

INTRODUCTION

Cough is a protective reflex, to clear the respiratory passages. It is among the commonest symptoms presenting to the out patient department.

Cough lasting less than 3 weeks is called acute cough. If the duration is 3 to 8 weeks, it is subacute.

Intractable cough is chronic cough, which is arbitrarily defined as any cough lasting for more than 8 weeks. This can be the presenting complaint in 20% - 40% of new patients.

This definition is based on the criteria that post infectious cough is unlikely to last for 8 weeks.¹

Cough is a natural defence mechanism of the airways and lungs. It helps clear secretions, noxious substances and foreign materials from the airways. So suppressing cough can result in infections, and excess cough can result in both physical and psychological complications.

The aetiology can arise anywhere along the tracheobronchial tree or from the systems, so a multidisciplinary approach is often needed.

Regardless of cause, chronic cough often worsens initially on lying down at night, while talking or with the hyperpnoea of exercise². It improves with sleep. In general, this cough is non productive.

Recently the term, 'Chronic cough hypersensitivity syndrome' is being used to label chronic cough, because it is being recognised as due to an abnormally sensitive cough reflex³, since, even after an extensive work up, the cause of the chronic cough may remain undiagnosed in as many as 46% of patients.⁴

Pathophysiology of cough

Cough receptors are present from the hypopharynx and larynx, upto the segmental bronchi. There are many types of sensory receptors which respond to mechanical, inflammatory, thermal and chemical stimuli. These are connected to the vagal afferent nerves. The cough centre located in the medulla and receives signals from these cough receptors. The efferent fibres reach the various muscles that produce the forced expiratory effort. Since the higher cortical centres have an influence over the cough centre, it is possible to produce or suppress cough, voluntarily.

CAUSES OF CHRONIC INTRACTABLE COUGH

Causes can be categorised as respiratory and non respiratory and systemic.

The most common respiratory causes of chronic cough include

Post nasal drip

Post infectious

Asthma

Environmental causes

Smoking, both active and passive – this is the commonest environmental factor

Particulate matter of 10micro meter or less

Occupational exposure to irritants

Drugs

ACE inhibitors

Beta blockers

NSAIDs

Drugs causing pulmonary fibrosis : Bleomycin, Busulphan, Methotrexate, Carmustine, Amiodarone, Cyclophosphamide, Hydralazine

Other respiratory causes include

Bronchiectasis

Bronchitis

COPD

Cystic fibrosis

Interstitial Lung Disease (ILD)

Primary or secondary lung tumours

Sarcoidosis

Tuberculosis

OTHER UPPER AIRWAY CONDITIONS TO BE RULED OUT

Chronic tonsillar enlargement

Obstructive Sleep Apnoea- wherein the apnoea may induce an increase in trans diaphragmatic pressure leading to decrease in lower oesophageal pressure, GERD and cough⁵.

Chronic snoring

Irritation of external auditory meatus

Laryngeal problems

Foreign bodies in the large airways

Non respiratory Causes

Common causes

GERD

Recurrent aspiration

Other systemic causes

Left Ventricular Failure

Mitral Stenosis

Pulmonary infarction

Psychogenic cough is a diagnosis of exclusion. The cough does not cause nocturnal awakening and is absent during positive distractions⁵.

Very rare conditions

Cardiac arrhythmias

Aortic aneurysm

Cough only when supine (due to collapse of large airways)⁶

Following complex involuntary tics (Tourette's syndrome), where patient may have paroxysms of cough⁷

Vit.B12 deficiency (probably due to sensory neuropathy)⁸

Of all these conditions: Cough Variant Asthma, GERD and UACS (Upper Airway Cough Syndrome) are called the Pathogenic Triad, and they constitute 90% cases.

Apart from the pathogenic triad, a fourth aetiology that deserves mention is, Non asthmatic Eosinophilic Bronchitis (NAEB). This condition is relatively common, easily amenable to early diagnosis and treatment.

POSTNASAL DRIP SYNDROME

It is not a disease per se, it is a syndrome. This condition arises commonly from rhinitis or rhinosinusitis. Rhinitis may be allergic or non allergic and sinusitis may be infectious or non infectious.

This is among the commonest causes of chronic cough. It has been renamed as Upper Airway Cough Syndrome, (UACS) by the guidelines committee of American College of Chest Physicians.

Symptoms of postnasal drip include: Throat clearing sensation, sneezing, rhinorrhoea, nasal congestion, cough triggered by deep breath, laughing or prolonged talking, nasal quality of voice due to concomitant nasal blockade and hoarseness of voice. Many may not experience cough at all.

Speculum examination of the nose reveals inflamed, oedematous nasal mucosa with or without polyps and cobble stoned appearance of mucosa along the posterior pharyngeal wall.

Improvement of cough with antihistaminic therapy, confirms the diagnosis.

POSTINFECTIOUS COUGH

Cough persisting for more than 3 weeks following an upper respiratory tract infection is considered to be post infectious cough. The patient usually has a normal chest X ray. This condition is particularly noted following outbreaks of Mycoplasma pneumoniae and Bordetella pertussis.

In children, the common organisms causing chronic cough are: Respiratory Syncytial Virus and Parainfluenza viruses apart from M.Pneumoniae, B.Pertussis and Chlamydia pneumoniae.

Among all the above respiratory infections, pertussis is a severe and debilitating disease, that can last for weeks or months, both in children and young adults.

Careful analysis of the history, physical examination as well as serology and sputum culture are essential, since this cough can be diagnosed only by exclusion.

GERD

This condition causes an intractable cough either through reflex pathways initiated in the oesophageal mucosa or due to a laryngo pharyngeal reflux, with consequent aspiration of the gastric contents, resulting in chemical bronchitis and pneumonitis.

Retrosternal burning sensation after meals or in the recumbent position, frequent eructations, hoarseness of voice, globus sensation and throat pain are indicators of GERD.

Again many patients with a symptomatic reflux may not experience cough. Upto 75% of patients with GERD induced cough may not have symptoms of heart burn and hence endoscopy may be non contributory⁵.

COUGH VARIANT ASTHMA

Asthma can cause cough in the absence of wheezing, shortness of breath and tightness of the chest. This is seen more commonly among children than in adults. This condition is known as cough variant asthma.

In these patients the history is very typical, wherein the cough starts following exposure to an asthma trigger.

Spirometry will reveal the airway obstruction which gets reversed with a bronchodilator.

NONASTHMATIC EOSINOPHILIC BRONCHITIS (NAEB)

This is again another cause of chronic cough with eosinophilic inflammation of the airways, in non smokers, with a normal chest X ray, with the characteristic sputum eosinophil count that is in excess of 3%. There is no airflow obstruction or bronchial hyper responsiveness and spirometric results are essentially normal. This condition can be successfully treated with inhaled steroids².

CHRONIC COUGH IN CHILDREN

In children, cough lasting more than 4 weeks is described as chronic. In the paediatric age group, commonest causes of chronic cough include infection and airway hyper reactivity followed by GERD⁹.

102 Pertussis is to be strongly considered in the paediatric age group, especially, if the cough is associated with long whoops, is troublesome at night and is associated with vomiting.

Foreign body aspiration also needs to be considered more commonly in children.

COMPLICATIONS OF CHRONIC COUGH

It is often the complications of cough which bring the patient to medical attention. It can cause devastating personal disturbance and social isolation. Common problems include: Sleep disturbances, musculoskeletal pain, emesis and syncope. Uncommon complications include: Pneumothorax, mediastinal emphysema, subconjunctival haemorrhage and stress incontinence.

MANAGEMENT OF CHRONIC COUGH

Cough needs to be assessed on the basis of:

Intensity

Severity

Frequency

Sensitivity

Some of the strong clues in the assessment of cough :

Cough worsening on supine posture: Post nasal drip, oesophageal reflux, chronic bronchitis, bronchiectasis and heart failure.

Presence of clear sputum: Hypersensitivity mechanism

Purulent sputum: Sinusitis, bronchiectasis (also, copious in quantity). To also rule out tuberculosis.

Blood tinged sputum: Malignancies, tuberculosis and bronchiectasis.

Non productive cough: ACE inhibitor therapy.

Improvement of cough with antihistaminic treatment confirms the diagnosis of UACS.

The red flag symptoms of chronic cough are:

Copious sputum (Bronchiectasis)

Haemoptysis (Malignancy, Tuberculosis)

Systemic symptoms (Tuberculosis, lymphoma, lung primary or secondaries)

Significant dyspnoea (CCF, COPD, fibrotic lung disease)

To evaluate the symptoms, the following questions may be useful:

1. What circumstances surround onset of cough?
2. What makes cough better or worse?
3. Whether it is productive?

History of fever, weight loss, night sweats and progressive fatigue should be enquired.

General examination should evaluate clubbing (maybe

indicative of vasculitis, sarcoidosis and malignancies), pedal oedema, lymphadenopathy,

Physical examination:

Physical examination findings should include search for deviated nasal septum, turbinate hypertrophy, polyps and sinusitis.

Examination of the ears for finding out inflammation of the tympanic membrane or the external canal.

Examination of the respiratory system : Bilateral wheeze in COPD, bronchial asthma or even heart failure.

Localised wheeze may occur in case of obstruction with a foreign body or tumor,

Other systems also to be examined thoroughly.

Chest X ray is mandatory in all cases.

Chronic cough with normal chest X ray occurs with ACE inhibitor therapy, post nasal drip, GERD and asthma. These account for 90% of the cases.

Diseases causing chronic cough but missed on chest X ray include tumors, early ILD, bronchiectasis and atypical mycobacterial pulmonary infection.

Sputum examination is essential, wherever possible.

Bacterial culture is needed if the sputum is purulent. Wherever feasible and in case of doubt, mycobacterial culture is also essential. Cytological examination is to identify malignant cells and to rule out eosinophilic bronchitis.

Blood investigations : To rule out infections, eosinophilia ESR and CRP may give a clue to the presence of infection, malignancy and connective tissue disorders.

Serological tests:

Cold agglutinin titre for M.Pneumoniae, in suspected cases.

HIV Elisa

Possible further investigations include:

B.Pertussis can be detected from the nasopharyngeal secretions.

Induced sputum analysis, when sputum is not easily available and it is mandatory to examine the sputum.

Bronchial provocation testing with methacholine or histamine is positive in bronchial asthma².

Bronchoscopy is to be done after excluding all common causes, if foreign body inhalation is suspected. Bronchoscopy is also indicated whenever there is abnormal chest X ray, haemoptysis, obstructive lesions and infiltrates, that otherwise elude diagnosis.

ECHO

24hour ambulatory oesophageal PH or oesophageal manometry for diagnosing GERD.

Radiology of the sinuses

HRCT – when no other diagnosis is made out.

Specialists needed in the evaluation of chronic, intractable cough:

Physician

ENT Surgeon

Pulmonologist

Medical Gastroenterologist

Allergist

Immunologist

Neurologist

Speech therapist

Patients who have isolated chronic dry cough, with normal physical examination, chest Xray and spirogram are unlikely to have serious pulmonary conditions.

TREATMENT OF CHRONIC COUGH

To stop smoking, in case of smokers. Cough should improve within 8 weeks of smoking cessation.

In case of ACE inhibitor therapy, to stop the therapy. Improvement occurs within 4 weeks. Persistence of cough after withdrawal of ACE inhibitors, raises the possibility of other causes of cough. Onset of asthma has been linked to its use.

Advising the patient to keep away from known environmental and occupational pollutants and irritants.

Treatment of UACS, depends on a presumed aetiology (infection, allergy or vasomotor rhinitis). So treatment includes first generation antihistaminics, antibiotics, nasal saline irrigation, nasal pump sprays with glucocorticoids with or without decongestants like pseudoephedrine.

Beta 2 agonists with inhaled corticosteroids give relief within a week's time in case of proven asthma. Negative response to a bronchoprovocative test, eg. Methacholine, rules out cough variant asthma. Peak Expiratory Flow Metre can be used as a cost effective method to assess therapeutic response.

A course of oral steroids for 2 weeks, or inhaled steroids, gives relief in case of NAEB.

Postinfectious cough can be treated with inhaled ipratropium, inhaled corticosteroids. Macrolide antibiotics with or without antitussives may be needed.

GERD therapy includes prokinetic agents, H₂ antagonists and proton pump inhibitors (PPIs). Appropriate dietary therapy, and proper positioning of the patient in bed are important aspects of management. PPIs should be tried for 8 to 12 weeks.

Role of antitussive therapy in patients with idiopathic, dry cough

Opiates may be advised for severe, distressing cough. Codeine and hydrocodeine, suppress the cough centre in the brainstem¹⁰. They may cause drowsiness, constipation and additive effect.

Dextromethorphan may be tried, but less effective.

Benzonatate¹⁵ is another non narcotic, oral cough suppressant acting through local anaesthetic effect on the stretch receptors in the lower airways and lungs.

Morphine is sparingly used, in patients with distressing cough and pain due to malignant disease¹.

Amitryptiline, gabapentin and carbamazepine are centrally acting drugs, which may be tried in intractable cough.

CONCLUSION

Chronic cough is a debilitating problem from a personal and social point of view. It is associated with physical and psychological consequences. The causes can range from trivial to fatal. It needs a systematic, multidisciplinary approach, focussing on history and physical examination, appropriate cost effective investigations and even therapeutic trials where necessary. Wherever there are diagnostic dilemmas and therapeutic failures, appropriate referrals and management will be needed.

REFERENCES

1. Irwin RS, Madison JM. The diagnosis and treatment of cough. *N Eng J Med* 2000; 343:1715-21.
2. Harrison's Textbook of Internal Medicine, 19th edition. Vol 1 ; 244 -245.
3. Ryan NM, Vertigan AE, Gibson PG; Chronic cough and laryngeal dysfunction improve with specific therapy of cough. *Cough* 2009; 5:4
4. Pavord ID, Chung KF. Management of chronic cough. *Lancet* 2008; 371:1375–84.
5. SP Rai. Chronic Cough. Supplement to *Journal of Association of Physicians of May* 2013; 61.
6. Madison JM, Irwin RS. Cough: A world wide problem; *Otolaryngeal Clin of North America* 2010; 43:1-13.
7. Duncan KL, Faust RA. Tourette Syndrome Manifesting as Chronic cough. *International J of Paediatric ORL*; 2002; 65-68.
8. Bucca CB, Culia B, Guida G, et al. Unexplained Chronic cough and Vit. B12 deficiency. *Am J Clinical Nutr* 2011; 93:542–8.
9. Harriden A, Grant C, Harison T, Perera R, et al. Whooping cough in school age child with persistent cough: prospective cohort study in primary care. *BMJ* 2006; 333:174 -177.
10. Morice AH, Menon MS, Mulrennan SA, et al. Opiate Therapy in Chronic cough. *Am J Respir Crit Care Med* 2007; 175:312–5.