Hiccups, an involuntary, spasmodic contraction of the diaphragm causing an initial inspiration and sudden closure of the glottis, are experienced by almost everyone, yet the etiology and mechanism remain elusive and debated. The most accepted theory is the “hiccup reflex”. The hiccup reflex arc is composed of three portions, the afferent, central, and efferent limbs. The afferent limb comprises the phrenic and vagus nerves and the sympathetic chain arising from thoracic segments T6–12. The efferent component consists mainly of the phrenic nerve and supraspinal coordination between the brainstem and midbrain areas. The central connection between the afferent and efferent limbs is attributed to a nonspecific anatomic location somewhere in the spinal cord between segments C3–5 and the brainstem. The most frequent benign causes include gastric distension, sudden change in temperature, alcohol, excess smoking, or psychogenic (sudden excitement or emotional stress); therefore, these hiccups are often brief, self-limiting episodes of no clinical significance.

When the hiccups last more than 48 hours (called persistent hiccups) or even 1 month (intractable hiccups), they may have a considerable impact on general health through disturbance of diet, sleep, and mood. Of most importance, these persistent or intractable hiccups might be secondary to underlying diseases. In the December 2010 issue of the Journal of the Chinese Medical Association, Lin and Huang reported an interesting case of sarcoidosis that presented solely as hiccups. In fact, although rare, this case is not surprising, because many reports have shown that hiccups are more common in those with underlying gastrointestinal tumors and can be the only presenting symptom of an underlying malignancy.

Because of the long course of the nerves and diffuse nature of central connection, many causes of hiccup have been reported. The report from Drs. Lin and Huang recalled our memory that very common but often neglected symptoms of patients might be the only initial presentation of curable benign or more severe diseases, for example, malignant diseases. Furthermore, based on the causes—vagal nerve/diaphragmatic irritation (including gastric distension, gastritis or gastroesophageal reflux, liver distension due to hepatomegaly or tumor and ascites/abdominal distension/intestinal obstruction); phrenic nerve (including mediastinal tumor and diaphragmatic irritation/tumor involvement), higher centers (including intracranial tumor (esp. brainstem) and meningeal infiltration), systemic causes (including hypokalemia, hyponatremia, hypocalcemia, hypocarbia, and infection/fever), and finally iatrogenic/drugs (including corticosteroids, benzodiazipines, antibiotics and opioids), treatment should be directed at a specific cause and might be more effective for these patients with hiccups. Many drugs with different mechanisms, such as antipsychotics (e.g. chlorpromazine), anticonvulsants (e.g. gabapentin), anesthetic agents (e.g. ketamine), calcium channel blockers (e.g. nifedipine), antidepressants (e.g. sertraline) and other medications (e.g. amantadine), might be effective for the treatment of hiccups.