AMERICAN THORACIC SOCIETY
Patient Information *Series*

Congenital Central Hypoventilation Syndrome (CCHS)

Congenital Central Hypoventilation Syndrome (CCHS) is a chronic disorder of the Autonomic Nervous System (ANS) and control of breathing. CCHS is caused by an abnormal gene (called a *gene mutation*). The abnormal gene leads to problems in the development of the ANS. The ANS is part of the body's nervous system that controls body functions that happen automatically (that is without thinking). Examples of what the ANS does include regulation of: breathing, heartbeat, digestion of food, and many other functions, all without our needing to think about it. In people with CCHS, the key concern is problems with the control of breathing while sleeping. If CCHS is severe, breathing is poorly controlled while awake and while asleep. With CCHS, the lungs, airways (breathing tubes) and the heart are normal, but the body does not signal breathing or the heart to beat as it should. CCHS is a rare condition that now affects nearly 1,000 people world wide. These numbers are likely to increase as CCHS is being diagnosed more often because of increased knowledge about CCHS and the availability of genetic testing.

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What kinds of signs or symptoms might I (or my child) have with CCHS?

CCHS is a life-long disease. Newborns with CCHS are often diagnosed soon after birth because they do not breathe effectively. Poor (ineffective) breathing can cause low oxygen levels (called *hypoxemia*). The infant's shallow breathing or pauses in breathing (called *apnea*) can result in the baby turning blue (called *cyanosis*). This poor breathing control also leads to high carbon dioxide levels in the blood. Both low oxygen levels and high carbon dioxide levels normally stimulate the ANS to "kick in" and tell us to breathe deeply or more often. People with severe CCHS, do not sense the need to breathe deeper or faster when they develop abnormal oxygen and/or carbon dioxide levels. For this reason, people with CCHS can hold their breath for a long period of time without knowing the potential harm this can cause. Swimming therefore, is a dangerous sport for individuals with CCHS.

In milder cases of CCHS, older infants, children, and adults may not be diagnosed until they have problems in situations that require the body to adjust breathing automatically. Therefore, a person may be discovered to have CCHS only after having problems during sedation for surgery, when taking medications that cause sleepiness (such as seizure or sedation medications), or when they have pneumonia or another respiratory illness.

How do I know if I have (or my child has) CCHS?

CCHS is often diagnosed during the newborn period when breathing problems may be immediately seen. Milder forms of CCHS, however, may go undiagnosed through infancy, childhood or even adulthood. If CCHS is suspected, a test for a gene mutation is recommended. Also, oxygen and carbon dioxide levels must be watched closely. Oxygen saturation levels can be measured either using a probe attached to a finger or toe (called a pulse *oximeter*) or by a blood test (called an *arterial blood gas*). Carbon dioxide levels can be measured by a monitor that measures the air exhaled (breathed out) or by a blood test (*arterial blood gas*). A sleep study (*polysomnogram*) can be used to look at breathing, oxygen saturation, and exhaled carbon dioxide levels during sleep. Often, other testing is done as well to be sure that the breathing abnormality is not due to abnormalities with the lungs, heart, brain or conditions which cause muscle weakness.

A simple blood test can be done to check if you or your child has CCHS. The most common gene mutations (changes in the gene) can be found with the "*PHOX2B* Screening Test". If the results from this test are normal and there is still a concern that you or your child has CCHS, then the "*PHOX2B* Sequencing Test" should be done to look for rare mutations in the *PHOX2B* gene. Because this gene mutation can be inherited, direct family members (parents and children) of people with CCHS, should have testing for *PHOX2B* mutations and work closely with their physician and a genetic counselor. It is important that the correct genetic test is performed for parents of a CCHS child and their physician should request the "*PHOX2B* Screening Test" as a start. Most often, though, a *PHOX2B* gene mutation occurs as a new mutation in a person with CCHS and is not inherited from someone else in the family.

What other problems can people with CCHS have?

There are other health problems that can happen in CCHS due to abnormalities with the ANS. The risk of developing these problems varies by the type of *PHOX2B*

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mutation present. Some individuals with CCHS have structural problems such as Hirschsprung disease and/or neural crest tumors. With Hirschsprung disease, certain nerve cells (ganglion cells) are not present so that a section of the intestines (gut) will not work properly. This abnormal section will not move stool properly through the intestines. The tumors (abnormal growths of neural crest tissue), are made up of cells that are usually seen very early in the development of the body. These tumors can appear at any age and include tumors called neuroblastoma, ganglioneuroma, or ganglioneuroblastoma. When present, they are found in the chest or abdomen. Other types of ANS abnormalities can lead to loss of "automatic" function of many other parts of the body. For example, people with CCHS may have heart rhythm abnormalities (such as pauses in the heart beat, called *asystoles*), abnormal temperature regulation with low body temperatures (*hypothermia*), and decreased sense of pain and anxiety. Some people have problems with slow movement of food and stool in the gut causing constipation even without Hirschsprung disease. Some people can have different types of eye abnormalities as well.

What is the treatment for CCHS?

There is no cure for CCHS and treatment depends on what parts of the body are affected and how severely they are affected. Most importantly, everyone with CCHS will need help with breathing during sleep (whether a daytime nap or night-time sleep). In severe cases, help with breathing is needed when the individual is awake **and** asleep (day and night). Infants with CCHS usually require a machine (called a *mechanical ventilator*) to help them breath. This machine helps the infant breathe by blowing air through a surgically made hole in the airway (tracheostomy). In some cases, older children and adults who only have problems breathing during sleep, may be able to be treated with the same machine but using a mask over the nose or nose/mouth (called non-invasive ventilation). In some cases, a special device called a diaphragm pacemaker can be used to assist breathing. This requires a surgical procedure for the placement of electrodes onto the nerves that stimulates the diaphragm. The diaphragm is the large, thin muscle that lies just under the lungs that is used for breathing. The diaphragm pacemaker works by stimulating the nerves that cause the diaphragm to move, causing air to be pulled into the lungs.

If a person with CCHS has asystoles (long pauses in the heart beat), a cardiac pacemaker may be needed. Medicines taken by mouth can be used to treat constipation. Neural crest cell tumors and parts of the intestine with Hirschsprung disease need to be removed with surgery. Because CCHS can involve many body functions, and the amount of involvement differs from person to person, it is important for people with this rare condition to be treated at a specialty center with a team experienced in diagnosing and treating many patients with CCHS. The goal of this team is to provide the best quality of life for you and your child, and to work closely with your local physicians.

How will CCHS affect my lifestyle or that of my child?

Early diagnosis and treatment can limit complications from CCHS. New technology has offered many options to children and families with CCHS. Home mechanical ventilators, portable oxygen saturation and carbon dioxide monitors, home care registered nurses and other support have allowed many infants and children to go home from the hospital and to stay out of the hospital. The result is that children with CCHS now have an excellent chance of growing up at home with their families, participating in normal activities including going to school (even college), and living to be productive adults.

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For additional information:

Congenital Central Hypoventilation Syndrome Family Network:
www.cchsnetwork.org

RADICA-FRE: Respiratory and Autonomic Disorders of Infancy, Childhood and Adulthood-Foundation for Research and Education, available in 2011.

Rx *Key Points*

If you have CCHS,

- ✔ Do not drink alcohol as it may cause you to not breathe enough.
- ✔ Do not use recreational drugs or any drugs like sleeping pills or narcotic pain medicines that may slow your breathing effort or cause you to stop breathing.
- ✔ Make sure you tell your health care provider that you or your child has CCHS, and remind your care provider again every time a new medicine is prescribed or if you need sedation/anesthesia for a test or surgery.
- ✔ To confirm the diagnosis of CCHS, get *PHOX2B* genetic testing from a specialist in CCHS (www.genetests.org).
- ✔ Use the ventilator as directed by your health care provider.
- ✔ Avoid swimming as you will be at risk for drowning.

Doctor's Office Telephone: