

CONSENSUS STATEMENT

Indian Consensus on Diagnosis of Cough at Primary Care Setting

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Abstract

Diagnosis of cough poses a common dilemma during consultations at primary care settings in India. This Expert Opinion document presents a diagnostic algorithm for primary care physicians to distinguish between cough conditions that can be treated at the community level and potentially serious cough that requires specialist care. The etiology and diagnostic work-up primarily depends on cough classification based on its duration as acute (<3 weeks), subacute (between 3 and 8 weeks), and chronic (>8 weeks). A targeted screening of numerous causes of cough through salient history, including smoking status, environmental exposure, and medication use is recommended. Aggressive investigations are recommended with presence of "red flag" signs. Confirming the diagnosis by monitoring treatment response is essential. If cough persists, frequent causes of acute cough such as infections, asthma, cardiac disease, and foreign body aspiration often overlap with causes of subacute and chronic cough. For cough duration >2 weeks, pulmonary tuberculosis should be ruled out. Subsequently, asthma, gastroesophageal reflux disease, upper airway cough syndrome, environmental cause, or post infectious cough should be suspected. Refer to specialist care if cardiac cause is suspected. Patients would be treated empirically after considering overlapping etiologies. Thus, this diagnostic strategy could bring in greater accuracy in the clinical assessment of cough and accelerate the process of appropriate referrals to specialty care.

Background

Cough is a sudden and repetitively occurring protective reflex, which helps clear the large breathing passages from fluids, irritants, foreign particles, and microbes. Normally, cough acts as a defense mechanism for the airways and the lungs; however, in some conditions, it may become excessive and potentially harmful to the airway mucosa.¹ The prevalence of cough in India is 5%-10%.² It is one of the most common presenting complaints (30%) at the primary care setting.³ Cough may adversely affect the quality of life, sleep, and productivity at work.⁴ Cough may also lead to urinary incontinence and depression.^{5,6}

The existing international guidelines on cough diagnosis and management^{7,10} are tailored to specialty care, and they do not address challenges encountered in developing countries like India. In our setting, a large proportion of patients (68.7%) with cough are

treated empirically without a definite diagnosis.³ Cough is a common manifestation of tuberculosis in India, with an incidence of 2.79 million.¹¹ Diagnosis of pulmonary tuberculosis is missed in about 25% of the cases.¹²

Following the recommended diagnostic criteria for cough management appears to be one of the major challenges faced by the primary care physicians in India. The diagnostic tests are either unavailable in the primary care setting or the patients cannot afford them; additionally, there is a longer waiting period for definitive diagnosis. Another concern is rampant self treatment of cough with

overthecounter medications. Thus, a symptom based approach would help mitigate these challenges for general practitioners (GPs) in India. A simple and specific algorithm can help GPs distinguish between conditions that could be managed with empirical treatment at the community level and potentially serious illnesses that require specialist care.

Hence the objective of this consensus document was to provide a structured and systematic approach for diagnosis of cough in the Indian scenario and to assist primary care physicians in effective cough management.

The Process

Experienced pulmonologists from across India discussed the existing national and international guidelines, current evidence on cough diagnosis and management, and the applicability of these guidelines for diagnosis of cough in the Indian primary care setting. Based on literature review, clinical practice, and feasibility, a simple holistic step-by-step approach for the diagnosis and management of cough as a symptom was proposed. The recommendations were finalized on the basis of the consensus among the experts. This consensus document is the first attempt toward providing a simplistic algorithm for diagnosing cough in India.

Diagnostic Approach Toward Cough

The recommended systematic approach toward cough diagnosis is presented as an algorithm. It involves

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Table 1: Causes of acute cough

- Upper respiratory tract infections (bacterial or viral)
- Pneumonia
- Asthma
- Congestive heart failure
- Pulmonary embolism
- Foreign body aspiration

Table 2: Red flag signs

- Hemoptysis
- Prominent dyspnea
- Systemic symptoms such as weight loss, fever, sore throat
- Hoarseness of voice
- History of tuberculosis (self or in a person who is in close contact)
- Immunosuppressive state
- Smokers' cough especially in patients >35 years of age
- Cough syncope

history taking for differential diagnosis, and then ruling out other causes using relevant investigations, and finally confirming the definite diagnosis.

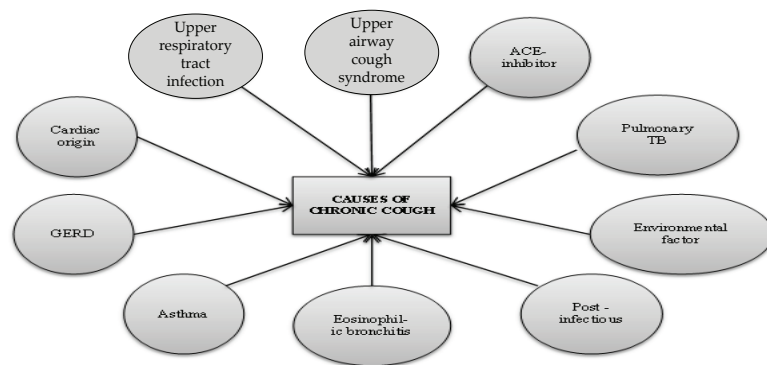
Duration of cough

Cough is classified into 3 categories on the basis of its duration in adults: acute (<3 weeks), subacute (between 3 and 8 weeks), and chronic (>8 weeks).⁷

Acute cough

Acute cough can set in due to infectious causes such as sinusitis, influenza, pneumonia, and infective bronchitis. Based on a survey in Indian patients visiting primary care clinics, upper and lower respiratory tract infections were the cause of cough in 12.2% and 8.1% of patients respectively.³ Other causes of acute cough could be asthma, congestive heart failure, and pulmonary embolism (Table 1).^{13,14} In the same Indian survey, these noninfectious causes for cough were observed in 7.4% (asthma) and 0.5% (congestive heart failure) patients in the primary care settings.³ Cough syncope is another cause of acute cough that should be aggressively investigated, especially in the elderly population, as it may have a cardiac or neurological origin.¹⁵ Foreign body aspiration (FBA) and pharyngeal incoordination should also be suspected in case of acute cough in children.¹⁶ Bronchoscopy is indicated if the medical history indicates FBA, as it requires referral to specialist care.¹⁷

Acute cough of viral origin should be treated empirically and may not require aggressive investigations unless



ACE inhibitor: Angiotensin-converting enzyme inhibitor; GERD: Gastroesophageal reflux disease; TB: Tuberculosis

Fig. 1: Causes of chronic cough

it is characterized by “red flag signs (Table 2).”

The expert group recommended that, in the primary care setting, the following red flag signs (Table 2) are important and relevant for any decision regarding diagnostic investigations or referral to a specialist:

The American College of Chest Physicians (ACCP), CHEST Expert Cough Panel, 2018 has also recommended these red flag signs. History of tuberculosis infection (self or in a person who is in close contact) is the India-specific addition made by the expert group, especially for the primary care setting. Similarly, expert group suggested that smokers' cough be considered especially in patients >35 years of age as a red flag sign. In addition, the red flag signs in pediatric age group are neonatal onset cough, abnormal voice or crying and cough while feeding (with dysphagia) and vomiting.¹⁸

Subacute cough

For a cough that has begun with an upper respiratory tract infection and has lasted for 3 to 8 weeks, the most common conditions to consider are postinfectious cough, bacterial sinusitis, postnasal drip, and asthma.¹⁹ Most causes overlap with causes of acute and chronic cough. Patients with subacute cough are recommended to be first treated symptomatically.

Postinfectious cough

Postinfectious cough is the most common etiology of subacute cough. Approximately 12% to 48% of adult patients with subacute cough have postinfectious cough.^{19,20} A self-limiting cough that persists after viral or

virus-like infections is termed as postinfectious cough. It lasts for no more than 8 weeks, and the chest radiograph is generally normal. The causative pathogens observed are *Mycoplasma pneumoniae* and *Bordetella pertussis*.²¹ Pathogenesis of postinfectious cough is unclear; however, the attributes are inflammation, epithelial damages of upper and lower airways, increased mucus secretion, and an increased reactivity of airways.

When cough is not associated with an obvious respiratory infection, the evaluation of patients is similar to that for chronic cough.

Chronic cough

Chronic cough could have multiple etiologies. Figure 1 shows the most common diseases observed in clinical practice in the primary care setting.²²

Clinical history and physical examination

Personal history taking is the key to identifying the cause of chronic cough. It should elicit history of smoking, exposure to irritants, and use of cough-inducing medications such as Angiotensin Converting Enzyme Inhibitors (ACEIs), β blockers, and Amiodarone.

In case of such history, reconsidering the medications such as ACEIs, β -blockers, or Amiodarone, smoking cessation, and prevention of exposure to irritants may relieve the cough (elaborated in Figure 2A).²³ Persistence of cough after discontinuation of ACEIs raises the possibility of gastroesophageal reflux disease (GERD), postnasal drip, and asthma.

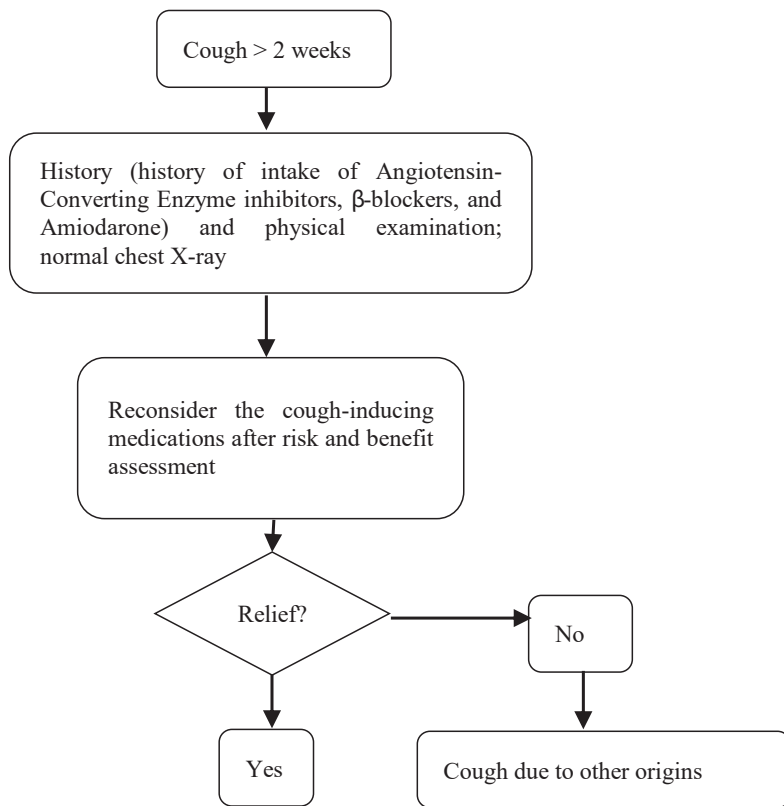
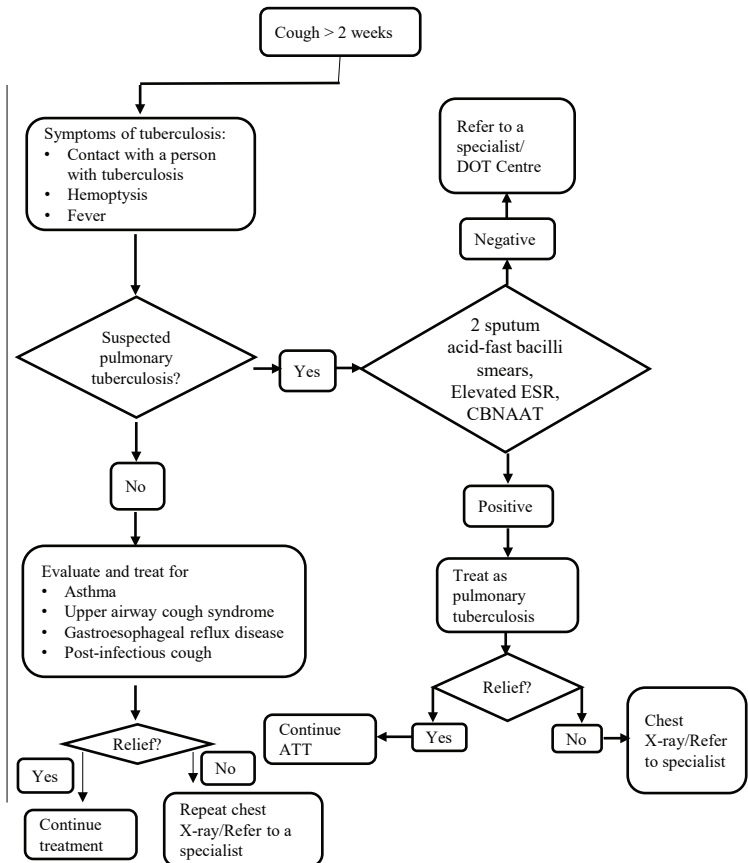


Fig. 2A: Algorithm for diagnosis of drug induced cough



CBNAAT: Cartridge Based Nucleic Acid Amplification Test; ESR: Erythrocyte Sedimentation Rate

Fig. 2B: Algorithm for diagnosis of pulmonary tuberculosis.

Key Messages: Clinical history and physical examination

Symptom-oriented physical examination (including cough sounds) is performed for the following:

- Classification of cough
- Identification of etiological factors
- Evaluation and ruling out of common causes of cough, e.g., gastroesophageal reflux disease, coughvariant asthma
- Provisional diagnosis
- Referral to a Cardiologist, if required

Key Message

- A history of intake of Angiotensin-Converting Enzyme Inhibitors will help diagnose drug-induced cough

Other differential diagnoses of cough

Pulmonary tuberculosis

Pulmonary tuberculosis should be suspected if cough persists beyond 2 weeks after the initiation of initial treatment and presence of suggestive signs and symptoms. The National Strategic Plan emphasizes on early diagnosis and management of patients with tuberculosis who seek care from healthcare providers.²⁴

All presumptive tuberculosis patients should be evaluated for sputum smear examination (spot-early morning or spot-spot). If the first sputum smear is positive and patient is not at risk for drug-resistant tuberculosis, it is categorized as microbiologically confirmed tuberculosis (Figure 2B).²⁴

Presumptive pulmonary tuberculosis refers to a person with any of the symptoms or signs suggestive of tuberculosis:

- Cough > 2 weeks
- Fever > 2 weeks
- Significant weight loss
- Hemoptysis

Key Messages:

- Pulmonary tuberculosis should be suspected in cases of patients having contact with persons with tuberculosis, or presence of hemoptysis or fever
- A positive test with 2 sputum acid-fast bacilli smears and elevated erythrocyte sedimentation rate will help diagnose pulmonary tuberculosis

Asthma

Asthma (25%) and nonasthmatic eosinophilic bronchitis (10%) are among the common causes of chronic cough.²⁵ Asthma was diagnosed among 7.4% of patients presenting with cough in an Indian study conducted with primary care providers.²⁶ Although rarely performed in the Indian primary health care setting,²⁷ spirometry can be employed to establish the diagnosis of asthma.²⁸

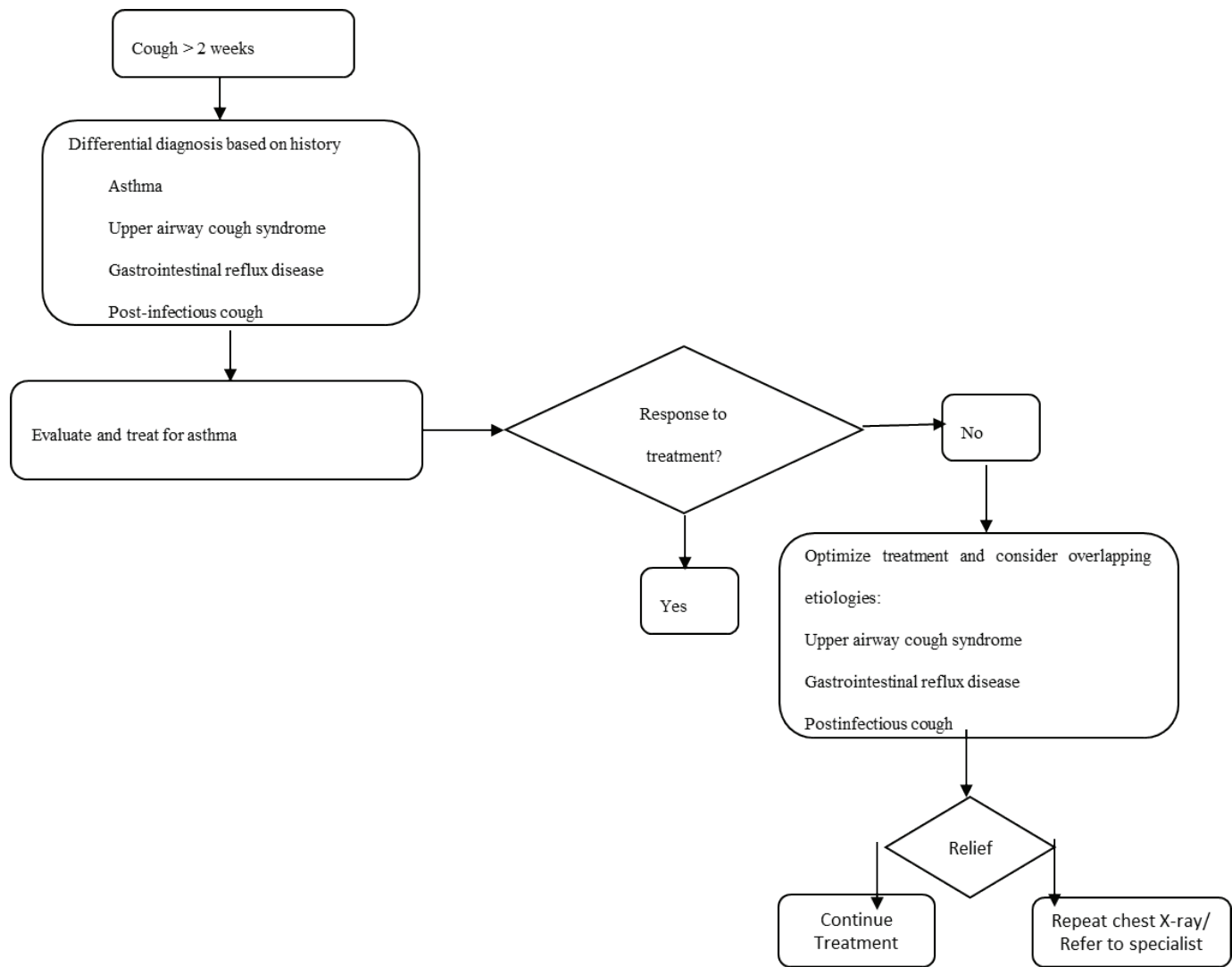


Fig. 2C: Algorithm for diagnosis of cough due to asthma, GERD, UACS, and postinfectious causes

Gastroesophageal reflux disease

GERD, singly or in combination with other conditions, can cause chronic cough.⁸ In patients with normal chest radiographic findings, GERD is the most likely cause of cough. However, accurate diagnosis of GERD-induced chronic cough is a major challenge. In addition, the consensus regarding the causal relationship between reflux and cough and the diagnostic approach to establish GERD etiology is lacking.^{7,29}

Cough due to GERD can be ruled out by administering proton pump inhibitor therapy and monitoring the patient; if the patient improves, the diagnosis is confirmed as GERD. However, it takes approximately 3 months for true GERD-related cough to improve. Chronic cough could be related to GERD if cough occurs at night time and/or postprandially, when

the patient reclines, not in association with activity, and/or without the presence of postnasal drip.³⁰

Key Messages

- Specialized investigations* may be required to rule out gastroesophageal reflux disease
- If empirical treatment for asthma or coughvariant asthma for approximately 4 weeks provides no relief, treatment with proton pump inhibitors for gastrointestinal reflux disease may be added.

* pH testing, pH impedance testing, and/or an upper endoscopy

Upper airway cough syndrome

Upper airway cough syndrome (UACS) is the cause of chronic cough in around 30% of patients,⁷ but disease pathogenesis is unclear.³¹ UACS is difficult to diagnose and treat because it often coexists with other disorders that contribute to chronic cough.³² In most cases, UACS is diagnosed on the basis of its clinical symptoms and the

patient's response to treatment with an H₁ receptor antagonist.³¹

In patients for whom a specific etiology of chronic cough is not apparent, empirical treatment can be initiated for about 15 days if UACS is considered as the etiology.⁷

Key Messages

Signs of upper airway cough syndrome:

History suggestive of allergic rhinitis, nasal examination

- Postnasal drip
- A cobblestone appearance of the posterior part of the pharynx

Environmental factors

Environmental pollutants can cause airways to become hyperactive. Irritants such as sulfur, ozone, nitrous oxides, and indoor air pollution because of biomass combustions can cause chronic cough and asthma as the exposures are persistent.^{33,34} The

Table 3: Approach to cough in primary care setting in India

Cough type	Acute Duration <3 weeks	Subacute Between 3 and 8 weeks	Chronic >8 weeks
Etiology	<p>Adult population</p> <ul style="list-style-type: none"> • Upper respiratory tract infections • Acute bacterial sinusitis • Influenza • Acute infective bronchitis • Pertussis • Exacerbations of chronic obstructive pulmonary disease • Allergic rhinitis • Exposure to environmental irritants • Asthma • Congestive heart failure • Pneumonia aspiration syndrome • Pulmonary embolism <p>Pediatric population</p> <ul style="list-style-type: none"> • Pneumonia • Foreign body aspiration 	<ul style="list-style-type: none"> • Postinfectious cough 	<ul style="list-style-type: none"> • Pulmonary tuberculosis • Asthma • Upper airway cough syndrome • Gastroesophageal reflux disease • Coughvariant asthma • Cough-inducing medications (ACEIs, beta-blockers, Amiodarone) • Psychogenic and idiopathic (or unexplained) cough • Cough of cardiac origin
Diagnostic objective	<ul style="list-style-type: none"> • Rule out serious illnesses • Identification of red flag signs and referral 	<ul style="list-style-type: none"> • Diagnosis of postinfectious cough 	<ul style="list-style-type: none"> • Rule out pulmonary tuberculosis • Identification of asthma gastroesophageal reflux disease, upper airway cough syndrome, coughvariant asthma • Referral for cough of cardiac origin
Investigations	<p>No aggressive investigations</p>	<ul style="list-style-type: none"> • Chest radiography • Routine investigations 	<ul style="list-style-type: none"> • Chest radiography • 2 sputum smears and ESR

ACEI: angiotensin-converting enzyme inhibitor; ESR: erythrocyte sedimentation rate

odds of cough (9.16), wheezing (10.3), and breathlessness (12.6) were very high in a study conducted in Mumbai, India in areas with a high level of suspended particulate matter.³⁵ The risk for chronic cough with sputum production is elevated in mining and refining areas.³⁶ Asbestos exposure can also cause respiratory symptoms such as chronic dry cough and dyspnea. Primary exposure to asbestos in India can be encountered in the form of asbestos mining, asbestos cement industries, asbestos processing units, and exposure to modern electrical as well as mechanical appliances in which asbestos is found. Construction workers, electricians, vehicle mechanics, and other workers are at risk of inhaling asbestos, which can cause lung damage.³⁷ Traffic police who are exposed to air pollutants are also at risk of contracting chronic cough. Effects are more prominent in children and the elderly. Family history of airway hyperactivity could be the deciding factor for cough caused due to pollution. Persons with comorbidities like chronic obstructive pulmonary disease are at more risk of cough due to environmental causes.

Key Messages

- Primary care providers should consider environmental factors as one of the important etiological factors for chronic cough
- Diagnostic investigations are not recommended at primary care settings for suspected gastroesophageal reflux disease, and upper airway cough syndrome

Cough of cardiac origin

Although rare (0.5%), cough is one of the presenting symptoms of cardiac failure with pulmonary congestion. In elderly patients, patients with past history of myocardial infarction, congestive heart failure, and in patients with paroxysmal nocturnal dyspnea, dry irritating cough, a cardiac cause, should be suspected and the patient should be referred to a specialist immediately.^{25,38}

Key Messages

- Cough of cardiac origin should be suspected based on the following:
 - o History of cardiac illness
 - o Presenting symptoms like paroxysmal nocturnal dyspnea
 - o Pulmonary tuberculosis, gastroesophageal reflux disease, upper airway cough syndrome, asthma, and post-infectious cause are ruled out and the patient has a normal repeat chest radiograph.
- Patient should be immediately referred to a cardiologist

Overlapping etiologies

Chronic cough may set in because of multiple causes, which, in turn, may have overlapping symptoms posing challenge in the differential diagnosis. Asthma, UACS, and GERD, alone or in combination, were reported to be responsible for 93.6% of the cases of chronic cough in Brazil, which were named as “pathogenic triad of chronic cough.”³⁹ In addition to the overlapping etiologies, smoking, asthma, and allergic rhinitis were found to be the risk factors for cough among the elderly in a Korean cross-sectional study. Moreover, comorbidities, constipation, and uncontrolled diabetes mellitus had positive associations with cough in the elderly.⁴⁰ The comorbidities may contribute to respiratory symptoms and, consequently, to poor asthma control. In addition, the presence of comorbidities complicates diagnosis. Cardiovascular disease or left ventricular failure can cause symptoms of breathlessness and cough.⁴¹ Hence, thorough history, physical examination, and investigations such as electrocardiogram and imaging play a crucial role in accurate diagnosis. Given the overlapping etiologies, asthma, GERD, and UACS should be managed with empirical treatment. Referral to a specialist is recommended if cough persists.

Figure 2C shows the approach for diagnosing common etiologies of chronic cough such as asthma, GERD, UACS, and postinfectious causes

Key Messages

- Evaluation based on history and differential diagnosis will help diagnose cough due to asthma, gastroesophageal reflux disease, upper airway cough syndrome, or postinfectious cough
- In case of no response to treatment, optimization of treatment should be done considering overlapping etiologies of gastroesophageal reflux disease, upper airway cough syndrome, or postinfectious cough

The overall approach and key recommendations for diagnosis of cough in primary care settings in India are presented in Table 3 and Box 1. A combined algorithm for diagnosis of cough in primary care settings in India is presented in Figure 3.

Summary and Conclusions

Clinical history including the presence of red flag signs and physical examination play a key role in the definitive diagnosis of cough in

the primary care setting. Empirical management and preventing exposure

Box 1: Recommendations for differential diagnosis of cough for the primary care setting

- Cough may be treated empirically and may not require aggressive investigations unless it is characterized by "red flag signs" or persists for > 2 weeks.
- Pulmonary tuberculosis should be excluded if the cough persists for > 2 weeks after the initial treatment with suggestive signs and symptoms.
- Upper airway cough syndrome, gastroesophageal reflux disease, and cough-variant asthma should be diagnosed based on medical history and nasal examination and treated empirically. Referral should be considered for spirometry and other specialized lung function tests.
- Cough of cardiac origin should be suspected based on history of cardiac illness, the use of angiotensin-converting enzyme inhibitors, β -blockers, and amiodarone, and the presence of orthopnea and/or dyspnea, and the patient should be referred to a specialist.
- Environmental factors should be considered as one of the significant causes for chronic cough.
- Any neonatal cough, until an etiology is established, should be suspected for pneumonia.

Referral for bronchoscopy is advised if foreign body aspiration is suspected.

to cough-inducing factors such as medications (ACEIs, β -blockers, and Amiodarone), smoking, and environmental irritants are recommended for cough >2 weeks old for patients with a normal chest radiograph and absence of red flag signs. If cough persists with suggestive symptomatology, pulmonary tuberculosis should be excluded and the diagnosis should be established on the basis of 2 sputum acid-fast bacilli smears and ESR. A chest radiograph can be repeated in case of sputum smear-negative patients. Patients in whom pulmonary tuberculosis is ruled out, asthma, GERD, UACS, or postinfectious cough should be suspected. If feasible, patients should be referred for spirometry to establish diagnosis of asthma. Chest radiographs can be repeated if cough persists after initial diagnostic work-up and treatment. In case the radiological findings persist, the patient should be referred to a specialist, where further investigations such as computed tomography scan, bronchoscopy, peak expiratory flow, or cardiac studies may be performed.

To conclude, this diagnostic

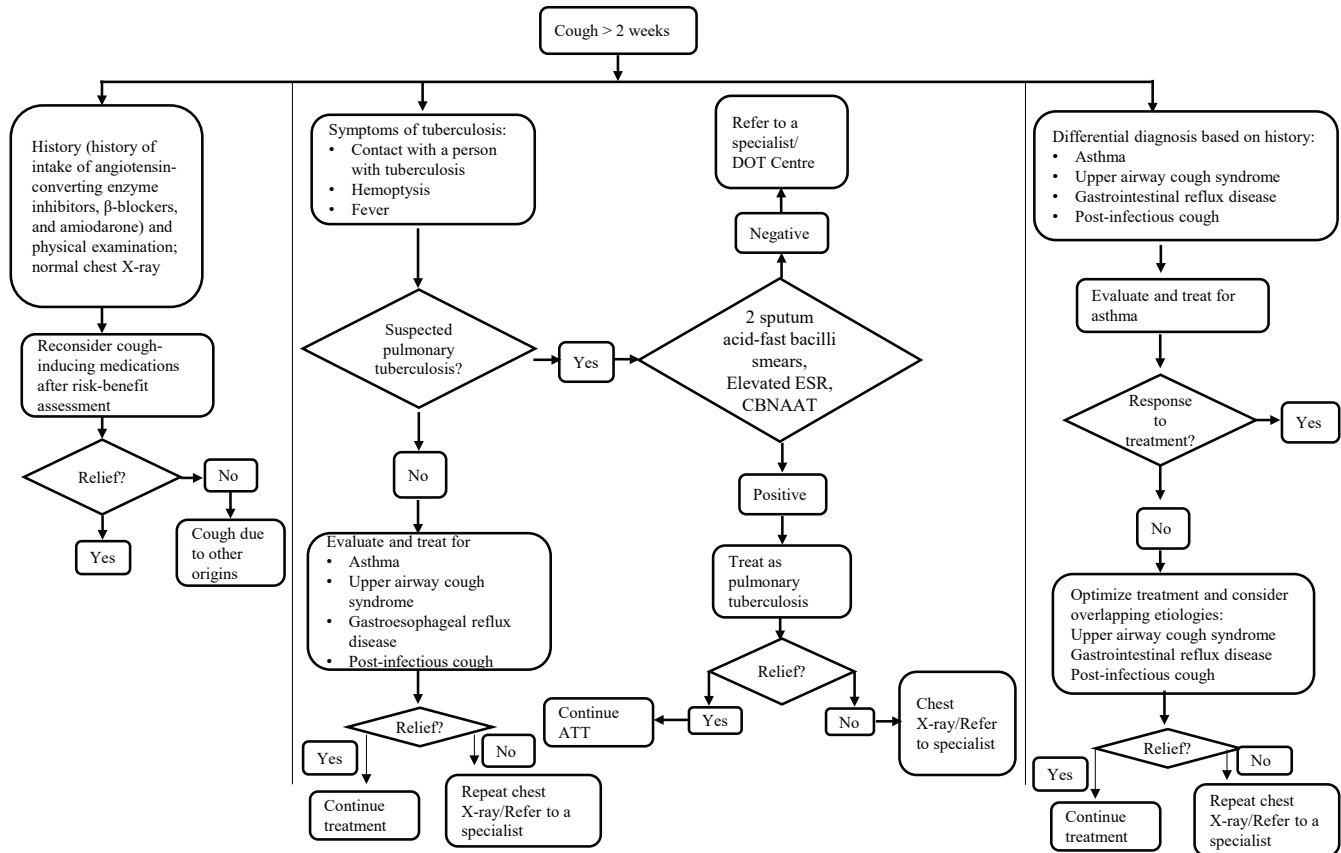
algorithm will facilitate early diagnosis and better management of patients with cough in India at a primary care level. Compliance to this recommended approach will aid in reducing the overall burden of the disease associated with cough at the community level and encourage appropriate referrals to specialty care for definitive treatment. A similar algorithm for the treatment at primary care setting will be a suitable add-on to this symptomatic approach for diagnosis of cough.

Disclosure

The expert meetings were done in association with Abbott Healthcare Pvt. Ltd. The views expressed and discussed in the meetings and stated in this consensus article are the views of the authors and not of Abbott Healthcare Pvt. Ltd.

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CBNAAT: Cartridge Based Nucleic Acid Amplification Test; ESR: Erythrocyte Sedimentation Rate

Fig. 3: Combined algorithm for diagnosis of cough

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