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THE PATHOPHYSIOLOGY OF ANOREXIA NERVOSA AND BULIMIA NERVOSA

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CONTENTS

Anorexia nervosa has been recognized as a distinct nosological syndrome for well over a century (23, 34), whereas bulimia has only recently been defined as a clinical entity (3). Descriptions of the phenomenology of both disorders date back to the Middle Ages and earlier (5). The onset of anorexia nervosa tends to be in early or middle adolescence, a time of accelerated physical and psychological growth and development. Bulimia occurs more commonly in late adolescence and young adulthood; females are predominantly affected in both disorders (14, 58). In mild cases, single episodes of anorexia nervosa and bulimia are common. More severely affected patients tend, without therapeutic

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intervention, to have a chronic deteriorating course that, in the case of anorexia nervosa, can result in death.

DIAGNOSTIC CRITERIA AND DIFFERENTIAL DIAGNOSIS

Other illnesses leading to food refusal and weight loss must be distinguished from anorexia nervosa. The loss of appetite and the aversion to food in organic illness, depression, hysterical disorders, and schizophrenia lack the drive for thinness, the fear of weight gain, and the pleasure in losing weight, all of which are typical features of anorexia nervosa. It is also important to note that even though the term anorexia nervosa connotes loss of appetite, hunger awareness and appetite are intact in anorexia nervosa unless the patient has reached a moribund state. Both Crohn's disease and ulcerative colitis have been reported in anorexia nervosa but are rare occurrences.

The morbid hunger and polyphagia of bulimia are not difficult to differentiate from the Klein-Levine syndrome, Froehlich's syndrome, and the Prader-Willi syndrome, all of which have their onset at a young age and are associated with multiple other symptoms, such as periodic somnolence, hypogonadism, and mental deficiency. In psychogenic vomiting (26) the regurgitation process reveals a symbolic meaning and, if present at all, the preoccupation with body weight or shape are not intense.

The attempt to outline concise diagnostic criteria in the DSM-III (3) has not been entirely successful. As a result most research centers retain a modification of the operational criteria originally proposed by Feighner et al (21).

1. Active refusal by the patient to eat enough or to maintain a normal body weight for age and height and/or sustained efforts to prevent food from being absorbed.
2. Intense fear of becoming obese, fear that does not diminish as weight loss progresses.
3. Loss of at least 25% of original body weight, or in children of 15% of weight- and height-adjusted body weight.
4. Body image disturbances (e.g. failure of the body image to adjust to the progressive emaciation).
5. Primary amenorrhea of at least three months duration.
6. No known physical illness that could account for the weight loss.

ANOREXIA NERVOSA

The prevalence of anorexia nervosa has been estimated to be slightly less than 1% in teenage girls (age 12–18 years) and seems to be on the rise (14). The condition is rare in boys, the female-to-male ratio being about 20:1. Boys are

typically affected during prepuberty or early puberty. Anorexia nervosa shows a familial and genetic pattern. Holland and associates (27) found nine of sixteen monozygotic twins concordant for anorexia nervosa as opposed to one of fourteen dizygotic twins. In the discordant pair the affected twin was more likely to reach menarche second and to be the less dominant one. An advanced maternal age at the patient's birth has been described (59) and relatives of patients seem to be more often affected than the general population.

The cause of anorexia nervosa is unknown. It seems to be a multifactorial disease. In a society with excess food, a high value is placed on thinness, which becomes representative of beauty, health, and self-control and hence efforts at weight control are culturally supported. The initial weight loss in anorexia nervosa is not always the result of a deliberate decision to diet. Physical illness, a gastrointestinal disorder, mononucleosis, or influenza can result in accidental weight loss that is then deliberately carried further. Individual personality traits that stand out include a drive for perfection and an excessive need for achievement; they are used to compensate for personal shortcomings and a low self-esteem. Bruch (8) has postulated perceptual disturbances in the recognition of hunger, satiety, or fatigue, and a sense of inadequacy. From a developmental viewpoint, anorexia nervosa can be conceived as avoidance of the adult female body, in particular avoidance of the sexual changes associated with puberty. Familial factors include excessive performance expectations and a tendency toward overweight among family members. A common denominator necessary to trigger the full syndrome is a starvation state with body weight dropping below the constitutional weight.

Nutritional Intake

Regardless of what stimulated the initial weight loss, a feature invariably found in anorexia nervosa is the patient's pleasure in the low weight for personal and emotional reasons. This promotes the deliberate decision to sustain and further the weight loss. The decision is also supported by a phobic attitude that the patient develops toward weight and food. Any weight gain generates severe anxiety; weight loss reduces this anxiety.

Weight loss maintenance and its promotion then become the overriding goal in the patient's life. To this end, thoughts about how to restrict calories are constantly on the patient's mind and determine her meals.

The type of food eaten depends largely on the patient's knowledge about the nutritional value of food. Initially, deleting carbohydrates from meals is considered the fastest way to lose weight, thus dessert and sweets are banned. Instead, low-calorie vegetables, fruit, and green salads are consumed in larger amounts. Next, fatty foods are eliminated. There is a taboo on gravy, butter, salad dressing, and whole milk. The food reduction occurs gradually but occasionally can be as drastic as a fast with no meals eaten; in either case it is done surreptitiously.

The low-calorie foods eaten may vary considerably and reflect individual preference. One patient may find it easier to prepare a concoction of 2% milk, cauliflower, and eggs and eat small amounts throughout the day, another lives exclusively on apricot juice, a third likes fish and eats swordfish steak each day, in addition to salads without dressing, cantaloupe, and plums.

Supplemental vitamin intake has been shown to be highly variable (12). Urged by concerned parents, many patients agree to take one or another kind of vitamin supplement. In our study (12) about half the patients regularly took vitamin preparations with or without mineral supplements. Given the general catabolic state of an anorectic patient the amount of vitamins taken may well exceed the need. Another half of the patients did not take any vitamins, either because they were not provided at home or patients believed that the fruit and vegetables supplied sufficient vitamins. Classical vitamin and trace mineral deficiency states are rare; if they occur, they are more often found in the chronic restricting or debilitated patient. For example, we found plasma zinc levels within the low normal range, but there are exceptions in which zinc levels drop to 50% of normal values (12, 19). The slow tissue catabolism associated with the reduced metabolic rate and the supplemental vitamins added to foodstuffs protect against full-blown deficiency states. However, minor signs indicative of a combined lack of vitamin and nutrient are not infrequently observed. Scalp hair loss is common, fine lanugo-like hair grows on the face and the trunk. The skin becomes rough and scaly and petechial, and ekchymoses may appear. Silverman (55) described hypovitaminosis A in 62% of teenage patients and hypercarotenemia in 52%.

Another factor that introduces considerable variation in the nutritional status is the preferred or practiced dieting pattern. Two types of dieting prevail: the fasting, abstaining, or restricting type and the so-called bulimic type (10).

In the bulimic type of diet, patients are unable to fast consistently and fall into a pattern of periodic overeating in binges. Binge eating initially occurs in spurts but gradually becomes a habit. A few patients compensate for the binge eating through prolonged abstinence but most seize upon self-induced vomiting either alone or in combination with laxative and/or diuretic abuse as a means to get rid of excess calories. There is good evidence that the two dieting types reflect different personality styles and constitute psychopathological subtypes of anorexia nervosa. Since many studies on medical complications in anorexia nervosa conducted before 1980 did not take note of these differences in the eating pattern, some of the findings need to be reconsidered in light of this new information.

The Consequences of Starvation

Each patient's body tolerates malnutrition in different ways, depending on such variables as (*a*) weight at onset, (*b*) speed of weight loss, (*c*) duration of illness, (*d*) self-induced vomiting, and (*e*) use of diuretics or laxatives.

The starvation effects observed in acute anorexia nervosa tend to be similar to but not altogether like those observed in famine, largely because protein deprivation is not predominant. Yet it must be realized that the caloric restriction generally is severe enough to lower body weight levels pathologically and to override the physiologic adjustments that normally result from the low caloric intake, for example lowering of the metabolic rate, decreased heat loss, lowered blood pressure, and hypothermia. The patient with acute anorexia nervosa presents a picture of both undernutrition and malnutrition to varying degrees for prolonged periods of time. Nevertheless, outright growth retardation leading to short stature is unusual, perhaps because most cases of restricted caloric intake start after age 13, when most girls have already had their first growth spurt.

Younger patients are at risk for growth retardation. Pugliese et al (48) recently described a group of children who fit a pattern of growth failure due to malnutrition. Because of their fear of becoming obese, these children had imposed chronic moderate dieting upon themselves, but they did not otherwise fit criteria for anorexia nervosa.

The starvation state of anorexia nervosa can perhaps best be compared to the semistarvation experiments conducted by Keys and Brozek (30) in Minnesota in the late forties. A group of 32 healthy young men, conscientious objectors, were subjected to semistarvation for 24 weeks, with normal physical activity being maintained despite a reduction in intake to an average of 1570 calories/day. Subsequently, the men were studied during 12 weeks of nutritional rehabilitation. A large amount of data was collected not only on the physiological but also on the intellectual and emotional effects of starvation. Table 1 contrasts the behavioral and psychological observations in these normal volunteers on a semistarvation diet with observations in anorexia nervosa patients.

Physiologic and Metabolic Abnormalities

The physiologic and metabolic changes in anorexia nervosa are a function of the duration and severity of the reduced intake and the degree to which body weight has been lost. Figure 1 illustrates how this can vary in patients. The 12-year-old was treated early on and recovered in a brief time, whereas the 14-year-old suffered a relapse and rebound excessive weight gain after refeeding before she settled to a lower weight. With body weight losses of 25% or more (calculated for height and age) or a body mass index [weight/(height)^2] under 16, the emaciation is obvious although the patient does her best to conceal the signs. The skin is cold and pale with acrocyanosis, the bony structure is prominent, and the patient looks old beyond her age.

CARDIAC STATUS The most common and frequent electrocardiographic (ECG) change is sinus bradycardia with a pulse below 60 beats per minute (31,

Table 1 Comparison of psychological and behavioral changes in semi-starvation and anorexia nervosa

Change	Starvation	Anorexia nervosa
Mood or feeling state	Lack of initiative; labile mood, quarrelsomeness; indecisiveness; deterioration of personal appearance; continuous hunger.	Initiative high; labile mood, alternating with feeling good; "strong-willed"; pride in personal appearance, occasional exhibitionistic tendencies; hunger present, but easily suppressed.
Mental content	Thinking and dreaming about food; concentration of interest on food with narrowing of unrelated interests; daydreaming, reading, and conversing about food.	Same as in starvation, but preoccupation with thoughts of food continues after weight gain.
Eating behavior	Bizarre tastes; preference for bulky foods and hot meals; dwelling a long time over meals; picking up crumbs; bulimia.	Same as in starvation, but low-calorie foods and fluids are preferred, and carbohydrates are avoided.
Activity level	Fatigue; avoidance of physical exertion; restlessness and periodic quickening effect.	Seemingly inexhaustible energy; physical exercise sought; overactivity; restlessness with periodic quickening.
Sexual activity	Decrease in sexual fantasies, feelings, and interests; impotence; amenorrhea.	Same as in starvation; amenorrhea can precede weight loss.

44, 60). We have observed heart rates as low as 34 beats per minute. S-T segment depression and T-wave morphological changes can be observed, mostly in those patients who use vomiting to lose weight. The blood pressure is usually low, below 100/50 mm Hg. Kalager and associates (29) found left ventricular functional impairment using systolic ejection time and cardiac output.

A systematic study of the effects of anorexia nervosa on body composition and body function in a fairly uniform population of thirty-one teenage patients (19 girls and 12 boys) was reported by Fohlin (22). The average weight loss in this group was 26% for the girls and 25% for the boys. Only four patients had heart rates faster than 60 beats per minute, with a mean heart rate of 53 beats per minute. Heart volume was significantly correlated to blood volume. Blood volume in turn and total body potassium correlated significantly with body weight. Glomerular filtration rate and renal plasma flow were reduced. Patients did not normalize their concentrating capacity following vasopressin adminis-

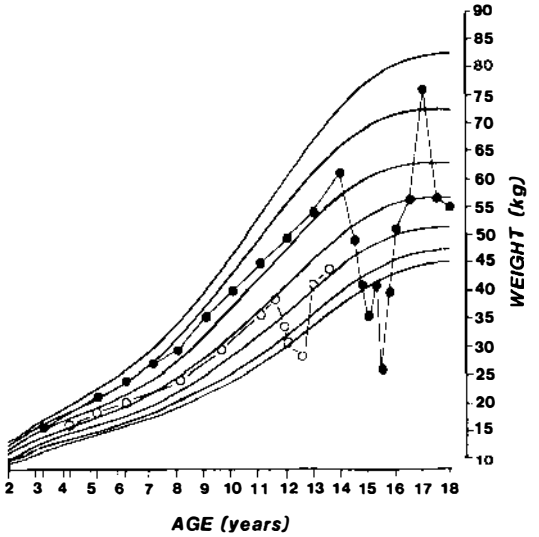

Figure 1 Body weight curves illustrating normal growth, weight loss during anorexia nervosa, and weight gain during and following nutritional rehabilitation and treatment.

tration, which suggests a concentrating defect of renal origin, reversible after rehabilitation. ECG abnormalities, such as low voltage, bradycardia, and T-wave inversion, were common. The maximal heart rate and maximal oxygen uptake in response to exercise were markedly decreased. Fohlin (22) concluded that all pathophysiological findings indicated a functional adaptation to the decreased caloric supply.

Other functional changes may include increased overall motility, which is surprising because, given the emaciation, a conservation of energy and fatigue would be expected. The continued high activity level probably plays a role in maintaining bone structure, because fractures are rarely observed (1% in our sample). Nevertheless, sophisticated methodology has revealed osteopenia (4) and osteoporosis (51). Changes in sleep structure occur (15), with early morning awakening and nocturia being common. Taste recognition and acuity are reduced; the taste for salty and sweet substances is preserved the longest (12, 33).

Gastric motility is significantly reduced with delayed gastric emptying (18, 54). Patients are at risk of superior mesenteric artery syndrome (57). The syndrome involves vascular compression of the distal portion of the duodenum (45), which leads to vomiting and abdominal pain. The compression can be alleviated through positional changes and is probably the result of weight loss.

Hematologic changes include mild anemia with anisocytosis, leukopenia (sometimes pronounced) with relative lymphocytosis, and on occasion thrombocytopenia resulting in ecchymoses. In young patients bone marrow hypopla-

sia is not uncommon. The 16-year-old patient in Figure 1, for example, had the following findings: red blood cells were reduced to 2.5×10^6 per μl, with a hemoglobin to 8.6 g% and a hematocrit to 25.3%. Morphologically there was anisocytosis and poikilocytosis. The white cell count was 3000 per μl of which 22% were granulocytes and 78% were lymphocytes, with 1 myelocyte. The fasting blood sugar was 47 mg%. Most of the time, blood glucose levels remain in the low normal range. Liver enzymes are often elevated. The BUN tends to be on the low side, unless there is superimposed fluid restriction. Plasma cholesterol and plasma carotene levels tend to be increased.

Endocrine Changes

Ever since Simmonds' publication on hypophyseal cachexia (56), anorexia nervosa had been considered a pituitary deficiency disease; but recently it became clear that virtually all endocrine changes were starvation induced. A full review of the endocrinology of anorexia nervosa is beyond the scope of this paper, and the reader is referred to the publications on this topic (6, 7, 62).

Once body weight drops below 60% of normal weight in the course of anorexia nervosa, virtually every endocrine system is affected.

THE HYPOTHALAMIC-PITUITARY-GONADAL AXIS (HPG) The hypothalamic-pituitary-gonadal system is usually involved the earliest. Originally it was believed that amenorrhea signalled a hypothalamic defect because in about a third of the cases menstruation ceases before a substantial weight loss has occurred. There is currently no evidence to support this hypothesis of a primary hypothalamic dysfunction (6). A more likely assumption is that initial dietary alterations in combination with emotional stress disrupt the HPG axis in patients vulnerable to such influences. For most patients the onset of amenorrhea occurs as body weight drops below the normal range. Subsequently, the luteinizing hormone (LH) secretion pattern regresses to continuously low LH plasma levels resulting in reduced ovarian stimulation, low estradiol levels, and nonmeasurable progesterone levels. In acute anorexia nervosa, LHRH stimulation fails to trigger a LH-follicle-stimulating (FSH) response.

HYPOTHALAMIC-PITUITARY-THYROID AXIS Clinically, anorexia nervosa patients display several signs of hypothyroidism, hypothermia, cold intolerance, bradycardia, constipation, a diminished basal metabolic rate, and raised levels of cholesterol and carotene. Nonetheless, TSH plasma levels remain in the normal range. Similarly, the TRH-induced TSH rise is normal in magnitude, albeit slightly delayed in occurrence (11) compared to normals.

The hypothyroidism in anorexia nervosa differs from true hypothyroidism since normal or low normal thyroxine (T_4) concentrations along with normal serum levels of protein-bound iodine are found along with depressed tri-

iodothyronine (T_3) levels. Moshang and coworkers (41) have demonstrated that in anorexia nervosa, as in conditions of starvation, there is reduced T_3 formation from T_4 and preferential deiodination to 3,3-5-triidothyronine (reverse T_3), a metabolically less active isomer of T_3. This combination of lowered T_3 and the rise in reverse T_3 probably accounts for the hypothyroid status in anorexia nervosa.

HYPOTHALAMIC-PITUITARY-ADRENAL AXIS (HPA) In anorexia nervosa, plasma cortisol levels tend to be increased with raised or normal urinary "free" cortisol levels (9). Weiner (62) has reviewed the reasons for the increased mean plasma cortisol concentrations. There is evidence that the low-T_3 syndrome (41) prolongs the half-life of cortisol in plasma by delaying its metabolic clearance. There also seems to be an activation of the HPA in anorexia nervosa. Calculated for body mass and body surface area, the cortisol production rate (CPR) is significantly elevated in anorexia nervosa and the number of secretory episodes of cortisol are increased. Thus when dexamethasone is administered to patients with anorexia nervosa, their plasma cortisol levels are not suppressed.

What accounts for the HPA activation is not known. Among the possibilities would be an increased release of corticotropin-releasing hormone (CRH) or hypersensitivity of adrenal cortical cells to CRH stimulation. Weight gain to the normal premorbid weight reverses these changes, as well as all other endocrine changes in anorexia nervosa.

Treatment

Because of the complexity of the disorder, anorexia nervosa requires a multivantage treatment approach: a supervised refeeding program supports body weight normalization; personality problems are explored in individual psychotherapy, which also assists the patient in becoming aware of the reasons for her exclusive attention to food and weight; and family therapy examines the kind of interaction and the relationships between family members that permitted the syndrome to develop.

In this section I focus on the nutritional rehabilitation programs. For obvious reasons, adequate nutrition is of utmost importance in the acutely ill, severely underweight patient. Moreover, without correcting the starvation state and the starvation-induced emotional and cognitive changes, the patient will physiologically and emotionally not be able to benefit from psychological treatment. Nevertheless, weight restoration and refeeding requires the patient's tacit or explict cooperation if it is to succeed, regardless of whether it is accomplished on an outpatient basis or, as is more often the case, in hospital. Even tube feeding or hyperalimentation cannot be performed unless the patient consents and complies, in principle.

The approach we have found useful is to discuss and negotiate a detailed

treatment contract with the patient and her parents before treatment begins or before hospitalization. This procedure allows the patients to express what is emotionally tolerable, it engages their active collaboration by leaving some control in their hands, and it presumes progress will be consistent and predictable.

Restoration of normal body weight is accomplished in two steps. The first is to correct the malnutrition until most physical signs of the acute starvation state, including sleep difficulties, restlessness, and morbid dwelling on food, have subsided. To this end, weight needs to be brought to about 80% of normal. This part is considered the medically necessary treatment. During the second phase, the patient is given more leeway to gain weight at her own pace. Both a short-term and long-term treatment outline are negotiated. The short-term plan is periodically revised and the long-term plan details the desirable weight and psychologic changes necessary for discharge and reducing the risk of relapse. It is expected that by virture of their pathology patients will at times undermine or challenge the treatment plan. However, if the reasons for their manuevering can be explored and understood patients usually abide by the arrangement.

For adolescents the desirable body weight is extrapolated from the Iowa Growth Charts. Parents are asked to obtain the pediatric weights; these are then plotted on the Iowa Growth Charts, and the respective growth curves form the basis for predicting optimal weight. We tend to prescribe a low rather than a high normal weight. In our sample only two of 85 patients had become pathologically overweight six years later.

For implementing the refeeding program, intense nursing care is mandatory, administered by trained, experienced, emotionally mature and infinitely patient nurses. The procedure itself is simple: Initially only a liquid nutrient (Meritene®, Ensure®, or Sustacal®) is offered at regular intervals in six divided meals.

Depending upon the patient's age, height, and physical condition, from 1400 to 1800 calories (250–300 calories per meal) are offered for the first three days. This calculation is based on the Boothby and Berkson Food Nomogram (17). Confronted with this liquid diet regime most patients will, despite having been informed beforehand, protest and claim they would prefer pizza or milk shakes. If offered these foods, however, they will refuse them. Eliminating food initially relieves the patient from agonizing over what and what not to order and then what and what not to eat. Between 30 and 45 minutes are allowed to finish each meal. Unless there is excessive dehydration with oliguria or excessive fluid loss through sweating, no extra fluids are permitted. A record of fluid and caloric intake and output is kept for at least two weeks. Subsequently, only the caloric input will be recorded until the patient has reached a normal weight. The patient is weighed every morning (or sometimes less often for therapeutic reasons) in a gown on the same scale after voiding and the weight is recorded.

Every aspect of the program is explained in detail to invite the patient's cooperation. If the patient ignores her meals or refuses to drink the nutrient, the treating physician is called and the reasons for her refusal are explored and the patient is encouraged to drink. The nursing staff praises the patient's efforts and meets attempts at subterfuge and sabotage with good-humored firmness. Much time is spent talking with the patient during the first week, persuading her to eat again. By the second week the patient usually has a good appetite and follows the schedule on her own. The emotional reactions to eating and weight gain are explored in individual psychotherapy and family therapy. Care is taken to monitor the patient's reactions in order to avoid overstressing her, which can trigger acute disintegration and self-destructiveness.

This broad outline is followed with some flexibility. Adjustments for individual patients or young patients may be necessary; however, the patients themselves will be the first to challenge individual special adjustments, arguing that equal treatment is fair and unequal treatment is unfair. If patients are known to have vomited after meals, they remain under supervision in the common area for 45 minutes after each meal or they go to school supervised. If this arrangement does not provide sufficient control, the bathroom doors are locked. Depending upon the patient's readiness, food is introduced as one meal at a time under dietary guidance. Patients are expected before discharge to eat three meals and not to skip meals. Deliberate attempts are made to involve the patient in hobbies, homework, or activities unrelated to eating. It is important that the dietary and nursing staff be knowledgeable about anorexia nervosa so that they answer patients' questions and be helpful. For example, the distorted sense for bodily proportions extends to meal size. Patients generally overestimate and complain about the size of meals. On the other hand, in order to gain weight at a reasonable rate, 3000 calories and often more eventually need to be consumed. Unless meals are offered frequently, this carries the risk of binge eating. For this reason we retain dietary supplements as snacks. Agras et al (2) observed a positive correlation between meal size and amount of food eaten by the patient. As a result, some hospitals offer double meals from the beginning. Such a policy can induce cardiac decompensation (47) and risks teaching the patient to overeat.

BULIMIA NERVOSA

Put in simplest terms, bulimia nervosa starts as an attempt at weight control and ends as a loss of self-control. The term *bulimia* denotes a ravenous appetite or literally "ox hunger" associated with powerlessness. *Kynorexia* ("fames canina," known to Xenophon about 400 BC) or "dog hunger" historically has been in use for a syndrome that closely resembles bulimia nervosa and in which large

quantities of food were devoured without any feeling of satiation, ultimately leading to fullness, abdominal pains, and vomiting.

The critical behavior in bulimia nervosa is binge-eating episodes and the experience of a distressing sense of loss of control during overeating. There is agreement that dieting is a precondition for the development of binge eating, i.e. there is an attempt to replace normal physiological controls with cognitive rules. Thus, the disorder starts with dieting attempts in which hunger feelings become ravenous and lead to binge eating as a result of prolonged abstinence. Once patients discover that they can undo the consequences of binge eating by vomiting out the ingested food, they tend to restrain their binge eating less and begin to resort to binge eating not only when they feel hungry, but also when they feel tense, anxious, or are experiencing other distressing emotions.

Bulimia is described in the Diagnostic and Statistical Manual (3) as an eating disorder separate from anorexia nervosa.

A. Recurrent episodes of binge eating (rapid consumption of a large amount of food in a discrete period of time, usually less than two hours).
B. At least three of the following:
   1. consumption of high-caloric, easily ingested food during a binge;
   2. inconspicuous eating during a binge;
   3. termination of such eating episodes by abdominal pain, sleep, social interruption, or self-induced vomiting;
   4. repeated attempts to lose weight by severely restrictive diets, self-induced vomiting, or use of cathartics and/or diuretics;
   5. frequent weight fluctuations of greater than ten pounds due to alternating binges and fasts.
C. Awareness that the eating pattern is abnormal and fear of not being able to stop eating voluntarily.
D. Depressed moods and self-deprecating thoughts following eating binges.
E. The bulimic episodes are not due to anorexia nervosa or any known physical disorder.

Strictly applied, the criteria tend to be overinclusive because severity parameters such as frequency of binge eating or vomiting are lacking, and binge eating alone suffices for the diagnosis. Furthermore, bulimia as a syndrome is not uncommonly associated with anorexia nervosa (10). Typically, however, it occurs in young college-age women of normal weight or slightly overweight women.

Epidemiological surveys (13, 25) using these criteria have found a high incidence of binge-eating behavior in college populations (between 46 and 79% in females and from 41 to 60% in males). If more restrictive criteria are applied, such as a daily occurrence and vomiting or laxative abuse, the rates drop to 2–13% for women and 1.4–6.1% for males (42, 49).

Eating Pattern and Abnormalities

Bulimic patients rarely eat normal meals. Forced by parents or by circumstances (for instance, by social occasions), most patients either consume very little or do not retain the ingested food. In the fully developed syndrome, binge eating is precipitated by a variety of conditions. Anxiety and tension (1), frustration (40), and depression in association with hunger (10) or simply the sight or smell of food or eating may trigger binge-eating episodes. During these episodes patients tend to consume "forbidden" food, high in carbohydrate and fat content such as ice cream, doughnuts, or bread and butter; others may eat leftovers or half-frozen unpalatable food. The food is consumed rapidly, without dwelling on the taste, and in secrecy. Patients are aware that the bulimic behavior pattern escapes voluntary control and takes on a life of its own; they describe it as an addiction to food.

The size of a binge varies considerably, with a range from 1,000 to 20,000 calories (38). Some patients begin to binge eat in the morning but the majority omit eating in the morning and begin to binge at midday. Most of the binge eating is done in the evening and at night when there is less of a chance of being interrupted. Following the binge, patients tend to feel uncomfortably full and become anxious and worried about any weight gain; they feel guilty and humiliated by the knowledge of having lost control and hence seek to undo the overeating, most commonly by regurgitating the ingested food. Vomiting eventually becomes coupled to binge eating; it can become a habit. Most patients overeat with the forethought of vomiting afterwards.

Impulse dyscontrol in bulimic patients is not limited to eating but is more generalized: shoplifting, particularly of food, is not infrequent, alcohol may be consumed to excess, and patients may be self-destructive. In severe cases the chaotic eating pattern tends to be a reflection of a severe personality dysfunction expressed in serious family problems and difficulties in personal relationships.

The weight of most bulimic patients varies considerably: weekly fluctuations of 5–25 lb are not unusual. Patients are extremely sensitive to such weight swings and react to the slightest weight gain with despair, a reaction that then sets off another bulimic cycle.

Medical Complications

The physiologic effects and the medical complications of bulimia are less well known than those of anorexia nervosa because until recently the incidence of bulimia was very low. Overeating alone causes weight gain. It leads to gastric dilatation (28, 52) and on rare occasions to gastric rupture. Most medical complications are the result of excessive vomiting; patients may vomit up to twenty times daily and can vomit between 2 and 3 liters of fluid during one episode (38). The excessive use of laxatives or diuretics also causes medical complications (See Table 2) (43).

Table 2 Medical complications of bulimia nervosa

Mouth	Gum disease, teeth decalcification, caries; swelling of salivary glands; pharyngitis—hoarseness
Gastrointestinal tract	Rumination
	Esophagitis
	Gastric dilation and rupture; elevated serum amylase
Liver	Abnormalities in liver function
Blood	Dehydration; hypokalemia; hypochloremia; alkalosis
Cardiac	S-T changes; arrhythmia; cardiac arrest
Renal	Polydipsia; polyuria; elevated BUN; kidney (tubular) damage
Skin	Ekchymoses on face and neck; dehydration—edema; bruises and lacerations over knuckles
CNS	EEG abnormalities

ELECTROLYTE AND FLUID DISTURBANCES The excess body fluid lost through vomiting results in fluctuations in the serum potassium levels, with hypokalemia, hypochloremia, and metabolic alkalosis (39). If vomiting episodes exceed five times daily, serum potassium concentrations can drop to dangerously low levels, usually around 2.5 meq/liter and rarely as low as 1.8 meq/liter. In such cases potassium supplements are indicated. Patients themselves rarely notice or mention cardiac symptoms such as irregular heart beats or palpitations because they seem to develop a high tolerance for feeling physically unwell. Thus potassium level monitoring becomes important and potentially life-saving.

With prolonged bulimia nervosa, esophageal reflex and herniation invariably occur. Rumination may occur with bulimia and persist after cessation of vomiting. To date little is known about the long-term effects of chronic induced vomiting upon the gastrointestinal tract. Dental enamel erosion and gingivitis occur. Swelling of the submaxillary salivary glands is common and may be diagnostic (16, 35) as might be a hoarse voice.

The irregular food intake results in constipation, which is cited as a reason for using laxatives. Laxative and diuretic use can become addictive behaviors, with patients developing tolerance to their effects and using ever-increasing amounts. Such patients are difficult to treat and generally require hospital supervision for withdrawal. Prolonged vomiting without diuretic abuse can result in kidney damage. In our follow-up investigation of 85 anorexia nervosa patients eight years after illness onset, two patients (whose vomiting started at age 12 and 16 years, respectively) had severe kidney damage with one patient requiring a kidney transplant.

Menstrual abnormalities in the form of oligomenorrhea, dysmenorrhea, and irregular menstruation are common. The endocrine investigations published so far, however (24), suffer from poor experimental control. Abnormal dexamethasone suppression tests have been reported, but in these studies the

overeating-vomiting pattern was not fully controlled. Initial reports of EEG abnormalities (a 14- and 6-per-second spike pattern) in compulsive eaters (50) were not confirmed in a recent study (37). Only four of 25 EEG tracings of bulimic patients were considered abnormal. Since bulimia has only recently come to clinical attention, little is known about its long-term course.

Treatment

The most immediate and manifest goal of treatment is to normalize the eating pattern. A variety of approaches have been used to assist the patient in regaining control over her eating.

PURELY PSYCHOLOGICAL STRATEGIES Most psychological approaches encourage the patient to make an explicit commitment to change. A combination of nutritional, educational, and self-monitoring techniques (63) are employed to increase awareness of the maladaptive behavior. An intervention program then seeks to change the eating behavior, to influence its antecedents and consequences, and to teach adaptive skills. A cognitive behavioral paradigm has been described by Fairburn (20), and recently the results of a behavioral self-monitoring approach combined with supportive psychotherapy were published by Lacey (32). Both approaches solicit the patient's active participation in the treatment program and seem to work well, provided that the patient is highly motivated and only moderately disturbed.

PHARMACOLOGICAL TREATMENTS The hypothesis that bulimia represented a depressive illness variant provided the rationale for the pharmacotherapy of bulimia. It was assumed that if the depressive-dysphoric states, anxiety, and tension that triggered bulimia would improve with antidepressant drugs, then patients would be less apt to use overeating to relieve these emotions. The following paragraph briefly summarizes the controlled drug trials.

Sabine et al (53) treated 50 bulimic patients with mianserine in a double-blind placebo-controlled trial over eight weeks. No differences in binge frequency, vomiting, or depression ratings were noted between drug and placebo groups. Imipramine given to 19 bulimic patients in a controlled study by Pope et al (46) markedly reduced the intensity of binge eating and decreased depressive symptoms. Mitchell & Groat (36) treated 32 bulimic outpatients with a behavioral program and amitriptyline (150 mg at night). The authors found a marked antidepressant effect in drug-treated patients and equal improvement in eating behavior for both groups. Walsh et al (61) recently published the results of a controlled 10-week treatment study with the monoaminoxidase inhibitor (MAOI) phenelzine sulfate (from 60 to 90 mg maximum) in 20 bulimic patients. Drug-treated patients dramatically reduced binge frequency from a mean of 12 per week to 2 per week as opposed to placebo-treated patients who

showed no change. Although eating attitude scores dropped significantly, Hamilton depression ratings, which were low initially (<17), showed little change. One third of the patients entered into this study were unable to tolerate the side effects such as orthostatic hypotension, diarrhea, and sleep problems or they could not observe the dietary restrictions.

These studies suggest that antidepressants have a place in the treatment of bulimia, but further studies are required to identify the patient who will benefit from medication.

With a combination then of nutritional counselling, psychologic family and social therapy, and pharmacotherapy most patients can improve; however, most bulimic patients have great difficulty following through with any treatment plan.

Literature Cited

1. Abraham, S. F., Beumont, P. J. V. 1982. How patients describe bulimia or binge eating. *Psychol. Med.* 12:625–35
2. Agras, W. S., Barlow, D. H., Chapin, H. N., Abel, G. G., Leitenberg, H. 1974. Behavior modification of anorexia nervosa. *Arch. Gen. Psychiatry* 30:249–86
3. American Psychiatric Association. 1980. *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: Am. Psychiatr. Assoc. 3rd ed.
4. Ayers, J. W., Gidwani, G. P., Schmidt, I. M., Gross, M. 1984. Osteopenia in hypoestrogenic young women with anorexia nervosa. *Fertil. Steril.* 41:224–28
5. Bell, R. M. 1985. *Holy Anorexia*. Univ. Chicago Press
6. Beumont, P. J. V. 1979. The endocrinology of anorexia nervosa. *Med. J. Austr.* 1:611–13
7. Brown, G. M. 1983. *Endocrine alterations in anorexia nervosa*. In *Anorexia Nervosa: Recent Developments in Research*, ed. P. L. Darby, P. E. Garfinkel, D. M. Garner, D. V. Coscina, pp. 231–34. New York: Liss. 455 pp.
8. Bruch, H. 1973. *Eating Disorders*. New York: Basic Books. 396 pp.
9. Casper, R. C., Chatterton, R. T., Davis, J. M. 1979. Alterations in serum cortisol and its binding characteristics in anorexia nervosa. *J. Clin. Endocrinol. Metab.* 49:406–11
10. Casper, R. C., Eckert, E. D., Halmi, K. A., Goldberg, S. C., Davis, J. M. 1980. Bulimia—its incidence and clinical importance in patients with anorexia nervosa. *Arch. Gen. Psychiatry* 37:1030–40
11. Casper, R. C., Frohman, L. A. 1982. Delayed TSH release in anorexia nervosa following injection of thyroptropin-releasing hormone (TRH) *Psychoneuroendocrinology* 7:59–68
12. Casper, R. C., Kirschner, B., Sandstead, H., Jacob, R. A., Davis, J. M. 1980. An evaluation of trace metals, vitamins, and taste function in anorexia nervosa. *Am. J. Clin. Nutr.* 33:1801–8
13. Cooper, P. J., Fairburn, C. G. 1983. Binge-eating and self-induced vomiting in the community—a preliminary study. *Br. J. Psychiatry* 142:139–44
14. Crisp, A. H., Palmer, R. L., Kalucy, R. S. 1976. How common is anorexia nervosa? A prevalence study. *Br. J. Psychiatry* 128:549–54
15. Crisp, A. H., Stonehill, E. 1976. *Sleep, Nutrition and Mood*, pp. 21–24. London/New York/Sydney/Toronto: Wiley. 173 pp.
16. Dawson, J., Jones, C. 1977. Vomiting-induced hypokalemic alkalosis and parotid swelling. *Practitioner* 218:267–68
17. Division of Biometry and Medical Statistics. 1933. *The Boothby and Berkson Food Nomogram*. Rochester, Ohio: Mayo Clinic
18. Dubois, A., Gross, H. A., Ebert, M. H., Castell, D. O. 1979. Altered gastric emptying and secretion in primary anorexia nervosa. *Gastroenterology* 77: 319–23
19. Esca, S. A., Brenner, W., Mach, K., Gschnait, F. 1979. Kwashiorkor-like zinc deficiency syndrome in anorexia nervosa. *Acta Dermatol. Venereol.* 59: 361–64
20. Fairburn, C. G. 1984. Bulimia nervosa. In *Epidemiology and Management in Eating Disorders*, ed. A. J. Stunkard, E.

Stellar, pp. 235–58. New York: Raven. 280 pp.
21. Feighner, J. P., Robins, E., Guze, S. B., Woodruff, R. A., Winokur, G., Munoz, R. 1972. Diagnostic criteria for use in psychiatric research. *Arch. Gen. Psychiatry* 26:57–63
22. Fohlin, L. 1977. Body composition, cardiovascular and renal-function in adolescent patients with anorexia nervosa. *Acta Paediatr. Scand.* 1977 (Suppl. 268):7–20
23. Gull, W. W. 1873. Anorexia hysterica (apepsia hysterica). *Br. Med. J.* 2:527–32
24. Gwirtsman, H. E., Roy-Byrne, P., Yager, J., Gerner, R. H. 1983. Neuroendocrine abnormalities in bulimia. *Am. J. Psychiatry* 140:559–63
25. Halmi, K. A., Falk, J. R., Schwartz, E. 1981. Binge-eating and vomiting: A survey of a college population. *Psychol. Med.* 11:697–706
26. Hill, O. W. 1968. Psychogenic vomiting. *Gut* 9:348–52
27. Holland, A. J., Hall, A., Murray, R. M., Russell, G. F. M., Crisp, A. H. 1984. Anorexia nervosa: a study of 34 twin pairs and one set of triplets. *Br. J. Psychiatry* 145:414–19
28. Jennings, K. P., Klidjian, A. M. 1974. Acute gastric dilatation in anorexia nervosa. *Br. Med. J.* 1:477–78
29. Kalager, T., Brubakk, O., Bassoe, H. H. 1978. Cardiac performance in patients with anorexia nervosa. *Cardiology* 63:1–4
30. Keys, A., Brozek, J., Henschel, A., Mickelson, O., Taylor, H. L. 1950. *The Biology of Human Starvation*. Minneapolis: Univ. Minn. Press. 1385 pp.
31. Kjellberg, J., Reizenstein, P. 1970. Effect of starvation on body composition in obesity. *Acta Med. Scand.* 188:171–77
32. Lacey, J. H. 1983. Bulimia nervosa, binge eating and psychogenic vomiting: a controlled treatment study and long-term outcome. *Br. Med. J.* 286:1609–13
33. Lacey, J. H., Stanley, P. A., Crutchfield, M., Crisp, A. H. 1977. Sucrose sensitivity in anorexia nervosa. *J. Psychosomat. Res.* 21:17–20
34. Lasègue, D. 1964. De l'anorexie hystérique. *Archives Générales de Medicine*. Reprinted in: Kaufman, R. M., Heiman, M., eds. 1964. *Evolution of Psychomatic Concepts. Anorexia Nervosa: A Paradigm*, pp. 141–55. Int. Univ. Press
35. Levin, P. A., Falko, J. M., Dixon, K., Gallup, E. M., Saunders, W. 1980. Benign parotid enlargement in bulimia. *Ann. Intern. Med.* 93:827–29
36. Mitchell, J. E., Groat, R. 1984. A placebo-controlled, double-blind trial of amitriptyline in bulimia. *J. Clin. Psychopharmacol.* 4:186–93
37. Mitchell, J. E., Hosfield, W., Pyle, R. L. 1983. EEG findings in patients with the bulimia syndrome. *Int. J. Eating Disorders* 2:17–23
38. Mitchell, J. E., Pyle, R. L., Eckert, E. D. 1981. Frequency and duration of binge-eating episodes in patients with bulimia. *Am. J. Psychiatry* 138:835–36
39. Mitchell, J. E., Pyle, R. L., Eckert, E. D., Hatsukami, D., Lentz, R. 1983. Electrolyte and other physiological abnormalities in patients with bulimia. *Psychol. Med.* 13:273–78
40. Morley, J. E., Levine, A. S. 1981. Stress-induced eating is mediated through endogenous opiates. *Science* 209:1259–62
41. Moshang, T., Parks, J. S., Baker, L., Vaidya, V., Utiger, R. D., et al. 1975. Low serum triidothyronine in patients with anorexia nervosa. *J. Clin. Endocrinol. Metab.* 40:470–73
42. Nogami, Y., Yabana, F. 1977. On kibarashi-gui (binge-eating). *Folia Psychiatr. Neurol. Jpn.* 31:159–66
43. Oster, J. R., Masterson, B. J., Rogers, A. I. 1980. Laxative abuse syndrome. *Am. J. Gastroenterol.* 74:451–58
44. Palossy, B., Oo, M. 1977. ECG alterations in anorexia nervosa. *Adv. Cardiol.* 19:280–82
45. Pentlow, B. D., Dent, R. G. 1981. Acute vascular compression of the duodenum in anorexia nervosa. *Br. J. Surg.* 68:665–66
46. Pope, H. G., Hudson, J. I., Jonas, J. M., Yurgelun-Todd, D. 1983. Bulimia treated with imipramine: A placebo-controlled double-blind study. *Am. J. Psychiatry* 140:554–58
47. Powers, P. S. 1982. Heart failure during treatment of anorexia nervosa. *Am. J. Psychiatry* 139:1167–70
48. Pugliese, M. T., Lifshitz, F., Grad, G., Fort, P., Marks-Katz, M. 1983. Fear of obesity: A cause of short stature and delayed puberty. *N. Engl. Med.* 309:513–18
49. Pyle, R. L., Mitchell, J. E., Eckert, E. D., Halvorson, P. A., Neuman, P. A., Goff, G. M. 1983. The incidence of bulimia in freshman college students. *Int. J. Eating Disorders* 2:75–85
50. Rau, J. H., Green, R. S. 1975. Compulsive eating. A neuropsychologic approach to certain eating disorders. *Compr. Psychiatry* 16:223–31
51. Rigotti, N. A., Nussbaum, S. R., Herzog, D. B., Neer, R. M. 1984. Osteoporosis in women with anorexia nervosa. *N. Engl. J. Med.* 311:1601–6

52. Russell, G. F. M. 1966. Acute dilation of the stomach in a patient with anorexia nervosa. *Br. J. Psychiatry* 112:203–7
53. Sabine, E. J., Yonace, A., Farrington, A. J., Barratt, K. H., Wakeling, A. 1983. Bulimia nervosa: A placebo-controlled double-blind therapeutic trial of mianserin. *Br. J. Clin. Pharmacol.* 15 (Suppl. 2):195S–202S
54. Saleh, J. W., Lebwohl, P. 1980. Metoclopramide-induced gastric emptying in patients with anorexia nervosa. *Am. J. Gastroenterol.* 74:127–32
55. Silverman, J. A. 1983. Medical consequences of starvation. See Ref. 7, pp. 293–99
56. Simmonds, M. 1916. Ueber Kachexie Hypophysaeren Ursprungs. *Dtsch. Med. Wochenschr.* 42:190–91
57. Sours, J. A., Vorhaus, L. J. 1981. Superior mesenteric artery syndrome in anorexia nervosa: A case report. *Am. J. Psychiatry* 138:519–20
58. Stangler, R. S., Printz, A. M. 1980. DSM-III: Psychiatric diagnosis in a university population. *Am. J. Psychiatry* 137:937–40
59. Theander, S. 1983. Research on outcome and prognosis of anorexia nervosa and some results from a Swedish long-term study. *Int. J. Eating Disorders* 2:167–74
60. Thurston, J., Marks, P. 1974. Electrocardiographic abnormalities in patients with anorexia nervosa. *Br. Heart J.* 36:719–23
61. Walsh, B. T., Stewart, J. T., Roose, S. P., Gladis, M., Glassman, A. H. 1984. Treatment of bulimia with phenelzine. *Arch. Gen. Psychiatry* 41:1105–9
62. Weiner, H. 1983. Abiding problems in the pychoendocrinology of anorexia nervosa. In *Understanding Anorexia Nervosa and Bulimia. Rep. 4th Ross Conf. on Med. Res.*, pp. 47–53. Columbus, Ohio: Ross Labs.
63. Willard, S. G., Anding, R. H., Winstead, D. K. 1983. Nutritional counseling as an adjunct to psychotherapy in bulimic treatment. *Psychosomatics* 24: 545–51