Cough is a common presenting symptom in primary care. It has a prevalence of 30% in the general European population, and in a US National Medical Case Survey in 1991 cough was the commonest presenting complaint. Between 10% and 38% of all new patient referrals to UK hospital chest clinics are for chronic cough. This article covers the physiological nature of cough and its role as an essential protective reflex, focuses on the differential diagnosis of cough in general practice in both adults and children, and discusses the use of treatment as a diagnostic tool.

All people cough at some point - either as a result of the cough reflex (when foreign bodies or smoke fumes enter the airway) or as a result of a straightforward viral upper or lower respiratory tract infection. However, what usually brings the patient to see the doctor or nurse is that they, or a family member, feel that the cough is ‘abnormal’ in some way. The cough may be troublesome in a number of ways - it could have persisted for an abnormal length of time and is affecting quality of life, it may be abnormally forceful, accompanied by the production of phlegm or mucus, or there may be other worrying features such as wheeze, shortness of breath, chest pain, or haemoptysis (coughing up blood).

PHYSIOLOGICAL COUGH
Cough is a powerful protective reflex and is the first line of defence if foreign bodies appear in the airway. In combination with the cilia lining the airway which sweep debris and secretions proximally, cough assists in keeping the airways clean by expelling mucus and debris which has been brought to the top of the airway by the ‘mucociliary staircase’. Cough enhances airway clearance in both healthy and diseased lungs, and the efficiency of the cilia and expulsion of debris is enhanced by cough, exercise and hyperventilation – this is the reason we frequently cough up mucus during and after exercise.

“Cough is a powerful protective reflex and is the first line of defence if foreign bodies appear in the airway”
Diagnosis

The ability to cough is important, and the consequences of not being able to cough can be serious; inability to cough can result in atelectasis (lung collapse), recurrent infection, aspiration lung disease and secondary pneumonia, bronchiectasis, and bronchiolitis obliterans (where inflamed bronchioles partially block the airways).

THE COUGH REFLEX

All reflexes require two main components: sensory receptors which transmit information via afferent sensory nerves to either the spinal cord or a nucleus in the brain (depending on which particular reflex it is); and efferent nerves which transmit a message to the effector muscles which then carry out the motor component of the reflex. For the cough reflex, there is abundant sensory innervation to receptors in the larynx, pharynx, trachea, bronchi and lung tissue provided by the vagus nerve. Airway irritation – either ‘mechanical’ stimulation by a foreign body or ‘chemical’ stimulation by smoke particles – triggers off the appropriate mechanical or chemical receptors and leads to impulses being transmitted along the vagus to the respiratory area of the brainstem (Figure 1). From the brainstem, the efferent motor nerves then initiate muscle contraction in the appropriate effector cough muscles – the muscles of the antero-lateral abdominal wall, the intercostals, the triangularis sterni, and the diaphragm. At the same time, there is reflex contraction of the external sphincters so that one can cough without there being urinary or faecal incontinence on every occasion.

Of course, there is some voluntary control over the cough reflex. We can make ourselves cough whenever we want. But the important thing is that the cough reflex is inherently an involuntary protective mechanism for the airways.

PATHOLOGICAL COUGH

When a patient presents with a cough they may well mention significant problems occurring as a result. These can include sleep loss (due to nocturnal cough which keeps the patient awake), exhaustion and irritability, urinary stress incontinence, cough syncope, social disability (“I can’t go to the concert, because I’ll be coughing all the way through the quiet bits…” ) and in the literature there are reports of rib fractures, pneumothorax, pneumomediastinum (air leaking into the chest cavity), and subcutaneous emphysema occurring solely as a result of prolonged severe coughing.

Definitions of pathological cough

Pathological cough can be acute (persisting for less than three or four weeks) or chronic (longer than three or four weeks), and productive (producing more than 30 ml of sputum a day) or non-productive (less than 30 ml of sputum a day).

Generally, in the absence of other worrying symptoms such as haemoptysis, shortness of breath, or wheeze, it is a chronic cough that patients find worrying. In one survey, the reasons for presenting with a chronic cough were:

- concern that “something’s wrong” (98%)
- exhaustion (57%)
- feeling self-conscious (55%)
- insomnia (45%)
- musculoskeletal pain (44%)
- fear of cancer (33%)
- fear of infection such as tuberculosis (TB) or AIDS (28%).

ACUTE COUGH

The most likely cause for an acute cough is a viral upper or lower respiratory tract infection. However, the history is important. Foreign body aspiration needs to be considered in the differential diagnosis, and if there is any suggestion that this may be the case, then the patient should be referred to hospital. Similarly, an acute allergic reaction or anaphylaxis presenting as cough needs to be managed appropriately.

There are several symptoms which, if they present at the same time as an acute cough, warrant an urgent chest X-ray (Box 1).

Box 1: Symptoms associated with acute cough which require an urgent chest X-ray

- Haemoptysis
- Breathlessness
- Persistent unremitting fever
- Chest pain
- Weight loss

CHRONIC COUGH

There are now British, European, and American guidelines for the management of chronic cough. In addition, the International Primary Care Respiratory Group (IPCRG) respiratory disease diagnosis guideline contains flow diagrams and questionnaires which can be used to assist the diagnostic process.
Diagnosis

COPD is a disease state characterised by progressive airflow limitation that is not fully reversible and which is associated with an abnormal inflammatory response of the lung. Persistent mucus production (the ‘hypersecretory form’ of COPD) used to be termed ‘chronic bronchitis’, and was defined as a daily cough with sputum production for three months a year for at least two consecutive years. The diagnosis of COPD needs to be considered in any patient presenting with cough, sputum production and dyspnoea, particularly if there is a history of risk factor exposure such as smoking. In older children, asthma exacerbations may occur secondary to recurrent bacterial infection and can present as recurrent episodes of productive cough. These children may need prophylactic antibiotics in order to manage their asthma.

### Chronic productive cough - adults

In adults, the most likely diagnosis is chronic obstructive pulmonary disease (COPD). However, bronchiectasis, congestive cardiac failure, TB, bronchiolitis, chronic pneumonia, and lung tumours need to be considered in the differential diagnosis (see Box 2).

#### Box 2: Most common differential diagnoses for chronic productive cough in adults

- COPD
- Bronchiectasis
- Congestive cardiac failure
- TB
- Bronchiolitis
- Chronic pneumonia
- Lung tumours

**COPD**

Chronic productive cough with purulent sputum, often with proven bacterial isolates on sputum analysis, and sometimes with coarse crackles in the chest. The pathophysiology is one of airway and lung parenchymal destruction, leaving open areas in the lung which accumulate mucus and debris which can then provide a focus for persistent infection. The definitive diagnosis is made on CT scanning. Therefore, any patient presenting with recurrent purulent chest infections needs to be considered for hospital referral.

**TB**

is becoming increasingly common, and for patients in high-risk groups the diagnosis must always be considered. A spumum sample, chest X-ray, and onward referral is obligatory if the diagnosis is confirmed or considered likely.

**Lung cancer**

Chronic cough in a middle-aged or elderly smoker, may be the first presentation of lung cancer. A productive cough may be due to persisting infection distal to partial airway obstruction caused by a bronchial carcinoma; investigation with a chest X-ray and subsequent referral if the cough persists, is essential.

### Chronic productive cough - children

The golden rule here is that a chronic productive cough in children – certainly lasting for longer than six weeks – is abnormal and always warrants referral preferably to a paediatric respiratory specialist. Particularly in the under-5s, the differential diagnosis list includes rhinosinusitis, bronchial or tracheal compression by lymphadenopathy (disease of lymph nodes), foreign body, cystic fibrosis, primary ciliary dyskinesia and systemic immunodeficiency (see Box 3).

**Box 3: Diseases which present as recurrent cough and/or wheeze in children (particularly the under-5s)**

- Upper airway disease (adenotonsillar hypertrophy, rhinosinusitis)
- Congenital structural bronchial disease
- Bronchial/facial compression - enlarged cardiac chamber, lymphadenopathy (TB/lymphoma)
- Foreign body
- Tumour
- Laryngeal cleft (opening between larynx and oesophagus), tracheo-oesophageal fistula
- Pulmonary suppuration; cystic fibrosis, primary ciliary dyskinesia, any systemic immunodeficiency
- Bronchopulmonary dysplasia
- Congenital or acquired tracheomalacia (collapse of tracheal wall)

In older children, asthma exacerbations may occur secondary to recurrent bacterial infection and can present as recurrent episodes of productive cough. These children may need prophylactic antibiotics in order to manage their asthma.

### Chronic non-productive cough - adults and children

The commonest causes of chronic non-productive cough are cough-variant asthma, gastro-oesophageal reflux, postnasal drip syndrome, post-viral cough, and idiopathic causes. Various drugs can cause cough - these include ACE inhibitors, beta-blockers, and non-steroidal anti-inflammatory drugs - and therefore a careful drug history must always be taken from any patient presenting with chronic non-productive cough. The diagnosis may well be suggested by the history and/or the examination findings. For example, if the cough is always worse after exercise and at night, and there is peak expiratory flow (PEF) variability, then asthma is a likely cause. If there is recurrent sneezing, rhinorrhea, and nasal congestion, worse during April and May, then the likely diagnosis is rhinitis with secondary postnasal drip.

The differential diagnosis in children is similar, except that one should be reluctant to diagnose asthma in the under-5s solely on the basis of a cough in the absence of any wheeze.

### TREATMENT AS A DIAGNOSTIC TOOL

The diagnosis of chronic non-productive cough is often not obvious despite some clues in the history. After excluding drugs and current upper or lower respiratory tract infections as a cause, and in the presence of a normal chest X-ray and normal spirometry, how does one then elucidate the diagnosis? An excellent paper by McGarvey et al. published in 1998 explored this question and used different treatment approaches, based on histories suggestive of asthma (inhaled corticosteroids, β2 agonists), postnasal drip syndrome (decongestants, antibiotics, inhaled corticosteroids) or GORD (dietary and postural advice, proton pump inhibitor), as a means of diagnosis.
The researchers found a cause for the cough in 35 out of the 43 patients (82%) who had persistent non-productive cough for over 5 years. In effect, these patients were cured following a successful trial of treatment. Some of the patients had more than one pathology contributing to their cough; postnasal drip syndrome was the commonest single cause in nine patients and was one of two causes in a further six patients, GORD was the cause in eight patients, and cough-variant asthma was the cause in 10 patients. Interestingly, six patients in the asthma group later went on to develop ‘typical’ asthma symptoms of wheeze and dyspnoea.

There are a number of important messages from this study which are relevant to us all in primary care:
1. When using treatment as a diagnostic tool, fairly high doses need to be used. Patients need to know that moderate to high doses of treatment have to be used to make a difference, and that treatment will stop after a period of time.
2. Think laterally. There may be more than one diagnosis contributing to the persistent cough.
3. Identifying a cause for the patient’s cough, and directing treatment at that cause, is the best approach. In particular, pay attention to the upper airway.

In children too – particularly pre-school children using a trial of treatment as a diagnostic tool can help to differentiate between asthma and viral-associated wheeze (and cough) (Figure 2).

However, if the trial of treatment does not work, then think again. As with many areas of medicine, if in doubt regarding the diagnosis, and the problem is not settling despite sound baseline investigation and appropriate treatment, the patient should be referred to hospital for further investigation and management.

**SUMMARY**
Cough is an important physiological mechanism and protective reflex. Pathological cough is an extremely common presenting symptom in primary care and it is vital to take a thorough history when patients present. Various accompanying symptoms such as haemoptysis, weight loss, chest pain or dyspnoea require immediate further investigation. The differential diagnosis of chronic productive cough in adults includes COPD, bronchiectasis, TB, heart failure, and lung cancer. Chronic productive cough in children is almost invariably abnormal, and warrants specialist referral. Assuming that drugs such as ACE inhibitors and beta-blockers have been excluded as a cause, the differential diagnosis of chronic non-productive cough in both adults and children includes cough-variant asthma, GORD, postnasal drip syndrome, and post-viral bronchial hyperreactivity. Using a trial of treatment as a diagnostic tool is a useful way of obtaining a diagnosis in selected patients. Think laterally, and do not forget the upper airway as a cause of persistent cough. If in diagnostic doubt, refer the patient for specialist investigation.

**Figure 2: Management strategy for diagnosis of non-productive cough in children**

- **Recurrent persistent symptoms**
  - Trial of treatment
  - Measure response
  - Response
  - Stop treatment
  - Recurrence
  - No recurrence
  - ASTHMA
    - For regular inhaled steroid +/- leukotriene receptor antagonists if needed
  - No asthma
    - Wait and see
  - ASTHMA
    - For regular inhaled steroid +/- leukotriene receptor antagonists if needed
  - Recurrence
  - No recurrence
  - Increase dosage
  - Review the diagnosis
  - Refer

**more information**

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