Study finds association between male birth defect and certain genetic mutations

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A small percentage of males born with cryptorchidism (failure of one or both testicles to descend into the scrotum), the most frequent congenital birth defect in male children, are more likely to have genetic mutations, including for a syndrome that is a common genetic cause of infertility, according to a study in the November 19 issue of JAMA.

Cryptorchidism occurs in 2-4 percent of full-term male births. "Although cryptorchidism is often considered a mild malformation, it can seriously affect men's health, representing the best characterized risk factor for infertility and testicular cancer in adulthood," the authors write. The cause of cryptorchidism remains mostly unknown.

Alberto Ferlin, Ph.D., of the University of Padova, Italy, and colleagues conducted a study to examine the frequency of genetic alterations in cryptorchidism. The study included 600 male infants with cryptorchidism, who were followed up for 2 to 3 years (through January 2008), and 300 male children who did not have cryptorchidism as controls.

The researchers found that the overall frequency of genetic alterations in boys with cryptorchidism was low (17/600 [2.8 percent]) and was statistically significantly higher than controls, both among children with persistent (since before birth) cryptorchidism (16/303 [5.3 percent] vs. 1/300 [0.3 percent] in controls) and among those with bilateral (both testes) cryptorchidism (10/120 [8.3 percent]). Children with persistent cryptorchidism had 17 times the odds of having a genetic alteration; the

odds were 27 times higher for boys with bilateral persistent cryptorchidism.

The most common genetic findings in those with cryptorchidism were eight cases of Klinefelter syndrome (a chromosome condition that is the most common genetic cause of male infertility) and five cases of mutations in the INSL3 receptor gene (a regulator of testicular descent). When considering birth weight and gestational age, genetic alterations were found exclusively in those with normal weight and gestational age.

"We found that chromosomal aberrations represent the most frequent genetic alteration in participants with isolated cryptorchidism, particularly in those with persistent cryptorchidism (1.6 percent in the unilateral forms and 4.2 percent in the bilateral forms), and that chromosomal alterations were exclusively represented by Klinefelter syndrome," the authors write.

"In this study, we found genetic alterations in a small percentage of boys with cryptorchidism. We found a significant association between bilateral and persistent cryptorchidism and genetic alterations, including mutations in the INSL3 receptor gene and Klinefelter syndrome. Genetic alterations were not found in participants with low birth weight or low gestational age …"

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