Gut microbes and poor artery health—researchers probe possible link

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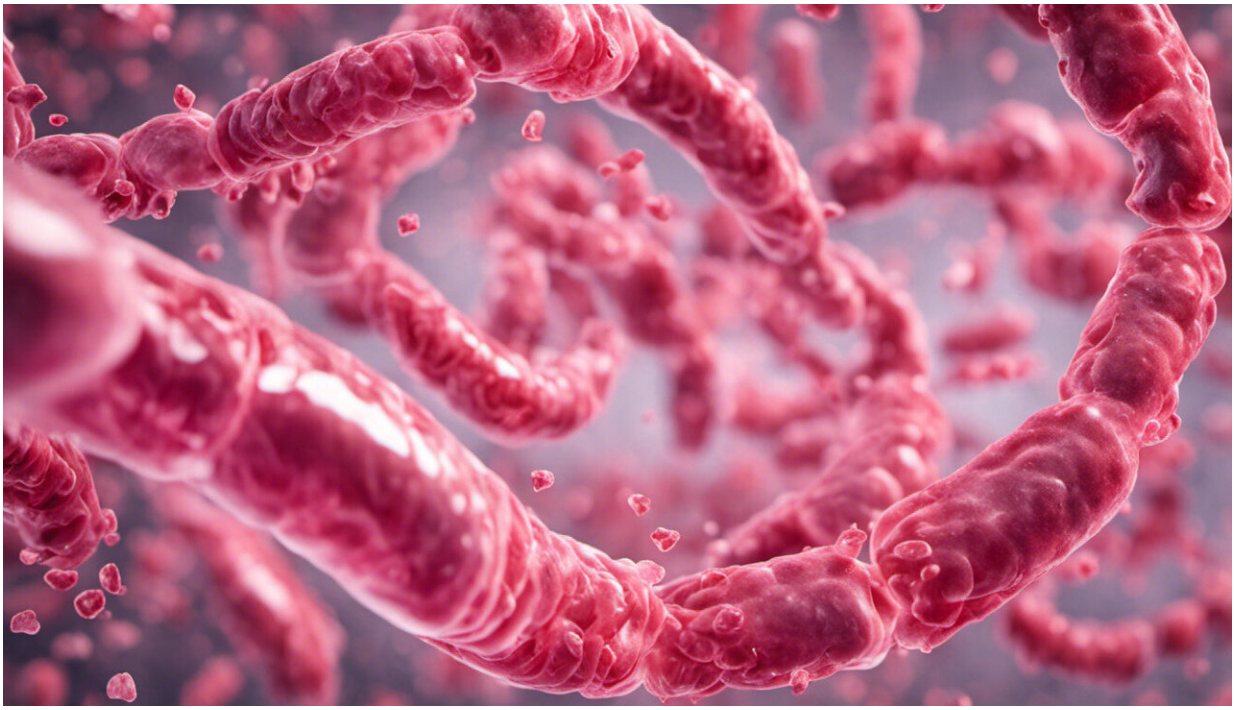

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Scientific evidence that the assortment of gut microbes in humans influences different and critical aspects of health is piling up: Researchers think our microbes may influence obesity, anxiety, depression, autism, cancer and gastrointestinal diseases.

A possible addition to the list: University of Colorado Boulder researchers recently reported preliminary evidence that changes in gut microbiota in mice contribute to poor artery health with aging. This condition is worsened by eating a "Western diet" high in fat and sugars and low in fiber. Artery dysfunction is the main reason our risk of developing cardiovascular diseases increases markedly as we age, said CU Boulder Professor Douglas Seals.

The Seals lab also has preliminary results showing that regular aerobic exercise may prevent the negative effects of both aging and lifelong consumption of a Western diet on artery health in mice.

Now, thanks to a four-year $3 million grant from the National Institutes of Health, Seals, postdoctoral fellow Vienna Brunt of the Department of Integrated Physiology and their team are deep-diving into the role of microbiota on arteries in both mice and humans. Their initial experiments show that treatment with a broad-spectrum antibiotic "cocktail" that eliminates much of the existing gut microbes reverses arterial dysfunction in old mice.

The two types of arterial dysfunction that develop with aging and cause increased risk of cardiovascular disease are the stiffening of some large arteries, and damage to the inner lining of the arteries, said Seals. Both changes are driven by oxidative stress (the excessive production of damaging "reactive oxygen species") and chronic, low-grade vascular inflammation, which develops in our arteries as we age.

"These two changes are conspiring partners that feed off each other, stimulating one another in a vicious cycle," said Seals.

While the researchers don't yet know what causes oxidative stress and inflammation to develop with aging, recent work in Seal's lab suggests gut bacteria affected by aging may in turn change the types of chemicals,

known as metabolites, that they produce.

"We believe the altered chemicals produced by gut bacteria with aging move from inside the intestines through a 'leaky gut' wall - also caused by aging - and enter the bloodstream," said Brunt. "Then they circulate and interact with the walls of the arteries to cause oxidative stress, inflammation and arterial dysfunction."

Part one of the new study will include mouse-to-mouse transplants in which gut microbiota will be transferred between mice differing in age, diet or exercise status to see if it induces changes in arterial function, said Brunt, who is overseeing day-to-day project operations. If successful, the study will provide important evidence that changes in the gut microbiome with aging are linked to increased cardiovascular risk, she said.

The second part of the study will be a clinical trial in about 120 adults divided into four groups: younger, older, exercising and non-exercising. Participants will change between eating a healthy diet and a Western-style diet to induce changes in the gut microbiome while their arterial function is monitored.

Part three of the study is to use a "humanized" mouse model in which stool samples containing gut microbiota from human subjects will be given to mice. The experiment will involve former CU Boulder Professor Rob Knight, now at the University of California San Diego, and will determine if characteristics present in human gut microbes with age, Western diet and exercise predictably influence arterial function.

The expected results have the potential to establish the gut microbiome as a key mechanism and therapeutic target for age-related arterial dysfunction, said Seals. The study also should help the team identify lifestyle or pharmacological strategies that may preserve microbial

health, enhance arterial function and reduce the risk of age-related cardiovascular disease.

The team includes University of Michigan medical student Rachel Gioscia-Ryan, who conducted key preliminary experiments as part of her doctorate under Seals at CU Boulder. The study is funded by NIH's National Heart, Lung and Blood Institute.

Provided by University of Colorado at Boulder