

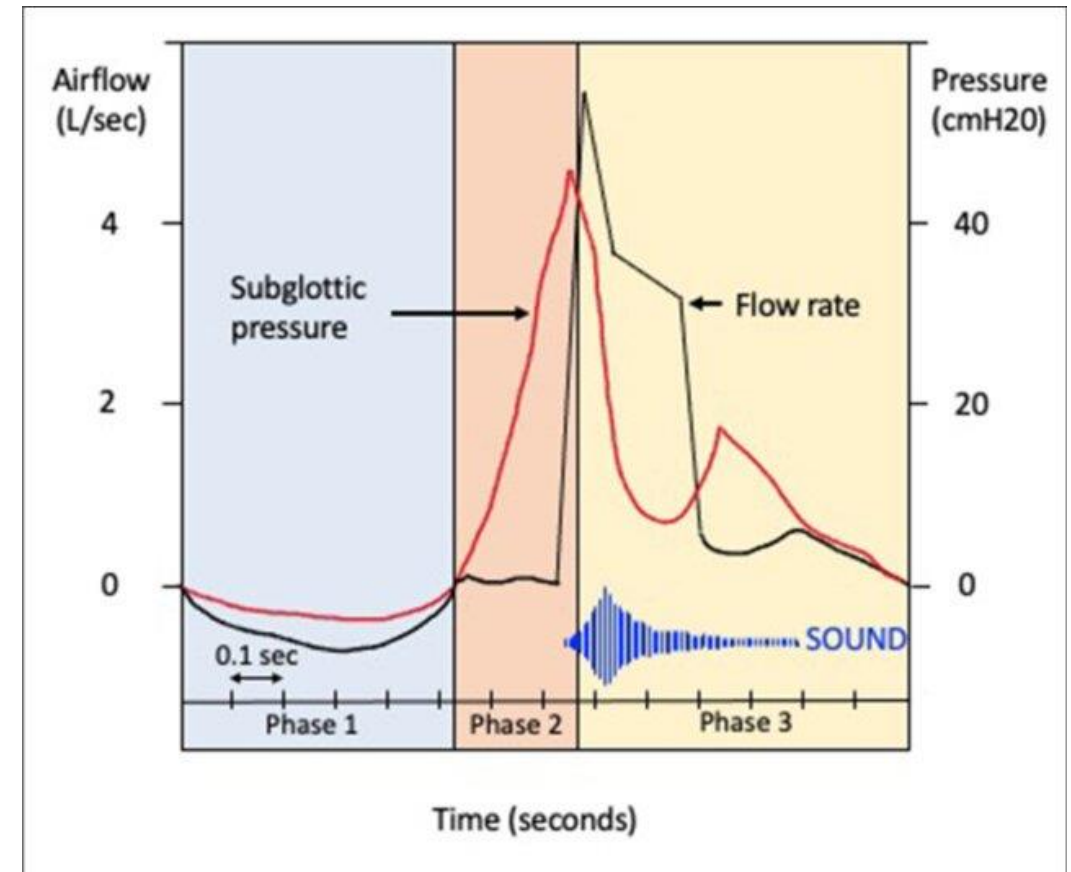
# Complication of Cough

한양대의대 호흡기알레르기내과  
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# Mechanism of Cough



- During vigorous coughing, intrathoracic pressures of up to **300 mmHg**
- Expiratory velocities of up to **280 m/s**

# Complications of Cough

## ACCP Evidence-Based Clinical Practice Guidelines

Richard S. Irwin, MD,

# Life-Threatening and Non-Life-Threatening Complications Associated With Coughing



## A Scoping Review

**Objectives:** To review the spectrum of complications associated with coughing.  
**Design/methodology:** Ovid MEDLINE, Embase, and Scopus databases were searched for English language articles published in the English language using MeSH terms “cough” and “complications of coughing.”  
**Results:** The complications of coughing include hemoptysis, pulmonary hypertension, cor pulmonale, and energy expenditure. An effective means of clearing the airways, providing cardiopulmonary rest, and addressing physical and psychosocial complications, such as constitutional, GI, genitourinary, musculoskeletal, and skin complications, are discussed.  
**Conclusions:** Knowledge of the spectrum of complications associated with coughing (1) the impact of cough on patient quality of life and (2) the available therapeutic options to eliminate the complaint of cough and/or advise patients on how to manage their cough.

Richard S. Irwin, MD, Master FCCP; Natasha Dudiki, MD; and Cynthia L. French, PhD, FCCP; on behalf of the CHEST Expert Cough Panel\*

**BACKGROUND:** This is an update of the section on complications that are associated with coughing in the 2006 CHEST cough guidelines that addresses two aims: (1) to systematically identify and thematically categorize the diverse complications of cough by providing a guide for future studies and (2) to identify gaps in the literature for future research.

**RESEARCH QUESTION:** What are the potential complications that are associated with the act of coughing that have been reported in infants, children, adolescents, and adults?

**STUDY DESIGN AND METHODS:** A scoping review was performed with the use of PubMed and SCOPUS databases that were searched from their beginning until September 6, 2019.

**Key words:** cardiovascular; constitutional symptoms; GI; genitourinary; musculoskeletal; neurological; ophthalmologic; psychosocial; quality of life; respiratory; skin

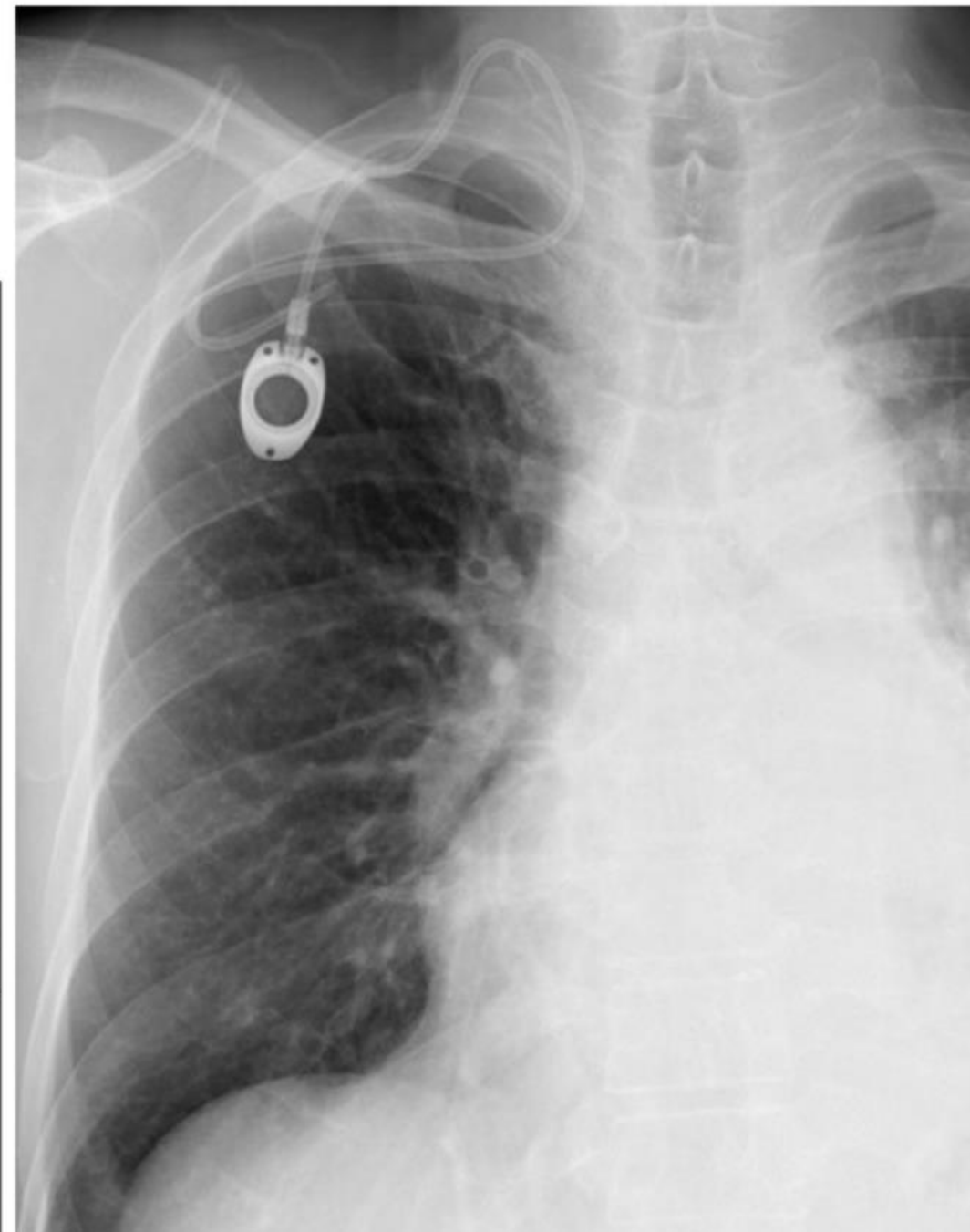
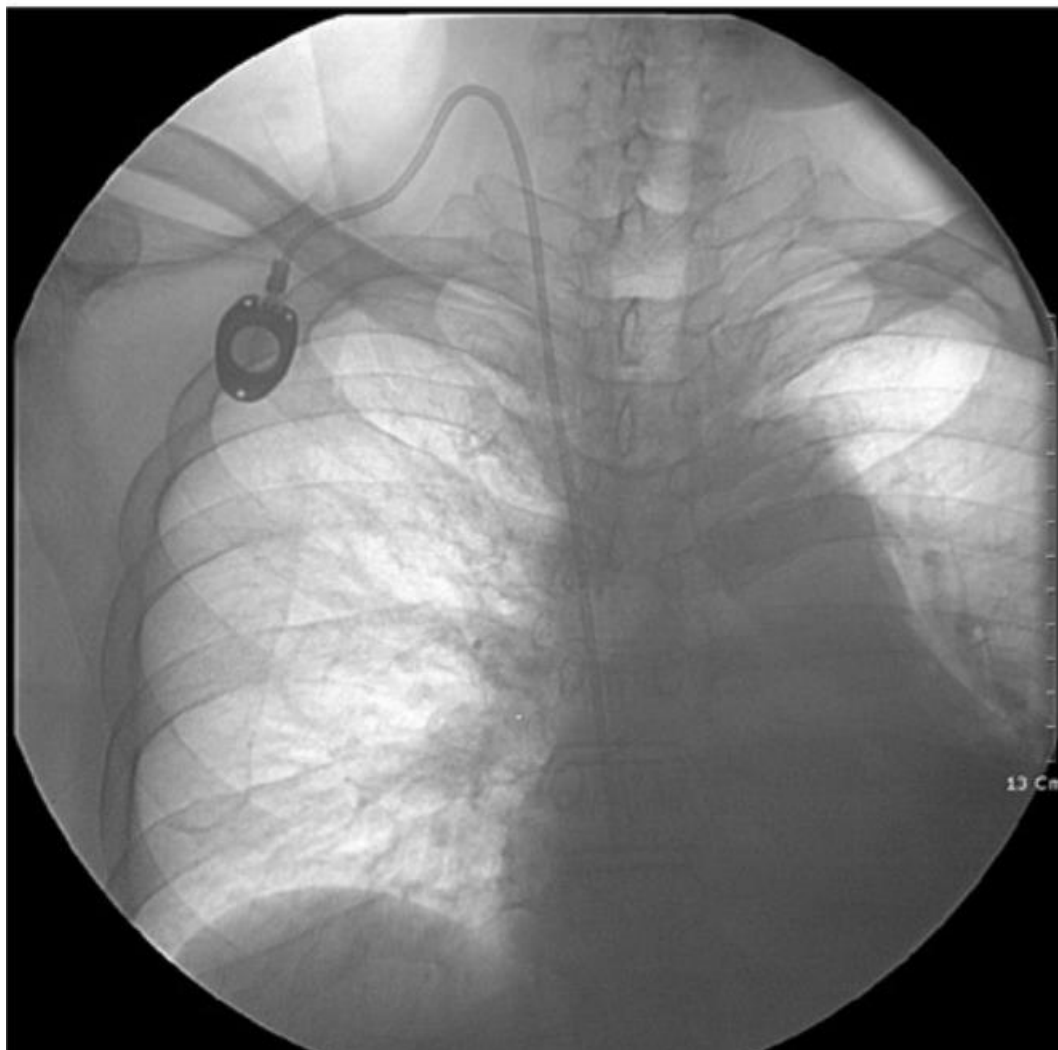
**Abbreviation:** CQLQ = cough-specific quality-of-life questionnaire

# Complication of Cough - Cardiovascular

- *Aortic dissection*
- Arterial hypotension
- Bradyarrhythmia and tachyarrhythmias
- *Coronary artery dissection*
- *Cardiac luxation after pneumonectomy*
- Dislodgement/malfunctioning of intravascular catheters
- Loss of consciousness
- *Pneumopericardium during coronary angiography*
- Rupture of subconjunctival, nasal, and anal veins, and massive intraocular suprachoroidal hemorrhage during pars plana vitrectomy



# Chemo-port dislodgement



**Cardiac luxation in ICU after coughing effort following right pneumonectomy**





# NEUROPHYSIOLOGY OF COUGH

## A $\delta$ -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:

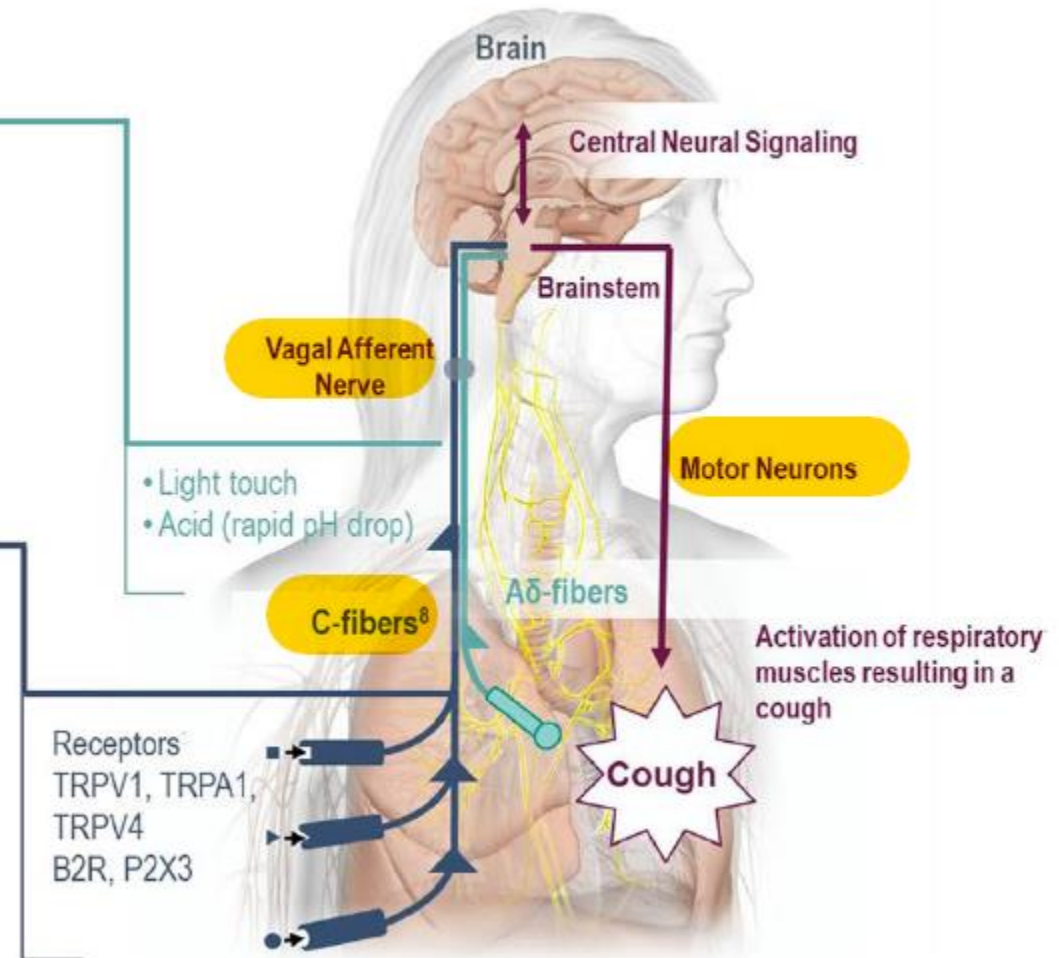
- Mechanical: light touch (eg, particulates or mucus)
- Acid, with a rapid drop in pH (eg, gastric fluid aspiration)

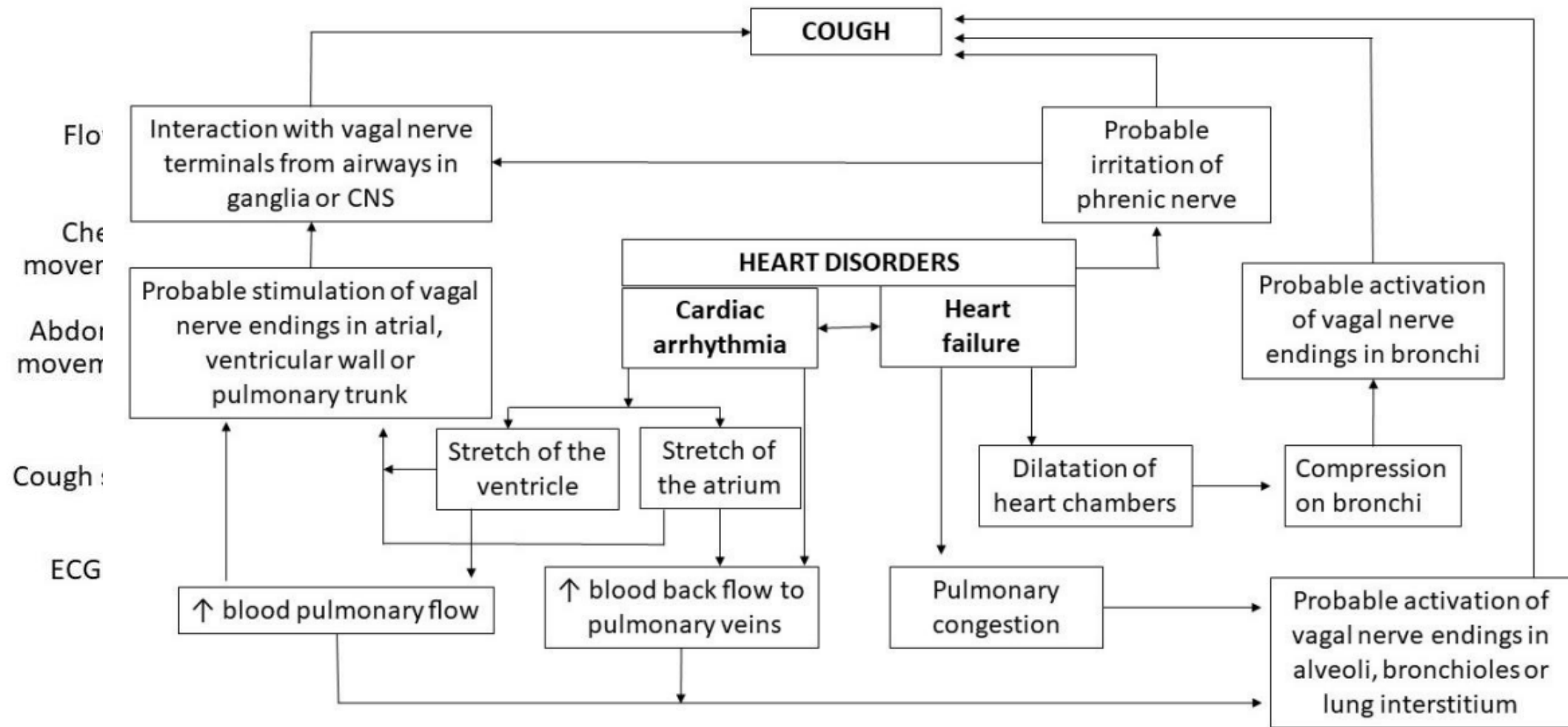
## C-fibers

- 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)

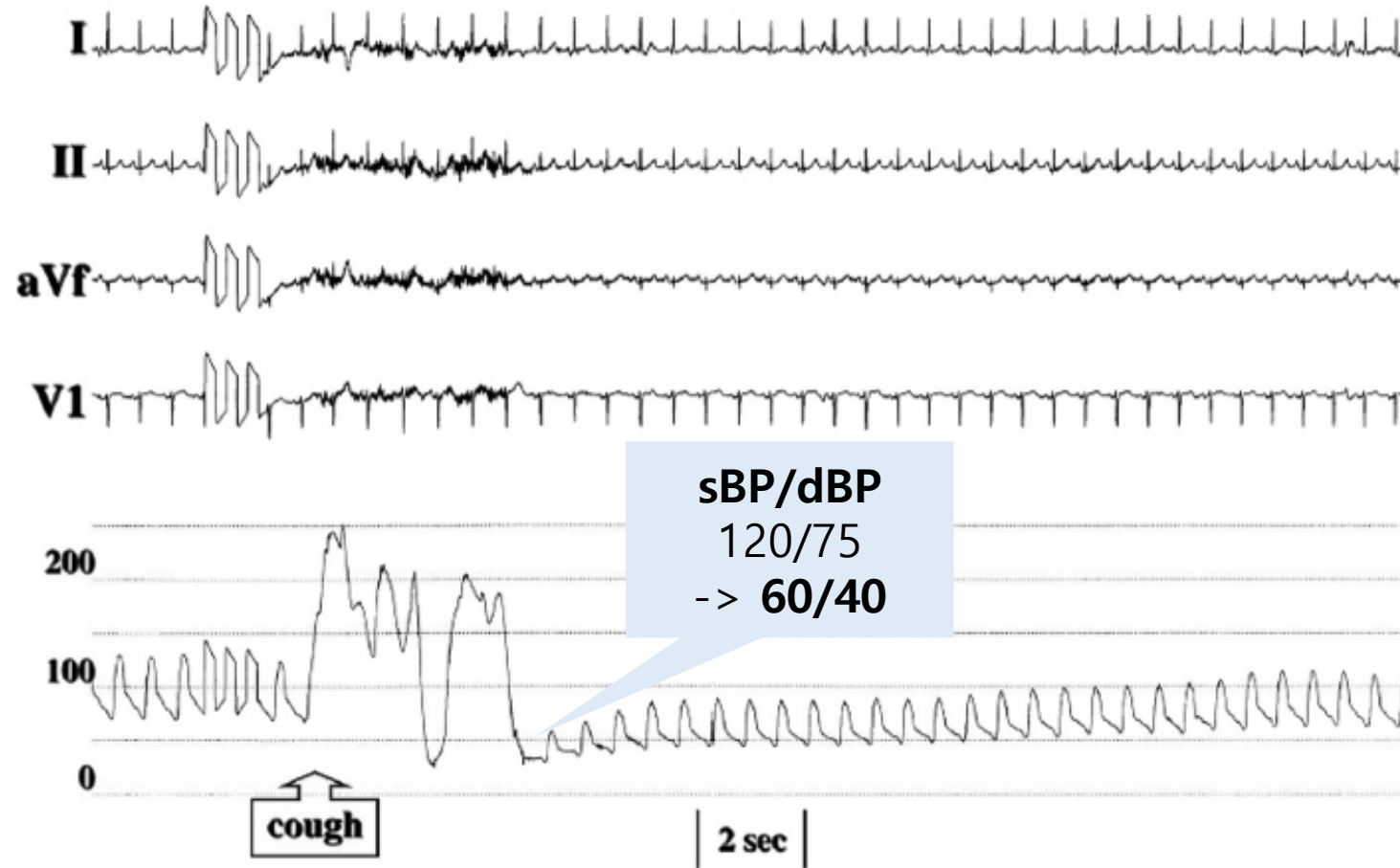




**Fig. 2.** Possible mechanisms of heart dysfunction-induced cough

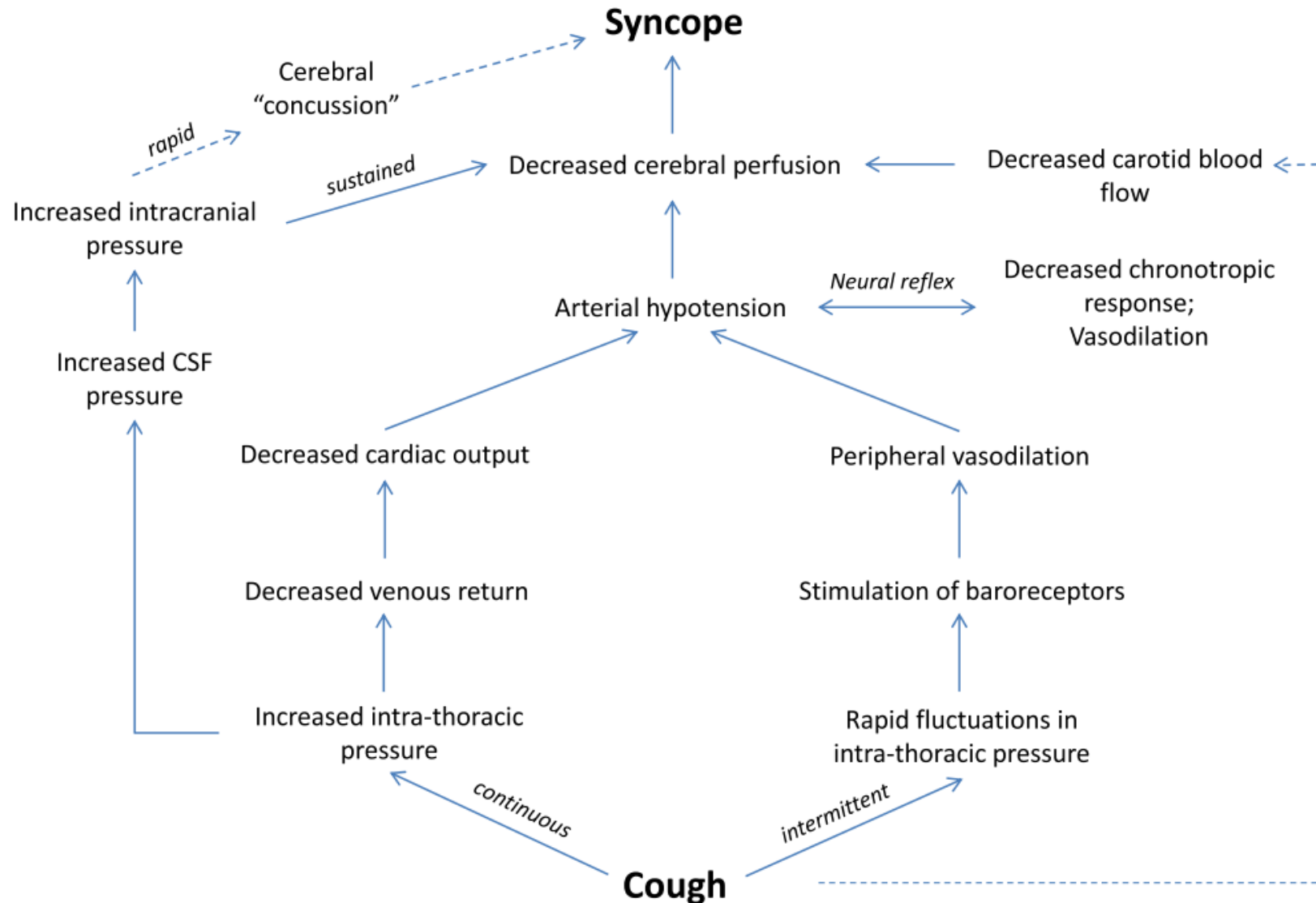
**Fig. 3.** Example of simultaneous record of nasal flow, chest and abdomen movements and ECG in a patient with arrhythmia-induced cough (possible connection between episodes of PACs and coughs marked with black arrow)

# During a cough test (supine position)



Recovery for 40s

# Mechanism of Syncope

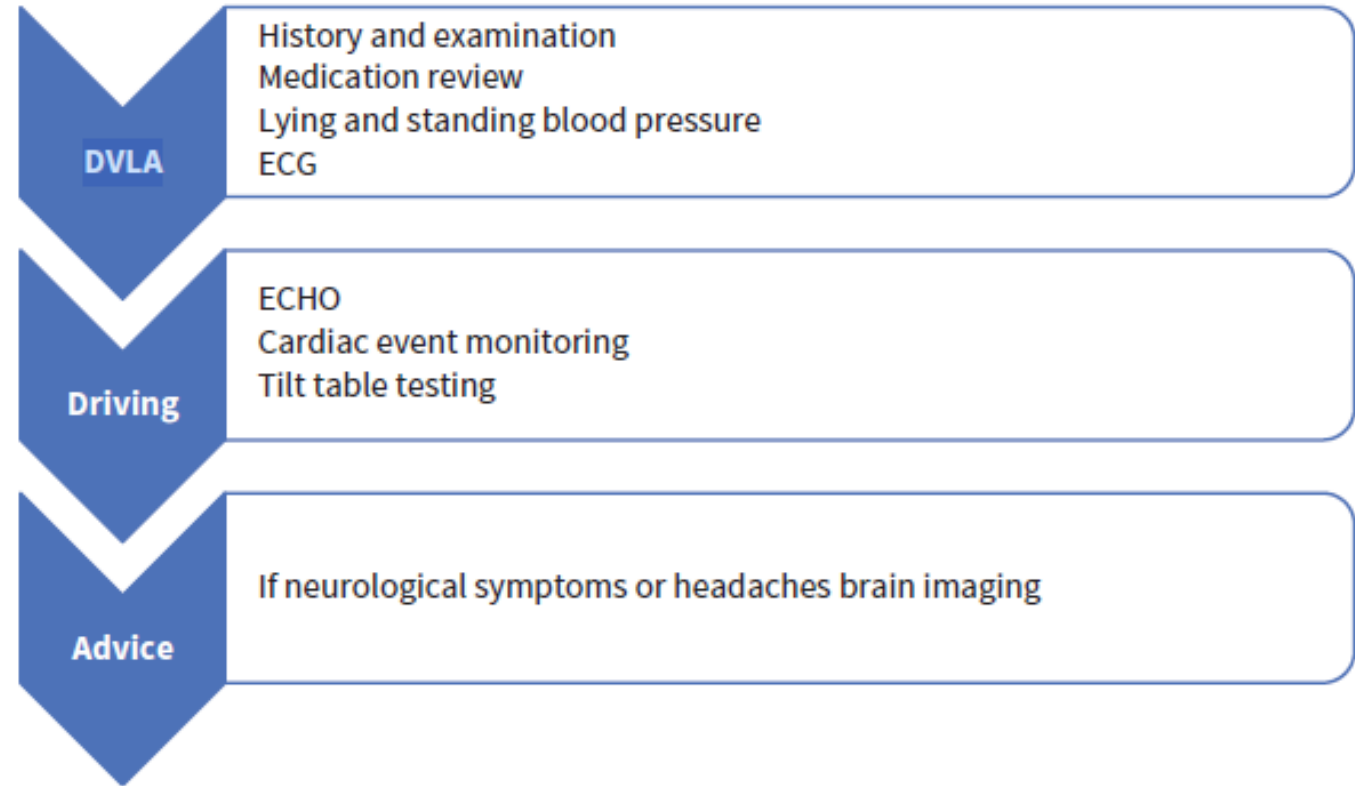


# Cough Syncope

**Table 3** EU standards for driving with recurrent cough syncope and DVLA guidance for group 1 (motorcycles, passenger cars and other small vehicles) and 2 (vehicles over 3.5 tonnes or vehicles designed for the carriage of more than nine passengers) drivers for patients with cough syncope

<b>EU standards [11]</b>	Group 1 drivers	Driving allowed if no recurrence in 6 months
	Group 2 drivers	Permanent ban
<b>UK DVLA guidelines [12]</b>	Group 1 Drivers	Must not drive for 6 months following a single episode and for 12 months following multiple episodes and must notify DVLA
	Group 2 Drivers (bus and lorry)	Must not drive for 12 months following a single episode and for 5 years following multiple episodes and must notify DVLA

If more than one episode of cough syncope occurs within a 24-h period, this will be counted as a single event. However, if the episodes of cough syncope are more than 24 h apart, these are considered as multiple episodes. Adapted from [11, 12].

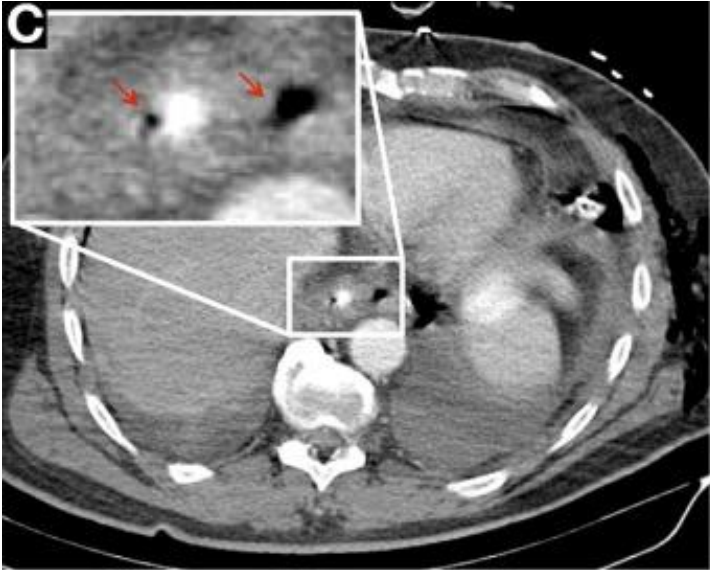


**Figure 4** Proposed set of investigations in all patients reporting cough syncope.

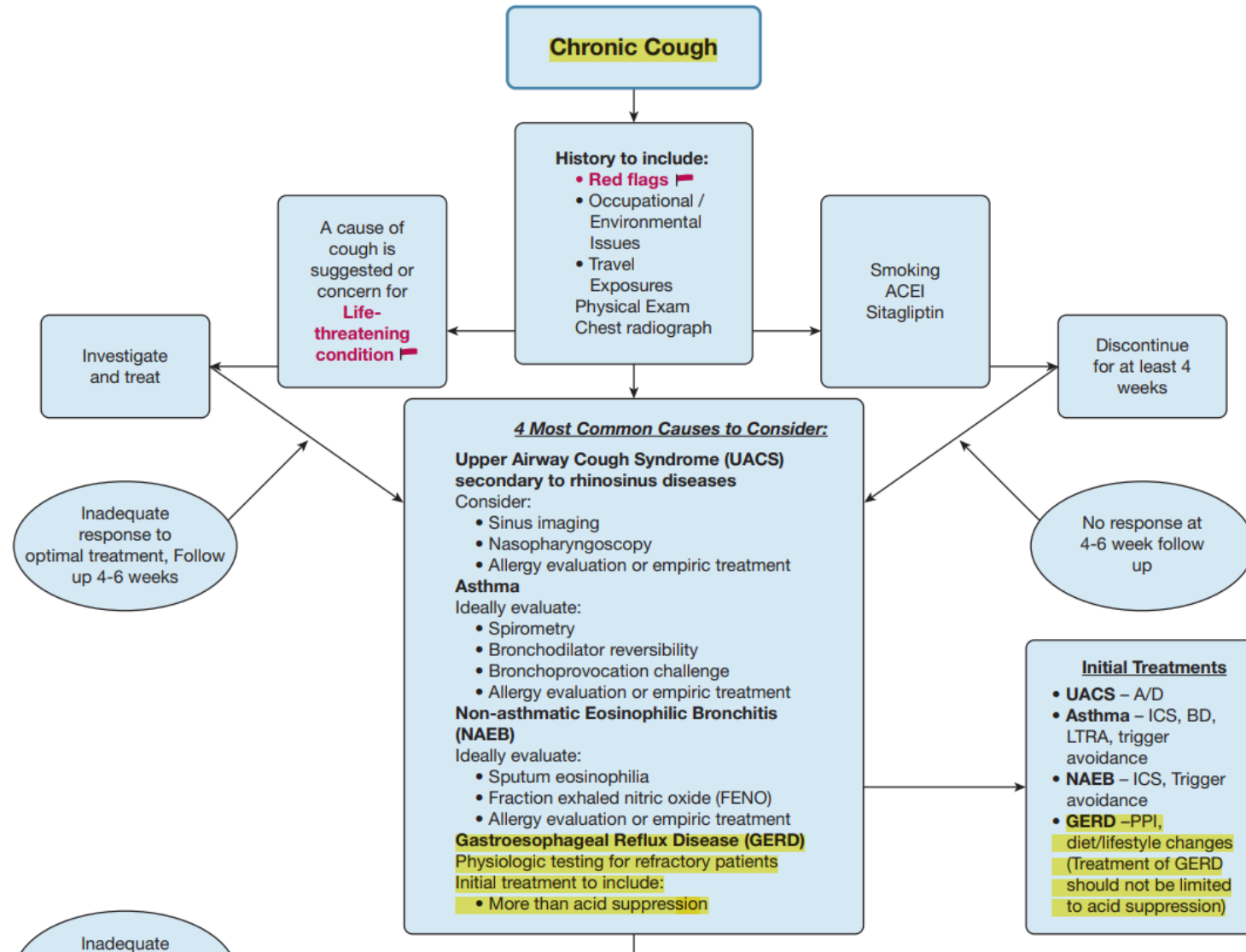
# Complication of Cough - GI

- Gastroesophageal reflux events
- Gastric hemorrhage following percutaneous endoscopic gastrostomy
- Hepatic cyst rupture
- *Laceration of stomach and spleen*
- Herniations (eg, inguinal, through abdominal wall, small bowel through laparoscopic trocar site)
- Malfunction of gastrostomy button
- Mallory-Weiss tear
- Splenic rupture
- *Spontaneous retroperitoneal bleed with hematoma*
- *Inguinal or femoral or umbilical or lumbar or abdominal wall hernia*

# Esophageal rupture

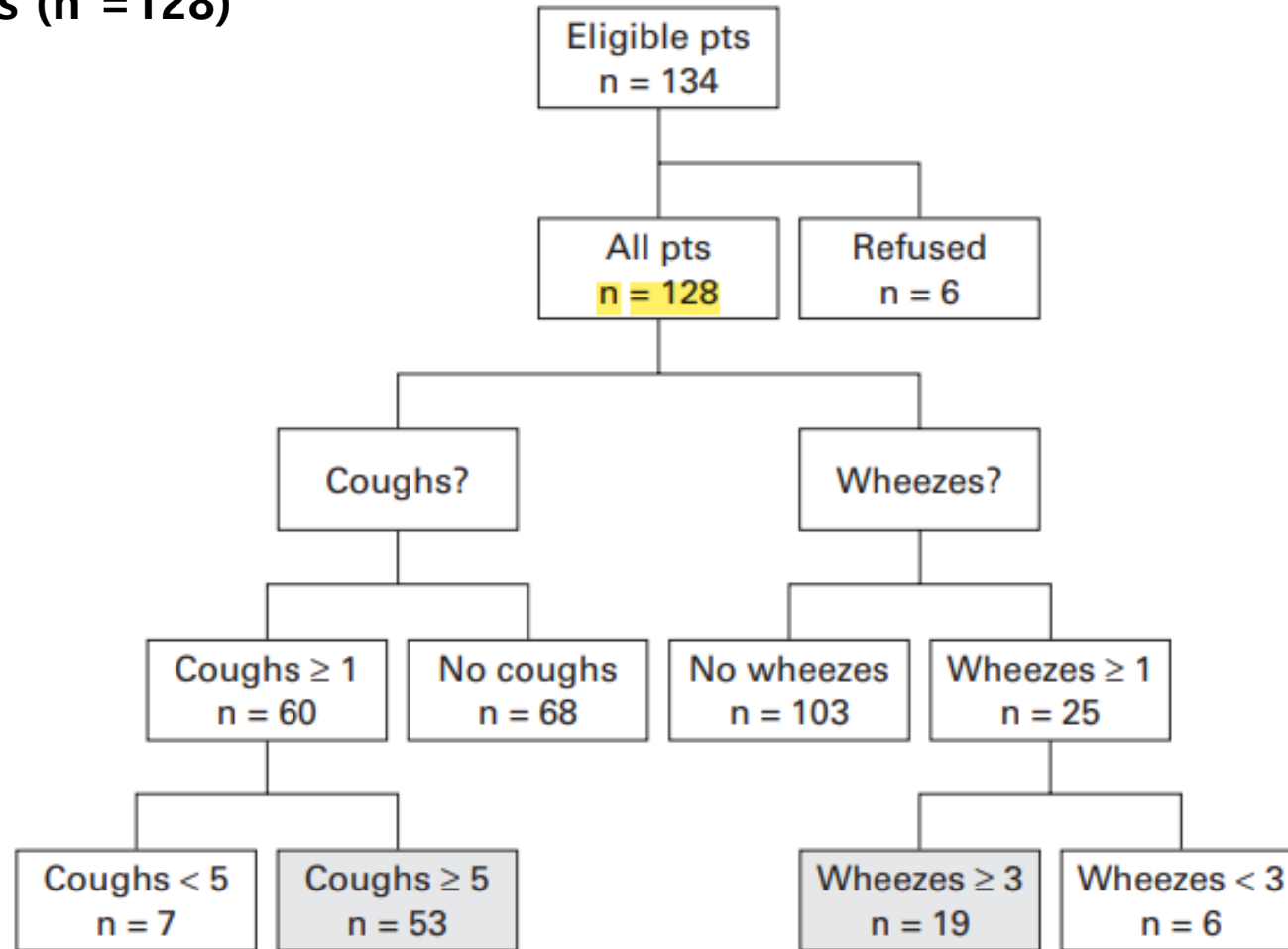


# GERD and Cough or Cough and GERD?



# GERD and Cough or Cough and GERD?

Asthmatics (n = 128)



- EGD
- Esophageal manometry
- pHmetry

Figure 1 Flow diagram of the study population.

Table 2 Relationships among coughing, wheezing, and reflux

Type of relationship	No patients	Observed* (SD)	Ratio† OBS/EXP	z Value	p Value
Cough and reflux	53				
Length of interaction: 0–2 min					
Cough precedes reflux	28	6% (1%)	3.21	1.71	0.043
Reflux precedes cough	49	40% (3%)	2.48	5.08	0.000
Association of reflux and cough	49	46% (3%)	2.25	5.35	0.000
Length of interaction: 0–5 min					
Cough precedes reflux	28	12% (2%)	2.70	2.18	0.014
Reflux precedes cough	50	50% (3%)	1.70	4.07	0.000
Association of reflux and cough	50	62% (4%)	1.61	4.17	0.000
Wheezes and reflux	19				
Association of reflux and wheezes (for 2 min)	16	48% (7%)	2.30	2.71	0.003
Association of reflux and wheezes (for 5 min)	17	56% (7%)	1.62	1.66	0.050

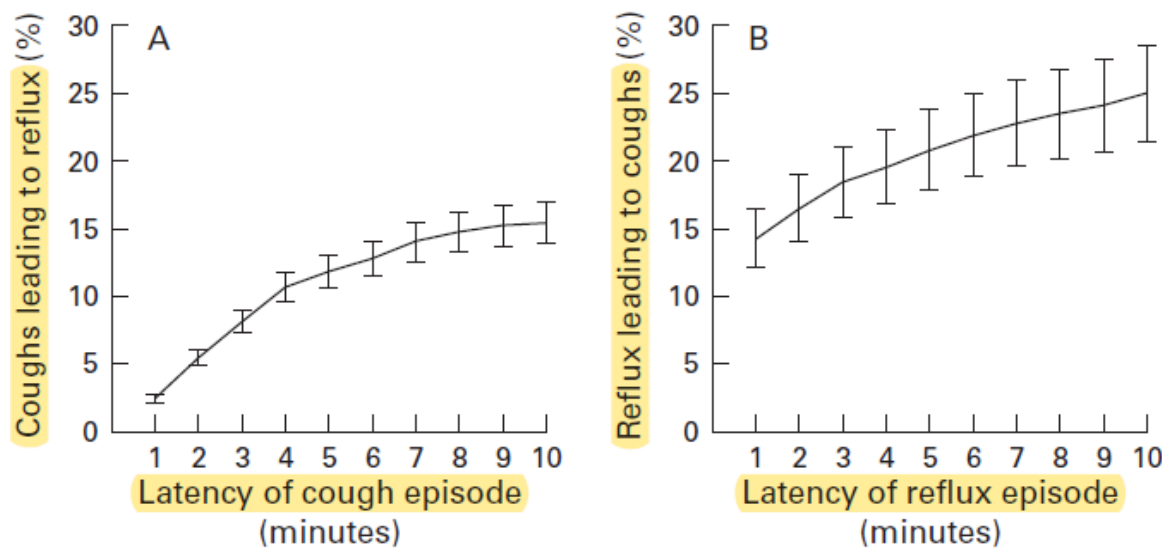


Figure 2 Fraction of coughs preceding reflux (A) and fraction of reflux episodes preceding coughs (B) dependent on the length of the latency period of coughing and reflux episodes, respectively. Each point represents the mean (SD) value calculated from the average values of 53 individual patients.

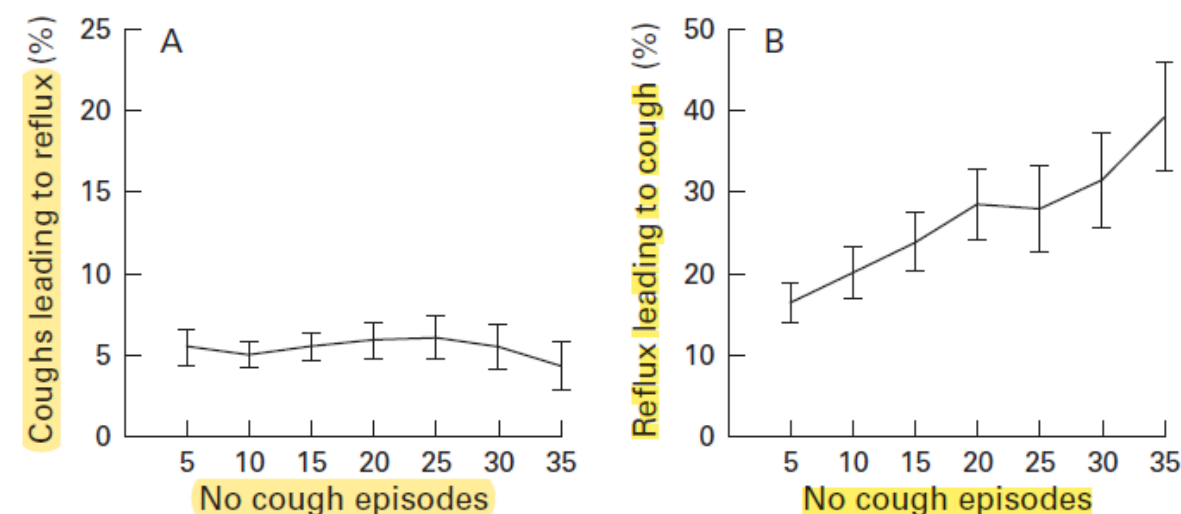
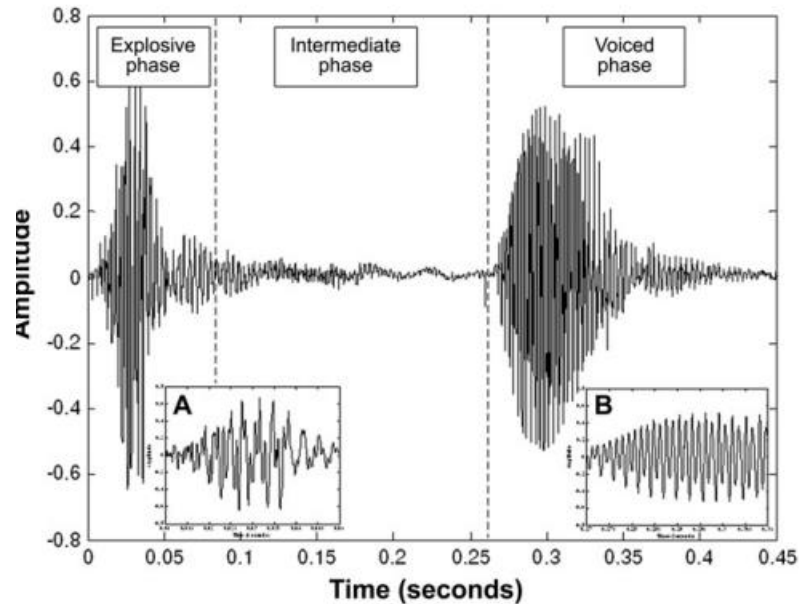


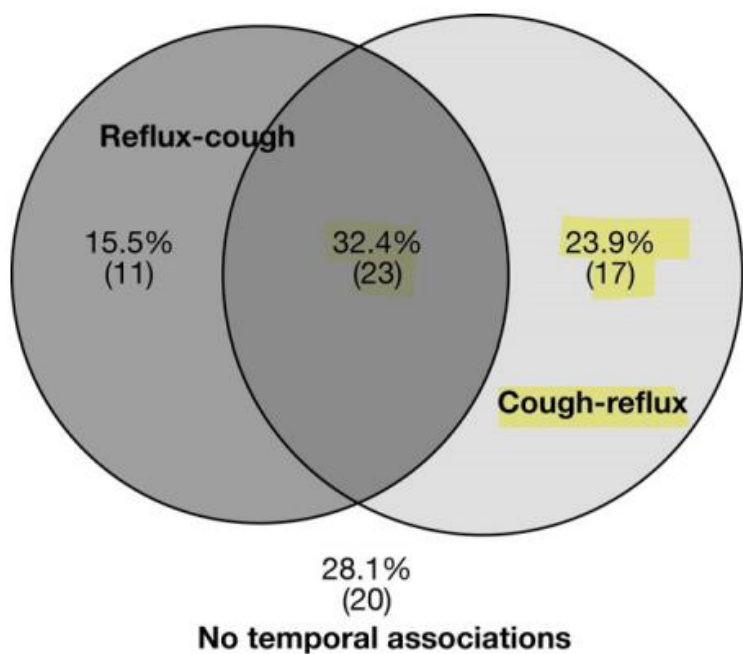
Figure 3 Influence of the number of coughing episodes on the fraction of coughs preceding reflux (A) and fraction of reflux episodes preceding coughs (B). Only patients with coughing episodes equal to or exceeding the threshold shown on the horizontal axes were included in calculating the mean (SD) value.

# GERD and Cough or Cough and GERD?

- 24 hours ambulatory acoustic cough monitoring with simultaneous impedance/pH recording
- 71 unselected patients with chronic cough
  - aged 51–64 years (47 female)



+ Esophageal Impedance/pH Monitoring



**Table 2.** Comparison of Reflux Parameters in Patients With a Positive and Negative Symptom Association Probability for Cough Preceding Reflux

	Positive SAP <sub>C-R</sub> n = 40	Negative SAP <sub>C-R</sub> n = 31	P value
Sex (% female)	62.5	71.0	.45
Age, y	59.0 (51.0–64.0)	58.0 (50.0–65.0)	.90
BMI	27.3 (25.7–29.7)	27.3 (23.6–31.1)	.68
Cough duration, y	6.0 (2.0–11.8)	4.0 (2.7–10.0)	.51
Cough reflex sensitivity to citric acid, mol/L (logC5)	–0.9 (–1.2 to –0.6)	–0.6 (–1.2 to –0.3)	.36
<b>Total number of reflux events</b>	70.5 (59.3–88.3)	62.0 (46.5–76.3)	.04
Acid	37.0 (24.3–48.5)	34.0 (19.0–51.5)	.45
Nonacid	24.0 (17.0–38.8)	20.0 (14.0–32.5)	.21
<b>Number of proximal reflux events</b>	11.0 (6.3–22.8)	7.0 (3.0–14.0)	.035
Proximal acid	0 (0–1.8)	0 (0–0)	.002
Proximal nonacid	11.0 (5.3–21.8)	6.5 (2.8–14.0)	.06
% Time pH <4	3.6 (0.6–9.0)	3.2 (1.2–5.7)	1.0
Nasal disease, %	44.4	30.0	.31
Eosinophilic bronchitis, %	15.0	6.5	.45
Asthma, %	5.1	9.7	.65
Bronchiectasis, %	5.0	0.0	.65

NOTE. Data expressed either as a percentage of whole group or as median and interquartile range. SAP<sub>C-R</sub>, symptom association probability for cough preceding reflux.

**Figure 3.** Venn diagram showing the percentage (number) of patients with significant reflux-cough associations (SAP<sub>R-C</sub> positive) and cough-reflex associations (SAP<sub>C-R</sub> positive).

# Complication of Cough - Neurological

- Acute cervical radiculopathy
- Cerebral air embolism
- Cerebral spinal fluid rhinorrhea
- Cervical epidural hematoma associated with oral anticoagulation
- Cough syncope
- Dizziness
- Headache
- Malfunctioning ventriculoatrial shunts
- Seizures
- Stroke due to vertebral artery dissection

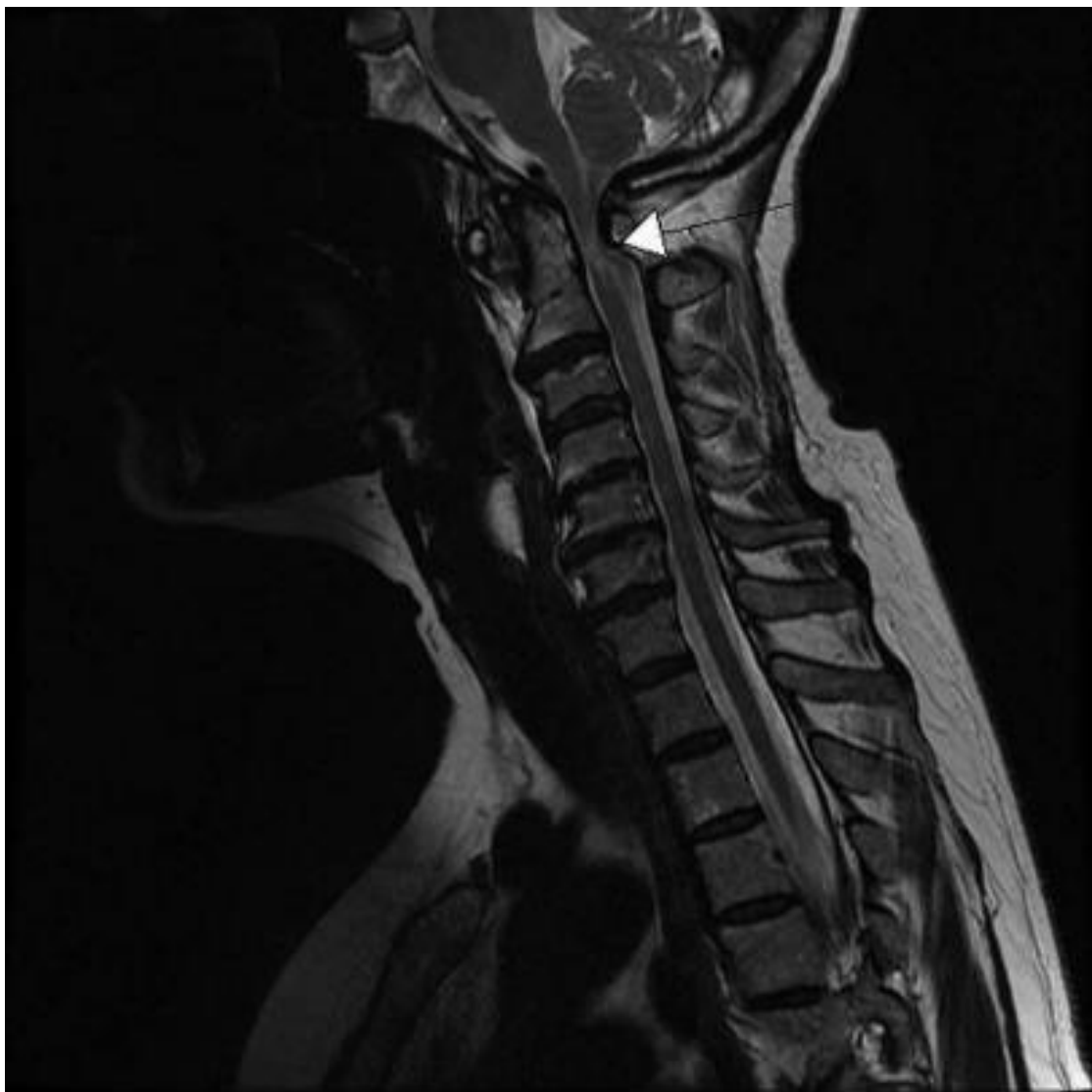
# Complication of Cough - Neurological

- *Carotid artery dissection and pseudoaneurysm*
- *Carotid artery dissection with stroke*
- *Cerebral air embolism causing stroke with and without death*
- *Cervicobrachial pain*
- *Cough induced anoxic cerebral injury in child*
- *Cough induced transient ischemic attack*
- *Cough induced nystagmus*
- *Cough induced recurrence of spinal anesthesia*
- *Cough induced vertigo*

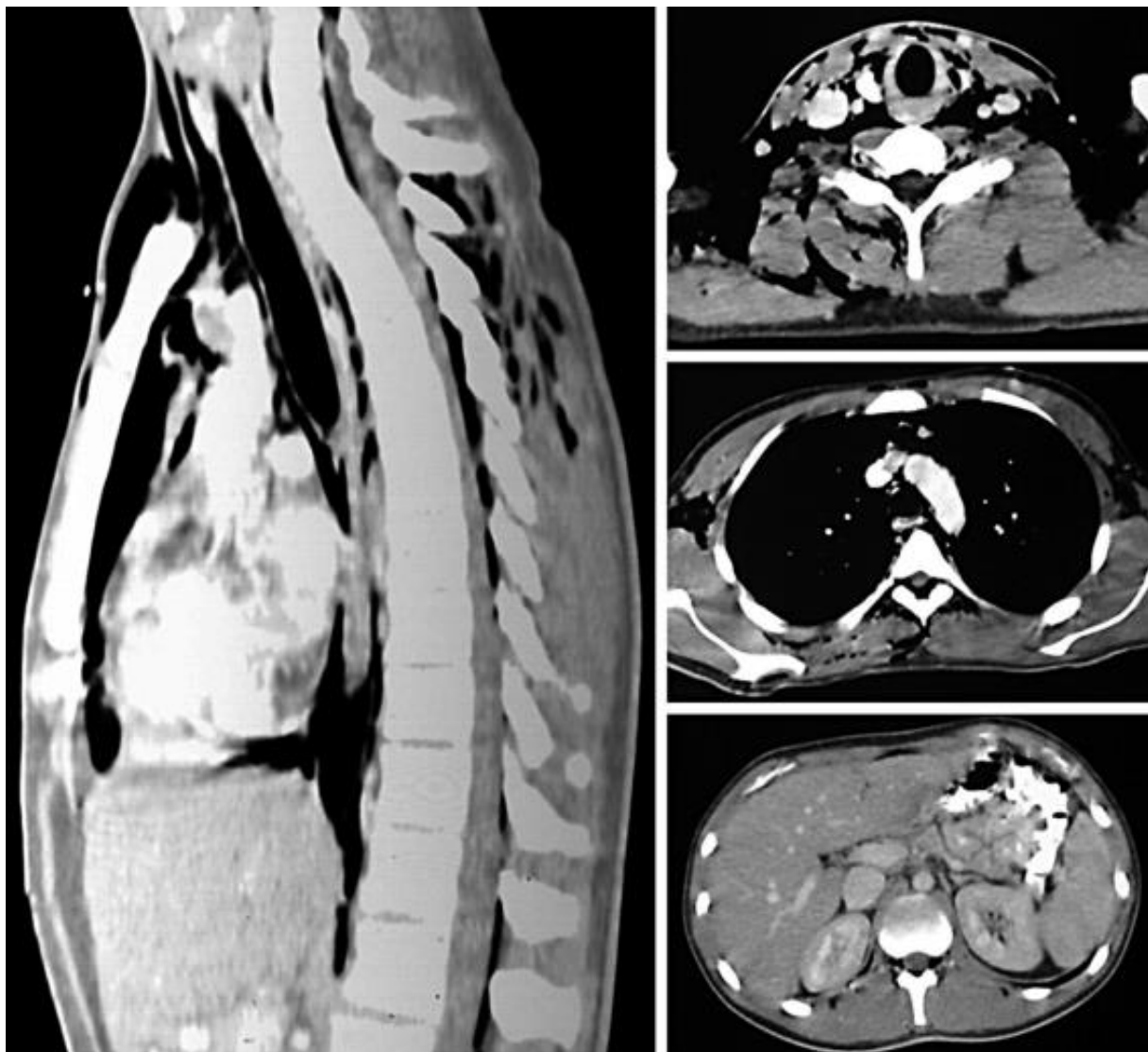
# Complication of Cough - Neurological

- *Cough-induced hemiparesis*
- *Cough-induced hemiplegic migraine*
- *Cough-induced myxoma embolism causing paraplegia*
- *Pneumocephalus*
- *Pneumorrhachis*
- *Spontaneous dissection of cerebral arteries*
- *Stroke due to bilateral carotid artery thrombus formation*

Cough-induced hemiparesis



Pneumorrhachis (=epidural emphysema)



# Complication of Cough - Musculoskeletal

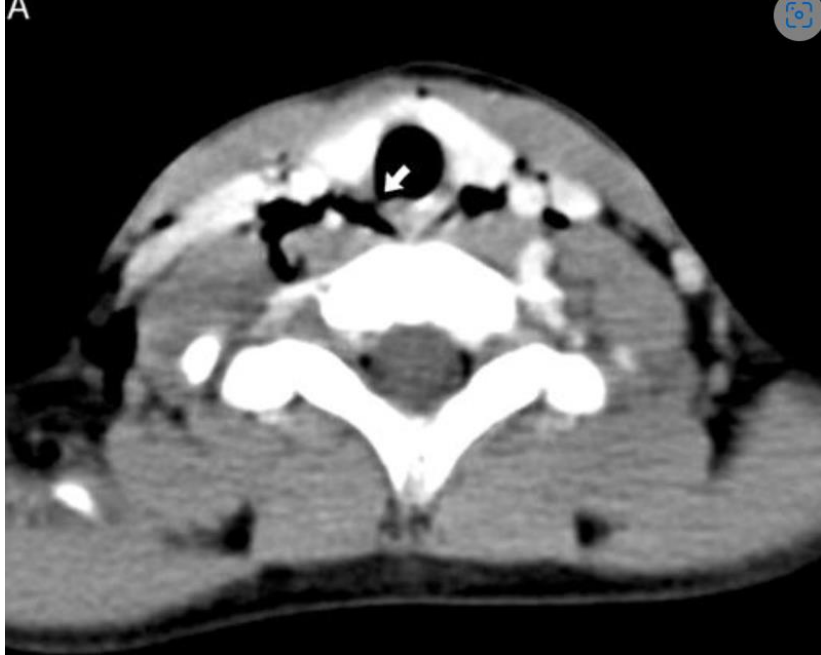
- From asymptomatic elevations of serum creatine phosphokinase to rupture of rectus abdominus muscles
- Diaphragmatic rupture
- Rib fractures
- Sternal wound dehiscence

# Complication of Cough – Respiratory

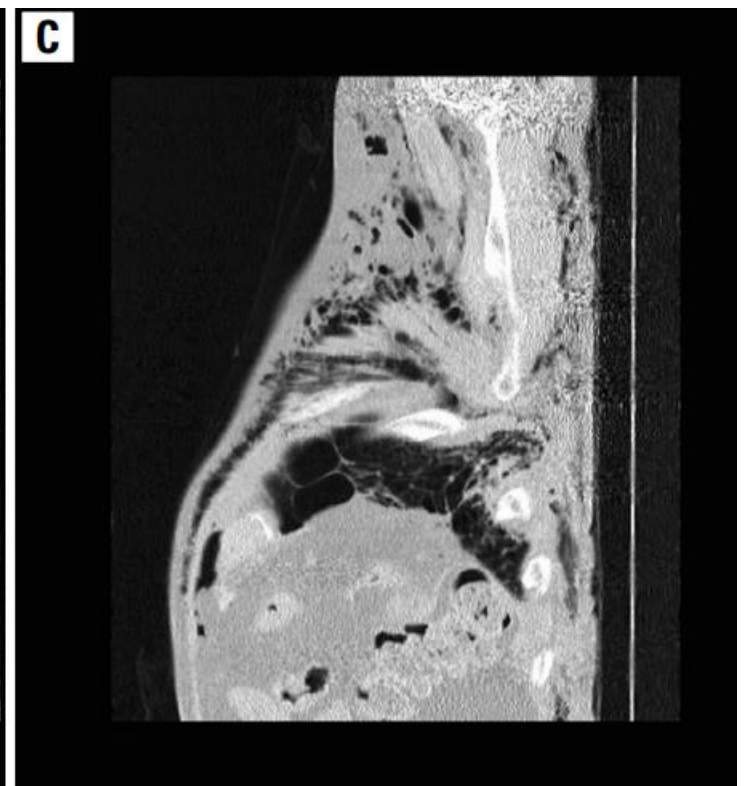
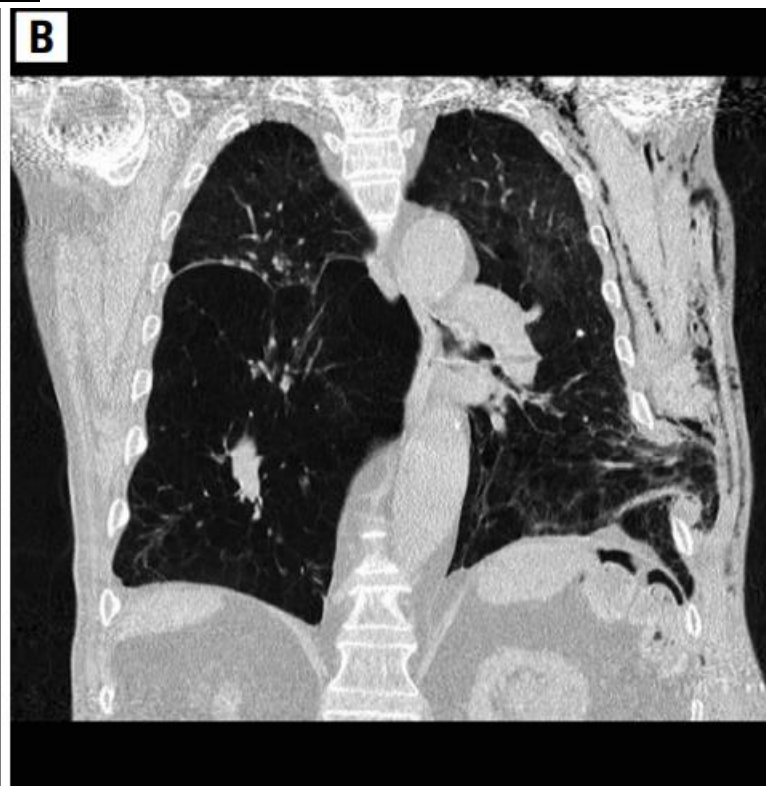
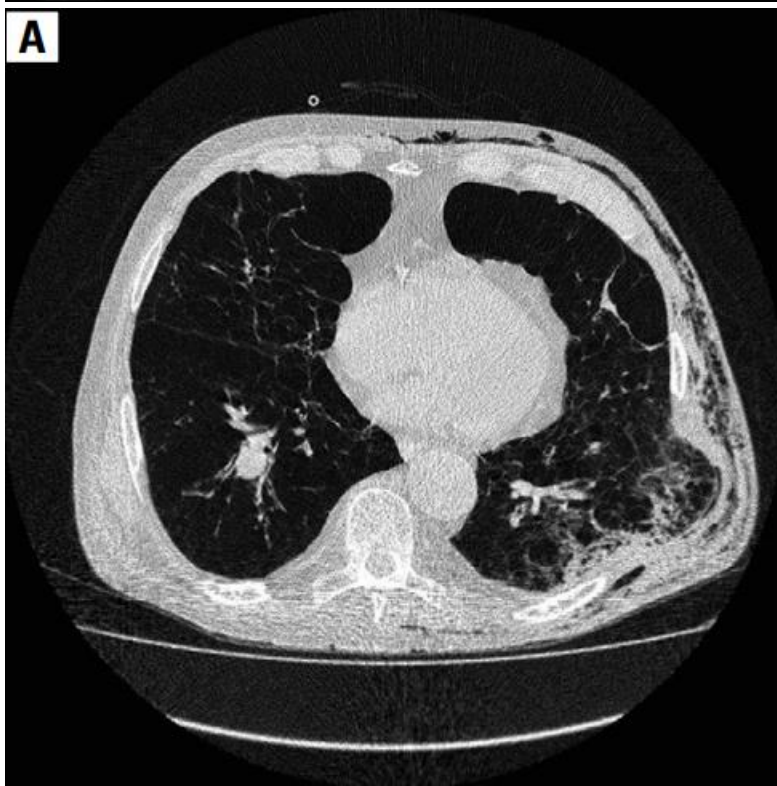
- Exacerbation of asthma
- Herniations of the lung (eg, intercostal and supraclavicular)
- Hydrothorax in peritoneal dialysis
- Laryngeal trauma (eg, laryngeal edema and hoarseness)
- Pulmonary interstitial emphysema, with potential risk of pneumatosis intestinalis, pneumomediastinum, pneumoperitoneum, pneumoretroperitoneum, pneumothorax, subcutaneous emphysema
- Tracheobronchial trauma (eg, bronchitis and bronchial rupture)

# Complication of Cough – Respiratory

- *Apical lung herniation with tracheal displacement*
- *Chylothorax*
- *Diaphragmatic rupture*
- *Hemothorax*
- *Hydropneumothorax and tension pneumothorax*
- *Rupture of bronchus or trachea*
- *Transmission of infectious disease*



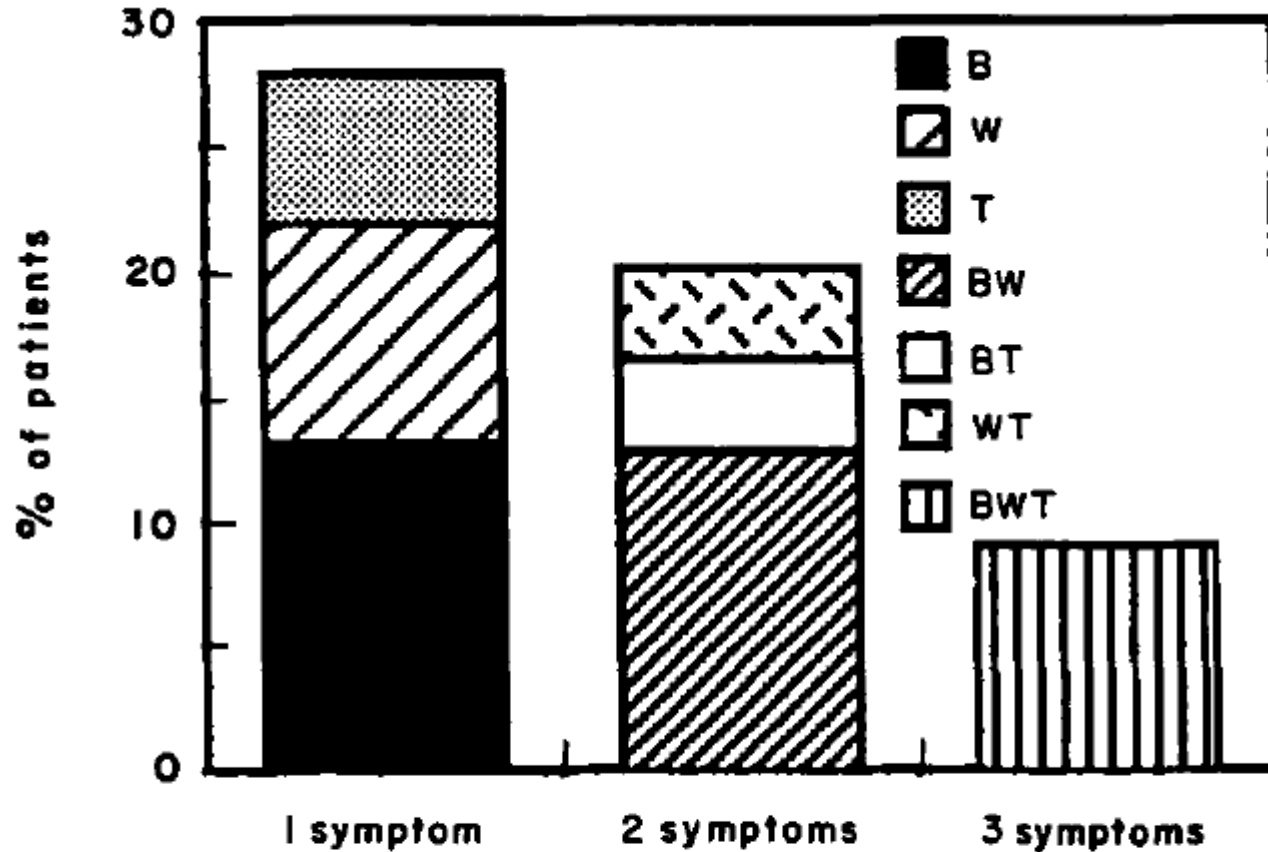
Trachea rupture



Lung intercostal herniation

# Exacerbation of asthma

- 187 patients
  - 41.7% coughing caused exacerbation
  - 29.9% coughing brought relief
  - 9.9% coughing had no effect
  - 18.7% coughing sometimes exacerbated their symptoms and sometimes brought relief



*Fig 3* Patterns of symptoms induced by coughing. B, breathlessness; W, wheezing; T, chest tightness; BW, breathlessness and wheezing; BT, breathlessness and chest tightness; WT wheezing and chest tightness; BWT, breathlessness, wheezing and chest tightness.

- The tone of smooth muscle
- The amount of edema
- The quantity of mucus
- Inspiration-induced bronchoconstriction
- Increase in specific airways resistance

# Complication of Cough – Etc. (I)

- Constitutional symptoms
  - Excessive sweating, anorexia, exhaustion
- Genitourinary
  - Inversion of bladder through urethra
  - Urinary incontinence

# Complication of Cough – Etc. (I)

- Ophthalmologic
  - Spontaneous compressive orbital emphysema of rhinogenic origin
  - *Orbital emphysema compressing the eyeball and the optic nerve*
  - *Periorbital ecchymosis (Panda sign)*
  - *Subconjunctival hemorrhages*
  - *Retinal detachmen*
  - *Subhyaloid hemorrhage*
  - *Suprachoroidal hemorrhage*
  - *Transient blindness*
  - *Postoperative Trabeculectomy bleb leak*

# Complication of Cough – Etc. (II)

- Psychosocial
  - Fear of serious disease
  - Lifestyle changes
  - Self-consciousness
  - *Adverse effects on quality of life*
- Skin
  - Petechiae and purpura
  - Disruption of surgical wounds
- *False-positive PET scan uptake in muscle related to cough*
- *Transmission of infectious disease*

**TABLE 2 ] Cough-Associated Complications That Lead to Death**

Cough-Associated Complication	Age/Sex	Comorbid Illness	Comment
<b>Death to self and others</b>			
Cough syncope in heavy goods-vehicle drivers causing serious traffic accidents resulting in death of two drivers and two pedestrians <sup>190</sup>	UA, UA	UA	Cough syncope can lead to death for the drivers and others.
<b>Death to self</b>			
Cough associated with spontaneous arterial gas embolism in patient with chronic necrotizing pneumonia, bullae, and brain infarct with death from complications <sup>160</sup>	78 y, M	COPD, smoker, chronic Enterobacter cloacae pneumonia, hypertension, atrial fibrillation, type 2 diabetes mellitus, hypothyroidism, dyslipidemia	Spontaneous arterial gas embolism resulted in brain infarcts and air in the cavernous sinuses, which led to death precipitated by coughing in a patient with preexisting chronic necrotizing pneumonia, blebs, and bullae. Proposed mechanism is likely weakened parenchyma that led to bleb rupture with entrainment of air into the pulmonary veins and left heart.
Paroxysms of cough followed by fainting in patients with asthma (four deaths in the series) <sup>173</sup>	UA, M (n = 281); F (n = 9) (N = 290)	Case series included patients with emphysema, bronchitis, TB, asthma, laryngitis, bronchiectasis, pneumoconiosis, sarcoidosis	Death reported as unequivocal cause after post-tussive syncope in four cases, which accounted for 1% mortality rate in the collective series included two in the literature and two personal cases

<p>Fatal rectus sheath hematoma<sup>102</sup></p>	<p>82 y, F</p>	<p>Polymyositis and related collagen disorders, well controlled with long-term corticosteroids (prednisone 5 mg daily), occult coronary artery disease</p>	<p>Rectus sheath hematoma in one of three patients reported may have been attributed to coughing associated with pneumonia. She was also on thromboprophylaxis with heparin and prednisone for polymyositis. Her course was complicated by a large hematoma, hypotension, and ultimately death.</p>
<p>Cough-induced lung intercostal (8th space) hernia with large abdominal hematoma in patient with COPD exacerbation and death<sup>49</sup></p>	<p>73 y, M</p>	<p>COPD, total laryngectomy for laryngeal cancer with tracheostomy</p>	<p>Cough-induced intercostal muscle rupture with lung hernia associated with hematoma of the left chest and abdomen, massive subcutaneous emphysema of the left chest and lumbar region in a patient presenting with an exacerbation of COPD that was improving before the coughing insult, which ultimately resulted in death.</p>
<p>Fatal gas cerebral embolism after heavy coughing while using noninvasive ventilation (bilevel positive airway pressure) for fibrotic lung disease<sup>162</sup></p>	<p>78 y, M</p>	<p>Severe restrictive lung disease due to fibrotic remodeling due to TB, MALT lymphoma</p>	<p>Cerebral air embolism precipitated by episodes of severe coughing that led to catastrophic stroke in a patient presenting with hemoptysis treated with left bronchial artery embolization, on noninvasive positive pressure ventilation and ultimately death due to intractable treatment of resistant cough.</p>
<p>Pneumomediastinum in children with cough with a death<sup>286</sup></p>	<p>4 y, M</p>	<p>Measles and pneumonia</p>	<p>In a case series of five patients with severe cough, one patient had refractory cough due to measles, bronchopneumonia that resulted in</p>

<p><b>Pneumomediastinum</b> secondary to coughing in an elderly patient with emphysema with death due to complications<sup>288</sup></p>	<p>96 y, M</p>	<p>Under custodial care in the geriatrics division</p>	<p>In this case series of three patients, the current patient experienced extensive subcutaneous emphysema and pneumomediastinum after an episode of coughing that resulted in progressive decline and death.</p>
<p>Prolapse of the rectum with spontaneous rupture of the distal colon and evisceration of the small intestine through the anus in an infant after a bout of coughing and death due to complications<sup>67</sup></p>	<p>4 Mo, F</p>	<p>Low birthweight</p>	<p>Severe bout of coughing putatively resulted in increased abdominal pressure that caused rectal prolapse, spontaneous rupture of visceral colon, and evisceration of the small bowel.</p>
<p><b>Cough-induced syncope</b> that resulted in death in the setting of <b>cor pulmonale</b> and obstructive lung disease<sup>198</sup></p>	<p>61 y, M</p>	<p>Anthracosilicosis, COPD, cor pulmonale, right ventricle myocardial infarction</p>	<p><b>Cough exacerbated the existing pulmonary hypertension and cor pulmonale</b> as measured by right heart catheterization which led to <b>hypotension, syncope, and ultimately death due to cardiac arrest.</b></p>

**TABLE 3 ] Reasons That Patients With Chronic Cough Seek Medical Attention**

Reason	Frequency, %	Most Troublesome, %
Something's wrong	98	12
Exhaustion	57	17
Self-conscious	55	10
Insomnia	45	4
Lifestyle change	45	12
Musculoskeletal pain <sup>a</sup>	44	3
Hoarseness	43	2
Excessive perspiration	42	1
Urinary incontinence <sup>b</sup>	39	9
Dizziness	38	0
Fear of cancer	33	11
Headache	32	3
Fear of AIDS or TB	28	11
Retching	21	4
Vomiting	18	1
Nausea	16	0
Anorexia	15	0
Syncope or near syncope	5	0

# Recommendations

- In patients complaining of cough, **evaluate for a variety of complications associated with coughing** (eg, cardiovascular, constitutional, GI, genitourinary, musculoskeletal, neurologic, ophthalmologic, psychosocial, and skin complications), which can lead to a decrease in a patient's health-related quality of life.
- Patients with cough should have a thorough diagnostic evaluation, according to the guidelines set forth in this document, to mitigate or prevent these complications.



**감사합니다.**

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