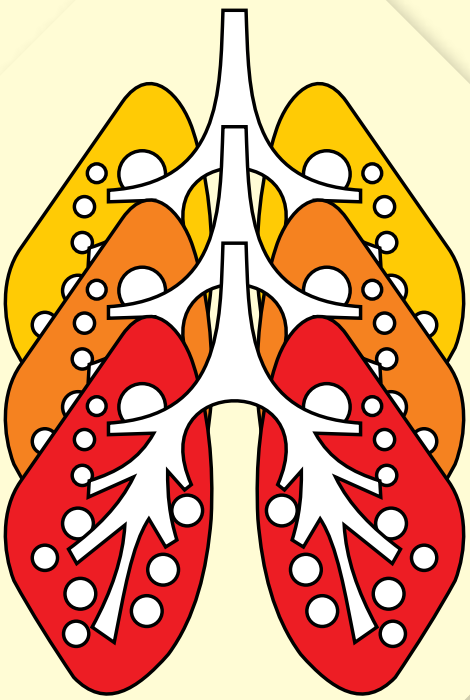
COUGHOLOGY

The art & science of navigating cough

MANAGING COUGH
A Pulmonologist's Perspective



DR. VIKRAM JAGGI

Published by

DocMode PUBLISHING
www.docmode.org

Edition 2

Educational grant by

Glenmark

COUGHOLOGY

The art & science of navigating cough

MANAGING COUGH

A Pulmonologist's Perspective

by

Dr. Vikram Jaggi

COUGHOLOGY

The art & science of navigating cough

MANAGING COUGH

A Pulmonologist's Perspective

Educational grant by

Glenmark
A new way for a new world

Glenmark Pharmaceuticals Limited (GPL),
Corporate Enclave, B. D. Sawant Marg,
Chakala, Andheri (E), Mumbai – 99.

Published by:

201, Kalpataru Plaza, Chincholi Bunder Road,
Nadiyawala Colony 2, Malad West, Mumbai - 400 064

Website: www.docmode.org

Preface

Cough is one of the most common reasons for a patient to come to the doctor. This seemingly simple symptom is often a complex interplay of reasons and sometimes foxes the doctor – both in reaching a correct diagnosis and in providing a treatment that works.

Cough concerns all specialties of doctors, whether they have a general practice, a pediatric practice, or a respiratory specialist practice. Even other specialty doctors should have a basic understanding of cough etiology and treatment.

This book is aimed at providing a comprehensive, yet simple, approach to the diagnosis and management of cough.

It is known for a fact that every complex task can be made easier by breaking it up into simpler steps. The same is true in solving the riddle of cough. What is required is:

- A basic understanding of cough physiology and all the best possible cough receptors and their locations to help in understanding where the cough is originating from.
- A systematic approach to categorize it into acute, subacute, or chronic cough.
- A thorough knowledge of the relatively common causes of cough of different durations.
- Listening to the patient carefully to elicit a good history. One must remember the old adage—"listen to the patient carefully; he is practically telling you his diagnosis."
- Formulating a working diagnosis as to the cause of the cough and remembering that oftentimes, there can be more than one cause of cough in a given patient.
- Remembering that "diagnosis must precede treatment." This is especially true for chronic cough.

- Be alert to the possibility of a serious underlying disease behind the cough (red flag signs).

The above was the doctor's perspective in dealing with cough. There is another perspective – the patient's perspective. She suffers because of social embarrassment, social isolation, headaches, and muscular chest pain that is due to prolonged cough and sometimes losing control of urination or even fainting (cough syncope). These issues need to be specifically asked for and dealt with.

In this book, you will find different chapters on cough physiology, categorization of cough, approach to cough and common reasons of cough. Some often neglected topics, like pollution and cough, and misuse of antibiotics and cough are also discussed. There are also chapters on home remedies of cough and one on what our traditional Indian alternative or complementary systems can offer to work of patience. I strongly feel that we Allopathic doctors must have a basic knowledge of these.

This is an attempt to bring a practical approach to cough management to your desk in the form of an easy-to-read book. I hope this book will serve as a practical guide to all your questions in the diagnosis and management of patients with cough and empower you with the requisite knowledge to recognize the complexity of this symptom and its effective management.

Dr. Vikram Jaggi
MD (Medicine), DNB
Medical Director
Asthma, Chest & Allergy Centres
New Delhi

Note of Thanks

I express my heartfelt appreciation to Glenmark Pharmaceuticals Ltd. for their support for this book through an educational grant. I am grateful to Dr. Salman Rizvi for his invaluable assistance in editing. Additionally, I extend my thanks to Dr. Ruchika Sharma and other members of DocMode Health Technologies Ltd. for their continuous efforts in editing, coordination, and publishing of this book.

About the Author

Dr. Vikram Jaggi is the Medical Director of **Asthma, Chest & Allergy Centres**. This is a premier institute, located in New Delhi, dealing with the diagnosis and treatment of asthma and allergy.

He did his schooling from Modern School, Barakhamba Road, New Delhi, where he was captain of the school basketball and football teams. A topper throughout, he secured the 3rd All India Rank in the 12th class CBSE examination. He is an alumnus and a double gold medalist from Delhi's Maulana Azad Medical College. He continues to play badminton regularly and finds time for his other hobbies, like wood carving.

He did his MD in Internal Medicine from Maulana Azad Medical College and later served as a Senior Registrar there. He was awarded with the prestigious Mohan Lal Nair award for the Best Senior Resident of the hospital.

His special interests have always been asthma and allergies. He is passionate about patient education and spreading awareness about asthma. He regularly contributes articles to national dailies, like Hindustan Times, The Times of India, etc., and has contributed over 35 such articles.

He has authored over 15 books/booklets on asthma and allergy. The latest book is titled "What patients REALLY want to know about Asthma." He has contributed the chapter "Allergen Immunotherapy" in the multi-author textbook "Pulmonary & Critical Care Medicine."

He has given over 100 lectures and chaired over 40 sessions, both nationally and internationally, on various topics of asthma and allergy.

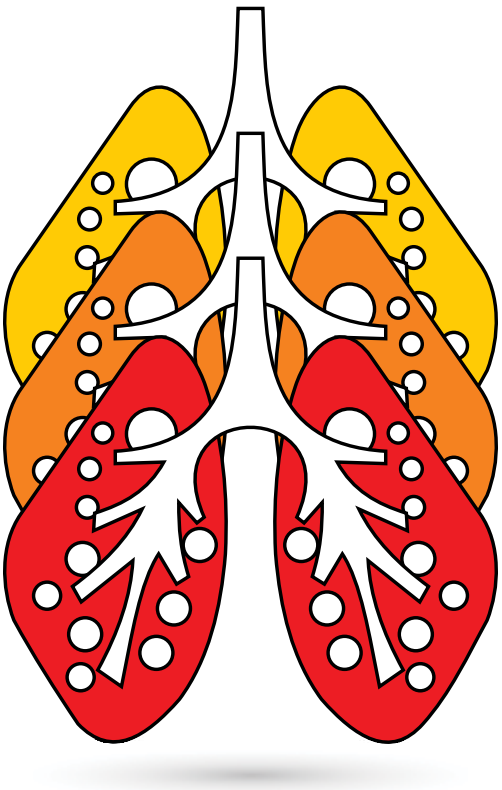
He has been successfully running a website www.acac.in since 2007 which is a rich source of helpful information for patients.

Dr. Jaggi's interest in 'cough' dates back to the 1990s, when he started a weekly Cough Clinic at his center. Recently, he was a member of the committee to formulate the Indian consensus on the management of cough, which was published in the *Journal of the Association of Physicians of India* in 2023.

CONTENTS

CHAPTER 1

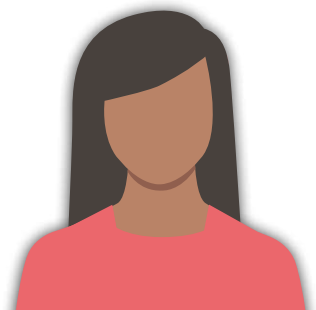
Importance of Cough



Cough and fever are probably the most common symptoms which make the patient seek a doctor's consultation. It would not be inaccurate to say that cough has increased in the last couple of decades. The reasons for this increase are many. Air pollution is increasing, and several Indian cities rank among the world's most polluted cities. A report in the Indian Express, dated March 15, 2023, stated that among the 50 most polluted cities in the world, 39 are from India.[1] In the presence of polluted air, most postviral coughs last weeks rather than days.

The incidence and prevalence of allergy in India is increasing. Data suggest that there has been a rise in allergic rhinitis prevalence in the county. A study from Mysuru noted an increasing prevalence of allergic rhinitis in children between 1998 and 2013.[2] This increase in allergy increases the chances of coughs lasting longer and being more troublesome. Modern living, with its unhealthy lifestyle, increasing obesity, poor food choices, and increasing incidence of gastroesophageal reflux disease (GERD), all contribute to the increasing incidence of cough.

Minor coughs, which occur after a viral respiratory infection and settle down within a couple of weeks, are not uncommon and do not pose problems. It is the prolonged cough, which lasts weeks and months, defies a clear diagnosis, and does not respond to the usual treatments, like cough syrups and lozenges, is the troublesome one. These coughs pose a different set of problems for patients and doctors alike. Let's take them up one by one.



Patient's perspective

- Embarrassment
- Fear of spreading infection
- Aches and pains
- Urinary incontinence
- Cough syncope
- Depression

Patient's perspective

Social embarrassment

The first and foremost problem the patient faces with prolonged cough is social embarrassment. Cough has a tendency to occur when the person is speaking in a meeting, or talking on the phone, or speaking in school or college, etc. When the cough starts, it is hard to control it, leading to a lot of embarrassment.

Fear of spreading infection

The fear and guilt of spreading infection are also quite high on the mind of a person having a cough. To add to that, people around the person who is coughing often view him/her with suspicion and hold him/her accountable for spreading infection. This problem became more acute during the coronavirus disease (COVID-19) times.

Aches and pains

Prolonged cough can cause headaches and pain in the ribs. Rib fractures have been known to occur with a violent cough.

Urinary incontinence

Elderly females, oftentimes, have involuntary leakage of urine because of violent coughing. Understandably, this is extremely embarrassing for them and severely restricts their social outings and interactions.

Cough syncope

Violent cough, especially that which comes without any pauses, can interfere with the circulation to the brain and can cause loss of consciousness. This is

called cough syncope. These patients, oftentimes, are misdiagnosed as having a neurological or a cardiac problem and undergo a lot of tests. A detailed history of very violent cough, without pauses, leading to gagging and choking, followed by slowly losing consciousness reveals the true diagnosis. This can save the patient a lot of unnecessary and costly testing.

I have personally seen patients with cough syncope getting electroencephalogram (EEG) and magnetic resonance imaging (MRI) brain and even undergoing coronary angiography.

Depression

Patients with cough that lasts months, or even years, often get depressed. Sometimes, this may require antidepressant pills.

Chronic cough adversely affects the quality of life (QoL) of the patients. A population-based study conducted in Japan noted that patients with chronic cough had worse health-related QoL (HRQoL) vs. respondents without cough. Additionally, chronic cough patients had higher work productivity and activity impairment (WPAI) as well as healthcare resource utilization (HRU) in comparison with non-cough respondents in the study. Patients with chronic cough also had more sleep issues compared to non-cough respondents. These patients also experienced more depression and anxiety.[3]

The effect of chronic cough on patients involves social isolation and emotional and economic impact. The patient's relationships with family and friends are hugely impacted. Patients face isolation for fear of spreading the infection to family, friends, and colleagues, feelings of guilt, uncontrollable cough at unpredictable times, and much more. Not just their personal life, but their work life is also affected.[4]

COVID-19 has fueled the fire and added to the stigma around coughing. People are now more cautious and immediately distance themselves from anyone who is coughing in their surroundings. As a result, many patients with cough avoid going out with their family or friends and fall deeper into the clutches of loneliness and isolation.

There is anxiety and low self-esteem among patients with cough which is uncontrolled. Failing to get the right diagnosis and the right treatment also instills the fear of death among some patients. As a clear diagnosis is not forthcoming, the patient starts to think of the worst. The fear that it may be because of a hidden cancer troubles the mind of the patient. All this can have a huge negative impact on the patient's emotional health.[4] Some patients might even face loss of productivity at work and some even lose their jobs due to cough, a problem that may seem trivial at first. The expenses for treatment can also be high for patients with prolonged cough. Overall, cough poses immense financial burden on the patients.[4] A study conducted among public service employees in Finland noted that cough heightens the likelihood of doctor consultations and absenteeism from work due to illness, thus posing a considerable socioeconomic burden.[5]

A study conducted among women with chronic cough noted stress urinary incontinence caused by episodes of cough in 63.3% of the study subjects.[6] In another study in adult women with chronic cough, 50.1% had urinary incontinence.[7] Clearly, urinary incontinence is not uncommon among women suffering from chronic cough and could negatively impact the patient's QoL. This is a delicate topic, but it must be addressed sympathetically during history taking.

Chronic cough, therefore, has a negative impact on the patients' physical and mental health as well as their overall well-being. With problems like stress urinary incontinence due to cough, cough syncope, anxiety, and depression, the QoL of a patient with chronic or refractory cough is considerably affected. Hence, it becomes important to evaluate the patient with a detailed history and physical examination and to establish a correct diagnosis based on relevant investigations, if required, in order to manage the cough with effective treatment options and avert the development of such issues.

- Diagnostic dilemma
- How much to investigate?
- Multiple causes
- Treatment discontinuation

Doctor's perspective

Diagnostic dilemma

The biggest dilemma that the doctor faces when dealing with a patient with a chronic cough is the likelihood that there is a serious condition behind the cough and, hence, the challenge of deciding which investigations to order. On the one hand, we do not want to miss a serious medical condition underlying the cough, and on the other hand, we do not want to impose the burden of a lot of tests on the patient.

How much to investigate?

While dealing with the diagnostic dilemma that a patient with a cough may pose, a clinician is often in a fix when it comes to deciding how many investigations are reasonable. Some diseases can have overlapping symptoms and thus make it difficult for the clinician to decide 'how many is too many'! Additionally, there may be cases where not investigating enough may lead to missing a diagnosis and delaying treatment.

Multiple causes of cough

Very often, the patient with a chronic cough that defies a diagnosis, has multiple reasons. For instance, the same patient may be having an allergic diathesis with bronchitis and a postnasal drip and also have GERD.

Treatment discontinuation

Even if the diagnosis is correct and appropriate treatment has been initiated for chronic cough, it still takes months to settle down. This should be clearly explained to the patient or else impatience and frustration will lead to discontinuation of therapy.

It is known that upper airway cough syndrome (UACS), asthma, GERD, and nonasthmatic eosinophilic bronchitis (NAEB) are the commonest causes of chronic cough. However, several other causes of chronic cough are also known.[8] For instance, in a country like India, cough is frequently seen in patients with tuberculosis (TB). Therefore, from the Indian perspective, TB must be suspected in patients with cough for more than 2 weeks following initial therapy and if there are symptoms and signs indicating TB.[9]

It is quite possible that even a thorough history may not be sufficient to determine the cause of cough.[10] Therefore, it is advisable to follow the region- or country-specific guidelines for the diagnosis and management of cough in order to have the best outcomes.

KEY MESSAGES

- Prolonged cough is troublesome for patients.
- Coughs that continue for a long time, remain unexplained, and do not respond to treatment, pose a different set of problems for patients as well as doctors.
- In patients, these coughs are a cause for social embarrassment and isolation, cause pains, are associated with urinary incontinence, particularly in women, and can lead to cough syncope. Overall, chronic cough can adversely affect a patient's QoL.

- Doctors, on the other hand, face a diagnostic dilemma while dealing with chronic cough patients, have to thoroughly assess all possible causes and underlying diseases that can lead to cough and also have to deal with the problem of treatment discontinuation when the cough fails to respond to therapy.

- Cough has great significance for both patients and doctors. Clinicians must follow evidence-based guidelines for the diagnosis and management of cough in order to have the best outcomes.

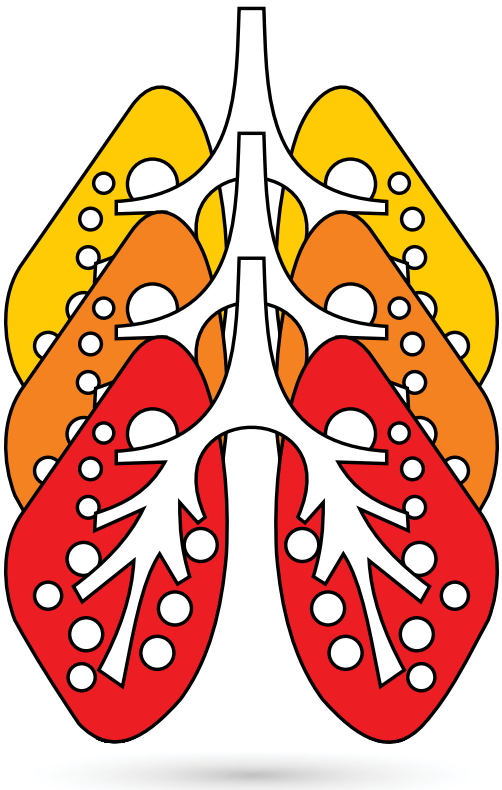
References

1. 39 out of world's 50 most polluted cities are in India: IQAir report [Internet]. Available from: https://indianexpress.com/article/india/iqair-report-indian-worlds-most-polluted-cities-39-8498146/. [cited August 28, 2023].
2. Chandrika D. Allergic rhinitis in India: an overview. *Int J Otorhinolaryngol Head Neck Surg.* 2017 Jan;3(1):1-6.
3. Kubo T, Tobe K, Okuyama K, Kikuchi M, Chen Y, Schelfhout J, *et al.* Disease burden and quality of life of patients with chronic cough in Japan: a population-based cross-sectional survey. *BMJ Open Respir Res.* 2021 Mar;8(1):e000764.
4. Won HK, Song WJ. Impact and disease burden of chronic cough. *Asia Pac Allergy.* 2021 Apr 28;11(2):e22.
5. Koskela HO, Lätti AM, Pekkanen J. The impacts of cough: a cross-sectional study in a Finnish adult employee population. *ERJ Open Res.* 2018 Nov 12;4(4):00113-2018.
6. Dicpinigaitis PV. Prevalence of stress urinary incontinence in women presenting for evaluation of chronic cough. *ERJ Open Res.* 2021 Feb 22;7(1):00012-2021.
7. Yang C, Feng Z, Chen Z, Xu D, Li Y, Lai K, Yi F. The risk factors for urinary incontinence in female adults with chronic cough. *BMC Pulm Med.* 2022 Jul 18;22(1):276.
8. Kaplan AG. Chronic Cough in Adults: Make the Diagnosis and Make a Difference. *Pulm Ther.* 2019 Jun;5(1):11-21.
9. Guleria R, Dhar R, Mahashur A, Ghoshal AG, Jindal SK, Talwar D, *et al.* Indian Consensus on Diagnosis of Cough at Primary Care Setting. *J Assoc Physicians India.* 2019 Jan;67(1):92-8.
10. Nantha YS. Therapeutic-diagnostic Evaluation of Chronic Cough Amongst Adults: Causes, Symptoms and Management at the Primary Care Level, Malaysia. *J Family Med Prim Care.* 2014 Jul;3(3):207-12.

CHAPTER 2

Prevalence of Cough

Why is cough increasing?



How often have you experienced cough in the past 6 months or a year? Quite a few times, right? You must be seeing many patients in your practice every day who present only with cough or cough as a significant symptom of some other disease they are diagnosed with.

We all know that cough is not infrequent. It is a very common presentation in daily clinical practice, possibly the commonest symptom for which a patient consults a doctor.[1] But what are the exact figures? We must know the prevalence of cough to acknowledge the burden it imposes, both from healthcare and financial perspectives.

In this chapter, let's look at the prevalence of cough globally as well as in Indian patients, and understand if, and why, cough is increasing as a standalone presentation and as a symptom of an underlying disease.

The prevalence of cough has been found to differ in different regions. The West has a comparatively higher prevalence of cough than the East. This could possibly be attributed to obesity and GERD, which seem to be more common in the Western population.[1,2]

The prevalence of acute cough (due to infection of the upper airways) was noted to be between 9% and 64% in a series of studies by Tyrrell *et al*,[3] while that of chronic cough has been reported to vary between 7.2% and 33% across various studies conducted between 1991 and 2006.[4] Analysis of data from participants in the Korean National Health and Nutrition Examination Survey 2010-2012 noted the point prevalence of acute cough as 2.5±0.2%, subacute cough as 0.8±0.1%, and chronic cough as 2.6±0.2%.[5] In the Rotterdam study including 9824 subjects, the prevalence of chronic cough was found to be 10.9%.[6]

A systematic review and meta-analysis published in 2015 by Song and colleagues estimated the epidemiology of chronic cough in adults. The prevalence of chronic cough was found to be 9.6%. The prevalence estimates across different regions are summarized in Table 1.[7]

Table 1. Prevalence of chronic cough across different regions

Region	Prevalence (%)
Oceania	18.1
Europe	12.7
America	11
Asia	4.4
Africa	2.3

Another systematic review and meta-analysis published in 2021, evaluating the prevalence of cough in primary care, included studies from 1969 to 2018. The researchers again noted differences based on regions. The prevalence of cough in the primary care setting in the West varied between 3.8% and 4.2%, with the incidence being 12.5%. On the other hand, the prevalence estimates were higher for Asia, Africa, and South America, ranging between 10.3% and 13.8%. However, the incidence estimates were lower for these regions – 6.3%-6.5%.[8]

In a recent review, including the Rotterdam study and the Korean National Survey study among others, the prevalence of chronic cough across some recent studies from different countries ranged from 2.6% to 18.5%.[9]

Talking of cough in children, it seems to be more common in the pediatric population compared to adults and is lower in adolescents compared to the younger age groups.[10]

The Indian scenario

In the systematic review by Song *et al*, the pooled prevalence of chronic cough in India was below 5%.[7] A point prevalence study involving pediatricians, general practitioners, and general physicians noted that in the primary care practice in India, cough was a commonly reported symptom (30%), second only to fever. Additionally, the prevalence of cough was higher among males.[11] A study conducted among South Asians (participants from India, Nepal, Bangladesh, Sri Lanka, and Pakistan) noted that the prevalence rate of chronic cough was 11% in India and was again higher among males.[12] An earlier study, published in 2014,

among people working in rice mills in India, showed that around 21.7% of the workers complained of cough. Other symptoms reported by the subjects included phlegm, dyspnea, chest tightness, burning of eyes, and nose irritation.[13] In the more recent Seasonal Waves Of Respiratory Disorders (SWORD) study, showing seasonal variations in outpatient visits by respiratory disease patients, cough was a common symptom among the participants – 37.1% had a productive cough and 31.5% had a dry cough.[14]

Clearly, there are wide variations in the prevalence estimates of cough, both globally and in the Indian scenario, but there is no denying the fact that the burden of cough is high.

Why is cough increasing?

We are living in a fast-changing world today. There has been an upheaval in people's lifestyles on a global level, pollution levels are increasing, obesity is on the rise, and allergies are increasing.

While the prevalence of cough in various studies conducted over the years varies widely and it may not be possible to compare these studies, on account of different patient populations or study methods, it is evident that the burden is high, and possibly the prevalence might even be increasing. Furthermore, some factors that are associated with cough appear to be on the rise.

For instance, there has been a marked **decline in air quality** over the past several years or decades. Air pollution has short- and long-term effects on our health.[15] Exposure to irritant gases, particulate matter, tobacco smoke, and mixed pollutants is linked to wheezing and cough.[16] Household air pollution is also tied to cough. Several indicators of household air pollution have been linked to persistent cough among children.[17] Additionally, traffic-linked pollution has been linked with cough incidence among adults.[18] Clearly, pollutant exposure, which has been on the rise, tends to increase cough.

Could age be a factor? Well, the number of older individuals is increasing in our country.[19] The prevalence of chronic cough appears to increase with age, as shown in several studies.[9] Therefore, increasing age could possibly be a factor that may increase cough.

As mentioned earlier, the prevalence of cough seems to be higher in the West, possibly due to conditions like **GERD and obesity**.[1,2] But with altered lifestyles, the scenario seems to be changing back home. An Indian Society of Gastroenterology (ISG) Task Force report in 2011, based on a questionnaire, reported that symptoms of GERD (heartburn and/or regurgitation) were noted in 7.6% of Indian patients once a week or more.[20] A later study published in 2019 found the prevalence of GERD to be 14% among the residents of a resettlement colony in Delhi.[21] A position statement by the ISG published in 2019 noted that GERD prevalence in the country varied between 7.6% and 30%.[22] It seems possible that with changes in our lifestyle, the prevalence of GERD is increasing and so is the prevalence of cough in the community.

Could that be the case with obesity as well? The risk of chronic cough has been reported to be higher in those with obesity.[23] Obesity has been increasing in prevalence for several years. The National Family Health Survey (NFHS)-5 has reported that abdominal obesity is prevalent in 40% of women and 12% of men in India.[24] Studies have shown that abdominal obesity, in particular, could potentially have a link with chronic cough. Moreover, reflux and asthma are also more severe in people living with obesity. Both reflux disorders and asthma are known to play a role in the development of chronic cough.[25] It seems plausible that increasing obesity among the general population could also be playing a role in increasing cough.

Allergy could also be a factor. India has witnessed an increase in the prevalence of asthma and allergic rhinitis in recent times.[26] The prevalence of asthma has been reported to rise to 54.9 per 1000 population from 41.9 from 2004-05 to 2011-12.[27] Likewise, the prevalence of allergic rhinitis has also increased and nearly 22% of the adolescents in India are estimated to have this allergic disease.[28] Cough is a presentation of both asthma and allergic rhinitis and could therefore be increasing in the population with a rise in these conditions.

KEY MESSAGES

- Cough is a common presentation in everyday clinical practice.
- The West has a comparatively higher prevalence of cough than the East, but the scenario could possibly be changing.
- A 2021 systematic review and meta-analysis noted the prevalence of cough in the primary care setting in the West to vary between 3.8% and 4.2%, while that in Asia, Africa, and South America ranged from 10.3% to 13.8%. It was definitely higher than the West.
- While a 2015 meta-analysis categorized India in the pooled prevalence range of below 5% for chronic cough, a 2017 study among South Asians noted the prevalence to be 11%.
- The SWORD study noted cough to be one of the most common symptoms (68.6%) among patients with respiratory diseases in Indian outpatient services.
- With factors like aging population, increasing air pollution levels, high prevalence of GERD and obesity, and increasing prevalence of allergy coming into play, it is possible that cough may be increasing in the population.

References

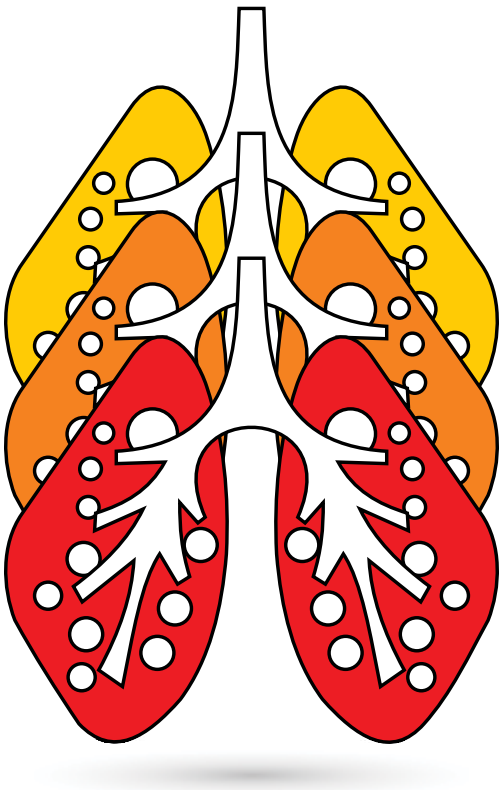
1. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
2. Song WJ, Faruqi S, Klaewsongkram J, Lee SE, Chang YS. Chronic cough: an Asian perspective. Part 1: Epidemiology. *Asia Pac Allergy.* 2015 Jul;5(3):136-44.
3. Tyrrell DA, Cohen S, Schlarb JE. Signs and symptoms in common colds. *Epidemiol Infect.* 1993 Aug;111(1):143-56.
4. Lai K, Pan J, Chen R, Liu B, Luo W, Zhong N. Epidemiology of cough in relation to China. *Cough.* 2013 Jul 8;9(1):18.

5. Kang MG, Song WJ, Kim HJ, Won HK, Sohn KH, Kang SY, *et al.* Point prevalence and epidemiological characteristics of chronic cough in the general adult population: The Korean National Health and Nutrition Examination Survey 2010-2012. *Medicine* (Baltimore). 2017 Mar;96(13):e6486.
6. Arinze JT, de Roos EW, Karimi L, Verhamme KMC, Stricker BH, Brusselle GG. Prevalence and incidence of, and risk factors for chronic cough in the adult population: the Rotterdam Study. *ERJ Open Res.* 2020 Apr 19;6(2):00300-2019.
7. Song WJ, Chang YS, Faruqi S, Kim JY, Kang MG, Kim S, *et al.* The global epidemiology of chronic cough in adults: a systematic review and meta-analysis. *Eur Respir J.* 2015 May;45(5):1479-81.
8. Bergmann M, Haasenritter J, Beidatsch D, Schwarm S, Hörner K, Bösner S, *et al.* Prevalence, aetiologies and prognosis of the symptom cough in primary care: a systematic review and meta-analysis. *BMC Fam Pract.* 2021 Jul 12;22(1):151.
9. Yang X, Chung KF, Huang K. Worldwide prevalence, risk factors and burden of chronic cough in the general population: a narrative review. *J Thorac Dis.* 2023 Apr 28;15(4):2300-13.
10. Bergmann M, Haasenritter J, Beidatsch D, Schwarm S, Hörner K, Bösner S, *et al.* Coughing children in family practice and primary care: a systematic review of prevalence, aetiology and prognosis. *BMC Pediatr.* 2021 Jun 4;21(1):260.
11. Apte K, Madas S, Barne M, Chhowala S, Gogtay J, Salvi S. Prevalence of cough and its associated diagnoses among 204,912 patients seen in primary care (PC) in India. *Eur Respir J.* 2016;48:PA864.
12. Bishwajit G, Tang S, Yaya S, Feng Z. Burden of asthma, dyspnea, and chronic cough in South Asia. *Int J Chron Obstruct Pulmon Dis.* 2017 Apr 6;12:1093-9.
13. Ghosh T, Gangopadhyay S, Das B. Prevalence of respiratory symptoms and disorders among rice mill workers in India. *Environ Health Prev Med.*2014;19:226-33.
14. Sharma BB, Singh S, Sharma KK, Sharma AK, Suraj KP, Mahmood T, *et al*; SWORD study group. Proportionate clinical burden of respiratory diseases in Indian outdoor services and its relationship with seasonal transitions and risk factors: The results of SWORD survey. *PLoS One.* 2022 Aug 18;17(8):e0268216.
15. Kaur R, Pandey P. Air Pollution, Climate Change, and Human Health in Indian Cities: A Brief Review. *Front Sustain Cities.* 2021;3:705131.
16. Joad JP, Sekizawa S, Chen CY, Bonham AC. Air pollutants and cough. *Pulm Pharmacol Ther.* 2007;20(4):347-54.
17. Coker E, Katamba A, Kizito S, Eskenazi B, Davis JL. Household air pollution profiles associated with persistent childhood cough in urban Uganda. *Environ Int.* 2020 Mar;136:105471.
18. Zhang J, Lodge C, Chang A, Knibbs L, Abramson M, Walters EH, *et al.* Associations between ambient air pollution and chronic cough in middle-aged adults. *Eur Respir J.* 2022;60:3357.
19. UN DESA Policy Brief No. 153: India overtakes China as the world's most populous country [Internet]. Available from: https://www.un.org/development/desa/dpad/publication/un-desa-policy-brief-no-153-india-overtakes-china-as-the-worlds-most-populous-country/. [cited August 23, 2023].
20. Bhatia SJ, Reddy DN, Ghoshal UC, Jayanthi V, Abraham P, Choudhuri G, *et al.* Epidemiology and symptom profile of gastroesophageal reflux in the Indian population: report of the Indian Society of Gastroenterology Task Force. *Indian J Gastroenterol.* 2011 May;30(3):118-27.
21. Yadav K, Saini NK, Patra S, Avasthi R. Prevalence of Gastroesophageal Reflux Disease And Its Correlates in Adults Residing in an Urban Resettlement Colony of East Delhi. *J Comprehensive Health.* 2019;7(2):43-9.
22. Bhatia SJ, Makharia GK, Abraham P, Bhat N, Kumar A, Reddy DN, *et al.* Indian consensus on gastroesophageal reflux disease in adults: A position statement of the Indian Society of Gastroenterology. *Indian J Gastroenterol.* 2019 Oct;38(5):411-40.

23. Landt EM, Çolak Y, Nordestgaard BG, Lange P, Dahl M. Risk and impact of chronic cough in obese individuals from the general population. *Thorax.* 2022 Mar;77(3):223-30.
24. Chaudhary M, Sharma P. Abdominal obesity in India: analysis of the National Family Health Survey-5 (2019-2021) data. *Lancet Reg Health Southeast Asia.* 2023 May 12;14:100208.
25. Guilleminault L. Chronic cough and obesity. *Pulm Pharmacol Ther.* 2019 Apr;55:84-8.
26. Krishna MT, Mahesh PA, Vedanthan P, Moitra S, Mehta V, Christopher DJ. An appraisal of allergic disorders in India and an urgent call for action. *World Allergy Organ J.* 2020 Aug 1;13(7):100446.
27. Kumar P, Ram U. Patterns, factors associated and morbidity burden of asthma in India. *PLoS One.* 2017 Oct 26;12(10):e0185938.
28. Moitra S, Mahesh PA, Moitra S. Allergic rhinitis in India. *Clin Exp Allergy.* 2023 Jul;53(7):765-76.

CHAPTER 3

Cough as a Natural Protective Mechanism



We come across many people on a daily basis, in our practice and otherwise, who might be coughing. Sometimes the children in our homes suddenly have a little cough and it settles down in a few minutes. We do not get concerned every time someone has a cough. Why is that?

Well, cough is a natural protective mechanism of our body to external stimuli. One could say that it is an important defense to protect our respiratory system against external irritants or foreign bodies and helps clear the airways of secretions in the respiratory tract.[1,2] When an external stimulus or a foreign body irritates the respiratory tract, the cough reflex springs into action.

The cough reflex therefore accomplishes two major things:[3]

- Acts as a protective mechanism against any foreign matter from being aspirated, be it particulate matter, pathogens, or secretions in the airways, and
- Helps clear the secretions accumulated in the airways.

Coughing could be voluntary or involuntary.[1] When an irritant or foreign body suddenly irritates the airway, one can initiate a cough voluntarily to get rid of the stimulus. Oftentimes, cough occurs involuntarily as a symptom of respiratory diseases and infections.

But what sounds so simple is actually a very complex mechanism. Several different muscles and specialized regions in the brain work in synchrony and in a meticulous way to stimulate cough. Let's understand this complex cough reflex.

Imagine you are sitting comfortably having your meal or drinking a smoothie and you accidentally aspirate a tiny bit of a food particle or a thin slice of cucumber from the smoothie. What will happen? You will feel a sudden urge to cough. And when that happens, several of your muscles, including the muscles of the chest wall, the abdominal muscles, the laryngeal muscles, the diaphragm, and certain regions of the brain are activated in a coordinated manner. What happens next is an inspiration, followed by a forceful expiration, either solitary or several, one after the other. The stimulus that irritated the airway momentarily is expelled. And

you feel fine. This represents a synchronized coordination of the brain and several different muscles.

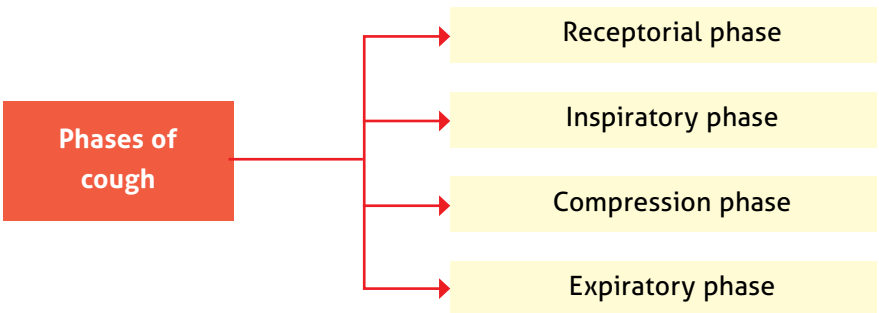
Let's understand this in detail.

Cough physiology

The cough reflex has three phases:[1]

- Inspiratory phase
- Compression phase
- Expiratory phase.

We could add one more phase in the beginning, which is the receptorial phase.[2]



Receptorial phase[2,3]

At the outset, the cough receptors are stimulated. Their activation transmits an impulse via the vagus nerve to the medullary center. Cough receptors are present in trachea, carina, at the bifurcation of large airways, small airways, and pharynx.

Inspiratory phase[1,2]

Air is inhaled and the glottis opens as the arytenoid cartilage contracts. During this phase, the expiratory muscles are elongated.

Compression phase[1,2]

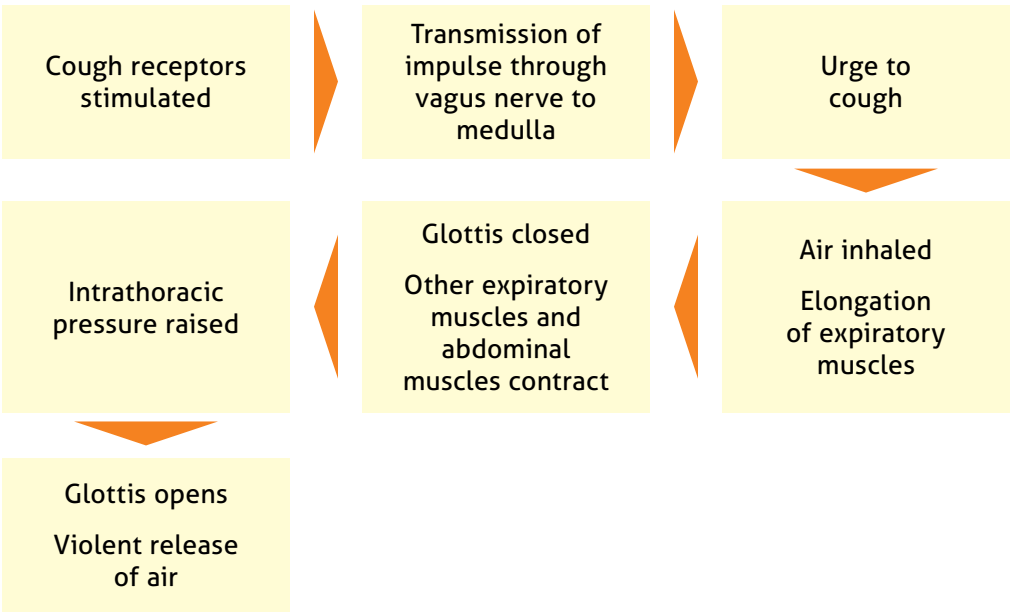
During this third phase, the adductor muscles of the arytenoid cartilage contract, and the vocal cords adduct. The glottis gets closed. Additionally, other expiratory muscles as well as the abdominal muscles contract. This is followed by a rise in intrapulmonary and intrathoracic pressure. The alveoli and bronchioles are constricted.

Expiratory phase[1-3]

In this phase, there is a sudden opening of the vocal cords and glottis followed by a violent release of air. The diaphragm is relaxed after this. As the air is expelled from the lungs at a high speed and the airways are constricted, the cough sound is produced. When someone has an intense cough, the expiratory velocity can reach as high as 800 km/h.

Figure 1 depicts the physiology of cough.

Figure 1. Physiology of cough



Cough, which is a motor activity, is, therefore, incited by chemical as well as sensory factors. This constitutes the cough reflex arc. The cough receptors in the respiratory tract are stimulated through the triggering factors which then stimulates the arc. Transmission of impulses by the afferent nerves to the cough center in the medulla followed by the vagus nerve carrying the signals to the spinal motor and phrenic nerves eventually ends up in cough.[4]

Let's understand the afferent and efferent pathways involved in the cough response.

Components of cough reflex arc

The receptorial phase involves the afferent pathway and the inspiratory, compressive, and expiratory phases involve the efferent pathway.[2]

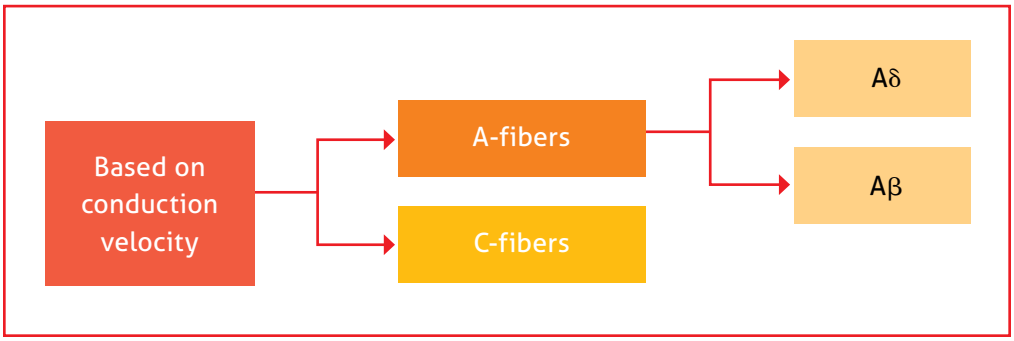
Afferent pathway—The afferent pathway comprises of vagal sensory nerve fibers. The sensory nerve fibers are distributed across the upper airway epithelium, besides the esophageal and cardiac branches from the diaphragm.[3]

Cough center or central pathway—This represents a central region present in the brainstem and pons.[3]

Efferent pathway—From the central unit, signals are transmitted to the abdominal wall, the muscles, and the diaphragm through the vagus nerve, phrenic nerve, and the spinal motor nerve.[3]

Categorization of airway neurons

Based on their speed of conduction or conduction velocity, to be specific, the airway afferent sensory neurons are categorized as follows:[1]



On the basis of their sensitivity, the afferents are categorized as:[1]

- Chemically-sensitive (nociceptors)
- Mechanically-sensitive (Aβ- or Aδ-fibers).

A specific group of Aδ-fibers [rapidly adapting receptors (RARs)] is also sensitive to acidic as well as mechanical stimuli (mechanoreceptors).[1]

Based on various characteristics, the afferents are divided into:[3]

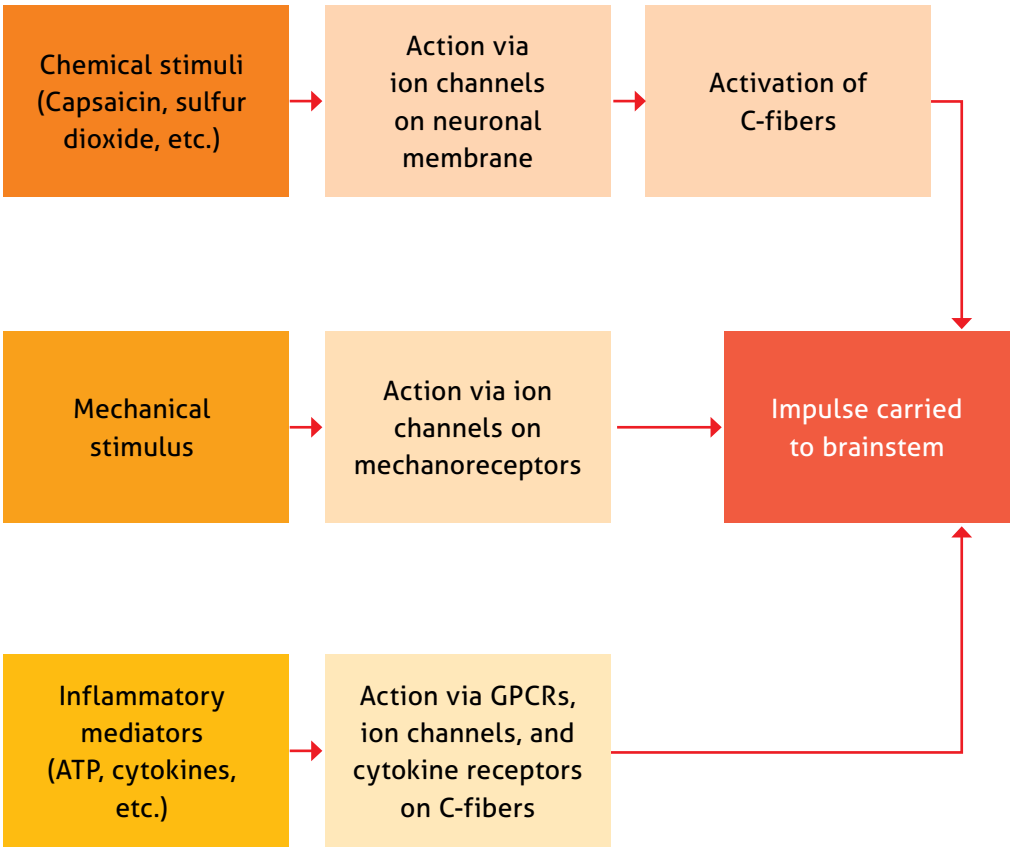
- RARs
- Slowly adapting stretch receptors (SARs)
- C-fibers.

RARs respond to mechanical changes in the airways and are activated by lung inflation, collapse, etc.[3]

SARs are mechanically-sensitive with their action rising while inhaling and attaining the highest level just before exhalation begins.[3]

C-fibers are unmyelinated fibers, not sensitive to mechanical changes and lung inflation. Bradykinin and capsaicin directly activate C-fibers. They are sensitized to them by prostaglandin E2 and adenosine. They are also activated by citric acid and sulfur dioxide.[3]

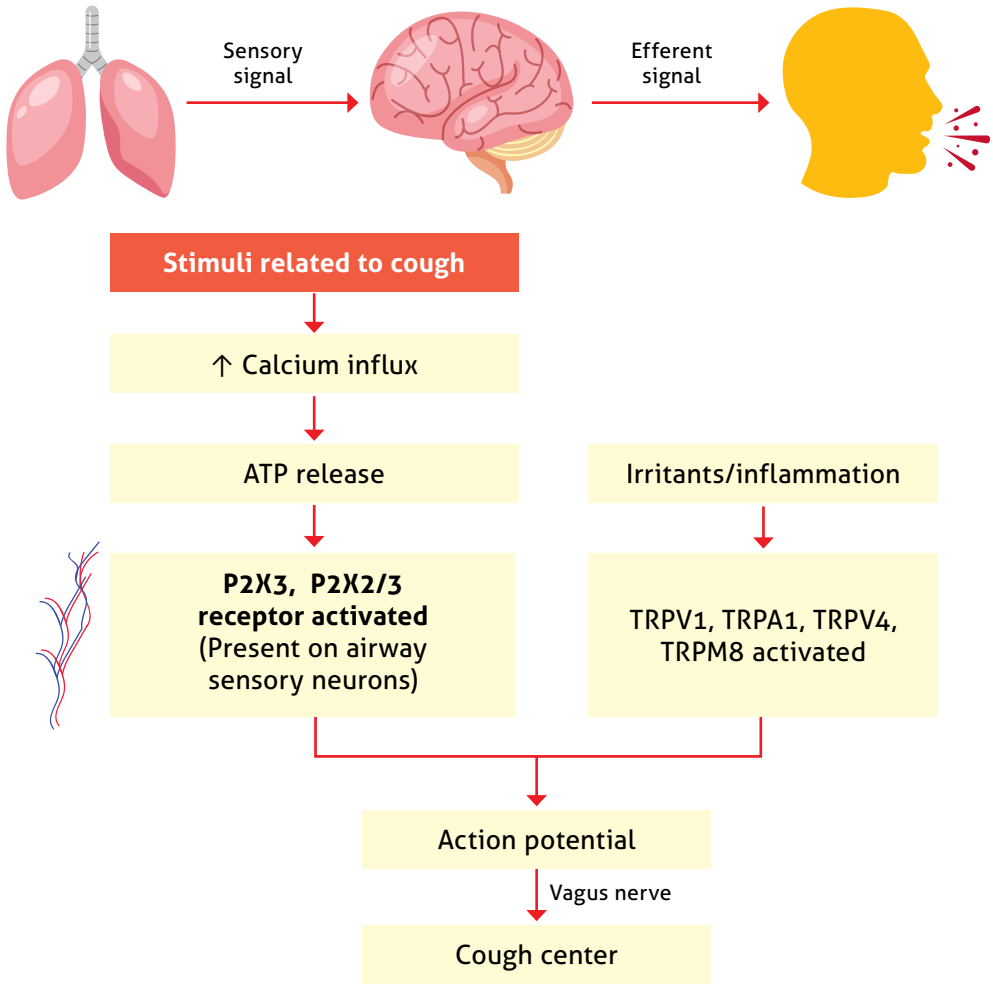
There are protein receptors on vagal afferents that communicate with the stimuli that induce cough and an action potential is generated.[1] Stimuli, whether mechanical or chemical, activate receptors on the neurons and evoke a cough response. Summarized below, in brief, is the description of how cough is evoked.[1]



ATP: Adenosine triphosphate; GPCR: G protein-coupled receptor

Figure 2 shows the regulation of the cough reflex.

Figure 2. Regulation of cough reflex



TRPV: Transient receptor potential vanilloid; TRPA1: Transient receptor potential ankyrin 1; TRPM: Transient receptor potential melastatin

Adapted from: Zhang M, Sykes DL, Sadofsky LR, Morice AH. ATP, an attractive target for the treatment of refractory chronic cough. *Purinergic Signal.* 2022 Sep;18(3):289-305.

To sum up, the vagal sensory signals are processed in the brainstem and converted to motor act of cough through the involvement of various receptors and sensory nerve fibers in the airways.

KEY MESSAGES

Let's go through the cough mechanism in brief:

Phases of cough

- **Receptorial phase—**Chemical and mechanical stimuli stimulate the cough receptors which transmits a signal to the medullary center through the vagus nerve
- **Inspiratory phase—**Air is inhaled and the glottis opens
- **Compression phase—**The glottis gets closed, adductor muscles of the arytenoid cartilage contract, other expiratory muscles as well as the abdominal muscles contract, intrathoracic pressure rises
- **Expiratory phase—**Vocal cords and glottis open, violent release of air, diaphragm is relaxed and cough is produced.

Pathways of cough reflex arc

- **Afferent pathway—**It includes vagal sensory nerve fibers
  - They can be chemically-sensitive (nociceptors) or mechanically-sensitive
  - RARs are activated by lung inflation, lung collapse, etc.
  - SARs are mechanically-sensitive receptors
  - C-fibers are activated by bradykinin, capsaicin, citric acid, and sulfur dioxide
- **Central pathway—**It is located in the brainstem and pons
- **Efferent pathway—**From the central pathway, signals are transmitted to the abdominal muscles and wall, and the diaphragm through the vagus nerve, phrenic nerve, and the spinal motor nerve.

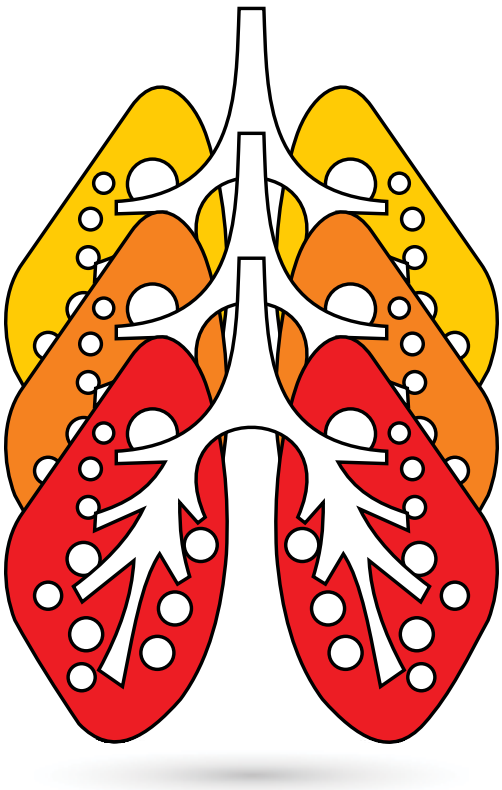
Mechanical and chemical stimuli activate receptors on the neurons and evoke a cough response.

References

1. Naqvi KF, Mazzone SB, Shiloh MU. Infectious and Inflammatory Pathways to Cough. *Annu Rev Physiol.* 2023 Feb 10;85:71-91.
2. Andrani F, Aiello M, Bertorelli G, Crisafulli E, Chetta A. Cough, a vital reflex. mechanisms, determinants and measurements. *Acta Biomed.* 2019 Jan 15;89(4):477-80.
3. Polverino M, Polverino F, Fasolino M, Andò F, Alfieri A, De Blasio F. Anatomy and neuropathophysiology of the cough reflex arc. *Multidiscip Respir Med.* 2012 Jun 18;7(1):5.
4. Dicpinigaitis P. Understanding the foundations of chronic cough. *Am J Manag Care.* 2020 Oct; 26(11 Suppl):S232-8.

CHAPTER 4

Classification of Cough



Cough is a common symptom for which patients present to the doctor on a daily basis and it could be caused by various diseases, both mild and serious. Sometimes, the etiology of cough remains obscure, thus posing significant challenges in diagnosis and management.

Classification of cough early during the course of illness may help determine the etiology and devise a targeted treatment plan for the patient. It is clinically useful for the clinician to have a mental framework of cough on the following lines:

- Based on duration: Acute, subacute, or chronic
- Wet/productive or dry
- Typical characters of the cough
- Based on its anatomical origin, e.g., arising from throat, trachea, airways, etc.

This chapter discusses all these different cough classifications. It also covers refractory cough.

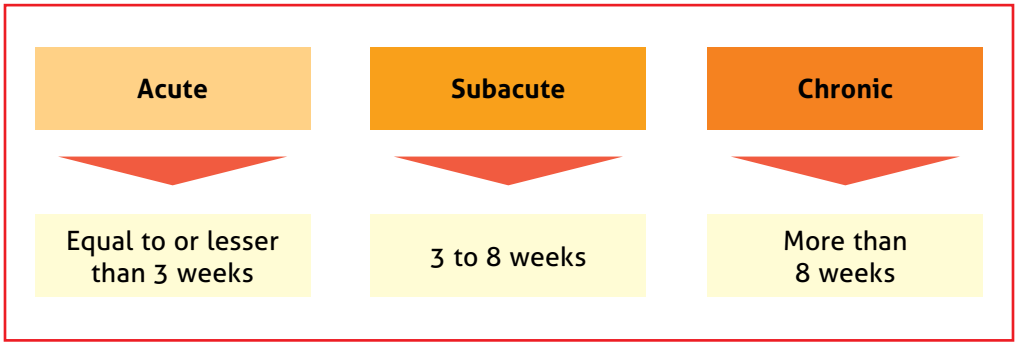
Classification based on duration

Cough is classified into three main categories on the basis of duration:[1]

- Acute
- Subacute
- Chronic.

Acute cough can occur as a result of an upper or a lower respiratory infection (URI/LRI) and exacerbations of asthma or chronic obstructive pulmonary disease (COPD). It could also occur as a result of foreign body aspiration.[2,3]

Subacute cough often occurs as a postinfectious cough or due to an exacerbation of COPD, asthma, or UACS.[3] It could also be incited by some drugs or could be due to postnasal drip.[2]



Chronic cough could be caused by asthma, GERD, COPD, chronic bronchitis, TB, heart failure, lung cancer, UACS, idiopathic pulmonary fibrosis, obstructive sleep apnea, etc.[2,3]

The classification of cough, based on duration, **in children** varies in different guidelines (Table 1). A statement of the Saudi Pediatric Pulmonology Association (SPPA), published in 2015, categorized cough for <4 weeks as acute cough and one that continues for more than 4 weeks as chronic cough.[4] In the British Thoracic Society (BTS) guidelines published in 2008, a recent onset cough of <3 weeks' duration was referred to as acute cough while that lasting for more than 8 weeks was termed chronic cough. A cough lasting for 3 to 8 weeks was termed prolonged acute cough.[5] The Australian cough guidelines categorized acute cough in general as one that lasts up to 2 weeks. It also defined protracted acute cough in children as one that lasts for 2 to 4 weeks, while cough for over 4 weeks was categorized as chronic cough.[6]

In the 2020 CHEST* guideline, chronic cough among children 14 years of age or below has been defined as daily cough for over 4 weeks.[7]

*American College of Chest Physicians

Table 1. Classification of cough in children in various guidelines, based on duration

Guideline	Cough classification
British Thoracic Society, 2008	Acute cough: <3 weeks Prolonged acute cough: 3-8 weeks Chronic cough: >8 weeks
Australian Cough Guidelines, 2010	Protracted acute cough: 2-4 weeks Chronic cough: >4 weeks
Saudi Pediatric Pulmonology Association, 2015	Acute cough: <4 weeks Chronic cough: >4 weeks
CHEST Expert Cough Panel, 2020	Chronic cough: >4 weeks

In general, most pediatricians are of the view that in children, a cough of greater than 4 weeks duration is considered to be chronic cough.

Classification based on nature of cough

Based on the nature of cough, it can be categorized into:[1,3]

- Dry/nonproductive cough
- Wet/productive cough
- Mixed.

Dry cough

When mucus or phlegm is not expectorated from the respiratory tract on coughing, it is dry or nonproductive cough.[1] Dry or irritant cough has a hacking sound.[3,8] Dry cough has a varied etiology ranging from viral upper respiratory tract infection (URTI), UACS, GERD, asthma, allergies, drug-induced, to heart failure, and pollutant exposure.[1,3]

Productive cough

A cough with expectoration of mucus or phlegm is termed productive or wet cough.[1] Productive cough is characterized by ≥30 ml of phlegm production over a period of 24 hours.[8] Pus or blood may also be mixed with phlegm sometimes.[3] Productive cough can be caused by flu, pneumonia, chronic bronchitis, TB, lung abscess, bronchiectasis, cystic fibrosis, COPD, and immunodeficiency.[3,9] A subgroup of asthma patients can also have productive cough.[9] Some features of sputum are summarized in Figure 1.[8]

Figure 1. Features of sputum

Mucus	Serous	Blood in sputum	Purulent	Cast
	Frothy, watery Seen in pulmonary edema	Seen in necrosis, tumor, infections, bronchiectasis, TB	Yellow or green in color Yellow – Infections, bronchiectasis, AECB Green – Asthma, eosinophilic bronchitis	Seen in bronchiectasis, COPD, uncontrolled asthma, allergic broncho-pulmonary aspergillosis

AECB: Acute exacerbation of chronic bronchitis

Mixed cough

Cough is termed as mixed when sometimes it is wet, with phlegm production, while on certain other occasions, it is nonproductive.[1]

While it is important to determine the nature of cough, as it can help the clinician in the differential diagnosis, the character of cough as a standalone feature lacks precise diagnostic value.

Classification based on features

Certain characteristics of cough can also help clinicians determine the underlying disease that may be causing the cough. These include whooping cough, staccato cough, honking cough, and barking cough.[3]

- **Whooping cough—**It presents as a spasmodic cough or paroxysms of cough ending in a gasp for air, thus producing the characteristic inspiratory whoop.[3,10] Pertussis is usually the condition associated with such cough.[3]
- **Staccato cough—**There is a series of explosive coughs with one inspiration between two successive bursts of cough. Staccato cough is characteristic of *Chlamydia* infection in infants.[3]
- **Barking cough—**Cough sounding like the barking of a seal is termed barking cough and is usually associated with stridor.[3] Barking cough and stridor occur as a result of the narrowing of subglottic trachea as a result of inflammation.[11] Such a cough is observed in croup and tracheomalacia.[3]
- **Honking cough—**Honking cough is observed in patients with psychogenic cough.[3]

Refractory cough

While discussing the classification of cough, one must not forget refractory cough. This is a type of cough that continues despite undergoing treatment based on guidelines.[2,12] Refractory cough is also known by the term unexplained chronic cough.[1] Chronic refractory cough can follow a viral infection.[13]

Cough hypersensitivity syndrome (CHS) has been implicated in refractory chronic cough. It has been suggested that CHS could be accountable for refractory cough in a patient following a disease condition that may have caused only mild cough in other patients.[14] CHS is probably the factor in patients having refractory cough experiencing worsening of symptoms on exposure to cold air, perfume, etc.[1]

Refractory chronic cough is characterized by a dry irritated cough. Patients may also complain of dyspnea, globus, and dysphonia,[13] and females are more commonly affected.[12] It is a diagnosis of exclusion. It can be diagnosed once the major causes of chronic cough have been investigated and ruled out.[12,15]

Etiology and features of cough based on the site of origin

The symptoms and characteristics of cough can differ based on the site of origin of cough. Knowing the anatomical site that is affected can help with timely diagnosis and appropriate management of the patient. For instance, when the cough originates from the pharynx, it could be attributed to postnasal drip and the cough is often persistent. When originating from the larynx, the cough is barking and painful and stridor usually accompanies this cough.[2] Summarized here are the etiologies and features of cough based on the origin site (Figure 2).[2,3]

Figure 2. Site of origin and the etiology and features of cough

Pharynx	**Etiology:** Postnasal drip **Features:** Persistent, dry cough
Larynx	**Etiology:** Laryngitis, whooping cough (pertussis), croup, tumor **Features:** Barking cough, painful and persistent, accompanied by stridor, paroxysmal cough in pertussis and parapertussis
Trachea	**Etiology:** Tracheitis, tracheomalacia **Features:** Painful cough, dry spasmodic cough, barking cough
Bronchi	**Etiology and features:** *Chronic bronchitis, COPD:* Productive/ non-productive cough, worse in morning *Asthma:* Usually dry cough, worse at night, usually accompanied by wheeze *Asthma-COPD overlap:* Productive cough *Bronchiectasis:* Productive cough, with blood *Bronchiolitis:* Persistent, dry cough *Bronchial cancer:* Persistent cough, usually with blood
Lung parenchyma	**Etiology and features** *TB:* Dry cough at first, productive afterwards ± blood *Pneumonia:* Dry cough at first, followed by productive cough *Pulmonary edema:* Productive cough (possibly), usually at night *Interstitial fibrosis:* Dry and irritant cough

KEY MESSAGES

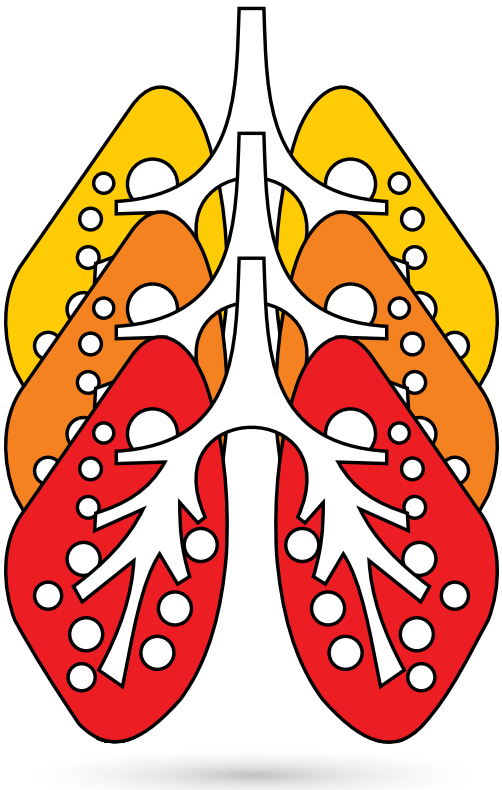
- It is important to classify cough early during the course of illness to determine the etiology and devise a targeted treatment plan for the patient.
- Cough is classified based on its duration into acute (≤3 weeks), subacute (3-8 weeks), and chronic (>8 weeks).
- The classification of cough, based on duration, in children differs in various guidelines with cough for <3-4 weeks referred to as acute and that lasting for >4 weeks termed as chronic in most guidelines.
- Based on its nature, cough is classified as dry/nonproductive cough, wet/productive cough, and mixed cough.
- On the basis of specific characteristics, cough can be categorized as whooping cough, staccato cough, honking cough, and barking cough. These cough characteristics can indicate the disease that could possibly be causing the cough.
- Cough that persists despite treatment based on guidelines is termed as refractory cough.
- It is possible that CHS is responsible for chronic refractory cough in some patients.
- Cough characteristics and symptoms can differ based on its site of origin. Knowing the anatomical site affected can help with diagnosis and appropriate management.

References

1. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al*. INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
2. Shankar PS, Korukonda K, Bendre S, Behera D, Mirchandani L, Awad NT, *et al*. Diagnoses and management of adult cough: An Indian Environmental Medical Association (EMA) position paper. *Respir Med.* 2020 Jul;168:105949.
3. Ijaz A, Nabeel M, Masood U, Mahmood T, Hashmi MS, Posokhova I, *et al*. Towards using cough for respiratory disease diagnosis by leveraging Artificial Intelligence: A survey. *Inform Med Unlocked.* 2022 Jan 1;29:100832.
4. Alsubaie H, Al-Shamrani A, Alharbi AS, Alhaider S. Clinical practice guidelines: Approach to cough in children: The official statement endorsed by the Saudi Pediatric Pulmonology Association (SPPA). *Int J Pediatr Adolesc Med.* 2015 Mar;2(1):38-43.
5. Shields MD, Bush A, Everard ML, McKenzie S, Primhak R; British Thoracic Society Cough Guideline Group. BTS guidelines: Recommendations for the assessment and management of cough in children. *Thorax.* 2008 Apr;63 Suppl 3:iii1-iii15.
6. Gibson PG, Chang AB, Glasgow NJ, Holmes PW, Katelaris P, Kemp AS, *et al*; CICADA. CICADA: Cough in Children and Adults: Diagnosis and Assessment. Australian cough guidelines summary statement. *Med J Aust.* 2010 Mar 1;192(5):265-71.
7. Chang AB, Oppenheimer JJ, Irwin RS; CHEST Expert Cough Panel. Managing Chronic Cough as a Symptom in Children and Management Algorithms: CHEST Guideline and Expert Panel Report. *Chest.* 2020 Jul;158(1):303-29.
8. Kardos P, Dinh QT, Fuchs KH, Gillissen A, Klimek L, Koehler M, *et al*. German Respiratory Society guidelines for diagnosis and treatment of adults suffering from acute, subacute, and chronic cough. *Respir Med.* 2020 Aug-Sep;170:105939.
9. Martin MJ, Harrison TW. Causes of chronic productive cough: An approach to management. *Respir Med.* 2015 Sep;109(9):1105-13.
10. Decker MD, Edwards KM. Pertussis (Whooping Cough). *J Infect Dis.* 2021 Sep 30;224(12 Suppl 2):S310-S320.
11. Patel JJ, Kitchin E, Pfeifer K. A Narrowing Diagnosis: A Rare Cause of Adult Croup and Literature Review. *Case Rep Crit Care.* 2017;2017:9870762.
12. Perotin JM, Launois C, Dewolf M, Dumazet A, Dury S, Lebargy F, *et al*. Managing patients with chronic cough: challenges and solutions. *Ther Clin Risk Manag.* 2018 Jun 6;14:1041-51.
13. Gibson PG, Vertigan AE. Management of chronic refractory cough. *BMJ.* 2015 Dec 14;351:h5590.
14. Morice AH, Millqvist E, Belvisi MG, Bieksiene K, Birring SS, Chung KF, *et al*. Expert opinion on the cough hypersensitivity syndrome in respiratory medicine. *Eur Respir J.* 2014;44(5):1132-48.
15. Kim SK. Chronic Refractory Cough. *Korean J Med.* 2016;91(1):18-27.

CHAPTER 5

Approach to Diagnosis of Cough



Diagnosis of cough can be challenging for a clinician, given the multitude of etiologies associated with this one symptom. Furthermore, when a cough begins, it is acute in all patients and there is no way to determine if it will resolve quickly or continue long enough to be categorized as subacute or chronic. But knowing the phase of cough in a patient when he/she presents can help us narrow down the possible causes behind it.

Additionally, the nature of cough and the cough sounds also give us crucial information about the likely cause. So, in other words, history is vital when approaching a patient with cough.

Following a standard approach can certainly help clinicians arrive at a diagnosis without any delays, thus paving the way for timely and appropriate management. Let us understand the diagnostic approach when dealing with acute, subacute, and chronic cough.

The first step in diagnosing the etiology of cough usually is to categorize it into acute, subacute, or chronic cough. The reason is that the medical conditions in each category are different, although some overlap can exist.

Diagnostic approach

The diagnostic approach toward cough involves a thorough history taking and physical examination to determine the differential diagnosis, followed by appropriate investigations – laboratory tests, and imaging – to reach a diagnosis.[1,2]

Diagnostic approach toward cough

Thorough history taking

Physical examination

Appropriate investigations – Laboratory as well as radiology

History taking

The inclusions of a good history taking encompass the following:[2,3]

- Duration of cough
- Cough features
- Any triggering factors
- Impact of changing position
- Any associated symptoms
- Timing of cough
- Details of sputum production—Volume, characteristics, if it is purulent, or has blood in it (hemoptysis), etc.
- Smoking, occupational, and environmental exposure
- Medication use, especially angiotensin-converting enzyme (ACE) inhibitors
- Personal and/or family history of allergic diseases
- Asthma, COPD
- History of acid reflux, heartburn, etc.

- Breathing difficulty
- History of respiratory infections, sinusitis, chronic bronchitis
- Rhinitis
- Presence of hoarse voice
- Associated pain
- Any comorbid conditions
- Family history of respiratory diseases.

A thorough history is of critical importance. It can provide valuable information to the clinician to identify or rule out the likely diagnoses. For instance, a cough that occurs mostly during the night indicates cough-variant asthma (CVA). However, when the cough is present only during the day and absent during sleep, especially in the case of a child, it suggests a psychogenic cough. The characteristics of sputum can also help narrow down the differential diagnoses. When there is sputum with blood, it can indicate TB, lung cancer, or bronchiectasis. When there are symptoms like heartburn and acid reflux, GERD-related cough is thought of.[2]

Differentiating between dry and wet cough can also help with the diagnosis. For instance, noninfectious causes can result in a dry cough while infections are usually associated with a productive cough.[2] Viral URTI, UACS, GERD, asthma, allergies, drugs, heart failure, and pollutant exposure have been linked to dry cough.[4,5] Flu, pneumonia, chronic bronchitis, TB, lung abscess, bronchiectasis, cystic fibrosis, COPD, and immunodeficiency can be associated with wet cough.[5,6]

Additionally, yellowish or greenish expectoration suggests that a bacterial infection is the likely cause.[7]

Cough sounds can also help with the differential diagnosis. For example, whooping cough points to pertussis, barking cough is suggestive of croup and tracheomalacia, and a honking cough indicates psychogenic cough.[5]

Warning signs

The presence of red flags or warning signs in the history calls for further investigations.[7] Box 1 summarizes the key red flags in the history of a patient with cough.[1,3,7,8]

Box 1. Red flags

- Dyspnea at rest
- Tachypnea
- Blood in sputum
- Pain in the thoracic region
- Raised body temperature (equal to or more than 38.5°C)
- Weight loss
- Tachycardia
- Arterial hypotension
- Hoarse voice
- Difficulty in swallowing
- Vomiting
- Peripheral edema along with gain in weight
- Cyanosis
- Suspicion of TB or pneumonia; history of TB
- Repeated episodes of pneumonia
- Signs of cardiac failure
- Smoking (over 35 pack-years); smoker's cough in people aged above 35
- Immunosuppression
- Cough syncope
- History of cancer
- Inhalational intoxication
- Abnormal findings on examination of respiratory system; abnormal findings on chest X-ray that complement cough duration

According to an Indian consensus, personal history of TB or positive TB history in a close contact is a red flag sign. Another red flag, according to the consensus, is smoker's cough, particularly among those aged over 35 years.[1] Among children, a cough that begins in the neonatal period, cough during feeding, vomiting, and abnormal voice/crying are some of the red flags.[1] The 2018 CHEST guideline states that a new-onset cough, change in cough, or an accompanying disturbance in voice in a person who smokes and is aged above 45 years and people 55-80 years of age, having a 30 pack-year smoking history and are current smokers or those who quit smoking within the past 15 years, are among the red flags.[8] A recent Indian consensus also included urinary stress incontinence in the alarm signs.[4]

Physical examination

Physical examination can also provide critical information in a patient with cough, which can help narrow down the differential diagnoses. It involves the examination of the nose, throat, and lungs, listening to lung sounds, and examination of the cardiovascular system.[2]

It also includes the examination of skin for pallor, cyanosis, sweating, etc. Based on the history and presentation, abdominal examination may also be needed. A patient's body type also needs to be evaluated as GERD-induced cough and cough associated with obstructive sleep apnea could be possible in obese individuals. The legs are also examined for signs of edema or thrombosis.[2,3]

Particular emphasis should be given to examination of the nose for inferior turbinate hypertrophy and polyp formation, postnasal drip at the back of the throat, and wheeze and rhonchi in the chest.

Investigations

In patients with acute cough with no red flags, further investigations are not routinely required. However, they may be needed in those with red flags and in patients with subacute and chronic cough.

The investigations include:[2,4]

- Complete blood count
- Chest X-ray
- Chest computed tomography (CT)
- Spirometry with bronchodilator reversibility
- Sputum analysis
- Bronchial provocation test
- Fractional exhaled nitric oxide (FeNO)
- 24-h esophageal pH-multi-channel impedance monitoring
- Bronchoscopy.

A chest X-ray is recommended as a routine investigation in patients with chronic cough and when an abnormal finding is detected on X-ray, further investigations are done. Interstitial pulmonary diseases and atypical bronchiectasis can be diagnosed early with the use of a high-resolution CT (HRCT) scan. A sinus CT can help when there is a suspicion of sinusitis.[2] The Indian consensus group suggests that HRCT be conducted when chronic cough does not respond to treatment and the common etiologies have been ruled out. This is applicable when there are bibasilar Velcro-like crackles or when there is a suspicion of the patient having bronchiectasis despite the findings on a chest X-ray being normal. The group emphasizes the use of HRCT when there is hemoptysis and when emphysema, interstitial collagen disease, or rheumatic disease are suspected.[4] The Chinese Thoracic Society (CTS) Asthma Consortium supports the use of pulmonary function tests to determine the underlying cause of chronic cough. A positive cough provocation test can be helpful in diagnosing CVA.[2]

Induced sputum analysis can also help identify the underlying cause of chronic cough. It also helps in the diagnosis of inflammation in the airways. The presence of eosinophilia points to eosinophilic bronchitis, CVA,[2] or asthma. Inadequate asthma control or having severe disease have been linked to higher levels of sputum eosinophils in patients.[9] FeNO also helps diagnose airway inflammation. Allergic or atopic conditions can be diagnosed with the help of skin prick and serum immunoglobulin (Ig)E tests. GERD can be diagnosed using the 24-h esophageal

pH-multi-channel impedance monitoring.[2] The Indian group of experts arrived at a near consensus for not recommending 24-h pH monitoring in all patients having chronic cough that appears to be due to GERD.[4]

Bronchoscopy is done when the cough does not respond to treatment or when the conventional investigations fail to ascertain the diagnosis,[2] and there is reasonable suspicion of a serious underlying disease. It can be useful in situations when we need to rule out a foreign body aspiration, lung cancer, or TB.[2]

A nasal endoscopy can help diagnose rhinosinusitis while a pharyngo-laryngoscopy can help identify pharyngitis and laryngitis.[7] Box 2 lists the recommendations from the Indian consensus group on the investigations in patients with cough.[4]

Box 2. Indian consensus group recommendations on investigations in patients having cough

- Sinus imaging recommended for patients having cough and features of chronic sinusitis or nasal hypertrophy
- Spirometry, bronchoprovocation challenge, allergy assessment, and FeNO recommended when there is suspicion of having asthma, CVA, or NAEB
- Cardiac tests, including, electrocardiography, echocardiography, and Holter when cough of cardiac origin is likely
- When there is a suspicion of infection or interstitial lung disease, bronchoscopy with bronchoalveolar lavage, is recommended, when there is no sputum
- Laryngoscopy for chronic cough patients with suspicion of an upper airway cause
- Gene Xpert Ultra test when *Mycobacterium tuberculosis* is suspected–Pulmonary TB must be excluded in all patients with subacute or chronic cough
- Sputum microscopic and culture examination when there is a suspicion of bacterial infection in a patient with chronic productive cough

- HRCT in cases of chronic cough not responding to therapy when the common causes have already been ruled out, and there are bibasilar Velcro-like crackles or there is a likelihood of bronchiectasis, and the chest X-ray is normal
- HRCT to be done when hemoptysis, emphysema, rheumatic disease, or interstitial collagen disease is suspected

Cough assessment tools

Assessment of the impact of cough is also an integral part of the overall approach toward cough. Therefore, the assessment of a patient with cough also involves evaluating the impact of cough using various scores and questionnaires. These tools can help us determine the impact of cough on the patient's QoL.

The CHEST guideline published in 2015 recommends the use of validated health-related QoL questionnaires, including the Leicester Cough Questionnaire (LCQ), the Cough-Specific Quality of Life Questionnaire (CQLQ), and the Parent Cough-Specific Quality of Life Questionnaire, to determine the impact of cough in patients with chronic cough. The use of acoustic cough counting has also been recommended to assess cough frequency.[10] However, the Indian consensus does not support routine assessment of QoL in chronic cough patients. It recommends such assessment in case of chronic idiopathic cough.[4]

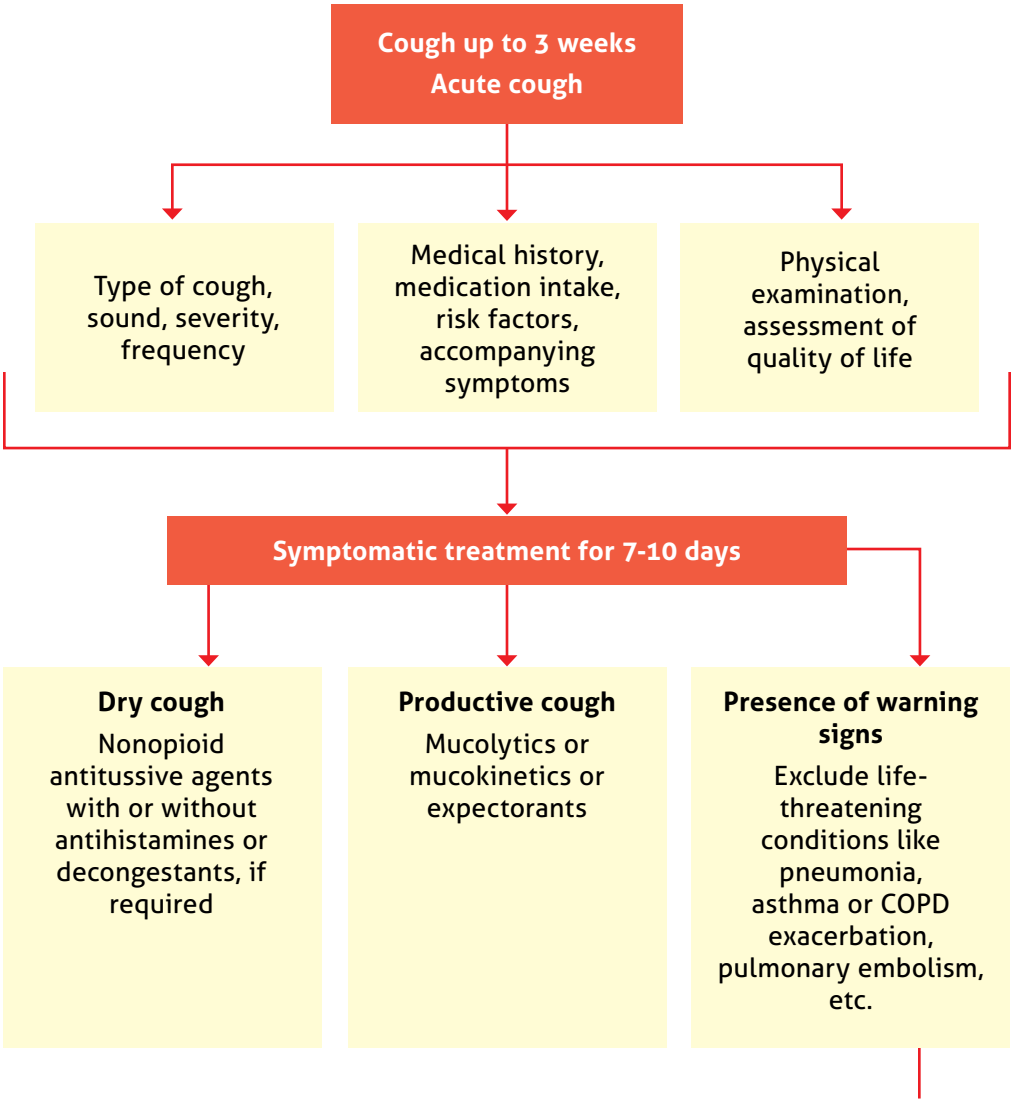
The tools that can help with the assessment of disease status and effectiveness of treatment include:[2]

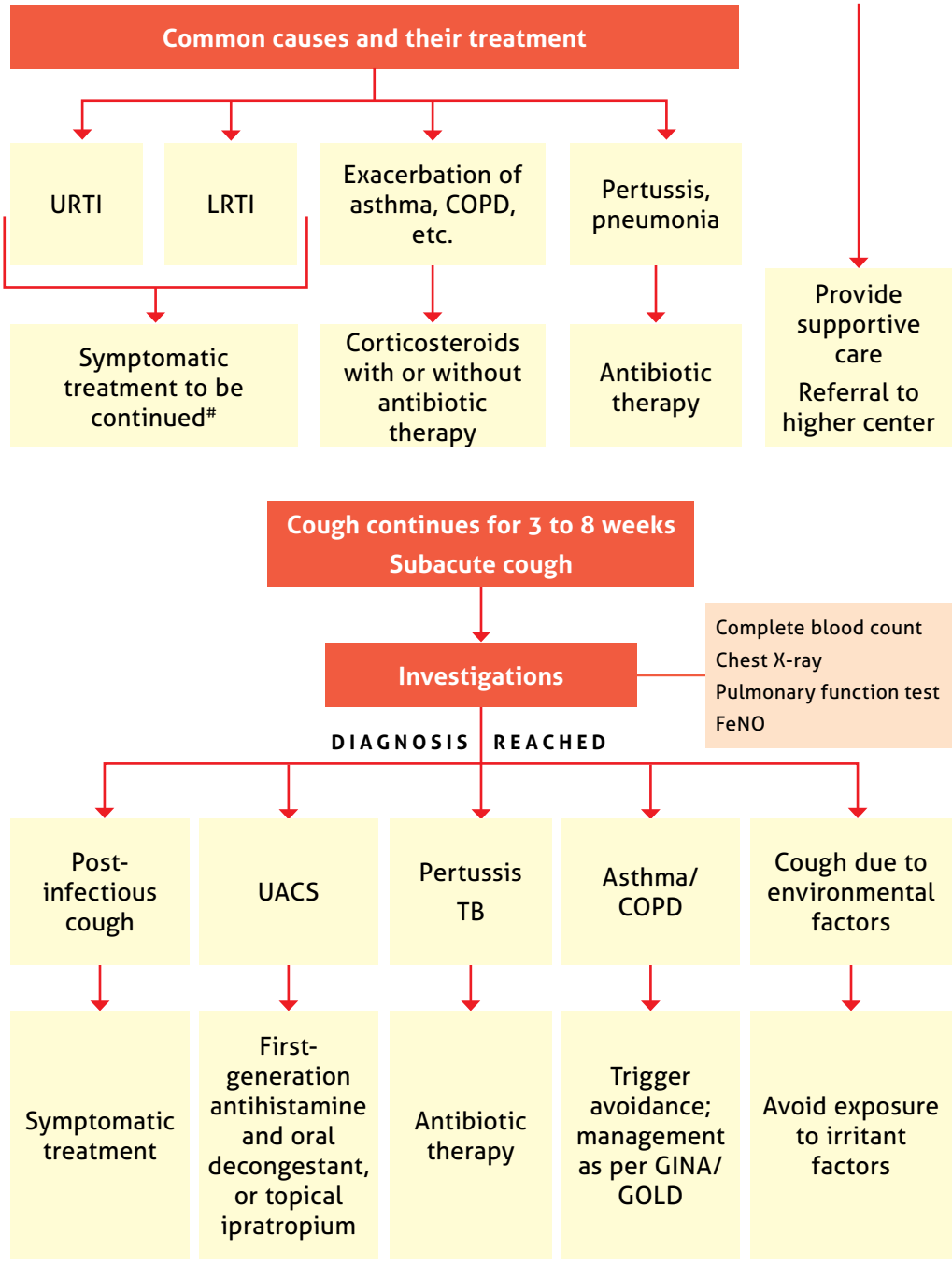
- Visual analogue scale (VAS)
- Cough symptoms score
- Questionnaires to assess QoL
- Monitoring of cough frequency
- Cough provocation test.

These cough scores are scientific and are available. It is my personal view that they are time-consuming and do not add much to the practical management of cough, except to show or document improvement. They can be useful research tools though.

Algorithms for approach to diagnosis and management of cough – The Indian consensus[4]

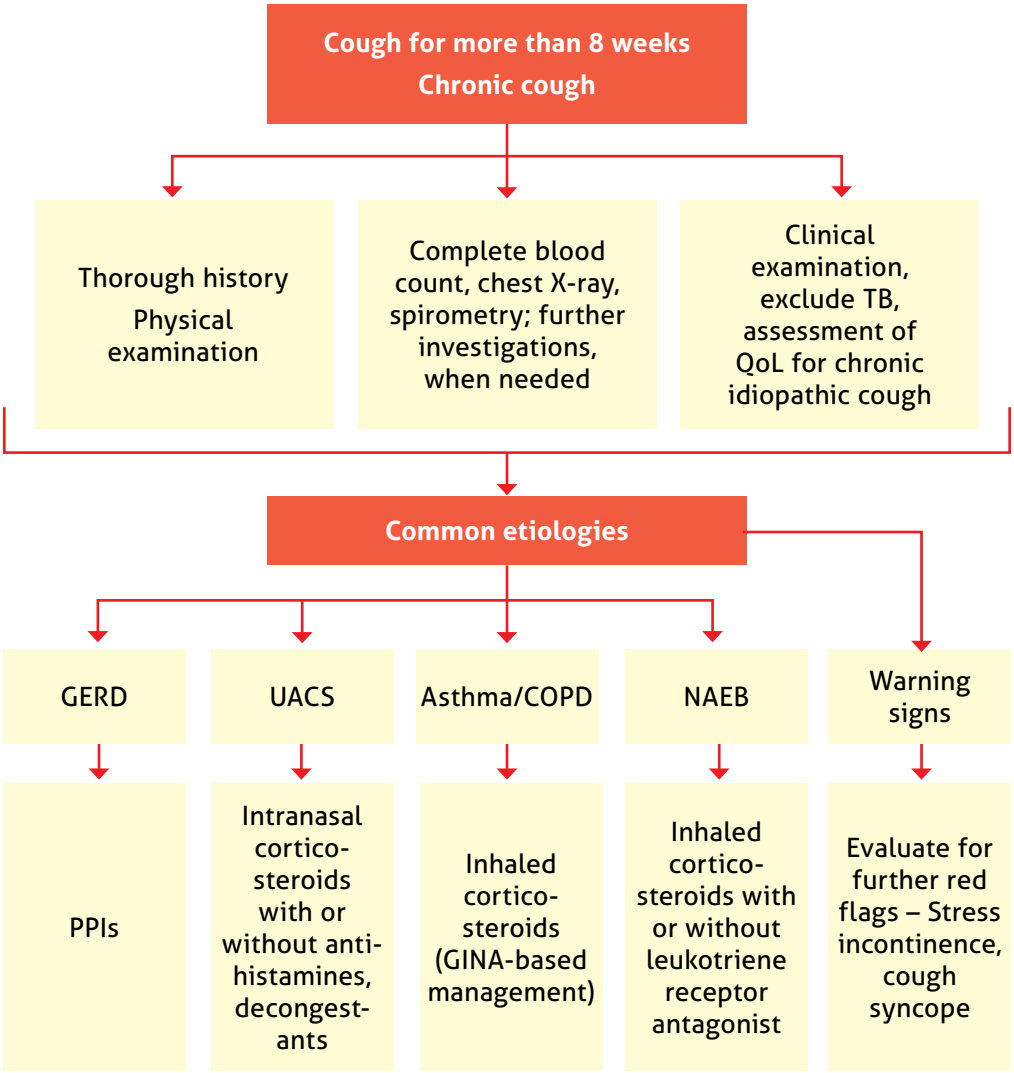
Diagnosis and management of acute and subacute cough





#Antibiotics to be avoided; can be given when there are systemic symptoms
LRTI: Lower respiratory tract infection; GINA Global initiative for asthma; GOLD: Global initiative for chronic obstructive lung disease

Diagnosis and management of chronic cough



PPI: Proton pump inhibitor. Further investigations are listed in Box 2.

In some cases, chronic cough may be refractory or unexplained and needs to be managed accordingly with speech or voice therapy, physical therapy, QoL assessment, re-evaluation of risk factors, counseling, and appropriate medication under the guidance of a specialist.

KEY MESSAGES

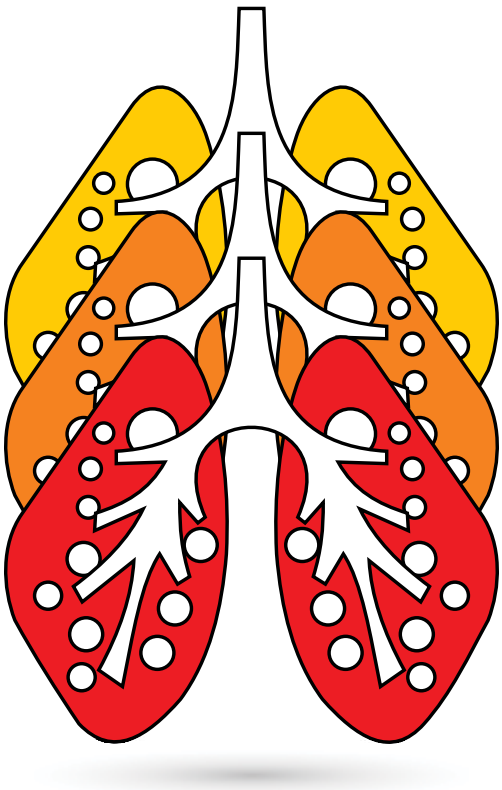
- The diagnostic approach toward cough involves a thorough history taking and physical examination to determine the differential diagnosis, followed by appropriate investigations – laboratory tests, and imaging – to reach a diagnosis.
- Unless there are any alarm signs or red flags, laboratory investigations and imaging studies are not required in a patient with acute cough.
- A thorough history can provide valuable information to the clinician to rule in and rule out the likely diagnoses.
- Differentiating between dry and wet cough can help with the diagnosis. Noninfectious causes can result in a dry cough while infections are usually associated with a productive cough.
- Presence of warning signs or red flags in the history calls for further investigations.
- Physical examination can also provide critical information in a patient with cough which can help narrow down the differential diagnoses.
- A chest X-ray is recommended as a routine investigation in patients with chronic cough; when an abnormal finding is detected on X-ray, further investigations are done.
- Investigations that help in a patient with cough include chest X-ray, CT, spirometry with bronchodilator reversibility, sputum analysis, bronchial provocation test, FeNO, 24-h esophageal pH-multi-channel impedance monitoring, and bronchoscopy.
- The assessment of a patient with cough also involves evaluating the impact of cough using various scores and questionnaires. These tools can help determine the impact of cough on the patient's QoL and treatment effectiveness.

References

1. Guleria R, Dhar R, Mahashur A, Ghoshal AG, Jindal SK, Talwar D, *et al*. Indian Consensus on Diagnosis of Cough at Primary Care Setting. *J Assoc Physicians India.* 2019 Jan;67(1):92-8.
2. Lai K, Shen H, Zhou X, Qiu Z, Cai S, Huang K, *et al*. Clinical Practice Guidelines for Diagnosis and Management of Cough—Chinese Thoracic Society (CTS) Asthma Consortium. *J Thorac Dis*. 2018 Nov;10(11):6314-51.
3. Holzinger F, Beck S, Dini L, Stöter C, Heintze C. The diagnosis and treatment of acute cough in adults. *Dtsch Arztebl Int.* 2014 May 16;111(20):356-63.
4. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al*. INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India*. 2023 Jun;71(6):62-77.
5. Ijaz A, Nabeel M, Masood U, Mahmood T, Hashmi MS, Posokhova I, *et al*. Towards using cough for respiratory disease diagnosis by leveraging Artificial Intelligence: A survey. *Inform Med Unlocked.* 2022 Jan 1;29:100832.
6. Martin MJ, Harrison TW. Causes of chronic productive cough: An approach to management. *Respir Med*. 2015 Sep; 109(9):1105-13.
7. Kardos P, Dinh QT, Fuchs KH, Gillissen A, Klimek L, Koehler M, *et al*. German Respiratory Society guidelines for diagnosis and treatment of adults suffering from acute, subacute, and chronic cough. *Respir Med.* 2020 Aug-Sep;170:105939.
8. Irwin RS, French CL, Chang AB, Altman KW; CHEST Expert Cough Panel*. Classification of Cough as a Symptom in Adults and Management Algorithms: CHEST Guideline and Expert Panel Report. *Chest.* 2018 Jan;153(1):196-209.
9. Demarche SF, Schleich FN, Paulus VA, Henket MA, Van Hees TJ, Louis RE. Asthma Control and Sputum Eosinophils: A Longitudinal Study in Daily Practice. *J Allergy Clin Immunol Pract.* 2017 Sep-Oct;5(5):1335-43.e5.
10. Boulet LP, Coeytaux RR, McCrory DC, French CT, Chang AB, Birring SS, *et al*; CHEST Expert Cough Panel. Tools for assessing outcomes in studies of chronic cough: CHEST guideline and expert panel report. *Chest.* 2015 Mar;147(3):804-14.

CHAPTER 6

Common Causes of Cough



A wide array of disease conditions can present with cough as a manifestation. In order to reach the correct diagnosis and provide appropriate treatment to the patient, it is important for clinicians to be aware of the causes of cough and their typical presentation.

After we classify a cough based on its duration at the time of presentation into acute, subacute, or chronic, and based on phlegm production into dry or productive, we are in a better position to determine what could be causing the cough in the patient. To be able to determine the exact cause, we need to be cognizant of the common causes known to be associated with different types of cough. So, let's look at the common causes of cough in adults and children.

Causes of acute cough

The most common cause of acute cough is an acute infection of the upper or lower respiratory tract.[1] A viral URTI is most often the cause of acute cough, probably 90% of the time.[2] Infections like influenza, sinusitis, bronchitis, and pneumonia can result in acute cough. There can be noninfectious causes as well, such as asthma, and congestive heart failure.[3] Bronchiolitis could also be a cause.[2] Exposure to allergens, environmental irritants like pollutants, smoke, etc., and to cold, dry wind can also cause acute cough.[2] One must also consider exacerbations of asthma, COPD, bronchiectasis, and UACS when dealing with acute cough.[2,4]

Some of the uncommon causes of acute cough include severe pneumonia and pulmonary embolism.[2] Infections with *Bordetella pertussis*, *Mycoplasma*, and *Chlamydia*, and irritant and allergic rhinitis can also cause acute cough.[5] COVID-19 is also associated with acute cough.[4]

In children, acute cough could occur as a result of foreign body aspiration. Pneumonia could also be a cause in children.[3] Box 1 summarizes the causes of acute cough.

Box 1. Causes of acute cough

- Upper and lower respiratory tract infections
  Influenza, sinusitis, bronchitis, pneumonia
- Allergic rhinitis
- Inhalation of irritants
- Asthma
- Bronchiolitis
- Exposure to allergens, cold and dry wind
- Exacerbation of asthma, COPD
- UACS
- Congestive heart failure
- Pulmonary embolism
- Foreign body aspiration
- COVID-19

Causes of subacute cough

When dealing with a patient who has had cough for 3 to 8 weeks, one must think of an infectious cause, or possibly a postinfectious cough.

A postinfectious cough, postnasal drip, bacterial sinusitis, and asthma can be the causes in a patient presenting with subacute cough that had its onset with a URI.[3] A subacute cough can also occur due to pertussis infection and following viral rhinosinusitis.[2] Drugs like ACE inhibitors could also cause subacute cough.[1] Exacerbations of pre-existing conditions like asthma and COPD, and *Mycoplasma* pneumonia can also be considered in subacute cough.[4] Adenovirus pneumonia can also cause subacute cough. Pleuritis can also be associated with a cough that lasts long.[6]

Box 2 lists the causes of subacute cough.

Box 2. Causes of subacute cough

- Postinfectious cough
- Bacterial sinusitis
- Postnasal drip
- Asthma
- *B. pertussis* infection
- Viral rhinosinusitis
- Drug-induced (ACE inhibitors)
- Exacerbation of asthma, COPD
- *Mycoplasma* pneumonia; adenovirus pneumonia
- Pleuritis

Causes of chronic cough

There can be several different causes for a cough that lasts longer than 8 weeks. There can be respiratory and nonrespiratory causes behind chronic cough.

UACS, GERD, and CVA have been reported to be the commonest etiologies in chronic cough cases.[4] It can also occur due to medication use, foreign body aspiration, chronic bronchitis, bronchiectasis, tracheobronchomalacia, smoker's cough, idiopathic pulmonary fibrosis, psychogenic cough, and obstructive sleep apnea.[1,4] Some serious conditions, like lung cancer, can also lead to chronic cough.[1]

Chronic cough is also caused by pulmonary TB, URTIs, cough due to congestive cardiac failure, NAEB, postinfectious cough, cystic fibrosis, and COPD.[2-4] Exposure to environmental irritants and indoor air pollution can also lead to chronic cough.[3]

Then, there are rarer causes of chronic cough. Endocarditis, retrotracheal mass, arteriovenous malformations, and premature ventricular contractions may also be associated with chronic cough.[1,6]

The causes of chronic cough are listed in Box 3.

Box 3. Causes of chronic cough

- UACS
- GERD
- CVA
- Pulmonary TB
- URTI
- NAEB
- Chronic bronchitis
- COPD
- Obstructive sleep apnea
- Foreign body aspiration
- Postinfectious
- Drug-induced
- Bronchiectasis
- Tracheobronchomalacia
- Smoker's cough
- Idiopathic pulmonary fibrosis
- Cystic fibrosis
- Cardiac origin
- Psychogenic cough
- Environmental irritants, indoor air pollution
- Lung carcinoma

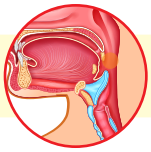
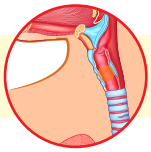
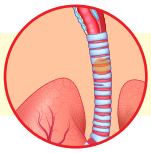
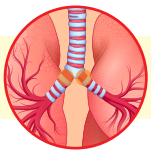
Some medications known to be associated with cough include:[2,3,6]

- ACE inhibitors
- β-blockers
- Leflunomide
- Amiodarone
- Inhaled corticosteroids (ICS)
- Methotrexate
- Busulfan
- Bleomycin
- Mitomycin C
- Inhaled drugs, such as ipratropium, tiotropium, β_2-adrenergic drugs
- Interferon alpha-2b and alpha-2a.

Cough etiology based on the site of origin

We can also describe the etiology of cough based on the affected site of the respiratory tract. Box 4 summarizes the various causes of cough based on the anatomical site affected.[4,7]

Box 4. Etiology of cough based on site affected

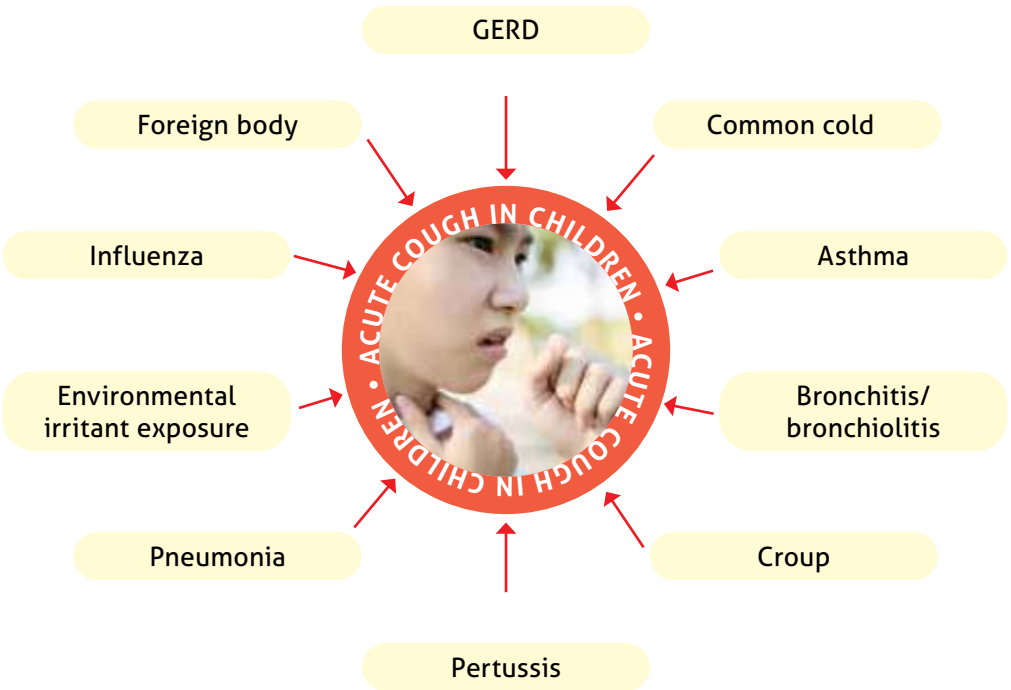
Site	Etiology
 Pharynx	Postnasal drip
 Larynx	Laryngitis, cancer, pertussis, parapertussis, croup
 Trachea	Tracheitis, tracheomalacia
 Bronchus	Chronic bronchitis, COPD, asthma, asthma-COPD overlap, bronchiectasis, bronchiolitis, bronchial cancer, allergic bronchopulmonary aspergillosis
Lung parenchyma	TB, pneumonia, interstitial fibrosis, pulmonary edema, atypical pneumonia

Causes of cough in the pediatric population

The causes of cough in children can be different from those in the adult population.

As mentioned earlier, foreign body aspiration and pneumonia can cause acute cough in children.[3] However, there can be several other causes. Some of these causes are mentioned in Figure 1.[8]

Figure 1. Causes of acute cough in children



A postinfectious or postviral cough is the commonest cause of prolonged acute cough in the pediatric population.[9]

Segregating children into two broad age categories – those aged below 5 years and those above 5 years of age – the various causes of chronic cough are summarized in Box 5.[10]

Box 5. Causes of chronic cough in children based on age

Children aged < 5

- Infections
- Asthma
- Gastroesophageal reflux (GER)
- Foreign body
- Protracted bacterial bronchitis
- Congenital anomaly
- Environmental pollutants
- Passive smoke exposure

Children aged > 5

- Infection
- Asthma
- Protracted bacterial bronchitis
- Postnasal drip
- Bronchiectasis
- Passive smoking
- Psychogenic cough

KEY MESSAGES

- It is important for clinicians to be aware of the causes of cough to be able to reach the correct diagnosis and provide appropriate treatment to the patient.
- We can divide the causes of cough based on its duration at the time of presentation.
- Acute cough is most frequently caused by a viral URTI. Acute cough can have both infectious as well as noninfectious etiology.
- It can be caused by influenza, sinusitis, bronchitis, pneumonia, asthma, congestive heart failure, bronchiolitis, exposure to allergens, irritants and cold, dry wind, UACS, bronchiectasis, and exacerbations of asthma or COPD. Irritant and allergic rhinitis and COVID-19 are also associated with acute cough.
- Subacute cough can be postinfectious. Postnasal drip, asthma, ACE inhibitor use, exacerbation of asthma and COPD, *Mycoplasma* or adenovirus pneumonia, and pleuritis can also be associated with subacute cough.
- UACS, GERD, and CVA seem to be the most frequent etiologies in patients with chronic cough. Other causes include URTI, TB, medication use, foreign body, chronic bronchitis, bronchiectasis, tracheobronchomalacia, smoker's cough, idiopathic pulmonary fibrosis, psychogenic cough, obstructive sleep apnea, congestive heart failure, NAEB, postinfectious cough, cystic fibrosis, COPD, and environmental factors, like pollutants. Lung cancer can also lead to chronic cough.
- In children, acute cough can be caused by common cold, foreign body aspiration, pneumonia, asthma, GERD, bronchitis, croup, pertussis, influenza, and environmental irritants.
- A postinfectious or postviral cough is the commonest cause of prolonged acute cough among children.

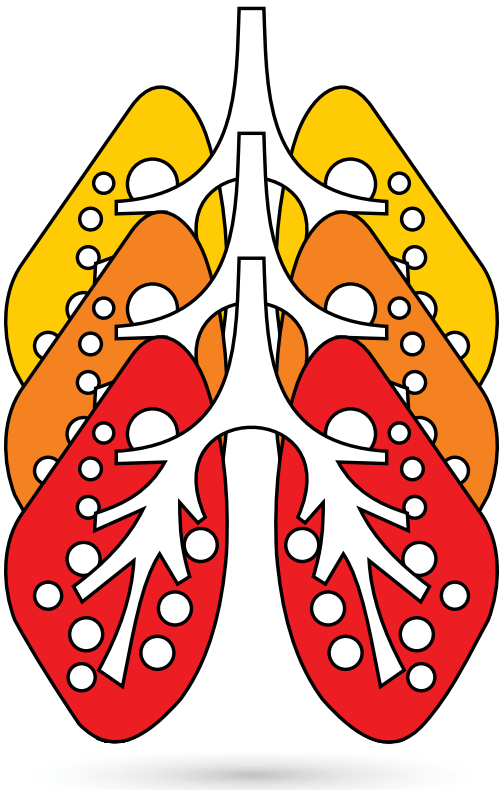
- In the pediatric population, chronic cough can develop as a result of infections, asthma, GERD, retained foreign body, protracted bacterial bronchitis, congenital defects, postnasal drip, bronchiectasis, passive smoking, environmental pollutants, and psychogenic cough.
- Causes of cough can also be described based on the anatomical site affected.
- Knowing the causes can help a clinician narrow down the differential diagnoses in a patient with cough.

References

1. Davis JA, Gudi K. Approach to the Patient with Cough. *Med Clin N Am.* 2021 Jan;105(1):31-8.
2. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
3. Guleria R, Dhar R, Mahashur A, Ghoshal AG, Jindal SK, Talwar D, *et al.* Indian Consensus on Diagnosis of Cough at Primary Care Setting. *J Assoc Physicians India.* 2019 Jan;67(1):92-8.
4. Ijaz A, Nabeel M, Masood U, Mahmood T, Hashmi MS, Posokhova I, *et al.* Towards using cough for respiratory disease diagnosis by leveraging Artificial Intelligence: A survey. *Inform Med Unlocked.* 2022 Jan 1;29:100832.
5. Boujaoude ZC, Pratter MR. Clinical approach to acute cough. *Lung.* 2010 Jan;188 Suppl 1(Suppl 1):S41-6.
6. Kardos P, Dinh QT, Fuchs KH, Gillissen A, Klimek L, Koehler M, *et al.* German Respiratory Society guidelines for diagnosis and treatment of adults suffering from acute, subacute, and chronic cough. *Respir Med.* 2020 Aug-Sep;170:105939.
7. Shankar PS, Korukonda K, Bendre S, Behera D, Mirchandani L, Awad NT, *et al.* Diagnoses and management of adult cough: An Indian Environmental Medical Association (EMA) position paper. *Respir Med.* 2020 Jul;168:105949.
8. Worrall G. Acute cough in children. *Can Fam Physician.* 2011 Mar;57(3):315-8.
9. Shields MD, Thavagnanam S. The difficult coughing child: prolonged acute cough in children. *Cough.* 2013 Apr 10;9(1):11.
10. Alsubaie H, Al-Shamrani A, Alharbi AS, Alhaider S. Clinical practice guidelines: Approach to cough in children: The official statement endorsed by the Saudi Pediatric Pulmonology Association (SPPA). *Int J Pediatr Adolesc Med.* 2015 Mar;2(1):38-43.

CHAPTER 7

Common Diseases that Present with Cough



It is quite well known that cough is not caused by a single factor but has a multifarious etiology. Cough, as a symptom, can be the presentation of various diseases, whether acute or chronic, whether self-limiting or life-threatening. Cough could be the major presenting symptom in a condition as common as viral URTI and also in a serious condition, such as pneumonia. It could be due to an acute condition, such as foreign body aspiration, and also due to a serious illness, like lung cancer.

In the previous chapter, we discussed the various causes of acute, subacute, and chronic cough in brief. In this chapter, we will discuss the common diseases that present with cough in detail. The diseases discussed in this chapter include the following:

Common diseases that present with cough

- Viral URTI
- Postinfectious cough
- Acute bronchitis
- Acute rhinosinusitis
- Exacerbation of existing lung disease
- Asthma
- CVA
- GERD
- UACS
- ACE inhibitor-induced cough
- CHS
- Psychogenic cough
- TB
- Heart diseases
- Smoker's cough
- Pollution-related cough
- Occupation-related cough

Besides these common conditions, there are some rare conditions that may also be associated with cough. Once we have evaluated all the common causes of cough in our patients, we must also consider the uncommon or rare causes, so that we do not miss out on a rare, but potentially serious underlying condition that may be contributing to the symptom of cough.

Let us have a look at all these conditions one by one.

1. Viral URTI

A URTI or common cold is among the most frequent causes of acute cough.[1,2] Around 200 different viruses have been linked to common cold.[3] These include rhinovirus, influenza and parainfluenza viruses, coronavirus, respiratory syncytial virus (RSV), enterovirus, adenovirus, and metapneumovirus.[1]

A paper published in 2021 estimated the prevalence of infections of the respiratory tract across various parts of India between 1970 and 2020. Researchers noted high prevalence rates for RSV, followed by influenza A virus. However, if all types of influenza were to be added together in this paper, it might become the most common cause of viral respiratory infections in the country. Other viruses included adenovirus, parainfluenza virus, rhinovirus, influenza B virus, and human metapneumovirus. Overall, the 3 most common respiratory virus infections across most Indian states were RSV, influenza, and parainfluenza.[4] Knowledge of the prevalence pattern of these viruses can help us devise appropriate plans to manage the infections promptly.

Did you know that adults can have around 2 to 5 episodes of URTIs in a year? This figure is way higher in the case of school children, at a staggering 7 to 10 episodes annually. They can experience cough for around 140 days out of the 365 days in a year.[5]

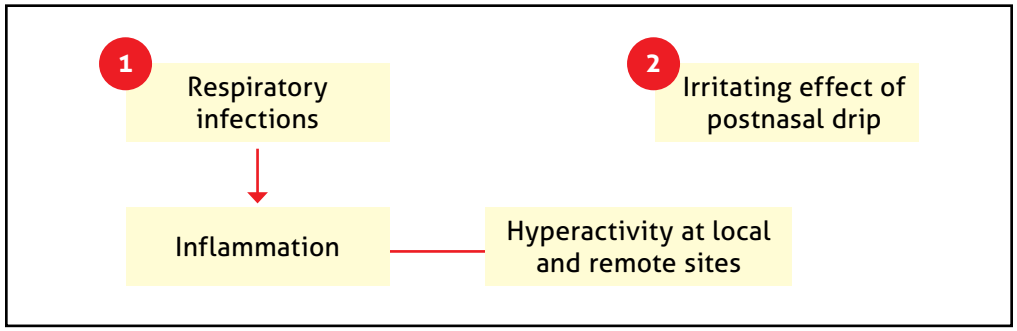
How is URTI-related cough regulated?

We have seen in a previous chapter that cough can be voluntary or involuntary. The feeling of an urge to cough occurs when something irritates the airways and ultimately leads to the actual act of coughing.

Besides the complex pathways involved in inciting cough where the signals are transmitted via the vagus nerve to the medulla, it is also known that stimulation of the pharynx can also incite cough. Hegland *et al* sought to assess whether stimulation of the oropharynx could evoke cough and noted that mechanical stimulation of the oropharynx led to an urge to cough and also evoked cough.[6] It thus appears that the pharyngeal sensory nerves might also contribute to the cough reflex in the presence of a URTI. It seems likely that in the case of

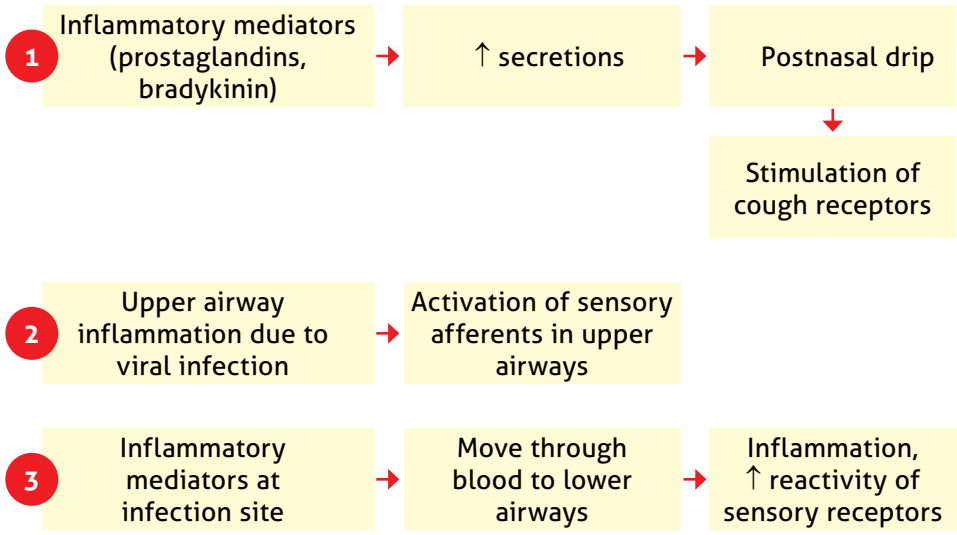
URTI-related cough, the voluntary pathway is at work.[5] Inflammation of the mucosa gives rise to an irritating stimulus in the upper airways. With the involvement of the cerebral cortex, a cough is voluntarily elicited.[5]

The potential mechanisms associated with the initiation and maintenance of cough in URTIs may include:[5]



The mechanisms proposed for viral infection-associated cough are shown in Box 1.[3,5]

Box 1. Proposed mechanisms for viral URTI-related cough



Presentation of URTI

The symptoms associated with a URTI or common cold are summarized in Box 2.[1-3,7]

Box 2. Symptoms of URTI

- Nasal congestion
- Discharge from nose
- Sore throat
- Muscle pain
- Chills
- Headache
- Raised body temperature
- Sneezing
- Cough
- Postnasal drip
- Throat clearing

Diagnosis

When the history and physical examination suggest common cold or a URTI and there are no red flags, no further investigations are required.[2] In the absence of warning signs and no signs of pneumonia, one must adopt a wait-and-watch approach for about 8 weeks.[1]

Acute respiratory viral infection presenting with cough often resolves on its own in 9 to 12 days' time.[1]

Management

A cold is usually a self-limiting condition and does not require any specific treatment. Symptomatic treatment can be given if necessary.

The first step in managing a URTI is preventing transmission. Cough hygiene is important, and the patient must be advised to wash hands frequently and cough into the elbow.[2]

Symptomatic treatment can be provided in the form of analgesics for pain. Antitussive agents may help with sleep but seem to have no major impact on the urge to cough.[2] Antipyretics can be given for fever. Antibiotics are not required in the treatment of common cold.[7] Decongestants can be helpful in cases of nasal

congestion in adult patients. Additionally, the use of decongestants and first-generation antihistamines in combination plays a role in improving sneezing, cough, and nasal discharge among adults and adolescents.[7] The CTS Asthma Consortium recommends the combined use of a first-generation antihistamine and an antitussive. It further states that a central or peripheral antitussive can be administered in case of severe cough but a central antitussive must not be used in isolation to manage cough due to common cold. Among adults and adolescents, an ipratropium bromide nasal spray may help with nasal discharge and sneezing, but its use can be associated with some side effects.[7]

2. Postinfectious cough

Subacute cough most commonly occurs due to postinfectious cough and the commonest triggering factor is a viral infection.[8] When cough follows an acute URTI or LRTI and continues for more than 2-3 weeks, it could be a postinfectious cough. Such a cough usually resolves on its own usually within 8 weeks.[1] Between 12% and 48% of adults experiencing a subacute cough have been reported to have postinfectious cough.[9]

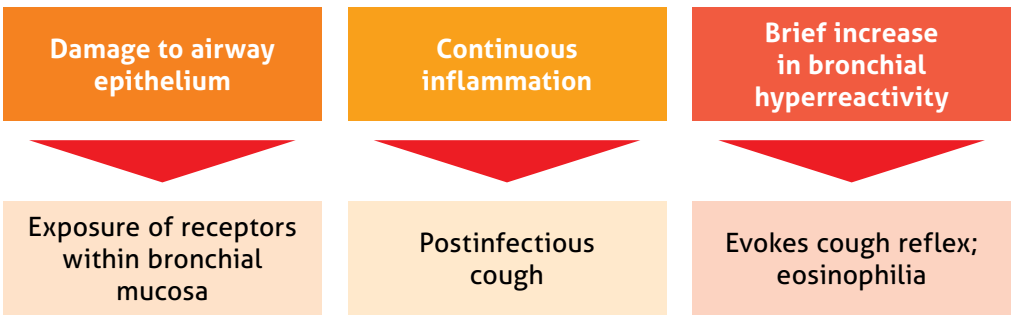
In my personal experience, postinfectious cough appears to be increasing in incidence, prevalence, severity, troublesomeness to the patient, as well as duration. This is primarily due to increasing pollution and rising incidence of allergy and atopy.

Postinfectious cough is quite common in patients who have had a viral infection. A study by Lin and colleagues among patients with H1N1 influenza infection noted that 8.5% of the patients had postinfectious cough. Interestingly, patients with postinfectious cough had increased cough sensitivity and a greater prior postinfectious cough prevalence.[10] A recent study by Chen *et al* evaluated the prevalence of postinfectious cough in patients with COVID-19 following discharge and noted postinfectious cough in 20.9% of the patients.[11]

The organisms noted to be associated with postinfectious cough include *B. pertussis* and *Mycoplasma pneumoniae*.[9] It is not clear as to how postinfectious cough occurs.

Inflammation, heightened secretions, damage to the airway epithelium, and airway hyperreactivity seem to contribute.[9] Figure 1 shows the likely mechanism behind postinfectious cough.[1]

Figure 1. Likely mechanism behind postinfectious cough



The causes of postinfectious cough can be three-fold:

Virus-related factors—Respiratory viruses cause denudation of the inner lining of airways and temporarily cause bronchial hyperresponsiveness. They expose cough receptors causing increased bronchial hyperreactivity and bronchial constriction. Additionally, there are increased secretions in the airways. Another virus-related factor is the postnasal drip caused by viruses.

Patient factors—A history of atopy or allergy plays a role in some patients. It has been seen in clinical practice that these patients have prolonged cough after viral respiratory infections. The patient may have GERD or may be a smoker. These patients usually have a more troublesome postinfectious cough.

Environmental factors—Most Indian cities are fighting increased air pollution these days. This is one factor that has the tendency to prolong postinfectious cough.

How does postinfectious cough present?

If a patient comes with a cough continuing for over 3 weeks that follows a URTI and the findings on a chest X-ray are normal, you are likely dealing with a postinfectious cough. Cough in the case of postinfectious cough is usually dry.[8]

So, I would describe the defining features of postinfectious cough as follows:

- ***It is caused by a viral respiratory infection.***
- ***The cough persists and lasts from 3 weeks to 8 weeks.***
- ***The cough resolves on its own.***
- ***X-ray chest is normal.***

A thorough history is, therefore, very important in establishing a diagnosis of postinfectious cough.

Diagnosis

As mentioned above, taking a detailed history of how the cough started can help determine the diagnosis. The patient gives a history of URTI or common cold followed by a cough that continues.[8] The patient may also provide a history of taking cough syrups or antibiotics and of cough persisting despite treatments.

X-ray chest is done in such cases, but it is usually normal. A spirometry can also be done.[8] A complete blood count may also be done.

While taking history, concentrate on where the cough is coming from. A runny nose, nasal congestion, throat irritation, and postnasal drip are characteristic symptoms of UACS. On the other hand, dry, irritating cough, wheezing, chest tightness, and cough while speaking point to lower airway involvement and are suggestive of bronchial hyperresponsiveness.

Treatment

While postinfectious cough is a self-limiting condition, one can consider the use of antihistamines, antitussive agents, and decongestants in certain patients.[7] According to the Indian Environmental Medical Association (EMA) guidelines, one can consider dextromethorphan in postinfectious cough.[8] The German Respiratory Society guidelines state that ICS therapy could work in patients having continuous inflammation. Additionally, in patients with bronchial hyperresponsiveness, β-2 sympathomimetics or ICS may help.[1]

As per my experience, treatment is guided by the part of the airways affected. In the case of UACS, older-generation antihistamines having anticholinergic action are effective. One can also consider nasal sprays, like azelastine, or ICS. If there are excessive secretions, one could use oxymetazoline.

When lower airways are affected, bronchodilators can be considered – anticholinergics or long-acting β_2-agonists (LABAs) may be considered. LABAs may also be useful when there is excessive secretion or when the constriction is more. These can be combined with ICS. ICS help with postinfectious bronchial hyperresponsiveness to some extent, but are not as effective as they are in allergy-related bronchial hyperresponsiveness.

Cough suppressants, like dextromethorphan, can also be used.

Postinfectious cough due to B. pertussis

Infection with *B. pertussis* in adults may not have a clear presentation. The patient can present with a dry cough.[2]

Paroxysmal cough, vomiting after cough, and inspiratory whoop suggest the diagnosis of pertussis if other causes have been ruled out.[12] The catarrhal stage of pertussis mimics a common cold and it is not until after week 1 or 2 that the paroxysmal cough begins.[2]

The diagnosis of pertussis is based on the detection of *B. pertussis* in a nasopharyngeal sample culture which has value only up to 2 weeks of infection. However, a polymerase chain reaction (PCR) can help detect the infection up to 4 weeks.[2] Additionally, it has higher sensitivity.[1,2] Serology helps with the diagnosis in the late phase.[2]

Treatment with macrolide antibiotics must be started early. Azithromycin or clarithromycin started in the catarrhal stage can speed up the recovery process.[2,7] Vaccination to prevent *B. pertussis* is also recommended.[2,12]

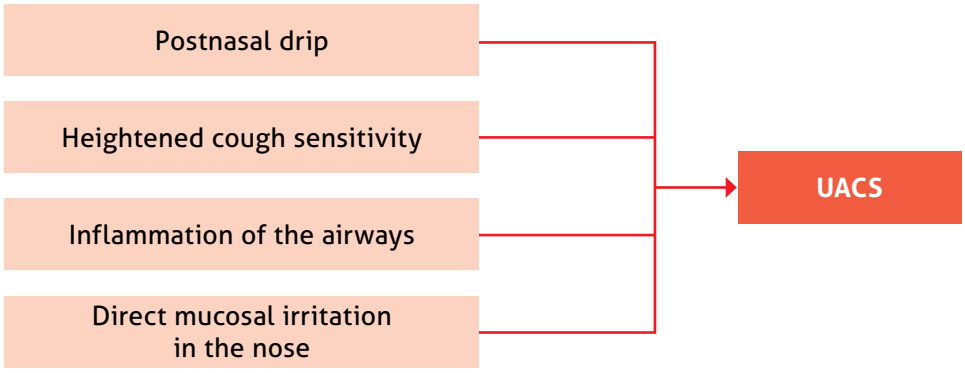
3. Upper airway cough syndrome

What was previously known as postnasal drip was later termed UACS in the American College of Chest Physicians (ACCP) 2006 guidelines on cough. The experts recommended that **UACS be the name used for cough that occurs in conditions affecting the upper airways**. The decision was taken as it is not clearly understood if the cough occurs as a result of postnasal drip, irritation, or inflammation of cough receptors in the upper airway.[13]

UACS is among the commonest causes of chronic cough. It involves diseases of the nose, sinus, throat, and pharynx. Cough in UACS may be associated with conditions like sinusitis, rhinitis, laryngopharyngitis, tonsillitis, nasopharyngitis, allergic rhinitis, etc.[7,14,15]

While the mechanisms behind UACS are not clearly understood, the probable mechanisms may include postnasal drip, direct mucosal irritation in the nose, inflammation of the airways – upper and lower, and heightened cough sensitivity (Figure 2).[15] A causal link with postnasal drip syndrome (PNDS) is not clear. Thus, the change in nomenclature from PNDS to UACS. It has been suggested that UACS-induced cough possibly occurs as a result of increased sensitivity of the sensory nerves of the upper airways or lower airways, or both.[15]

Figure 2. Probable mechanisms of UACS



Clinical presentation

Patients with UACS can present with the following symptoms:[7,14]

- Cough
- Expectoration
- Nasal congestion
- Nasal discharge
- Sensation of secretions trickling down the throat
- Frequent clearing of the throat.

Patients with rhinosinusitis can have purulent nasal discharge. Their sense of smell may be affected, and they may sometimes also have pain or swelling over the face.[7]

Diagnosis of UACS

Diagnosis of UACS involves a thorough history, examination, and investigations.

History

History may suggest the presence of conditions affecting the nose or throat, such as allergic rhinitis.[7,9] UACS-induced cough may occur in paroxysms or may be continuous. Additionally, it usually occurs during the day. It is quite uncommon to experience cough after sleeping in UACS.[7,8]

Physical examination

Physical examination in a patient with UACS may show signs of the underlying conditions. We may find secretions in the nasopahrynx and cobblestone posterior pharynx.[9,14]

UACS may be present along with other conditions known to be associated with chronic cough. Therefore, diagnosis may be challenging in some patients. Furthermore, due to atypical symptoms or symptoms which are not clearly defined, response to first-generation oral antihistaminics helps establish the diagnosis.[9,14,16]

Investigations

Additional investigations like CT scan of sinuses for sinusitis and allergy tests for allergic rhinitis may help establish a definitive diagnosis.[17]

Box 3 summarizes the key points to make a diagnosis of UACS.[7]

Box 3. Key points for UACS diagnosis

- Cough in paroxysms or continuous cough, usually during the day, rarely after sleeping
- History and presentation suggestive of diseases affecting the nose or throat
- Additional investigations pointing to diseases of the nose or throat
- Response to specific treatment directed at the throat – Improvement of cough

Treatment

As mentioned in the section on postinfectious cough, older-generation antihistamines with anticholinergic action can be helpful.[18,19] ICS may also help.

The treatment of UACS-induced cough is based on the underlying etiology, i.e., allergic rhinitis, nonallergic rhinitis, sinusitis etc. For allergic rhinitis, one can consider intranasal ICS and second-generation antihistamines orally. In patients

with nonallergic rhinitis and common cold, first-generation antihistamines and decongestant therapy should be given.[8] Table 1 summarizes the treatment approach for UACS.[7,8]

Table 1. Treatment of UACS

Underlying etiology	Treatment
Allergic rhinitis	• Avoiding allergen exposure • Intranasal ICS • Oral second-generation antihistamines • Leukotriene receptor antagonists (LTRAs)
Severe allergic rhinitis not responding to usual therapy	Allergen-specific immunologic therapy
Nonallergic rhinitis; common cold	• First-generation antihistamines • Decongestants
Chronic sinusitis	• Amoxicillin-clavulanic acid, cephalosporins, quinolones • Combined treatment with nasal ICS (>3 months) • Mucolytic agents may help • Chronic sinusitis with nasal polyps – ICS; oral steroids followed by inhaled ones seem to be more effective

Clinical points to consider[7,8]

✓ Nasal decongestants help with congestion and swelling; they should be used for less than 7 days.

✓ Long-term use of nasal decongestants may be associated with 'rhinitis medicamentosa' and is therefore not recommended.

✓ Combined first-generation antihistamines and decongestants should be given for a duration of 2-3 weeks.

4. Acute bronchitis/tracheobronchitis

Acute bronchitis is an inflammatory condition affecting the lower airways and the trachea.[20] However, its symptoms can be similar to various other conditions, such as common cold, asthma, etc.

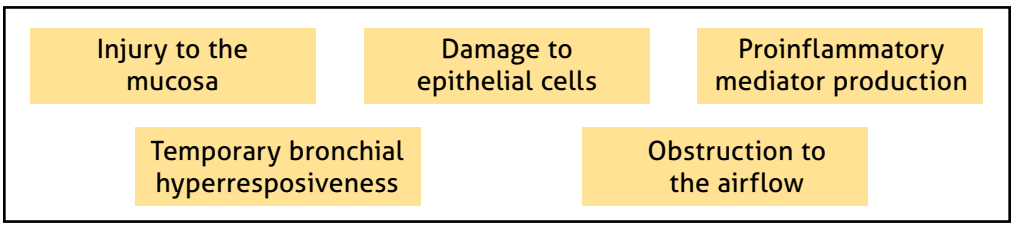
Therefore, it is a diagnosis of exclusion and is diagnosed when common cold, acute asthma, pneumonia, and COPD exacerbation have been ruled out.[8,20]

Acute bronchitis is also a self-limiting condition, like the common cold, and differentiating between these two conditions is quite challenging.[20,21] Acute bronchitis is an infection of the lower respiratory tract, namely the bronchial tubes, that presents with cough with sputum or without sputum, which lasts for up to 3 weeks. Additionally, there are no clinical signs or evidence on radiographs of other diagnoses. **Particularly, there is no evidence of pneumonia.**[8,20] It is most commonly caused by respiratory viruses.[8] Bacterial infection may be evident in less than 10% of the patients with acute bronchitis.[3] This fact is clinically important. Only 10% of the patients would genuinely need antibiotics. The viruses and bacteria known to be associated with acute bronchitis include:[3]

- Influenza A
- Influenza B
- Parainfluenza virus
- RSV
- Rhinovirus
- Coronavirus
- Adenovirus
- *Chlamydophila pneumoniae*
- *M. pneumoniae*
- *B. pertussis*
- *B. parapertussis.*

Acute tracheobronchitis can also occur due to exposure to dust, cold air, and irritating gases.[7]

In acute bronchitis, the cough could occur as a result of the following mechanisms:[21]



Clinical presentation[2,3,7,16,21]

- Acute bronchitis presents mainly with a cough which may or may not be productive and lasts for about 3 weeks
- In acute bronchitis, the cough may initially be dry and later become productive
- Sputum may be purulent, suggesting bacterial etiology
- Dyspnea
- Wheezing
- Fever
- Headache
- Pain in muscles
- Sore throat
- Sneezing and runny nose.

Diagnosis

The diagnosis of acute bronchitis or acute tracheobronchitis is largely clinical. As mentioned earlier, the diagnosis of acute bronchitis/tracheobronchitis is based on the clinical presentation of cough and fever with or without sputum, for up to 3 weeks, when the absence of any clinical signs or signs on radiographic assessment rule out pneumonia, and other conditions, like common cold, asthma, and acute COPD exacerbation, have also been excluded.[7,8,21]

The chances of the patient having pneumonia are decreased if the following are not present:[21]

- Heart rate of over 100 beats/min
- Respiratory rate of over 24/min
- Temperature of more than 38°C (oral)
- Focal consolidation, fremitus, or egophony on chest examination.

Culture for virus, serology, and sputum investigations do not have much significance in cases of acute bronchitis and must **NOT** be done as a routine as the causative pathogen is not usually detected.[21]

Treatment

- Symptomatic treatment is given in acute bronchitis.[7]
- Acute bronchitis is usually due to viral etiology. Antibiotic therapy is therefore not required.[3] However, in cases with purulent sputum, antibiotics should be prescribed.[7]
- Antitussive agents, like levodropropizine, dextromethorphan, etc., seem to be beneficial in dry cough.[8]
- Mucolytics or expectorants are helpful in patients who face issues with sputum expectoration.[7] Ambroxol is effective in patients having cough with sputum production.[8] Drinking plenty of fluids also helps in hydration.
- Guaifenesin, an expectorant, has action on the cough receptor hypersensitivity caused by viruses, and helps relieve the symptoms of acute infection.[1,7]
- There is no need for routine use of β_2-agonists but they may have a role in patients with acute bronchitis and asthma,[7] or those who clearly have a wheeze.
- When dealing with patients having bronchospastic conditions, one can use preparations having a short-acting bronchodilator, a mucolytic, and an expectorant.[8]

Dextromethorphan and ambroxol have been shown to decrease the severity and duration of cough in acute bronchitis.[1]

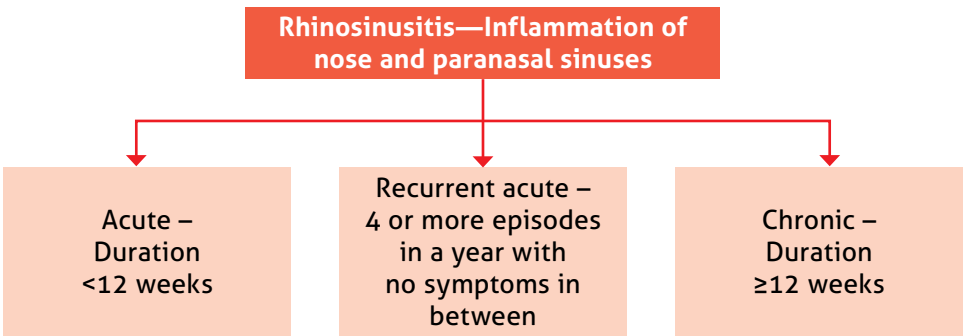
Point to consider

According to the CHEST expert panel report 2020 for acute bronchitis-associated acute cough in immunocompetent adults, routine use of antibiotic or antiviral agents, antitussive agents, inhaled β-agonists or anticholinergics, oral corticosteroids or ICS, oral nonsteroidal anti-inflammatory drugs, or any other agents, is not suggested unless clearly indicated.[20]

5. Acute rhinosinusitis

Rhinosinusitis is a term that combines rhinitis and sinusitis – rhinitis refers to inflammation of the nose, while sinusitis is the inflammation of paranasal sinuses.[22] The 2020 European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020) classifies rhinosinusitis as acute, recurrent acute, and chronic (Figure 3).[23]

Figure 3. Classification of rhinosinusitis



Acute rhinosinusitis (ARS) is an inflammation of the nose and the paranasal sinuses that lasts for up to 12 weeks.[24] The maxillary sinuses are most commonly affected.[25]

ARS is a common condition. A study conducted at a North Indian tertiary care center noted that 29.7% of the patients attending the ear-nose-throat (ENT) outpatient department (OPD) had ARS.[26]

Rhinosinusitis is described as follows:[23]

- Presence of ≥2 symptoms, one being nasal congestion/obstruction/blockage or discharge from the nose – with or without facial pressure or pain or decreased sense of smell/loss of smell

AND, either

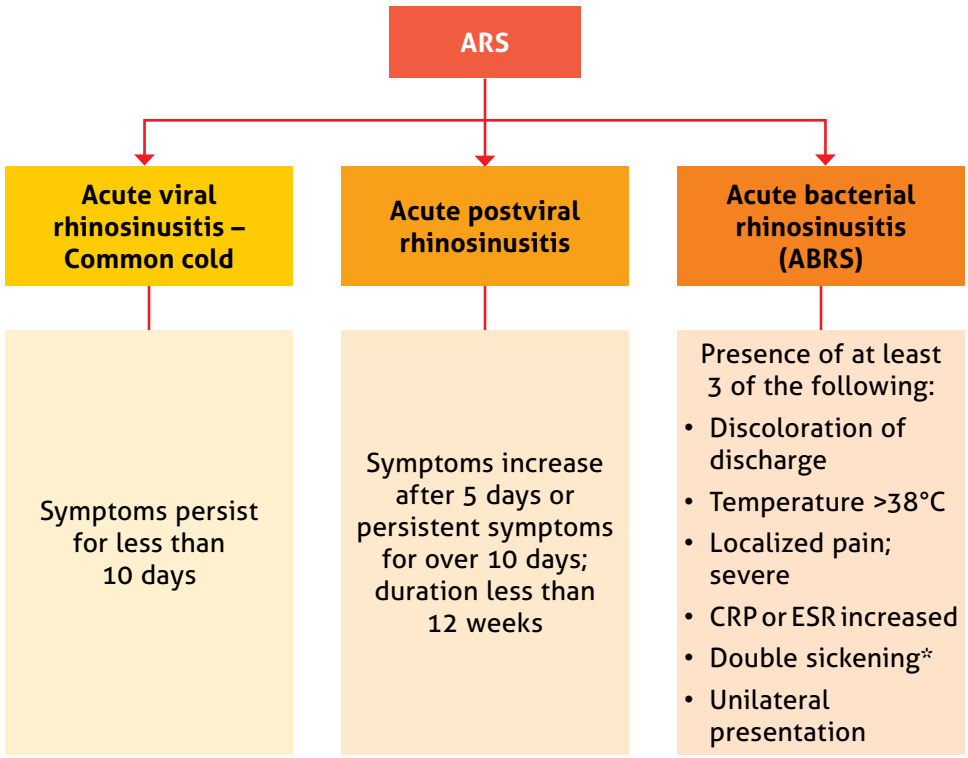
- Findings on endoscopy showing
  - Mucopurulent discharge from middle meatus and/or
  - Nasal polyps and/or
  - Swelling or mucosal obstruction in the middle meatus and/or

- Findings on CT scan showing mucosal changes in the sinuses and/or the ostiomeatal complex.

In children, decreased sense of smell/loss of smell is replaced by cough.

ARS is most commonly caused by viruses; however, bacteria and fungi have also been associated with ARS.[24] It has been noted that in patients suspected of having ARS, about a third have acute bacterial rhinosinusitis (ABRS).[25] ARS can be categorized as acute viral rhinosinusitis, acute postviral rhinosinusitis, and ABRS (Figure 4).[23] Postviral rhinosinusitis is a common cause of subacute cough while UACS after rhinosinusitis is commonly seen in cases of chronic cough.[18]

Figure 4. Categories of ARS



CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate

* Worsening following a mild disease phase

Children have a higher incidence of acute viral rhinosinusitis, while adults have a higher incidence of acute postviral rhinosinusitis. Additionally, cough is more prominent in children.[24]

Clinical presentation

As mentioned above, the symptoms of ARS include congestion or obstruction of nose, nasal discharge, facial pressure or pain, and loss of smell or reduced sense of smell.

The nasal discharge may be mucopurulent and with facial pain or pressure, the patient can experience headache.[23] In addition to these symptoms, the patient may also have a sore throat, cough, fever, malaise, and drowsiness.[23]

Infection of the maxillary sinus can be associated with dental pain and tenderness over the molar region. Swelling, tenderness, and pain around the eyes may be evident when the ethmoid sinus is affected.[22]

Diagnosis of ARS

ARS is diagnosed based on the clinical presentation. CT may be required if the symptoms persist even after appropriate therapy or a complication is likely.[23]

The diagnosis requires sudden onset of 2 or more symptoms including nasal blockage, nasal discharge, pain or pressure over the face, and decreased sense of smell/loss of smell.[23,24] ARS is further categorized as mentioned in Figure 4.

Findings on endoscopic examination support the diagnosis.[24] Examinations such as anterior rhinoscopy may show inflammation, swelling of the mucosa, purulent discharge, nasal polyps, etc. CRP is a potential investigation that can indicate bacterial infection when elevated. ESR and plasma viscosity are also increased in ABRS. It has been reported that ESR levels of more than 10 could predict sinus fluid levels or sinus opacity on CT.[23]

Treatment of ARS

- In case of acute viral rhinosinusitis (common cold), the treatment is symptomatic. It includes the use of paracetamol, non-steroidal anti-inflammatory drugs, combined analgesics and nasal decongestants, second-generation antihistamines (short-term beneficial effects), ipratropium bromide to manage runny nose, and vitamin C in deficient patients. Antibiotics and intranasal corticosteroids are not recommended in acute viral rhinosinusitis.[24]
- Postviral rhinosinusitis can be managed with intranasal corticosteroids based on symptom severity. Antibiotics, second-generation antihistaminics, nasal decongestants, and corticosteroids (systemic) are not recommended in postviral ARS.[24]
- In patients with ABRS, symptomatic treatment along with antibiotic therapy is recommended. In particular, β-lactams have known efficacy in adults. Sodium hyaluronate and saline solution may serve as a potential adjuvant to antibiotic therapy.[24]
- Using oral corticosteroids with antibiotics may have a role in decreasing facial pain.[24]
- Even if ABRS is suspected in a patient, the decision of antibiotic therapy must be individualized.[24]

Points to consider

✓ Cough can occur as a result of viral, bacterial and allergic rhinosinusitis.

✓ One must consider viral and postviral rhinosinusitis and postinfectious transient bronchial hyperresponsiveness in patients with subacute cough.[1]

Figure 5 summarizes the treatment recommendations for ARS.[23]

Figure 5. Treatment of ARS

Viral ARS	Postviral ARS	ABRS
• Short-term benefit of antihistamines • Use of nasal corticosteroids not supported • Antibiotic therapy not recommended • Nasal obstruction and discharge may be improved with paracetamol • Antihistamine/ decongestant/ analgesic combination beneficial • Ipratropium bromide beneficial for runny nose	• Antibiotic use not advised • Nasal corticosteroids have a small beneficial effect in symptom reduction • Systemic corticosteroids not advised • Nasal decongestants may help enhance mucociliary clearance • Antihistamines cannot be advised	• Antibiotic therapy can be effective in selected patients • Antihistamines cannot be advised

6. Acute exacerbation of chronic bronchitis

Chronic bronchitis is a condition described as the presence of cough and phlegm production on most days for 3 months or more in a year and for a minimum of 2 years in a row, provided there are no other conditions that could be responsible for these symptoms.[27] Chronic bronchitis, along with emphysema, is a key element in COPD.[27] COPD is a condition of progressive and continuous airflow limitation which presents with symptoms of cough, dyspnea, phlegm, and exacerbations. This occurs as a result of airway abnormalities, i.e., bronchitis, and (or) abnormalities of the alveoli, i.e., emphysema. In COPD, the airflow obstruction is not reversible completely.[28]

The burden of these diseases is quite high in the Indian population. The Global Burden of Disease Study 1990-2016 noted that India had 55.3 million cases of COPD in 2016.[29] A systematic review and meta-analysis published in 2021 noted the prevalence of COPD in India in people aged ≥30 years to be 7%. The risk factors associated with COPD included the following:[30]

- Smoking – Active and passive
- Exposure to environmental tobacco smoke
- Exposure to biomass fuel
- Occupational exposure to dust
- Indoor and outdoor pollution
- Advancing age.

Another recent systematic review and meta-analysis estimated the prevalence of chronic bronchitis and COPD across 8 South Asian countries. The estimated pooled prevalence for COPD was 11.1% and that for chronic bronchitis was 5% in India.[31] Overall, the burden of chronic respiratory disorders is high in our country.[29]

Acute exacerbation of chronic bronchitis

Acute exacerbation of chronic bronchitis is a state when there is a sudden worsening of a patient's condition who had stable chronic bronchitis, with an increase in the amount of sputum, increased purulence of sputum, patient's cough is aggravated,

and/or the patient's dyspnea worsens. This is a state of acute tracheobronchitis and it is usually observed that an exacerbation follows URTI.[27] A vast majority (~80%) of the cases of AECB are caused by infections.[32] A study noted that around 30% of the exacerbations are caused by viruses, which may or may not be associated with a superimposed bacterial infection.[33] Another study found that in most of acute exacerbation of COPD (AECOPD) cases, viruses and atypical bacteria were the causes.[34] The noninfective causes for acute exacerbations may include nonadherence to treatment, environmental factors, like pollution, etc.[32]

A combination of viral and bacterial etiology can also be seen in cases of AECB.[35] Viral infections seem to pave the way for a secondary bacterial infection.[27] AECB has been linked to pathogens like *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* in data obtained from Asia.[7]

One must ensure that other potential etiologies, apart from acute tracheobronchitis, like pulmonary embolism, pneumonia, pneumothorax, exacerbation of bronchiectasis, congestive heart failure, have been ruled out as the cause of the patient's worsening condition, before labeling it as AECB.[27]

Various factors have to be evaluated while establishing a diagnosis of AECB. These include potential triggers for the worsening condition, patient's age, any comorbidities, any prior exacerbations and their nature and intensity, etc.[32] Exacerbation can be ascertained based on the worsening symptoms.[27,32] History can help us identify the potential cause of the worsening condition. Noninfectious triggers must also be assessed as a cause for exacerbation, such as smoke exposure, allergen exposure, etc.[32] Additionally, while the symptoms of sore throat and cold suggest a viral etiology, increased purulent sputum or increase in sputum volume along with increase in inflammatory parameters, like neutrophils, could point to a bacterial exacerbation.[32]

A sputum culture may not be very helpful as the causative pathogens may be present in culture in stable patients as well.[32,35] Culture examination may help in case of recurrent exacerbations and for treatment with antibiotics.[32] A chest X-ray is also not particularly useful in diagnosing exacerbations. It rather detects any other conditions that might be responsible for the worsening of symptoms. Spirometry may help determine the extent of airflow limitation. Oxygen saturation evaluation can also provide valuable information.[32]

Advise the patient, who is a smoker, to quit smoking if he/she hasn't already done that. Antibiotic therapy is recommended in patients with AECB.[27] Patients with increased dyspnea, heightened sputum production and purulence appear to have an edge when it comes to treatment with antibiotics.[32] Macrolides and fluoroquinolones are potential agents.[32] Levofloxacin and moxifloxacin are often used.[7]

Depending on the antibiotic agent used, treatment duration may range from 5 to 10 days.[32]

Besides antibiotic therapy, adjuvant therapy for patients with AECB includes avoidance of irritants, oxygen therapy, bronchodilators, corticosteroids, proper hydration, and physical therapy.[32]

According to the 2006 ACCP guidelines, patients with AECB should receive short-acting β-agonists (SABAs) or anticholinergics. Furthermore, if the response is suboptimal with the maximum dose of the initial drug, the second agent must be added to it. ICS should be considered in case of recurrent exacerbations. A short course of systemic corticosteroids could be administered in AECB.[27]

7. Gastroesophageal reflux disease

Gastroesophageal reflux disease, a common condition, has a prevalence in the Indian population ranging anywhere between 7.6% and 30%.[36] GERD has been reported to be associated with chronic cough.[9] GERD presents with esophageal as well as extra-esophageal symptoms. Heartburn and regurgitation constitute the esophageal symptoms, while the extra-esophageal symptoms include hoarseness and cough.[8] However, all patients with GERD do not develop cough. Who are these patients? It has been reported that reflux leads to cough only if the cough reflex sensitivity is increased.[1]

Mechanism of GERD-related chronic cough

GERD-related chronic cough can be attributed to 3 factors:[37]

- Reflux theory
- Reflex theory
- Esophageal dysmotility.

The reflux theory states that defects in the structure and function of the lower esophagus result in reflux. Cough receptors can be directly stimulated by reflux of gastric contents. Reflux may also result in mucus secretion in the lower respiratory tract and cough receptor activation via the vagal reflex.[37]

It has been suggested that GER can result in microaspiration. Regurgitation of the gastric contents into the proximal esophagus and the pharynx irritates the upper respiratory tract cough receptors and can also result in aspiration of the fluid into the lower respiratory tract. This evokes cough. Airway reflux has also been implicated in GERD-related cough. Airway reflux is composed of a nonacidic gas mist.[1,37]

The reflex theory states that reflux into the distal esophagus stimulates the esophageal cough receptors, thus evoking cough. This is also known as the esophagus-tracheobronchial reflex mediated by the distal esophageal afferent nerve.[1,37]

Impaired esophageal motility has also been linked with GERD-related chronic cough.[37] Li and colleagues have shown that reflux-associated cough can be attributed to both proximal acidic reflux and distal reflux-reflex. The study by Li *et al* noted that low esophageal pressure during primary peristalsis and synchronous contraction at the time of secondary peristalsis may contribute to GERD-related cough.[38]

Characteristics of GERD-related cough[7,16]

- Dry or nonproductive
- Occurs at night
- Associated with hoarseness of voice
- Acidic or fatty foods may incite or worsen the cough
- Cough usually starts following a meal.

Diagnosis

A large proportion of patients with GERD-related chronic cough do not present with characteristic reflux symptoms.[37] Therefore, a careful history is important

when a patient with a chronic cough presents to you. In addition to thorough history taking, a clinician must rule out other potential causes of cough.[37]

A cough that occurs during the night or usually following a meal, and after the patient lies down, suggests a GERD-related cough.[9] However, as mentioned earlier, most patients may not have the defining symptoms of reflux. In that case, some features have been put forward that can help a clinician ascertain that the patient's cough is possibly a result of reflux despite the fact that he/she has no symptoms of the gastrointestinal tract. These include:[39]

- Presence of cough for over 8 weeks
- Patient is not on ACE inhibitor therapy
- No evidence of exposure to environmental irritants
- Patient is not a current smoker
- Asthma, UACS secondary to a rhinosinus condition, and NAEB have been excluded
- Normal findings on chest X-ray, or only stable inconsequential scars.

Hence, we can see that this diagnosis is often a diagnosis of exclusion.

The diagnostic tools for GERD-related chronic cough include impedance pH monitoring, symptom index (SI) and symptom association probability (SAP), endoscopic evaluation and biopsy, salivary pepsin evaluation, frequency of symptoms of gastroesophageal reflux scale (FSSG), mean nocturnal baseline impedance (MNBI), mucosal impedance, postreflux swallow-induced peristaltic wave (PSPW), MRI, narrow-band imaging, and PPI trial. Impedance pH monitoring appears to be the most accurate test to assess GERD.[37] However, it is not widely available.

When there is a suspicion of GERD-related chronic cough, PPI therapy should be given. Significant improvement in cough or complete resolution of cough after therapy points to reflux-related cough. But even if PPI therapy does not improve or resolve cough, it does not rule out reflux-related cough.[7]

There are varied views on the investigations for GERD-related cough in different guidelines. According to the German Respiratory Society guidelines, endoscopic finding of reflux esophagitis is not sufficient to determine that the cough is caused by reflux. They further state that impedance pH monitoring should be done after

endoscopy and motility assessment when other causes for cough have been ruled out. The guidelines also state that if there is no indication for PPI therapy, diagnosis of cough due to reflux using PPI therapy is not recommended.[1] According to the CTS guidelines, normal ambulatory esophageal pH monitoring results do not rule out GERD. They state that together, esophageal pH monitoring and intraluminal impedance monitoring can play a role in detecting nonacid reflux.[7] The CTS guidelines also recommend PPI therapy when GERD-related cough is the likely cause. It states that a PPI trial is more economical and easier to execute than 24-h ambulatory esophageal pH monitoring or multi-channel intraluminal impedance-pH monitoring (MII-pH), though the specificity is lesser.[7]

Indian experts made a near consensus to not recommend 24-h pH monitoring in all patients likely to have GERD-related chronic cough. Additionally, the experts did not reach a consensus to monitor pH prior to PPI therapy.[18]

The CTS guidelines suggest that in the absence of 24-h ambulatory esophageal pH monitoring or MII-pH, GERD-related chronic cough can be determined using the following findings:[7]

- Cough during or after eating
- Presence of reflux symptoms, such as heartburn and regurgitation, or a GERD Questionnaire score of 8 or above
- CVA, UACS, and eosinophilic bronchitis have been ruled out and there is no improvement in cough with treatment for these conditions.

GERD-related cough appears likely in these patients and one must begin diagnostic or empirical therapy for GERD-associated chronic cough in these patients.[7]

Treatment

Treatment of GERD-related cough includes lifestyle modifications, pharmacotherapy, and surgery (after careful consideration).

Lifestyle modifications for GERD patients encompass raising the patient's bed from the head end, avoiding meals for at least 3 hours before going to bed, changes in diet to help with weight loss in overweight and obese patients, avoiding spicy, fatty, and acidic foods and beverages, avoiding coffee, smoking cessation, and avoiding vigorous exercise.[7,39]

PPIs and H_2 receptor antagonists can be used for acid suppression. Alginates (mucosal protection) and prokinetic agents are also helpful in GERD.[7,37] The CTS guidelines recommend acid suppression and the use of prokinetic agents in GERD-related cough.[7]

While the characteristic reflux symptoms may improve quickly, cough may take up to **3 months** to improve with PPI treatment.[1] The Indian expert panel recommends PPI therapy for a minimum of 2 months when GERD is the likely cause of chronic cough in the presence of reflux symptoms.[18]

To specifically address cough, levocloperastine can be safely given for up to 14 days in GERD patients and has been reported to be effective.[8]

Anti-reflux surgery can be considered in a limited number of patients not responding to pharmacotherapy. It should not be considered if there is a major motility disorder or the acid exposure time in the distal esophagus is normal.[39] It has to be thought of when the inadequately controlled cough has a major effect on QoL of the patient and 24-h ambulatory esophageal pH monitoring or MII-pH monitoring identifies residual reflux even after acid suppression therapy.[7]

8. Psychogenic cough

Psychogenic cough, as we commonly know it, is known by a new term now – somatic cough disorder, in line with the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) classification. Furthermore, the term tic cough has been suggested for habit cough.[40] Cough has been described as habit/tic/psychogenic cough when there is no identifiable medical cause for the cough and medical therapy does not resolve the cough.[40]

When the patient's cough impacts his/her life markedly and the patient gives too much importance to the cough, becomes anxious, and responds to it in an inordinate manner, it is considered as somatic cough syndrome.[1]

As we know, a honking/barking cough, present only during the day and disappearing during sleep, which is associated with a psychiatric disorder and does not respond to treatment has been regarded as a psychogenic cough.[41] However, barking cough can be present in other conditions as well, like in tracheomalacia. Therefore, such features cannot reliably establish the diagnosis of psychogenic cough.

The updated CHEST guideline states that the diagnosis of somatic cough syndrome or psychogenic cough should not be established or ruled out on the basis of the mere presence or absence of nocturnal cough or barking or honking cough. The guideline also states that psychogenic cough should not be diagnosed on the basis of the presentation of depression or anxiety in a patient.[40]

Causes and clinical presentation

Psychogenic cough has been more commonly reported among children and the knowledge about the presentation of this condition in adults is not very clear.[7,42] Lai and colleagues conducted a retrospective study among patients with somatic cough syndrome. The psychiatric conditions noted in these patients were anxiety, obsessive-compulsive disorder, somatoform disorders, depression, and cognitive bias. Patients with somatic cough syndrome had a dry cough and had a lower incidence of night-time cough, compared to the nonpsychogenic cough patients. The commonest initial triggering factor for cough in somatic cough syndrome patients was common cold. The cough was also associated with itchiness in the throat, throat clearing, postnasal drip, tightness of the chest, sensation of a foreign body in the pharynx, and shortness of breath.[42]

Diagnosis

Owing to a lack of set criteria to diagnose psychogenic cough, it must be considered in patients in whom both the common and the infrequent causes of cough have been ruled out.[7]

Additionally, once all the causes for chronic cough have been ruled out, a clinician must differentiate between refractory cough or chronic idiopathic cough and somatic cough syndrome.[1]

According to the updated CHEST guideline, when tic disorders and rare causes of cough have been excluded through a thorough evaluation and the DSM-5 criteria for a somatic symptom disorder is fulfilled, somatic cough syndrome can be diagnosed.[40] Tic cough is diagnosed when the cough cannot be explained even after an extensive evaluation and there are key characteristics of tics – distractibility, suppressibility, variability, suggestibility, and premonitory sensation. This can be done when the cough cannot be explained through an extensive evaluation.[40]

The existence of comorbid psychiatric disorders can help in the diagnosis of somatic cough syndrome.[42]

Management

In children with somatic cough disorder, the updated CHEST guideline advocates hypnosis or suggestion therapy trials or reassurance and counseling. It also suggests referral to a psychologist or psychiatrist.[40] Short-term antitussive therapy can serve as an additional treatment option. Among adults with somatic cough syndrome, antidepressants or antianxiety drugs along with psychological interventions may have some benefit.[7,18]

The Indian consensus panel recommends that a short counseling session be given to patients with psychogenic cough.[18]

9. Asthma

Asthma is a common reason for chronic cough in the adult population.[43] The burden of asthma in the Indian population is quite high. Around 35 million individuals in India have asthma, according to the Global Asthma Report 2022. However, it has been found in the Global Asthma Network (GAN) phase 1 study that the prevalence of asthma was lower than that noted in the International Study of Asthma and Allergies in Childhood (ISAAC) phase 3 study.[44] Yet, the GAN phase 1 study noted that 68-70% of the individuals having severe asthma were never diagnosed with asthma by a clinician.[45] This gap needs to be addressed urgently in order to better manage our patients with asthma.

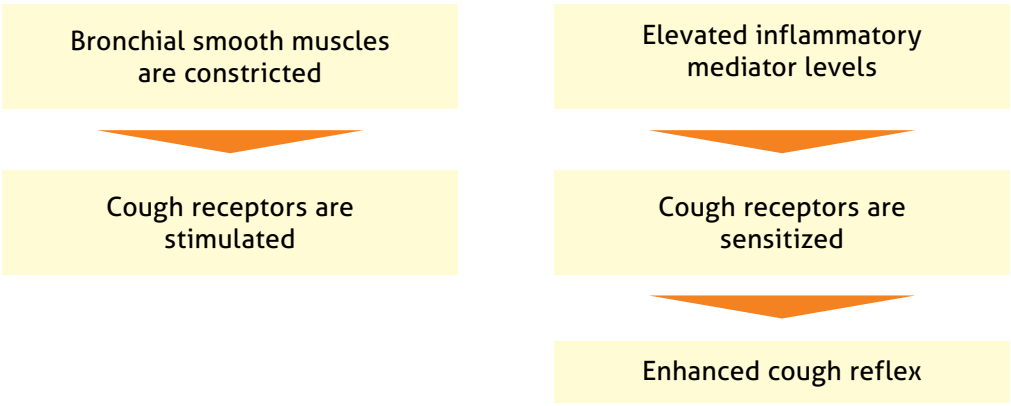
The updated GINA report defines asthma as having a heterogeneous presentation and often described by inflammation of the airways and restriction of the airflow that varies.[46] The respiratory symptoms of asthma fluctuate with time as well as in severity. The symptoms include dyspnea, wheezing, tightness of the chest, and cough.[46]

Cough in asthma usually occurs at night.[14] Sometimes, cough may be the only symptom in an asthma patient. This is referred to as CVA.[43]

In cases of classic asthma, there is bronchial hyperresponsiveness and variable airflow restriction. However, in CVA, spirometry does not show any signs of airway obstruction.[14]

The mechanisms behind cough in asthma patients are shown in Figure 6.[47]

Figure 6. Mechanisms associated with cough in asthma



Clinical presentation

The latest GINA report of 2023 has clearly summarized the characteristic symptoms and characteristics of asthma, the presence of which heightens the odds of the patient having asthma. These include:[46]

- Symptoms – Dyspnea, wheezing, cough, chest tightness
- Presence of more than one of the symptoms
- Variability in symptoms over time and in severity
- Symptoms worsen usually at night or early morning hours
- Factors like a viral infection, exposure to allergens or weather changes, exercise, laughing, exposure to irritating stimuli, such as strong smells, fumes or smoke, can provoke the symptoms.

Diagnosis of asthma

I have discussed the diagnosis and management of asthma here largely based on the updated GINA report, and also on the updated National Institute for Health and Care Excellence (NICE) guidelines.

According to the GINA report, asthma is diagnosed on the basis of characteristic symptoms and expiratory airflow limitation. As the patient presents with respiratory

symptoms, a clinician must first determine if the symptoms are characteristic of asthma. The symptoms and features that point to asthma have been mentioned above.[46] The variability of symptoms, daily or seasonal, should be determined. One must also determine if there is a personal or family history of atopy.[48]

Look for expiratory wheeze (polyphonic) on physical examination of the patient presenting with features suggestive of asthma. Also, check for any evidence of other causes for the patient's symptoms.[48] However, physical examination can reveal normal findings too.

If the history and physical examination point to asthma, spirometry and peak flow variability should be done.[46,48] The characteristics of variability in expiratory airflow limitation, as mentioned in the GINA report, include disproportionate lung function variability and confirmed expiratory airflow obstruction. Excessive lung function variability can be confirmed with positive bronchodilator responsiveness, increased forced expiratory volume in 1 second (FEV_1) following 4 weeks of therapy, extreme variability in peak expiratory flow (PEF) (twice a day) over a duration of 2 weeks, positive result on exercise challenge test and bronchial challenge, and excessive variation in FEV_1 between the visits.[46]

Expiratory airflow restriction is confirmed when FEV_1/forced vital capacity (FVC) ratio is decreased in comparison with the lower limit of normal.[46]

Allergy testing with skin prick test or specific IgE test can help determine atopy or the factors that trigger the patient's symptoms once asthma has been diagnosed.[46,48] FeNO test can also be done when asthma seems likely in a patient.[48] FeNO may have limited utility though as according to the GINA report, it has not been found to contribute to excluding or ruling in an asthma diagnosis. It can be elevated in asthma but also in conditions like allergic rhinitis, atopy, etc.[46] Additionally, it can be lower in patients who smoke.[46,48]

Management of asthma

An ICS is the key to the management of asthma patients. Treatment with ICS, with or without inhaled bronchodilators, has been recommended by the Indian consensus panel for patients with chronic cough when asthma is suspected. Additionally, if the response to ICS is inadequate, one can consider adding an antileukotriene agent.[18]

The GINA report describes the agents used to manage asthma in the categories of controllers and relievers. Controller therapy involves the use of low-dose ICS-formoterol (LABA) when symptoms appear. The patient may also take controller maintenance therapy, aka maintenance and reliever therapy (MART), with daily or twice a day ICS-formoterol. Reliever therapy includes SABA-only treatment, ICS-formoterol as-needed, and ICS-SABA as-needed. It also mentions add-on medications for those who have severe asthma.[46]

The use of SABA-only therapy is not recommended in the GINA report. It recommends ICS-based therapy for the control of symptoms and reduction of exacerbations.[46] Maintenance therapy is given continuously despite the absence of symptoms and involves the use of ICS, ICS-LABA, and ICS-LABA-long-acting muscarinic antagonist (LAMA). It can also include LTRAs and biologicals.[46]

10. Cough-variant asthma

Cough-variant asthma is a type of asthma in which cough is the only symptom and there are no signs of any obstruction of the airways on investigation.[14] Dyspnea and wheeze are absent in patients with CVA but bronchial hyperresponsiveness is noted.[7]

Clinical presentation of CVA

- Patients with CVA usually have night-time or early morning cough.[7,8]
- The cough is dry, severe, and irritating.[7]
- Cough on laughing or speaking loudly is a very typical symptom.

Diagnosis of CVA

CVA can be diagnosed on the basis of patient's history, physical examination, findings on bronchial provocation test, and response to asthma treatment.[7] Spirometry cannot diagnose CVA.[1]

While response to bronchodilator therapy is observed in CVA patients, it cannot be used to diagnose this condition. Variability in PEF can also help with the diagnosis. Additionally, raised FeNO and eosinophilia on sputum analysis point to CVA.[7]

The CTS Asthma Consortium recommends certain criteria for the diagnosis of CVA (Figure 7).[7]

Figure 7. Criteria for diagnosis of CVA

Presentation	Investigations	Treatment
Chronic irritating cough, often nocturnal	Bronchial challenge test – Positive, OR Bronchodilator reversibility test – Positive, OR Average daily PEF variability of 10% or more during 2 weeks duration	Resolution of cough with asthma therapy

Management of CVA

The treatment of CVA and classic asthma is the same.[7] CVA patients respond to the usual treatment, including ICS, β_2-agonists and LTRAs.[1]

Combined use of ICS and β-2 receptor agonist is recommended (ICS/formoterol). The treatment duration has been recommended as over 8 weeks. Treatment with oral corticosteroid (short duration) may be needed in case of no or inadequate response to ICS, or when there is severe airway inflammation.[7] Antitussive agents, like levodropropizine, levocloperastine,[8] or dextromethorphan can also help.

According to the CTS cough guidelines, LTRAs can be beneficial for inflammation and cough and may be helpful in some patients not responding to ICS therapy.[7] The 2020 CHEST guideline suggests the use of ICS as the first-line therapy in patients with CVA. ICS dose step-up approach and leukotriene inhibitor trial can be considered when response to ICS therapy is inadequate in CVA patients or if cough alone persists after ICS therapy in asthma patients. This should be considered after other causes of cough have been evaluated again. ICS can be combined with β-agonists, as per the CHEST guideline.[43]

11. Pulmonary TB

Tuberculosis is a very common disease in India. Around 21.4 lakh cases of TB were notified in India in the year 2021.[49] In a national survey conducted between 2019 and 2021, microbiologically confirmed pulmonary TB prevalence was noted as 316 per lakh population among those aged 15 years and above. In 2021, the prevalence of all types of TB was 312 per lakh population in the country.[50]

Box 4 lists the risk factors for TB.[51,52] Many of these risk factors are seen in the Indian setting and must raise the suspicion of TB when any of these factors coexist with persistent cough in a patient.

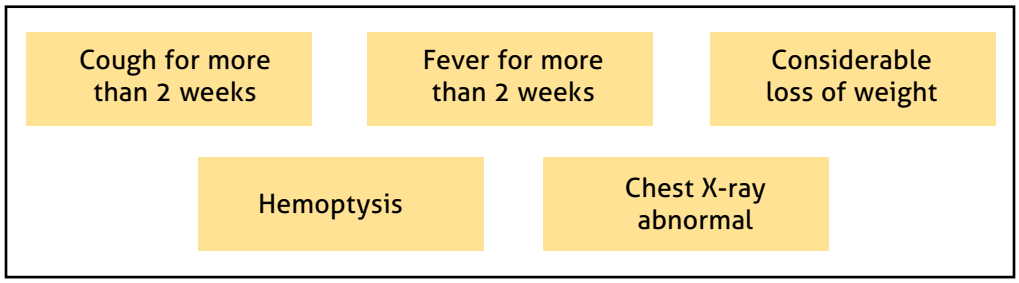
Box 4. Risk factors for TB

- Overcrowded places/households
- Malnutrition
- Illicit drug use
- Low socioeconomic status; people in shelter homes or prisons
- Close contact with infectious TB patient
- Healthcare workers
- Diabetes
- Immunosuppressive state (Human immunodeficiency virus infection)
- Smoking
- Alcohol
- Children
- Chronic lung conditions
- Silicosis
- Indoor air pollution

The Indian expert consensus is of the opinion that when a patient presents with a subacute or chronic cough to a clinician, pulmonary TB must be excluded.[18] A cough that has been there for over 2 weeks since treatment was started along with typical clinical presentation should raise the suspicion of TB.[9]

What is presumptive pulmonary TB?

An individual presenting with any of the following features pointing to TB is considered a case of presumptive pulmonary TB:[51]



Cough in TB is productive. Another symptom observed in TB patients is night sweats.[8,16]

Diagnostic tests for TB

In patients with signs and symptoms suggesting TB infection, diagnosis should be confirmed using specific tests.

The tests to confirm the diagnosis include culture, smear microscopic evaluation to detect acid-fast bacilli (AFB), cartridge-based nucleic acid amplification tests (CBNAAT), such as Xpert MTB/RIF* assay, line probe assays to identify *M. tuberculosis* and drug resistance, whole genome sequencing (WGS), drug sensitivity testing (DST), biomarkers, and chest X-ray.[8,53] Bronchial TB can be confirmed with the help of bronchoscopy.[8] Two sputum AFB smear positive tests and a raised ESR support the diagnosis of pulmonary TB.[9]

When a patient has a positive result on the first sputum smear examination and there is no evident risk for drug-resistant TB, the patient is said to have microbiologically-confirmed TB.[9] The Indian consensus panel recommends the use of Gene Xpert Ultra test to exclude *M. tuberculosis* infection in suspected patients.[18]

Management

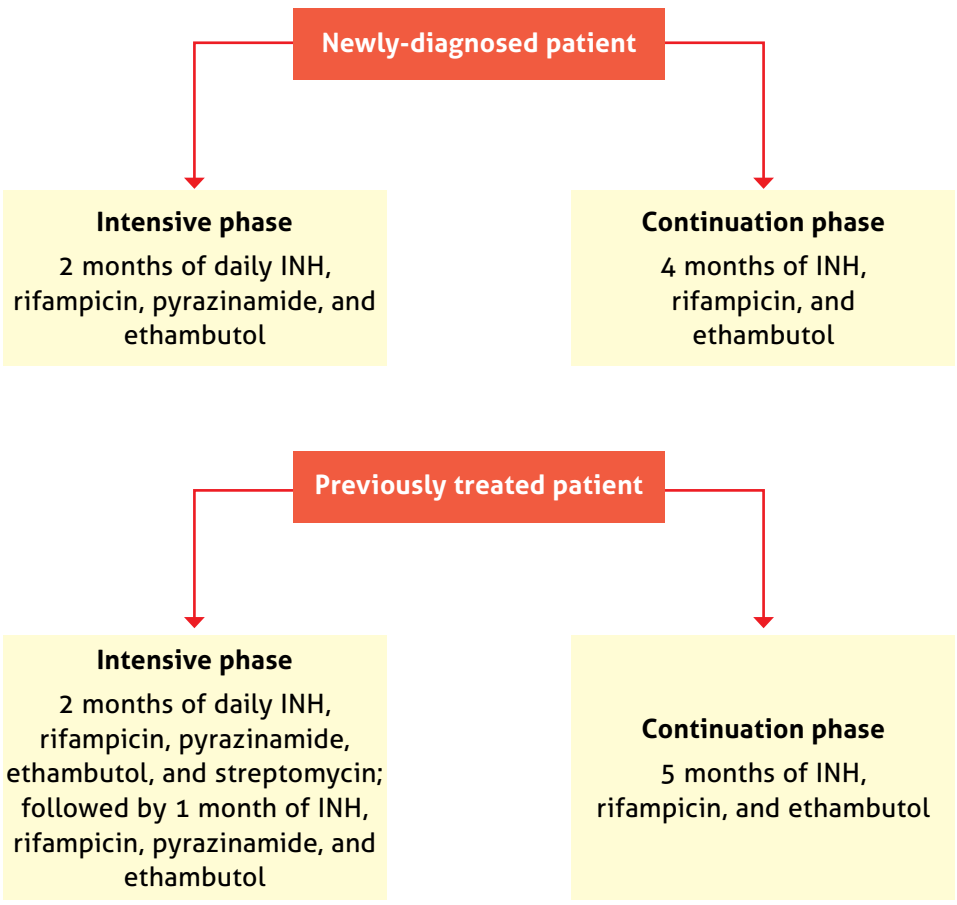
The drugs used for the treatment of TB include rifampicin, pyrazinamide, isoniazid (INH), ethambutol, levofloxacin/moxifloxacin, bedaquiline, linezolid, clofazimine, cycloserine, delamanid, aminoglycosides, ethionamide/prothionamide, p-Aminosalicylic acid, and amoxicillin-clavulanic acid with meropenem or imipenem-cilastatin.[53]

*_M. tuberculosis_/Rifampicin

The treatment of TB according to the Revised National Tuberculosis Control Programme (RNTCP) guidelines is described in Box 5.[51]

Additionally, levodropropizine could have benefit in dry cough related to pulmonary TB. Dextromethorphan can also be beneficial in cases of chronic cough, such as those due to TB.[8]

Box 5. Treatment of newly-diagnosed TB patients and previously treated patients



12. ACE inhibitor-induced cough

ACE inhibitors are well known for their cardioprotective role. These drugs are commonly used in the management of cardiovascular diseases as well as renal disorders.[54,55] While they have been found to be beneficial across a range of patients, such as those with hypertension, myocardial infarction, heart failure, coronary artery disease, and renal diseases, they have certain adverse effects, one of them being cough.[54,55]

Drug-induced cough must be ruled out in a patient presenting with a cough. If there is a history of ACE inhibitor use, the medication should be discontinued.[9,16] However, if ACE inhibitor discontinuation does not resolve the cough, alternative diagnoses should be considered.[9]

It is not well understood how ACE inhibitor use leads to the development of cough. It has been speculated that these drugs inhibit the degradation of bradykinin and substance P, thus resulting in their aggregation in the respiratory tract – both upper and lower. Neurokinin A and substance P are released as bradykinin stimulates the sensory nerves in the airways through RARs and C-fiber receptors, eventually resulting in constriction of the smooth muscles in the airways and cough.[55] ACE inhibitors heighten the cough reflex sensitivity.[1]

Some other mechanisms have also been postulated, such as a history of asthma, increased bronchial reactivity, heightened sensitivity of the airway sensory nerves that depend on bradykinin, lung congestion, reduced bradykinin breakdown, and genetic polymorphism of bradykinin receptor.[55]

Presentation of ACE inhibitor-induced cough

- Drug-induced cough is dry.[8]
- The patients may also have a tickling sensation or a scratchy feeling in the throat.[8,55]
- The cough usually resolves within a few days of discontinuation of the drug.[55] However, it may take up to 2 months to resolve after discontinuation in some patients.
- The cough starts within a week or a month of initiating the medication.[55]

Improvement in cough within a week to 4 weeks of treatment discontinuation points to drug-induced cough.[16]

How to manage ACE inhibitor-induced cough?

Discontinuation of treatment with the ACE inhibitor is recommended.[8] There are other drugs that can also induce cough. As with ACE inhibitors, these drugs must be discontinued if they seem to cause cough.[1,8]

A recent article by Borghi and colleagues states that cessation of ACE inhibitor therapy should be guided by the severity of cough.[55] Furthermore, the CTS cough guidelines suggest that angiotensin II receptor blockers (ARBs) can be used in place of ACE inhibitors.[7] But Borghi and colleagues argue that some patients can develop cough even with ARB therapy and switching to ARBs can also diminish the cardiovascular benefits. Therefore, they suggest that a challenge-rechallenge test be done in patients with ACE inhibitor-induced cough that can help ascertain whether introducing ACE inhibitor again would lead to cough.[55]

If ACE inhibitor cannot be stopped, one could consider using sodium cromoglycate, theophylline, indomethacin, sulindac, ferrous sulfate, picotamide, amlodipine, and nifedipine. Levocloperastine also seems to be beneficial in cough due to ACE inhibitor use.[8]

Pinto and colleagues, in a paper published in 2020 in the *Indian Heart Journal*, stated that in a patient presenting with cough, we can transiently withdraw the ACE inhibitor and reintroduce the drug after cough resolves. If there is worsening of cough, one may consider an ARB or some other agent. A calcium channel blocker (CCB) can also be added to ACE inhibitor to diminish the cough reflex. In moderate to severe cough, one should discontinue ACE inhibitor therapy and prescribe an alternative agent. In case cough still continues, and stopping the ACE inhibitor therapy is not possible and other agents are not indicated, the ACE inhibitor therapy be reintroduced and an additional drug be added. If there is an indication, one may switch to an ARB or an angiotensin receptor neprilysin inhibitor (ARNI).[54]

The decision to continue or discontinue the ACE inhibitor would depend on the benefit and risk assessment: What was the indication on starting it, how important is it to continue, whether or not alternatives are there, and how troublesome is

the cough. This decision is best taken in co-consultation with the cardiologist who initiated the treatment with the ACE inhibitor.

When the history is suggestive of cough-inducing drug use and the chest X-ray is normal, one must reconsider the use of the offending medication based on risk-benefit evaluation.[9]

Some important clinical points of ACE inhibitor-induced cough:

- It occurs in around 15% of the patients.
- It is observed more in Indian and Chinese patients.
- It is more frequently seen in females.
- It is more common in people with atopy.
- Spirometry or pulmonary function test is normal.
- It usually starts within 1-4 weeks of starting the drug; sometimes longer.
- On stopping the drug, the cough stops within a few weeks; sometimes longer.
- It is a class effect; changing to another ACE inhibitor does not help.

13. Cough hypersensitivity syndrome

There are many patients that we come across in our clinical practice who have cough but there is no identifiable cause for it. The cough may be refractory to treatment or may be idiopathic. A clinician would do various investigations, ranging from chest X-ray to spirometry, and administer therapeutic trials, give antibiotics, cough suppressants, etc., but to no avail.

Are these patients hypersensitive to irritants and noxious stimuli? Well, the term 'cough hypersensitivity syndrome' has been proposed relatively recently which corresponds to a condition where a cough occurs as a result of airway sensory neuron hypersensitivity.[56] CHS represents a hypernym that includes a range of

patients presenting with chronic cough – for some an identifiable cause may be known, while for others, the cough could be due to hypersensitivity to stimuli. In CHS, the patient develops a cough from exposure to even low levels of mechanical, chemical, or thermal stimuli.[56] So, CHS represents a state where cough is the key presentation regardless of what the underlying condition is.[57] According to the CHS paradigm, the conditions considered to be the causes of cough, such as GER, asthma, rhinosinusitis, etc., are instead the triggering factors.[57]

Increased cough receptor expression has been noted in the airways of cough patients.[47] Peripheral as well as central mechanisms seem to be involved in cough hypersensitivity.[58] TRPV1 is upregulated in the nerves of bronchial epithelium and there is enhanced activity in midbrain areas. Additionally, the potential for cough suppression is diminished as the activation of brain areas involved in cough suppression is reduced.[57,59]

To put it simply, CHS is similar to pain hypersensitivity syndrome. In both, the nerves and the receptors are oversensitive. In pain hypersensitivity, it is the pain receptors and in cough hypersensitivity, it is the cough receptors.

Box 6 summarizes the key characteristics of CHS.[47]

Box 6. Characteristics of CHS

Chronic cough	No or very little phlegm	Cough reflex challenge test—Positive
Presence of triggers of cough reflex—Speaking, eating, exposure to cold air, perfumes	Tickling or itching in the throat (Urge to cough)	Patient's QoL affected by cough

Presentation of CHS[56]

- Cough
- Sensation of tickling or irritation in the throat or chest
- Dysphonia
- Hoarseness of voice
- Feeling of obstruction in the larynx following exposure to low levels of irritating stimuli, like smoke, fragrances, etc.

The clinical picture that backs neuropathology as the culprit in CHS includes coughing provoked even on exposure to low levels of stimuli, feeling of the urge to cough and itching in throat, and hypertussia. Some clinical studies have also shown that agents associated with neuromodulation, such as gabapentin, pregabalin, etc., are effective in patients with unexplained cough or refractory chronic cough.[57] Chronic idiopathic or refractory cough could therefore be explained by heightened cough reflex sensitivity.[1]

Normal individuals can tolerate capsaicin concentration of up to 500 µmol/ml; however, those with a hypersensitive cough reflex may have cough at a concentration of 1-10 µmol/ml.[1] Hypersensitivity of the cough reflex in patients with chronic idiopathic or refractory cough can be diagnosed clinically.[1] So, in order to make such a diagnosis, one must rule out the established etiologies of chronic cough and must ascertain that treatment approach targeting the cause has been unsuccessful. These patients tend to have chronic dry cough, sensation of itchiness in the throat, sensitivity to stimuli like odors, dust, smoke, and cold air, and even talking. This is how one can diagnose unexplained cough due to hypersensitivity of cough reflex.[7]

If the initial investigations (chest X-ray and pulmonary function test) do not suggest a diagnosis in a patient with chronic cough, there may be a possibility of cough reflex hypersensitivity. Cough triggers like CVA, UACS, GER, and NAEB should be ruled out. Once these conditions have been excluded, bronchoscopy and CT may help determine an alternate etiology. If the cause is still not confirmed, it is termed chronic idiopathic cough.[1]

We have limited choices for the treatment of CHS. The European Respiratory Society (ERS) guidelines suggest that targeting cough hypersensitivity instead of the treatable traits leading to increased sensitivity could be helpful. A trial of pregabalin or gabapentin has also been suggested for these patients in the guidelines.[58] These agents with neuromodulatory potential can benefit patients with CHS.[7] Clinicians may also think of physiotherapy or speech and language therapy in patients with refractory chronic cough.[58] Physical cough suppression therapy can have beneficial effects in terms of hypersensitivity, frequency of cough, and cough-related QoL.[7]

Points to consider

- CHS includes chronic idiopathic cough as well as other conditions where the patient has an escalated response to stimuli known to evoke cough.[56]
- Hypersensitivity of the cough reflex can be seen in a large number of patients having chronic cough.[58]
- CHS is probably the factor in patients having chronic idiopathic or refractory cough where temperature, odors, and cold air seem to intensify the symptoms.[18]

14. Smoker's cough

Tobacco or cigarette smoke is a commonly inhaled irritating stimulus in the respiratory tract. Furthermore, smoking is known to increase the risk of chronic cough and COPD.[60] While acute exposure to tobacco smoke can induce cough, long-term exposure tends to alter the sensitivity to various cough-evoking stimuli.[61] Certain components of cigarette smoke, namely reactive oxygen species, nicotine, and α,β-unsaturated aldehydes, are known to result in activation of TRPA1 channels.[60] Smoking is associated with inflammation in the lung parenchyma.[16]

The Indian expert consensus suggests that smoker's cough be regarded as a warning sign, particularly in those aged over 35 years.[9] When taking history, one must document the patient's smoking history and the nature of sputum. In smokers, there may be productive cough with mucoid or mucopurulent sputum. This could

be attributed to chronic bronchitis. In some, the irritating effects of the smoke could result in a dry cough.[62]

Smoker's cough is observed in chronic smokers which is a chronic, persistent cough.[16] Chronic bronchitis can develop in people who smoke too much, which usually happens beyond the age of 40 years. The cough in these patients usually occurs in the morning.[63] Chronic bronchitis is described as the presence of cough and sputum on most days for a minimum of 3 months in a year for at least 2 successive years when other conditions responsible for cough have been ruled out. Chronic bronchitis as a result of smoking appears to be a common cause of chronic cough. The cough occurs as a result of mucosal inflammation and heightened mucus secretion.[1]

Chronic bronchitis and emphysema are both parts of COPD, which is a condition with progressive obstruction of the airflow.[16,28] When there is no obstruction, chronic bronchitis is diagnosed through the history of exposure and the presenting symptoms. Smoking history or exposure to occupational pollutants points to a likely diagnosis of chronic bronchitis in such cases.[1]

Symptoms

In COPD, patients may have both productive cough and dry cough. Productive cough is often present during the morning. Cough is largely caused by increased mucus secretion and also as a result of decreased mucociliary clearance caused by factors like smoking.[1] Patients with COPD can have cough with small or moderate sputum production, which is mucoid, tightness of chest, dyspnea on exertion, expiratory wheezing, restriction of activity, and fatigue.[16,28]

Diagnosis

Physical examination may not reveal any signs of airflow obstruction unless the lung function is considerably impaired. A diagnosis of COPD is confirmed when spirometry shows FEV_1/FVC ratio of below 0.7 after bronchodilator use. This suggests airflow obstruction which is not completely reversible. Chest X-ray does not have a role in diagnosing COPD but can help rule out other conditions. Chest CT can be considered in select patients.[28]

Treatment

Abstinence from smoking and avoiding exposure to passive smoking and workplace pollutants can help relieve cough.[27] Nicotine replacement therapy can also help COPD patients.[28] Inhaled bronchodilators given with or without ICS can help improve cough. Mucoactives may have a beneficial role when there is normal lung function in chronic bronchitis patients. In chronic bronchitis with dry cough, levodropropizine and levocloperastine have favorable effects. Dextromethorphan can also help at high doses. When there is productive cough, preparations that have short-acting bronchodilators with mucoactives can be used. One can also consider the use of a preparation that contains a bronchodilator, a mucolytic, and an expectorant.[8]

Drugs used to manage COPD include SABAs and LABAs, anticholinergics, combined SABA and anticholinergic or LABA and anticholinergic, LABA and ICS combination, methylxanthines, mucolytics, and LABA-LAMA-ICS combination.[28]

15. Occupation-related cough

Documenting details about the patient's occupation is a vital part of history when dealing with a patient with chronic cough. Occupational exposure to several different pollutants or noxious stimuli can provoke cough in an individual.

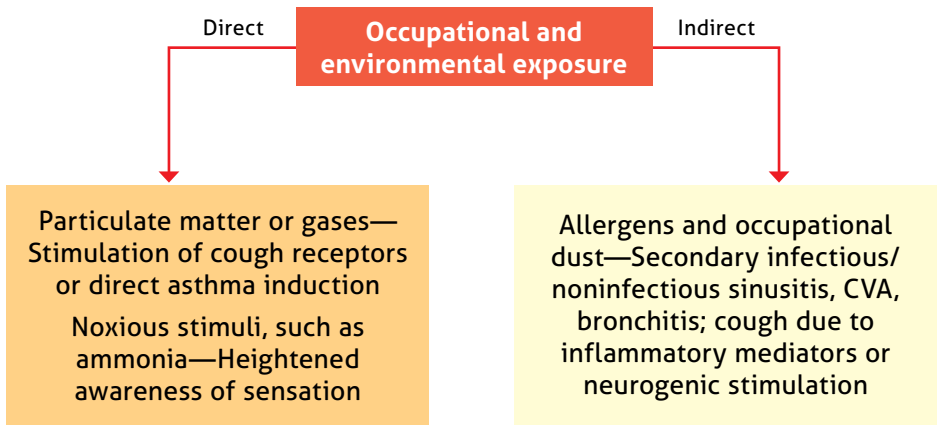
Chronic cough is a common condition associated with occupation-related exposure. Coal mining, hard-rock mining, concrete manufacturing, and working in tunnels have been linked to cough.[64] Exposure to sulfur, nitrous oxide, and indoor air pollution are associated with chronic cough and asthma.[9] Cough due to occupational exposure can be present as the only symptom or it could be a sign of a more serious condition.[65]

People working in mines and refineries have an increased risk of chronic productive cough. Working with asbestos has been linked with chronic dry cough and breathlessness.[9] Working in the food industry or farming, and wood industry may also be associated with chronic cough.[64] According to the European Community Respiratory Health Survey, chronic phlegm production and chronic bronchitis are linked to occupational exposures, particularly to mineral dust and metals.[66]

An Indian study conducted among carpenters noted symptoms like chronic phlegm, chest tightness, chronic cough, dyspnea, and irritation in the nose.[67]

Occupational and environmental factors can cause cough through direct and indirect effects (Box 7).[65] Certain exposures may lead to behavioral changes which may present with somatic cough syndrome. Phonation can also incite cough.[65]

Box 7. Direct and indirect effects of occupational and environmental factors



The risk of environmental factors-related cough is high in people who have conditions like COPD.[9] Dusts, gases, vapor, etc., can lead to the development of chronic bronchitis, COPD, and asthma. Furthermore, smokers are at a higher risk.[65]

Exposure to environmental triggers can cause chronic cough through non-IgE antibody-mediated mechanisms.[65] Eosinophilic bronchitis is a condition where the patient is particularly sensitive to dust, odors, smoke, etc. Occupational history has to be considered when diagnosing eosinophilic bronchitis.[7] A patient with occupational eosinophilic bronchitis can have chronic cough that is aggravated at work.[68] The cough is dry or may produce small amounts of mucoid sputum.[7] There is no dyspnea or wheezing. There is eosinophilia on sputum examination, absence of airflow limitation, and the PEF variation is normal. There is no airway hyperresponsiveness.[68] Therefore, while diagnosing eosinophilic bronchitis, besides occupational history, one must also check for induced sputum eosinophils

or eosinophils in bronchoalveolar lavage, airway responsiveness, and improvement with steroid therapy.[7]

When a patient presents with a history of occupational exposure to a noxious stimulus, occupation-related or occupational cough must be thought of. **When there is improvement after the occupational or environmental exposure is avoided or removed, it ascertains the diagnosis of occupational cough or cough due to environmental factors.**[7] Therefore, history is vital to determine a work-related cause of cough. Both short-term and long-term history of occupational exposure is required as exposure several years prior to symptom onset may also be valuable. This is because cough could be a manifestation of another condition with a long period of dormancy.[65]

Besides avoiding workplace exposure, using protective equipment may help but is only a temporary solution.[65] The 2016 CHEST expert panel report made some suggestions regarding chronic cough due to occupational and environmental exposures (Box 8).[65]

Box 8. Suggestions from the CHEST expert panel report

- When the history points to occupational or environmental cause for chronic cough, it should be confirmed using objective tests, like pulmonary function and rhinolaryngoscopy
- In patients having a history of occupational or environmental exposure, objective tests to ascertain the link between the exposure and chronic cough include metacholine challenge, induced sputum, before and after tests, and immunologic studies to check for hypersensitivity
  - Sputum or induced sputum cytology to look for eosinophilia
  - Metacholine challenge test to determine cough from occupation-related asthma/eosinophilic bronchitis
  - Before and after exposure tests–To assess the causal link
  - Immunologic tests–Skin test, specific IgE antibodies, specific IgG antibodies in serum

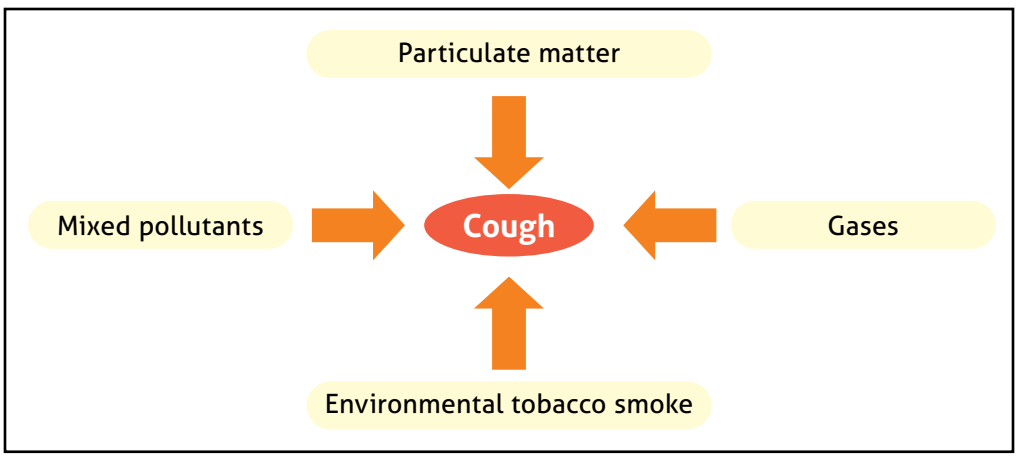
16. Pollution-related cough

Air pollution is a growing problem globally and the scenario is similar in India as well. Vehicle exhaust and pollution from industries are rising and the effects of these pollutants on human health are perilous.

Air pollution is known to affect respiratory health and can increase cough incidence or prevalence.[69] The situation of air pollution in our country is abysmal with 39 cities from India making it to the list of 50 most polluted cities in the world.[70]

Poor air quality and air pollution have been associated with impaired lung function, asthma, allergy, various respiratory symptoms, COPD, bronchitis, and respiratory infections.[71] Air pollution worsens COPD, asthma, respiratory infections, and lung cancer. Ozone, particulate matter, and nitrogen oxides seem to have the most impact.[72] Exposure to particulate matter has been linked to cough and sputum production.[73] Particulate matter tends to activate TRPA1 and TRPV1 ion channels, thus playing a role in the cough reflex. Exposure to particulate matter can alter the cough reflex, decrease the urge to cough threshold, and adversely affect lung function.[73] Air pollution can be associated with dry cough.[16]

Various air pollutants, including particulate matter, gases, mixed pollutants, and environmental tobacco smoke tend to increase cough to varying extents.[74] While particulate matter and mixed pollutants increase cough and wheezing, gases seem to have a greater impact in increasing wheezing, compared to cough. Environmental tobacco smoke can have a permanent impact, with childhood exposure linked to wheezing and cough in adults.[74]



17. Heart diseases/Congestive heart failure

Cough can occur as a result of extrapulmonary diseases, such as heart disease.[1] It has been reported in arrhythmia and heart failure.[75] Cough, particularly nocturnal, has been reported as a symptom of heart failure, though in the category of not-so-typical symptoms.[76] Congestive heart failure is associated with pulmonary congestion and edema, and results in cough.[16] Bronchial obstruction and increased bronchial reactivity as well as cough can occur due to acute left heart failure.[1] Heart diseases can be associated with both acute and chronic cough.[1]

Cough triggered by cardiac disorders may possibly be explained by the neural reflex hypothesis and the hemodynamic hypothesis (Box 9).[75]

Box 9. Mechanisms proposed for cough due to cardiac disorders

Neural reflex	Hemodynamics
Vagal reflex Interaction of afferent nerves of the heart and cough neural pathways	Disorders of heart function can lead to hemodynamic changes in pulmonary circulation as well as the heart

Presentation of cough due to arrhythmias and heart failure

Cough due to arrhythmia is usually dry and continues all through the day. However, the cough is not very severe and may affect sleep. It appears that premature ventricular contraction (PVC)-related cough is reduced at night. Patients may also have dyspnea on exertion and palpitations.[75] Besides causing chronic cough, PVCs can also lead to cough syncope.[77,78]

A sudden urge to cough has been reported by patients after a tickling feeling in the throat or cough following a feeling of a thump in the chest, as described by Neil

Brandon in his patients with premature atrial contraction (PAC).[75,79] There may be solitary episodes or bouts of cough in patients with arrhythmia-induced cough.[75]

In congestive heart failure, the patient may have dyspnea, orthopnea, lower limb edema, and fatigue, in addition to cough. The cough in these cases may be productive with pink straw-colored phlegm production.[16] In acute pericarditis, a patient may have a dry cough with dyspnea.[80]

Diagnosis

History is important when diagnosing a case of cough related to heart disease/dysfunction. A history of heart failure or myocardial infarction should raise the suspicion of cough due to heart disease. Additionally, when the patient complains of paroxysmal dyspnea at night and a dry irritating cough, cardiac etiology should be considered.[9]

With such history and presentation, if infections like TB, GERD, UACS, asthma, and postinfectious cough have all been excluded, one must think of heart disease-related cough.[9]

A detailed history, physical examination, and investigations can help establish an appropriate diagnosis. Patients having evidence of pulmonary congestion, arrhythmia, or heart murmurs should undergo a thorough cardiologic evaluation.[18]

Examination may reveal basal crepitus in the early stages of congestive heart failure. Investigations like chest radiography, electrocardiography, echocardiography, B-type natriuretic peptide (BNP), cardiac stress test, and Holter monitoring can help confirm the diagnosis of heart disease-related cough.[16,18]

Arrhythmia-triggered cough may not be associated with any abnormal findings on auscultation or X-ray. A history of palpitations and cough all through the day (including night) is indicative of arrhythmia-related cough. Cough immediately after premature beats is important for diagnosing such cough etiology. This may be observed on pulse examination, electrocardiogram, echo, or rhythm Holter evaluation while recording of cough at the same time.[75]

Additionally, when antiarrhythmic therapy is given, cough and arrhythmia are resolved, thus confirming that the cough is due to arrhythmia.[75]

As soon as a cough of cardiac origin is suspected, based on the history, presentation, examination, and/or investigations, the patient should be referred to a cardiologist.

18. Rare diseases that cause cough

We are aware of various common etiologies that can cause acute, subacute, or chronic cough. However, there are some uncommon conditions as well that can lead to cough. In a significant proportion of patients, the cause of cough remains unexplained. This poses a major healthcare burden. Without a known etiology despite all necessary investigations, it becomes challenging to devise an appropriate treatment plan for the patient. This adds to the patient's as well as the treating physician's agony.

Therefore, it is important to be aware of the uncommon or rare causes of cough so that we do not miss looking for those when the common causes do not seem likely to be the factors in a particular patient.

Lai and colleagues conducted a retrospective study among patients with chronic cough. Among more than 1500 patients, common causes of cough were identified in 1,055 cases and rare causes were evident in 235 cases. Protracted bacterial bronchitis, somatic cough syndrome, diffuse panbronchiolitis, obstructive sleep apnea syndrome, and interstitial lung disease were the leading 5 rare causes of cough in the study. The investigations that helped identify the rare causes included bronchoscopy or nasopharyngoscopy, HRCT scan of the chest, sinus CT, and pulmonary diffusing capacity.[81]

In this section, I have attempted to list the rare or uncommon causes of cough which should be considered when every other disorder or cause seems to have been ruled out.

Rare causes of cough

The rare causes of cough, as described in the published literature, are mentioned in Box 10, segregated into pulmonary and extrapulmonary causes.[1,7,82]

Box 10. Rare causes of cough

Pulmonary	Extrapulmonary
Tracheobronchomalacia	Tracheoesophageal fistula
Tracheobronchopathia osteoplastica	Bronchoesophageal fistula
Airway strictures or stenosis	Connective tissue disorders
Tracheobronchomegaly	Inflammatory bowel disease
Tracheobronchial amyloidosis	Thyroid disease
Foreign body	Vasculitides
Broncholithiasis	Esophageal cyst
Lymphangioleiomyomatosis	Esophageal cancer
Ossifying bronchopathy	Cervical spondylosis
Relapsing polychondritis	Celiac disease
Obstructive sleep apnea syndrome	Cerumen in the external auditory canal
Pulmonary alveolar proteinosis	Hepatic cavernous hemangioma
Pulmonary alveolar microlithiasis	Pleural endometriosis
Pulmonary fibrosis	Tourette syndrome
Pulmonary Langerhans cell histiocytosis	Left heart failure
Tonsillar enlargement	Arrhythmia

Pulmonary	Extrapulmonary
Endobronchial hamartoma	Relapsing polychondritis
Heterotopic salivary gland	Hodgkin's lymphoma
High altitudes	
Mediastinal mass	
Tracheal diverticulum	
Pulmonary embolism	
Pulmonary edema	
Laryngeal cancer	
Epiglottic hypoplasia	
Tracheal adenoid cystic cancer	
Pericardial cyst	
Post-traumatic pseudo-aneurysm	
Reactive airway dysfunction syndrome	
Cystic fibrosis	
Others • Vocal cord dysfunction • Surgical sutures	

Summarized below are some recommendations from the ACCP guidelines on rare causes of cough.[82]

- Among patients presenting with chronic cough, if there is continuation of cough after the common etiologies have been assessed, and the evaluation points that an uncommon etiology may be responsible, one must look at the uncommon causes.
- A CT scan should be done as well as a bronchoscopic evaluation must be performed, if required, when cough continues after the most common etiologies for cough have been considered.
- Foreign body aspiration should be considered in patients with sudden onset cough.
- The likelihood of drug-induced cough should be assessed among patients with unexplained cough.

KEY MESSAGES

- When the history and physical examination suggest common cold or a URTI and there are no red flags, no further investigations are required.
- Acute respiratory viral infection presenting with cough often resolves on its own in 9 to 12 days' time. It may take longer if the person has an allergic disposition or resides in a very polluted city.
- A cold is usually a self-limiting condition and does not require any specific treatment. Symptomatic treatment can be given if required.
- Postinfectious cough is quite common in patients who have had a viral infection.
- A thorough history is therefore very important in establishing a diagnosis of postinfectious cough.

- A runny nose, nasal congestion, throat irritation, and postnasal drip are characteristic symptoms of UACS. A dry, irritating cough, wheezing, chest tightness, and cough while speaking point to lower airway involvement and are suggestive of bronchial hyperresponsiveness.
- In postinfectious cough, one can consider the use of antihistamines, antitussive agents, and decongestants in certain patients.
- UACS is among the commonest causes of chronic cough. It may be present along with other conditions known to be associated with chronic cough. Therefore, diagnosis may be challenging in some patients.
- Treatment of UACS-induced cough is based on the underlying etiology. Nasal decongestants help with congestion and swelling, but should be used for less than 7 days.
- Acute bronchitis presents with a cough with sputum or without sputum, that lasts for up to 3 weeks.
- The diagnosis of acute bronchitis/tracheobronchitis is based on the clinical presentation of cough and fever with or without sputum, for up to 3 weeks, when the absence of any clinical signs or signs on radiographic assessment rule out pneumonia, and other conditions like common cold, asthma, and acute COPD exacerbation have also been excluded.
- Symptomatic treatment is given in acute bronchitis.
- ARS is diagnosed based on the clinical presentation. The diagnosis requires sudden onset of 2 or more symptoms including nasal blockage, nasal discharge, pain or pressure over the face, and decreased sense of smell/loss of smell; endoscopic examination can support the diagnosis.
- In case of acute viral rhinosinusitis, the treatment is symptomatic. Postviral rhinosinusitis can be managed with intranasal corticosteroids based on symptom severity. In patients with ABRS, symptomatic treatment along with antibiotic therapy is recommended.

- A vast majority (~80%) of the cases of AECB are caused by infections. Exacerbation can be ascertained based on the worsening symptoms. Sore throat and cold suggest a viral etiology, while increased purulent sputum or increase in sputum volume along with increase in inflammatory parameters, like neutrophils, could point to a bacterial exacerbation.
- Antibiotic therapy is recommended in patients with AECB; adjuvant therapy for patients with AECB includes avoidance of irritants, oxygen therapy, bronchodilators, corticosteroids, proper hydration, and physical therapy.
- A cough that occurs during the night or usually following a meal, and after the patient lies down, suggests a GERD-related cough.
- When there is a suspicion of GERD-related chronic cough, PPI therapy should be given. Significant improvement in cough or complete resolution of cough after therapy points to reflux-related cough.
- PPI therapy has been recommended for a minimum of 2 months when GERD is the likely cause of chronic cough in the presence of reflux symptoms.
- Psychogenic cough must be considered in patients in whom both the common and the infrequent causes of cough have been ruled out. Once all the causes for chronic cough have been ruled out, one must differentiate between refractory cough or chronic idiopathic cough and somatic cough syndrome.
- Antidepressants or antianxiety drugs along with psychological interventions may have some benefit in adults with somatic cough syndrome.
- Asthma is a common cause of chronic cough in adults. It can be diagnosed on the basis of characteristic symptoms and expiratory airflow restriction. If the history and physical examination point to asthma, spirometry and peak flow variability should be done.
- ICS is the key to the management of asthma patients.
- CVA can be diagnosed on the basis of history, physical examination, findings on bronchial provocation test, and response to asthma treatment.

- ICS is the first-line therapy in patients with CVA.
- When a patient presents with a subacute or chronic cough to a clinician, pulmonary TB must be excluded. A cough that has been there for over 2 weeks since treatment was started along with typical clinical presentation should raise the suspicion of TB.
- Use of Gene Xpert Ultra test is recommended to exclude *M. tuberculosis* infection in suspected patients.
- The key drugs used for the treatment of TB include rifampicin, pyrazinamide, isoniazid (INH), and ethambutol.
- Improvement in cough within a week to 4 weeks of treatment discontinuation points to drug-induced cough. Discontinuation of treatment with the ACE inhibitor is recommended in patients with ACE inhibitor-induced cough.
- In CHS, the patient develops a cough from exposure to even low levels of mechanical, chemical, or thermal stimuli.
- Chronic idiopathic or refractory cough could be explained by heightened cough reflex sensitivity.
- Agents with neuromodulatory potential can benefit patients with CHS.
- Smoker's cough should be regarded as a warning sign, particularly in those aged over 35 years. Chronic bronchitis as a result of smoking appears to be the commonest cause of chronic cough.
- When a patient presents with a history of occupational exposure to a noxious stimulus, occupation-related or occupational cough must be thought of. When there is improvement after the occupational or environmental exposure is avoided or removed, it ascertains the diagnosis of occupational cough or cough due to environmental factors.
- Various air pollutants, including particulate matter, gases, mixed pollutants, and environmental tobacco smoke tend to increase cough.

- A history of myocardial infarction or congestive heart failure should raise the suspicion of cough of cardiac origin.
- As soon as a cough of cardiac origin is suspected, based on the history, presentation, examination, and/or investigations, the patient should be referred to a cardiologist.
- There are several uncommon or rare causes of cough that should be considered when nothing else seems to be the cause of the patient's cough, before labeling it as unexplained cough.

References

1. Kardos P, Dinh QT, Fuchs KH, Gillissen A, Klimek L, Koehler M, *et al.* German Respiratory Society guidelines for diagnosis and treatment of adults suffering from acute, subacute, and chronic cough. *Respir Med.* 2020 Aug-Sep;170:105939.
2. Holzinger F, Beck S, Dini L, Stöter C, Heintze C. The diagnosis and treatment of acute cough in adults. *Dtsch Arztebl Int.* 2014 May 16;111(20):356-63.
3. Boujaoude ZC, Pratter MR. Clinical approach to acute cough. *Lung.* 2010 Jan;188 Suppl 1(Suppl 1):S41-6.
4. Waghmode R, Jadhav S, Nema V. The Burden of Respiratory Viruses and Their Prevalence in Different Geographical Regions of India: 1970-2020. *Front Microbiol.* 2021 Aug 31;12:723850.
5. Murgia V, Manti S, Licari A, De Filippo M, Ciprandi G, Marseglia GL. Upper Respiratory Tract Infection-Associated Acute Cough and the Urge to Cough: New Insights for Clinical Practice. *Pediatr Allergy Immunol Pulmonol.* 2020 Mar;33(1):3-11.
6. Hegland KW, Pitts T, Bolser DC, Davenport PW. Urge to cough with voluntary suppression following mechanical pharyngeal stimulation. *Bratisl Lek Listy.* 2011;112(3):109-14.
7. Lai K, Shen H, Zhou X, Qiu Z, Cai S, Huang K, *et al.* Clinical Practice Guidelines for Diagnosis and Management of Cough—Chinese Thoracic Society (CTS) Asthma Consortium. *J Thorac Dis.* 2018 Nov;10(11):6314-51.
8. Shankar PS, Korukonda K, Bendre S, Behera D, Mirchandani L, Awad NT, *et al.* Diagnoses and management of adult cough: An Indian Environmental Medical Association (EMA) position paper. *Respir Med.* 2020 Jul;168:105949.
9. Guleria R, Dhar R, Mahashur A, Ghoshal AG, Jindal SK, Talwar D, *et al.* Indian Consensus on Diagnosis of Cough at Primary Care Setting. *J Assoc Physicians India.* 2019 Jan;67(1):92-8.
10. Lin L, Yang ZF, Zhan YQ, Luo W, Liu BJ, Pan JY, *et al.* The duration of cough in patients with H1N1 influenza. *Clin Respir J.* 2017 Nov;11(6):733-8.
11. Chen Y, Zhang X, Zeng X, Xu T, Xiao W, Yang X, *et al.* Prevalence and risk factors for postinfectious cough in discharged patients with coronavirus disease 2019 (COVID-19). *J Thorac Dis.* 2022 Jun;14(6):2079-88.
12. Braman SS. Postinfectious cough: ACCP evidence-based clinical practice guidelines. *Chest.* 2006 Jan;129(1 Suppl):138S-146S.

13. Irwin RS, Baumann MH, Bolser DC, Boulet LP, Braman SS, Brightling CE, *et al.* Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. *Chest.* 2006 Jan;129(1 Suppl):1S-23S.
14. Vally M, Irjuma MOE. Management of Cough: a practical approach. *S Afr Fam Pract.* 2016;58(4):35-9.
15. Lucanska M, Hajtman A, Calkovsky V, Kunc P, Pecova R. Upper Airway Cough Syndrome in Pathogenesis of Chronic Cough. *Physiol Res.* 2020 Mar 27;69(Suppl 1):S35-42.
16. Ijaz A, Nabeel M, Masood U, Mahmood T, Hashmi MS, Posokhova I, *et al.* Towards using cough for respiratory disease diagnosis by leveraging Artificial Intelligence: A survey. *Inform Med Unlocked.* 2022 Jan 1;29:100832.
17. Kaplan AG. Chronic Cough in Adults: Make the Diagnosis and Make a Difference. *Pulm Ther.* 2019 Jun;5(1):11-21.
18. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
19. Bolser DC. Older-generation antihistamines and cough due to upper airway cough syndrome (UACS): efficacy and mechanism. *Lung.* 2008;186 Suppl 1(Suppl 1):S74-7.
20. Smith MP, Lown M, Singh S, Ireland B, Hill AT, Linder JA, Irwin RS; CHEST Expert Cough Panel. Acute Cough Due to Acute Bronchitis in Immunocompetent Adult Outpatients: CHEST Expert Panel Report. *Chest.* 2020 May;157(5):1256-65.
21. Braman SS. Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines. *Chest.* 2006 Jan;129(1 Suppl):95S-103S.
22. Masood A, Moumoulidis I, Panesar J. Acute rhinosinusitis in adults: an update on current management. *Postgrad Med J.* 2007 Jun;83(980):402-8.
23. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, *et al.* European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology.* 2020 Feb 20;58(Suppl S29):1-464.
24. Jaume F, Valls-Mateus M, Mullol J. Common Cold and Acute Rhinosinusitis: Up-to-Date Management in 2020. *Curr Allergy Asthma Rep.* 2020 Jun 3;20(7):28.
25. Ebell MH, McKay B, Dale A, Guilbault R, Ermias Y. Accuracy of Signs and Symptoms for the Diagnosis of Acute Rhinosinusitis and Acute Bacterial Rhinosinusitis. *Ann Fam Med.* 2019 Mar;17(2):164-72.
26. Khan AR, Siddiqui F. Regional prevalence of different types of sinusitis at a tertiary care centre in Northern India. *Int J Otorhinolaryngol Head Neck Surg.* 2020 May;6(5):969-73.
27. Braman SS. Chronic cough due to chronic bronchitis: ACCP evidence-based clinical practice guidelines. *Chest.* 2006 Jan;129(1 Suppl):104S-15S.
28. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy For the Diagnosis, Management, And Prevention Of Chronic Obstructive Pulmonary Disease: 2023 REPORT [Internet]. Available from: https://goldcopd.org/2023-gold-report-2/. [cited September 23, 2023].
29. India State-Level Disease Burden Initiative CRD Collaborators. The burden of chronic respiratory diseases and their heterogeneity across the states of India: the Global Burden of Disease Study 1990-2016. *Lancet Glob Health.* 2018 Dec;6(12):e1363-74.
30. Verma A, Gudi N, Yadav UN, Roy MP, Mahmood A, Nagaraja R, Nayak P. Prevalence of COPD among population above 30 years in India: A systematic review and meta-analysis. *J Glob Health.* 2021 Aug 21;11:04038.
31. Jarhyan P, Hutchinson A, Khaw D, Prabhakaran D, Mohan S. Prevalence of chronic obstructive pulmonary disease and chronic bronchitis in eight countries: a systematic review and meta-analysis. *Bull World Health Organ.* 2022 Mar 1;100(3):216-30.
32. Brunton S, Carmichael BP, Colgan R, Feeney AS, Fendrick AM, Quintiliani R, Scott G. Acute exacerbation of chronic bronchitis: a primary care consensus guideline. *Am J Manag Care.* 2004 Oct;10(10):689-96.

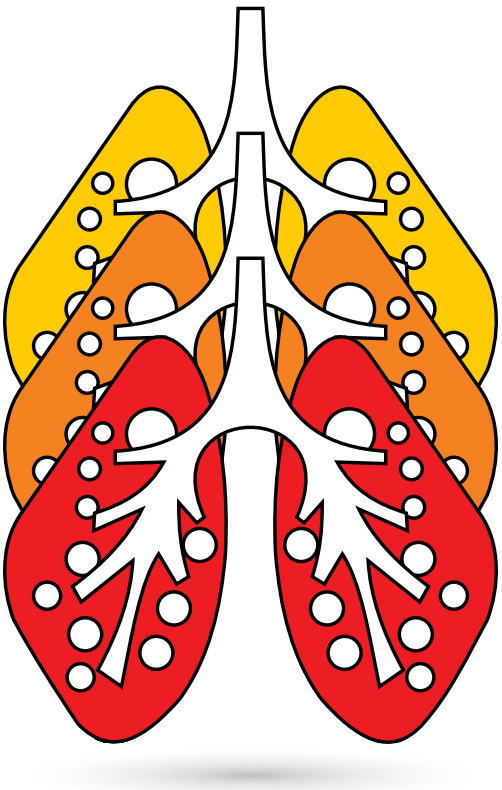
33. Sethi S. Infectious etiology of acute exacerbations of chronic bronchitis. *Chest.* 2000 May;117(5 Suppl 2):380S-5S.
34. Lieberman D, Lieberman D, Ben-Yaakov M, Lazarovich Z, Hoffman S, Ohana B, *et al.* Infectious etiologies in acute exacerbation of COPD. *Diagn Microbiol Infect Dis.* 2001 Jul;40(3):95-102.
35. Sohy C, Pilette C, Niederman MS, Sibille Y. Acute exacerbation of chronic obstructive pulmonary disease and antibiotics: what studies are still needed? *Eur Respir J.* 2002 May;19(5):966-75.
36. Bhatia SJ, Makharia GK, Abraham P, Bhat N, Kumar A, Reddy DN, *et al.* Indian consensus on gastroesophageal reflux disease in adults: A position statement of the Indian Society of Gastroenterology. *Indian J Gastroenterol.* 2019 Oct;38(5):411-40.
37. Wu J, Ma Y, Chen Y. GERD-related chronic cough: Possible mechanism, diagnosis and treatment. *Front Physiol.* 2022 Oct 20;13:1005404.
38. Li X, Lin S, Wang Z, Zhang H, Sun X, Li J, *et al.* Gastroesophageal reflux disease and chronic cough: A possible mechanism elucidated by ambulatory pH-impedance-pressure monitoring. *Neurogastroenterol Motil.* 2019 Dec;31(12):e13707.
39. Kahrilas PJ, Altman KW, Chang AB, Field SK, Harding SM, Lane AP, *et al*; CHEST Expert Cough Panel. Chronic Cough Due to Gastroesophageal Reflux in Adults: CHEST Guideline and Expert Panel Report. *Chest.* 2016 Dec;150(6):1341-60.
40. Vertigan AE, Murad MH, Pringsheim T, Feinstein A, Chang AB, Newcombe PA, *et al*; CHEST Expert Cough Panel. Somatic Cough Syndrome (Previously Referred to as Psychogenic Cough) and Tic Cough (Previously Referred to as Habit Cough) in Adults and Children: CHEST Guideline and Expert Panel Report. *Chest.* 2015 Jul;148(1):24-31.
41. Vertigan AE. Somatic cough syndrome or psychogenic cough-what is the difference? *J Thorac Dis.* 2017 Mar;9(3):831-8.
42. Lai K, Peng W, Zhan W, Xie JX, Tian J, Zuo XP, *et al.* Clinical characteristics in adult patients with somatic cough syndrome. *Ther Adv Respir Dis.* 2022 Jan-Dec;16:17534666221092993.
43. Côté A, Russell RJ, Boulet LP, Gibson PG, Lai K, Irwin RS, Brightling CE; CHEST Expert Cough Panel. Managing Chronic Cough Due to Asthma and NAEB in Adults and Adolescents: CHEST Guideline and Expert Panel Report. *Chest.* 2020 Jul;158(1):68-96.
44. The Global Asthma Report. *Int J Tuberc Lung Dis.* 2022;26:S1-102.
45. Singh S, Salvi S, Mangal DK, Singh M, Awasthi S, Mahesh PA, *et al.* Prevalence, time trends and treatment practices of asthma in India: the Global Asthma Network study. *ERJ Open Res.* 2022 May 30;8(2):00528-2021.
46. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Updated July 2023 [Internet]. Available from: www.ginasthma.org. [cited on September 27, 2023].
47. Mahashur A. Chronic dry cough: Diagnostic and management approaches. *Lung India.* 2015 Jan-Feb; 32(1):44-9.
48. NICE. Asthma: diagnosis, monitoring and chronic asthma management [Internet]. Available from: https://www.nice.org.uk/guidance/ng80/resources/asthma-diagnosis-monitoring-and-chronic-asthma-management-pdf-1837687975621. [cited September 27, 2023].
49. WHO Global TB Report 2022 [Internet]. Available from: https://pib.gov.in/PressReleasePage.aspx?PRID=1871626. [cited September 28, 2023].
50. National TB prevalence survey in India (2019-2021). Summary report [Internet]. Available from: https://tbcindia.gov.in/WriteReadData/l892s/25032022161020NATBPSReport.pdf. [cited September 28, 2023].
51. Behera D, Pandey MK, Kant S. RNTCP Guidelines for TB and Extra-Pulmonary Tuberculosis. NMO Journal [Internet]. 2020 Jul 24; 12(01):56-9. Available from: https://nmojournal.org/index.php/nmojournal/article/view/27. [cited September 28, 2023].

52. Narasimhan P, Wood J, Macintyre CR, Mathai D. Risk factors for tuberculosis. *Pulm Med.* 2013;2013:828939.
53. Gill CM, Dolan L, Piggott LM, McLaughlin AM. New developments in tuberculosis diagnosis and treatment. *Breathe* (Sheff). 2022 Mar;18(1):210149.
54. Pinto B, Jadhav U, Singhai P, Sadhanandham S, Shah N. ACEI-induced cough: A review of current evidence and its practical implications for optimal CV risk reduction. *Indian Heart J.* 2020 Sep-Oct;72(5):345-50.
55. Borghi C, Cicero AF, Agnoletti D, Fiorini G. Pathophysiology of cough with angiotensin-converting enzyme inhibitors: How to explain within-class differences? *Eur J Intern Med.* 2023 Apr;110:10-5.
56. Morice AH, Millqvist E, Belvisi MG, Bieksiene K, Birring SS, Chung KF, *et al.* Expert opinion on the cough hypersensitivity syndrome in respiratory medicine. *Eur Respir J.* 2014 Nov;44(5):1132-48.
57. Song WJ, Morice AH. Cough Hypersensitivity Syndrome: A Few More Steps Forward. *Allergy Asthma Immunol Res.* 2017 Sep;9(5):394-402.
58. Morice AH, Millqvist E, Bieksiene K, Birring SS, Dicpinigaitis P, Domingo Ribas C, *et al.* ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. *Eur Respir J.* 2020 Jan 2;55(1):1901136.
59. Chung KF, McGarvey L, Song WJ, Chang AB, Lai K, Canning BJ, *et al.* Cough hypersensitivity and chronic cough. *Nat Rev Dis Primers.* 2022 Jun 30;8(1):45.
60. Kanezaki M, Ebihara S, Gui P, Ebihara T, Kohzuki M. Effect of cigarette smoking on cough reflex induced by TRPV1 and TRPA1 stimulations. *Respir Med.* 2012 Mar;106(3):406-12.
61. S M, A M, Dubuis E, G M. Tobacco Smoke Induced Cough: Mechanisms Driving Acute and Chronic Cough Pathology [Internet]. Advanced Topics in Environmental Health and Air Pollution Case Studies. InTech; 2011. Available from: http://dx.doi.org/10.5772/21907. [cited September 29, 2023].
62. Morice AH, Fontana GA, Sovijarvi AR, Pistolesi M, Chung KF, Widdicombe J, *et al;* ERS Task Force. The diagnosis and management of chronic cough. *Eur Respir J.* 2004 Sep;24(3):481-92.
63. Poulose V, Tiew PY, How CH. Approaching chronic cough. *Singapore Med J.* 2016 Feb; 57(2): 60-3.
64. Groneberg DA, Nowak D, Wussow A, Fischer A. Chronic cough due to occupational factors. *J Occup Med Toxicol.* 2006 Feb 2;1:3.
65. Tarlo SM, Altman KW, Oppenheimer J, Lim K, Vertigan A, Prezant D, Irwin RS; CHEST Expert Cough Panel. Occupational and Environmental Contributions to Chronic Cough in Adults: Chest Expert Panel Report. *Chest.* 2016 Oct;150(4):894-907.
66. Lytras T, Kogevinas M, Kromhout H, Carsin AE, Antó JM, Bentouhami H, *et al.* Occupational exposures and incidence of chronic bronchitis and related symptoms over two decades: the European Community Respiratory Health Survey. *Occup Environ Med.* 2019 Apr;76(4):222-9.
67. Das B. Prevalence of respiratory symptoms and respiratory disorders among carpenters in India. *J Hum Ergol.* 2019;48:83-91.
68. Xie J, Chung KF, Lai K. Uncommon causes of chronic cough associated with airway eosinophilia. *J Thorac Dis.* 2021 May;13(5):3191-6.
69. Jiang XQ, Mei XD, Feng D. Air pollution and chronic airway diseases: what should people know and do? *J Thorac Dis.* 2016 Jan;8(1):E31-40.
70. 39 out of world's 50 most polluted cities are in India: IQAir report [Internet]. Available from: https://indianexpress.com/article/india/iqair-report-indian-worlds-most-polluted-cities-39-8498146/. [cited October 2, 2023].
71. Kaur R, Pandey P. Air Pollution, Climate Change, and Human Health in Indian Cities: A Brief Review. *Front Sustain Cities.* 2021;3:705131.

72. Kurt OK, Zhang J, Pinkerton KE. Pulmonary health effects of air pollution. *Curr Opin Pulm Med.* 2016 Mar;22(2):138-43.
73. Sato R, Gui P, Ito K, Kohzuki M, Ebihara S. Effect of Short-Term Exposure to High Particulate Levels on Cough Reflex Sensitivity in Healthy Tourists: A Pilot Study. *Open Respir Med J.* 2016 Dec 30;10:96-104.
74. Joad JP, Sekizawa S, Chen CY, Bonham AC. Air pollutants and cough. *Pulm Pharmacol Ther.* 2007;20(4):347-54.
75. Grabczak EM, Stec S, Dabrowska M, Plevkova J, Krenke R. Cough as a Cause and Consequence of Heart Dysfunction—Current State of Art. *Physiol Res.* 2020 Mar 27;69(Suppl 1):S105-21.
76. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al*; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021 Sep 21;42(36):3599-726.
77. Hu Y, Hua W, Li N, Huang H. Case Report: Premature Ventricular Beats-Induced Chronic Cough and Cough Syncope. *Front Med* (Lausanne). 2021 Mar 10;8:641948.
78. Stec S, Dabrowska M, Zaborska B, Bielicki P, Maskey-Warzechowska M, Tarnowski W, *et al.* Premature ventricular complex-induced chronic cough and cough syncope. *Eur Respir J.* 2007 Aug;30(2):391-4.
79. Brandon N. Premature atrial contraction as an etiology for cough. *Chest.* 2008 Mar;133(3):828.
80. Rao KNM. Diagnosis and management of chronic cough due to extrapulmonary etiologies. *Indian J Clin Pract.* 2014 Oct;25(5):437-42.
81. Lai K, Tang J, Zhan W, Li H, Yi F, Long L, *et al.* The spectrum, clinical features and diagnosis of chronic cough due to rare causes. *J Thorac Dis.* 2021 Apr;13(4):2575-82.
82. Prakash UBS. Uncommon causes of cough: ACCP evidence-based clinical practice guidelines. *Chest.* 2006 Jan;129(1 Suppl):206S-19S.

CHAPTER 8

Red Flags in Cough



We all know the significance of a thorough history when a patient first presents with a cough. An in-depth history of the events preceding the occurrence of cough, like a viral infection or any triggering factors, can sometimes help us determine the cause of cough. The onset of cough, whether sudden or gradual, can also assist us in determining what could have caused it.

While knowing if the cough is productive or nonproductive helps us rule out certain etiologies, the timing of cough also guides the determination of the likely diagnosis in certain cases. As discussed in a previous chapter, **history is critical while evaluating a patient presenting with cough**.

An integral part of history-taking is the evaluation of the patient for the presence of any warning signals or **"red flags"**.

Red flags are the signs that there is a possibility of a serious or even life-threatening cause behind the cough and should prompt specific diagnostic workup or referral to a specialist. One must never miss asking about or evaluating for red flags in a patient with cough, as missing something so crucial will make you misdiagnose the patient.

Red flags in the patient's history can indicate a serious condition such as pneumonia, pulmonary embolism, TB, etc.[1,2] A clinician must evaluate for red flags in the history of a patient with cough, irrespective of its classification, whether acute, subacute, or chronic. The presence of such warning signals can help us identify any underlying conditions that might endanger the patient's life.[3]

The red flags that one must screen for are mentioned below:[3-6]

Red flag signs

Noticeable dyspnea, particularly at rest	Peripheral edema and increase in weight
Tachypnea	Cyanosis
Blood in sputum	Suspicion of TB or pneumonia; history of TB; repeated episodes of pneumonia

Pain in thorax	Smoker's cough in people aged above 35
Weight loss	Immunosuppression or immunodeficient state
Elevated body temperature	History of cancer
Arterial hypotension	Inhalational intoxication
Tachycardia	Acute cardiac failure
Hoarse voice	Cough syncope
Swallowing difficulty	Urinary incontinence
Vomiting	Abnormal findings on chest X-ray that complement cough duration; abnormal findings on respiratory system examination

The presence of any of these warning signs should raise an alarm and must prompt further investigations.[4] The added investigations can help exclude various serious conditions, such as pulmonary embolism, pneumonia, exacerbation of an existing disease, etc.[2] For instance, hemoptysis can be seen in pulmonary embolism and bronchiectasis.[6]

If required, the patient presenting with cough and having any red flags should be referred to a specialist.

The Indian expert consensus group is of the opinion that urinary incontinence during cough and cough syncope should also be regarded as alarm signs.[2] Additionally, in areas endemic for TB, a history of TB must be assessed in patients with cough.[3] Considering the Indian scenario, Guleria and colleagues also advocate including a personal history of TB or history of TB in a close contact in the red flags.[4]

Concerning smoking, the CHEST guideline states that a new-onset cough, change in cough, or an accompanying disturbance in voice in a person who smokes and is aged above 45 years, be considered a red flag. Another alarm sign is current smokers or those who quit smoking within the past 15 years, 55 to 80 years of age, having a 30-pack-year history.[3]

Red flags in children

Children can also present with certain specific red flag signs. These include:[4,7,8]

- Cough beginning in the neonatal period
- Abnormality of voice/crying and cough during feeding; difficulty feeding
- Vomiting
- Pain in chest
- Feeling of choking
- Productive cough on a daily basis
- Dyspnea/tachypnea; exertional dyspnea
- Clubbing
- Deformity of the chest wall
- Pain in the face
- Purulent discharge from the nose
- Growth failure
- Hemoptysis
- Hoarseness of voice
- Cyanosis or hypoxia
- Frequent infections
- Neurodevelopmental issues
- Prior esophageal disease or lung disease
- Wheeze, crepitations.

Prominent red flags in the history of a child with cough can indicate the probable cause and require further evaluation.

KEY MESSAGES

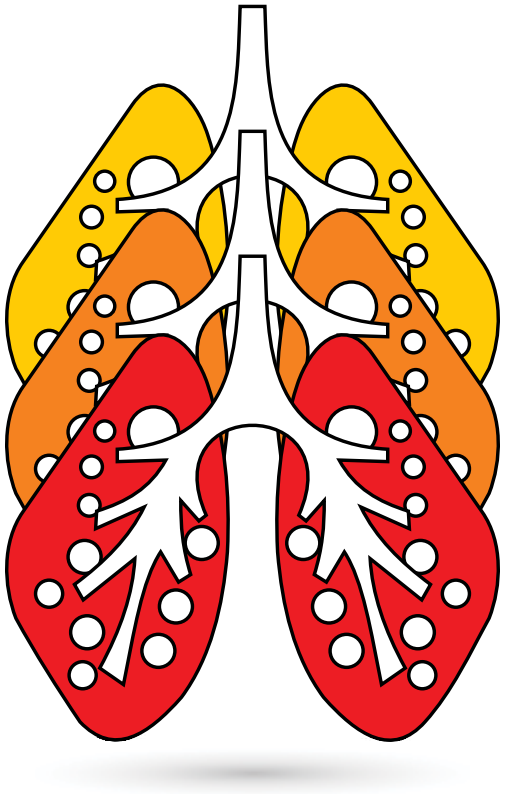
- Red flags in the patient's history can indicate a serious condition such as pneumonia, pulmonary embolism, TB, etc.
- The presence of any of the warning signs should prompt further investigations.
- The Indian expert consensus group opines that urinary incontinence during cough and cough syncope should also be regarded as alarm signs and considering the Indian scenario, including a personal history of TB or history of TB in a close contact in the red flags has been advocated.

References

1. Irwin RS, Oppenheimer JJ, Dunlap W, Lieberman JA, Chang AB. Yardstick for managing cough, part 1: In adults and adolescent patients older than 14 years of age. *Ann Allergy Asthma Immunol.* 2023 Mar;130(3):379-91.
2. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
3. Irwin RS, French CL, Chang AB, Altman KW; CHEST Expert Cough Panel*. Classification of Cough as a Symptom in Adults and Management Algorithms: CHEST Guideline and Expert Panel Report. *Chest.* 2018 Jan;153(1):196-209.
4. Guleria R, Dhar R, Mahashur A, Ghoshal AG, Jindal SK, Talwar D, *et al.* Indian Consensus on Diagnosis of Cough at Primary Care Setting. *J Assoc Physicians India.* 2019 Jan;67(1):92-8.
5. Holzinger F, Beck S, Dini L, Stöter C, Heintze C. The diagnosis and treatment of acute cough in adults. *Dtsch Arztebl Int.* 2014 May 16;111(20):356-63.
6. Kardos P, Dinh QT, Fuchs KH, Gillissen A, Klimek L, Koehler M, *et al.* German Respiratory Society guidelines for diagnosis and treatment of adults suffering from acute, subacute, and chronic cough. *Respir Med.* 2020 Aug-Sep;170:105939.
7. Cheng ZR, Chua YX, How CH, Tan YH. Approach to chronic cough in children. *Singapore Med J.* 2021 Oct;62(10):513-9.
8. Chang AB, Oppenheimer JJ, Irwin RS; CHEST Expert Cough Panel. Managing Chronic Cough as a Symptom in Children and Management Algorithms: CHEST Guideline and Expert Panel Report. *Chest.* 2020 Jul;158(1):303-29.

CHAPTER 9

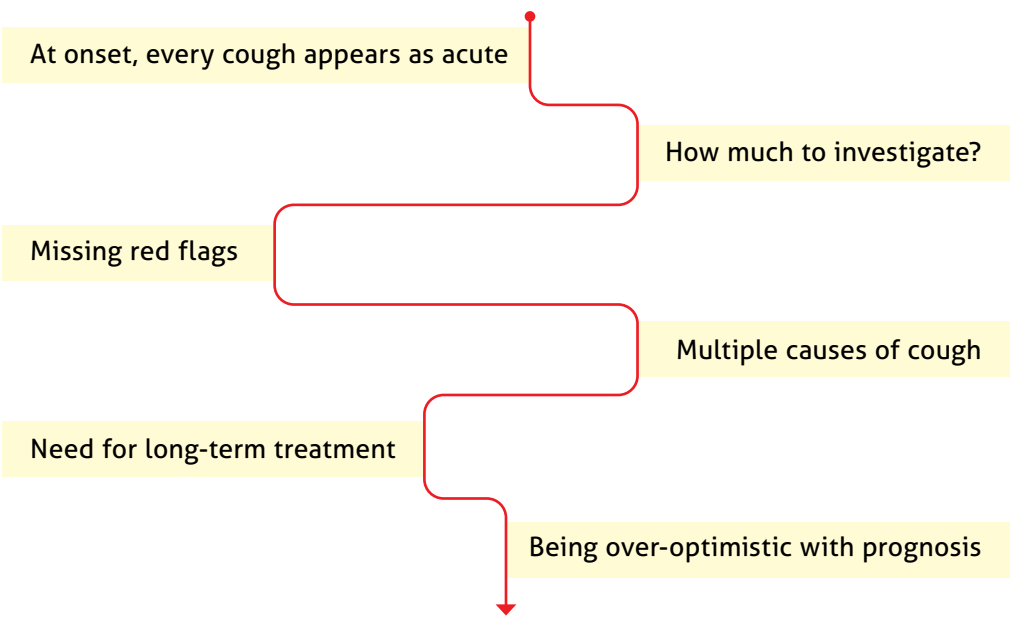
Pitfalls in Diagnosis and Management



Despite the advancements in the understanding of cough physiology and etiology, as well as its diagnostic workup and management, the diagnosis of cough continues to be a challenge, particularly in situations where there is no apparent cause or no significant radiological finding, the findings on physical examination are normal, and the history does not reveal anything specific.

A thorough history, physical examination, and investigations are all significant when approaching a patient with a cough. Despite following the recommended approach, clinicians sometimes fail to establish the correct diagnosis. Many times, multiple causes or conditions coexist in a patient that together cause cough. Failing to diagnose and address all the conditions can result in inadequate treatment and the cough can persist in the patient despite treatment.

Several pitfalls or errors can occur at the end of the clinician in diagnosis and management of cough which lands the clinician in a tough situation and plays a role in the patient losing faith in the doctor. These pitfalls should be avoided so that a diagnosis is made in time and adequate treatment can be initiated. Some common pitfalls are discussed in this chapter.



1. Every cough appears acute at the onset

When a patient comes to the clinician with a cough of 2 weeks' duration, it is addressed and treated as acute cough and the commonly known causes of acute cough are considered as the culprits, such as a viral URTI. The most likely cause of acute cough is considered to establish the diagnosis and the treatment is initiated based on that. Although this seems to be the correct approach at that point, we tend to forget that at the beginning, even chronic cough will appear as acute. It is only after the cough persists for over 8 weeks that we label it as chronic in an adult.[1] Even if the reason is a serious one, it may not come out in the beginning.

Therefore, it is important to take a detailed history, perform a thorough physical examination, and order the required investigations in order to determine the most likely causes of cough and then ascertain whether the cough in a particular patient would likely resolve in a few days or has the tendency to become chronic.

Additionally, if a patient presents with cough of a few days' duration, it is important to ascertain if the patient is suffering from a chronic disease, such as COPD or asthma. What may look like an acute cough might actually be a symptom of an acute exacerbation of a pre-existing chronic illness. Thinking that the cough is acute and will resolve on its own would be a mistake in such a situation as this acute exacerbation needs to be managed with appropriate medications.

At this stage, red flags should be carefully asked for and if present, appropriate investigations should be ordered.

2. The dilemma of how much to investigate

As discussed in Chapter 1, a clinician faces the challenge of deciding how many investigations are too many. The overlapping symptoms of various conditions can make it difficult for the doctor to decide which and how many investigations are needed. Also, even a remote possibility of a serious disease may warrant investigations.

In a country like ours, people in resource-poor settings or belonging to the lower socioeconomic group cannot afford too many or expensive investigations. The treating doctor must minimize this burden. This is where the knowledge and skill of identifying the cause of cough and reaching a diagnosis with minimal investigations come in handy.

Not ordering the relevant tests can also result in misdiagnosis or missing a diagnosis. For example, a chest X-ray reveals normal findings, and the history is not suggestive of an infectious disease. Rather, there is a history of anxiety disorder in the patient. Without differentiating it from a refractory cough or chronic idiopathic cough, the clinician diagnoses it as somatic cough and refers the patient. This is a mistake. One must follow a diagnostic protocol and all possible causes of cough, both common and rare, must be ruled out using relevant investigations before labeling it as somatic cough.

It is crucial not to be dogmatic in the beginning. One must always explain a differential diagnosis to the patient so that investigations can be suggested based on the same and the patient also understands the process of diagnosis and treatment. Often, it is prudent to explain to the patient that he/she is "under observation" and it is an evolving situation.

3. Missing red flags

Looking for the warning signs or red flags should be a part of the initial assessment of a patient with cough.[2] Identifying the red flags can help determine further investigations and failing to do so may render the diagnosis more challenging.

We have discussed the red flags in Chapter 8. Evaluation of red flags is a crucial part of history, whether it is acute, subacute, or chronic cough.[3] The presence of red flags in history can indicate a serious or even a life-threatening condition. Therefore, identifying such a warning signal in a patient with a cough can save time and assist in decision-making regarding further investigations.

Besides the well-known red flags, such as hemoptysis, weight loss, tachycardia, hoarseness of voice, cyanosis, etc., the Indian consensus groups also advocate the inclusion of a personal history of TB or history of TB in a close contact, urinary incontinence during cough, and cough syncope in the list of red flags.[1,4]

Missing the warning signs is a major pitfall in the diagnosis of cough and may prove fatal in certain situations. It can also open the floodgate of litigation.

4. Failure to identify multiple causes of cough

Another pitfall while approaching a patient with cough is not being able to recognize the fact that there can be more than one cause of cough in a patient, even if one cause is clearly apparent. Several studies have shown multiple causes of cough in patients with chronic cough. A recent study found multiple causes of cough in around 18.5% of the patients with chronic cough.[5]

There can be a patient with a cough who has a history of allergic disease, and simultaneously have GERD, postnasal drip, and bronchitis. Failing to recognize all of these underlying conditions and not treating all these conditions concurrently can lead to the persistence of cough.

5. Not treating for the appropriate duration

Stopping the treatment earlier than the required duration is another error that clinicians make. Several diseases known to cause chronic cough require long-term treatment. For example, in the case of GERD, it takes 2-3 months for the cough to resolve, although the symptoms of GERD may resolve early.

Guidelines recommend that PPI therapy should be given in patients with chronic cough when characteristic reflux symptoms are present. While reflux symptoms may improve early, cough may show improvement only after about 3 months of PPI therapy.[6]

It is, therefore, important to be aware of the actual duration of treatment required for cough to resolve, and also to explain this to the patient upfront.

6. Being over-optimistic with the prognosis

A clinician must recognize that in today's day and age, the prognosis of a disease is not what it was a decade ago. We live in times of increasing prevalence of lifestyle disorders. The cities are getting more and more polluted. Amid such situations, a cough may take longer than expected to resolve. While a cough due to a common cold usually resolves quickly, in some patients, it may take longer than usual. This could be attributed to the associated underlying diseases, the patient's environment and/or occupation, etc.

Therefore, a clinician must consider the history, presentation, differential diagnosis, associated comorbid conditions, and environmental factors while explaining the prognosis to the patient. He/she must steer clear of being too dogmatic about providing an exact timeline for the cough to resolve and rather explain all the factors that may play a role in making the prescribed treatment a success.

KEY MESSAGES

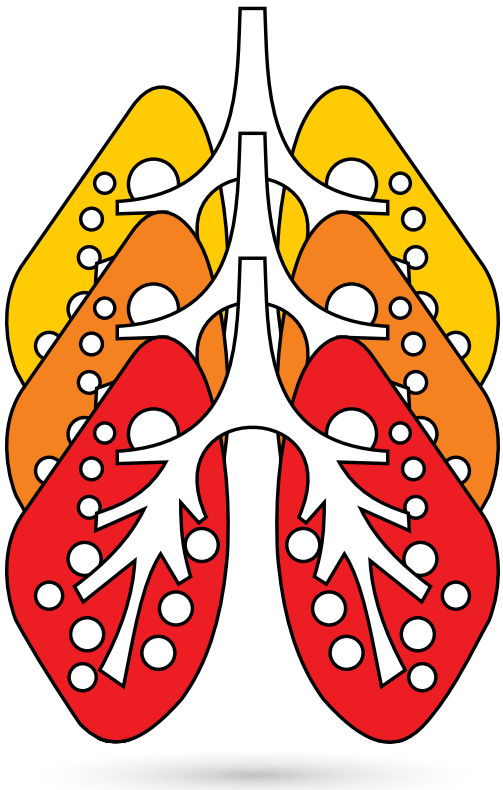
- Several pitfalls occur at the end of the clinician in diagnosis and management of cough which leads to negative outcomes. These pitfalls should be avoided for timely diagnosis and adequate management.
- Some common pitfalls include:
  - Every cough appears acute at the onset
  - Not being able to decide how much to investigate
  - Failing to identify the red flags
  - Failing to recognize multiple causes of cough
  - Treating for a shorter duration than needed
  - Being over-optimistic with the prognosis.
- At the onset, the cough will appear as acute and if there is a serious cause behind the cough, it will not surface unless the clinician digs deeper into the history and performs a thorough examination and orders the requisite investigations.
- It is important not to be dogmatic in the beginning and explain a differential diagnosis to the patient.
- Never miss red flags in the history of a patient with cough. Ask relevant questions and perform a thorough examination to determine if there are any warning signs with cough.
- Be cognizant of the fact that multiple causes of cough can coexist in a patient and need to be managed together in order to relieve cough.
- One must provide treatment for the appropriate duration to resolve cough.
- Recognize that in the times that we live in, prognosis of a disease is not what it was a few years ago. Be careful while discussing the prognosis with the patient and his relatives.

References

1. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
2. Perotin JM, Launois C, Dewolf M, Dumazet A, Dury S, Lebargy F, *et al.* Managing patients with chronic cough: challenges and solutions. *Ther Clin Risk Manag.* 2018 Jun 6;14:1041-51.
3. Irwin RS, Oppenheimer JJ, Dunlap W, Lieberman JA, Chang AB. Yardstick for managing cough, part 1: In adults and adolescent patients older than 14 years of age. *Ann Allergy Asthma Immunol.* 2023 Mar;130(3):379-91.
4. Guleria R, Dhar R, Mahashur A, Ghoshal AG, Jindal SK, Talwar D, *et al.* Indian Consensus on Diagnosis of Cough at Primary Care Setting. *J Assoc Physicians India.* 2019 Jan;67(1):92-8.
5. Supapannachart KJ, Fryd AS, Shelly S, Warrier A, Tkaczuk A, Hatcher JL, *et al.* Chronic cough etiology within a tertiary care center: A retrospective chart review. *Int J Adv Med Health Res.* 2022 Jul 1;9(2):101-6.
6. Kardos P, Dinh QT, Fuchs KH, Gillissen A, Klimek L, Koehler M, *et al.* German Respiratory Society guidelines for diagnosis and treatment of adults suffering from acute, subacute, and chronic cough. *Respir Med.* 2020 Aug-Sep;170:105939.

CHAPTER 10

Pollution and Cough



Air pollution is a problem that is widespread across the globe. Both indoor and outdoor air pollution are a health threat. Every year, as the winter approaches, the northern part of our country fights dense smog from the burning of crop residue. Vehicular pollution, emissions from industries, *chulhas* being used to cook food in rural areas and some parts of urban areas – all contribute to the rising air pollution and its devastating effects on human health.

The danger of air pollution looms both indoors and outdoors with an estimated 6.7 million deaths occurring due to outdoor or ambient and household air pollution annually. Around 99% of the people of the world, in other words, nearly everyone on the planet, resides in areas with pollution levels beyond the threshold set by the World Health Organization (WHO).[1] In the year 2022, India ranked 8th among the most polluted countries across the globe. The average $PM_{2.5}$* concentration was 53.3 µg/m^3, way exceeding the annual threshold set at 5 µg/m^3 by the WHO.[2]

There are several types of air pollutants, such as particulate matter, dust, ammonia, sulfur oxide, nitrogen oxide, carbon monoxide, smog, ozone, etc. Air pollution can be associated with respiratory infections and chronic diseases of the respiratory system.[3] Air pollution has been linked to respiratory symptoms and impaired lung function. Pollutants tend to heighten wheezing and cough. The effects of pollutants can be so harmful that exposure during childhood could be associated with cough and wheeze later in life.[4]

How do pollutants cause cough? Activation of TRPA1 and TRPV1 channels by particulate matter plays a role in the cough reflex. Exposure to elevated levels of particulate matter is associated with a decreased cough reflex threshold as well as urge to cough threshold.[5]

An article by Joad and colleagues noted that pollutants like particulate matter, gases, mixed pollutants, and environmental tobacco smoke increase cough to varying degrees. Particulate matter and mixed pollutants seem to increase cough and wheezing, while gases predominantly increase wheezing, compared to cough.[4]

*Particulate matter

Evidence showing a link between air pollution and cough

Several studies have shown a link between air pollutants and cough. Let us have a look at the findings from some of the studies.

A study by Doiron and colleagues evaluated the association of ambient air pollution exposure with chronic bronchitis and symptoms of cough or sputum. Pollutants were found to be associated with prevalent cough or sputum symptoms in the study.[6]

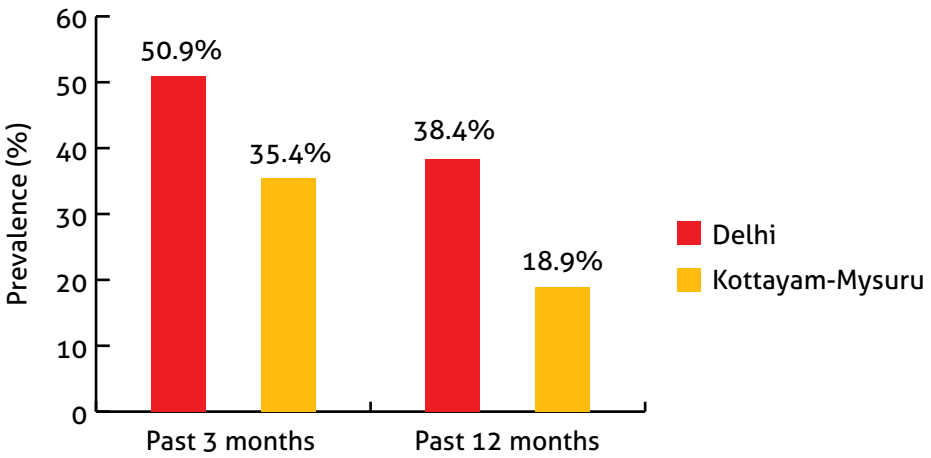
Sato and colleagues evaluated the impact of exposure to high levels of particulate matter over a short duration on cough reflex threshold, urge to cough, lung function, and QoL associated with cough among healthy individuals who visited Beijing (residing in Japan). The investigators noted that the cough reflex thresholds were reduced during the Beijing visit in comparison with prior to and after the visit. Lower vital capacity, FVC, FEV_1, and FEV_1/FVC were noted while the participants were in Beijing, compared to preceding the visit. Threshold for urge to cough and the Leicester Cough Questionnaire-acute (LCQ-acute) score were also reduced during the visit.[5] The study shows that even short-term exposure to elevated levels of particulate matter can alter the cough reflex, urge to cough, and lung function parameters.

Zhang *et al* evaluated the link between cough phenotypes and air pollution in adults from Australia. Pollution linked to traffic was found to be linked to cough incidence as well as phenotypes. A link was noted between residing within 200 meters of a major road and escalated risk of incident chronic cough and having a frequent wheezy cough phenotype at 53 years of age.[7]

A study conducted among healthy children found that exposure to environmental tobacco smoke affected cough reflex sensitivity, particularly in females. Environmental tobacco smoke exposure was associated with higher cough reflex sensitivity among girls. Dry cough of over 3 weeks' duration had a greater incidence in girls having exposure to environmental tobacco smoke compared to girls not having such exposure.[8] Salvi and colleagues conducted a study among adolescents in Delhi to determine the prevalence of respiratory and allergic symptoms and asthma. This was compared with data for children from Mysuru and

Kottayam (comparatively less polluted). The prevalence of asthma was high among Delhi children. Self-reported prevalence of cough was higher in Delhi children (Figure 1).[9]

Figure 1. Prevalence of self-reported cough over the past 3 and 12 months in children in Delhi and Kottayam-Mysuru



An individual's occupation can expose him/her to air pollution, for example, traffic police personnel. A study from Bengaluru noted that traffic police officers struggle with respiratory issues. The study included 217 traffic police officers. Among these, 12.9% were found to have chest symptoms, including cough and difficulty in breathing. Additionally, exacerbation of symptoms at work was evident in 20.3% of the participants.[10]

All these studies, and many more, from various parts of the world, have shown that air pollution has an adverse impact on the respiratory health of an individual. Elevated levels of air pollution can be associated with symptoms like cough and wheeze. Therefore, a good clinician is one who never misses asking the patient about exposure to environmental pollutants. Asking about occupational exposure to air pollutants and ambient air pollution in general right at the time of history taking will avert misdiagnosis and unnecessary medications.

What can you do to help patients with cough related to air pollution?

- To begin with, advise your patients to wear a mask when venturing out. COVID-19 has taught us an important lesson, although in a very harsh way. But learning from our experiences during the pandemic, wearing an N-95 mask when going out is a good option to minimize exposure to pollutants.
- To limit the pollution indoors, advise your patients to install air purifiers.
- People in rural areas must be encouraged to use clean fuels for cooking.
- Treatment can be initiated based on the symptoms and the underlying disease diagnosed after thorough evaluation.

KEY MESSAGES

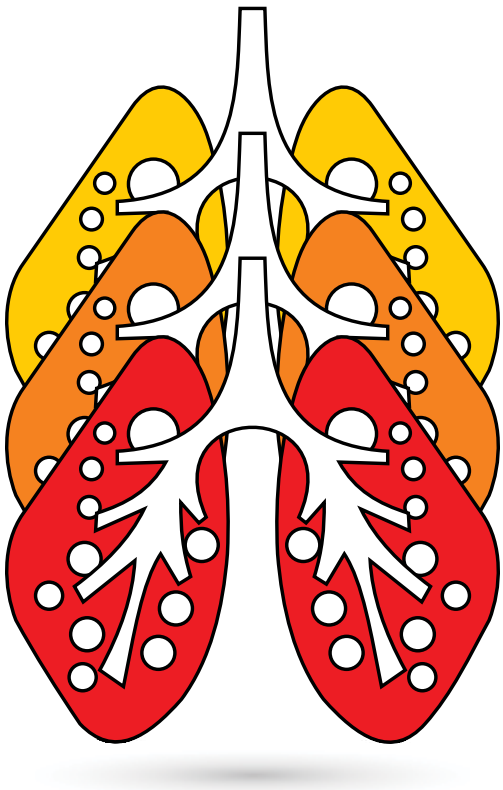
- Air pollution can be associated with respiratory infections and chronic respiratory diseases and has been tied to various respiratory symptoms and impaired lung function.
- Effects of pollutants can be so harmful that exposure during childhood could be associated with cough and wheeze later in life.
- Exposure to high levels of particulate matter have been linked to a decreased cough reflex threshold as well as urge to cough threshold.
- Published literature has shown a link between air pollutants and cough.
- Exposure to high levels of particulate matter even for a short duration can alter the cough reflex, urge to cough, and lung function parameters.
- It is important to assess a history of indoor and outdoor pollution exposure in a patient presenting with cough to prevent misdiagnosis and provide appropriate treatment.

References

1. Air pollution data portal [Internet]. Available from: https://www.who.int/data/gho/data/themes/air-pollution. [cited October 18, 2023].
2. India 8th most polluted country in the world, Delhi country in the world, Delhi 4th most polluted city [Internet]. Available from: https://timesofindia.indiatimes.com/city/delhi/india-8th-most-polluted-country-in-world-delhi-4th-most-polluted-city/articleshow/98643631.cms?from=mdr. [cited October 18, 2023].
3. Kaur R, Pandey P. Air Pollution, Climate Change, and Human Health in Indian Cities: A Brief Review. *Front Sustain Cities.* 2021;3:705131.
4. Joad JP, Sekizawa S, Chen CY, Bonham AC. Air pollutants and cough. *Pulm Pharmacol Ther.* 2007;20(4):347-54.
5. Sato R, Gui P, Ito K, Kohzuki M, Ebihara S. Effect of Short-Term Exposure to High Particulate Levels on Cough Reflex Sensitivity in Healthy Tourists: A Pilot Study. *Open Respir Med J.* 2016 Dec 30;10:96-104.
6. Doiron D, Bourbeau J, de Hoogh K, Hansell AL. Ambient air pollution exposure and chronic bronchitis in the Lifelines cohort. *Thorax.* 2021 Jan 28;76(8):772-9.
7. Zhang J, Lodge C, Chang A, Knibbs L, Abramson M, Walters EH, *et al*. Associations between ambient air pollution and chronic cough in middle-aged adults. *Eur Respir J.* 2022 Sep;60 (suppl 66):3357.
8. Demoulin-Alexikova S, Plevkova J, Mazurova L, Zatko T, Alexik M, Hanacek J, Tatar M. Impact of Air Pollution on Age and Gender Related Increase in Cough Reflex Sensitivity of Healthy Children in Slovakia. *Front Physiol.* 2016 Feb 23;7:54.
9. Salvi SS, Kumar A, Puri H, Bishnoi S, Asaf BB, Ghorpade D, *et al*. Association between air pollution, body mass index, respiratory symptoms, and asthma among adolescent school children living in Delhi, India. *Lung India.* 2021 Sep-Oct;38(5):408-15.
10. Gowda G, Thenambigai R. A Study on Respiratory Morbidities and Pulmonary Functions among Traffic Policemen in Bengaluru City. *Indian J Community Med.* 2020 Jan-Mar;45(1):23-6.

CHAPTER 11

Multiple Cause Cough



It is well known that cough can be a presenting symptom in various respiratory diseases as well as nonrespiratory disorders, for instance, GERD. Cough is a symptom with a multifactorial etiology.

While we are well aware of the common causes of acute, subacute, and chronic cough, there are times when the most obvious cause or the commonest known cause is not actually the cause in our patient, or it may not be the only cause of cough in a particular case. However, we, as clinicians, tend to settle down for the most obvious cause of the cough, start treating the same, and fail to get a positive outcome. There can be more than one cause of cough in a patient and the symptoms of various conditions may overlap in the same patient, thus making it difficult to establish the correct diagnosis.

So, when cough defies a clear diagnosis, multiple causes could be simultaneously causing cough. In such cases, all the causes must be addressed together rather than treating them one after the other, sequentially.

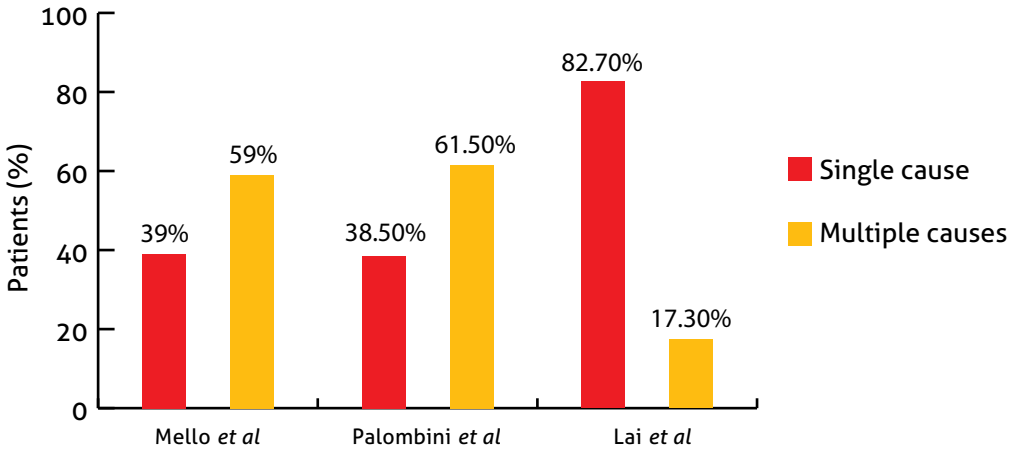
Let us understand this with the help of an example. A patient presents with a severe, nonproductive cough. The patient is obese and has features suggestive of CVA and GERD. History reveals that the patient is also prone to allergies and has postnasal drip too. In such a case, all these factors might collectively be responsible for the patient's cough. If the clinician tries to address the most common cause, it is likely that the patient will not get relief. However, if the clinician successfully identifies all the factors that could be responsible for the patient's cough and initiates treatment for all the causes simultaneously, the odds are quite high that the patient will be relieved of cough.

As another example, in a patient with cough, the clinician identifies UACS as the cause and starts treatment. However, despite the best possible treatment, the cough persists. Eventually, the clinician takes the history again and realizes that he/she missed the history of environmental exposure, smoking, and ACE inhibitor use. Unless all these factors are also addressed along with UACS, the cough will not resolve.

How common is multiple cause cough?

It is not uncommon for a patient to have a cough due to more than one underlying etiology. Irwin and colleagues published a report wherein they found that in about 73% of the patients, chronic cough occurred as a result of one condition. In around 23% of the patients, it was due to two disorders, and in about 3% of the patients, three conditions were responsible for causing cough.[1] A study by Smyrnios *et al* noted that 38% of the patients who had chronic cough and history of excessive expectoration had cough from one cause. Around 36% had cough due to two causes, while in 26% of the patients, there were three causes behind cough.[2] In a study by Mello and colleagues, conducted among patients with chronic cough, 39% of the patients had only one cause of cough, while 59% had several causes (Figure 1), with GERD, PNDS, and asthma being the three commonest causes.[3] Palombini *et al* noted in their study that 38.5% of the patients with chronic cough had one cause while 61.5% of the patients had several causes of cough (Figure 1).[4] Another study by Lai and colleagues noted a single reason for chronic cough in 82.7% of the patients and multiple reasons in 17.3% of the patients (Figure 1).[5]

Figure 1. Patients with single and multiple causes of cough in different studies



It is clear from the available evidence that though the frequency varies across studies, cough due to a multitude of etiologies is not a rare occurrence. A clinician must therefore approach a patient with a cough with an open mind and consider multiple causes where the cough seems to evade a clear diagnosis, especially if it fails to respond adequately to the treatment.

Failure to address multiple causes of cough

Failing to treat multiple cause cough appropriately can have some serious consequences. First, initiating treatment for the most common or the most obvious cause may not resolve the cough completely. This is because other etiologies are also at play simultaneously.

Second, the patient tends to lose faith in the treating physician and the treatment overall, as despite taking medications, the cough persists.

Hence, the treatment should also be multifaceted, addressing the multiple causes of cough simultaneously in the patient. In my opinion, all the causes should be treated together to have the best outcome and once the cough is relieved or resolved, treatment for the cause least likely to have a major contributory effect should be stopped sequentially.

KEY MESSAGES

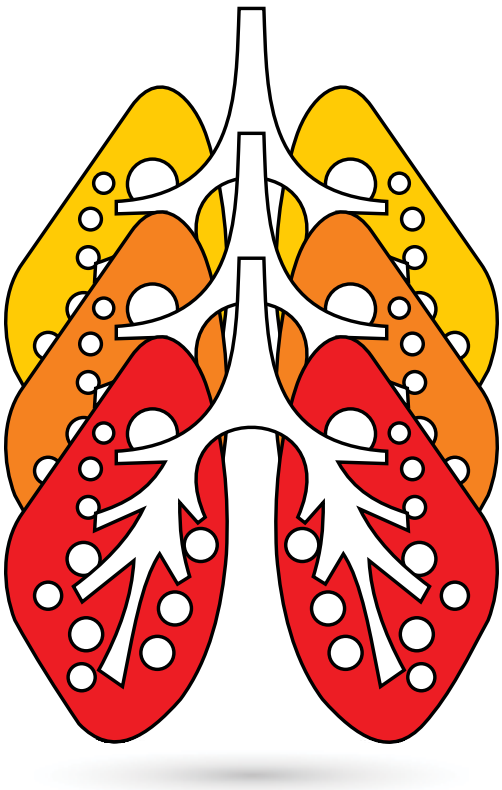
- There can be more than one cause of cough in a patient and the symptoms of various conditions may overlap in the same patient, thus making it difficult to establish the correct diagnosis.
- Published literature shows that it is not uncommon for a patient to have a cough due to more than one underlying etiology.
- The treatment for multiple cause cough should address the myriad causes **simultaneously and not one after the other as an afterthought**.

References

1. Irwin RS, Curley FJ, French CL. Chronic cough. The spectrum and frequency of causes, key components of the diagnostic evaluation, and outcome of specific therapy. *Am Rev Respir Dis.* 1990 Mar;141(3):640-7.
2. Smyrnios NA, Irwin RS, Curley FJ. Chronic cough with a history of excessive sputum production. The spectrum and frequency of causes, key components of the diagnostic evaluation, and outcome of specific therapy. *Chest.* 1995 Oct;108(4):991-7.
3. Mello CJ, Irwin RS, Curley FJ. Predictive values of the character, timing, and complications of chronic cough in diagnosing its cause. *Arch Intern Med.* 1996 May 13;156(9):997-1003.
4. Palombini BC, Villanova CA, Araújo E, Gastal OL, Alt DC, Stolz DP, Palombini CO. A pathogenic triad in chronic cough: asthma, postnasal drip syndrome, and gastroesophageal reflux disease. *Chest.* 1999 Aug;116(2):279-84.
5. Lai KF, Chen RC, Liu CL, Luo W, Zhong SQ, He MZ, *et al.* [Etiology and a diagnostic protocol for patients with chronic cough]. *Zhonghua Jie He He Hu Xi Za Zhi.* 2006 Feb;29(2):96-9.

CHAPTER 12

Misuse of Antibiotics in Cough



We are now familiar with the common causes of cough. We, therefore, also recognize that the majority of coughs do not stem from bacterial infections. Regrettably, individuals frequently resort to antibiotics to treat a cough even though such treatment is unnecessary. This misapplication of antibiotics can result in more harm than benefit, as it may lead to undesirable side effects and contribute to the issue of antibiotic resistance.

Acute viral URTI or common cold and acute bronchitis are frequently associated with acute cough in the adult population. Acute bronchitis is generally caused by viruses, although bacterial infections account for around 10% of cases. There are other causes as well, such as acute rhinosinusitis, exacerbation of COPD, etc.[1] These have been discussed in a previous chapter. In cases without major coexisting health issues, acute cough resolves on its own.[2]

Chronic cough is often a prominent feature of various chronic respiratory illnesses and can also be the only symptom in certain extrapulmonary diseases, like gastrointestinal disorders.[2] Managing such cases can be a challenge for physicians and can seriously impair the patient's QoL. However, antibiotics may not be useful in such situations.

It is important to determine the cause of cough to treat it appropriately and avoid using unnecessary antibiotics that may have no particular role in treating the patient's cough.

Is there a need for antibiotics in the treatment of cough?

A cough is usually linked to a viral infection, commonly caused by viruses like influenza, parainfluenza, rhinovirus, coronavirus, RSV, and adenovirus. However, infection with pathogens other than viruses, including *B. pertussis* and *M. pneumoniae*, is also possible. In certain cases, secondary bacterial infections may also occur, often involving *H. influenzae* and *S. pneumoniae*.[3]

Distinguishing viral from bacterial infections based solely on symptoms is difficult.[3] Clinicians are, therefore, faced with the challenge of whether to prescribe antibiotics for cough or not.

So, to address the question of whether antibiotics are necessary for treating cough, let us look at a systematic review of randomized controlled trials. Researchers investigated the effectiveness of antibiotics in treating acute cough in community settings. The results showed that antibiotics did not perform any better than placebo in resolving cough at 7-11 days. Antibiotics were not associated with any significant improvement in the resolution of illness. Around 19% of the subjects reported side effects from antibiotic treatment.[3]

This review indicates that antibiotics do not contribute to the improvement of acute cough. On the contrary, antibiotic treatment may lead to side effects in some patients.[3]

In a study involving 416 adults with acute bronchitis and discolored sputum, antibiotics or ibuprofen did not appear to be more effective than placebo in reducing the duration of cough. None of the two could increase the likelihood of resolution of cough when compared with placebo. However, adverse effects were notably more common with antibiotic treatment (12%) compared to ibuprofen (5%) or placebo (3%).[4]

Despite the apparent inefficacy of antibiotics in treating cough, as evidenced by the aforementioned data, more than half of the patients presenting with acute cough or LRTIs are given antibiotic prescriptions in primary care settings.[5]

Even in patients with exacerbation of COPD, where antibiotics are prescribed, a Cochrane review noted that the effects of antibiotics appear to be small and inconsistent for certain outcomes, such as treatment failure, while there seems to be no effect for certain other outcomes like duration of stay in the hospital

and mortality. Antibiotics, however, appear to be beneficial for patients in the intensive care unit (ICU).[6]

Misuse of antibiotics

Antibiotic misuse is quite common in clinical practice for conditions like cough and cold, even though their use is not advised in such conditions.

A survey of clinicians in Kolkata hospitals revealed unanimous agreement that antibiotics were irrationally used. Over half of the respondents (55.4%) considered this misuse frequent and in need of significant correction. About 50.76% believed that oral antibiotics were more commonly misused than injectable or topical preparations. Cough and cold (78.46%) were identified as the most common conditions associated with antibiotic misuse.[7]

In a hospital-based Tanzanian study involving 384 children with diarrhea and cough, 84.9% were prescribed antibiotics, including penicillins, aminoglycosides, sulphonamides, and macrolides. Alarmingly, 68.9% of the children having common cold received inappropriate antibiotic prescription.[8]

In an analysis of prospective observational data, 52.7% of patients having acute cough or LRTI were prescribed antibiotics. According to the ERS/European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines, antibiotics could have been validated for 71.2% of these patients based on their clinical presentation.[9]

While antibiotics are used inappropriately in healthcare settings by clinicians, patients also contribute to misuse of antibiotics. When prescribed antibiotics, patients must follow the doctor's advice and take the antibiotics appropriately. Failure to take the prescribed treatment appropriately can have an adverse impact in terms of health outcomes, unnecessary expenditure, and frustration if the patient's condition does not improve. Unused antibiotics due to incomplete antibiotic course, lying around in the house, is also a health hazard.

A study with 2520 patients with cough or LRTIs revealed that a large proportion of patients do not adhere to antibiotic prescriptions. Around 41.2% of the patients prescribed immediate antibiotics did not take the medication. About 44.2% completed the prescribed course. Of note, around 30.4% of the patients took

no antibiotic during the study follow-up. Among those who did not receive an antibiotic prescription at the initial consultation, 11.6% took an antibiotic.[5] This represents a gross misuse of antibiotics on the part of the patients.

What do the guidelines recommend?

The ACCP guidelines do not advocate the use of antibiotics for patients with acute bronchitis. The guidelines recommend antibiotic use in patients with whooping cough.[10]

The Indian consensus group favors antibiotic use in case of productive cough or the presence of purulent sputum. Additionally, a subacute cough caused by bacteria should be treated with antibiotics.[11] The CTS guidelines also recommend antibiotic use when the patient has purulent sputum.[12]

Additionally, according to the NICE guidelines, when dealing with acute cough related to acute bronchitis, routine antibiotic use is not recommended in individuals who are not severely unwell or have a higher complication risk. This approach acknowledges several important considerations. Firstly, antibiotics do not generally contribute to an overall improvement in the clinical condition of individuals suffering from acute bronchitis. Secondly, while they may marginally reduce the duration of cough symptoms by approximately half a day on average, the benefit is limited. Lastly, the use of antibiotics can lead to potential adverse effects.[13] Antibiotic therapy should be given to patients who are too unwell or have an increased risk of complications.[13]

Need for antibiotic stewardship program

Antibiotic stewardship is crucial for combating antibiotic resistance. It focuses on ensuring the appropriate use of antibiotics by considering drug selection, dosing, and duration to improve patient care. Evidence shows that stewardship programs increase the likelihood of patients receiving relevant guideline-based treatment. With such programs, patients have been found to have higher odds of being cured and lesser odds of experiencing treatment failures.[14]

KEY MESSAGES

- The majority of coughs do not result from bacterial infections, and the misuse of antibiotics for treating cough can lead to undesirable side effects and antibiotic resistance.
- Acute cough typically resolves on its own, and the primary causes include viral URIs, acute bronchitis, and other respiratory conditions.
- Antibiotics do not significantly improve acute cough, and their use can lead to side effects, making their prescription for cough treatment questionable.
- Misuse of antibiotics, both at the end of the doctor and the patient, can have adverse health outcomes and result in antibiotic resistance, which is a significant global health threat.

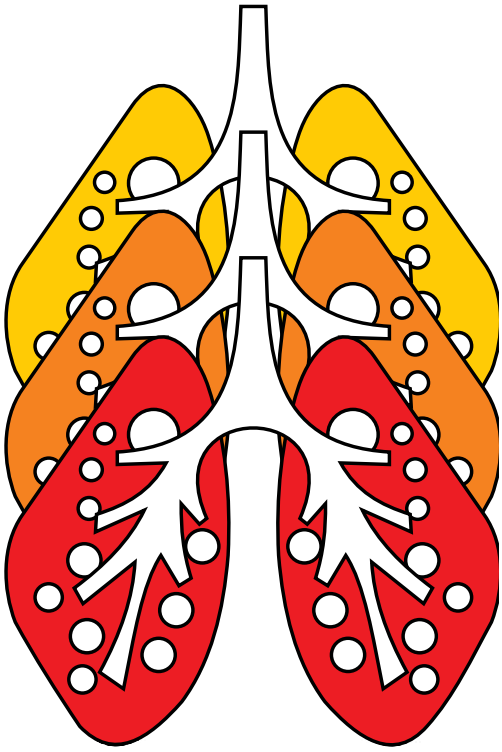
References

1. Sharma S, Hashmi MF, Alhajjaj MS. Cough. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493221/. [cited October 28, 2023].
2. Morice AH, McGarvey L, Pavord I; British Thoracic Society Cough Guideline Group. Recommendations for the management of cough in adults. *Thorax.* 2006 Sep;61 Suppl 1(Suppl 1):i1-24.
3. Fahey T, Stocks N, Thomas T. Quantitative systematic review of randomised controlled trials comparing antibiotic with placebo for acute cough in adults. *BMJ.* 1998 Mar 21;316(7135):906-10.
4. Llor C, Moragas A, Bayona C, Morros R, Pera H, Plana-Ripoll O, *et al*. Efficacy of anti-inflammatory or antibiotic treatment in patients with non-complicated acute bronchitis and discoloured sputum: randomised placebo controlled trial. *BMJ.* 2013 Oct 4;347:f5762.
5. Francis NA, Gillespie D, Nuttall J, Hood K, Little P, Verheij T, *et al*; GRACE Project Group. Antibiotics for acute cough: An international observational study of patient adherence in primary care. *Br J Gen Pract.* 2012 Jun;62(599):e429-37.
6. Vollenweider DJ, Frei A, Steurer-Stey CA, Garcia-Aymerich J, Puhan MA. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2018 Oct 29;10(10):CD010257.
7. Chatterjee D, Sen S, Begum SA, Adhikari A, Hazra A, Das AK. A questionnaire-based survey to ascertain the views of clinicians regarding rational use of antibiotics in teaching hospitals of Kolkata. *Indian J Pharmacol.* 2015 Jan-Feb;47(1):105-8.
8. Gwimile JJ, Shekalaghe SA, Kapanda GN, Kisanga ER. Antibiotic prescribing practice in management of cough and/or diarrhoea in Moshi Municipality, Northern Tanzania: cross-sectional descriptive study. *Pan Afr Med J.* 2012;12:103.

9. Wood J, Butler CC, Hood K, Kelly MJ, Verheij T, Little P, *et al*. Antibiotic prescribing for adults with acute cough/lower respiratory tract infection: congruence with guidelines. *Eur Respir J.* 2011 Jul;38(1):112-8.
10. Braman SS. Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines. *Chest.* 2006 Jan;129(1 Suppl):95S-103S.
11. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al*. INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
12. Lai K, Shen H, Zhou X, Qiu Z, Cai S, Huang K, *et al*. Clinical Practice Guidelines for Diagnosis and Management of Cough-Chinese Thoracic Society (CTS) Asthma Consortium. *J Thorac Dis.* 2018 Nov;10(11):6314-51.
13. National Institute for Health and Care Excellence. Cough (acute): antimicrobial prescribing. NICE guideline [Internet]. [London]: NICE;2019 [cited October 29, 2023]. [NG120]. Available at: https://www.nice.org.uk/guidance/ng120.
14. Butt MA, Peicher M, Nguyen AP, Sheikh AB. Antibiotic Stewardship in Patients With Acute Bronchitis: A Case Report of Doxycycline-Induced Esophagitis. *Cureus.* 2022 Jun 26;14(6):e26354.

CHAPTER 13

Drugs for Cough



Pharmacological treatment of cough should be based on the underlying etiology. It is crucial to make a diagnosis in a patient with chronic cough and then initiate pharmacotherapy in order to have the best outcomes. Not diagnosing the cause behind the patient's cough can result in inappropriate and inadequate treatment.

Furthermore, acute cough usually resolves on its own and does not require pharmacotherapy. But in some patients, who complain of distressing cough, symptomatic treatment can be considered.

The Indian consensus group reached a near consensus that pharmacotherapy is not required in patients with an acute cough that is mild. If the cough increases, the group of experts opined that the patient can be given medication therapy.[1] Among patients who are being given etiological or causal treatment, symptomatic treatment can also be added.[2,3]

Drugs used for the management of cough

The medications used to manage cough can be divided into two groups:

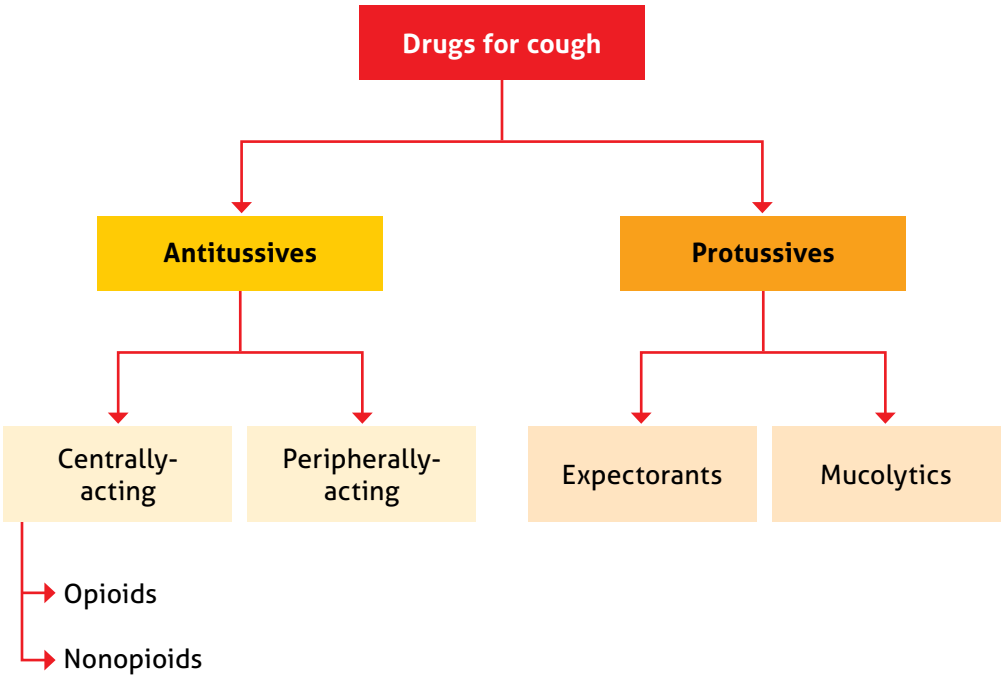
- Antitussive agents
- Protussive agents.

Antitussives are drugs that suppress cough (cough suppressants). Protussives are agents that help with the expectoration of sputum.[3] Figure 1 summarizes the categories of antitussives and protussives in cough management.[1,3,4]

Besides the aforementioned agents, other agents are also available for cough management, including:[1]

- Antihistamines
- Decongestants
- Bronchodilators
- Antibiotics
- Steroids.

Figure 1. Antitussives and protussives in cough management



Let us have a look at these agents one by one.

Antitussive agents

The action of antitussives can be on the cough receptors present on the afferents and efferents and on the cough reflex arc, or they may act centrally on the cough center in the medulla.[4] Antitussives are indicated in dry cough.[5]

As mentioned above, antitussives are divided into centrally-acting and peripherally-acting agents.[4] The central antitussives are further subdivided into opioids and nonopioids.[3]

Central antitussives

Opioid antitussives—Opioid agents bind to the opioid receptors present in the cough center and have an inhibitory action.[3,4] These include morphine, codeine, and pholcodine.[4,6] These antitussives can be addictive.[4] Codeine can be metabolized to morphine at a fast pace in some patients, thus increasing its levels in the body, which can be deleterious. Opioids can interfere with psychomotor activity and can also affect cognitive function.[7] They may also depress breathing.[3] As a result, the use of opioid agents is generally not recommended.

Codeine is known to have sedative and analgesic actions and can help in cases of severe cough and in cases of refractory cough or nonproductive cough associated with pain in the chest.[4] Opioids do not have a role in productive cough.[3]

The evidence is not in favor of using codeine in cases of acute cough and the Indian consensus group is also opposed to the use of codeine for acute and subacute cough patients.[1] The use of codeine is not allowed in children below 12.[7]

Nonopioid antitussives—Nonopioid drugs are rather favored in the antitussive class of agents, with dextromethorphan being the choice in cases of acute cough (nonproductive).[1] Dextromethorphan has central action but does not cause sedation, as opposed to codeine.[4] It can suppress acute cough and has a lower addictive potential.[1,3] The CTS cough guidelines also recommend the use of dextromethorphan in adults for chronic cough.[4] Dextromethorphan has a prolonged effect, thanks to its slow penetration across the blood-brain barrier. It has a slow onset of action.[8]

Peripheral antitussives

Levodropropizine is a peripheral antitussive that has an action on the peripheral receptors. It regulates the sensory neuropeptides in the respiratory tract. It has also been reported to have an inhibitory effect on the vagal C-fibers.[6,7]

The drug can be used to manage dry cough.[1] Published literature has found it to be superior to centrally-acting antitussives in decreasing cough frequency and severity and has efficacy in both adults and children. It is also better than the central antitussives when it comes to the patient waking up at night.[9] The Indian expert group was also able to make a near consensus for the use of levodropropizine in acute nonproductive cough.[1]

Points to consider

- ✓ Formulations containing codeine should not be used in patients with acute and subacute cough.[1]
- ✓ Nonopioid antitussive agents should be used for empiric treatment of cough.[1]
- ✓ Dextromethorphan is the choice of antitussive for acute nonproductive cough.[1]

Protussive agents

Protussive or mucoactive agents work in multiple ways. They tend to reduce the excessive mucus secretion, decrease the viscosity of mucus, and facilitate the clearance of mucus.[1,3] They increase the secretion amount and decrease cough receptor irritation.[3,6]

Guaifenesin

Guaifenesin is an expectorant that increases the secretion volume and decreases the viscosity of mucus. It reduces the amount of viscous mucus and is known to dilate the bronchi.[1,4] Guaifenesin is useful in conditions like acute URTIs and stable chronic bronchitis where increased secretion of mucus is evident.[10] In acute bronchitis, guaifenesin is reported to have an action on cough receptor hypersensitivity caused by viruses.[3] The agent is safe to be used both in adults and children.[10]

The drug is combined with antitussives, decongestants, and antihistamines to manage cough.[4]

Ambroxol and bromhexine

Bromhexine and its metabolite ambroxol tend to reduce the secretion of mucus. Ambroxol reduces mucus viscosity and enhances the expiratory flow, thus improving the clearance of cough.[1,2] It also enhances the activity of cilia.[4] These agents also have anti-inflammatory action.[1]

Ambroxol seems to have favorable effects in managing productive cough in acute bronchitis.[2] Using bromhexine along with antibiotics seems to enhance the antibiotic's action.[1]

N-acetylcysteine

N-acetylcysteine is a mucolytic agent that seems to reduce the viscosity of secretions.[1] It has an impact on the production of mucus and also enhances mucociliary transport. It is also known to have antioxidant and anti-inflammatory actions.[2]

The Indian EMA position paper states that mucolytics such as N-acetylcysteine may have a role in patients with chronic sinusitis. It further states that N-acetylcysteine could contribute to symptomatic relief in patients with chronic bronchitis.[2] This agent may be of particular help for patients who find it difficult to expectorate.[1]

Points to consider

- ✓ Guaifenesin and N-acetylcysteine may be helpful for patients having difficulty in coughing up the sputum.[1]
- ✓ The Indian consensus group advocates short-term use of mucolytic agents. It recommends bromhexine or ambroxol and either guaifenesin or N-acetylcysteine for productive cough.[1]
- ✓ Mucolytic agents may have a favorable role in chronic sinusitis.[2]

Antihistamines

First-generation antihistamines appear to have a role in managing cough.[8] However, they are not recommended as monotherapy. Rather, their use along with decongestants can be beneficial in cough with common cold.[4] According to the Indian EMA position paper, the use of first-generation antihistamines and

decongestants has been advocated for managing UACS due to nonallergic rhinitis and common cold. However, in the case of allergic rhinitis, the paper recommends oral second-generation antihistamine and intranasal ICS.[2]

Diphenhydramine, a first-generation antihistamine, has the potential to suppress cough reflex sensitivity.[11] The Indian consensus group reached a near consensus for levocetirizine in managing dry cough.[1]

Decongestants

Decongestants, combined with histamine type 1 receptor (H_1) antihistamines with anticholinergic effect, seem to have a favorable effect on cough in UACS.[3] Their use has been recommended only as combination preparations when combined with an antihistamine or antitussive for managing cough in patients with rhinitis or common cold.[1] Nasal decongestants should be used for a short duration of <1 week and the use of combined oral antihistamine and decongestant should not exceed 2 to 3 weeks.[4]

Bronchodilators

Bronchodilators appear to have a role in acute and chronic bronchitis. In acute bronchitis, one can use a preparation of a mucolytic, an expectorant, and a SABA. In chronic bronchitis, inhaled bronchodilator in combination with inhaled corticosteroid, or without it, can be beneficial for cough.[2] In case of asthma, ICS along with inhaled bronchodilators or without them should be used. If the response to corticosteroids is inadequate, LTRAs can be used.[1]

The Indian EMA position paper states that clearance of cough can be enhanced using SABAs and that their use can improve the impact of mucoactives.[2]

SABAs, like levosalbutamol and terbutaline, can be helpful in patients with chronic bronchitis having a productive cough. These agents, besides dilating the airways, can also decrease mucus viscosity.[2] Both levosalbutamol and terbutaline affect mucociliary clearance.[2] Analyses conducted in India by Vora and Bhargava revealed that cough preparations that contain levosalbutamol are effective and safe in both adult and pediatric populations for the treatment of cough associated with allergic rhinitis, COPD, and asthma.[12]

Bronchodilators are also beneficial in CVA.[2] Additionally, the Indian consensus group recommends the use of SABAs, ICS, short-acting muscarinic antagonists, as well as antibiotics in acute exacerbations of COPD and asthma.[1]

ICS and bronchodilator combination can effectively improve cough in CVA.[4] Combinations like budesonide/formoterol and fluticasone/formoterol are recommended in this condition.[2]

Antibiotics

Antibiotics have no particular role in the absence of a bacterial infection. However, when a bacterial infection is identified or there is purulent sputum or mucus discharge from the nose, antibiotics can be administered. They are indicated in conditions like bronchiectasis, exacerbation of COPD, exacerbation of chronic bronchitis, sinusitis, etc.[1,4,6] The antibiotics commonly used in sinusitis include amoxicillin-clavulanic acid, quinolones, and cephalosporins.[4] In AECB, the frequently used antibiotics include moxifloxacin and levofloxacin.[4]

Macrolide antibiotic therapy is needed in pertussis. Treatment initiated early in the catarrhal phase is beneficial.[4] The Indian consensus group recommends antibiotic use for 5 to 10 days in case of purulent sputum and bacterial infection-associated subacute cough.[1] A recent Cochrane review noted that macrolide antibiotics can potentially limit severe exacerbations and decrease symptoms in patients with chronic asthma.[13]

However, antibiotic misuse is a growing problem and can have devastating effects on the patient's overall health in the short as well as the long run. Therefore, one must refrain from prescribing antibiotics when not indicated.

Demulcents

Demulcents like honey, glycerol, menthol, etc., are agents that enhance the production of saliva and form a coating on the cough receptors, thus altering the cough reflex, while also decreasing the irritation of pharyngeal cough receptors.[1,3]

The Indian consensus group recommends the use of demulcents to manage acute nonproductive cough. Demulcents do not seem to be helpful in chronic cough cases.[1]

KEY MESSAGES

- Acute cough does not usually require pharmacotherapy, except for cases with distressing or severe cough.
- The drugs used for cough include antitussive agents, mucoactive drugs, antihistamines, decongestants, bronchodilators, antibiotics, and steroids.
- Codeine, an opioid antitussive, is not indicated in acute cough. It can be helpful in severe cough and refractory cough or dry cough associated with pain in the chest, where its sedative and analgesic effects can be beneficial.
- Dextromethorphan, a nonopioid, central antitussive, does not cause sedation and can suppress acute cough.
- Dextromethorphan is the choice of antitussive for acute nonproductive cough; levodropropizine can also be used.
- Guaifenesin can be helpful in conditions like acute URTIs, stable chronic bronchitis, and acute bronchitis. It is used in combination with antitussives, decongestants, and antihistamines.
- Bromhexine and ambroxol reduce the secretion of mucus and have anti-inflammatory potential.
- Ambroxol or bromhexine and N-acetylcysteine or guaifenesin can be used for productive cough for a short duration.

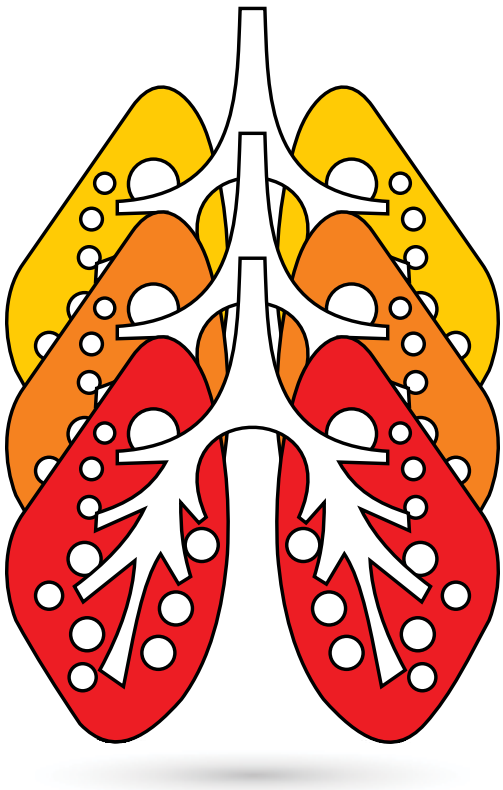
- First-generation antihistamines should be used along with decongestants; nasal decongestants should be used for a short duration.
- Bronchodilators can be beneficial in several conditions, such as acute and chronic bronchitis, asthma, CVA, and COPD.
- Antibiotics should be used judiciously, only when indicated.

References

1. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
2. Shankar PS, Korukonda K, Bendre S, Behera D, Mirchandani L, Awad NT, *et al.* Diagnoses and management of adult cough: An Indian Environmental Medical Association (EMA) position paper. *Respir Med.* 2020 Jul;168:105949.
3. Kardos P, Dinh QT, Fuchs KH, Gillissen A, Klimek L, Koehler M, *et al.* German Respiratory Society guidelines for diagnosis and treatment of adults suffering from acute, subacute, and chronic cough. *Respir Med.* 2020 Aug-Sep;170:105939.
4. Lai K, Shen H, Zhou X, Qiu Z, Cai S, Huang K, *et al.* Clinical Practice Guidelines for Diagnosis and Management of Cough—Chinese Thoracic Society (CTS) Asthma Consortium. *J Thorac Dis.* 2018 Nov;10(11):6314-51.
5. Vally M, Irjuma MOE. Management of Cough: a practical approach. *S Afr Fam Pract.* 2016;58(4):35-9.
6. Bakhtiar A, Juwita PM. Management of Cough. *Jurnal Respirasi.* 2020 Sep;6(2):85-96.
7. Shirsat A, Trailokya A, Wankhede S. Levodropropizine: A promising peripherally acting antitussive agent. *IP Indian J Immunol Respir Med.* 2023;8(2):53-61.
8. Morice A, Kardos P. Comprehensive evidence-based review on European antitussives. *BMJ Open Respir Res.* 2016 Aug 5;3(1):e000137.
9. Zanasi A, Lanata L, Fontana G, Saibene F, Dicpinigaitis P, De Blasio F. Levodropropizine for treating cough in adult and children: a meta-analysis of published studies. *Multidiscip Respir Med.* 2015 May 31;10(1):19.
10. Albrecht HH, Dicpinigaitis PV, Guenin EP. Role of guaifenesin in the management of chronic bronchitis and upper respiratory tract infections. *Multidiscip Respir Med.* 2017 Dec 11;12:31.
11. Dicpinigaitis PV, Dhar S, Johnson A, Gayle Y, Brew J, Caparros-Wanderley W. Inhibition of cough reflex sensitivity by diphenhydramine during acute viral respiratory tract infection. *Int J Clin Pharm.* 2015 Jun;37(3):471-4.
12. Vora A, Bhargava A. A Cross-sectional Cohort Analyses Assessing Response to Levosalbutamol Bronchodilatory Cough Formulations in Outpatient Community Settings of India: 'BUS' analyses. *J Assoc Physicians India.* 2016 Sep;64(9):45-8.
13. Undela K, Goldsmith L, Kew KM, Ferrara G. Macrolides versus placebo for chronic asthma. *Cochrane Database Syst Rev.* 2021 Nov 22;11(11):CD002997.

CHAPTER 14

Home Remedies for Cough



Symptomatic treatment is to be considered in most patients presenting with cough in order to provide them some relief from the disturbing symptom of cough.

Patients also seek immediate relief from cough as it is considered to be a curse by them and the people around them alike. No one wants to cough in the middle of a meeting or presentation, and no one wants to sit beside a person who is constantly coughing. A common symptom like cough can make someone unwelcome in a room. Hence, people want to put a stop to coughing as soon as it begins, basically to avert embarrassment and isolation.

The best management of cough is to first determine the reasons or diseases causing it and then treat the disease. The role of cough suppressants is after that.

We are aware that there are various agents available to manage cough. Besides the over-the-counter and prescription medications discussed in the previous chapter, there are some home remedies as well that can provide symptomatic relief to patients with cough, though the evidence supporting these remedies is limited.

In a country like ours, our mothers and grandmothers have always been the first physicians for the family. They always cook up some decoction when someone catches a cold, has a fever, or develops a cough. They would put various herbs into the decoction, ranging from *tulsi*, cloves, black pepper, and cinnamon, to turmeric, and honey, in various permutations and combinations. Even several cough syrups available in the market also contain ingredients like honey and *tulsi*. Although these ingredients seem to work on certain occasions and appear not to be helpful on certain others, the data on their effectiveness seems to be scarce. This should not detract us from using these time-tested and safe home remedies.

The common home remedies for cough, as we know from day-to-day experience, and advise our patients to follow, include:

- Avoiding foods and beverages that are cold or sour
- Avoiding the intake of pickles
- Consuming ginger water and honey
- Consuming plenty of warm fluids.

Honey

Honey is a natural substance with multiple beneficial properties. It has antioxidative and antimicrobial actions and acts as a demulcent. Demulcents act by coating the sensory receptors involved in cough. Irritation of the pharyngeal cough receptors is decreased and the impulses reaching the cough center are diminished.[1-3] Besides antioxidant and demulcent activity, honey seems to enhance the generation of cytokines and seems to have antimicrobial potential.[4]

According to the 2017 CHEST expert panel report, it might be more favorable to give honey rather than diphenhydramine or no treatment at all in those with cough as a result of common cold; however, this has been suggested only for children and adolescents in the age group of 1 to 18 years. Additionally, honey does not seem to be superior to dextromethorphan in children as well as adults.[5] Honey could be beneficial for symptomatic relief in patients with acute postviral cough.[2]

In children with URI, honey taken before bed may be helpful in relieving night-time cough and improve sleep.[6] In children with nonspecific acute cough, the effect of a mix of honey and milk has been reported to be comparable to dextromethorphan and levodropropizine.[7] The WHO also advocates that honey may have the potential to manage cough and cold in the pediatric population.[4] However, as per a Cochrane review, robust data does not exist either favoring or against the use of honey.[8]

While numerous studies have been conducted among children evaluating the effect of honey in cough, data seem to be scarce in adults. A study conducted among adults with persisting postinfectious cough of over 3 weeks' duration compared a combination of honey and coffee, steroid therapy, and guaifenesin (control) and noted honey and coffee to have a better effect compared to the other two interventions in terms of frequency of cough.[9]

A study conducted among adults with acute nonproductive cough evaluated the effect of a honey-based cough syrup and noted that it effectively decreased daytime and night-time cough frequency and led to a significant reduction in

irritation in throat. It was superior to a marketed cough syrup for cough relief while not leading to the adverse effect of drowsiness.[10]

A relatively recent systematic review and meta-analysis noted that in comparison with routine care, use of honey was better at improving URTI symptoms. Its use has been reported to be associated with improvement in cough intensity and frequency.[11]

While the data is limited, it seems to put forward the beneficial effect of honey in patients with cough and is worth trying to provide symptomatic relief to the patients.

Ginger

Ginger is another natural substance found in every kitchen that is believed to relieve cough to some extent. It is a common practice to drink warm ginger water in many Indian households and this practice gained pace during the COVID-19 era when everyone was readily drinking this decoction to keep the infection at bay.

In Ayurveda, ginger is used extensively to manage several conditions, including, but not limited to, common cold, cough, fever, sinusitis, rhinitis, and bronchitis.[12] Ginger and its active constituents have been found to have airway smooth muscle relaxing potential. They also seem to diminish airway hyperresponsiveness and seem to have a potential role in the management of conditions like asthma.[13] Ginger appears to have favorable effects in patients having cough and those with RTIs.[13]

A study revealed that a mixture of honey and ginger along with standard treatment could improve cough in children with a productive cough. Another study noted that its use along with standard treatment was associated with a lesser time to recovery. Additionally, adverse effects of sedation and drowsiness were not observed with honey and ginger mix as opposed to dextromethorphan in children with dry cough. The authors concluded that honey and ginger mix possessed anticough and antimicrobial properties and soothes the irritable throat.[14,15]

Hydration

Hydration is also often advised when someone has a cough or a cold. The patient is asked to drink adequate amounts of fluids, particularly warm fluids, like tea, warm water, chicken soup, etc.

Dehydration has an adverse impact as it may promote inflammation through proinflammatory mediator generation and can adversely affect the airways. Adequate hydration, on the other hand, helps with mucociliary clearance.[2] Maintaining hydration is advisable in order to decrease the viscosity of sputum.[16]

However, one must be wary of drinking fluids in extreme as it may lead to hyponatremia.[17]

Hence, maintaining 'adequate' hydration is the key.

Others

There are many other natural substances or herbs available in our kitchens that are often used to relieve cough or soothe the throat, such as *tulsi*, turmeric, etc.

In Ayurveda, *tulsi* is used to manage fever, cough, bronchitis, etc. *Tulsi* is known for its antioxidative, antimicrobial, anti-inflammatory, and antipyretic activities, among various other properties.[18] A decoction made from the leaves of *tulsi* can be helpful in conditions of cold and cough. It is also helpful in eliminating mucus.[19] A decoction made with honey, ginger, and *tulsi* leaves could be beneficial in cold, cough, bronchitis, asthma, and influenza.[20]

Turmeric, a commonly used spice in Indian homes, is also considered a magic remedy for many ailments by Indian people. Everyone must have had warm turmeric milk at least once in their lives for some reason or the other.

Turmeric has various actions, including antioxidant, anti-inflammatory, and antimicrobial properties. It has been used for cough, coryza, and sinusitis in traditional medicine.[21]

According to the BTS cough management recommendations in adults, a home remedy in the form of honey and lemon is an economical option.[22]

The Indian consensus panel makes a strong recommendation for adequate hydration in the management of productive cough.[2]

Guidelines from the Indian Academy of Pediatrics state that hydration, ventilation, honey with lime, hot water taken in sips, hot water gargles, and sitting in an upright position can be helpful in cough.[3]

In acute cough or cough due to an acute viral infection, it is not required to prescribe any medications. The illness resolves on its own in most cases. However, based on the evidence available, limited guideline recommendations, and our own experience, we can advise the patients to try some home remedies that may help relieve cough, soothe the throat, and make the patient feel better overall.

KEY MESSAGES

- Honey has antioxidant and demulcent activity and seems to have antimicrobial potential.
- Honey has been reported to be associated with improvement in cough intensity and frequency.
- Ginger and its active constituents have been found to have airway smooth muscle relaxing potential.
- Ginger has favorable effects in patients having cough.
- Adequate hydration helps with mucociliary clearance and maintaining hydration is advisable to decrease the viscosity of sputum.
- A decoction made with honey, ginger, and *tulsi* leaves could be beneficial in cough and cold.
- Honey has been recommended in some guidelines as well for cough relief.

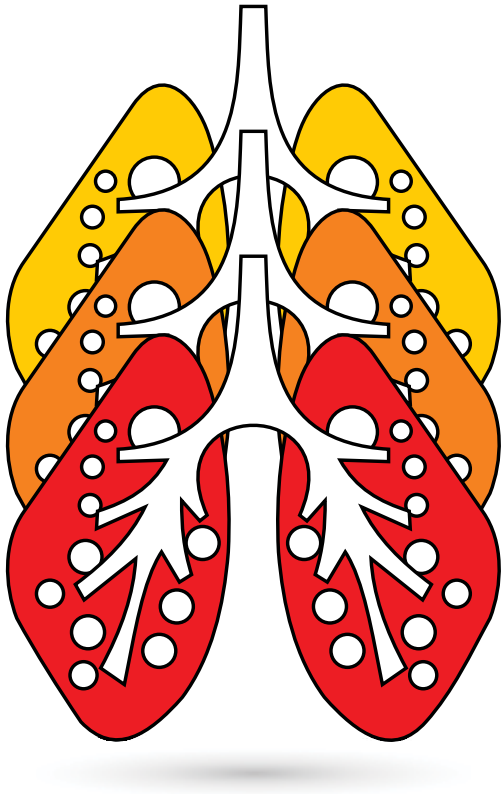
References

1. Ashkin E, Mounsey A. PURLs: a spoonful of honey helps a coughing child sleep. *J Fam Pract.* 2013 Mar;62(3):145-7.
2. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
3. Amdekar Y, Chokhani R, Palaniraman R. IAP Standard Treatment Guidelines 2022. Management of cough in office practice. [Internet] Available from: https://iapindia.org/pdf/Ch-150-Management-of-Cough-in-Office-Practice.pdf. [cited October 10, 2023].
4. Goldman RD. Honey for treatment of cough in children. *Can Fam Physician.* 2014 Dec; 60(12):1107-10.
5. Malesker MA, Callahan-Lyon P, Ireland B, Irwin RS; CHEST Expert Cough Panel. Pharmacologic and Nonpharmacologic Treatment for Acute Cough Associated With the Common Cold: CHEST Expert Panel Report. *Chest.* 2017 Nov;152(5):1021-37.
6. Cohen HA, Rozen J, Kristal H, Laks Y, Berkovitch M, Uziel Y, *et al.* Effect of honey on nocturnal cough and sleep quality: a double-blind, randomized, placebo-controlled study. *Pediatrics.* 2012 Sep;130(3):465-71.

7. Miceli Sopo S, Greco M, Monaco S, Varrasi G, Di Lorenzo G, Simeone G; Milk Honey Study (M&HS) Group. Effect of multiple honey doses on non-specific acute cough in children. An open randomised study and literature review. *Allergol Immunopathol* (Madr). 2015 Sep-Oct;43(5):449-55.
8. Oduwole O, Udoh EE, Oyo-Ita A, Meremikwu MM. Honey for acute cough in children. *Cochrane Database Syst Rev.* 2018 Apr 10;4(4):CD007094.
9. Raeessi MA, Aslani J, Raeessi N, Gharaie H, Karimi Zarchi AA, Raeessi F. Honey plus coffee versus systemic steroid in the treatment of persistent post-infectious cough: a randomised controlled trial. *Prim Care Respir J.* 2013 Sep;22(3):325-30.
10. Gupta A, Gaikwad V, Kumar S, Srivastava R, Sastry J. Clinical validation of efficacy and safety of herbal cough formulation "Honitus syrup" for symptomatic relief of acute non-productive cough and throat irritation. *Ayu.* 2016 Jul-Dec;37(3-4):206-14.
11. Abuelgasim H, Albury C, Lee J. Effectiveness of honey for symptomatic relief in upper respiratory tract infections: a systematic review and meta-analysis. *BMJ Evid Based Med.* 2021 Apr;26(2):57-64.
12. Sultana S, Khan A, Safhi MM, Alhazmi HA. Cough Suppressant Herbal Drugs: A Review. *Int J Pharm Sci Invent.* 2016 Aug;5(5):15-28.
13. Townsend EA, Siviski ME, Zhang Y, Xu C, Hoonjan B, Emala CW. Effects of ginger and its constituents on airway smooth muscle relaxation and calcium regulation. *Am J Respir Cell Mol Biol.* 2013 Feb;48(2):157-63.
14. Jaybhaye DL, Chandra S, Johar S, Nagre AS. Effect of honey and ginger mixture on productive cough in pediatrics patients. *Int J Basic Clin Pharmacol* [Internet]. 2022 Apr. 22;11(3):237-41. Available from: https://www.ijbcp.com/index.php/ijbcp/article/view/4970. [cited October 11, 2023].
15. Jaybhaye DL, Chandra S, Johar S, Nagre AS. Comparative effect of mixture of ginger and honey with dextromethorphan in dry cough in children. *Int J Basic Clin Pharmacol* [Internet]. 2021 Apr. 26;10(5):545-51. Available from: https://www.ijbcp.com/index.php/ijbcp/article/view/4645. [cited October 11, 2023].
16. Vally M, Irhuma MOE. Management of Cough: a practical approach. *S Afr Fam Pract.* 2016;58(4):35-9.
17. Holzinger F, Beck S, Dini L, Stöter C, Heintze C. The diagnosis and treatment of acute cough in adults. *Dtsch Arztebl Int.* 2014 May 16;111(20):356-63.
18. Mohan L, Amberkar MV, Kumari M. Ocimum sanctum linn (TULSI)—an overview. *Int J Pharm Sci Rev Res.* 2011 Mar 1;7(1):51-3.
19. Kumar R, Saha P, Lokare P, Datta K, Selvakumar P, Chourasia A. A Systemic Review of Ocimum sanctum (Tulsi): Morphological Characteristics, Phytoconstituents and Therapeutic Applications. *Int J Res Appl Sci Biotechnol.* [Internet]. 2022 Apr 7;9(2):221-6. Available from: https://www.ijrasb.com/index.php/ijrasb/article/view/251. [cited October 11, 2023].
20. Sethi L, Bhadra P. A Review Paper on Tulsi Plant (Ocimum sanctum L.). *Indian Journal of Natural Sciences.* 2020;10(60):20854-60.
21. Rathaur P, Raja W, Ramteke PW, John SA. Turmeric: The golden spice of life. *Int J Pharm Sci Res.* 2012 Jul 1;3(7):1987-94.
22. Morice AH, McGarvey L, Pavord I; British Thoracic Society Cough Guideline Group. Recommendations for the management of cough in adults. *Thorax.* 2006 Sep;61 Suppl 1(Suppl 1):i1-24.

CHAPTER 15

Alternative Systems of Medicine for Cough



Cough is a common symptom in general as well as in specialist practice. However, many patients do not present to the doctor for cough and try to use various alternative systems or treatments to manage it on their own.

Conventional or Allopathic system of medicine and complementary and alternative medicine go hand-in-hand when it comes to common diseases and symptoms like common cold and cough. It is not only the patients who use alternative systems of medicine to manage cough. The practicing doctors also sometimes agree with the patients in the use of such treatment approaches, given the fact that any specific pharmacotherapy is usually not recommended in acute cough that is mild.[1] Sometimes, the patients resort to alternative therapies when they do not get relief from over-the-counter or prescription cough formulations and other drugs.

Even the experts advocate the use of natural remedies like honey in cases of cough from common cold, though in children only.[2] While the data on the use of alternative systems for cough relief may be lacking, some remedies are backed by evidence. This chapter discusses some such therapeutic options from the alternative systems of medicine used in our country which may be helpful for patients with cough. Delving into the details of all the systems and all the therapeutic approaches is beyond the scope of this chapter.

Ayurvedic treatment

Ayurveda is an age-old traditional medicinal system of India. Herbs are extensively used in this system of medicine.[3] In Ayurveda, it has been stated that the bodily functions are regulated by three doshas, namely *Vata, Pitta*, and *Kapha*.[3] An imbalance of any of the three doshas is said to result in disease.[4] *Kasa* or cough is a manifestation of impaired *Vata* dosha.[3,4] Published literature has shown the benefits of various Ayurvedic preparations for cough. Ginger, a household spice in India, is reported to have an antitussive or *Kaphahara* action. It is used in asthma and COPD. Ginger has anti-inflammatory action.[3] Liquorice is used in Ayurvedic medicine for cough, TB, and to relieve hoarseness of voice. Peppermint is also reported to have antitussive properties.[3]

Several Ayurvedic formulations and procedures have also been shown to have benefits in relieving cough. A study investigated the effects of a polyherbal

formulation containing *Solanum xanthocarpum* Schrad. and Wendl. (*Kantakari*) and *Terminalia chebula* (*Haritaki*) in chronic bronchitis. Use of this formulation significantly improved the primary and secondary outcomes. There was 97.62% relief in nasal congestion and 68.9% relief in productive cough. Around 89.52% of the patients had marked improvement.[5]

Other formulations with ingredients like *Zingiber officinale* (ginger), *Piper nigrum*, and *Piper longum* or *Cinnamomum zeylanicum* Blume., *Elettaria cardamomum* Maton., *C. tamala* Ness., and *Mesua ferrea* Linn. have also been found to be helpful in *Kasa*.[5]

A study evaluated the effect of oil enema or *Sneha Basti* in two children with pertussis. *Sneha Basti* was done along with administering conventional treatment. It was found to reduce cough and was associated with quicker recovery.[4] Another case series evaluated the effectiveness of Ayurvedic treatment of *Vatik Kasa* in the COVID-19 times. All the patients had cough in addition to other symptoms. There was rapid improvement with Ayurvedic treatment, and the symptoms improved significantly.[6]

Different case reports also demonstrate the beneficial effects of Ayurvedic treatment in the management of cough in conditions like chronic bronchitis in adults and recurrent cough in children.[7,8]

Ayurvedic treatment seems to have a potential role in the management of cough, both in children and adults.

Homeopathic treatment for cough

A system of medicine based on the principle of 'let like be cured by like' or *'Similia similibus curantur'*, Homeopathy was introduced by a German physician Dr. Christian Friedrich Samuel Hahnemann. Homeopathic practice involves the prescription of medicines at very low doses.[9,10] This system of medicine follows the principle that an agent that gives rise to certain symptoms in a healthy individual treats similar symptoms in a disease condition, i.e., a drug would be prescribed to a patient that would cause the symptoms that the patient presents with, when given to a healthy person.[11,12]

Various Homeopathic medicines may help manage cough, such as *Arsenic album, Bryonia alba, Spongia tosta, Hepar sulphuricum, Sanguinaria canadensis, Causticum,* etc.[13] Homeopathic drugs that seem to have a role in postviral cough include *Aconite, Arsenicum album, Ambra grisea, Belladonna, Ignatia, Ipecac, Senega, Bryonia, Phosphorus, Kali brom, Spongia,* and many more.[14]

Let us look at some of the evidence from trials of Homeopathic treatment for cough.

A randomized trial evaluated the effect of a Homeopathic syrup on cough due to infections of the upper respiratory tract. The severity of cough was found to be lesser in the patients receiving Homeopathic treatment compared to placebo following 4 and 7 days of treatment. Sputum viscosity was also lower among the patients receiving the Homeopathic treatment.[15] A multicenter study assessed the utility of Homeopathic medications in acute tracheobronchitis (patients having coryza, irritable dry or productive cough, chest oppression, and neutrophilic leukocytosis). Symptom score was noted to be significantly decreased in 24 hours of treatment initiation and around 91% of the patients reported being cured or having marked improvement after study follow-up ended.[16] A study conducted in children with acute dry cough noted that the improvement in Cough Assessment Score was higher with a Homeopathic formulation compared to placebo.[17] A prospective cohort study evaluated the role of a Homeopathic preparation alone or combined with other medicines, in managing cough caused by various conditions. Over the initial 3 days of treatment, the symptoms improved significantly in about half of the patients (45%). By the termination of the treatment or observation period, there was a significant improvement in subjective well-being and symptoms for most of the patients.[18]

Other systems

Unani system of medicine originated in Greece,[19] although it is commonly practiced in the Indian subcontinent. Unani medicine has been reported to be beneficial in lung diseases and coughs of different types. In this system of medicine, *Su'āl* or *Surfa* or cough refers to the movement of the respiratory organs to remove harmful substances from the body. Different forms of medications are used in Unani medicine for cough, including syrups, tablets, linctus, lozenges, etc. Treatment

modalities include pharmacotherapy, regimental therapy like steam inhalation, fomentation, massage with oils, and dietary therapy. Pharmacotherapy involves various agents such as starch, *Plantago ovata, Cydonia oblonga, Acacia arabica, Prunus amygdalus, Vitis vinifera, Glycyrrhiza glabra, P. nigrum*, to name a few. Cold-tempered medications are given when the accumulations in the lungs are thin, while hot-tempered medicines are given when the accumulation is thick.[20]

Siddha is a traditional system of medicine of India, followed in South India, with its origin from Tamil Nadu. This system of medicine largely includes mineral and metal-based drugs. Drugs of plant origin are also used in Siddha medicine.[19,21,22] In Siddha medicine, *Irumal* (cough) has been described as a disease.[22] Various medicinal plants are used in Siddha system of medicine to manage cough, such as *Adhatoda vasica* Nees., *Borassus flabellifer, Crocus sativus, Ocimum sanctum, P. longum, P. nigrum, S. xanthocarpum, T. bellirica* Roxb, *Acalypha indica,* etc.[21,22] A study involving patients with productive cough evaluated the effects of *A. indica* and noted that it decreased the bouts of cough, sputum volume, irritation in the throat, and nasal discharge.[22]

Yoga is another traditional science that has been practiced in our country since ages. Yoga involves the practice of *asanas*. It also includes the practice of *pranayama* which plays a role in control of breathing. Also included in yoga practice is the principle of meditation. Yoga has been shown to improve lung parameters, such as vital capacity, FEV_1, FEV_1/FVC ratio, tidal volume, etc. Thus, it could have a potential role in some pulmonary disorders.[23] A study conducted in patients with bronchial asthma who were subjected to training in yoga practice noted that the patients improved significantly. Besides several other parameters, the patients also had improvement in cough.[24]

Overall, it seems that the alternative systems of medicine and yoga practice have evidence to back their use in respiratory disorders and cough, in particular. The practitioners of conventional medicine must be aware of the alternative systems of therapy prevalent in our country so that if their patients are employing any of the alternative systems or intend to use the same, the clinician can guide them appropriately of the pros and cons. At the same time, if a clinician feels that an alternative system of treatment can help their patient, he/she must not shy away from allowing their patient to follow the same if the safety of the treatment is known.

KEY MESSAGES

- A lot of alternative systems of medicine are practiced in India, including but not limited to, Ayurveda, Homeopathy, Siddha, Unani, Yoga, and Naturopathy.
- Published literature shows that several treatment agents or practices of these alternative systems are beneficial in respiratory diseases.
- Clinicians should gain knowledge about the prevalent alternative systems of medicine and their benefits and risks so that they can make decisions with their patients that are in their best interests.

References

1. Desai PP, Thomas PK, Abhyankar N, Vora A, Jaggi V, Jog P, *et al.* INDIan Consensus on the mAnagemenT of cOugh at pRimary care setting (INDICATOR). *J Assoc Physicians India.* 2023 Jun;71(6):62-77.
2. Malesker MA, Callahan-Lyon P, Ireland B, Irwin RS; CHEST Expert Cough Panel. Pharmacologic and Nonpharmacologic Treatment for Acute Cough Associated With the Common Cold: CHEST Expert Panel Report. *Chest.* 2017 Nov;152(5):1021-37.
3. Wardani RS, Schellack N, Govender T, Dhulap AN, Utami P, Malve V, Wong YC. Treatment of the common cold with herbs used in Ayurveda and Jamu: monograph review and the science of ginger, liquorice, turmeric and peppermint. *Drugs Context.* 2023 Jun 14;12:2023-2-12.
4. Gujarathi RH, Gokhale VM, Tongaonkar JN. Effect of Basti (oil enema) therapy for the management of cough in pertussis. *Ayu.* 2013 Oct;34(4):397-400.
5. Ram J, Baghel MS. Clinical efficacy of Vyaghriharitaki Avaleha in the management of chronic bronchitis. *Ayu.* 2015 Jan-Mar;36(1):50-5.
6. Sharma A, Kaur H. Ayurvedic management of vatik kasa in era of COVID 19—A case series. *Int J Ayur Pharma Research.* 2022 Jan;10(1):40-4.
7. Vasundhara J, Patgiri B, Bedarkar P. Chronic Bronchitis and its Ayurvedic Management: A single Case Report. *International Journal of AYUSH Case Reports.* 2019;3(1):94-9. Available from https://ijacare.in/index.php/ijacare/article/view/70. [cited October 27, 2023].
8. Dethe SK, Kale AB, Swami TY, Gupta D. Management of Recurrent Cough in Children with Ayurvedic Regimen a Case Study. *International Journal of Pharmaceutical Research and Applications.* 2022 May-Jun;7(3):248-52.
9. Dutta A, Sehrawat N. Homoeopathy for Upper Respiratory Tract Infection in Children: A Narrative Review of Research Evidence. *Homoeopathic Links.* 2021;34(03):206-13.

10. Fisher P. What is Homeopathy? An Introduction. *Front Biosci.* (Elite Ed) 2012;4(5): 1669-82.
11. Kurd R, Freed Y, Jarjoui A, Izbicki G, Levin P, Helvitz Y, *et al*. Homeopathic Treatment for COVID-19-Related Symptoms: A Case Series. *Complement Med Res.* 2022;29(1):83-8.
12. Vickers A, Zollman C. ABC of complementary medicine. Homoeopathy. *BMJ.* 1999 Oct 23;319(7217):1115-8.
13. Banswal S, Jangada S. Cough During Covid: Keynote Prescription with Fast Recovery. *Journal of Medical and Pharmaceutical Innovation.* 2022;9(46):49-51.
14. Lakshmi GL. Persistent cough after COVID-19 Pathophysiology and homoeopathic management. *Int J Hom Sci.* 2021;5(3):221-3.
15. Zanasi A, Mazzolini M, Tursi F, Morselli-Labate AM, Paccapelo A, Lecchi M. Homeopathic medicine for acute cough in upper respiratory tract infections and acute bronchitis: a randomized, double-blind, placebo-controlled trial. *Pulm Pharmacol Ther.* 2014 Feb;27(1):102-8.
16. Nayak C, Singh V, Singh H, Siddiqui VA, Gupta J, Mishra A, *et al*. A Prospective Multicentre Observational Study to Evolve the usefulness of Group of Homoeopathic Medicines in the Management of Acute Tracheobronchitis. *Indian J Res Homoeopathy.* 2011 Jul-Sep;5(3):20-6.
17. Voß HW, Michalsen A, Brünjes R. Efficacy and tolerability of a complex homeopathic drug in children suffering from dry cough-A double-blind, placebo-controlled, clinical trial. *Drug Res* (Stuttg). 2018 Aug;68(8):444-9.
18. Rabe A, Ludwig J, Weiser M. Modern Homeopathic Therapy for Coughs: Results of a Prospective Cohort Study. *Biologische Medizin.* 2001;30(5):234-8. Available from: https://www.biopathica.co.uk/documents/studies/Husteel.pdf. [cited October 27, 2023].
19. Ravishankar B, Shukla VJ. Indian systems of medicine: a brief profile. *Afr J Tradit Complement Altern Med.* 2007 Feb 16;4(3):319-37.
20. Huma, Kalam MA, Ahmad R, Avid M, Azmi F. Su'āl (cough): Concept and its management in the light of classical unani literature—A review. *International Journal of Research and Analytical Reviews.* 2023;10(2):858-63.
21. Ram A, Joseph DA, Balachandar S, Singh VP. Medicinal plants from Siddha system of medicine useful for treating respiratory diseases. *International Journal of Pharmaceuticals Analysis.* 2009 Jan;1(2):20-30.
22. Paheerathan V, Nazlam MNM, Piratheepkumar R. Effectiveness Acalypha indica on the Management of Cough. *Sch Int J Tradit Complement Med.* 2021;4(5):61-6.
23. Agnihotri S, Gaur P, Bhattacharya S, Kant S, Pandey S. Benefits of Yoga in Respiratory Diseases. *Indian J Pharm Biol Res.* 2018;6(4):10-3.
24. Bhatt AA, Pandey S, Singh B, Vyas G, Shukla GD, Gulati U. The role of yoga therapy in the management of bronchial asthma (Tamaka shwasa). *Asian J Pharm Clin Res.* 2019;12(12):27-33.

Educational grant by

Glenmark Pharmaceuticals Limited (GPL),
Corporate Enclave, B. D. Sawant Marg,
Chakala, Andheri (E), Mumbai – 99.

Published by

MAJE/1223/01