

**Editorial**

# Cough is a Significant Public Health Concern

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## Introduction

Cough is forceful push of air that body uses to clear irritants, mucus and germs out of airways. Cough is the single most common reason for seeking medical attention and lack of suitable antitussive makes this a major unmet clinical need. Cough is one of the most common symptom encountered in medical practice and leading cause of outpatient and emergency department visits worldwide and also represents a significant public health concern.

Cough is among the most frequent complaints among patients visiting respiratory clinics. Symptom duration classifies cough into acute (<3 weeks), subacute (3–8 weeks), and chronic (>8 weeks). This classification has crucial diagnostic implications, making thorough history-taking essential in the table below.<sup>1</sup> Chronic cough (CC) is prevalent in adults in developed countries (10–20%), with global rates varying from 3.9% to 30% depending on geography, demographics, and environmental exposures (e.g., air pollution, occupational hazards).<sup>2</sup> For patients, CC can be distressing due to symptom severity, its complications, and lifestyle modifications required to avoid triggers. The impact extends beyond physical symptoms (e.g., stress incontinence, sleep disturbance, chest pain) to psychological (e.g., disappointment, depressive states) and social domains (e.g., social anxiety/isolation, decreased quality of life).<sup>3</sup>

### Classifications and etiologies of cough

Acute	Subacute	Chronic
• Upper respiratory tract infections	• Post-infectious	• Upper airway cough syndrome
• Lower respiratory tract infections	• Cough	• Gastroesophageal reflux
• Hay fever, allergic rhinitis	• Pertussis	• Asthma
• Inhalational exposure	• Angiotensin converting enzyme inhibitors	• Angiotensin-converting enzyme inhibitors • Chronic bronchitis • Tracheobronchomalacia • Bronchiectasis • Lung cancer

## Etiology

The etiology of CC is complex and multifactorial, often involving cough variant asthma (CVA), gastroesophageal reflux cough (GERC), and upper airway cough syndrome (UACS). Some patients may progress to refractory chronic cough (RCC) or unexplained chronic cough (UCC), both significantly impair quality of life. CC also imposes a substantial societal burden through healthcare costs and productivity losses. Therefore, developing strategies to manage symptoms, mitigate underlying causes, and enhance timely and accurate diagnosis and treatment is critical for CC research.<sup>4</sup>

Upper and lower respiratory tract infections most commonly cause an acute cough. However, clinicians must remain alert to potentially life-threatening conditions that can also present acutely, including asthma or chronic obstructive pulmonary disorder (COPD) exacerbations, pulmonary embolism, and acute heart failure. Common causes of acute cough include viral respiratory infections (e.g., influenza), acute bronchitis, pneumonia, pertussis, and tuberculosis in endemic areas, as well as upper airway inflammatory conditions such as acute rhinosinusitis and allergic rhinitis. Additional etiologies include aspiration syndromes, inhalation of environmental irritants, trauma, pleural irritation, and, less commonly, medication effects or malignancy.<sup>5,6,7</sup>

Subacute cough most often develops following a respiratory infection and is typically driven by persistent irritation of cough receptors due to ongoing or resolving airway or paranasal sinus inflammation. Many causes of subacute cough overlap with both acute and chronic etiologies, reflecting a transitional phase in the disease process. Chronic cough has a broader and more complex differential diagnosis. Asthma is a significant cause in adults and the leading cause in children, along with other eosinophilic airway disorders such as cough-variant asthma and nonasthmatic eosinophilic bronchitis.

Upper airway conditions, including upper airway cough syndrome and chronic rhinosinusitis, and lower airway diseases such as chronic bronchitis, COPD, bronchiectasis, and tracheo-bronchomalacia are also common contributors. Clinicians should also consider gastroesophageal and laryngopharyngeal reflux, chronic infections (e.g., tuberculosis, nontuberculous mycobacteria, fungal or parasitic infections), prolonged post-pertussis cough, structural airway abnormalities, and medication-related causes. Less common but

important causes include obstructive sleep apnea, interstitial lung disease, malignancy, and somatic cough disorder, underscoring the need for a systematic and comprehensive evaluation.<sup>8,9</sup>

### Types of Cough

1. **Dry Cough:** no mucus, tickling throat, irritating cough, viral infection, allergy and asthma.
2. **Wet / Productive Cough:** Produces sputum, chest congestion, bronchitis, pneumonia and respiratory infection.
3. **Whooping Cough:** Severe coughing fits, “whoop” sound after coughing, pertussis infection
4. **Barking Cough:** Harsh barking sound, croup
5. **Night Cough:** Worse at night, asthma, postnasal drip, Gastroesophageal Reflux Disease (GERD)
6. **Chronic Cough:** Lasts >8 weeks, smoking, Chronic Obstructive Pulmonary Disease (COPD), Chronic Lung Disease.

### Epidemiology / Prevalence

Cough is among the most common complaints in primary care, with chronic cough affecting approximately 8% to 10% of the global population; however, reported prevalence ranges from 2% to 18% across regions.<sup>10</sup> Rates are higher in North America, Europe, and Oceania than in Asia and Africa, likely reflecting environmental and lifestyle differences.

In the United States (US), more than 12 million individuals are affected annually.

In Pakistan, the prevalence of chronic cough varies significantly by age and urban exposure, with regional studies showing an estimated 12% among adults aged 40 and older in urban areas like Karachi. In contrast, the rate drops to around 3% to 5% among younger, broader demographics.

The high variation and concentration of chronic cough cases in Pakistan stem from several specific environmental and demographic factors:

**Age & Demographics:** Chronic cough prevalence is notably higher in older adults and females, largely driven by a lifetime of cumulative environmental exposures.

**Urban Air Quality:** Rapid urbanization in metropolitan cities like Karachi and Lahore has exposed populations to poor air quality and high levels of particulate matter.

### Evaluation

History and Physical Examination plays a crucial role in the evaluation. Cough is a symptom rather than a diagnosis, and a thorough history and physical examination are fundamental steps in the evaluation. The clinical presentation varies based on the underlying etiology. The following discusses the presentations of some of the most common causes of cough, but is not all-inclusive.

#### Acute Cough

- **Acute bronchitis:** Dry or productive cough lasting less than 3 weeks, often following an upper

respiratory infection; associated with wheezing and rhonchi that typically clear with coughing.

- **Acute decompensated heart failure:** Dyspnea, orthopnea, paroxysmal nocturnal dyspnea, bibasilar crackles, peripheral edema, S3 gallop, and possible hypotension or tachyarrhythmias.
- **Acute Rhinosinusitis:** Nasal congestion or discharge, facial pain or pressure, decreased smell, and postnasal drip.<sup>11</sup>
- **Allergic rhinitis:** Rhinorrhea, nasal itching, sneezing, cough, allergic conjunctivitis, and fatigue; exam findings include pale, edematous nasal mucosa, clear rhinorrhea, pharyngeal cobblestoning, and infraorbital darkening or edema.<sup>12</sup>
- **Asthma:** Episodic cough, wheezing, or dyspnea triggered by cold air, exercise, infections, or environmental exposures; cough may be the predominant or sole symptom in cough-variant asthma.<sup>13</sup> Intermittent expiratory wheezing is typical, whereas fixed or unilateral wheezing suggests an alternative pathology.
- **Bronchiolitis:** Primarily affects children younger than 2; begins with upper respiratory symptoms followed by wheezing, crackles, tachypnea, retractions, and sometimes fever.
- **COPD Exacerbation:** Worsening cough, wheezing, tachypnea, tachycardia, accessory muscle use, difficulty speaking, altered mental status, or signs of hypercapnia such as asterixis.<sup>14</sup>
- **Foreign body aspiration:** Acute cough, stridor, focal wheezing, tachypnea, or decreased air entry; severe cases present with respiratory distress, cyanosis, or altered mental status.
- **Pertussis:** Progressive cough that worsens after an initial catarrhal phase, followed by paroxysmal coughing fits with inspiratory “whoop,” posttussive vomiting, and possible cyanosis; gradual resolution during the convalescent phase.
- **Pulmonary embolism:** Acute cough with dyspnea, pleuritic chest pain, tachypnea, hemoptysis, wheezing, or signs of deep vein thrombosis.

#### Chronic Cough

- **Bronchiectasis:** Chronic productive cough with daily mucopurulent sputum, recurrent infections, dyspnea, fatigue, wheezing, and occasional hemoptysis.
- **Chronic aspiration:** Cough associated with eating or drinking, especially thin liquids; may include focal wheezing, hemoptysis, or foul-smelling sputum.
- **Chronic Rhinosinusitis:** Nasal congestion or drainage, facial pressure, reduced or absent smell; cough is particularly prominent in children.
- **Cystic fibrosis:** Persistent productive cough with multisystem involvement, including failure to

thrive, pancreatic insufficiency, sinus disease, hepatobiliary disease, rectal prolapse, and nephrolithiasis.

- **Gastroesophageal reflux disease:** Cough associated with dysphonia, heartburn, regurgitation, or sour taste.
- **Interstitial lung disease:** Chronic cough and progressive dyspnea with fine inspiratory crackles, often in dependent lung zones.
- **Medication-induced cough:** Typically dry; angiotensin-converting enzyme inhibitor-associated cough develops within 1 week to 6 months of initiation, resolves within weeks of discontinuation, and recurs on rechallenge.
- **Nonasthmatic eosinophilic bronchitis:** Chronic nonproductive cough in patients with atopic tendencies, elevated sputum eosinophils, airway inflammation, and no airway hyperresponsiveness.
- **Obstructive sleep apnea:** Chronic cough accompanied by loud snoring, excessive daytime sleepiness, and morning headaches.
- **Protracted bacterial bronchitis:** Chronic wet cough lasting 4 weeks or longer, normal spirometry and chest radiography (aside from possible peribronchial cuffing), and resolution with a 2-week course of appropriate antibiotics.
- **Upper airway cough syndrome:** Frequent throat clearing, postnasal drip sensation, nasal discharge; exam findings include pharyngeal cobblestoning and visible secretions.

### Treatment / Management

#### Acute Cough

##### Acute upper respiratory tract infection

Management of acute cough due to an upper respiratory tract infection is primarily supportive. Short-term use of acetaminophen or nonsteroidal anti-inflammatory drugs effectively relieves fever, headache, myalgias, arthralgias, ear pain, and malaise, with similar efficacy and good tolerability.<sup>15</sup> In adults and children older than 12, combination antihistamine–decongestant products may provide greater symptom relief than either agent alone. Antibiotics, antihistamines used alone, and antiviral therapies do not improve outcomes and may cause harm.

##### Acute Rhinosinusitis

Only 0.5% to 2% of cases of acute rhinosinusitis (ARS) are bacterial.<sup>16</sup> Some experts recommend saline nasal irrigation with buffered, physiologic, or hypertonic saline using sterile or bottled water. The actual benefit of saline irrigation is unclear.<sup>17</sup> However, irrigation has minimal adverse effects, and anecdotal reports indicate that it may improve nasal symptoms in some patients. Likewise, clinicians can also offer topical nasal steroids for patients with both ARS and acute bacterial rhinosinusitis (ABRS).<sup>18</sup>

If symptoms fail to improve or worsen, amoxicillin or amoxicillin–clavulanate is first-line therapy for 5 to 7 days.

#### Influenza

Influenza is typically self-limited. However, infection is associated with increased morbidity and mortality in select populations. The treatments of these patients with antivirals:

Oseltamivir is the antiviral medication of choice for influenza. Additional alternatives are baloxavir, zanamivir, and peramivir.

#### Pertussis

The following patients should receive antimicrobial treatment for pertussis:

- All individuals older than 1 year with a clinical or lab-confirmed diagnosis who present within 3 weeks of the onset of cough
- All individuals younger than 1 year, pregnant individuals, patients with asthma, COPD, or an immunocompromising condition, and those aged 65 and older who present within 6 weeks of cough onset.

Preferred treatment is azithromycin or clarithromycin; trimethoprim-sulfamethoxazole is an alternative, except in infants younger than 2 months due to the risk of kernicterus. Early treatment (within 7 days) may shorten symptom duration. Patients are most contagious during the first 3 weeks of illness or the first 5 days of treatment.

#### Acute lower respiratory tract infections

Like most upper respiratory tract infections, acute bronchitis is most commonly viral in etiology, and management is supportive. Antivirals and antibiotics have not shown benefit in the treatment of acute bronchitis.<sup>19</sup>

#### Bronchiolitis

Management of mild bronchiolitis consists of nasal suctioning and adequate hydration. Medications are unnecessary unless caregivers elect to treat fever when present. Moderate to severe symptoms will likely need evaluation in an emergency department. Treatment consists of supplemental oxygen when necessary and nasal suctioning. Clinicians do not routinely use bronchodilators to manage bronchiolitis; however, they may trial nebulized epinephrine or albuterol in infants and children who present with wheezing and respiratory distress.

#### Pneumonia

The choice of antibiotic therapy for community-acquired pneumonia depends on the expected pathogen, patient age, risk factors, comorbidities, and local resistance patterns.<sup>20</sup> According to the 2019 American Thoracic Society/Infectious Diseases Society of America guidelines, the preferred empiric antibiotic regimen for community-acquired pneumonia in healthy outpatients 64 and younger is high-dose amoxicillin. Monotherapy with doxycycline or a macrolide, such as azithromycin or clarithromycin (if the local S

pneumoniae macrolide resistance rate is below 25%), is an acceptable alternative. Macrolide resistance rates among *S pneumoniae* are often greater than 30% in the United States and exceed 25% in nearly the rest of the world.

Patients 65 and older or with chronic lung, liver, or kidney disease, asplenia, a history of cancer, alcohol use disorder, patients who smoke, or those treated with antibiotics within the last 3 months, should receive amoxicillin-clavulanic acid and a macrolide or doxycycline. Patients who are unable to tolerate amoxicillin-clavulanate should receive a third-generation cephalosporin such as cefpodoxime in combination with a macrolide or doxycycline. Clinicians prescribe a respiratory fluoroquinolone for patients who cannot tolerate a third-generation cephalosporin.

Hospitalized individuals with pneumonia are treated with a respiratory fluoroquinolone or  $\beta$ -lactam antibiotics, along with doxycycline or a macrolide.<sup>21</sup>

#### **Asthma exacerbation**

Clinicians manage an acute asthma exacerbation with short-acting inhaled bronchodilators and steroids. Patients with severe symptoms (respiratory rate greater than 30 breaths per minute, pulse greater than 120 beats per minute, use of accessory muscles, drowsiness, diminished breath sounds, and hypoxia) should receive treatment in the emergency department.

#### **Heart failure**

Supplemental oxygen, noninvasive ventilation when indicated, loop diuretics, and sodium restriction for volume overload are the cornerstones of the treatment of acute decompensated heart failure. Vasodilators such as nitroprusside lower systemic vascular resistance and left ventricular afterload in patients with severe hypertension, acute mitral regurgitation, or acute aortic regurgitation. Nitroglycerine lowers venous tone to relieve respiratory distress when the diuretic response is inadequate.

Intravenous inotropes such as dobutamine or milrinone may be necessary in patients with severe systolic dysfunction and end-organ hypoperfusion; however, the use of inotropes in the setting of acute decompensated heart failure with preserved ejection fraction is not appropriate.

#### **Pulmonary embolism**

Hemodynamic status and bleeding risk guide treatment of a pulmonary embolism. High-risk patients with low bleeding risk receive systemic thrombolysis followed by anticoagulation. High-risk individuals with a high bleeding risk undergo catheter-directed therapy or surgical embolectomy.

#### **Subacute and Chronic Cough**

Management of subacute and chronic cough targets the underlying cause. In children, watchful waiting for 2 to 4 weeks is appropriate, as most cases are postviral and self-limited. Inhaled steroids, bronchodilators, and oral medications do not benefit postinfectious cough. A

short trial of bronchodilators or inhaled corticosteroids may be considered for suspected cough-variant asthma, while a 4-week trial of acid suppression is appropriate when GERD features such as recurrent regurgitation, dystonic neck posturing in infants, or heartburn in older children or adults are present.

Tuberculosis requires standard multidrug therapy. Clinicians should discontinue ACEIs and other cough-inducing medications when possible and strongly encourage smoking cessation. Asthma and COPD therapy should be optimized if present.

Intranasal glucocorticoids are the mainstay of therapy for upper airway cough syndrome with antihistamines, ipratropium, or azelastine as adjuncts. Lack of improvement after 2 to 3 weeks makes this diagnosis unlikely.

### **Differential Diagnosis**

#### **Acute**

The following are common differential diagnoses for patients presenting with an acute cough:

Acute bronchitis, Acute exacerbations of COPD or asthma, ARS, Acute viral upper respiratory infection, Allergic rhinitis, Aspiration syndromes, Bronchiolitis, Cerebrospinal fluid leak, Chemical or inhalation injury, Congestive heart failure, Croup, Pertussis, Pneumothorax, Pneumonia and Pulmonary embolism

#### **Subacute**

The following are common differential diagnoses for patients presenting with a subacute cough:

Bronchiectasis, Chlamydia pneumoniae, Mycoplasma pneumoniae, Pertussis, Post-infectious cough and Tuberculosis

#### **Chronic**

The following are common differential diagnoses for patients presenting with a chronic cough:

Asthma, Chronic aspiration, Chronic bronchitis, Chronic rhinosinusitis, COPD, GERD, Interstitial lung diseases, Malignancy, Medication effects, Neurogenic cough, Nonasthmatic eosinophilic bronchitis, Obstructive sleep apnea, Somatic cough syndrome and Upper airway cough syndrome

The following are additional but less common potential causes of cough:

Amyloidosis, Cerumen impaction, causes stimulation of the auricular branch of the vagus nerve or Arnold nerve, Esophageal achalasia, Tracheoesophageal fistula, Esophageal-tracheobronchial reflex, Holmes-Adie syndrome (anisocoria, abnormal deep tendon reflexes, and patchy areas of hyperhidrosis or anhidrosis, along with chronic cough), Inflammatory bowel disease, Ortner syndrome or compression of the left recurrent laryngeal nerve caused by enlarged vascular structures, such as an enlarged left atrium due to mitral stenosis, Paradoxical vocal fold motion, Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci,

causing motor tics, Peritoneal dialysis due to GERD, pulmonary edema, or pleuroperitoneal communication, Pneumonitis, Premature ventricular contractions, Relapsing polychondritis, Sarcoidosis, Syngamus laryngeus infection, Tracheobronchial collapse, Sensory neuropathy due to B12 deficiency and Zenker or distal esophageal diverticulum

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