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My46 Trait Profile

Congenital central hypoventilation syndrome

Other Names: Ondine's Curse

Congenital central hypoventilation syndrome is a genetic condition that affects the body's central nervous system's control over breathing. It is due to mutations in the PHOX2B gene that makes the paired mesoderm homeobox protein 2B.

Characteristics of Congenital central hypoventilation syndrome

Central hypoventilation describes a problem with the central nervous system's control over breathing. People with congenital central hypoventilation syndrome (CCHS) take shallow breaths (or 'hypoventilate') because their brain cannot properly regulate the breathing process. Hypoventilation most often occurs during sleep, but can also happen while awake.

CCHS affects the autonomic nervous system. The autonomic nervous system controls body processes that are involuntary, such as breathing, heart rate, sweating, pupil dilation, and blood pressure. CCHS typically presents with hypoventilation and apneic spells (episodes where one stops breathing) in the newborn period. However, symptoms can also begin later in childhood or adulthood. Longstanding hypoventilation leads to learning difficulties and other neurological problems due to chronic oxygen deprivation. Since it affects the autonomic nervous system, people with CCHS can also have abnormalities of other organs regulated by this system. These can include heart rhythm problems, episodes of increased sweating, eye problems, and low blood pressure when standing up after sitting. CCHS may also cause Hirschsprung disease and certain tumours, such as neuroblastoma.

CCHS can range from severe hypoventilation and Hirschsprung disease (a condition that involves the large intestine and causes severe constipation or blockage in the intestine) in newborns to barely noticeable symptoms in adults. Affected people with few symptoms may go undiagnosed, but they can develop serious health problems, such as pulmonary hypertension (high blood pressure affecting the arteries to the lung), and polycythemia (an increased volume of red blood cells). These health risks make proper diagnosis important.

Diagnosis/Testing

CCHS can be confirmed by PHOX2B genetic testing. This is the only gene known to cause this condition. Most (over 90%) affected individuals have a particular type of mutation called a polyalanine repeat expansion mutation (PARM). A small number of individuals with CCHS have non-PARM mutations (frameshift and nonsense mutations) in PHOX2B and are at increased risk of having Hirschsprung disease and neuroblastoma (a type of cancer).

Management/Surveillance

Current recommendations for infants and young children with CCHS is to have a tracheostomy and be on a ventilator to support breathing. Older children and adults may be able to use mask ventilators that go over the mouth. Whether a person with CCHS needs ventilation all day or just at night depends on how severely they are affected. For heart rhythm problems, a pacemaker may be needed.

Infants with CCHS should have comprehensive breathing evaluations every six months until age three. After that, evaluations of breathing, heart assessments, and blood analyses to rule out polycythemia should be done yearly.

Evaluations for learning problems should also be done regularly. For children with non-PARM mutations, evaluations should be done to look for Hirschsprung disease and tumors.

People with CCHS should avoid taking alcohol, recreational drugs, and medications that could depress breathing. They should also avoid swimming and wear a Medic Alert bracelet.

Mode of inheritance

CCHS is inherited in an autosomal dominant pattern. This means inheriting one PHOX2B mutation is enough for an individual to be affected and show signs of CCHS. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

Risk to family members

The risk to family members depends on whether or not the individual with CCHS has a parent affected with CCHS. If a parent also has CCHS, the risk of having a child with CCHS is 50% with each pregnancy. If a parent does not have CCHS, the risk of other siblings being affected is very low.

Special considerations

None

Resources

Genetics Home Reference: Congenital Central Hypoventilation Syndrome
http://ghr.nlm.nih.gov/condition/congenital-central-hypoventilation-syndrome
CCHS Family Network
http://www.cchsnetwork.org

References

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