

Cough in the palliative care setting

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Jennifer, a 62-year-old married woman with bronchogenic lung carcinoma, presented in the emergency room 2 days ago because of severe dyspnea, despite having home oxygen at 2 L/min. Initial measurements of her vital signs revealed the following: temperature of 37.2°C, blood pressure of 97/61 mm Hg, heart rate of 116 beats/min, respiratory rate of 27 breaths/min, and oxygen saturation of 88%. She looked pale and distressed, and was using her accessory muscles of respiration to improve her breathing. Her chest was dull to percussion on the left side, with no substantial air entry. An x-ray scan revealed a massive left-sided pleural effusion. Respiratory staff drained the effusion and left a drain in place for further use. A subsequent bronchoscopy showed narrowing in one of the left-sided bronchi and substantial inflammation of most of her bronchial tree. A stent was placed over the narrowing to facilitate expansion of the left lower lobe.

Jennifer received 45 mg of sustained-release morphine every 12 hours for metastatic bone pain. She was also prescribed 50 µg/d of thyroxine and 150 mg/d of venlafaxine, with scheduled laxatives to prevent constipation.

These treatments gave Jennifer great relief from the dyspnea, but subsequently she developed a distressing, dry cough. She even vomited on her unsuspecting husband, Gerry, after a bout of uncontrolled coughing. Jennifer asked that you do something about her cough, which was driving her "crazy."

Cough is a normal but complex physiological mechanism that protects the airways and lungs by removing mucus and foreign matter from the larynx, trachea, and bronchi, and is under both voluntary and involuntary control. Pathological cough is common in malignant and non-malignant disease. Cough can be classified in various ways, and several causes might coexist in one patient.

The cough reflex is mediated by the vagus nerve in the airways and the glossopharyngeal nerve in the pharynx. These afferents are excited by mechanical stimuli, endogenous chemicals in mucus, and external stimuli like cigarette smoke. Excitatory information is sent from the brainstem to spinal motor neurons, innervating the respiratory muscles. Closure of the vocal cords, which usually enhances the effectiveness of cough, is not essential for effective cough, as demonstrated by patients with tracheotomies.

Ineffective cough can be the result of pulmonary disease decreasing the amount of airflow or creating

excessive amounts of mucus and secretions. Cough can also be impeded by central and peripheral neuromuscular diseases. Understanding the pathophysiology of abnormal cough aids in targeting therapy to the nervous, muscular, and pulmonary systems responsible for it. (A full discussion of this topic is beyond the scope of this article but can be found within the references.¹⁻¹⁰) The American College of Chest Physicians recommendations for chronic cough⁵ were last updated in 2006, but they do not reflect the usual causes of chronic cough seen in palliative care.

Ineffective cough is a major disruption in quality of life for patients, and it can cause life-threatening complications.²⁻⁴ The pressures and air velocities can cause a variety of profound physical and psychosocial occurrences, which have the potential to lead to a substantial decrease in quality of life.⁹

Loss of appetite, headaches, dizziness, sweating, insomnia, and overall exhaustion can be common with abnormal cough. Psychosocial issues for patients include their families' inability to tolerate the excess noise or repetitive nature of the cough, difficulty speaking on the telephone, embarrassment, self-consciousness, and social isolation. Knowledge of these complications should help clinicians appreciate the substantial effects of the cough and why it is imperative to consider and try all reasonable therapeutic options to control it.

The evaluation of cough begins with a history and physical examination, concentrating on the afferent limb of the cough reflex. Chest x-ray scans are very useful in ranking the possibilities shown in the differential diagnosis.⁴ **Table 1**⁴⁻⁸ shows the differential diagnoses of cough in palliative care. In almost all cases, cough is a complication of the primary pathology, but unrelated causes should not be automatically excluded.

Treatment

If the cough is primarily caused by airway obstruction or compression due to lung cancer or metastatic lung disease, treating the primary pathology might resolve or reduce the cough. Endoscopically placed stents for airway obstruction, radiotherapy of compressing lymph nodes, and drainage of pleural effusion might be useful.

Nonpharmacologic treatment. Nonpharmacologic therapy is directed at the symptom rather than the underlying etiology, and it aims to control rather than eliminate cough: proper positioning reduces coughing secondary to reflux or aspiration. Saline via nebulizer reduces dryness and irritation of airways. Chest physiotherapy helps

expectorate mucus. These nonpharmacologic treatments can be used in addition to medications.

Table 1. Differential diagnosis of cough in palliative care

COUGH CATEGORY	DIFFERENTIAL
Noncancerous state	Neuromuscular pathology* <ul style="list-style-type: none"> • Multiple sclerosis • Amyotrophic lateral sclerosis • Hereditary ataxia • Late-stage dementia (irrespective of type) • Cerebrovascular disease Immunocompromised host† <ul style="list-style-type: none"> • Prolonged neutropenia • Organ transplant recipients • HIV infected (with CD4 lymphocyte count at <200 cells/μL) End-stage heart failure End-stage respiratory failure End-stage kidney failure
Cancerous state	<ul style="list-style-type: none"> • Directly caused by cancer <ul style="list-style-type: none"> Pulmonary parenchymal involvement (primary or secondary) Lymphangitic carcinomatosis Intrinsic or extrinsic airway obstruction by tumour Pleural effusion Pleural tumour (primary or implant) Multiple tumour microemboli Pulmonary leukostasis Superior vena cava syndrome • Indirectly caused by cancer <ul style="list-style-type: none"> Anorexia-cachexia syndrome Pulmonary aspiration Pulmonary embolus Paraneoplastic syndrome Radiotherapy sequelae Chemotherapy induced (eg, bleomycin, cyclophosphamide) Chemotherapy-induced cardiomyopathy (eg, adriamycin)
Unrelated to primary disease‡ (Chronic§)	Upper airway cough syndrome Asthma Gastroesophageal reflux disease Chronic bronchitis Bronchiectasis Angiotensin-converting enzyme inhibitor drugs

*Cough caused mainly by dysphagia and repeated aspiration.

†The nature and the severity of the immune defect must always be considered in the evaluation of patients with suspected opportunistic infections.

‡Cough unrelated to primary disease is from the American College of Chest Physicians cough guidelines⁵; these guidelines divide cough in 3 categories, according to the cough's duration in time.

§More than 8 weeks or not postinfectious in nature.

||Formerly called postnasal drip syndrome, upper airway cough syndrome—a result of rhino sinus conditions—has an extensive differential diagnosis in itself.

Data were derived from Madison and Irwin,⁴ Irwin et al,⁵ Kvale,⁶ Dudgeon,⁷ and Rosen.⁸

Pharmacologic treatment.

Oral drugs: Drugs that suppress cough by modifying the excitability of the afferent receptors in the airways are defined as peripheral antitussive agents. Central antitussive agents suppress cough by controlling the excitability of neural elements in the brainstem that produce cough. There is no evidence (ie, no double-blind trial with an adequate number of patients to have a sufficient statistical power) that cough suppressant therapy can prevent coughing.²

Opioids suppress cough, but there is no scientific evidence allowing comparison of one opioid with another. For those patients already using substantial doses of opioids, one might increase the dose by 20% every 24-hour period, until control of coughing is obtained or side effects become unacceptable. The addition of dextromethorphan to the opioid might have a synergistic effect.¹⁰

Table 2 recommends doses of peripheral- and central-action drugs for treatment of cough.

Nebulizers: There is very little scientific evidence to support the use of nebulizers in the symptomatic management of patients with breathlessness or cough related to primary or secondary malignancy, or in chronic cardiac, pulmonary, neuromuscular, and neurodegenerative disorders. Doses and schedules have been partly derived from experience in patients with chronic obstructive pulmonary disease (COPD) and from practitioners' experience.¹ Nebulizers can be valuable for other symptoms as well. When using nebulizers, patients should be sitting in an upright position of at least 45°.

Because Jennifer was unable to talk without provoking an uncontrollable episode of coughing, her husband had to speak for her. Gerry confirmed that for the past 2 days she had not slept much. Whenever she ate, she vomited, and therefore restricted herself to small sips of fluid. Gerry continued to explain that Jennifer had confessed to him that she would rather die than be afflicted with such a terrible symptom.

Upon examination, you found that Jennifer was a frail woman, looking older than her stated age. She was cachectic, but her respiratory rate was 12 breaths/min despite the cough. Between the coughing bouts, you auscultated bilateral wheezing, a pleural rub on the left lateral chest, and good air entry on both sides. The remainder of the examination revealed a hard, nontender liver edge.

Her last chest x-ray scan, done at the bedside, was read as suboptimal by the radiologist. A repeat film in the x-ray department revealed pulmonary lymphangitic carcinomatosis.

From your history and physical examination, you diagnosed the following as responsible for Jennifer's cough: intrinsic airway obstruction, pulmonary

Table 2. Drug doses for treatment of cough

DRUGS	DOSE
Peripheral action	
• Sodium cromoglycate	20 mg inhaled 2 to 4 times daily
Central action	
• Dextromethorphan	15 to 30 mg orally every 4 to 8 hours (120 mg is maximum daily dose)
• Codeine	20 mg orally every 4 hours as needed
• Hydrocodone*	5 to 10 mg every 4 to 6 hours as needed
• Normethadone–p-hydroxyephedrine compound†	15 drops orally twice daily
• Paroxetine	Begin with 10 mg daily‡

*Five mg of hydrocodone is equivalent to 30 mg of codeine.

†This compound is a combination of 10 mg/mL of normethadone and 20 mg/mL of p-hydroxyephedrine.

‡Anecdotal cases; response in a few days.

lymphangitis, pleural effusion, and uncontrolled COPD. The following therapies were used: ensuring proper positioning; humidifying her airways with saline via nebulizer; continuing oxygen; treating COPD with nebulized β_2 -agonists and anticholinergics; adding steroids (ie, 4 to 8 mg of dexamethasone) to address inflammatory airway response; and increasing her opioid to 60 mg of sustained-release morphine every 12 hours with a breakthrough dose of 15 mg every 1 hour as needed.

When you visited Jennifer the following morning, she was still coughing a little; however, she was doing much better and was able to drink half a glass of water without stopping. She was also able to say “thank you” without coughing.



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Competing interests

None declared

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BOTTOM LINE

- The main explanation for the patient's cough is usually a complication of the primary pathology.
- Intractable coughing has a profound effect on quality of life.
- Remember the nonpharmacologic modalities of treatment.
- There is not much evidence to support pharmacologic treatment of cough, yet some clinically effective treatments do exist.
- Multiple concurrent therapies are often needed to control intractable coughing.

POINTS SAILLANTS

- Habituellement, la toux du patient s'explique principalement par une complication de la pathologie première.
- La toux rebelle affecte profondément la qualité de vie.
- N'oubliez pas les modalités thérapeutiques non pharmacologiques.
- Peu de données probantes justifient le recours aux traitements pharmacologiques de la toux et pourtant, il existe certains traitements efficaces sur le plan clinique.
- Il faut souvent des thérapies simultanées multiples pour contrôler la toux réfractaire.

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