

Central Adrenal Insufficiency in Individuals with Prader-Willi Syndrome

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A recent article in the Journal of Clinical Endocrinology and Metabolism by de Lind van Wijngaarden et al indicated that there may be a high frequency of central adrenal insufficiency (CAI) in individuals with Prader-Willi syndrome. Morning salivary cortisol levels and cortisol profiles were normal in all the children studied, leading the authors of the study to conclude that CAI in individuals with PWS only becomes apparent during stress. Therefore, the presence or absence of CAI cannot be determined by measuring an 8 AM cortisol level – the individual must be tested while stressed (e.g. with febrile illness) or using a stimulation test.

Given this information, we (at the University of Florida) recommend that all individuals with PWS should be screened for the presence of CAI. The two ways to test for CAI are (1) to measure a cortisol and ACTH level while the child is sick or (2) to perform a stimulation test which will evaluate the hypothalamic-pituitary-adrenal axis. Because some children with PWS do not have fevers when ill, it can be difficult for parents and physicians to know when the child is sick enough to put the body under significant stress to accurately assess the presence of CAI. Thus, a stimulation test may be the best way to detect adrenal insufficiency. The metyrapone stimulation test was used in the above-mentioned research study, but this test is not usually done in the United States. A low-dose ACTH stimulation test (1 mcg ACTH) has ~ 95% sensitivity for diagnosing impaired adrenal function, but may miss mild CAI; a glucagon stimulation test has equal sensitivity for diagnosing CAI but may pick up more subtle abnormalities of the hypothalamic-pituitary-adrenal axis, and an insulin-tolerance test is the gold standard for evaluating for the presence of CAI.

Please present this information to your endocrinologist and discuss testing for CAI with him/her. It is important to discuss the fact that the presence or absence of CAI in an individual with PWS cannot be determined by measuring an 8 AM cortisol level – the individual must be tested under a stressful condition (e.g. illness) or using a stimulation test. If your child does have adrenal insufficiency your endocrinologist will determine the best course of treatment. In general, your child can most likely be treated with stress-dose steroids (hydrocortisone) during times of illness. You will be given a Solu-cortef emergency kit which is an injection to be used if your child is vomiting or unconscious. If you have to use the emergency injection your child needs to go to the Emergency Room immediately for further evaluation.

Precautions to Take when Starting Growth Hormone with PWS

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We advocate a sleep study before the start of growth hormone (GH) on infants, children and adults with Prader Willi syndrome, and then a follow up study 6-8 weeks later. If there is worsening of obstructive sleep apnea (OSA) on GH temporarily stopping the GH is recommended until the cause is understood. Frequently the OSA can be corrected by removing the adenoids and tonsils or lowering the dose of GH (in the face of an abnormally high IGF-1). We also recommend taking precautions during bouts of upper respiratory infections.

Dr. Merlin Butler also recommends obtaining a thyroid function test and cortisol levels (in AM) before starting growth hormone treatment. He has done a recent study on cortisol levels in 63 subjects with PWS and found one of four infants with PWS had a low cortisol level. There has been some discussion about adrenal hypofunction in a subset of PWS.

Studies have shown that in most individuals with sleep-disordered breathing due to PWS, GH can actually improve (or at least doesn't worsen) the apnea (Haqq et al, 2004; Miller et al, 2006; Festen et al, 2006). Withholding GH from those with sleep apnea may be detrimental on several levels, thus monitoring the child with PWS closely when starting GH to make sure that they do not worsen is the recommended approach.
