Upper airway reflexes are of great practical importance to anaesthetists. Coughing during anaesthesia may often be only a minor problem, but can occasionally be a serious danger. Aspiration of foreign material into the lungs when pharyngeal coordination and airway reflexes are impaired can cause serious sequelae. Fortunately, although aspiration may be a relatively frequent event after anaesthesia [1], serious complications appear to be rare [2]. Much is known of the components of airway reflexes, but the application of this knowledge to everyday practice is surprisingly patchy. How can we learn more about the impact of anaesthesia on these reflexes?

At first sight, the reflex appears simple. Irritation of receptors in the upper respiratory tract causes a reflex motor response. The receptors of the respiratory tract include slowly adapting ("stretch") receptors responsible for the Hering-Breuer reflex, and rapidly adapting ("irritant") receptors, which are activated briefly by light touch, dust, chemical stimuli and cold air [3]. It is the rapidly adapting receptors that are responsible for the cough reflex. Their afferent impulses run in the vagus nerve, the superior laryngeal branch of which carries afferents from within the upper larynx; the central reflex site is in the medulla, and the efferent impulses are again carried in the vagus to the laryngeal muscles, and by the appropriate nerves to respiratory muscles (diaphragm, intercostal, accessory and abdominal muscles). Some other reflexes involving the larynx are well known by anaesthetists: the "Brewer-Luckhardt" reflex [4] is quoted in old anaesthetic textbooks. This is the response of vocal cord adduction ("laryngeal spasm") that occurs frequently after surgical stimuli such as anal dilatation. However, it is unlikely that any reflex is simple [5]. Further examination of the components of the upper airway reflexes may emphasize this.

Laryngeal afferent neurones with receptive fields in the epiglottis can be activated by a range of stimuli, but mechanical stimuli are most effective, particularly a light touch that moves over several receptive fields [6]. The sensory units consist of free nerve endings that lie between the mucosal cells of the airway epithelium [7]. They can respond faithfully up to high frequencies [8]. More than 50% of laryngeal afferent fibres also respond to cooling or, more exactly, to rate of heat loss from the airway [9]. They also respond to the presence of fluids, particularly water [10], and a variety of chemicals. The response to fluids appears to have a considerable degree of chemical discrimination: isotonic sodium chloride causes very little in the way of stimulation, whereas water, or solutions that are isosmolar but free of chloride ions, are potent stimuli for the laryngeal mucosal receptors [11]. The pattern of nerve firing from epiglottic receptors depends on the nature of the fluid causing the stimulation: low osmolality fluid contact leads to a longer delay and a longer period of activity than a solution that contains no chloride. Similarly, the response after ammonium chloride solution, for example, causes a more high-frequency and rapidly adapting response in a single superior laryngeal nerve fibre than most other substances [12], and it has been suggested that an "afferent portal" in the brainstem decodes these activity patterns before further central projection occurs. Inhalation of isosmolar solutions that lack chloride causes cough; if the solution is not isosmolar, then it causes not only cough, but also bronchoconstriction in susceptible subjects. This latter response is not affected by inhaled lignocaine, suggesting that the mechanisms for these two airway responses are different, despite stimulation of neurally similar receptors [13].

Sensory units appear to be particularly abundant over the arytenoid cartilages and are also found on the laryngeal side of the epiglottis [14]. The superior laryngeal nerve carries a large proportion of small diameter myelinated fibres (group III, A delta or B sensory fibres) [9], which carry afferent impulses from rapidly adapting receptors from structures such as the epiglottis [15].

The recurrent laryngeal nerve also carries sensory fibres [16], mainly from rapidly adapting receptors that are activated by light touch. These receptors are particularly numerous at the anterior and posterior extremities of the inferior surface of the vocal cords. Stimulation of these receptors results in vocal cord movement [17]. Afferent fibres in the laryngeal nerves project centrally to the nucleus tractus solitarius, particularly the caudal and posterior parts [6].

The vagal nerves do not represent the only pathway for airway protective reflexes: for example, potassium chloride applied to the lungs of anaesthetized dogs results in ipsilateral expiratory muscle activity despite section of the vago, suggesting a spinal reflex via sympathetic afferent nerves [18].

Cough consists of an initial laryngeal opening, followed by a closure of both the glottis and the supraglottic structures; the structures then open and vibrate, and the epiglottis may move forcibly backwards and then forwards again [19].

Laryngeal closure is a complex muscular event, involving activity of muscles that are considered to have abductor effects when active alone. Activation of...
of the laryngeal muscles by stimulation of the internal branch of the superior laryngeal nerve, which causes a reflex laryngeal closure, results in a more forceful closure than stimulation of the recurrent laryngeal nerve, which activates the laryngeal muscles directly, but presumably in a less coordinated way [20].

Cough does not always follow stimulation of laryngeal receptors, even in susceptible species [21]. In sleeping infants, introduction of small quantities of warm saline into the pharynx, sufficient to cause pooling posterior to the larynx, rarely leads to cough, and more commonly to apnea and a swallow reflex [22].

The strength of reflex response to laryngeal stimulation appears experimentally to vary with the depth of anaesthesia [23]. The reaction of airways to inhaled substances is reduced by increased mucus secretion, presumably because the mucus protects the airway surface [24]. In contrast, viral infection of the lungs leads to increased airway responsiveness, with amplification of reflex bronchoconstriction involving both afferent and efferent pathways, as discussed by Jacoby and Hirshman [25]. Changes in inspiratory flow rate alter the reaction to inhaled irritant aerosol [26] and may alter the reaction to inhaled ammonia, as discussed by Murphy and coworkers [27].

Using inhaled dilute concentrations of ammonia, Duckett and Hirsh [28] studied 23 patients before surgery, of whom 11 agreed to a repeat study either 24 h after surgery or 24 h after removal of a tracheal tube. Treatment was not allocated randomly and did not appear comparable, but their abstract concluded that tracheal intubation was responsible for a significant reduction in the competence of the glottic reflex.

The motor response to inhalation of a small concentration of ammonia consists of temporary inhibition of inspiration—probably phrenic—and a brief partial adduction of the vocal cords, although inspiratory flow does not cease completely. Greater concentrations can cause coughing. How good a paradigm is this response for the cough reflex?

First, the exact location of the receptors involved is unclear. Although receptors that respond to ammonia have been detected on the epiglottis, and within the larynx, the lower airways are also well supplied with receptors that respond to irritant substances with a rapidly adapting pattern of discharge [29]. Ammonia in concentrations about 100–200 p.p.m. stimulates both continuously active and normally silent laryngeal receptors, but only after a delay of between 2 and 4 s [30]. In lightly anaesthetized patients, insufflation into the nose of a 5% concentration of volatile anaesthetics such as halothane, and particularly enfurane and isoflurane, can cause reflex responses. The duration of expiration increases and the larynx tightens [31].

Thus it is likely that all parts of the airway are involved in the response to inhaled ammonia: the sensation of ammonia inhalation is subjectively localized generally within the larynx and trachea. The sensitivity of the reflex was reduced by local anaesthesia of the airway, but the anaesthesia was extensive, involving injection via the cricothyroid membrane, and thus did not localize any particular receptive field [32].

Second, the stimulus used does not closely resemble a natural stimulus such as foreign material in the airway; finally, the response used as an endpoint is not a cough.

Commonly, coughing is caused by entry of foreign material into the larynx and lower airways—that is "something going down the wrong way". The term laryngeal competence is often taken to imply, not only an adequate cough response in response to foreign material, but also that the upper airway is sufficiently well co-ordinated to prevent material getting down into the larynx and lower airways in the first place. Impairment of this co-ordination is a frequent accompaniment of recovery from general anaesthesia, and is of particular concern when regurgitation is likely, such as after lower oesophageal resection. The ability to protect the airway returns as central reflex impairment decreases; it is probable that the reflex response to ammonia inhalation does the same. Do interventions such as sedation or general anaesthesia specifically impair airway co-ordination or responsiveness, and the reflex response to inhaled foreign material, more than other reflexes or other indices of central depression such as reaction time? The influences of different anaesthetics appear to vary considerably.

For example, the effects of inhaled anaesthetic vapour depend upon the circumstances. A conscious patient can usually breathe 5% halothane vapour without coughing, when requested to do so for the purpose of inhalation induction, but after a "sleep dose" of thiopentone the same patient would cough vigorously if even 1% halothane were inhaled. Since barbiturates do not obviously affect the activity of the airway receptors, it seems that in the conscious state the central reflex is less easily activated. In contrast, the gag reflex is equally vigorous in awake and thiopentone-anaesthetized subjects. Other anaesthetic agents such as propofol have a more depressant effect on upper airway reflexes [33], and animal studies have shown changes in patterns of laryngeal muscle activity with sleep state and barbiturate anaesthesia [34]. The cough reflex is more easily elicited in some species than in others [21].

In consequence of all these factors, it appears unlikely that there will be a constant relationship between tests such as reaction time, and tests of airway reactivity such as ammonia inhalation, when different agents such as barbiturates, benzodiazepines and propofol are investigated, particularly if different species are used. The ideal anaesthetic in this regard would suppress reflex responses such as cough, whatever the stimulus, during anaesthesia and allow rapid recovery after emergence. At first sight, propofol might appear to be valuable, but it appears to have a surprisingly prolonged effect on other respiratory reflexes [35], and it may be that the reflex protection of the airway is similarly impaired for a prolonged period. Indeed, volatile anaesthetics may finally prove to be superior. Cough responses remain, at least at light levels of anaesthesia. During
anesthesia with enflurane (1.5% end-tidal), instillation of small quantities of water into the trachea can evoke reflex responses such as forceful expiration, coughing, panting and apnoea. I.v. lignocaine reduces the panting, coughing and respiratory reflexes, probably by a central action [36]. However, the central actions of different anaesthetics can result in widely different laryngeal responses [37].

Clearly, further study of "laryngeal competence", its components and the effects of anesthesia and sedation are required. This would be aided by a test of how well a patient can prevent "things going down the wrong way", and of how well things can be coughed out if they do. Ideally this test should not require invasive measurements, patient co-operation or ionizing radiation. The method refined by Langton and his colleagues [38] is a step in the right direction, but it may be necessary to use several paths to reach the goal.

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REFERENCES