Cough remains one of the most common complaints that motivate patients to seek medical attention.

Assessment of cough

Cough is caused by stimulation of irritant receptors in the central airways and/or stretch receptors in the distal airways or the lung interstitium. It is a normal protective mechanism, which may be lost with local or general anaesthesia, other causes of decreased level of consciousness, or neuromuscular problems (especially bulbar). Cough is abnormal if it is persistent, painful or productive.

History and examination

If a patient presents with a cough, the following features should be clarified on history:

- duration – days, weeks, months or years
- course – constant, worsening, intermittent, diurnal variation
- triggers – allergens, irritants, swallowing, position
- dry or productive (nature and volume of sputum) – clear/white/grey (mucoid), yellow/green (purulent) or bloody (haemoptysis)
- other – shortness of breath, chest pain, wheeze/tightness, loss of weight, fever, sweating.

On examination, one should listen to the type of cough (Table I) and look for signs, particularly the following:

- general – distress, fever, sweating, loss of weight, cyanosis, clubbing
- respiratory – respiratory rate, hyperinflation, dullness, crackles, wheeze, bronchial breathing, pleural rub.

Investigations will depend on the most likely cause determined clinically (Table II).

Chronic cough

Chronic cough as the only symptom can account for up to 10% of all referrals to general respiratory clinics and occurs in 3-40% of the general population. Unsurprisingly, cigarette smoking has a dose-related influence on the prevalence of productive cough. Smokers who cough usually feel that their cough is due to smoking and therefore rarely seek medical advice specifically for it. Most patients referred to specialists for cough are women, possibly because they smoke less and because of an intrinsically heightened cough response.

By definition, chronic persistent cough lasts for >8 weeks in a non-smoking, immunocompetent patient who has a normal chest X-ray (CXR), is not receiving therapy with an angiotensin-converting enzyme (ACE) inhibitor, and has not been exposed to an environmental irritant.

It is advised that the following two common causes should be considered first:

Table I. Common causes of cough

<table>
<thead>
<tr>
<th>Common causes/types of cough</th>
<th>Description and associated features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic bronchitis ('smokers' cough')</td>
<td>Cough productive of sputum for most days for at least 3 months of a year for at least 2 years, usually mucoid, but may be purulent during infective exacerbations</td>
</tr>
<tr>
<td>Acute bronchitis/tracheitis</td>
<td>Dry or purulent, with central burning chest pain; short duration</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Purulent or rusty, often with associated pleuritic chest pain, shortness of breath and fever; short duration</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Usually large volumes of purulent sputum, sometimes offensive, often associated with clubbing and coarse crackles transmitted to the mouth; long duration</td>
</tr>
<tr>
<td>Lung abscess</td>
<td>Usually large volumes of purulent sputum, sometimes offensive, often associated with fever, clubbing and aphonic breathing; usually long duration</td>
</tr>
<tr>
<td>Tuberculosis (TB)</td>
<td>Dry, purulent or bloody, often associated with fever, night sweats, loss of weight (LOW); long duration</td>
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<tr>
<td>Lung cancer</td>
<td>Dry, purulent or bloody, occasionally 'bovine' (vocal cord palsy) or 'brassy' (central airway compression), often associated with LOW</td>
</tr>
<tr>
<td>Interstitial lung disease (ILD)</td>
<td>Usually dry, often associated with fine crackles; long duration</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>Dry or productive (pink froth or blood), often associated with orthopnoea and paroxysmal nocturnal dyspnoea</td>
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</tbody>
</table>
An ACE-inhibitor cough is associated with the use of ACE inhibitors and occurs in up to 15% of patients. It has a very variable onset and course. After discontinuing ACE inhibitors, it may take several months in the case of some individuals for the cough to settle. Alternative agents such as angiotensin II antagonists may be used.

Post-infectious cough sometimes occurs after a relatively minor respiratory tract infection, and is especially prolonged after Bordetella pertussis and some viral infections. Post-infectious coughs usually last <3 weeks but can occasionally persist for 8 - 12 weeks.

If these causes have been excluded, the three most common causes of cough are:
- postnasal drip (41 - 58%)
- asthma (24 - 59%)
- gastro-oesophageal reflux disease (GORD) (21 - 41%).

### Diagnostic strategies for chronic cough

There is no consensus as to the best diagnostic strategy for chronic cough. Many protocols combine empiric trials of treatment with laboratory investigations, as the former can substitute for specific diagnostic testing in some circumstances. Systematic evaluation remains the most effective approach. Utilising a diagnostic protocol allows the cause of the cough to be identified in 88 - 100% of patients. Several studies have supported the utility of the diagnostic protocol in patients with chronic persistent cough, not only in the academic tertiary-care setting but also in the community. Current diagnostic protocols for chronic cough have been based on the work of Irwin and colleagues first reported over 20 years ago. Approximately 20 - 40% of chronic cough is due to more than one cause, often making careful, persistent follow-up and further evaluation necessary. Despite comprehensive evaluation and treatment, up to 20% of patients remain symptomatic.

<table>
<thead>
<tr>
<th>Clinical investigations</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray (CXR)</td>
<td>All chronic cough or if suspect pneumonia/cancer</td>
</tr>
<tr>
<td>Sputum M, C and S or acid-fast bacilli staining and TB culture</td>
<td>If purulent sputum produced</td>
</tr>
<tr>
<td>Pulmonary function tests (pre- and post-bronchodilator spirometry, serial peak flows)</td>
<td>If suspect asthma or chronic obstructive pulmonary disease (COPD)</td>
</tr>
<tr>
<td>Bronchial challenge tests (metacholine, exercise)</td>
<td>If suspect asthma</td>
</tr>
<tr>
<td>Gastrointestinal tests (24-h oesophageal pH)</td>
<td>If suspect GORD</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>If suspect cancer, foreign body or sputum -ve TB</td>
</tr>
<tr>
<td>High-resolution computed tomography (HRCT)</td>
<td>If suspect bronchiectasis or ILD</td>
</tr>
<tr>
<td>Electrocardiogram (ECG) and echocardiography</td>
<td>If suspect cardiac disease</td>
</tr>
</tbody>
</table>

### History and examination

A careful history and thorough physical examination are critical in the evaluation of a patient with chronic cough.

Postnasal drip usually causes symptoms such as the sensation of ‘something dripping into the throat’, frequent throat clearing, nasal congestion, itch or nasal running. Asthma might be suggested if the cough is present or worse at night or in the early morning only. It is usually associated with dyspnoea and wheeze or tight chest but these may be absent in cough-variant asthma.

GORD is more likely if there are symptoms such as heartburn, acid regurgitation, a bitter taste in the mouth, dysphagia, dysphonia or globus (oesophageal spasm). Classically, there is a relation between coughing and eating but another helpful clue is a cough that starts in the morning after rising or sitting (because the upright position is accompanied by relaxation of the lower oesophageal sphincter).

However, the characteristics and associated symptoms of the cough can be misleading as symptoms of postnasal drip may be due to coincidental rhinitis, in a patient with asthma, and the absence of dyspepsia does not rule out GORD. Examination is often completely normal, but seeing nasal blockage or hearing wheezes or crackles on chest auscultation may influence the subsequent investigation or treatment choice.

### Clinical investigations

A few baseline investigations should be performed routinely and there are a range of more complex tests often limited by availability, time and expense.

#### Chest X-ray (CXR)

Most patients referred to specialist cough clinics have a normal CXR. However, review of a recent radiograph is critical, as any significant abnormality will alter the investigation algorithm.

### Pulmonary function tests (PFTs)

When available, these should be performed with bronchodilator reversibility testing in all patients with chronic cough. If they are not available, serial peak expiratory flow (PEF) measurement twice daily over 2 weeks may diagnose airflow obstruction with diurnal variability.

### Bronchial challenge testing

Bronchial challenge testing (usually done with methacholine) can provide very useful clinical information regarding patients with chronic cough. Bronchial hyper-reactivity in a patient with cough and normal spirometric measurements may be due to cough-variant asthma. However, a definitive diagnosis cannot be made until the cough responds to specific asthma treatment. Cough may persist for many weeks after an acute viral upper respiratory tract infection, and a positive challenge test in this circumstance may be diagnosed misleading because transient airway hyper-reactivity may develop. A negative bronchial challenge off therapy effectively excludes asthma as the diagnosis but does not eliminate a cough that may respond to steroid treatment.

### Sinus imaging

In a prospective study of patients with chronic cough, routine CT sinus imaging had no better predictive value than ear, nose and throat examination in proving that the cough was due to upper airway disease. In patients diagnosed with cough caused by sinusitis only 29% had abnormalities of the plain sinus radiographs. CT imaging of the sinuses revealed abnormalities in two-thirds of children with cough, but there was no proof that these abnormalities caused the cough.

**HRCT should not be an early routine investigation in chronic cough, but it may show parenchymal lung disease.**
Cough

In asthma, empiric therapy with inhaled bronchodilators and steroids may be attempted. However, the treatment may take several weeks to be effective.

Gastrointestinal investigations

GORD-related cough can be diagnosed easily if the patient has oesophageal manifestations of GORD, but prominent oesophageal GORD symptoms occur in only 6 - 10% of chronic cough patients. In these patients GORD should be treated aggressively. However, it may be clinically silent in 50 - 75% of cough patients. Barium swallow has a low sensitivity and specificity and is of little value in the evaluation of chronic cough. While not freely available, 24-hour oesophageal pH monitoring is currently the best single test to help characterise any link between GORD and cough. A cost-effective alternative may be an empiric trial of medical anti-reflux therapy (see below). It should be remembered that up to one-third of reflux episodes in GORD patients are not acid related, which may be diagnosed with intra-oesophageal impedance measurement.

Chest high-resolution computed tomography (HRCT)

HRCT should not be an early routine investigation in chronic cough, but it may show parenchymal lung disease (e.g. interstitial lung disease or bronchiectasis) or endobronchial lesions not seen on the CXR. In a prospective study of patients with chronic cough, all of whom had an HRCT in their diagnostic protocol, bronchiectasis was identified in nearly 25%, but this might also have been suggested by history, examination and/or CXR. If there are suggestive clinical findings or CXR abnormalities, HRCT has a diagnostic yield of 17%.

Bronchoscopy

Bronchoscopy has a very low yield (5%) in the routine evaluation of chronic cough because of the low number of smokers and CXR abnormalities in this group of patients. In a review of patients referred with refractory cough, bronchoscopic diagnoses were found in one-quarter of cases and included aspirated foreign bodies, tumours, and other very rare conditions (broncholithiasis, tracheobronchopathia, laryngeal dyskinesia). In certain indicated cases, fiberoptic bronchoscopy may be necessary to perform bronchial lavage/washings/brushings or endobronchial or transbronchial lung biopsies.

Empiric treatment

Empiric treatment can be used as a ‘diagnostic trial’ in patients with cough. Patients reporting symptoms suggestive of postnasal drip syndrome or GORD may first be offered a trial of empiric treatment.

In postnasal drip syndrome, empiric treatment with older (first-generation) antihistamines together with nasal decongestants and nasal steroids may be tried. As mentioned above, in patients with GORD a proton-pump inhibitor (i.e. omeprazole 40 mg before breakfast daily or twice daily) for 8 weeks can produce an effective and sustained resolution of symptoms. It may take up to 12 weeks to become effective. Therapy should also include lifestyle measures, such as weight reduction, elevation of head of bed, not smoking, small meals, and a high-protein, low-fat anti-reflux diet with avoidance of caffeine and chocolate. A prokinetic agent may be added to the regimen if dysphagia is present or if initial therapy with a proton-pump inhibitor is less successful than expected. Surgical fundoplication may be tried in those with proven significant GORD and poor response to medical therapy.

In asthma, empiric therapy with inhaled bronchodilators and steroids may be attempted. However, the treatment may take several weeks to be effective. The term cough-variant asthma to describe asthma associated with cough was originally used to describe patients with chronic cough, bronchial hyper-responsiveness, and a response to anti-asthma medication but without wheezing and airflow obstruction. Subsequently, the term cough-predominant asthma was suggested because cough is not a separate entity but part of the spectrum of asthma together with dyspnoea and airflow obstruction. All symptoms of the cough/asthma syndrome usually improve with inhaled corticosteroids. The early symptomatic response to inhaled corticosteroids that often occurs in ‘classic asthma’ may be delayed in chronic asthmatic cough, similar to the slow improvement in airway hyper-responsiveness seen with inhaled corticosteroids. In patients who remain symptomatic on inhaled corticosteroids and bronchodilators a course of oral steroids or a leukotriene-receptor antagonist may be effective.

Other

Several recent series suggest that 7 - 46% of patients have idiopathic cough despite thorough investigation. The mechanism is unclear but these patients are usually middle-aged women and their cough often starts around menopause.

Psychogenic cough should only be considered after exclusion of a physical cause. These patients classically complain of a persistent tickling/irritating feeling in the throat or chest, often leading to coughing paroxysms. These are often triggered by temperature change, cigarette smoke, strong smells, eating crumbly food, deep breaths, laughing or talking on the phone.

References

In a nutshell

- Cough is a normal protective mechanism.
- Cough is abnormal if it is persistent, painful or productive.
- Chronic cough as the only symptom can account for up to 10% of all referrals to general respiratory clinics and occurs in 3 - 40% of the general population.
- Cigarette smoking has a dose-related influence on the prevalence of productive cough.
- The two most common causes of chronic cough, apart from smoking, are ACE inhibitor-associated cough and post-infectious cough.
- The three next most common causes are postnasal drip, asthma and gastro-oesophageal reflux disease.
- There is no consensus as to the best diagnostic strategy for chronic cough.
- Systematic evaluation remains the most effective approach to chronic cough. Utilising a diagnostic protocol allows the cause of cough to be identified in 88 - 100% of patients.
- A careful history and thorough physical examination are critical in the evaluation of a patient with chronic cough.
- A few baseline investigations should be performed routinely and there are a range of more complex tests often limited by availability, time and expense.
- Many protocols combine empiric trials of treatment with laboratory investigations, as the former can substitute for specific diagnostic testing in some circumstances.

Single suture

Monthly shot to stay on the wagon

Alcoholics generally struggle to keep off the hard stuff and temptation over holiday periods can sometimes just be too much, resulting in relapses. Now they may be able to take a monthly injection that keeps them sober.

For people battling alcoholism, holidays and family events are particularly difficult. Some people take pills containing naltrexone, a substance that reduces the desire to drink by blocking receptors in the brain that are responsible for the high that alcohol can bring. But during holiday periods, some alcoholics stop taking the tablets. To prevent people having to make the daily decision to take a tablet, a slow-release formulation of naltrexone was developed in the USA, which is injected into muscle once a month. Sandra Lapham at the Behavioural Health Research Center, Albuquerque, New Mexico looked at 28 patients who received full-dose naltrexone shots compared with 28 who were given placebos.

The naltrexone shots reduced the frequency of drinking days, the number of drinks and the percentage of days classed as heavy drinking sessions – 5 or more drinks a day for men and 4 for women. The drug was just as effective during the holiday season as it was for the rest of the year. However, the injection must be given with care as it can cause abscesses if the drug is deposited into fatty tissue.

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