High-Risk Infections: Influence of Down-Regulation and Up-Regulation of Cough Using Airway Reflexes and Breathing Maneuvers

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Acute respiratory failure • Aspiration pneumonia • Aspiration reflex • Expiration reflex • Coughing • Flu A (H1N1) • Breathing maneuvers

Coughing is a watchdog of the lungs. It represents the most important airway defensive reflex and one of the main symptoms of respiratory disease. During coughing and sneezing, particles of mucus can be expelled for a distance of up to 9 m [1]. Various pathogens, if present, may therefore infect nearby people and animals, contributing to massive dissemination of airborne infections. In addition to using various protective measures, down-regulation of coughing plays a substantial role in preventing dissemination of respiratory infections. For example, about 80 % of passengers on a 3-h airplane trip may be infected by the cough of an individual carrying the flu virus. These newly infected passengers then disseminate the viral infection at their destinations worldwide.

Protective and therapeutic actions are particularly urgent during a pandemic of influenza A (H1N1 virus), which mainly affects the most marginal and immunocompromised members of a population, including children. There are several pathophysiological forms of cough down-regulation [2] that can be applied during a flu pandemic.

The *D222G* mutation of the 2009 pandemic virus A (H1N1) caused destruction of the tracheobronchial ciliated cells as well as the bronchiolar and alveolar cells. This, in turn, disabled the clearing mechanisms of the lungs, which in Spain caused a 3.5-fold increase in the fatal outcome of the 2009 flu pandemic [3, 4].

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During the breathing cycle, the lung volume at the moment determines the actions of two alternating tendencies—inspiration and expiration—mediated by two distinct ventilatory reflexes. The reflexes are induced by stimulation of the airway and lung receptors, again depending on the lung volume and local pressure at the moment. At the early phase of inspiration, the lung volume is very low, just starting to increase gradually from its functional residual capacity (FRC). There is a strong general tendency to inspire at this point [5].

Inspiratory efforts can be provoked by various methods for stimulating airway rapidly adapting receptors (RARs). In cats, rapid inspiratory efforts can be evoked by nasopharyngeal stimulation, manifesting as the sniff- and gasp-like aspiration reflex (AspR) [1, 6–8] and by rapid lung inflation [5], which decreases the frequency and intensity of the subsequent expiratory efforts of cough and postpones them [9]. During gastroesophageal reflux or inhalation of irritant substances to the larynx, there is a strong "urge to cough" that can be voluntarily suppressed. To prevent aspiration of irritant substances into the lower airways, the necessary effort of coughing may be postponed by a previous, very slow voluntary inspiration followed by breath-holding and swallowing of the bolus to the esophagus. Only then can the effort to cough be initiated for expulsion of irritants from the airways [10–12]. Similar voluntary cough suppression commonly decreases the disturbing effect of coughing during a concert. It can similarly strongly inhibit dissemination of airborne infections due to coughing. Such ventilatory maneuvers might be usefully applied to the fight against flu pandemics and other widespread respiratory infection outbreaks.

On the other hand, the increasing lung volume at and above the tidal volume (V_T) stimulates the slowly adapting receptors (SARs). Also, because of the Hering Breuer inspiration inhibiting reflex (HBIIR), after inspiratory "switch-off" the V_T induces the expiratory phase. The tendency to expire is strong at the end of tidal inspiration [5]. Therefore, stimulation of laryngeal RARs interrupts the inspiration and evokes laryngoconstriction and the expiration reflex (ExpR) [1, 7, 8]. Additionally, an inspired or inflated volume above the normal V_T or blockade of lung deflation at the beginning of expiration by positive pressure can adequately speed up and increase the intensity of the subsequent expiratory effort. It is caused by stimulation of airway receptors and manifests as the Hering Breuer expiration facilitating reflex (HBEFR) [5].

Hyperinflation or occlusion of airways and hindering lung deflation by a ventilator or a pressure pulse provokes the ExpR and the cough reflex (CR). Such rapid expiratory efforts might promote expulsion of infected mucus, preventing its protrusion from the larynx to the lungs and preclude, or at least postpone, the development of dangerous aspiration pneumonia [13]. A proposed voluntary breathing maneuver consists of several rapid sniffs with a closed mouth of 0.5 s duration, each followed by forced expiration lasting about 3 s. Such a maneuver might save many lives and improve the quality of life of millions of people worldwide during imminent flu pandemics or other widespread respiratory infections. The early inspiratory sniffs and other spasmodic inspirations, including provocation of the AspR, result in down-regulation of coughing and may substantially retard a flu or other respiratory infection pandemic.

Rapid reflex or voluntary hyperinflation or occluded lung deflation—started at the early expiratory phase by pressure pulses—may result in reflex up-regulation of cough due to stimulation of airway receptors and mediated by HBEFR [5]. Such up-regulation may prevent, or at least postpone, the development of mostly fatal aspiration pneumonia. The sniff- and gasp-like AspR provoked by nasopharyngeal stimulation in anesthetized cats decreased the number and intensity of cough efforts provoked in the tracheobronchial region [9]. Similarly, the urge to cough may be suppressed, and even the motor act of coughing might be inhibited or at least postponed by voluntary action, helping to decrease the dissemination of airborne infections [11, 12]. Rapid, deep breaths through the nose, but not through the mouth, have bronchoprotective and bronchospasmolytic effects in probands and patients with mild bronchial asthma. This bronchoprotective effect in humans requires rapid inspiratory airflow [14, 15]. The sniff-like voluntary inspiration decreases the bronchoconstriction detected by one-second forced expiratory volume (FEV_1), induced by metacholine inhalation in adult asthmatics [16] and decreased the number of coughs provoked by capsaicin inhalation in young asthmatics [17]. These results indicate a reflex origin of the bronchodilator effect of nasopharyngeal stimulation, which decreases in parallel with bronchodilation and bronchoconstrictor-triggered coughing [18]. Taking advantage of voluntary airway reflexes and ventilatory maneuvers have many important practical applications [19]. They include detection of preparatory movement activity in the premotor area in persons in a vegetative state [20, 21]. The control of wheelchairs by trained paraplegics [22] can be reproduced by voluntary performance of aspiration and expiration reflexes, representing binary signals [19]. Gasping respiration developing in animals can provide autoresuscitation for few minutes even during cardiac arrest [23]. Therefore, provocation of the gasp-like AspR persisting even in agonal state or voluntary sniffs, might provide autoresuscitation in emergency situations [7, 19].

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