

## Cough and Wheezing — Definition and Treatments

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**A cough is one of the common presenting symptoms in the clinic and is associated with a number of respiratory and non-respiratory diseases. It can have a number of distinguishing characteristics such as quality, sputum production, timing, onset, duration, and associated symptoms. The physiological mechanisms underlying cough involve a reflex arc with a command center in the medulla. Common non-respiratory causes include gastroesophageal reflux disease and postnasal drip, whereas, the most common respiratory etiologies are infectious diseases, chronic obstructive pulmonary disease, asthma, and interstitial lung disease. Wheezes are high-pitched, loud sounds that usually accompany asthma, while stridor is most prominent with upper respiratory obstruction. In this article, physiology, different causes of cough and wheezing will be discussed in detail.**



### Physiology of Cough

The **cough reflex arc** starts with sensory nerve fibers in ciliated epithelial cells in the upper and lower respiratory systems. A number of factors can trigger the cough mechanism and they include **chemicals, irritants and mechanical pressure from bodies or masses**.

Furthermore, humans have the ability to voluntarily cough, which can be explained by the presence of **afferent neuronal circuits** emanating from **higher centers in the brains**. The cough center is located in the **medulla** and all **cough afferents** ultimately converge there. The medulla integrates all afferent input and acts as a control center that coordinates and commands activity in the efferent portion of the circuit.

**Efferent conductors** of cough include the **vagus nerve**, reaching the **tracheobronchial tree**, and the **phrenic and spinal nerves** ultimately controlling **intercostal muscles**, the abdominal wall, the **diaphragm**, and the pelvic floor. The **physiological mechanisms** underlying cough can be divided into three distinct phases: inspiratory phase, compressive phase, and expiratory phase.

## 3 Phases of Cough

### 1. Inspiratory phase

The inspiratory phase describes the **initial and sudden expansion of the chest** corresponding to the filling of the **lungs** with air.

### 2. Compressive phase

The second phase corresponds to the closing of the **glottis and the supraglottic level** in the **larynx**. This is accompanied by a significant contraction of the chest wall, **diaphragm**, and pelvic floor, causing a large increase in air pressure within the thorax.

### 3. Expiratory phase

The expiratory phase starts with an opening of the **larynx**, leading to a sudden decrease in air pressure. This is accompanied by a decrease in the cross-sectional area of the larynx, generating a “tussive squeeze” and subsequent clearance of secretions from the **tracheobronchial tree**.

## History Taking of Cough

When evaluating patients with cough, it is important to pay attention to several aspects in the history that involve the duration, quality, severity, and timing of the cough. An **acute cough** lasts less than 3-weeks and the most common causes are the common cold, **pneumonia** and **whooping cough**.

A **subacute cough** lasts from 3 to 8-weeks and usually follows **upper respiratory viral infections**. A chronic cough lasts more than 8-weeks and responsible etiologies are usually **asthma** and **gastroesophageal reflux disease**. Cough characteristics are important and can be productive (with sputum), involve blood (**hemoptysis**) or hacking.

It is also important to ask about alleviating symptoms and triggers, such as over-the-counter or prescription drugs, and whether it occurs only at work or when mowing the lawn. Associated symptoms can include **fever, chills, sweats, weight loss, dyspnea, chest pain, sneezing, postnasal drip or heartburn**.

The physician should also ask about the severity of the cough, whether it affects work or sleep, and whether it is accompanied by **syncope** or incontinence. The timing can be acute or chronic, constant or intermittent and one should also know the onset and the duration of the symptoms.

Finally, it is important to gather relevant medical, social and family histories, such as a history of **asthma**, **atopy**, drug allergies, recent medication intake, **TB exposure**, travel or immigration, hobbies, and occupation, as well as any new pets or rugs.

## Etiology of Cough

### Gastroesophageal Reflux Disease

There are two proposed mechanisms for the pathophysiology of cough associated with **gastroesophageal reflux disease (GERD)**:

- The first mechanism involves exposure of the distal **esophagus** to acid, stimulating the **vagus nerve** and leading to **cough reflux**.
- The second mechanism consists of **aspiration of gastric content** into the **respiratory airways**.

Recent studies seem to favor the first mechanism as acid exposure of the **distal esophagus** has been more tightly correlated with cough than that of the **proximal esophagus**.

Other physical findings, common with reflux disease, include laryngeal edema and **erythema** and **pachydermia**, which consist of posterior commissure hypertrophy. Important clues in the history can help in establishing the diagnosis.

In particular, **hoarseness** that is especially severe in the morning, throat clearing and **globus sensation** have been associated with **GERD**. The cough usually occurs after meals or when lying down at night. It can also be triggered by talking or laughter.

Medical treatment is the initial step for GERD treatment and takes place with **PPI** administration. Treatment duration continues for 3-months after the cough disappears and it usually takes about 6-months for the cough to resolve. Thus, patience and encouragement are of paramount importance.

PPIs exert their effects by blocking the **H<sup>+</sup>/K<sup>+</sup> adenosine triphosphatase enzyme (ATP)** in the parietal cells of the **stomach**, ultimately decreasing acid secretion. The addition of an **anti-histamine H2 blocker** such as **ranitidine** can also be required in certain instances. H2 blockers are particularly effective in decreasing acid level breakthroughs at night, usually related to a peak in histamine concentration.

Failure of medical treatment or lifetime medical symptoms sometimes requires surgical intervention through the **Nissen Fundoplication procedure**. Studies have shown that Nissen fundoplication is able to effectively control classical symptoms of GERD such as **heartburn**, but fares much worse with non-classical symptoms such as cough or hoarseness.

## Asthma

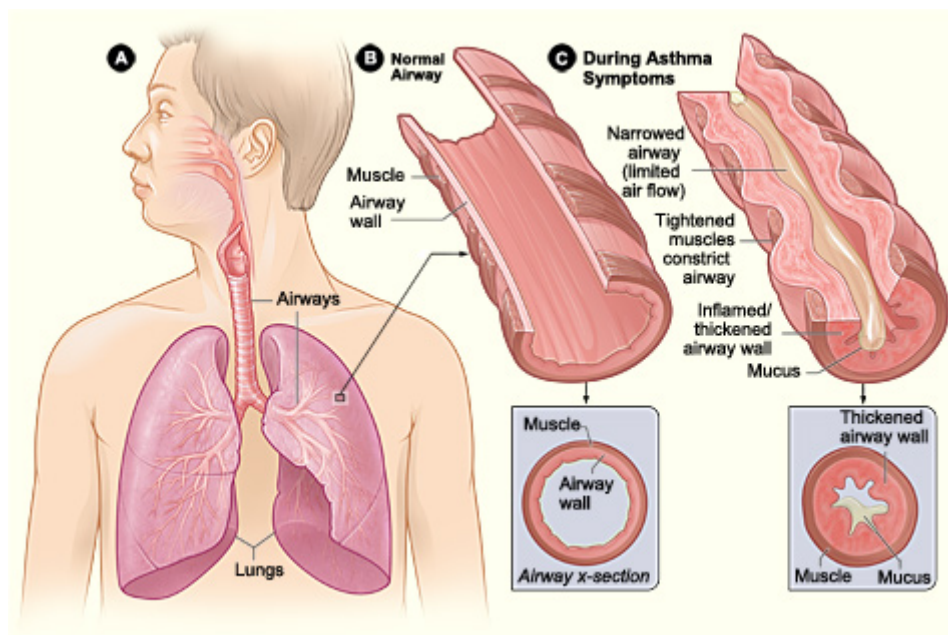
**Asthma** is caused by airflow obstruction due to inflammatory factors and manifests principally with **wheezing and shortness of breath**, but also with cough in cough-variant asthma (CVA).

Cough in **asthma** is most of the time **non-productive and non-paroxysmal**. Additionally, it can be the only symptom in patients presenting with exercise-induced asthma. Usually, the patient cannot take a deep breath without coughing. A

distinguishing feature in children with nocturnal asthma is cough after midnight associated with **chest tightness**.

Diagnosis of asthma is usually established with pulmonary function tests after one of either: 1) a decrease of 20% in forced expiratory volume in 1 second, after **methacholine inhalation** or 2) an increase of 15% in forced expiratory volume in 1 second, after inhalation of **albuterol** or another bronchodilator.

Sometimes, however, pulmonary function tests are not sensitive enough to detect patients with **cough variant asthma**. In these cases, clinicians can use an empiric treatment of 4 to 8-weeks with an **inhaled corticosteroid**. Leukotriene inhibitors, such as **montelukast and zafirlukast**, can also aid in treatment and diagnosis.



**Image:** "Figure A shows the location of the lungs and airways in the body. Figure B shows a cross-section of a normal airway. Figure C shows a cross-section of an airway during asthma symptoms." by United States-National Institute of Health: National Heart, Lung, Blood Institute. License: [Public Domain](#)

## Postnasal Drip

A postnasal drip is one of the most causes of cough in adults. However, rather than representing a single disease entity, it is more of a **"wastebasket" diagnostic category**, with many involved disease mechanisms that include **reflux disease, allergic rhinitis, and chronic sinusitis**.

The cough in the postnasal drip is usually dry and accompanied by a feeling that mucus is dripping down the throat. One of the major distinctive characteristics for post-nasal drip is its positive response to combinations of **decongestants and antihistamines**.

Sedating antihistamines, such as **azatidine and brompheniramine**, are, in general, more effective than newer non-sedating antihistamine medications.

## Angiotensin-Converting enzyme Inhibitors (ACE Inhibitors) Induced Cough

ACE inhibitor intake is associated with a dry non-productive cough. Up to 10% of patients who regularly take ACE inhibitors can develop a cough. It mostly occurs within weeks or days of starting therapy, but, in some cases, the cough may develop after months or even years.

ACE inhibitors need to be stopped when a patient develops a **cough**, regardless of the time they were started and symptoms should resolve in four weeks if indeed the cough was caused by the medication. Substitution with other ACE inhibitors is not advised, but rather a course of **Angiotensin II inhibitor** treatment (with Losartan for example) should be attempted.

In some instances, such as severe **congestive heart failure**, it will be impossible to stop the medication and adjuvant treatment is recommended. Studies have shown that **hydrochlorothiazide and cromolyn sodium** can be used for the treatment of ACE inhibitor-induced cough.

## Whooping Cough (Bordetella Pertussis Infection)



[Image](#): "This image depicts a young boy who presented to a clinic suffering from what was diagnosed as pertussis." by CDC. License: [Public Domain](#)

It begins with non-specific respiratory symptoms such as **cough, rhinorrhea, post-nasal drip, throat clearing, and irritation.**

Initial symptoms last for two weeks and are followed by the cough accompanied by whooping inspiratory noises.

The cough episodes can be extremely severe and result in vomiting or patients dropping to their knees.

In most cases, the coughing episodes last for 2 to 4-weeks but may continue up to months in the most severe cases.

One potential complication of extended episodes of whooping cough is **gastroesophageal reflux disease**.

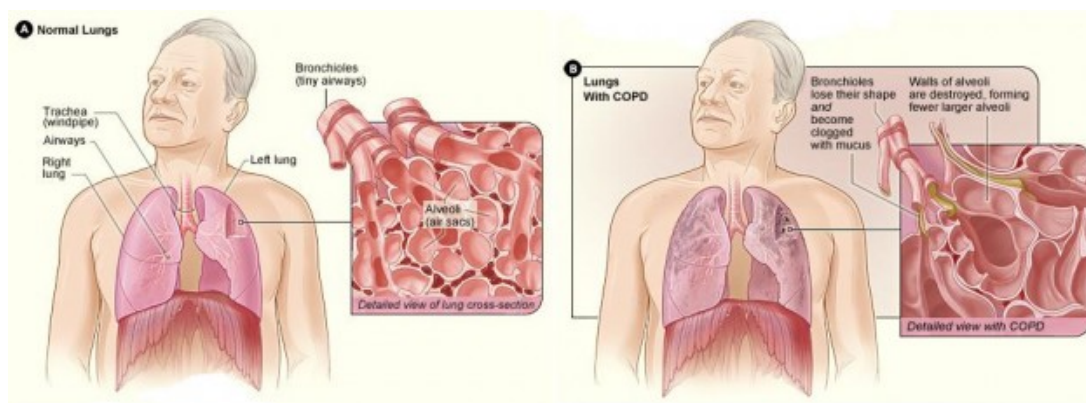
The diagnosis of pertussis can be difficult because the bacteria do not easily grow in culture. In the early phases of the disease, a PCR of a swab culture from the **pharynx** is favored and, in later stages, when patients are most likely to present in the clinic, diagnosis can be established with serology for the **pertussis toxin**.

The fundamental principle of treatment for pertussis is the prophylaxis of close contacts to avoid the spread of the disease. **Macrolide antibiotics** or, in case of allergy, **trimethoprim-sulfamethoxazole** are best suited for prophylactic treatment. Nonetheless, **antibiotics** are not effective for the disease after the development of a distinctive cough.

## Chronic Bronchitis

Chronic bronchitis is one of the most common causes of cough in the elderly population. It usually develops after a prolonged smoking history. Cough in **chronic obstructive pulmonary disease (COPD)** usually produces small amounts of colorless **sputum** and is especially worse in the mornings.

Pathophysiology is complex, but usually involves loss of ciliated cells and an increase of **goblet cells** in the epithelium. The cough starts in the second or third decade after starting smoking and gets significantly worse with time. Smoking cessation is the cornerstone for treatment and antibiotics can be used during acute exacerbations.



**Image:** "Figure A shows the location of the lungs and airways in the body. The inset image shows a detailed cross-section of the bronchioles and alveoli. Figure B shows lungs damaged by COPD. The inset image shows a detailed cross-section of the damaged bronchioles and alveolar walls." by National Heart Lung and Blood Institute. License: [Public Domain](#)

# Interstitial Lung Disease

There are many causes of interstitial lung diseases and they include environmental factors such as silica, bird droppings, **mold and asbestos**, drugs such as **amiodarone**, radiation therapy and autoimmune diseases like systemic **lupus erythematosus**, **rheumatoid arthritis**, and scleroderma.

Symptoms are usually limited to shortness of breath, and a dry, non-productive cough. The cough begins gradually and worsens with time. Chronic interstitial lung disease that has been present for a significant period of time is accompanied by clubbing of the digits and heart failure.

Non-specific symptoms can also be present such as **fever, weight loss, and fatigue**. Diagnosis is established most commonly with pulmonary function tests, which usually show a restrictive pattern and biopsy is sometimes needed for a definitive diagnosis.

Treatment involves avoidance behaviors, **immunosuppressive agents such as corticosteroids** and, in some cases, no treatment can be available.

## Psychogenic Cough

Psychogenic cough is a diagnosis of exclusion and manifests mostly in children and adolescents. It is only diagnosed after the most common diagnoses are excluded and the necessary laboratory tests are done.

It is usually associated with anxiety, but it is unknown if the cough is the cause or the result of **psychiatric disease**. Treatment is focused on psychotherapy, relaxation techniques, breathing exercises, and speech therapy. Referral to an expert speech and language pathologist can be necessary.

## Other Causes

The following are the major causes of cough in the pediatric population with associated characteristics:

- Barking or brassy cough: croup or **tracheomalacia**
- Staccato cough: **chlamydia infection**
- Wet cough: **sinusitis or pneumonia**
- Spasmodic or paroxysmal cough: Pertussis
- Barking/honking cough in adolescence: psychogenic

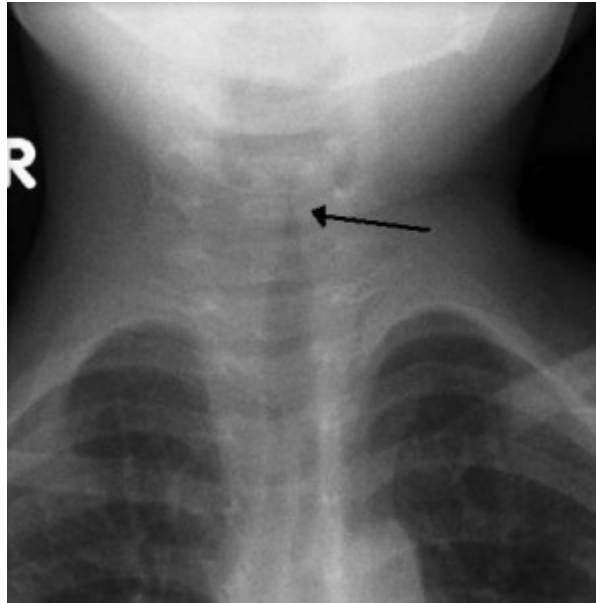


Image: "Steeple Sign in Croup." by Frank Gaillard. License: [CC BY-SA 3.0](#)

Other important causes of cough in adults and their associated characteristics are:

- Rust colored sputum: **Streptococcus pneumoniae infection**
- Foul smelling sputum: aspiration pneumonia
- Current jelly sputum: **Klebsiella pneumoniae infection**
- Suppressed cough: **Mycobacterium avium intracellulare infection**

## Wheezing

Wheezes are high-pitched, continuous loud sounds. They can be inspiratory or expiratory although most commonly they are expiratory. They are caused by a narrowing of the airways, resulting in the oscillation of opposing airway walls. Diseases that result in obstruction usually lead to the development of wheezing, most commonly [asthma](#).

**Stridor** is a specific kind of wheezing that has a constant pitch and is most commonly heard in upper respiratory obstruction. Inspiratory stridor is usually related to laryngeal obstruction, whereas expiratory stridor is associated with **tracheobronchial obstruction**.

The following are the common causes of wheezing and their associated characteristics:

- Symmetric wheezing: [asthma](#)
- Unilateral wheezing: foreign body aspiration, [pulmonary embolism](#), airway compression from a tumor or mass
- Wheezes heard more without the stethoscope: dysfunction of the vocal cords
- Wheezes after eating: aspiration or food allergy

## Review Questions

The answers are below the references.

### 1. Where is the cough command center in the central nervous system?

A. Pons



- B. Medulla
- C. Cervical Spinal Cord
- D. Midbrain
- E. Hypothalamus

**2. Which of the following is a characteristic of cough associated with GERD?**

- A. Productive cough
- B. Foul-smelling cough
- C. Dry cough that follows a meal
- D. Paroxysmal dry cough
- E. Barking cough

**3. Which of the following correctly associates the disease with cough characteristics?**

- A. Pertussis → barking cough
- B. Croup → whooping cough
- C. Klebsiella pneumonia → cough with rust-colored sputum
- D. Pertussis → whooping cough
- E. Foul-smelling sputum → GERD

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**Correct answers:** 1B, 2C, 3D

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