

Looking Farther Afield

The Decreasing Distance between the Male Fetus and Phthalates

Julie Ross, Senior Editor

Phthalates are used extensively in a wide variety of products, e.g., plastic bags, cling film, plastic toys, cosmetics, soaps, paint, and pesticides. A number of phthalate esters have been shown to have antiandrogenic effects and to disrupt reproductive tract development in male rats. However, there have been few human studies and these have been open to the criticism that the phthalate levels described could have been due to contamination. A paper by Swan et al. (1) describes a very well conducted study of prenatal phthalate levels in mothers and the subsequent risk of a short anogenital distance in their male offspring. Anogenital distance (presented in this study as an index: anogenital index = anogenital distance / body weight) has been shown in animal studies to be a measure of androgenization and it is sexually dimorphic in rodents and humans (male/female = 2:1). Thus, reduced anogenital distance is a measure of fetal hypoandrogenization.

Swan et al. clearly show that four individual phthalate monoesters were associated with a higher risk of shorter anogenital distance with odds ratio for high versus low exposures from 3.8 to 9.1 (all $P < 0.05$). They further show that there was a relationship between anogenital index and the risk of incomplete testicular descent and finally that a summary phthalate exposure score was strongly (albeit with wide confidence limits) associated with a short anogenital index: high versus low (odds ratio = 90.0; 95% confidence interval = 4.9-1,659) and high versus medium (29.4; 3.4-251).

As Sharpe (2) notes in an accompanying editorial, this finding is an observational association not an experimental result. However, coupled with animal experimental data and the internal corroborative finding of the association between short anogenital index and testicular maldescent, there is an exigent need to replicate the study. Crucially, although it has previously been thought that the exposures in humans were lower than the deleterious doses in animal studies, Swan et al. note that exposure to phthalates in the mothers of the short-anogenital index boys is at a level seen in 25% of the U.S. population (3).

There is an urgent need to establish the sources of exposure in women of reproductive age to make appropriate public health recommendations. If this is a causal association, there is a need to begin the search for alternatives.—John D. Potter

References

1. Swan SH, Main KM, Liu F, et al. Decrease in anogenital distance among male infants with prenatal phthalate exposure. *Environ Health Perspect* 2005;113:1056–61.
2. Sharpe RM. Phthalate exposure during pregnancy and lower anogenital index in boys: wider implications for the general population? *Environ Health Perspect* 2005;113:A504–5.
3. Centers for Disease Control and Prevention. Second national report on human exposure to environmental chemicals. Atlanta (Georgia): Centers for Disease Control and Prevention, National Center for Environmental Health, Division of Laboratory Sciences; 2003.