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Results of large study of genetic imprinting disorders and ART presented

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Further confirmation of a link between genetic imprinting disorders and assisted reproduction techniques (ART) was provided to the 21st annual conference of the European Society of Human Reproduction and Embryology held in June 2005.

Alastair Sutcliffe, from the Department of Child Health, University College, London, U.K., reported results of the world's largest study into the relation between ART and four disorders known to be associated with aberrant genomic imprinting patterns.

Genetic imprinting is a mechanism in which gene expression depends upon parental origin. Mutations can alter normal imprinting, thus causing genetic abnormalities. Beckwith-Widemann syndrome (BWS), transient neonatal diabetes (TND), Angelman syndrome (AS), and Prader-Willi syndrome (PWS) are all acquired because of either a maternal or paternal deletion on a chromosome or from inheritance of both chromosomes of a pair from one parent.

"It has been known for some time that BWS, for example, was associated with ART," said Sutcliffe, "and we set out to look at the association of all four disorders and assisted conception."

Sutcliffe and his team contacted patients throughout the U.K. who were in support groups for the disorders and obtained family histories and details of whether or not they had had ART, and if so, which kind.

Of 82 replies from families who had had a child with BWS, 10 had used ART in order to conceive (12%). Families with children with TND, AS, and PWS were also contacted and asked the same questions.

"We found that BWS was the only disorder where there was a significant risk for children conceived by ART," reported Sutcliffe. "However, we found that all affected children apart from those with BWS had a mixture of genomic mutations, whereas those with BWS had a suggested mechanism: maternal loss of methylation."

Methylation is a mechanism used to inactivate parts of a chromosome to prevent problems.

Sutcliffe says that the findings are encouraging. "Not only have we found a possible mechanism for the occurrence of BWS, but we found no significantly higher rate of any disorder in children born after ART apart from BWS. Neither did we find that any particular method of ART was implicated. The problem with BWS could be in the culture media, or it could simply be that the parents are naturally infertile because of a genetic abnormalities.

"We are now planning to do a further study on the childhood eye cancer, retinoblastoma, where it is believed that imprinting is involved. What would help us enormously would be in the U.K. Human Fertilization and Embryology Authority and the cancer registries were to link their databases to enable us to study this condition," he said.

Although such disorders are unusual, Sutcliffe continued, "to a parent of a child with a rare disorder, this is irrelevant. They simply have a sick child, and it is just as important for us to try and find treatments and cures for these conditions as for those that are more common."

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