Chronic Cough

guidance on investigation, management and referral
ABHUB, Department of Respiratory Medicine

- Chronic cough is defined as one lasting more than eight weeks
- It is reported in 10-20% of adults – commoner in females and obese
- Most present with a dry or minimally productive cough
- The presence of significant sputum production usually indicates primary lung pathology

**URGENT REFERRAL (Red Flag Features)**

- If a chest x-ray suggests lung cancer - including effusion or non-resolving consolidation
- Persistent haemoptysis, weight loss, progressive breathlessness, signs of superior vena caval obstruction or stridor
- History of aspiration of a foreign body

**IF LUNG CANCER SUSPECTED PLEASE REFER TO RAPID ACCESS LUNG CANCER CLINIC**

Causes of chronic cough:

**Most common:**
- Smoking
- Asthma
- Chronic obstructive pulmonary disease (COPD)
- GORD
- Postnasal drip (including allergic rhinitis, vasomotor rhinitis)
- ACE inhibitors
- Whooping cough

**Less common:**
- Chronic lung infections:
  - Bronchiectasis, TB, Cystic fibrosis, lung abscess
- Parenchymal lung disease:
  - Interstitial lung disease (fibrosis), Sarcoid
- Cancer:
  - Primary lung cancer, metastases to the lung, lymphomas and other cancers causing mediastinal lymphadenopathy
- Upper airway conditions:
  - Obstructive sleep apnoea, chronic snoring, irritation of the external meatus
- Cardio-vascular causes:
  - Left ventricular failure, arrhythmias, aortic aneurysm, pulmonary emboli
- Vitamin B12 deficiency
- Iron deficiency
- Thyroid dysfunction

This guideline is online at: [http://www.wales.nhs.uk/sites3/page.cfm?orgid=814&pid=48819](http://www.wales.nhs.uk/sites3/page.cfm?orgid=814&pid=48819)

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Where a cough is chronic with no obvious features pointing to an underlying disease, the commonest causes of a chronic cough are:

- Gastro-oesophageal reflux related cough [37%]
- Asthma and asthma-like syndromes [33%]
- Rhinitis, sinusitis, post-nasal drip [10%]

See diagnostic algorithm on page 3

Specific considerations:
- ACE Inhibitor therapy:
  16% of patients on these drugs develop cough, for the majority of patients with ACE associated cough this improves within 1 month of cessation of ACE inhibitors.
- ARB’s are a rare cause of cough and may be used instead of ACE inhibitors.
- Smoking: cough frequency is related to the number of cigarettes smoked

Smoking cessation is an important and effective intervention

- It is not uncommon for a number of causes to be present at the same time

<table>
<thead>
<tr>
<th>Characteristics of cough / associations</th>
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<tbody>
<tr>
<td>Talking, laughing, singing precipitates cough</td>
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<tr>
<td>Associated metallic taste in the mouth</td>
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<tr>
<td>Worse on bending, lying</td>
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<td>Eases at night (worse during the day, present on rising)</td>
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<td>Dyspepsia, present on eating or ~10 minutes after eating</td>
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<td>Chronic nasal congestion</td>
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<td>Catarrhal symptoms and persistent throat clearing</td>
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<tr>
<td>Mucous at the back of the throat</td>
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<tr>
<td>Nocturnal cough</td>
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<tr>
<td>Onset on exercise ± Peripheral blood eosinophilia</td>
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<tr>
<td>Associated wheeze, dyspnoea</td>
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<tr>
<td>Reversibility/airflow obstruction on spirometry (NB. The absence of this does not exclude asthma or asthma-like syndromes)</td>
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All patients with unexplained cough should have the following tests as a minimum:

- Chest x-ray
- Spirometry (with reversibility)
- Serial peak flow readings
Supporting information:

Chronic cough is a common presenting complaint, patients are often concerned about chronic cough being due to lung cancer, however this is a relatively uncommon cause accounting for less than 2% of patients presenting with chronic cough. It is important to reassure patients that for the majority chronic cough is not a symptom of cancer.

One review found that out of 77 patients diagnosed with lung cancer who presented with cough as one of their main symptoms 7.8% had an x-ray which was reported as normal, and a further 14.3% had an abnormal chest x-ray where lung cancer was not suspected. If clinical suspicion is high that a patient may have lung cancer referral to the rapid access lung cancer service is recommended.

ACE inhibitor associated cough:

Generally resolves 1-4/52 after cessation of an ACE inhibitor but can take up to 3 months. ARBs are only rarely associated with cough and if indicated an ACE can be swapped to an ARB. As ACE inhibitors are thought to lower the threshold of cough receptors ACE inhibitors should be avoided in any patient complaining of a chronic cough.

Smoking and chronic cough:

There is a dose response effect seen for number of cigarettes smoked and cough, generally cough improves and may resolve within about 1-3 months after stopping smoking.

Asthma and asthma type syndromes and chronic cough:

Cough variant asthma, asthma and eosinophilic bronchitis are all associated with chronic cough. Cough may be the only symptom, particularly in eosinophilic bronchitis where there is often a lack of measurable airflow obstruction and/or diurnal variation. No test has sufficient sensitivity or specificity to exclude asthma or asthma type syndromes as a cause of chronic cough.

Cough may be the first symptom of asthma and may present months or years before patients exhibit more classic symptoms of asthma (wheeze, reversible airflow obstruction etc).

Treatment recommendations:

First line would be a two month trial of 400 micrograms b.d of budesonide (or equivalent) as this is the recommended starting dose for the treatment of eosinophilic bronchitis.

It is vital to ensure patients are taught how to correctly use an inhaler, and in terms of delivery device the recommendation would be a dry powder inhaler or an MDI via an aerochamber or volumatic. Some patients may find that paradoxically their cough worsens with inhaled therapy this is generally due to poor technique or a constituent in the aerosol, use of an alternative delivery device should be considered, or a volumatic or aerochamber.

Where there is a partial response or no response stepping up to a combination inhaler with 400 micrograms of budesonide (or equivalent) plus long acting beta agonist for a further two-month trial is recommended.
Where there is doubt about a patients compliance with inhaled therapy or potential treatment resistance then a 2 week trial of 30 mg of oral corticosteroids can be considered\textsuperscript{10}

In patients whose cough successfully responds to inhaled corticosteroids consider stepping down inhaled therapy after 3 months, as you would in patients whose asthma is well controlled.

**Postnasal drip (PND)/rhinitis**

PND refers to the sensation of nasal secretions at the back of the throat (or of a ‘drip’), often resulting in the need to clear the throat and is associated with nasal stuffiness or nasal discharge. Sometimes, the patient may describe the sensation of ‘something running down the back of the throat’. It is also often referred to as ‘nasal catarrh’ or ‘mucus in the throat’ by patients in the UK. There are numerous rhinological conditions that can give rise to PND including allergic, non-allergic (vasomotor) and infective rhino sinusitis.

**Allergic rhinitis** responds well to intranasal steroids +/- antihistamines either nasally or orally. **Non-allergic rhinitis** especially if rhinorrhoea is a predominant feature may respond to ipratropium bromide intranasally\textsuperscript{11} in addition to nasal steroids. Oral antihistamines are generally ineffective in non-allergic rhinitis however intranasal antihistamines especially azelastine is effective in non-allergic rhinitis\textsuperscript{11}

The following may be trialled either altogether\textsuperscript{12} or in a stepwise fashion in patients where post nasal drip appears to be a trigger for their cough, but other intranasal therapies have not been successful\textsuperscript{12}.

1) Intranasal steroid – once a day nasal steroids are recommended to aid compliance.

2) Intranasal antihistamine

3) Intranasal Ipratropium bromide

**Oral antihistamines:**

Older generation sedating antihistamines are lipophilic and so cross the blood–brain barrier and may be helpful in supressing a central component to cough. Additionally with the older agents it is well recognised that they have anticholinergic properties\textsuperscript{13}

**Reflux associated cough**

Observational studies suggest a link between chronic cough and reflux. Two mechanisms have been proposed to explain why people with GORD develop chronic cough. The most intuitive theory is called the reflux theory, whereby reflux rises above the esophagus and upper oesophageal sphincter, resulting in microaspiration as microdroplets land in the larynx or occasionally enter the bronchial tree, directly causing cough as a protective mechanism against reflux. The other theory is known as the reflex theory. Because of the common embryologic origin of the respiratory tract and the digestive tract, a little bit of reflux in the oesophagus can lead to an oesphago-bronchial reflex that causes cough. In addition, some investigators have found that cough can lead to reflux, which then leads to a cycle of cough (the cough-reflux-cough cycle).

Randomized controlled trials assessing the efficacy of proton pump inhibitors (PPI’s) to reduce cough have been hampered by small sample sizes, and often chronic cough has been one of a number of symptoms assessed rather than cough reduction being the primary end point\textsuperscript{14}. In studies of patients with isolated chronic cough empiric trials of PPI’s have proven effective in a proportion of patients.\textsuperscript{15} An empiric trial of

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PPI's are therefore recommended in chronic cough either where features of GORD are present and GORD is thought to be a trigger for cough or as part of a therapeutic step wise trial where an obvious trigger for chronic cough is not apparent on history, investigation, or investigations.

We recommend a 2 month trial of high dose PPI’s b.d (20-40mg b.d), ensuring patients are aware of the need to take them on an empty stomach.

References: