"Arginine infusion is advantageous because it is a well-established procedure that is already in widespread use for the diagnosis of growth hormone deficiency."

The authors found that arginine-stimulated copeptin measurements are a reliable test to diagnose diabetes insipidus. As arginine infusion is much easier to perform than hypertonic saline infusion, and because it was associated with fewer adverse effects, it could become the standard test to diagnose diabetes insipidus.

"As a next step, we are planning a randomized cross-over diagnostic international multicentre study with the aim to investigate the diagnostic accuracy (and tolerability as a second endpoint) of hypertonic saline-stimulated and arginine-stimulated copeptin measurements in a head-to-head comparison," concludes Winzeler.

*Alan Morris*

> "arginine-stimulated copeptin measurements are a reliable test to diagnose diabetes insipidus"

**ORIGINAL ARTICLE** Winzeler, B. et al. Arginine-stimulated copeptin measurements in the differential diagnosis of diabetes insipidus: a prospective diagnostic study. *Lancet* https://doi.org/10.1016/S0140-6736(19)31255-3 (2019)

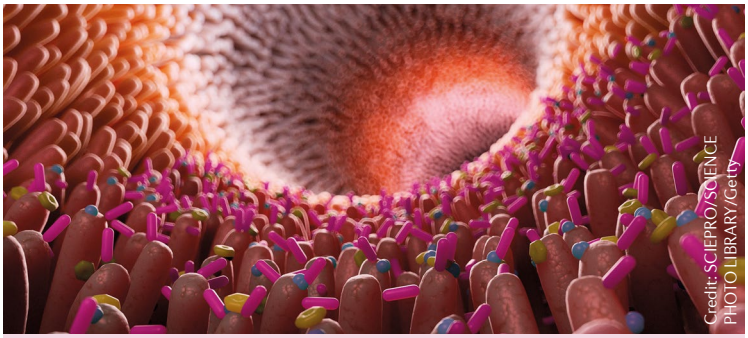
Credit: Andrew Brookes/Getty

In summary, the researchers identified an early novel molecular signature in children who went on to develop T1DM-associated autoantibodies or T1DM at a young age. "We will validate and expand our study on a larger cohort of prediabetic children as well as study the role of IL-32 and other molecules identified in this study in the pathogenesis of T1DM," concludes Lahesmaa.

*Shimona Starling*

> "One upregulated example was *IL32*, which encodes a proinflammatory cytokine"

**ORIGINAL ARTICLE** Kallionpää, H. et al. Early detection of peripheral blood cell signature in children developing beta-cell autoimmunity at a young age. *Diabetes* https://doi.org/10.2337/db19-0287 (2019)



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REPRODUCTION

## IL-22 links gut microbiota to PCOS

Polycystic ovary syndrome (PCOS) is associated with dysfunctional ovulation, ovarian cysts and elevated androgen levels. The causes of PCOS are not fully understood and there is currently no aetiological cure.

Previous human studies, with limited ethnic breadth, have shown that the composition of the gut microbiome in individuals with PCOS differs from that of individuals without the disease. Furthermore, PCOS often occurs with metabolic disorders, including insulin resistance and obesity, which are also characterized by gut microbial dysbiosis. Now, a new study from Yanli Pang, Changtao Jiang, Jie Qiao and colleagues provides insight on the mechanisms that link the gut microbiota to PCOS-associated ovarian and metabolic dysfunction.

"Exploring novel targets for therapeutic strategies is still a key challenge in PCOS research," Jie Qiao points out. "In the lead up to this work we speculated that intestinal flora disturbance could be involved in the pathogenesis of PCOS."

To test this hypothesis, the researchers analysed the gut microbiome composition, as well as metabolic function, of 43 healthy women and 50 women with PCOS. This analysis revealed that the composition of the microbiomes of participants in the PCOS group shared more similarities than the composition of the microbiomes from participants within the control group. Interestingly, *Bacteroides vulgatus* was notably increased in individuals with PCOS.

The scientists then transplanted the gut microbiota from study participants into mice. The microbiome transplants from women with PCOS resulted in insulin resistance and disrupted oestrous cycle and cyst-like follicles, thus mimicking the human symptoms. The administration of live *B. vulgatus* had similar effects on the mice as microbiome transplants from human participants with PCOS, indicating that *B. vulgatus* contributes to the pathogenesis of PCOS.

The researchers also investigated the mechanisms that mediate the observed effects of *B. vulgatus* and report that *B. vulgatus* colonization alters bile acid metabolism, reducing certain species of bile acids that induce IL-22-secreting group 3 innate lymphoid cells (ILC3s) in the intestinal lamina propria. The number of ILC3s was reduced in mice transplanted with *B. vulgatus*, and IL-22 serum concentrations were decreased in both mice and humans with PCOS.

Insulin resistance, disrupted oestrous cycle and morphological changes to the ovaries in *B. vulgatus*-treated mice were rescued by supplementation with IL-22 or the bile acid glycodeoxycholic acid. These data demonstrate that targeting the identified bile acid–IL-22 signalling axis presents a possible treatment strategy for patients with PCOS.

The authors are now planning to build on this work. "We want to recruit more volunteers with PCOS to join the large-scale multicentre clinical trial to verify the effect of gut microbiota, bile acids or IL-22 on PCOS," Jie Qiao concludes.

*Anna Kriebs, Associate Editor,*
Nature Communications

**ORIGINAL ARTICLE** Qi, X. et al. Gut microbiota–bile acid–interleukin-22 axis orchestrates polycystic ovary syndrome. *Nat. Med.* **25**, 1225–1233 (2019)