Impairment of Cough and its Consequence

강동경희대학교병원

호흡기-알레르기내과. 이정미

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Introduction

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- **Definition of cough**
  - ✓ **Natural defense mechanism** that effectively protect the respiratory tract from inhaling foreign bodies and by clearing excessive bronchial secretions
  - ✓ **Important defensive reflex** that occurs through the stimulation of a complex reflex arc

  - ✓ One of the **most common symptoms** for which outpatient care is asked

Introduction

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- **Classification based on during of Cough**

1. Acute cough

- ✓ Persists for **<3 weeks**
- ✓ most frequently upper airway infection and bronchitis
- ✓ physiological response to a foreign body, irritant dust or noxious chemicals

2. Subacute cough

- ✓ Persists for 3 to 8 weeks
- ✓ Most frequently caused by post-infectious cough

3. Chronic cough

- ✓ Persists for **>8 weeks**
- ✓ peaks in patients in their 50s and 60s
- ✓ twice as common in women

Epidemiology

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PLOS ONE

Cough in the Elderly Population: Relationships with Multiple Comorbidity

Woo-Jung Song[1,2], Alyn H. Morice[3], Min-Hye Kim[1,2], Seung-Eun Lee[1,2,4], Eun-Jung Jo[1,2,4], Sang-Min Lee[5], Ji-Won Han[6], Tae Hui Kim[6], Sae-Hoon Kim[1,2,4], Hak-Chul Jang[4], Ki Woong Kim[6,7], Sang-Heon Cho[1,2], Kyung-Up Min[1,2], Yoon-Seok Chang[1,2,4*]

- ✓ Cross-sectional analysis
- ✓ Using a baseline dataset from the KLoSHA(Korean Longitudinal Study on Health and Aging), a community-based elderly population cohort study
- ✓ From September 2005 to August 2006
- ✓ Persons aged ≥65 years old

PLoS ONE 8(10): e78081

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① **Frequent cough**

"Do you usually cough as much as four to six times a day, four or more days a week?"

② **Chronic persistent cough**

"Do you usually cough like this on most days for three consecutive months or more during the year?"

③ **Nocturnal cough**

"Have you been wakened by an attack of coughing at any time in the last 12 months?"

PLoS ONE 8(10): e78081

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- **Prevalence of cough**
  - ✓ **Frequent cough** : 9.3%
  - ✓ **Chronic persistent cough** : 4.6%
  - ✓ **Nocturnal cough** : 7.3%

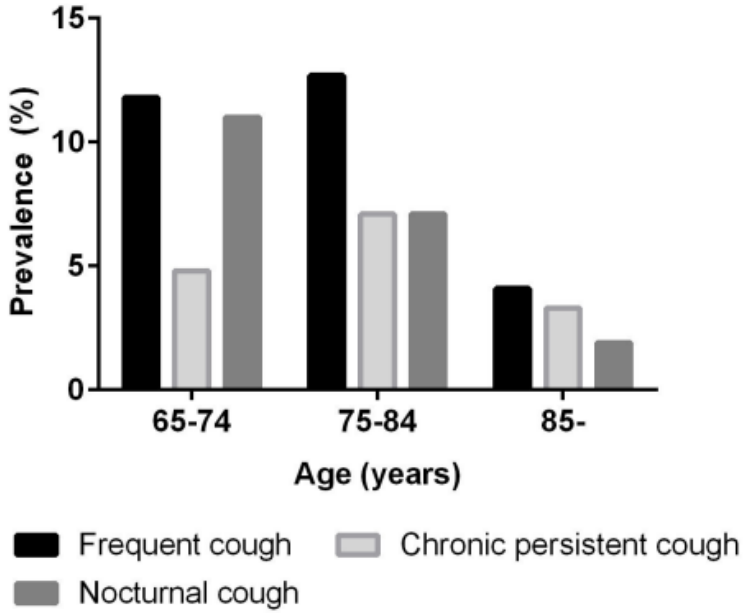

Figure 1. Prevalence of cough according to age groups.

Epidemiology

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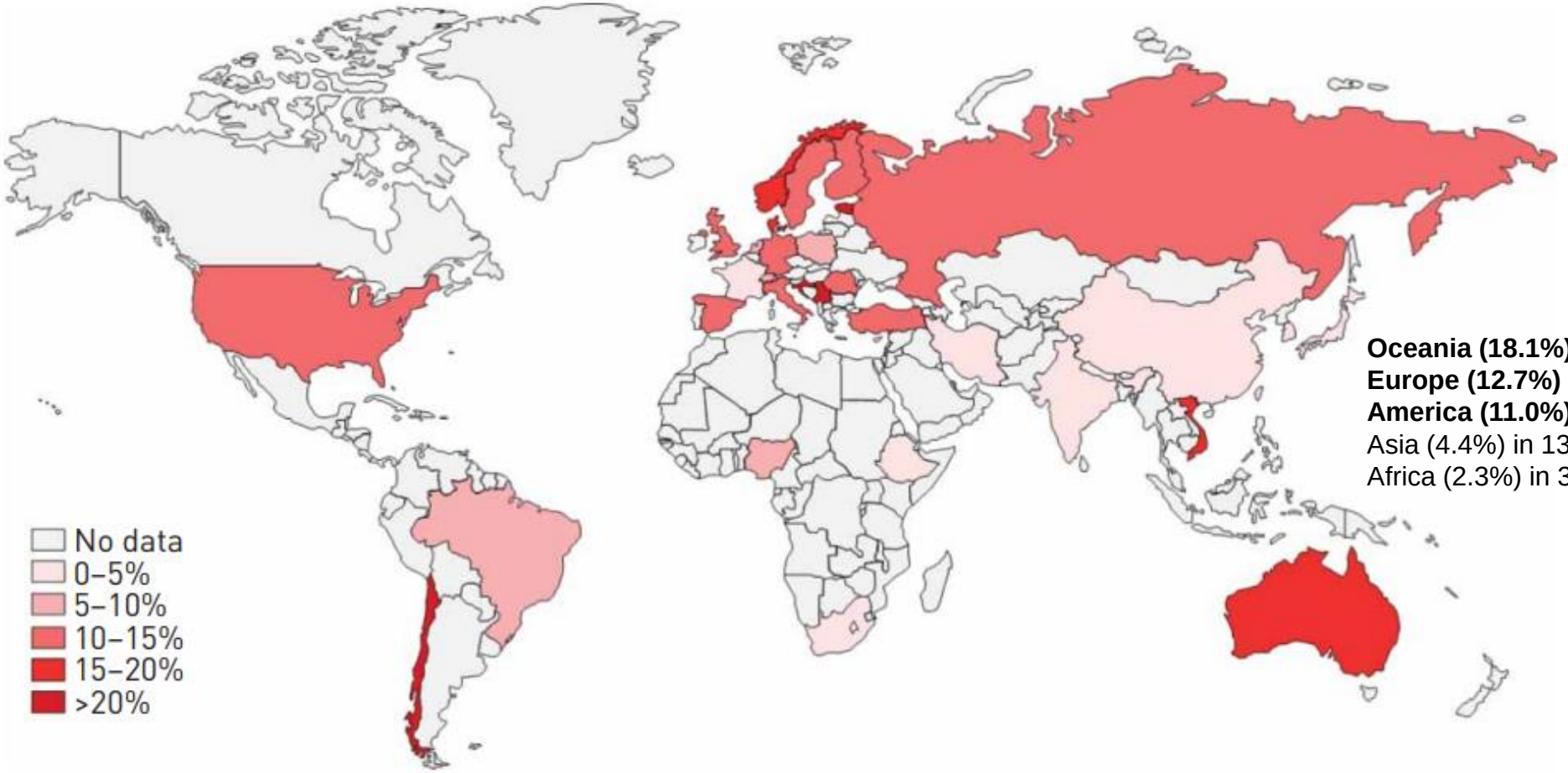
- **Map showing the pooled prevalence of chronic cough by country**



Oceania (18.1%) in 5541 subjects
Europe (12.7%) in 344522 subjects
America (11.0%) in 60585 subjects
Asia (4.4%) in 131566 subjects
Africa (2.3%) in 34625 subjects

✓ **Overall prevalence** of chronic cough : **9.6%** (95% CI 7.6–11.7%; I^2=99%; 576 839 subjects)

Eur Respir J 2015; 45: 1479–1481

Mechanism of cough

Mechanism

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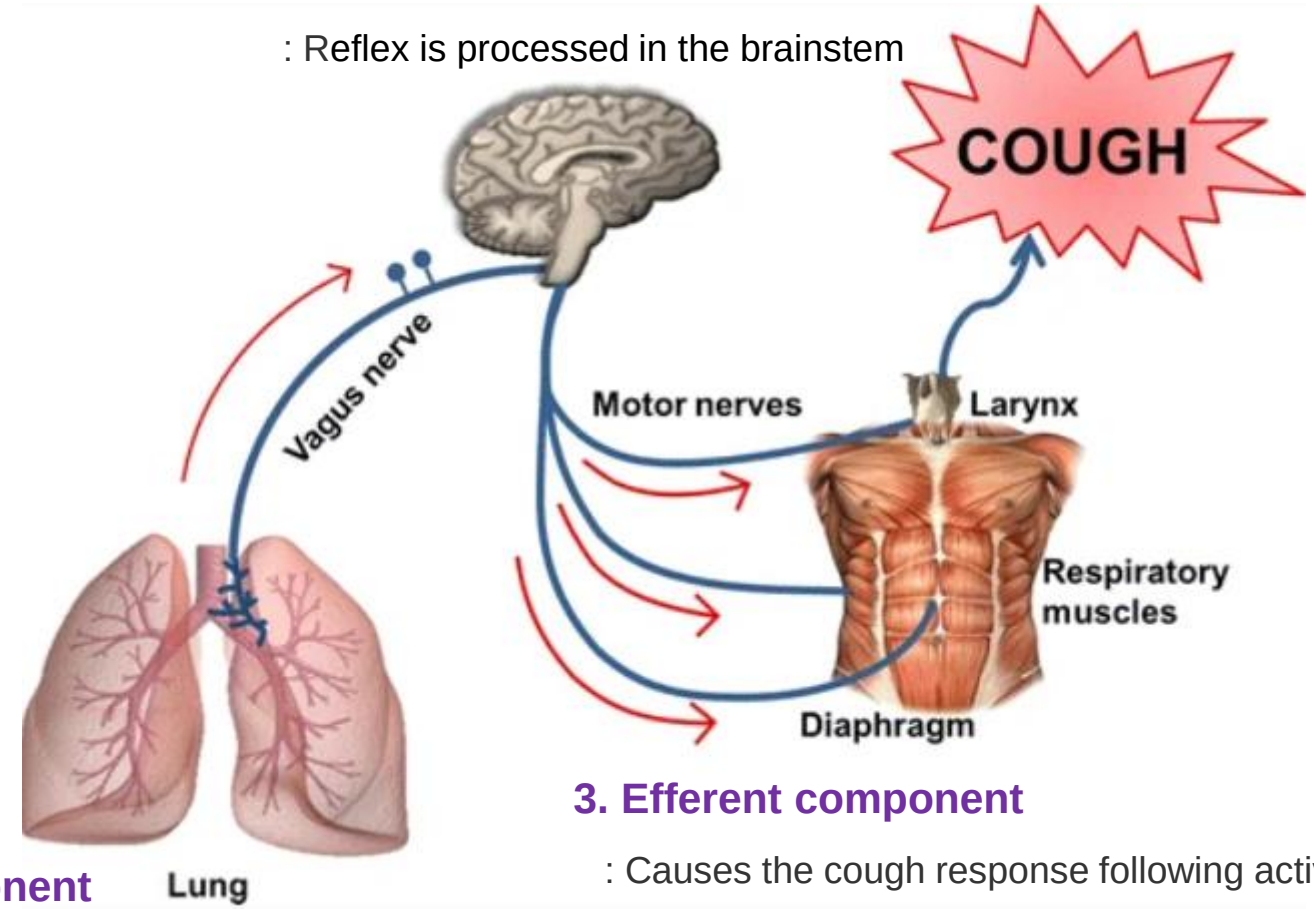
- **The cough reflex**

2. Central component

: Reflex is processed in the brainstem



3. Efferent component

: Causes the cough response following activation of motor nerves

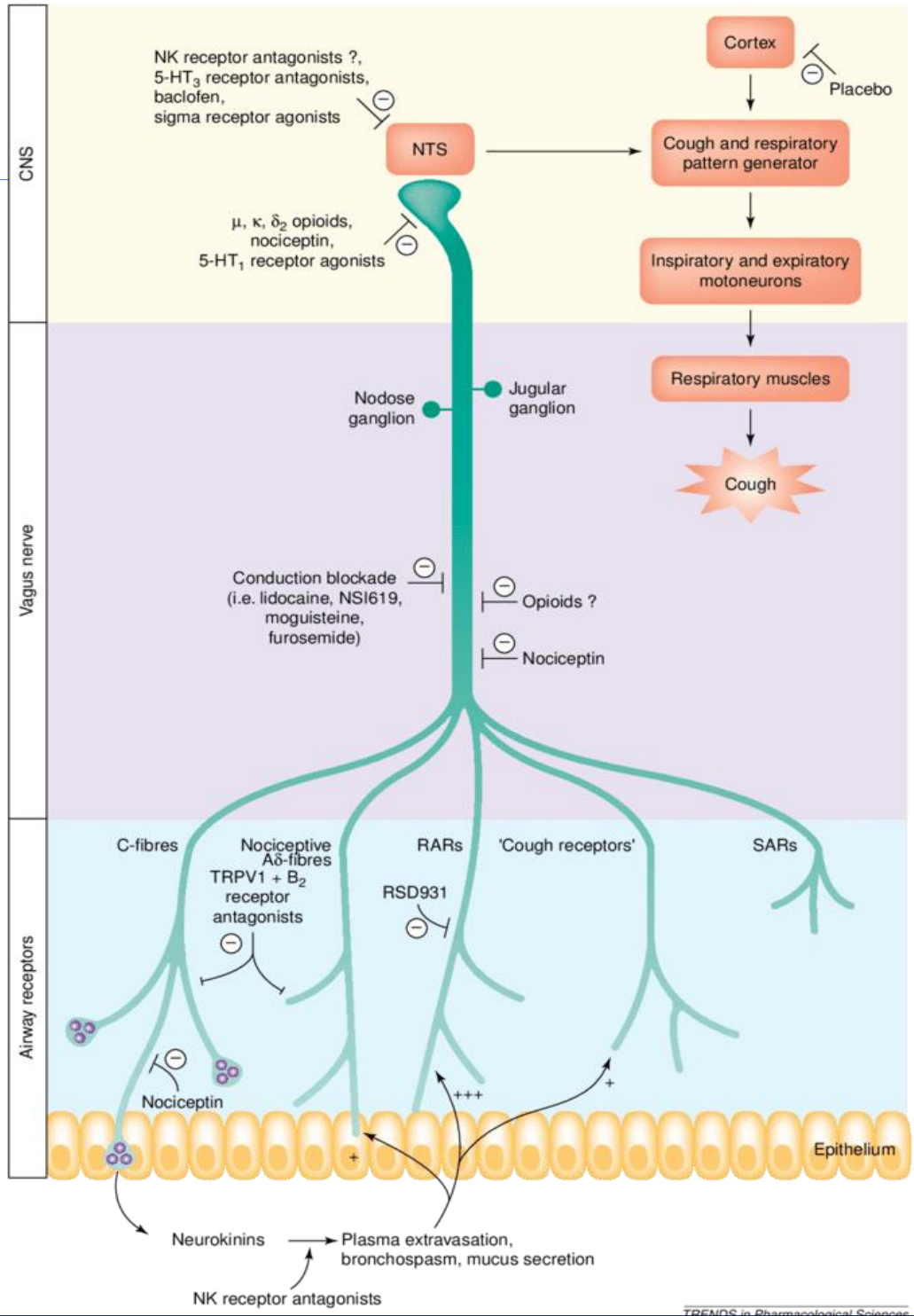
1. Afferent component

: Initiates the reflex following sensory nerve activation

Naunyn-Schmiedeberg's Archives of Pharmacology volume 388, 401–420 (2015)

Mechanism

1. **Afferent pathway**
   - **Sensory nerve fibers** (branches of the vagus nerve) located in the ciliated epithelium of the upper airways and the diaphragm
   - **Ion channel → action potential**
   - Afferent impulses go to the medulla diffusely
2. **Central Pathway (cough center)**
   - Located in the upper brain stem and pons
   - **NTS(nucelus tractus solitaries)**
3. **Efferent pathway**:
   - Impulses from the cough center travel via the vagus, phrenic, and spinal motor nerves to diaphragm, abdominal wall and muscles



Mechanism – (1) Afferent pathway

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- **Two type of vagal sensory neurons by conduction velocity**

Aδ-fibers

- Suggested to be involved in the protective cough reflex
- Nerve terminals mainly in large airways (larynx, trachea, main bronchi)
- Thinly myelinated, faster-conducting fibers (~5 m/sec)
- Characteristic subepithelial branching structure

Stimuli:

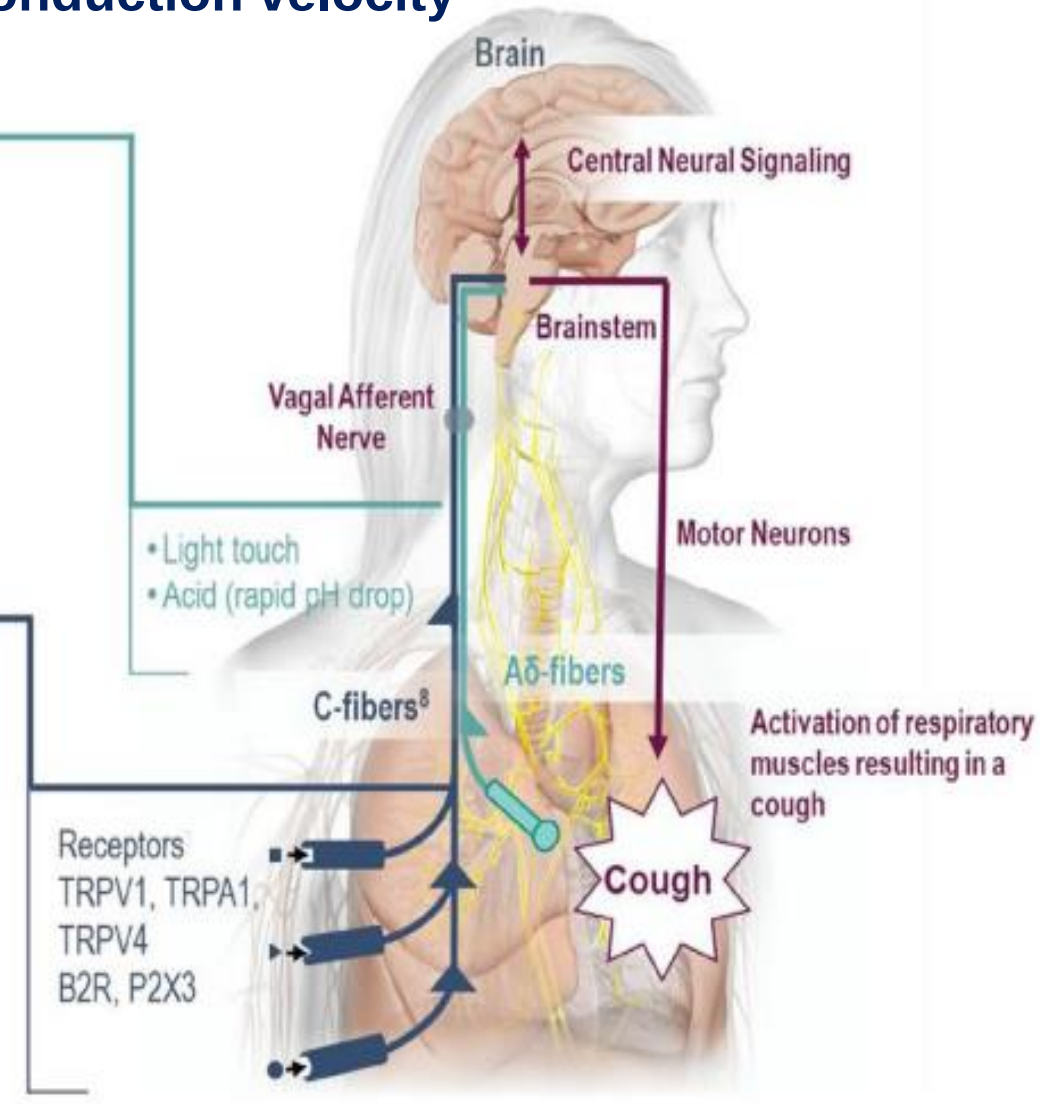
- Mechanical: light touch (eg, particulates or mucus)
- Acid, with a rapid drop in pH (eg, gastric fluid aspiration)

C-fibers

- Unmyelinated, slower-conducting fibers (~1 m/sec)
- Nerve terminals more in peripheral airways
- Extensive network (plexus) just under and projecting into the airway mucosal epithelium

Stimuli:

- Chemical irritants (eg, cigarette smoke, pollutants, ozone)
- Inflammatory mediators (eg, bradykinin)



Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, Volume 5, 2021 - Issue 6

Mechanism – (1) Afferent pathway

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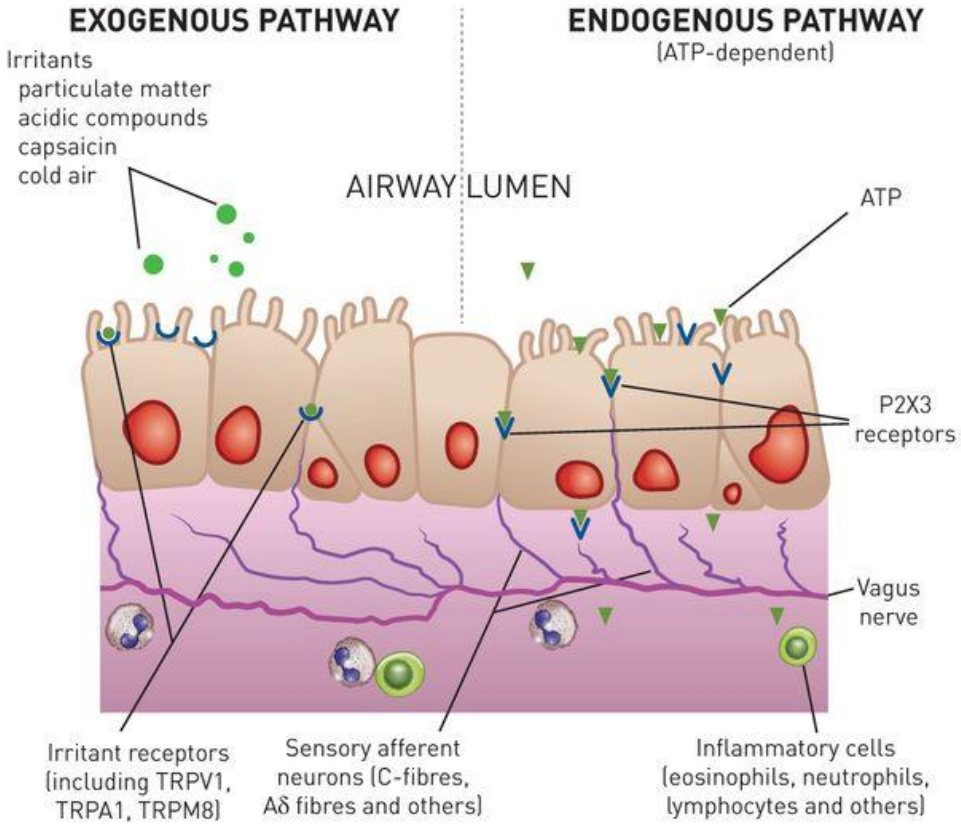
1. Exogenous pathway

- Triggered by **physical and chemical stimuli** originating external to the lung (e.g. cold air, aspirated food, acids)
- Receptors : **TRPV1, TRPA1, TRPM8**

2. Endogenous pathway

- Triggered by **ATP** originating from within the lung itself (possibly in response to inflammation or other causes of tissue stress)
- ATP interacts with **P2X3**
- Greater importance in **chronic refractory cough**



Eur Respir J 2019; 54: 1900889

Mechanism – (1) Afferent pathway

Tussive stimuli from various sources

→ Increase the calcium influx

→ Leading to ATP release from the open pannexin-1 channel

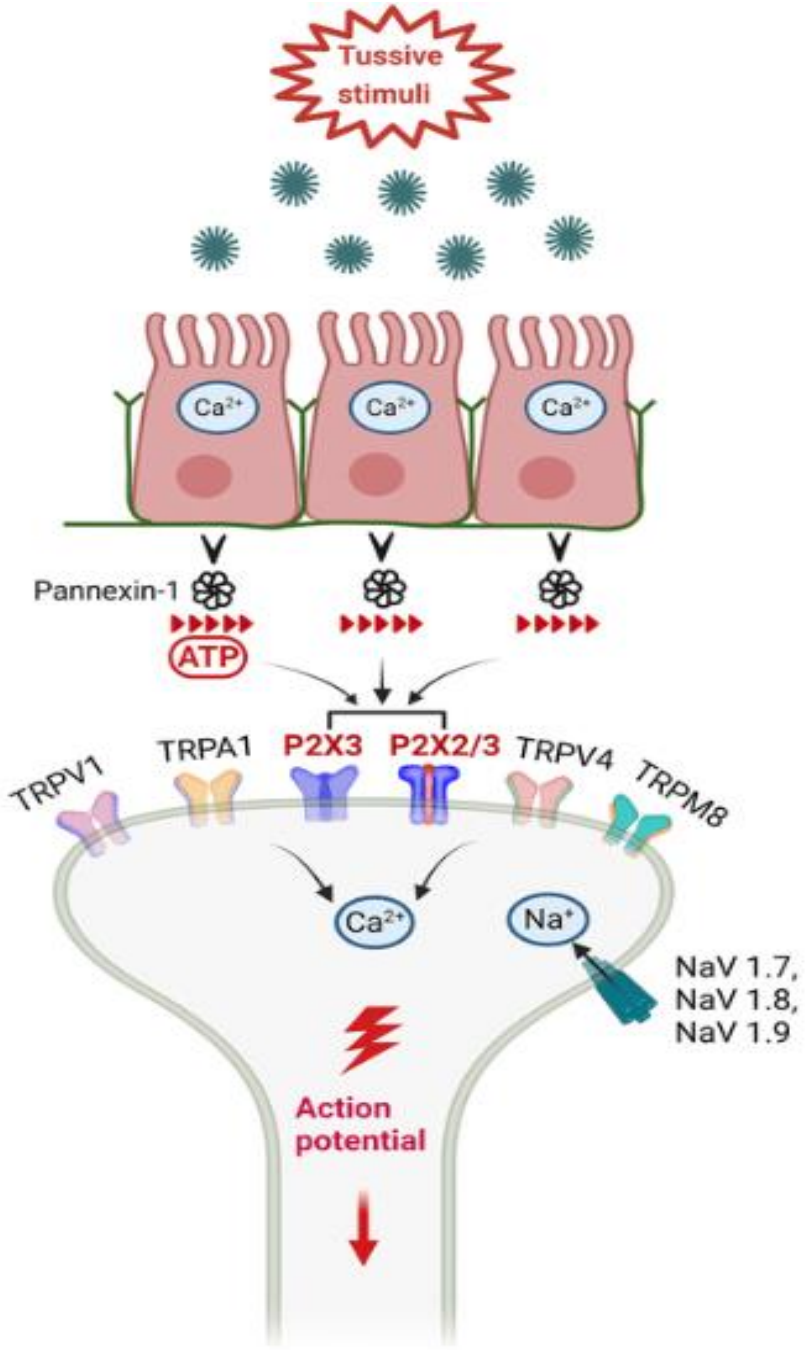
→ Activates **P2X3, P2X2/3** receptors on sensory neurone within the airway mucosa

+

TRPV1,TRPA1, TRPV4, TRPM8 activated by irritants

↓

Action potential



Purinergic Signalling (2022) 18:289–305

Mechanism – (2) Central pathway

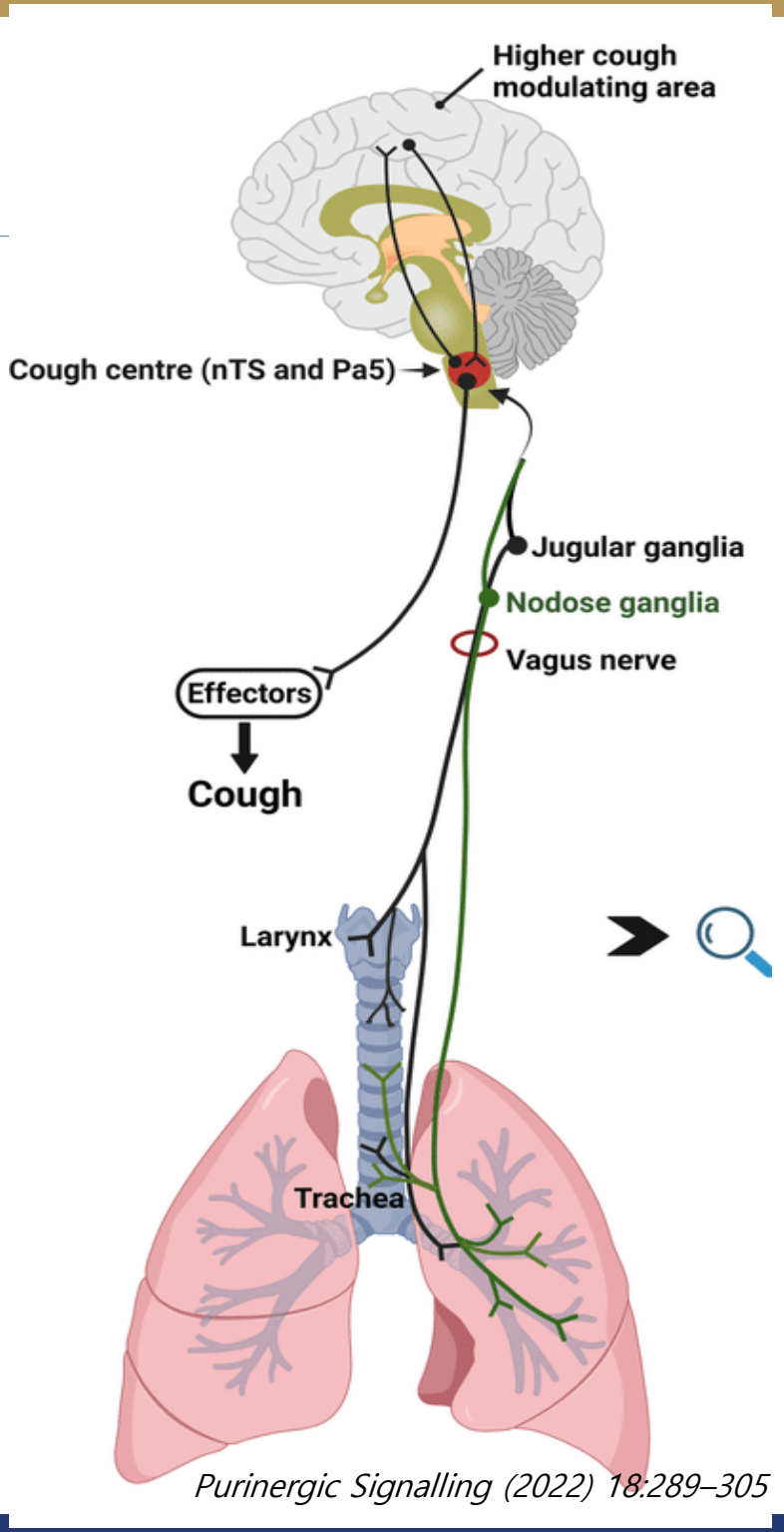
✓ Most of the lung sensory neurons come from the **vagal innervation**

① **Nodose ganglia**

- Innervates most of **intrapulmonary sites**
- Communicates with the **NTS(nucelus tractus solitaries)**

② **Jugular ganglia**

- Innervate most of **extrapulmonary sites**
- Reaches the **paratrigeminal center (Pa5)**



Purinergic Signalling (2022) 18:289–305

Mechanism – (2) Central pathway

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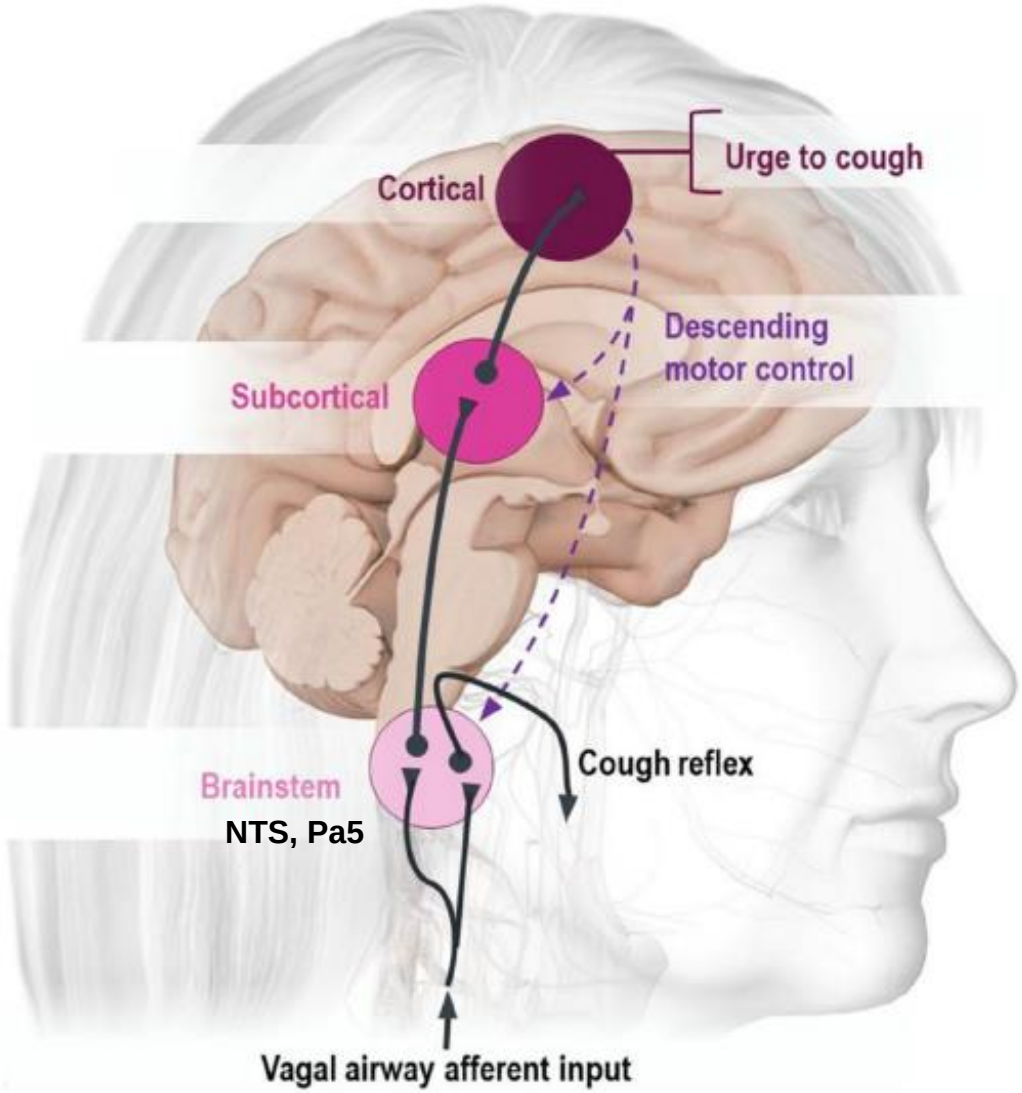
Signal reaches the first order synapse in the NTS(nucleus tractus solitarius) and Pa5 (paratrigeminal nuclei)

→ Second order neurons relay the signal to the **thalamus**

→ Third order neurons to the primary **somatosensory cortex**

→ Urge to cough

→ If strong enough, will evoke coughing



Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, Volume 5, 2021 - Issue 6

Impairment of cough

Impairment of cough

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- **Weak or ineffective cough** compromised the ability to clear lower respiratory tract infection, predisposing to **more serious infections and their sequelae**

- **Causes of impaired cough**
  - ① Decreased respiratory muscle strength
  - ② Chest wall deformity
  - ③ Impaired glottic closure
  - ④ Abnormal airway secretion
  - ⑤ Central respiratory depression (anesthesia, sedation or coma)

Impairment of cough

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- **Aspiration**
  - ✓ Oropharyngeal or gastric contents into the lower respiratory tract

- **Loss of normal functioning of the cough reflex**
  - ✓ Cause of a significant proportion of mortality in the elderly
    - → Primarily through the development of **aspiration pneumonia**

SHORT PAPER

Impaired cough reflex in patients with recurrent pneumonia

A Niimi, H Matsumoto, T Ueda, M Takemura, K Suzuki, E Tanaka, K Chin, M Mishima, R Amitani

Thorax 2003;**58**:152–153

- ✓ **Recurrent pneumonia**
  - At least two episodes of pneumonia in 1 year
  - Three or more episodes at any time

- ✓ **7 patients** with recurrent pneumonia but **no underlying condition**

  → They may have unknown defects in host defence mechanisms such as cough reflex

  → **Capsaicin cough sensitivity**

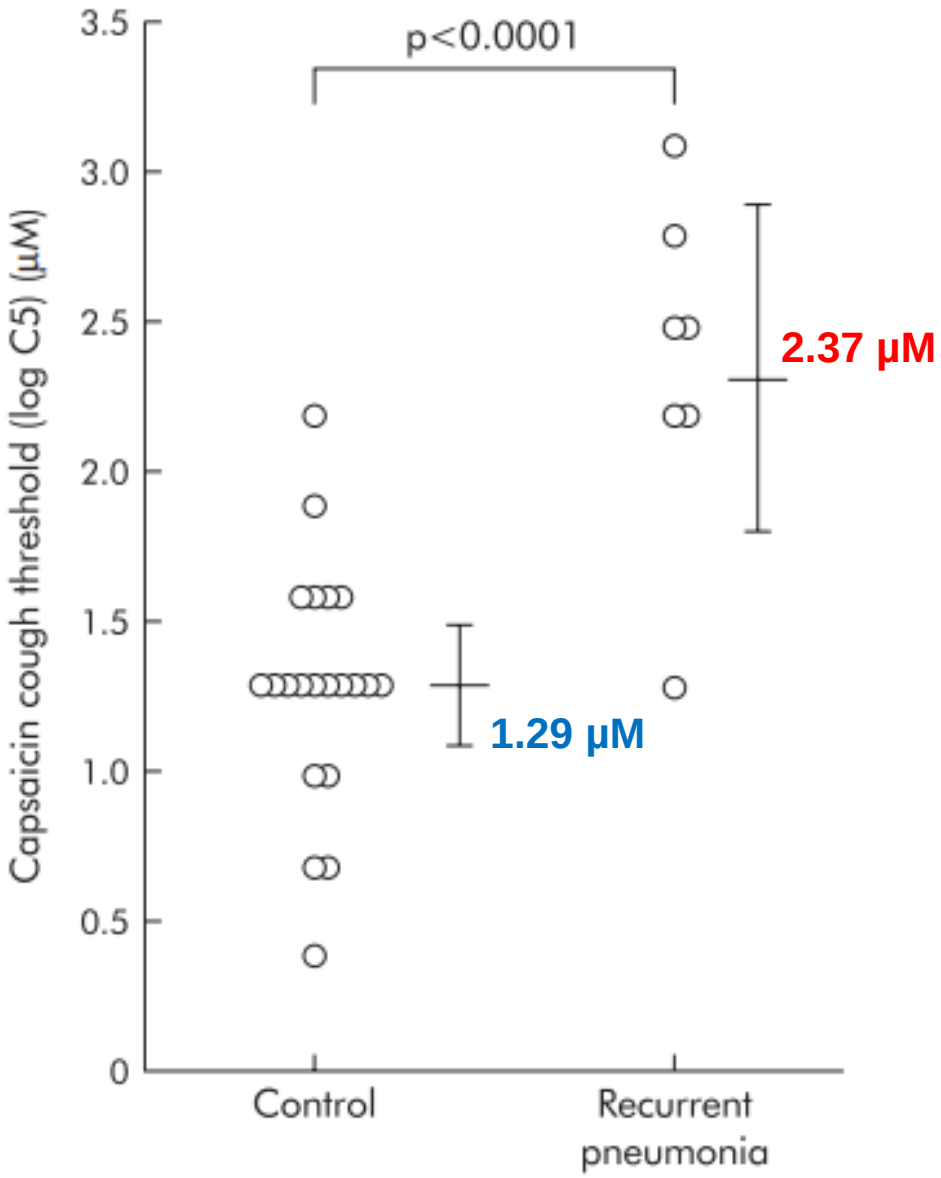


Figure 1 Capsaicin cough threshold (log C5) in patients with recurrent pneumonia and control subjects. Bars indicate mean (95% CI).

- Ten doubling concentrations of capsaicin solution (1.22–625 µM) were inhaled until five or more coughs were induced

- Log C5 was significantly higher in patients than in control subjects (mean 2.37 µM (95% CI 1.84 to 2.90) v 1.29 µM (95% CI 1.11 to 1.47); p<0.0001, fig 1)

➔ **Impaired cough reflex** may be involved in the **pathogenesis of recurrent pneumonia**

Thorax 2003;58:152–153

CHEST Volume 124, Issue 3, September 2003, Pages 1009-1015

Clinical Investigations

MISCELLANEOUS

Impaired Efficacy of Cough in Patients With Parkinson Disease

Ebihara Satoru MD, PhD [a], Saito Hiroshi MD, PhD, FCCP [b], Kanda Akio MD [a], Nakajoh Mizue MD, PhD [a], Takahashi Hidenori MD, PhD [a], Arai Hiroyuki MD, PhD [a], Sasaki Hidetada MD, PhD, FCCP [a]

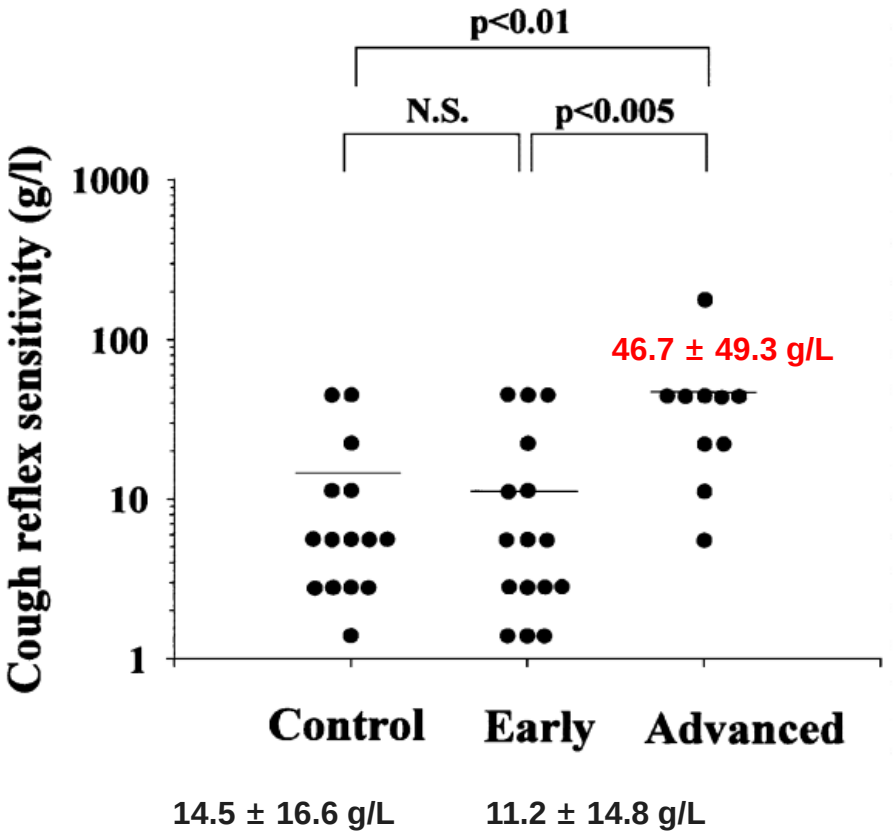
- ✓ Aspiration pneumonia is a leading cause of death in patients with PD

- ✓ 15 patients with early stages of PD
- ✓ 10 patients with advanced stages of PD
- ✓ 15 age-matched control subjects

→ **Sensory component** : cough reflex sensitivity to citric acid inhalation

→ **Motor component** : monitoring voluntary maximal cough peak flow

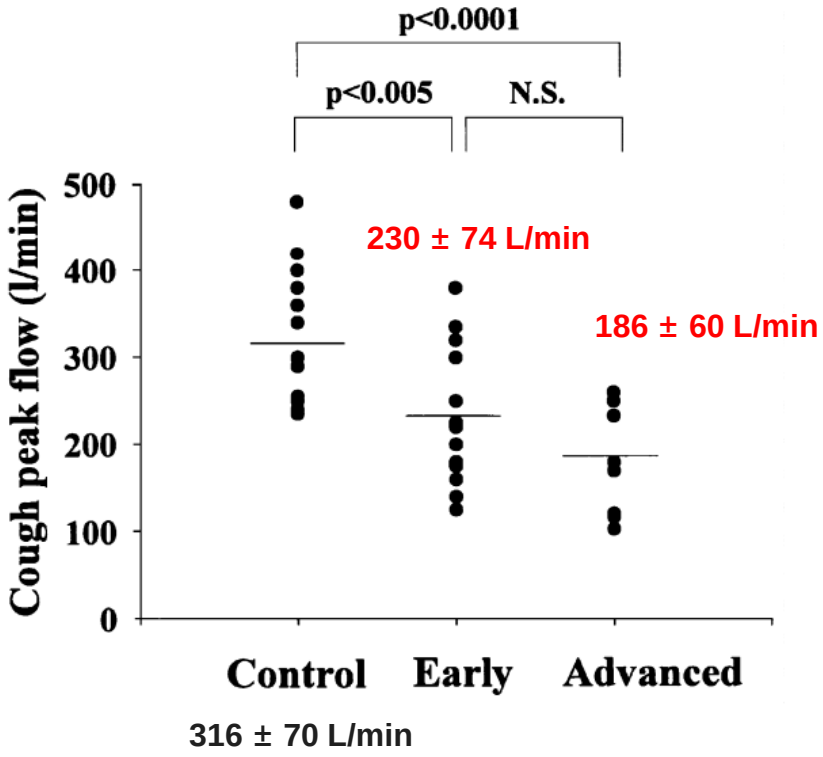
- **Sensory component**
  - Cough reflex sensitivity to citric acid inhalation
  - Citric acid was evaluated with tidal breathing of a nebulized solution → Cough was recorded
  - Concentration at which the patients coughed at least five times during 1 min of breathing the citric acid aerosol



- Cough reflex sensitivity in patients with advanced PD (46.7 +/- 49.3 g/L) was significantly lower compared to control subjects (14.5 +/- 16.6 g/L; $p < 0.01$) and patients with early PD (11.2 +/- 14.8 g/L; $p < 0.005$)

CHEST / 124/3/ SEPTEMBER, 2003

- **Motor component**
  - sitting subjects were instructed to take a full inspiration and to cough into the face mask connected to a peak flowmeter



- The mean cough peak flow rates in patients with both early PD (230 +/- 74 L/min; p < 0.005) and advanced PD (186 +/- 60 L/min; p < 0.0001) were significantly weaker than that in control subjects (316 +/- 70 L/min)

➔ Early stages of PD, mainly the **motor component of cough was impaired**.

➔ Advanced stages of PD, both the **motor and sensory components of cough were impaired**.

CHEST / 124/3/ SEPTEMBER, 2003

RESPIRATORY CARE
Research Article | Original Research

Cough Impairment and Risk of Postoperative Pulmonary Complications After Open Upper Abdominal Surgery

Daniela B Bonfim Colucci, Julio F Fiore, Denise M Paisani, Thais Telles Risso, Marcelo Colucci, Luciana Dias Chiavegato and Sonia Maria Faresin
Respiratory Care May 2015, 60 (5) 673-678; DOI: https://doi.org/10.4187/respcare.03600

- ✓ Prospective cohort study
- ✓ 101 patients admitted for elective upper abdominal surgery

- ✓ Measurements of **peak cough flow**
  - → Day before surgery and repeated on postoperative days 1, 3, 5
- ✓ **Postoperative pulmonary complications(PPCs)** were assessed daily

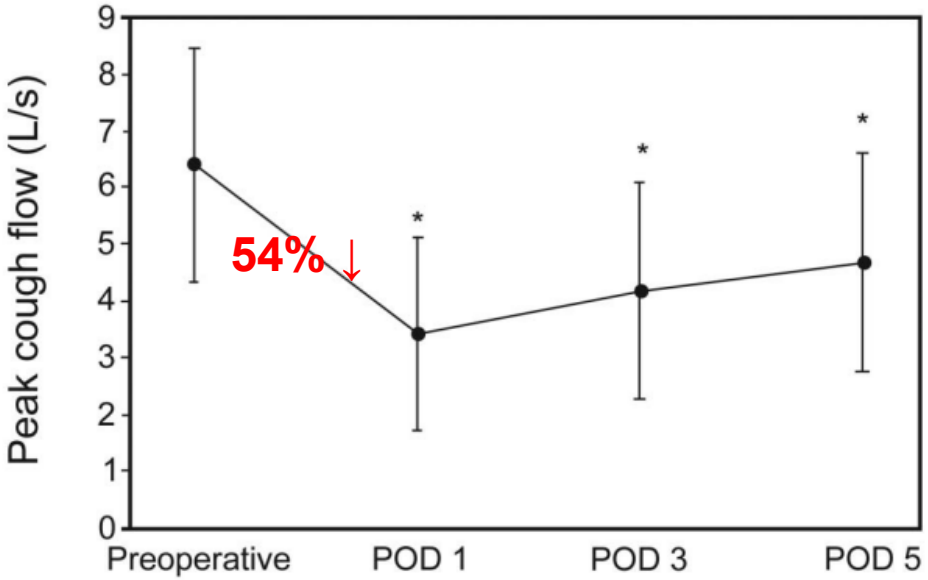


Fig. 1. Progression of peak cough flow over the perioperative period. POD = postoperative day. * $P < .001$ compared with previous measurements. Data are shown as mean ± SD.

- Peak cough flow dropped to 54% of the preoperative value on postoperative day 1
- Peak cough flow gradually increased on postoperative days 3 and 5
- Postoperative day 5, peak cough flow was still significantly lower (72%) in relation to the preoperative value

➔ Cough is impaired after upper abdominal surgery.

- Postoperative pulmonary complications were diagnosed in 6 subjects (6%)

Table 2. Univariate and Multivariate Logistic Regression Estimating the Relationship Between Peak Cough Flow on Postoperative Day 1 and Risk of Postoperative Pulmonary Complications

	Odds ratio (95% CI)	*P*
Univariate analysis	0.80 (0.45–1.40)	.44
Multivariate analysis†	0.66 (0.32–1.38)	.41

† Multivariate analysis was adjusted for preoperative peak cough flow, sex, age, body mass index, and presence of respiratory comorbidities.

- The association between peak cough flow on postoperative day 1 and risk of PPCs was **not** statistically significant in the unadjusted analysis (odds ratio of 0.80, 95% CI 0.45–1.40, P = .44) or in the adjusted analysis (odds ratio of 0.66, 95% CI 0.32–1.38,P = .41)

Take home messages

Take home messages

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- **Cough** is defined as **natural defense mechanism** that protect the respiratory tract from inhaling foreign bodies and by clearing excessive bronchial secretions

- The **cough reflex** is constituted by:
  1. **Afferent pathway**
  2. **Central Pathway (cough center)**
  3. **Efferent pathway**

- **Weak or ineffective cough** compromised the ability to clear lower respiratory tract infection → **Aspiration pneumonia**


Thank you