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Primary Testicular Dysfunction Is a Major Contributor to Abnormal Pubertal Development in Males with Prader-Willi Syndrome

Harry J. Hirsch, Talia Eldar-Geva, Fortu Benarroch, Orit Rubinstein and Varda Gross-Tsur

Neuropediatric Unit (H.J.H., O.R., V.G.-T.), Department of Pediatrics; and Department of Obstetrics and Gynecology (T.E.-G.), Shaare Zedek Medical Center, the Hebrew University, Jerusalem 91031, Israel; and Child and Adolescent Psychiatry (F.B.), Hadassah Mount Scopus Hospital, Jerusalem 91120, Israel

Address all correspondence and requests for reprints to: Harry J. Hirsch, M.D., Neuropediatric Unit, Department of Pediatrics, Shaare Zedek Medical Center, the Hebrew University, POB 3235, Jerusalem 91031, Israel. E-mail: hirschmd@gmail.com .

Background: Recent studies challenge the assumption that hypogonadism in Prader-Willi syndrome (PWS) is due only to hypothalamic dysfunction.

Objectives: The aims of the study were to characterize sexual development and reproductive hormones in PWS males and investigate the etiology of hypogonadism.

Methods: Physical examination and blood sampling were performed on 37 PWS males, ages 4 months to 32 yr.

Results: All had a history of undescended testes; age at orchiopexy ranged from 2 months to 6 yr. Pubertal signs were variable, but none achieved full genital development. Anti-Mullerian hormone (AMH) levels in PWS boys were near the lower limits of normal, decreasing from 44.4 ± 17.8 ng/ml (mean ± SD) in young children to 5.9 ± 4.7 ng/ml in adolescents, similar to normal males. In contrast, inhibin B was consistently low (27.1 ± 36.1 pg/ml) or undetectable in all age groups. In adult males, FSH levels were high (20.3 ± 18.3 IU/liter), LH levels were normal (4.2 ± 4.3 IU/liter), and testosterone levels were low (1.87 ± 1.17 ng/ml). Only two adults had severe hypogonadotropic hypogonadism with undetectable levels of LH and FSH and high AMH levels (34.9 and 36.7 ng/ml), unlike the other nine adults with AMH levels 2.6 ± 2.1 ng/ml. Androstenedione (1.06 ± 0.30 ng/ml) and DHEAS (281.1 ± 143.6 μg/dl) in adult PWS were normal.

Conclusions: Pubertal development in PWS is characterized by normal adrenarche, variable hypothalamic dysfunction, and hypogonadism due to a unique testicular defect. Primary testicular dysfunction is a major component of hypogonadism in PWS.