Hormone treatment to prevent ambiguous genitalia in baby girls spurs debate

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Each year in the United States, perhaps a few dozen pregnant women learn they are carrying a fetus at risk for a rare disorder known as congenital adrenal hyperplasia. The condition causes an accumulation of male hormones and can, in females, lead to genitals so masculinized that it can be difficult at birth to determine the baby's gender.

A hormonal treatment to prevent ambiguous genitalia can now be offered to women who may be carrying such infants. It's not without health risks but, to its critics, they are of small consequence compared to this notable side effect: the treatment also might reduce the likelihood that a female with the condition will be homosexual. Further, it seems to increase the chances that she will have what are considered more feminine behavioral traits.

That such a treatment would ever be considered, even to prevent genital abnormalities, has outraged gay and lesbian groups, troubled some doctors and fueled bioethicists' debate about the nature of human sexuality.

The treatment is a step toward "engineering in the womb for sexual orientation," said Alice Dreger, a professor of clinical medical humanities and bioethics at Northwestern University and the most outspoken opponent of the treatment.

The ability to chemically steer a child's sexual orientation has become increasingly possible in recent years, with evidence building that

homosexuality has biological roots and with advances in the treatment of babies in utero. Prenatal treatment for congenital adrenal hyperplasia is the first to test - unintentionally or not - that potential.

The hormonal treatment "theoretically can influence postnatal behavior, not just genital differentiation," said Ken Zucker, psychologist-in-chief of the Centre for Addiction and Mental Health in Toronto who studies gender identity. "Some people refer to girls with CAH as experiments of nature because you've got this condition and you can take advantage of studying it."

Complicating the picture is the fact that the daily hormone pill does nothing to treat or cure the underlying condition, caused in this case by a defective enzyme in the adrenal gland.

Dreger and critics - which include the National Center for Lesbian Rights, Advocates for Informed Choice (an organization that works to protect the rights of people with intersex conditions), and some pediatric endocrinologists and parents of children with the condition - say far too little is known about the safety of the hormone, the steroid dexamethasone, when used prenatally. They say it should be used sparingly, in closely monitored clinical trials, or not at all. They're even more concerned that some doctors might tell parents that a reduced chance of homosexuality is one of the therapy's benefits.

"Most clinicians speak about this treatment as ambiguous-genitalia prevention," said Dreger, who co-wrote an editorial about the treatment in a July publication of the Hastings Center, a bioethics organization. "Others suggest that you should prevent homosexuality if you can. But being gay or lesbian is not a disease and should not be treated as such."

To that end, in September, a consortium of medical groups led by The Endocrine Society, will release updated guidelines on treatment of

congenital adrenal hyperplasia that acknowledge the controversy. The guidelines are expected to describe prenatal dexamethasone therapy - first used about 20 years ago, but now with increasing frequency - as experimental and reiterate that the standard approach for cases of ambiguous genitalia is to perform corrective surgery.

But they're not expected to discourage research on the treatment.

Congenital adrenal hyperplasia, caused by a defect in an enzyme called 21-hydroxylase, affects about 1 in 15,000 infants, and almost all newborns are screened for it. Undetected, the abnormality can make male and female infants critically ill within a few weeks of birth because of an associated salt loss through the urine. The defective enzyme also causes a deficiency of the hormone cortisol, which can affect heart function, and an increase in androgens produced by the adrenal glands.

The excess testosterone has little effect on a male fetus' genitalia. Even in females, the anatomical defect may be mild, involving nothing more obvious than a slightly enlarged clitoris. However, in severe cases, girls are born with male-like sexual organs although they usually have ovaries and a uterus.

The treatment of such disorders has long been the subject of debate. Early surgery to assign a child's gender is controversial, but prenatal treatment for congenital adrenal hyperplasia is even more alarming, said Anne Tamar-Mattis, executive director of Advocates for Informed Choice. She adds that the complicated surgery carries risks, including infection and nerve damage, and that parents may not be adequately counseled beforehand. The group favors allowing children born with intersex conditions to participate in decisions about their gender identity, including delaying a decision until adolescence.

Most couples don't know their offspring are at risk for the condition

until one child is born with it; prenatal dexamethasone treatment is offered in subsequent pregnancies. The drug is an anti-inflammatory medication used most often for arthritis. Prenatal use is considered off-label.

In animal studies, the treatment appears to cause an increased risk of high blood pressure, plus changes in glucose metabolism, brain structure and brain function, leading to memory problems, for example. Long-term studies in humans are lacking.

"There is not a lot of information on its long-term safety," said Dr. Phyllis Speiser a pediatric endocrinologist with the Cohen Children's Medical Center in New York who chaired the Endocrine Society task force writing the new treatment guidelines. "The efficacy has been demonstrated in case reports - a fairly sizable number of cases that used untreated siblings for comparison _ but not in randomized, controlled clinical trials."

Carriers of the gene mutation that causes this form of hyperplasia have roughly a 12.5 percent chance of having a daughter with the condition. The treatment must be started as soon as possible, before the gender of the child is determined, for it to have an effect on genital development.

"It would be much less of a controversy if the treatment was just given to CAH girls," said Heino Meyer-Bahlburg, professor of clinical psychology at Columbia University Medical Center and a prominent researcher on disorders of sexual development in children. "To effectively treat one fetus, you have to treat seven others."

There have been only a few hundred cases of prenatal dexamethasone treatment in the world. But the emerging data on those cases has captured researchers' and activists' attention.

Dr. Maria New, a highly regarded pediatric endocrinologist at Mount Sinai Medical Center in New York, is among a handful of physicians worldwide who have studied the treatment. New does not offer the treatment in her current position at Mount Sinai, but continues to follow children she treated previously or who have had the treatment provided by other doctors. She declined to be interviewed for this story, but on her website and in publications, New says the data so far show the treatment is safe and effective in preventing ambiguous genitalia.

However, New's more recent studies have caused more consternation, because - as she describes it - treated girls behave in ways that are considered more traditionally girlish.

In a 2008 study in the Archives of Sexual Behavior, New and her colleagues administered a sexual behavior assessment questionnaire to 143 women with congenital adrenal hyperplasia who were not treated prenatally. They found that most were heterosexual, but the rates of homosexual and bisexual women were markedly higher in women with the condition _ especially those with the most severe conditions - compared to a control group of 24 female relatives without congenital adrenal hyperplasia.

And, in a paper published earlier this year in the Annals of the New York Academy of Sciences, New and her colleagues reported on data from 685 pregnancies in which the condition was diagnosed prenatally, acknowledging the potential effects of the treatment for reducing traditionally masculine behavior in girls. Prenatally treated girls were more likely to be shy, they wrote, while untreated girls were "more aggressive."

Moreover, the authors said, failure to provide prenatal therapy seems to lead to traditionally masculine gender-related preferences in childhood play, peer association and career and leisure time choices.

"The majority, no matter how severe, are heterosexual," said Meyer-Bahlburg, who has collaborated with New on some of the studies. "But the rate of CAH women attracted to females increases with their degree of androgen exposure during prenatal life."

Studies have not yet been conducted to examine whether such treatment would reduce the rate of lesbianism, Meyer-Bahlburg said.

"I would never recommend treatment in order to take lesbianism away if that is someone's predisposition," he said. "Any treatment can be misused. That could happen here. But this is not the focus of the treatment. The focus is to make surgery unnecessary."