Stem-cell therapy may provide new approach to fight infection

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A new study from researchers in Ottawa and Toronto suggests that a commonly used type of bone marrow stem cell may be able to help treat sepsis, a deadly condition that can occur when an infection spreads throughout the body. The study, published in the *American Journal of Respiratory and Critical Care Medicine*, shows that these cells can triple survival rates in an experimental model of sepsis.

This work was a collaboration between research groups led by Dr. Duncan Stewart at the Ottawa Hospital Research Institute (OHRI), Dr. Arthur Slutsky at St. Michael's Hospital and Dr. W. Conrad Liles at the University Health Network in Toronto.

The cells used in this study are called mesenchymal stem cells. In addition to their stem cell properties, they are also known to influence the immune system and help repair tissue damage. They are found in adult bone marrow and they have been used extensively in clinical trials for other diseases.

The researchers tested these cells in mice with sepsis. Bacteria from the gut were released into the abdomen, resulting in severe infection, inflammation and organ damage throughout the body. Six hours after inducing the infection, approximately half the mice were given an intravenous injection of mouse mesenchymal stem cells, while the other half received a control injection of a salt solution. Both groups of animals also received antibiotics, which is the standard treatment for sepsis in the clinic. After five days, 50 per cent of the animals that

received the cells were alive, compared to just 15 per cent of the control animals that did not receive the cells.

Other experiments showed that mice that were treated with mesenchymal stem cells had healthier lungs and other organs, lower levels of bacteria and a more moderate level of inflammation. Further analysis revealed that the treatment caused a global change in the expression of genes that are associated with inflammation, such that the damaging effects of inflammation were reduced while the ability to clear the infection was increased.

"Our results suggest that mesenchymal stem cells may provide a promising new approach for treating organ damage caused by severe infection and we are looking to test this in patients in the near future," said Dr. Stewart.

"Sepsis is a life-threatening medical condition caused by the body's response to infection," said Dr. Slutsky. "About a quarter of patients with severe sepsis die, and there are very few specific therapies for this devastating condition. That's why this study is potentially important."

"To achieve approximately 70 per cent reduction in mortality is pretty remarkable, even in a mouse model," said Dr. Liles. "By using a cell therapy, we can target multiple pathways that feed into this complex physiology rather than just one single pathway or factor."

Sepsis is the second leading cause of mortality in Canadian and U.S. intensive care units, resulting in more than 200,000 deaths each year and more than $16 billion in health care costs.

More information: Mesenchymal Stem Cells Reduce Inflammation while Enhancing Bacterial Clearance and Improving Survival in Sepsis. Mei SH, Haitsma JJ, Dos Santos CC, Deng Y, Lai PF, Slutsky AS, Liles

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WC, Stewart DJ. Am J Respir Crit Care Med. 2010 Jun 17. (Abstract available in PubMed)

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