Infant daughters already show signs of reproductive disease

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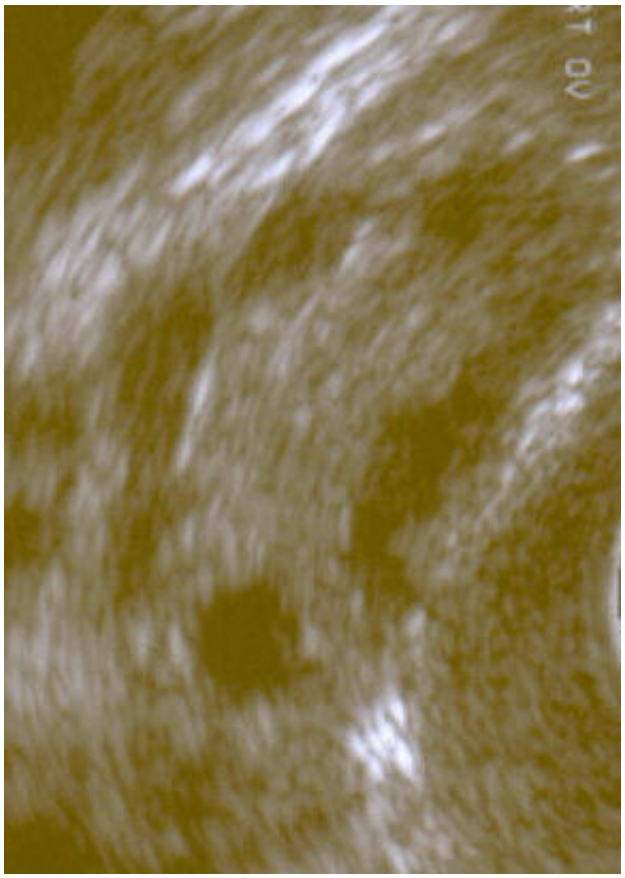

Polycystic Ovary by Sonography. Credit: ekem/ Wikipedia.

The infant daughters of women with polycystic ovary syndrome (PCOS) show a higher level of an enzyme that activates testosterone and may be an early sign of developing the complex genetic disease, according to a new Northwestern Medicine study.

PCOS is one of the leading causes of hormonally related infertility and type 2 diabetes in young women. It affects about 5 million women in the U.S.

Scientists have long sought the primary driver of the disease. Catching it early may enable the development of early treatment or improved prevention. The daughters of affected women are at increased risk to develop PCOS.

The study shows infants whose mothers have PCOS have a higher level of an enzyme that activates androgens—the best known of which is testosterone—than infants whose mothers don't have the disease. That could mean the girls are being exposed to higher levels of testosterone in utero and during infancy, both critical times for development.

"Increased activity of this enzyme, called 5-alpha-reductase, would lead to a higher activation of and greater exposure to testosterone in these daughters, which could contribute to the development of PCOS," said lead author Dr. Laura Torchen, assistant professor of pediatrics at Northwestern University Feinberg School of Medicine and a pediatric endocrinologist at Ann & Robert H. Lurie Children's Hospital of Chicago.

PCOS, a serious metabolic disorder, has long-term health risks throughout a woman's lifespan, including obesity, prediabetes and diabetes. Affected women also have other risk factors for heart disease.

The enzyme 5-alpha-reductase is the most important for converting testosterone to the much more potent androgen, dihydrotestosterone (DHT). Increased levels of testosterone and DHT cause the symptoms of PCOS including excessive hair growth and fertility problems.

"We wondered, when do changes in hormone production or metabolism begin in these daughters?" Torchen said. In early infancy, the ovaries in infant girls are very active and produce sex hormones, Torchen noted.

When female animals are exposed to testosterone

early in development—in utero or early in infancy—they develop what looks like PCOS with insulin resistance, high testosterone levels and irregular menstrual periods.

"Because PCOS can't be diagnosed until after puberty, we've been trying to look for early changes that may signal its development," said senior author Dr. Andrea Dunaif, the Charles F. Kettering Professor of Endocrinology and Metabolism at Feinberg and a Northwestern Medicine endocrinologist. "We hope we may be able to develop early treatment or improved prevention, if we can catch it early."

Scientists measured 5-alpha-reductase activity in the urine of infant girls (1 to 3 years old), 21 of whose mothers had PCOS and 36 control girls. The goal was to determine if daughters of women with PCOS have altered androgen metabolism in early childhood. The study showed the daughters of women with PCOS had a 30 percent higher level of the enzyme activity.

The study was published recently in The *Journal of Clinical Endocrinology & Metabolism*.

More information: Laura C Torchen et al. Evidence for Increased 5?-Reductase Activity During Early Childhood in Daughters of Women with Polycystic Ovary Syndrome, *The Journal of Clinical Endocrinology & Metabolism* (2016). DOI: 10.1210/jc.2015-3926