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Achalasia: Pathogenesis, clinical manifestations, and diagnosis

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INTRODUCTION

Achalasia results from progressive degeneration of ganglion cells in the myenteric plexus in the esophageal wall, leading to failure of relaxation of the lower esophageal sphincter (LES), accompanied by a loss of peristalsis in the distal esophagus. This topic will review the etiology, pathogenesis, clinical manifestations, and diagnosis of achalasia. The management of achalasia is discussed separately. (See "Overview of the treatment of achalasia" and "Pneumatic dilation and botulinum toxin injection for achalasia" and "Surgical myotomy for achalasia".)

EPIDEMIOLOGY

Achalasia has been regarded as an uncommon disorder with an annual incidence of approximately 1.6 cases per 100,000 individuals and prevalence of 10 cases per 100,000 individuals [1]. Although epidemiologic data on achalasia are limited, its frequency appears to be rising, with one study suggesting that, from 2004 to 2014, the incidence and prevalence of achalasia in central Chicago were two- to threefold greater than estimates from earlier years would have predicted [2]. Males and females are affected with equal frequency. The disease can occur at any age, but onset before adolescence is rare. Achalasia is usually diagnosed in patients between the ages of 25 and 60 years.

Achalasia may occur in association with adrenal insufficiency and absent lacrimation in patients with triple A syndrome or Allgrove syndrome, a rare autosomal recessive genetic disorder [3,4].

ETIOLOGY

The etiology of primary or idiopathic achalasia is unknown. Secondary achalasia is due to diseases that cause esophageal motor abnormalities similar or identical to those of primary achalasia (table 1). In Chagas disease, which occurs predominantly in Central and South America, esophageal infection with the protozoan parasite *Trypanosoma cruzi* can result in loss of intramural ganglion cells, leading to aperistalsis and incomplete lower esophageal sphincter (LES) relaxation [5]. Other diseases that have been associated with achalasia-like motor abnormalities include amyloidosis, sarcoidosis, neurofibromatosis, eosinophilic esophagitis, multiple endocrine neoplasia type 2B, juvenile Sjögren's disease, chronic idiopathic intestinal pseudo-obstruction, and Fabry disease [6-12]. (See "Chagas gastrointestinal disease".)

PATHOGENESIS

Achalasia has been assumed to result from inflammation and degeneration of neurons in the esophageal wall (figure 1) [13]. The cause of the inflammatory degeneration of neurons in primary achalasia is not known. The observations that achalasia is associated with variants in the HLA-DQ region and that affected patients often have circulating antibodies to enteric neurons suggest that achalasia is an autoimmune disorder [14-16]. Some investigators have proposed that the inflammatory attack on esophageal neurons in achalasia is triggered by an antibody response to viral infections (eg, herpes zoster, measles viruses), but data have been inconclusive [17,18]. A study evaluating T cells in patients with achalasia found reactivity to HSV-1, suggesting that achalasia may be triggered by HSV-1 infection [19]. A genetic predisposition to the inflammatory degeneration of ganglion cells in achalasia is suggested by its association with variants in the HLA-DQ region and by its occurrence in genetic syndromes such as Allgrove syndrome (see 'Epidemiology' above). It has also been suggested that there may be an allergy-driven form of achalasia [20].

Histologic examination of the esophagus in patients with achalasia typically reveals decreased numbers of neurons (ganglion cells) in the myenteric plexuses, and the ganglion cells that remain often are surrounded by lymphocytes and, less prominently, by eosinophils [21,22]. This inflammatory degeneration preferentially involves the nitric oxide-producing, inhibitory neurons that affect the relaxation of esophageal smooth muscle; the cholinergic neurons that contribute to lower esophageal sphincter (LES) tone by causing smooth muscle contraction may

be relatively spared [23]. In some patients, degenerative changes are also found in the ganglion cells of the dorsal motor nucleus of the vagus in the brainstem, and Wallerian degeneration has been observed in the vagal fibers that supply the esophagus (figure 1) [24]. However, the disordered motility that characterizes achalasia is believed to result primarily from the loss of inhibitory neurons within the wall of the esophagus itself. Loss of inhibitory innervation in the LES causes the basal sphincter pressure to rise and renders the sphincter muscle incapable of normal relaxation. In the smooth muscle portion of the esophageal body, the loss of inhibitory neurons results in aperistalsis [25]. The manifestations of achalasia depend on the degree and location of ganglion cell loss [26]. Loss of peristalsis in the distal esophagus and a failure of LES relaxation with swallowing both impair esophageal emptying; however, most of the symptoms and signs of achalasia are due primarily to the defect in LES relaxation (esophagogastric junction outflow obstruction).

In addition, patients with achalasia may also have a subtle defect in reflex relaxation of the upper esophageal sphincter (UES) [27]. The abrupt esophageal distention that results when gas from the stomach suddenly enters the esophagus normally triggers a reflex relaxation of the UES, thereby allowing the gas to escape through the mouth in the form of a belch. The UES belch reflex can be demonstrated experimentally by injecting air into the esophagus. In normal subjects, esophageal air injection causes UES relaxation that is accompanied by an audible belch. In patients with achalasia, however, air injected into the esophagus frequently causes a paradoxical increase in UES pressure without a belch. This abnormal reflex presumably results from the loss of inhibitory neurons, although the precise neural pathways that affect the reflex are not clear. The inability to burp in some patients with achalasia may contribute to the esophageal distention and chest pain that often accompany the disease. Patients with achalasia may also have impaired gastric relaxation [28].

CLINICAL FEATURES

Achalasia has an insidious onset, and disease progression is gradual. Patients typically experience symptoms for years prior to seeking medical attention. In one series of 87 consecutive patients with newly diagnosed achalasia, the mean duration of symptoms was 4.7 years prior to the diagnosis [29]. The delay in diagnosis was mainly due to misinterpretation of typical clinical features. Patients are often treated for other disorders including gastroesophageal reflux disease (GERD) before the diagnosis of achalasia is established [30].

Clinical manifestations — Dysphagia for solids (91 percent) and liquids (85 percent), and regurgitation of bland undigested food or saliva (76 to 91 percent) are the most frequent symptoms in patients with achalasia (figure 2) [31,32]. Regurgitation of retained material in

the esophagus, especially while recumbent, may result in aspiration (8 percent). Patients may also induce vomiting to relieve a sensation of retrosternal fullness after a meal. Up to 85 percent of patients have difficulty belching, which may be due to a defect in relaxation of the upper esophageal sphincter (UES). Substernal chest pain and heartburn occur in approximately 40 to 60 percent of patients [30]. The etiology of chest pain in patients with achalasia is unclear as it does not always correlate with radiographic or manometric findings [31]. Chest pain is more common in younger patients and often fails to respond to treatment, but tends to diminish over the course of several years. (See 'Pathogenesis' above and "Evaluation of the adult with chest pain of esophageal origin".)

Patients frequently report retrosternal burning discomfort similar to the heartburn typical of GERD. This may in fact be due to gastroesophageal reflux, or to direct irritation of the esophageal lining by food, pills, or lactate production by bacterial fermentation of retained carbohydrates [33,34]. Abnormal esophageal motor activity also might trigger the sensation of heartburn.

Patients may have hiccups due to obstruction of the distal esophagus [35]. In order to overcome the distal obstruction, affected patients eat more slowly and often adopt specific maneuvers such as lifting the neck or throwing the shoulders back in order to enhance esophageal emptying. Uncommonly, patients may present with a globus sensation. Weight loss is usually mild, although significant weight loss may be seen in some patients [30]. Rapid progression of dysphagia and profound weight loss are suggestive of pseudoachalasia due to a malignancy. (See "Globus sensation", section on 'Clinical manifestations' and 'Differential diagnosis' below.)

Radiographic findings — A plain radiograph of the chest may reveal widening of the mediastinum due to the dilated esophagus. The normal gastric air bubble may be absent due to the failure of lower esophageal sphincter (LES) relaxation that prevents swallowed air from entering the stomach (image 1). Findings on barium esophagram in patients with achalasia are discussed below. (See 'Barium esophagram' below.)

DIAGNOSTIC EVALUATION

Diagnostic approach — Achalasia should be suspected in the following patients:

- Dysphagia to solids and liquids
- Heartburn unresponsive to a trial of proton pump inhibitor therapy
- Retained food in the esophagus on upper endoscopy

- Unusually increased resistance to passage of an endoscope through the esophagogastric junction

Esophageal manometry is required to establish the diagnosis (algorithm 1). Diagnostic manometric findings of achalasia are incomplete relaxation of the lower esophageal sphincter (LES; manifested as integrated relaxation pressure [IRP] above the upper limit of normal) and aperistalsis in the distal two-thirds of the esophagus. In patients with equivocal esophageal manometry results, barium esophagram can help to assess esophageal emptying and esophagogastric junction morphology. In addition, measuring esophagogastric junction (EGJ) distensibility with the functional lumen imaging probe (FLIP) may help to clarify equivocal manometric findings, and this is discussed separately. (See "Functional lumen imaging probe (FLIP) for adults with esophageal disorders".)

Endoscopic evaluation with upper gastrointestinal endoscopy should be performed in patients with suspected achalasia to exclude a malignancy at the esophagogastric junction that can mimic achalasia. (See 'Esophageal manometry' below and 'Upper endoscopy' below.)

We perform additional evaluation with endoscopic ultrasonography and fine-needle aspiration to definitively rule out a malignancy at the esophagogastric junction in patients with any one of the following [36,37]:

- Clinical features suggestive of a malignancy (eg, symptoms of less than six months duration, new onset of dysphagia in patients >60 years, rapid or marked weight loss)
- Abnormal endoscopic evaluation (eg, unusually increased resistance to passage of endoscope through the esophagogastric junction or mucosal changes suggestive of a malignancy)

Our approach (algorithm 1) is largely consistent with guidelines from the American College of Gastroenterology and the American Gastroenterological Association [37,38].

Esophageal manometry — Both conventional and high-resolution manometry (HRM) can diagnose achalasia, but HRM is preferred and has essentially replaced conventional manometry entirely [39,40]. HRM is used to categorize achalasia into one of three distinctive subtypes, which can guide prognosis and management [41-46]. (See "High resolution manometry", section on 'Disorders of EGJ outflow obstruction' and "Overview of the treatment of achalasia", section on 'Choice of treatment'.)

High-resolution manometry — Achalasia is diagnosed on HRM by an elevated median IRP, which indicates impaired esophagogastric junction relaxation, and absence of normal

peristalsis. The IRP is the median of the maximal relaxation pressures of the esophagogastric junction in four seconds during the 10-second window of esophagogastric junction relaxation that follows a swallow. The upper limit of normal median IRP value varies among manometry systems; for the most widely used system at this time, an elevated median IRP is identified as ≥15 mmHg. (See "High resolution manometry", section on 'Integrated relaxation pressure (IRP)'.)

According to the Chicago Classification (CC, version 4.0 [CC-4]) of patterns of esophageal pressurization on HRM, achalasia is subtyped into the following (figure 3) [47]:

- **Type I (classic achalasia)** – Swallowing results in no significant change in esophageal pressurization. By CC-4 criteria, type I achalasia has 100 percent failed peristalsis as indicated by a distal contractile integral (DCI, an index of the strength of distal esophageal contraction) <100 mmHg·s·cm.

- **Type II** – Swallowing results in simultaneous pressurization that spans the entire length of the esophagus. According to CC-4, type II achalasia has 100 percent failed peristalsis and pan-esophageal pressurization seen in ≥20 percent of swallows.

- **Type III (spastic achalasia)** – Swallowing results in premature and often lumen-obliterating contractions or spasms. By CC-4 criteria, type III achalasia has no normal peristalsis and premature (spastic) contractions with distal latency <4.5 seconds and DCI >450 mmHg·s·cm seen in ≥20 percent of swallows.

These subtypes have important implications for management, and HRM is preferred over conventional manometry for the diagnosis of achalasia. (See "Overview of the treatment of achalasia", section on 'Treatment approach'.)

Barium esophagram — Findings on barium esophagram that are suggestive of achalasia include:

- Dilation of the esophagus. In patients with late- or end-stage achalasia, the esophagus may appear significantly dilated (megaesophagus), angulated, and tortuous, giving it a sigmoid shape.

- Narrow esophagogastric junction with "bird-beak" appearance caused by the persistently contracted LES (image 2A-B).

- Aperistalsis.

- Delayed emptying of barium [48].

However, barium esophagram is not a sensitive test for achalasia, as it may be interpreted as normal in up to one-third of patients [30]. In some patients, purposeless, spastic contractions are observed in the esophageal body.

A timed barium esophagram (TBE) can be useful for documenting bolus retention for patients with untreated achalasia in addition to assessing response to treatment. To perform TBE, the patient drinks approximately 100 ml of low-density barium sulphate suspension, and oblique films are taken in the upright position at 1, 2, and 5 minutes after barium ingestion [49]. Most patients with untreated achalasia exhibit barium retention (measured by the height of the barium column) at one or more of these time points. After treatment, complete esophageal emptying at one minute post-barium ingestion is consistent with treatment success.

Upper endoscopy — Upper endoscopy may reveal a dilated esophagus that contains residual material, sometimes in large quantities. The appearance of the LES may range from normal to a thickened muscular ring with a rosette configuration on retroflexed view. In patients with achalasia, the LES typically does not open spontaneously to allow effortless passage of the endoscope into the stomach but, unlike obstruction caused by neoplasms or fibrotic strictures, the contracted LES can usually be traversed easily with gentle pressure on the endoscope. The esophageal mucosa usually appears normal in patients with achalasia [30]. Nonspecific changes that may be seen include erythema and ulceration due to inflammation, secondary to retained food and pills. Stasis may predispose to esophageal candidiasis, which may be seen as adherent whitish plaques. (See "Esophageal candidiasis in adults", section on 'Epidemiology'.)

Endoscopic ultrasound — Findings of achalasia on endoscopic ultrasound (EUS) can include a thickened circular muscle layer at the LES and through the smooth muscle esophagus. Although the accuracy of EUS in distinguishing achalasia from pseudoachalasia has not been established, EUS is useful for characterizing tumors of the distal esophagus and gastric cardia [50]. EUS findings of marked (>10 mm) and/or asymmetric esophageal wall thickening are suggestive of an underlying malignancy that may be confirmed by fine-needle aspiration. (See "Endoscopic ultrasound-guided fine needle aspiration in the gastrointestinal tract", section on 'Upper GI tract lesions'.)

Functional lumen imaging probe — Functional lumen imaging probe (FLIP) is a catheter-based instrument with an attached, fluid-filled balloon that surrounds a series of impedance planimetry electrodes. The FLIP catheter is passed into the esophagus, and it displays the diameter of various esophageal segments in real-time images. In addition, FLIP provides real-time information about the distensibility of the esophageal segments in the form of a distensibility index, and information about esophageal motility in the form of FLIP topography. In achalasia, FLIP reveals a narrowed esophagogastric junction segment that has a low

distensibility index, and inflation of the FLIP balloon results in abnormal or no esophageal contractions. FLIP may provide useful data to establish the diagnosis of achalasia in equivocal cases [51]. (See "Functional lumen imaging probe (FLIP) for adults with esophageal disorders".)

DIAGNOSIS

The diagnosis of achalasia is established by the presence of aperistalsis in the distal two-thirds of the esophagus and incomplete lower esophageal sphincter (LES) relaxation on manometry (elevated median integrated relaxation pressure [IRP] by high-resolution manometry [HRM]). In patients with typical achalasia symptoms (dysphagia to solids and liquids and regurgitation of bland undigested food or saliva) and equivocal manometric findings, the diagnosis is supported by aperistalsis, dilation of the esophagus, narrow esophagogastric junction, and poor emptying on barium esophagram. Pseudoachalasia due to cancer at the esophagogastric junction should be excluded by endoscopic evaluation as discussed above. (See 'Diagnostic approach' above.)

DIFFERENTIAL DIAGNOSIS

Achalasia may be misdiagnosed as gastroesophageal reflux disease (GERD), especially in patients with chest pain of a burning quality typical of heartburn. The differential diagnosis of achalasia also includes other esophageal motility disorders and pseudoachalasia due to a malignancy. The differential diagnosis of dysphagia is discussed in detail, separately. (See "Approach to the evaluation of dysphagia in adults", section on 'Symptom-based differential diagnosis'.)

- **Gastroesophageal reflux disease** – In patients with GERD, regurgitated food is typically sour tasting due to the presence of gastric acid. In contrast, in patients with achalasia, food and saliva are regurgitated from the esophagus and are therefore bland. Esophageal manometry is diagnostic of achalasia. Unlike the incomplete lower esophageal sphincter (LES) relaxation and aperistalsis that characterize achalasia, patients with GERD often have nonspecific manometric findings including ineffective esophageal motility and hypotensive LES. (See 'Esophageal manometry' above.)

- **Pseudoachalasia** – Malignancy can cause pseudoachalasia either by invading the esophageal neural plexuses directly (eg, adenocarcinoma of the esophagogastric junction) or through the release of uncharacterized humoral factors that disrupt esophageal function as part of a paraneoplastic syndrome. In addition to gastric carcinoma, other tumors that can produce the syndrome include cancer of the esophagus, carcinoma of the

lung, lymphoma, and pancreatic carcinoma [52,53]. Patients with pseudoachalasia can have the same manometric findings as those with achalasia but can be differentiated by upper endoscopy and endoscopic ultrasound (EUS). (See 'Esophageal manometry' above and 'Upper endoscopy' above and 'Endoscopic ultrasound' above.)

- **Other esophageal motility disorders** – Patients with distal esophageal spasm and jackhammer esophagus may also present with dysphagia to solids and liquids. Esophageal manometry testing can distinguish achalasia from these esophageal motility disorders as LES relaxation (integrated relaxation pressure [IRP]) is normal in these conditions. (See 'Esophageal manometry' above and "Distal esophageal spasm and hypercontractile esophagus".)

NATURAL HISTORY AND PROGNOSIS

Disease course — Without treatment, patients with achalasia can develop progressive dilation of the esophagus. Late- or end-stage achalasia is characterized by esophageal tortuosity, angulation, and severe dilation or megaesophagus (diameter >6 cm). Approximately 10 to 15 percent of patients who have undergone treatment for achalasia will develop late- or end-stage achalasia, and up to 5 percent of patients in some series require esophagectomy [54,55].

Cancer risk — Patients with achalasia are at increased risk for developing esophageal cancer; however, the absolute risk for esophageal cancer is low [56-61]. In one study in which 448 patients with achalasia were followed for a median of 9.6 years, esophageal cancer developed in 15 patients (3.3 percent) after mean symptom duration of 13 years [59]. While the risk of esophageal cancer was increased 28-fold (95% CI 17-46) as compared with controls, the annual incidence of esophageal cancer was only 0.34 percent (95% CI 0.20-0.56).

Esophageal cancer is typically squamous cell type, although some studies have also demonstrated an increased risk of esophageal adenocarcinoma. Endoscopic surveillance in patients with achalasia is controversial and is not routinely recommended. In a population-based study in Sweden in which 1062 patients with achalasia were followed for up to 24 years, the risk of esophageal cancer was increased 16-fold (95% CI 8.8-28.3) above that of population controls [56]. Esophageal cancer was diagnosed an average of 14 years following the diagnosis of achalasia. It was estimated that annual surveillance endoscopy after the first year would be required in 406 males and 2200 females to detect one cancer. (See "Overview of the treatment of achalasia", section on 'Surveillance'.)

There are limited long-term data on the incidence of esophageal cancer following a Heller myotomy for achalasia. However, available data suggest that patients remain at increased risk for esophageal cancer [61]. (See "Surgical myotomy for achalasia", section on 'Other complications'.)

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: Achalasia".)

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 topics (see "Patient education: Achalasia (The Basics)" and "Patient education: Upper endoscopy (The Basics)")
- Beyond the Basics topics (See "Patient education: Achalasia (Beyond the Basics)".)

SUMMARY AND RECOMMENDATIONS

- **Pathogenesis** – Achalasia is thought to result from progressive degeneration of ganglion cells in the myenteric plexus in the esophageal wall leading to failure of relaxation of the lower esophageal sphincter (LES) accompanied by a loss of peristalsis in the distal esophagus. The etiology of primary or idiopathic achalasia is unknown. Secondary

achalasia is due to diseases that cause esophageal motor abnormalities similar or identical to those of primary achalasia (table 1). (See 'Pathogenesis' above.)

- **Epidemiology** – Achalasia has been regarded as an uncommon disorder with an annual incidence of approximately 1.6 cases per 100,000 individuals and prevalence of 10 cases per 100,000 individuals. Achalasia can occur at any age, but is usually diagnosed in patients between 25 and 60 years. Males and females are affected with equal frequency. (See 'Epidemiology' above.)

- **Clinical manifestations** – Dysphagia for solids and liquids and regurgitation of bland undigested food or saliva are the most frequent symptoms in patients with achalasia. Other symptoms include chest pain, heartburn, and difficulty belching. (See 'Clinical manifestations' above.)

- **Diagnostic approach** – Achalasia should be suspected in the following patients (see 'Diagnostic approach' above):

  - Dysphagia to solids and liquids
  - Heartburn unresponsive to a trial of proton pump inhibitor therapy for four weeks
  - Retained food in the esophagus on upper endoscopy
  - Unusually increased resistance to passage of an endoscope through the esophagogastric junction

  Esophageal manometry is required to establish the diagnosis (algorithm 1). Achalasia is diagnosed on high-resolution manometry (HRM) by an elevated median integrated relaxation pressure (IRP) and absence of normal peristalsis. (See 'Esophageal manometry' above.)

  In patients with equivocal esophageal manometry results, barium esophagram should be performed to assess esophageal emptying and esophagogastric junction morphology. Upper endoscopy should be performed in all patients with achalasia to exclude an esophagogastric malignancy.

  We perform additional evaluation with endoscopic ultrasound (EUS) and fine-needle aspiration to definitively rule out a malignancy at the esophagogastric junction in patients with any one of the following:

  - Clinical features suggestive of a malignancy (eg, symptoms of less than six months duration, new onset of dysphagia in patients >60 years, rapid or marked weight loss)

- Atypical endoscopic evaluation (eg, unusually increased resistance to passage of endoscope or mucosal changes suggestive of a malignancy)

- **Natural history and prognosis** – Patients with achalasia are at an increased risk for developing esophageal cancer; however, the absolute risk is low. Surveillance for esophageal cancer is therefore not routinely performed for patients with achalasia. (See 'Cancer risk' above and "Overview of the treatment of achalasia", section on 'Surveillance'.)

  Without treatment, patients with achalasia can develop progressive dilation of the esophagus. Late- or end-stage achalasia is characterized by esophageal tortuosity, angulation, and severe dilation or megaesophagus (diameter >6 cm). Approximately 10 to 15 percent of patients who have undergone treatment for achalasia will develop late- or end-stage achalasia, and up to 5 percent of patients may require esophagectomy. (See 'Disease course' above.)

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Topic 2268 Version 33.0

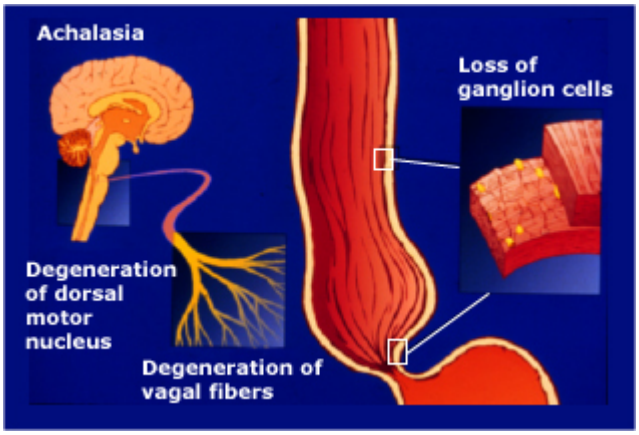
GRAPHICS

Diseases with manometric findings of achalasia

Malignancy, especially gastric carcinoma
Chagas disease
Amyloidosis
Sarcoidosis
Neurofibromatosis
Eosinophilic esophagitis
Multiple endocrine neoplasia, type 2B
Juvenile Sjögren's syndrome with achalasia and gastric hypersecretion
Chronic idiopathic intestinal pseudo-obstruction
Anderson-Fabry disease

Graphic 71111 Version 3.0

Pathophysiology of achalasia



Schematic representation of the pathophysiology of achalasia which results from the degeneration of neurons in the esophageal wall. Histologic examination reveals decreased numbers of neurons (ganglion cells) in the myenteric plexuses, and the ganglion cells that remain often are surrounded by lymphocytes and, less prominently, by eosinophils. This inflammatory degeneration preferentially involves the nitric oxide-producing, inhibitory neurons that effect the relaxation of esophageal smooth muscle, resulting in an elevation in basal lower esophageal sphincter (LES) pressure and an inability of the sphincter muscle to relax normally; the cholinergic neurons that contribute to LES tone by causing smooth muscle contraction are relatively spared[1]. In some patients, degenerative changes also are found in the ganglion cells of the dorsal motor nucleus of the vagus in the brainstem, and Wallerian degeneration has been observed in the vagal fibers that supply the esophagus.

Reference:

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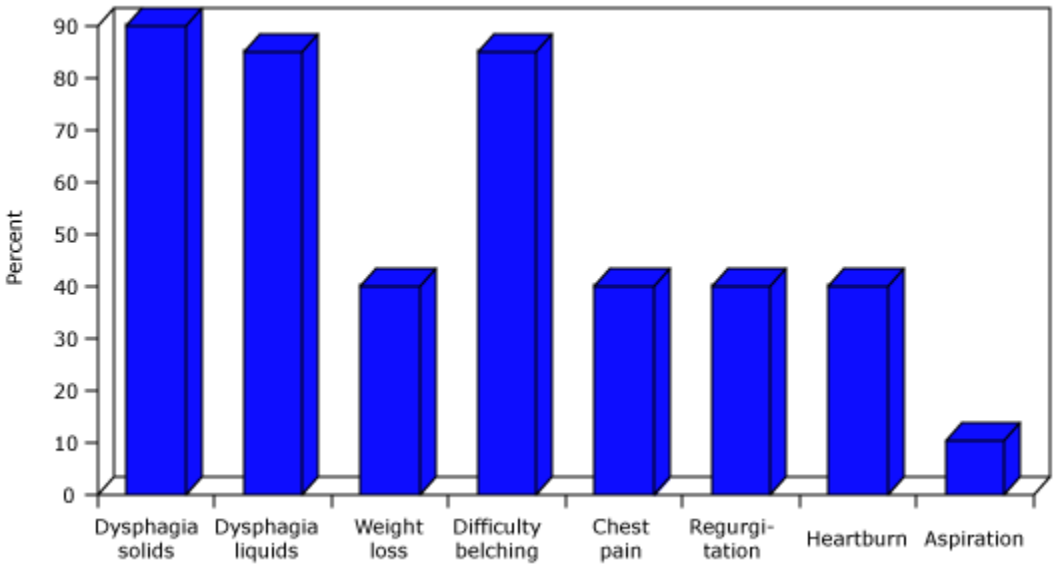
Frequency of the symptoms of achalasia



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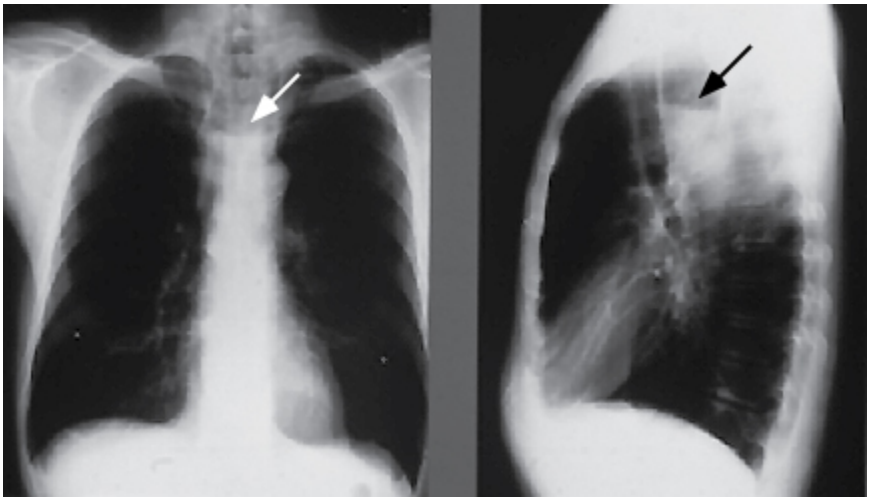
Achalasia



PA and lateral chest x-rays from a patient with achalasia. The major findings are a widened mediastinum caused by the dilated esophagus, an air-fluid level in the upper chest due to retained fluid in the dilated esophagus (arrows), and absence of the gastric air bubble.

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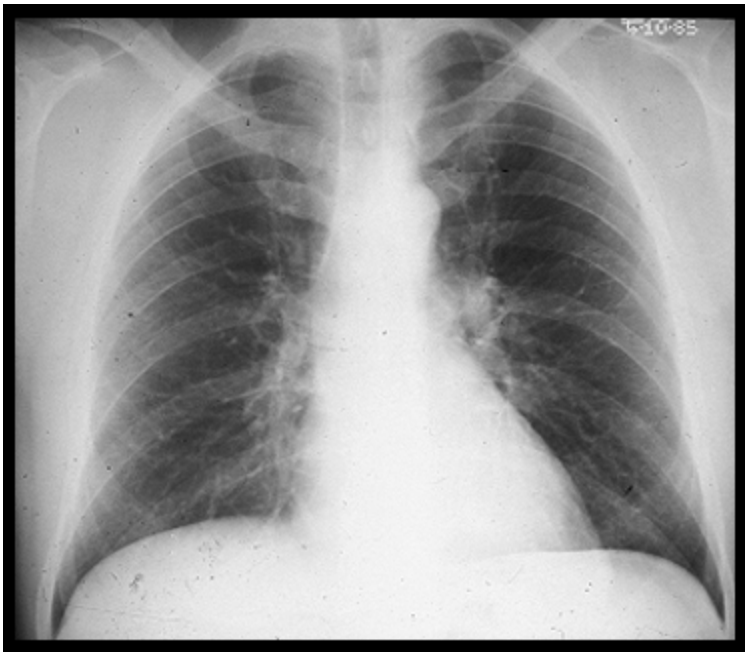
Normal chest radiograph

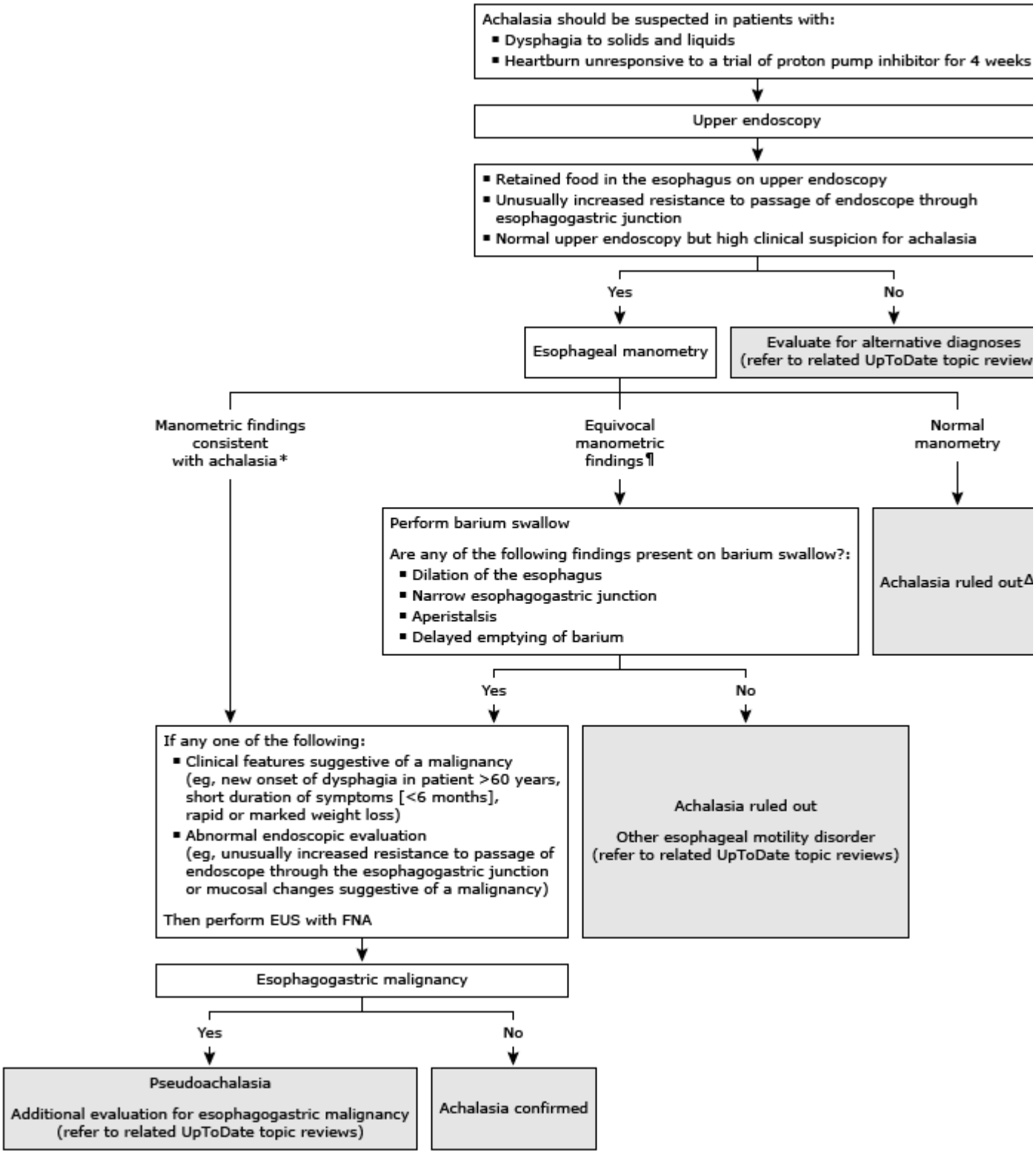


Posteroanterior view of a normal chest radiograph.

Courtesy of Carol M Black, MD.

Graphic 65576 Version 5.0

Diagnostic evaluation in patients with suspected achalasia



LES: lower esophageal sphincter; EUS: endoscopic ultrasound; FNA: fine needle aspiration; IRP: integrated relaxation pressure.

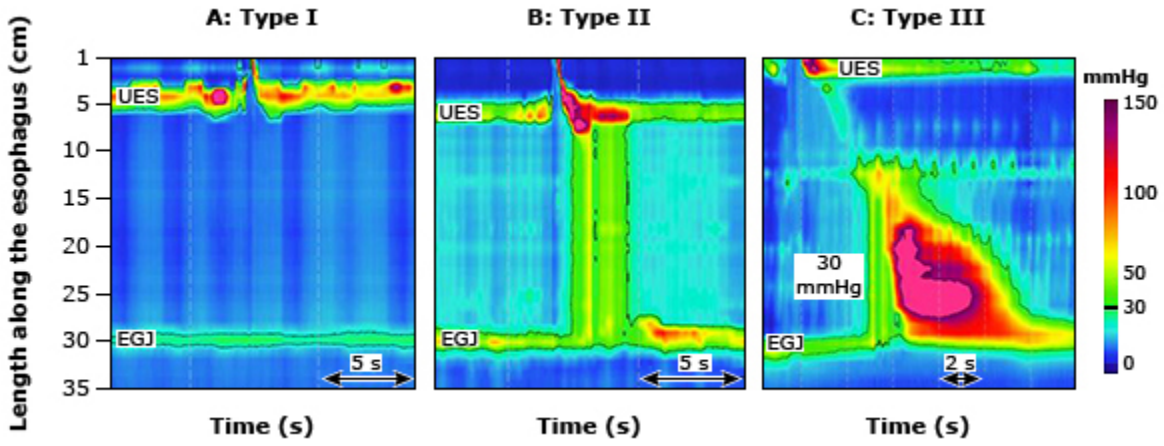
* Diagnostic manometric findings of achalasia are incomplete relaxation of the LES (IRP above the upper lim of normal) and aperistalsis in the distal two-thirds of the esophagus.

¶ Equivocal manometric findings include incomplete LES relaxation but some preserved peristalsis; some complete LES relaxation with aperistalsis.

Δ Additional evaluation should be based on patient symptoms.

Graphic 110069 Version 1.0

Esophageal pressure topography plot of achalasia subtypes in the Chicago Classification



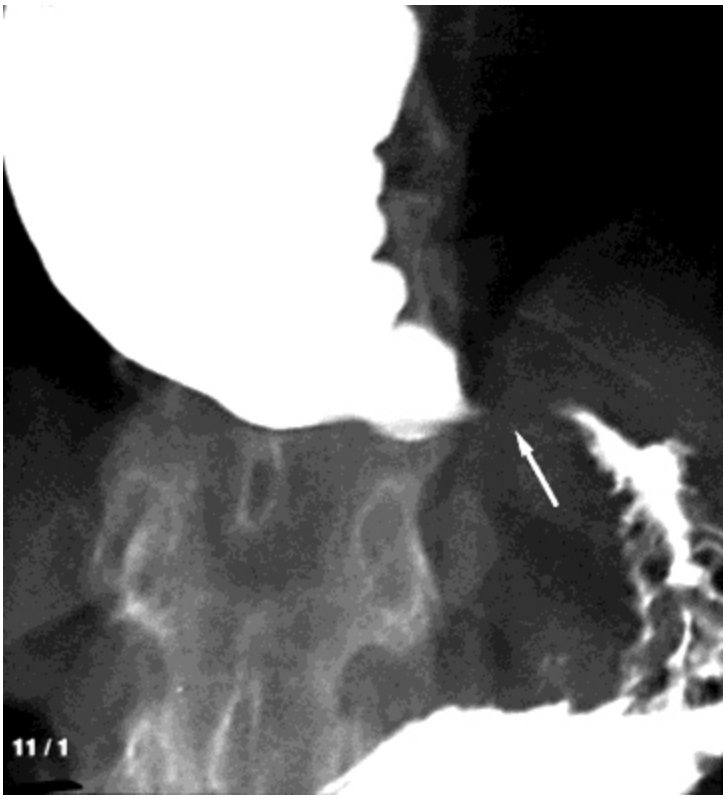
In each case, the 30 mmHg isobaric contour is highlighted in black and there is impaired EGJ relaxation evident by the EGJ never relaxing to less than 30 mmHg in any panel. With type I achalasia, there is minimal contractile activity between the UES and EGJ. Type II is defined by ≥20 percent of swallows (supine posture, 5 mL water) with panesophageal pressurization to ≥30 mmHg. With type III, there is ≥20 percent of swallows with either premature contractions or fragments of peristalsis.

EGJ: esophagogastric junction; UES: upper esophageal sphincter.

Original figure modified for this publication. Pandolfino JE, Kwiatek MA, Nealis T, et al. Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology 2008; 135:1526. Illustration used with the permission of Elsevier Inc. All rights reserved.

Graphic 86439 Version 2.0

Dilation of the esophagus in a patient with achalasia (barium esophagram)



Barium esophagram in a 62-year-old man demonstrates a dilated, barium-filled esophagus with a region of persistent narrowing (arrow) at the gastroesophageal junction, producing the so-called bird's beak appearance. Achalasia was confirmed with manometry and the patient underwent successful dilation of the esophagus.

Courtesy of Jonathan Kruskal, MD.

Graphic 54252 Version 4.0

Achalasia

Barium esophagram showing a dilated esophagus and bird's beak appearance typical of achalasia. Retained food is also visible.

Courtesy of Ram Dickman, MD.

Graphic 53672 Version 4.0

Contributor Disclosures

Stuart J Spechler, MD Consultant/Advisory Boards: Castle Biosciences [Barrett's esophagus]; Interpace Diagnostics [Barrett's esophagus]; Ironwood Pharmaceuticals [GERD]; ISOThrive, LLC [GERD]; Phathom Pharmaceuticals [GERD]; Takeda Pharmaceuticals [GERD]. All of the relevant financial relationships listed have been mitigated. **Nicholas J Talley, MD, PhD** Patent Holder: Australian Provisional Patent [Diagnostic marker for functional gastrointestinal disorders]; Biomarkers of irritable bowel syndrome [Irritable bowel syndrome]; Mayo Clinic [Dysphagia questionnaire]; Mayo Clinic [Bowel Disease questionnaire]; Nepean Dyspepsia Index [Dyspepsia]; Nestec [Irritable bowel syndrome]; Singapore Provisional Patent [BDNF Tissue Repair Pathway]. Grant/Research/Clinical Trial Support: Alimetry [Gastric mapping device research collaboration]; Allakos [Gastric eosinophilic disease]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; Intrinsic Medicine [Bowel syndrome with constipation]; NHMRC Centre for Research Excellence in Digestive Health [NHMRC Investigator grant]. Consultant/Advisory Boards: Adelphi Values [Functional dyspepsia]; Allakos [Gastric eosinophilic disease, AK002]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; AusEE [Eosinophilic gut diseases]; Bayer [Inflammatory bowel syndrome]; BluMaiden [Microbiome Ad Board]; Comvita Mānuka Honey [Digestive health]; Dr Falk Pharma [Eosinophilia]; GlaxoSmithKline Australia [Educational speaker eosinophilic gut disease]; Glutagen [Celiac disease]; International Foundation for Functional Gastrointestinal Disorders [Advisory board, functional GI disorders]; Intrinsic Medicine [Human milk oligosaccharide]; IsoThrive [Esophageal microbiome]; Planet Innovation [Gas capsule, inflammatory bowel syndrome]; Progenity Inc [Intestinal capsule]; Rose Pharma [IBS]; Viscera Labs [Inflammatory bowel syndrome, diarrhea]. Other Financial Interest: Elsevier textbook royalties [Medical education]. All of the relevant financial relationships listed have been mitigated. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

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