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Diagnostic test helps find bloodstream infections before they appear

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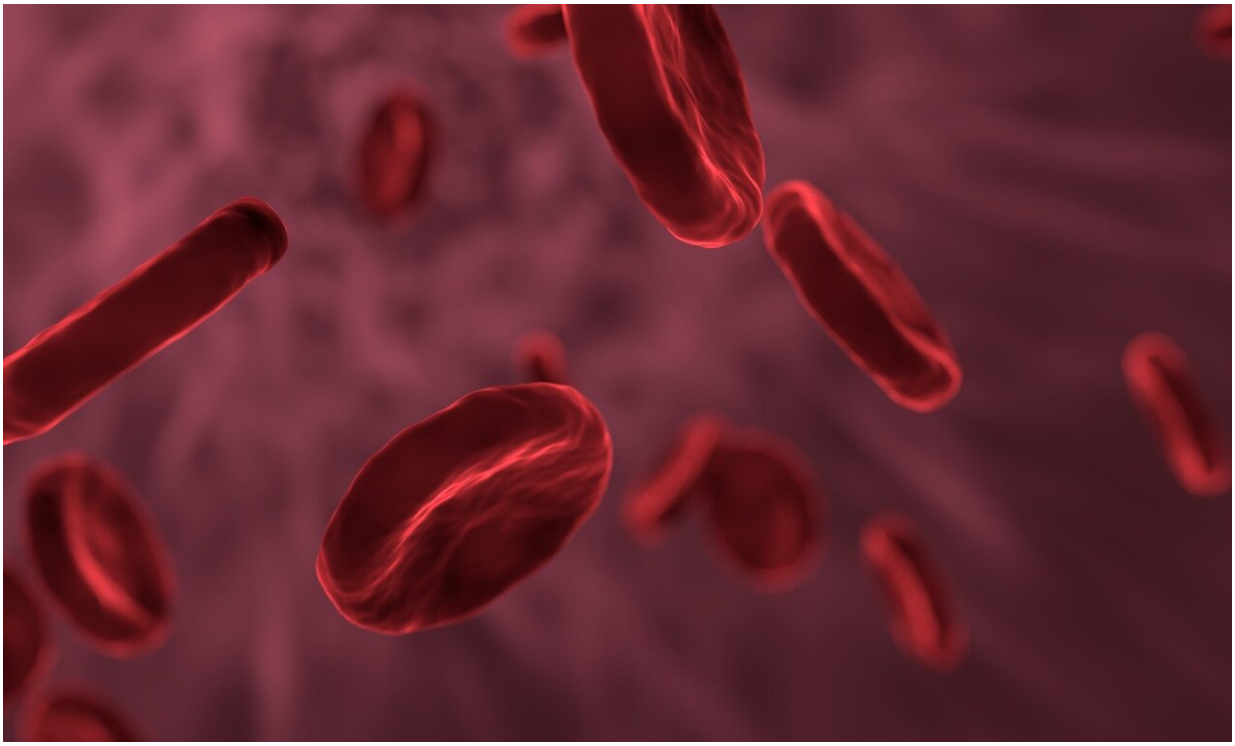

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A test called microbial cell-free DNA identified potentially lethal bloodstream infections in children with relapsed leukemia days before symptoms appeared, according to investigators at St. Jude Children's Research Hospital. The work appears as an advance online publication today in *JAMA Oncology*.

Infections are the most common cause of death for children treated in the U.S. for leukemia. Children with leukemia are at high risk for infection because treatments weaken their immune systems. For children with relapsed leukemia, the risk of infection is even greater.

"This work gets to the heart of something families desperately want: to know what is coming next and to be able to do something about it," said co-senior author Joshua Wolf, MBBS, Ph.D., an associate member of the St. Jude Department of Infectious Diseases.

Currently, prophylactic antibiotics are used in certain high-risk patients to try to prevent infections. However, this approach is effective only half of the time, and exposure to antibiotics may cause gastrointestinal symptoms or contribute to antibiotic resistance.

"We know that early intervention against infection can make a difference clinically," said first author Kathryn Goggin, M.D., a St. Jude Infectious Diseases clinical fellow. "Microbial cell-free DNA testing has the potential to create a paradigm shift in the way infections are diagnosed and treated in people with compromised immune systems."

The study is the first to test the usefulness of microbial cell-free DNA for pre-emptive diagnosis of bloodstream infection. Researchers focused on patients with high-risk relapsed leukemia. When the patients gave blood samples for clinical use, leftover blood was stored. If patients developed bloodstream infections, the researchers could analyze the previously collected samples for the DNA of specific pathogens.

The study enrolled 47 patients, 12 of whom developed a total of 19 bloodstream infections. The microbial cell-free DNA test, performed by Karius Inc., predicted the bloodstream infection in 75% of cases as far out as three days before patients showed symptoms. The researchers are conducting an expansion of this study to analyze the test's ability to

detect infection in more patients.

To improve outcomes for our patients, we need a test that detects infection in advance while reliably discriminating between those who are about to get sick versus those who aren't," said co-senior author Charles Gawad, M.D., Ph.D., formerly of St. Jude and now of Stanford University. "These initial results suggest that analyzing microbial cell-free DNA has enormous potential for overcoming these obstacles to enable the diagnosis and treatment of bloodstream infections before our patients show symptoms."

More information: Kathryn P. Goggin et al. Evaluation of Plasma Microbial Cell-Free DNA Sequencing to Predict Bloodstream Infection in Pediatric Patients With Relapsed or Refractory Cancer, *JAMA Oncology* (2019). DOI: 10.1001/jamaoncol.2019.4120

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