

Anatomy of Hiccups and its Relations to its Nonpharmacological Management

Marjadi Hardjasudarma

Abstrak

Cegukan masih merupakan teka-teki medis karena tidak mempunyai manfaat dan cara-cara pengobatannya jauh lebih banyak daripada penyebab-penyebabnya. Cara-cara pengobatan ini berkisar antara pengobatan-pengobatan tradisional yang telah terkenal sejak dahulu kala sampai obat-obat sintetik baru. Pengetahuan yang tepat dan rinci tentang asal dan sifat cegukan belum banyak, meskipun akhir-akhir ini telah diusulkan suatu lengkung refleks cegukan dengan koordinasi supraspinal. Makalah ini dimaksudkan untuk mengungkapkan aspek-aspek anatomi cegukan dikaitkan dengan mekanisme kerja penanganan-penanganan non farmakologikanya.

Abstract

Hiccups remain a medical enigma, as they serve no useful purpose and have much more cures than etiologies. These cures may range from universally known time-honored remedies to new synthetic pharmacologic agents. Little is known about the exact nature of hiccups, although recently a hiccup reflex with supraspinal coordination is proposed. The purpose of this paper is to reveal the anatomical aspects of hiccups and to relate them to the mechanisms of action of many non pharmacologic managements of hiccups.

Keywords : Hiccup reflex, Supraspinal coordination, Nonpharmacological management of hiccups.

INTRODUCTION

Hiccup is usually a transient and benign annoyance experienced occasionally by most people as a sudden contraction of the inspiratory muscles terminated by abrupt closure of the glottis to produce the characteristic sound, from which it derives its onomatopoeic name ("hoquet" in French, "hik" in Dutch, "Hipo" in Spanish, "geehouk" in Hebrew, "hicka" in Swedish, "hikke" in Norwegian and Danish).^{1,2}

Most hiccups occur as brief, self-limited episodes lasting only a few seconds or minutes; they are often caused by overdistention of the stomach, excitement, a sudden change in temperature or alcohol ingestion.²

Hiccups that last more than 48 hours or recur at frequent intervals, are referred as "persistent" and often imply a serious underlying pathologic disorder such as myocardial infarction,³ uremia or intracranial neoplasms.^{1,2} Occasionally hiccups are "intractable", occurring continuously for months or years, causing insomnia, exhaustion, wound dehiscence after surgery, dehydration and weight loss resulting from inability to swallow fluids and food, and ventricular dysrhythmias as a result of disturbance in serum potassium;^{1,2} all this

may result in high morbidity and even death.⁴ Although hiccups are a frequent and nearly universally experienced phenomenon, they serve no known useful or protective function.^{1,2}

In some cases, despite exhaustive investigations, their etiologies cannot be determined, so that therapeutic recommendations for management of hiccups encompass a spectrum of approaches ranging from universally known home remedies to new synthetic pharmacological agents.¹ No wonder that Charles Mayo⁵ in a discussion about 60 years ago commented: "Perhaps one is justified in saying that there is no disease which has had more forms of treatments and fewer results from treatment than has persistent hiccup".

Many of these home remedies are time-honored and although many of them are ancient and obscure, some have sound anatomical and physiological bases.^{1,2}

On the other hand, the exact nature of hiccups is still not satisfactorily explained. On the anatomical part, the role of two nerves, the phrenic and the vagus, is firmly established; while on the physiological part there is little doubt that hiccups have a reflex arc.^{1,2,6}

In this context, the author tried to review the literatures on the anatomical aspects of hiccups and relate these to the many non pharmacological approaches used in the management of hiccups.

DISCUSSION

Anatomical and physiological considerations

a) Anatomy of the phrenic and vagus nerves^{7,8}

The anatomy of these nerves will be briefly reviewed, as they are intimately related to the "hiccup reflex".

- The phrenic nerve (see Fig.1) usually arises from the third, fourth and fifth cervical nerves, so that it is derived from both cervical and brachial plexuses; it passes downward in front of the anterior scalene muscle, between the muscle and the prevertebral fascia, and is commonly attacked surgically as it lies in this position.

At operations, the vagus nerve and the cervical sympathetic chain have both been mistaken for the phrenic nerve. The vagus nerve lies within the carotid sheath, anterior to the phrenic nerve, and the cervical sympathetic chain lies somewhat more medially, posterior to the carotid sheath, but not upon the anterior scalene muscle.

At the root of the neck, the phrenic nerve passes between the subclavian artery and the subclavian vein and so enters the thorax. Within the thorax, it descends nearly vertically in front of the root of the lung, and then between the pericardium and the mediastinal pleura (where it is accompanied by the pericardiophrenic vessels) to the diaphragm which it innervates. In 30% of the cases in which the phrenic nerve is crushed to alleviate intractable hiccups, there is an **accessory phrenic nerve**. It arises most frequently from the fifth cervical nerve (in common with the nerve to the subclavius muscle) and runs usually lateral to the normal phrenic to join it at about the level of the first rib, but it may not unite with it until the level of the root of the lung or even until close to the diaphragm. The accessory phrenic nerve may account for the occasional failure to obtain diaphragmatic paralysis after crushing of the phrenic nerve.

If the phrenic nerve is avulsed from the well within the thorax, it is probable that all accessory phrenic nerves will also be torn out. However, if the phrenic nerve is simply crushed in its normal surgical position (as it lies on the anterior scalene muscle), it may be prudent to locate and crush the nerve to the subclavius muscle and to seek all other branches descending from the brachial plexus

along the lateral border of the anterior scalene muscle.

- The vagus nerve (Latin : vagus = wanderer), or the tenth cranial nerve, has an extensive course and distribution, since it passes through the neck and the thorax to the abdomen.

The vagus nerve (see Fig.2) makes its exit through the jugular foramen; within the foramen it bears its jugular (or superior) ganglion, from which arise the meningeal branch to the duramater in the posterior cranial fossa, and the auricular branch (nerve of Arnold) which passes through the tympanomastoid fissure to innervate parts of the external acoustic meatus and the outer surface of the tympanic membrane.

After its exit from the jugular foramen, the vagus nerve enlarges into a second swelling, the nodose (or inferior) ganglion, from which arise the pharyngeal branch (principal motor nerve of the pharynx), branches to the carotid body and the carotid sinus, and the superior laryngeal nerve which innervate the cricothyroid muscle and the mucous membrane of the larynx as far down as the level of the vocal folds.

The right recurrent laryngeal nerve arises in the neck, while the left one arises in the thorax; both nerves ascend to the tracheoesophageal groove and end in the larynx where they innervate almost all laryngeal intrinsic muscles and the mucous membrane of the larynx below the level of the vocal folds.

Cardiac branches arise in the neck and in the thorax, to join branches from the cervical sympathetic ganglions to form the cardiac plexus at the base of the heart.

In the thorax, both vagus nerves pass behind the roots of the lungs, here they give off pulmonary branches to both lungs. Both nerves then descend on the esophagus, giving off esophageal branches and then enter the abdomen through the esophageal opening in the diaphragm to the stomach. Here it distributes gastric branches for the stomach and celiac branches for the celiac plexus and ganglion, from here twigs are sent to the splenic, hepatic, renal, suprarenal and superior mesenteric plexuses, so the parasympathetic vagal nerves can be traced in the large intestine as far as the left colic (splenic) flexure.

b. Anatomy of the "hiccup reflex"

The precise pathophysiological mechanisms responsible for hiccuping eluded anatomists, physiologists and neurologists for centuries.² Scientists of the early cen-

turies mentioned several pathological processes associated with hiccups, such as inflammation of the liver and inflammation of the stomach due to spoiled food. In the latter, it was thought that hiccups occurred as a convulsive motion of the stomach to dislodge what is impacted in its body.^{1,2}

The first anatomical structure related to hiccups was found by Short⁹ in 1833, when he recognized the relationship between irritation of the phrenic nerve and hiccups.

In 1943, Bailey¹⁰ proposed the existence of a "hiccup reflex", a principal component of which was a "hiccup center" located somewhere in the upper cervical segments of the spinal cord. Since then Bailey's findings have been modified and expanded, it is now known that hiccups result from stimulation of one or more components of the hiccup reflex arc.

The afferent portion of the hiccup reflex are comprised of the phrenic and vagus nerves and the sympathetic chain arising from the thoracic segments T6-T12, while the efferent portion was then thought to be exclusively from the phrenic nerve.

The central connections between the afferent and efferent limbs of the reflex, as well as the center of the reflex, were anatomically not so clear, but it was thought that the center was located somewhere in the spinal cord, between segments C3 and C5, which was the origin of the phrenic nerve.

Bailey's findings were confirmed by subsequent investigators, such as Salem and others¹¹, who contributed that besides the phrenic nerve as the primary efferent limb of the reflex, other efferents to the glottis and accessory muscles of respiration were also thought to be involved in hiccupping. These contributions were based on findings in patients in whom hiccups were still present even after transection of both phrenic nerves. Electromyographic studies done during hiccupping, have demonstrated simultaneous firing of motor neurons to the anterior scalene muscles (C5-C7), external intercostal muscles (T1-T11) and glottis (recurrent laryngeal nerve). It was also recently noted that normal esophageal contractile tone and lower esophageal sphincter pressure were reduced during hiccupping, suggesting the existence of a simultaneous inhibitory autonomic process.^{11,12}

All these findings and the finding of the bilateral hemi-diaphragm involvement during hiccupping, pointed to a complex supraspinal coordination of the efferent limb which included brainstem and midbrain areas such as the respiratory center, phrenic nerve nuclei, medullary reticular formation and hypothalamus.^{1,11,12}

Nathan and others⁶ went even further by proposing that the center of the hiccup reflex was in the brain

stem itself, independent of the respiratory center, its afferent limbs consisted of the pharyngeal plexus, branches of sympathetic thoracic ganglions, phrenic and recurrent laryngeal (vagus) nerves, while the efferent limb consisted of the nerves to the anterior scalene muscle, and external intercostal muscles, the phrenic and the recurrent laryngeal (vagus) nerves.

So, in this theory, the vagus and phrenic nerves supply both afferent and efferent pathways to and from the hemi diaphragms and the laryngeal musculature (see Fig.3).

It was thought for many years, that the origin of the hiccup reflex was respiratory in nature (hence the term "hiccough"). This thinking was recently challenged, by Davis¹³ who monitored diaphragmatic and intercostal electromyographic recordings and pulmonary spirometric function simultaneously, to demonstrate that hiccups have only a minimal effect on ventilation. He arrived at this conclusion by determining that glottic closure was noted to be very transient and occur only 35 ms after the onset of respiratory muscle motor discharge.

Mechanisms involved in the non pharmacological managements of hiccups

Most mechanisms of action of the many time-honored remedies still used in the non pharmacological management of hiccups are readily explained by anatomical knowledge of the hiccup reflex arc.

Some of these mechanisms are :

1. Stimulation of vagal afferents of the hiccup reflex arc, thereby interrupting the vagal limb of the arc.^{1,2} According to the "gate control" theory,^{6,14} impulses arising in response to vagal stimulation (e.g by pharyngeal stimulation), may block or inhibit other afferent impulses being transmitted through the vagus and thus interrupting the hiccup reflex. Hiccup remedies which use this mechanism are:^{1,2,15}
 - a. manipulation of an aberrant hair irritating the tympanic membrane (mediated via the auricular branch of the vagus nerve).
 - b. forcible traction of the tongue, gargling with water sipping ice water, swallowing granulated sugar, hard bread or crushed ice, biting on a lemon wedge (soaked with something noxious, such as vinegar), inhaling noxious agents (e.g. ammonia), drinking from the far side of the glass, direct pharyngeal stimulation either orally or nasally with a rubber catheter, lifting of the uvula with a spoon or cottontip applicator, instillation of ice water into the nostril (all these

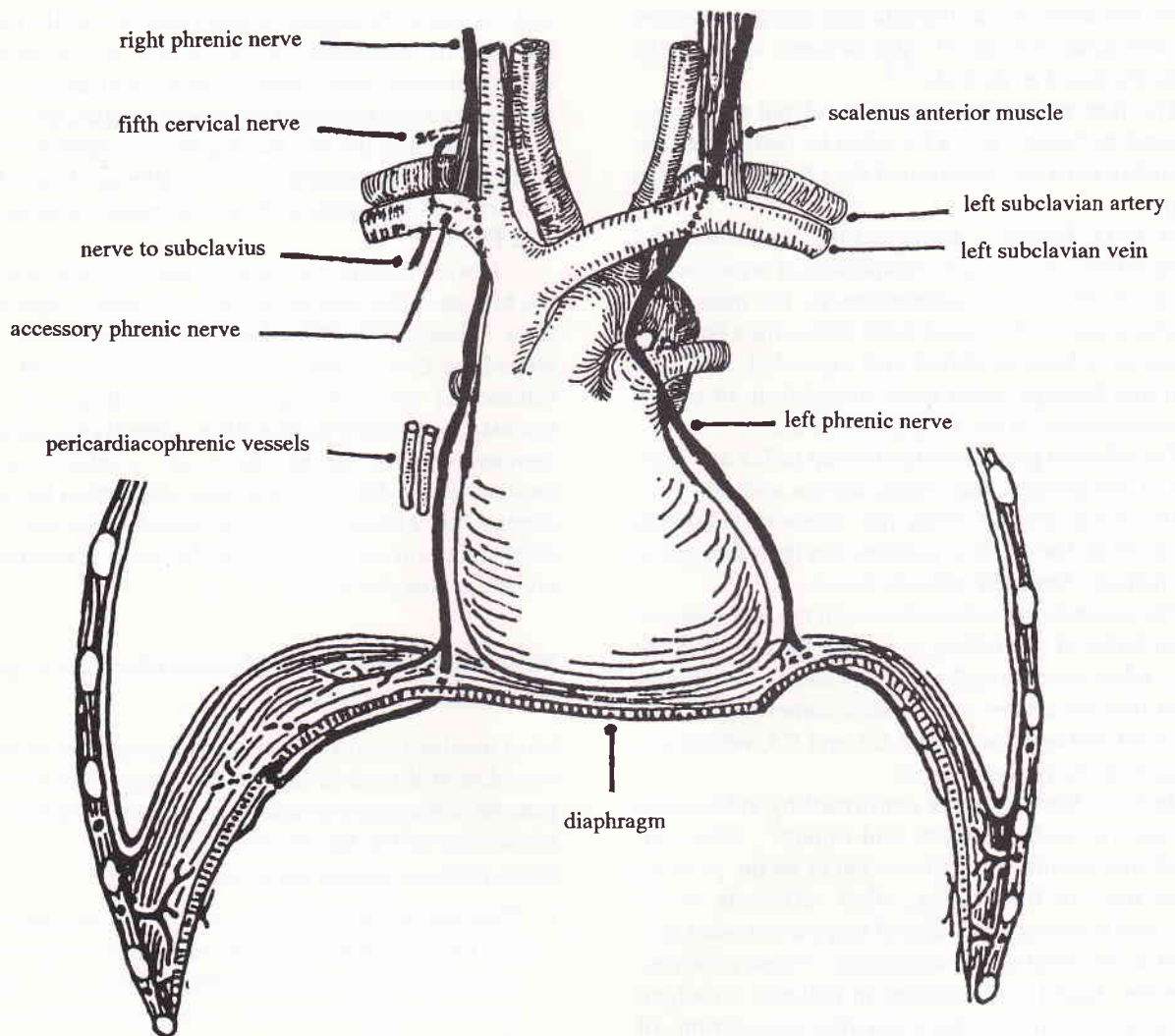


Fig 1. The course and distribution of the phrenic nerves. The phrenic nerve is commonly attacked surgically as it lies in front of the scalenus anterior muscle, beneath the prevertebral fascia. On the right side, an accessory phrenic nerve arises from the fifth cervical nerve in common with the nerve to the subclavius muscle and after leaving this, it joins the phrenic nerve. This accessory nerve may account for the occasional failure to obtain diaphragmatic paralysis after crushing of the phrenic nerve.

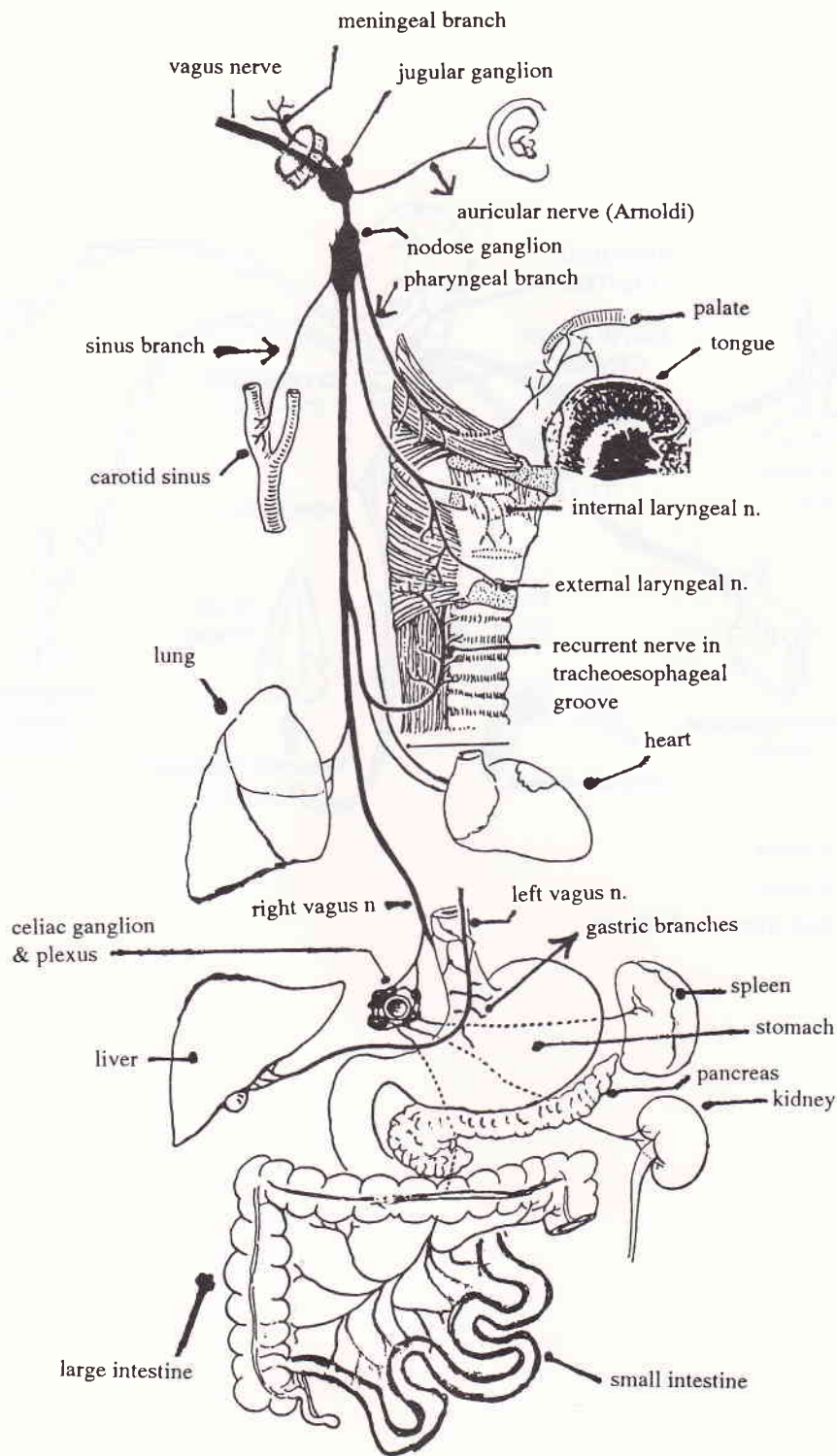


Fig 2. The extensive course and distribution of the vagus nerves render it possible to be used in many nonpharmacological remedies of hiccups, by stimulating branches of the nerves at different locations (see arrows : the pharyngeal, sinus, auricular and gastric branches).

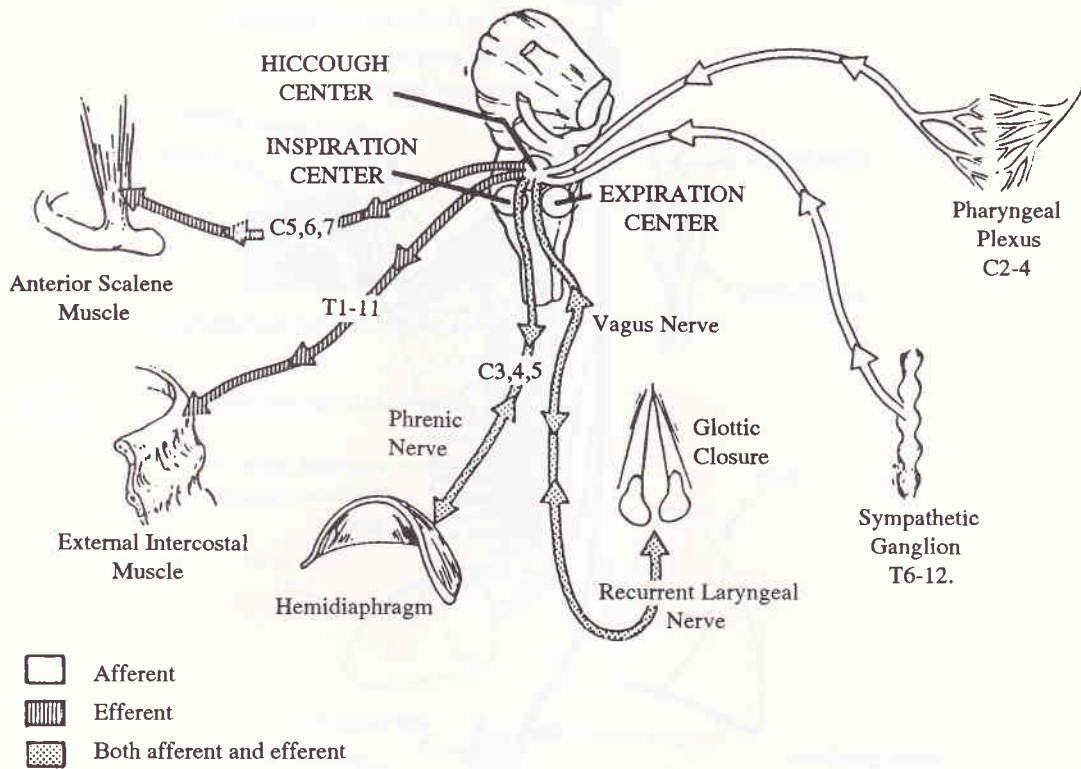


Fig 3. Schematic representation of the hiccup reflex arc as proposed by Nathan et al.⁶. The center of the reflex is located in the brain stem, independent of the respiratory center. Branches of the pharyngeal plexus and the thoracic sympathetic chain supply afferent pathways, while the efferent ones consist of nerves to the anterior scalene and intercostal muscles. The phrenic and the vagus nerves supply both afferent and efferent pathways to and from the hemidiaphragms and the laryngeal musculature.

remedies are mediated via the pharyngeal branch of the vagus nerve).

- c. nasogastric suction and iced gastric lavage (these remedies are mediated via the gastric branches of the vagus nerve, but some authors believe that direct diaphragmatic stimulation may play a role).
- d. other vagomimetic procedures such as carotid massage and digital ocular globe pressure.

2. Interruption of the phrenic limb of the hiccup reflex are :^{1,2}

Remedies using this mechanism are :

Cervical (C5) dermatome stimulation, done by rhythmic tapping over the fifth cervical vertebra level at the origin of the phrenic nerve, spraying the area with vapocoolants, acupuncture, galvanic (electric) stimulation, direct phrenic nerve stimulation by operative placement of electrodes and surgical phrenic nerve interruption (crushing or transection of the nerve).

Some remedies are explained on a physiological basis, such as creating a respiratory acidosis which inhibits the diaphragm contractility by : sneezing or coughing by various means, breath holding, hyperventilation, grasping (like that precipitated by fright or sudden pain) and breathing in a paper bag (use of a plastic bag is not recommended and is in fact dangerous, as it may stick to the face causing asphyxia).^{1,2}

Despite all efforts to explain these mechanisms on an anatomico-physiological basis, for some remedies there is still no satisfying explanation available, e.g. :

- a. auriculo-acupuncture and auriculo-pressure : according to TCM (Traditional Chinese Medicine), in hiccups the normal stomach function of sending food down is disturbed, resulting in reversed upward surge of stomach Qi to attack the diaphragm.¹⁶
- b. hypnosis : although Kirkner and West¹⁷ felt that hypnosis may inhibit the cerebral cortex (as seen by the influence of voluntary action, relaxation and sleep on the magnitude of reflexes), the exact mechanism by which hypnosis cures hiccups is still obscure.
- c. some bizarre remedies, such as :
 - prayers to St.Jude, the patron of lost causes, which were ultimately successful in a patient who hiccuped for more than 8 years and reportedly received 60.000 letters containing possible cures.^{1,2}

- a financial reward of US \$ 10 offered by Kirkman¹⁸ to a hiccuper if he could voluntarily continue to hiccup on demand. Kirkman stated, that this approach worked among his family, friends and a few patients; leading him to postulate that the "neural energy" was suddenly drained from the hiccup pathway after he offered the reward.

Acknowledgement

The author wishes to thank Dr. Mardjohan Hardjasudarma (Shreveport-LA, USA) for providing some references used in this review.

REFERENCES

1. Kolodzik PW, Eilers MA. Hiccups (singultus) : Review and approach to management. *Ann Emerg Med* 1991;20(5):565-73.
2. Lewis JH. Hiccups, causes and cures. *J Clin Gastroenterol* 1985;7(6):539-52.
3. Swan HR, Simson LH. Hiccups complicating myocardial infarction. *N Eng J Med* 1952;247:726-8.
4. Fleet WF, Morgan HJ, Morello PJ. A fatal case of hiccups (Vanderbilt morning report). *J Tenn Med Assoc* 1990; Febr;79-80.
5. Mayo CW. Hiccup. *Surg Gynecol Obstet* 1932;55:700-8.
6. Nathan MD, Leshner RT, Keller Jr AP. Intractable hiccups (singultus). *Laryngoscope* 1980;90:1612-8.
7. Hollinshead HW. *Anatomy for surgeons*. Tokyo : Hoeber Harper first reprint edition, 1966;(1):496-8.
8. Johnston TB, Davies DV, Davies F. *Gray's Anatomy, descriptive and applied*. Glasgow : Longman's Green & Co 32nd. edition, 1958;1130- 6.
9. Lewis JH. Hiccup, its causes and cure. *J Clin Gastroenterol* 1985;7(6):539-52.
10. Lewis JH. Persistent hiccup. *J Clin Gastroenterol* 1985; 7(6):539- 52.
11. Salem MR, Baraka A, Rattenborg CC, Holaday DA. Treatment of hiccups by pharyngeal stimulation in anesthetized and conscious objects. *JAMA* 1967;202:126-30.
12. Rosenberg J, Hansen BJ. Possible role of autonomic afferents in treatment of postoperative hiccups. *Lancet* 1989;Oct;7:873.
13. Kolodzik PW, Eilers MA. An experimental study of hiccup. *Ann Emerg Med* 1991;20(5):565-73.
14. Wall PD, Sweet WH. Temporary abolition of pain in man. *Science* 1967;155:08.
15. Cardi E. Hiccups associated with hair in external auditory canal-successful treatment by manipulation. *N Eng J Med* 1961;265-59.
16. Li X, Yi J, Qi B. Treatment of hiccough with auriculo-acupuncture and auriculo-pressure. *J Tradit Chin Med* 1990;10(4):257-9.
17. Bendersky G, Baren M. Hypnotic treatment of persistent hiccup; a case report. *Retracted by Arch Int Med* 1959; 104:417-20.
18. Kirkman R. Discussion in Nathan et al. Intractable hiccups (singultus). *Laryngoscope* 1980;90:1618.