

Hiccups

Maxime Coles MD

It is very common to terminate a large meal in family or in company of your friends and suddenly hear one of you deliver a “Hic”. And you simply excuse yourself in saying highly that you have a hiccup and being uncomfortable, you turn on your seat to make them go away. You have certainly witnessed a friend of yours, drinking excessively his beer or his glasses of alcohol, and starting having hiccups without being able to stop them. I wonder if you ever asked yourself why an individual produce such a funny noise? I want to explore the phenomenon and try to understand their origin.

A common “Hiccup” is a universal reflex that everyone will experience through life. One may compare it to sneezing or even coughing but in those last two reflexes, we know well that these reflexes have a purpose to simply clear the airways. With a hiccup, we do not know well what the advantages we take from a common hiccup.

I remember being a young extern (4th year) rotating in the service of Internal Medicine and I was assigned to a senior resident at the State University Hospital of Haiti, whom, that day, in his desire to teach, asked me if I have ever witnessed a gentleman suffering from an advanced liver cancer with an intractable hiccup? He was planning to perform a procedure on his patient to relieve him of his problems. I was eager to learn on the symptomatology and to discover any new technique as well. I followed him to the patient room and proceed to help in his planned procedure.

I realize that the plan was simple, with the introduction of a rectal sound, meaning the introduction of an instrument, consisting in a large rubber catheter with a balloon, to probe and dilate the rectum and the sigmoid colon. In performing such maneuver, the patient will pass tremendous number of gases under pressure, relieving the intestinal tension and indirectly alleviate the hiccups.

He proceeded to placing the very uncomfortable patient in a sitting position, on his bed while leaning him over my left shoulder for comfort and for better

access to the rectum. Gloved and holding on a large red catheter, my teaching resident de regrettee memoire, (RS) used “K-Y” Jelly to lubricate the catheter and introduce it into the rectum. Instantly, we were able to hear the passage of audible and fool-smelling gases. The patient stopped hiccupping but I did not realize that he had also stopped breathing and has expired over my left shoulder. It looks like my senior resident knew that the patient expired but he left me in the room, still holding on the dead patient, without saying any word. I realized later that it was his way in dealing with the situation.

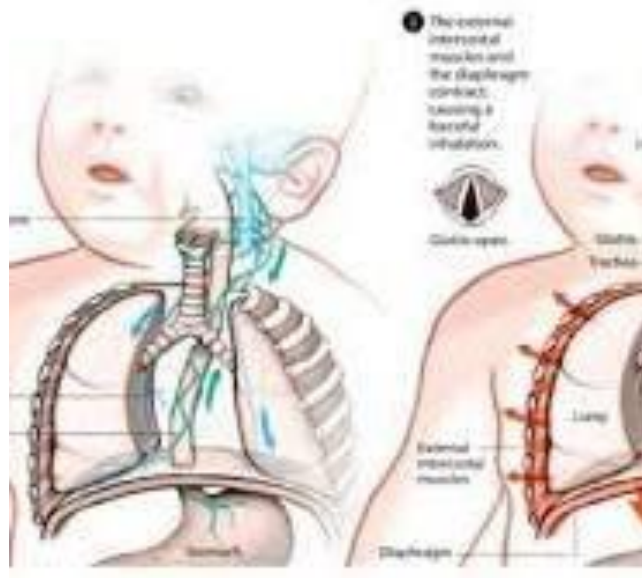
It seems to me that my senior resident realized that he never told me anything that he decided to return in the room to explain to me that the older gentleman that we were trying to relieve of his hiccup (probe), has passed.

I was mortified, knowing that I was holding on a dead body for a while, so close. I rapidly allowed the body slide on the bed but I remained in a state of shock. The life of a medical student is always full of such surprises. I have learned that day, a lesson that I was not about to forget soon and for most of the medical students, interns and residents I taught in Medicine, this is an example that I bring to the surface to show the impact that such case had on my life as a young medical student.

In anyway, one needs certainly to ask why we are having hiccups and where they come from. Hiccups are associated to your diaphragm. Let us explore the phenomenon and look at the remedies. There is always a reason why these funny noises are heard. Although, they may not be considered as a rudimentary reflex, but many would argue that hiccups may be part of a “complex reflex” to remove air from the gastro-intestinal tract, especially the stomach.

Hiccups seems to happen in most animals, cats, rats, rabbits, horses, dogs and humans are not an exception. Often, they maybe unnoticed or maybe considered as a minimal annoyance but if they become persistent and last more than 48 hours, they may be signs of underlying and serious diseases. In pregnant women getting an ultrasound, the rhythmic movement of the hiccups, can be recorded before any swallowing or respiratory reflexes can be observed in the fetus (in Utero). This is a most prevalent reflex among newborns who spend a lot of their time hiccupping, until they diminish during infancy.

Most of what is known about “Hiccup reflex” derive from studying pathological hiccups due to infections or malignancies near the diaphragm or from lesions of the brain. We will see also the impact of distal esophagus, stomach and the abdominal side of the diaphragm, the Phrenic nerve and the Valgus nerve as well as the sympathetic chain branches (T6-T12), responsible to initiate the reflex. A drop in the intrathoracic pressure is experienced by the lungs, heart, great vessels, lymphatics, the thymus and the esophagus. The stomach is in the abdominal cavity, under the diaphragm.



Hiccup reflex in the newborn

The central component of the reflex lies in the Medulla. Electrophysiological studies have demonstrated that the center for the “hiccup reflex” is completely separated from the pathways involved in rhythmic breathing. It has been demonstrated that patients with lateral medullary infarction (Wallenberg’s Syndrome) can induce hiccups as well as others with middle and dorsolateral lesions. Hiccups can then be suppressed by elevation in Carbon Dioxide (CO₂) but can be triggered by gastric distention, rapid eating or drinking carbonated beverages.

Efferent nerves travel from the hiccup center to the diaphragm, the external intercostals, the glottic structure and the esophagus. The diaphragm is the most

significant muscle involved. It is a dome shaped muscular structure separating the thorax and the abdominal cavity in most mammals. It plays a major role in breathing as its contraction increase the volume of the thoracic cavity by helping in inflating the lungs. It works rhythmically and continually, so every time you breathe in air, the diaphragm contracts and flattens. This creates a vacuum, pulling air out of the lungs. In exhalation, the diaphragm relaxes and turn back to its dome-shape, forcing the air out of the lungs. Several studies have shown that hiccups are often unilateral, involving only the left hemi-diaphragm.

Hiccup is also known as a synchronous diaphragmatic “flutter” (SFD) or “singultus”, completely harmless and temporary. It can become very annoying at time. What causes this reaction?

Various factors can trigger hiccups:

- a- Eating or drinking too quickly allow us to swallow sufficient amount of air capable of irritating the diaphragm especially when alcohol or soft drinks like soda are ingested rapidly. As well, hot food and especially spicy food can irritate the nerve stimulating the diaphragm. This will generate hiccups.
- b- An excitement or any emotional stress can also stimulate the ending of the Vagus nerve. This nerve represents the main component of the parasympathetic nervous system overseeing a vast array of crucial bodily functions including mood control, immune response, digestion and heart rate. The vagal nerves carry signals between the brain, heart and digestive system. Any damage to such system can lead to “gastroparesis” food not moving into the intestines. Some with vasovagal reflexes may cause fainting from a low blood pressure. Vagus nerve stimulation may be used to treat disease like Epilepsy and Depression. The Vagus nerve is the 10th cranial nerve “X”.

The phrenic nerve controls also the diaphragm which is essential to our breathing mechanism. It sends signals that cause the diaphragm to contract or relax meaning getting thicker or thinner in contracting or relaxing. It plays a critical role in the respiratory system to aid breathing. It is the only nerve in our nervous system that provide motor function (movement) to your diaphragm. It

sends signals that cause the diaphragm to expand and contract, allowing the lungs to inhale and exhale.

The phrenic nerve also provides touch and pain sensory to the diaphragm, the diaphragmatic pleura, the mediastinal pleura, the pericardium and the peritoneum. It starts at the C3 level, in alignment with the jaw to help you bend or rotate your neck/head.

The phrenic nerve connects to the C3 and C5 cervical nerve roots and travel to the neck and the chest, to reach the diaphragm passing by the heart and the lungs. A cervical spinal cord injury at the C3-C4 level can cause an injury making the person unable to breath on their own.

- c- An excitement or an emotional distress can stimulate the Vagus nerve which oversee most of the bodily functions, including the mood, the digestion, the heart rate, the immune responses. This nerve establishes the relation between the brain and the intestine, and play a role in the hiccup process.
- d- Some carbonated beverages mixed with other drinks may cause the stomach to expand, imposing some pressure on the diaphragm. Temperature changes by example, taking a hot meal and then drink cold drinks, can trigger hiccups. People can develop hiccups acutely or in a chronic way lasting days. I gave the story of that patient with a gastrointestinal malignancy with his intractable hiccup for which we inserted a rectal probe.
- e- There are also rare and unusual cases of hiccups showing sporadically and never left, or they may be due to an accident or one special case has been recorded in the Guinness World Record because it lasted the longer. A gentleman of the name of Charles Osbourne, working on his farm near Union in Nebraska, on the year 1922, and while he was ready to butcher a hog. He fell down and started developing hiccups. His physicians discovered that he injured a tiny vessel inside his brain stem and this accident left him with a long-life incurable hiccup. He tried to look for a cure and seen many physicians in different countries, a cure was not passible but a special breathing techniques provided him with relief just by forcing him to conceal the “hiccup “sounds. He learned further, how-to breath while having the hiccups. He managed 20 to 40 spasms per minute on his diaphragm with an estimated 460 million times he experienced hiccupping during his lifetime. Charles Osbourne died at the age of 97, on May 1991. Although it is rare that such a case can be so extreme, it exists

remedies to help people get relief from hiccups whenever you breathe wrongly or eat too fast.

Holding your breath as long as possible can allow your diaphragm to relax and give secondary relief to the hiccups. Drinking water, preferably cold in a sip or in little quantity can eventually stop the hiccup reflex. Many had relief with granulated sugar like a tea spoon of white or brown sugar may stimulate the vagus nerve and bring relief. Other may breathe in a paper bag as a technique which is often used in an airplane by the one developing discomfort or being airsick or seasick. This mechanism will increase Carbon dioxide levels in the blood and may help reset the diaphragm. Gargling with cold water also can stimulate the Vagus nerve and stop the hiccup reflex.

Any episode of hiccup lasting more than 48 hours may indicate an underlying medical condition and we may have to identify any disease affecting the diaphragm. Diseases of the lungs like pneumonia or disease of the chest cavity, brain infection or injuries, tumors or strokes may trigger hiccups. Diseases of the liver or the kidneys may generate hiccups. Medications like the one given in Oncology with chemotherapy, Corticosteroids, even pain medication like Morphine, or other intravenous narcotics, can trigger hiccups. Morphine is the drug of choice for analgesia because its reliable effects, safety and the ease of reversibility with Naloxone. Your body can also break down certain nutrients into energy, causing a build-up and then leading to hiccups.

Medications have been used in the treatment of hiccup. Baclofen, a muscle relaxant has demonstrated its efficacy in the treatment. Chlorpromazine
Any medications have been used in the treatment of hiccups. Baclofen, a muscle relaxant has demonstrated its efficacy in treating Hiccups by inducing the hyperpolarization of the afferent's terminals and in inhibiting both monosynaptic and polysynaptic reflexes at the spinal level. Chlorpromazine appears to be the medication of choice. Haloperidol and metoclopramide have also demonstrated their efficacy in hiccups associated with esophageal lesions. Several anticonvulsant agents like phenytoin (Dilantin), valproic acid (Depakote), and carbamazepine have effectively treated intractable hiccups and may be doing so in by blocking the post-tetanic potentiation by reducing summation of temporal stimulation. Gabapentin was found effective in patients with lesions in the central nervous system. Other muscle relaxants, sedatives,

analgesics, and even stimulants or other various agents like dexamethasone, amantadine, and nifedipine have shown their efficacy, but benzodiazepines should be avoided. Anesthetics affect the muscle contractions and may be effective. Ketamine works on the cortex and limbic system decreasing muscle spasms.

Chlorpromazine remains the treatment of choice. It is an antipsychotic medication that help restore the balance of certain natural substances in the brain. The mechanism of action is not well known. It has sedative and psychotropic activity at all level of the central nervous system. It acts antidopaminergic agent that blocks the post synaptic mesolimbic dopamine receptors (D2). It is also an anti-adrenergic receptor and depresses the release of hypophyseal and hypothalamic hormones. This drug is used in the treatment of schizophrenia, bipolar disorders and acute psychosis.

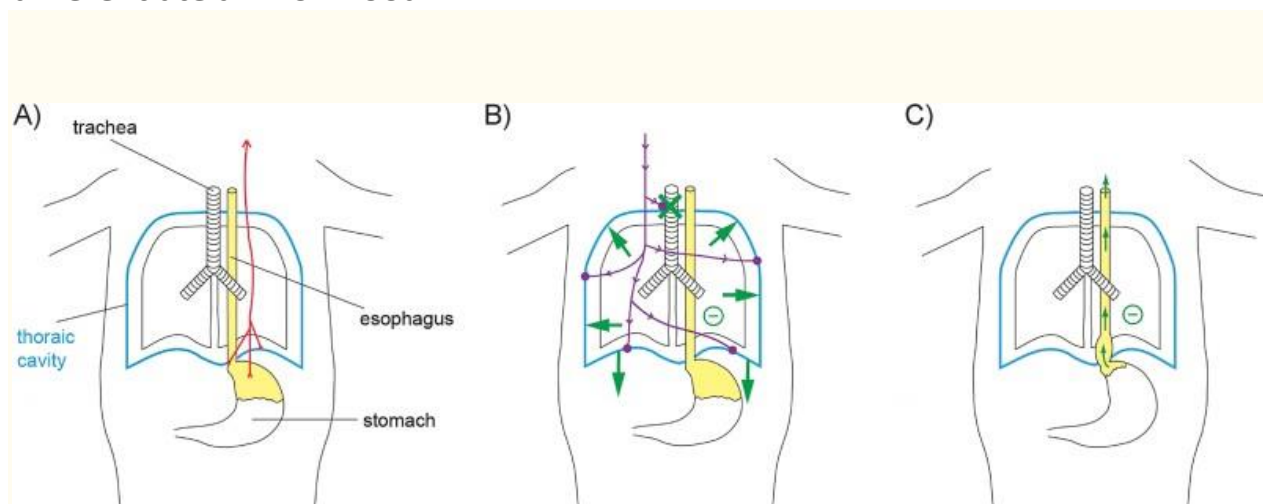
Metoclopramide (Reglan) blocks also the dopamine receptors in the chemoreceptors in the CNS. It is used in the treatment of gastroesophageal reflux. It can also treat gastroparesis in patients with Diabetes. Unfortunately, metoclopramide may cause a muscle problem called tardive dyskinesia, especially involving muscle in your face.

Intractable hiccups can't be inherited because there is nothing genetic in their origin but in some cases, it may never be known what is the cause. You may hear people with their specific tricks to stop hiccups but it appears only accidental with no backup from science. In growing back home, one may tell you that if you find a way to scare the one who has the hiccup, he will stop hiccupping. In fact, we all tried tricks to alleviate the symptoms to realize that most of the time, they will stop naturally.


It has been suggested that "hiccups" were a prodrome of Epilepsy or a failure of supraspinal inhibition. Others have explained it as a dysfunction in the inspiratory breathing also present in absence of swallowing. In 1899, Ferroni suggested that perhaps the fetus was using hiccups to strengthen their respiratory muscles. Others like Kahri and Shi have revisited this theory but failed to associate the afferent limb to the reflex. A theory of meconium inducing hiccups via a strong contraction of the respiratory muscles was also introduced. A hypothesis on an evolutionary remnant that originated with the

gill ventilation theory of evolution. A mechanical reflex able to move boluses of food. A drop in the intra-thoracic pressure with the closure of the glottis. The trachea has also been named as an area of interest to explain hiccups but airways were found already to be well protected by gag, cough and sneeze reflexes. Finally, the esophagus in which any negative pressure from the hiccups may move the content from the mouth or the stomach toward the mid-section of the esophagus. This suggested the hiccups to be more related to the lower esophagus instead the upper esophagus or the mouth.

It is possible that Hiccups work as a “burping reflex” to remove swallowed gas from the stomach. The presence of gas or air bubble in the stomach could stimulate a burping reflex, activating the afferent limb of the reflex, to remove the air bubble from the distal esophagus or the stomach. Ventilation of the stomach via the esophagus is known as “Belching” or “ructus”, coming from a combination of reflux symptoms and dyspepsia after food absorption. The explanation may satisfy a burping reflex which appeared to be supported by the suppression (relaxation) of the distal esophagus peristaltic movement. This “burping reflex” seems to provide a significant survival importance especially when “suckling” needs to be coordinated with breathing resulting in air swallowing. It can easily explain why it is seen more often during infancy. If this theory is true, there must be something in the stomach capable of differentiate air from food. Further hypothesis will be needed to identify how the reflex differentiate air from food.



This “burping reflex” theory may explain the way air is removed from the stomach of young suckling mammals. The presence of air (yellow) in the stomach beneath the diaphragm

triggers the afferent limb of the reflex, sending signals to the medulla (shown in red). **B:** Activation of the reflex efferent limb (purple) causes the muscles of respiration to expand the chest (green arrows), while simultaneously closing the opening of the trachea (green X). The result is a sharp drop in pressure in the chest (symbolized by ). **C:** The negative intra-thoracic pressure moves the air bubble to the thoracic esophagus. With relaxation after the hiccup, the air can pass up the esophagus and out the mouth, leaving more room for milk.

To conclude, if many of the hypothesis were exposed, we can understand that a “Hiccup “must represent a very common reflex triggered by the presence of air in the stomach, stimulating the “Burping” mechanism seen in infants consuming milk, or the belching in adults with solid foods. Such reflex (Burping) may represent the persistence of this infantile reflex or a reminder that one is eating or drinking too much or too quickly. Further studies are needed to try to elucidate this puzzle of “Hiccapping”.

Maxime Coles MD

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