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REVIEWS

Cough, expiration and aspiration reflexes: possible anesthetic implications – a brief review

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Abstract

Systematic study in animals indicated, that in addition to cough there are 2 distinct airway reflexes. The aspiration reflex (AspR) characterized by rapid and strong gasp-like inspiration provoked by stimulation of nasopharynx, nasal phyltrum or auricle of ear. The expiration reflex (ExpR) manifests by prompt expiration, induced by laryngeal stimulation. Both reflexes strongly activate the brainstem inspiratory or expiratory generators, respectively, and inhibit the opposite respiratory and various functional disorders.

This paper indicates several functional disorders occurring during manipulation with airways in anaesthesiological practice, which can be influenced positively or negatively by application of these special reflexes (asphyxia, breath-holding, laryngospasm, bronchospasm, sleep apnoea episodes, arrhythmia, collapse, etc.). The AspR, ExpR and CR (cough reflex) have important clinical relevance in anaesthesia and emergency medicine applicable also in domestic therapy and in hardly accessible places particularly by application of ICT (Information & Communication Technologies) using a mobile connection of the patient with the remote hospital centre.

Keywords: aspiration reflex, breath-holding, bronchospasm, expiration reflex, cough

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Introduction

Airway stimulation evokes well described reactive responses, such as cough [1-6], laryngospasm [7-11] and bronchospasm [12-15]. These reflex responses may also occur during light anesthesia. Additionally to these, two other reflexes, the expiration and aspiration reflexes have been described, though their precise mechanisms of action and implications in clinical practice have not been clearly identified. Nonetheless, both expiration reflex (ExpR) and aspiration reflex (AspR) might have important implications in various pathological processes in the anesthetized patients and in other conditions unrelated to anesthesia.

The purpose of this brief review is to familiarize the anesthesiologists with the possible implications of ExpR, AspR and cough reflex (CR) in various situations encountered in anesthesia practice.

Disclosure: Part of the text content relies on clinical observation and assumptions rather than being based on evidence or other published literature.

Description and basic pathophysiology

Table 1 lists the ten main components of AspR, ExpR and CR and Figure 1 schematically illustrates and compares them with quiet breath.

The ExpR has been described as a solitary, short-lasting activity of the abdominal muscles, indicating a prompt expiratory effort with no preceding inspiration, with reflex interruption of an occasional inspiration. It

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Table 1. Main parameters of aspiration, expiration and cough reflexes

Aspiration Reflex	Expiration Reflex	Tracheo-Bronchial Cough
1) a short-lasting high-frequency activity in phrenic nerve and inspiratory muscles, indicating a rapid, and strong, spasmodic sniff; 2) no subsequent active expiration, but even a reflex interruption of spontaneous activity of the abdominal muscles, suggesting an inhibition of active expiration and passive exhalation; 3) marked inspiratory decrease of P_{pl} (-4 kPa), followed by a passive return of intrathoracic pressure to values slightly above zero, promoting an increased venous return to the heart, supporting blood supply to various organs and tissues; 4) a rapid inspiratory airflow (280-420 ml.s^{-1}); 5) marked positive increase in transmural pressure; 6) passive inspiratory dilation of intrathoracic airways; 7) a rapid short-lasting inspiratory reflex dilation of the pharyngeal lumen with opening of the glottis, allowing lung inflation, followed by a glottal narrowing during the post-inspiratory phase, inhibiting subsequent lung deflation; 8) a sniff-like sound; 9) reflex inhibition of bronchoconstrictor fibre activity, resulting in transient bronchodilation; 10) a moderately increased V_T [2].	1) no preceding inspiration or even a reflex interruption of an occasional inspiration; 2) a solitary, short-lasting activity in the abdominal and intercostal muscles, indicating a prompt expiratory effort; 3) sudden marked expiratory increase in the intrathoracic pressure (Ppl + 2.2 kPa), contributing to systolic ejection of the blood from the heart; 4) rapid and marked expiratory airflow (~130 ml.s^{-1}); 5) a negative transmural pressure; causing; 6) an expiratory compression of the intrathoracic airways; 7) a reflex glottal closure, promoting a pressure increase during the compressive phase, followed by reflex glottal opening allowing a rapid expulsion of airflow together with any irritants or fluids during the expulsive phase; 8) a brisk explosive sound; 9) a reflex bronchoconstriction, indicated by ~2-fold increase of baseline bronchoconstrictor fibre activity; 10) a moderately increased expiratory tidal volume.	1) a strong activity of the phrenic nerve, the diaphragm and other inspiratory muscles, causing deep longer-lasting initial inspiration; 2) a very strong activation of the abdominal and other expiratory muscles, resulting in a successive powerful expiratory effort; 3) a considerable decrease followed by a large increase in intrathoracic (Pleural) pressure (+4 kPa), promoting an increased venous return to the heart, followed by marked ejection of blood to various tissues; 4) very rapid expiratory airflow (~500 ml.s^{-1}); 5) a highly negative transmural pressure; promoting; 6) a dynamic expiratory compression of the intrathoracic airways; 7) after inspiratory dilation a reflex glottal closure in the compressive phase, causing an intrathoracic pressure increase, followed by prompt glottal opening, allowing a powerful expulsion of air with any irritants; 8) an explosive cough sound; 9) reflex bronchoconstriction indicated by ~ 3-fold increase in bronchoconstrictor fibre activity; 10) a large (~5-fold) increase in expired tidal volume.

is accompanied by transient bronchoconstriction in addition to prompt activation of expiratory muscles [2, 6, 16-18].

The AspR has been described as a short-lasting, high-frequency activity in the phrenic nerve and the inspiratory muscles, indicating a rapid and strong, spasmodic sniff- and gasp-like inspiration with no subsequent active expiration. It is accompanied by a reflex interruption of any spontaneous activity of the abdominal muscles, suggesting an inhibition of active expiration [2, 18-22].

ExpR, AspR and CR are defensive reactions, which can manifest both in normal and various pathological situations. ExpR provides tracheal protection against aspiration of foreign bodies. Upon irritation by a foreign body, primarily of the vocal folds and the larynx, or less often the trachea and bronchi [17], a forceful expiration accompanied by transient laryngo-constriction and followed immediately by swallowing expels the foreign body away from the airways. Unlike the ExpR, the CR provides cleaning of the airways from particles that already entered them. The CR comprises a deep inspiratory phase, followed by a short lasting laryngeal closure and forceful expiration. AspR, ExpR and CR are the main airway defensive reflexes evoked by irritation of the nasopharynx, oro-pharynx, larynx and lower airways, respectively (Figure 1, 2).

They are normal, prompt reactions to airway irritation. CR and ExpR are expulsive reflexes, designated to prevent distal dispersion of various particles in the airways and their elimination. They are accompanied by transient broncho-constriction, to further block airway penetration by irritants. Their main components are listed in Table 1 and compared with quiet Breath in Figure 1. The reflex arch, mechanism and various resuscitation potentials of these powerful airway reflexes are indicated in Figure 2 and discussed later.

Clinical relevance of airway reflexes

Possible implications of ExpR, CR and AspR in anesthetic scenarios

In an awake or a lightly anesthetized patient, breath-holding "on the endotracheal tube" occasionally called by some authors as "cough and strain afterward" [9] is a well known clinical problem. This "strain after-ward" is best explained by an ExpR activity.

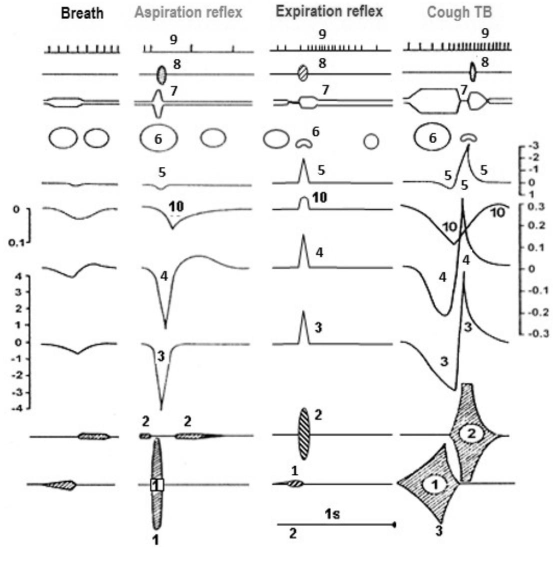

Fig. 1. The 10 main components of AspR, ExpR, CR compared with quiet breath. Abbreviations: 1) EMG_d – diaphragmatic electromyogram, 2) EMG_{ab} – abdominal electromyogram, 3) P_{pl} – pleural pressure, 4) V' – airflow, 5) P_{tm} – transmural pressure, 6) Tr – tracheal lumen, 7) Gl – glottal lumen, 8) Phono – acoustic signal of breathing, 9) ENG_b – electroneurogram of a bronchoconstrictor fiber activity, 10) V_T – tidal volume. The axis for airflow and P_{tm} is on the right side of the figure, but the P_{pl} label is on the left (with permission from: Z. Tomori, I. Poliacek, J. Jakus, J. et al. Distinct generators for aspiration and expiration reflexes: localization, mechanisms and effects. J Physiol Pharmacol 2010; 61(1): 5-12)

Breath holding with desaturation is also not uncommon after extubation of the trachea. A typical clinical picture is convulsive expiratory movements ("strain") of chest and abdomen and difficulty to ventilate the patient through a facemask. Often, this is related to laryngospasm though the manifestations of ExpR and laryngospasm seem to be different. This is especially evident with partial laryngeal closure often manifested by stridor which is absent in the case of ExpR. We thus speculate that in post extubation breath holding, similarly to a "strain" on the endotracheal tube, the patient holds his breath during expiration and cannot generate inspiration effort supposedly owing to an active ExpR, whereas during laryngospasm the patient cannot drive gas into the lungs because of upper airway obstruction.

ExpR may also be activated as an exaggerated response to aggressive upper airway manipulations. In our clinical experience, this can be encountered in lightly anesthetized pediatric patients and morbidly obese patients, especially in those suffering from obstructive sleep apnea.

The AspR, another defensive airway reflex, might explain the mechanism of post-obstructive negative pressure pulmonary edema following a laryngospasm, because it manifests by strong, gasping movements that can create excessive negative pressures in the chest cavity.

Manifestation of ExpR, CR and AspR in emergency medicine scenarios

The ExpR may play an important role in children suffering from "Breath-holding spells", where breath-holding and desaturation occur at the end of expiration, instead of normally starting an inspiratory effort. Remarkably many of these children suffer from ENT (ear throat and nose) problems and improve significantly after adenoidectomy [12, 24].

Additionally, about 15% of the drowning victims have no water in the lungs (the dry-drowning phenomenon) [25-30]. The mechanism behind these phenomena may be a breath-holding, also involving ExpR.

The management of post-extubation breath holding seems to be similar to that of post-extubation laryngospasm. We empirically but successfully use rapid, shallow mask ventilation along with CPAP. Recently, Al-Metwalli [31], successfully managed post-extubation laryngospasm (or ExpR?) with gentle chest compressions. All these management tools promote air

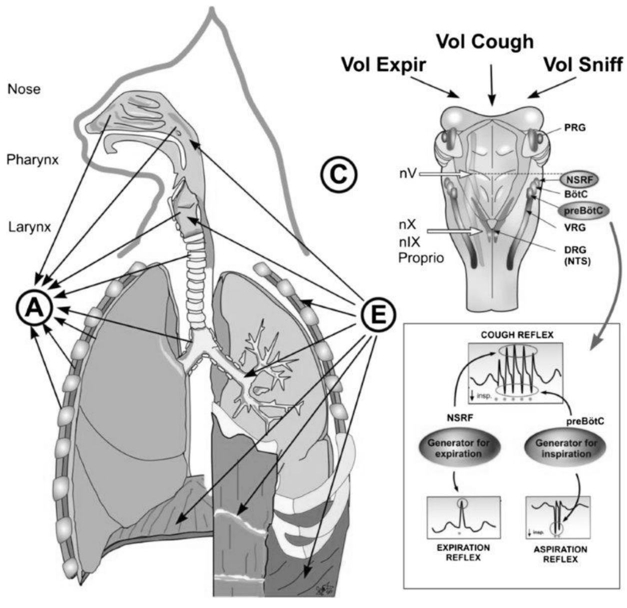

Fig. 2. Afferent (A), efferent (E) and central (C) components of AspR, ExpR and CR and their voluntary equivalents (Cough, Expiration, Sniff). Abbreviations: nV – nervus trigminus, nX – nervus vagus, nIX – nervus glossopharyngicus, PRG – Pontine Respiratory Group, NSRF – Nucleus Sub Retro Facialis, PreBotC – Pre Botzinger Complex, VRG – Ventral Respiratory Group, DRG – Dorsal Respiratory Group, NTS – Nucleus Tractus Solitarius (with permission from: Tomori Z, Donic V, Benacka R, et al. Reversal of functional disorders by aspiration, expiration, and cough reflexes and their voluntary counterparts. Front Physiol 2012, 3: Article 467. doi: 10.3389/fphys.2012.00467)

movement within the chest and thus, supposedly help brake the ExpR and/or laryngospasm.

Revitalization and resuscitation effects of airway reflexes

Gasping respiration observed in infants in critical conditions before death has a strong resuscitation potential. Survival or death depends on the prevalence of either the gasps or the inhibitory effect on vital organs with morphological destruction or functional impairment of control mechanisms, such as in SIDS (Sudden Infant Death Syndrome [32]. Contact stimulation of the nasopharynx in cats provokes strong impulses (~200 Hz) in the glossopharyngeal afferents [33], which activate the brainstem inspiratory generator located in the pre-Botzinger complex [34]. This provokes a rapid and strong inspiratory effort, the gasp-like aspiration reflex [19-23]. The AspR has similar resuscitation and revitalization potential as gasping, proved mostly in animals [21]. Stimulation and suction by a nasopharyngeal catheter, proved to interrupt supraventricular tachycardia in 4 from 12 infants [35], similarly as in adults observed accidentally during introduction of a naso-gastric catheter for gastric juice collection [36]. Nasopharyngeal stimulation could also interrupt hiccough attacks [37]. Provocation of AspR proved to interrupt hypoxic apnoea in cats [23]. Therefore, it can speed up normalization of breathing also in artificially ventilated patients, resulting from reflex activation of the brainstem inspiratory generator [34].

Rapid sniff through the nose for one second with closed mouth, representing a voluntary equivalent of AspR has a broncho-protective and broncho-dilatory effect in patients with asthma, chronic obstructive pulmonary disease, smokers and healthy people [38, 39]. Strong activation of brainstem inspiratory generator during rapid sniffs may be transferred to other central structures and may dilate the airway lumen [39], or inhibit various pathological states such as laryngospasm, bronchospasm, Parkinson's tremor, epileptic seizure, etc.

Sudden hypotension with imminent loss of consciousness caused by anaphylactic reaction or other reasons such as ventricular arrhythmias can be prevented by cough "on demand" [40]. The deep inspiration of cough ("sniff and expire") increases venous return and the successive strong expiratory effort provides prompt brain perfusion to prevent a collapse.

The persisting AspR might allow differentiation of patients in a vegetative state by the presence of activity in the pre-motor area of brain in fMRI on the instruction to move the hand, from non-reacting patient with brain death [41]. Similar activities might also be observed by fMRI after provocation of AspR by mechanical means even in more severe disorders of consciousness without voluntary but persisting reflex signs. Since AspR persists even in the stage of pre-mortal gasping at least in cats, the procedure might allow exclusion of brain death in selected cases of moribund patients [22].

The persisting AspR and ExpR, representing diametrical different reactions, as binary signals allow for paraplegics to communicate using a computer and control their wheelchair, as described by Plotkin et al. [42].

Conclusion: In this review we tried to familiarize the anesthesia and intensive care medicine specialties readers with the concepts of ExpR, CR and AspR and their possible clinical relevance, including in the field of anesthesia and emergency medicine.

Conflict of interest

Nothing to declare

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Tusea, reflexul expirator şi de aspiraţie: implicaţii anestezice

Rezumat

Studii sistematice pe animale au arătat că există două reflexe suplimentare ale căii aeriene pe lângă reflexul de tuse. Reflexul de aspiraţie (AspR) este caracterizat printr-o inspiraţie rapidă şi puternică ("gasp-like") provocată de stimularea nazofaringelui, filtrului nazal sau a pavilionului urechii. Reflexul expirator (ExpR) se manifestă printr-o expiraţie promptă indusă de stimularea laringiană. Ambele reflexe activează puternic centrii respiratori care generează inspiraţia, respectiv expiraţia, inhibând reflexul opus precum şi alte variate tulburări funcţionale.

Această lucrare semnalează câteva tulburări funcţionale care apar pe parcursul manipulării instrumentale a căii aeriene în timpul practicii anestezice şi care pot fi influenţate pozitiv sau negativ prin aplicarea acestor reflexe particulare (asfixia, apneea voluntară, laringospasmul, bronhospasmul, episoadele de apnee de somn, aritmii, colaps etc.). AspR, ExpR şi reflexul de tuse au o importanţă particulară în practica anestezică şi în medicina de urgenţă, cu aplicabilitate şi în terapia la domiciliu, chiar şi în locuri aflate la distanţă mai mare de spital, prin utilizarea unei legături telefonice mobile cu pacientul.

Cuvinte cheie: reflex de aspiraţie, apnee, bronhospasm, reflex expirator, tuse