

# Perioperative Antitussive Considerations

## Learning Objectives

- Understand the mechanism of coughing.
- Understand the initiation and activation of the cough reflex arc pathway.
- Discuss antitussive agents and their application in anesthetic management.

## Introduction

Involuntary coughing is a protective reflex that forcefully expels air from the lungs. The respiratory tract is highly responsive to airway irritants leading to the initiation of the cough reflex arc pathway in order to remove the offending agents. However, chronic diseases such as asthma and chronic obstructive pulmonary disease (COPD) can increase the release inflammatory mediators, increase mucus secretion, and sensitize the sensory nerves of respiratory system to the cough reflex. In the perioperative setting, coughing can be undesirable after the completion of certain procedures due to increasing the risk of acute hemorrhaging, increasing intraocular pressure and intracranial pressure. Many ENT, cranial, and vascular surgeries require stringent control of cough suppression. Opioids have been the mainstay for antitussive therapy for many decades. However, adverse effects are associated with opioids, such as respiratory depression. The cough reflex has many afferent pathways leading to the initiation of a cough, and many sites for antitussives to enact their effect. Antitussives are categorized by their site of action either centrally or peripherally.

## Case Presentation

A 68 y.o. female weighing 110 kg with a BMI of 44 presented to the OR for a right temporal artery biopsy due to concern for giant cell arteritis, also referred to as temporal arteritis. The patient had bilateral blurry vision secondary to a left occipital CVA approximately 1 year prior to surgery. She subsequently had improvement in the left eye with little improvement in the right eye. Prior CT scan was negative, however, her visual acuity continued to decline. Her present symptoms included headache, right eye blurriness, and a dull right-sided temporal pain radiating to her occiput. Other past medical history includes insulin-dependent diabetes mellitus, essential hypertension, migraine, obesity, obstructive sleep apnea, and no prior history of tobacco use.

## Intraoperative Course

The patient was placed under moderate sedation and kept spontaneously breathing with 2 mg midazolam, a ketamine-propofol infusion (often referred to as "ketofol") with 40 mg ketamine in a 500 mg propofol vial and set at an infusion rate of 50 mcg/kg/min, and intermittent boluses of 25 mcg fentanyl with a total of 100 mcg. A nasal cannula was placed and taped in an appropriate manner as to avoid the surgical site. The patient was positioned supine, with slight reverse-Trendelenburg, head slightly tilted to the left, and surgical bed rotated 45 degrees. The goal of the anesthetic was to maintain normotension, provide adequate analgesia, while maintaining spontaneous respirations. The patient required the use of an oropharyngeal airway (OPA) and a nasopharyngeal airway (NPA) due obstructive apnea and oxygen desaturation. Intraoperative events were otherwise unremarkable.

Once skin closure occurred and dressings were applied, the ketofol infusion was halted, the OPA removed with NPA remaining, and the patient was transferred onto the transport bed. Shortly after, the patient emerged with profuse coughing. The NPA was immediately removed. The surgeon subsequently removed the dressings and observed a small hematoma at the surgical site. Pressure was maintained while the decision to re-prepare the OR bed for further evaluation. The surgeon noticed minor pulsatile bleeding and corrected it with sutures. The patient was awoken in a similar manner and transported to the recovery area in stable condition.

## Cough Reflex

The afferent pathway of the cough reflex arc involve mechanoreceptors and chemoreceptors providing sensory information to the nucleus tractus solitarius (NTS) of the medulla oblongata via the vagus nerve. The larynx and the tracheobronchial tree are of the most highly innervated regions that will stimulate this reflex. The efferent pathway innervates respiratory muscles including the laryngeal muscles, diaphragm, external intercostal muscles, and rectus abdominis.

The initiation of the cough reflex produces a sharp inspiration with expansion of the chest cavity via the diaphragm and external intercostal muscles. The laryngeal muscles will then contract and close the glottis. The contraction of expiratory muscles against a closed glottis will lead to the compression of air within the lungs and increase intrapleural pressure. Glottic relaxation will then cause a rapid expulsion of air and potential harmful substances.

Risk factors for the stimulation of the cough reflex in the perioperative setting include the use of inhalational anesthetics, airway instrumentation or irritation, reactive airways, and history of smoking.

## Antitussives

The aim for antitussives is to either desensitize the cough reflex or raise the cough threshold. Antitussives act either centrally at the level of the NTS or peripherally by targeting neuronal pathways.

Opiates such as remifentanyl and fentanyl act at the central mu opioid receptors exhibiting its antitussive properties. Codeine is considered the gold standard for antitussive therapy due to its favorable side-effect profile. Dextromethorphan is an NMDA antagonist that also works centrally by inhibiting cough reflex, although the mechanism is poorly understood. Other centrally acting antitussives include diphenhydramine, an H1 receptor antagonist, and dexmedetomidine, an alpha-1 receptor agonist.

Peripherally acting antitussives primarily exert their effects by anesthetizing the local nerves and decreasing the initiation of the cough reflex arc or acting as demulcents. Local anesthetics are the most consistently effective peripherally acting antitussive pharmacological agents. However, perioperative usage is limited due to its transient effects and tachyphylaxis with repeated doses.

## Discussion

The anesthetic management of a temporal artery biopsy necessitates MAC sedation at a plane of anesthesia to which the patient does not make much movement while still maintaining spontaneous respirations. The anesthetic required for this sedation abolishes the cough reflex until emergence. With the patient's history and the lack of inhalational anesthetic use or airway instrumentation, there were no major indications that would suggest an increased risk of coughing on emergence. Due to coughing and bucking on emergence, there was minor hemorrhaging at the surgical site causing a delay. After the NPA was removed on the second emergence, the likely cause of the cough was due to mechanical irritation of the pharynx by the NPA or use of excessive lubricant causing irritation of the vocal cords. Antitussive management is an important consideration in general anesthetics, however it is also imperative to remain vigilant of potential offending factors during MAC sedation cases.

## References

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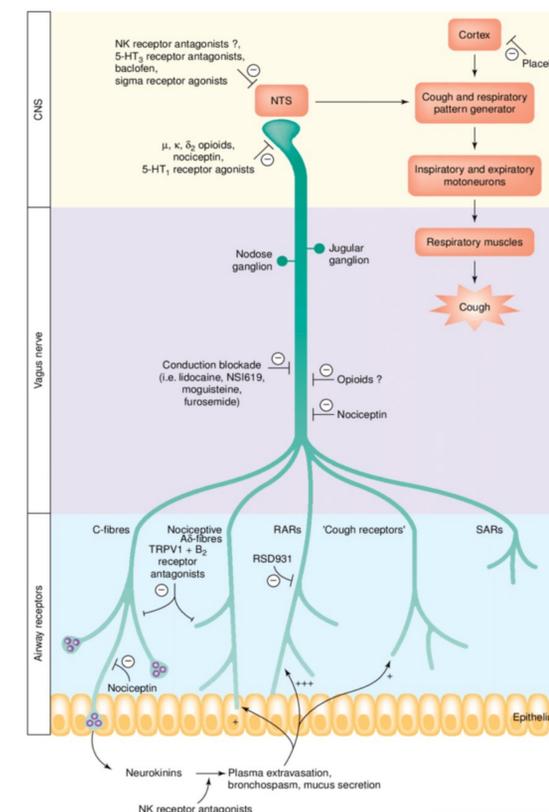


Figure 1. The cough reflex and sites of action of antitussive agents.