Eunice Kennedy Shriver **National Institute of Child Health and Human Development (NICHD)**

Polycystic Ovary Syndrome (PCOS) and Women's Health

Advancing Diagnosis and Treatments to Improve Outcomes

What is PCOS?

PCOS describes a group of symptoms related to a hormonal imbalance that can affect women and girls of reproductive age. A PCOS diagnosis means at least two of the following features are present: 1) sporadic ovulation, resulting in irregular or no menstrual periods; 2) high levels of androgen hormones, or signs of high androgen levels, such as acne that does not respond well to usual treatments; 3) growths in one or both ovaries, often clumps of ovarian follicles that have stopped developing. People with PCOS can also be at higher risk for infertility, diabetes and metabolic conditions, and cardiovascular disease. They may also have unwanted hair growth, weight gain, dark skin patches, acne, and heavy menstrual bleeding.

How does NICHD support PCOS research?

NICHD has a long history of supporting research on PCOS. Decades ago, institute researchers were instrumental in helping to define the diagnostic features of PCOS. NICHD-supported projects on PCOS include understanding the disorder's underlying causes, discovering how cellular and molecular processes altered by PCOS cause symptoms, identifying predictors of PCOS in adolescents, developing animal models of PCOS, finding new therapies to treat symptoms, and learning about the effects of the disorder on later generations.

Success Snapshots

Clarifying the Role of Genetics in PCOS

PCOS is usually viewed as a disorder of the ovaries, but NICHD-funded research showed that genes associated with PCOS can act independently of the ovaries to cause certain PCOS symptoms. By studying men and women, the researchers found that men who have PCOS-associated genes also have cardiometabolic conditions like those experienced by women with PCOS. Findings like these help illuminate the true effects of PCOS beyond the ovaries, while focusing efforts on development of effective treatments.

Defining Subtypes of PCOS

Because symptoms and features of PCOS can vary widely, it can be difficult to get a diagnosis. A relatively new classification system of genetic subtypes, developed by NICHD-supported researchers, may improve PCOS diagnosis and treatment. Knowing the genetic risk factors for PCOS can help identify girls who may benefit from earlier diagnosis, interventions, and lifestyle changes to reduce symptoms. Knowledge of genetic subtypes may also help healthcare providers tailor treatments based on a person's genetic profile and symptoms.

Selected NICHD-Funded Polycystic Ovary Syndrome (PCOS) Projects

Genetic & Mechanistic Advances

Identifying New PCOS-Related Genes

Advances in genetic sequencing have expanded our knowledge about PCOS. In one NICHD-funded study, researchers identified variations in genes expressed in the ovaries, where androgen hormones are produced. The findings suggest that certain variations in the *PA2G4* and *ERBB3* genes prompt the ovaries to make more androgens, leaving people with these variations at higher risk for PCOS. Identifying this genetic pathway and understanding its downstream effects opens possibilities to develop more personalized treatments.

Defining PCOS Subtypes

Several NICHD-funded projects applied genetic sequencing tools to PCOS to define subtypes using genome-wide data. One research group, which identified reproductive and metabolic subtypes, is working to determine whether these subtypes are consistent among diverse populations. Another group identified four subtypes: obesity/insulin resistance, hormonal/menstrual cycle changes, blood markers/inflammation, and metabolic changes. These distinct genetic profiles could explain the different symptoms and disease trajectories observed in PCOS.

Expanding Research Models

Having accurate research models is essential for studying PCOS. NICHD-funded researchers created an animal model to explore how PCOS develops and affects future generations. A study using this model showed that exposure to high levels of androgens during fetal development caused symptoms in offspring nearly identical to those seen in humans with PCOS. Follow-up efforts may use this model to evaluate potential treatments.

Learn More About NICHD PCOS Projects

NICHD's PCOS Website:
https://go.nih.gov/ct6Mxme

Treatment & Diagnostic Progress

Studying the Effects of Weight-Loss Drugs on PCOS Symptoms

The drug semaglutide (brand names: Ozempic and Wegovy) is a treatment for type 2 diabetes that has become popular for helping people lose weight. Weight loss is known to improve ovulation in people with PCOS, who often have overweight and metabolic conditions, such as insulin resistance. NICHD-supported researchers are exploring benefits of this drug for people with PCOS, including its effects on reproductive and metabolic symptoms. The study will also help assess the relationship between weight loss and reproductive health in people with PCOS.

Identifying Early Diagnostic Measures

Daughters whose mothers have PCOS are much more likely to develop PCOS than those whose mothers don't have it. In an NICHD-supported study, researchers are evaluating whether these at-risk girls have detectable hormonal differences early in life, specifically during the "mini puberty of infancy," a developmental phase in which sex hormone levels temporarily increase. A predictive marker, detectable in infancy, would improve our understanding of when and how PCOS begins. Early detection would also enable early interventions and other changes to help reduce the likelihood of symptoms as these girls grow.