The Surviving sepsis campaign

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The incidence of severe sepsis (sepsis with organ dysfunction) is increasing [1]. Several recent published studies have demonstrated decreased mortality and morbidity as a result of interventions and therapeutics applied to patients with sepsis [2-5]. These new data, resulting from rigorously performed, randomized controlled trials, combined with previous data for beneficial interventions not specific to sepsis management [6-10], such as DVT and stress ulcer prophylaxis, lend significant weight to the belief that critical care clinicians can now significantly reduce mortality in patients with severe sepsis and septic shock.

Protocolized care now exists for a heart attack or a stroke, which is based on recent advances as demonstrated by the medical literature. Up to now there has been no attempt to reproduce such an approach in severe sepsis. The Surviving Sepsis Campaign hopes to change that. The Surviving Sepsis Campaign is administered by the Society of Critical Care Medicine (SCCM), the European Society of Intensive Care Medicine (ESICM), and the International Sepsis Forum (ISF), and is open to be funded by unrestricted educational grants from industry. Thus far Baxter Bioscience, Edwards Lifesciences, and Eli Lilly and Company have provided funding. The campaign, initiated in 2002, is comprised of three phases.

The first phase was the introduction of the campaign at several major international critical care medicine conferences, beginning with the ESICM meeting in Barcelona in 2002, and followed by the Society of Critical Care Medicine meeting in 2003. The overall goal of the campaign is to increase clinician and public awareness of the incidence of sepsis, severe sepsis, and septic shock, to develop guidelines for the management of severe sepsis, and to foster a change in the standard of care in sepsis management.

Phase 2 of the campaign was aimed at producing guidelines for the management of sepsis. In 2003, critical care and infectious disease experts representing 11 international organizations developed management guidelines for severe sepsis and septic shock that would be of practical use for the bedside clinician, under the auspices of the Surviving Sepsis Campaign. A modified Delphi methodology for grading recommendations, built on a 2001 publication sponsored by the International Sepsis Forum was used. The process included a consensus conference, several subsequent smaller meetings of subgroups and key individuals, teleconferences, and electronic-based discussion among subgroups and among the entire committee. A systematic review of the literature graded along five levels to create recommendation grades from A to E, with A being the highest grade. Pediatric considerations were provided to contrast adult and pediatric management. Lead authors on recent positive clinical trials were excluded from the process to avoid potential bias. All participants fully disclosed potential financial conflicts of interest. The recommendations that resulted represent an attempt to facilitate a rapid change in the standard of care for management of sepsis, based on the quality of available published data and expert opinion where no literature guidance is available. The guidelines manuscript has recently been published in both *Critical Care Medicine* and *Intensive Care Medicine* [11,12]. The publication of this manuscript represents an historic step for critical care, worldwide. These guidelines represent an international consensus on the best available standard for management of sepsis.

Key recommendations, listed by category and not by hierarchy, include early goal-directed resuscitation of the septic patient during the first 6 hours after recognition; appropriate diagnostic studies to ascertain causative organisms before starting antibiotics; early administration of broad-spectrum antibiotic therapy; reassessment of antibiotic therapy with microbiology and clinical data in order to narrow coverage, when appropriate; a usual 7 to 10 days of antibiotic therapy guided by clinical response; source control with attention to the method that balances risks and benefits; equivalence of crystalloid and colloid resuscitation; aggressive fluid challenge to restore mean circulating filling pressure; vasopressor preference for norepinephrine and dopamine; cautious use of vasopressin pending further studies; avoiding low-dose dopamine administration for renal protection; consideration of dobutamine inotropic therapy in some clinical

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situations; avoidance of supranormal oxygen delivery as a goal of therapy; stress-dose steroid therapy for septic shock; use of recombinant activated protein C in patients with severe sepsis and high risk for death; with resolution of tissue hypoperfusion and in the absence of coronary artery disease or acute hemorrhage, targeting a hemoglobin of 7-9 g/dl; appropriate use of fresh frozen plasma and platelets; a low tidal volume and limitation of inspiratory plateau pressure strategy for acute lung injury and acute respiratory distress syndrome; application of a minimal amount of positive end expiratory pressure in acute lung injury/acute respiratory distress syndrome; a semi-recumbent bed position unless contraindicated; protocols for weaning and sedation/analgesia, using either intermittent bolus sedation or continuous infusion sedation with daily interruptions/lightening; avoidance of neuromuscular blockers, if at all possible; maintenance of blood glucose <150 mg/dl after initial stabilization; equivalence of continuous veno-veno hemofiltration (CVVH) and intermittent hemodialysis; lack of utility of bicarbonate use for pH 7.15 or greater; use of deep vein thrombosis/stress ulcer prophylaxis; and consideration of limitation of support where appropriate. Pediatric considerations included a more likely need for intubation due to low functional residual capacity; more difficult intravenous access; fluid resuscitation based on weight with 40-60 ml kg or higher needed; decreased cardiac output and increased systemic vascular resistance as the most common hemodynamic profile; greater use of physical examination therapeutic endpoints; unsettled issue of high-dose steroids for therapy of septic shock; and greater risk of hypoglycemia with aggressive glucose control.

Unfortunately, clinicians change very slowly. Historically, transfer of research from the bench to the bedside is a long, tortuous process – one that is not driven by anything very clear and seems to be based more on fad and coincidence than on a keen, evidence-based evaluation of the literature. What motivates clinicians to change? There are several obvious factors, including quality of the evidence, magnitude of the treatment effect, precision of the treatment effect, risk/benefit ratio, and cost/benefit analysis. In addition, there are intangible factors that drive the rate at which clinicians adapt research into new standards of care. These include physiological rationale for a new intervention, peer pressure, and how easy it is to use or apply a new intervention. Changing clinicians' behaviors in response to published data has long been a glaring failure in medicine. We would like to believe that, with the dawn of the information age, this lag time between the publication of rigorous data and incorporation into routine practice at the bedside would finally be reduced.

The next step for the campaign will be Phase 3, which aims to operationalize the guidelines in order to create a global standard of care for sepsis management. The guidelines will be transformed into user-friendly tools that will allow clinicians to easily incorporate these new recommendations into bedside care. The first step in this next phase will be a joint effort with the Institute of Healthcare Improvement to deploy a "change bundle" based on a core set of the previous recommendations into the Institute of Healthcare Improvement collaborative system. Chart review will identify and track change in practice and clinical outcome. Engendering evidence-based change through motivational strategies while monitoring and sharing impact with healthcare practitioners is the key to improving outcome in severe sepsis.

The Surviving Sepsis Campaign represents an important step for international critical care societies. Recognizing the long history of delay in incorporating research into bedside care, these critical care societies have committed to working together to facilitate bench-to-bedside transfer of recent research. Thus, the campaign represents an ongoing commitment to excellence in patient care. The Surviving Sepsis Campaign has established a target of a 25% reduction in mortality worldwide from sepsis over the next five years. If the Surviving Sepsis Campaign is able to bring the guidelines into routine use, it is possible to achieve this goal. In order for the campaign to be successful, it will require more than good publicity. It will require a further commitment from bedside clinicians to critically appraise new research and rapidly adopt interventions proven to be effective.

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