Chronic Cough

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Chronic Cough

- Background
- Mechanism
- Evaluation
- Chronic Cough Hypersensitivity Syndrome
- On the Horizon
Chronic Cough

Common reason to seek medical attention
- 30 million visits/year

Patient perspective
- exhaustion, pain, fear, embarrassment, sleep deprivation

Family/co-worker/fellow traveller
- Annoying, disruptive, “I don’t want to catch that”

A $6.8 billion dollars in OTC medications

Defined as > 8 weeks/ > 12 weeks

Cause identified 75-90%
Chronic Cough

Provide hope
Expectation management

Pulm

1° Care

GI

ENT
What is a cough?

Respiratory tract defense: Triphasic
- Inspiratory phase
- Forced exhalation effort against closed glottis
- Glottic opening with rapid expiration

Chronic cough
- Too much of a good thing
Cough receptors:
  Upper/lower respiratory tract
  Esophagus
  Diaphragm
  Stomach
  Pericardium

Afferent nerve:
  Vagus

Cough Center:
  Medulla

Efferent nerves:
  Vagus
  Phrenic
  Spinal Motor
Sensory receptors

**Chemoreceptors**
- unmyelinated/slow
- noxious stimuli
- chemicals
- inflammatory molecules

**Mechanoreceptors**
- myelinated/fast
- touch
- ↓ pH
- Hypotonic solutions

**Supratentorial Volitional Control**
Cough: Gender

Women have lower cough thresholds

↑ ACE cough
↑ Postmenopausal

Capsaicin challenge (n=100)
- Increasing concentration
- 2 and 5 coughs
Distribution of 5 coughs for female and males

(Chest 1998, 113:1319)
Where does your cough start?
Chronic Cough: Etiology

- Asthma / Airway hyperresponsiveness (AHR) (24%)
- GERD (21%)
- Post-nasal drip / Upper airway cough syndrome (41%)
- Smoking
- ACEi

Irwin, Chest 2014
Asthma

- Wheezing (may be absent)
  - cough-variant asthma
  - eosinophilic bronchitis
- Prolonged cough after URI
- Sense of chest tightness
- Cough with environmental changes
- Atopic history

I HAS TEH AZMAH
Asthma: Diagnosis

Spirometry
- \(\text{FEV}_1/\text{FVC} < 70\%\)
- Bronchodilator response \(\geq 12\%\) or 200 ml
- Frequently \(> 20\%\)
- Can be normal

Bronchoprovocation Testing
- Methacholine
- \(\text{FEV}_1 \downarrow 20\%\)

Fractional Exhaled Nitric Oxide (\(\text{F}_{\text{ENO}}\))
# Methacholine Challenge

<table>
<thead>
<tr>
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<th>Pre DILULENT</th>
<th>1MG/ML</th>
<th>5MG/ML</th>
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<tr>
<td><strong>Dose</strong></td>
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<td>5.000</td>
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<tr>
<td><strong>Dose Units</strong></td>
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<td>25.000</td>
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<tr>
<td><strong>C.D.U.'s</strong></td>
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<td>5.000</td>
<td>30.000</td>
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**SPIROMETRY**

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<tbody>
<tr>
<td><strong>FVC (L)</strong></td>
<td>3.52</td>
<td>3.40</td>
<td>3.09</td>
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<tr>
<td><strong>FEV1 (L)</strong></td>
<td>2.66</td>
<td>2.42</td>
<td>1.91</td>
<td>2.61</td>
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<tr>
<td><strong>FEF 25-75% (L/sec)</strong></td>
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<td>1.48</td>
<td>0.70</td>
<td>1.93</td>
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<td>%Change</td>
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<td>-67</td>
<td>-8</td>
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<tr>
<td><strong>FEF Max (L/sec)</strong></td>
<td>6.84</td>
<td>6.77</td>
<td>4.86</td>
<td>7.24</td>
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<td>%Change</td>
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<td>-29</td>
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Asthma Diagnosis

Fractional Exhaled Nitric Oxide (F\textsubscript{E}NO)

- Tracks eosinophilic inflammation
- Range (ppb)
  - $< 25$ no eosinophilic inflammation
    - additional glucocorticoids may not help
  - $> 50$ eosinophilic inflammation
    - suggests glucocorticoid responsiveness
- 25-50 clinical context
  - Symptomatic
  - On therapy
  - ? Smoking (↓ 70%)

(Am J Respir Crit Care Med 2005;171:912)
Asthma: Empiric treatment
(Cough variant/ Eosinophilic bronchitis)

Inhaled corticosteroids
  • 2-4 weeks at least

If ICS “makes my cough worse”
  • Change delivery system
  • HFA propellant vs dry powder

Add leukotriene receptor antagonist

Trial of oral glucocorticoids
  • Prednisone 40 mg x 5 days, 20 mg x 5 days
GERD

- Heartburn, sour taste, water brash, regurgitation
- Chest pain
- Throat clearing! (also with post-nasal drip)
- Globus sensation
- Hoarseness (non-specific)
- Symptoms absent up to 40%
GERD: Cough

- Stimulation of upper airway receptors
- Aspiration of gastric contents
  - Stimulation of lower tract receptors
- Esophageal-tracheobronchial cough reflex
  - Acid in lower esophagus
Larygopharyngeal reflux (LPR)

Upper esophageal sphincter
- Physical exertion, bending over, Valsalva
- Classic GERD is lower esophageal sphincter

Only 35% report heartburn

Direct laryngoscopy
- Arytenoid erythema and edema
GERD: Emperic treatment

**Acid suppression**
- PPI – BID – for 2-3 months!
- PPI alone unlikely benefit

**Lifestyle modification:**
- HOB elevation
- Weight loss, intake modification

**Consider OSA**
- up to 30% have cough

Smith, NEJM 2016
Kahrilas, Chest 2016
If you see this

Consider an esophagagram
Intractable Cough

Esophagram: Tracheoesophageal fistula
Post Nasal Drainage / UACS

Throat clearing
Mucus pooling
Sniffing/ nose blowing
No symptoms common

Causes:

Rhinitis
- Allergic
- Perennnial nonallergic
- Vasomotor

Sinusitis
Post Nasal Drainage/UACS:

**Empiric treatment**
- Nasal steroids
- Antihistamine (first generation)
  
  chlorpheniramine SR 12 mg BID

**Consider**
- Sinus irrigation BID
- Nasal ipratropium
- Sinus CT
ACE Inhibitors: Cough

- 10-15%
- Starts 1 week- 6 months
- Upper airway “tickle”
- ? Accumulated bradykinin
  - Simulate afferent C receptors
- Women > men
- No correlation with asthma
- Stops in 1-30 days
- Angiotensin II receptor antagonists tolerated

Irwin, Chest 2006
Chronic Cough
Hypersensitivity Syndrome

Chronic persistent cough despite appropriate investigation and treatment

Proposed mechanism

• $\Delta$ in peripheral and/or central sensory neural processing for a given stimulus (sensitization)
• Peripheral inflammation alters the activation profiles of cough-evoking sensory fibers

Keller et al Chest 2017 (in press)
Chronic Cough Hypersensitivity Syndrome

AKA

- Vagal neuropathic cough
- Laryngeal sensory neuropathy

Treatment

- **Gabapentin**
  - 100 mg TID up to 600 mg TID
- **Amitriptyline**
  - 10- 25 mg Daily
  - Superior to guaifenesin + codeine
- **Speech Pathology Consult**
Chronic Cough Hypersensitivity Syndrome

Won’t hurt, might help
• Cough drops with pectin
• Dextromethorphan
• Honey
• Zinc

Might help, could hurt
• Narcotics
**Additional considerations**

- *Cancer (lung, metastases, laryngeal)*
- *Chronic aspiration (including foreign body)*
- *Occupational exposures*
- *ILD – Sarcoidosis, IPF*
- *Bronchiectasis*
  - loose cough
- *LV failure*
- *External ear disease*
  - cerumen, foreign body
On the Horizon

Balance: Suppress/Protect

Neurotransmitter level:
- Voltage gated sodium channels
- Transient receptor potential (TRP) channel blockers
- Neurokinin Antagonists
- Neuromodulators
- Purinergic Antagonists (ATP P2X3)
Chronic Cough

Investigate and Treat

A cause of cough is suggested

History, examination, chest x-ray

Smoking, ACE-I

Discontinue

Inadequate response to optimal Rx

Upper Airway Cough Syndrome (UACS)
empiric treatment

Asthma
ideally evaluate (spirometry, bronchodilator reversibility, bronchial provocation challenge) or empiric treatment

Non-asthmatic eosinophilic bronchitis (NAEB)
ideally evaluate for sputum eosinophilia or empiric treatment

Gastroesophageal reflux disease (GERD)
empiric treatment

(for initial treatments see box below)

No response

Inadequate response to optimal Rx
Further Investigations to Consider:
- 24h esophageal pH monitoring
- Endoscopic or videofluoroscopic swallow evaluation
- Barium esophagram
- Sinus imaging
- HRCT
- Bronchoscopy
- Echocardiogram
- Environmental assessment
- Consider other rare causes

Important General Considerations
- Optimize therapy for each diagnosis
- Check compliance
- Due to the possibility of multiple causes
- Maintain all partially effective treatment

Initial Treatments
- UACS: A/D
- Asthma: ICS, BD, LTRA
- NAEB: ICS
- GERD: PPI, diet/lifestyle

Figure 3. Chronic cough algorithm for the management of patients aged ≥15 years with cough lasting >8 weeks. ACE-I = ACE inhibitor; BD = bronchodilator; LTRA = leukotriene receptor antagonist; ICS = inhaled corticosteroid.
References

References


References


WHERE COUGH SYRUP COMES FROM.

Cough! Cough! Cough!

Cough! Cough!