YU:MC 영남대학교병원

Drug induced cough

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- **Drug with a secondary or indirect effect**
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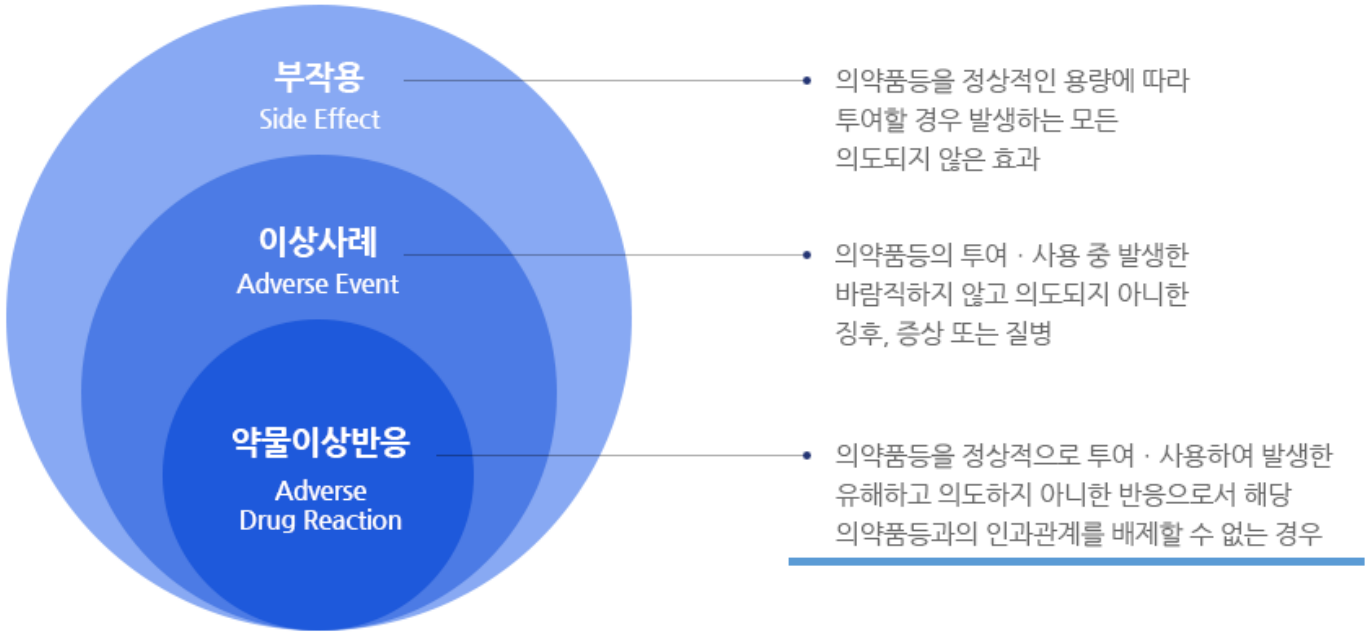
    - Drug-induced esophagitis
- **Low evidence drugs (CASE reports)**

Drug induced cough

- Primary cause : Drug
- Sx. : cough
- 약제의 복용 후 시작
- 약제의 중단 후 호전
- Adverse drug reaction



WHO ADR system VigiBase

- 110개 이상의 국가, 국가 약물 당국이 수집하고 100,000개 이상의 다양한 의약품에 걸쳐 의심되는 ADR에 대한 보고서를 보관하는 저장소

- Sitagliptin : 28574건의 ADR → cough 337 (1.18%)
- Metformin : 75718건의 ADR → cough 643 (0.85%)
- Dextromethorphan : 9589건의 ADR → cough 155 (1.62%)
- Lisinopril(ACE-i) : 52500건의 ADR → cough 10178 (**19.4%**)

Lung. 2020 Apr;198(2):271-273.

Incidence

Supplementary Table S1. Causes of patients with chronic cough (n = 1,822, cases = 1,972)

Diagnosis	No. of patients
CVA	288 (15.8)
EB	389 (21.4)
GERC	321 (17.6)
UACS	313 (17.2)
AC	102 (5.6)
Unexplained	136 (7.5)
Others	423 (23.2)

Data are presented as number (%).
CVA, cough-variant asthma; EB, eosinophilic bronchitis; GERC, gastro-esophageal reflux related cough; UACS, upper airway cough syndrome; AC, atopic cough. Other causes included 73 chronic obstructive pulmonary disease, 71 bronchiectasis, 68 post-infectious cough, 61 chronic bronchitis, 61 classic asthma, 21 protracted bacterial bronchitis, 20 interstitial pneumonia, 11 obstructive sleep apnea syndrome, 8 angiotensin-converting enzyme inhibitor-induced cough, 6 bronchiolitis, 6 diffuse panbronchiolitis, 4 fungus-associated chronic cough, 4 cardiac arrhythmia induced cough, 3 postoperative cough, 2 cervical spondylosis related cough, 1 Kartagener's syndrome, 1 thyroid enlargement induced cough, 1 vocal cord amyloidosis related cough, 1 menstrual periods cough.

0.5%
China, single-center, observational study

Korea, 19 multi-center,
Observational study, 427명

Final diagnosis	
UACS	229 (53.6)
CVA	200 (46.8)
EB	34 (8.0)
GERD	63 (14.8)
Psychogenic cough	25 (5.9)
Others	12 (2.8)

Allergy Asthma Immunol Res. 2019 Nov;11(6):871-884.
Tuberc Respir Dis (Seoul). 2020 Jan; 83(1): 31–41.

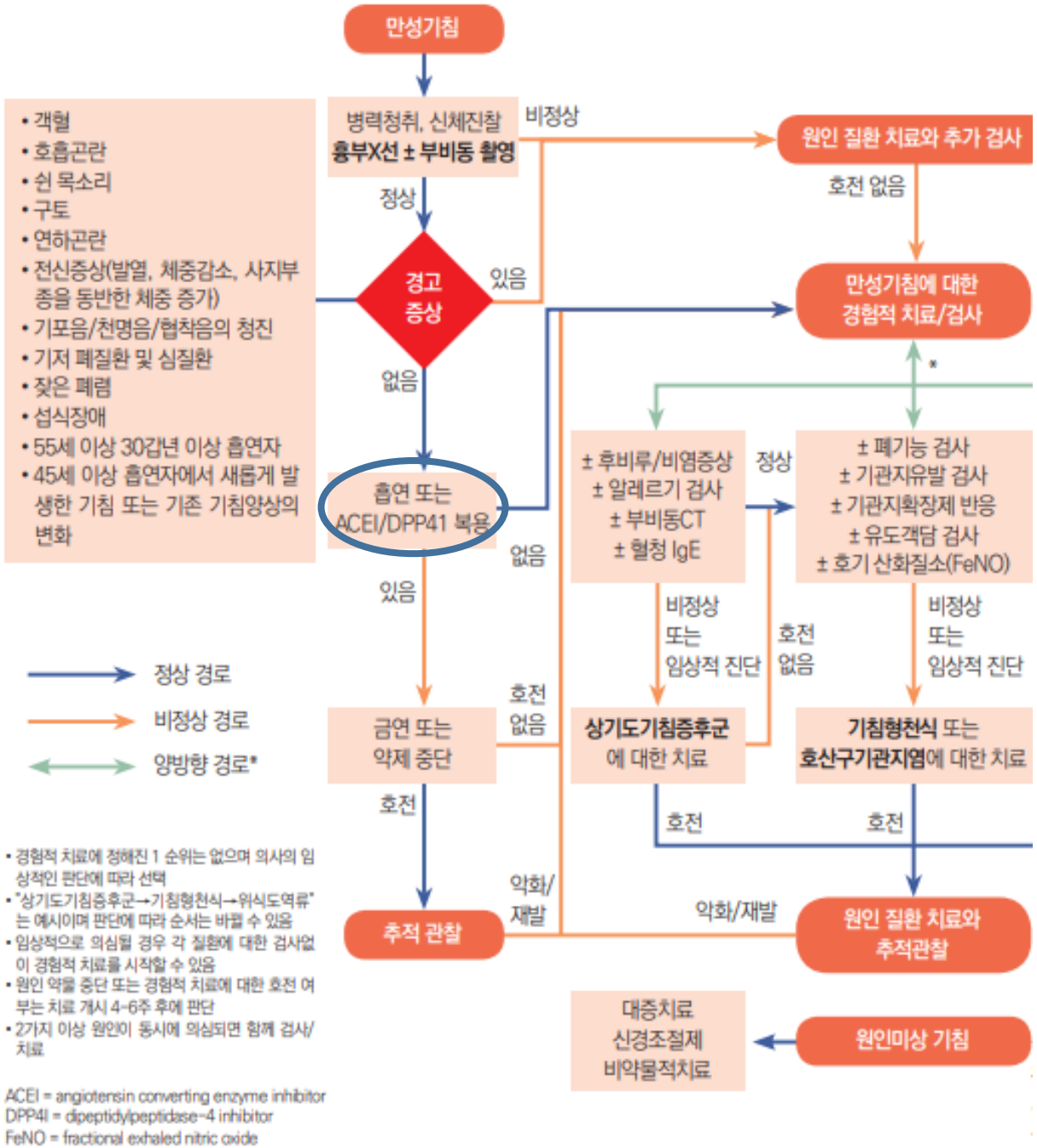


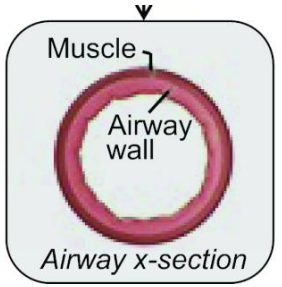
그림 4. 만성기침의 진단적 접근

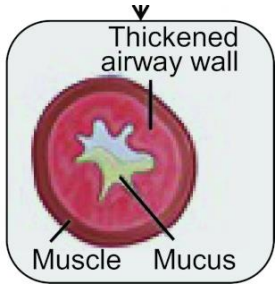
History taking and physical examination on presentation
- Cough duration
- Cough impact and triggers
- Family history
- Cough score (using VAS or verbal out of 10)
- HARQ
- Associated symptoms: throat, chest, gastrointestinal
- Risk factors: ACE inhibitor, smoking, sleep apnoea
- Physical examination: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

TRD, 2020 기침진료지침
Eur Respir J. 2020 Jan 2;55(1):1901136

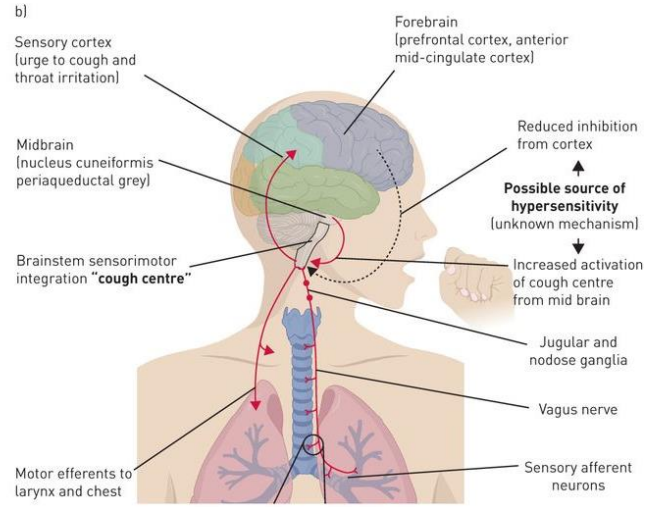
Pathophysiological phenomena of cough

- 1. Airway hyperresponsiveness

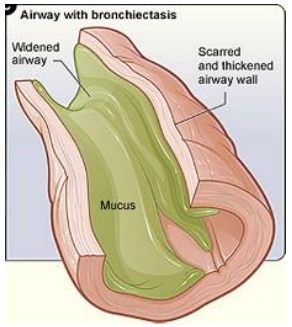




- 2. <u>Hypersensitivity of cough reflex arc</u>



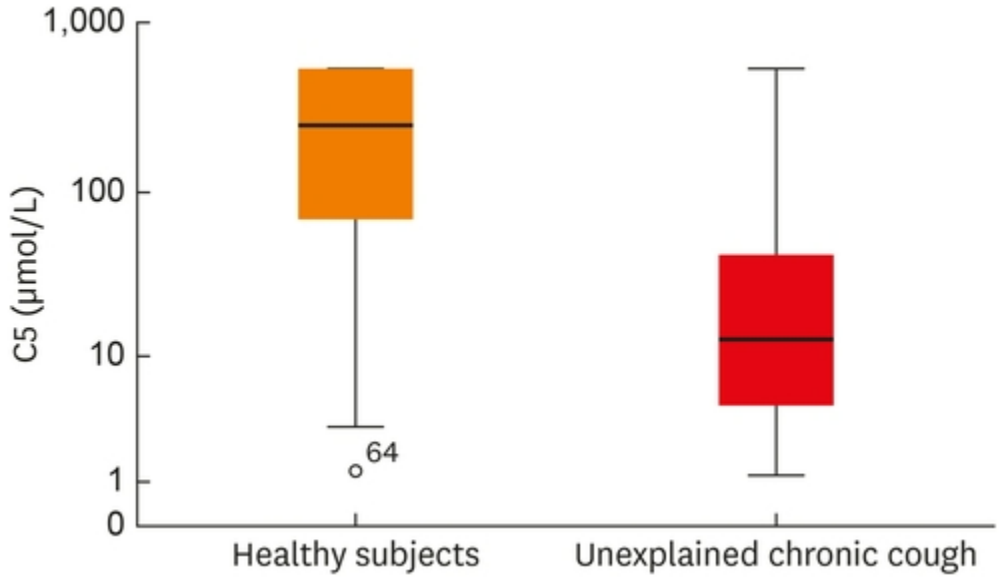
- 3. Airway mucus production ↑



Eur Respir J. 2019 Jul 4;54(1):1900889.
N Engl J Med. 2004 Aug 5;351(6):531-2.
National Heart Lung and Blood Institute

Cough provocation test
- hypersensitive cough reflex -

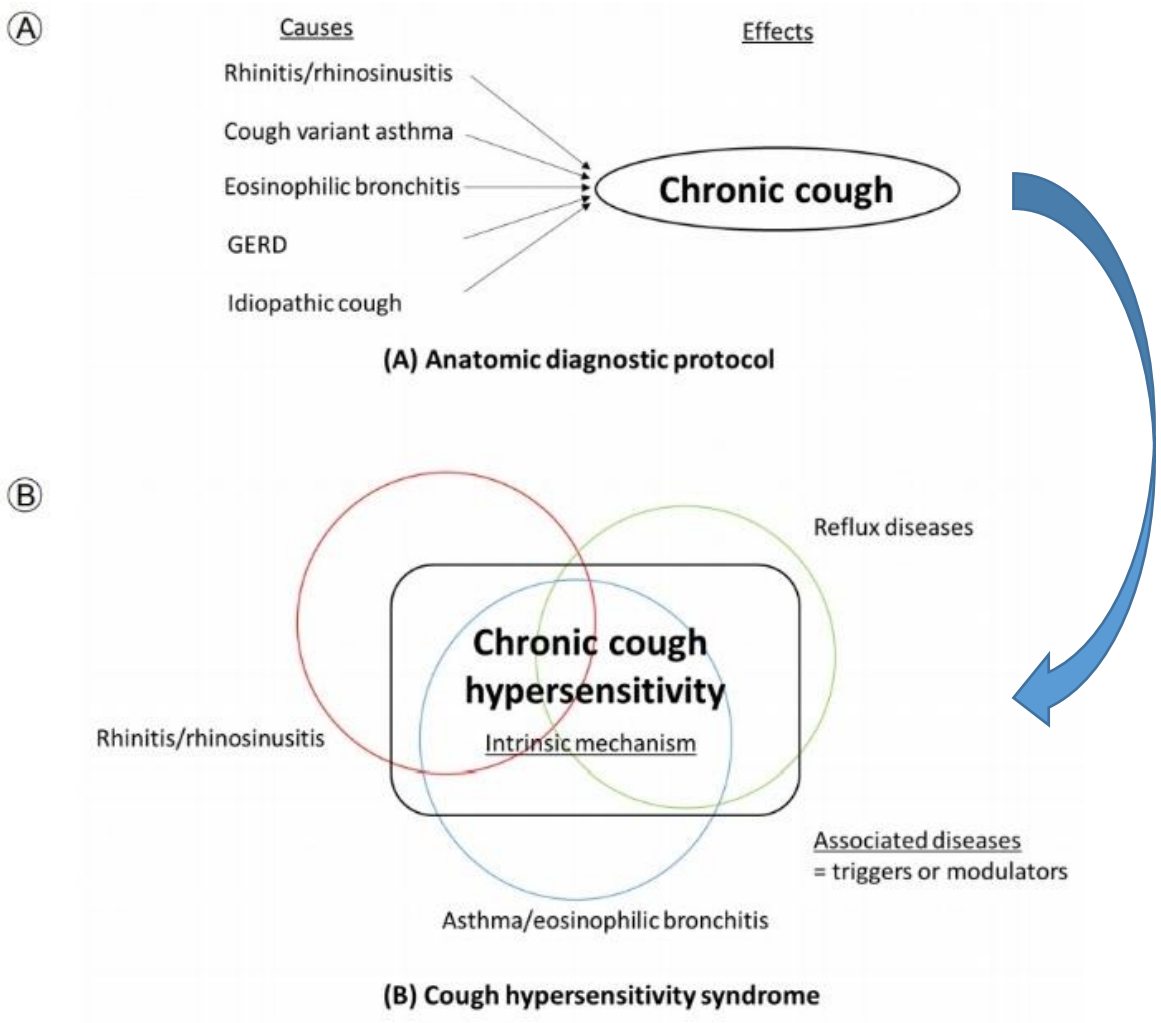
- Capsaicin, Citric acid, Tartaric acid..

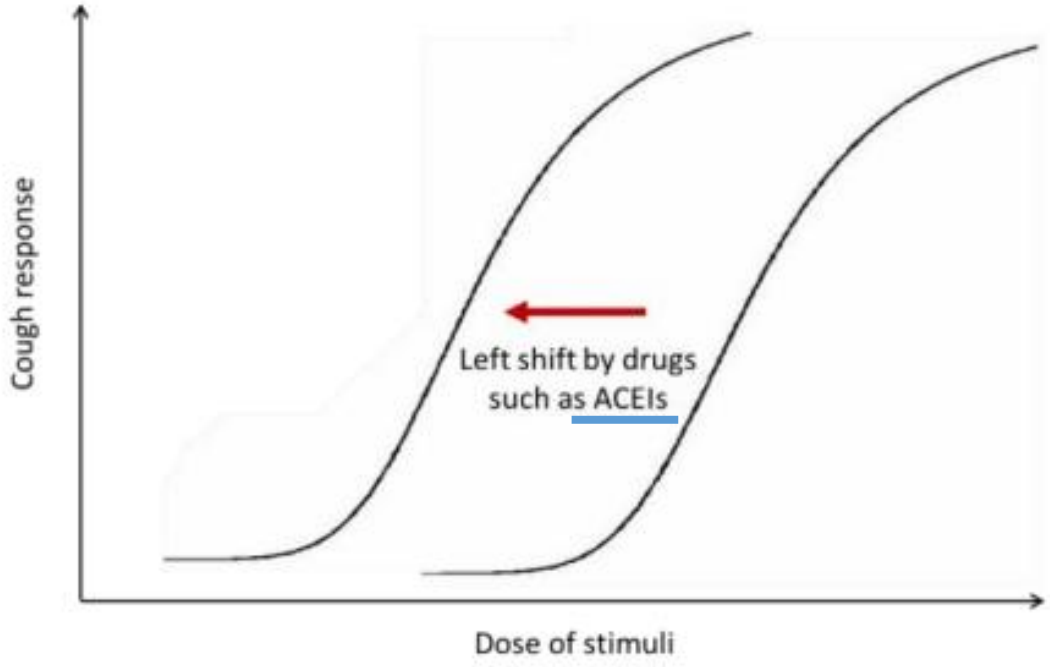


Chemical irritant (solvent, perfume)
Refractory cough
Unexplained cough
GERD associated cough
Cough variant asthma

Eur Respir J. 2019 Jul 4;54(1):1900889.
N Engl J Med. 2004 Aug 5;351(6):531-2.
National Heart Lung and Blood Institute

Two concepts of cough





Physiol Res. 2020 Mar 27;69(Suppl 1):S81-S92.
Korean J Med 2019;94(6):471-484.

Drug	Disease	Route	Clinical manifestation	Possible mechanism
ACE-i	HTN, HF	PO	Dry cough	Bradykinin, Substance P → cough reflux ↑
ARB?	HTN, HF	PO	Dry cough?	ACE-i 와 유사한 기전?
DPP4i?	DM	PO	Cough, rhinorrhea, wheezing	Aggravation of underlying allergic conditions?
Statin	DL	PO	Dry cough	NO production, Bradykinin (in vitro) ↑
CCB	HTN	PO	Cough c/s reflux sx.	Aggravation of underlying reflux conditions
Fentanyl	Analgesia	IV	Bronchoconstriction	Central sympathetic tone ↓ & Vagal tone ↑
Latanoprost	Glaucoma	Optahlmic	Dry cough	Cough reflux ↑?
Miscellaneous				
Topiramate	Migraine	PO	Dry cough	Unknown
Phenytoin	Epilepsy	PO, IV	Nocturnal dry cough	Unknown
MTX	RA	PO	Dry cough	Unknown
MMF	KT	PO	Dry cough	Unknown
PPI(Omeprazole)	GERD	PO	Nocturnal dry cough	Unknown
Leflunomide	RA, PsA	PO	Dry cough	Unknown

Physiol Res. 2020 Mar 27;69(Suppl 1):S81-S92.
Ann Palliat Med. 2020 Sep;9(5):3562-3570.

Strong evidence drug

ACE-I (Angiotension converting enzyme inhibitor)

ACE-I (Angiotensin-converting enzyme inhibitor)

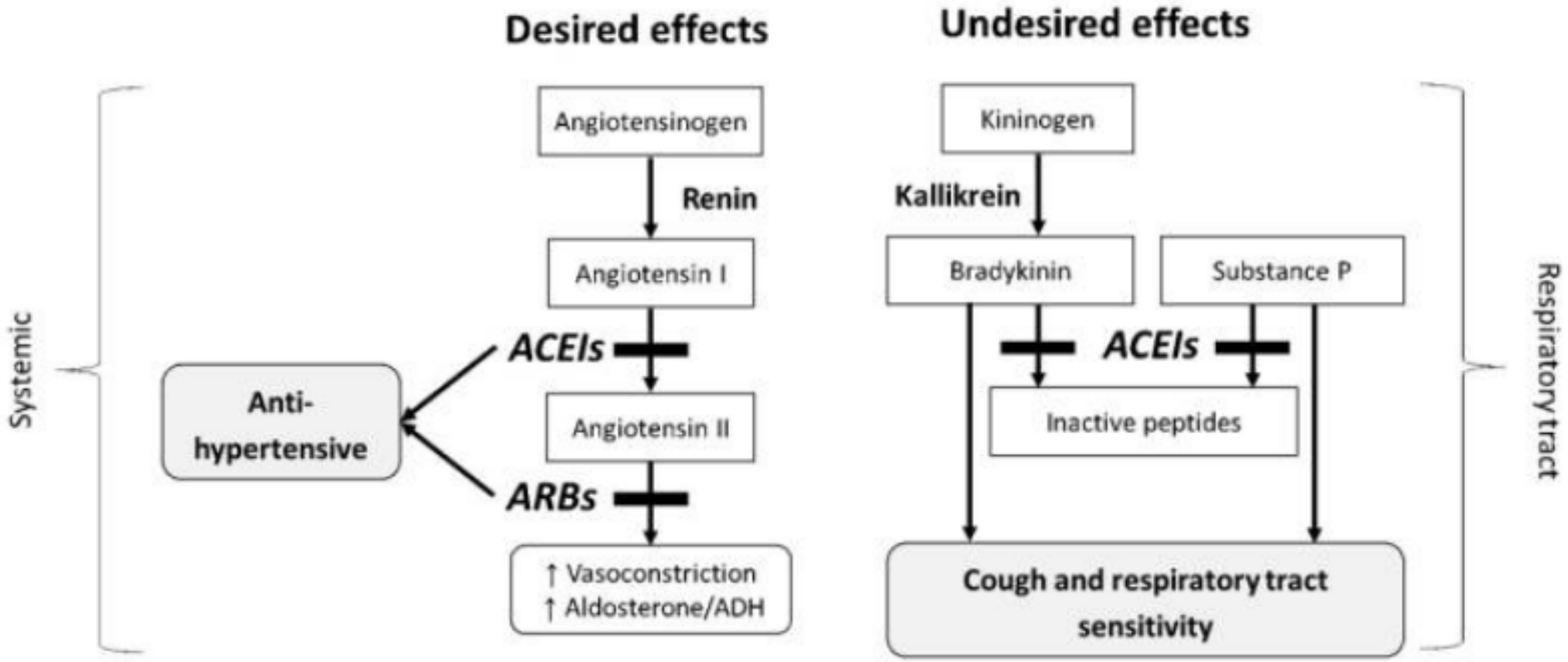
- 특징: 마른 기침, 목구멍의 간질거림, 기침약에 반응하지 않음
- 대표 질환: HTN, CHD, HF(특히 **HFpEF**), CKD, CVA
- 발생 비율: 약 10% (5~37%)
- 발생 시기

- 약제 복용 후 몇 일 ~ 몇 개월(Several Months)

- 호전 시기: 1~4주 이내
- 위험군: 고령(>65세), 여성, 비흡연자, 동아시아인
- 질환군에 따른 발생 비율: HTN>CHD>HF

Physiol Res. 2020 Mar 27;69(Suppl 1):S81-S92.
Clin Pharmacol Ther. 2019 Mar;105(3):652-660.

Mechanism of ACE-I induced cough



Physiol Res. 2020 Mar 27;69(Suppl 1):S81-S92.
Clin Pharmacol Ther. 2019 Mar;105(3):652-660.

Frequency of cough on ACE-I

- 45,420 pts., 135 RCT Meta-analysis

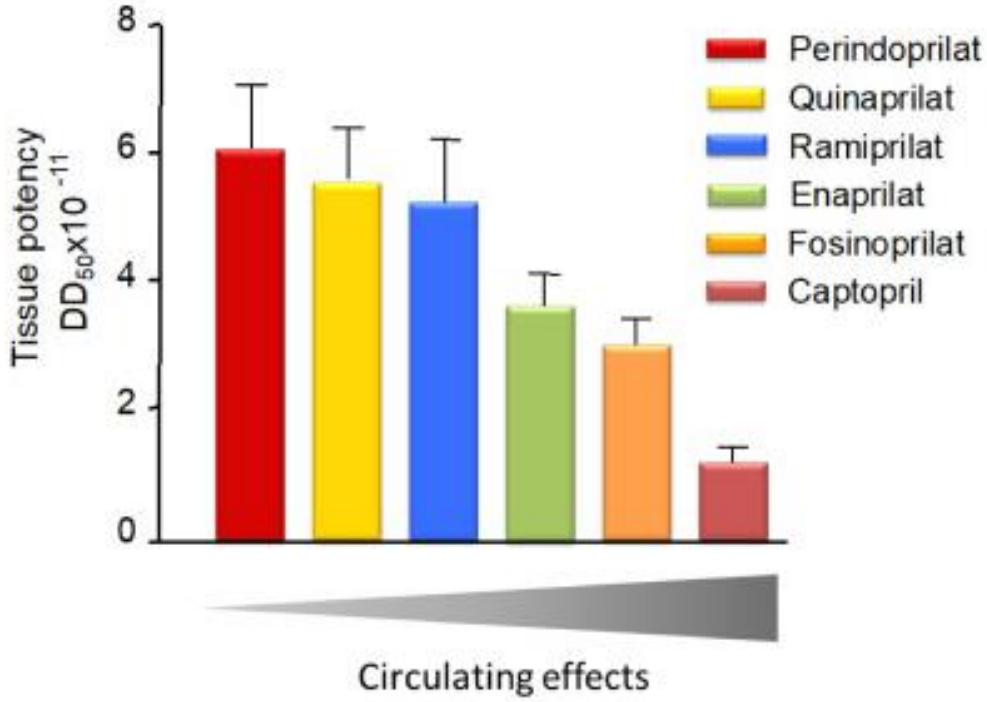
ACEI (100%)	0.45 (0.41, 0.49)	0.31 (0.28, 0.34)	0.15 (0.12, 0.20)
2.24 (2.06, 2.34)	PLACEBO (66.7%)	0.70 (0.62, 0.79)	0.34 (0.27, 0.44)
3.20 (2.90, 3.53)	1.43 (1.26, 1.62)	ARB	0.49 (0.38, 0.64)
6.50 (5.07, 8.34)	2.91 (2.25, 3.76)	2.03 (1.56, 2.66)	CCB

J Clin Hypertens (Greenwich). 2023 Aug;25(8):661-688.

Class differences of cough on ACE-I

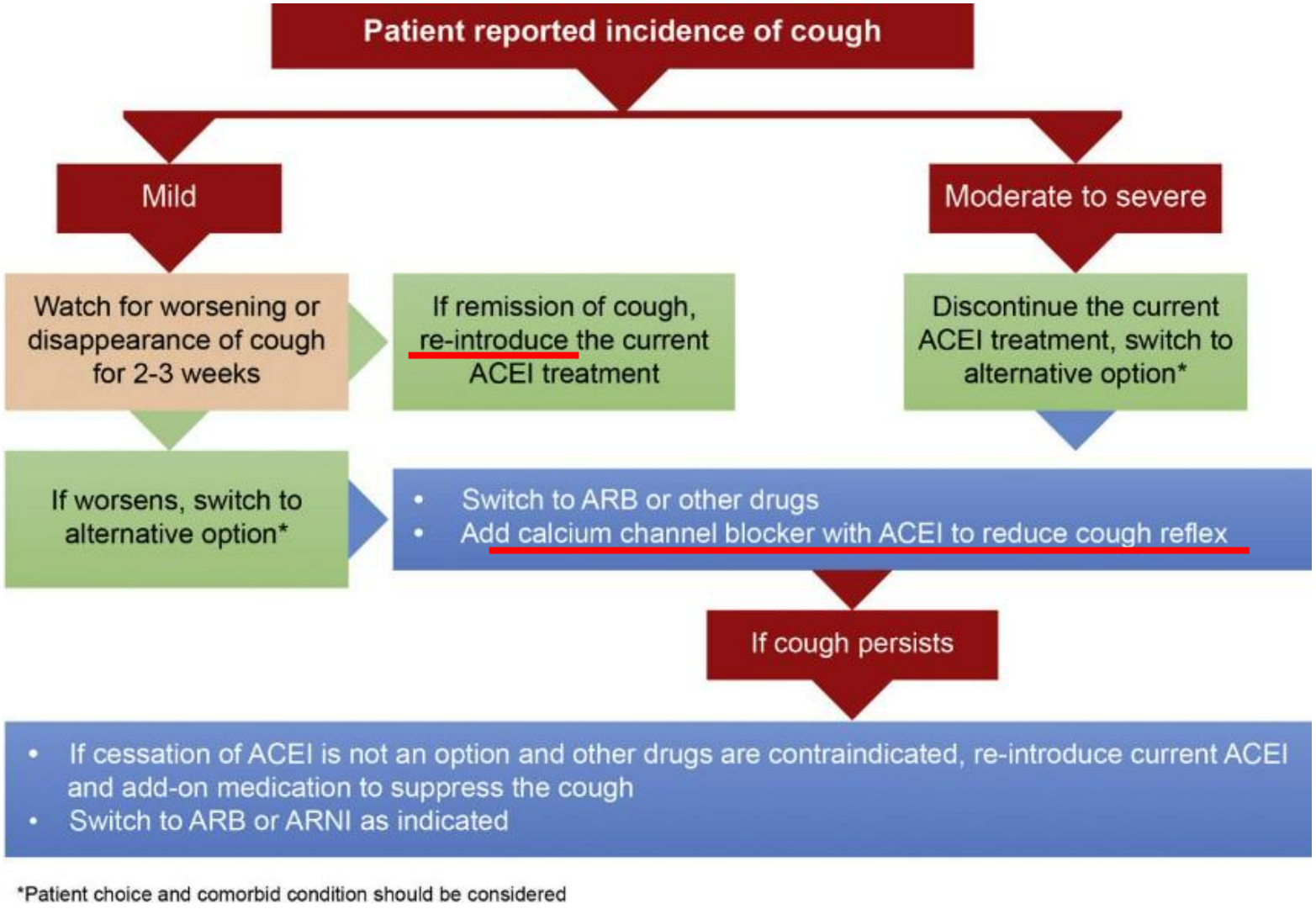
Ranking of ACEI induced cough compared to placebo based on SUCRA.

ACE inhibitor	SUCRA value
Ramipril	76.4%
Fosinopril	72.5%
Lisinopril	64.7%
Benazepril	58.6%
Quinapril	56.5%
Perindopril	54.1%
Enalapril	49.7%
Trandolapril	44.6%
Captopril	13.7%
Spirapril	12.3%



J Clin Hypertens (Greenwich). 2023 Aug;25(8):661-688.
Eur J Intern Med. 2023 Apr;110:10-15.

NEXT STEPs of ACE-I induced cough

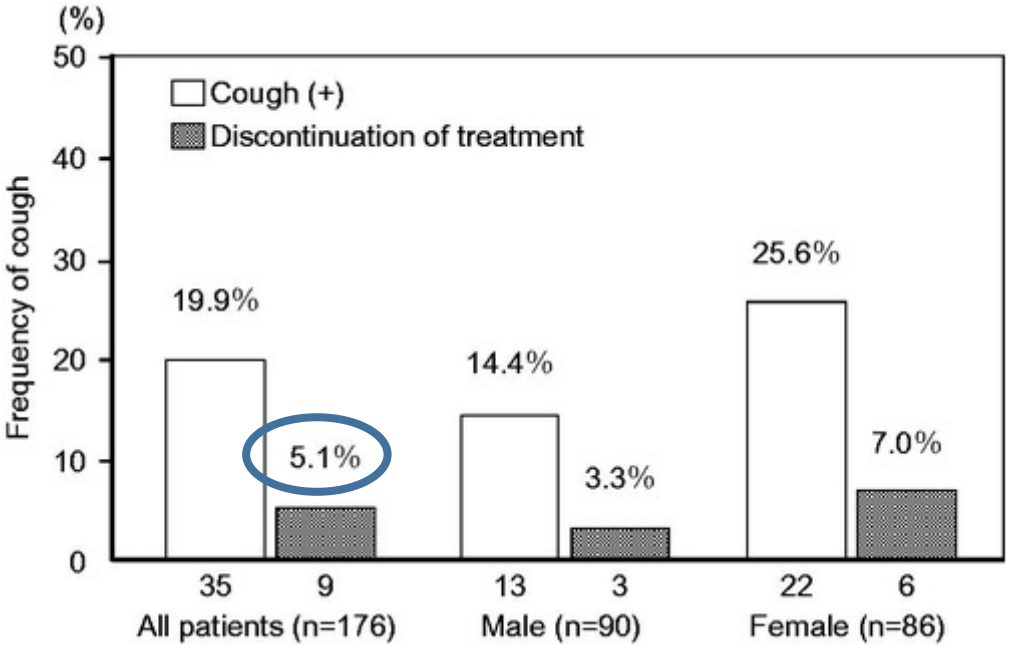


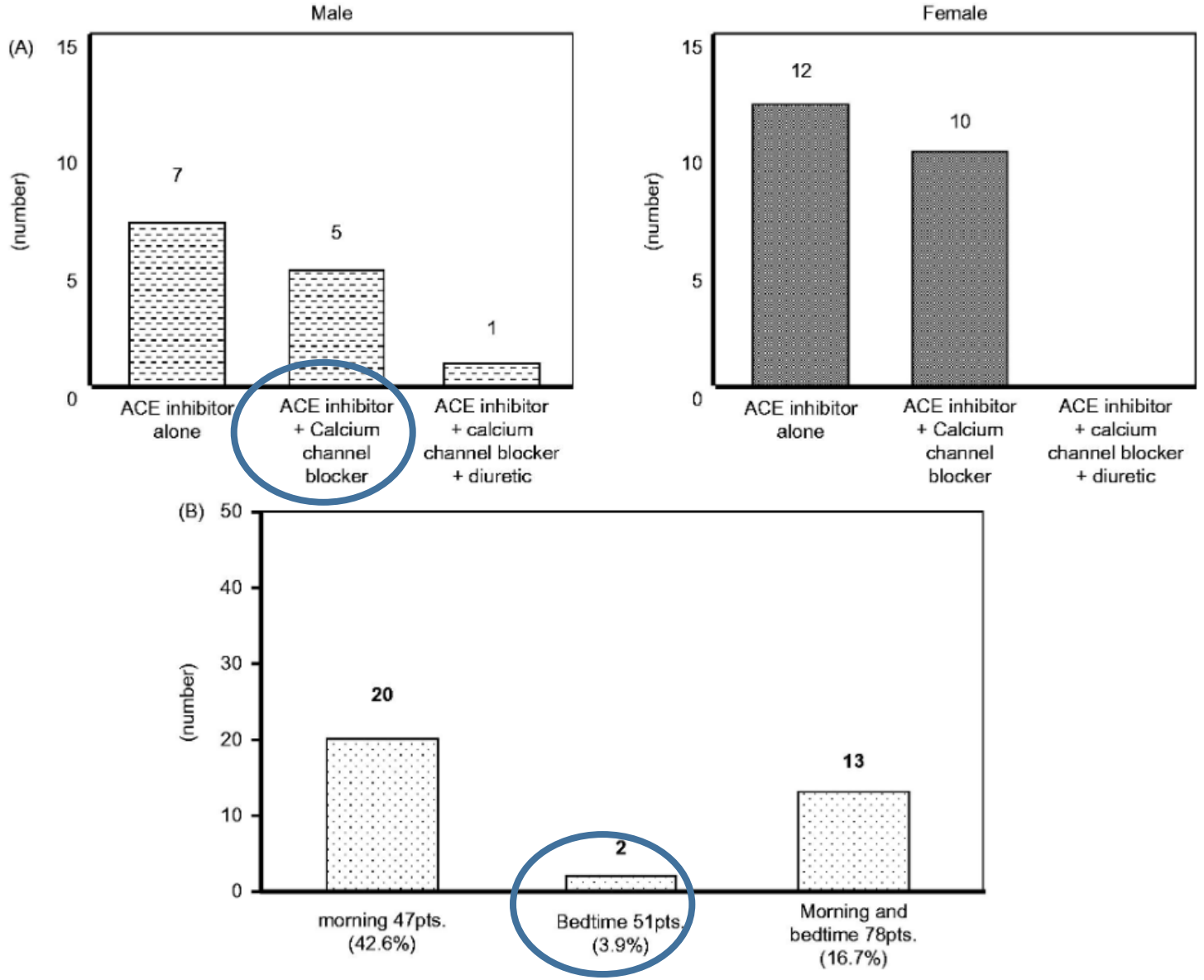
HTN, CHD, CVA → ARB

HFpEF
HTN(Low BP) → ACE-I retry or change

Indian Heart J. 2020 Sep-Oct;72(5):345-350.

- RCT, japan, 176명





Clin Exp Hypertens. 2015;37(7):563-8..

Interesting research of ACE-I Side effect

Elderly stroke pt. & Pneumonia prevention

TABLE 1 The association of angiotensin-converting enzyme (ACE) inhibitor use and the rate of pneumonia in different trials

	van de Garde [1]	Sekizawa [2]	Arai [3]	Teramoto [4]	Ohkubo [5]	Ohkubo [5]
Race	Caucasian	Asian	Asian	Asian	Asian	Caucasian
Age yrs	67	76–77	75.3–76.5	>65	64	64
Subjects n	4925	440	576	358	2352	3753
Observation period yrs	6	2	3	3	3.9	3.9
History of stroke	No	Yes	No	No	Yes	Yes
Pneumonia incidence %						
Without ACE inhibitors		9	2.77–2.97	0.25	1.04	1.3
With ACE inhibitors		3.5	1.1	0.56	0.56	1.24
Pneumonia prevention by ACE inhibitors	No	Yes	Yes	No	Yes	No

ERj 2007 29: 218-219.

Interesting research of ACE-I Side effect

Elderly stroke pt. & Pneumonia prevention (meta-analysis)

Summary of findings: A comparison between angiotensin converting enzyme inhibitor treatment and control treatment (cohort and case–control studies)

Patient or population: Adults, Setting: Anywhere, Intervention: ACE-I, Comparison: Control treatment

Outcomes	Anticipated absolute effects [c] (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	Risk with ACE-I			
Risk of pneumonia	115 per 1,000 [d]	99 per 1,000 (92 to 107) [d]	OR 0.85 (0.78 to 0.92)	60,832 cases/272,584 controls, 1,178,746 exposed /192,868 unexposed (34 observational studies) [e]	⨁◯◯◯ Very low [Link], [Link]
Mortality	113 per 1,000	177 per 1,000 (168 to 184)	OR 1.43 (0.97 to 2.09)	1,170,449 exposed/183,144 unexposed (4 observational studies)	⨁◯◯◯ Very low [b]

J Gen Fam Med. 2022 Mar 10;23(4):217-227.

Interesting research of ACE-I Side effect

Elderly stroke pt. & Pneumonia prevention (meta-analysis)

Summary of findings: A comparison between angiotensin converting enzyme inhibitor treatment and control treatment (randomized control trials)

Patient or population: Adults, Setting: Anywhere, Intervention: ACE-I, Comparison: Control treatment

	Anticipated absolute effects [a] (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
Outcomes	Risk with placebo	Risk with ACE-I			
Risk of pneumonia	69 per 1,000	52 per 1000 (44–62)	OR 0.75 (0.62–0.90)	8704 (7 RCTs)	⨁⨁◯◯ Low [a]
Mortality	165 per 1,000	165 per 1000 (117–226)	OR 1.00 (0.67–1.48)	8704 (7 RCTs)	⨁⨁◯◯ Low [a]
Withdrawal because of adverse effects	20 per 1,000	49 per 1000 (27–88)	OR 2.51 (1.35–4.68)	6601 (6 studies)	⨁⨁◯◯ Low [a]

CVA pt.
Asian
Elderly pt.
RAS inhibitor indications

J Gen Fam Med. 2022 Mar 10;23(4):217-227.

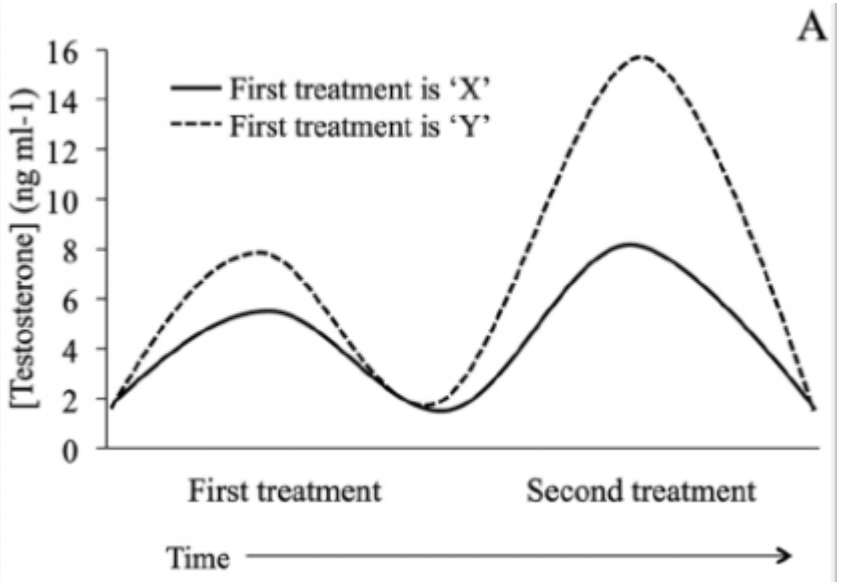
Strong evidence drug

ARB (Angiotensin II receptor blocker)

DPP4-I (Dipeptidyl peptiase-4 inhibitor)

"ARB와 DPP4-I는 Drug induced cough를 일으킬 가능성이 매우 낮다."

Carry over effect (confounder)

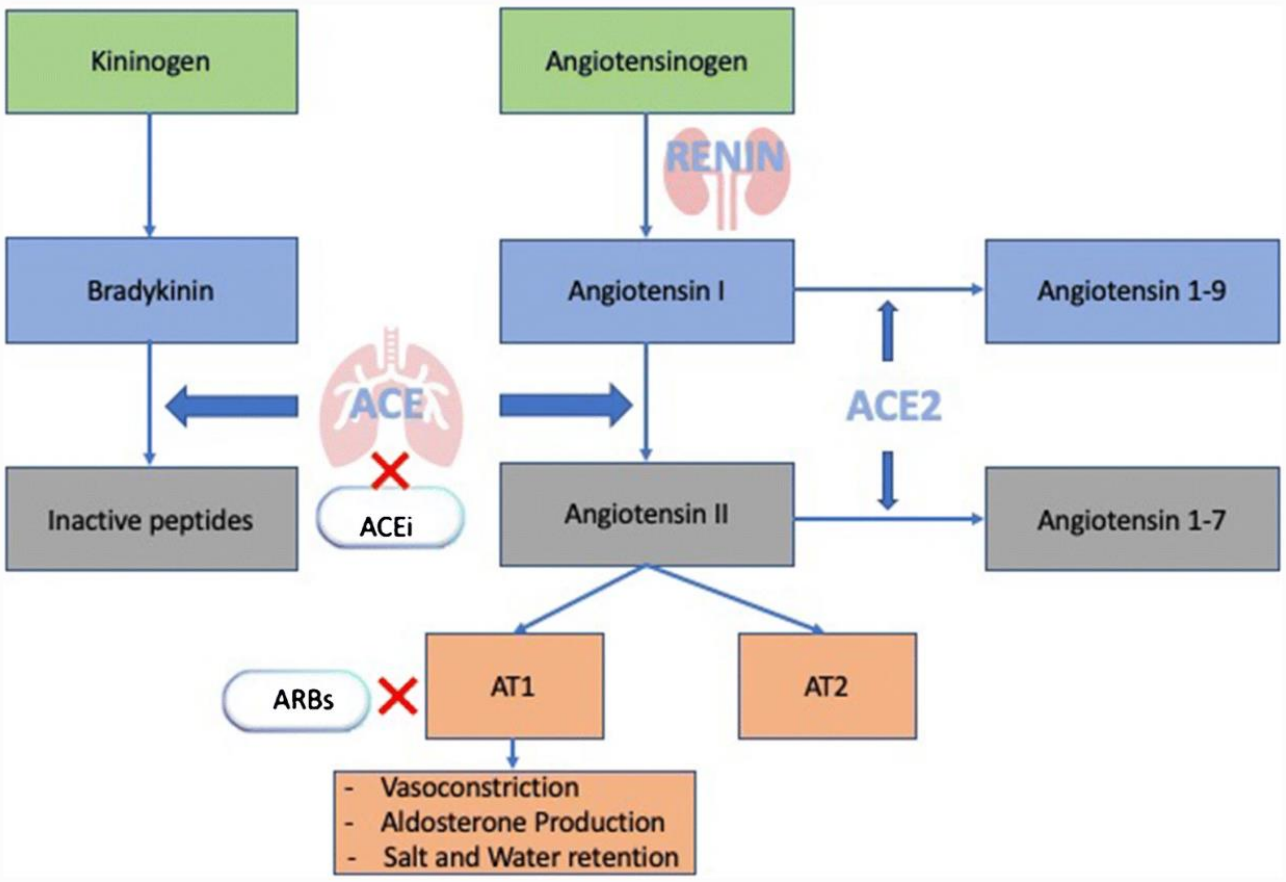


Drug	*Number of patients with cough*	*Patient-months of exposure*	*Rate per 1000 patient-months*	*95% confidence limits*
Enalapril	86	21 983	3.9	3.1–4.8
Lisinopril	270	18 749	14.4	12.7–16.2
Perindopril	210	12 751	16.4	14.3–18.8
Losartan	64	20 533	3.1	2.4–4.0

- ACE-I(236명) → Rosartan → ARB(Rosartan) STOP(101명, 43%)
  - 7건 data missing
  - 94건 (81명, 86%/81% → ACE-i induced cough)

Br J Clin Pharmacol. 1999 Jan;47(1):111-4.
Ecosphere 5(3):28.

Mechanism of ARB



- Kinin hypothesis

→ Bradykinin / Substance P level에 영향을 주지 않음

Curr Cardiol Rep. 2020 Jul 9;22(9):95

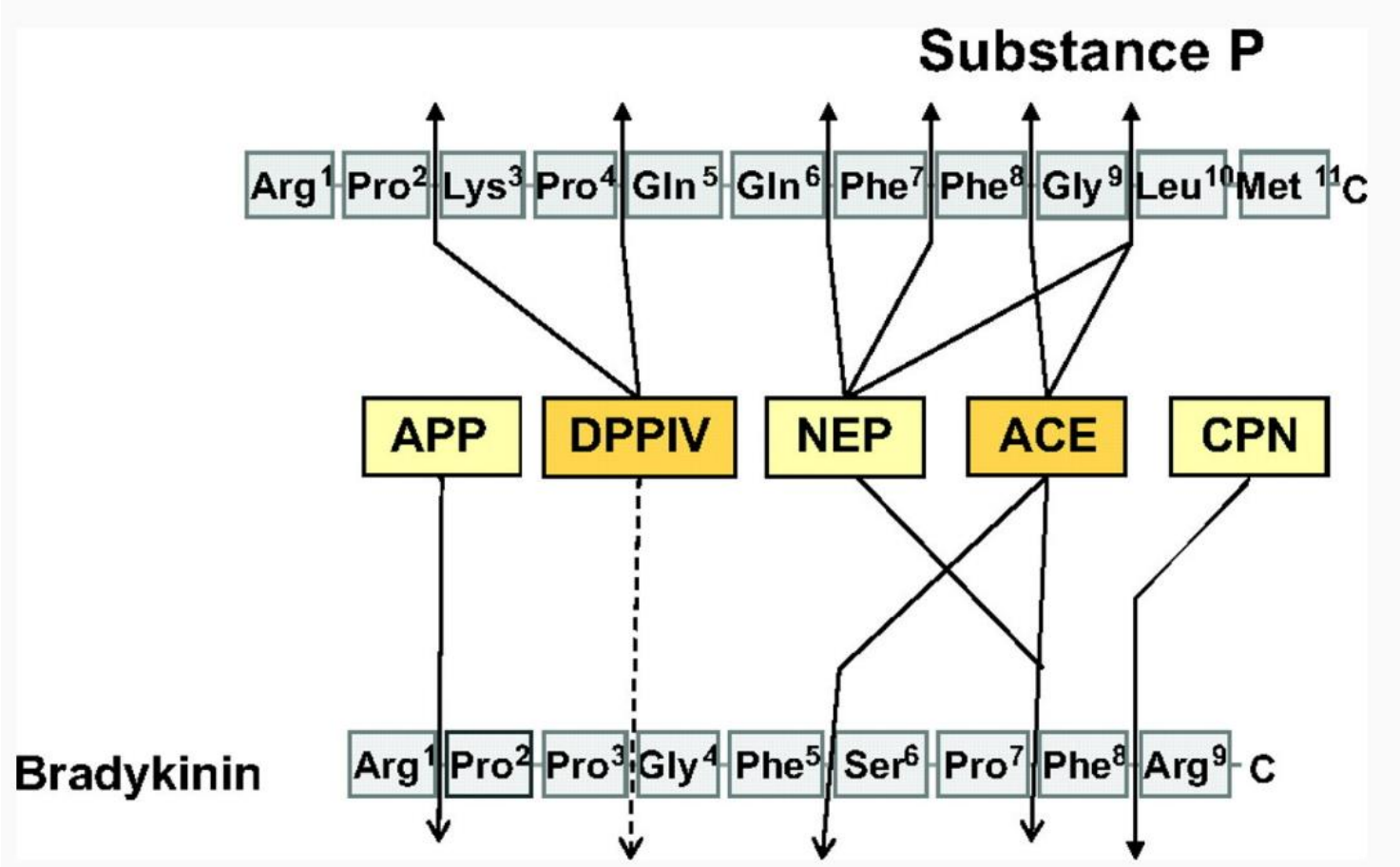
Frequency of cough on ARB (meta-analysis)

Table II. Summary of study results

ARBs vs other drugs/placebo	RCTs	References	Patients	RR (95% CI)
Discontinuation due to adverse events (figure 2)				
ARBs vs ACE inhibitor	5	18-20, 22, 23	428	0.47 (0.18, 1.23)
ARBs vs placebo/diuretics	9	12, 18-20, 22-26	9015	0.99 (0.85, 1.15]
ARBs vs diuretics	2	18, 19	140	1.50 (0.26, 8.52)
ARBs vs placebo	7	12, 20, 22-26	8875	0.99 (0.84, 1.17)
Cough (figure 3)				
ARBs vs ACE inhibitor	7	15-23	564	0.37 (0.28, 0.48)
ARBs vs placebo/diuretics	10	12, 15-24, 26	8845	1.01 (0.76, 1.34)
ARBs vs diuretics	2	18, 19	140	1.00 (0.51, 1.95)
ARBs vs placebo	8	12, 15-17, 20-24, 26	8339	1.01 (0.74, 1.39)

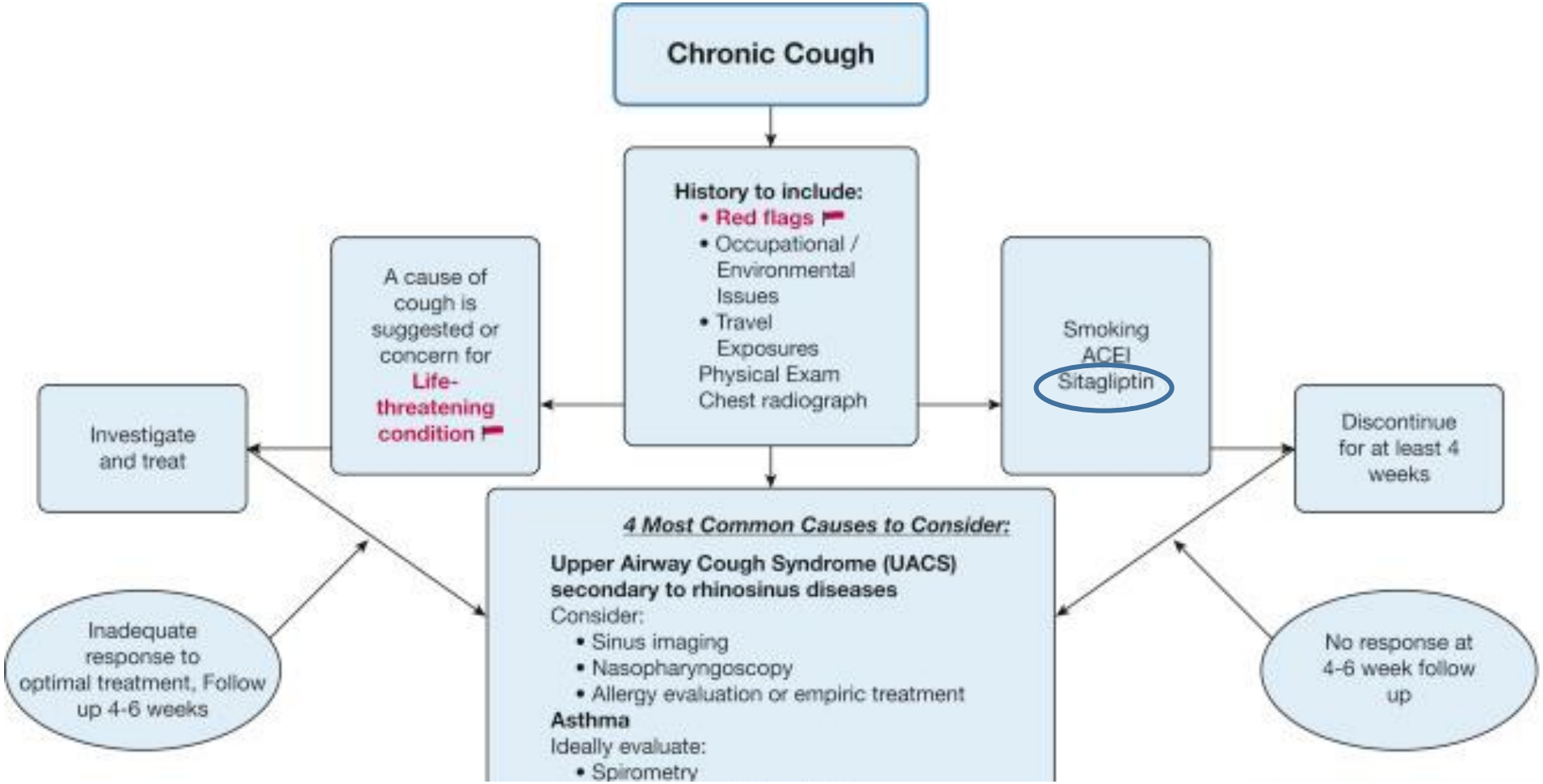
Am J Cardiovasc Drugs. 2012 Aug 1;12(4):263-77.

DPP4-i(Dipeptidyl peptiase-4 inhibitor)



Hypertension. 2009;54:516-523.

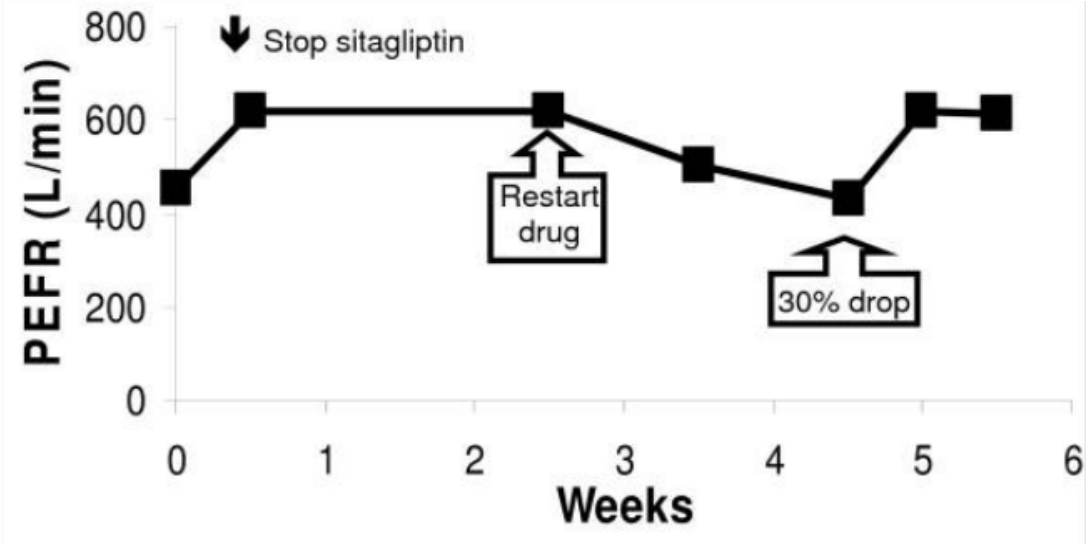
CHEST Guideline and Expert Panel Report



Chest. 2018 Jan;153(1):196-209.

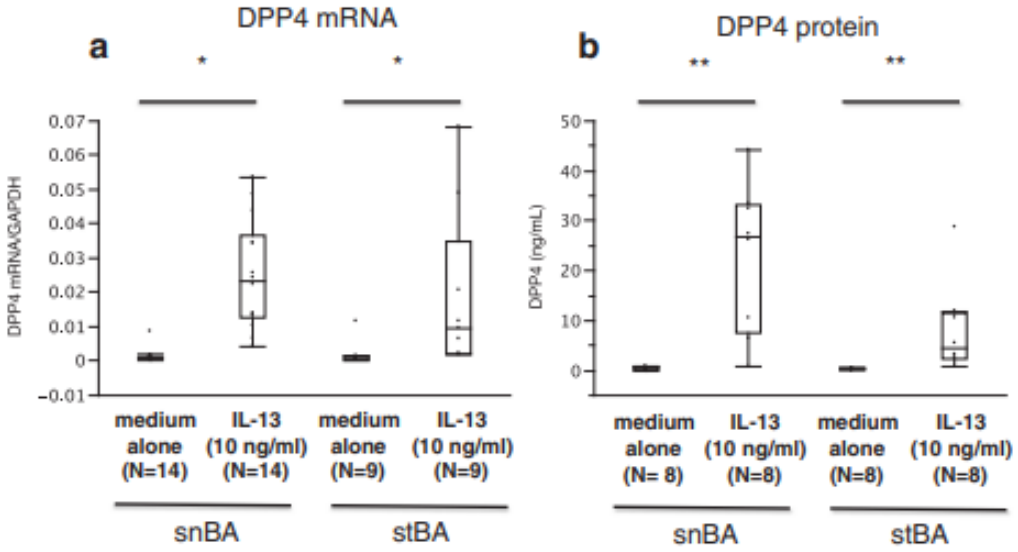
CASE series

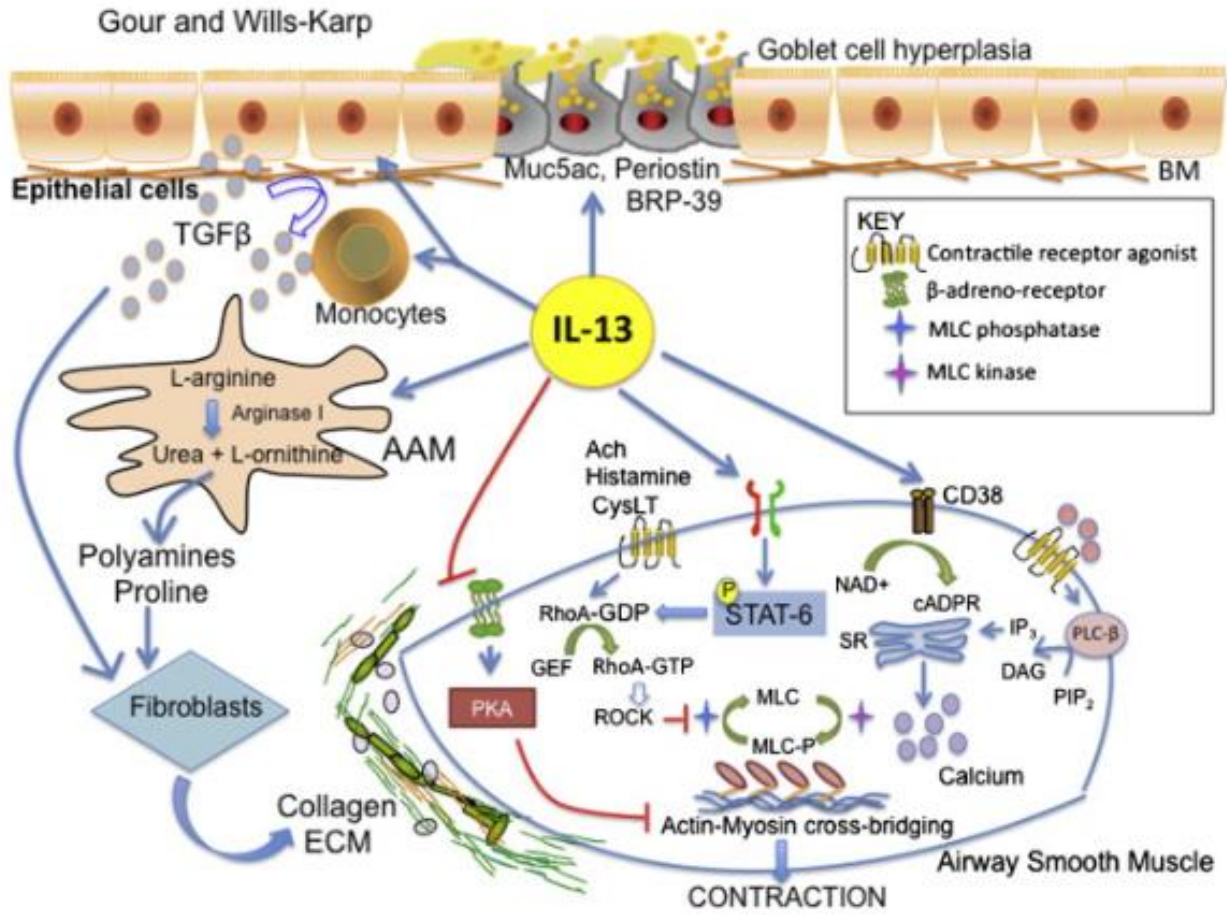
- Sitagliptin intolerance, 15명
- 13명 콧물, 호흡곤란/천명 등을 동반한 기침 (ACE-i 복용)
- All Underlying allergic ds.
- 5명의 intolerance 환자에게 재 투여 → 4명 기침 재발



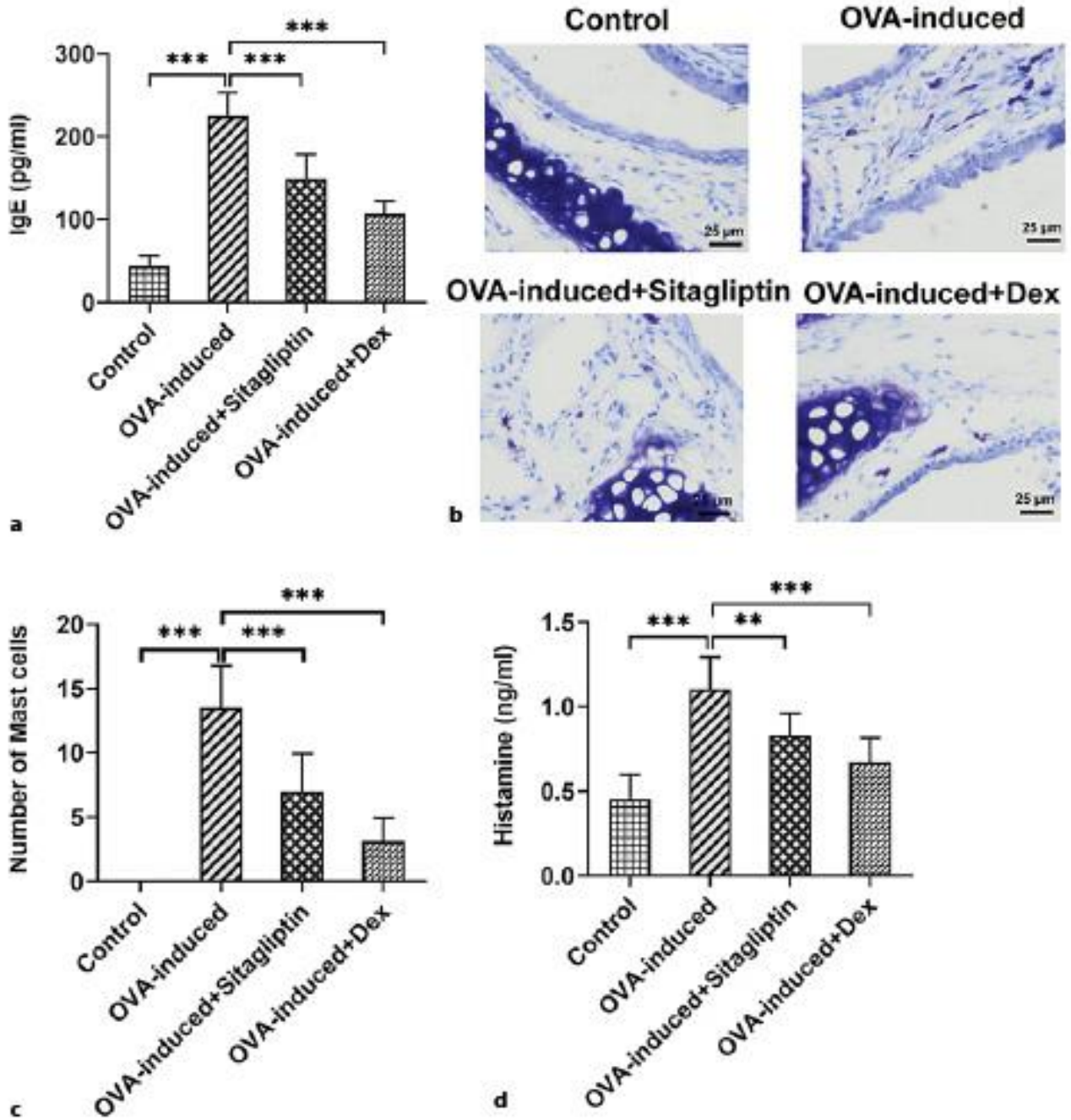
Allergy Asthma Clin Immunol. 2010 May 12;6(1):8.

DPP4-i(Dipeptidyl peptiase-4 inhibitor)





Respir Res. 2016 Mar 14;17:28.
Cytokine. 2015 Sep;75(1):68-78.



Mouse model

Allergic rhinitis를 유발하는 Ovalbumin(OVA)

Nasal mucosal biopsy

Pharmacology. 2023;108(2):166-175.

Frequency of cough on DPP4-I
(25 RCT pooled analysis)

Adverse event	Incidence rate per 100 patient-years[a]		
	Sitagliptin 100 mg	Non-exposed	Difference between sitagliptin and non-exposed (95% CI)[b]
Neck pain	0.6	0.9	−0.3 (−0.7, −0.0)
Neurodermatitis	0.0	0.1	−0.1 (−0.2, −0.0)
Peripheral edema	2.2	3.0	−0.8 (−1.4, −0.2)
Pharyngeal erythema	0.0	0.1	−0.1 (−0.2, −0.0)
Sepsis	0.0	0.1	−0.1 (−0.2, −0.0)
Sinus headache	0.1	0.3	−0.2 (−0.4, −0.1)
Suicidal ideation	0.0	0.1	−0.1 (−0.2, −0.0)
Thrombophlebitis	0.0	0.2	−0.1 (−0.3, −0.0)
Urine ketone body present	0.0	0.1	−0.1 (−0.3, −0.0)
Weight increased	0.8	1.4	−0.6 (−1.0, −0.2)
White blood cell count increased	0.1	0.3	−0.2 (−0.4, −0.0)
Upper airway cough syndrome	0.0	0.1	−0.1 (−0.3, −0.0)
Vitreous detachment	0.0	0.1	−0.1 (−0.2, −0.0)
Wheezing	0.0	0.1	−0.1 (−0.3, −0.0)

N=14,611명

Diabetes Ther. 2013 Jun;4(1):119-45.

Drug with a secondary or indirect effect

Esophageal reflux related drugs

CCB

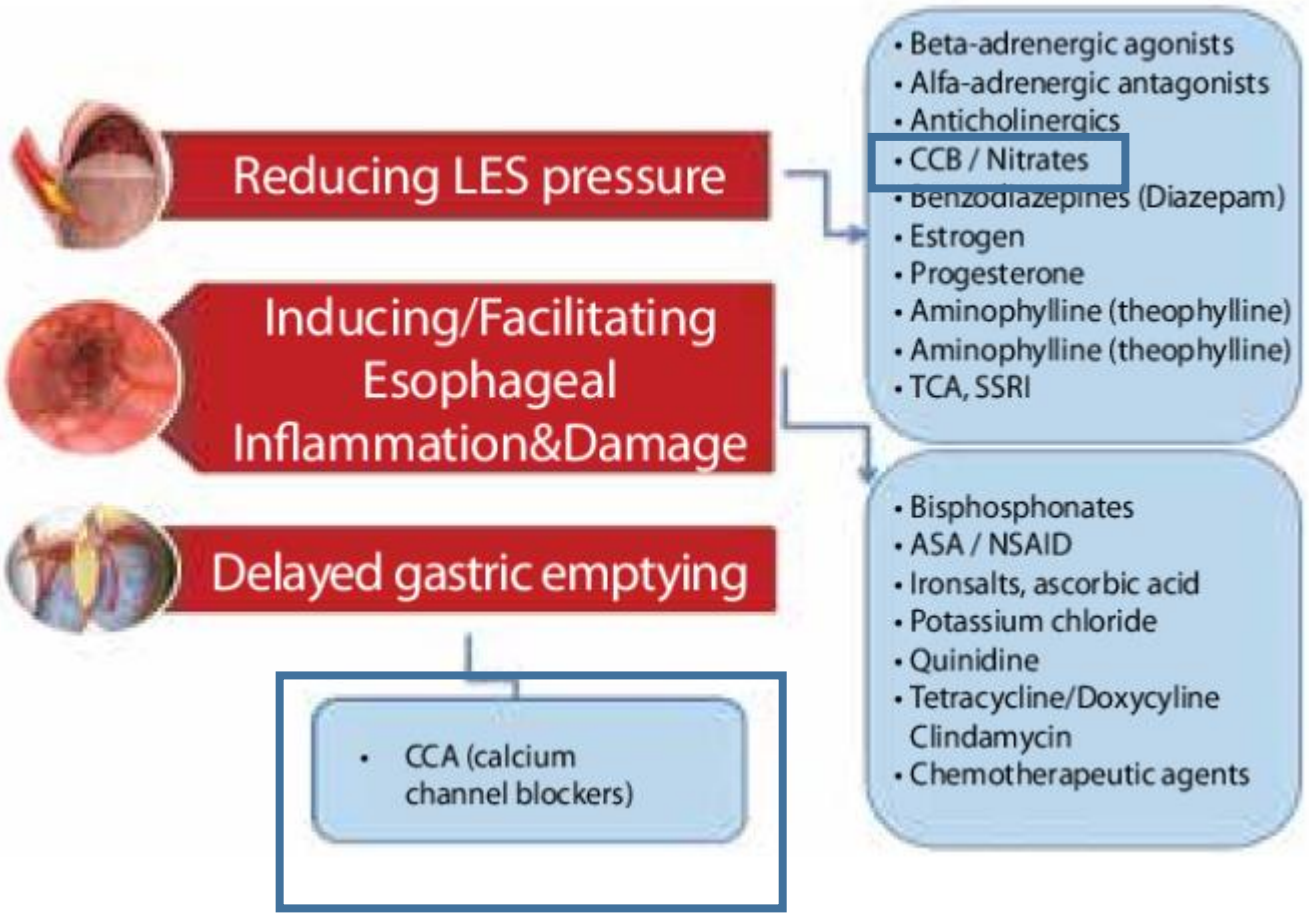
Drug-induced esophagitis

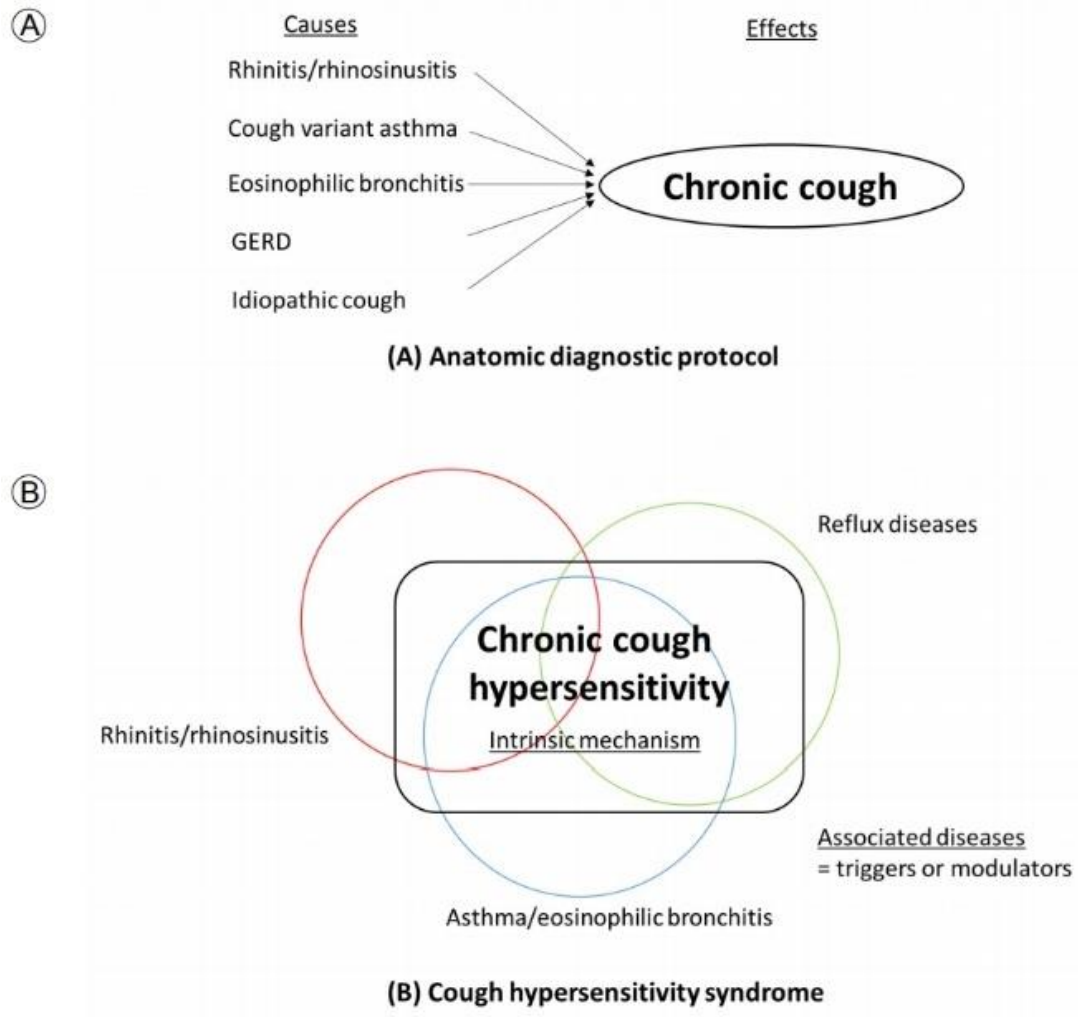
Reflux esophagitis

- Incidence
  - Western country: 10~20%
  - Asian: 5%
- Risk factor
  - 50세 이상
  - BMI ≥ 30
  - Smoking
  - Depression
  - Nitrate, **CCB**
- **Sx.**
  - 작열감, 쓴맛 혹은 신맛, 인후통, **기침**, 이물감(Lump sensation)

StatPearls Publishing; 2023 Apr 17.

Mechanism of cough on CCB (Calcium channel blocker)





Korean J Med 2019;94(6):471-484.
Turk J Gastroenterol. 2017 Dec;28(Suppl 1):S38-S43

Reflux related symptoms on CCB

Precipitation of reflux-related symptoms during calcium ant

	Precipitation of reflux-related symptoms			
CA	*n*	Total	%	*P*-value
Nifedipine	23	51	36.5	0.043
Amlodipine	19	50	35.8	0.005
Felodipine	17	45	32.0	0.118
Verapamil	18	45	39.1	0.001
Diltiazem	8	24	30.7	0.107
Total	85	215	35.3	

Exacerbation of reflux-related symptoms after calcium antagonist (CA) exposure

	Patients with pre-existing symptoms prior to CA therapy		Patients with symptom exacerbation after CA therapy		
CA	*n*	%	*n*	%	*P*-value, McNemar's test for paired proportions
Nifedipine	28	21.5	15	53.6	<0.0001
Amlodipine	31	23.8	19	61.3	<0.0001
Felodipine	28	21.5	15	53.6	<0.0001
Verapamil	27	20.8	8	29.6	<0.0160
Diltiazem	16	12.4	2	12.5	<0.5000
Total	130	100.0	59	45.4	

최대 3개월간 약제 중단을 고려
Single center, Retrospective observational study
N= 371

Br J Clin Pharmacol. 2007 Jul;64(1):83-9.

Considerations for Withdrawing CCBs

Table 1.

Major recommendations and nemarics in recent guidelines for chronic cough in adults

Proton pump inhibitors	In adult patients with suspected chronic cough due to reflux-cough syndrome, but without heartburn or regurgitation, we recommend against using PPI therapy alone because it is unlikely to be effective in resolving the cough (Grade 1C). In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).	We suggest that clinicians do not routinely use anti-acid drugs in adult patients with chronic cough (conditional recommendation, low-quality evidence).

8.3.1.2. 약물요법

속쓰림과 역류 증상을 호소하는 역류성 기침 환자에게는 증상조절을 위해 PPI가 1차 약물이다[34,35]. PPI 상용량의 2~3개월 용법이 추천되고 있다[8,36]. PPI의 짧은 반감기를 고려한다면, 하루에 한 번 투여로 치료효과가 만족스럽지 않는 경우, 두 번 투여를 시도해볼 수 있다[37–39]. 속쓰림과 역류증상을 호소하지 않는 역류성 기침이 의심되는 환자에서는 PPI 단독치료는 증상호전에 도움이 될 가능성이 낮으므로 제한적으로 사용한다[24,40].

다른 질환이 모두 배제된 경우 or
cough + reflux symptoms + CCB
→ 약제 중단 고려

Korean J Med 2019;94(6):471-484.
TRD, 2020 기침진료지침

Drug(pill)-induced esophagitis

- Sx. : retrosternal **pain**, dysphagia, odynophagia, cough
- Related drugs
  - 항생제: Doxycycline..
  - NSAIDs
  - **Bisphosphate**: Alendronate, Ibandronate, Risedronate
  - **Vit-C (Ascorbic acid)**
  - Potassium chloride and ferrous sulfate
  - **Sustained-release drugs**
  - Glimepride / Tiropramide
  - CTx. & RTx.

Low evidence drugs
(CASE reports)

Statin

Therapeutic Advances in Respiratory Disease
Volume 6, Issue 4, August 2012, Pages 243-246

https://doi.org/10.1177/1753465812452192

Reviews

Chronic cough as a complication of treatment with statins: a case report

- CHD → stent
- Simvastatin→Fluvastatin→Simbastatin (기침)
- ACE-i 복용하지 않음

Ther Adv Respir Dis. 2012 Aug;6(4):243-6.

Statin

- 미국, 캐나다, 호주 3개국 database 이용, cough ADR report
- 기침을 호소한 환자 중 88%는 폐 손상이나 폐기능 이상이 없었다

Table 1 Reports of statin-induced cough in three international databases (years 2004–2012)

Statin	Adverse event reporting System database FDA (AERS) (N. reports)	Canada vigilance ADR database (N. reports)	Australian Database of Adverse Event Notifications (DAEN-TGA) (N. reports)	Total N. reports of statin-induced cough
Rosuvastatin	399	26 (Three with lung injury)=23	3	425
Atorvastatin	315	24 (Two in therapy with ACE inhibitors indicated as suspected drugs; two with lung injury)=20	11 (One with lung injury and in therapy with ACE inhibitors indicated as suspected drugs; one in therapy with ACE inhibitor indicated as suspected drugs)=9	344
Simvastatin	140	2	2	144
Pravastatin	35	–	4	39
Fluvastatin	34	–	–	34
Lovastatin	9	–	–	9
Pitavastatin	–	–	–	–

Eur J Clin Pharmacol. 2014 Dec;70(12):1529-31.

Statin

- Observational study

Table 1. Oral symptoms and evolution after interruption of the treatment with statins.

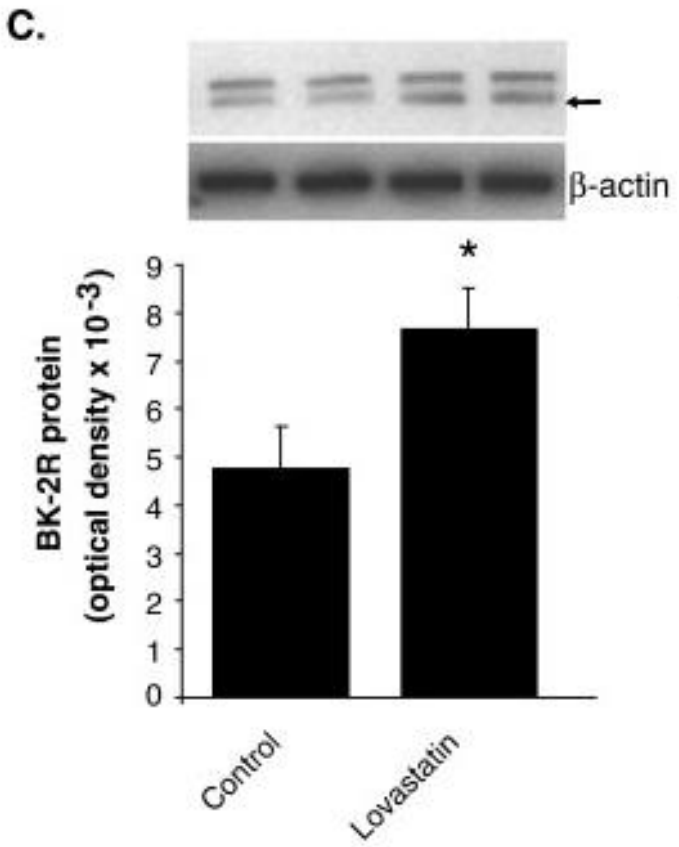
		First visit	Second visit		
SYMPTOM	Total		No change	II	RI
Dryness	26	23 (88.5%)	6 (26.1%)	17 (73.9%)	0 (0%)
Itch	26	15 (57.7%)	2 (13.3%)	6 ((40.0%)	7 (46.7%)
Bitterness	26	14 (53.8%)	1 (7.1%)	0 (0%)	13 (92.8%)
Cough	26	12 (46.1%)	1 (8.3%)	11 (91.7%)	0 (0%)

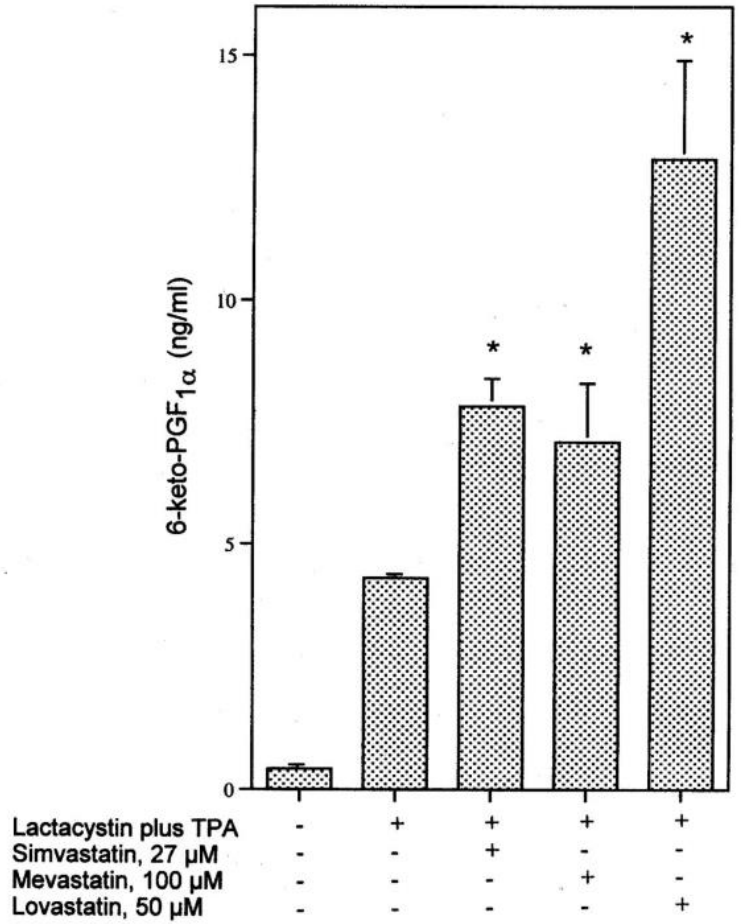
1~2wks

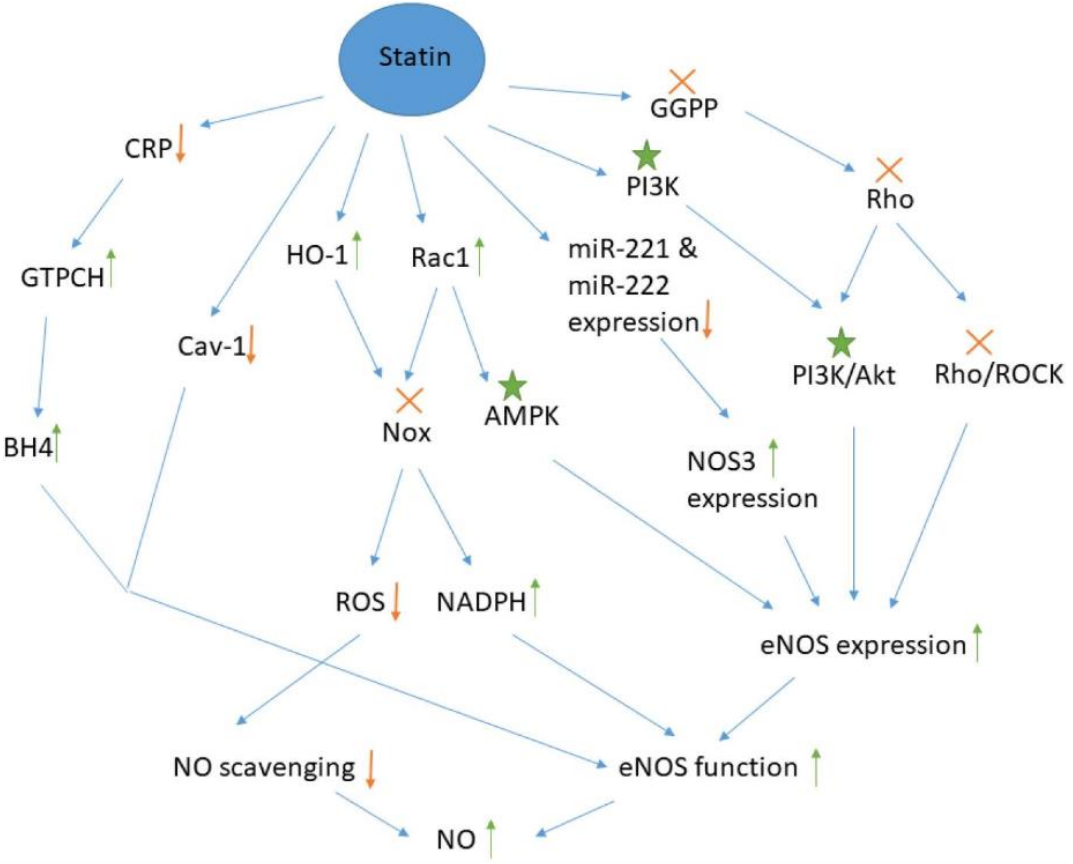
증상호전 **Remission**

Med Oral Patol Oral Cir Bucal. 2008 Feb 1;13(2):E98-101.

Mechanism of cough on Statin







mouse model

J Clin Med. 2019 Dec; 8(12): 2051.
J Mol Cell Cardiol. 2007 Nov;43(5):593-600.
Lipids Health Dis. 2003 Mar 12;2:1.

Fentanyl

- Opioid induced cough
- **IV bolus** (18~65%)
- Patch → 천식환자의 증상 악화
- RCT, 400명, elective surgery

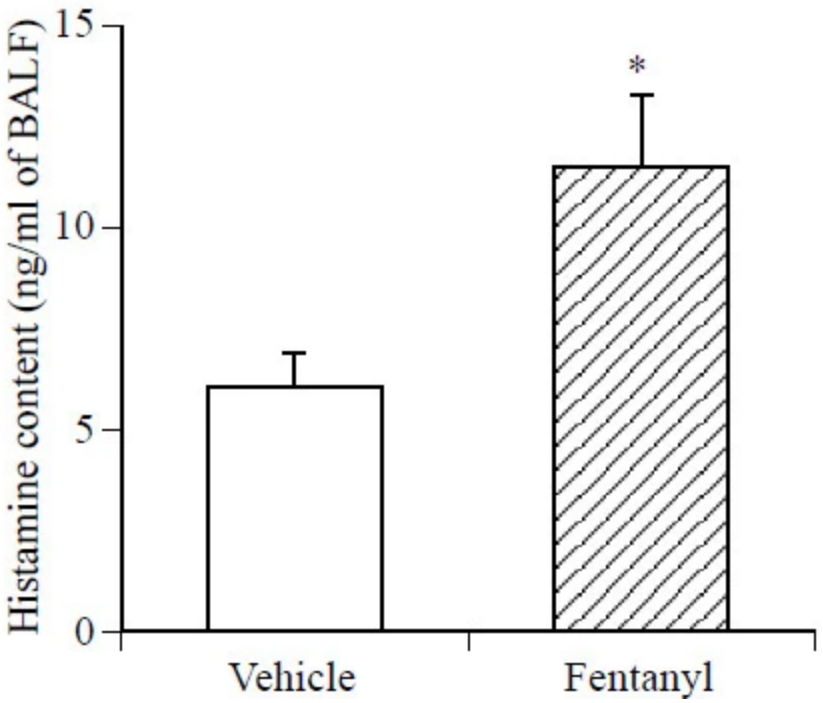
Incidence of coughing and its severity after fentanyl injection.

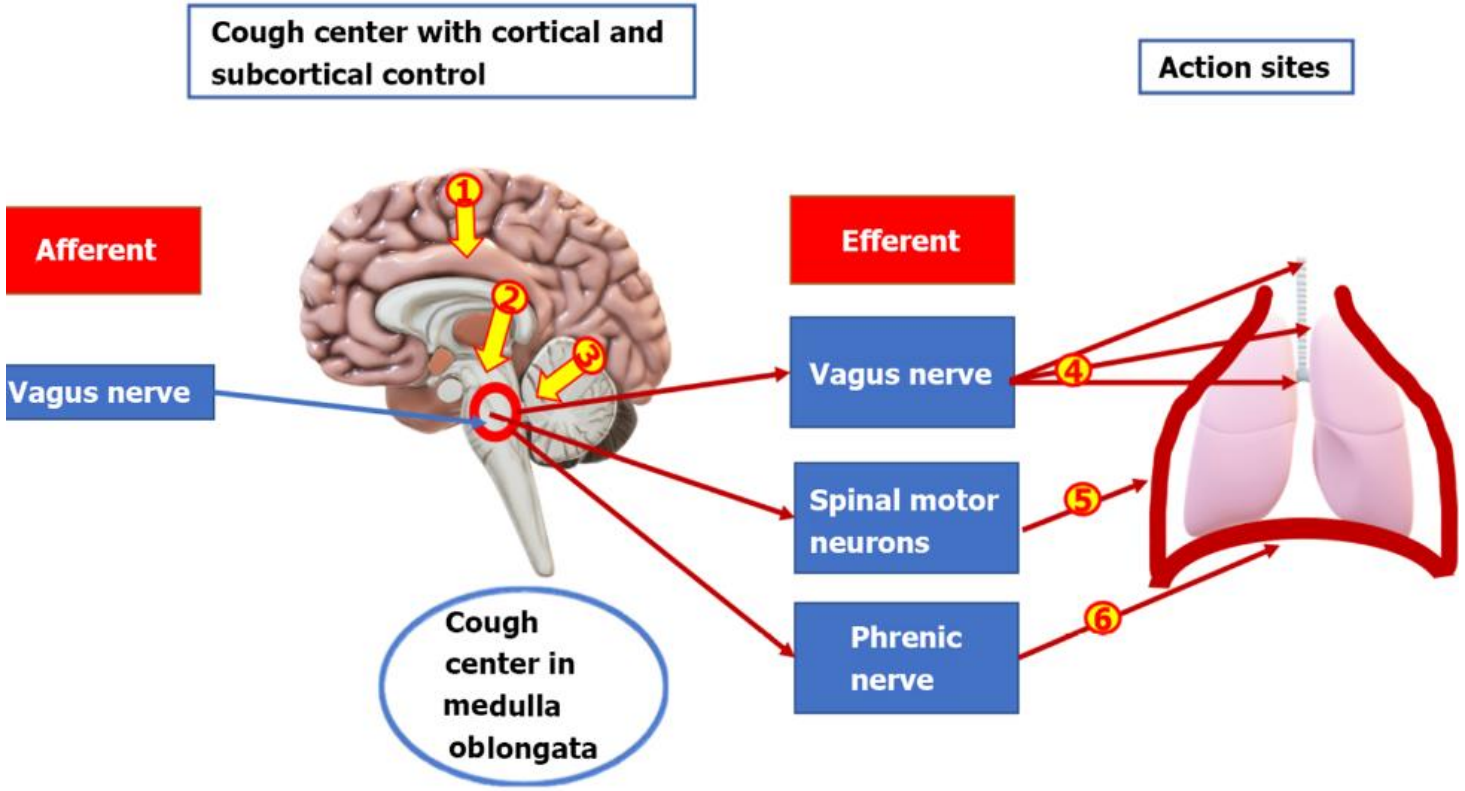
Groups	Incidence (%)	Onset (s)	Severity of cough (%)				
			Mild	Moderate	Severe	Total	No cough (%)
Placebo	53/100 (53)	15.7 ± 3.9	25 (25)	17 (17)	11 (11)	53	47
KET	20/100 (20)	18.6 ± 3.3	10 (10)	6 (6)	4 (4)	20	80
DEX	34/100 (34)	18.2 ± 3.2	16 (16)	11 (11)	7 (7)	34	66
KETODEX	9/100 (9)	25.8 ± 3.8[b]	6 (6)[b]	3 (3)	0 (0)[a]	9	91

- effective: lidocaine, ketamine, dexamethasone, **propofol**, dextromethorphan...
- ineffective: salbutamol, tramadol, **midazolam**...

J Clin Anesth. 2016 Nov;34:440-7.
Ups J Med Sci. 2014 Nov;119(4):333-7.

Mechanism of cough on Fentanyl





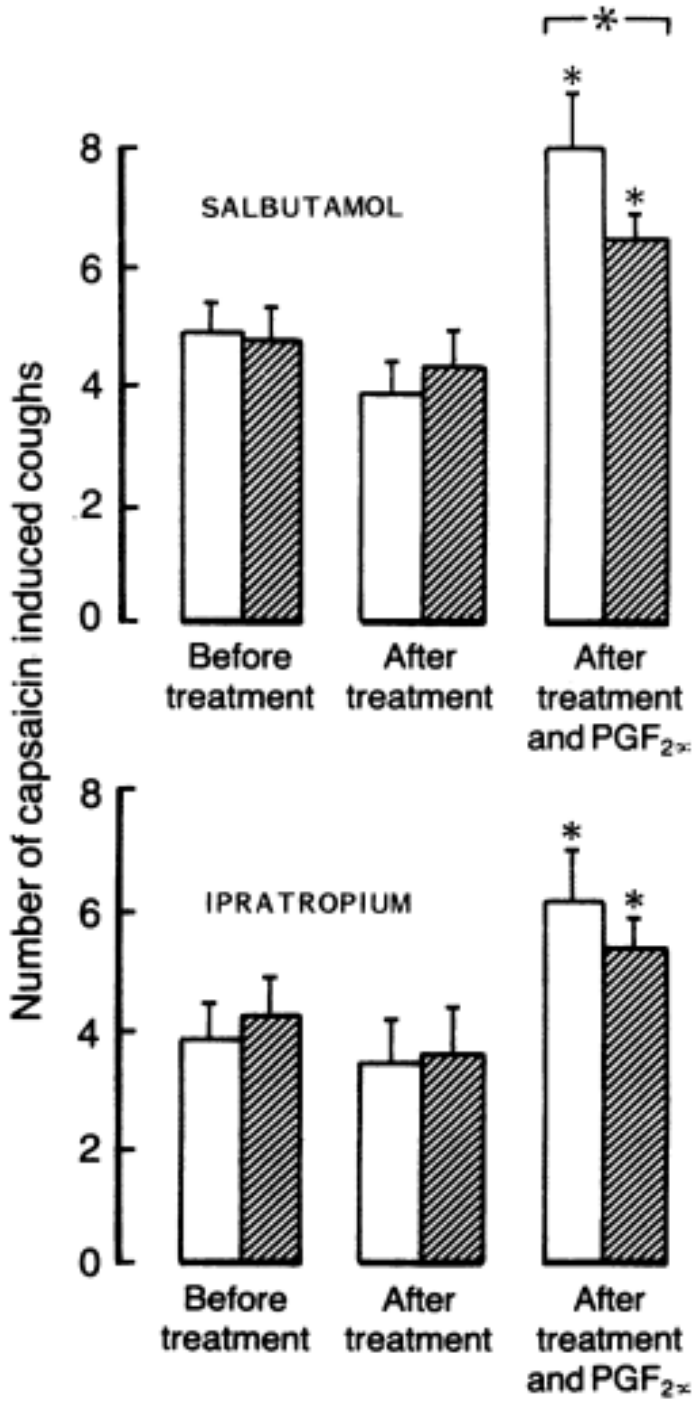
World J Crit Care Med. May 9, 2022; 11(3): 115-128
Cough. 2013 Feb 1;9(1):3.

Latanoprost (PGF2 analog)

Table 1. Cough Reflex Sensitivity Following Citric Acid Challenge

Concentration, mmol/L	Visit 1	Visit 2	Visit 3
C2	10.4	75	10.5
C5	14.3	113	14.3

Visits 1 and 3 = patient receiving latanaprost; visit 2 = patient not receiving latanaprost; C2 = citric acid concentration to produce two coughs; C5 = citric acid concentration to produce five coughs.



Chest. 2009 Nov;136(5):1406-1407.
Thorax. 1990 Sep;45(9):694-8.

Rare case reports of other drugs

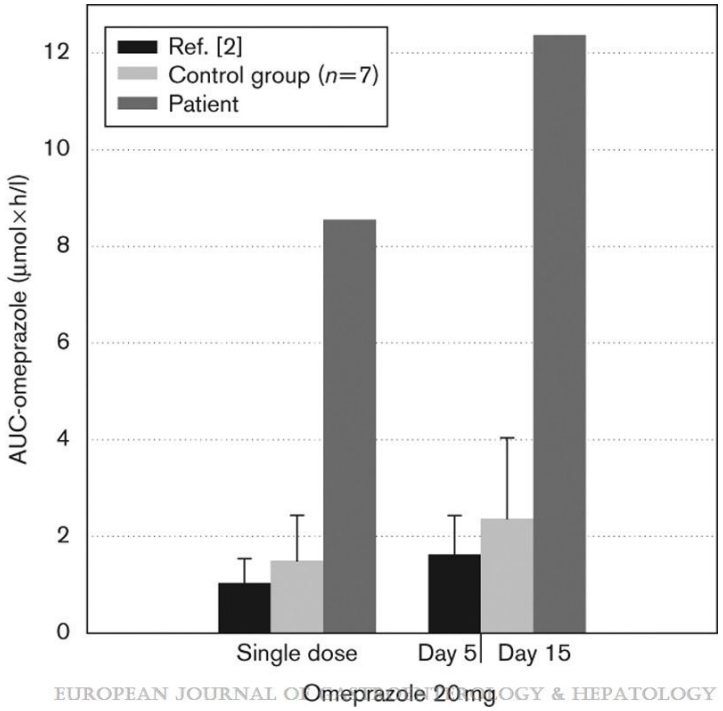
- **Topiramate**
  - 2 cases, 투여 직후 기침, 중단 후(1주 이내) 소실
  - 기침약, Steroid, Bronchodilator에 반응하지 않음
- **Phenytoin**
  - 1 case, 투여 직후 기침, 중단 후 6개월간 지속 후 소실
- **MTX**
  - 10 cases(All RA pts.), Lung parenchymal dx. X, BSC로 기침 호전
- **MMF**
  - 5 cases(All KT pts.), 약물 투여 후 30~90일에 발생, 약제 중단 후 호전

Acta Neurol Belg. 2012 Jun;112(2):217-20.
Headache. 2010 Feb;50(2):301-4.
Epilepsy Behav Case Rep. 2016 Mar 16;5:44-5.
Clin Rheumatol. 1996 May;15(3):277-82
Transplantation. 1998 Aug 15;66(3):409

Rare case reports of other drugs

- **Omeprazole**
  - 2 cases
  - 개개인에 따른 혈중 약물 농도와의 관련?

- **Leflunomide**
  - 1 case, RA c pul. TB pt.
  - 결핵 치료 종결 후에도 불구 하고 기침 지속
  - Leflunomide STOP후 기침 호전됨.



Eur J Gastroenterol Hepatol. 2010 Jul;22(7):880-2.
BMJ Case Rep. 2013; 2013: bcr2012008373.

Summary

- 약물 유발 기침은 만성 기침의 일반적인 원인 중 하나는 아니지만 일부를 차지 할 수 있다.
- 약물은 기침 반사가 더 잘 일어날 수 있는 상태를 만들 수 있다.
- 아직까지는, ACE-I를 제외하고는 약제 유발 기침의 대부분의 임상 증거는 부족한 상태이다.
- 그러나, 약물로 인한 기침을 인지 한다면 추가적 진단이나 노력 없이도 기침을 해결 하는데 도움이 될 수 있다.

감사합니다.