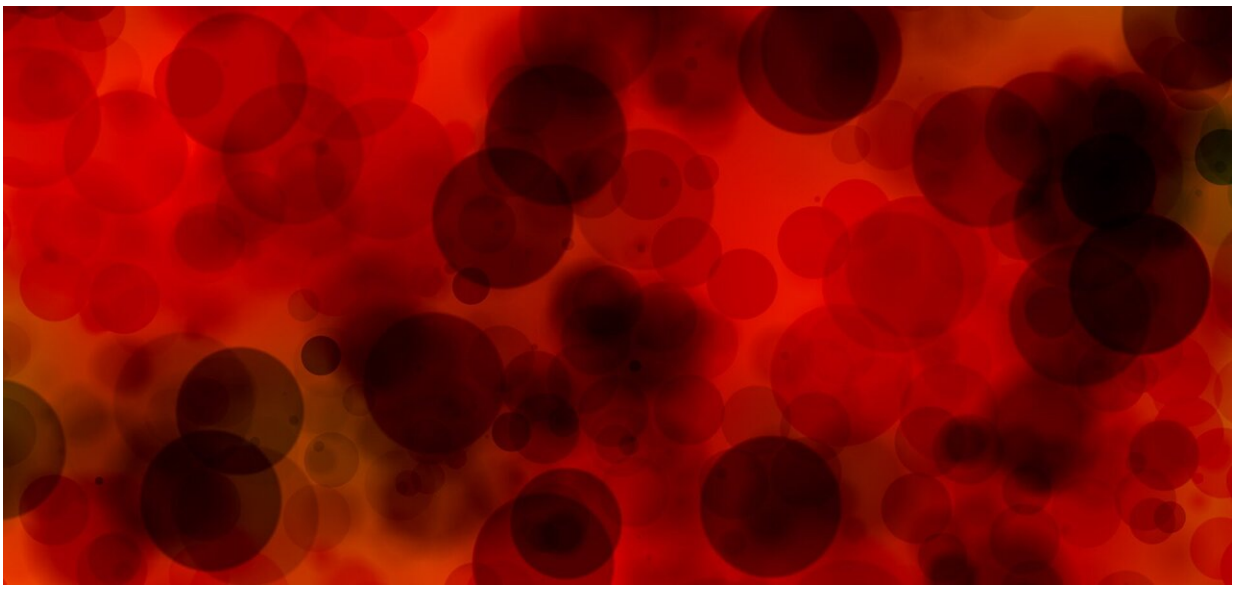
New way of measuring white blood cell function offers better insights to help patients with sepsis

November 11 2019



Credit: CC0 Public Domain

Caring for a patient with sepsis requires walking a treatment tightrope. Clinicians must identify the pathogen that is causing a patient's infection, carefully monitor the patient's response to antibiotics and supportive measures and race against the clock to prevent potential organ failure and death. Most of the time, physicians can control the infection itself. What ultimately leads to multi-organ system injury and fatality is the

patient's immune system's over-exuberant response. Current testing and bedside diagnostics do not provide clinicians with precise and timely information needed to rapidly change their therapeutic approach. To address this unmet need, investigators from Brigham and Women's Hospital, in collaboration with colleagues at MIT, have developed a technology advance to enable measurement of the activation and function of white blood cells—the immune system's sentinels—from a small aliquot of blood from patients with sepsis. The team's new approach, results and clinical implications are detailed in a paper published in *Nature Biomedical Engineering*.

"Our idea was to develop a point-of-care diagnostic test that, instead of focusing on the white blood cell count, would inform us about white blood cell activation state and function," said corresponding author Bruce Levy, MD, chief of the Division of Pulmonary and Critical Care Medicine at the Brigham. "It's been exciting for us, as translational scientists, to work on a solution with outstanding bioengineer colleagues. Together, we're able to address a truly important clinical problem."

The team's technological advancements are two-fold. The new approach uses microfluidics—tiny channels that aligns cells by their size, allowing investigators to sort out larger white blood cells from smaller red blood cells and other elements of the blood. This requires only microliter quantities of blood instead of milliliters—in other words, drops of blood instead of vials of it. This sample sparing approach, in turn, could reduce the risk of iatrogenic anemia among patients.

Secondly, working with the MIT team, the authors utilized a novel technology for measuring the electrical activity of cells, which changes when white blood cells are activated and can distinguish patients with and without inflammation, such as in sepsis. This electrical measurement—known as isodielectric separation—gave the team important information about the function and activation state of white

blood cells.

The team assessed samples from 18 hospitalized patients and 10 healthy subjects, looking at the collected samples over the course of seven days. Both the activation state and function of white blood cells were significantly more predictive of the patient's clinical course than were white blood cell counts.

The authors note that their findings may have implications beyond sepsis. Having a way to accurately and precisely measure the immune system's response in microliter aliquots of blood could be useful in monitoring patients receiving immune modulating therapies, including treatment with immune checkpoint inhibitors for cancer or treatment with immunosuppressive drugs after an organ transplant. A more precise diagnostic test for the immune system's activity would enable clinicians to adjust their immune modulating therapies to maximize benefit and minimize risk for individual patients.

"We're excited to take the next steps forward," said co-first author Bakr Jundi, MD, MMSc, a researcher in the Levy lab. "As physicians try to understand how sepsis affects patients and how we can better monitor patients, we hope this technology will help to address some of the main issues clinicians face."

More information: Leukocyte function assessed via serial microlitre sampling of peripheral blood from sepsis patients correlates with disease severity, *Nature Biomedical Engineering* (2019). DOI: 10.1038/s41551-019-0473-5 , nature.com/articles/s41551-019-0473-5

Provided by Brigham and Women's Hospital