Chronic Dry Cough in Allergic Respiratory Diseases: Diagnostic and Management Approach

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ABSTRACT
Cough is considered as a single most common complaint for which patients globally seek medical attention. A multitude of allergic etiologies contribute to the development of chronic cough in adults, which makes the diagnosis and treatment quite challenging. Allergic cough is a distinct entity where there is no respiratory obstruction and there is presence of a family history, past history and/or concomitant allergic conditions. Sensitivity to allergens is readily demonstrable by skin testing. It is also characterized by a therapeutic response to epinephrine and a periodic nature. The intention of this article is to highlight the common causes of chronic dry cough associated with allergic diseases, to differentiate allergic cough from various other causes of chronic cough associated with asthma syndromes (which include related airway disorders like ‘classic’ asthma [cough-variant asthma], nonasthmatic eosinophilic bronchitis and atopic cough) and to discuss its management strategies.

Keywords: Chronic cough, allergic cough, occupational and environmental causes, mechanisms, management options

CHRONIC COUGH: A WORLDWIDE PROBLEM
Cough is a forceful expiration against closed glottis. This maneuver prevents the entry of harmful substances into the lungs and movement of secretions and other airway constituents upward from mouth. Coughing, apart from being a physiological barrier against irritant substances that reach the respiratory tract, is also a symptom of diseases of both respiratory and nonrespiratory origin. Cough is considered as the single most common complaint globally for which patients seek medical attention. An individual’s lifestyle, quality-of-life and sense of well-being can be significantly affected by the presence of cough.

A cough can be arbitrarily classified as acute (that lasts for <3 weeks), subacute (that lasts between 3 and 8 weeks) and chronic (that lasts for >8 weeks). Cough lasting longer than this duration can be precluded as being post-infectious cough. The estimated prevalence of chronic cough is between 11 and 20%. This type of cough is observed commonly in females and in obese individuals. Chronic cough is the fifth most common symptom reported by patients who visit the outpatient clinics. Morbidities associated with chronic cough include lack of sleep, exhaustion, urinary incontinence and syncope. There can also be socioeconomic encumbrances due to work absenteeism.

Rib fractures, pneumothorax, pneumomediastinum and subcutaneous emphysema are some serious side effects associated with chronic cough.

LINK BETWEEN COUGH AND ALLERGY: WHAT EVIDENCES SAY?
Chronic Cough and Allergy
Chronic cough has been linked to the presence of asthma and allergic rhinitis. Cough can occur as a symptom of allergic diseases such as seasonal allergic rhinitis, which is an inflammatory condition of the nasal mucous membranes. This type of cough is usually associated with rhinorrhea, nasal stuffiness/congestion, nasal itching and sneezing. Occupational and environmental factors such as cigarette smoking and pollutants are known aggravating factors or triggers for cough and these may also exacerbate cough that was initially caused by other mechanisms.

Presence of high levels of particulates has been linked to productive or chronic nocturnal dry cough in adults and school children. People, especially children living in localities which are close to areas of heavy traffic have been known to suffer from increased respiratory symptoms including cough and increased symptoms from respiratory viral infections.

Causes of Allergic Cough
The most common causes of chronic cough in non-smoking adults (who have not received treatment with angiotensin-converting enzyme inhibitors and have
RESPIRATORY DISEASES

Upper Airway Cough Syndrome

Upper airway cough syndrome is a common condition that occurs in 20-40% (up to 87%) of patients who present with cough. This syndrome incorporates many diagnoses in the upper respiratory tract, including allergic rhinitis, nonallergic rhinitis, post-infectious (post-viral) cough, sinusitis and anatomic abnormalities of the nose and sinuses. All these conditions are linked to retention of mucosal secretions that drain into the posterior pharynx.

Cough-variant Asthma

In referral populations of adult nonsmokers, cough-variant asthma accounts for about 24-29% of diagnoses for chronic cough. Chronic and/or recurrent respiratory symptoms associated with reversible airflow obstruction and airway inflammation are the characteristic features of asthma. Stimulation of airway sensory nerves by inflammation is thought to be responsible for the occurrence of cough in these patients. Heightened cough sensitivity has been observed in patients with both asthma and chronic obstructive pulmonary disease.

In contrast, allergic cough is not associated with any airflow obstruction.

Eosinophilic Bronchitis

Chronic cough is also an important entity in patients with eosinophilic bronchitis and the condition has two important similarities with asthma:

- Presence of an eosinophilic airway infiltrate
- Response to corticosteroids.

There is no evidence of variable airflow obstruction or bronchial hyper-reactivity in patients with eosinophilic bronchitis but there is evidence of basement membrane thickening and elevated levels of exhaled nitric oxide that is reflective of airway eosinophilia. Patients with eosinophilic bronchitis, by definition, have sputum eosinophilia >3%.

Atopic Cough

This type of cough has clinical features of chronic nonproductive cough, sputum eosinophilia and lacks bronchial hyper-responsiveness. In contrast to eosinophilic bronchitis, atopic cough has eosinophilia only in the upper airway and the condition usually does not respond to inhaled corticosteroids.

The Japanese Cough Research Society criteria for recognizing atopic cough include:

- Nonproductive cough lasting for >8 weeks without wheezing or dyspnea.

normal chest radiogram) include upper airway cough syndrome, gastroesophageal reflux disease and asthma syndromes. In this review, we will be discussing in detail about the association of cough with asthma syndromes and allergic diseases.

Asthma syndromes represent a collection of related airway disorders including;

- ‘Classic’ asthma, the so-called cough-variant asthma
- Nonasthmatic eosinophilic bronchitis
- Atopic cough.

Both upper and lower respiratory causes of cough such as allergic rhinitis, asthma, allergic bronchopulmonary mycoses can be triggered by exposure to allergens such as dust mite, animal or cockroach allergens, fungi and pollen at indoor or outdoor environments (see Table 1).

Cough and Allergic Diseases

Allergic cough has certain characteristics that are common to all allergic diseases such as:11

- Presence of a family history of allergy
- History of past and/or concomitant allergic conditions (such as urticaria, eczema)
- Sensitivity to allergens that can be elicited by skin testing
- Therapeutic response to epinephrine
- Periodic nature of the allergic condition.

Cough is essentially produced on exposure to allergens and relieved on removing them. The sensitivity can be decreased by immunizing with the ‘concerned’ allergen, if the allergen is an inhalant. Important characteristic features of common allergic diseases have been described as follows.11

Table 1. Occupational and Environmental Causes of Allergic Cough

<table>
<thead>
<tr>
<th>Occupational factors</th>
<th>Environmental factors</th>
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<tr>
<td>Occupational rhinitis</td>
<td>Exposure to dust mite, animal or cockroach allergens, fungi and pollen</td>
</tr>
<tr>
<td>Occupational asthma</td>
<td>Exposure to cigarette smoking or other respiratory irritants</td>
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<tr>
<td>Occupational eosinophilic bronchitis</td>
<td>Exposure to indoor particulate pollution from biomass combustion</td>
</tr>
<tr>
<td>Hard metal disease</td>
<td>Exposure to air pollutants such as nitrogen oxides from gas cooking stoves or outdoor traffic</td>
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Presence of one or more findings indicative of an atopic constitution, including a past history and/or complications of allergic diseases excluding asthma.
- No bronchial reversibility (defined as less than a 10% increase in forced expiratory volume in 1 sec (FEV\textsubscript{1}) after inhalation of 300 μg salbutamol sulfate
- Normal bronchial responsiveness.
- Increased cough reflex.
- Cough-resistant to bronchodilator therapy.
- No abnormal findings indicative of cough etiology on chest X-ray.
- Normal FEV\textsubscript{1} (≥80% of predicted value) and normal forced vital capacity (FVC) and FEV\textsubscript{1}/FVC ratio.

**Characteristics of Allergic Cough**

Allergic cough is characterized by a loud barking sound with intensity and force that is similar to sneezing in hay fever. This type of cough is paroxysmal and nonproductive in nature, and may last from a few minutes to hours or days.\textsuperscript{11} In contrast, cough associated with cough-variant asthma is dry and nocturnal in nature while atopic cough is isolated in nature with cough hypersensitivity and normal airway responsiveness. Eosinophilic bronchitis, on the other hand, is characterized by a troublesome cough that is devoid of asthma symptoms and hyper-responsiveness.\textsuperscript{8}

Pathophysiological events, following allergen exposure are generally biphasic.\textsuperscript{6}
- The early phase is mediated by mast cell-derived mediators.
- The late phase response that occurs from 4 to 12 hours after exposure and persists up to 24 hours, involves increased recruitment and activation of inflammatory cells such as T cells, neutrophils, macrophages and eosinophils.

**Evaluation and Diagnosis**

**Evaluation and History Taking**

The trigger for chronic cough can be gleaned from a detailed history of the patient. The evaluation should include a number of key components. The British Thoracic Society Cough Guidelines recommendations for evaluating a patient with chronic cough include:\textsuperscript{5}
- A detailed history (including a thorough occupational history) should be taken in all patients.
- Physical examination should be performed with focus on the afferent sites of the vagus nerve most commonly associated with irritation leading is chronic cough.
- An assessment of health status and cough severity should be done.
- Chest radiograph and spirometry which are considered as mandatory should be advised.
- Bronchial provocation testing should be performed in patients with chronic cough without a clinically obvious etiology and normal spirometry.
- Bronchoscopy should be performed in all patients with chronic cough and suspected foreign body inhalation.
- High resolution computed tomography may be helpful in patients with chronic cough in whom other more targeted investigations are normal.
- Optimal management strategies should be chosen based on the most likely aggravator(s) by using a combination of diagnostic testing and treatment trials.
- Effects of treatment should be quantified.

**Diagnosis**

With respect to allergic cough, the radiographic as well as physical examination of the chest and sputum analysis may be within normal limits. Patients with allergic cough may not look or feel sick, but may complain of an itchy, scratchy or rubbing sensation deep in the throat, leading to an irritation which can reflexly cause coughing spells.\textsuperscript{11}

**Differential Diagnosis of Common Allergic Respiratory Conditions Causing Cough**

Although allergic cough may resemble asthmatic cough, it can be differentiated by a normal chest examination and the lack of sibilant and sonorous rales and prolonged expiration that is observed in asthmatic cough.

Additionally, patients with asthmatic cough have dyspnea and complaints of pressure over the sternum, whereas in patients with allergic cough there is no obstruction to respiration and other complaints.\textsuperscript{11}

A negative result of methacholine challenge may rule out asthma as a cause of chronic cough.\textsuperscript{3} Differentiating features of the asthma syndromes have been presented in Table 2.\textsuperscript{8,11}

**Managing Chronic Dry Cough in Patients with Allergic Respiratory Diseases**

For cough associated with allergic conditions such as allergic rhinitis, in addition to avoidance of the offending allergen, oral antihistamines such as loratadine,
10 mg once a day is recommended. Nasal cromolyn, corticosteroids and azelastine may also be helpful. Upper airway cough syndrome can be managed with a trial of H1 antihistamines and decongestants for a period of 1-2 weeks. Patients who respond or partially respond to this treatment are advised to continue on the same for one more week and nonresponders are cough-variant asthma can be managed with the use of inhaled steroids by metered-dose inhaler with spacer or salbutamol by metered-dose inhaler with spacer as needed. Improvement of cough is usually noted within 1 week and resolution may take 6-8 weeks. Patients with this type of cough may require long-term maintenance therapy with an anti-inflammatory agent. For managing eosinophilic bronchitis, inhaled budesonide, 400 μg twice-daily for a period of 1-2 weeks is recommended; equivalent doses of other inhaled corticosteroids are also effective. Patients with this condition may require long-term therapy. Avoidance of aggravants is advised if the condition is found to be associated with an environmental irritant such as acrylic resin.3

**Value of Antitussive Agents**

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.13 Most antitussives available are combinations of dextromethorphan or codeine with antihistamines, expectorants, decongestants and/or antipyretics. Codeine is a commonly used, centrally-acting cough suppressant and its effectiveness in suppressing artificially-induced, disease-related and chronic cough has been established from animal models and in humans. Codeine has analgesic and sedative effects in addition to its antitussive property, which may be useful in relieving painful cough. The American College of Chest Physicians (ACCP) evidence-based clinical practice guidelines recommend cough suppressants such as codeine and dextromethorphan for short-term symptomatic relief of cough in patients with chronic bronchitis.14

**CONCLUSIONS**

Allergic cough is characterized by the presence of marked familial history, past history and/or concomitant allergic conditions, sensitivity to allergens readily demonstrable by skin testing, therapeutic response to epinephrine and its periodic nature. Chronic cough is a common symptom in a multitude of allergic diseases in adults, which makes the diagnosis and treatment quite challenging. Differential diagnosis and
a systematic therapeutic approach might simplify the management of cough related to allergies. Avoidance of offending allergen is the first-line of defense to reduce the possibility of an allergic attack. Various therapeutic options available for the management of cough associated with allergic conditions. Use of antitussive agent such as codeine or dextromethorphan is suggested for the short-term symptomatic relief of dry cough.

Key Messages
- Chronic cough is a common symptom in a multitude of allergic diseases in adults, which makes the diagnosis and treatment quite challenging.
- Differential diagnosis and a systematic therapeutic approach might simplify the management of cough related to allergies.

REFERENCES

Healthcare

2 patients every minute get
confident cough relief

In Persistent Dry Cough

PHENSEDYL
Codeine Phosphate IP 10 mg and Chlorpheniramine Maleate IP 4 mg per 5 ml

The Expert’s Confidence in Cough Relief