constraints. Regrettably, therefore, although showing risks at the level one might expect, these studies are subject to criticism because of small sample size, simplified exposure determination, lack of compensation for confounders, and so on.

The paper by Dutt *et al.* in this issue[1] is a step forward in the progression of evidence. By careful sample selection and correction for important potential confounding risk factors, they provide evidence of higher confidence than most previous studies by comparing respiratory disease/symptoms and lung function in non-smoking women cooking with biomass with those using kerosene and liquid petroleum gas.

Given the large vulnerable populations involved, if the widespread existence of such health effects were to be generally accepted, there would be important implications for health, energy, housing, and environmental policies and investments in a number of nations. For these reasons, the World Bank in 1992 classed indoor air pollution in developing countries as one of the foremost critical global environmental problems.

Nevertheless, there is yet no research programme directly addressing this problem in any national or international organization concerned with development, health, housing, or environment. One consequence of this inattention is the strange sight of health scientists extrapolating effects from low doses, where most air pollution work has been done, to high doses, where most of the people are. That this is the reverse of the usual direction of health research may be indicative of what one day might be seen as shocking public health neglect of a serious problem for a large population with relatively little political and economic clout to protect itself.

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Causes and Treatment of Persistent Hiccups

Hiccups consist of involuntary brief bursts of intense, coordinated inspiratory activity involving the diaphragm and inspiratory intercostal muscles with reciprocal inhibition of the expiratory intercostals. Sudden closure of the glottis occurs almost immediately after the onset of diaphragmatic contraction thus minimizing the ventilatory effect as well as generating the characteristic grunt and sense of discomfort.[1] It is usually a transient phenomenon resolving spontaneously or with simple measures and is often associated with gastric distension, sudden changes in temperature, emotion or alcohol ingestion.[2] They have no known physiological function and can occur in the foetus, child or adult. Hiccups may be present during all stages of sleep and the amplitude and frequency of sleep hiccup have stage-dependent characteristics.[3] Chronic or intractable hiccups may be defined as lasting longer than 24 hours or recurring in repetitive attacks. They are rare and may indicate serious underlying pathology; they may also produce deleterious effects including sinus pause with atrioventricular asystole due to an excessive vagal response,[4] postoperative wound dehiscence or infection, fatigue, dehydration, sleep deprivation, weight loss, and in extreme cases, death.[5]

Intractable hiccups may be the result of gastrointestinal, metabolic and endocrine disorders, structural or functional disturbances of the medulla, disturbances affecting afferent or efferent nerves to the respiratory muscles, drugs, general anaesthesia and psychogenic causes.

Disorders of the oesophagus and other parts of the gastrointestinal tract are associated with protracted hiccup due to stimulation of the visceral afferent fibres of

the vagus nerve. In particular, hiccups occur with gastroesophageal reflux, achalasia, gastric distension, oesophageal or small bowel obstruction and pancreatic or biliary disease.[1,6] Similarly, involvement of the auricular branch of the vagus may explain the association with a foreign body in the external auditory meatus[7] and, by a similar mechanism, mediastinal pathology including tumours and thoracic aortic aneurysms may cause hiccup by involvement of the thoracic afferent fibres.[8] Protracted hiccup may also be associated with diaphragmatic irritation caused by subphrenic and hepatic pathology,[9] pleural or pericardial effusion and lateral myocardial infarction[10] possibly due to involvement of efferent phrenic nerve fibres.

Hiccups occur as a consequence of structural lesions of the medulla in the region of the vagal nuclei and the nucleus tractus solitarius;[11] these include infarction in the territory of the posterior inferior cerebellar artery (pica), brainstem haemorrhage, saccular aneurysms or ectasia of the pica,[12] tumour,[13] tuberculoma,[14] abscess,[15] Arnold–Chiari malformation and syrinx,[16] haematoma and demyelination.[9] They may also be a feature of infections of the central nervous system such as viral encephalitis and less commonly meningitis, encephalitis lethargica and syphilis.[17] HIV encephalopathy, toxoplasma infection and progressive multifocal leukoencephalopathy are also increasingly recognized as important causes of chronic hiccup.[18,19] Neurogenic hiccups indicate involvement of the medullary region intimately associated with automatic respiratory control. Their occurrence may anticipate the development of irregularities of respiratory rhythm culminating in respiratory arrest.[20] However, neurogenic hiccup rarely occurs in isolation and associated brainstem or long tract signs are usually evident.

Hiccups are common during light anaesthesia and may interfere with the surgical procedure and the efficiency of ventilation. They are also common in the postoperative period.[21] They are associated with systemic disorders such as diabetes mellitus, uraemia, hypocalcaemia, and Addison's disease.[2,9,22] Several reports have described intractable hiccup as a manifestation of hyponatraemia, often due to psychogenic polydipsia.[23–25] In an important recent study, Thomas *et al.* [26] have reported a clear and strong association between hyponatraemia and hiccup. This paper suggests that hyponatraemia may be causal or may exacerbate hiccups present for another reason and in some patients therefore may be easily treated. Iatrogenic causes include short-acting barbiturates, ceftriaxone, etopiside, alpha methyldopa and steroids. Hiccups may also be a distressing and painful manifestation in terminal disease.

More than one hundred forms of physical or pharmacological treatment for intractable hiccups have been described, including acupuncture, hypnosis and prayers to St. Jude.[27,28] This vast array of anecdotal and uncontrolled reports reflects both the self-limiting nature of hiccups and the lack of any consistently satisfactory and reliable treatment.

The first line of management is to reverse or treat any underlying cause, including relief of oesophageal obstruction or gastric distension. Hiccup frequency is reduced by elevated pCO_2 and amplitude is increased with a fall in pCO_2.[1] This may be the mechanism by which breath-holding, rebreathing and other techniques designed to interrupt the respiratory rhythm are effective. However, if the patient has a tracheostomy bypassing the glottis, the vigorous and uninterrupted inspiratory spasm may produce hyperventilation, respiratory alkalosis and thereby exacerbate the hiccups.[29,30]

Stimulation of the pharynx reliably controls hiccups although the effect may be only temporary. Salem [31] described the use of frictional movement of a catheter sited in the pharynx opposite the second and third cervical vertebrae. Presumably, similar pharyngeal stimulation is achieved by the passage of a nasogastric tube, sipping iced water, gargling, swallowing granulated sugar and a variety of other manipulations of the uvula or nasopharynx. Hiccups may also be inhibited by stimulation of other areas of the upper respiratory tract and external auditory meatus.[2] Modulation of phrenic nerve function either by transection, anaesthetic block or stimulation (electrical and mechanical) is often unsuccessful because associated inspiratory bursts persist in intercostal and accessory respiratory muscles.[29] Furthermore, blocking of both phrenic nerves causes complete diaphragmatic paralysis and may precipitate severe

respiratory impairment. A recent report has described successful non-descriptive microvascular decompression of the vagus nerve from the pica for the treatment of intractable idiopathic hiccup.[32]

Many drugs have been used to treat prolonged hiccups resistant to physical methods. Chlorpromazine remains the most consistently effective agent but haloperidol is also valuable. There are a number of alternative drugs including metoclopramide, clonazepam and antiepileptics (carbamazepine, sodium valproate or phenytoin), intramuscular glucagon and dexamethasone, which may also help, particularly in the management of neurogenic hiccup. Recent reports have described resolution of prolonged hiccup with amitriptyline, nifedipine, amantidine, lignocaine, cisipride and baclofen. Many other classes of agents have been beneficial in single cases or short reports; these include tricyclic antidepressants, anticholinergics, benzodiazepines, CNS stimulants, H_2 receptor antagonists and dopamine agonists.

When faced with a patient with intractable hiccup it is necessary to exclude or treat any underlying pathology. If simple physical measures fail to abort the attack the most valuable drugs include chlorpromazine, metoclopramide and baclofen.

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