

# The Antiseptic

Estd.1904

Indexed in  
IndMED

A MONTHLY JOURNAL OF MEDICINE AND SURGERY

Email: [admin@theantiseptic.in](mailto:admin@theantiseptic.in)

[www.theantiseptic.in](http://www.theantiseptic.in)

Vol. 113 • No. 12

DECEMBER 2016

ISSN 003-5998 • ₹ 100



**Indians to get free 50 essential medicines**

- Page No : 12

**Cardiac surgery associated acute kidney injury**

- Page No : 20

# Recent Advances in Management of Cough & Cold

**SANJAY AGRAWAL**

## **Introduction**

Cough is a forced expulsive maneuver, usually against a closed glottis and which is associated with a characteristic sound. Cough frequently presents as a troublesome symptom to clinicians working in both primary and secondary care settings.

## **Acute cough**

Acute cough is defined as lasting less than 3 weeks. Acute cough is the commonest new presentation in primary care and is most commonly associated with viral upper respiratory tract infection. In the absence of significant co-morbidity, an acute cough is normally benign and self-limiting. It is the commonest symptom associated with acute exacerbations and hospitalizations with asthma and COPD.

## **Chronic cough**

Chronic cough is defined as one lasting more than 8 weeks. It is reported by 10–20% of adults, commoner in females and obese. Cough accounts for 10% of respiratory referrals to secondary care. Most patients present with a dry or minimally productive cough. Decrement in quality of life is comparable with severe COPD. The presence of significant sputum production usually indicates primary lung pathology. In chronic cough a heightened cough reflex is the primary abnormality.

## **Treatment Strategy of cough and cold**

Since there is no cure for the common cold, treatment has two goals: to make one feel better and to help him/her fight off the virus.

Lots of rest is the key treating a cold. It may require taking 12 hours of sleep each night, so the patients should not set the alarm. Patients may be most comfortable in a warm, humid environment. It's also important to stay hydrated by drinking lots of water and avoiding alcohol and caffeine. This makes mucus flow more freely and helps to relieve congestion.

No specific treatment exists for the virus that is causing cold, but in treating the symptoms one can find relief. For aches and pains accompanied by a fever of 100 degrees or higher, Tylenol rather than aspirin helps to avoid the risk of Reye syndrome, a sometimes fatal condition that occurs in children with viral illnesses, especially if they have taken aspirin. If throat is sore, gargle as often as patient likes with salt water (1/2 teaspoon salt in 1 cup water) will be useful.

One should think twice before using heavily advertised over-the-counter cold and flu medications, which likely to contain drugs for symptoms one may not have and therefore may result in needless overtreatment. The FDA and manufacturers now say that over-the-counter cough and cold drugs should not be given to children under age 4.

Over-the-counter decongestants containing pseudoephedrine can help dry and clear nasal passages, but only temporarily. Decongestant

nasal sprays can help, too, but if they're used for more than three to five days, they may cause a "rebound" effect. This means more mucus and worse congestion. Pseudoephedrine may increase blood pressure and heart rate. Drugs should not be taken without first checking with a doctor if patients have heart disease, high blood pressure, prostate problems, diabetes, or thyroid problems.

Over-the-counter decongestants containing phenylpropanolamine have been pulled voluntarily from the shelves because they increase the risk of stroke.

Over-the-counter cough suppressants, such as those containing dextromethorphan, can be helpful if cough is so severe that it interferes with sleeping or talking.

Antihistaminics seem to help some people, but their effect during colds remains controversial.

Good nutrition is essential for resisting and recovering from a cold. Eat a balanced diet. Taking supplements as needed to ensure one is receiving the recommended dietary allowances for vitamin A, the vitamin B complex (vitamins B1, B2, B5, B6, folic acid), and vitamin C, as well as the minerals zinc and copper is essential. Both vitamin C and zinc are essential for production of infection-fighting neutrophils; without adequate levels, one may be an easy mark for all types of infections. Evidence shows zinc may shorten the duration of a cold, especially in adults if taken within 24 hours of the onset of symptoms. Zinc nasal spray should be avoided as it may lead to permanent loss of smell.

Dr. Sanjay Agrawal,  
Leading Pharmaceutical Consultant and Editor-in-  
Chief of IJMToday,  
6/146, Malviya Nagar, Jaipur - 302 017,  
Rajasthan.

Specially Contributed to "The Antiseptic"  
Vol. 113 No. 12 & P : 17 - 19

After much research, vitamin C is believed to have a small effect in preventing colds, and no benefit in treating a cold. There have been several large studies in adults and in children, but the results have been inconclusive. Taking a lot of vitamin C over a long period of time can be harmful.

Chicken soup has been heralded as a cold therapy since the 12th century. Recent scientific evidence shows mild support for the notion that chicken soup reduces cold symptoms, especially congestion.

Asian healing treatments often use hot soups to treat upper respiratory infections, making use of red pepper, lemongrass, and ginger, in particular.

To ease cold symptoms, the essential oils of aromatherapy may be rubbed on the body, inhaled with steam, diffused into the air, or poured on a cloth to be used as a compress. Rubbing diluted eucalyptus oil on the chest as a decongestant, or inhalation of eucalyptus or peppermint oil to clear stuffiness may be helpful. Adding lavender, cedar, or lemon to steam may also soothe the nasal passages. Inhaling menthol not only provides relief from nasal congestion, but might help inhibit infection as well. Rosemary, thyme, mint, basil, and tea tree oils can also provide relief from symptoms of a cold.

Antitussive therapies should be considered in patients with chronic dry cough when the cause of the increased cough reflex is unexplained and treatment against the potential aggravating factors is not satisfactory<sup>1</sup>. Antitussives can be categorized as acting centrally or peripherally. The common centrally acting antitussive agents used in clinical practice include codeine, pholcodine, dextromethorphan, methadone, and morphine. They exhibit their action directly on the cough center

in the brain and decrease the nerve impulse discharges to the muscles that produce cough. Peripherally acting antitussives may inhibit the responsiveness of the afferent or efferent nerves of the cough reflex that evoke cough<sup>2</sup>. Peripherally acting agents are further grouped as demulcents, local anesthetics (lidocaine, benzocaine, hexylcaine hydrochloride, and tetracaine), and humidifying aerosols<sup>3</sup>.

In India, several cough formulations are available. Most antitussives are combinations of dextromethorphan or codeine, with antihistamines, expectorants, decongestants, and/or antipyretics. These antitussives are useful in the symptomatic relief of dry or non-productive cough. Codeine is one of the most commonly preferred centrally acting cough suppressants. Its efficacy has been proven in animal models<sup>4,5,6</sup> and also in humans,<sup>7,8</sup> where it suppresses artificially induced, disease-related, and unexplained chronic cough. In addition to its antitussive property, codeine has analgesic and sedative effects, which may be useful in relieving painful cough<sup>3</sup>. Dextromethorphan has also been shown to be effective in suppressing cough in animal models as well as in humans<sup>3</sup>. It is non-addictive and does not depress respiration in the usual doses. However, it has no significant analgesic or sedative properties. Pholcodine has a comparable efficacy to codeine, with a longer duration of action and an equivalent or safer toxicity profile<sup>9</sup>.

#### **Potential new treatments for cough**

##### **Recommendations**

There is an urgent need for multicentre phase II trials on new drugs carried out across specialist centers using objective methods of cough counting as well as subjective quality of life and symptom indices.

## **Background**

Chronic cough is associated with many inflammatory airways diseases such as asthma, COPD, post-viral infections, pulmonary fibrosis, and bronchiectasis. In some cases certain drugs can be used to inhibit the underlying inflammatory process that, under certain conditions, cause coughs—for example, corticosteroids for the treatment of asthma or COPD, or PPIs as treatment for gastroesophageal reflux. However, there are patients who cough and do not respond to treatments directed at the cause of the cough, and there are patients in whom there is no identifiable cause to treat. Therefore, there is also a requirement to develop compounds that are targeted to inhibit sensory nerve activity directly (by inhibition of peripheral or central mechanisms), which should in theory inhibit cough of any etiology.

## **New treatments under investigation**

### **Opioids**

Attempts have been made to improve the therapeutic index by topical administration of a peripherally acting polar enkephalin analogue, BW443C81, which was shown to inhibit citric acid induced cough in guinea pigs.<sup>2,1,5</sup> However, in humans there was no effect on capsaicin induced cough in normal volunteers.<sup>2,1,5</sup> A novel opioid peptide, nociceptin, which binds to the opioid receptor-like 1 receptor (NOP) has been shown to suppress capsaicin induced cough in guinea pigs and mechanically induced cough in the cat, but so far no data exist in humans<sup>10,11</sup>.

### **Neurokinin receptor (NK) antagonists**

The NK2 receptor antagonist SR 48968 has been shown to inhibit citric acid induced cough in conscious guinea pigs and

an antitussive effect of NK1 receptor antagonists is still under debate. Although there is a report suggesting an antitussive effect of a dual NK1/NK2 receptor antagonist (FK224) on bradykinin induced cough in asthmatics other studies have failed to demonstrate any antitussive action of compounds of this type. Recent data have implicated a role for NK3 receptor activation in evoking a tussive response possibly via a peripheral mechanism of action, even though there have been no reports of the presence of functional NK3 receptor antagonists in the human lung.

#### **Gamma-aminobutyric acid (GABAB) receptor agonists**

GABAB agonists (such as baclofen) have been shown to inhibit capsaicin induced cough in the conscious guinea pig<sup>12,13</sup> and in normal volunteers and provided some benefit in patients with chronic cough.

#### **Cannabinoid CB2 receptor agonists**

CB2 receptor agonists inhibit guinea pig and human sensory nerve activation in vitro and the cough reflex in guinea pigs, which suggests that the development of CB2 agonists, devoid of CB1 mediated central effects; will provide a new and safe antitussive treatment for chronic cough. No clinical data exist in humans.

#### **Local anesthetics**

Local anesthetics such as lignocaine are delivered locally to the airways and have been shown to attenuate capsaicin induced cough in man<sup>14</sup>. However, the effect is transient and the antitussive effect is accompanied by oropharyngeal anesthesia leading to an increased risk of aspiration of airway secretions and food.

#### **Transient receptor potential (TRP) channels**

The cold and menthol sensitive

receptor (CMR1) has recently been characterized and cloned. Interestingly, menthol has been proposed as an antitussive therapy and has been shown to inhibit citric acid induced cough in normal volunteers. The heat sensitive channel TRPV1 is activated by capsaicin, the main pungent ingredient in hot chilli peppers, and capsazepine, a blocker of this channel, inhibits capsaicin and citric acid induced cough in the guinea pig. An increase in epithelial nerve profiles expressing TRPV1 has been reported in patients with non-asthmatic chronic cough. Compounds of this type are currently in clinical development.

#### **Potassium channel openers**

NS1619, an opener of large conductance calcium activated potassium (BKCa) channels, has been shown to inhibit sensory nerve function and cough induced by citric acid in the guinea pig. ATP sensitive potassium channels may also be a good target.

#### **REFERENCES**

1. Pavord ID, Chung KF. Management of chronic cough. *Lancet*. 2008;371:1375-84.
2. Reynolds SM, Mackenzie AJ, Spina D, Page CP. The pharmacology of cough. *Trends Pharmacol Sci*. 2004;25:569-76.
3. Padma L. Current drugs for the treatment of dry cough. *J Assoc Physicians India*. 2013;61(Suppl 5):9-13.

4. May AJ, Widdicombe JG. Depression of the cough reflex by pentobarbitone and some opium derivatives. *Br J Pharmacol Chemother*. 1954;9:335-40.
5. Chou D, Wang SC. Studies on the localization of central cough mechanism: Site of action of antitussive drugs. *J Pharmacol Exp Ther*. 1975;194:499-505.
6. Bolser DC, Hey JA, Chapman RW. Influence of central antitussive drugs on the cough motor pattern. *J Appl Physiol* (1985) 1999;86:1017-24.
7. Sevelius H, McCoy JF, Colmore JP. Dose response to codeine in patients with chronic cough. *Clin Pharmacol Ther*. 1971;12:449-55.
8. Sevelius H, Colmore JP. Objective assessment of antitussive agents in patients with chronic cough. *J New Drugs*. 1966;6:216-23.
9. Blanchard E, Tunon de Lara M. New insights into the role of pholcodine in the treatment of cough in 2013? *Therapie*. 2013;68:85-91.
10. Bolser DC, Mcleod RL, Tulshian DB, et al. Antitussive action of nociceptin in the cat. *Eur J Pharmacol* 2001;430:107-11.
11. Advenier C, Girard V, Naline E, et al. Antitussive effect of SR 48968, a nonpeptide tachykinin NK(2) receptor antagonist. *Eur J Pharmacol* 1993;250:169-71.
12. Bolser DC, Aziz SM, DeGennaro FC, et al. Antitussive effects of GABAB agonists in the cat and guinea-pig. *Br J Pharmacol* 1993;110:491-5.
13. Bolser DC, DeGennaro FC, O'Reilly S, et al. Peripheral and central sites of action of GABA-B agonists to inhibit the cough reflex in the cat and guinea pig. *Br J Pharmacol* 1994;113:1344-8.
14. Choudry NB, Fuller RW, Anderson N, et al. Separation of cough and reflex bronchoconstriction by inhaled local anaesthetics. *Eur Respir J* 1990;3:579-83.



Self-monitoring of blood glucose can trigger both positive and negative emotional responses. For instance, people may feel reassured when self-monitoring results are in range, but may feel distressed or worried when self-monitoring outcomes are incongruous with expectations, or when proposed actions to target (unexpected) outcomes are unclear.

**Diabetic Medicine.**