

Critical Care CME Program

Module 4

CSA's Critical Care CME Program will consist of eight modules. The fourth module appears in this issue of the *Bulletin*, and Modules 5 through 8 will appear in upcoming consecutive issues of the *Bulletin*. The test questions and evaluation for this module are at the end of this article. Submit answers to the nine questions to the CSA office with the registration page to receive the CME credit. Your CME certificate will be mailed from the CSA office. Alternatively, the full text of each module of this CME program will be accessible through the CSA Web Site, www.csahq.org, in the Online CME Program section, and as part of the online *CSA Bulletin*. Instructions to complete Module 4 online are given in the Information pages. After completing the assessment, print your CME certificate. Members will need their usernames and passwords to do the modules online.

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Important Information about Critical Care Module 4

The following information must be read and acknowledged before proceeding to the rest of the module. Check the acknowledgement box on the registration page.

Faculty/Disclosures

All faculty participating in continuing medical education activities sponsored by the CSA are required to disclose any real or apparent conflict(s) of interest related to the content of their presentation(s) or any of the industry sponsors of the meeting. In addition, speakers must disclose when a product is not labeled for the use under discussion or when a product is still investigational.

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Dr. Shah has received honoraria from Masimo, Abbott, and Baxter for his role as speaker. He owns stock in Masimo Corporation.

Registration/Instructions

Method of Participation: The physician will read and study the materials and complete a quiz and evaluation of the module. Some modules may have slides available online. To register for and complete this module: Read and study all of the module pages, complete the registration page, go to the test questions that can be found after the article, complete the quiz and the evaluation that follows, submit your quiz to the CSA office by mail or fax (650-345-3269). Your CME certificate will be mailed to you.

Estimated Time to Complete the Module: One hour

Availability

Module 4: Sepsis Bundles Including Early Goal-Directed Therapy

Release Date: December 31, 2008

Expiration Date: December 31, 2011

CME Sponsor/Accreditation

The California Society of Anesthesiologists is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

The California Society of Anesthesiologists Educational Programs Division designates this critical care program for a maximum of 8 *AMA PRA Category 1 Credit(s)*[™]. The program consists of eight modules with 1 credit per module. Physicians should claim credits commensurate with the extent of their participation in the activity.

Fees

The modules are free to CSA members. Nonmembers pay \$30 for each module. Each module is worth one *AMA PRA Category 1 Credit*[™].

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Target Audience

This program is intended for all licensed physicians, including residents.

Evaluation

An evaluation of each module of this series is offered after the test questions.

Privacy Policy

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Acknowledgement

To proceed with this module, please acknowledge that you have read everything on these introductory pages by checking the box on the registration page.

Objectives

Upon completion of this CME activity, participants will be able to:

- Discuss the clinical impact of severe sepsis/septic shock in the intensive care unit.
- Describe the initial monitoring modalities and laboratory tests recommended for a workup of severe sepsis/septic shock.
- Discuss the initial interventions and time course recommended for the management of severe sepsis/septic shock.
- Describe the clinical endpoints currently utilized in the resuscitation of a patient with severe sepsis/septic shock.
- Discuss some of the new adjuvant therapies in the management phase of severe sepsis/septic shock.

Sepsis Bundles Including Early Goal-Directed Therapy

By Scott Ahlbrand, M.D., and Fred Mihm, M.D.

Scott M. Ahlbrand, M.D., is currently a fellow in the Division of Critical Care Medicine of the Department of Anesthesia at Stanford University. Originally from Northern California, he received his medical degree from the Keck School of Medicine at the University of Southern California before completing his anesthesia residency at Stanford University. His main area of

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interest is resident and fellow education and he is currently a member of the Graduate and Resident Education Committee for the Society of Critical Care Medicine.

Fred Mihm, M.D., trained in Anesthesia at Stanford University and Critical Care Medicine at Stanford and Harvard Universities. He has been practicing Anesthesia and CCM at Stanford University since 1979, and is currently Professor of Anesthesia, Chief of the Division of CCM and Co-Director of the ICU. Dr. Mihm's two areas of research interest involve cardiorespiratory monitoring techniques and applications and the perioperative management of patients with pheochromocytoma. Away from Stanford, he has participated in 27 overseas medical missions to Central/South America, Africa, and Southeast Asia.

Introduction

The intensive care unit is a place where critically ill patients walk a tight rope between life and death. Patients are admitted to intensive care units for a variety of reasons, including respiratory failure, altered mental status, and low blood pressure. One of the most common causes of all these diagnoses is sepsis. Sepsis can be defined as simply the body's own reaction to infection. There are different levels to which the body reacts to these infections. Uncomplicated sepsis can be caused by something as simple as the flu or other viral infections, gastroenteritis, or even dental caries. This form of sepsis occurs to millions of people each year, and is typically self-limiting. Severe sepsis, defined as a process that involves one or more of the vital organs, such as the lungs, heart, liver, or kidney, is estimated to afflict more than 750,000 people each year in North America alone. Severe sepsis is associated with a mortality rate of 30 percent to 35 percent, as compared to uncomplicated sepsis, which rarely even requires hospitalization. Lastly there is septic shock, which occurs when severe sepsis is accompanied by low blood pressure that is refractory to initial fluid resuscitation and results in the failure of more than one vital organ system. Not surprisingly, the 50 percent mortality rate associated with septic shock is greater than that for severe sepsis. Due to the relatively common occurrence of sepsis in the intensive care unit, and the strikingly high mortality associated with this condition, much attention has been directed to developing therapeutic guidelines for the management of sepsis.

In 2003, the Surviving Sepsis Campaign, an international effort to increase awareness and improve outcome in severe sepsis, brought together critical care and infectious disease experts from 11 international organizations to develop management guidelines for severe sepsis and septic shock. What resulted from this campaign were evidence-based recommendations regarding the many aspects of the acute management of severe sepsis and septic shock that are hoped to translate into improved outcomes for the critically ill patient. These

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recommendations were then updated in 2006 and 2007 using a new evidence-based methodology system for assessing quality of evidence and strength of recommendations.⁴ The following pages will describe the guidelines included in this campaign.

Surviving Sepsis Campaign—Resuscitation Phase

The Surviving Sepsis Campaign is broken into two phases: resuscitation and management. The **Resuscitation Phase** involves the first six hours after identification of severe sepsis or septic shock. Severe sepsis and septic shock are characterized by the presence of confirmed or suspected infection, evidence of a systemic inflammatory response syndrome (SIRS), and a low blood pressure and/or an elevated serum lactate. SIRS by definition includes at least two of the following: temperature $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$; heart rate $> 90/\text{min}$, a respiratory rate > 20 breaths per minute (or a $\text{PaCO}_2 < 32$ mmHg), or a WBC $> 12,000$ or $< 4,000$ cells per cubic millimeter of blood, or the presence of $> 10\%$ bands.

- **Notification and Monitoring**

Once identification has occurred, appropriate *notification and monitoring* needs to be initiated. *Notification* includes making the physicians most responsible for the patient's care aware of the patient's clinical state. At Stanford, this includes the Emergency Department Attending, the Critical Care fellow, and the primary medical team, depending on where this identification occurs.

The next step is to ensure that there is proper *monitoring* of the patient. This includes an EKG to evaluate the patient's cardiac rhythm, a noninvasive blood pressure cuff set to inflate at least every five minutes until mean blood pressure reaches baseline level, or a continuous intra-arterial monitor is placed. Additional monitors include continuous pulse oximetry with supplemental oxygen, at least two large bore (18 G or larger) peripheral IVs, an indwelling urinary catheter to monitor hourly urine output, and an initial patient weight.

Baseline laboratory evaluations should be the next step. These must be drawn from the patient within the first hour of identification and should include complete blood count with differential, complete metabolic panel, serum lactate, amylase, lipase, blood cultures, a coagulation panel, and a urinalysis/urine culture. Additional optional tests include sputum gram stain and culture, blood type and screen, arterial blood gas analysis, venous blood gas analysis, and a chest x-ray. This concludes the evaluative portion of the resuscitative phase. We now move on to the interventional portion.

Sepsis Bundles (cont'd)

- **Initial Resuscitation Interventions**

Initial interventions should also occur within the first hour following identification. These include normal saline or balanced salt solution (i.e., lactated ringer's) intravenous bolus every 15 minutes until the mean arterial pressure is greater than 65 mmHg or a target central venous pressure is obtained. The CVP can be used to assist with the evaluation of the patient's volume status.

At the same time, and equally important, is the first dose of an appropriately broad spectrum intravenous antibiotic that should now be administered. Antibiotic selection is of ongoing debate, but it is divided into two general categories. These two categories are based on whether or not the target is a community-acquired or hospital-acquired organism. In our institution, if the target antibiotic therapy is to treat community-acquired organisms, ceftriaxone would be started for sepsis thought to originate from a urinary tract infection, ceftriaxone and moxifloxacin for sepsis thought to originate from a pneumonia source, and ertapenem for sepsis of unknown cause. Additional coverage with vancomycin or linezolid is added if skin or soft tissue infection is suspected to be the source.

If the target antibiotic therapy is to treat hospital-acquired organisms, including *Pseudomonas* and methicillin-resistant *Staphylococcus aureus*, a different regimen is used, which typically includes piperacillin/tazobactam, ciprofloxacin, vancomycin, and anidulafungin if *Candidemia* is suspected. If there is a history of recent exposure to or failure of piperacillin/tazobactam within the last 10 days, then imipenem or meropenem is substituted.

- **Further Resuscitation Interventions**

The second part of the interventional portion involves the placement of more invasive monitors if not already done. These typically include an intra-arterial catheter for continuous mean arterial pressure measuring, a central venous catheter for CVP measurement, and a means to measure either central or mixed venous oxygen saturation. This can be accomplished either by obtaining a central venous blood sample from the aforementioned central venous catheter ($ScVO_2$), or by placing a pulmonary artery catheter and obtaining a mixed venous blood sample (SVO_2). Both PA and CVP catheters equipped with continuous oxygen saturation monitoring may be used. Lastly, serial serum lactate levels should be monitored on a q4 – q6 hour basis.

Once these data points have been obtained, one can use them to navigate through the hemodynamic “storm” that may ensue. Beginning with the CVP, if the value is < 8 mmHg in the spontaneously breathing patient, administration

Sepsis Bundles (cont'd)

of either normal saline or lactated ringer's bolus every 15 minutes should be initiated until either the MAP > 65 mmHg **and** ScVO₂ > 70% or a total volume of 60 ml/kg has been given. Once the fluid limit or CVP target has been met, the MAP becomes the next primary focus if not goal. If the MAP remains < 65 mmHg even after these interventions, intravenous infusions of either norepinephrine or dopamine should begin up to a maximum of 20 mcg/min or 20 mcg/kg/min, respectively. If this is not adequate to bring the MAP > 65 mmHg, then intravenous infusions of either epinephrine or vasopressin should be started.

After the MAP has been raised to greater than 65 mmHg, attention is then directed to making sure that venous oxygenation is within normal limits. If the ScVO₂ or SVO₂ is less than 70 percent, then the cause is usually anemia or a cardiac output that is not adequate to meet the high metabolic demands created by this septic physiology. If so, one can either administer packed red blood cells to achieve a hematocrit > 30 percent or initiate an intravenous infusion of dobutamine and titrate that to a ScVO₂ /SVO₂ > 70 percent.

At this point in the resuscitation, it is important to step back and reassess the situation. Have all of the indicators of adequate resuscitation been met at this time? Is the MAP > 65 mmHg, CVP > 8-12 mmHg, Urine Output > 0.5 mg/kg/hr, **and** ScVO₂ > 70 percent? Are the serial lactate levels decreasing? Does the patient exhibit signs of improved perfusion? If these are not all present, readdress their needs before moving forward.

Assuming adequacy of resuscitation has been achieved, or at least approached, one must then make sure appropriate diagnostic imaging and consultation has been obtained to define the source of the infection and treat accordingly. One must also consider ventilatory support if necessary at this time. If initiated, tidal volumes of 6 ml/kg and peak plateau pressures < 30 cmH₂O should be attempted.

Surviving Sepsis Campaign—Management Phase

The **Management Phase** encompasses the following 18 hours. The management phase can be thought to fill in the gaps of the resuscitation phase. Some of these “gaps” include the administration of steroids to patients whose MAP < 65 despite adequate fluid resuscitation and vasopressor administration; hydrocortisone 50 mg IV every six hours is recommended.

Another area is glucose control. The literature supports tight glucose control in the setting of severe sepsis or septic shock. Ideally, blood glucose values should remain < 130 mg/dl by either a glucose protocol or insulin drip.

Sepsis Bundles (cont'd)

As for any critically ill patient, deep vein thrombosis and stress ulcer prophylaxis should be included in the management of a patient with severe sepsis/septic shock. Prophylaxis against deep vein thromboses should be determined according to the risk level of the patient, while GI stress ulcer prophylaxis should be administered to most all critically ill patients. Additionally, sedation/analgesia should be administered to all mechanically ventilated patients, and muscle relaxation should be considered when adequate oxygenation or ventilation cannot be achieved.

The final topic is the topic of recombinant human activated protein C (rhAPC) within the first 24 hours of identification of sepsis. The typical dose at our institution is 24 mcg/kg/hr for 96 hours if the patient meets the established criteria, which include an Acute Physiology and Chronic Health Evaluation (APACHE) II score of > 25 or the presence of multiple organ failure. Whether the patient is a candidate for rhAPC or not should be documented in the medical record in addition to the contraindication if not used.

Conclusion

We have attempted to present a brief, yet concise overview of the evidence-based recommendations created by the Surviving Sepsis Campaign. Although there exist many differences between how individual institutions manage severe sepsis/septic shock, the principles outlined here should be included in each hospital's sepsis management protocols. The importance of establishing standards of care for this disease is to improve outcome by early identification and aggressive resuscitation.

References

1. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008, *Crit Care Med* 2008 Vol. 36, No. 1, pages 296-327
2. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock, *Crit Care Med* 2004 Vol. 32, No. 3, pages 858-873
3. Stanford Hospital and Clinics Critical Care Sepsis Management Guidelines
4. Surviving Sepsis Campaign: <http://www.survivingsepsis.org>

ABA Numbers for Reporting CME credits!

CSA will report CME credits earned to the American Board of Anesthesiology. These credits will be counted as Lifelong Learning and Self-Assessment activities toward your Maintenance of Certification in Anesthesiology (MOCA) requirement. In order to report these credits, doctors need to provide their ABA number. To obtain an ABA number, visit www.theABA.org and create a personal portal account.

Questions

1. Septic shock differs from severe sepsis in that septic shock is associated with a greater mortality and is refractory to fluid resuscitation.
 - a. True
 - b. False
2. Systemic inflammatory response syndrome by definition includes all of the following except:
 - a. temperature $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$
 - b. heart rate $> 90/\text{min}$
 - c. MAP < 60 mm Hg
 - d. respiratory rate > 20 BPM (or a $\text{PaCO}_2 < 32$ mmHg)
 - e. WBC $> 12,000$ or $< 4,000$ cells per cubic milliliter of blood, or the presence of $> 10\%$ bands
3. Which of the following is the most reliable physiologic parameter of adequate tissue perfusion?
 - a. MAP > 65 mmHg
 - b. CVP $> 8\text{-}12$ mmHg
 - c. HR < 80 bpm
 - d. Urine Output > 0.5 mg/kg/hr
 - e. $\text{ScVO}_2 > 70$ percent
4. SVO_2 and ScVO_2 values are not interchangeable. An SVO_2 value is usually 5 percent lower than ScVO_2 , due to the fact that blood that drains from the lower part of the body into the IVC has a higher venous saturation level than the blood in the superior vena cava. This difference is mainly due to the high venous saturation of what organ?
 - a. Liver
 - b. Small intestine
 - c. Large intestine
 - d. Kidney
 - e. Brain
5. A 49-year-old female is admitted to the intensive care unit gravely ill with a recurrent pneumonia for which she was recently discharged from the hospital six days prior. An appropriate broad spectrum antimicrobial regimen might include all of the following except:
 - a. piperacillin/tazobactam
 - b. ceftriaxone
 - c. ciprofloxacin
 - d. vancomycin
 - e. anidulafungin

Sepsis Bundles (cont'd)

6. The same patient mentioned above presents with a HR of 109 bpm, ABP 87/43, CVP 14, SVO₂ of 53 and hematocrit of 29. The most appropriate next step would be to:
 - a. Transfuse the patient two units of PRBCs
 - b. Administer one L normal saline
 - c. Perform a rapid sequence endotracheal intubation
 - d. Begin an infusion of dopamine or norepinephrine

7. Four hours later, that same patient mentioned above then exhibits a HR of 84, ABP 110/69, CVP 7, hematocrit of 30, and an SVO₂ of 59. The most appropriate next step would be to:
 - a. Transfuse the patient two units of PRBCs
 - b. Administer one L normal saline
 - c. Perform a rapid sequence endotracheal intubation
 - d. Begin an infusion of epinephrine

8. An additional 4 hours pass and the same patient mentioned above then exhibits a HR of 92, ABP 89/41, CVP 13, hematocrit of 31, and an SVO₂ of 51. A pulmonary artery catheter is placed, which reveals a PCWP of 20 and a CO of 2.1. The most appropriate next step would be to:
 - a. Transfuse the patient two units of PRBCs
 - b. Administer one L normal saline
 - c. Insert an intra-aortic balloon pump
 - d. Begin an infusion of epinephrine

9. Over the next 48 hours, the patient develops bilateral patchy infiltrates on chest radiograph, the requirement for renal replacement therapy (hemodialysis or venovenous dialysis), elevated transaminase levels, and becomes difficult to arouse during their daily sedation vacation. According to the Surviving Sepsis Campaign, the use of recombinant human activated protein C (rhAPC) at this point would be appropriate.
 - a. True
 - b. False

Critical Care CME Program

In this issue of the *Bulletin*, Module 4 of the new Critical Care CME Program is available. There will be eight modules for this program. After each module is published in the *CSA Bulletin* (one per season), it is posted on the CSA Web Site at www.csaHQ.org. Each online module uses a self-assessment and evaluation; once these are completed, you may print your CME certificate. You may also contact the CSA office at 800-345-3691 to obtain the materials by fax or mail.

Sepsis Bundles (cont'd)

Registration

Complete this form, the test, and the evaluation, and **mail or fax** all three to the CSA office at 951 Mariner's Island Boulevard #270, San Mateo, CA 94404 or FAX to 650-345-3269. The CSA CME journal courses are also available on the CSA Web Site at www.csahq.org.

Critical Care CME Course, Module 4

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I acknowledge that I have read the Important Information about Module 4.