmonary function, including sleep apnea, and progressing to the obesity/hypertension (pickwickian) syndrome.<sup>8</sup> Overweight men have significantly higher mortality rates for colorectal and prostate cancers, and overweight women have significantly higher rates of endometrial, cervical, ovarian, gall bladder, and breast cancers.<sup>2</sup> The incidence of osteoarthritis and gout increases with increased weight, even in non-weight-bearing joints. Furthermore, all risks associated with obesity are increased with increasing weight and are very high in patients with severe obesity, who have a body mass index (BMI) that is >40 or who weigh 100% above ideal body weight.<sup>9</sup>

As important as the overall level of obesity in obesity-related diseases is the distribution of body fat.<sup>10,11</sup> This distribution is often measured by the waist-hip ratio, with upper-body obesity defined as a waist-hip ratio of more than 1.0 for men and 0.8 for women. Risk, however, is directly proportional to the size of the waist-hip ratio, independent of gender; the greater mortality of men is a function of their greater waist-hip ratio. Some authorities believe that waist circumference and sagittal diameter are more accurate indicators of body-fat distribution than the waist-hip ratio.<sup>11</sup>

To the ill effects of obesity has been added, in recent years, concern about the effects of the regain of body weight following weight reduction, so-called "weight cycling." Such regain is all too common.<sup>12</sup> Drenick and Johnson<sup>13</sup> found that only 2% of severely obese persons who had reduced their weight by fasting and semistarvation had not returned to pretreatment weight after 9 years. Goodrick and Foreyt<sup>14</sup> reported that only about 5% of patients trained in the behavioral self-management of obesity achieved long-term success.

It has been reported that weight cycling increases upper-body fat, alters metabolic rate to make later efforts at weight reduction more difficult, and even increases mortality rates. Fortunately, more recent studies have not supported these dire predictions. Reviews of the studies on animals by Prentice<sup>15</sup> and Reed and Hill<sup>16</sup> and on humans by Wing<sup>17</sup> indicate that weight cycling has no effect on metabolic variables. Wadden et al<sup>18</sup> have confirmed that weight cycling has no long-term metabolic effects, nor does it increase upper-

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body obesity, and Jeffery et al<sup>19</sup> have found no effect on cardiovascular risk factors. Existing data on the relationship between weight loss and mortality are limited because they have not distinguished between voluntary and involuntary weight loss.<sup>3,20</sup>

### **WHY OBESITY SHOULD BE CONSIDERED A CHRONIC DISEASE**

Despite the acknowledged association between obesity and chronic disease, relatively little recognition has been given to the fact that obesity is itself a chronic disease. And a very common disease it is! It has increased by 30% in the last 10 years, and now afflicts 35% of American women and 31% of American men.<sup>21</sup>

A chronic disease is a disruption of bodily function that develops slowly, sometimes insidiously, and persists for an extended period, often for the life of the affected individual.<sup>22</sup> Treatment for a chronic disease aims at alleviating symptoms rather than curing it.<sup>23</sup> Obesity is now beginning to be characterized as a chronic disease,<sup>23-25</sup> and a review by Bray and Gray<sup>23</sup> stands out. It compares the obese patient with one having asymptomatic hypertension. Both require chronic treatment but may be unwilling to seek medical help, follow a prescribed regimen, or continue treatment when treatment-related side effects are experienced.

Another noteworthy discussion of obesity as a chronic disease is the 1993 review by Yanovski.<sup>26</sup> She argues that, although it fits the model of a chronic disease, obesity is rarely considered to be a disease at all. When it is acknowledged to be a disease, obesity tends to be considered more like a subacute illness that will respond to a time-limited course of treatment and eventually be cured. The fallacy of this approach is indicated by the fact that most well-motivated patients treated with current techniques regain most of their weight within 5 years. Yanovski asserts that regarding obesity as a chronic disease of multifactorial origin has several benefits: it decreases the stigma associated with obesity; recognizes it as a heterogeneous disorder that, like hypertension, should be treated on an individualized basis; and encourages physicians and their patients to develop realistic treatment goals.

Kral<sup>9</sup> has proposed that the impact of obesity on quality of life is comparable to that of a number of chronic diseases, while Gortmaker et al<sup>27</sup> showed that its impact on social functioning is as devastating. Seven years after adolescent girls were identified as being overweight, they had completed fewer years of school, were less likely to be married, and had higher rates of household poverty than did women who had not been overweight. These effects were more pronounced than those of several other types of chronic illness.

### **ATTITUDES OF HEALTH CARE PROFESSIONALS TOWARDS PERSONS WITH OBESITY**

Discrimination against obese persons is said to be the last acceptable form of prejudice, and, it is sad to say, this prejudice occurs even among physicians and other health care professionals.<sup>28</sup> Bray<sup>29</sup> has reported that questions about the moral worth of obese persons appear as long ago as the writings of Hippocrates and that more overtly negative attitudes were expressed by Galen and many eminent 18th- and 19th-century European physicians.

At the beginning of their medical careers, as medical students, physicians harbor negative, moralistic attitudes towards obese persons,<sup>30,31</sup> and such attitudes persist throughout their careers.<sup>32,33</sup> Frank<sup>34</sup> contends that discrimination extends even to physicians who specialize in the treatment of obesity, who are viewed by their peers as ethically suspect, engaged in tedious and ultimately futile treatment of unappealing patients. It has been proposed that these negative attitudes stem from the belief that lack of will-power is a cause of obesity<sup>35</sup> and that obese persons are weak-willed and self-indulgent.

Patients are fully aware of their physicians' negative attitudes. Murphree<sup>36</sup> found that obese patients may feel that their physicians' treatment methods are unrealistic. More disturbing was Rand and Macgregor's survey<sup>37</sup> of severely obese gastric surgery patients: 78% reported having been "always or usually" treated disrespectfully by their doctors because of their weight.

### **THE ETIOLOGY OF OBESITY**

The ultimate cause of obesity is an imbalance between caloric intake and energy expenditure, but the pathologic mechanisms that lead to this imbalance are still not understood.<sup>38</sup> Obesity is believed to be of both genetic and environmental origin, involving excess caloric intake, decreased physical activity, social and economic forces, and metabolic and endocrine abnormalities.<sup>1,4,39</sup>

#### **Genetic Factors**

The role of inheritance in obesity was first suggested by the ease with which adiposity can be produced by the selective breeding of farm animals and later by the occurrence of several forms of genetic obesity in rodents.<sup>40</sup> The genes coding for several of these forms of obesity have been localized and two have recently been cloned. The product of one of them, the *ob* gene, may form part of a signalling pathway from adipose tissue to brain centers controlling food intake.<sup>41</sup>

Studies of humans have begun to extend the role of heredity to human obesity.<sup>42</sup> The first studies, using the classic twin method, estimated very high levels of heritability—approximately 80%. Even studies

of identical twins separated at birth, a method that avoids some of the bias of classic twin studies, estimated heritability at about 66%. Although these studies are still widely cited, there is a growing consensus that they overestimate the influence of heredity. Adoption studies and complex segregation analyses agree on a heritability of the BMI of about 33%, a value now viewed as a more reasonable estimate than that of the twin studies.<sup>43,44</sup>

If only 33% of the variance in body weight is due to genetic influences, environmental influences are clearly of great importance. The most systematic studies of environmental factors are those of socioeconomic status. There is a strong inverse relationship between socioeconomic status and the prevalence of obesity, particularly among women, with lower socioeconomic status favoring the development of obesity.<sup>45</sup> A recent review cites two large longitudinal studies that have shown that causation underlies this correlation and concludes that one of the most powerful risk factors for obesity is growing up in a lower-class environment.<sup>45</sup>

Environmental influences on obesity include both energy intake and energy output. After years of uncertainty about the contribution of excessive food intake to the development of obesity, the introduction of doubly labelled water to measure energy expenditure, and so energy intake, has made it clear that obesity is associated with increased food intake.<sup>46,47</sup> Although diet histories have been shown to be inaccurate records of the amounts and types of food actually consumed,<sup>48</sup> it appears that this increased food intake is facilitated by fat in the diet, the content of which has risen from 32% to 40% or more in the past half century. Not only does fat increase the palatability of food, but it is also converted into body fat far more efficiently than are carbohydrate and protein. Furthermore, unlike carbohydrate and protein, dietary fat is poorly regulated<sup>49</sup>; excessive intake of fat at one meal is not followed by decreased intake at the next meal.

The second environmental factor promoting obesity is the sedentary lifestyle so prevalent in the United States today.<sup>50</sup> This lifestyle has resulted from the proliferation of labor-saving devices that have transformed the nature of work and of leisure-time activities. It is the rare person today who works the long hours at heavy labor, and even the home presents fewer opportunities for physical activity. The lessened physical activity contributes significantly to the obesity of genetically predisposed persons.

## TREATMENT

The goals of treating obesity have been radically revised by the evidence that weight losses of 10% or less of body weight are sufficient to greatly reduce the medical complications of obesity. Accordingly,

we no longer seek to reduce patients to "ideal" weight, but instead focus attention on losses of 5% to 10% of body weight and on long-term maintenance of body weight.<sup>51,52</sup>

The recent review, "Weighing the Options," by the Institute of Medicine, divides methods of treatment into three categories: (1) "do-it-yourself" programs that include diet books and articles and self-help ("lay-led") approaches such as Overeaters Anonymous and Take Off Pounds Sensibly (TOPS); (2) "non-clinical" (commercial) programs such as Weight Watchers and Jenny Craig; and (3) "clinical" programs that provide medical care as well as more aggressive therapies, such as very-low-calorie diets, medication, or surgery.<sup>53</sup>

A primary task of physicians is to manage the health complications of their obese patients. They may also manage their patients' efforts at weight control, particularly with highly motivated patients who are only mildly overweight and require only infrequent contact.<sup>1,23</sup> Significantly obese persons, however, usually require greater structure and support. For them, the physician may be most useful in helping them select from among the many treatment options and in encouraging them to continue treatment.<sup>53,54</sup>

We consider four treatment modalities for obesity: (1) behavior therapy, (2) very-low-calorie diets, (3) medication, and (4) surgery.

### Behavior Therapy

As applied to obesity, behavior therapy refers to a set of principles and techniques designed to modify eating habits and physical activity. Behavior therapy for obesity is based on the assumptions that all behavior is acquired and maintained according to certain definable principles, that people are more accurately described by their behavior than by dispositional tendencies, that treatment measures should be specified as precisely as possible and outcomes evaluated as objectively as possible, that treatment should be individualized, and that progress should be assessed throughout the course of treatment.<sup>55</sup>

In most behavioral weight-control programs, treatment occurs in a group format, with 5 to 12 persons in clinical programs and groups of 80 or more in some lay-led programs.<sup>56</sup> Treatment, which usually consists of weekly, hour-long sessions, tends to be more didactic than is traditional group therapy. These sessions focus on facilitating adherence to dietary and exercise regimens. Exercise can enhance the effect of dieting, perhaps because obese people who exercise do not compensate for their increased energy expenditure by increasing their food intake. They thus lose weight at a rate that is directly related to the amount of energy expended during exercise.<sup>57,58</sup> Treatment usually continues for 10 to 20 weeks, al-

TABLE

Appetite-Suppressant Agents Currently Available in the United States<sup>70,71</sup>

| Therapeutic Class and Agent | Daily Dose<br>DEA <sup>*</sup> Schedule | Trade Names                              | Range (mg) |
|-----------------------------|---|--|------------|
| Noradrenergic agents        |   |  |            |
| Benzphetamine               | III                                     | Didrex                                   | 25-150     |
| Diethylpropion              | IV                                      | Tenuate, Tepanol                         | 75         |
| Mazindol                    | IV                                      | Mazanor, Sanorex                         | 1-3        |
| Phentermine                 | IV                                      | Adipex, Fastin, Ionamin, Obenix, Zantryl | 12-37.5    |
| Phenylpropanolamine         | Over the counter                        | Acutrim, Dexatrim                        | 25-75      |
| Serotonergic agent          |   |  |            |
| Fenfluramine                | IV                                      | Pondimin                                 | 60-120     |

\*DEA = Drug Enforcement Agency.  
Adapted from Bray.<sup>70</sup>

though programs lasting for 6 months or more are increasingly used. Attrition rates tend to be low, averaging less than 20%, although attrition tends to increase with time.<sup>56</sup>

Behavior therapy programs are most helpful for mildly to moderately obese patients.<sup>1,59</sup> In recent years, these programs have produced weight losses that average 8 kg in 15 to 20 weeks or about 0.5 kg (1 lb) per week. Longer therapy produces larger weight losses, but they rarely exceed 15 kg, even in treatments that last 1 year.

During the first year after treatment, patients in behavioral programs typically regain about one third of the weight they had lost. Weight regain can be minimized if patients maintain frequent, regular contact with their provider following treatment and particularly if they engage in regular physical activity for 2 to 3 hours a week. In a notable study of 160 male police officers, those who continued to exercise largely maintained their 12-kg weight loss for at least 18 months, while those who did not regained almost all of the weight that they had lost.<sup>60</sup>

The best long-term results have been obtained by Björvell and Rössner,<sup>61</sup> who treated severely obese patients initially in a 5-d/wk, 6-week hospital outpatient program and then in regularly scheduled "booster sessions." The mean weight loss of 68 subjects remained at 12.6 kg at 4 years and in the 43 who continued, at 10.6 kg at 10 years. This study showed that long-term maintenance is possible, but it was achieved only with a very heavy investment of time and money.

### Very-Low-Calorie Diets

Very-low-calorie diets, which usually provide 400 to 800 kcal/d, are designed for patients who are at least 30% overweight and who have failed to lose weight by conservative measures. They produce weight losses of 20 to 25 kg at a rate of approximately 1.5 kg/week in women and 2.0 kg/week in men.<sup>62,63</sup> These diets provide 45 to 100 g/d of high-quality pro-

tein, sufficient to maintain lean body mass, and are generally safe when limited to 12 to 16 weeks under careful medical supervision. Candidates for these diets should be referred to programs that combine medical supervision with comprehensive efforts at behavior change. Patients regain about one third of the weight they have lost in the year following treatment and most of the rest in the next 2 years.

The chief shortcomings of very-low-calorie diets are the intensity of the required medical supervision, which is expensive and inconvenient for patients, and the regain of the weight that has been lost. For these reasons, very-low-calorie diets are losing the popularity they once enjoyed.

### Medication

After years of neglect, pharmacotherapy of obesity is attracting increasing interest and there is every reason to believe that it will become a major modality in the treatment of obesity.<sup>64,65</sup> This interest has arisen partly from the growing awareness of the limitations of behavior therapy and partly from a revision of the views on medication that had led to its virtual abandonment. These views had two causes. Although the potential for abuse of amphetamines has been known since shortly after the drugs were introduced, it was renewed attention to these abuses by unscrupulous "diet doctors" in the Hart hearings of 1968 that led to the banning of amphetamines, and a concurrent disinclination on the part of physicians to use other, safe and effective, medications.<sup>66,67</sup> The other cause for the abandonment of medication was the widespread, mistaken belief that tolerance developed to the effects of appetite-suppressant medication. Because of this belief, state medical boards severely limited the duration of use of these medications.<sup>68</sup>

It is now clear that this belief was inaccurate. Although there are, of course, persons who do not respond to appetite-suppressant medication, in most patients it retains its effectiveness for as long as it is used. As soon as it is discontinued, however, weight

rebounds to pretreatment levels. Newer findings reverse the old argument favoring short-term treatment and suggest that appetite-suppressant medication should be used on a long-term basis or not at all.<sup>69</sup> A list of the agents currently available for the treatment of obesity in the United States is shown in the **Table**.

In an early large-scale, 6-month study, *dl*-fenfluramine was used, either in comparison or in combination with behavior therapy.<sup>72</sup> The medication alone produced weight losses of 14.5 kg, and combined with behavior therapy, 15.3 kg; behavior therapy alone produced losses of 10.9 kg. When medication was discontinued, weight was promptly regained. More recently, a double-blind, placebo-controlled trial combined *dl*-fenfluramine with phentermine and behavior therapy in various combinations and for various periods of time over 3.5 years.<sup>73</sup> Overall, weight losses of 14 kg were achieved and well maintained for as long as patients received medication. Again, when medication was discontinued, weight returned to pretreatment levels, reinforcing the view that medication should be used on a long-term basis or not at all.

No new medication for the control of obesity has been introduced in the United States for 20 years, and the practitioner is confined to the use of the agents listed in the Table. Nevertheless, drug development has continued and new and potentially more effective medications may be introduced in the near future. Prominent among them is *d*-fenfluramine, the dextrorotatory isomer of the agent described above, which acts by enhancing the release of serotonin into the synapse and inhibiting its reuptake.<sup>74</sup> *d*-Fenfluramine has been used extensively in Europe and was the subject of a large multicenter, placebo-controlled trial.<sup>75</sup> In this trial, patients receiving *d*-fenfluramine lost 11% of their body weight and maintained this loss for a period of 1 year, compared with a weight loss of 8% by placebo patients, who regained part of the weight they had lost.

Another investigational agent is sibutramine, which blocks the reuptake of norepinephrine and, to a lesser extent, serotonin and dopamine.<sup>76</sup> In an 8-week double-blind, placebo-controlled trial, patients who received a low dose (5 mg) lost 1.5 kg more than patients who received placebo and those who received 20 mg lost 3.6 kg more. Both losses were statistically significant.

Another approach to the pharmacologic treatment of obesity is provided by lipase inhibitors, designed to reduce the absorption of dietary fat by preventing the hydrolysis of triglycerides.<sup>77</sup> In a 12-week, double-blind, placebo-controlled trial of the lipase inhibitor orlistat, patients in the treatment group lost 4.3 kg, compared to 2.1 kg in the placebo group.<sup>78</sup> The difference was statistically significant, although of questionable clinical importance in weight control.

The agent may, however, be useful in the reduction of dietary fat.

### Surgery

The treatment of choice for severely obese persons is surgery. Candidates are those who are more than 100% overweight or whose BMI is >40.<sup>79</sup> Persons may also be considered for surgical treatment at lesser degrees of overweight if they also suffer from significant comorbidity. The first operation, jejunoileal bypass, has been replaced by two gastric restriction procedures.<sup>80</sup> In the vertical-banded gastroplasty, a pouch of 15- to 30-mL capacity with a narrow stoma into the remainder of the stomach is constructed, which greatly reduces the amount of food that can be eaten at any one time. In the gastric bypass, a larger pouch, which empties into the jejunum, is created. Nutrients thus bypass the duodenum and much of the stomach. A "dumping" syndrome, characterized by weakness, nausea, and sweating, caused by too-rapid absorption of carbohydrate into the jejunum, is often the result. This dumping may be the cause of the somewhat greater weight losses with gastric bypass.

Weight losses following surgery depend upon the extent of the initial overweight and average from 40 to 70 kg.<sup>81</sup> Weight losses reach their maximum at about 2 years and are reasonably well maintained for another 2 to 3 years.

Surgical treatment is surprisingly well tolerated, even by extremely obese persons. In centers that specialize in this treatment, perioperative mortality does not exceed 1% and morbidity is less than 10%. Such good results depend upon highly skilled teams, and surgery should be undertaken only in programs that specialize in this treatment and that have demonstrable records of safety and efficacy.

The benefits of surgical treatment are impressive, with major reductions in comorbidity and prevention of further complications of the obesity. There is a marked decrease in noninsulin-dependent diabetes mellitus, hypertension, hyperlipidemia, respiratory distress and, in fact, in almost all complications of obesity.<sup>80</sup> The most striking indication of improvement is the increased life expectancy of operated persons, which approaches actuarial standards of the general population.<sup>81</sup> The psychological benefits of surgery are comparable, with marked improvement in psychosocial functioning, rate of employment, annual income, and other quality-of-life measures.<sup>82</sup>

### CONCLUSION

The view that obesity is a chronic disease is increasingly accepted, with major benefits to many obese persons who suffer from the complications of this disorder. Recent advances in the understanding of the origins of obesity, particularly its genetics,

promise significant help in the future. In the meantime, treatment will improve as it is increasingly viewed as a lifetime endeavor that requires careful individualization. The long-term use of medication is a particularly favorable prospect.

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