

# Translocation Chromosome Associated With Both Angelman and Prader-Willi Syndromes in a Single Family

The Angelman and Prader-Willi syndromes have been associated with a deletion in the same region of chromosome 15. Almost all cases of Angelman and Prader-Willi are sporadic; thus, it had not been possible to prove unequivocally that a 15q deletion was responsible for the different phenotypes seen in these 2 syndromes. Hulten et al<sup>1</sup> have now reported a translocation chromosome transmitted within a family in which both Angelman and Prader-Willi children are seen.

Other studies have shown that the only apparent cytogenetic difference between patients with the 2 syndromes is that Angelman is associated with a deletion in the maternal chromosome 15q, while Prader-Willi is associated with a deletion in the paternal chromosome.<sup>2</sup> Thus, it has been postulated that these 2 syndromes represent an example of genomic imprinting, the process by which a gene or chromosomal region produces a different phenotype depending upon whether it is inherited from the mother or from the father. Genetic contributions from both parents usually play complementary but sometimes opposing roles, and both are necessary for normal phenotype. In regions that are imprinted, the phenotype produced by a mutation is determined by the sex of the parent transmitting the mutant allele. In the Hulten et al study, the index child with classic Angelman syndrome had a maternally derived unbalanced 15;22 translocation leading to a deletion 15pter→q13. Another branch of the same family had 2 children with Prader-Willi syndrome who had the same unbalanced translocation but of paternal derivation.

The authors note that the unbalanced translocation in the index children was overlooked at first and classified as the

typical 15q11-q13 deletion. The detection of this translocation was achieved only through the application of more specialized in situ cytogenetic techniques. The authors stress the importance of obtaining detailed pedigree information and for the cytogenetic reinvestigation of apparently sporadic cases of both syndromes to look for familial chromosomal translocations.

## References

1. Hulten M, et al. *Lancet* 1991;338:638.
2. Magenis ER, et al. *Am J Med Genet* 1990;35:333.

**Editor's comment:** *This report further supports the theory of genomic imprinting. The fact that both Angelman and Prader-Willi syndromes occur in a single family and are associated with the same chromosomal translocation provides striking evidence for parent-of-origin differences in phenotypic expression for certain areas of the genome. It seems likely that there are actually 2 different closely linked genes on the 15q11-q13 region, one maternally imprinted and one paternally imprinted, with both deleted by the translocation in this family. However, the mechanism of imprinting is unknown at this time. It suggests other chromosomal translocations may produce 2 phenotypes, depending upon parent of origin. Particular care may need to be given to submicroscopic deletions with translocations.*

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