How to treat cough associated with common cold

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Pneumology around the clock
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Common Cold Centre

Part of Cardiff University, Wales, UK

Main interest is in understanding mechanisms of symptoms and symptomatic treatments

Common Cold centre established 1988 to conduct clinical trials on new treatments for common cold and flu
Cough ---- a vital protective reflex

Cerebral cortex

NTS respiratory area of brainstem

Voluntary control

Urge to cough

Sensation of irritation

Vagus nerve

Voluntary control

Respiratory muscles

Cough!

Aspirated food and fluid

Mechanical osmotic pH
Acute cough due to common cold is the most common type of cough and one of the most common symptoms. Defined as cough < 3 weeks.


Acute cough is caused by respiratory viral infection which causes hypersensitivity of airway receptors.
Our study demonstrates that spontaneous, presumably viral, upper respiratory tract infections cause striking increases in bronchial reactivity to inhaled histamine and citric acid aerosols in otherwise normal subjects. This bronchial hyperreactivity was present during infection and for several weeks after recovery, but all the subjects returned to normal within 7 weeks.


Fig. 1. Effect of colds on change in airway resistance (Raw) after inhalation of histamine aerosol (1.6 percent, 10 breaths). Each point is the mean of 9 measurements in one subject. The line of identity is drawn; points above this line indicate bronchoconstriction, and points on the line indicate no change in the Raw after histamine. In healthy subjects (left panel, ▲), histamine aerosol caused only mild bronchoconstriction. Subjects with colds (right panel, ○) showed increased bronchoconstriction after inhalation of histamine aerosol. Seven weeks after the onset of their colds these same subjects (right panel, ●) had responses to histamine that were similar to those of the control subjects (P > 0.5).
In summary, PIV3 infection leads to elevations in TRPV1 expression in the two key cough evoking nerve subtypes in the guinea pig trachea, and this is associated with a hypertussive state with respect to various TRPV1 activating stimuli.
Acute cough

cerebral cortex

Urge to cough

Voluntary control

sensation of irritation

NTS respiratory area of brainstem

+ve / -ve

vagus nerve

hypersensitivity

TRPV1

INFECTION airway inflammation and irritation

respiratory muscles

cough!
Treatments for acute cough can work at three levels:

- Cerebral cortex (psychological)
- Brainstem (cough control)
- Peripheral actions
Treatments for acute cough

peripheral actions
1 peripheral actions

NORMAL COUGH (reflex?)

MECHANICAL CHEMICAL pH

ACUTE HYPERSENSITIVE COUGH (voluntary?)

INCREASED TRPV1 EXPRESSION

VIRAL INFECTION

inflammatory mediators bradykinin, prostaglandins, cytokines, Substance P etc.
Peripherally acting treatments

**ACUTE COUGH**

**EFFECT ON NERVE ENDINGS**
- guaifenesin
- levodropropozine

**EFFECT ON MEDIATORS**
- NSAID’s (nonsteroidal anti-inflammatory drugs)
- corticosteroids
- leukotriene antagonists

**HYPERSENSITIVITY**
Efficacy of levodropropizine

“This analysis indicates that levodropropizine is an effective antitussive drug in children and adults”

Cough scores over 3 evenings, honey and milk, dextromethorphan, levodropropizine

Milk and honey mixture seems to be at least as effective as DM or LDP in non-specific acute cough in children.
Treatments for acute cough

brainstem (cough control)
TREATMENTS acting on brainstem

- Urge to cough
- Voluntary control
- Sensation of irritation
- NTS respiratory area of brainstem
- +ve / -ve
- Respiratory muscles cough!

- Codeine
- Dextromethorphan
- Antihistamines
- Sweet syrups
Mean cough frequency before and after treatment with a single dose of codeine syrup B.P (30mg/10ml) n= 46 and placebo syrup vehicle n = 45
Journal of Clinical Pharmacy and Therapeutics, 17, 175-180.
Subjective scores for cough placebo versus 30mg codeine

Fig. 2. Mean visual analogue scores before and after treatment with a single dose of codeine syrup B.P. (30 mg/10 ml) (●), and syrup vehicle (○). Forty-six subjects received codeine and 45 were treated with vehicle alone. The extremes of the visual analogue scale were labelled ‘no cough’ (maximum score, +50 mm) and ‘worst cough I can imagine’ (maximum score, −50 mm).

Eccles R, Morris S, Jawad M
Severity scores over 3 days for cough, placebo versus 30mg codeine

Table 1. Cough severity scores from home phase diaries expressed as the area under the curve for eight measures over 5 days. Cough severity was scored on a five-point scale from 0 = cough not present to 4 = very severe. A paired t-test on the data showed no difference between the means ($P = 0.23$).

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Placebo</th>
<th>Codeine</th>
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</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>40</td>
<td>41</td>
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<tr>
<td>Mean</td>
<td>18.8</td>
<td>17.2</td>
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<tr>
<td>SD</td>
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<td>6.3</td>
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<tr>
<td>Minimum</td>
<td>5.0</td>
<td>5.7</td>
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<tr>
<td>Maximum</td>
<td>31.0</td>
<td>29.0</td>
</tr>
</tbody>
</table>

Eccles R, Morris S, Jawad M
“Recent placebo-controlled studies have shown that codeine is no more effective than placebo in suppressing cough caused by either upper respiratory disorders or chronic obstructive pulmonary disease. These recent reports are not consistent with several older placebo-controlled studies that demonstrated the efficacy of codeine.”
Sweet taste may modulate cough by generation of endogenous opioid compounds in brainstem. This mechanism is accepted for analgesic effects of sweet substances.

Antitussive effect of sweet taste

Rinsing mouth with sweet solution inhibited capsaicin induced cough but rinsing with bitter tasting solution had no effect.
Treatments for acute cough

cerebral cortex (psychological)
TREATMENTS acting on cerebral cortex

Urge to cough

Voluntary control

sensation of irritation

NTS respiratory area of brainstem

vagus nerve

INFECTION airway irritation

respiratory muscles cough!

Placebo effect of ALL cough treatments

+ve / -ve
Placebo

The placebo is the “most effective medication known to science, subjected to more clinical trials than any other medicine yet nearly always does better than anticipated”

O’ Donnel M, Monitor Weekly 1995
Patients were told that the study was designed to investigate the effects of vitamin E on cough associated with common cold.

Lee et al 2005 Psychosomatic Medicine 67 314-7
Factors influencing psychological effects of cough medicine

- Side effects of medicine
- Environment
- Doctor-patient interaction
- Culture
- Advertising and branding
- Conditioned response
- Formulation and dose
- Physiological effect
- Personality of patient
- Faith, hope, belief
Treatments for acute cough can work at three levels:

- Cerebral cortex (psychological)
- Brainstem (cough control)
- Peripheral actions
ALL SWEET SYRUPS ARE EFFECTIVE ANTITUSSIVES FOR ACUTE COUGH

Sweet placebo syrups containing honey etc. are effective antitussives and until we have a safe and effective pharmacological treatment to reverse cough hypersensitivity associated with viral infection, sweet syrups are still my preferred treatment for pediatric and adult acute cough.
THANK YOU

Cardiff bay