

Gut bacteria may be a trigger for antiphospholipid syndrome

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The gut microbiomes of patients with antiphospholipid syndrome show higher levels of phospholipid-producing bacteria, and this findings point to microbes being a trigger for this life-threatening disease, according to new research findings presented this week at the American College of Rheumatology Annual Scientific Meeting in Washington.

Antiphospholipid syndrome (APS) is an autoimmune disease that mostly affects younger women. Antiphospholipid antibodies are present in some cases of [deep vein thrombosis](#) and new strokes in people under age 50, as well as a cause of recurrent miscarriages and pregnancy complications for many women.

Pathogens have been associated with transient antiphospholipid antibodies, so researchers at the Kriegel Lab at Yale University School of Medicine in New Haven, Conn., looked for clues for the source of chronic stimulus of these antibodies in the fecal matter [bacteria](#) of people with APS.

"Transient antiphospholipid antibodies have long been associated with infections, but are not considered disease-related," said Martin A. Kriegel, MD, PhD, Assistant Professor of Immunology and Medicine and the study's lead author. "We hypothesized that commensals (the microbes normally present in one's gut) that chronically colonize us, instead of acute infections that resolve over time, might be the persistent triggers of APS in [patients](#)."

APS' exact cause is still unknown. Blood thinners, the current treatment option, only target the blood clots that occur at the end phase of disease, said Dr. Kriegel. This study aimed to find earlier triggers for the disease to possibly prevent deadly strokes and miscarriages. "There's still significant mortality associated with this syndrome compared to other rheumatic diseases in which we can largely prevent mortality nowadays. So there is a huge need to better understand and treat this syndrome," he said.

The researchers collected and analyzed 60 stool samples of 22 APS patients, 13 samples of six control subjects with non-autoimmune, thrombophilic states, and 49 samples of 19 healthy donors, each at baseline, four and eight weeks. Peripheral blood mononuclear cells (PBMCs) from the APS patients responded preferentially to β 2-glycoprotein I (GPI), a major auto-antigen in APS, compared to the controls. In addition, the fecal microbiomes of APS patients showed a significant decrease in *Bifidobacteria* bacteria and an increase in *Slackia* bacteria. Fifty-nine percent of the APS patients, but none of the controls, were persistently positive for anti-domain I (DI) antibodies. Increased *Slackia* and decreased *Butyrivibrio*, a genus of bacteria that produces butyrate, were also significantly correlated to anti-DI IgG positivity in the APS patients. *Slackia* can produce phospholipids, including cardiolipin, one of the target lipids in APS. The researchers speculated that cardiolipin derived from these [gut bacteria](#) could promote autoreactivity against the major B-cell epitope in β 2GPI.

"The study's findings are early, but suggest that certain gut microbes are enriched across time in APS patients compared to control subjects. Since we performed not only a cross-sectional microbiome study, but sampled our patients at three monthly time points and tested how much microbes are coated with IgA antibodies from the patients, we believe that the gut microbes we identified as promising candidates should be studied further," said Dr. Kriegel. "These eventually may become biomarkers of

disease or even treatment targets, but we're still far away from these goals."

One day, doctors may be able to identify APS biomarkers in patients' fecal microbiomes. Dr. Kriegel's laboratory is currently testing functional links between these microbes and APS.

"The immediate next step is to culture the candidate bacteria that emerged from the study and put them together with immune cells from the patients," he said. "In particular, we would like to test if cardiolipin could be derived from our candidate bacteria and, therefore, be recognized by the patients' immune cells that are known to target these lipids."

Provided by American College of Rheumatology

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