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Microbiome Disruption Ups Sepsis Risk in Hospitalised Patients

A new University of Michigan and VA study shows that older adults are three times more likely to develop sepsis — a body-wide catastrophic response to infection — in the first three months after leaving a hospital than at any other time. Notably, the risk of sepsis is 70 percent higher for those who received care that is likely to alter the balance of microbes in the gut.

In fact, one in 10 gut infection (Clostridium difficile) survivors end up with sepsis within 90 days of hospitalisation, according to the new study published online by the *American Journal of Respiratory and Critical Care Medicine* .

"Our findings could mean that disruption to the microbiome in the hospital may predispose older people to get sepsis later, which is different from what we already know about the acute and chronic effects of microbiome disruption," says lead author Hallie Prescott, MD, MSc, a U-M critical care physician and healthcare researcher. "While more work is needed to explore this further, it also opens the possibility that we might be able to prevent sepsis — by doing something as simple as helping the microbiome recover rapidly from a hospitalisation."

Dr. Prescott and colleagues examined the relationship between hospitalisation and sepsis because of a growing understanding that antibiotics and other infection treatments disrupt the body's microbiome — the natural community of bacteria and other organisms that is vital for healthy body function. In turn, C. difficile preys upon hospital patients who have a disrupted gut microbiome.

Caused by a body-wide over-reaction to any kind of infection, sepsis can lead to damage of vital organs and now kills one in every six people diagnosed with it. More people die from sepsis than die from breast cancer, prostate cancer and AIDS combined.

For the study, the team analysed data from more than 43,000 hospital stays by nearly 11,000 older Americans over a 12-year period. All took part in the U-M-based Health and Retirement Survey, and allowed researchers access to their Medicare records so they could see what happened after each of their hospitalisations. The researchers also analysed a subset of the patients to see what their odds of sepsis were during other times.

"What is really new here is that we studied dysbiosis — disruption of the microbiome — on the population level rather than on the level of the individual patient," explains Robert Dickson, MD, a co-author of the study and U-M critical care physician and microbiome researcher. "Virtually all sepsis research to date has focused on only the host or the pathogen. This paper raises the possibility that we've been ignoring a key third factor: the microbial communities living on and in our vulnerable patients."

Antibiotic use is known to be a major cause of microbiome disruption. This study also hints that "profligate use of antibiotics might not just be bad because of antibiotic resistance," according to senior author Theodore J. Iwashyna, MD, PhD. "Profligate use of antibiotics might also, via the microbiome, put patients at increased risk of both all kinds of other infections, and to having a particularly bad response ('sepsis') to those infections," says Dr. Iwashyna, a physician-scientist at both the U-M and the Veterans Affairs Ann Arbor Center for Clinical Management Research.

The team says further studies should include direct monitoring of the microbiomes of hospitalised patients, followed by long-term follow-up to see which develop sepsis after going home. They also hope to test diet-based interventions to encourage faster recovery of the microbiome after hospitalisation. "There are nearly no strategies proven to prevent sepsis," Dr. Prescott points out. "This unusual collaboration between physicians, social scientists, and microbiome researchers at Michigan offers new hope of an approach to preventing sepsis."

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