

**GUIDE NO. 2** 

# Evaluation of Odynophagia in Persons with HIV

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# **ABOUT THIS HIV SYMPTOM EVALUATION GUIDE**

The HIV Symptom Evaluation Guide addresses the initial diagnostic evaluation of common problems that occur in persons with HIV. The goal of this decision guide is to provide a practical approach to the initial evaluation and diagnosis of odynophagia in persons with HIV.

Clinical judgment should be used to determine whether hospitalization is required. If needed, clinicians should seek expert consultation for assistance with the diagnostic evaluation or management.

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# **DEFINITION OF ACUTE ODYNOPHAGIA**

Odynophagia is typically defined as retrosternal chest pain felt with or just after swallowing; acute odynophagia is defined as symptoms present for less than 14 days.

# **KEY CLINICAL QUESTIONS**

#### Does the individual have odynophagia or pharyngitis?

It is important to first clarify if the person's symptoms originate from the esophagus, the pharynx, or both. Individuals with an esophageal disorder typically present with odynophagia (retrosternal chest pain felt with or just after swallowing) and/or dysphagia (difficulty swallowing, with a sensation of food sticking in the throat or chest). In contrast, discomfort originating from the pharynx will usually be described as discomfort in the throat region.

#### What is the person's most recent CD4 cell count?

Current or recent low CD4 cell count raises the likelihood of certain HIV-associated disorders that may cause odynophagia. In persons with a CD4 count less than 100 cells/mm<sup>3</sup>, HIV-related causes include esophageal candidiasis, herpes simplex virus (HSV)-related ulcerations, and gastrointestinal Kaposi sarcoma. If the CD4 count is less than 50 cells/mm<sup>3</sup>, additional consideration should include cytomegalovirus (CMV)-induced ulcers and aphthous lesions (ulcers). Oral candidiasis, or oral thrush, may occur at CD4 less than 200 cells/mm<sup>3</sup>, but esophageal involvement typically occurs only when the CD4 declines to less than 100 cells/mm<sup>3</sup>.

# Does the individual have a history of gastroesophageal reflux?

Gastroesophageal reflux is a common cause of odynophagia and can occur at any CD4 cell count. It is important to know if the person has classic "heartburn" symptoms or a past diagnosis of reflux disease. A history of worsening symptoms when recumbent and/or a history of response to acid-suppressive therapy supports the diagnosis of reflux disease.

#### Has the person swallowed any toxic substances?

Although most individuals would provide this history, it is important to rule out intentional (or unintentional) ingestion of substances, such as cleaning products or bleach, that could cause esophagitis.

#### Has the person recently taken any oral medication known to cause pill esophagitis?

Certain oral medications, such as aspirin, bisphosphonates, doxycycline (and tetracycline), iron, nonsteroidal antiinflammatory drugs (NSAIDs), or potassium chloride, can cause pill esophagitis and odynophagia.

# Are there any abnormalities on oral examination?

Esophageal candidiasis is by far the most common cause of odynophagia in persons living with HIV who have a CD4 count less than 100 cells/mm<sup>3</sup>, and the presence of oral candidiasis is a good predictor of esophageal candidiasis in persons with odynophagia but is not diagnostic of esophageal involvement. Similarly, the presence of oral HSV lesions makes the presence of this disorder in the esophagus more likely, but diagnosis is usually through endoscopy.

#### DIAGNOSTIC APPROACH TO ODYNOPHAGIA IN PERSONS WITH HIV

#### **INITIAL EVALUATION OF ALL PERSONS ADDITIONAL STEPS IF REGARDLESS OF CD4 COUNT** CD4 COUNT <100 CELLS/MM<sup>3</sup> Obtain initial history and perform physical examination: If no cause already identified: History of toxic ingestion • Initiate empiric treatment for esophageal candidiasis with oral Symptoms or history of reflux fluconazole (if not pregnant)\* · Taking medication known to cause pill esophagitis Abnormalities on oropharyngeal examination **REVIEW RESULTS AND REEVALUATE IN 3-7 DAYS** Toxic ingestion Symptoms compatible Suspected pill with reflux esophagitis If symptoms If symptoms improved: not improved:^ Complete 14- to 21-day course Prompt referral Severe symptoms: Immediate referral to Empiric trial with acidof oral to GI specialist specialist and request for suppressing therapy; Refer for endoscopy fluconazole or for EGD. Testing always assess for drug endoscopy other systemic via EGD should Mild symptoms: interactions with include: antifungal antiretrovirals Discontinue offending medication if possible Fungal stain and culture of any superficial white lesions Biopsy of any ulcerative lesions to evaluate tissue pathology for CMV and to perform HSV PCR test

ABBREVIATIONS: CMV = cytomegalovirus; EGD = esophagogastroduodenoscopy; GI = gastrointestinal; HSV = herpes simplex virus; PCR = polymerase chain reaction

<sup>\*</sup> Treating esophageal candidiasis during pregnancy should be done in consultation with an expert due to potential teratogenicity from fluconazole and other systemic antifungal drugs.

<sup>^</sup> If local expert consultation is not available, consultation can be obtained through the National Clinician Consultation Center (http://nccc.ucsf.edu/ or 800-933-3413).

# **COMMON CAUSES AND INITIAL DIAGNOSTIC EVALUATION FOR ODYNOPHAGIA IN PERSONS WITH HIV**

<b>CAUSE</b> (in alphabetical order)	RISK FACTORS AND CHARACTERISTICS	TYPICAL CD4 CELL COUNT	INITIAL DIAGNOSTIC EVALUATION
Acid reflux	Heartburn symptoms History of reflux Worse when recumbent and after eating certain foods	Any	Response to empiric treatment, dietary modifications, and/or lifestyle changes Characteristic findings on endoscopy
Aphthous lesion(s)	Cause/trigger unknown Typically, 1–2 large esophageal ulcers	<50 cells/mm³	Visible ulcer(s) on endoscopy without identifiable cause Biopsy shows inflammatory cells Diagnosis of exclusion
Candida esophagitis	Multiple yellow-white esophageal patches and plaques Oral candidiasis usually present (but not always)	<100 cells/mm³	Response to empiric treatment Visual appearance on endoscopy +/- confirmation with culture
Cytomegalovirus (CMV)	Typically, 1–2 large esophageal ulcers CMV retinitis often present	<50 cells/mm³	Endoscopy with biopsy:  Diagnosis confirmed by tissue sample showing inclusion bodies  Diagnosis should not be made based on culture or PCR alone
Herpes simplex virus (HSV)	Multiple small, shallow esophageal ulcers or vesicles May have concurrent orolabial ulcers	<100 cells/mm³	Endoscopy with biopsy: Sample should include HSV PCR and culture
Pill esophagitis	Recent ingestion of medication known to cause esophagitis Improvement with ingesting pill with a large glass of water or after discontinuing medication	Any	Endoscopy with one or more findings: Solitary ulcer or kissing ulcers Mucosal erythema and erosion Bleeding ulcer Ulcer with visible medication coating
Toxic ingestion	Severe acute pain following ingestion	Any	Immediate evaluation and expert referral if toxic ingestion suspected Prompt endoscopy to evaluate severity of esophageal damage

ABBREVIATIONS: PCR = polymerase chain reaction

#### **KEY SUMMARY POINTS**



- It is important to distinguish odynophagia—typically described as retrosternal pain felt after swallowing—from other similar symptoms, including dysphagia (difficulty swallowing), pharyngeal disorders (e.g., pharyngitis, tonsillitis, retropharyngeal abscess), and chest pain, including from cardiac origin. The causes of odynophagia and dysphagia overlap, and a person may experience both concurrently.
- Persons living with HIV most often develop odynophagia from causes not related to HIV, such as gastroesophageal reflux and pill esophagitis.
- The most common HIV-related causes of odynophagia are esophageal candidiasis and HSV-associated esophageal ulcers; these typically occur only in persons with a CD4 count less than 100 cells/mm<sup>3</sup>. In addition, persons with a CD4 count less than 50 cells/mm<sup>3</sup> may develop CMV-induced ulcers or aphthous lesions. The most common etiology when the CD4 cell count is low is esophageal candidiasis.
- Unless the history indicates a clear alternate cause of the odynophagia, the initial recommended approach in a person with HIV and a CD4 count less than 100 cells/mm<sup>3</sup> is to empirically treat for esophageal candidiasis with systemic antifungal therapy (such as fluconazole, assuming the individual is not pregnant). This approach has both diagnostic and treatment utility.
- Persons with a CD4 count less than 100 cells/mm³ who do not respond to antifungal therapy within 3 to 7 days should be promptly referred for gastroesophageal endoscopy. The endoscopic procedure should include a biopsy of any visible ulcers. Ulcers caused by CMV and aphthous lesions are typically large and few in number, whereas HSV-related ulcers typically are generally small and numerous.
- For persons who have dysphagia (difficulty swallowing food and/or the sensation of food stuck in the chest), the most common causes (at any CD4 cell count) include esophageal stricture, esophageal cancer, or eosinophilic esophagitis. Gastrointestinal Kaposi sarcoma, which is caused by the human herpesvirus-8, can cause esophageal lesions and gastrointestinal bleeding but typically only occurs in persons with a CD4 count less than 100 cells/mm<sup>3</sup>. Diagnosis of all of these causes requires endoscopy.

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