Understanding the risks for hypospadias

In the previous articles in this issue of TreatmentUpdate, we mentioned that some studies have found a possible link between the use of certain medicines in pregnancy and a risk of male genital birth defects, or hypospadias. In this article, we discuss hypospadias and research findings from pregnant HIV-negative women. This information puts the risk for hypospadias in context.

What is hypospadias?

In males, the opening of the urethra, through which urine leaves the body, is on the tip of the penis. However, with hypospadias, this opening can form on other parts of the shaft of the penis, on the scrotum or even close to the anus. This can be corrected in infancy with surgery.

Points to consider

1. Hypospadias incidence

Hypospadias can occur in about one in every 300 boys born to HIV-negative mothers. Reports from East Asia, Western Europe and the U.S. suggest that in the past two decades hypospadias may have become more common.

The reasons for this trend are not clear but may be due to better monitoring of infants as well as better reporting and collection of data about birth defects. There are also studies that suggest that there are several factors that may affect the potential risk for hypospadias, including the following:

- certain medicines
- some chemicals and pesticides
- certain health issues encountered by pregnant women and the fetus
- genes

We explore some of these issues next.

2. Pregnancy-related complications and issues

As a result of pregnancy, some women develop temporarily higher-than-normal blood pressure (hypertension) and kidney dysfunction. These are part of a syndrome called preeclampsia and require monitoring and in some cases treatment. Elevated blood pressure during pregnancy can affect the blood supply to the fetus and potentially restrict its growth.

A British study explored the issue of birth defects in 12,821 infants born to HIV-negative women between the years 1998 to 2010. It found that the use of medicines during the first trimester of pregnancy to lower blood pressure in women with hypertension was associated with an increased risk for hypospadias. It also found that women diagnosed with preeclampsia, whether or not they were treated for this condition, were at heightened risk for giving birth to children with birth defects, including hypospadias.

Another study from the U.S. also found an increased risk for hypospadias among infants of HIV-negative women with higher-than-normal blood pressure, regardless of whether they received treatment.

Taken together, the results from these two studies point to the fact that changes in the environment that surrounds the fetus can affect its development.

Research has also found that male babies who are born prematurely and/or who are born underweight are at
increased risk for having hypospadias. This may be related to a condition whereby the placenta (the physical connection between the mother and fetus), which supplies oxygen and nutrients to the fetus and helps to remove wastes, is not working properly. Researchers are not certain why this might cause hypospadias.

3. Seizure medication

Researchers in Australia reviewed reports of birth defects collected between 1999 and 2012 among women who took anti-seizure drugs. They found that women who took, on average, higher doses of the drug valproate (valproic acid) during the first trimester of pregnancy were at increased risk for giving birth to infants with birth defects, particularly hypospadias. Women whose physicians decreased their dose of valproate had a reduced risk for infants being born with birth defects. Valproic acid can interfere with male hormones.

4. Obesity

Several studies have found that very overweight women were at increased risk for giving birth to male infants with hypospadias. However, not all researchers agree about the impact of obesity on the risk of hypospadias.

5. Genes and the environment

Hypospadias can occur in infants whose parents have a family history of this condition, suggesting that there is a genetic link.

In some cases, the genes in question have to do with receptors for the hormone estrogen or sensitivity to the hormone testosterone. Some researchers suspect that there are possible interactions between genes in the fetus and chemicals or hormone-like compounds in the environment.

One theory is that certain pollutants in the environment, called endocrine disruptors or hormone disruptors, interact with the fetus. Examples of these pollutants are:

- PCBs (polychlorinated biphenyls)
- PCDFs (polychlorinated dibenzofurans)
- dioxins (polychlorinated dibenzo-p-dioxins, or PCDD)
- some pesticides

The hormone testosterone is essential for the formation of male genitals. But it is possible that some of these pollutants or other chemicals could mimic the effect of estrogen and affect the development and formation of the penis. This theory about the impact of environmental contaminants is controversial. Indeed, while results of some experiments in animals may support the link between some pollutants and genital malformation, there is no clear proof of this link in humans.

Note well

As mentioned earlier in this issue of *TreatmentUpdate*, ART is very valuable when it comes to helping HIV-positive women deliver healthy, HIV-negative infants who generally have normal development as children.

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—Sean R. Hosein

REFERENCES:


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