PAKISTAN CHEST SOCIETY

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STRIVING FOR PULMONARY CARE

Clinical Practice Guidelines

# Chronic Cough

PAKISTAN CHEST SOCIETY-2026

Guidelines On

# Chronic Cough

March 2026

PAKISTAN CHEST SOCIETY

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# Preface

Cough is one of the most common symptoms encountered in clinical practice and remains a major reason for seeking medical attention. Most of the time, it is self-limiting but a persistent cough can indicate underlying respiratory, gastrointestinal, or systemic disorders and may lead to considerable physical and psychosocial distress. Considering the importance and day-to-day issue in our practice, this guideline has been developed to provide clinicians with a structured, evidence-based approach for the evaluation and management of cough, with special focus on chronic cough that significantly impacts quality of life.

This document combines the latest scientific knowledge with practical recommendations suited to our local needs. It explains the definition, causes, pathophysiology and mechanisms of cough. It also describes how to investigate both acute and Chronic Cough; and gives step-by-step guidance on management. Special focus has been given to common and treatable causes such as asthma, GERD, and upper airway cough syndrome, along with newer concepts like cough hypersensitivity syndrome and refractory Chronic Cough.

The guideline also highlights the complications and emotional impact of Chronic Cough, stressing the importance of treating the patient as a whole.

Each section is based on international recommendations from ERS, BTS, and CHEST guidelines, adapted to suit local clinical practice and available resources.

It is hoped that this guideline will serve as a concise yet comprehensive reference for physicians, pulmonologists, and healthcare professionals in the management of their difficult to treat cough patients. This will ultimately improve diagnostic accuracy, rational use of investigations, and patient outcomes in the management of cough.

**Prof. Nisar Ahmed Rao**
Chair, Chronic Cough Guideline Working Group
Pakistan Chest Society

# Message by the President

## Pakistan Chest Society

Chronic cough is defined as a cough lasting more than eight weeks and requires proper medical evaluation.Patients should seek consultation with a qualified healthcare professional for accurate diagnosis.Common causes include asthma, gastroesophageal reflux disease, and post-nasal drip.Self-medication, especially unnecessary antibiotics, must be avoided.Smoking cessation is essential for symptom control.Exposure to dust, smoke, and allergens should be minimized.Medications should be taken strictly as prescribed.Maintain adequate hydration and a healthy lifestyle.

I appreciate the efforts of working group for Chrinic Cough Guidelines under leadership of Prof Nisar Rao for a comprehensive task.

**Prof. Shereen Khan**

President
Pakistan Chest Society

# Message by the Chairman

## Guideline Committee, Pakistan Chest Society

It gives me great pleasure to present the Guidelines for the Management of Chronic Cough by the Pakistan Chest Society. These guidelines are an important step toward improving and standardizing the care of patients who suffer from long-lasting cough—a problem that is often ignored but affects thousands of people across Pakistan.

A chronic cough is defined as a cough that lasts for more than eight weeks. Although coughing is a common symptom, when it becomes long-term, it can be troubling for patients and challenging for doctors to diagnose. In Pakistan, the causes of chronic cough are often different from those in Western countries. Conditions such as old tuberculosis, repeated chest infections, asthma, and Interstitial Lung Diseases. Allergies, environmental pollution, and smoking are common triggers in our population. Understanding these local factors is essential to planning effective and affordable care.

The Working Group for Chronic Cough, led by Prof. Nisar Ahmed Rao has reviewed international recommendations and adapted them to fit Pakistan's healthcare system. These guidelines highlight the possible causes, proper evaluation, and best management strategies for Chronic Cough in our setting.

A key message of these guidelines is the importance of identifying the underlying cause. A detailed medical history, physical examination, chest X-ray, lung function tests, assessment for asthma, reflux disease, postnasal drip, and evaluation for previous tuberculosis are strongly recommended. When needed, further tests such as HRCT chest, allergy testing, or sputum cultures may help find hidden or treatable causes.

Management of chronic cough must be patient-centered and systematic. Treatment should target the root cause—whether it is asthma, allergies, acid reflux, infection, or environmental exposure. Supportive measures like avoiding smoke and pollutants, quitting smoking, staying hydrated, and using prescribed inhalers or medications are also emphasized.

These guidelines highlight the importance of early diagnosis, correct treatment, and patient education. Our goal is to reduce suffering, prevent complications, and improve the quality of life for people living with Chronic Cough across Pakistan.

On behalf of the Guidelines Committee, we extend heartfelt appreciation to all members who contributed to these recommendations. Together, we remain committed to promoting better respiratory care and evidence-based medicine throughout the country.

**Prof. Muhammad Ashraf Jamal**
Chairman Guideline Committee
Pakistan Chest Society

# Pakistan Chest Society

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# Chapter 01: Overview of Cough:
## Definition, Mechanisms and Causes

**Introduction**

Cough is a vital protective reflex preventing aspiration and enhancing airway clearance by expelling mucus, irritants, or foreign material from the respiratory tract.[1] It is described as a forced expulsive maneuver against a closed glottis, associated with a characteristic sound or sounds.[2]

**Pathophysiology**

The airways are innervated by sensory neurons, activation of which is carried via the vagus nerve to the brain stem and higher centers.[3] Airway nerves sense irritant, noxious or mechanical stimuli through receptors on the nerve terminals (eg, TRPV1 and TRPA1), stimulation of these receptors may lead to an 'urge to cough', associated with a tickle sensation in the throat leading to coughing in normal individual (Figure 1). However, pathologically excessive and protracted cough is a common and disabling complaint, affecting perhaps 5– 10% of the adult population.[1]

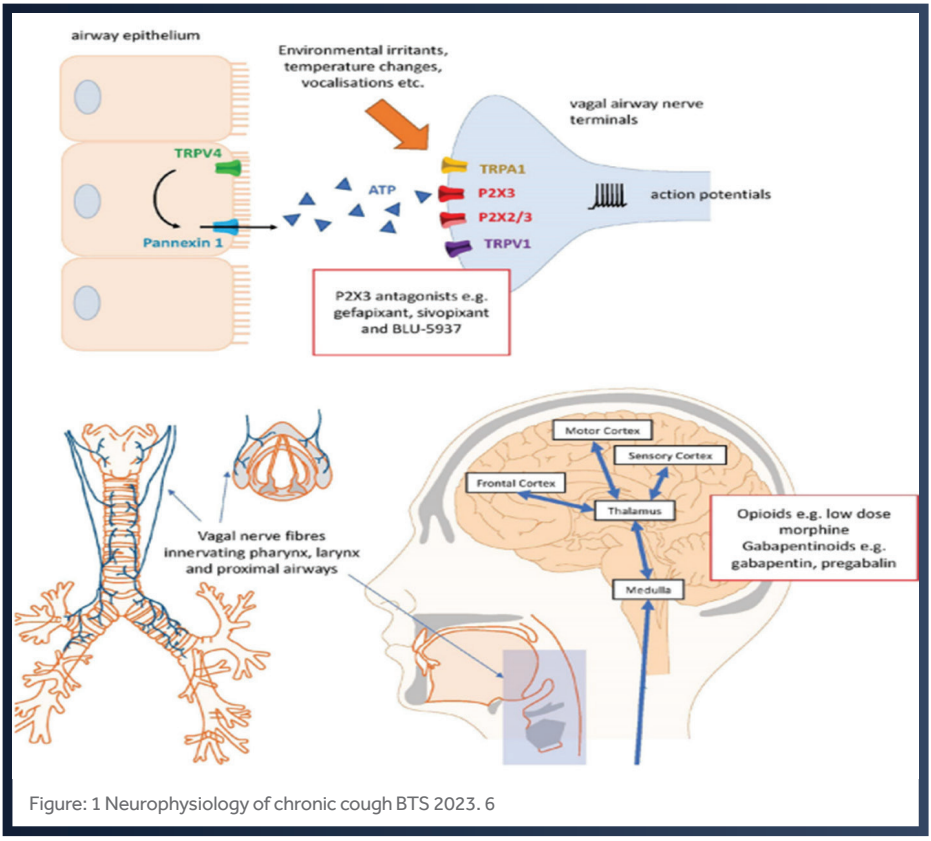



Figure: 1 Neurophysiology of chronic cough BTS 2023. 6

An international survey of 10032 adult patients attending specialist cough clinics, two-thirds were female and the most common age for presentation was in the sixth decade.[3]

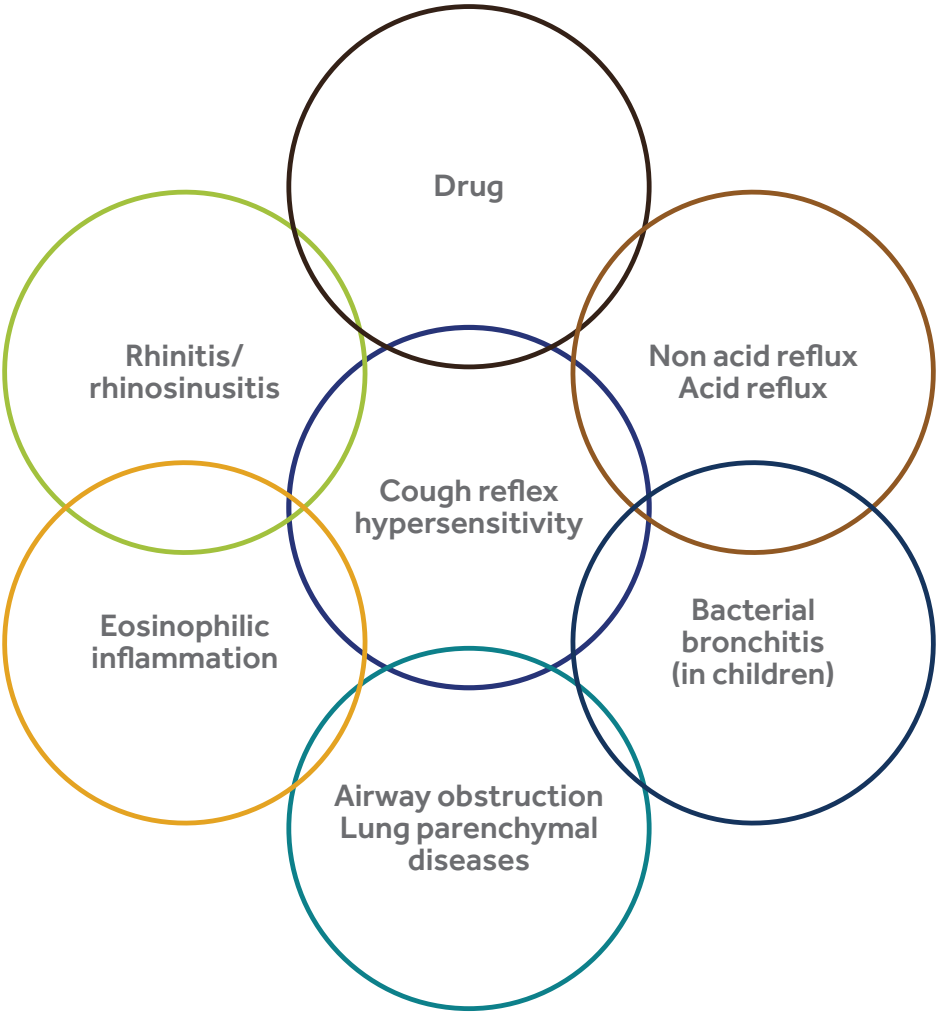
It has become increasingly clear that the majority of adult patients presenting with chronic cough as the primary complaint have a common clinical presentation. When severe, it causes a major decrement in the quality of life, with comorbidities such as incontinence, cough syncope and dysphonia leading to social isolation, depression and difficulties in relationships.[4]

They often complain of exquisite sensitivity to inhalation of environmental irritants such as perfumes, bleaches and cold air which result in sensations of tickling/irritation in the throat and an urge to cough; features suggestive of heightened sensitivity of the neuronal pathways mediating cough.[5] It has been seen that 2/3 of these patients are female in their fifties and sixties which leads to concept of cough hypersensitivity syndrome. In contrast in children Chronic Cough presents in different fashion and in different etiologies.

**Following terminologies are used in describing various types of cough.**

| Type of cough | Definition | Common causes |
|---|---|---|
| Acute cough | Lasts ≤3 weeks | Viral URTI(most common), acute bronchitis, pneumonia, allergic rhinitis, environmental irritants |
| Subacute (Post-infectious) Cough | Lasts 3–8 weeks after a respiratory infection | Post-viral inflammation or transient bronchial hyperreactivity |
| Chronic Cough (Adults) | Lasts >8 weeks | Postnasal drip (Upper Airway Cough Syndrome), asthma, GERD, chronic bronchitis, bronchiectasis, ACE inhibitors, smoking, lung cancer |
| Chronic Cough (Children) | Lasts >4 weeks | Asthma, protracted bacterial bronchitis, post-viral cough, airway malformations |
| Refractory Chronic Cough (RCC) | Persists despite identification and management of treatable traits | May show features of cough hypersensitivity |
| Unexplained Chronic Cough (UCC) | Chronic cough with no identifiable cause after thorough evaluation | Often neurogenic or hypersensitivity-related |
| Cough Hypersensitivity Syndrome (CHS) | Troublesome cough triggered by low-level irritants (thermal, mechanical, or chemical) due to neuronal sensitization | Often associated with laryngeal hypersensitivity and dysphonia |

**Treatable traits of chronic cough[5]**




**Reference:**
**1.** Song WJ, Chang YS, Faruqi S, Kim JY, Kang MG, Kim S, et al. The global epidemiology of chronic cough in adults: a systematic review and meta-analysis. Eur Respir J. 2015;45(5):1479–1481.
**2.** Morice AH, Fontana GA, Belvisi MG, Birring SS, Chung KF, Dicpinigaitis PV, et al. ERS guidelines on the assessment of cough. Eur Respir J. 2007;29(6):1256–1276.
**3.** Morice AH, Jakes AD, Faruqi S, Birring SS, McGarvey LP, Smith JA, et al. A worldwide survey of chronic cough: a manifestation of enhanced somatosensory response. Eur Respir J. 2014;44(5):1149–1155.
**4.** Chamberlain SA, Garrod R, Douiri A, Masefield S, Powell P, Bücher C, et al. The impact of chronic cough: a cross-sectional European survey. Lung. 2015;193(3):401–408.
**5.** Morice AH, Millqvist E, Bieksiene K, Birring SS, Dicpinigaitis PV, Ribas CD, et al. ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. Eur Respir J. 2020;55(1):1901136.
**6.** Pavord ID. New statement and new hope for patients with refractory chronic cough. Thorax. 2023;78(Suppl 6):s1–s2.

# Chapter 02:
## Causes and work up of Chronic Cough

Chronic Cough (CC) is common in adults. It is reported in 10-20% of adults, commonly seen in females and obese patients. Gastro-oesophageal reflux disease GERD, asthma, and allergic or chronic rhinitis are frequently seen in patients with Chronic Cough.[1] The Rotterdam study showed GERD, smoking, asthma, and chronic obstructive pulmonary disease (COPD), are independent risk factors for Chronic Cough in adult population.[2] Another study showed that 66% of patients had esophageal dysmotility in refractory respiratory symptoms and contributed to respiratory diseases such as asthma, Chronic Cough and interstitial lung disease.[3] Here are enlisted causes of chronic cough Table 1.

**Table 1: Causes of Chronic Cough**

| Diseases | Treatable traits |
|---|---|
| Asthma /COPD | Gastro-oesophageal reflux disease |
| Infection | Smoking |
| ILD | Drugs ( ACEI) |
| Bronchiectasis | Chronic rhinosinusitis/ UACS |
| Heart failure | Irritant exposure |
| Cancer | Anxiety |
| Non-Asthmatic Eosinophilic Bronchitis (NAEB) | Inducible laryngeal obstruction |
| | Obstructive sleep apnoea |

**ILD:** interstitial lung disease, **ACEI:** angiotensin-converting enzyme inhibitors, **UACS:** upper airway cough syndrome

**Asthma / Cough-Variant Asthma (CVA)**

Accounts for ~14–41% of Chronic Cough.[5] Characterised by Dry cough, especially at night/exercise; wheeze/dyspnea may be absent in CVA. Diagnosis is usually made with Spirometry (bronchodilator trial), methacholine challenge and skin prick or IgE for allergy. The clinical management of cough variant asthma does not differ from that of usual form of asthma.

**Non-Asthmatic Eosinophilic Bronchitis (NAEB)**

NAEB accounts for 10–30% of cases of Chronic Cough.[5] It is characterised by chronic dry cough with no airflow limitation or hyperresponsiveness with sputum eosinophil ≥3%. FeNO measurement may not be useful to predict NAE.[6] Spirometry is typically normal. Inhaled corticosteroids (4–8 weeks); oral steroids is recommended for severe disease; relapse is common up to 60% after treatment cessation.[7]

**Upper Airway Cough Syndrome (UACS) – Postnasal drip PND / rhinosinusitis**

UACS is common cause of CC, prevalence is variable from 9% and 82%.[8] It is usually diagnosed after ruling out other causes of CC. Cough results from PND inducing mechanical

or chemical stimulation of the afferent nerves innervating the pharynx, larynx or lower airways.[5] Patients usually have rhinorrhea, nasal congestion, throat clearing history. Diagnosis is based on history/ear, nose, throat exam and nasal endoscopy if needed. Flexible nasendoscopy and laryngoscopy indicated in selected patients with CC: **(a)** symptoms of rhinosinusitis/rhinitis despite treatment, **(b)** hoarseness of voice and **(c)** where inducible laryngeal obstruction (ILO) is suspected.[9] Treated usually with antihistamines and Nasal decongestants.

**Gastro oesophageal reflux disease (GERD)**

GERD is frequently seen in CC. GERD is reported to contribute to the severity of several respiratory tract diseases including sinusitis, Chronic Cough, laryngeal disorders, asthma, bronchiectasis, COPD, idiopathic pulmonary fibrosis, cystic fibrosis, and bronchiolitis obliterans post lung transplant.[4] A study from Karachi Pakistan showed 71.6% prevalence of GERD among asthmatic patients with a negative impact on quality-of-life QoL.[10] Treatment with PPI is indicated only if patient has heartburn or reflux. Medical and surgical treatment options for GERD are available, but data are limited on effectiveness.[4] Proton pump inhibitors (PPIs) are superior to histamine-2 receptor antagonists in control of GERD symptoms, but some patients are PPIs refractory.[11] Laparoscopic fundoplication is preferred over long-term PPI therapy due to better cost-effectiveness, symptom control, and quality-of-life outcomes. This approach is supported by guidelines from the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), the National Institute for Health and Care Excellence (NICE), the American College of Gastroenterology (ACG), and the American Gastroenterological Association (AGA), particularly for PPI-refractory GERD. (12) A reduction in BMI of ≥3.5 $kg/m^2$ has also been associated with a 40% decrease in GERD symptoms among women.[11]

**Malignancy / Lung Tumor**

Suspect when red flags are present like Persistent cough (>8weeks), weight loss, hemoptysis, abnormal chest X-ray and Smoker >40 yrs. CT scan chest is recommended and bronchoscopy if suspicion remains.

**Drug-Induced Cough**

Common offenders are ACE inhibitors; others include opioids, prostaglandin eye drops, beta-blockers, statins, NSAIDs. When a patient with CC presents, medication history should be reviewed in detail. Treatment is to stop offending drug and observe for resolution.

**Obstructive sleep apnea (OSA)**

Between 44% and 68% of individuals with CC have been found to have OSA.[13,14] Two mechanisms have been proposed to underlie OSA-associated CC. Firstly, repetitive upper airway obstruction and snoring contribute to local airway inflammation, which may enhance cough reflex sensitivity. Secondly, there is an increased incidence of GERD in patients with OSA-related cough, with GERD serving as an independent predictor of cough in this cohort.[15] Assessment for OSA should be considered in patients with refractory Chronic Cough or when clinical signs of OSA are present. Continuous positive airway pressure (CPAP) therapy has demonstrated effectiveness, with reports showing cough improvement in 93% of patients and complete cough resolution in 67% following treatment with CPAP.[15,16].

**Cough Hypersensitivity Syndrome (CHS)**

CHS is associated with hypersensitivity of the larynx and upper airways to benign stimuli (perfume, cold air, voice). Usually presents as dry tickling cough, laryngeal paraesthesia, dyspnoea, dysphonia, or laryngeal spasm. Commonly seen in middle-aged women. The Hull Airway Reflux Questionnaire (HARQ) has been developed to aid in the diagnosis of chronic hypersensitivity syndrome (CHS), demonstrating high sensitivity (94%) and specificity (95%).[17] The diagnosis necessitates ruling out other potential causes as mentioned in Table 1.

**Infections**

- **Pertussis (Bordetella pertussis)**
  Can cause Chronic Cough. Whooping and post tussive vomiting are key clues. Diagnosis usually made via culture, PCR, serology. CDC recommends Tdap (diphtheria pertussis tetanus) Vaccination in adults any time who were not vaccinated previously. There are 2 types of combination vaccines that include protection against whooping cough: DTaP/ Tdap The letter "T" in DTaP and Tdap shows they also help protect against tetanus. The letter "D/d" in DTaP and Tdap shows they also help protect against diphtheria. Post exposure prophylaxis recommended in high-risk group to prevent serious life-threatening infection.

- **Chronic infection/bronchiectasis**
  TB, Fungus, Nocardia, consider with chronic history and productive cough. Consider sputum testing and HRCT where indicated.

**Other Respiratory Causes**

- **Bronchiectasis**
  Produces chronic productive cough, chest examination showed bilateral crackles; HRCT chest is required for confirmation of diagnosis.

- **Interstitial Lung Disease**
  Sarcoidosis, Bronchiolitis, Tracheomalacia: HRCT chest is required for confirmation of diagnosis.

- **Psychogenic / Habit cough**
  A cough with a "honking" or "barking" character and which disappears with sleep has been suggested as typical of a psychogenic or habit cough. Especially seen in younger patients and frequently reported in paediatric population. Diagnosed when organic causes excluded. Treatment includes behavioural therapy.

**Environmental & Occupational Exposure**

- **Smoking**
  Active and passive smoking both are major risk factor of cough. Smoking cessation helps in cough management as bronchitis resolves. Some patients may experience rebound cough on smoking cessation. Nicotine replacement therapy may prevent a rebound in cough hypersensitivity and worsening symptoms. Also, Nicotine suppresses the cough reflex.[18]

- **Workplace irritants**
  Dust, chemicals, gases in industries like mechanics, cleaning, and mining.

**Workup of Chronic Cough**

**Initial assessment:**

A systemic approach is mentioned in Table 1. All patients should undergo detailed history and examinations. History should include occupation, workplace environment, Smoking and drug history should be taken in detail. Crackles on examination suggest ILD, bronchiectasis should be referred to pulmonologist and Urgent HRCT chest should be done to confirm the diagnosis.

**Basic Investigation**

All patients with Chronic Cough should undergo chest x-ray and spirometry testing (preferably with reversibility testing). If infection is suspected spirometry should be avoided. Sputum test should be ordered for appropriate infection and treat accordingly. If patient presents with red flag features as shown in Table 1 require urgent CXR and hospital referral. Normal CXR does not rule out malignancy, CT scan chest (low dose CT scan chest) is recommended for screening of such patients.

| Step | Category | Key actions/Notes |
|---|---|---|
| 1 | **Define Chronic Cough** | >8 weeks duration |
| 2 | **Initial Screening** | **Detailed history**<br>Duration, pattern (diurnal/nocturnal), smoking, ACE inhibitors (Drug history), occupation, GERD symptoms, nasal symptoms, wheeze<br>Physical exam: ENT (PND), chest auscultation, signs of chronic disease |
| 3 | **Rule Out Red Flags** | Hemoptysis<br>Weight loss, fever, night sweats<br>Dyspnea or hypoxia<br>Abnormal chest X-ray<br>Smoker >40 yrs (exclude malignancy) |
| 4 | **Basic Investigations** | **Chest x-ray**<br>Spirometry with bronchodilator reversibility<br>Trial of ACE inhibitor/drug withdrawal (if applicable) |
| 5 | **Empiric Sequential Trials (if normal CXR + spirometry)** | **A. UACS (Postnasal drip)**<br>• Antihistamines (non-sedating)<br>• Intranasal corticosteroids<br>**B. Asthma/Cough variant asthma**<br>• ICS ± LABA trial<br>• Consider methacholine challenge |

| Step | Category | Key actions/Notes |
|---|---|---|
| | | **C. Non-asthmatic Eosinophilic Bronchitis (NAEB)**<br>• Normal spirometry + sputum eosinophilia- ICS monotherapy<br>**D. GERD**<br>• PPI 8-week trial<br>• Lifestyle: elevate bed head, avoid late meals |
| 6 | **Persistent or Atypical Cough** | • **CT chest:** to rule out ILD, bronchiectasis, malignancy<br>• **Bronchoscopy:** if concern for airway lesion, aspiration, or foreign body<br>• **Induced sputum** for eosinophilia,FeNO<br>• **ENT** referral if upper airway symptoms predominate<br>• **pH monitoring or esophageal manometry** if GERD is refractory<br>• **Empirical** trial of gabapentin or speech therapy for chronic refractory cough |
| 7 | **Special Conditions** | **Refractory Chronic Cough:**<br>• Consider gabapentin, amitriptyline, or speech therapy (laryngeal hypersensitivity)<br>**Consider less common causes:**<br>• ILD, TB, bronchiectasis, malignancy<br>• Cardiac (HF), aspiration (especially elderly or stroke patients)<br>• Habit cough (especially in children, young people) |
| 8 | **Refer or Investigate Further** | **Multidisciplinary team or specialised cough clinic referral if**<br>• Workup is unrevealing<br>• Cough impacts QoL<br>• Suspicion of rare pathology |

**Reference:**
**1.** Chen W, Schatz M, Zhou Y, et al. Prediction of persistent chronic cough in patients with chronic cough using machine learning. ERJ Open Res 2023; 9(2): 00471-2022.
**2.** Arinze JT, de Roos EW, Karimi L, et al. Prevalence and incidence of, and risk factors for chronic cough in the adult population: the Rotterdam Study. ERJ Open Res 2020; 6(2): 00300-2019
**3.** Sykes DL, Crooks MG, Hart SP, et al. Investigating the diagnostic utility of high-resolution oesophageal manometry in patients with refractory respiratory symptoms. Respir Med 2022; 202: 106985
**4.** McDonnell MJ, Hunt EB, Ward C, et al. Current therapies for gastro-oesophageal reflux in the setting of chronic lung disease: state of the art review. ERJ Open Res 2020; 6(4): 00190-2019
**5.** Perotin JM, Launois C, Dewolf M, Dumazet A, Dury S, Lebargy F, Dormoy V, Deslee G. Managing patients with chronic cough: challenges and solutions. Ther Clin Risk Manag. 2018;14:1041-1051(https://doi.org/10.2147/TCRM.S136036)
**6.** Song WJ, Kim HJ, Shim JS, et al. Diagnostic accuracy of fractional exhaled nitric oxide measurement in predicting cough-variant asthma and eosinophilic bronchitis in adults with chronic cough: a systematic review and meta-analysis. J Allergy Clin Immunol. 2017;140(3):701–709. doi: 10.1016/j.jaci.2016.11.037

**7.** Lai K, Liu B, Xu D, et al. Will nonasthmatic eosinophilic bronchitis develop into chronic airway obstruction? A prospective, observational study. Chest. 2015;148(4):887–894. doi: 10.1378/chest.14-2351
**8.** Donaldson AM. Upper Airway Cough Syndrome. Otolaryngol Clin North Am. 2023 Feb;56(1):147-155. doi: 10.1016/j.otc.2022.09.011. Epub 2022 Oct 22. PMID: 36283869.
**9.** Halvorsen T, Walsted ES, Bucca C, et al. Inducible Laryngeal obstruction: an official joint European Respiratory Society and European Laryngological Society statement. Eur Respir J 2017;50:1602221.
**10.** Iqbal N, Amirali A, Lail GU, Khan MA, Sial R, Irfan M. Correlation of gastro-esophageal reflux disease with asthma control and quality of life: a cross-sectional study from a low-middle income country. Ther Adv Respir Dis. 2024 Jan-Dec;18:17534666241297879. doi: 10.1177/17534666241297879. PMID: 39512235; PMCID: PMC11544649.
**11.** Katz PO, Dunbar KB, Schnoll-Sussman FH, et al. ACG clinical guideline for the diagnosis and management of gastro-oesophageal reflux disease. Am J Gastroenterol 2022; 117: 27–56.
**12.** Lata T, Trautman J, Townend P, et al. Current management of gastro-oesophageal reflux disease-treatment costs, safety profile, and effectiveness: a narrative review. Gastroenterol Rep (Oxf) 2023; 11: goad008.
**13.** Sundar KM, Daly SE, Pearce MJ, Alward WT. Chronic cough and obstructive sleep apnea in a community-based pulmonary practice. Cough. 2010;6(1):2. doi: 10.1186/1745-9974-6-2.
**14.** Sundar KM, Daly SE. Chronic cough and OSA: a new association? J Clin Sleep Med. 2011;7(6):669–677. doi: 10.5664/jcsm.1482
**15.** Wang TY, Lo YL, Liu WT, et al. Chronic cough and obstructive sleep apnoea in a sleep laboratory-based pulmonary practice. Cough. 2013;9(1):24. doi: 10.1186/1745-9974-9-24
**16.** Sundar KM, Daly SE, Willis AM. A longitudinal study of CPAP therapy for patients with chronic cough and obstructive sleep apnoea. Cough. 2013;9(1):19. doi: 10.1186/1745-9974-9-19.
**17.** Morice AH. Chronic cough hypersensitivity syndrome. Cough. 2013;9(1):14. doi: 10.1186/1745-9974-9-14.
**18.** Parker SM, Smith JA, Birring SS, Chamberlain-Mitchell S, Gruffydd-Jones K, Haines J, Hennessey S, McGarvey LP, Marsden P, Martin MJ, Morice A, O'Hara J, Thomas M. British Thoracic Society Clinical Statement on chronic cough in adults. Thorax. 2023 Dec 6;78(Suppl 6):s3-s19. doi: 10.1136/thorax-2023-220592. PMID: 38088193.

# Chapter 03:
## Management of Chronic Cough

Effective management of chronic cough requires identifying and treating the underlying cause, along with addressing cough hypersensitivity and improving quality of life.

A systematic, stepwise approach guided by clinical evaluation and targeted investigations is suggested:

**Clinical Assessment:** In the history following points should be noted:

- Duration, character, and timing of the cough
- Associated symptoms: sputum, wheeze, dyspnea, heartburn, nasal discharge, etc.
- Drug history like ACE inhibitors
- Smoking history
- Environmental/occupational exposure

**Examination Findings:**

- **Upper airway:** nasal mucosal swelling, postnasal drip, oropharyngeal cobble stoning (Allergic rhinitis, non-allergic rhinitis, sinusitis, UACS)
- **Chest:** wheeze (asthma, COPD), crackles (bronchiectasis, ILD), decreased breath sounds (effusion, mass)
- **Cardiac:** signs of left heart failure (S3 gallop, edema, basal crackles)
- **Others:** digital clubbing (bronchiectasis, ILD, bronchogenic carcinoma), lymphadenopathy, oral ulcers (connective tissue disease)

**Initial Investigations:**

- Routine laboratory tests like CBC, IgE (allergy, anemia, infection)
- Chest X-ray: (malignancy, tuberculosis, ILD, bronchiectasis etc)
- Spirometry with bronchodilator reversibility
- Consider exhaled nitric oxide (FeNO) if available

**If CXR and spirometry are normal, then three most common causes should be considered:**

- Upper airway cough syndrome (UACS) / postnasal drip
- Asthma or eosinophilic airway disease
- Gastroesophageal reflux disease (GERD)

## Management of Common Causes

**A. Upper Airway Cough Syndrome (UACS):**
These patients present with nasal congestion, postnasal drip, frequent throat clearing, cobble stoning of pharyngeal mucosa. Sinus imaging is indicated if chronic rhinosinusitis is suspected.

**Treatment:** It should be treated with Intranasal corticosteroids (fluticasone, mometasone), oral or intranasal antihistamines, saline nasal irrigation. An ENT referral is indicated if symptoms persist despite adequate therapy (2-6 weeks).

**B. Asthma and Eosinophilic Bronchitis:**
These patients present with nocturnal cough, wheeze, chest tightness, cough after exercise or exposure to allergens. Spirometry with bronchodilator reversibility is indicated as initial diagnostic test. If spirometry is normal then methacholine challenge test is indicated especially in cough variant asthma. Induced sputum eosinophilia (>3%) or elevated FeNO may be helpful in eosinophilic bronchitis.
**Treatment:** The mainstay of treatment is inhaled corticosteroids (ICS) with bronchodilator (LABA/LAMA). In acute cases short course of oral steroid is indicated. Non-asthmatic eosinophilic bronchitis can be treated with ICS alone.

**C. Gastroesophageal Reflux Disease (GERD):** These patients present with heartburn, regurgitation, cough after meals or lying down, hoarseness. Up to 40% of GERD-related cough cases may occur without typical reflux symptoms. Clinical examination is normal.
**Treatment:** It includes lifestyle modification: elevate head of bed, avoid late meals, reduce caffeine, alcohol and fatty foods. A therapeutic trial of proton pump inhibitors (PPIs) for 8–12 weeks is recommended. Addition of prokinetics sometimes help. In refractory cases, 24-hour pH monitoring or impedance studies is recommended.

**D. ACE Inhibitor-Induced Cough:**
These patients develop dry cough 1–6 weeks after starting ACE inhibitor.
**Treatment:** discontinue ACE inhibitor and replace with an angiotensin receptor blocker (ARB). Cough typically resolves within 1–4 weeks after cessation.

**E. Chronic Bronchitis / COPD:**
These patients present with chronic productive cough, smoking history, airflow limitation on spirometry.
**Treatment:** It includes: smoking cessation, bronchodilators (LABA, LAMA) ± inhaled corticosteroids, pulmonary rehabilitation, vaccination.

**F. Bronchiectasis:**
These patients present with daily copious sputum, recurrent infections, coarse crackles.
**Treatment:** It includes: airway clearance techniques (postural drainage, oscillatory PEP devices), antibiotics in exacerbation, Treat underlying causes (e.g., post-infective, immunodeficiency, ABPA). Long-term antibiotics (macrolides) is indicated in selected cases

**G. Post-Infectious Cough:**
It often follows viral infection and usually lasts for 3–8 weeks. It is self-limiting, but bothersome.
**Treatment:** Reassurance. Short course (2-4 weeks) of inhaled corticosteroids or antitussives like dextromethorphan if severe.

**H. Obesity:** Obesity may be associated with Chronic Cough (CC). Weight loss should be recommended in obese patients and might improve CC.

**I. Obstructive sleep apnea:**
It may be a potential treatable trait in refractory cough. Continuous positive airway pressure (CPAP) treatment might improve CC if there is objective evidence of OSA on a sleep study.

**J. Psychogenic/Somatic cough syndrome:**
It is often triggered or maintained by psychological factors such as stress or anxiety. It typically disappears during sleep or distraction and may follow a mild respiratory infection. Diagnosis is by exclusion of other causes. Management includes reassurance, behavioral therapy, and counseling. Medications e.g. antidepressants are rarely needed.

**How to proceed in patient with refractory or unexplained Chronic Cough?**
After thorough evaluation if no cause is identified then such cases be labelled as Cough Hypersensitivity Syndrome or Resistant Chronic Cough (RCC).

**Treatment Options:** It includes:
**Neuromodulator drugs:** Gabapentin (up to 1800 mg/day), Pregabalin (150–300 mg/day), Low-dose morphine (5–10 mg BID; use cautiously due to its depressive effect on respiratory center).

**Speech therapy (Cough Control Therapy):** Focuses on cough suppression, vocal hygiene, and breathing exercises.

**Emerging therapies:** Recent advances in the management of refractory Chronic Cough (RCC) have shifted from nonspecific symptomatic therapy toward mechanism-based treatments targeting cough hypersensitivity pathways. It has focused on novel neuropharmacological pathways, particularly those involving ATP-mediated purinergic signaling.

**P2X3 Receptor Antagonists:** Geoffrey Burnstock's hypothesis that ATP acts via purinergic receptors has identified P2X3 receptors as key mediators of cough hypersensitivity through sensory nerve activation in the vagus nerve. Excess ATP release or increased receptor activity may trigger exaggerated cough reflexes.

Gefapixant is the first-in-class P2X3/P2X2/3 antagonist, which significantly reduces cough frequency and severity in RCC but causes frequent taste disturbances (dysgeusia in ~60%) due to poor receptor selectivity.

Newer, more selective P2X3 antagonists like eliapixant, filapixant and sivopixant show promise in reducing cough with fewer taste-related side effects, though results are complicated by substantial placebo effects and heterogeneous study designs. Further large-scale, comparative trials are needed to confirm the efficacy and safety of newer agents.

**Investigational Pathways:**

In addition to the purinergic pathway, several other neuroreceptors are being explored:

- Neurokinin-1 (NK-1) receptor antagonists: Orvepitant demonstrated reductions in cough frequency and severity in early studies.
- Transient receptor potential (TRP) channels: TRPV1, TRPV4, and TRPA1 antagonists have shown limited or no benefit. Capsaicin (a TRPV1 agonist) is under evaluation for potential symptom relief.
- Voltage-gated sodium channel (NaV1.7) and α7 nicotinic receptor agents (e.g. bradanicline) have not demonstrated efficacy in phase II studies.

**Symptomatic / Supportive Treatment:**

- Try to avoid cough triggers like smoke, strong odors, cold air etc.
- Maintaining adequate hydration is important.
- Honey-based syrups may provide transient relief.
- Short-term use of centrally acting antitussives (e.g. dextromethorphan, codeine) if cough is distressing.

**Follow-Up:** It is important to regularly reassess the patient for symptom resolution or evolution of new findings. Also review medication adherence and response to empiric therapy. Besides, reinforce smoking cessation and environmental control measures.

**Reference:**

**1.** Morice AH, McGarvey L, Pavord I; European Respiratory Society Cough Guideline Group. ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. Eur Respir J. 2020;55(1):190113.

**2.** Irwin RS, French CL, Chang AB, Altman KW; CHEST Expert Cough Panel. Classification of cough as a symptom in adults and management algorithms: CHEST guideline and expert panel report. Chest. 2018 Jan;153(1):196-209.

**3.** Parker SM, Smith JA, Birring SS, et al. British Thoracic Society Clinical Statement on chronic cough in adults. Thorax 2023;78(suppl 6):3–19

**4.** Burnstock G, Campbell G, Satchell D, et al. Evidence that adenosine triphosphate or a related nucleotide is the transmitter substance released by non-adrenergic inhibitory nerves in the gut. Br J Pharmacol 1970; 40: 668–688.

**5.** Aw Yong PY, Islam F, Harith HH, Israf DA, Tan JW, Tham CL. The potential use of honey as a remedy for allergic diseases: a mini review. Front Pharmacol. 2021;11:599080. doi:10.3389/fphar.2020.599080.

# Chapter 04:
## Complications of Chronic Cough

Chronic Cough can lead to a range of complications, both physical and psychosocial. These complications arise primarily from its physiologic effects of forceful coughing. The magnitude of pressures and energy generated during bouts of coughing can lead to a variety of physical and psychosocial complications. These include breathlessness, fatigue, sleep disturbance, speech impairment (e.g., vocal cord dysfunction, hoarseness), retching and vomiting[1].

One significant complication is stress urinary incontinence seen predominantly in women, affecting 55-66% in comparison to 5% in men. This complication has significant impact on their quality of life (QoL).[2]

Cough syncope: It occurs due to a sudden rise in intrathoracic pressure during a severe bout of coughing. This pressure triggers the cardioinhibitory baroreflex. As a result, there is peripheral vasodilation and a reduced ability to respond to low blood pressure. These changes lead to decreased cerebral blood flow, ultimately causing syncope.[3] Around 10% of patients,[4] almost exclusively male, develop cough syncope which adversely affects their ability to drive.[5]

If the cough is sufficiently severe, it can generate very high intra-abdominal and intrathoracic pressures, producing muscle strain especially of intercostal and abdominal muscles[6] and, less commonly, rib fractures[7] (especially in elderly or osteoporotic patients) and hernias.

Gastroesophageal reflux can be both a cause and a complication.[8] Besides, Hiatal hernia can develop due to repetitive high intrathoracic pressure.[9]

Less commonly complications may involve the cardiovascular, neurologic, ophthalmologic, respiratory, and dermatological systems.[10]

The psychosocial effects include disrupted daily activities, social embarrassment especially during meetings, anxiety/depression, fear of serious disease etc. Anxiety and depression have been reported in 33–52% and 16–91% of patients with Chronic Cough, respectively.[1]

Additionally, occupational and social impairments are common. Patients often experience disruption of work, Sleep deprivation affecting daytime functioning and Avoidance of public places due to fear of embarrassment or social stigma.[11]

## Complications of Chronic Cough

| Domain | Complication/Manifestation | Mechanism |
|---|---|---|
| **Respiratory and Musculoskeletal** | • Breathlessness, fatigue<br>• Muscle strain (intercostal, abdominal)<br>• Rib fractures<br>• Hernias (inguinal, umbilical, hiatal) | • Result from repeated bouts of coughing causing increased respiratory effort and energy expenditure.[1]<br>• High intrathoracic and intra-abdominal pressures lead to strain of respiratory and abdominal muscles.[6]<br>• Repetitive forceful coughing can cause fractures, especially in elderly or osteoporotic patients.[7]<br>• Repeated increases in intrathoracic pressure predispose to hernia formation.[8,9] |
| **Upper Airway / ENT** | • Speech impairment, vocal cord dysfunction, hoarseness<br>• Retching and vomiting | • Chronic irritation and laryngeal trauma from coughing.[1]<br>• Due to intense stimulation of the cough reflex and associated emetic pathways.[1] |
| **Cardiovascular / Neurologic** | Cough syncope | Severe coughing elevates intrathoracic pressure → cardioinhibitory baroreflex→ vasodilation→decreased cerebral perfusion →transient loss of consciousness; affects ~10%, mostly men.[3,4,5] |
| **Gastrointestinal** | Gastroesophageal reflux disease (GERD) | May be both a cause and complication of Chronic Cough; repeated pressure promotes reflux.[8] |
| **Genitourinary** | Urinary stress incontinence | Common in women (55–66% vs. 5% in men); due to raised intra-abdominal pressure; markedly impacts QoL.[2] |
| **Psychosocial / Quality of Life** | • Anxiety and depression<br>• Sleep disturbance, daytime fatigue<br>• Social embarrassment, occupational impact | • High prevalence—anxiety 33–52%, depression 16–91%; linked to chronic symptoms and social stigma.[1]<br>• Cough disrupts sleep, leading to poor daytime functioning.[1,11]<br>• Fear of coughing in public, avoidance of social gatherings, work disruption.[10,11] |

| Domain | Complication/Manifestation | Mechanism |
|---|---|---|
| **Other Organ** | Cardiovascular, | Rarely, severe or prolonged coughing can |
| **Systems** | neurologic, | affect multiple systems (e.g., conjunctival |
| | ophthalmologic, | hemorrhage, arrhythmias, subcutaneous |
| | respiratory, dermatologic | emphysema)[10]. |
| | complications | |

**Reference:**
**1.** Morice AH, Millqvist E, Bieksiene K, Birring SS, Dicpinigaitis PV, Ribas CD, et al. ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. Eur Respir J. 2020;55(1):1901136. doi:10.1183/13993003.01136-2019.
**2.** Dicpinigaitis PV. Prevalence of stress urinary incontinence in women presenting for evaluation of chronic cough. ERJ Open Res. 2021;7(1):00012-2021.
**3.** Waldmann V, Combes N, Narayanan K, Jaïs P, Haïssaguerre M. Cough syncope. Am J Med. 2017;130(3):e295–6.
**4.** Arinze JT, Verhamme KMC, Luik AI, Hofman A, Stricker BH, Brusselle GG. The interrelatedness of chronic cough and chronic pain. Eur Respir J. 2021;57(1):2002651.
**5.** Dicpinigaitis PV, Lim L, Farmakidis C. Cough syncope. Respir Med. 2014;108(2):244–51.
**6.** Irwin RS, French CL, Chang AB, Altman KW; CHEST Expert Cough Panel. Complications of cough: ACCP evidence-based clinical practice guidelines. Chest. 2006;129(1 Suppl):54S–60S.
**7.** Hanak V, Hartman TE, Ryu JH. Cough-induced rib fractures. Mayo Clin Proc. 2005;80(7):879–82. doi:10.4065/80.7.879.
**8.** Gibson PG, Vertigan AE. Management of chronic refractory cough. BMJ. 2015;351:h5590. doi:10.1136/bmj.h5590.
**9.** Kahrilas PJ, Kim HC, Pandolfino JE. Approaches to the diagnosis and grading of hiatal hernia. Best Pract Res Clin Gastroenterol. 2008;22(4):601–16. doi: 10.1016/j.bpg.2007.12.007.
**10.** Young EC, Smith JA. Quality of life in patients with chronic cough. Ther Adv Respir Dis. 2010;4(1):49–55.
**11.** Pulli T, Sutinen S, Sovijärvi A, Uitti J, Tammilehto L, Toskala E, et al. The impacts of cough: a cross-sectional study in a Finnish adult employee population. Eur Respir J. 2018;52(4):1801067.

# Chapter 05:
## Future research and gaps

Chronic Cough is a challenging clinical issue. There are a lot of gaps in the understanding of chronic cough which need to be addressed first for the fruitful outcome.

The current research on Chronic Cough is limited by heterogeneous definitions and inconsistent phenotyping, due to which comparisons across studies become difficult. The clinical trials have used varied outcome measures like cough frequency, subjective scores, quality of life etc. due to which meta analyses and evidence synthesis become difficult. There is no proper and complete understanding of peripheral and central mechanisms of cough hypersensitivity. There are no reliable noninvasive biomarkers to identify treatable traits or predict therapeutic response. There is no standardized diagnostic algorithms regarding the most efficient and cost-effective sequence of tests. Besides, pharmacologic options are limited. There is insufficient long-term data on the safety and efficacy of emerging agents such as P2X3 antagonists and neuromodulators. Evidence for non-pharmacologic interventions, including speech, behavioral, and physiotherapy based therapies is variable.

At present we do not have reliable method to predict which treatment will work best for the individual patient. Moreover, most studies have short follow-up so we are not sure about the long-term outcomes like recurrence, safety etc.

**What is the way forward?**

It is suggested that future studies should focus on standardized universally accepted definitions along with core outcome measurement. Cellular and molecular studies on airway sensory neurons, purinergic (P2X3) & TRP channel pathways and neuroimmune interactions will help in identifying reliable biomarkers that can differentiate eosinophilic, reflux-related, and neurogenic cough. Long-term multicenter prospective studies, randomize control trials and national registries are needed to assess disease burden, evaluate safety profiles, and determine the sustained effectiveness of emerging therapeutic interventions.