

Findings suggest that severe sepsis can lead to impairment of immune system

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An analysis of lung and spleen tissue from patients who died of sepsis revealed certain biochemical, cellular and histological findings that were consistent with immunosuppression, according to a study in the December 21 issue of *JAMA*.

"Sepsis is responsible for more than 225,000 deaths annually in the United States. Developing new therapies for sepsis has been particularly challenging, with more than 25 unsuccessful drug trials. Characterized by an initial intense [inflammatory response](#) or 'cytokine storm,' patients with sepsis may present with fever, shock, altered mental status, and [organ dysfunction](#)," according to background information in the article. "Whether this hyperinflammatory phase is followed by immunosuppression is controversial. Animal studies suggest that multiple immune defects occur in sepsis, but data from humans remain conflicting."

Jonathan S. Boomer, Ph.D., of the Washington University School of Medicine, St. Louis, and colleagues conducted a study to assess evidence of immunosuppression in sepsis and to determine mechanisms that might be responsible for the presumed impaired immunity. For the study, to characterize their immune status at the time of death (2009-2011), postmortem [spleen](#) and [lung tissue](#) harvest was performed on 40 patients who died in intensive care units (ICUs) with active severe sepsis. Control spleens (n = 29) were obtained from patients who were declared brain-dead or had emergency splenectomy due to trauma; control lungs (n = 20) were obtained from transplant donors or from lung cancer

resections. Various tests were performed on the [tissue samples](#) to identify potential mechanisms of immune dysfunction.

The average ages of patients with sepsis and controls were 72 and 53 years, respectively. The median (midpoint) number of ICU days for patients with sepsis was 8, while control patients were in ICUs for 4 or fewer days. The median duration of sepsis was 4 days. Among the results of the researchers were that patients who died of sepsis had biochemical, flow cytometric (cell analysis), and immunohistochemical (process of detecting antigens in cells of a tissue section) findings that were consistent with immunosuppression, compared with the patients who died of nonsepsis causes.

"The present study has a number of important therapeutic implications. Most investigative agents in sepsis have been directed at blocking inflammation and immune activation. Although such therapies may be successful if applied early, they may be harmful if applied later in the immunosuppressive phase. As supportive therapies of sepsis have improved, early deaths have decreased and most patients enter a more protracted phase, with evidence of impaired immunity made manifest by infections with relatively avirulent organisms. An important part of implementing more targeted therapies will be to accurately determine the immune status of individual [patients](#) during their disease," the authors write.

Peter A. Ward, M.D., of the University of Michigan Medical School, Ann Arbor, comments on the findings of this study in an accompanying editorial.

"Boomer and colleagues have presented an informative report documenting immunosuppression in humans with septic shock, along with the broad array of cellular changes that can be linked to the loss of immune competence. A next step might be to determine why during

sepsis immune cells switch from a phenotype with proimmune receptors and ligands to a phenotype featuring anti-immune receptors and ligands. Another important research question is whether such derangements in [sepsis](#) involving humans can be reversed by treatment with agents such as interleukins 7 or 15. These agents in some settings may restore immune responsiveness by increasing the number of competent T cells."

More information: *JAMA*. 2011;306[23]:2594-2605.
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