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Anorexia nervosa in adults: Evaluation for medical complications and criteria for hospitalization to manage these complications

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INTRODUCTION

Anorexia nervosa is associated with numerous medical complications that are directly attributable to caloric restriction and weight loss (table 1) [1]. A medical evaluation is necessary to assess patients for these complications and determine whether hospitalization is necessary.

Among patients with anorexia nervosa, medical complications account for more than half of all deaths and the rate of mortality is high [2]. A meta-analysis of 35 studies (n >12,000 individuals with anorexia nervosa) found that the annual all-cause mortality rate was 5 per 1000 person years of follow-up [3]. Standardized mortality ratios show that the rate of death in anorexia nervosa is approximately 5 to 10 times greater than the rate in the general population [3-6]. Among all psychiatric disorders, anorexia nervosa has one of the highest mortality rates.

The evaluation for medical complications and criteria for hospitalization of patients with anorexia nervosa is reviewed here. The medical complications of anorexia nervosa and their management; the epidemiology, pathogenesis, clinical features, treatment, and outcome of anorexia nervosa; the refeeding syndrome in patients with anorexia nervosa; and the medical complications of bulimia nervosa and binge eating disorder are discussed separately.

- (See "Anorexia nervosa in adults and adolescents: Medical complications and their management".)
- (See "Anorexia nervosa in adults: Clinical features, course of illness, assessment, and diagnosis".)
- (See "Eating disorders: Overview of epidemiology, clinical features, and diagnosis".)
- (See "Eating disorders: Overview of prevention and treatment".)
- (See "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)
- (See "Bulimia nervosa and binge eating disorder in adults: Medical complications and their management".)

DIAGNOSIS OF ANOREXIA NERVOSA

A diagnosis of anorexia nervosa, according to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), requires each of the following criteria (table 2) [7]:

- 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 clinical features and diagnosis of anorexia nervosa are discussed separately. (See "Anorexia nervosa in adults: Clinical features, course of illness, assessment, and diagnosis".)

MEDICAL EVALUATION

Patients with anorexia nervosa, restricting subtype, should be evaluated for medical complications (table 1) [2,8]. The complications and their signs and symptoms are secondary to caloric restriction and weight loss. The evaluation of all patients with anorexia nervosa should include a history, physical examination, and laboratory testing.

Patients with medical complaints due to anorexia nervosa often attempt to mask their thinness and conceal their eating disorder from clinicians by wearing bulky clothes [9]. In addition,

patients may inflate their body weight by hiding objects in their clothes and drinking water.

Findings from the medical evaluation help determine whether the patient requires initial medical hospitalization for stabilization. (See 'Treatment setting' below.)

Medical history — The most common medical symptoms of anorexia nervosa are [2,9]:

- Amenorrhea
- Exertional fatigue
- Weakness
- Cold intolerance
- Palpitations
- Dizziness
- Abdominal pain and bloating
- Early satiety
- Constipation

Irritability is often present as well.

Physical examination — Within the context of a complete physical examination, key portions include weight and height; vital signs including heart rate, blood pressure both supine and standing, and temperature; cardiovascular assessment; and skin examination.

Common physical signs — Common signs in patients with anorexia nervosa are [9,10]:

- Low body mass index (BMI; <17.5 kg/m²)
- Emaciation (body weight less than 85 percent of ideal body weight)
- Hypothermia (core temperature <35°C or 95°F)
- Bradycardia (pulse <60 beats per minute)
- Hypotension (systolic blood pressure <90 mmHg and/or a diastolic blood pressure <50 mmHg)
- Hypoactive bowel sounds
- Xerosis (dry, scaly skin)
- Brittle hair and hair loss
- Lanugo hair growth
- Abdominal distention
- Proximal muscle weakness.

Other signs that are often present include brittle nails, pressure sores, yellow skin (hypercarotenemia, especially palms), cyanotic and cold hands and feet, edema (ankle and

periorbital), and heart murmur from mitral valve prolapse.

Laboratory assessment — Laboratory tests indicated for all patients with anorexia nervosa include [2,8,11-15]:

- Serum electrolytes
- Blood urea nitrogen
- Serum creatinine
- Serum glucose
- Serum calcium, phosphorous, and magnesium
- Serum albumin and prealbumin
- Liver function tests (aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase)
- International Normalized Ratio
- Complete blood count including differential
- Thyroid stimulating hormone
- 25-hydroxyvitamin D
- Pregnancy test (females)
- Testosterone (males)
- Electrocardiogram

Other tests may be indicated, based upon symptoms and findings on the physical examination.

Echocardiography is indicated for patients with anorexia nervosa who have syncope, orthopnea, dyspnea, pulsus paradoxus, elevated jugular venous pressure, pulmonary and peripheral edema, gallop, murmur suggestive of valve disease, or unexplained hypotension [16]. For patients with a BMI <14, and the presence of epigastric pain that develops 15 to 20 minutes after starting to eat, we suggest diagnostic studies to rule out superior mesenteric artery syndrome. (See "Superior mesenteric artery syndrome", section on 'Diagnostic studies'.)

In addition, patients amenorrheic for greater than nine months warrant dual-energy x-ray absorptiometry. Patients with atypical features, an unremitting course, or significant cognitive impairment may warrant imaging of the brain [8].

Excluding medical disorders — Anorexia nervosa is the most common cause of substantial weight loss in young adolescent females in Western countries, and the diagnosis is usually clear because patients present with emaciation in conjunction with self-induced starvation and intense fear of fatness [11]. However, if the diagnosis of anorexia nervosa is not clear, the evaluation should account for general medical illnesses that can present with weight loss

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(table 3), malabsorption, or secondary amenorrhea (table 4 and table 5). These include [2,17]:

- Neoplasm
- Chronic infections (eq., tuberculosis or acquired immunodeficiency syndrome)
- Uncontrolled diabetes mellitus
- Hyperthyroidism
- Malabsorption syndromes (eg, celiac disease)
- Inflammatory bowel disease (eg, Crohn disease)

Among Asian populations, the patient's condition may in part be due to constitutional thinness [18,19].

Findings from the medical evaluation of anorexia nervosa overlap with findings obtained from the evaluation of other illnesses that cause weight loss. However, there are a few important differences. As an example, most starving patients describe lethargy and inability to exercise, whereas patients with anorexia nervosa may exercise excessively in an attempt to lose weight. Patients with anorexia nervosa are often not concerned about their marked weight loss, whereas patients who lose weight from other causes usually express concern. In addition, weight loss due to malabsorption usually presents with diarrhea or symptoms of adrenergic excess, such as diaphoresis and rapid pulse, which are typically absent in anorexia nervosa (purging may lead to dehydration and tachycardia, and laxative abuse to diarrhea). Further, the diet of patients with anorexia nervosa usually contains protein and vitamins even though their total caloric intake is very low. Thus, patients are often spared the starvation-related complications of malnutrition observed in resource-limited countries (eg, kwashiorkor and marasmus).

Illnesses other than anorexia nervosa can be diagnosed or excluded through the history, physical examination, and laboratory screening tests. The guiding principle is that a complex and expensive workup to rule out numerous medical disorders is rarely, if ever, indicated. The etiology and evaluation of weight loss; clinical features and diagnosis of malabsorption; and etiology, diagnosis, and treatment of secondary amenorrhea are discussed separately. (See "Approach to the patient with unintentional weight loss" and "Approach to the adult patient with suspected malabsorption" and "Evaluation and management of secondary amenorrhea".) See other topics for a review of individual illnesses.

TREATMENT SETTING

Determining the treatment setting for patients with medical complications of anorexia nervosa requires a general medical evaluation, and the decision about disposition rests upon careful assessment of the risks and benefits of each option. Clinical judgment and some degree of individualization is required.

Based upon our clinical experience, most severe medical complications of anorexia nervosa are managed as inpatients or in residential care facilities. Other treatment settings that may be available include intensive outpatient (eg, two to three hours per weekday) and partial hospital (day program that provides six to eight hours of outpatient care per weekday) (table 6) [8]. Patients with a body mass index (BMI) (calculator 1) <14 kg/m² should generally not initiate treatment in a partial hospital program or a residential treatment center.

Inpatient hospitalization — Patients with anorexia nervosa who are not medically stable (table 7) should first be hospitalized for medical stabilization. In addition, some medical complications of anorexia nervosa require inpatient treatment on an internal medicine, psychiatric, or combined unit. The choice depends upon the patient's weight, medical and psychiatric status, and available resources. As an example, a BMI <14 kg/m² necessitates initial stabilization on an inpatient medical unit located in a medical hospital [20]. To help inform the decision regarding inpatient hospitalization, clinicians can use the severity index for anorexia nervosa in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [7]. The severity index is based upon the patient's BMI (calculator 1):

- Mild BMI 17 to 18.49 kg/m²
- Moderate BMI 16 to 16.99 kg/m²
- Severe BMI 15 to 15.99 kg/m²
- Extreme BMI <15 kg/m²

Anorexia nervosa is associated with numerous general medical complications that are directly attributable to weight loss and malnutrition. The complications affect most major organ systems and often include physiologic disturbances such as hypotension, bradycardia, hypothermia, and amenorrhea. (See "Anorexia nervosa in adults and adolescents: Medical complications and their management".)

There are no evidence-based criteria indicating which patients with anorexia nervosa need initial hospitalization. Based upon clinical practice guidelines, we suggest inpatient hospitalization in a medical facility with specialized expertise and immediate availability of urgent medical-surgical services for adult patients with any one or more of the following [2,8,9,12,16,21-24]:

- Unstable vital signs:
 - Bradycardia less than 40 beats per minute
 - Blood pressure <80/60 mmHg or symptoms of lightheadedness
- Cardiac dysrhythmia (eg, QTc >0.499 msec) or any rhythm other than normal sinus rhythm or sinus bradycardia.
- Weight <70 percent ideal body weight or BMI (calculator 1) <14 to 15 kg/m², especially if weight loss was rapid. Ideal body weight for females is the weight at which normal ovulation occurs and for males is the weight at which gonadal function is normal. Ideal body weight can also calculated using the Hamwi method [25].

Extenuating circumstances may rarely lead us to not hospitalize patients with a weight <70 percent ideal body weight or BMI <15 kg/m². As examples, we do not hospitalize patients who are coherent and refuse admission, who do not meet criteria for involuntary hospitalization (certification), are classified as having severe and enduring anorexia nervosa, do not have severe general medical comorbidity, and are willing to be treated in a less restrictive setting that can adequately monitor the patient.

- Cardiovascular, hepatic, or renal compromise requiring medical stabilization.
- Marked dehydration.
- Serious medical complication of malnutrition (eg, syncope, seizures, cardiac failure, liver failure, pancreatitis, hypoglycemia, or marked electrolyte disturbance).
- Refeeding syndrome:
 - Critical acid-base and electrolyte disorders
 - Marked edema
 - Serum phosphorous <2 mg/dL
- Poor response to outpatient treatment, or major recent and rapid weight "disruption" even when current weight is not severely low [26].

The refeeding syndrome is discussed separately. (See "Anorexia nervosa in adults and adolescents: The refeeding syndrome".)

Clinicians treating patients on an internal medicine unit should obtain consultation from the psychiatry service. A clinical practice guideline from one institution for treating patients with restrictive anorexia nervosa during medical hospitalization is available [13].

Follow-up care — There are no empirically tested guidelines that direct the frequency of follow-up visits for medical complications or the time intervals for testing. Based upon clinical experience, we suggest outpatient general medical follow-up within three days for patients discharged after an acute care hospitalization for severe emaciation and nutritional rehabilitation. These patients are at risk for the refeeding syndrome for the first few weeks after consistent weight restoration and weight gain have started. Initially, weekly primary care follow-up is prudent to examine patients for:

- Signs of the refeeding syndrome (see "Anorexia nervosa in adults and adolescents: The refeeding syndrome")
- Check phosphate, other electrolyte levels, and liver function tests
- Monitor weight gain

However, for those with a BMI $<14 \text{ kg/m}^2$ who are initially stabilized on an inpatient medical unit, we suggest transfer to a residential eating disorder treatment center for ongoing care.

For patients who remain ill with anorexia nervosa, we suggest a repeat dual-energy x-ray absorptiometry scan every one to two years to monitor bone mineral density and response to treatment for osteoporosis. Repeat electrocardiogram and echocardiograms are not required unless cardiac symptoms persist despite weight restoration, or if new cardiac symptoms develop, or if there were significant abnormalities present on the initial tests.

Outpatient — Medical complications of anorexia nervosa usually can be treated in an outpatient setting if the patient's weight is \geq 85 percent of ideal body weight or if the BMI (calculator 1) is \geq 17 kg/m², and the complications are correctly diagnosed and responding to treatment [1]. The clinician treating these complications should have expertise in managing them and is often part of a team that includes specialists in psychiatry and nutrition [8].

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".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

• Basics topic (see "Patient education: Anorexia nervosa (The Basics)")

SUMMARY

- Medical complications in anorexia nervosa Anorexia nervosa is associated with numerous medical complications that are directly attributable to caloric restriction and weight loss (table 1). A medical evaluation is necessary to assess patients for these complications and determine whether hospitalization is necessary. (See 'Introduction' above.)
- Medical evaluation The history and physical examination that occur as part of the
 medical evaluation should be accompanied by laboratory blood testing. All patients with
 anorexia nervosa should receive an initial set of serum electrolytes, blood urea nitrogen,
 creatinine, glucose, calcium, phosphorous, magnesium, albumin, prealbumin, liver
 function tests, International Normalized Ratio, complete blood count, thyroid stimulating
 hormone, 25-hydroxyvitamin D, electrocardiogram, and urinalysis. (See 'Medical history'
 above and 'Physical examination' above and 'Laboratory assessment' above.)
- Rule out medical illnesses that mimic anorexia nervosa For patients presenting with atypical features of anorexia nervosa, clinicians should rule out general medical illnesses that mimic anorexia nervosa by causing weight loss, malabsorption, or secondary amenorrhea (table 3 and table 4 and table 5). (See 'Excluding medical disorders' above.)

• **Criteria for hospitalization** – Patients with anorexia nervosa who are not medically stable (table 7) should be hospitalized for medical stabilization. Criteria for hospitalization include unstable vital signs, cardiac dysrhythmia other than normal sinus bradycardia, weight less than 70 percent of ideal body weight or body mass index (calculator 1) <14 to 15 kg/m², serious medical complication of malnutrition (eg, syncope, seizures, cardiac failure, liver failure, pancreatitis, hypoglycemia, or electrolyte disturbance), moderate to severe refeeding syndrome, and poor response to outpatient treatment. (See 'Inpatient hospitalization' above.)

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