

The Korean Cough Guideline: Recommendation and Summary Statement

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Cough is one of the most common symptom of many respiratory diseases. The Korean Academy of Tuberculosis and Respiratory Diseases organized cough guideline committee and cough guideline was developed by this committee. The purpose of this guideline is to help clinicians to diagnose correctly and treat efficiently patients with cough. In this article, we have stated recommendation and summary of Korean cough guideline. We also provided algorithm for acute, subacute, and chronic cough. For chronic cough, upper airway cough syndrome (UACS), cough variant asthma (CVA), and gastroesophageal reflux disease (GERD) should be considered. If UACS is suspicious, first generation anti-histamine and nasal decongestant can be used empirically. In CVA, inhaled corticosteroid is recommended in order to improve cough. In GERD, proton pump inhibitor is recommended in order to improve cough. Chronic bronchitis, bronchiectasis, bronchiolitis, lung cancer, aspiration, angiotensin converting enzyme inhibitor, habit, psychogenic cough, interstitial lung disease, environmental and occupational factor, tuberculosis, obstructive sleep apnea, peritoneal dialysis, and idiopathic cough can be also considered as cause of chronic cough. Level of evidence for treatment is mostly low. Thus, in this guideline, many recommendations are based on expert opinion. Further study regarding treatment for cough is mandatory.

Keywords: Cough; Guideline; Korean

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Introduction

Cough is one of the most common symptom of many respiratory diseases. Although cough guidelines from various countries are available, there has been no Korean cough guideline. The Korean Academy of Tuberculosis and Respiratory Diseases organized cough guideline committee at March 2013. From March 2013 to October 2014, cough guideline was developed by the members of this committee. The purpose of this guideline is to help clinicians to diagnose correctly and treat efficiently patients with cough. The content of this guideline is confined to adult patients only. This guideline is developed based on evidence. The committee developed key questions and searched evidence in three medical databases, Medline, Embase, Cochrane library and also in three Korean journals, *Tuberculosis and Respiratory Diseases*, *Korean Journal of Medicine*, and *Allergy, Asthma & Respiratory Disease*. The level of evidence was evaluated by the Grading of Recommendations Assessment, Development and Evaluation approach¹. The strength of recommendation was assigned by formal voting rules from expert committee. The Korean cough guideline is written in Korean and published October 2014. In this article, we have stated recommendation and summary of Korean cough guideline.

1. Definition, Mechanism, and Epidemiology of Cough

1) Summary

Cough is normal defense mechanism. However, severe or long-standing cough is the most common symptom that results in visit of hospital.

2. Classification of cough

1) Summary

- Cough can be classified as acute (<3 weeks), subacute (3 to 8 weeks), and chronic (>8 weeks) according to the duration.
- Classification of cough according to the duration helps to differentiate cause of cough.

3. Acute and subacute cough

1) Recommendation

- Beta-2 agonist should not be used to improved cough symptom (evidence, low; recommendation, strong).
- Considering adverse effect of antibiotics, empirical therapy of antibiotics can be considered only in patients with purulent sputum (evidence, high; recommendation, weak).

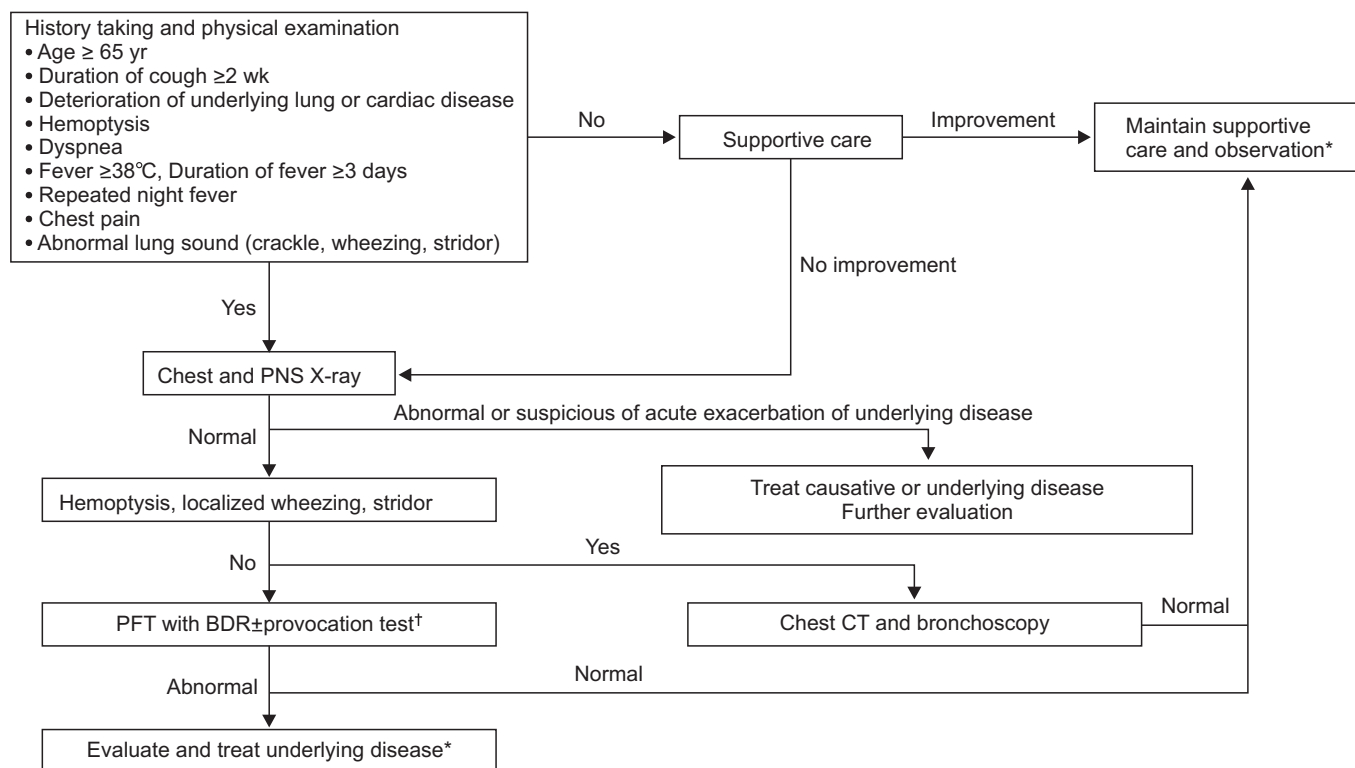


Figure 1. Algorithm for evaluation of acute cough. *If symptom maintains, follow algorithm for subacute and chronic cough evaluation. †May consider empirical therapy when evaluation is not possible. PNS: paranasal sinus; PFT: pulmonary function test; BDR: bronchodilator response; CT: computed tomography.

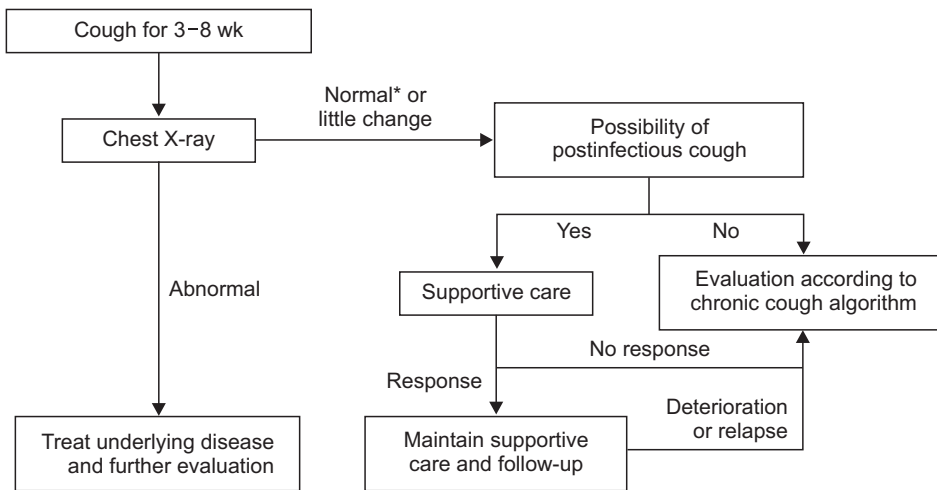


Figure 2. Algorithm for evaluation of subacute cough. *When clinical manifestations are suspicious of *Bordetella pertussis* or *Mycoplasma* infection, evaluation and treatment can be performed to these pathogens.

2) Summary

- Acute cough can be early symptom of serious diseases such as acute exacerbation of interstitial lung disease (ILD), congestive heart failure, tuberculosis (TB), endobronchial neoplasm, or foreign body aspiration. Thus, these diseases should be included in the differential diagnosis of acute cough (Figures 1, 2).
- Considering prevalence of TB in Korea, chest X-ray should be checked in patients with acute cough whose duration is more than 2 weeks.
- Chest X-ray can be checked in acute cough patients with old age, since symptoms of serious diseases may be non-specific in them.
- For acute cough due to upper respiratory infection (URI), first generation antihistamine is effective², while second generation is not^{3,4}.
- In acute cough due to URI, paranasal sinus X-ray or antibiotics may not be necessary during first 1 week^{2,5-7}.

4. Chronic cough

1) Summary

- Chronic cough is defined as a cough lasting more than 8 weeks.
- History including smoking, accompanying symptom, and medication is helpful for differential diagnosis and should be taken first and enough.
- Test for upper airway cough syndrome (UACS), cough variant asthma (CVA), and gastroesophageal reflux disease (GERD) should be performed (Figure 3).
- Chest X-ray should be performed first⁸⁻¹⁰. Then, other tests can be performed step by step according to symptom of patient and facilities of hospital.

5. Upper airway cough syndrome

1) Recommendation

- In UACS, intranasal steroid can be considered in order to improve cough (evidence, very low; recommendation, weak).
- In UACS, oral anti-histamine is recommended to improve cough (evidence, very low; recommendation, strong).
- In UACS, using nasal decongestant only is not recommended to improve cough (evidence, expert opinion; recommendation, strong).
- In UACS, intranasal anti-histamine is not considered to improve cough (evidence, very low; recommendation, weak).
- In UACS, antibiotics is not recommended to improve cough (evidence, expert opinion; recommendation, strong).

2) Summary

- UACS is syndrome of which various upper airway disease cause cough.
- UACS is diagnosed based on symptom, physical examination, radiologic finding, and response to empirical treatment.
- If UACS is diagnosed, adequate treatment should be initiated.
- If UACS is suspicious, first generation anti-histamine and nasal decongestant can be used empirically.

6. Cough variant asthma

1) Recommendation

- In CVA, leukotriene antagonist (LTRA) can be considered in order to improve cough (evidence, low; recommendation, weak).
- In CVA, inhaled corticosteroid (ICS) is recommended in order to improve cough (evidence, expert opinion; recommendation, strong).

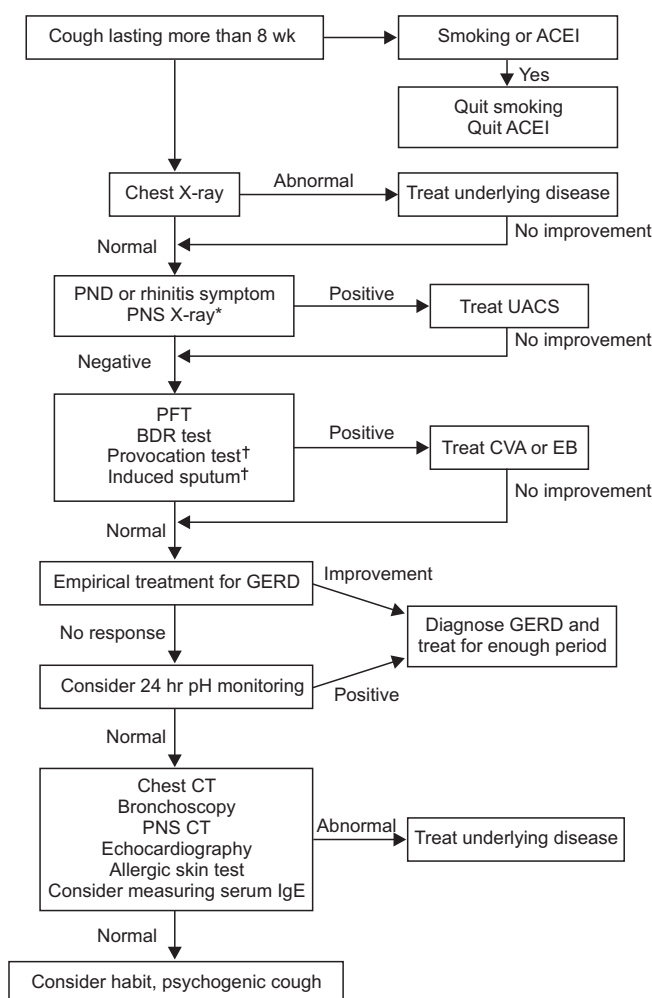


Figure 3. Algorithm for evaluation of chronic cough. *When clinical manifestation is suspicious for UACS, empirical treatment can be tried even if PNS X-ray is normal. †Empirical treatment can be considered when evaluation is not feasible. ACEI: angiotensin converting enzyme inhibitor; PND: postnasal drip; PNS: paranasal sinus; UACS: upper airway cough syndrome; PFT: pulmonary function test; BDR: bronchodilator response; CVA: cough variant asthma; EB: eosinophilic bronchitis; GERD: gastroesophageal reflux disease; CT: computed tomography.

2) Summary

- CVA is defined as symptoms mainly confined to cough, bronchial hyperresponsiveness, and improvement of cough after asthma treatment.
- Key medication for CVA is ICS and bronchodilator, same as in asthma.

7. Eosinophilic bronchitis

1) Recommendation

- In eosinophilic bronchitis (EB), LTRA is not recommend-

ed in order to improve cough (evidence, expert opinion; recommendation, strong).

- In EB, ICS is recommended in order to improve cough (evidence, expert opinion; recommendation, strong).

2) Summary

- EB is defined as symptoms limited only to cough, no bronchial hyperresponsiveness, and eosinophilic inflammation in airway^{11,12}.
- Key medication for EB is ICS.

8. Gastroesophageal reflux disease

1) Recommendation

- In GERD, proton pump inhibitor is recommended in order to improve cough (evidence, low; recommendation, weak).
- In GERD, prokinetic is not recommended in order to improve cough (evidence, expert opinion; recommendation, weak).

2) Summary

- If GERD is suspicious as cause of cough, empirical therapy can be performed.
- Treatment option for cough due to GERD includes dietotherapy^{13,14}, life style modification¹⁵⁻¹⁹, and medication at least 4-8 weeks.

9. Chronic bronchitis

1) Recommendation

- In chronic bronchitis (CB) with normal lung function, smoking cessation is recommended in order to improve cough (evidence, expert opinion; recommendation, strong).
- In CB with normal lung function, mucoactive agent can be considered in order to improve cough (evidence, expert opinion; recommendation, weak).

2) Summary

- Treatment for CB with decreased lung function should follow chronic obstructive pulmonary disease guideline.
- Smoking cessation is most effective treatment in CB with decreased lung function^{20,21}.
- CB is the most common cause of cough in smokers.
- Mucoactive agent is effective on improvement of cough in CB with decreased lung function²².
- Inhaled short acting beta agonist (SABA)²³, theophylline²⁴, ICS/long acting beta agonist²⁵, and codeine can be used to treat cough in CB with decreased lung function.

10. Bronchiectasis

1) Summary

- When bronchiectasis is suspicious, high resolution computed tomography (HRCT) is needed even if chest X-ray

is normal²⁶.

- Long-term treatment of antibiotics should be considered cautiously since it can decrease acute exacerbation by infection; however, it also can develop adverse effect²⁷⁻³⁰.

11. Bronchiolitis

1) Recommendation

- In diffuse panbronchiolitis, low-dose macrolide antibiotic is recommended in order to improve cough (evidence, expert opinion; recommendation, strong).

2) Summary

- Bronchiolitis should be preferentially considered when there are irreversible airflow obstruction, suspicion of small airway disease in HRCT, and purulent sputum in patients with cough³¹.

12. Lung cancer

1) Summary

- Chest X-ray should be performed in case of risk factor for lung cancer or metastatic lung cancer.
- Bronchoscopy should be performed when suspicious of endobronchial invasion by tumor even if chest X-ray is normal³².
- In lung cancer, the reason of cough may not come from cancer. Thus, further evaluation is needed.
- In lung cancer, cough should be managed actively since it can affect quality of life and prognosis³³.
- In lung cancer, stepwise treatment based on mechanism of drug should be considered in order to control cough³⁴.

13. Aspiration

1) Summary

- Oropharyngeal dysphagia and aspiration should be checked in case of cough being developed when eating or swallowing food³⁵.

14. Angiotensin converting enzyme inhibitor

1) Recommendation

- In cough due to angiotensin converting enzyme inhibitor (ACEI), cessation of ACEI is recommended in order to improve cough (evidence, expert opinion; recommendation, strong).

2) Summary

- To diagnose cough due to ACEI, detailed history including ACEI administration is needed.
- Generally, cough subsides 1–4 weeks after cessation of ACEI. However, cough can last more than 3 months in some patients^{36,37}.

15. Habit, psychogenic cough

1) Summary

- Habit, psychogenic cough is unconsciously persistent cough without underlying disease. It can be considered when there is no obvious reason for cough or cough does not respond to conventional therapy³⁸.
- Habit, psychogenic cough is developed mostly during pediatrics and adolescent. When developed in adult, it may accompany with psychological problem^{39,40}.
- Habit, psychogenic cough is characterized by aggravation during emotional stress and social activity and disappearance during sleep.
- Habit, psychogenic cough can be diagnosed only if other causes are ruled out³⁸.
- Psychological consultation and therapy can be considered⁴⁰⁻⁴².

16. Interstitial lung disease

1) Summary

- Chronic cough is common symptom in ILD.
- ILD should be included in the differential diagnosis of chronic cough since chest X-ray can be normal in 5%–10% of early ILD patients.
- Progression of cough can vary according to cause and underlying disease.

17. Cough due to environmental and occupational factor

1) Summary

- Environmental and occupational factors can evoke cough in itself, or can aggravate cough due to other causes. Thus, consideration for environmental and occupational factors is mandatory.
- Detailed history taking of exposure and occupation is important to find environmental and occupational factors.

18. Cough due to TB and other infection

1) Summary

- Considering prevalence of TB in Korea, active TB should be suspected and evaluated in cough lasting more than 2 weeks.
- Respiratory infection should be considered as cause of unexplained chronic cough.

19. Obstructive sleep apnea

1) Summary

- In unexplained or unresponsive chronic cough, obstructive sleep apnea should be included in the differential diagnosis^{43,44}.

20. Cough and peritoneal dialysis

1) Summary

- Cough is common symptom in patient with peritoneal dialysis⁴⁵⁻⁴⁷. The cause of cough may be GERD^{47,48}, ACEI, infection⁴⁹, and pulmonary edema.

21. Cough in immunocompromised patient

1) Summary

- The cause of cough in immunocompromised patient is similar with those of immunocompetent.
- Opportunistic infection should be included in the differential diagnosis.

22. Uncommon causes of cough

1) Summary

- In the diagnosis of uncommon causes of cough, knowledge of disease, clinical suspicion, and adequate evaluation are very important.

23. Idiopathic cough

1) Recommendation

- In idiopathic cough, antitussive can be considered in order to improve cough (evidence, expert opinion; recommendation, weak).

2) Summary

- Diagnosis of idiopathic cough should be made when after cough is not improved by adequate therapy and other causes are ruled out^{10,50}.

24. Treatment agent of cough: antitussive and mucoactive agent

1) Summary

Antitussive is classified as central and peripheral^{51,52}.

- Narcotic central antitussive: morphine, codeine
- Nonopioid central antitussive: dextromethorphan, levopropoxyphene
- Peripheral antitussive: benzonatate, benproperine, theobromine
- Etc.: amitriptyline, baclofen, gabapentin

Mucoactive agent can be classified as expectorants, mucoregulatory agents, mucolytics, and mucokinetics^{53,54}.

- Expectorants: hypertonic saline, iodinated glycerol, domidol, guaifenesin, ion channel modifiers
- Mucoregulatory agents: carbocysteine, anticholinergics, glucocorticoid, macrolide antibiotics
- Mucolytics
 - Classic mucolytics: N-acetylcysteine, nacystelyn, bromhexine, erdosteine, fudosteine
 - Peptide mucolytics: dornase alfa, gelsolin, thymosin β 4
 - Nondestructive mucolytics: dextran, heparin
- Mucokinetics: inhaled SABA, methylxanthine, surfactant, ambroxol, acebrophylline

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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