Immune system protein accurate predictor of survival in pediatric septic shock

August 1 2008

About 4,000 children in the United States die every year from uncontrolled infections of the body known as septic shock, and researchers are pushing the boundaries of molecular science to find new therapies that can stem the condition. But a simple measure of an immune system protein within 24 hours of being admitted to the hospital for septic shock can predict survival in children, yielding a powerful tool for diagnostics and clinical trials of new septic shock therapies, according to a research team led by Cincinnati Children's Hospital Medical Center in the Aug. 1 *American Journal of Respiratory and Critical Care Medicine*.

The protein, interleukin-8 (IL-8), is secreted into the blood as part of the body's immune system response, the chief defense mechanism against infection-related conditions like septic shock. Previous research by the authors showed that higher blood levels of IL-8 are associated with more severe cases of pediatric septic shock and a greater chance of death. That research also pointed to the potential value of IL-8 as an early diagnostic marker of systemic bacterial infections.

The new study reports an IL-8 blood level at or below 220 pg/ml (picograms per milliliter) should allow doctors to predict with 95 percent accuracy which children with septic shock can survive through conventional antibiotics and therapies for at least 28 days following admission. Additionally, measuring IL-8 levels would make it possible to screen lower risk patients out of interventional clinical trials of experimental therapies, said Hector Wong, M.D., a physician and

researcher of Critical Care Medicine at Cincinnati Children's and the study's lead author.

"Using IL-8 as a biomarker to screen low-risk septic shock patients from clinical trials of experimental or potentially high-risk therapies is an effective strategy to improve the risk-to-benefit ratio of a given intervention," said Dr. Wong, who also is professor of pediatrics at the University of Cincinnati College (UC) of Medicine. "Excluding patients who respond to standard care would enable investigators to focus clinical trial enrollment on patients least likely to respond well to conventional methods and find the most effective new therapies."

Because the reagents to measure IL-8 are available and blood samples can readily be obtained from patients, Dr. Wong wants to develop a "point-of-care" test that can be used to detect the Il-8 biomarker in septic shock patients, especially patients being considered for clinical trials. He has submitted a provisional patent application with the United States Patent and Trademark Office through the Cincinnati Children's Research Foundation for IL-8 as a stratification biomarker in pediatric septic shock.

Despite today's potent antibiotics and pediatric intensive care units, septic shock remains a serious public health challenge. Sepsis sets off a chain reaction of events that can ultimately lead to uncontrolled inflammation in the body and puts a person's entire immune system into overdrive.

When infections spread throughout the bloodstream, known as sepsis, the immune system makes certain proteins called cytokines, including IL-8 and other interferons, to help fight the infection. The presence of cytokines and toxins from the infection dilates blood vessels, dropping blood pressure to dangerously low levels. Blood flow to vital organs, including the kidneys and brain, becomes inadequate. The heart tries to

compensate, but it weakens as blood vessels walls may leak, allowing fluid into tissues and the lungs, which can cause difficulty breathing. The resulting condition, in which multiple organs malfunction, is called septic shock.

Apart from antibiotics, supportive care and vaccination strategies, no specific therapies are approved by the FDA for pediatric septic shock.

For their study, Dr. Wong and colleagues obtained blood serum measurements and other patient information from two separate databases that included a total of 332 septic shock patients younger than 10 years old. Using statistical analyses of IL-8 levels obtained within 24 hours of hospital admissions, the researchers projected that a threshold of 220 pg/ml blood serum would have sensitivity for predicting rates of deaths in patients 75 percent of the time. The subsequent analyses, conducted separately on patient data from both databases, revealed a much higher validation of 95 percent accuracy when using an IL-8 level of 220 pg/ml or less to predict septic shock survivability at 28 days following hospital admission.

Source: Cincinnati Children's Hospital Medical Center