Introduction

Cough is the most common complaint of patients who present to primary care physicians.\(^1\) It has been recently identified as the sixth common reason for hospital outpatient department visits.\(^2\) In most of the cases, cough occurs as part of a brief, self-limiting illness. Cough is a defensive reflex mechanism that clears secretions from the upper airways of the respiratory tract; it is triggered by the stimulation of a complex reflex arc.\(^3\)

Approach

Dry cough is usually classified as three types: acute, subacute or chronic based on duration. Acute cough lasts up to three weeks, subacute cough lasts three to eight weeks and chronic cough lasts longer than eight weeks.\(^4\) Acute cough is most commonly caused by a viral infection of the upper respiratory tract, but it may also be secondary to an acute underlying cardiorespiratory disorder. Other causes include exacerbation of chronic obstructive pulmonary disease or asthma and occupational or environmental exposure to irritants.\(^5\)

Subacute cough often has a postinfectious origin and will typically resolve without treatment. It is usually secondary to asthma or bacterial sinusitis.\(^6\) Bordetella pertussis infection can cause acute, subacute or chronic cough and should be considered in patients with cough lasting longer than two weeks that is accompanied by an inspiratory whooping sound (in young children), coughing paroxysms or post-tussive emesis.\(^5\)

Most episodes of chronic cough in adults are caused by upper airway cough syndrome (UACS, also known as postnasal drip syndrome), asthma or gastroesophageal reflux disease (GERD), alone or in combination (Table I).\(^1-9\) Chronic cough has two or more causes in 18 to 62 percent of patients, and three causes in up to 42 percent of patients.\(^10,11\)
If an immunocompetent adult presents with chronic cough, meticulous history and physical examination is warranted. If history points out any drug such as Angiotensin-converting enzyme inhibitor or irritant exposure then stoppage of exposure is the first step. If stoppage of exposure fails with resolution of cough, or no such fact is found in history then chest radiography should be advised. If chest radiography is normal, then patient should be treated without any further investigations. Normal chest radiography usually excludes bronchiectasis, persistent pneumonia, sarcoidosis and tuberculosis.\textsuperscript{6, 12-15}

If the chest radiography is abnormal and related to cough then further testing based on clinical judgment should include sputum analysis, modified barium esophagography, pulmonary function testing, high resolution computed tomography (HRCT), fibre optic bronchoscopy (FOB), cardiac studies.

But when the initial chest radiography abnormality is not related to cough, the best approach is to evaluate for the three most common conditions: upper airway cough syndrome, asthma, gastroesophageal reflux disease. If cough persists after adequate measures, then further thorough investigations mentioned as above are needed. If even after adequate treatment cough persists, then adequacy of treatment regimens must be reevaluated before considering habitual or psychogenic cough. This is the point where one should consider referral to a pulmonologist.\textsuperscript{14, 15}

### Individual Approach
Management of chronic cough is challenging at times. Patience is required which should be shown by both patients and doctors. Before embarking on treatment, a detailed plan regarding options should be discussed with patients.

### Postnasal Drip Syndrome/Upper Airway Cough Syndrome
In general, adults produce about 20-30 mL of nasal mucus every day, which is either expectorated or

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### Table I
**Etiology Of Chronic Cough In Adults And Children**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Common causes</th>
<th>Less common causes</th>
<th>Rare causes</th>
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<tr>
<td>Adults</td>
<td>Angiotensin-converting enzyme inhibitor use</td>
<td>Bronchiectasis</td>
<td>Arteriovenous malformation</td>
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<td></td>
<td>Asthma</td>
<td>Chronic bronchitis</td>
<td>Aspiration</td>
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<td>Gastroesophageal reflux disease</td>
<td>Irritants (e.g., cigarette smoke)</td>
<td>Bronchiolitis</td>
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<td>Upper airway cough syndrome</td>
<td>Laryngopharyngeal reflux</td>
<td>Bronchogenic carcinoma</td>
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<td>Nonasthmatic eosinophilic bronchitis</td>
<td>Chronic interstitial lung disease</td>
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<td>Postinfectious cough</td>
<td>Irritation of external auditory meatus</td>
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<td>Persistent pneumonia</td>
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<td>Psychogenic cough</td>
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<td>Sarcoidosis</td>
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<td>Tuberculosis</td>
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<td>Children</td>
<td>Asthma</td>
<td>Foreign body (young children)</td>
<td>Aspiration</td>
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<td>Gastroesophageal reflux disease</td>
<td>Pertussis</td>
<td>Congenital abnormalities</td>
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<td></td>
<td>Upper or lower respiratory tract infection</td>
<td>Postinfectious cough</td>
<td>Cystic fibrosis</td>
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<td>Immune deficiencies</td>
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<td>Psychogenic cough</td>
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<td>Tourette syndrome</td>
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<td>Tuberculosis</td>
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swallowed with saliva. Very often, patients complain of a sensation of secretions from the nose or paranasal sinuses into the pharynx, leading to throat clearing, coughing or both.\textsuperscript{16} Postnasal drip syndrome is considered as one of the most common causes of chronic cough with reported incidence between 6\% and 73\% of a studied population.\textsuperscript{17} It is also commonly associated with the common cold (acute cough). Upper airway cough syndrome may result from a number of distinct etiologies, but it commonly arises from rhinitis or rhinosinusitis.\textsuperscript{18}

**Post Infectious Cough**

Post infectious cough is suspected when a patient with a normal chest radiograph complains of persistent cough (>3 weeks) after an upper respiratory tract infection. It occurs in about 11\%-25\% of patients with persistent cough. Increased frequency of post infectious cough (between 25\% and 50\%) has been observed during outbreaks of *Mycoplasma pneumoniae* and *Bordetella pertussis* infections. Common pathogens that cause chronic cough in children include respiratory viruses (particularly respiratory syncytial virus and parainfluenza), *M. pneumoniae*, *Chlamydia pneumoniae* (strain TWAR) and *B. pertussis*. The cough in adult patients with *B. pertussis* infection is spasmodic in nature and occurs more frequently at night. Although cough generally lasts for 4-6 weeks, it can persist longer in some patients.\textsuperscript{11}

Post infectious cough is believed to occur as a result of airway inflammation with or without transient airway hyperresponsiveness.\textsuperscript{11}

**Diagnosis**

Diagnosis of post infectious cough by a careful history, physical examination, as well as serology and sputum culture (if positive) can provide important clues to the diagnosis.\textsuperscript{11,19,20}

When a patient complains only of cough after a respiratory tract infection for at least 3 weeks, but not more than 8 weeks and has a normal chest radiograph, a diagnosis of post infectious cough should be considered. In case of suspected *M. pneumoniae* infection, a high cold agglutinin titer or acute and convalescent specific serologic studies could help confirm the diagnosis.

When a patient has a cough lasting for >2 weeks without any other apparent cause and is associated with post-tussive vomiting and/or an inspiratory whooping sound, the diagnosis of *B. pertussis* infection should be made. The confirmatory diagnosis of *B. pertussis* infection can be made by detection of the organism from nasopharynx secretions.

**Asthma**

Cough is the most commonly reported symptom in patients with chronic asthma, and it is the only manifestation in up to 57\% (i.e., cough-variant asthma). Cough-variant asthma should be considered when per-sistent cough is exacerbated by cold or exercise, or is worse at night. In patients suspected of having cough-variant asthma but who have no demonstrable abnormality on physical examination and spirometry, methacholine inhalation challenge testing may be an option.\textsuperscript{21} But as the diagnosis is established only after the resolution of cough with specific asthma therapy, a trial of inhaled bronchodilators or corticosteroids can be considered.

**Gastroesophageal Reflux Disease (GERD)**

GERD is the third leading cause of chronic cough in adults.\textsuperscript{11} Acid reflux can stimulate the afferent limb of the cough reflex by irritating the upper respiratory tract without aspiration or by irritating the lower respiratory tract through aspiration. GERD can also cause chronic cough by stimulating an esophageal-bronchial cough reflex.\textsuperscript{22} Daily heartburn and regurgitation suggest a GERD-induced chronic cough. These symptoms sometimes may be absent in “silent” GERD.\textsuperscript{23}

A definitive diagnosis of GERD-related cough requires that the cough nearly or completely disappears with treatment. The most sensitive and specific test for acid-induced GERD is 24-hour esophageal pH monitoring. This test may be performed if therapeutic trials are ineffective.\textsuperscript{15}

**Atopic Cough**

This is characterized by chronic nonproductive cough, sputum eosinophilia and lacks bronchial hyperresponsiveness. In contrast to eosinophilic bronchitis, atopic cough has eosinophilia only in the upper airway and the condition usually does not respond to inhaled corticosteroids.\textsuperscript{24}

The Japanese Cough Research Society criteria for recognizing atopic cough include:\textsuperscript{24, 25}

1. Nonproductive cough lasting for >8 weeks without wheezing or dyspnea
2. Presence of one or more findings indicative of
an atopic constitution including a past history
and/or complications of allergic diseases
excluding asthma

3. No bronchial reversibility defined as less than a
10% increase in forced expiratory volume in one
second (FEV₁) after inhalation of 300 µg
salbutamol sulfate

4. Normal bronchial responsiveness

5. Increased cough reflex sensitivity

6. Cough resistant to bronchodilator therapy

7. No abnormal findings indicative of cough etiology
on chest X-ray

8. Normal FEV₁ (≥80% of predicted value) and
normal forced vital capacity (FVC) and FEV₁/
FVC ratio

Psychogenic Or Habitual Cough
A habitual cough is a diagnosis of exclusion.³ Many
patients with this condition do not cough during sleep,
are not awakened by cough and generally do not
cough during enjoyable distractions. Failure to cough
during sleep is not specific for this condition. Common
triggers include changes in ambient temperature;
taking a deep breath; laughing; talking on the
telephone for more than a few minutes; exposure to
cigarette smoke, aerosol sprays or perfumes; or
eating crumbly, dry food.¹⁰

ACE Inhibitors (ACEI)
ACE inhibitors cause a nonproductive cough in 5 to
20 percent of patients, affecting women more often
than men. This effect is not dose related and the cough
may begin one to six months after therapy is
initiated. The cough should spontaneously resolve a
few days to several weeks after the ACE inhibitor is
discontinued; therefore, a four-week trial of withdrawal
is usually sufficient to determine whether the
medication caused the cough.²⁶

Non asthmatic Eosinophilic Bronchitis
Non asthmatic eosinophilic bronchitis has been
defined as a chronic cough in patients with normal
airway hyper responsiveness, sputum eosinophilia
and no symptoms or objective evidence of variable
airflow obstruction. The lack of bronchial hyper
responsiveness in non asthmatic eosinophilic
bronchitis differentiates it from asthma, because
asthma also may result in the presence of reactive
cells in the sputum. Patients with non asthmatic
eosinophilic bronchitis have normal spirometry and
respond to inhaled and systemic corticosteroids.²⁷-²⁹
This condition usually can be ruled out if induced
sputum contains insufficient eosinophils (less than 3
percent) or if corticosteroid therapy does not improve
the cough. The condition may be transient, episodic
or persistent unless treated.³⁰ Rarely, patients may
require long-term treatment with prednisone.

Advanced Considerations In Chronic Cough
Aetiology
The growing numbers of patients with unexplained
cough, who are resistant to treatment has put forward
many questions.³¹ This has also led to significant
progress in the field of cough during the past decade
and identified a number of conditions associated with
unexplained chronic cough.

Non-Acid Reflux And Chronic Cough
The importance of non-acid reflux events in chronic
cough has been highlighted in several studies.³²-³⁶
These studies have reported that a subgroup of
patients with chronic cough have failed to respond to
intense acid suppression treatment and improved
chronic cough after antireflux surgery, suggesting
the involvement of a non-acidic gastric component in
the refluxate.³⁷,³⁸

Chronic cough due to non-acid reflux causes a
hypersensitive cough reflex, possibly by stimulation
of the neurogenic airway inflammation and mast cell
activation.³⁹

Impedance-pH monitoring is a powerful tool that helps
in detecting acid and non-acid reflux events in patients
on PPI therapy. The current treatment approaches
are limited; however, therapeutic options for non-acid
GERD are largely dietary modifications, prokinetic
drug therapy and antireflux surgery in selected
patients.⁴⁰

Laryngopharyngeal Reflux And Cough
The concept of laryngopharyngeal reflux (LPR)
causing upper airway symptoms has gained
increased attention in recent years by
otolaryngologists despite failure to gain widespread
recognition among pulmonologists.⁴¹
Laryngopharyngeal reflux does not have any specific
pathognomonic symptoms, signs or endoscopic
findings. Generally, the diagnosis of LPR is based
on the laryngoscopic findings of erythema, edema and thickening of the posterior pharynx. Limited evidence supports the use of PPIs in patients with cough due to LPR.

**Sleep Apnea And Chronic Cough**
Several recent studies have suggested a possible association between chronic cough and obstructive apnea with a reported prevalence of 33 and 44%, in two different studies. Two proposed mechanisms of cough in OSA are, an increase in trans-diaphragmatic pressure during apnea episodes, which causes lower esophageal sphincter insufficiency leading to GERD. Another potential mechanism is cough that results from upper airway inflammation secondary to epithelial injury, associated with snoring and apnea. A trial of continuous positive airway pressure therapy is reported to reduce or resolve the cough in patients with OSA.

**Vocal Cord Dysfunction And Chronic Cough**
Patients with vocal cord dysfunction commonly experience stridor and dysphonia, owing to episodic, uncontrollable narrowing of the cords during inspiration. These patients also occasionally experience dyspnoea and cough. The diagnosis of vocal cord dysfunction can be made with the use of direct laryngoscopy and flattening of the inspiratory flow-volume loop on spirometry. In acute cases, continuous positive airway pressure can be used to treat vocal cord dysfunction, while in longer-term voice therapy, psychological counseling along with reassurance, irritant avoidance and supportive care are useful. Evidences suggest that a number of patients with vocal cord dysfunction are commonly misdiagnosed with asthma and hence, receive overtreatment with inhaled corticosteroids.

**Chronic Cough In Children**
In children, a cough lasting longer than four weeks is considered chronic. The most common causes of chronic cough in children are asthma, respiratory tract infections and GERD. The differential diagnosis for chronic isolated cough without associated wheezing in an otherwise healthy child includes recurrent viral bronchitis, postinfectious cough, pertussis-like illness, cough-variant asthma, UACS, psychogenic cough and GERD. Signs suggestive of serious underlying lung disease include neonatal onset of cough, chronic moist or purulent cough, cough starting with and persisting after a choking episode, cough occurring during or after feedings, or associated failure to thrive.

Children with chronic cough should undergo chest radiography and spirometry at minimum. Foreign body aspiration should be considered in young children. Congenital conditions, cystic fibrosis and immune disorders are possible diagnoses in children with chronic cough and recurrent infections. Congenital abnormalities, although rare, can include vascular rings, tracheoesophageal fistulas and primary ciliary dyskinesia.

**Treatment Of Dry Cough**
Treatment of dry cough should be individualized. After careful evaluation, treatment should always be directed towards the underlying cause. Recent guidelines published by the American College of Chest Physicians (ACCP) recommend the use of a first-generation antihistamine in combination with a decongestant for the treatment of chronic cough due to upper airway cough syndrome. Non pharmacological approach such as nasal breathing exercises may also be useful in patients with upper airway cough syndrome.

In patients with post infectious cough, if cough persists despite use of inhaled ipratropium, then use of inhaled corticosteroids can be considered. Use of macrolides is recommended in patients with *B. pertussis* or *M. pneumoniae* infection. ACCP also recommends use of antitussive agents such as codeine and dextromethorphan in the management of post infectious cough when the cough adversely affects the patient’s quality-of-life despite all other measures. Codeine, in addition to antitussive effect, possesses analgesic and minor sedative effects, which can be especially beneficial in relieving painful cough.

Current recommendation for non surgical management of GERD are as follows: Lifestyle modification: Raising head end of the bed, Avoiding meals within 3 hours of bedtime and Weight loss. Medical management: Antacids, Gaviscon, Proton pump inhibitors, *H₂* receptor antagonists, Prokinetics, Baclofen and Carafate. In "Atopic cough", complete relief of cough has been documented after treatment with histamine *H₁*.
For managing eosinophilic bronchitis, inhaled budesonide, 400µg twice-daily for a period of 1-2 weeks is recommended; equivalent doses of other inhaled corticosteroids are also effective. Avoidance of aggravants is advised if the condition is found to be associated with an environmental irritant such as acrylic resin. In general, a trial of antitussive therapy is generally indicated for patients with chronic dry cough when the cause of an increased cough reflex is not known.

**Conclusion**

In general, a trial of antitussive therapy is generally indicated for patients with chronic dry cough when the cause of an increased cough reflex is not known or when the treatment against potential aggravating factors remains unsatisfactory. Common antitussives available in most countries are combinations of dextromethorphan or codeine with antihistamines, expectorants, decongestants and/or antipyretics. Codeine has analgesic and sedative effects in addition to its antitussive property, which may be useful in relieving painful cough. But cough management can become difficult in countries where codeine is not available like Bangladesh due to risk of abuse.

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**Conflict Of Interest:** The authors of this paper have declared that there is no conflict of interest to any of the authors.

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