Abstract

Male reproductive tract abnormalities such as hypospadias and cryptorchidism, and testicular cancer have been proposed to comprise a common syndrome together with impaired spermatogenesis with a common etiology resulting from the disruption of gonadal development during fetal life, the testicular dysgenesis syndrome (TDS). The only quantitative summary estimate of the link between prenatal exposure to estrogenic agents and testicular cancer was published over 10 years ago; other reviews of the link between estrogenic compounds, other than the potent pharmaceutical estrogen diethylstilbestrol (DES), and TDS end points have remained inconclusive. We conducted a quantitative meta-analysis of the association between the end points related to TDS and prenatal exposure to estrogenic agents. Inclusion in this analysis was based on mechanistic criteria, and the plausibility of an estrogen receptor (ER)-mediated mode of action was specifically explored. Eight studies were included, investigating the etiology of hypospadias and/or cryptorchidism that had not been identified in previous systematic reviews. Four additional studies of pharmaceutical estrogens yielded a statistically significant updated summary estimate for testicular cancer. Results of the subset analyses point to the existence of unidentified sources of heterogeneity between studies or within the study population.

Keywords
Cryptorchidism, DES, Estrogen, Hypospadias, Oral contraceptives, Testicular cancer