

Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) is a rare disorder of respiratory control and autonomic nervous system (ANS) regulation, with endocrine system abnormalities. Respiratory control is the automatic function of breathing in response to varied activities of daily living (ex. exercise, sleep, eating), so within the context of the ANS. The ANS is the portion of the nervous system that controls or regulates many involuntary body functions including heart rate, blood pressure, temperature regulation, bowel and bladder control, breathing, and more. The endocrine system is regulated by the hypothalamus, and through hormones it controls growth, energy and water balance, sexual maturation and fertility as well as response to stress. The diagnosis of ROHHAD is currently based on clinical criteria and though investigation of genetic mutations is underway, no specific cause for ROHHAD has been found to date. ROHHAD is a very rare disorder with approximately 100 cases reported in the literature and clinically to date. Though first described under a different name in 1965, it was not re-named until 2007 nor shown to be distinct from CCHS (documented absence of CCHS-related PHOX2B mutations). Therefore, as ROHHAD is a relatively “new” disorder without many cases identified thus far, it is not yet clear if any certain population is at greater risk for developing ROHHAD. Because of the explosion of exogenous obesity worldwide, a very high level of vigilance in consideration of ROHHAD is essential. Congenital central hypoventilation syndrome (CCHS) is a disorder of the ANS caused by a gene mutation in the PHOX2B gene that affects the embryologic development of the ANS. Similar to ROHHAD, the “automatic” control of breathing, heart -beat, digestion, and other features of ANSD are among the affected features. In CCHS, the hallmark is hypoventilation while sleeping and, in severe cases, hypoventilation while awake and asleep – despite anatomically normal heart, lung, and airways. Both CCHS and ROHHAD fall within the rubric of respiratory and autonomic disorders of infancy, childhood, and adulthood (RADICA). CCHS is a rare disorder with approximately 1,000 cases described worldwide. Numbers of reported CCHS cases continue to grow, likely because of increased awareness and introduction of a clinically available genetic test (in 2003) – allowing for early diagnosis and improved treatment. CCHS is often diagnosed in the newborn period because of breathing problems, but milder forms of CCHS may go undiagnosed through infancy, childhood, and even adulthood. A simple blood test can be done to look for a PHOX2B gene mutation (PHOX2B is the disease-defining gene for CCHS). Different types of mutations can occur in this gene which will determine how severely an individual with CCHS is affected. Stepwise testing for PHOX2B mutations should be done with close involvement by a physician and genetic counselor. (For more information about this disease, choose “CCHS” as your search term in the Rare Disease Database.)