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Congenital Central Hypoventilation Syndrome

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Description: Congenital central hypoventilation syndrome (CCHS) is a life long condition characterized by generally adequate alveolar ventilation awake but hypoventilation, with typically normal respiratory rates and diminished tidal volume, during sleep. The diagnosis is made in the absence of primary neuromuscular, lung, or cardiac disease, or of an identifiable brainstem lesion. More severely affected children hypoventilate while awake also. CCHS is increasingly recognized as a more global disorder of the autonomical nervous system and is associated with Hirschsprung disease, pupillary response abnormalities, decreased heart rate variability, feeding difficulties, and tumors of neural crest origin (ganglioneuroma, neuroblastoma, and ganglioneuroblastoma).

Epidemiology and diagnosis: CCHS is considered very rare although its exact prevalence is unknown. Individuals typically present during the newborn period with duskiness or cyanosis on falling asleep. They may appear to apnoea. Investigations will include tests for primary neurological, metabolic, neuromuscular, cardiac and lung diseases (to exclude other diagnoses) together with polysomnography demonstrating progressive hypoxia and hypercarbia during sleep. A specific diagnosis is achieved through gene testing of blood or tissue. Most cases involve de novo mutations of the PHOX2b gene on chromosome 4p12. It has autosomal dominant inheritance and Weese-Mayer et al found 10% of the parents of children with CCHS were (asymptomatic) mosaics for the PHOX2B mutation. Half of the offspring of these parents (and of those with CCHS) would therefore be expected to have the CCHS phenotype. Prenatal testing is possible.

Management: Goals of therapy include the normalisation of ventilation, long-term survival, the minimization of neurodevelopmental impairment, the avoidance of complications, and the minimization of psychosocial impact on the affected individual and their family. As with many complex chronic conditions, frequent multidisciplinary review is recommended. This condition demands particularly meticulous and diligent care as affected individuals will not respond normally to hypoxia or hypercarbia (ie they will not experience or demonstrate dyspnoea/respiratory distress).

Typically individuals require invasive (tracheostomy) ventilation, at least to begin with. Those who consistently only require support during sleep may be candidates for non-invasive ventilation (i.e. may be weaned off tracheostomy ventilation). Ventilatory targets include a SpO2 □ 95% and pCO2 between 4-6kPa (30-45mmHg). Relative hyperventilation is achieved in health to avoid hypoventilation during intercurrent illness.

References:

Idiopathic congenital central hypoventilation syndrome: diagnosis and management. American Thoracic Society.American Journal of Respiratory and Critical Care Medicine (1999) vol. 160 (1) pp. 368-73

Weese-Mayer. Genetics of Congenital Central Hypoventilation Syndrome: Lessons from a Seemingly Orphan Disease. American Journal of Respiratory and Critical Care Medicine (2004) vol. 170 (1) pp. 16-21