Chronic Cough

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March 4, 2014

Speak Up!!

Cure for a Cough

The owner of a drugstore walks in to find a guy leaning heavily against a wall with an odd look on his face.
The owner asks the clerk, "What's with that guy over there by the wall?"
The clerk says, "Well, he came in here at 7 A.M. to get something for his cough. I couldn't find the cough syrup, so I gave him an entire bottle of laxatives."
The owner says, "You idiot! You can't treat a cough with laxatives!"
The clerk says, "Oh yeah? Look at him—he's afraid to cough!"

Importance

Cough is the most common presenting symptom in primary practice.
UK general practice data suggests:
- 2 consultations per year for every adult
- 6 consultations per year for each child under 4
Importance

In 2004, Acute cough accounted for 26 million office visits
Leads to decreased patient quality of life and decreased school and work productivity
Over-the-counter medicines are often inadequate for symptom relief.
Still a 2 Billion dollar industry
Chronic cough may account for up to 40% of visits to a Pulmonologist

Cough

• Vital protective mechanism
• Four steps:
  – inspiratory gasp
  – Valsalva maneuver
  – expiratory maneuver as cords abduct
  – post-tussive prolonged inspiration

Cough is a forceful expulsion of air from the lungs

It is normally a protective reflex for removing foreign bodies, environmental irritants, or accumulated secretions from the respiratory tract.
The cough reflex involves central and peripheral mechanisms. Centrally, the cough center in the medulla oblongata receives stimuli and initiates the reflex response (deep inspiration, closed glottis, buildup of pressure within the lungs, and forceful exhalation). Peripherally, cough receptors in the pharynx, larynx, trachea, or lungs may be stimulated by air, dryness of mucous membranes, or excessive secretions.

Complications of Cough

Cardiovascular
  - Arterial hypotension
  - Loss of consciousness
  - Closure of intracranial, nasal and anal veins
  - Dislodgment/malfunction of intravascular catheters

Neurologic
  - Cough syncope
  - Headache
  - Cerebral air embolism
  - CSF rhinorrhea
  - Seizures
  - Stroke due to vertebral artery dissection

Gastrointestinal
  - Gastroesophageal reflux events
  - Hydrothorax in peritoneal dialysis
  - Malfunction of gastrostomy button
  - Splenic rupture
  - Inguinal hernia

Complications of Cough

Cough Receptors/Cough Reflex
Complications of Cough

Genitourinary
- Urinary incontinence
- Inversion of bladder through urethra

Musculoskeletal
- Acute asymptomatic elevations of serum creatine phosphokinase to rupture of rectus abdominis
- Fractures

Respiratory
- Pulmonary interstitial emphysema, with potential risk of pneumatosis intestinalis, pneumatosis gastroduodenum, pneumoperitoneum, pneumomediastinum, subcutaneous emphysema
- Laryngeal trauma
- Tracheobronchial trauma (e.g., bronchitis, bronchial rupture)
- Tracheal perforation
- Intestinal lung herniation

Miscellaneous
- Retching and purging
- Swelling of genital wounds
- Lymphoid changes
- Gastrointestinal, hoarseness, dizziness
- False sense of serious illness
- Decrease in quality of life

Classification of Cough

Three Categories of Cough
- Acute Cough = < 3 Weeks Duration
- Subacute Cough = 3 – 8 Weeks Duration
- Chronic Cough = > 8 Weeks Duration

Etiology

- Acute cough (<3 weeks)
  - Is most often due to upper respiratory infection (common cold, acute bacterial sinusitis, and pertussis). Serious disorders, such as pneumonia, pulmonary emboli, and congestive heart failure, can also present in this fashion.

- Sub acute cough (between 3 and 8 weeks)
  - Is commonly post-infectious, resulting from persistent airway inflammation and/or postnasal drip following viral infection, pertussis, or infection with Mycoplasma or Chlamydia.

- Chronic cough (>8 weeks)
  - In a smoker raises the possibilities of asthma, COPD or bronchogenic carcinoma, Eosinophilic Bronchitis, Esophageal Disease, Post Nasal Drip, ACEI, Smoking.

Managing Acute Cough

Identify High Risk groups

Acute Cough Can be 1st Indicator of Serious Disease
- Eg Lung ca, TB, Foreign Body, Allergy, Interstitial Lung disease
- Chronic cough always preceded by acute cough.

Threatening symptoms

- Cough with increasing intensity that lasting above week
- Cough accompanied by hyperthermia above 38 °C during 3 days or more
- Cough accompanied by dyspnea and thoracic pain on breathing
- Cough of pus
- Blood spitting
- Cough and weakness and weight loss
- Excessive sweating, shivering
- Sudden attack of severe cough

Tenor

- Can you tell the cause of a cough by its sound?
Upper Airway Cough Syndrome

UACS is considered the most common cause of chronic cough (87%)

- PNDS
- Acute bacterial sinusitis
- Allergic fungal sinusitis
- Allergic rhinitis
- Nonallergic rhinitis
- Nonallergic rhinitis with eosinophilia (NARES)
- Occupational rhinitis
- Postinfectious rhinitis
- Rhinitis due to anatomic abnormalities
- Rhinitis due to physical or chemical irritants
- Rhinitis medicamentosa
- Rhinitis of pregnancy
- Vasomotor rhinitis
9

Allergy

Mechanism

Direct PND
Irritant receptors
Histamine enhances cough reflex

8

Smoking

Mechanism

Increased mucus production
Paralyzed ciliary escalator
Irritant receptors
Direct irritation
Asthma

Mechanism

- Irritant reflexes
- Muscarinic reflex
- Parasympathetic reflex

GER

Reflux Esophagitis

Esophageal-tracheobronchial cough reflex & GERD

- 22 pts with reflux & cough, 12 controls
- Instilled acid into distal esophagus
- Looked at effects of:
  - Esophageal lidocaine
  - Esophageal ipratropium
  - Inhaled ipratropium

Ing et al 1994

Ing 1994

Figure 2: Results of distal esophageal acid perfusion testing, comparing the number of coughs precipitated by saline and acid in patients with reflux vs. control subjects.
Laryngopharyngeal Reflux (LPR)

Also known as Extraesophageal GERD
Microaspiration of esophageal contents into the laryngopharynx and tracheobronchial tree
Differs from traditional GERD in that it does not manifest as heartburn and tends to occur when the patient is upright as opposed to lying flat.
This silent GERD can be present in as many as 75% of patients with chronic cough.
Symptoms of LPR include throat clearing, hoarseness, and globus sensation. Empiric treatment includes acid suppression and lifestyle and dietary modifications.

Top 3 Causes of Chronic Cough

1. Upper airway cough syndrome (UACS), previously referred to as postnasal drip syndrome (PNDS)
2. Asthma
3. GERD
   - Account for the etiologic cause of chronic cough in 92-100% of immunocompetent, nonsmoking patients with normal CXR.

Whooping Cough

- Also known as Pertussis
- Outbreaks first described in the 16th Century
- Major cause of childhood fatality prior to vaccination

Pertussis

Clinical Features

- Incubation period 4-21 days
- 3 Stages
  - 1st Stage - Catarrhal Stage
  - 2nd Stage - Paroxysmal Stage
  - 3rd Stage - Convalescent Stage
Diagnosis

- Isolation by culture
- PCR
- Direct fluorescent antibody
- Serological testing

ACE-inhibitor therapy

- Angiotensin converting enzyme (ACE) inhibitors (enalapril, captopril, lisinopril, ramipril, etc.)
- Dry cough in 3-30% patients
- Begins 1 week to 6 months after drug started
- Usually resolves 1-7 days after stopping therapy, but can take 4 weeks

Mechanism

- Bradykinin or Substance P increase
- Usually metabolized by ACE
- PGE2 accumulates and vagal stimulation.

Iatrogenic

Sinusitis

Factitious

Trust Me, I'm a Doctor

Mechanism

Direct PND
Bacterial seeding
Neurologic reflex
   balloon inflation
Psychogenic Cough

- A diagnosis of exclusion
- Most common in adolescents with concomitant emotional disorders
- Does not produce sputum
- Usually does not occur at night
- Not affected by commonly used cough suppressants

Causes and estimated frequencies of acute cough in the adult

- **Common**
  - Common cold
  - Acute bacterial sinusitis
  - Pertussis
  - Exacerbations of COPD
  - Allergic rhinitis
  - Environmental irritant rhinitis

- **Less common**
  - Asthma
  - Congestive heart failure
  - Pneumonia
  - Aspiration syndromes
  - Pulmonary embolism


Chronic Cough

- Common things are common
- Patients who do not respond frequently have more than one cause
- GERD causes cough
- Post-infectious cough is common

Table 6. Common Patterns in Managing the Most Common Causes of Chronic Cough

<table>
<thead>
<tr>
<th>Number of Causes of Cough</th>
<th>Patients %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
</tr>
</tbody>
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Smyrnios et al Arch Intern Med 1998 158:1222

Number of causes of cough
Case Study 1

- 55 yo school secretary
- C/O cough for 3 years
- Non-smoker
- Cough:
  - Often productive, wax/wane
  - Better c abx, but comes back
  - “no better” with asthma meds
  - worst in AM

Nasal voice, afebrile, looks well
- Mild “cobblestoning”
- No facial tenderness
- normal heart and lungs
- normal spirometry

Chronic Sinusitis

- Often paucity of symptoms
- Often improvement with antibiotics
- Dx: Clinical & Sinus CT scan

Case Study 2

- 35 yo woman
- Yearly cough
  - starts only after a “cold” in fall or winter, lasts until mid-summer
  - Severe coughing FITS
  - goes away by itself
  - has happened last 4 years.
- Tried “everything”

Denies: wheezes, PND sx, allergies heartburn, aspiration
- No: pets, exposures, current meds
- Family hx negative
- PMH: negative
- Physical exam and CXR normal
- Normal spirometry, no bronchodilator effect
- “I can’t take it any longer!”
Methacholine Challenge Testing

Cough Variant Asthma

- Cough is sole symptom
- Spirometry is normal
- Up to 25% of asthmatics
- Diagnosis:
  - Positive methacholine challenge
  - Response to therapy
- Mechanism

Case Study 3

- This 49-years-old lady has had a dry cough for a few months.
- Her BMI is 36
- She doesn’t smoke
- She takes Gaviscon plus a tablet for her blood pressure which she can’t recall

Cough and Reflux

GERD causes cough & lowers cough threshold

abdominal pressure

Cough & GERD

- May be silent (up to 75%)
- May complicate other causes
- Diagnosis can be difficult
  - pH probe vs. therapeutic trial
- Treatment must be aggressive
- Bland reflux can still cause cough
- Surgery effective in some patients

Case Study 4

46 yo woman
Secretary in College Infirmary
3 wks severe cough
Followed mild “cold”
Cannot talk, sleep
Cough comes in “fits”
Otherwise very healthy
**B. pertussis**  
“The hundred Day Cough”

- *Bordatella pertussis, parapertussis*  
  Immunity wanes 12 yrs after vaccine  
  Phases:  
  - catarrhal, paroxysmal, convalescent  
  Abx ↓ infectivity, no effect on cough  
  Prophylaxis

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**Why diagnose pertussis?**

- Treatment:  
  - does not ↓ paroxysmal phase  
  - does ↓ infectivity  
  Prophylaxis  
  To reassure patient  
  Minimize further work-up

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**Case Study 5**

Cough productive of white sputum most days over the past 2 years  
Lifelong smoker (30 per day)  
Gets breathless going up stairs

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**Case Study 5**

Unwell!  
- He becomes unwell with fevers, sweats, increasing cough and sputum volume.  
- Sputum is now green  
- He also complains of right sided pleuritic chest pain and had a few crackles at the right base on chest auscultation

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**CXR**

![CXR Image](https://www.meddean.luc.edu/pulmonar/cxr/segm.htm)
Case Study 6

6 YO male previously healthy
Several week history of “that cough”
Well adjusted
Normal examinations except for the cough

No response to antibiotics
No response to anti-tussives
Negative methacholine challenge
CXR showed significant atelectasis

To pediatric pulmonology for evaluation
Chest CT scan
Abnormal vessel in lung

15 YO male who is acting well
Chest examination
– Profuse rales
– Wheezing

No response to antibiotics and bronchodilators

CXR showed severe bilateral pneumonia
Repeat CXR shows no change

Pediatric and then adult pulmonary evaluation
Pulmonary Alveolar Proteinosis
– Anti-GMCSF antibody
– Repeated pulmonary lavages to wash out exudate
### Chronic Cough: Conclusions

Common things are STILL common  
Many patients have > 1 cause  
Most patients respond to therapy

### Managing Acute Cough

“Don’t just do something stand there.”  
*Alice in Wonderland*

### Antitussives

- Antitussive agents suppress cough by depressing the cough center in the medulla oblongata or the cough receptors in the throat, trachea, or lungs.
- **Centrally acting** antitussives: narcotics (e.g., codeine, hydrocodone) and non-narcotics (e.g., dextromethorphan).
- **Locally acting** agents (e.g., throat lozenges, cough drops) may suppress cough by increasing the flow of saliva and by containing demulcents or local anesthetics to decrease irritation of pharyngeal mucosa.

### Tessalon

- Local anesthetic
- Numbs stretch receptors
- Do Not Chew!!

### Indication for use of antitussives

A dry, hacking, nonproductive cough that interferes with rest and sleep.  
**It is not desirable to suppress a productive cough** because the secretions need to be removed.  
Although antitussives continue to be used and some people report beneficial effects, some research studies indicate that cough medicines are no more effective than placebos in children or adults.

### Expectorants

- Expectorants are agents given orally to liquefy respiratory secretions and allow for their easier removal.
- **Guaifenesin** is the most commonly used expectorant. It is available alone and as an ingredient in many combination cough and cold remedies, although research studies do not support its effectiveness and many authorities do not recommend its use.
Oral cough suppressants

- **Codeine** and hydrocodone are narcotic oral cough suppressants that require a doctor’s prescription. **Dextromethorphan** is an oral cough suppressant that is available OTC. Dextromethorphan is chemically related to codeine and acts on the brain to suppress cough, but
- **Diphenhydramine** is another non-narcotic medication that acts on the brain to suppress cough. It is also an antihistamine.

Oral expectorants

- **Guaifenesin** is an oral expectorant that is believed to increase the leaking of fluid out of the lung tissue and into the airways. This action thins (liquefies) the thick mucous in the airways and facilitates the clearing of the mucous by coughing. Clearing of mucous from the airways decreases cough.

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Number of causes of cough

-Chronic Cough

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