Early and innovative interventions for severe sepsis and septic shock: Taking advantage of a window of opportunity
Emanuel P. Rivers, Lauralyn McIntyre, David C. Morro, Kandis K. Rivers

PURPOSE
Severe sepsis and septic shock are common, accounting for about 2.9% of hospital admissions and 10% of admissions into the intensive care unit (ICU). Combined, these conditions have a mortality rate greater than 30%. Improved understanding of the pathogenesis of severe sepsis and septic shock has led to the development of new therapies that emphasize early identification and aggressive management. This article reviews the most contemporary and practical approaches to the early recognition, diagnosis, and therapeutic management of sepsis.

INTRODUCTION
Delays in the identification, transfer, and management of critically ill patients during the first six hours after admission with sepsis to the ICU have been associated with higher mortality rates. The timeliness of onset of treatment became a more important issue when Rivers and colleagues were able to demonstrate a significant mortality benefit when hemodynamic optimization was provided within the first few hours of sepsis identification. If left untreated, sepsis can progress to septic shock, and this transition occurs most often within the first 24 hours of hospitalization.

TREATMENT
Because the disease progresses so rapidly, early and aggressive treatment is essential. Early antimicrobial therapy is recommended with broad coverage initially that is tailored to the potential source of infection and according to local hospital sensitivity and resistance patterns.

Early goal-directed therapy (EGDT) aims to restore the balance between oxygen supply and demand in cases of severe sepsis or septic shock within the first six hours of care. EGDT is an algorithmic approach of hemodynamic optimization and targets adequate oxygen delivery by optimizing:

- intravascular volume (preload) with the use of central venous pressure (CVP) monitoring,
- blood pressure (afterload) with mean arterial pressure monitoring,
- contractility with use of monitoring to avoid tachycardia, and
- restoration of the balance between systemic oxygen delivery and oxygen demand (aided by ScvO\textsubscript{2} measurements) to resolve global tissue hypoxia.

Early hemodynamic monitoring requires the monitoring of CVP, arterial blood pressure, and ScvO\textsubscript{2}. ScvO\textsubscript{2} can be measured intermittently from venous gas samples taken from the distal port of a standard central venous catheter or continuously by use of a fiber-optic central venous catheter and monitor.

FIGURE 1. A normal SvO\textsubscript{2} or ScvO\textsubscript{2} and serum lactate level suggest that oxygen supply meets demand.

| Decreased | Increased |
|-----------|-----------|
| SvO\textsubscript{2} (ScvO\textsubscript{2}) | 70-75% of normal |
| VO\textsubscript{2} | DO\textsubscript{2} | VO\textsubscript{2} | DO\textsubscript{2} |
| Stress | PaO\textsubscript{2} | PaO\textsubscript{2} | Hyperthermia |
| Pain | Hemoglobin | Hemoglobin | Anesthesia |
| Hyperthermia | Cardiac output | Cardiac output | Decrease work of breathing |
| Shivering | | | |
| Work of breathing | | | |
Other forms of treatment include volume therapy, vasoactive agents, administration of erythrocytes, inotropic therapy, and decreasing oxygen consumption.

ADJUNCTIVE THERAPIES
Several additional therapies initiated within the first 24 hours after identification of severe sepsis and septic shock have demonstrated a mortality benefit. Early implementation of these therapies may improve patients’ survival, since they may wait several hours or even days before transfer to an ICU. These therapies include steroid therapy, activated protein C, protective lung strategies, and tight glycemic control.

CONCLUSION
Outcomes are optimized through early recognition during the first several hours of severe sepsis and septic shock along with prompt resuscitation. Other therapies that can provide a mortality benefit include the administration of corticosteroids, activated protein C, mechanical ventilation with low tidal volumes, and tight glycemic control. Emphasizing appropriate triage to ensure prompt diagnosis of the high-risk patient is vital to launch a coordinated and cooperative effort by the care team. The pathogenic, diagnostic, and therapeutic landscape of sepsis is no longer limited within the ICU, as many patients from other portals of entry to care progress to severe disease.

Summarized from the study originally published in the Canadian Medical Association Journal in October 2005

References
1. Angus DC, Linde-Zwirble WT, Lidicker J, et al. Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29:1303-10.
2. Lundberg JS, Perl TM, Wiblin T, et al. Septic shock: An analysis of outcomes for patients with onset on hospital wards versus intensive care units. Crit Care Med 1998;26:1020-4.
3. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-77.

© 2012 ICU Medical Inc.