



Voluntary and reflex cough and the expiration reflex; implications for aspiration after stroke

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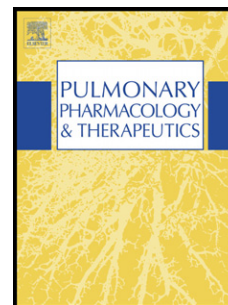
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Review article**Voluntary and reflex cough and the expiration reflex; implications for aspiration after stroke**

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Abstract

Aspiration is a common result of stroke, and may lead to lung infections and pneumonia. Cough may prevent this aspiration and thus prevent the pneumonia.

We review the four types of cough usually used to assess aspiration risk:

voluntary cough (VC), reflex cough (RC), the laryngeal expiration reflex (LER), and cough on swallow (CoS). VC is easy to test but starts with an inspiration that may cause aspiration, and is controlled by cortico-brainstem pathways that may not be involved in influencing aspiration. RC also starts with an inspiration, and requires instrumental intervention, but is more relevant to protecting the lungs.

The LER starts with an expiration, so is 'anti-aspiration', and is easy to test, but its neural mechanisms have not been fully analysed. CoS can be tested at the same time as direct observations of aspiration, but little is known about its neural mechanisms. Each method has its advocates, and the purpose of the review is to discuss how each may be applied and how the information from each may be assessed and valued.

1. Introduction

Aspiration, possibly followed by lung infections including pneumonia, is a serious risk after central nervous disorders such as stroke [1,2]. Tests to determine the risk of aspiration are therefore important to prevent, by appropriate care and treatment, its occurrence. These tests assess the normality or otherwise of the various physiological mechanisms that prevent aspiration.

The site of aspiration into the lungs is the larynx. There are two main types of laryngeal mechanism that prevent aspiration: those that close the glottis and those that expel material that might be inhaled into the lungs. Both are usually present and synchronized. The glottal closure reflex, in response to mechanical stimulation of the vocal fold region, can occur in isolation without involvement of the respiratory muscles [3], but usually is accompanied by the laryngeal expiration reflex (LER) [4,5]. 'True cough', either voluntary (VC) or reflex (RC), starts with an inspiration that might draw material into the lungs (aspiration) before expelling it [4-6]

Different studies use different end-points: (A) aspiration/risk of aspiration, also assessed by methods such as barium (or other material) swallow or videofluoroscopy; or (B) chest infections/pneumonia or their risk, assessed clinically. There have been many studies on the use of cough in assessing the risk of aspiration in patients with dysphagia, not necessarily due to stroke, and some of these will be quoted here. When the end result is pneumonia, its occurrence will depend on prior treatment of the patient, which in turn depends on provisional assessment of its risk. These relationships are complex.

This review will deal only with the protective and defensive reflexes under the general heading ‘cough’. However it cannot deal in detail with all the vast literature on cough, stroke and the risk of aspiration. The use of methods to test the LER will be emphasized, because of all the cough tests it is theoretically the most ‘anti-aspiration’; it is also the most neglected, although simple to test. We have developed and are using such a method to test the LER in stroke patients [7]. In this review we compare the use of LER with other cough tests. More sophisticated methods involving intubation (e.g. videofluoroscopic swallowing examination; fiberoptic endoscopic examination of swallowing; fiberoptic endoscopic evaluation of swallowing with sensory testing) may include cough induced by mechanical stimulation of the laryngeal mucosa. These important methods will not be reviewed here, where the primary concern is with cough mechanisms, although some of them have been claimed as ‘gold standard’ for the assessment of risk of aspiration. (‘Only alchemists believe in gold standards’; anon).

A problem with assessing the information on cough and aspiration in patients after stroke is that most studies involve *subjective* identification or estimation of the ‘strength’ of the cough. They usually lack measurements of the cough itself. Cough is portrayed as present or absent, or subjectively graded usually on a three point scale (present, weak, absent). However *objective* analyses of cough (by airflow, gastric pressure, expiratory muscle EMGs, chest wall acceleration and sound generation) are available and not only allow identification of the different types and patterns of cough [8-13], but also provide valuable information of the way neurological disease may disco-ordinate the neural mechanisms of cough (see later). Fig. 1 illustrates

some parameters that can be derived from airflow and gastric pressures in voluntary cough [10].

(Fig. 1 near here)

Thus cough is a highly complex process, and few would agree that all we need to measure is a recording of cough sounds, or to listen to them [14]. However cough sound intensity has been shown to correlate with some other parameters of cough [9].

2. Types of cough, including after stroke

Three different types of cough are described in the textbooks: voluntary and reflex cough (VC and RC), and the expiration reflex (ER). (Speaking semantically the ER is not a cough because it does not start with an inspiration, but it is convenient to include it as a 'cough'). There are probably further subdivisions. There are at least five different types of vagal afferent sensors which can cause cough [15-16], and they and their interactions would be expected to produce different patterns of cough. Visual observation of cough might identify these different patterns, but this subjective analysis has not been applied to cough after stroke, except to measure cough frequency.

Voluntary cough (VC). This has inspiratory, compressive and expulsive phases. It originates in the cerebral cortex; decerebrate animals have a vigorous RC [17] but,

obviously, no cough from the cortex. VC intensity can be measured by airflow, gastric/oesophageal pressures, expiratory muscle EMGs and sound intensity .

VC is related to urge-to-cough (UtC), a sensation that often precedes cough caused by a reflex stimulus [18,19]. However VC is preceded by an 'intention-' but not an 'urge' - to-cough. To elicit VC the patient is instructed to 'take a deep breath and cough'. But if you tell them just to 'cough', they will still start with a deep inspiration (G. Fontana, personal communication). The response is usually assessed subjectively by an observer, but quantitative methods have been applied [8,9-12, and see below].

VC is extensively used to test the risk of aspiration in patients with conditions like stroke, and for good reasons. If assessed subjectively it is quick and involves no apparatus. Objective measures of VC after stroke (airflows, pressures, expiratory muscle EMGs) give better predictive values of the risk of aspiration than do subjective measures [1,8-10]. However, although the apparatus needed is fairly simple, it may get in the way of patient assessment and treatment. A face mask and flowmeter, an inductance vest or an accelerometer [20] is required and, for more comprehensive analysis, expiratory muscle EMGs and gastric or oesophageal pressures are needed. If the patient is conscious but can't respond to a request for a VC, this may suggest damage to the cortical descending pathways for cough, although it does not follow that the LER and CR are weakened (see below).

There are good correlations between the objective strength of VC and the risk of aspiration [9]. However the results for individual patients may not be definitive. An important illustration of an objective method of assessing VC in stroke patients (Fig.

2 [8]) shows that, whatever the statistical analysis for the whole group of patients, a mild aspiration patient had *no* VC and a severe aspiration patient had only a *weakened* VC. Of course this variability between individual patients, compared with mean results, applies to other methods of assessing the risk of aspiration.

(Fig. 2 near here)

One complication of the use of VC to assess risk of aspiration in stroke patients is that the effect on VC will depend on the site of the main lesion and whether the patient is left- or right-handed [21-23]. In a study on 30 right-handed stroke patients, all of whom had a normal LER, 11 of 14 with a left-sided infarct had depression of VC, while none of 16 with a right-sided infarct did [21]. Risk of aspiration was not assessed, but this result is clearly relevant to the use of VC to assess this risk. This complication did not apply to the LER [21], and should not to the RC. It does not follow that VC is controlled from only one side of the cortex, although one side may be dominant.

A digression. It is difficult to see why *voluntary* cough has emerged during evolution of humans. Its only functions are to attract attention or to feign illness, and there are far more effective ways to do this than coughing. Nonhuman mammals, including primates, do not cough to attract attention, although they often vocalize to do so and can sneeze to express welcome and love—rare in humans who cannot voluntarily sneeze. Could animals be trained to cough? Guinea pigs can be conditioned to cough to non-tussive stimuli [24], but although the cortex may be involved we don't know what they are thinking or if they have UtC.

Reflex cough (RC). This is the ‘classical’ cough seen with lung diseases and airway irritation. It consists of an initial deep inspiration (inspiratory phase), followed by glottal closure and an expiratory effort (compressive phase), and then opening of the glottis with forced expiration (expulsive phase). Thus it mimics the general pattern of VC. However objective tests show clear differences in the neurological patterns of VC and RC [6,10,25]. There may be several glottal closures and expiratory efforts in one cough (a cough bout or epoch) [12]. The teleological advantage of RC is clear. It will tend to expel material which has reached the lower airways and may block, damage or irritate them; the initial inspiration may draw the material deeper into the airways, but it will provide a more substantial volume and flow of air with which then to expel it. But there is a teleological disadvantage to RC; like VC it starts with an inspiration, so is a form of ‘pro-aspiration reflex’.

RC is usually tested by making the patient inhale, either during tidal breathing or with deep voluntary breaths, an aerosol of a tussogenic agent such as capsaicin, citric or tartaric acids or distilled water [10-12,26-29]. Usually the concentrations are increased until the patient gives two coughs (C2—‘threshold’) and then five coughs (C5—‘sensitivity’), and the results are usually determined subjectively, although objective methods have also been used [10-12].

Assessment of RC has been applied to stroke patients [10,27-29]; it involves rather cumbersome apparatus (including a face mask and aerosol administration apparatus) that may interfere with patient assessment or treatment; and it may give no

better information on the risk of aspiration than the use of VC, except in patients where the stroke lesion has abolished or diminished VC with RC intact.

Laryngeal expiration reflex (LER). This is set up when solid or liquid material, or a chemical irritant, touches the vocal folds [4,5,13]. It consists of prompt closure of the glottis, together with a strong reflex expiratory effort with opening of the glottis and expulsion of gas from the lungs, interrupted by further closures of the glottis and expiratory efforts, the whole complex comprising an epoch or bout. There is no preliminary inspiration before the ER; this would invalidate its function which is to prevent solid or liquid material from entering the lungs, although after the bout of expiratory efforts there will be a compensatory inspiration. The ER can be elicited from the trachea (TER) [30,31], but here we will consider only the laryngeal ER (LER) which has an anti-aspiration effect.

The LER can be elicited voluntarily, as seen with throat clearing. It is usually tested experimentally by asking the patient first to breathe out and then inhale a small volume of a concentrated aerosol of 20 % tartaric acid [7,21]. A single controlled dose can be given from a 'puffer' (dosimeter) placed in the patient's mouth; he first breathes out deeply and when he subsequently begins to inspire the stimulus is applied [7,32-36]. The patient responds with a prompt reflex closure of the glottis and a forced expiratory effort; the glottis then opens with expiratory airflow, and the process may be repeated several times.

For stroke patients, only subjective methods (three-four point scale) of assessing the LER have been reported [7,32-34]. However the method has been used

extensively in patients with stress urinary incontinence (SUI), with measurements of gastric and vesicular pressures [35-36].

A potentially useful method to assess the LER is to vibrate the larynx from outside the neck [37,38]. This stimulus causes cough, probably the LER (N. K. Robinson, personal communication), and could be a good non-invasive and quantitative method.

Cough on swallow (CoS). In patients with central nervous disorders such as stroke cough may occur on swallowing. This may be reported during natural swallowing (CSE, clinical swallowing examination), and is usually tested by injecting some liquid into the back of the pharynx (MWST, modified water swallowing test). Presumably the pharyngeal material enters the glottis and the 'cough' prevents its aspiration. The modified barium swallow (MBS) is often used as a test, and has the advantage that radiographic techniques can show the presence of aspiration if it occurs. Presumably CoS is the same as the LER, but this has never been established. We are unable to find any objective records of CoS.

A paradox. If a patient swallows and *does not cough*—good and normal; if he swallows *and coughs*, not so good since material has entered the glottis (although it may not be aspirated); if he swallows and *does not cough*—bad if the material has passed the glottis and has been aspirated without cough. So an absent cough can be good or bad. Of course the use of X-radiography helps to answer this question as it applies at the time of the test, but we don't know if the objective recording of CoS would help the assessment.

We have described above four ‘types of cough’, and there may be subtypes yet to be identified. The choice of the type of cough tested in stroke patients may not only give different assessments of the risk of aspiration, but may point to quite different neural mechanisms and different abnormalities due to the disease process.

4. Comparisons between methods

It is not practical, for reasons of space, to summarize all the many results of comparing any two different methods for assessing ‘cough’ after stroke. No-one seems to have compared three (or four) methods in the same patients. Often the results include sensitivity, selectivity and specificity values for the two methods chosen, but space does not allow these important values to be detailed here. The general impression is that any of the methods is valuable in pointing to the risk of aspiration, and the use of two methods increases the value. In an acute stroke setting (aspiration may not be a problem in the kind of patients fit enough to come to an outpatient clinic) an important consideration must be simplicity of application of a method. Subjective VC assessment involves no apparatus; LER only the introduction of a ‘puffer’ into the mouth; RC and CoS quite complicated apparatus.

VC and LER. In a comparison between VC and LER in assessing the risk of pneumonia (due to aspiration) in patients after stroke, Addington et al. [7,32,33] studied 400 patients assessed by both VC and LER (both assessed subjectively, with appropriate anti-aspiration precautions taken if necessary). For LER, a depressed response was seen in 40 (11 %), and for VC in 81 (25%). Only 5 patients (1%)

developed pneumonia. A further 204 patients were assessed by VC alone, and 27 (13%) developed pneumonia. The results show that by assessing LER as well as VC and applying appropriate treatment, the risk of pneumonia was 1 %, compared with 13% when VC was used alone. In addition about half the patients who had a depressed VC had a normal LER. The studies have been criticised because of the subjective element in the assessments, the inevitable lack of a no-patient control group and the fact that the two studies were separate [39].

VC and LER produce very similar increases in intra-abdominal pressure, but the LER causes a much greater elevation of the diaphragm during the expiratory phase [34,35]. This seems surprising since the LER starts at a considerably lower lung volume than the VC, and indicates that the neural expiratory muscle input during LER must be much greater than that during VC.

LER and CoS. An important study assessed subjectively both LER and CoS (MBS) in 78 post-stroke patients [7,33]. This showed that of 53 patients with a normal LER 26 (49%) had an abnormal MBS but none developed pneumonia; whereas of the 25 patients with a depressed LER, 11 (44%) had an abnormal MBS but 5 (20%) developed pneumonia (Table 1). This indicates that a depressed LER is a better indicator of pneumonia risk than is the CoS due to MBS.

(Table 1 near here)

VC and RC. Several studies have compared VC and RC in assessing the risk of aspiration or pneumonia [10, 27-29]. In general both were shown to be depressed after

stroke. An important recent study by Ward et al. [10] assessed VC and RC by measurements of airflow and gastric pressure. They found that after stroke gastric pressure increases were much more depressed for VC than for RC (by 53 and 14%) while expiratory airflows were equally depressed (by 42 and 46 % (Table 2, Fig. 3). This must show that the stroke has not only 'depressed' cough, but has also caused discoordination of the respiratory muscles, presumably in the upper airways, that determine the rate of airflow for any given abdominal expiratory pressure.

(Table 2 and Fig 3 near here)

VC and CoS. Daniels et al. [40] looked at aspiration risk in patients after stroke, assessing VC and CoS. They found that the use of both indices had much better predictive value than either alone, and that VC alone was a more specific but less sensitive test than CoS alone; these results have been confirmed [41]. Similar results were found with patients with dysphagia due to parkinsonism [42]. Smith Hammond et al. [8,9] used objective quantification of cough (airflows and sound 'pressures') to compare VC and CoS with the risk of aspiration. They found that VC had greater sensitivity and specificity than CoS as an indicator of the risk.

RC and CoS. Several studies have compared RC with CoS, as indicators of the risk of aspiration or pneumonia [e.g. 41,42] Usually capsaicin or citric acid aerosol was used as the RC stimulant. An increase in the threshold to citric acid correlated well with an increased risk of aspiration and pneumonia.

RC and LER. We can find no examples of these two tests being compared in the same patients.

Discussion

We have described and briefly assessed four methods using cough for the assessment of the risk of aspiration and pneumonia after stroke. Each has its advocates who provide evidence to support their views (although none claims a method to be a gold standard!). The choice of test may depend on other features: the condition of the patient, the practicality of use in different clinical environments, and the availability and desirability of invasive techniques to assess risk. Most authors agree, and present evidence to support their view, that the use of two cough tests gives a better prediction of aspiration risk than does one test alone.

We have been developing and using the test of the LER to assess aspiration and pneumonia risk. It is more effective in this respect than VC and CoS alone [7,33] but, in relation to stroke, it has seldom been assessed objectively and quantitatively (unlike stress urinary incontinence [35,36]). We are influenced by the consideration that, unlike VC and RC which start with an inspiration that would cause aspiration, LER prevents inspiration and is an ‘anti-aspiration reflex’.

The last decade has seen two important advances in our understanding of cough mechanisms in stroke and other neurological disorders.

The first is the introduction of objective quantitative methods to measure cough in patients after stroke [1,9,10]. This is important, not only because the tests become more sensitive in assessing the risk of aspiration, but because they show that cough and its different types are very complex motor activities (which seems obvious). This is well established for healthy experimental animals [13,17] and humans [10,11,12]. To put it at its simplest, the muscular contraction patterns of VC and RC in healthy subjects are different [6,10,25]. The implication is that in terms of understanding disease mechanisms, it is insufficient to say that cough is normal, enhanced or weakened; one should try to determine which of the many complex motor outputs are affected. This is especially true for central nervous disorders such as stroke where the site, extent and influence of the lesion may cause many different patterns of activity in different types of cough. We have moved far from saying that cough is only a sound to that there are different types of cough, and that there are different patterns of sensory and motor activities in the different types of cough.

The second important advance is the demonstration that the various motor outputs of cough can be ‘disco-ordinated’—affected in different degrees [10-12]. In retrospect this is obvious; one would not expect these outputs—to different respiratory muscles and the glottis (not to mention mucus glands and the cardiovascular system)—to be distorted equally by neurological diseases.

It is uncertain whether this complex approach will be relevant to assessing the risk of aspiration after stroke, but it could be a valuable research tool in mapping out what is happening in the brainstem. Smith Hammond [9] and Ward et al. [10] have shown that flow pattern analysis in VC, in particular the volume acceleration in the

expiration phase, is a valuable clue to the risk of aspiration. Fig 3 illustrates the components of the flow pattern of VC and compares them with gastric pressures.. These components, together with the muscular activities that produce them, need further analysis and, in particular, need to be extended to the LER and the CoS.

We appreciate that the approaches advocated in this review may not always be applicable in a busy stroke ward or unit, but we suggest that as research tools they would tell us much about the pathophysiology of cough in stroke patients. And there is an important gap to be filled. Urge-to-Cough (UtC), in response to a cough stimulus, has been much studied recently in healthy humans, and is telling us much about the neural mechanisms of voluntary and reflex cough [18,19]. It seems important, and would be relatively easy, to include it in studies on the pathology of cough after stroke. After all, UtC links the sensory cough pathways to the cerebral cortex, and it is the disruption of these pathways that plays a major role in the changes in cough after stroke.

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Table 1. LER vs MBS; assessing risk of pneumonia in patients after stroke.

	No. of pts.	MBS		
		Normal	Abnormal	Pneumonia
Normal LER	53	27 (51 %)	26 (49 %)	0 (0 %)
Depressed LER	25	14 (56 %)	11 (44 %)	5 (17 %)

MBS; modified barium swallow. LER; laryngeal expiration reflex.

Note that with a depressed MBS patients were considerably more likely to develop pneumonia, whereas an abnormal MBS was a much less reliable indication. [From 7]

Table 2. Voluntary cough and reflex cough in healthy subjects and in patients after stroke.

	Voluntary cough		Reflex cough	
	Healthy	Stroke	Healthy	Stroke
Gastric pressure (cm H ₂ O)	209	99 (-53%)**	208	179 (-14 %) ^{NS}
Peak expir. airflow (l.min ⁻¹)	497	287 (-42%)**	379	204 (-46%)**

Values are for gastric pressure and peak expiratory airflow for healthy subjects and those after stroke. Reflex cough was induced by tartaric acid aerosol. Note that the expiratory flows were about equally depressed for both voluntary and reflex cough, but that gastric pressure increases were only significantly reduced with voluntary cough.

^{NS} Not significant. ** P < 0.001. (From [10]).

Figure legends.

Fig.1. Some of the variables which can be measured from airflow and gastric pressure during cough in normal subjects and in patients after stroke. [From 10]

Fig.2. Airflow measurements in a healthy subject (1) and in three patients after stroke (2-4). The severity of aspiration is indicated. Vertical lines indicate timing points for inspiratory phase, glottal closure and increase in expiratory flow. [From 8]

Fig 3. Airflow (above) and gastric pressure (below) in a healthy subject (left) and a post-stroke patient (right). Not that in the patient there is still an elevation of gastric pressure, but the airflow change is minimal. [From 10]

Figure1

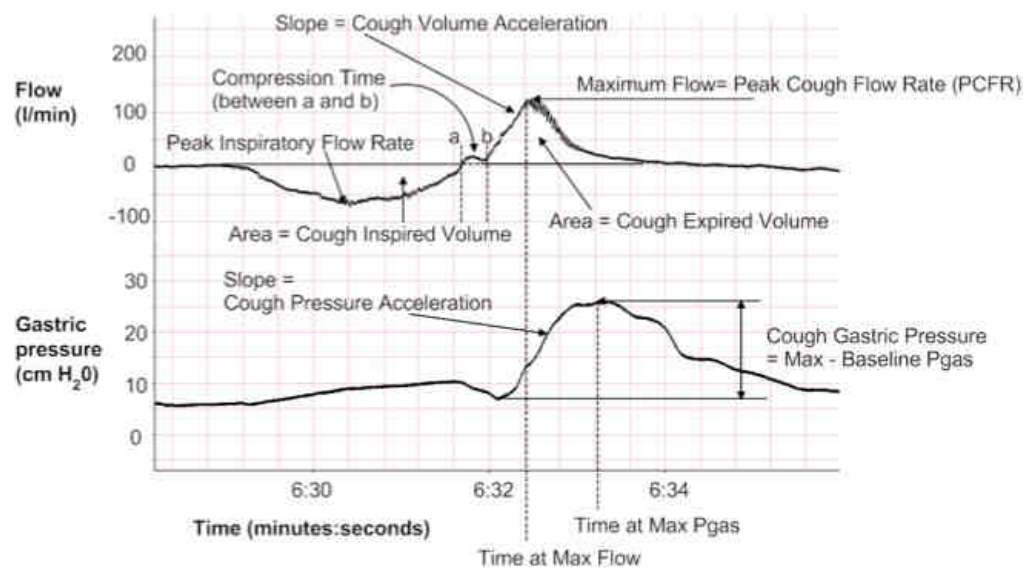


Figure 2

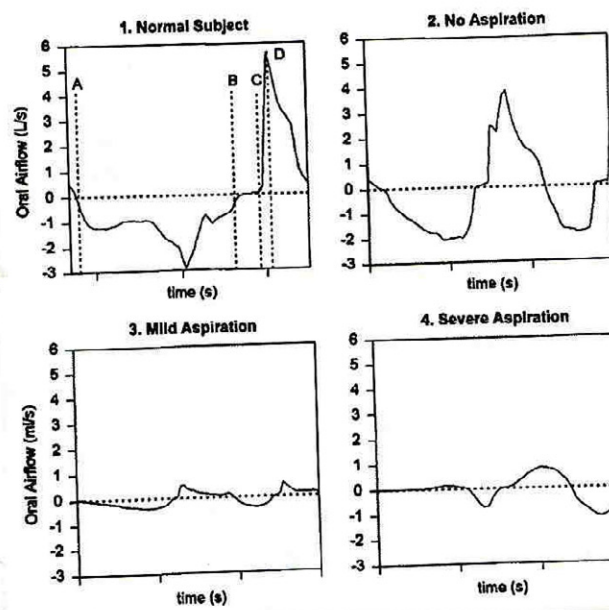


Figure. 3.

