



API Delhi Chapter 2025



Modern Day Cough Conundrums : *Role of Codeine*

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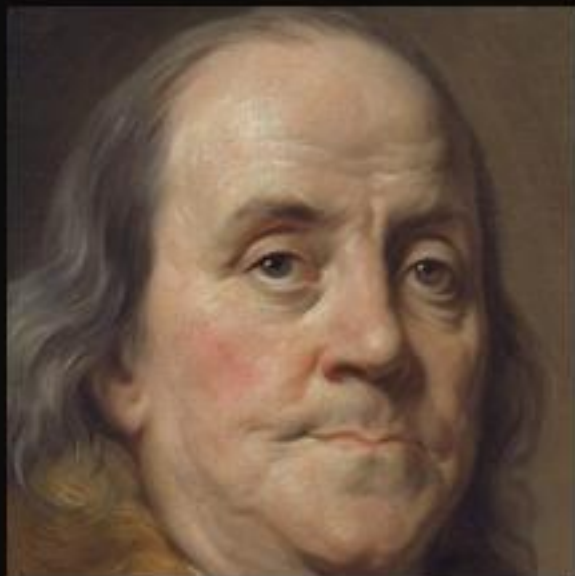
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Love, Cough, & a Smoke, can't
well be hid.

~ Benjamin Franklin

AZ QUOTES

Ben Franklin, 1706 - 1790

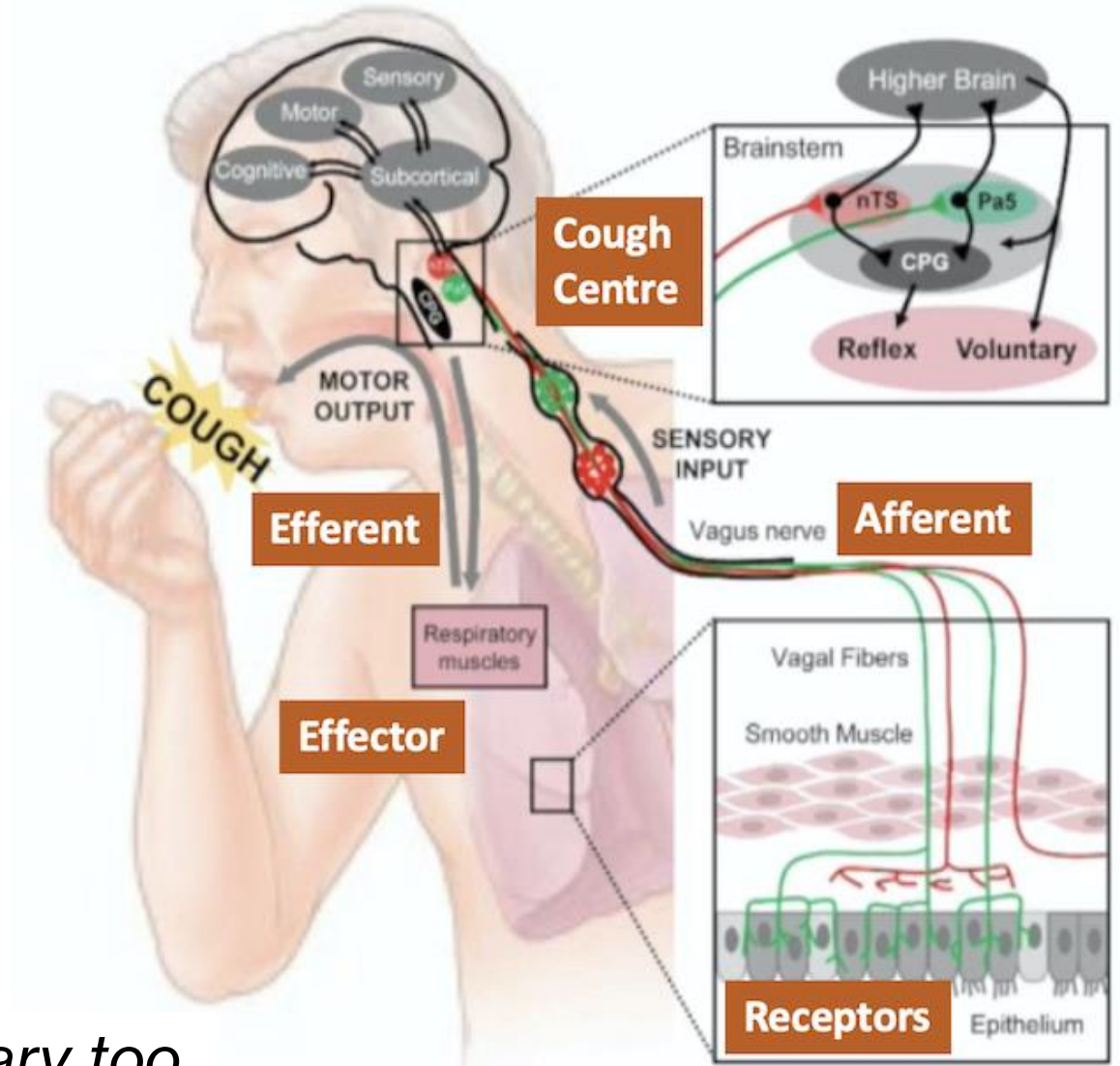
Protective reflex:

- Receptor
- Afferent
- Cough Centre
- Efferent
- Effector

*When at loss to
continue speaking,
Cough'*

It can be voluntary too

Cough Reflex



*Greek proverb

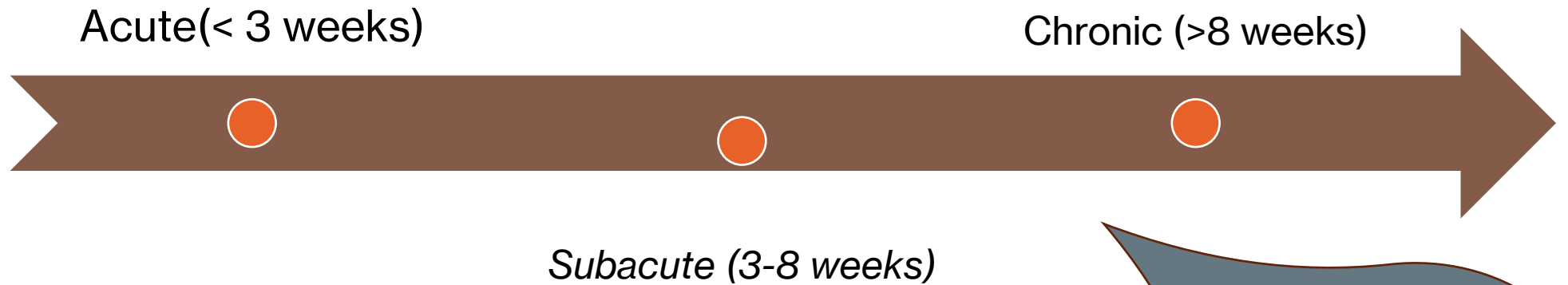
Why Cough is Important to Patient ?



Arch Intern Med 1998;158(10);1657



Classification of Cough : '*Duration*'



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

Chronic Cough :

Why Need Physician ?

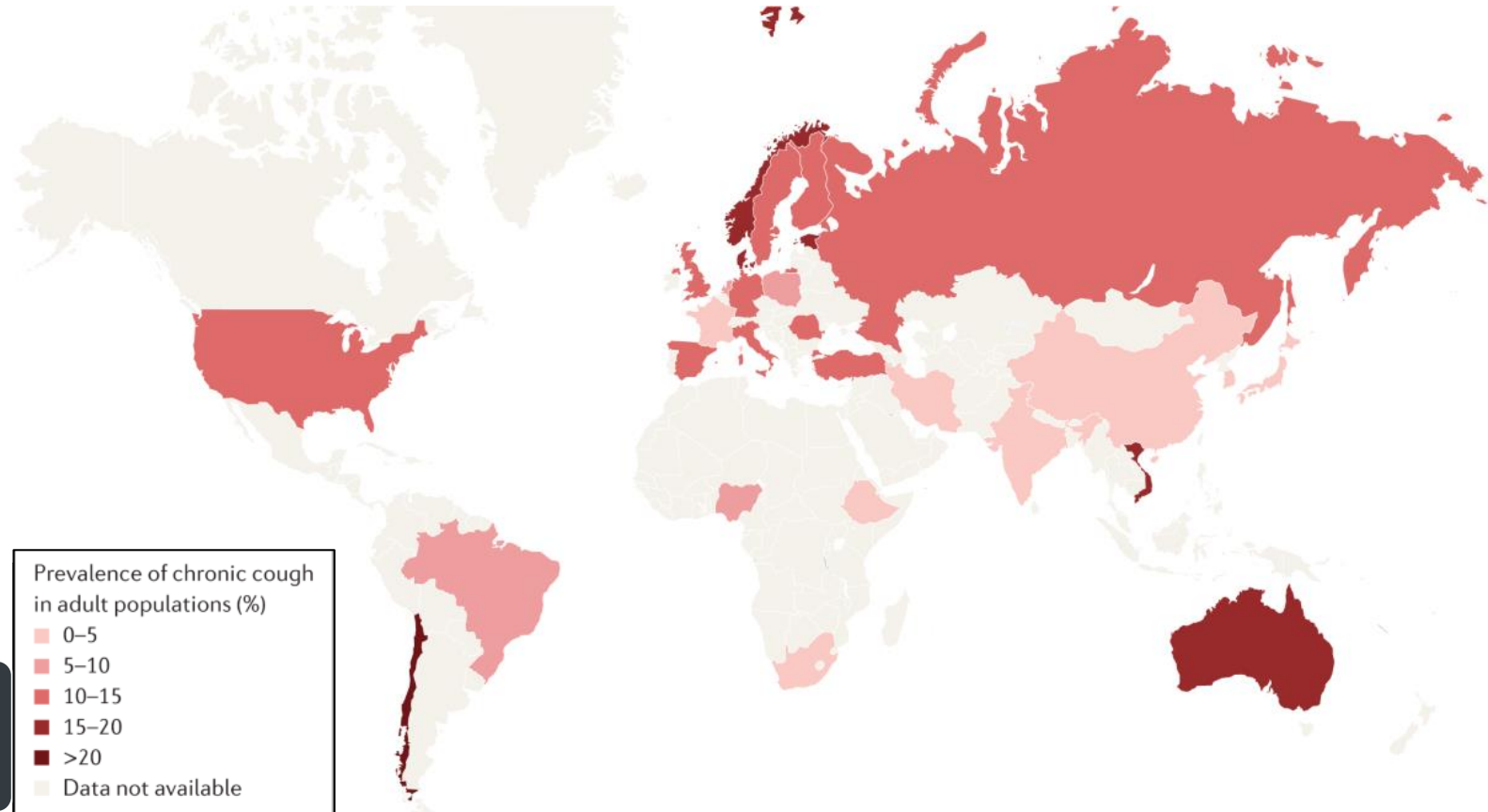
57% treated with ineffective therapies

70% patients remain unsatisfied by treatment given

Average patient sees 3 physicians, still no diagnosis

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

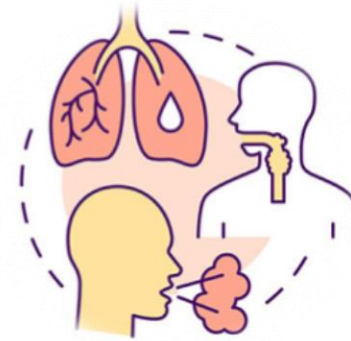
- Affects 10% of population
- Less in Asians and nonsmokers
- Common in females, around 60 years of age



Dry vs Productive Chronic Cough

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

Productive but not dry chronic cough is associated with a higher risk of mortality.²



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***)



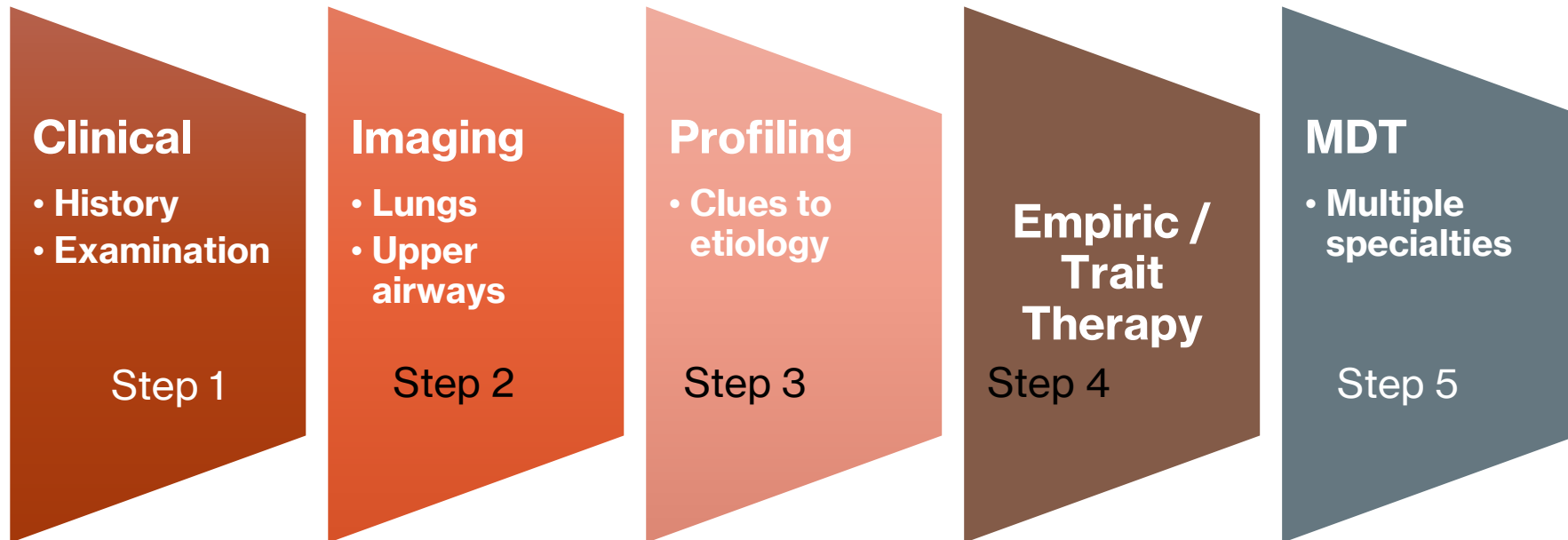
*Vagal sensory fibres
represent potential
sites for generation of
chronic cough*

ERS OFFICIAL DOCUMENT
ERS GUIDELINES

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

Alyn H. Morice¹, Eva Millqvist², Kristina Bieksiene³, Surinder S. Birring^{4,5}, Peter Dicipinaitis⁶, Christian Domingo Ribas⁷, Michele Hilton Boon⁸, Ahmad Kantar⁹, Kefang Lai^{10,21}, Lorcan McGarvey¹¹, David Rigau¹², Imran Satia^{13,14}, Jacky Smith¹⁵, Woo-Jung Song^{16,22}, Thomy Tonia¹⁷, Jan W. K. van den Berg¹⁸, Mirjam J.G. van Manen¹⁹ and Angela Zacharasiewicz²⁰

Evaluate Chronic Cough : 5 Steps



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

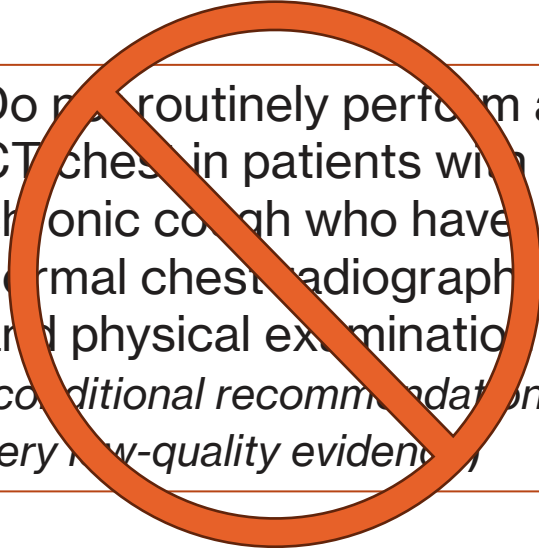
History taking and physical examination on presentation
Cough duration
Cough impact and triggers
Family history
Cough score (using VAS or verbal out of 10)
HARQ
Associated symptoms: throat, chest, gastrointestinal
Risk factors: ACE inhibitor, smoking, sleep apnoea
Physical examination: throat, chest, 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 H₂-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

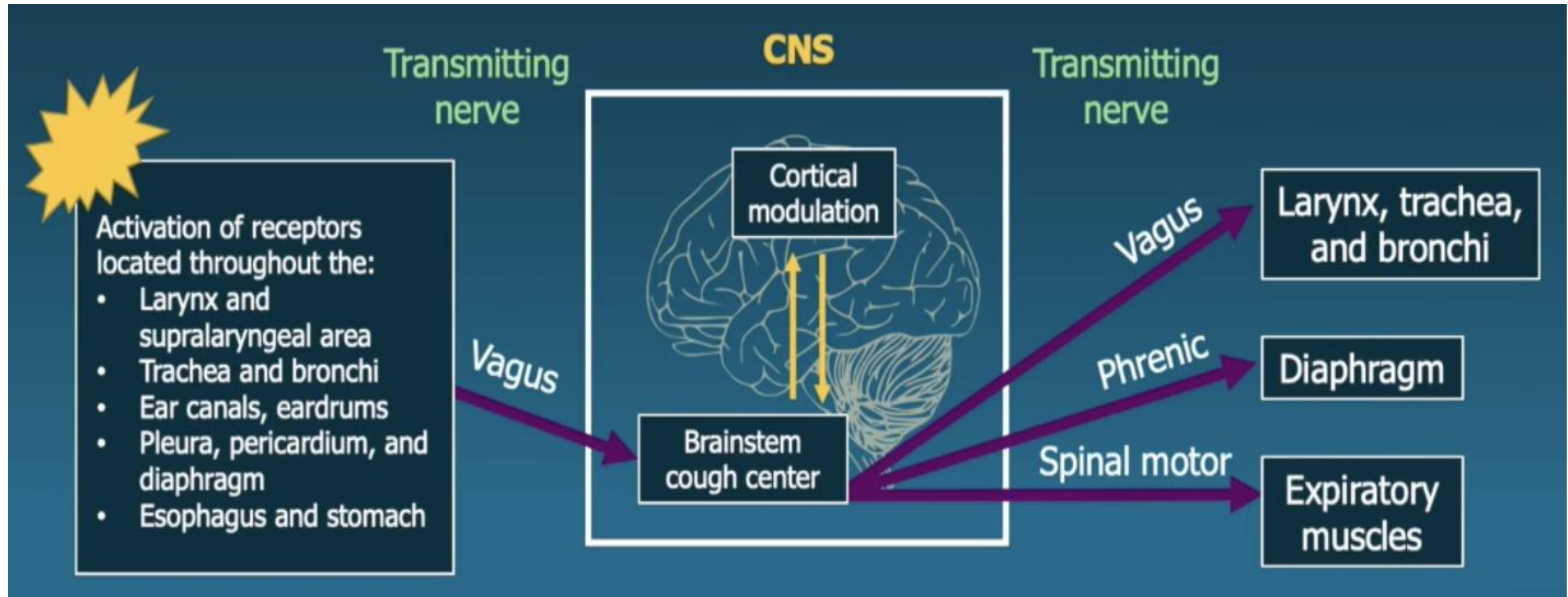
For ACE inhibitor-induced cough, discontinuation of the ACE inhibitor resolves cough in 3-4 weeks after the drug is discontinued.

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 (2–4weeks) 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 ^a	±	✓
Gabapentin ^b	✓	✓
Proton pump inhibitor ^c	±	±
Morphine ^d	±	✓

^dCodeine is useful in treating various etiologies producing chronic cough

Codeine :



An Antitussive via μ -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



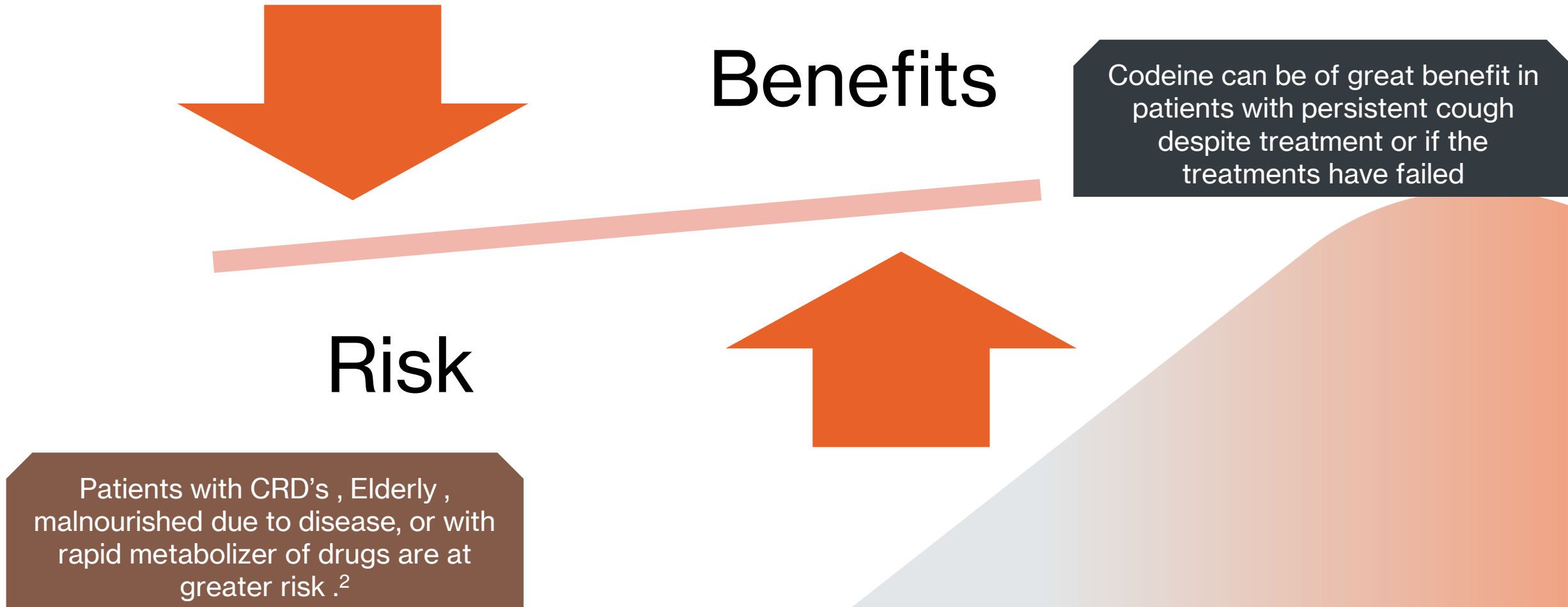
Naloxone is specific antidote to reverse overdose

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



Cough Syndrome Profiles for Codeine Use

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

Patient Symptom Profiles for Codeine Use

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

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^{1*}, Surinder K Jindal², Deepak Talwar³, Nitin Abhyankar⁴, H Paramesh⁵, Murali Mohan⁶, Balamurugan Santhalingam⁷

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