

## Commentary

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### Why do we hiccup?

Considering the fact that almost everyone experiences hiccups at one time or another, remarkably little is known about them. The name itself is onomatopoeic, which is appropriate considering that the only common understanding of the hiccup is of the characteristic sound. Hiccups can be predictably elicited in some individuals by overindulgence of food, alcohol, or both, sometimes providing evidence of such behaviour and making them a common object of humour. There are, however, instances in which hiccups become intractable (singultus) causing insomnia, wasting, exhaustion, and even death, prompting scientific scrutiny of this otherwise harmless curiosity.<sup>1</sup> In this issue Fass *et al* (see page 590) present original investigative work on the afferent limb of the hiccup reflex.

Fass *et al* used a barostat to characterise the parameters of oesophageal distention that could elicit hiccups in normal volunteers. They report that rapid phasic distension of the proximal, but not distal, oesophagus could reproducibly induce hiccups in four of 10 subjects. Hiccups occurred during rapid inflation of the barostat bag and immediately resolved with deflation, strongly implicating oesophageal mechanoreceptors as the critical afferents. The authors speculatively generalise this observation to the population as a whole, but in this one needs to be circumspect, recognising the long list of stimuli that have been reported to cause prolonged bouts of hiccups. A partial inventory of hiccup aetiologies encompasses trauma (skull fracture, closed head trauma, surgery), mass lesions (aneurysms, tumours, goitres, diverticuli), infections (subdiaphragmatic abscess, cholecystitis, pleurisy, meningitis, encephalitis), irritative stimuli (heartburn, spicy food, gastritis, peptic ulcers, pancreatitis), luminal distension (achalasia, gastric distension, oesophageal rings and strictures), central nervous system pathology (multiple sclerosis, cerebrovascular accidents, psychogenic), and metabolic aberrations (uraemia, drugs).<sup>2–4</sup> One individual is described in whom a hair tickling the tympanic membrane was ultimately revealed to be the cause of singultus. In view of this great diversity of causative stimuli, defining the afferent limb of the hiccup reflex is no simple task and there is reason to suspect substantial intersubject variability. In the broadest sense, relevant afferents can course with the vagus or phrenic nerves, the pharyngeal plexus from C2 to C4, and the sympathetic chain from T6 to T12.<sup>3,5</sup> In all likelihood, there is no universal stimulus for hiccups in adults, but rather, a long list of potential stimuli in susceptible individuals.

The central elements and efferent limbs of the hiccup reflex have been better characterised than the afferent limb. The hiccup is an involuntary medullary reflex influenced by, but independent of, the respiratory centre of the medulla. In a meticulous investigation, Davis demonstrated that hiccup frequency could be modulated or completely suppressed by inhalation of CO<sub>2</sub> (the physiology behind the remedies of rebreathing into a paper bag and breath holding).<sup>6</sup> Furthermore, the whole array of inspiratory muscles are activated on the efferent side of the reflex: the phrenic nerves to the diaphragm, the external intercostal nerves (T1–T11) to the intercostal muscles, and the

scalenus anticus nerve to the scalene muscles which elevate the clavicles.<sup>4,6</sup> These inspiratory efferents are activated far more vigorously during hiccups than during cyclic respiration. Thirty five milliseconds after inspiratory activation, the recurrent laryngeal nerve effects glottic closure, resulting in the characteristic “hic” and eliminating any ventilatory effect of the reflex. The large volume changes which would occur in hiccups were it not for the associated glottal closure is evident in tracheostomised individuals in whom hiccups can cause severe hyperventilation; Davis reports such a case in which hiccups resulted in an arterial pH of 7.58 and a minute ventilation exceeding 20 litres.<sup>6</sup> Thus, although the hiccup reflex results in repetitive, essentially maximal stimulation of the inspiratory musculature, it normally serves no respiratory function.

As detailed earlier, the hiccup has minimal impact on ventilation because of the prompt glottic closure following the intense inspiratory drive. Thus, speculation regarding the purpose of the hiccup naturally shifted to the gastrointestinal tract because of the numerous gastrointestinal stimuli observed to elicit them.<sup>6</sup> However, although a spell of hiccups may interfere with eating, it is not a protective reflex (despite the speculation presented by Fass *et al* that it may prevent the entry of large food boluses into the gastrointestinal tract). Whereas vomiting, gagging, and coughing are effective (at times life saving) protective reflexes of the gastrointestinal and respiratory tracts, the hiccup has no discernible survival value. More likely than not, spells of hiccups in adults result from activation of a vestigial reflex that once served some purpose in ontogeny or phylogeny. Since it is equally difficult to construe a scenario in which hiccuping is of use to mature beasts, the more likely candidate would seem to be ontogeny. Hiccuping is observed in utero and the tendency to hiccup continues after delivery. Fetal hiccuping can be demonstrated ultrasonographically in utero as large inward and outward movements of the chest occurring 1–6 times per minute with spells lasting an average of eight minutes.<sup>7</sup> Premature infants spend an average of 2.5% of their time hiccuping.<sup>4</sup> Hiccuping spells occur in utero and in premature babies without any identifiable stimulus for initiation or for cessation. This suggests that during the perinatal period, when the respiratory tract needs to mature rapidly, hiccuping does have a survival value. Perhaps, hiccuping is essentially a programmed isometric exercise of the inspiratory muscles which are superfluous in utero, but afforded no time for maturation after birth. Beyond the perinatal period, however, hiccuping is a vestigial reflex, incidentally elicited by a wide and variable range of autonomic stimuli.

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