Correspondence

COMMENT ON MATERNAL ALCOHOL CONSUMPTION—RE: “CRYPTORCHIDISM AND HYPOSPADIAS AS A SIGN OF TESTICULAR DYSGENESIS SYNDROME: ENVIRONMENTAL CONNECTION”

To the editor:

Toppari and co-authors recently published a review on “the environmental connection” of cryptorchidism and hypospadias, including the potential adverse effect of alcohol (Toppari et al., 2010). Based on an article by Damgaard et al., 2007, they conclude that: “mothers’ alcohol consumption caused a dose-dependent increase in the risk of cryptorchidism” (Damgaard et al., 2007). We are not convinced that the article by Damgaard and co-authors actually present data that indicate a dose-response relation, and furthermore, it is not the only paper published on this topic (Jensen et al., 2007; Mongraw-Chaffin et al., 2008; Strandberg-Larsen et al., 2009).

The study by Damgaard et al. (2007) is a follow-up study ($n = 2496$) with prospective exposure information and clinical assessment of cryptorchidism at birth and at 3 months of age. They report an association between average maternal alcohol consumption during pregnancy and transient cryptorchidism, but this association was apparently driven by an excess risk among few highly exposed boys. Compared with unexposed boys, those exposed to 0.1 to 8.9 drinks per week had an adjusted odds ratio (OR) of cryptorchidism of 0.96 (95% confidence interval [CI], 0.62–1.49). Exposure to nine or more and exposure to 9 or more drinks per week (among 5 boys) resulted in an OR of 31.89 (95% CI, 3.96–256.93). The authors regrouped the exposure categories by consecutively lowering the cut value by one drink per week, and thus admixed an increasing number with lower exposure to the highly exposed open-ended category. For example, boys exposed to five drinks or more per week had an attenuated OR of 3.10 (95% CI, 1.05–9.10). A true dose-response relation should also be present for the medium exposure groups (e.g., 0.1–4.9 and 0.1–8.9), which was not seen. In fact, the association appears to be driven entirely by few outlying observations, which probably results in an unstable statistical model.

Since Damgaard’s study in 2007, three new studies with prospective alcohol exposure classification have been published: two follow-up studies (Jensen et al., 2007; Strandberg-Larsen et al., 2009), and one matched case-control study (Mongraw-Chaffin et al., 2008). None of these studies corroborate an increased risk of cryptorchidism with average weekly alcohol consumption. Two of the studies addressed persisting cryptorchidism and were conducted on older cohorts with higher alcohol exposure contrast than in Damgaard’s study (Jensen

et al., 2007; Mongraw-Chaffin et al., 2008). Damgaard’s findings included transient cryptorchidism, which could explain the incongruences if transient and persisting cryptorchidism do not share this risk factor. This is to our knowledge not supported by experimental or epidemiologic data. There is evidence to indicate that maternal and environmental risk factors do contribute to the occurrence of persisting cryptorchidism (Jensen et al., 2010). A large cohort study ($n = 41,268$) on both maternally reported cryptorchidism (which will include both transient and persisting cases) and persisting cases from treatment reports showed no association with average weekly prenatal alcohol exposure (Strandberg-Larsen et al., 2009). In our view, the combined body of evidence does not support the conclusion by Toppari et al., (2010) on maternal alcohol consumption and cryptorchidism.

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