Cough Originating from the Esophaus and Larynx

충북의대 내과
양범희

Contents

- Introduction
- Anatomy and Physiology of the Esophagus and Larynx
- Pathophysiology of Cough Originating from the Esophagus
- Pathophysiology of Cough Originating from the Larynx

Contents

Definition and Importance of Cough

- **Definition of Cough**
  - A cough is **a protective reflex** that clears the airways of mucus, secretions, foreign particles, or irritants.
  - It plays a crucial role in **protecting and maintaining the cleanliness of the respiratory system.**

CHEST guideline and expert panel report. Chest 149 (1), 27–44. doi:10.1378/chest.15-1496

Types of Cough

Feature	Voluntary Cough	Reflex Cough
Trigger	Conscious decision	Involuntary response to irritation
Central Nervous System Involvement	Cerebral cortex (conscious decision)	Medulla (reflex response)
Typical Examples	Clearing food, throat irritation	Dust, smoke, mucus irritation
Cough Development Process	Cognition → Inhale → Cough	Stimulation → Nerve Signal → Cough

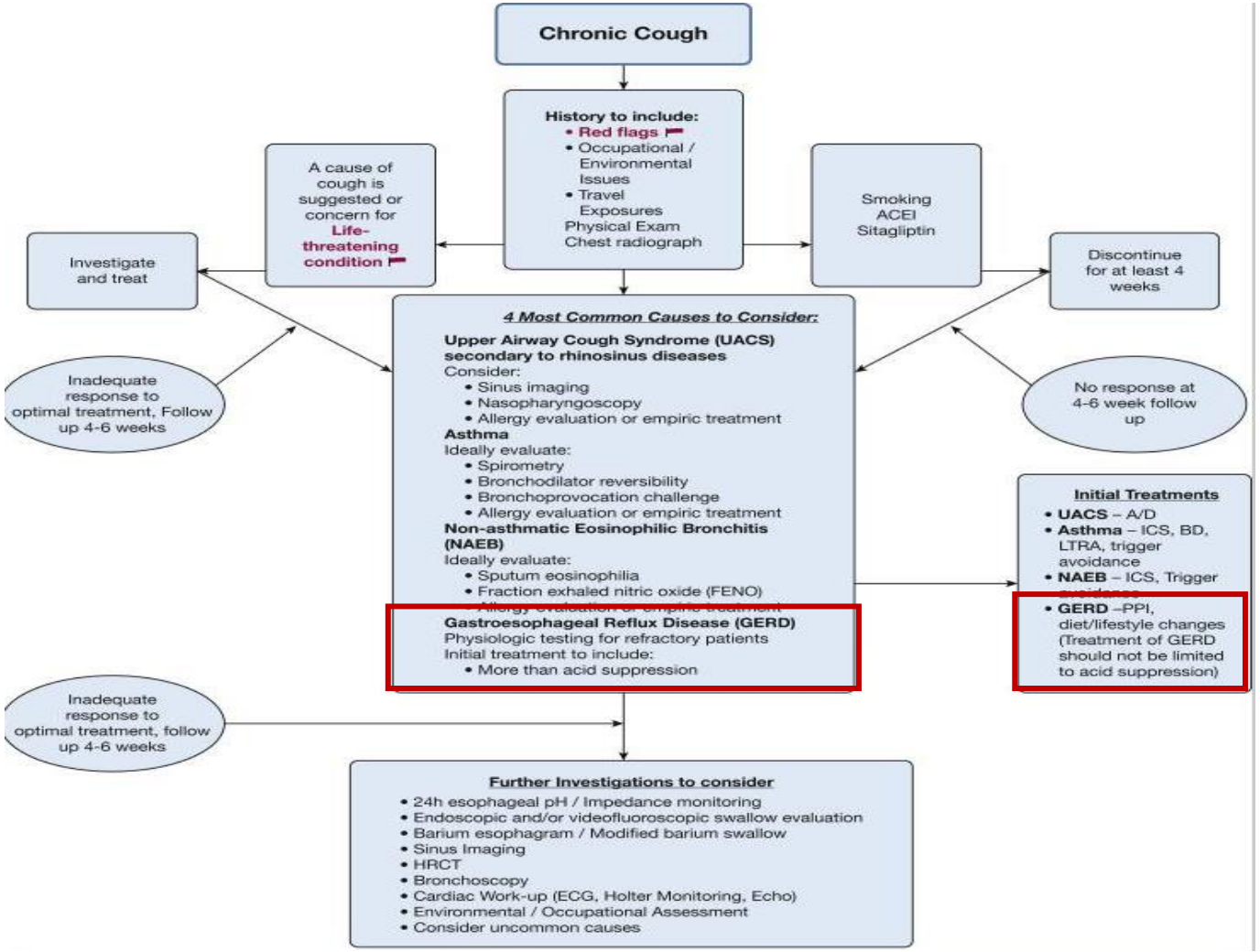
CHEST guideline and expert panel report. Chest 149 (1), 27–44. doi:10.1378/chest.15-1496

Classification of Cough by Duration

- Cough can be classified into three types based on how long it lasts
  - Acute Cough : A cough that lasts less than **3 weeks**
  - Subacute Cough: A cough that lasts between **3 and 8 weeks**
  - Chronic Cough: A cough that lasts longer than **8 weeks**

CHEST guideline and expert panel report. Chest 149 (1), 27–44. doi:10.1378/chest.15-1496

GERD and cough

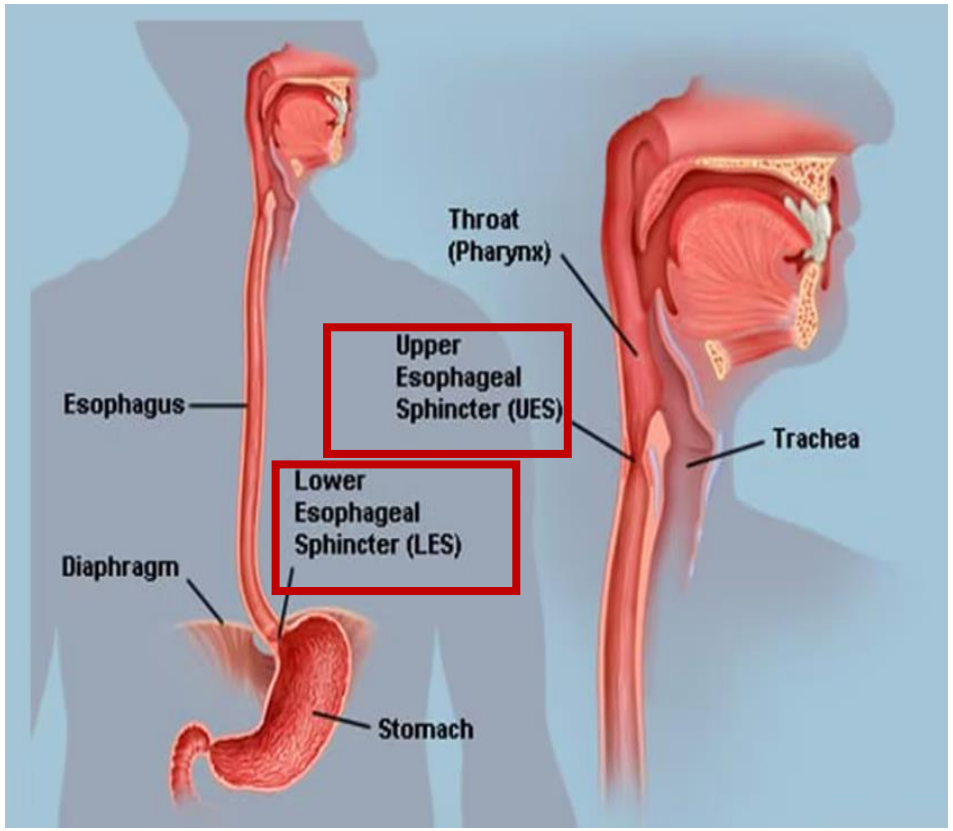


- Approximately 10–59% of chronic cough cases are caused by GERD

CHEST guideline and expert panel report. Chest 149 (1), 27–44. doi:10.1378/chest.15-1496

Contents

Anatomy of the Esophagus

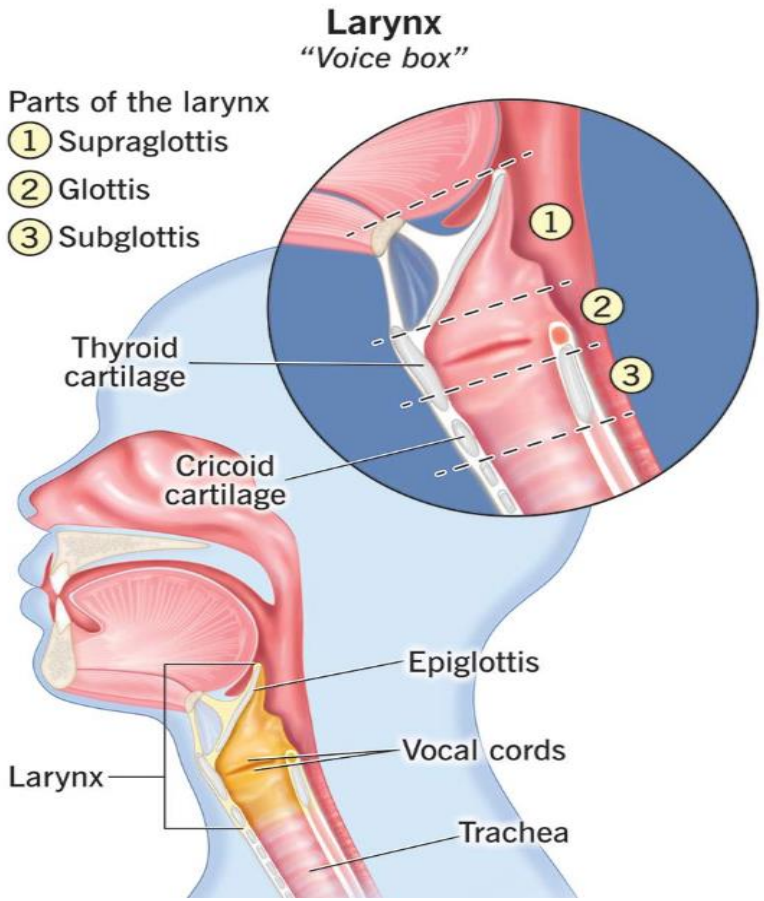


- Key Features
  - Upper Esophageal Sphincter
  - Lower Esophageal Sphincter

- Although **primarily for swallowing**, the esophagus can play a role in **cough reflex when reflux (GERD) occurs, irritating the esophageal lining and triggering a reflex.**

World J Crit Care Med. May 9, 2022; 11(3): 115-128Al-Biltagi M, Bediwy AS, Saeed NK. Cough as a neurological sign: What a clinician should know.

Anatomy of the Larynx

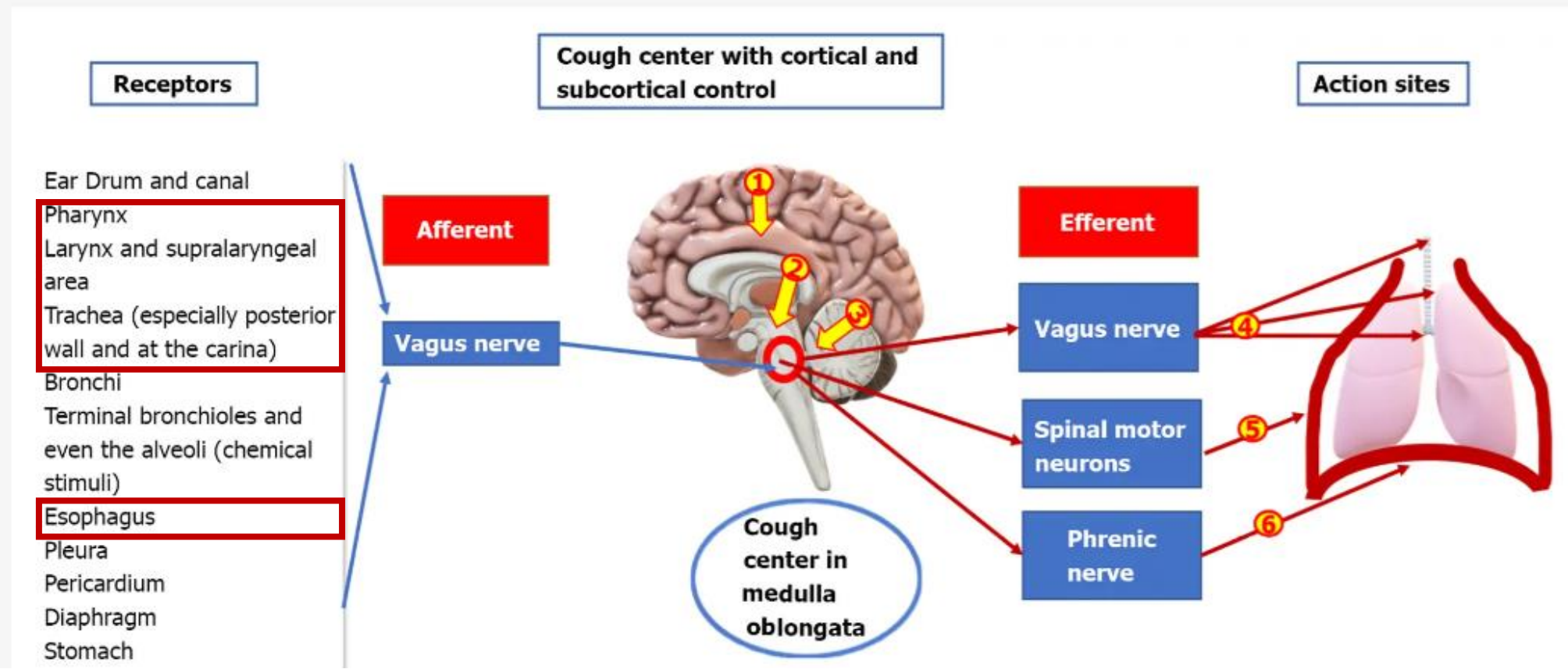


- Key Features
  - Epiglottis
  - Vocal Cords

- The larynx, particularly the vocal cords and surrounding structures, is **highly sensitive to irritants and can trigger a cough reflex when stimulated.**

World J Crit Care Med. May 9, 2022; 11(3): 115-128Al-Biltagi M, Bediwy AS, Saeed NK. Cough as a neurological sign: What a clinician should know.

Physiology of the Cough Reflex



Contents

Cough Originating from the Esophagus

- **GERD (Gastroesophageal Reflux Disease)**
  - **Acid Reflux Irritation:** The acidic content from the stomach irritates the esophagus and can stimulate the cough reflex.
  - **Vagal Reflex Pathway:** Acidic irritation activates sensory receptors in the esophagus, which send signals via the vagus nerve to the cough center in the brainstem.
  - **Microaspiration**

Respir. Med. 105 (8), 1257–1261.
Am. J. Gastroenterol. 115 (9), 1412–1428.
Gastroenterology 154 (2), 302–318
Laryngoscope 124 (10), 2375–2379.

Cough Originating from the Esophagus

- **Eosinophilic Esophagitis:** an allergic/immune condition characterized by eosinophil accumulation in the esophagus, leading to inflammation and symptoms.

less common but should be considered in cases of **unexplained chronic cough with other esophageal symptoms, such as dysphagia or food impaction**

Respir. Med. 105 (8), 1257–1261.
Am. J. Gastroenterol. 115 (9), 1412–1428.
Gastroenterology 154 (2), 302–318
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Cough Originating from the Esophagus

- **Structural Abnormalities and Cough:**
  - **Zenker's Diverticulum:** An outpouching of the esophageal wall that can trap food and cause regurgitation and cough.
  - **Esophageal Strictures:** Narrowing of the esophagus due to inflammation or scarring that can lead to retained food, causing irritation and cough.

Structural abnormalities may present with other symptoms, such as difficulty swallowing

Respir. Med. 105 (8), 1257–1261.
Am. J. Gastroenterol. 115 (9), 1412–1428.
Gastroenterology 154 (2), 302–318
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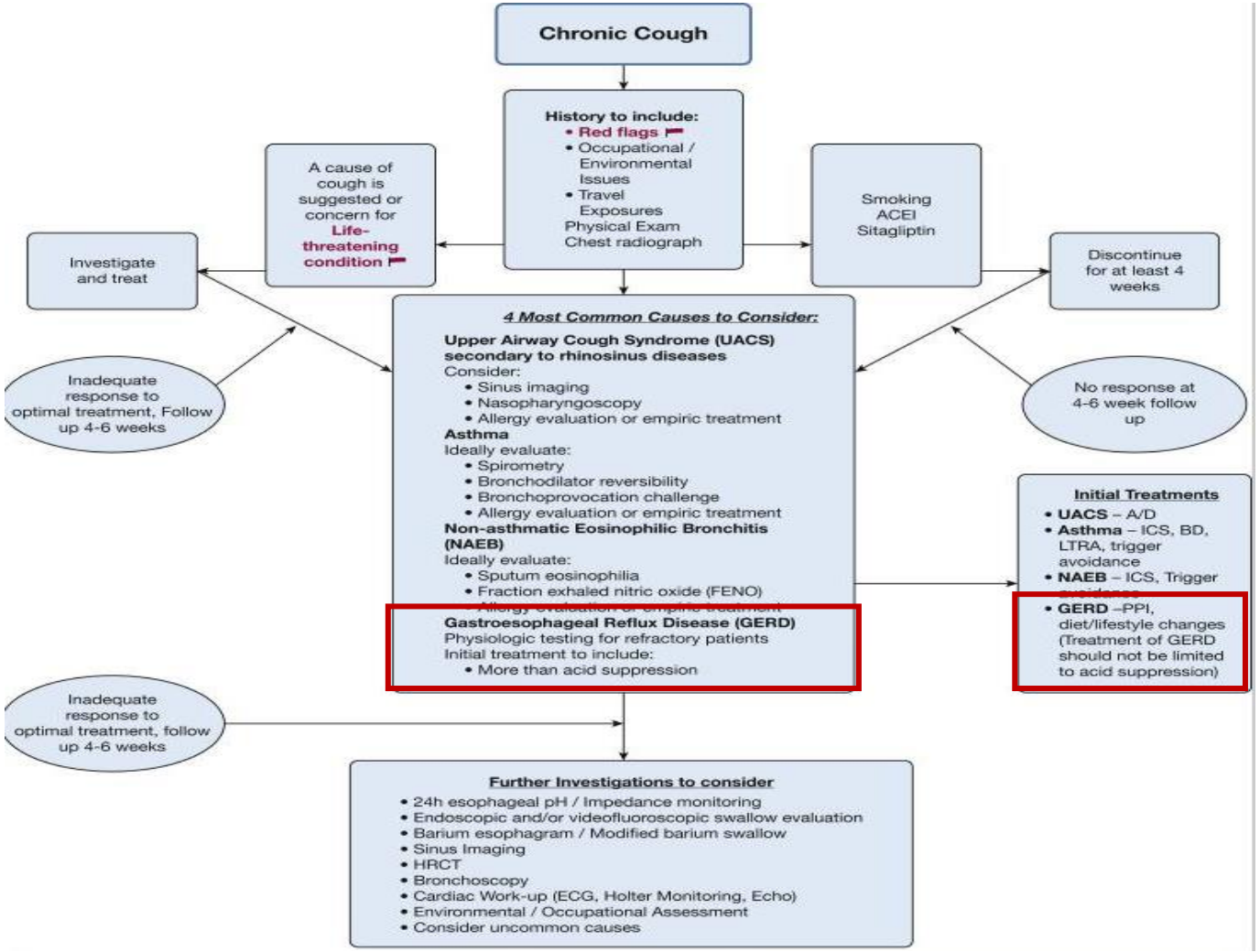
Gastroesophageal reflux disease related cough (GERC)

GERD and cough



- Approximately 10–59% of chronic cough cases are caused by GERD

CHEST guideline and expert panel report. Chest 149 (1), 27–44. doi:10.1378/chest.15-1496

Pathophysiology

Figure 1

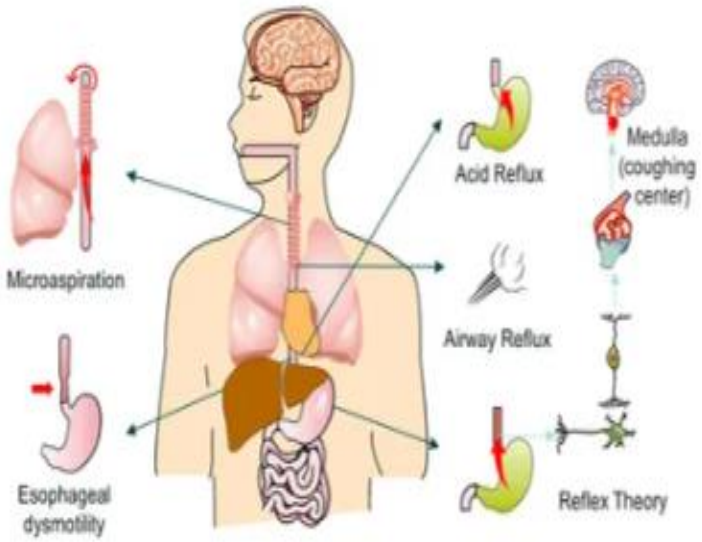


FIGURE 1. Possible mechanism of GERC.

- reflux theory
- reflex theory
- esophageal dysmotility

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Pathophysiology

Figure 1

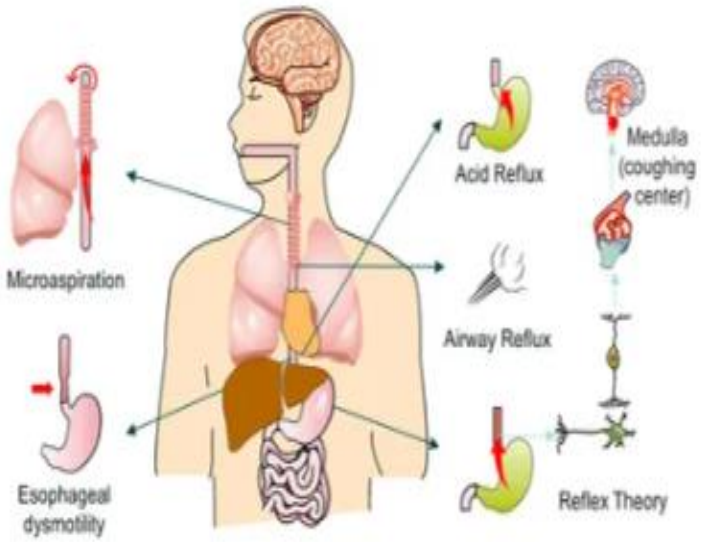

FIGURE 1. Possible mechanism of GERC.

- reflux theory
  - Acid reflux
  - Microaspiration
  - Airway reflux

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Pathophysiology

Figure 1

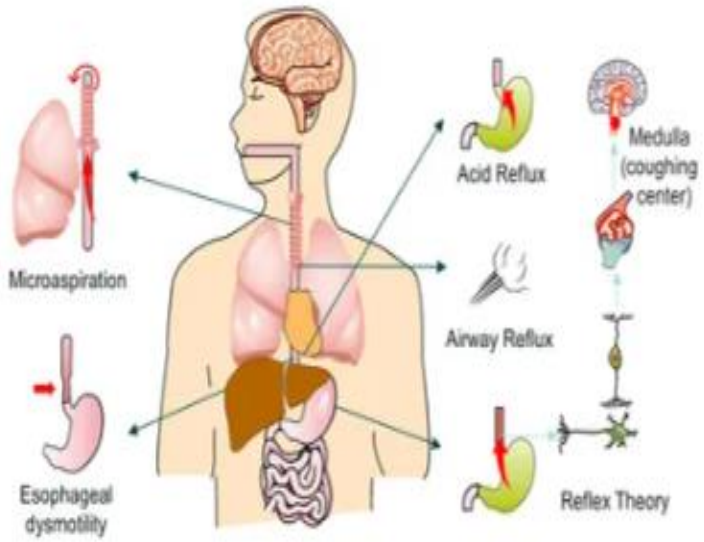

FIGURE 1. Possible mechanism of GERC.

- reflex theory
  - the distal esophageal afferent nerve-mediated esophagus-tracheobronchial reflex

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Am. J. Gastroenterol. 115 (9), 1412–1428.
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Pathophysiology

Figure 1

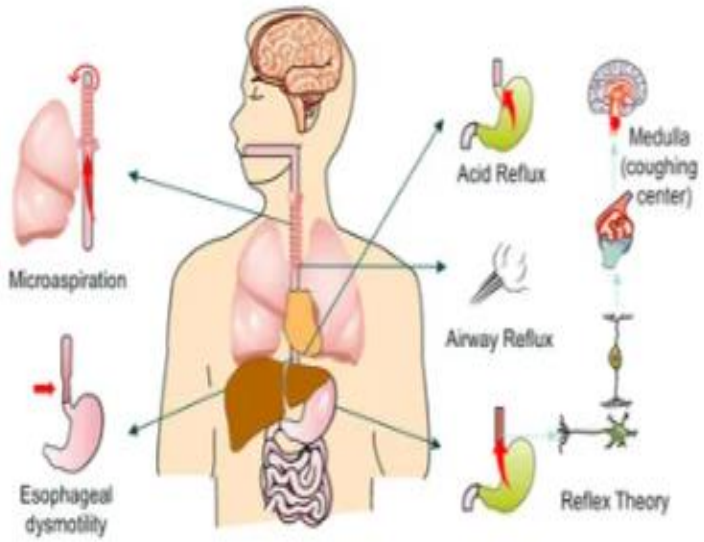

FIGURE 1. Possible mechanism of GERC.

- esophageal dysmotility
  - ineffective esophageal motility
  - massive esophageal ruptures

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Am. J. Gastroenterol. 115 (9), 1412–1428.
Gastroenterology 154 (2), 302–318
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Diagnosis

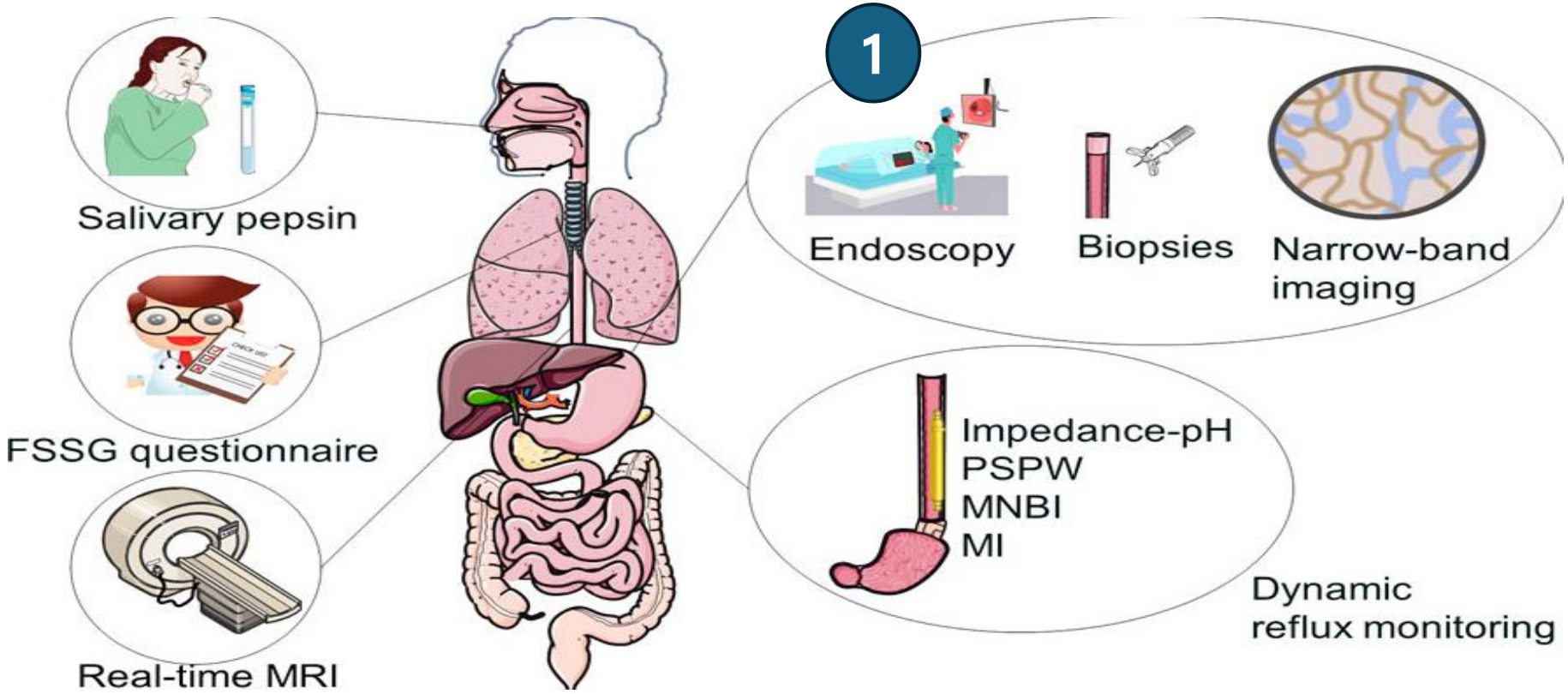
- When patients have no signs of reflux, it might be difficult to identify GERC (GERD related cough)

- about 70% of GERC patients do not have typical gastrointestinal reflux symptoms

Diagnosis

- **Endoscopy and biopsies**
- Dynamic reflux monitoring
  - **Impedance pH detection**
  - Symptom index (SI) and symptom association probability (SAP)
- Other impedance parameters
  - Mean nocturnal baseline impedance (MNBI)
  - DeMeester score
  - Post-reflux swallow-induced peristaltic wave (PSPW)
  - Mucosal impedance (MI)
  - Real-time magnetic resonance imaging (MRI)
  - **Proton pump inhibitor trial**
  - Salivary pepsin
  - Frequency of symptoms of gastroesophageal reflux scale (FSSG)

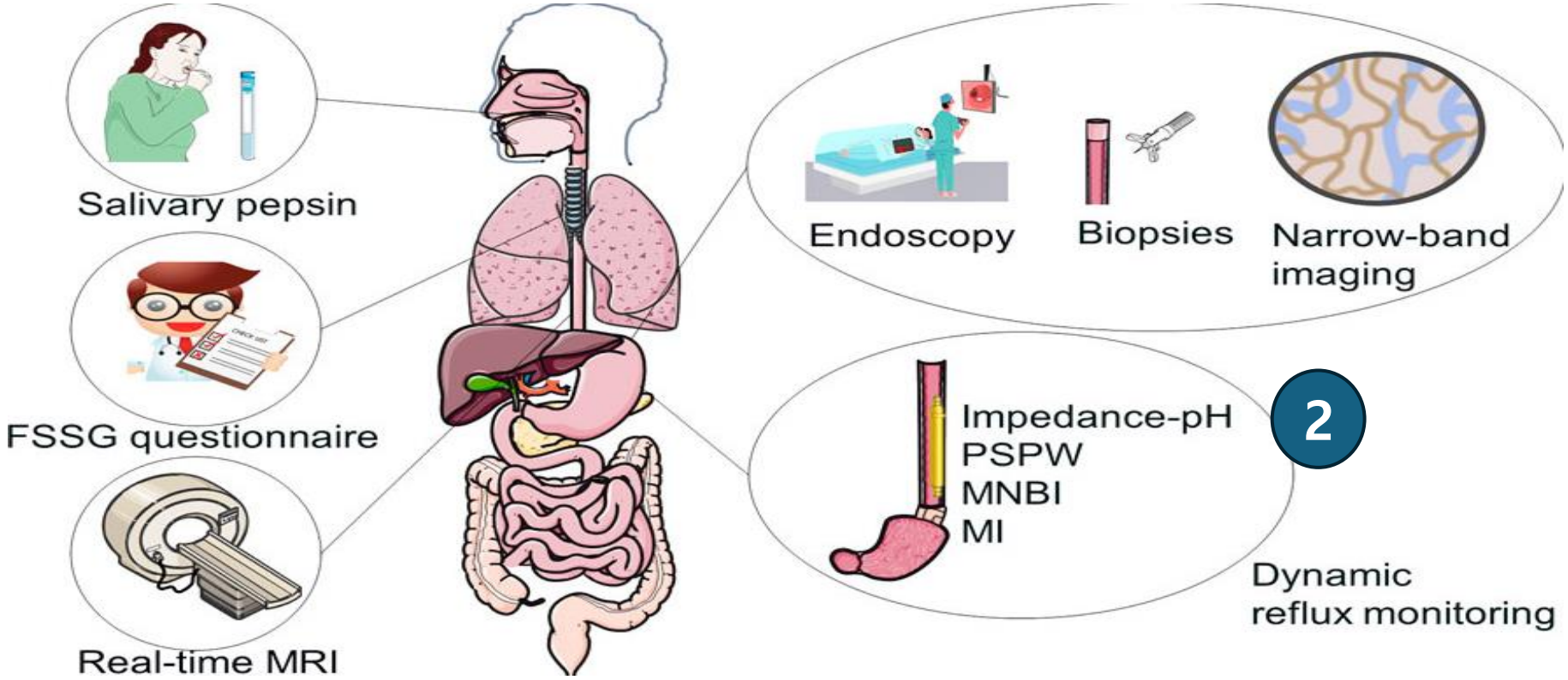
Diagnosis



Endoscopy is the preferred screening method for suspected GERD syndrome. However, so far, endoscopy has not shown great advantages in the detection of GERC due to **its low diagnostic rate and low patient tolerance.**

Clin. Gastroenterol. Hepatol. 13 (6), 1082–1088.

Diagnosis



Impedance-pH monitoring is often regarded as the most precise and thorough tool for evaluating GERD and has greatly improved the diagnosis of GERD patients.

Clin. Gastroenterol. Hepatol. 13 (6), 1082–1088.
Respir. Med. 109 (8), 963–969.

Diagnosis

- Proton pump inhibitor trial
  - A practical approach, but response to PPI therapy is not equivalent to the diagnosis of GERD, especially since GERD has many atypical extraesophageal symptoms
  - the low specificity, high placebo response and the low cost of empirical PPI treatment compared with diagnostic tests it leads to **overdiagnosis and overuse of PPI**.

Treatment

- **Lifestyle changes**
- Medications
  - Baclofen
  - Gabapentin
  - Acid suppression therapy
  - **Proton pump inhibitor (PPI)**
  - H+/K+-ATPase blockers (P-CAB)
  - Prokinetic therapy
  - Anti-reflux surgery

Contents

Cough Originating from the Larynx

- **Postnasal Drip Syndrome (Upper Airway Cough Syndrome)**
- **Laryngopharyngeal Reflux (LPR)**
- Vocal Cord Dysfunction (VCD)
- Chronic Laryngitis

Definition of LPRD

Laryngopharyngeal reflux disease (LPRD) refers to the retrograde flow of gastric content to the laryngopharynx, where it comes in contact with tissues of the upper aerodigestive tract.

- 위산을 포함한 위의 내용물이 인두와 후두로 역류하여 임상 증상을 나타내거나,
  인후두 조직의 형태학적 변화를 초래하는 경우를 위식도 역류질환과 구분하여
  인후두 역류질환(laryngopharyngeal reflux disease, LPRD)이라고 한다.
  [인후두 역류질환 표준진료지침서 권고수준 1]

Korean J Otorhinolaryngol-Head Neck Surg 2014;57(10):698-702

GERD ≠ LPRD

Gastroesophageal reflux disease

Laryngopharyngeal reflux disease

Table. Summary of typical differences between GERD and LPR*

	GERD	LPR
Symptoms		
Heartburn and/or regurgitation	++++	+
Hoarseness, cough, dysphagia, globus	+	++++
Findings		
Esophagitis	++++	+
Laryngeal inflammation	+	++++
Test results		
Erosive or Barrett's esophagitis	+++	+
Abnormal esophageal pH monitoring	++++	++
Abnormal pharyngeal pH monitoring	+	++++
Esophageal dysmotility	+++	+
Abnormal esophageal acid clearance	++++	+
Pattern of reflux		
Supine (nocturnal) reflux	++++	+
Upright (daytime) reflux	+	++++
Both	+	++
Response to treatment		
Effectiveness of dietary and lifestyle modifications	++	+
Successful treatment with a single-dose PPI†	+++	+
Successful treatment with a twice-daily PPI	++++	+++

✓ **Symptoms**

LPRD : 인후통, 만성적인 헛기침, 애성, 인후두 이물감 등의 비특이적인 증상

✓ **Periods of acid**

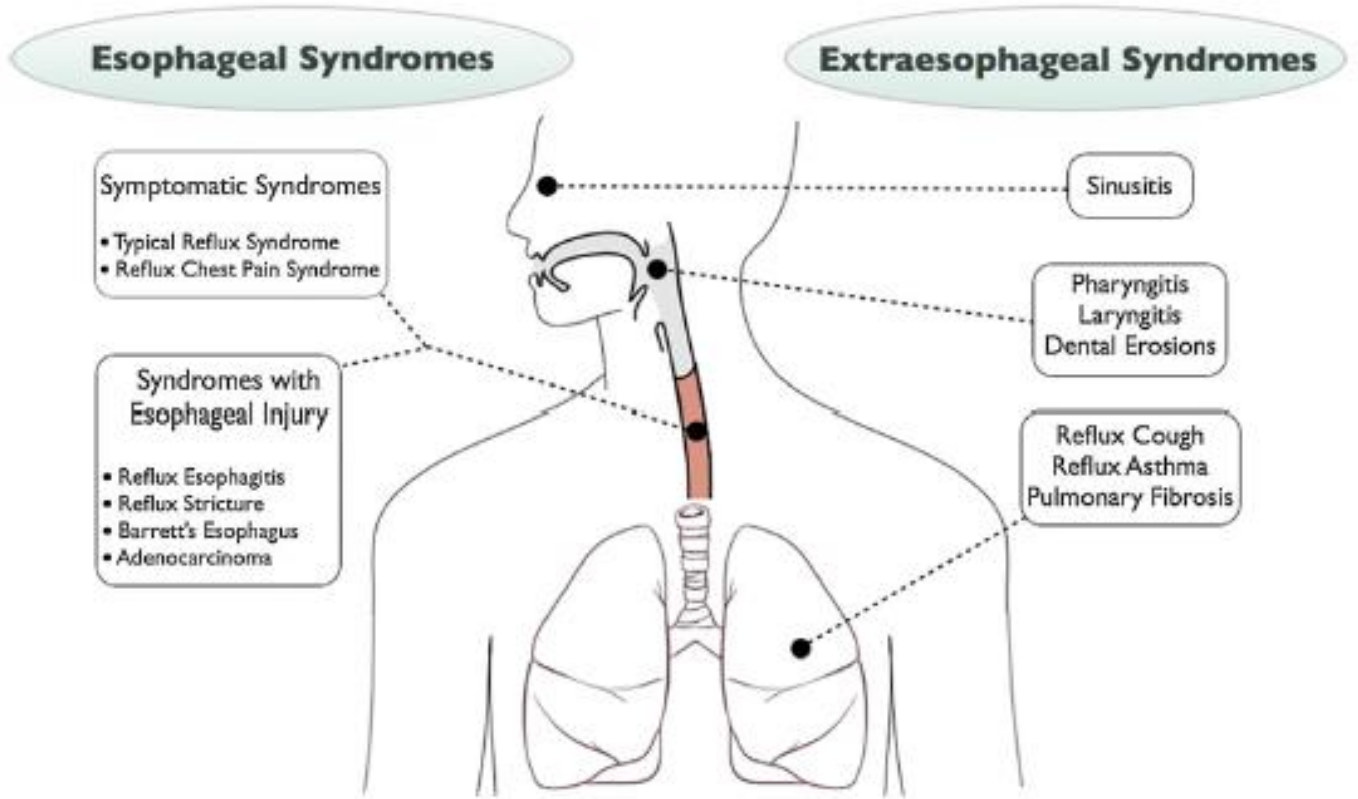
More prolonged periods of acid exposure in GERD

✓ **Position of acid**

- LES in GERD
- UES in LPR

Korean J Otorhinolaryngol-Head Neck Surg 2011;54:519-25

GERD is a condition that develops when reflux of stomach contents causes troublesome symptoms and/or complications



Korean J Otorhinolaryngol-Head Neck Surg 2011;54:519-25

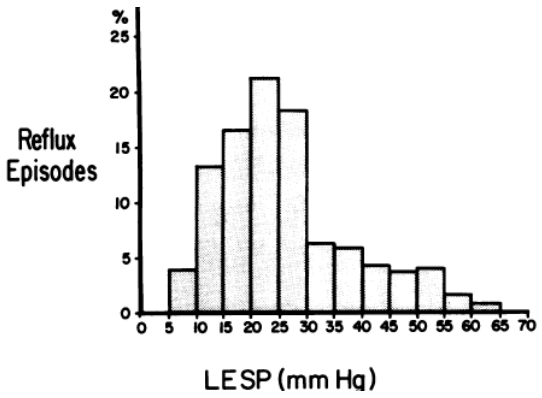
Symptoms of LPRD

- Hoarseness/dysphonia (71%)
- **Chronic cough (51%)**
- Globus pharyngeus (47%)
- Chronic throat clearing (42%)
- Dysphagia (35%)
- Heartburn (10~13%)/ no heartburn (↑ 50%)

Koufman JA., The Laryngoscope 1991; 101(4 Pt 2 Suppl 53): 1-78

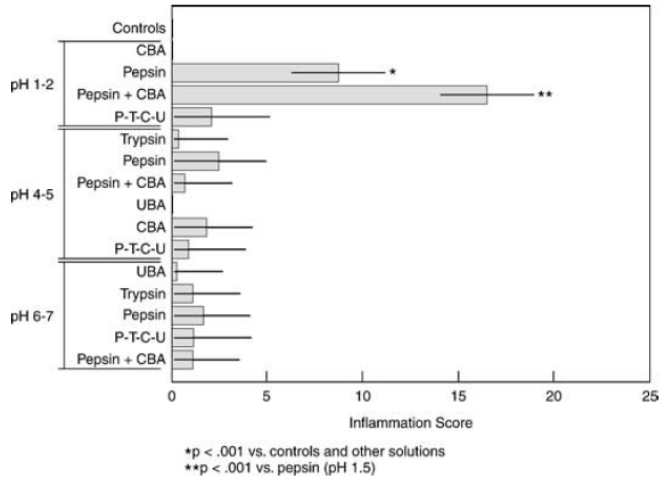
Pathophysiology

1. 하부 식도 괄약근의 일시적인 이완



- 70~100%의 역류 현상이 일시적이고 불규칙한 하부 식도 괄약근 (LES, Lower esophageal sphincter)의 이완시 발생

2. 위와 십이지장의 분비물의 영향



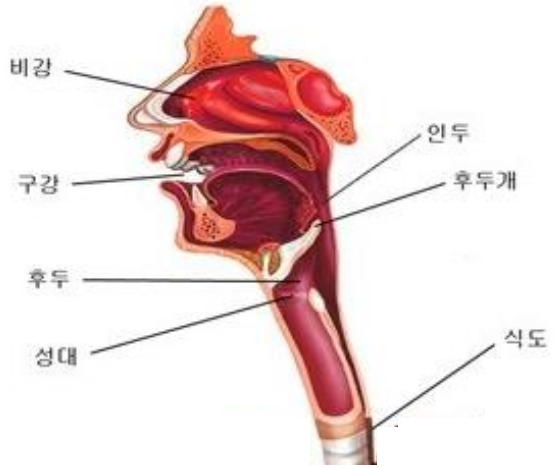
- 낮은 pH에서, 펩신과 담즙산이 후두의 발적과 조직학적인 염증 등의 손상을 가장 많이 일으킴

Sang Hyuk Lee et al, Korean J Otorhinolaryngol-Head Neck Surg 2011; 54: 519-25
J Dent et al, J Clin Invest 1980; 65(2): 256-67,
Adhami T, et al, Am J Gastroenterol 2004; 99: 2098-2106

Pathophysiology

3. 후두 점막의 민감성

- 일반적으로 후두는 식도에 비하여 위산 역류에 보다 더 쉽게 손상을 받는 것으로 알려져 있음
- 한 연구에서, 산도 검사상 식도의 경우 정상 성인은 하루에 50회 정도의 위산 역류를 견딜 수 있지만 후두의 경우 식도와는 다르게 1주일에 단 3차례의 후두 역류로도 심각한 후두의 염증과 손상을 일으킬 수 있다고 보고함



Korean J Otorhinolaryngol-Head Neck Surg 2011;54:519-25, Koufman JA. Laryngoscope. 1991 Apr;101(4 Pt 2 Suppl 53):1-78

Diagnosis

✓ 식도 외 증상을 호소하는 환자의 50% 가량은 가슴 쓰림과 위산 역류 등의 전형적인 역류 증상을 호소하지 않을 수 있음

✓ It is important for physicians to appreciate the potential significance of hoarseness and the relative nonspecificity of laryngitis.

Table. Clinical Clues to Distinguish LPR From Other Causes of Hoarseness

	LPR	Infection	Rhinosinusitis (Postnasal Drip)	Allergy	Benign Vocal Fold Lesion	Malignant Vocal Fold Lesion
Hoarseness characteristic	Fluctuates	Acute, resolves	Acute/chronic or recurrent	Fluctuates	Constant	Progressive
Throat pain	Common (with cough, throat clearing)	Yes	Uncommon	No	From secondary muscle tension	Late (local and referred)
Laryngeal findings	Edema, granuloma, erythema, pseudosulcus	Erythema, edema	Secretions (thick, discolored), edema	Edema, clear secretions, bluish mucosa	Nodules, polyps, cysts, scars	Ulcerative or exophytic (red-white mass), stiff
Aggravating factors	Smoking, obesity, diet/lifestyle	Systemic infection, immunosuppression	LPR, allergy, smoking	Environment, seasonal	Smoking, vocal trauma, LPR	Smoking (common), LPR, ethanolism

Abbreviation: LPR, laryngopharyngeal reflux.

✓ 흡연과 음주 여부, 식도 역류를 일으킬 수 있는 환자의 음식물 섭취 취향과 약물 복용 등의 선행요인 조사 필요

Ear Nose Throat J 2002;81(9 suppl 2):7-9. JAMA. 2005;294:1534-1540

Laryngoscopy

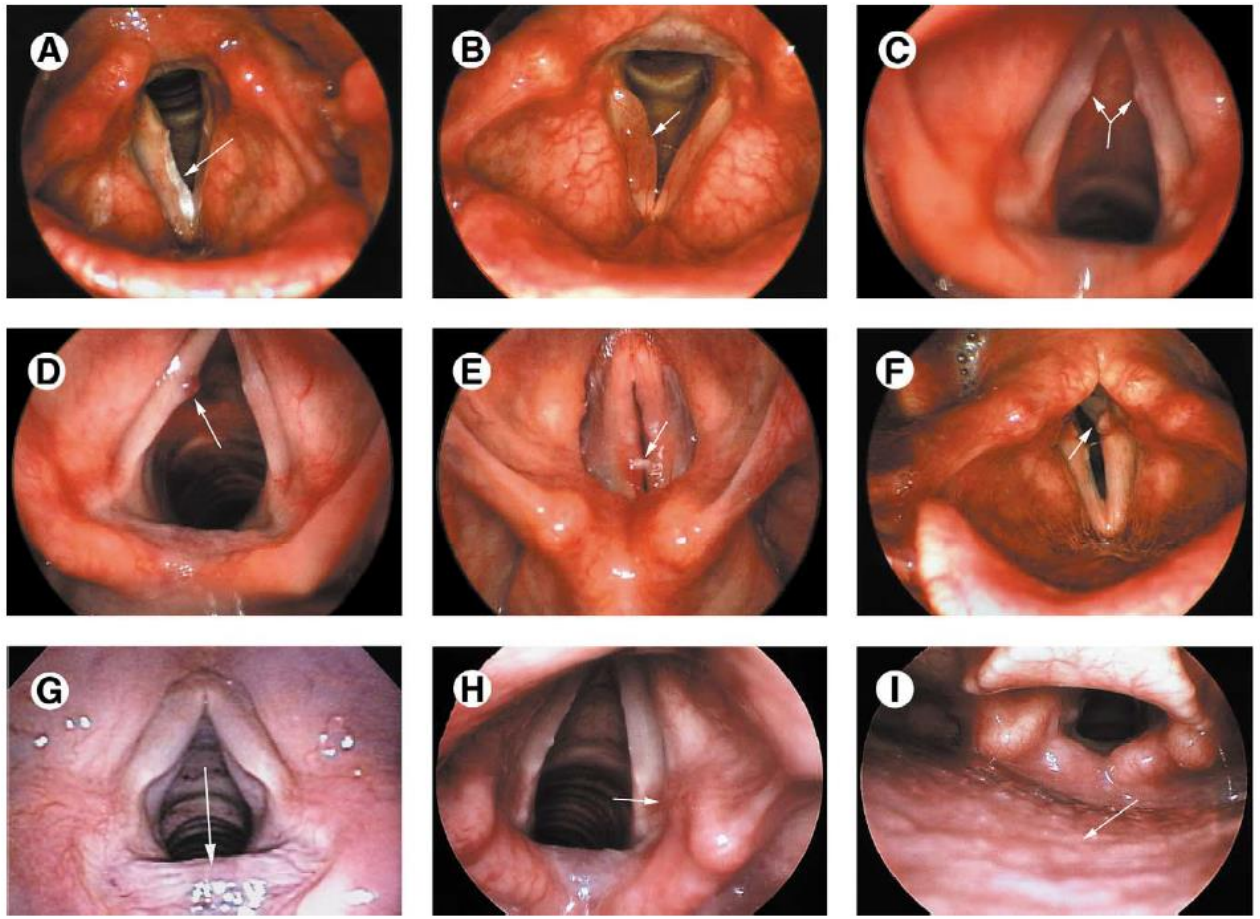


Figure 3. Abnormal larynx. (*A*) Leukoplakia; (*B*) Reinke's edema; (*C*) bilateral true vocal fold nodules; (*D*) true vocal fold hemorrhagic polyp; (*E*) true vocal fold erythema; (*F*) vocal fold granuloma; (*G*) interarytenoid bar; (*H*) arytenoid medial wall erythema; (*I*) posterior pharyngeal wall cobble stoning.

MICHAEL F. et al, CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2003;1:333–344

RSI (Reflux Symptom Index)

1	쉰목소리가 난다. 거칠거나 고르지 않은 목소리가 난다. (목소리에 문제가 있다).
2	목청을 가다듬는다(하루에 네 번 이상 목청을 가다듬는다). (헛기침을 한다).
3	후비루가 있다(코에서 목구멍으로 점액이나 분비물이 넘어간다).
4	음식물을 삼키기 어렵다(연하곤란).
5	식사 후나 누우면 기침이 나온다.
6	숨쉬기 힘들거나 가끔 사래가 든다.
7	성가시거나 문제가 되는 기침이 난다.
8	목구멍에 이물감을 느낀다 (목구멍에 덩어리가 걸려있는 느낌이 든다).
9	가슴이 쓰리거나, 가슴이 아프거나, 소화가 안 되거나, 위산이 넘어오는 것을 느낀다.

RFS (Reflux finding score)

TABLE I.
Reflux Finding Score (RFS).

Subglottic edema	성문하 부종	0 = absent 2 = present
Ventricular	후두실 부종	2 = partial 4 = complete
Erythema/hyperemia	후두 홍반	2 = arytenoids only 4 = diffuse
Vocal fold edema	성대 부종	1 = mild 2 = moderate 3 = severe 4 = polypoid
Diffuse laryngeal edema	범발성 후두부종	1 = mild 2 = moderate 3 = severe 4 = obstructing
Posterior commissure hypertrophy	후연합부 점막비후	1 = mild 2 = moderate 3 = severe 4 = obstructing
Granuloma/granulation tissue	육아종 혹은 육아조직	0 = absent 2 = present
Thick endolaryngeal mucus	후두 내 진한 점액	0 = absent 2 = present

Peter C et al, Symptoms and findings of laryngopharyngeal reflux. Ear Nose Throat J. 81(Suppl 2):10,2002

Management of LPRD

Behavioral modification

Medical treatment

Surgical treatment

Lifestyle modification

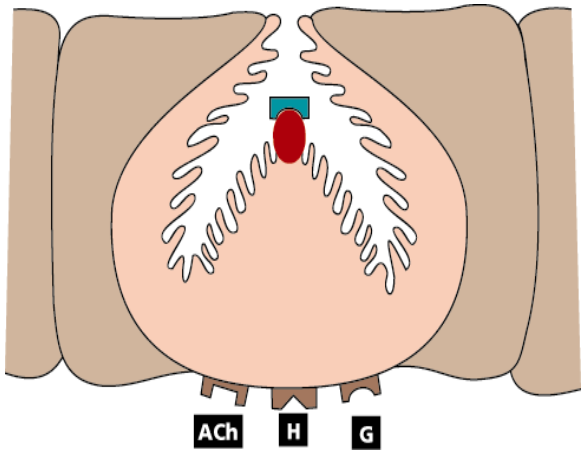
- Avoidance : heavy meals, smoking, alcohol, late meals, fat intake
- Avoidance of food and liquid before bedtime
- Sleeping with the head of bed elevated
- Reducing body weight
- Addictive benefit in patients receiving medical Tx.

Medical treatment

- H2 receptor antagonist
- Prokinetic agent
- Mucosal cytoprotectant
- Antacids
- Proton pump inhibitor

Proton Pump Inhibitor

- Blocking the final step of gastric acid production



- Proton pump inhibitors are considered the mainstay of medical treatment, although there is some controversy regarding their efficacy.

- A 3-month empirical trial is a cost-effective approach to initial assessment and management.

Charles N, JAMA. 2005;294(12):1534-1540

감사합니다