Published in final edited form as:

Lancet. 1985 October 12; 2(8459): 828–829.

BIRTH SEASONALITY IN PRADER-WILLI SYNDROME

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SIR,—The Prader-Willi syndrome (PWS), generally sporadic in occurrence, is characterised by infantile hypotonia, early childhood obesity, mental deficiency, small hands and feet, short stature, and hypogonadism.^{1–3} A deletion of chromosome 15 has been found in 50% of individuals clinically diagnosed with PWS.^{4–6}

Parental studies to determine the origin of the chromosome deletion in 13 families made use of variants affecting the stalk length and satellite region of chromosome 15. In all 13 families the chromosome 15 from the father was identified as the chromosome in which the deletion had occurred.⁶ Both sets of parents' chromosomes were normal; thus all chromosome deletions were de novo. Paternal origin of the chromosome deletion in PWS has been supported by others.⁷ Paternal origin of de novo chromosome rearrangements has also been reported.⁸

Proliferation of gonial cells is continuous in the male, whereas in females, meiosis is arrested at the diacytote stage of meiosis I during fetal life. If the replication of chromosome 15 is sensitive to environmental effects, there may be more chances for chromosomal deletions which involve breakage and reunion to occur during gametogenesis. Therefore factors such as drugs, occupational exposures, and irradiation, which are known to cause chromosome breakage, need to be examined in relation to paternal chromosomal errors.

We now have further evidence suggesting environmental causation of the chromosome deletion in PWS. In a survey of 124 PWS subjects (63 with normal chromosomes and 61 with chromosome 15 deletion) from three medical centres, we have identified birth seasonality in PWS (figure). Monthly variation in the incidence of birth of patients with Down, Turner, and Klinefelter syndromes has also been noted.^{9,10} PWS individuals grouped according to chromosome finding and season of birth (autumn, winter, spring, and summer) resulted in a significant difference ($p < 0.01$; a two-tailed χ^2 test with three degrees of freedom). 46% of chromosome 15 deletion PWS individuals were born in the autumn (September, October, November), 7% in the winter (December, January, February), 16% in the spring (March, April, May), and 31% in the summer months (June, July, August)

compared with 22% of non-deletion PWS individuals born in the autumn, 22% in the winter, 32% in the spring, and 24% in the summer.

For comparison with the general population, a survey by Sherrets of 7312 live births in a midwestern community was used.¹¹ Sherrets found that 25·8% of births were in the autumn months, 24% in the winter, 24·7% in the spring, and 25·9% in the summer. The seasonal birth pattern of PWS individuals with normal chromosomes thus did not differ from that in the general population, but seasonality was identified for chromosome deletion PWS. A greater number of PWS individuals with the chromosome deletion were born in the autumn and fewer than expected were born in the winter. Epidemiological studies are in progress to identify possible causative factors in the chromosome 15 deletion in PWS.

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Birth months of 63 individuals with Prader-Willi syndrome and normal chromosomes and 61 individuals with chromosome 15 deletion.