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Esophageal Disorders

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 - Clinical and research focus: Esophageal disorders, gastrointestinal motility



Disclosures

- Scientific Advisory Board (Regeneron Pharmaceutical)

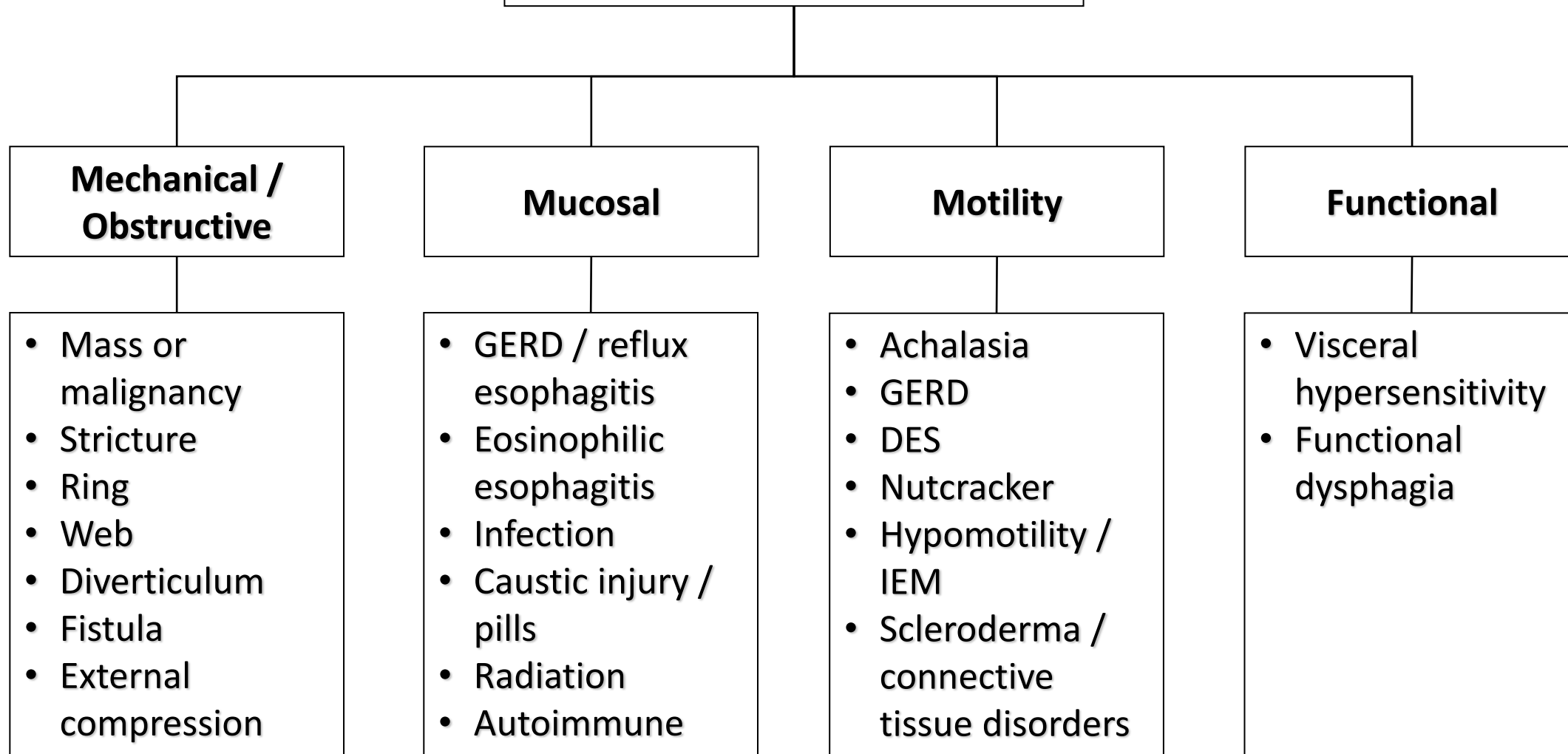


Objectives

- Overview of the diagnostic approaches to esophageal and swallowing symptoms
- Review common esophageal disorders
 - Gastroesophageal reflux disease and complications
 - Esophageal motility disorders
 - Eosinophilic esophagitis
 - Other esophagitis (infectious, pill-induced)



Etiologies of Esophageal Symptoms



Diagnostics for Esophageal and Swallowing disorders



Case 1

A 75 years old woman with a history of diabetes, hypertension, coronary artery disease, and cerebral vascular accident, and gastroesophageal reflux disease who presents for evaluation of swallowing symptoms. She describes a sensation of food sticking in her throat region when swallowing. The symptoms may occur with both liquids and solids. She also notices frequent coughing with eating as well. She denies odynophagia. She reports some heartburn after meals that improved with the use of proton pump inhibitors.



Case 1

What is the most appropriate next step in evaluation of this patient's symptoms?

- A. Barium swallow.
- B. Upper endoscopy.
- C. Chest CT.
- D. Esophageal manometry.
- E. Modified barium swallow.



Imaging

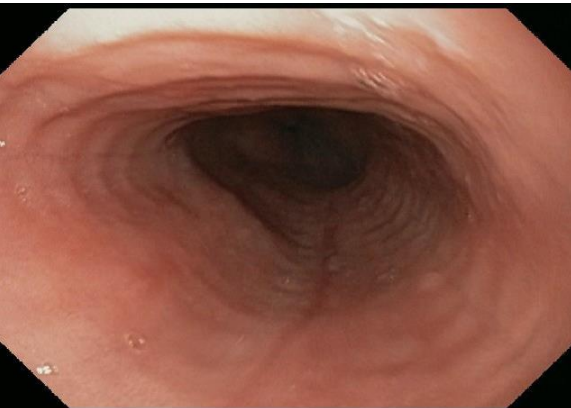
- Videofluoroscopic swallow study/modified barium swallow
 - Assess oropharyngeal bolus transport
 - Evaluate structural abnormalities of oropharynx and upper esophagus
- Barium swallow
 - Evaluate for high-grade esophageal obstructive lesion, strictures, diverticuli, or retained foreign body
 - May demonstrate characteristic changes of certain motility disorders, hiatal hernia, or reflux



Endoscopy



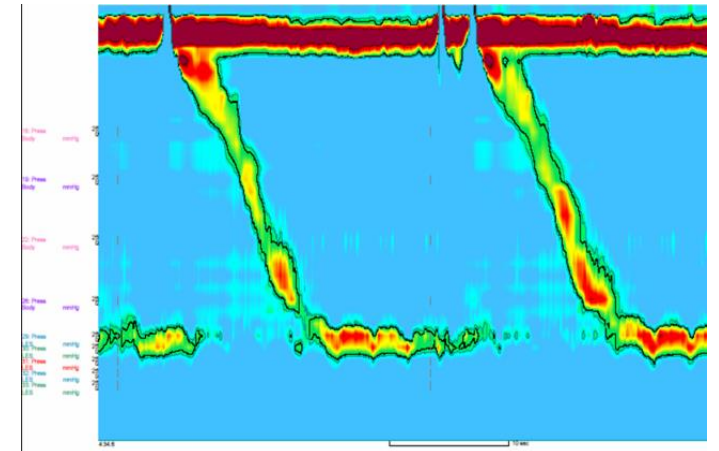
- Rule out mechanical obstruction
 - Malignancy
 - Foreign body
 - Stricture, ring, web



- Assess and biopsy abnormal mucosa
 - Infection (viral, fungal)
 - Inflammation (GERD, caustic)
 - Eosinophilic esophagitis

Esophageal Manometry

- Transnasal passage of catheter with pressure sensors into the esophagus and stomach
- Indications
 - Assess esophageal contractile activity and anatomical landmarks => diagnosis of motility disorders
 - Assist in placement of pH probe
 - Pre-operative evaluation for anti-reflux surgery or other esophageal/chest surgeries



Ambulatory Reflux Monitoring

- Continuous monitoring to quantify reflux over study period (24-96 hrs)
- Modalities:
 - Transnasal pH probe or endoscopically placed capsule (wireless monitoring)
 - pH + impedance monitoring (evaluate acid + nonacid reflux)
- A battery-powered device records reflux data and patient-reported symptoms
 - Correlation between symptoms and reflux events



Case 1

What is the most appropriate next step in evaluation of this patient's symptoms?

- A. Barium swallow.
- B. Upper endoscopy.
- C. Chest CT.
- D. Esophageal manometry.
- E. Modified barium swallow.



Case 1: Answer

E. Modified barium swallow.

The patient in question presented with symptoms suspicious for oropharyngeal dysphagia, with a sensation of food sticking in the throat region and coughing with eating that may suggest aspiration. The most useful test for evaluating oropharyngeal symptoms is videofluoroscopic modified barium swallow. Full column barium swallow, upper endoscopy, and esophageal manometry (answer A, B, D) are all esophageal evaluations, but provide little information on oropharyngeal function. Chest CT (answer C) may provide be helpful for evaluation of extraluminal malignancy that may contribute to swallowing symptoms. However, it is generally not a first-line diagnostic tool for swallowing symptoms, particularly for oropharyngeal symptoms.



Esophageal Disorders: Gastroesophageal Reflux Disease



GERD

- 25-40% healthy adults in US experience GERD symptoms at least once per month
 - 7-10% of adults experience symptoms daily
 - Likely underestimated due to self-treatment/OTC PPI
- Gender: Male \approx Female
 - Reflux esophagitis: 2-3:1 (M:F)
 - Barrett's esophagus: 10:1 (M:F)
- GERD prevalence increases with age
 - Mean \approx 40 years old
 - Intensity of symptoms may \downarrow after age 50, but prevalence of erosive esophagitis \uparrow with age



GERD: Pathophysiology

- Gastroesophageal reflux is physiologically normal
 - Normally with meals
 - Refluxate
 - **Gastric acid**, bile, pancreatic secretion, food matter
 - Pathologic reflux results when irritation of the esophagus (symptom \pm inflammation) occurs from refluxate exposure
 - Increased acid/refluxate exposure
 - Decreased barrier to irritation
- Factors associated with GERD
 - Esophagus: Impaired esophageal motility or epithelial barrier function
 - LES: Weak LES or inappropriate relaxation
 - Stomach: \uparrow acid production, delayed emptying, hiatal hernia
 - Others:
 - Obesity
 - Pregnancy / hormonal changes
 - Medications
 - Ingestions: Food, alcohol, tobacco



GERD: Clinical Presentation

- Esophageal Symptoms

- Typical

- Heartburn
 - Regurgitation

- Atypical

- Chest pain
 - Dysphagia
 - Odynophagia
 - Nausea
 - Globus sensation
 - Epigastric pain

- Extraesophageal Manifestations

- ENT

- Hoarseness, sorethroat, cough, post-nasal drip

- Pulmonary

- Asthma
 - COPD
 - Interstitial lung disease

- Dental erosions

- Waterbrash



Case 2

A 70 years old man with a history of Alzheimer's presents for evaluation reflux symptoms for 2 months. He describes a heartburn sensation and regurgitation that is worse with eating or lying down at night. He denies dysphagia, odynophagia, abdominal pain, or nausea. He has never had similar symptoms in the past. He has tried taking over-the-counter antacids and histamine-2 receptor antagonists without adequate relief of his symptoms.



Case 2

Which of the following is an appropriate next step in management?

- A. Start omeprazole 20 mg at bedtime for nocturnal symptoms.
- B. Trial of metoclopramide.
- C. Avoid proton pump inhibitor due to history of Alzheimer's.
- D. Upper endoscopy.
- E. 24-hour pH monitoring.



GERD: Management

- Lifestyle modification
 - Dietary modification
 - Avoid trigger food items
 - Spicy food, citrus food, chocolate, caffeine, carbonated drinks, alcohol, peppermint
 - Multiple, small meals
 - Avoid recumbency for 2-3 hours after eating
 - Tobacco cessation
 - Elevating the head of bed
 - Weight loss



Strategies with the best evidence for improving GERD symptoms



GERD: Management

- Empiric acid suppression therapy
 - Trial x 8 weeks and titrate dose to severity of symptoms
 - Administer ~30 min before meals
 - Always try to taper to lowest possible dose when symptoms respond
- Risk factors for PPI failure: longer duration of disease, hiatal hernia, extraesophageal symptoms, low compliance
- Pregnancy: Antacids, H2 receptor antagonists, PPI (except omeprazole – category C) are safe to use



GERD: Management

- PPI Adverse Effects?
 - Acute side effects in <2%: headache, diarrhea, constipation, abdominal pain
 - Increased risk for community-acquired pneumonia in elderly with short term usage (upon initiation)
 - Chronic PPI use:
 - Malabsorption of B12 (elderly), calcium, magnesium
 - Osteoporosis and hip fractures in high risk groups
 - Bacterial gastroenteritis and *C. difficile* → Only significant adverse effect identified in RCT
 - Small intestinal bacterial overgrowth
 - Suggested association
 - Cardiovascular events?? => *no evidence on further investigation*
 - Chronic renal insufficiency?? => *further investigation needed*
 - Dementia?? => *no evidence on multiple subsequent studies*



GERD: Management

- When should endoscopy and further diagnostic testing be performed to evaluate GERD?
 - Alarming features
 - Dysphagia / odynophagia
 - Weight loss
 - Signs of GI bleeding/anemia
 - Vomiting
 - Abnormal imaging
 - Family history of upper GI malignancy
 - Age > 50
 - Nonresponder to medical therapy



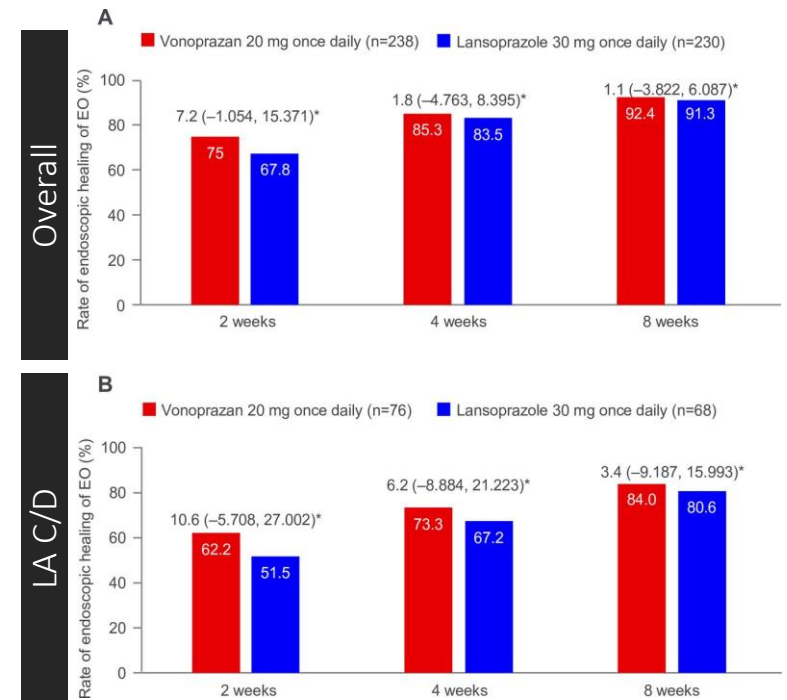
GERD: Management

- Options for PPI nonresponders:
 - Optimize timing of PPI and compliance
 - Potassium channel acid blockers (PCAB)
 - Esophageal function testing (manometry, pH monitor)
 - Addition of H2 blockers for nocturnal symptoms
 - Most beneficial if pH testing shows overnight acid reflux
 - No role for metoclopramide without gastroparesis
 - Neuromodulator for hypersensitivity: TCA, Trazodone
 - Consider GABA-B receptor agonists as reflux inhibitors
 - Baclofen 5-20 mg tid (not FDA approved for GERD)
 - Decreases acid exposure, reflux episodes, symptoms, and TLESR
 - Side effects: dizziness, somnolence, constipation



GERD: Management - PCAB

- P-CAB competitively binds to K⁺-binding site of proton pump
 - Inhibits H⁺/K⁺ exchange and acid release
- Differences from PPI
 - Not pro-drug -> pH-independent and does not require activation
 - Binds to both active (luminal) and inactive (cytoplasmic) proton pumps
- Non-inferior to PPI in treating:
 - Erosive esophagitis
 - GERD symptoms



Ashida K et al. Aliment Pharmacol Ther 2015

Xiao Y et al. Gut 2019

Oshima T. Aliment Pharmacol Ther 2019

GERD: Management

- Anti-reflux Surgery
 - Indications
 - Failed/intolerant of medical therapy, medication dependence
 - Fundoplication
 - Relieves GERD symptoms in over 90% of patients
 - Laparoscopy has comparable 10-year outcome to laparotomy
 - Adverse events: gas-bloat syndrome (15-20%), dysphagia
 - Bariatric surgery may be more effective patients with obesity
 - RYGB >> adjustable gastric band and sleeve gastrectomy
 - Gastric banding and sleeve gastrectomy associated with increased reflux



Case 2

Which of the following is an appropriate next step in management?

- A. Start omeprazole 20 mg at bedtime for nocturnal symptoms.
- B. Trial of metoclopramide.
- C. Avoid proton pump inhibitor due to history of Alzheimer's.
- D. Upper endoscopy.
- E. 24-hour pH monitoring.



Case 2: Answer

D. Upper endoscopy.

The patient in question presented with acute, new-onset reflux symptoms at advanced age. This is an indication for early upper endoscopy to rule out any potential foregut malignancies that may contribute to symptoms. Proton pump inhibitors (PPI) for further acid suppression to control symptoms is appropriate, even patients with history of Alzheimers, as there is no evidence proving causative relationship between PPI and dementia, and multiple population studies have demonstrated no link between them. (answer C). PPI should be used before meals for optimal efficacy, rather than bedtime (answer A). Use of prokinetic agents has not been shown to provide benefit and is not recommended in the absence of gastroparesis (answer B). Objective reflux monitoring may be helpful in PPI-refractory reflux symptoms, especially with normal endoscopy, but it would not be first-line evaluation (answer E).



Case 3

A 40 year-old woman with no significant past medical history presented to the Emergency Department with chest pain over the past week. She described a sharp pain in her substernal region, with no association with exertion, positional changes, or eating. Cardiac evaluations, including an exercise stress test, were negative. Her symptoms were felt to most likely be of an esophageal origin. She denied any dysphagia, odynophagia, nausea, vomiting, heartburn, reflux, or regurgitation symptoms. Her other laboratory evaluations were unremarkable and she had no other complaints.



Case 3

What is the most appropriate next step for the management of this patient?

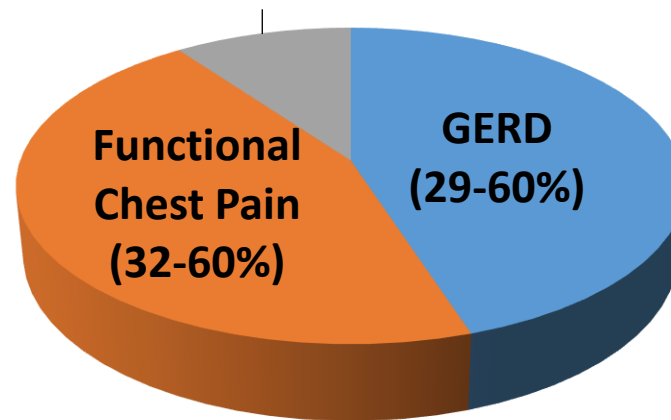
- A. Barium swallow.
- B. Empiric trial of proton pump inhibitor.
- C. Upper endoscopy with mucosal biopsies.
- D. Esophageal manometry with impedance study.
- E. Trial of smooth muscle relaxant (calcium channel blockers).



Non-Cardiac Chest Pain

- Etiologies

Esophageal Motor Disorders (10-18%)



Esophageal motility disorder or spasm only accounts for a small minority of patients with non-cardiac chest pain!

- Evaluation:

- **RULE OUT CARDIAC CAUSE**
- Lifestyle modification, empiric PPI
- EGD, pH study, manometry



Case 3

What is the most appropriate next step for the management of this patient?

- A. Barium swallow.
- B. Empiric trial of proton pump inhibitor.
- C. Upper endoscopy with mucosal biopsies.
- D. Esophageal manometry with impedance study.
- E. Trial of smooth muscle relaxant (calcium channel blockers).



Case 3: Answer

B. Empiric trial of proton pump inhibitor.

The patient in question presented with chest pain symptoms and her cardiac evaluation was unremarkable. The most common cause of non-cardiac chest pain is gastroesophageal reflux disease (GERD), which should be evaluated/treated next. In a young and healthy patient without alarming signs/symptoms, the initial steps of GERD management include lifestyle modification and an empiric trial of proton pump inhibitor (PPI). Diagnostic studies (answers A, C, D) should be considered only after the patient fails her PPI trial or if she has any alarming signs/symptoms. An empiric trial of smooth muscle relaxant (answer E) would not be appropriate without an objective diagnosis of hypercontractile motility disorder, as GERD is a significantly more common cause of non-cardiac chest pain than esophageal dysmotility, and smooth muscle relaxants would worsen reflux.



Esophageal Disorders: Barrett's Esophagus



Case 4

A 45 years old African American woman with a history of gastroesophageal reflux disease presents for annual physical examination. She has been doing well with no complaints. Her reflux symptoms are well-controlled with the use of omeprazole 20 mg once daily. She has previously tried coming off the omeprazole, but her symptoms later recurred. She denies any dysphagia, odynophagia, abdominal pain, nausea, or vomiting. She has been eating a normal, healthy diet and her weight is stable. She denies tobacco or alcohol use. Her family history is unremarkable. Physical examination revealed a thin, healthy-appearing woman with no abnormalities.



Case 4

The patient asked about screening for Barrett's esophagus. Which of the following strategy would you recommend?

- A. Upper endoscopy now and every 10 years thereafter.
- B. Upper endoscopy now and every 5 years thereafter.
- C. Upper endoscopy now and every 3 years thereafter.
- D. Upper endoscopy now and every 1 year thereafter
- E. Start screening with upper endoscopy at age 50.
- F. No endoscopy indicated.



Barrett's Esophagus

- Replacement of normal esophageal squamous epithelium by specialized intestinal metaplasia
 - Chronic GERD -> esophagitis -> metaplastic change -> dysplasia -> adenocarcinoma
- Overall prevalence in US: ~5.6%
 - Patients with GERD: ~5-10%
- Risk factors: Caucasian, age, male, obesity, tobacco, alcohol



Barrett's Esophagus

- Barrett's screening
 - No screening recommended for general population
 - Screening indicated in patients with multiple risk factors associated with Barrett's (AGA recommendations):
 - Age 50 or older
 - Male sex
 - White race
 - Chronic GERD
 - Hiatal hernia
 - Elevated BMI
 - Intra-abdominal distribution of body fat



Barrett's Esophagus

- Barrett's surveillance
 - Endoscopic surveillance with biopsies is indicated for signs of dysplastic progression
 - All biopsies should be examined by pathologists with expertise in esophageal histopathology

No Dysplasia	Low-grade Dysplasia	High-grade Dysplasia
Surveillance every 3-5 years	* Referral for endoscopic therapy <i>or</i> Surveillance every 6-12 months if therapy not performed	* Referral for endoscopic therapy <i>or</i> Referral for surgery <i>or</i> Surveillance every 3 months if therapy not performed



Barrett's Esophagus

- Treatment
 - Endoscopic therapy
 - Endoscopic mucosal resection, radiofrequency ablation
 - Indication: Dysplastic Barrett's
 - All post-endoscopic therapy patients require continued surveillance
 - Chemoprevention
 - PPI: reduced neoplastic progression in patients with Barrett's
 - Aspirin and NSAIDs: reduced risk for esophageal cancer
 - Combination high-dose PPI + aspirin: decreased time to mortality, esophageal cancer, or high-grade dysplasia



Case 4

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- C. Upper endoscopy now and every 3 years thereafter.
- D. Upper endoscopy now and every 1 year thereafter
- E. Start screening with upper endoscopy at age 50.
- F. No endoscopy indicated.



Case 4: Answer

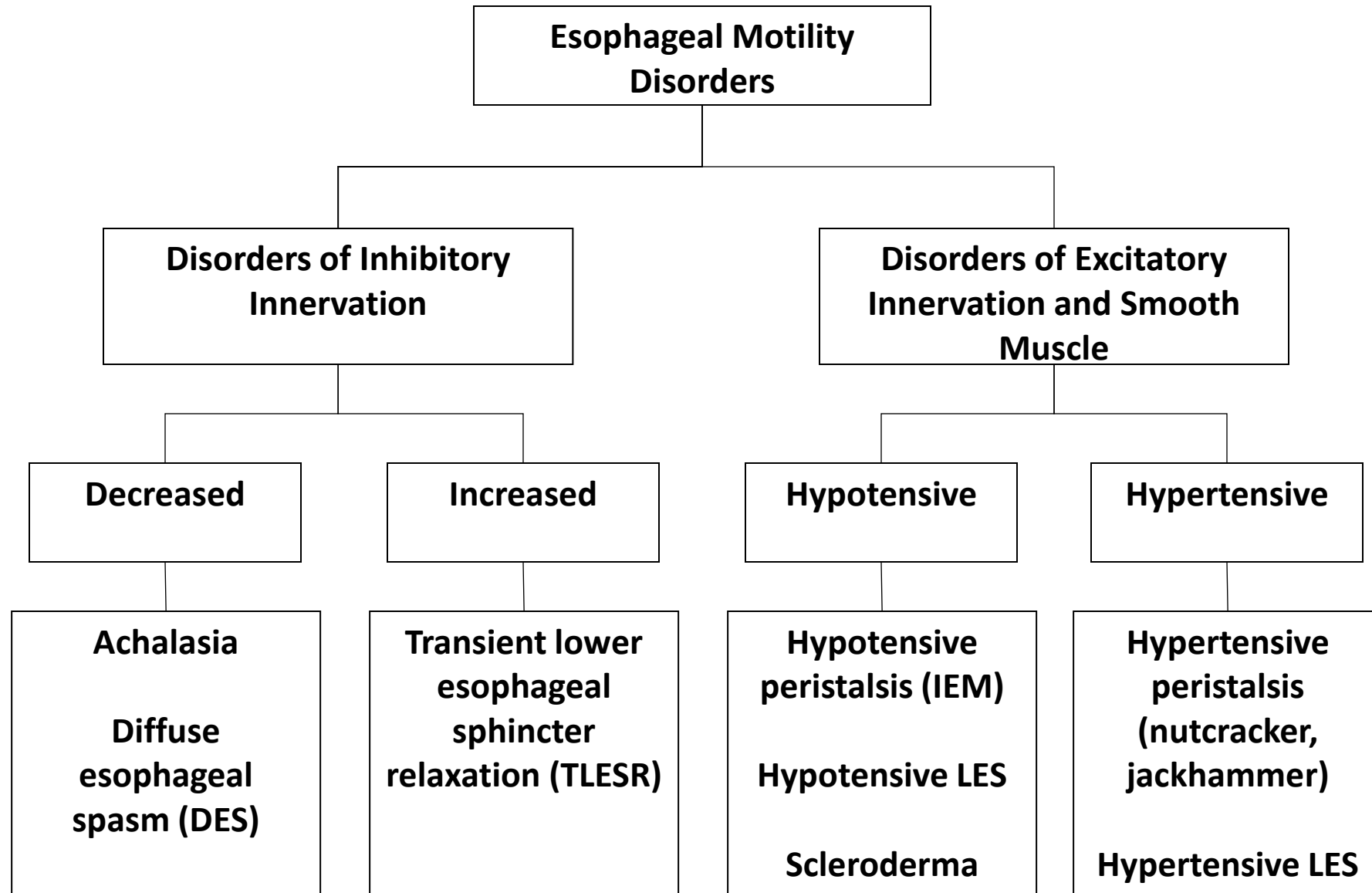
F. No upper endoscopy indicated.

The patient in question is young with well-controlled reflux symptoms. She has no significant risk factors for Barrett's (Caucasian race, male, overweight, smoking, alcohol, family history, obesity). Therefore, routine screening for Barrett's esophagus is not indicated at this time per current guidelines. In patients with known Barrett's esophagus but no dysplasia, surveillance every 3-5 years is indicated (answers B, C). In patients with Barrett's esophagus with low-grade dysplasia, surveillance every 6 months may be considered, although endoscopic ablative therapy is now the preferable strategy.



Esophageal Disorders: Motility Disorders





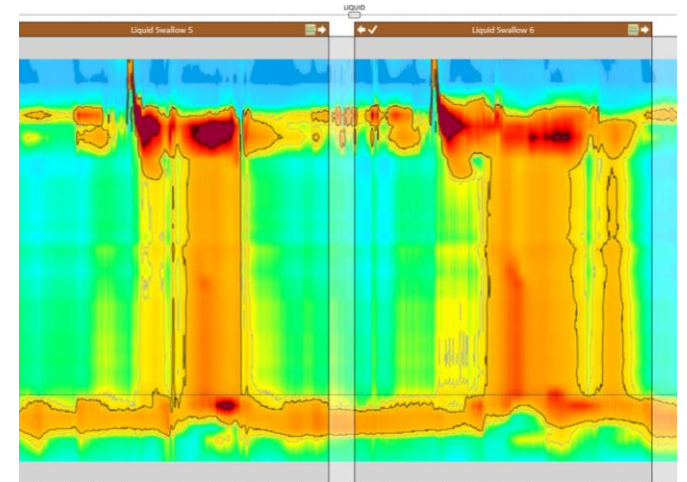
Achalasia

- Preferential degeneration of post-ganglionic inhibitory neurons
 - Insufficient LES relaxation with swallowing and aperistalsis
- Primary achalasia: **Idiopathic**, ? viral, ? Autoimmune
 - Gradual onset and insidious progression
 - Mean duration of symptoms -> diagnosis = 4.7 years
- Secondary achalasia: Chagas disease, malignancy, amyloidosis, sarcoidosis, eosinophilic gastroenteritis, neurofibromatosis
 - Often acute onset and more rapidly progressive




Achalasia

- Signs/symptoms
 - Dysphagia (nearly 100%), regurgitation (60-90%)
 - Difficulty belching (85%), chest pain/heartburn (40%), weight loss, airway symptoms
- Diagnosis
 - Endoscopy
 - Rule out mechanical obstruction
 - Barium swallow
 - Bird's beak, Dilated esophagus, No peristalsis, Poor emptying
 - Manometry
 - Abnormal relaxation of the LES with swallowing
 - Aperistalsis of the esophageal body



Achalasia Treatment

	Pneumatic dilation	Surgical myotomy	POEM	Botulinum toxin injection	CCB / Nitrates
Response	60-90% at 1 year 86% at 2 years 82% at 5 years	90-93% at 1 year 90% at 2 years 85% at 5 years	98% at 1 year 91% at 2 years	90% at 1 mo 60% at 1 year	50-70% initial <50% at 1 year
Complications	2-5% perforation	10% symptomatic reflux; 11% mucosal tear	37% increased reflux on 24-hr pH; 18% reflux esophagitis	20% rash, transient chest pain	30% headache, hypotension
Advantages	Good response rates	Excellent, prolonged response; Laparoscopic	Excellent response; Less invasive than surgery; Long myotomy	Low morbidity	Rapidly initiated
Disadvantages	Risk of perforation; ~25% require re-treatment	Surgical risk	Lack of controlled and long-term data	Frequent repeat; Loss of response; Fibroinflammatory reaction at LES	Poor effect on esophageal emptying; Tachyphylaxis



Low Surgical Risk Patients

High Surgical Risk Patients

Other Motility Disorders

Motor Disorders	Pathology	Etiologies	Clinical Presentation	Study Findings	Treatment
Hypomotility Disorders <ul style="list-style-type: none"> • Hypotensive LES • Absent contractility • Ineffective Esophageal Motility (IEM) 	<ul style="list-style-type: none"> • Impaired excitatory innervation or muscle contractility 	<ul style="list-style-type: none"> • Idiopathic • Medications <ul style="list-style-type: none"> - Anticholinergic - Smooth muscle relaxant - Hormone • Pregnancy • CTD (Scl) • GERD 	<ul style="list-style-type: none"> • GERD <ul style="list-style-type: none"> - Esophagitis - Stricture • Dysphagia • Chest pain 	<ul style="list-style-type: none"> • Decreased contraction • Increased failed peristalsis • Impaired esophageal clearance 	<ul style="list-style-type: none"> • Anti-reflux therapy • Avoid offending meds • Baclofen • Bethanechol
Hypermotility Disorders <ul style="list-style-type: none"> • Distal Esophageal Spasm (DES) • Hypertensive LES • Hypercontractile LES • Nutcracker/Jackhammer 	<ul style="list-style-type: none"> • Overactive excitatory nerves or smooth muscle response • Impaired inhibitory innervation 	<ul style="list-style-type: none"> • CNS stress • GERD 	<ul style="list-style-type: none"> • Chest pain • Dysphagia 	<ul style="list-style-type: none"> • Increased contraction • Normal peristalsis • Nutcracker esophagus • Elevated LES pressure 	<ul style="list-style-type: none"> • Anti-reflux therapy • Anticholinergic • Smooth muscle relaxant • TCA • Cognitive-behavioral therapy



Esophageal Disorders: Eosinophilic Esophagitis



Eosinophilic Esophagitis

- Clinically characterized by symptoms related to esophageal dysfunction
- Pathologically, ≥ 1 biopsy specimens must show eosinophil-predominant inflammation
 - ≥ 15 eos/hpf on esophageal biopsies
- Disease is isolated to the esophagus and other causes of esophageal eosinophilia are excluded



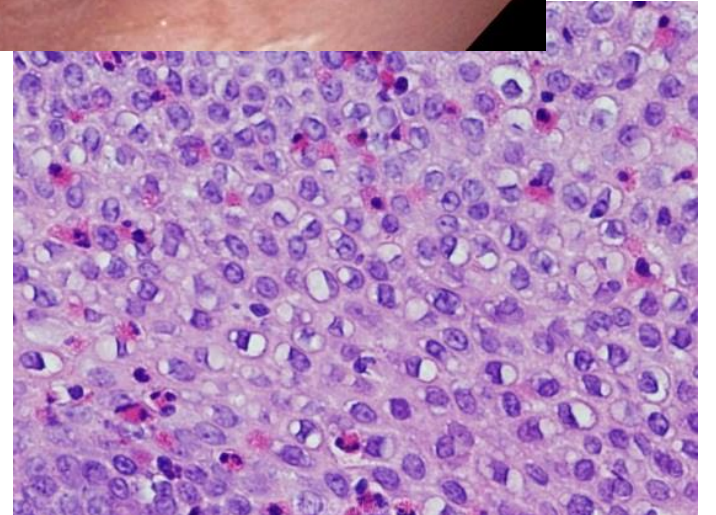
Eosinophilic Esophagitis

- Mean age: 37 years
- Gender: 72% Male
- Mean symptom duration: 5 years
- Atopic history: 74%
- Food allergy history: 19%
- Symptoms:
 - Dysphagia 82%
 - Heartburn: 29%
 - Chest pain: 8%



Eosinophilic Esophagitis

- Food impaction
 - EoE found in 11-55% of adult with food impaction
 - 30-55% of EoE patients experience food impaction
- Endoscopy
 - Ringed esophagus
 - Longitudinal furrows
 - White patches
 - Small caliber esophagus
 - Strictures



Treatment for EoE

	Drugs			Dietary	Dilation
	Proton Pump Inhibitors (PPI)	Steroid	Immunomodulator		
Indication / Target	Active Inflammation	Active Inflammation	Active Inflammation	Active Inflammation	Fibrostenotic disease
Formulation / Regimen	Twice daily dosing	<u>Topical</u> Fluticasone Budesonide <u>Systemic</u> Prednisone	Dupilumab 300 mg SQ weekly	<u>Elemental</u> <u>Targeted</u> Allergy test-guided <u>Elimination</u> SFED, 4FED, 2FED	Gradual bougie dilator or balloon dilation

Maintenance therapy is recommended after remission is achieved over treatment cessation due to risk of recurrence



Esophageal Disorders: Other Esophagitis



Infectious Esophagitis

- Odynophagia is the most common symptoms
- Most often develops in immunosuppressed patients
 - HIV infection, chemotherapy, organ transplantation, chronic immunosuppression
- Candidial esophagitis
 - Most frequent cause of infectious esophagitis
 - Often associated with oral candidiasis
 - Upper endoscopy with biopsy is the most sensitive and specific test
 - Characteristic appearance: whitish plaques
 - Treatment typically involves systemically active oral azoles (e.g. fluconazole)



Infectious Esophagitis

- Viral esophagitis
 - Herpes simplex virus, cytomegalovirus
 - Most often seen in transplant recipients
 - Diagnosis requires upper endoscopy with esophageal brushing, viral culture, or biopsies
 - Characteristic appearances: mucosal ulcerations
- Treatment:
 - HSV: acyclovir, foscarnet
 - CMV: ganciclovir, foscarnet, cidofovir



Pill Esophagitis

- Dysphagia or odynophagia
- Most common drugs:
 - Antibiotics, NSAIDs, bisphosphonates, potassium chloride, quinidine, ferrous sulfate
- Most patients have normal underlying esophageal structure and function
- Risk factors: advanced age, esophageal dysmotility, extrinsic esophageal compression, large pill size, swallowing pills without water and in supine position



Take Home Points

- In management of GERD symptoms, endoscopy and other diagnostic studies should be reserved for patients with alarm features, older age individuals (>50), or those who fail medical therapy.
- Dose tapering of acid suppression should be attempted when symptoms respond.
- The most common cause of non-cardiac chest pain is GERD.
 - Management strategies for GERD should be followed once cardiac cause has been ruled out.



Take Home Points

- Secondary or pseudoachalasia should be ruled out in patients diagnosed with achalasia.
- Management strategy of primary achalasia depends on the patient's surgical risk.
 - Low surgical risk patients should undergo pneumatic dilation or myotomy (surgical or endoscopic).



Take Home Points

- Esophageal biopsies to assess for eosinophilia should be performed for work-up of dysphagia.
- Recommended treatment options for EoE include: **D**rugs (PPI, topical steroids, immunomodulator), elimination **D**iet, **D**ilation.
- Maintenance therapy is indicated for EoE due to high risk of recurrence.



Take Home Points

- Odynophagia is the most common symptom for infectious esophagitis.
- Infectious esophagitis usually occur in immunosuppressed patients, with candida being the most common agent.
- Medications at highest risk for causing pill esophagitis include NSAID, antibiotics, bisphosphonate, potassium tablets.

