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Anorexia nervosa in adults and adolescents: Nutritional rehabilitation (nutritional support)

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INTRODUCTION

Anorexia nervosa is characterized by dietary restriction that causes an abnormally low body weight, and can be life threatening and require hospitalization [1,2]. An essential first step in acute treatment is nutritional rehabilitation (refeeding malnourished patients) and restoring a healthy body weight. Normalization of weight can reverse nearly all of the general medical sequelae of the underweight state, with the exception of bone health [3-5]. In addition, nutritional rehabilitation can improve psychological sequelae of the underweight state, including depression, anxiety, and cognitive impairment.

This topic reviews nutritional rehabilitation for anorexia nervosa. An overview of treatment for anorexia nervosa, the refeeding syndrome, and the medical complications of anorexia nervosa are discussed separately:

- (See "Eating disorders: Overview of prevention and treatment", section on 'Anorexia nervosa'.)
- (See "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)
- (See "Anorexia nervosa in adults and adolescents: Medical complications and their management".)
- (See "Anorexia nervosa: Endocrine complications and their management".)

DIAGNOSIS OF ANOREXIA NERVOSA

According to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), the diagnosis of anorexia nervosa requires each of the following criteria (table 1) [1]:

- Restriction of energy intake that leads to a low body weight, given the patient's age, sex, developmental trajectory, and physical health
- Intense fear of gaining weight or becoming fat, or persistent behavior that prevents weight gain, despite being underweight
- Distorted perception of body weight and shape, undue influence of weight and shape on self-worth, or denial of the medical seriousness of one's low body weight

Additional information about the diagnosis of anorexia nervosa is discussed separately. (See "Anorexia nervosa in adults: Clinical features, course of illness, assessment, and diagnosis", section on 'Diagnosis'.)

Definition of low body weight — Whether an individual is underweight is generally determined by a measure of weight that is standardized for height. Body mass index (BMI) is the most common measure of weight in relation to height and is calculated as weight in kg divided by height in m² (calculator 1). According to DSM-5, low body weight is defined as "weight that is less than minimally normal"; the World Health Organization and the United States Centers for Disease Control and Prevention define low body weight as a BMI <18.5 kg/m² [1]. Another means for determining whether someone is underweight are tables that present ideal body weight for height.

INDICATION

Nutritional rehabilitation (nutritional support) is indicated as the first step of treatment for all patients who are acutely ill with anorexia nervosa and underweight [6]. This approach is consistent with practice guidelines from the American Psychiatric Association [6], United Kingdom National Institute for Health and Care Excellence [7], and the Academy for Eating Disorders [8]. In addition, some patients who are technically not underweight may nevertheless require nutritional rehabilitation due to recent rapid weight loss that was significant.

GENERAL PRINCIPLES

Goals and outcomes — The goals of nutritional rehabilitation (refeeding) for anorexia nervosa are to stabilize the patient's general medical status, reverse the medical complications that ensue from the underweight state, and restore weight and normal eating patterns [3,6]. Normalization of eating aims to interrupt problematic behaviors, such as purging and other actions that are used to compensate for eating, and can help patients regain the ability to perceive hunger and satiety.

Nutritional replenishment often reverses the general medical complications that can occur in anorexia nervosa due to starvation and malnutrition. As an example, weight restoration can ameliorate electrolyte, cardiac, gastrointestinal, and endocrine disturbances [6,9]. Nutritional rehabilitation can also improve psychiatric symptoms such as mood and anxiety [10], cognitive function [3,11], apathy, and lethargy [6]. Although osteoporosis is less amenable to acute nutritional rehabilitation, achieving a normal weight and the resumption of menses can improve osteoporosis, especially in adolescents [12]. The medical complications of anorexia nervosa and their management are discussed separately. (See "Anorexia nervosa in adults and adolescents: Medical complications and their management" and "Anorexia nervosa: Endocrine complications and their management".)

Treatment response is measured primarily as successful weight gain, and behavioral management is the most successful approach for helping patients to achieve normal weight. Behavioral therapy is used to reinforce healthy eating and weight gain, and to avoid reinforcing behaviors that do not promote health [13]. For patients who do not achieve expected weight gain, we suggest prescribing more calories and/or decreasing physical activity. In addition, patients will likely require monitoring during and after meals for a range of behaviors that undermine weight restoration (eg, vomiting, exercising, and hiding food that is not consumed). (See 'Number of calories' below and 'Behavioral management' below.)

Approach to the patient — Patient engagement in weight restoration may be aided by education about the body's nutritional needs and the physical and psychological sequelae of low body weight. The discussion includes information about caloric needs, the importance of fat intake, the plan to initiate weight gain by increasing caloric intake from the patient's baseline, and the likely need to continually increase caloric intake as weight gain progresses.

Clinicians should explain to patients and families that treatment is intended to keep the patient alive. If treatment is experienced as punitive or a struggle over control, clinicians can explain that behavioral treatment aims to reinforce only those behaviors that promote health [3,6]. It is frequently necessary for clinicians to set parameters around behavior in order to enforce the treatment plan.

Patient assessment — Assessment of the patient's general medical status, including body mass index (BMI) (calculator 1), determines treatment recommendations. The evaluation should address:

- Current weight, and height For adolescents, the growth chart and BMI percentile need to be consulted.
- Current caloric intake.
- Weight history Has weight recently been stable, declining, or increasing?
- Engagement in treatment Does the patient accept the need for treatment? Is the patient motivated? How ambivalent is the patient about increased energy intake?
- Behavioral reinforcements that will motivate healthy eating behaviors. (See 'Behavioral management' below.)

Additional information about assessing patients with anorexia nervosa, as well as assessing the dietary and nutritional status of primary care patients, is discussed separately. (See "Anorexia nervosa in adults: Clinical features, course of illness, assessment, and diagnosis", section on 'Assessment' and "Dietary assessment in adults".)

Setting — Nutritional rehabilitation (refeeding) for anorexia nervosa is generally started during an inpatient hospitalization, and completed on an inpatient or outpatient basis. Other settings that may be available include intensive outpatient clinics (eg, two to three hours per weekday), partial hospitals (eg, six hours of outpatient care per weekday), and residential care (table 2) [14,15]. The decision to discharge patients from the hospital is based upon their general medical status, ability to feed themselves, and motivation to participate in aftercare, as well as the availability of aftercare [6].

Randomized trials suggest that after inpatients with anorexia nervosa are medically stabilized with nutritional rehabilitation, ongoing refeeding and treatment in a partial (day) hospital or outpatient clinic may be as effective as continued inpatient hospitalization:

An open-label trial enrolled 172 female adolescents with anorexia nervosa who were
initially treated on an inpatient unit for three weeks, and then randomly assigned to
continued inpatient care or day hospital care (eight hours per day, five days per week) [16].
The inpatient hospitalization represented the first lifetime admission to a hospital for
anorexia nervosa; continued inpatient hospitalization and day hospital care each provided
the same multimodal specialized care program of nutritional rehabilitation (including
nutritional counseling), cognitive-behavioral therapy (CBT), and family therapy. At the

- follow-up assessment 12 months after admission for inpatient care, BMI in the group who received day hospital was comparable to continued inpatient care (18.1 and 17.8 kg/m²).
- A second trial compared shorter inpatient hospitalization for the purpose of medical stabilization with longer hospitalization for restoring weight to 90 percent of expected body weight in 82 medically unstable adolescents with anorexia nervosa [17]. In both groups, hospitalization included nutritional rehabilitation and other specialist treatments; following discharge, both groups received outpatient family therapy. Remission 12 months after treatment was comparable for shorter and longer hospitalizations (30 and 33 percent of patients).

Behavioral management — Inpatient nutritional rehabilitation typically involves behavioral management, which includes [3,6,18,19]:

- Regular structured meal plans Nutritional support staff should be consulted to determine caloric intake, help patients plan meals, and establish regular eating patterns. (See 'Nutritional counseling' below.)
- Monitoring
 - Meals Patients are observed as they eat to ensure that they do not surreptitiously
 discard their food, and to interrupt abnormal eating behaviors (eg, cutting food into
 small pieces or refusing to mix different types or colors of food on the plate) as they
 occur. For one hour after meals, patients are observed to prevent compensatory
 behaviors such as exercise or vomiting, and access to the bathroom is denied. In
 addition, fluid intake is monitored to prevent fluid loading.
 - Exercise During acute weight restoration, physical activity is generally restricted. As medical status improves, mild exercise (eg, yoga and stretching) is often introduced. For patients who can safely exercise, the activity should focus upon pleasure, rather than burning calories; group activities and time-limited activities (eg, classes) are preferable to solitary exercises.
- Behavioral reinforcement Behavioral reinforcements increase the probability of desired responses:
 - Positive reinforcements encourage healthy eating behaviors with desirable consequences such as off unit privileges or increasing choice in meal selection.
 - Negative reinforcements remove undesirable or aversive contingencies such as enforced bed rest, or restrictions of exercise or off-unit privileges. If patients lose

weight, privileges and autonomous control may need to be reduced (eg, bed rest imposed) until weight gain is again achieved. While this may be experienced by patients as an aversive consequence, it can be reframed as a necessary step to restore the balance of energy in a positive, healthy direction. Of note, weight may not increase or may even be lost during the first several days (eg, five to seven) of nutritional rehabilitation, as the body shifts from a catabolic state to an anabolic state.

Nutritional counseling — Nutritional rehabilitation for anorexia nervosa includes nutritional counseling provided by registered dieticians who [9,18,20]:

- Assess the patient's nutritional status, nutritional knowledge, and motivation to get better
- Determine the number of calories to administer
- Provide information about food, meal preparation, and eating behavior
- Supervise patients in selecting foods and planning meals
- Support patients in coping with eating and weight gain (eg, discourage dieting and reassure patients that their weight gain is not out of control)

Although nutritional counseling is an important component of nutritional rehabilitation for anorexia nervosa, dietary counseling is not sufficient as a stand-alone intervention for post hospitalization management. A one-year randomized trial compared 50 individual outpatient sessions of nutritional counseling with CBT in patients with anorexia nervosa who successfully completed inpatient treatment (n = 33) [21]. Relapse occurred in more patients treated with nutritional counseling than CBT (8 out of 15, 53 percent) versus (4 out of 18, 22 percent).

Support and psychotherapy — Nutritional rehabilitation for anorexia nervosa is accompanied by support and psychotherapy to help patients overcome their reluctance to increase caloric intake and to manage dysphoria that can occur as patients gain weight [6]. The increase in caloric intake that occurs during weight restoration is physically and psychologically uncomfortable. Patients draw support from patience, empathy, and flexibility in the treatment plan, as well as acknowledgement of small successes [20]. Several psychotherapies can be useful, including CBT. (See "Anorexia nervosa in adults: Cognitive-behavioral therapy (CBT)".)

CBT techniques include cognitive restructuring, which helps patients identify and challenge distorted, maladaptive beliefs (cognitive distortions) about themselves and food (eg, "I can't eat eggs because they make me fat"). [9,18]. The clinician questions the patient's maladaptive thoughts, and the clinician and patient consider challenges to the thoughts; the process includes examining the evidence for the thoughts and discussing alternative, rational

explanations. In addition, more functional thoughts may be substituted (eg, "Eating protein will help restore muscle mass").

Patients with anorexia nervosa may be disturbed by the distribution of body fat that occurs as they gain weight; counseling should address any such concerns (eg, "My stomach looks bigger and fat"). Observational studies have found that immediately after patients normalized their weight, adipose tissue was disproportionately distributed in the trunk (including the waist) [19,22]. However, during follow-up in which normal weight was maintained for approximately one year, the abnormal fat distribution appeared to resolve [23].

REFEEDING REGIMEN

Overview — Patients with anorexia nervosa should be prescribed a standard diet; for most patients, initial caloric prescriptions are 1500 to 1800 kcal/day (see 'Number of calories' below). Nutritional support staff should be consulted to determine the initial daily calories to be ingested and to help patients plan their meals and establish regular eating patterns [6,9,18,20]. Although patient preferences should be considered in developing meal plans and genuine food allergies addressed, it is necessary to ensure that the diet is nutritionally adequate and includes all major food groups. Reduced calorie, low-fat, or calorie free foods are not indicated [9].

Meal plans can be based upon an exchange system that consists of food categories (eg, dairy, fat, fruit, meat, starches, sweets, and vegetables) [9,24]. Each category includes specified portions of individual foods that can be exchanged for each other, which provides flexibility and a variety of foods.

More severely underweight patients initially receive fewer calories at the beginning of refeeding (eg, 1200 to 1500 kcal/day), and the number of calories is increased more slowly over time, to prevent refeeding complications [20]. (See "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)

Weight gain targets — The goal of nutritional rehabilitation for anorexia nervosa is to restore weight to a healthy range; patients who do not fully restore their weight are at risk for relapse [6,20,25]. (See 'Goals and outcomes' above and 'Evidence of efficacy' below.)

Many patients can restore weight to within normal limits in a structured treatment setting (eg, inpatient or partial hospital program) that includes behavioral contingencies [26] (see 'Behavioral management' above). The treatment team needs to discuss the target weight with patients when they are capable of processing this information; for some patients the ultimate weight goal is not a priority at the onset of treatment.

There is no single standard for what constitutes a minimally normal weight [1,27]. However, one reasonable measure for an acceptable minimal weight is a body mass index (BMI) ≥19.5 kg/m². BMI is calculated by dividing weight in kg by height in m² (calculator 1). Additional information about the definition of normal weight in anorexia nervosa is discussed separately. (See "Anorexia nervosa in adults: Clinical features, course of illness, assessment, and diagnosis", section on 'Diagnostic and Statistical Manual'.)

The weekly target for controlled weight gain generally varies according to the setting [3,6,7,9,19,20]:

- Inpatient 2 to 3 pounds (0.9 to 1.4 kg) per week
- Partial hospital 1 to 2 pounds (0.5 to 0.9 kg)
- Outpatient 0.5 to 1 pound (0.2 to 0.5 kg)

Early in the refeeding process, patients may gain weight rapidly because of fluid retention and a low baseline metabolic rate [28]. Weight gain >3 pounds (1.4 kg) per week should prompt highly vigilant monitoring for the refeeding syndrome and fluid retention. (See 'Monitoring general medical status' below.)

Number of calories — Caloric intake at the beginning of inpatient nutritional rehabilitation for anorexia nervosa is typically 30 to 40 kcal/kg body weight/day (eg, 1500 to 1800 kcal/day) [3,6,9,18,19,29]. Support for this approach includes the following:

- A randomized trial compared higher-calorie refeeding with lower-calorie refeeding in 111 hospitalized adolescents and young adults with anorexia nervosa or atypical anorexia nervosa [30]. Participants had vital sign instabilities (bradycardia, hypotension, orthostatic hypotension, and/or hypothermia) and low BMI. Higher-calorie refeeding commenced at 2000 kcal/day and increased by 200 kcal/day, whereas lower-calorie refeeding started at 1400 kcal/day and advanced by 200 kcal every two days. Higher-calorie refeeding restored medical stability in less time (7 versus 10 days) and produced greater weight gain, compared with lower-calorie refeeding. Safety (incidence of electrolyte abnormalities) and other adverse events were comparable between the two groups. In addition, mean length of stay was shorter with higher-calorie refeeding than lower-calorie refeeding (8 versus 12 days), indicating that higher-calorie refeeding is cost-effective.
- A review of observational studies in hospitalized adolescents found that lower calorie refeeding, starting at 1000 to 1200 kcal/day, was associated with weight loss at the beginning of treatment, followed by slow weight gain of 0.7 to 0.9 kg/week [15].

A subsequent retrospective study of an adolescent, inpatient nutritional rehabilitation program compared a lower-calorie diet (n = 64) with a higher-calorie diet (n = 61) [31]. The lower-calorie diet, used from 2010 to 2014, started at 1400 to 1500 kcal/day and was titrated to 2600 to 2700 kcal/day. The higher-calorie diet, used from 2016 to 2017, started at 1600 to 1800 kcal/day and was titrated to 3000 to 3600 kcal/day. The higher-calorie group gained weight more quickly, and moderate to severe hypophosphatemia was comparable in the two groups. However, mild hypophosphatemia occurred in more patients with the higher-calorie than the lower-calorie diet (46 versus 22 percent).

• A retrospective study of 119 adult inpatients compared a diet starting at 1000 kcal/day with a diet starting at 1500 kcal/day, and found that the lower calorie diet was associated with more episodes of hypoglycemia [32].

Nevertheless, outpatient treatment teams often start with fewer calories (eg, patient's current daily intake plus 400 kcal/day) because they cannot supervise meals and patients are more likely to agree to small increases over their current diet. In addition, more severely underweight patients (eg, BMI <15 kg/m²) are started with fewer calories to help prevent the refeeding syndrome.

The risks of inadequate intake are more common than the risks of the refeeding syndrome. Four studies found that caloric intake or rate of weight gain was not associated with refeeding hypophosphatemia [15]. Nevertheless, caution is still recommended as these studies generally prescribed a relatively lower calorie diet and were conducted with rigorous medical monitoring. Additional information about the refeeding syndrome and hypophosphatemia is discussed separately. (See "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)

Some patients are adamantly opposed to initially consuming 1000 kcal/day [6]. For patients who are medically stable, it is reasonable to start refeeding at a level that is approximately 200 to 300 kcal above their baseline intake, to facilitate the treatment alliance.

As nutritional status improves and patients gain weight, the number of calories that patients require to continue gaining weight increases [20]. Thus, daily calories are advanced by approximately 200 to 400 kcal every two to four days; caloric intake may progress up to 70 to 100 kcal/kg body weight/day (eg, 3000 to 3600 kcal/day) [3,6,9,20]. At the peak of weight gain, energy intake reaches approximately 3500 to 5000 kcal/day [3,20]. To achieve weight gain of 1 pound (0.5 kg) requires approximately 3500 kcal in excess of maintenance requirements.

A review of 27 studies (nearly all observational; total n >2600 patients) supports relatively aggressive rates of refeeding (eg, starting with at least 1500 kcal/day) in patients who are mildly to moderately malnourished (eg, BMI \geq 15 kg/m²) [15]. The review found that higher calorie

refeeding, accompanied by monitoring and replenishing of phosphorous as needed, is associated with better weight gain and shorter hospital stays, and is not associated with increased rates of complications. As an example, a prospective observational study compared higher calorie diets with lower calorie diets in 56 adolescents admitted for moderate anorexia nervosa (mean BMI 16 kg/m²) [33]. Higher calorie diets initiated refeeding with a mean of 1764 kcal/day and were advanced by approximately 120 kcal/day; lower calorie diets initiated refeeding with a mean of 1093 kcal/day and were advanced by approximately 100 kcal/day. Weight gain was greater with higher calorie diets than lower calorie diets (0.27 versus 0.14 kg/day), length of stay was shorter (12 versus 18 days), and the refeeding syndrome did not occur in any patients. A second review concluded that patients with anorexia nervosa who are moderately malnourished can safely begin refeeding with at least 1500 kcal/day; that diets can be advanced by 250 kcal every day or every other day, reaching approximately 2500 to 3000 kcal/day by day 14; and that such diets can lead to weekly weight gains of at least 1.5 kg with little risk of the refeeding syndrome [34].

Macronutrients — In standard diets for the United States general population, it is recommended that calories be distributed among macronutrients as follows [9,19,35]:

- Carbohydrates 45 to 65 percent of calories
- Fat 20 to 35 percent
- Protein 10 to 35 percent

Patients commonly fear that consuming fat leads to weight gain that consists entirely of adipose tissue; thus, it is important to tell patients that dietary fat is associated with gaining lean body mass.

Additional information about macronutrients is discussed separately. (See "Healthy diet in adults".)

Micronutrients — Patients with anorexia nervosa are frequently low in vitamins and minerals, which reverses with oral nutrition [9]. Nonetheless, we typically provide a daily oral multiple vitamin and mineral supplement [19], which is consistent with treatment guidelines [6,7]. In addition, we prescribe thiamine 100 mg/day, and folate 100 micrograms/day (not to exceed 1 mg/day) upon initiation of refeeding, which may help prevent refeeding syndrome [36]. Selenium and zinc may also benefit patients at risk for the refeeding syndrome and are generally included in standard multiple mineral supplements [9,36,37].

Electrolyte imbalances need to be monitored, and supplementation (eg, potassium) may be necessary. For more severely underweight patients (eg, BMI <16 kg/m²), phosphorous may be

required to prevent the refeeding syndrome. (See "Hypophosphatemia: Evaluation and treatment" and "Clinical manifestations and treatment of hypokalemia in adults".)

Administration — Nutritional rehabilitation can be achieved by:

- Oral refeeding typically indicated
- Enteral (nasogastric) refeeding occasionally indicated
- Total parenteral nutrition rarely indicated

Oral — Nutritional rehabilitation (refeeding) of anorexia nervosa is typically accomplished solely through oral intake of regular food, which helps patients resume healthy eating patterns (eg, three meals and one or two snacks per day) [9]. Energy dense liquid dietary supplements may be prescribed if patients cannot consume enough food to meet their caloric goals [3,20]. Supplements are commonly required at the peak of weight gain, when nutritional requirements are high. These supplements can be consumed during or between meals. After patients restore their weight and transition to a weight maintenance diet, supplements are discontinued.

Enteral — Enteral (nasogastric tube) feeding is occasionally indicated for extremely underweight patients (eg, BMI <15 kg/m²) or highly refractory patients who are unable to eat a sufficient amount of food to gain weight [20]. Enteral feeding is preferable to parenteral feeding (see 'Parenteral' below) because enteral feeding normalizes gastrointestinal function (comparable to oral intake) [6,9]. The risk of the refeeding syndrome may be greater with enteral feeding compared with oral refeeding; however, some data suggest that the risk of refeeding syndrome is primarily related to the nutritional status of the patient (eg, lower BMI at baseline) [6,15]. An alternative to the nasogastric tube for enteral feeding is a percutaneous endoscopic gastronomy tube, but this is rarely indicated.

Some nutritional rehabilitation programs augment oral intake with nasogastric tube feeds [9,38,39]. A review of nine observational studies and one randomized trial (total n = 899 patients) found that supplementing oral meals with nasogastric tube feeding posed no additional risks; however, most studies used prophylactic supplemental phosphate to prevent refeeding hypophosphatemia [15]. In addition, weight gain may perhaps be faster with nasogastric plus oral refeeding than oral refeeding alone. As an example, an open-label, two-month randomized trial compared tube refeeding plus oral refeeding with oral refeeding alone in 81 malnourished inpatients with anorexia nervosa; BMI at baseline was approximately 12.5 kg/m² [40]. All patients received psychotherapy and dietary counseling in the context of behavioral management. Mean weight gain was greater in the tube feed group than the control group (1.4 versus 0.9 kg/week). In addition, a BMI ≥18.5 kg/m² was achieved by more patients treated with tube feeding than the control group (39 versus 8 percent). During the one year

follow-up after discharge, time to relapse was longer in the group that received tube feedings, compared with the controls (34 versus 27 weeks). However, patients may have an aversion to the tube (which can cause nasal irritation and epistaxis) and complaints of gastric fullness with enteral feeding; also, one goal of nutritional rehabilitation is to restore normal eating behavior [20].

Based upon clinical experience, enteral feeding is better tolerated (with less gastric discomfort and diarrhea) and poses less danger of metabolic abnormalities when it is administered continuously over 24 hours, rather than in three to four daily boluses, each of which requires approximately 10 minutes to administer [6,20]. However, continuous enteral feeding requires patients to be connected to the pump all day. In the uncommon situation that enteral refeeding is a life-saving necessity and the patient is repeatedly pulling out the nasogastric tube, it may be necessary to place patients in restraints, in compliance with regulations concerning restraints.

Parenteral — Total parenteral (intravenous) nutrition is rarely indicated for extremely underweight patients (eg, BMI <15 kg/m²) or highly refractory patients who are unable to eat a sufficient amount of food to gain weight [20]. Parenteral nutrition is a treatment of last resort when no other alternatives exist, including cases in which enteral feeding is precluded (eg, following gastrointestinal surgery) or patients with acute hepatitis or pancreatitis [15]. The benefits of parenteral feeding almost never outweigh the risk of serious complications, which include catheter related infection and air embolism if patients disconnect the parenteral solution from the indwelling catheter, as well as the risks of disseminated intravascular coagulation and death [15,20,41,42]. In addition, the risk of the refeeding syndrome may be greater with parenteral feeding compared with oral refeeding; however, the risk of refeeding syndrome may be primarily related to the nutritional status of the patient [6].

EVIDENCE OF EFFICACY

Nutritional rehabilitation in the context of acute inpatient and/or outpatient treatment can facilitate weight restoration. As an example, a one-year prospective observational study assigned female patients (n = 90) to one of four treatment conditions: hospitalization (multimodal specialized care program including various psychotherapies) for several months followed by outpatient treatment, an outpatient program based upon individual and family psychotherapy, an outpatient group psychotherapy program, or no treatment [43]. The three active treatment conditions included nutritional rehabilitation (including nutritional counseling). Mean weight gain at one year was greater in patients who received active treatment than patients who received no treatment (9 to 10 kg versus 3 kg).

However, successful nutritional rehabilitation and weight restoration in anorexia nervosa is often followed by relapse. One review found that in the first year after inpatient nutritional rehabilitation, relapse occurred in approximately 50 percent of patients [3].

Based upon retrospective studies of patients with anorexia nervosa who are treated with nutritional rehabilitation, relapse and rehospitalization may be less likely to occur in patients who are closer to their ideal body weight at the time of discharge, compared with patients with lower weights at discharge [6]:

- One study of inpatients (n = 59) found that the risk of postdischarge relapse was four times greater among patients with a body mass index (BMI) ≤19 kg/m² at the time of discharge, compared with a BMI >19 kg/m² [44].
- A second study consisted of inpatients who initially gained comparable amounts of weight, and were discharged either fully weight recovered (n = 14; mean weight 96 percent of ideal body weight) or with lower discharge weights (n = 8, mean weight 76 percent of ideal body weight) [5]. After discharge, rehospitalization occurred in fewer patients who were fully weight recovered at discharge, compared with lower weight patients (7 percent [1 out of 14] versus 63 percent [5 out of 8]) [5].
- In a prospective observational study of 168 inpatients with anorexia nervosa, who were assessed yearly after discharge for up to five years, higher weight at discharge was associated with maintaining a healthy weight [45].

Relapse may also be the result of unresolved pathological attitudes about weight and ongoing problematic eating behaviors [3]. Cognitive-behavioral therapy can help prevent relapse. (See "Anorexia nervosa in adults: Cognitive-behavioral therapy (CBT)", section on 'Maintenance treatment'.)

COMPLICATIONS

Medical complications and concerns that can occur during nutritional rehabilitation (nutritional support) include the refeeding syndrome, refeeding edema, and constipation. Complications associated with refeeding are most likely related to the severity of the patient's low weight at presentation. Clinicians should remain vigilant for the refeeding syndrome, especially among the most severely underweight patients (eg, body mass index <16 kg/m²).

Refeeding syndrome — The refeeding syndrome is a rare but potentially fatal complication that can occur when nutritional rehabilitation is too aggressive. The clinical features, general

medical complications, and management of the refeeding syndrome are discussed separately. (See "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)

Refeeding edema — Refeeding edema is common during the refeeding process in anorexia nervosa [6]. The clinical significance of refeeding edema is usually minor; occasionally it produces discomfort [20]. Nevertheless, monitoring ankle and pretibial edema during refeeding is important because edema may serve as a harbinger of the refeeding syndrome [20]. Edema (including abdominal edema) may be more likely to occur in patients who purged and/or used laxatives.

In the absence of the full-blown refeeding syndrome, refeeding edema probably results from the increased release of insulin that is associated with increased caloric intake. Increased insulin causes sodium retention through increased reabsorption of sodium in the renal distal tubules [20,46]. In addition, hypoalbuminemia rarely contributes to the development of peripheral edema during the early refeeding phase.

It is important to discuss with patients the presence of excess fluid and its relationship to the underweight state because patients may be alarmed by rapid increases in weight that come with fluid retention. Clinicians should explain that the high rate of weight gain is unlikely to continue as fluid gets reabsorbed and the general medical status stabilizes, and that nutritional rehabilitation must continue for edema to stabilize and resolve.

Refeeding edema is usually managed conservatively with bed rest, leg elevation, and monitoring fluid intake. Low-sodium diets may also be helpful. In a retrospective study that included patients managed with low-sodium diets (n = 176; 4 to 5 grams NaCl/day per 2000 kcal/day) or normal sodium diets (n = 42; 10 to 12 grams NaCl/day), peripheral edema occurred in fewer patients who received low-sodium diets (6 versus 21 percent) [47]. Although diuretics are typically not used, if edema becomes severe such that tissue breakdown is a concern, we cautiously use furosemide (eq, 10 mg twice per day for a few days).

Additional information about the clinical manifestations, diagnosis, and treatment of edema are discussed separately. (See "Clinical manifestations and evaluation of edema in adults" and "General principles of the treatment of edema in adults".)

Constipation — Patients commonly experience abdominal bloating and constipation during weight gain due to slowed gastric motility and prolonged colon transit time [20]. Constipation generally resolves with continued oral intake. Additional information about managing constipation in anorexia nervosa is discussed separately. (See "Anorexia nervosa in adults and adolescents: Medical complications and their management", section on 'Constipation'.)

MONITORING GENERAL MEDICAL STATUS

The general medical status of patients with anorexia nervosa who are receiving nutritional rehabilitation should be monitored, and more severely underweight patients (eg, body mass index $<16 \text{ kg/m}^2$) require more intensive monitoring [3,6,7,20]:

- **Vital signs** For inpatients, vital signs are monitored one to three times daily, for partial hospital patients once each day, and for outpatients, vital signs are monitored each visit. Patients with anorexia nervosa are at high risk for orthostatic hypotension. In addition, patients are usually bradycardic, and a sudden, sustained, increased pulse greater than 70 beats per minute may be a sign of cardiac overload and harbinger of the refeeding syndrome. (See "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)
- **Weight** For inpatients and partial hospital patients, weight is measured several (eg, three) times per week or on a daily basis, and for outpatients at each visit. Weighing is preferably conducted at the same time each day with the same scale, typically in the morning, post voiding, with patients in hospital gowns (when appropriate). These procedures can increase the reliability and validity of recorded weights by preventing patients from falsely elevating their weight through water loading, wearing heavy clothing, or surreptitiously carrying extra weights in pockets. Weight gain targets are discussed separately. (See 'Weight gain targets' above.)

Weighing patients may cause distress if they are gaining weight [2]. If a mechanical beam scale is used, discomfort can be reduced by having patients stand with their backs facing the beam and counterweights.

- **Physical examination** The physical examination focuses upon the cardiovascular (including signs of lower extremity edema), gastrointestinal, and pulmonary systems. Early in the refeeding process (eg, first two weeks), clinicians should examine inpatients and partial hospital patients daily and outpatients at each visit, looking for signs of the refeeding syndrome.
- Laboratory tests Once nutritional replenishment commences, clinicians should regularly check serum electrolytes, glucose, phosphorous, magnesium, and liver function tests. The frequency of laboratory testing depends upon the severity of the patient's general medical status. We usually perform tests on hospital days 1, 3, 7, and 10, and weekly thereafter. For patients whose general medical status is severely compromised, laboratory tests are performed daily or every other day for at least one to two weeks [20]. Hypophosphatemia can signal the need to slow down the refeeding process;

hypophosphatemia is the hallmark of the refeeding syndrome, and most commonly appears on day 3 or 4 of refeeding. Hypokalemia, hypoglycemia, hyponatremia, hypomagnesemia, and elevated liver enzymes can also occur. Hyponatremia may necessitate fluid restriction.

The frequency of laboratory tests can be decreased progressively as patients consistently gain weight, provided serum electrolyte levels remain stable.

It is worth noting that hypokalemia can occur in patients who persistently vomit. If clinicians suspect that patients are fluid loading to artificially increase their weight, a urine specific gravity should be checked.

MAINTENANCE DIETARY REGIMEN

Patients with anorexia nervosa who have restored their weight have higher daily caloric requirements than healthy controls [48]. Whereas a healthy woman of normal weight requires approximately 30 kcal/kg/day, patients who have recently normalized their weight require 45 to 50 kcal/kg/day. It is unclear whether this greater caloric requirement for patients reflects metabolic demand and/or increased physical activity [49,50]. The increased caloric requirements may persist for six months after weight restoration [51].

Observational studies suggest that in patients with anorexia nervosa who have recently restored their weight, relapse is less likely to occur with diets that include highly caloric foods and a greater variety of food [9,52]. In two studies of patients who had successfully gained weight (body mass index $\ge 20 \text{ kg/m}^2$, n = 47 and 16) and were then followed for up to one year after hospital discharge, diets marked by low energy density and a limited variety of food were associated with poor outcomes [53,54].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Eating disorders".)

SUMMARY

• Anorexia nervosa is diagnosed according to the criteria in the table (table 1). (See "Anorexia nervosa in adults: Clinical features, course of illness, assessment, and

diagnosis", section on 'Diagnosis'.)

- Nutritional rehabilitation is indicated for all malnourished patients with anorexia nervosa.
 (See 'Indication' above.)
- The assessment of patients with anorexia nervosa for nutritional rehabilitation (refeeding) should address current weight, height, and caloric intake; weight history; engagement in treatment; and behavioral reinforcements that will motivate healthy eating behaviors. (See 'Patient assessment' above and "Anorexia nervosa in adults: Clinical features, course of illness, assessment, and diagnosis", section on 'Assessment'.)
- The goal of nutritional rehabilitation is to restore a minimally normal weight (eg, body mass index ≥19.5 kg/m²) (calculator 1). The weekly target for controlled weight gain generally varies according to the setting:
 - Inpatient 2 to 3 pounds (0.9 to 1.4 kg) per week
 - Partial hospital 1 to 2 pounds (0.5 to 0.9 kg)
 - Outpatient 0.5 to 1 pound (0.2 to 0.5 kg)

(See 'Weight gain targets' above.)

- Caloric intake at the beginning of nutritional rehabilitation is typically 30 to 40 kcal/kg body weight/day (eg, 1500 to 1800 kcal/day). Daily calories are advanced by about 200 to 400 kcal every two to four days; caloric intake may eventually progress up to 70 to 100 kcal/kg/day (eg, 3000 to 3600 kcal/day). (See 'Number of calories' above.)
- Nutritional rehabilitation is typically accomplished solely through oral intake of regular food; energy dense liquid dietary supplements may be prescribed if patients cannot consume enough food to meet their caloric goals. Enteral (nasogastric tube) feeding is occasionally indicated and total parenteral (intravenous) nutrition is rarely indicated for extremely underweight patients or highly refractory patients who steadfastly refuse to eat a sufficient amount of food to gain weight. (See 'Administration' above.)
- The refeeding syndrome is a rare but potentially fatal complication that can occur when nutritional rehabilitation is too aggressive. Other complications of nutritional rehabilitation include refeeding edema and constipation. (See 'Complications' above and "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)
- Clinicians administering nutritional rehabilitation should monitor vital signs; weight; cardiovascular, gastrointestinal, and pulmonary systems; and laboratory tests (serum

electrolytes, glucose, phosphorous, magnesium, and liver function tests). (See 'Monitoring general medical status' above.)

• Patients with anorexia nervosa who restore their weight initially require a maintenance diet of approximately 45 to 50 kcal/kg of body weight/day, which is eventually tapered to 30 kcal/kg/day. Relapse is less likely to occur with maintenance diets that include highly caloric foods and a greater variety of food. (See 'Maintenance dietary regimen' above.)

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