

Approach to the Patient with Chronic Cough

Case related questions.

Scenario:

A 67-year-old woman with a history of hypertension presents with a cough over the past year. She was in her usual state of health until she developed an upper respiratory infection with rhinorrhea, a sore throat, and a productive cough. All of her symptoms resolved after a few days except her cough. The cough slowly changed in nature and became non-productive.

Question 1: What is the definition of chronic cough?

Question 2: What are the two reversible causes of a chronic cough that should be ruled out or addressed before moving on to further work-up?

Question 3: What are the most common causes of a chronic cough? What symptoms would you want to ask about as you continue to take a more detailed history?

Scenario cont.:

The patient has intermittent sinus congestion with an associated sensation of a tickle in the back of her throat. She has tried saline nasal spray without improvement in her symptoms. However, she feels that her cough persists even when she does not have sinus congestion. She denies any associated shortness of breath or wheezing and her exercise capacity has not changed although she does note some coughing when she runs on the treadmill. She does have intermittent heartburn when she eats large meals but denies any coughing after eating or drinking. She doesn't think her cough increases at night.

Question 4: What would you like to do next?

Scenario cont.:

She did not have any other concerning symptoms. Her chest x-rays obtained two weeks and six months ago were normal.

Question 5: What would you recommend next?

Question 6: How would you treat upper airway cough syndrome?

Scenario cont.:

She first tries an intranasal steroid and then adds a systemic antihistamine without improvement. You ask her to try the saline nasal spray before intranasal steroid. She notes improvement in her sinus congestion but no change in her cough.

Question 7: Does this patient have upper airway cough syndrome?

Scenario cont.:

You decide to obtain pulmonary function testing before and after bronchodilator therapy. Her pulmonary function tests are normal without any significant change following administration of albuterol.

Question 8: Does this patient have asthma as the cause of her cough?

Scenario cont.:

You prescribe a short acting bronchodilator which she takes before exercise and if she develops a particularly severe episode of coughing. She notes no change in her cough.

Question 9: Would you try an inhaled steroid?

Scenario cont.:

She does not respond to inhaled steroids. You would like to consider GERD as a possible cause of her chronic cough.

Question 10: How would you determine if GERD is the cause of her chronic cough?

Scenario cont.:

You decided to obtain a 24-pH monitoring study that did show rare episodes of reflux, but they do not correlate with her documented episodes of coughing. It is also acceptable to proceed with empiric treatment for GERD. Along with acid suppression, diet and lifestyle modifications are very important.

Question 11: What are your options for further evaluation at this point?

Scenario cont.:

Her work-up was completely negative and you consider that she has chronic idiopathic cough syndrome.

Question 12: What patients typically present with idiopathic cough syndrome?

Question 13: How would you diagnose and treat idiopathic cough syndrome?

Approach to the Patient with Chronic Cough

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*Literature review current through June 2025
Last updated June 2025*

Citation

Anandaiah A, Jagana R, et al., Approach to the Patient with Chronic Cough. In: Dine C. Palakshappa J. Association of Pulmonary and Critical Care Program Directors Ambulatory Care Teaching Scripts. 2025. <https://apccmpdscholars.org/tool/ambulatory-care-curriculum/>.

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Educational Objectives:

1. Define chronic cough and the potential underlying etiologies
2. Discuss the diagnostic workup of chronic cough
3. Review the treatment approach to the three most common etiologies: upper airway cough syndrome, asthma, and gastroesophageal reflux disease (GERD)
4. Define idiopathic cough syndrome

Scenario:

A 67-year-old woman with a history of hypertension presents with a cough over the past year. She was in her usual state of health until she developed an upper respiratory infection with rhinorrhea, a sore throat, and a productive cough. All of her symptoms resolved after a few days except her cough. The cough slowly changed in nature and became non-productive.

Question 1: What is the definition of chronic cough?

Acute: Less than 3 weeks (most commonly due to an acute upper respiratory infection (URI))

Subacute: 3 to 8 weeks

Chronic: More than 8 weeks¹

Question 2: What are the two reversible causes of a chronic cough that should be ruled out or addressed before moving on to further work-up?

Angiotensin converting enzyme (ACE) inhibitors and smoking¹

Question 3: What are the most common causes of a chronic cough? What symptoms would you want to ask about as you continue to take a more detailed history?

Upper airway cough syndrome, asthma and gastroesophageal reflux disease explain 90% of the cases of chronic cough.¹ These causes correlate to cough receptors, which are located in the larynx, lower airway bifurcations, and the distal esophagus (Figure 1).

Figure 1. Cough Receptors and Neural Pathways of Cough²

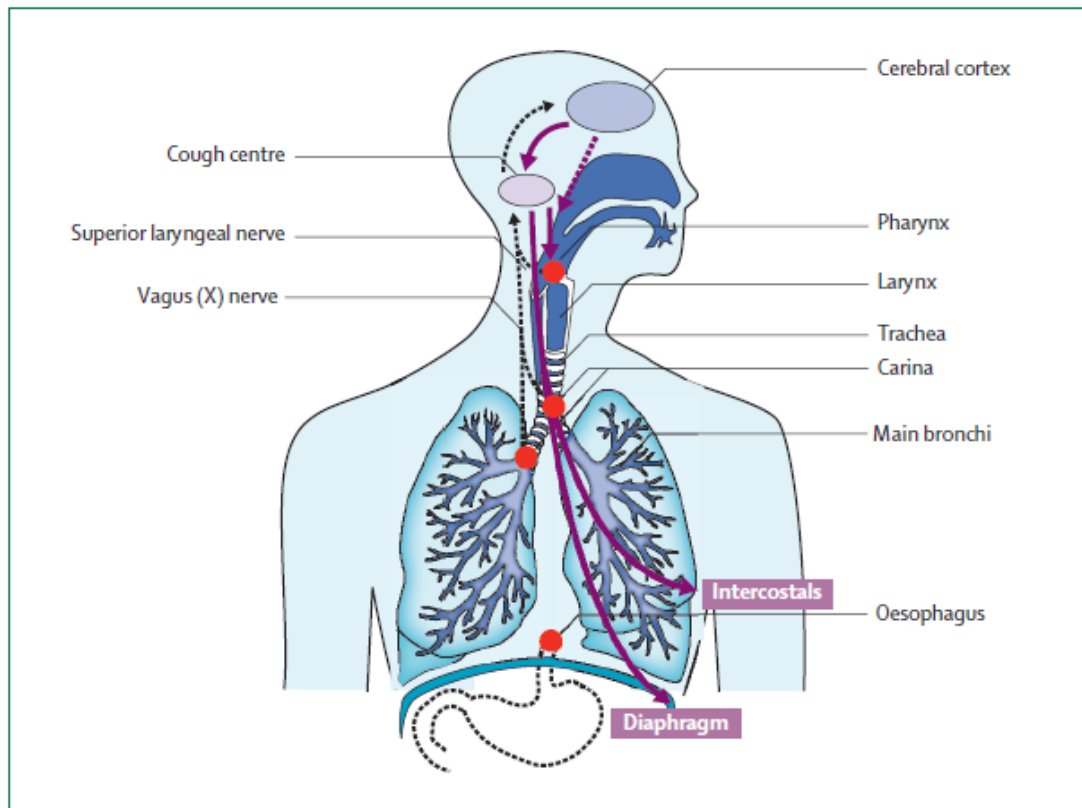


Figure 1: Anatomical representation of neural pathways for cough

Cough receptors (shown in red colour) at the airway bifurcations, in the larynx and at the distal oesophagus, link to cough afferents through the vagus and superior laryngeal nerves to the cough centre and cerebral cortex. Efferent pathways coordinate the muscle response that leads to a cough.

Common causes of chronic cough can be remembered by the **mnemonic “COUGH”** in Figure 2.³

Figure 2. Common Causes of Chronic Cough³

“COUGH”	
C:	Cigarette smoking, CHF
O:	Obstructive lung disease [Asthma, COPD/chronic bronchitis, non asthmatic eosinophilic bronchitis (NAEB)]
U:	Upper airway inflammation (sinusitis, pharyngitis, otitis) Upper airways cough syndrome (UACS/PNDS), Urban irritants (Pollutants, dry heat, dusts etc),
G:	GERD
H:	HTN Medication (ACE inhibitor)

Scenario cont.:

The patient has intermittent sinus congestion with an associated sensation of a tickle in the back of her throat. She has tried saline nasal spray without improvement in her symptoms. However, she feels that her cough persists even when she does not have sinus congestion. She denies any associated shortness of breath or wheezing and her exercise capacity has not changed although she does note some coughing when she runs on the treadmill. She does have intermittent heartburn when she eats large meals but denies any coughing after eating or drinking. She doesn't think her cough increases at night.

Question 4: What would you like to do next?

Before considering the most common causes of a chronic cough, one should first make sure that there are no red flags like hemoptysis, weight loss etc., and a chest x-ray should be obtained. (Detailed list of “Red Flags” are listed in Figure 3 on p. 6).⁴

Scenario cont.:

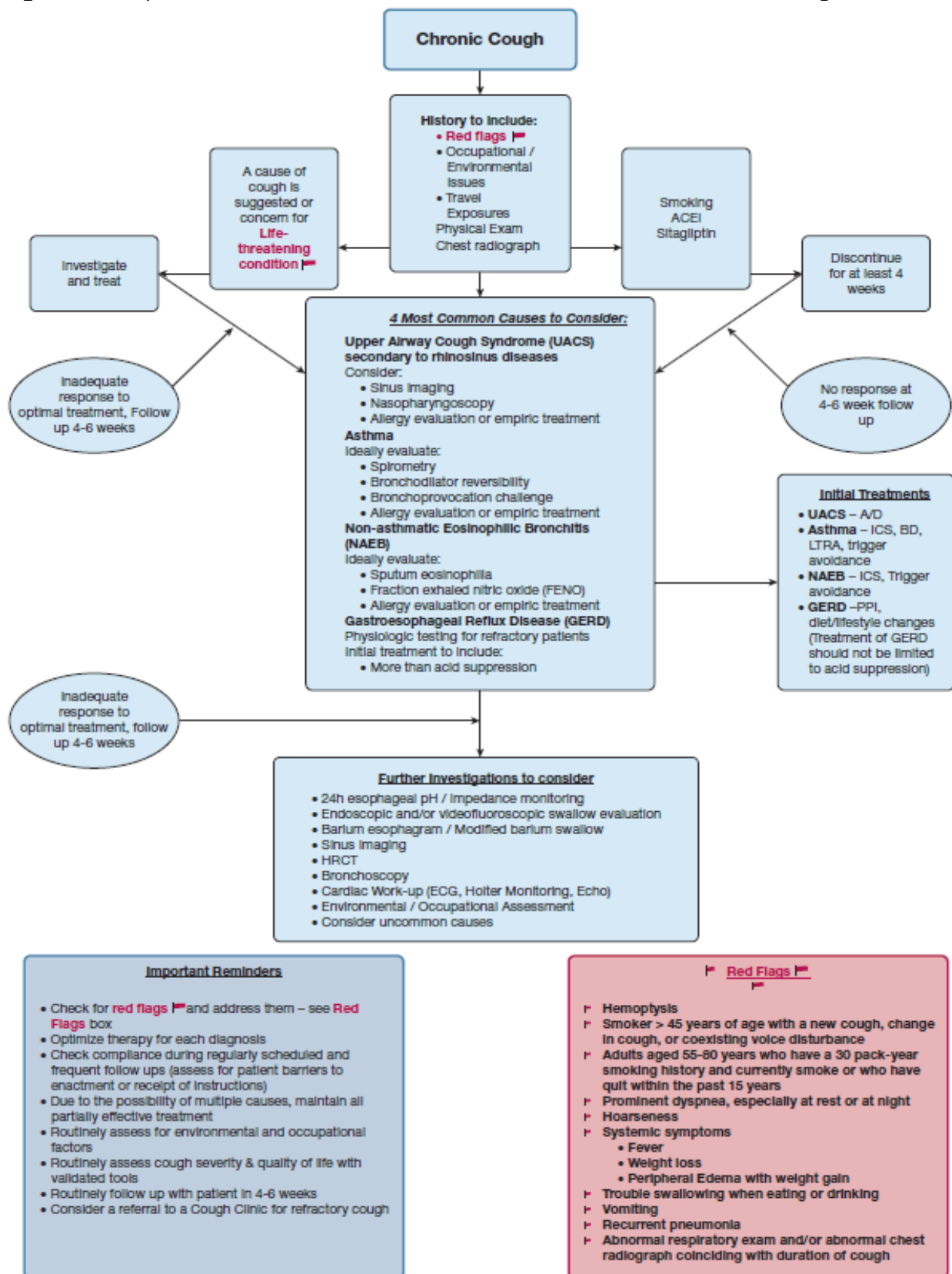
She did not have any other concerning symptoms. Her chest x-rays obtained two weeks and six months ago were normal.

Question 5: What would you recommend next?

The work-up for chronic cough is often difficult. Testing can show abnormalities that are not necessarily related to the symptoms. For example, evidence of reflux on a swallowing study does not necessarily mean that the cough is due to reflux. Therefore, the diagnostic work-up often includes treating the most common causes to see if the patient improves.⁵

Given that her symptoms are most consistent with upper airway cough syndrome, you decide to treat that first.

Figure 3. Steps for the Evaluation and Treatment of Patients with Chronic Cough⁴



Question 6: How would you treat upper airway cough syndrome?

Options include:

- Intranasal steroids
- Standing topical antihistamine (azelastine)
- Ipratropium nasal spray (especially if rhinorrhea is the only symptom or gustatory rhinitis)
- Consider systemic antihistamines (second and third generation may be less effective but are not sedating)⁵

Scenario cont.:

She first tries an intranasal steroid and then adds a systemic antihistamine without improvement. You ask her to try the saline nasal spray before intranasal steroid. She notes improvement in her sinus congestion but no change in her cough.

Question 7: Does this patient have upper airway cough syndrome?

Probably not, but guidelines suggest obtaining a sinus CT at this point to more confidently rule out chronic sinusitis including allergic fungal sinusitis.⁵

Scenario cont.:

You decide to obtain pulmonary function testing before and after bronchodilator therapy. Her pulmonary function tests are normal without any significant change following administration of albuterol.

Question 8: Does this patient have asthma as the cause of her cough?

Cough variant asthma can have normal pulmonary function tests just like any other asthma variants. One could obtain a bronchoprovocation test but even those can result in false negative testing. A trial of bronchodilator therapy may be more diagnostic in determining if asthma is the cause of her cough. Detailed history about triggering factors and avoidance of those factors should be done along with bronchodilator therapy.⁵

Scenario cont.:

You prescribe a short acting bronchodilator which she takes before exercise and if she develops a particularly severe episode of coughing. She notes no change in her cough.

Question 9: Would you try an inhaled steroid?

Global Initiative for Asthma (GINA) guidelines for asthma recommend an inhaled corticosteroid (ICS)-containing inhaler for asthma as inflammation is an important pathogenic factor.⁶ Similarly, Non-Asthmatic Eosinophilic Bronchitis (NAEB) may respond to ICS and not an inhaled bronchodilator. NAEB has been reported in up to 14% of patients who present to specialty cough clinics. NAEB occurs due to eosinophilic infiltration into the epithelial cells rather than smooth muscles and requires a bronchial mucosal biopsy as a confirmatory test. A trial of high dose inhaled steroids is reasonable in a patient with a chronic cough.^{5,7}

Scenario cont.:

She does not respond to inhaled steroids. You would like to consider GERD as a possible cause of her chronic cough.

Question 10: How would you determine if GERD is the cause of her chronic cough?

You can proceed with empiric treatment versus confirmatory testing. A barium swallow is not the ideal test in that many patients with GERD have a normal barium swallow study. In addition, the presence of GERD does not necessarily mean it is the cause of her cough. Thus, 24-hour pH monitoring may be more helpful since it may correlate episodes of reflux with symptoms.^{5,8}

Scenario cont.:

You decided to obtain a 24-pH monitoring study that did show rare episodes of reflux, but they do not correlate with her documented episodes of coughing. It is also acceptable to proceed with empiric treatment for GERD. Along with acid suppression, diet and lifestyle modifications are very important.

Question 11: What are your options for further evaluation at this point?

- *Chest CT*– to look for early interstitial lung disease, mild bronchiectasis, or other airway abnormalities
- *NPL* – to look for vocal cord lesions or other upper airway abnormalities such as laryngeal hyperfunction
- *Bronchoscopy* – to look for airway lesions
- *Trial of systemic steroids*^{5,8}

Scenario cont.:

Her work-up was completely negative and you consider that she has chronic idiopathic cough syndrome.

Question 12: What patients typically present with idiopathic cough syndrome?

This disorder is more common in women who are either peri- or post-menopausal. It typically starts after an upper respiratory infection which may have led to a heightened cough reflex through an unknown mechanism. Cough hypersensitivity is not completely understood but appear to be neuronal dysregulation at both peripheral and central cough reflex pathway leading to heightened response to thermal, chemical and mechanical stimulation.⁹

Question 13: How would you diagnose and treat idiopathic cough syndrome?

The diagnosis is made if the patient responds to neuromodulator therapy. Amitriptyline, gabapentin, pregabalin and baclofen have been studied with some success.⁸ In one RCT, cough control therapy with physiotherapy and speech pathology treatment with four components (education, reduction of laryngeal irritation, cough-control techniques, and psychoeducational counseling) was also shown to reduce cough severity and improve quality of life in patients with refractory chronic cough.⁷ Superior laryngeal nerve block therapy has shown improvement in the recent studies in patients with idiopathic cough syndrome.¹⁰

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Approach to the Patient with Chronic Cough

Post-Test Case Related Questions

1. A 31-year-old otherwise healthy female comes to your office for evaluation of a persistent cough. She notes that her cough has been ongoing for the last 4 months and has been unrelenting. She denies any sputum production or shortness of breath. She is not currently taking any medications. She had a CXR performed last month that was normal. On review of systems she notes some occasional acid reflux at night but has no other symptoms of note. You suspect that gastroesophageal reflux may be the cause of her chronic cough. Which of the following would be the most appropriate next step in her management?
 - a. Empiric treatment trial with a proton-pump inhibitor
 - b. Barium swallow
 - c. 24-hour pH monitoring
 - d. Any of the above
 - e. Either A or C
 - f. Either A or B
2. A cough is considered chronic if present for more than
 - a. 6 weeks
 - b. 8 weeks
 - c. 10 weeks
 - d. 12 weeks
3. A 55-year-old female with a history of hypertension comes to your office for evaluation of a cough that has persisted for 6 months. She has tried multiple therapies including a variety of inhalers, treatment for acid reflux and nasal steroids without improvement. She has had a CT chest that was unremarkable as well as a trial of steroids without improvement. You consider a diagnosis of idiopathic cough syndrome. Which of the following is not an accepted treatment for this entity?
 - a. Sertraline
 - b. Gabapentin
 - c. Baclofen
 - d. Amitriptyline

Approach to the Patient with Chronic Cough

Post-Test Case Related Questions with Answer Key

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 - c. 24-hour pH monitoring
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