

Researchers devise test to predict sepsis in burns patients

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Researchers have created a potentially life-saving new test that will allow clinicians to predict which burn victims will develop sepsis during their treatment.

Their findings, published in *Annals of Surgery*, show that using just three biomarkers of neutrophil function on the day of injury can determine which <u>patients</u> with major burn injuries are likely to become septic.

In addition to its potential as a diagnostic marker for sepsis, the data highlights burn-induced neutrophil dysfunction as a potential therapeutic target to reduce susceptibility to bacterial infections and sepsis.

The research was funded by the Healing Foundation Birmingham Centre for Burns Research, a partnership including University of Birmingham and University Hospitals Birmingham NHS Foundation Trust (UHBFT).

Centre Director, Mr Naiem Moiemen, a consultant in burns and plastics at Queen Elizabeth Hospital Birmingham (QEHB) and Birmingham Children's Hospital, said, "The researchers have shown that burn patients who may suffer life threatening systemic infections, which occur in 30 percent of major burns at around day six following their injury, could be identified with a 98.6 percent certainty.

"Burn patients who suffer systemic infection have a high probability of non-surviving their injury. This discovery will enable the clinicians to stratify the care of these patients and improve their outcomes."



Professor Janet Lord, Director of the University of Birmingham's Institute of Inflammation and Ageing, who jointly led the research, added, "Major burn injuries result in a systemic <u>inflammatory response</u> syndrome (SIRS) and reduced immune function, which increases the risk of patients developing sepsis or infections in hospitals."

"A delay in diagnosis of sepsis of only a few hours leads to a rapid increase in risk of death. The administration of antibiotics within three hours after sepsis recognition is recommended, but only when positive blood cultures are present."

"However, the majority of clinical studies report negative cultures in as many as 40% of severe sepsis patients - so many cases will be missed. As such, the identification of novel, accurate biomarkers is crucial."

The diagnosis of sepsis represents a major clinical challenge as many classical diagnostic biomarkers are masked by the ongoing systemic inflammatory response syndrome following major burn injury.

The Birmingham team identified neutrophil function and the production of neutrophil extracellular traps (NETs) as potential biomarkers of sepsis.

Neutrophils provide frontline protection against rapidly dividing bacterial and fungal infections, common in burn-injured patients. Their antimicrobial functions include phagocytosis, the generation of toxic intracellular intermediates, and the ability to produce NETs.

Sixty-three patients admitted to the QEHB Burns Centre with 39 percent burns on average were recruited into the study within 24 hours of their injury.

Peripheral blood neutrophil function and biomarkers of NET production



were measured and the patients monitored for the development of sepsis in the weeks following.

Three potentially novel biomarkers of sepsis in burn injury were tracked—immature granulocyte (IG) count, neutrophil phagocytosis and plasma cell free DNA—with the combination of measurements displaying good discriminatory power to predict later development of sepsis, especially at one day after injury.

Professor Lord added, "Our data showed that IG count could accurately discriminate between septic and non-septic patients, even with the complications that systemic inflammatory response syndrome has caused for other potential biomarkers. In addition to this, when we used a combination of two or more of our biomarkers, the discriminatory power was further enhanced."

The team will now look to carry out a trial in patients to see if the use of this new test will help to reduce the incidence of <u>sepsis</u> by allowing doctors to give antibiotics to patients promptly.

More information: Peter Hampson et al, Neutrophil Dysfunction, Immature Granulocytes, and Cell-free DNA are Early Biomarkers of Sepsis in Burn-injured Patients, *Annals of Surgery* (2016). <u>DOI:</u> 10.1097/SLA.0000000000001807

Provided by University of Birmingham

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