



API Delhi Chapter 2025



# Modern Day Cough Conundrums : Role of Codeine

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***Director & Chair***

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Metro Group of Hospitals, INDIA



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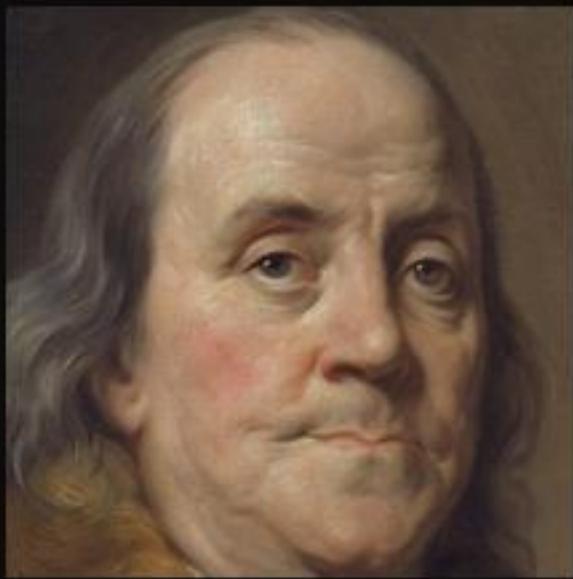
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Love, Cough, & a Smoke, can't  
well be hid.

~ Benjamin Franklin

AZ QUOTES

Ben Franklin, 1706 - 1790

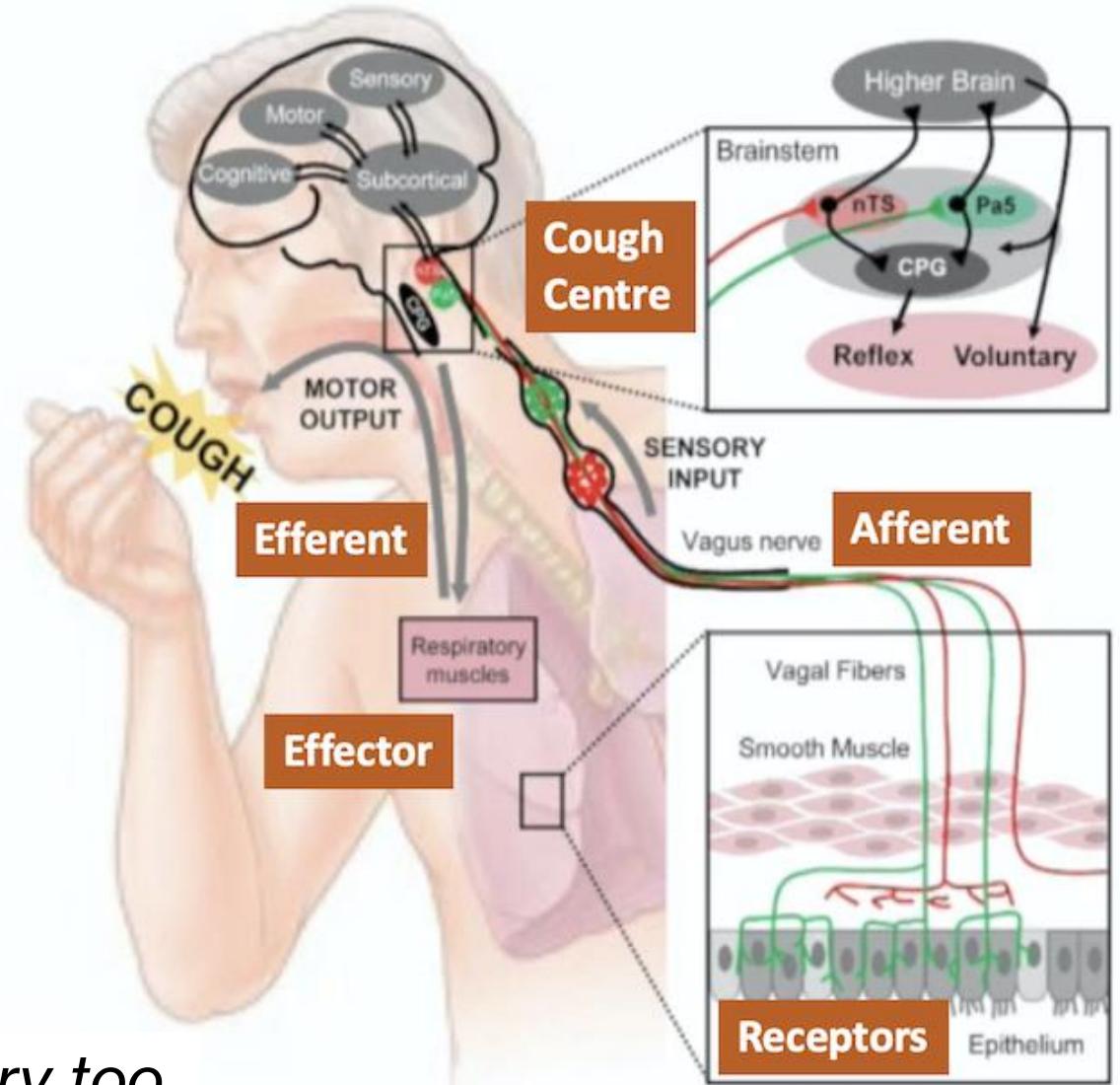
## Protective reflex:

- Receptor
- Afferent
- Cough Centre
- Efferent
- Effector



*It can be voluntary too*

# Cough Reflex

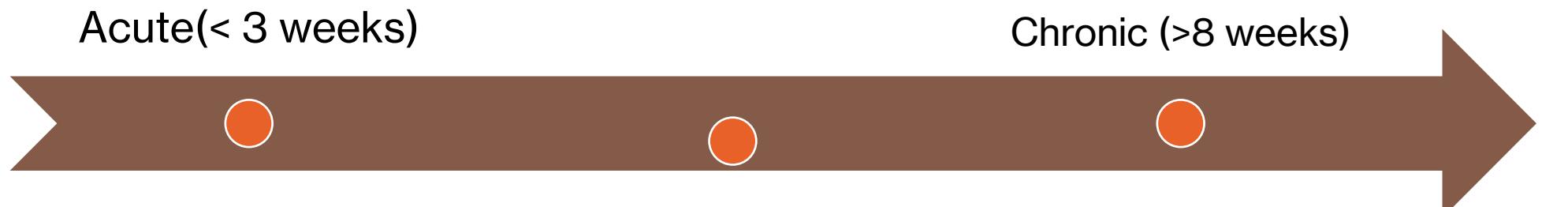


\*Greek proverb

# Why Cough is Important to Patient ?



# Classification of Cough : '*Duration*'



*69% with cough  
are treated for  
the symptoms  
without a  
diagnosis*

Cough of > 8 weeks in adults and > 4 weeks in children

# Chronic Cough :

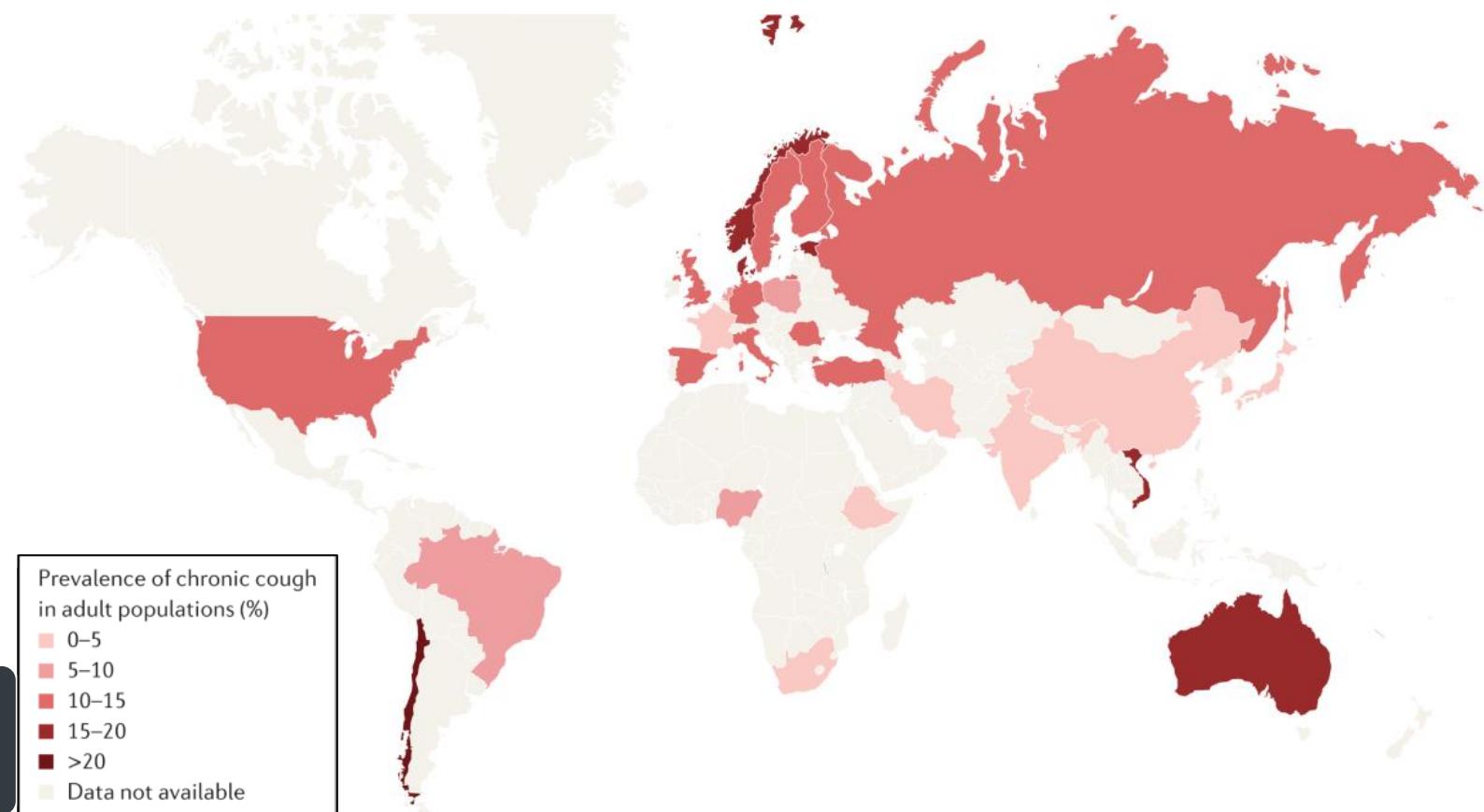
## *Why Need Physician ?*

57% treated with ineffective therapies

70% patients remain unsatisfied by treatment given

Average patient sees 3 physicians, still no diagnosis

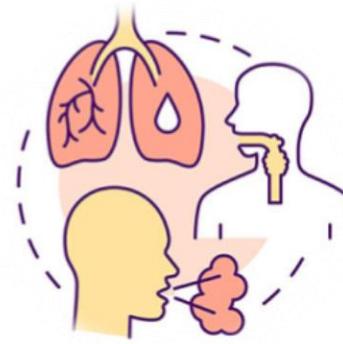
- Affects 10% of population
- Less in Asians and nonsmokers
- Common in females, around 60 years of age



# Dry vs Productive Chronic Cough

Dry **cough incidence** in the adult age group is between 3-12%.<sup>1</sup>

**Productive but not dry chronic** cough is associated with a higher risk of mortality.<sup>2</sup>



1. Bilgin G. General approach to dry cough. Journal of Pulmonology and Intensive Care. 2023 Aug 29;1(3):65-9.
2. Satia I, Mayhew AJ, Sohel N, et al. Respiratory Medicine. 2023 Nov 1;219:107431.

# Chronic Cough : Phenotypes

Chance of treatment of cough is better when the cause of the cough is determined, and specific treatment is given

- Eosinophils Related Cough – OAD
- Smokers Cough – Nicotine / Tobacco Related
- Reflux Cough – Esophageal disorders
- PNDS : Upper Airway Disorders
- Iatrogenic : Drugs
- Idiopathic : Refractory
- Chronic Hypersensitivity Syndrome
  - (***Allotussa or Hypertussia***)



*Vagal sensory fibres  
represent potential  
sites for generation of  
chronic cough*

ERS OFFICIAL DOCUMENT  
ERS GUIDELINES

**ERS guidelines on the diagnosis and  
treatment of chronic cough in adults  
and children**

Alyn H. Morice<sup>1</sup>, Eva Millqvist<sup>2</sup>, Kristina Bieksiene<sup>3</sup>, Surinder S. Birring<sup>4,5</sup>,  
Peter Dicpinigaitis<sup>6</sup>, Christian Domingo Ribas<sup>7</sup>, Michele Hilton Boon<sup>10,8</sup>,  
Ahmad Kantar<sup>11,9</sup>, Kefang Lai<sup>10,21</sup>, Lorcan McGarvey<sup>11</sup>, David Rigau<sup>12</sup>,  
Imran Satia<sup>13,14</sup>, Jacky Smith<sup>15</sup>, Woo-Jung Song<sup>16,22</sup>, Thomy Tonia<sup>17</sup>, Jan W.  
K. van den Berg<sup>18</sup>, Mirjam J.G. van Manen<sup>19</sup> and Angela Zacharasiewicz<sup>20</sup>

# Evaluate Chronic Cough : 5 Steps

## Clinical

- History
- Examination

Step 1

## Imaging

- Lungs
- Upper airways

Step 2

## Profiling

- Clues to etiology

Step 3

## Empiric / Trait Therapy

Step 4

## MDT

- Multiple specialties

Step 5

*Chest X ray is abnormal in only < 7% of cases*

*Absence of heartburn does not exclude reflux as the cause of the cough*

# Cough Assessments

Routine evaluation  
Chest radiography  
Pulmonary function test  
 $?F_{eNO}$   
 $?Blood$  count for eosinophils

History taking and physical examination on presentation  
Cough duration  
Cough impact and triggers  
Family history  
Cough score (using VAS or verbal out of 10)  
HARQ  
Associated symptoms: throat, chest, gastrointestinal  
Risk factors: ACE inhibitor, smoking, sleep apnoea  
Physical examination: throat, chest, ear

# Imaging

Question 1 : Should chest CT be performed routinely on chronic cough patients with normal chest radiograph and physical examination?

- CT findings seen in 6.5% - 58%
- Relationship to chronic cough – ? Questionable
- Potential radiation risk

Do not routinely perform a CT chest in patients with chronic cough who have normal chest radiograph and physical examination  
*(conditional recommendation, very low-quality evidence)*

# Refractory Cough :

Additional evaluation where indicated

- High-resolution oesophageal manometry
- Induced sputum for eosinophils
- Sputum AAFB
- Laryngoscope
- Methacholine challenge
- Chest CT
- Bronchoscopy

Question : Should anti-acid drugs (PPIs and H<sub>2</sub>-antagonists) be used to treat patients with chronic cough?

Recommendation : Suggest that clinicians do not routinely prescribe anti-acid drugs in adult patients with chronic cough

*(conditional recommendation, low-quality evidence)*

# Chronic Cough Management

Proton pump inhibitors are the most effective drugs used in GER coughs. Other drugs used are prokinetic agents, H2 receptor blockers

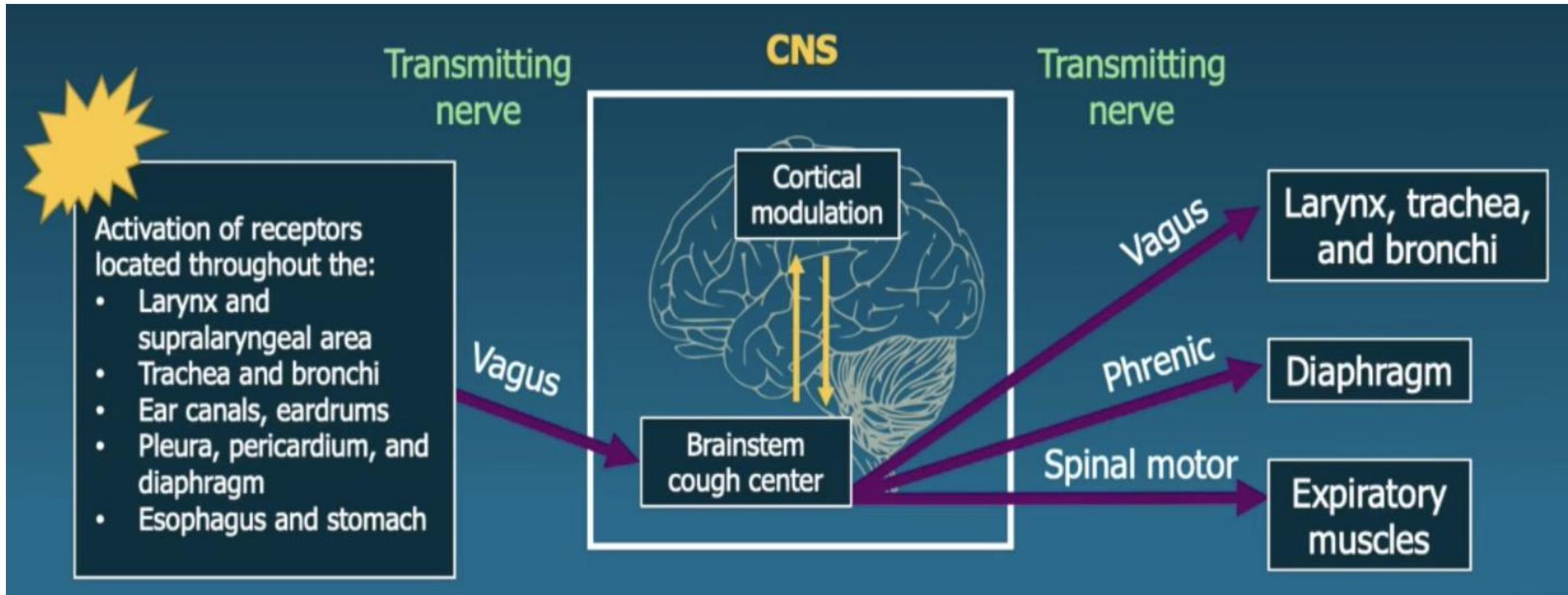
For ACE inhibitor-induced cough, discontinuation of the ACE inhibitor resolves cough in 3-4 weeks after the drug is discontinued.

Question : Should anti-asthmatic drugs (anti-inflammatory or bronchodilator drugs) be used to treat patients with chronic cough ?

Recommendation : We suggest a short-term ICS trial + LRTA's (2–4 weeks) in adult patients with chronic cough

*(conditional recommendation, low-quality evidence)*

# Management of Chronic Cough : *Drugs & Non Drugs Therapy*



**Neuromodulators**

**Narcotics & Non Opioids**

**Cough Control Therapy**

# Guideline Recommendations for Management :

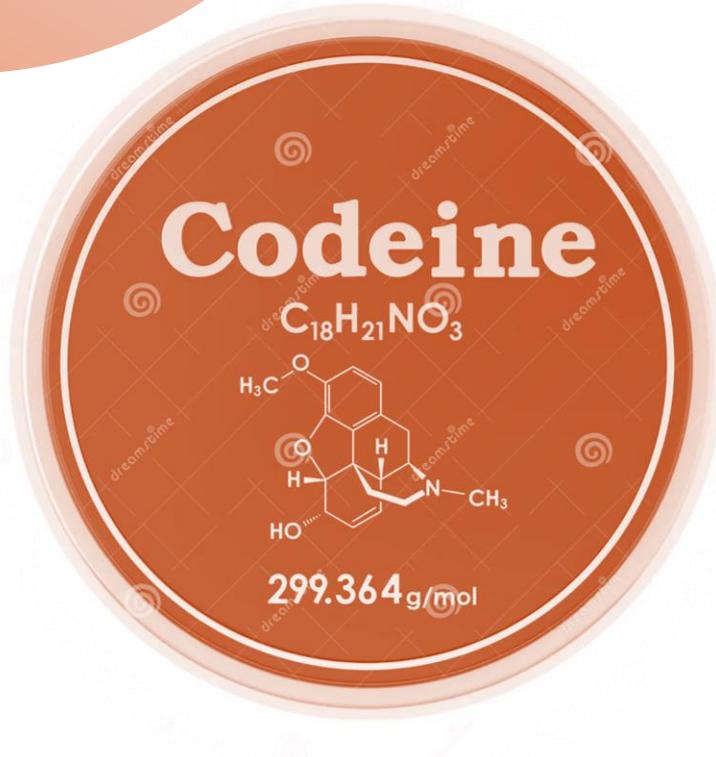
## Comparison of CHEST and ERS Guideline Recommendations

Recommendation	2016 CHEST Guidelines	2020 ERS Guidelines
Speech pathology therapy	✓	✓
Inhaled corticosteroid <sup>a</sup>	±	✓
Gabapentin <sup>b</sup>	✓	✓
Proton pump inhibitor <sup>c</sup>	±	±
Morphine <sup>d</sup>	±	✓

<sup>d</sup>Codeine is useful in treating various etiologies producing chronic cough

CHEST 2018; 153(1):196-209

# Codeine :



An Antitussive via  $\mu$ -opioid receptor in the central nervous system & approved

Naturally occurring opium alkaloid

Prodrug metabolized by cytochrome P450

Less toxic to humans

Peak in an hour and  $\frac{1}{2}$  life is 33.5 hours

Metabolized in liver

Potential for abuse : Physical and Psychological

# Potential Adverse Effects of Codeine

**Constipation** most common **on initiation or ↑dose**

➤ **Increased fluid intake** : and stool softeners

**Nausea/vomiting diminishes** within days

➤ **Anti-emetics** : oral and rectal for treatment

**Sedation** : **fade over time**

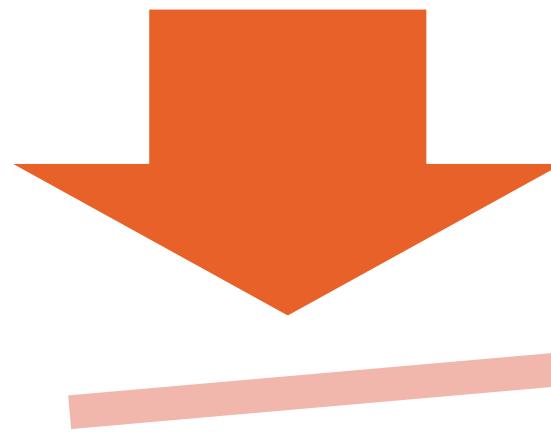
➤ **Naloxone** is specific antidote to reverse overdose

The concomitant use of codeine with other known sedatives, such as alcohol or benzodiazepines, can significantly increase the risk of adverse effects.

# Safety Considerations

- **In less than 12 years**
- **Hypersensitivity Reaction** to codeine
- **Respiratory Depression** due to comorbid respiratory disorders
- **Paralytic ileus**
- **Intestinal Obstruction**
- **Box Warning** : Pediatric patients with obesity or impaired respiration, and with a history of tonsillectomy or adenoidectomy.
- **Box Warning** : **Concomitant use of opioids with benzodiazepines or other CNS depressants**, including alcohol, **may result in respiratory depression, profound sedation, coma, and death**
- MAOi : CI

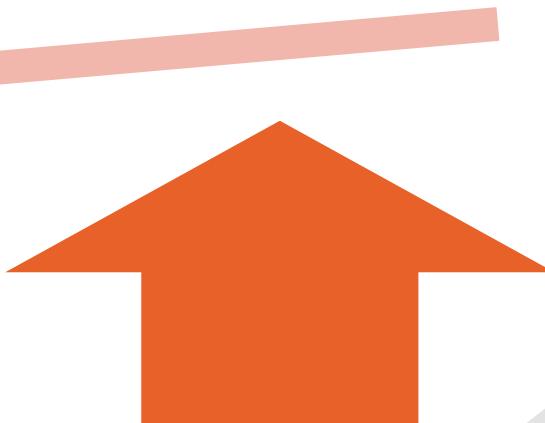
# Potential Benefits vs Risks Needs Review



## Risk

Patients with CRD's , Elderly , malnourished due to disease, or with rapid metabolizer of drugs are at greater risk .<sup>2</sup>

## Benefits



Codeine can be of great benefit in patients with persistent cough despite treatment or if the treatments have failed

# Cough Syndrome Profiles for Codeine Use

Cough	Indication
<b>Acute cough</b>	Cough lasting for <b>&lt;3-week</b> duration and associated with viral URTI
<b>Subacute cough</b>	Cough lasting for <b>&gt;3weeks but &lt;8 weeks</b> duration. <sup>1</sup>
<b>Chronic cough (unexplained)</b>	Defined in adults as cough lasting for <b>&gt;8 weeks</b>
<b>Cough hypersensitivity syndrome</b>	Cough induced by <b>innocuous stimuli</b> (ambient temperature, laughing, talking, and exposure to aerosols)
<b>Postinfectious Cough</b>	Coughs that persist after a common cold or other upper respiratory infection are called post-infectious or post-viral coughs. <sup>3</sup>
<b>Idiopathic chronic cough</b>	Cough that remained <b>unexplained</b> despite extensive investigation. Now replaced with the preferred term “unexplained chronic cough”
<b>Refractory chronic cough</b>	Cough that <b>persists despite optimal treatment</b> according to published best practice guidelines

# Patient Symptom Profiles for Codeine Use

Cough	Indication
<b>Allotussia</b>	Cough triggered at stimulus levels that is insufficient to induce cough in healthy subjects
<b>Hypertussia</b>	<b>Excessive cough</b> to stimuli that are normally cough inducing
<b>Urge to cough</b>	Sensation of <b>airway irritation or “itch” that is not satiated by coughing</b> (sometimes termed “laryngeal paresthesia”). <sup>1</sup>
<b>Nocturnal Cough</b>	Nocturnal cough from reversible airflow limitation and bronchial hyper-responsiveness is a common cough in children with asthma. <sup>2</sup>
<b>Postinfectious Chronic Cough</b>	Coughs that persist after a common cold or other upper respiratory infection are called post-infectious or post-viral coughs. <sup>3</sup>
<b>Hemoptysis</b>	Hemoptysis is the expectoration of blood due to bleed from lung parenchyma or airways. <sup>4</sup>

# Conclusions :

Codeine has multimodal action of antitussive, analgesic, and sedative

Codeine suppresses cough reflex in idiopathic, postinfectious cough, cancer or IPF

Codeine dependence responsible for 2% of admissions to substance abuse

Codeine must be prescribed and dispensed with the utmost caution

Physicians need to balance ethics vis a vis necessity when QoL is impaired



# Thank You

## REVIEW ARTICLE

### Expert Opinion on the Management of Acute and Chronic Cough: An Indian Perspective in Primary Care Setting

Raja Dhar<sup>1\*</sup>, Surinder K Jindal<sup>2</sup>, Deepak Talwar<sup>3</sup>, Nitin Abhyankar<sup>4</sup>, H Paramesh<sup>5</sup>, Murali Mohan<sup>6</sup>, Balamurugan Santhalingam<sup>7</sup>

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