Gut bacteria could protect cancer patients and pregnant women from Listeria, study suggests

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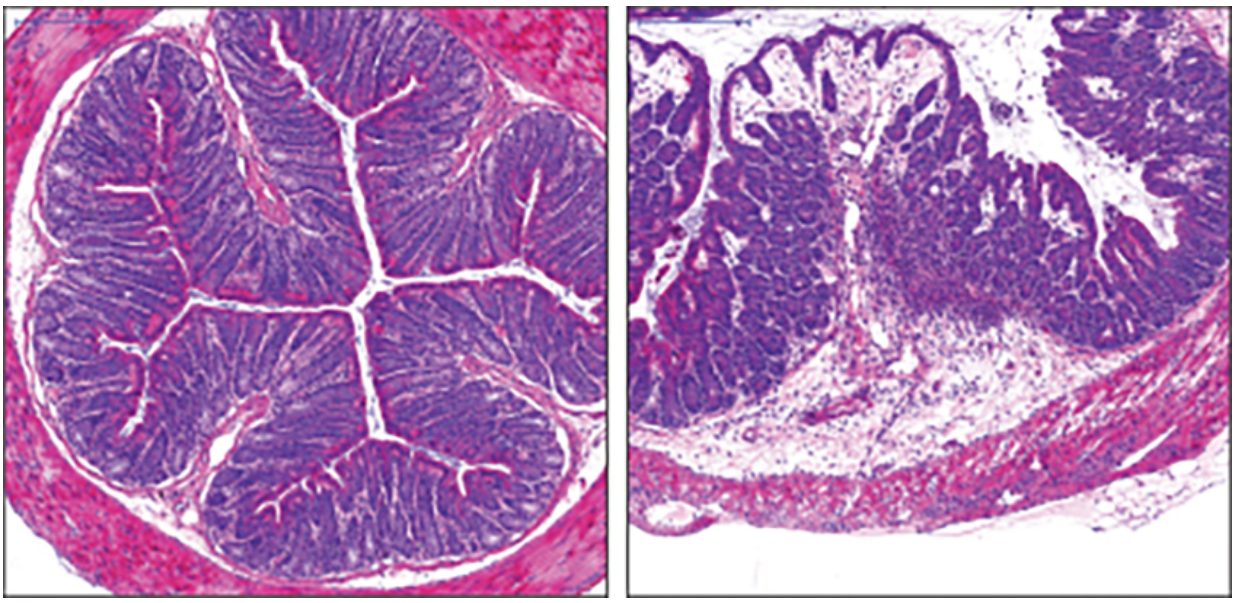

Listeria infection causes swelling and inflammation in the intestine of a mouse pretreated with antibiotics (right) but has little effect in the presence of an intact microbiome (left). Credit: Becattini et al., 2017

Researchers at Memorial Sloan Kettering Cancer Center in New York have discovered that bacteria living in the gut provide a first line of defense against severe *Listeria* infections. The study, which will be published June 6 in *The Journal of Experimental Medicine*, suggests that

providing these bacteria in the form of probiotics could protect individuals who are particularly susceptible to *Listeria*, including pregnant women and cancer patients undergoing chemotherapy.

Listeria monocytogenes is a major pathogen acquired by eating contaminated food, but healthy adults can generally fend off an infection after suffering, at worst, a few days of gastroenteritis. However, some individuals, including infants, pregnant women, and immunocompromised cancer patients, are susceptible to more severe forms of listeriosis, in which the bacterium escapes the gastrointestinal tract and disseminates throughout the body, causing septicemia, meningitis, and, in many cases, death.

Patients with some forms of cancer are as much as 1,000 times more likely to develop listeriosis, possibly because chemotherapy drugs can suppress a patient's immune system. But a team of researchers led by Simone Becattini and Eric G. Pamer wondered whether the gut microbiome—the community of bacteria that naturally lives in the gastrointestinal tract—might also play a role in limiting *L. monocytogenes* infection. Chemotherapy disrupts the microbiome, and gut bacteria are known to prevent other food-borne pathogens from colonizing the gastrointestinal tract by, for example, secreting antibacterial toxins.

The researchers found that disrupting the microbiome with antibiotics made laboratory mice more susceptible to *L. monocytogenes* infection, increasing the pathogen's ability to colonize the gastrointestinal tract and spread into the circulatory system to cause the animals' death. The effect of antibiotics was even more noticeable in immunocompromised mice lacking key immune cells; these animals succumbed to even small doses of *L. monocytogenes* if their microbiomes were disrupted by antibiotic treatment.

Mice treated with the common chemotherapy drugs doxorubicin and cyclophosphamide were vulnerable to *Listeria* infection, and they became even more susceptible when they were also treated with antibiotics.

The researchers identified four species of gut bacteria—all members of the Clostridiales order—that together were able to limit *L. monocytogenes* growth in laboratory cultures. Transferring these probiotic bacteria into germ-free mice protected the rodents from *Listeria* infection by limiting the pathogen's ability to colonize the gastrointestinal tract and disseminate into other tissues. "Thus, augmenting colonization resistance functions in immunocompromised patients by introducing these protective bacterial species might represent a novel clinical approach to prevent *L. monocytogenes* infection," says Becattini.

"Our results also raise the possibility that in other at-risk categories for listeriosis, such as infants or pregnant women, disruptions to the gut microbiome could be a contributing factor to susceptibility," Becattini continues. "Pregnant women in their third trimester, the phase in which susceptibility to *Listeria* is known to be highest, show an altered microbiome, with a marked reduction in Clostridiales species."

More information: Becattini et al., 2017. *J. Exp. Med.* jem.rupress.org/cgi/doi/10.1084/jem.20170495

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