Approach and Treatment of Cough in Adult

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cough, also known as tussis, is a voluntary or involuntary act that clears the throat and breathing passage of foreign particles, microbes, irritants, fluids, and mucus; it is a rapid expulsion of air from the lungs.
There are three phases to a cough:

- Inhalation (breathing in).
- Increased pressure in the throat and lungs with the vocal cords closed.
- An explosive release of air when the vocal cords open, giving a cough its characteristic sound.
Pathogenesis: Mechanism of Cough

Irritation phase
- Neural activation from solitary nucleus
- Can be cortically suppressed

Inspiratory phase
Brief inspiration:
- Glottis opens
- Diaphragms contract
- Thoracic cage expands

Compressive phase
Abdominal and thoracic muscles compress air against a closed glottis

Expulsive phase
- Abrupt glottis opens
- Rapid exhalation
- High velocity and shear force allow airway clearance

Middleton's 8th edition
Types of cough

- Chesty cough
- Tickly cough
- Dry cough
- Nervous cough
- Night cough
- **Persistent cough**
- Croup cough
- Whooping cough
- Choking
Coughing complications

Acute complications of coughing include:

- fainting spells after coughing fits (cough syncope)
- insomnia from coughing at night
- cough-induced vomiting
- red eyes caused by subconjunctival hemorrhages which is in turn caused by forceful coughing
- involuntary urination due to coughing.

Chronic complications include:

- Fatigue
- abdominal and pelvic hernia
- fractures of lower ribs
- inflammation of the chest wall (costochondritis)
Specific Cough Pointers

Associated symptoms or conditions

- Cardiac disease .... tracheomalacia, primary ciliary dyskinesia
- Neurological disease .... aspiration
- Feeding intolerance .... laryngeal/tracheal disorder, aspiration
- Failure to thrive .... severe lung disease, cystic fibrosis, indolent infection
- Autoimmune disease .... Interstitial lung disease (ILD)
- Immunodeficiency .... opportunistic infections, deep infections
- Chronic fever .... indolent infections

Common serious conditions presenting with isolated cough

- Neoplasm
- Infection, e.g. tuberculosis
- Foreign body inhalation
- Acute allergy – anaphylaxis
- Interstitial lung disease
classification

Acute :
< 3 weeks
Most common cause: acute respiratory tract infection
Other: acute exacerbation of an underlying lung disease, pneumonia, and pulmonary embolism

Subacute :
3-8 weeks

Chronic:
>8 weeks
Symptoms associated with acute cough prompting a chest radiograph

- Hemoptysis
- Breathlessness
- Fever
- Chest pain
- Weight loss
Causes of acute cough with a normal chest radiograph

- Viral respiratory tract infection
- Respiratory syncytial virus
- Rhinovirus
- Influenza
- Parainfluenza
- Adenovirus
- Respiratory corona virus
- Metapneumovirus
- Bacterial infection (acute bronchitis)
- Inhaled foreign body
- Inhaled toxic fume
Causes of chronic cough in patients with a normal chest radiograph

- Reflux disease
- Gastro-oesophageal reflux
- Laryngopharyngeal reflux
- Oesophageal dysmotility
- Asthma syndromes
- Cough variant asthma
- Eosinophilic bronchitis
- Rhinitis
Diagnostic approach

History:
Cigarette smoking, the use of ACE inhibitors, the presence of an upper respiratory tract infection at the onset of the cough.
A history of coexisting symptoms might suggest an underlying diagnosis (eg, asthma, PND, GERD, chronic bronchitis, bronchiectasis).

Surprisingly, one study found that the character and timing of the cough and the presence or absence of sputum production do not appear to aid in the differential diagnosis.
In patients whose cough lasted > 8 weeks: chest radiograph should be considered as part of initial evaluation, Upper airway cough syndrome, asthma, and gastroesophageal reflux, alone or in combination, are responsible for approximately 90 percent of cases of chronic cough.
Metacholine challenge and esophageal pH monitoring are useful diagnostic studies in the evaluation of selected patients with chronic cough.

If empiric therapy of postnasal drip in unsuccessful, a stepwise approach should be initiated that emphasizes sequential diagnostic test and/or empiric therapy for asthma, non-asthmatic eosinophilic bronchitis, and gastroesophageal reflux disease.
Evaluation of subacute or chronic cough in adults

Cough ≥3 weeks

- History, physical exam suggest post-nasal drip, asthma or GERD
  - Treat accordingly
  - Cough resolved
  - Cough persists

- History, physical exam do not strongly suggest cause or do suggest pulmonary parenchymal disease
  - Chest radiograph
  - Normal (or old unrelated abnormality)
  - Evaluate based on the nature of the radiographic abnormality
    - Treat accordingly
    - Cough persists
    - Cough resolved

- Purulent sputum OR Smoker OR ACE inhibitor treatment OR Immunocompromised host
  - Evaluate and treat accordingly (e.g., antibiotics; smoking cessation; stop ACE inhibitor)
  - Cough persists
  - Cough resolved

Sequentially treat (or evaluate) for the most common causes of cough*:
- Upper airway cough syndrome (allergy skin testing, sinus CT)
- Asthma (PFTs)
- Non-asthmatic eosinophilic bronchitis (sputum eosinophilia)
- GERD (esophageal pH monitoring)

- Treat accordingly
  - Cough resolved
  - Cough persists

Evaluate for less common conditions (e.g., sputum tests, HRCT scan, esophageal pH probe monitoring, esophagoscopy, flexible bronchoscopy, cardiac studies)

- Treat accordingly
  - Cough resolved
  - Cough persists

Always reconsider adequacy of treatment regimens before considering cough to be psychogenic.

GERD: gastroesophageal reflux disease; ACE: angiotensin-converting enzyme.
* Also consider post-infectious etiology for subacute cough (3 to 8 weeks duration).

Graphic 67147 Version 5.0
The initial step in the algorithm identifies patients who are immunosuppressed, smoke cigarettes, or have purulent sputum.

Immunosuppressed patients should have a rapid evaluation for infection.

Smokers need counseling to quit smoking and often a chest radiograph to exclude bronchogenic carcinoma.

Patients with significant production of purulent sputum need evaluation for pulmonary and possibly sinus infection, and treatment of identical infectious, prior to proceeding with the algorithm.
Specific treatment

- Upper airway cough syndrome

Etiologies: allergic, nonallergic, and vasomotor rhinitis, acute nasopharyngitis, and sinusitis.

When an environmental precipitant for allergic rhinitis can be identified, exposure to this precipitant should be eliminated if all possible.

For allergic rhinitis: intranasal glucocorticoid (effective in reducing cough within the first few days, but may take up to 2 weeks to achieve the maximum effect.)

If the patient responds, therapy is continued for approximately three months.

In addition intranasal glucocorticoids are effective for several types of nonallergic rhinitis including nonallergic rhinitis with eosinophilia (NARES) and vasomotor rhinitis.
Additional therapy for allergic rhinitis: oral and nasal antihistamines, oral decongestants, oral leukotriene receptor antagonists, and other agents.
Among patients without evidence for allergic rhinitis in whom nonallergic rhinitis is more likely, our approach is to perform a diagnostic trial with an oral first generation antihistamine. (eg, chlorpheniramine, clemastine) or a combined antihistamine-decongestant (eg, brompheniramine-pseudoephedrine).

First generation antihistamines are preferred over second generation ones. (eg, cetirizine, fexofenadine, loratadine) due to stronger anticholinergic effect, but concern over the sedating effect may limit their use.
For patients with suspected nonallergic UACS who are not candidates for use of an oral first generation antihistamines (eg, due to excess somnolence), other options include intranasal administration of one of the following: azelastine, glucocorticoid, and ipratropium bromide. azelastine may cause somnolence even with intranasal use. Intranasal ipratropium bromide significantly reduces the rhinorrhea associated with perennial nonallergic rhinitis and has few side effects.
Cough variant asthma

Similar to therapy for asthma, the mainstays of therapy for cough variant asthma are regular use of inhaled glucocorticoids and as needed use of inhaled bronchodilators.

The leukotriene receptor antagonists (LTRA) have also been shown to improve cough variant asthma. LTRAs are an alternative among patients who wish to avoid or who have not responded to glucocorticoids. For patients who are disabled by their cough, a short (one or two) course of oral prednisone can be given, generally with excellent results.
Nonasthmatic eosinophilic bronchitis

The usual treatment for nonasthmatic eosinophilic bronchitis (NAEB) is an inhaled glucocorticoid.

When an acting agent (eg, occupational allergen) is identified, further exposure should be avoided. Rarely, oral glucocorticoids are needed for refractory symptoms.
Gastoeophageal reflux

- Lifestyle modifications:
  - Weight loss for patients who are overweight
  - Elevation of the head of the bed three to four inches
  - Cessation of smoking
  - Avoidance of reflux-inducing foods (e.g., fatty foods, chocolate, excess alcohol)
  - Avoidance of very acidic beverages (e.g., colas, red wine, orange juice)
  - Avoidance of meals for two or three hours before lying down (except medications)

- Acid-suppression medication
Cough following an upper respiratory tract infection may be due to postnasal drip or a direct effect of the viral infection to increase bronchial reactivity or cough receptor sensitivity. Patients in whom postnasal drip (ie, upper airway cough syndrome or UACS) seems to be contributing to the prolonged cough following a viral upper respiratory. First generation antihistamines

In patients with postviral cough without upper airway cough syndrome, These patients often have transient bronchial hyperreactivity and a positive methacholine challenge test.
• in patients with postviral cough who have no evidence of airway hyperreactivity, inhaled ipratropium bromide has been reported to produce improvement in the cough.

• Infection due to **Bordetella pertussis** (whooping cough) may be responsible for approximately 20 percent of cases of prolonged cough in adolescents and adults. It is therefore important to consider this diagnosis in the patient with an apparent postinfectious cough, especially if post-tussive vomiting is present. Patients are treated with a macrolide antibiotic, or trimethoprim-sulfamethoxazole, if a macrolide cannot be given.
Angiotensin converting enzyme inhibitors and receptor blockers

Angiotensin converting enzyme (ACE) inhibitors produce a cough in 3 to 20 percent of patients, an effect that may be mediated by increased availability of kinins. The cough usually begins within one to two weeks of starting therapy, but may be delayed for as long as six months. The cough will typically resolve within one to four weeks after stopping the ACE inhibitor, but occasionally will last up to three months.

Angiotensin II receptor antagonists are alternatives to ACE inhibitors (acting via a related mechanism) that do not affect kinin metabolism.
Nonspecific therapy should be reserved for those patients who do not respond to the algorithm. These patients may have another underlying airway or parenchymal disease as the cause of their cough. More often, however, they have what many now term “unexplained chronic cough”, “chronic idiopathic cough”, or “cough hypersensitivity syndrome”.

This disorder may in part be due to an abnormally sensitive cough reflex, perhaps in the form of heightened sensory nerve receptor sensitivity due to alterations in receptor ion channels, such as transient receptor potential vanilloid 1 (TRPV1) or transient receptor potential ankyrin 1 (TRPA1).
Centrally acting antitussive agents

A number of agents, both opioid and non-opioid, are thought to suppress cough via an action on the central cough center.

We usually start with dextromethorphan, due to its better side effect profile. If that is ineffective, then codeine or long-acting morphine are tried.

Use of gabapentin for cough is “off-label”, but may be tried for cough refractory to other measures, as described below.
Dextromethorphan is probably the most common non-opioid agent used for cough. In a systematic review that analyzed studies of dextromethorphan versus placebo, the quality of the studies was generally felt to be fair to poor. Nonetheless, dextromethorphan was found to modestly decrease cough severity (five studies) and frequency (two studies).
Codeine is the traditional opiate used for cough. In our practice, when prescribing codeine, we start at 30 mg every 4 to 6 hours as needed and increase to 60 mg, if the lower dose is insufficient. We caution patients about potential adverse effects such as somnolence and constipation.
Morphine

In a double-blind crossover trial, 27 patients who had a persistent cough of greater than three months duration and failed specific treatment were randomly assigned to receive slow-release morphine (5 mg twice daily) or placebo for four weeks. Morphine improved daily cough severity scores, cough reflex was unaltered. Among those patients who did not respond to 5 mg twice daily, improvement was detected when the dose was increased to 10 mg twice daily. Patients should be warned about potential somnolence and constipation.
inhaled ipratropium bromide

in patients with postviral cough who have no evidence of airway hyperreactivity, has been reported to produce improvement in the cough. Blocking the efferent limb of the cough reflex Decreasing stimulation of cough receptors by alteration of mucociliary factors a beneficial effect of ipratropium has been noted in a small group of patients with persistent cough following upper respiratory tract infection The usual dose of ipratropium is 2 inhalations by metered dose inhaler, four times a day.
Benzonatate is a peripherally acting antitussive agent that presumably acts by anesthetizing stretch receptors in the lungs and pleura.

One report showed that a combination of 200 mg of benzonatate and 600 mg of guaifenesin significantly suppressed capsaicin-induced cough compared to guaifenesin alone. There are case reports of effective use of benzonatate in the palliative treatment of cough in advanced cancer. It may be tried as an adjunctive treatment to narcotics in such cases.
Thalidomide has been evaluated as an antitussive agent for patients with cough due to idiopathic pulmonary fibrosis (IPF). The mechanism by which thalidomide might suppress cough in IPF is not known anti-inflammatory or antifibrotic properties or to its inhibition of pulmonary sensory nerve fibers.

Nebulized lidocaine may be helpful in a minority of patients with refractory chronic cough.
The observation that chronic cough is associated with airway inflammation even in nonasthmatic patients, has prompted use of inhaled glucocorticoids (GCs) for nonspecific management of chronic cough.
Macrolide antibiotics

Patients with chronic cough tend to have increased levels of neutrophils in their induced sputum, which led to the hypothesis that macrolide antibiotics, which have antineutrophil effects independent of antimicrobial effects, might be efficacious in treating chronic cough.
The role of herbal medicines

♣ Herbal medicine has been used for several thousands of years.

♣ A majority of the world’s population in developing countries still relies on herbal medicine to meet its basic health service.

♣ Even in areas where modern medicines is available, the interest on herbal medicines & their utilization have been increasing rapidly in recent years.

( WHO 1998 )
Non-pharmacologic interventions

Modalities such as speech therapy, breathing exercises, cough suppression techniques, and patient counseling have been tried in the management of chronic cough. A systematic review reported that studies of such interventions showed improved cough severity and frequency.
Thank You