

# Assessment and Treatment of Mucus Hypersecretion in COPD: A Case Study

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Received September 02, 2021; Revised October 05, 2021; Accepted October 13, 2021

**Abstract** Mucus hypersecretion is a debilitating feature of COPD that is often overlooked and under treated by clinicians despite its contribution to declining lung function and quality of life. This case study explores the use of the COPD Assessment Test in the evaluation of mucus hypersecretion and improvements in quality of life related to this symptom after the addition of guaifenesin as part of a comprehensive COPD care plan.

**Keywords:** COPD, exacerbation, mucus hypersecretion, mucociliary clearance, guaifenesin, chronic bronchitis

**Cite This Article:** Kami Whitney PA-C, "Assessment and Treatment of Mucus Hypersecretion in COPD: A Case Study." *American Journal of Medical Case Reports*, vol. 9, no. 12 (2021): 730-733. doi: 10.12691/ajmcr-9-12-18.

## 1. Introduction

Primary care clinicians are estimated to manage approximately 80% of patients with chronic obstructive pulmonary disease (COPD), [1] a chronic, progressive disease process characterized by dyspnea, chronic cough, and excess mucus production. Airway mucus hypersecretion is one of the most important features of COPD. [2] Clinically, it results in cough and expectoration, but it is also a marker of disease progression and prognosis. [2] COPD complicated with mucus hypersecretion results in progressive decline of lung function, [2] diminished quality of life, [2,3] exacerbations, and hospitalizations. [4] It may also be predictive of respiratory and all-cause mortality. [4] Treatment of airway mucus hypersecretion should therefore be a critical component of overall management of COPD in the primary care setting. The COPD Assessment Test (CAT), a self-administered symptom severity assessment tool, consists of eight items, rated from 0-5, that impact patient quality of life including those of mucus hypersecretion. CAT scores range from 0-40 with higher scores denoting more severe impact on quality of life. [5] A CAT score of  $\geq 2$  for the two questions related to cough and phlegm effectively identifies chronic mucus hypersecretion in patients with COPD. [6] Guaifenesin, an over the counter (OTC) expectorant has shown improvements in mucociliary clearance and cough in chronic bronchitis patients, [7] and may improve quality of life when added to standard COPD therapy. [8,9,10]

## 2. Case Report

A 64 year old male presented in the fall of 2020 with complaints of increasing cough and excess mucus over the past two weeks, causing him to wake frequently at night coughing up large amounts of phlegm which continued through most of the morning. He also reported increased difficulty with his regular daily activities due to frequent coughing. He denied increased dyspnea, fever, chills, myalgias, wheezing, chest pain, abdominal complaints, or exposure to COVID-19. His total CAT score was 22. On a scale of 0-5 he rated chest phlegm at 4 and cough at 5. (Figure 1).

He has a history of stable COPD diagnosed 4 years ago, Global Obstructive Lung Disease (GOLD) 3 Group D.

He reports regular use of his maintenance inhalers: budesonide/formoterol 160 mcg/4.5 mcg (Symbicort® Astra Zeneca, Wilmington; DE), tiotropium bromide 2.5 mcg (Spiriva® Respimat® Boehringer Ingelheim, Ridgefield; CT) and is currently using his albuterol HFA inhaler twice daily.

He has a  $>60$  pack year smoking history and recently decreased smoking from 2-3 packs per day to 1 pack daily.

On physical examination, the patient was an overweight (BMI, 26.2) white male in no apparent distress, with intermittent cough throughout the visit. Temporal temperature 97.4, pulse 96 bpm and regular. Pulse oximetry at rest: 98% on room air.

Lung sounds were distant to auscultation without appreciable wheezing, rales or rhonchi. Chest x-ray revealed decreased lung markings and hyperinflation, without consolidation. COVID-19 rapid nasal antigen test was negative.



**How is your COPD? Take the COPD Assessment Test™ (CAT)**

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

<b>Example:</b> I am very happy	0	X 1	2	3	4	5	I am very sad	1
								Score
I never cough	0	1	2	3	4	X 5	I cough all the time	5
I have no phlegm (mucus) in my chest at all	0	1	2	3	X 4	5	My chest is completely full of phlegm (mucus)	4
My chest does not feel tight at all	X 0	1	2	3	4	5	My chest feels very tight	0
When I walk up a hill or one flight of stairs I am not breathless	0	1	X 2	3	4	5	When I walk up a hill or one flight of stairs I am very breathless	2
I am not limited doing any activities at home	0	1	X 2	3	4	5	I am very limited doing activities at home	2
I am confident leaving my home despite my lung condition	X 0	1	2	3	4	5	I am not at all confident leaving my home because of my lung condition	0
I sleep soundly	0	1	2	3	4	X 5	I don't sleep soundly because of my lung condition	5
I have lots of energy	0	1	2	3	X 4	5	I have no energy at all	4

**Total Score: 22**

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**Figure 1.** CAT assessment - Baseline

Pulmonary function testing was not done due to COVID-19 restrictions.

The patient had received his flu shot earlier in the season and Pneumococcal polysaccharide vaccine a year earlier.

A diagnosis of COPD exacerbation was made. The patient was commenced on 40 mg of prednisone for 5 days and advised to increase his albuterol use to 4 times daily. To address his concerns of increased mucus production, OTC guaifenesin extended release 600 mg BID (Mucinex® Extended-Release Bi-Layer Tablets Reckitt, Parsippany,NJ) was advised. Follow up was planned for 2 weeks, with direction to return sooner if symptoms did not improve in 2-3 days.

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For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

<b>Example:</b> I am very happy	0	X 1	2	3	4	5	I am very sad	1
								Score
I never cough	0	1	2	X 3	4	5	I cough all the time	3
I have no phlegm (mucus) in my chest at all	0	X 1	2	3	4	5	My chest is completely full of phlegm (mucus)	1
My chest does not feel tight at all	0	X 1	2	3	4	5	My chest feels very tight	1
When I walk up a hill or one flight of stairs I am not breathless	0	1	X 2	3	4	5	When I walk up a hill or one flight of stairs I am very breathless	2
I am not limited doing any activities at home	0	X 1	2	3	4	5	I am very limited doing activities at home	1
I am confident leaving my home despite my lung condition	0	1	X 2	3	4	5	I am not at all confident leaving my home because of my lung condition	2
I sleep soundly	0	1	X 2	3	4	5	I don't sleep soundly because of my lung condition	2
I have lots of energy	0	1	2	X 3	4	5	I have no energy at all	3

**Total Score: 15**

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**Figure 2.** CAT assessment post 14-days guaifenesin

At two weeks follow up the patient reported much less coughing and was no longer waking at night coughing and expectorating mucus. His CAT score improved from 22 to 15. Notable changes included a decrease in his rating of chest phlegm to 1, and a cough score of 3. (Figure 2) He continues to use his controller medications and guaifenesin twice daily. Review of the patient's chart revealed frequent exacerbation of mucus production in the fall and early winter months. A recommendation to continue guaifenesin through the fall and winter was made based on a COPD case study by Storms et al and a small number of similar published cases suggesting that daily administration of guaifenesin might improve respiratory mucus removal. [8,9,10] At the patient's regularly

scheduled health maintenance follow up three months later, he had experienced no further exacerbations and his CAT score remained stable at 16. COVID-19 vaccination was advised as soon as available.

### 3. Discussion

COPD is a disease wrought with relapsing and remitting episodes of increased cough, shortness of breath and increased mucus production. Exacerbations can cause significant disruption to quality of life.

The key intervention for any COPD patient who is still smoking is to achieve complete cessation. Another is to maintain an active lifestyle and engage in physical activities including pulmonary rehabilitation, which has been shown to improve exercise tolerance, dyspnea, and overall health status. [11]

It is also recommended that all individuals with COPD be vaccinated annually for influenza, as well as receive pneumococcal vaccinations per Centers for Disease Control and Prevention guidelines. [11]

Pharmacologic therapy is used to reduce both symptoms and the frequency and severity of COPD exacerbations. Treatment selection is based on the patient's GOLD classification as well as availability, cost and insurance coverage of the medications. Commonly used maintenance medications include short-acting beta-2

agonists (SABAs), long-acting beta-2 agonists (LABAs), short-acting muscarinic antagonists (SAMAs), long-acting muscarinic antagonists (LAMAs), combination medications and mucolytics. [11]

Of these, only mucolytics address airway mucus hypersecretion. The 2021 GOLD Guidelines include two such medications: carbocysteine, and N-acetylcysteine (NAC), which are briefly noted to improve health status and possibly reduce exacerbations for patients not on inhaled corticosteroids. [11]

NAC liquefies mucus by opening disulfide bonds in the mucoproteins. [12] Carbocysteine reduces the viscosity of bronchial secretions by breaking disulphide crosslinks between mucin monomers as well as reducing goblet cell hyperplasia. [13] However, there is no evidence that either improve the ability to expectorate sputum. Guaifenesin, an over-the-counter, oral expectorant may therefore be a useful addition as at least one study has suggested that therapies targeting mucus hypersecretion in COPD could be beneficial regardless of the presence of chronic cough and sputum production. [14]

Guaifenesin's exact mechanism of action is not completely understood, but several studies have suggested that it works by: increasing hydration of the mucus layer through parasympathetic glandular secretion of the submucosal glands and goblet cells; decreasing mucin production and secretion; and reducing mucus viscoelasticity, all of which may contribute to mucociliary clearance. [15]

**Table 1. Mechanism of Action and Effects of Guaifenesin on Mucus**

Authors	Observed action of guaifenesin	Effect	Reference(s)
Seagrave J, Albrecht H, Park YS, et al.	Indirect activation / stimulation of gastrointestinal vagal afferent nerves	Triggers reflex parasympathetic glandular secretion from submucosal glands and goblet cells, increasing hydration of mucus layer	[16]
Seagrave J, Albrecht HH, Hill DB, et al.	Decreased mucin production and secretion	Increased mucociliary transport. Decreased mucus viscoelasticity	[17]
Thomson ML, Pavia D, McNicol MW, Bennett WD, Kala A, Zeman KL, et al.	Reduced viscoelasticity of mucus	Increased mucociliary clearance	[18,19]
Robinson R, Cummings WB, Deffenbaugh ER		Makes cough more productive	[20]
Chodosh S.	Reduced surface tension and adhesiveness of mucus	Improves expectoration	[21]

Although guaifenesin has a professional indication for stable chronic bronchitis it is not currently included in the GOLD guidelines. A review of the use of guaifenesin in CMH with stable bronchitis concluded that guaifenesin was likely excluded because the four studies [22,23,24,25] that formed the basis of the approval were all published prior to 1983, involved small numbers of patients and do not meet today's scientific, methodological, statistical or regulatory evidence-based medicine standards. [7]

### 4. Conclusion

COPD with CMH contributes to decreased quality of life due to increased symptom burden and serves as a marker of disease progression and prognosis. [2] CAT is a screening tool that primary care providers can use to identify COPD symptom burden including those related to mucus. [5,4] Currently there are only two medications included in the 2021 GOLD Guidelines that address airway mucus hypersecretion. [5] Guaifenesin is not,

however several case studies, including this one, suggest that its daily use may improve CMH and its associated symptoms. Further study into the effectiveness of guaifenesin in both acute exacerbations of COPD and stable COPD with symptoms of CMH should be considered.

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