DECREASE IN ANOGENITAL DISTANCE AMONG MALE INFANTS WITH PRENATAL PHTHALATE EXPOSURE
Prenatal phthalate exposure and male anogenital distance

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[Anogenital distance (AGD) is the measured distance from the center of the anus to the anterior base of the penis]

FROM ABSTRACT:

Prenatal phthalate exposure impairs testicular function and shortens anogenital distance (AGD) in male rodents.

We present data from the first study to examine AGD and other genital measurements in relation to prenatal phthalate exposure in humans.

The age-adjusted AGD decreased significantly with increasing phthalate score.

The associations between male genital development and phthalate exposure seen here are consistent with the phthalate-related syndrome of incomplete virilization that has been reported in prenatally exposed rodents.

The median concentrations of phthalate metabolites that are associated with short AGD and incomplete testicular descent are below those found in one-quarter of the female population of the United States, based on a nation-wide sample.

These data support the hypothesis that prenatal phthalate exposure at environmental levels can adversely affect male reproductive development in humans.

THESE AUTHORS ALSO NOTE:

“Phthalates are widely used in industry and commerce; they are used in personal care products (e.g. makeup, shampoo and soaps), plastics, paints and some pesticide formulations.”
Several phthalates have been shown to disrupt reproductive tract development in male rodents.

Studies have reported significant reductions in anogenital distance (AGD) in rats after prenatal exposure to phthalates because they are antiandrogenic [which means they interrupt the normal release of male sex hormones].

There is a growing body of literature on phthalate reproductive toxicity and data demonstrating extensive human exposure.

Phthalate exposure can be accurately assessed by looking for its “monoester metabolites” in the urine.

Studies have shown that phthalate exposure reduces sperm motility, sperm concentration, sperm concentration, and increases sperm DNA damage. These problems are noted in men attending infertility clinics.

In newborn male rodents, the distance from the anus to the penis, the AGD, is androgen-dependent [male sex hormone] and about twice as long in males as females.

The AGD is a sensitive measure of prenatal anti-androgen exposure, which included phthalates.

The measured distance from the anus to the base of the scrotum in human males and from the anus to the base of the genitals (the fourchette) in females is about twice as long in males as females.

In this study, “boys’ genital examinations included a description of the testes and scrotum, location and size of each testicle, and measurement of the penis.” Penis width and length were recorded. The anogenital distance (AGD), measured from the center of the anus to the anterior base of the penis was recorded.

Urinary phthalate metabolite analyses was carried out. The metabolite concentrations reported are from 214 prenatal maternal urine samples.

The mean age of the 134 boys in this study was 15.9 months.

25 boys were classified as having a short AGD. Their AGD was on average 18.3% (range 10% - 32%) shorter than expected.

The researchers also assessed the degree of testicular descent, the size of the scrotum, and penile volume.
DISCUSSION

“In the recent National Health and Nutrition Examination Survey (NHANES 1999–2000), the majority of the general population in the United States had measurable exposure to multiple phthalates.”

In this study, phthalate “metabolite concentrations for mothers of boys with short AGD were consistently higher than those of other mothers.”

“It is likely that the doses to which our participants were exposed are lower than those used in toxicologic settings, suggesting that humans may be more sensitive to prenatal phthalate exposure than rodents.” [Important] It has already been shown that humans are more sensitive to other toxicants than rodents because rodents have a higher metabolic rate and more rapid inactivation of toxicants.

“A boy with short AGD has, on average, an AGD that is 18% shorter than expected based on his age and weight as well as an increased likelihood of testicular maldescent, small and indistinct scrotum and smaller penile size.”

Masculinization of external male genitalia, represented by longer AGD, is controlled by dihydrotestosterone, a metabolite of testosterone, which is markedly decreased by prenatal administration of phthalates, suggesting that phthalates act as an anti-androgen.

In male rodents, “some phthalate-induced changes have been shown to be permanent.”

Phthalate concentrations in humans are fairly stable, “reflecting habitual use of phthalate-containing household and consumer products.”

The authors note that phthalate “levels were highly correlated and the majority of women were exposed to all metabolites at detectable levels.”

Researchers “refer to a ‘phthalate syndrome’ characterized by testicular, epididymal, and gubernacular cord agenesis as well as decreased AGD.”

“It has recently been suggested that this ‘phthalate syndrome’ shares many features with the human Testicular Dysgenesis Syndrome (TDS)” proposed to be caused by “chemically-induced disruption of embryonic programming and gonadal development during fetal life.” “The current findings, though based on small numbers, provide the first data in humans linking measured levels of prenatal phthalates to outcomes that are consistent with this proposed syndrome.” [Important]

This study was “motivated by toxicologic studies showing that genital morphology is altered by anti-androgens, including some phthalates.”
“We report that AGD, the most sensitive marker of anti-androgen action in toxicologic studies, is shortened and testicular descent impaired, in boys whose mothers had elevated prenatal phthalate exposure.”

“These changes in male infants, associated with prenatal exposure to some of the same phthalate metabolites that cause similar alterations in male rodents, suggest that commonly used phthalates may undervirilize humans as well as rodents.”

BACKGROUND FROM DAN MURPHY

I first learned about phthalates from reading:
1) Out Stolen future: Are we Threatening Our Fertility, Intelligence, and Survival? by Theo Colborn, A Plume Book, 1997, and
2) Detoxified Or Die by Sherry Rodger’s (MD), Sand Key Co. In her book, Dr. Rodgers cites numerous studies that note phthalates are human-made toxins that can now be found in the cell of every living organism on planet earth.

KEY POINTS FROM DAN MURPHY:

1) Phthalates are widely used in industry and commerce; they are used in personal care products such as makeup, shampoo and soaps, plastics, paints and some pesticide formulations.

2) Phthalate exposure can be accurately assessed by looking for its “monoester metabolites” in the urine.

3) Prenatal phthalate exposure impairs male reproductive development and testicular function, reduces sperm motility and sperm concentration, and increases sperm DNA damage. These problems are noted in men attending infertility clinics.

4) Prenatal phthalate exposure also reduces the size of the penis, testicles, and scrotum, and causes testicular maldescent.

5) 25% of the female population of the United States have concentrations of phthalate that are associated with impaired male reproductive development and testicular function.

6) Phthalates interfere with testosterone and its metabolites.

7) Some phthalate-induced changes are permanent.

8) Phthalate concentrations in humans reflect habitual use of phthalate-containing household and consumer products.

9) Commonly used phthalates undervirilize humans and rodents.