Congenital Central Hypoventilation Syndrome

Do you consciously think about every breath you take? For almost everyone, the answer is no. This is because breathing is a subconscious process that is controlled by a branch of the nervous system that regulates automatic processes: the autonomic nervous system. Other processes regulated by the autonomic nervous system include sweating, shivering, blood pressure, salivation and heart rate. These functions are crucial to maintaining life: the autonomic nervous system is active before we are born and its inactivity is used to define brain death in life support situations.

It's well known that breathing transfers oxygen into the bloodstream and eliminates carbon dioxide from our blood. Both of these gases are important in providing energy to cells: oxygen helps to convert sugars to energy, and carbon dioxide is a bi-product of that conversion. What's less appreciated is that the levels of blood carbon dioxide, not oxygen, are the main driver of breathing – increases in blood carbon dioxide (for example during physical exertion) make us breathe more deeply and rapidly, and reductions in carbon dioxide (e.g. during inactivity and rest) slow down our rate of breathing. Although we can exert some control over our breathing – we can hold our breaths or adapt our breathing to speak or sing – the influence of carbon dioxide is so strong that we cannot overcome it by willpower alone: carbon dioxide build-up is responsible for 'breathe-hunger' when we hold our breaths.

It could be said therefore that the main function of breathing is to keep carbon dioxide levels within a narrow range; if carbon dioxide levels are too low we reduce breathing to retard its expulsion, allowing blood carbon dioxide to build up, and if too high we facilitate its expulsion by breathing quickly. In order to match the level of breathing with the level of carbon dioxide special sensors have evolved to relay information about blood carbon dioxide to the parts of the brain that control breathing. These 'chemoreceptors' (i.e. chemical receptors) provide constant feedback to the respiratory centres which in turn control the muscles responsible for inflation of the lungs.

Congenital central hypoventilation syndrome (CCHS) is a rare disorder of the central nervous system where the body's ability to sense blood carbon dioxide is either absent or impaired. As a result CCHS patients breathe too slowly or even stop breathing altogether. This normally only occurs during sleep, but in more severe cases it occurs during both sleep and wakefulness. When asleep this 'hypoventilation' causes a progressive build up of carbon dioxide and a reduction in the amount of oxygen in the blood. Although prolonged exposure to low oxygen can cause brain damage and death in some cases, the major risk posed by CCHS is actually respiratory infection due to poor lung inflation. There is no difference in the occurrence of CCHS based on sex or race; it affects about 1 in 200,000 people and is therefore quite rare.

Congenital central hypoventilation syndrome is a confusing name that makes sense when broken down into fragments: congenital = something you're born with (as opposed to something you develop); central = caused by the central nervous system, not a problem with the lungs; hypoventilation = not breathing enough; syndrome = it describes a set of symptoms, not the cause of the disease. CCHS used to be known as "Ondine's Curse", after a German myth in which a water nymph named Ondine cursed an unfaithful lover with the responsibility of remembering to breathe.

In >90% of cases the cause for CCHS is genetic – a crucial gene that is needed by chemoreceptors (Phox2B) is not functional in CCHS patients. CCHS is also associated with general neurological

conditions that involve the brainstem, and symptoms similar to CCHS can result from brainstem injury in previously healthy adults. CCHS is commonly associated with other neurological conditions such as Hirschsprung's Disease, seizures, learning difficulties, fainting and temperature control problems.

In most cases CCHS is diagnosed in early infancy. There is no cure, so treatment is supportive and depends on the severity of the patient's symptoms. Treatments include drugs that increase breathing, facemasks that help the lungs to inflate, long-term ventilator support, and electronic 'pacemakers' that make the diaphragm contract. As children with CCHS grow, the condition may stabilise due to the development of the lungs and ventilatory muscles, but the problem will never go away entirely. In most cases patient will require insertion of a breathing tube (tracheostomy) for life in order to allow ventilation while sleeping.

New technological innovations such as devices that can monitor blood oxygen and carbon dioxide levels, and home ventilation, are increasing the quality of life and life expectancy of patients with CCHS. However, the condition is serious and is associated with considerable mortality; a French study published in 2005 found that around 20% of patients died within their first year of life, and that a further 20% may die before adulthood (Treng et al, 2005). A proportion of children that die from Sudden Infant Death Syndrome (SIDS) are likely to be undiagnosed CCHS patients.

However, those statistics should be interpreted with caution; the rarity of CCHS makes accurate and up-to-date data difficult to obtain; there are only about 1000 people with CCHS alive worldwide. The study by Treng et al. is one of the largest so far performed, but subjects included in that study were born from the early 1980s onwards; the influence of current treatment and diagnosis on outcomes are yet to be determined; the fact remains that most children born with CCHS survive until adulthood.

Further reading

US National Institute of Health: http://ghr.nlm.nih.gov/condition/congenital-central-hypoventilation-syndrome

Trang et al., CHEST January 2005 vol. 127 no. 1 72-79
http://chestjournal.chestpubs.org/content/127/1/72.full

CCHS Family Network http://www.cchsnetwork.org/