NURSING CONSIDERATIONS TO COMPLEMENT THE SURVIVING SEPSIS

CAMPAIGN GUIDELINES

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NURSING CONSIDERATIONS TO COMPLEMENT THE SURVIVING SEPSIS CAMPAIGN GUIDELINES

ABSTRACT

Objective: To provide a series of recommendations, based on the best available evidence, to guide clinicians providing nursing care to patients with severe sepsis.

Design: Modified Delphi method involving international experts and key individuals in subgroup work and electronic-based discussion among entire group to achieve consensus.

Methods: We used the Surviving Sepsis Campaign Guidelines (SSC) as a framework to inform the structure and content of these guidelines. We used the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system to rate the quality of evidence from high (A) to very low (D) and to determine the strength of recommendations, with *grade1* indicating clear benefit in the septic population and *grade 2* indicating less confidence in the benefits in the septic population. In areas without complete agreement between all authors a process of electronic discussion of all evidence was undertaken until consensus was reached. This process was conducted independently of any funding.

Results: Sixty-three recommendations relating to the nursing care of severe sepsis patients are made. Prevention recommendations relate to education, accountability, surveillance of nosocomial infections, hand hygiene and prevention of respiratory, central-line related, surgical site and urinary tract infections, while infection management recommendations related to both control of the infection source and transmission based precautions. Recommendations related to initial resuscitation include improved recognition of the deteriorating patient, diagnosis of severe sepsis, seeking further assistance and initiating early resuscitation measures. Important elements of hemodynamic support relate to improving both tissue oxygenation and macrocirculation. Recommendations related to supportive nursing care incorporate aspects of nutrition, mouth and eye care and pressure ulcer prevention and

management. Pediatric recommendations relate to the use of antibiotics, steroids,

vasopressors and inotropes, fluid resuscitation, sedation and analgesia and the role of

therapeutic end points.

Conclusion: Consensus was reached regarding many aspects of nursing care of the severe

sepsis patient. Despite this, there is an urgent need for further evidence to better inform this

area of critical care.

BACKGROUND

Sepsis, including severe sepsis and septic shock, continues to be a major healthcare problem internationally. Although mortality related to severe sepsis and septic shock have reduced slightly in the past decade, it remains above 20% (1, 2). As part of the response to optimize care for this group of patients evidence-based clinical practice guidelines have been published by the Surviving Sepsis Campaign (SSC) to facilitate clinicians to improve the outcomes of patients with sepsis and septic shock (3, 4).

Although the SSC Guidelines (4) provide a comprehensive review of the medical management of patients with sepsis and septic shock, they are frequently silent on the nursing care that is essential for optimal outcome of these patients. Expert nursing knowledge and skill is required for both the identification of the deteriorating patient as a result of newly developed sepsis and the ongoing implementation of competent care for the known severe sepsis patient. The World Federation of Critical Care Nurses (WFCCN), as the premier organization for critical care nurses worldwide, consequently formed an international group of interested experts in the area to provide guidance for nursing care of severe sepsis patients.

This care is provided by every registered nurse, as well as many of the advanced practice nurses (e.g. Nurse Practitioner, Clinical Nurse Specialist or Consultant) who practice in the acute hospital setting. Internationally, advanced practice nursing roles vary in scope, education and authorization. Although the scope and requirements for some of these roles are designated by legislation, for example, the scope of practice of the nurse practitioner, many of the roles are professional extensions of the registered nurse role. Given this variation in nursing roles from one region or country to another, we have not attempted to limit the recommendations contained within this document to care provided only by registered nurses, but have extended it to cover the practice of all nurses, regardless of their specific role.

Most of these recommendations relate to the adult septic patient, with the majority of interventions not tested in the pediatric patient. Despite this, many of the recommendations are likely to be applicable to the pediatric setting. Throughout the document we have identified where specific information confirming or denying application to patients in specific age groups exists. Recommendations specific to the pediatric septic patient are contained within section IV late in the document.

While this document is designed to provide guidance for every nurse who cares for patients with severe sepsis, we have also provided recommendations regarding practice in areas of joint responsibility with other members of the healthcare team. For example, nurses frequently influence which central venous catheters or endotracheal tubes are purchased and used, as well as provide care related to the device following insertion. In addition, although most nurses do not order drugs, they do participate in protocol development and often advocate for the timely ordering and administration of medications important to patient outcomes in severe sepsis. Consequently, it is essential that nurses are familiar with the best available evidence.

Of note, this document is not designed to provide information regarding strategies for implementation to ensure practice is based on these recommendations. Rigorous and comprehensive implementation and evaluation strategies are essential, but constitute a separate body of knowledge and as such are not reviewed in this document. Clinicians are encouraged to become familiar with appropriate strategies prior to implementing the recommendations outlined throughout this document.

The aim of this review is therefore to provide a series of recommendations, based on the best available evidence, to guide clinicians providing nursing care to patients with severe sepsis.

METHODS

Sepsis, including severe sepsis and septic shock, has been well defined in the literature and inform these guidelines (Table 1). These guidelines for nursing care are designed to augment, not to replicate or replace, the current SSC Guidelines (4) and have been developed using the following methodology:

- WFCCN formed a team to develop guidelines for the nursing care of patients with sepsis; the organization appointed a coordinator (LMA) and an organizational sponsor (GW)

- Known experts in the field of sepsis care were invited to contribute to the guidelines

- Authors worked in sub-groups of two or three; wherever possible these authors represented different geographical regions of the world

- The broad structure of the SSC guidelines (4) was used to inform the structure and content of these guidelines for nursing care

- An additional section relating to prevention of infection and subsequent sepsis was added in recognition of the pivotal role that nurses provide in this area

- Each sub-group of authors undertook searches to locate any published literature that informed the nursing care of patients with severe sepsis

- Authors searched the literature referred to in the SSC guidelines (4), with searches expanding based on the section topics

- Analogous to the SSC guidelines (4), the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system (5), was used to rate the quality of the evidence (Table 2)

- Initial discussion of relevance and quality of the evidence was undertaken electronically within the sub-groups

- All recommendations were reviewed by the coordinator as well as an independent reviewer (GRB), queries were discussed electronically with the sub-group, then with the entire author team where necessary

- The evidence supporting each recommendation, as outlined in the rationale, and the associated level of recommendation, was then forwarded to all authors who confirmed, or not, their support for each recommendation based on the rationale and summary of evidence in line with the GRADE system (5)

- Every recommendation that did not receive 100% agreement for the grade of support was subject to email discussion and exploration of additional evidence until consensus by all members of the author team was achieved.

I. INFECTION PREVENTION

A. Education

1. We recommend interactive, multifaceted, longitudinal educational programs and educational outreach to enhance guideline implementation. Traditional education approaches, such as incorporated passive education and information dissemination through conferences, web sites and didactic lectures, are often not effective (grade 1A).

2. We recommend educational initiatives to reduce healthcare-associated infection rates (grade 1C).

Rationale. Education is generally considered as a first step to increase awareness of a problem and as crucial for processes of change. A systematic review found that interactive, multifaceted, longitudinal educational programs and educational outreach enhance guideline implementation (6). More specifically, a systematic review that investigated the effect of education on the reduction in infection rates concluded that the implementation of educational interventions may considerably reduce healthcare associated infections (7).

B. Accountability

1. We suggest the promotion of a culture of patient safety and individual accountability (grade 2D).

Rationale. Recent trends have seen a transition from accepting healthcare-associated infection as an inevitable outcome of admission to the Intensive Care Unit (ICU) (8) towards personal accountability and a goal of zero tolerance in relation to hospital-acquired infections (9, 10). A systematic review of 30 reports of nosocomial infection found that at least 20% could be preventable (11). A major impediment to achieving zero tolerance towards hospital-

acquired infection has been a lack of accountability of all levels of hospital staff (9). This attitude is shifting, with recognition that hospital management, as well as every healthcare worker, is responsible and accountable for ensuring patient safety including infection prevention and control (9, 10). Educating and empowering nurses to ensure infection control guidelines are followed by all staff has the potential to positively impact on hospital-acquired infections (12, 13).

C. Surveillance of nosocomial infections

1. We recommend a continuous surveillance program for the detection of nosocomial infection (grade 1B).

   Rationale. Local surveillance systems (eventually integrated in a national surveillance program) allow benchmarking of nosocomial infection data and are therefore essential to guide and evaluate interventions to reduce infection rates. Surveillance systems combined with appropriate feedback contribute to reduced nosocomial infection risk (14-19).

D. Hand hygiene

1. We recommend hand antisepsis, irrespective of the use of gloves, between caring for different patients or between different care activities for the same patient, immediately before and after each episode of direct patient contact, and after any activity or contact that potentially results in hands becoming contaminated (grade 1B).
2. We recommend hand antisepsis by means of an alcohol-based hand rub (grade 1A).
3. We recommend hand washing with soap and water when hands are visibly soiled (grade 1A).

4. We recommend the use of gloves when contact with blood or other potentially infectious materials, secretions, mucous membranes and non-intact skin could occur (grade 1D).

Rationale. Adequate hand antisepsis has proven to result in reduced infection rates (20, 21). The use of alcohol-based hand rub is particularly effective; in contrast with hand washing, it kills susceptible bacteria more rapidly and to a greater extent, is less time consuming, and skin health is better preserved when moisturizers are added. Hand disinfection after glove removal is necessary because gloves may have imperceptible defects or may be torn during use, resulting in contamination of hands. Hand washing is necessary when hands are visibly dirty because alcohol-based hand rub is ineffective in the presence of organic material. However, after hand washing, the use of alcohol-based hand rub remains mandatory (20, 21).

As a rule of thumb, a first step towards adequate hand hygiene consists of avoiding direct contamination of hands. The use of non-sterile, well fitting gloves is recommended whenever the risk of contamination exists. Gloves must be changed between separate tasks on one patient (when going from a dirty/contaminated to a clean body site) and in between different patients (20-22).

E. Site-specific considerations

Most healthcare associated infections in the ICU are related to the use of therapeutic devices. These include ventilator-associated pneumonia (VAP), catheter-related bloodstream infection (CR-BSI), surgical site infection (SSI), and urinary tract infection (UTI) (23, 24). Recommendations for their prevention are outlined below.

E1.   Prevention of respiratory infections

The development of pneumonia in patients mechanically ventilated with an artificial airway may affect 10–48% of patients (25-27). VAP is associated with a higher mortality rate, and significantly longer ICU length of stay and hospital costs (24, 27). However, VAP is often preventable, and application of practices such as education strategies (28, 29) and ventilator bundles (30, 31) have contributed to a reduction in VAP incidence. Strategies to prevent VAP should be considered in all patients with severe sepsis (32).

1. We recommend head-of-bed elevation 30–45° for all critically ill and mechanically ventilated patients (grade 1B). Special attention should be given to maneuvers in which it is difficult to achieve a 30° head-of-bed elevation, such as during bed bath or changing sheets. In such circumstances we recommend backrest elevation of at least 10° should be maintained.

Rationale. Aspiration of upper airway secretions is a common event even in normal healthy adults (33). Semi-recumbent position in mechanically ventilated patients has been associated with lower levels of aspiration into the lower airways (34-36) and lower VAP incidence than the supine position (37-39). In patients receiving enteral nutrition, head-of-bed elevation is especially effective in reducing the risk of VAP (37). However, the feasibility of maintaining head-of-bed elevation in daily practice has been questioned by some authors (40, 41). Van Nieuwenhoven et al (41) achieved average head-of-bed elevation of only 28° despite a target of 45°, while Song et al (40) achieved head-of-bed elevation >30° in 43.4% of patients.

2. We recommend the use of an endotracheal tube with subglottic secretion drainage in patients expected to require mechanical ventilation for more than 72 hours (grade 1A).

Rationale. Impaired gag reflex leads to pooling of secretions in the posterior part of the oropharynx (42), with microaspiration of subglottic secretions leading to VAP. Subglottic secretion drainage is accomplished through use of a specially designed endotracheal or tracheotomy tube with a separate dorsal lumen that opens directly above the endotracheal tube cuff. Subglottic secretions drainage appears to be effective in preventing VAP (relative risk [RR] 0.51, 95% confidence interval [95% CI] 0.37–0.71) in patients expected to be mechanically ventilated for more than 72 hours (43).

3. We suggest the use of a silver-coated endotracheal tube be considered (grade 2A).

Rationale. In multicenter randomized controlled trials, a silver-coated endotracheal tube was demonstrated to reduce bacterial airway colonization as well as VAP in patients intubated 24 hours or more (44, 45). More studies that confirm the current findings are required.

4. We suggest the use of an endotracheal tube with a polyurethane cuff (grade 2B).

Rationale. In a single center randomized controlled trial, an endotracheal tube with a polyurethane cuff was shown to significantly reduce early onset post-operative pneumonia in cardiosurgical patients (46). More studies that confirm this result are required.

5. We recommend endotracheal cuff pressure be maintained at least 20 cm H_2O, but not more than 30 cm H_2O (grade 1C).

Rationale. Inadequate cuff pressure is a risk factor for microaspiration of oropharyngeal secretions and subsequent pneumonia. One observational study among intubated patients not receiving antibiotic therapy showed that a persistent intracuff pressure below 20 cm H_2O was an independent predictor of VAP (RR 4.2, 95% CI 1.1–15.9) (47). Cuff pressure should be maintained at the lowest pressure above 20 cm H_2O that prevents cuff leak.

6. We suggest heat and moisture exchangers (HME) should be changed between patients, every 5–7 days, or as clinically indicated (grade 2C).

Rationale. Humidification of inspired air to prevent mucosal injury may be achieved by using a heated humidifier, a heated humidifier with a heated-wire circuit, or passively using a HME. There are insufficient data to demonstrate a benefit in VAP reduction for any humidification device (48). No benefit in infection rates or functionality of ventilator circuits has been demonstrated when HMEs are changed every day compared to 5–7 days (49, 50).

7. We recommend ventilator circuits should not be changed routinely, except between patients (grade 1B).

Rationale. There is no evidence that routine ventilator circuit changes can reduce the incidence of VAP (25, 51). New ventilator circuits should be used for each patient, and circuit changes performed only if the circuit becomes visibly soiled or damaged (32).

8. We recommend the aspiration of endotracheal secretions in response to clinical signs, i.e. visible or audible signs of respiratory secretions, respiratory deterioration or other changes

in the patient's condition that may be due to respiratory secretions, in intubated patients

(grade 1C).

Rationale. Critically ill patients mechanically ventilated via a tracheal tube frequently

require removal of tracheobronchial and upper airway secretions due to increased mucus

production and a decreased ability to clear secretions (52, 53). Secretion removal may reduce

infectious, respiratory and tube patency complications (54-56).

Suctioning should only be performed when necessary, using the lowest possible suction

pressure, take no longer than 15 seconds, use continuous rather than intermittent suctioning;

the suction catheter should occlude less than half the lumen of the endotracheal tube and be

inserted no further than the carina; hyperoxygenation should be provided before and after

suctioning, and saline lavage should be avoided (55, 57).

The optimum frequency of endotracheal suctioning has not been clearly determined, but

should be in response to clinical signs (56). There is insufficient evidence to recommend the

benefits of either an open or closed suctioning system (57).

9. We recommend regular mouth care and oral cavity assessment be provided to all critically

    ill and intubated patients (grade 1C).

Rationale. Colonization of the oropharynx by pathogens is a potential risk factor for the

development of VAP (58-60). Critical illness contributes to changes in the oral flora, and an

increase in gram-negative flora that includes more virulent organisms may occur (61, 62).

Providing regular oral care, incorporating oral cavity assessment, is an important part of

providing comfort to the critically ill patient (63) and is also demonstrated to contribute to a

decrease in VAP (63-67). Assessment should include the condition of the teeth, gums, tongue,

mucus membranes and lips, and barriers to mouth care delivery (63). The use of a designated oral care protocol, in association with an education program for nurses in its importance in preventing VAP, can increase compliance and assessment of mouth care (68).

10. We recommend the use of chlorhexidine-based antiseptic for oral care in intubated patients (grade 1A).

Rationale. Chlorhexidine is widely used and investigated in the oral care of intubated patients (69-72). Chlorhexidine effectively decontaminates the oropharynx (73, 74), and its use in oral care has been proven to decrease dental plaque (75) and incidence of respiratory infections (76), and substantially decrease the incidence of VAP (77-79). The optimal concentration of chlorhexidine solution (0.12%, 0.2% or 2%) remains undetermined. The optimum frequency for oral care with chlorhexidine has not been demonstrated. In general, a frequency of 3–4 times daily is proposed (69, 80, 81). The benefit of tooth brushing in critically ill patients as a component of oral care protocols has demonstrated efficacy but additional research is indicated (65, 66). Tap water is not recommended for oral care in the critically ill (63).

E2.   Prevention of central line-related bloodstream infections (CR-BSI)

1. We recommend the implementation of a central line care bundle including staff education, creation of a catheter insertion cart, implementation of a checklist to ensure adherence to evidence based guidelines, empowering nurses to stop catheter insertion procedures when a guideline violation is observed, and daily assessment of possible catheter removal (grade 1B).

Rationale. A bundle approach to central venous catheter (CVC) insertion and care (12, 13, 82, 83) has proven to be effective in substantially reducing the rate of CR-BSI. Nurses play a key role in preventing CR-BSI through the activities outlined above.

2. We recommend the use of maximal sterile barriers during CVC insertion (grade 1A).

Rationale. During the CVC insertion procedure, all healthcare personnel involved must wear a mask, cap, sterile gown, and sterile gloves and the patient is to be covered with a large sterile drape (84-88). Use of maximal sterile barrier precautions during CVC insertion have led to reduced infection rates (87, 89, 90).

3. We recommend the use of a chlorhexidine-based antiseptic for skin preparation before insertion and subsequent catheter care (grade 1A).

Rationale. As the risk of CR-BSI increases with the density of microorganisms at and around the insertion site (21), site antisepsis is crucial in the prevention of infection. Aqueous chlorhexidine (2%) solution has consistently been found to be superior to both 10% povidone iodine and 70% alcohol for preventing CR-BSI (91-93).

4. We suggest the replacement of administration sets every 96 hours (grade 2A), except when used for the administration of blood, blood products or lipids, in which case sets must be changed within 24 hours (grade 1A).

Rationale. A Cochrane systematic review found no increase in the risk for CR-BSI when the interval for administration set replacement was increased from 72 hours to 96 hours (94).

When a fluid that enhances microbial growth is infused (lipid emulsions, blood products) more frequent changes of administration sets are indicated because these products have been identified as independent risk factors for CR-BSI in both adults and neonates (95-100).

5. We recommend the use of minocyclin-rifampin impregnated catheters (grade 1B).

Rationale. Studies have repeatedly demonstrated a significant reduction in CR-BSI with the use of impregnated CVCs in comparison with standard catheters (101-104); this reduction in infection rates has been greatest with minocycline-rifampin coated CVCs when compared to other impregnated CVCs (105). Minocycline-rifampin impregnated CVCs are approved for use in the pediatric population by the Food and Drug Administration (USA); however, studies have not been conducted in children.

E3.   Prevention of surgical site infections (SSI)

1. We recommend that antimicrobial prophylaxis be administered within one hour before incision to maximize tissue concentration. Two hours are allowed for the administration of vancomycin and fluoroquinolones (grade 1A).

Rationale. In 2003, the Surgical Infection Prevention Guideline Writers Workgroup meeting reviewed the various guidelines for antimicrobial prophylaxis in surgery (106). On the basis of published evidence, the workgroup concluded that infusion of the first antimicrobial dose should begin within 60 minutes before incision, and when a fluoroquinolone or vancomycin is indicated the infusion should begin within 120 minutes before incision to prevent antibiotic-associated reactions (106, 107).

2. We recommend that only hair that will interfere with the operation be removed, and that, if hair removal is necessary, it should be removed by using electric clippers (grade 1B).

   Rationale. Although several authors have reported pre-operative hair removal is associated with increased SSI rates (108-111), a Cochrane systematic review compared a variety of hair removal methods (depilatory cream, razors, clippers) versus no hair removal and reported no difference in SSI rates among patients who had hair removal prior to surgery and those who did not (112). The same review found that shaving led to statistically significantly more SSIs compared with clipping or depilatory cream (112). The increased infection risk associated with the technique of shaving is attributed to the formation of microscopic cuts in the skin that later act as foci for bacteria (108). Although the use of depilatories has been associated with a lower SSI risk than shaving or clipping (113, 114) they can produce hypersensitivity reactions (114).

3. We recommend that blood glucose levels be controlled during the immediate post-operative period for patients undergoing cardiac surgery: controlled blood glucose level (lower than 200 mg/dL) on post-operative day 1 and post-operative day 2, with procedure day being post-operative day 0 (grade 1C).

   Rationale. Increased glucose levels (>200 mg/dL) in the immediate post-operative period (≤48 hours) are associated with increased SSI risk (115, 116). One study found that patients with a blood glucose level more than 300 mg/dL within 48 hours of surgery had more than three times the likelihood of a wound infection (117). Regular monitoring of glucose levels and timely administration of insulin and hyperglycemic agents is a direct nursing

responsibility, therefore nursing education should stress the importance of glucose control in preventing SSI.

4. We recommend the identification and treatment of infections remote to the surgical site before elective surgery (grade 1B).

   Rationale. Concurrent remote site infections are considered to increase SSI risk (118-120). Therefore, whenever possible, all infections remote to the surgical site should be identified and treated before elective operation, and elective operations on patients with remote site infections should be postponed until the infection has resolved (108).

E4.   Prevention of urinary tract infections (UTI)

1. We recommend that all attempts should be made to limit the duration of urinary catheterization (grade 1C).

   Rationale. The urinary tract is the most prevalent source of nosocomial infection and there are several recommendations to prevent or reduce the incidence of UTI (121). Duration of catheterization is the most important risk factor for developing UTI (121). Post-operative urinary catheterization >2 days is associated with an increased likelihood of UTI and 30-day mortality, as well as a decreased likelihood of discharge to home (122). Nurses should advocate for prompt removal of urinary catheters (123) and discourage long-term catheterization, if possible.

2. We recommend that a sterile, continuously closed drainage system be maintained (grade 1A).

Rationale. Closed urinary drainage systems are pivotal in preventing UTI (21, 123). The risk of infection reduces from 97% using open systems to 8–15% when sterile closed systems are used (124-126). Errors in maintaining sterile closed drainage and opening the closed drainage system have been well documented to predispose patients to infection (124, 126-129).

3. We recommend regular perineal hygiene measures (grade 1C).

Rationale. Most episodes of UTI are caused by the patient's own flora (121). Daily cleansing of the urethral meatus using soap and water or perineal cleanser is recommended (123, 130).

4. We suggest the maintenance of unobstructed urine flow (grade 2C).

Rationale. Reflux of urine is associated with infection; therefore, drainage bags should be positioned below the level of the bladder at all times to prevent urine back-flow and unobstructed urine flow should be maintained (21, 131, 132).

II. INFECTION MANAGEMENT

A. Infection source control issues

1. We recommend prompt removal of intravascular catheters and subsequent catheter tip culturing in patients with proven bloodstream infection associated with severe sepsis as well as in hemodynamically unstable patients with suspected CR-BSI (grade 1C).

Rationale. Prompt removal of contaminated invasive devices is a cornerstone in the management of device-related infection. Failure to remove the catheter was demonstrated to be an independent predictor of mortality in an epidemiological study on CR-BSI (OR 0.22, 95% CI 0.10–0.86) (133). If the catheter is removed for suspected CR-BSI, guidewire exchange is acceptable in circumstances where catheter insertion is problematic as this reduces the risk for mechanical complications (134). If, however, the catheter tip culture appears to be positive, the newly inserted catheter should be replaced a second time because bacterial contamination can be expected and guidewire exchange on itself was shown to be an independent risk factor for the development of CR-BSI in an observational study (OR 4.59, 95% CI 2.28–9.3) (133).

B. Transmission-based precautions

1. We recommend transmission-based precautions for patients who are known or suspected to be infected or colonized with infectious agents including certain epidemiologically important pathogens (grade 1A).

Rationale. Standard precautions are required for all patients. In addition, patients colonized or infected with epidemiologically important pathogens, including methicillin-resistant Staphylococcus aureus; vancomycin-resistant enterococci, glycopeptide-resistant Staphylococcus aureus, extended-spectrum beta-lactamase producing Enterobacteriaceae, multidrug-resistant non-fermenting Gram-negative bacteria, and Clostridium difficile, may pose a potential threat to patients in their vicinity (135), and require additional precautions to prevent cross-infection. There are three categories of transmission-based precautions: contact, droplet and airborne precautions (136). For diseases with multiple routes of transmission, more than one transmission-based precautions category may be recommended. Transmission-

based precaution categories and the particular measures they include are described in detail elsewhere (136).

III.   INITIAL RESUSCITATION

As the SSC Guidelines (4) for initial resuscitation (six-hour resuscitation bundle) are operational only from the point that severe sepsis/septic shock is diagnosed, the processes that lead to early diagnosis are pivotal. Many of the processes that support compliance with the six-hour resuscitation bundle such as recording and interpreting clinical observations, seeking further assistance, and initiating early resuscitation measures are often the domain of nurses. The role of the nurse in initial resuscitation will vary according to the clinical area concerned. On a general ward nurses will be responsible for monitoring clinical observations, and giving antibiotics and fluid challenges, whereas in a critical care area nurses may be also be involved in monitoring hemodynamic status and administering vasoactive agents. The nurse's role in initial resuscitation does not end when medical staff arrive on the scene. Successful resuscitation depends on collaborative integration of the skills and expertise of all members of the multidisciplinary team.

A. Recognizing deterioration and diagnosing severe sepsis

1. We recommend that all staff with a direct responsibility for patient care (including nursing assistants and health care assistants) be educated to recognize the Systemic Inflammatory Response Syndrome (SIRS) criteria and signs of severe sepsis or septic shock (grade 1C).

Rationale. All staff with a direct responsibility for patient care, including the taking of vital signs, must be able to recognize the clinical findings of SIRS and sepsis (Table 3). The definitive diagnosis of sepsis or severe sepsis in hospital patients will often be made by a

medical officer, but the clinical review leading to diagnosis will usually be facilitated by a nurse who recognizes signs and symptoms indicative of the onset of SIRS and/or sepsis (137).

Nurses therefore play a pivotal role in the early identification of deteriorating patients and prompt management of sepsis to enhance recovery (138). Numerous studies have demonstrated the relationship between nursing and failure-to-rescue (139, 140). The effect on patient outcomes of providing sepsis education for all nurses including nursing assistants is inconclusive. A national sepsis education program in Spain for medical and nursing staff marginally improved guideline compliance and hospital mortality rates (44.0% vs. 39.7%; P = .04) but did not demonstrate sustained improvement after one year (141). However a more recent multi-national performance improvement study demonstrated sustained improvement in both compliance and patient mortality at two years (142).

2. We recommend the use of early warning systems (EWS) to assist in the early recognition of sepsis in order to promote prompt treatment to enable best patient outcomes (grade 1C).
3. We suggest the use of sepsis screening tools to assist in the early recognition of sepsis in order to promote prompt treatment to enable best patient outcomes (grade 2C).

Rationale. Early diagnosis of sepsis is linked to improved outcomes and survival from sepsis. The recognition of patient deterioration and diagnosis of sepsis relies on the detection of abnormalities in physiological data. The collection and documentation of clinical observations is an important nursing role (143, 144). Despite this, there is evidence that clinical observations sometimes are performed poorly or not at all, are not documented, are not interpreted correctly, or are not reported when abnormalities are found (145). Early warning systems (EWS), also known as 'Track and Trigger' systems, have been promoted to aid in the detection of deterioration by highlighting abnormalities in clinical observations

(146), however, the evidence of their effectiveness is inconclusive (147, 148). Additional

verification of the usefulness of EWS is needed in order to recommend consistent use in

clinical care.

The addition of sepsis screening tools have been recommended in promoting early

recognition of patients at risk for developing or those who have SIRS criteria, indicating the

early onset of severe sepsis (146, 149). Sepsis screening can be added to observation charts or

EWS charts, prompting nurses to use a sepsis screening tool if the patient triggers one or more

of the SIRS criteria of temperature, heart rate and respiratory rate (149). One study reported a

decrease in mortality of one-third following the introduction of a three-step sepsis screening

tool (150).

B. Seeking further assistance

1. We suggest that communication tools (e.g. SBAR, RSVP) be used to improve

   communication and promote prompt identification and treatment of patients with

   suspected or confirmed sepsis (grade 2D).

Rationale. Summoning medical assistance is crucial in implementing the resuscitation

bundle, and communication delays can result in poorer outcomes for patients with severe

sepsis. There is evidence that nurses and medical staff do not always communicate effectively

with each other (145, 151). Communication between disciplines can be improved by using

structured communication tools such as SBAR (Situation, Background, Assessment,

Recommendations) (152, 153), RSVP (Reason, Story, Vital signs, Plan) (154) and EWS (155)

that incorporate objective, unambiguous language to convey patient information. Sepsis

screening tools may also be incorporated into the Assessment (SBAR) or Vital Signs (RSVP)

to ensure the nurse cogently relays the message that the patient meets the consensus definition for severe sepsis and needs immediate attention to implement the resuscitation bundle.

C. Initiating early resuscitation measures

1. We suggest that the initial resuscitation of patients with sepsis be provided through the use of rapid response systems (grade 2B).

Rationale. Early recognition of sepsis can improve patient outcomes if a rapid response is initiated (156, 157). Early goal-directed therapy (EGDT) and the SSC guidelines have demonstrated efficacy in improving mortality outcomes in severe sepsis (4, 158, 159). Despite this, compliance with the six-hour resuscitation bundle is poor, ranging from 19–52% (160, 161). A number of studies have explored the poor uptake of EGDT and suggest barriers to implementation include inadequate facilities (162) and inadequate numbers of nurses (163).

Nurses must be able to recognize signs of severe sepsis and be knowledgeable about the six-hour bundle components in order to begin prompt implementation of therapy. The focus then should be on identifying patients eligible for EGDT (those not responding to fluid resuscitation and/or having a lactate >4 mmol/L) and arranging prompt transfer to a higher level of care area such as the High Dependency Unit and Intensive Care Unit to ensure timely treatment for severe sepsis. Table 5 outlines additional strategies for integrating the SSC guidelines in nursing practice (138).

2. We suggest the provision of adequate resources to enable prompt identification of patients with actual or suspected sepsis (grade 2D).

Rationale. A recent UK survey of acute medical units found that only 12% appeared to have the minimum facilities to comply with the six-hour resuscitation bundle (162). Carrying out EGDT can be labor intensive and may require a minimum of two nurses in the initial phase (164), although some clinical settings can incorporate EGDT into their regular clinical duties without the allocation of additional staff (165). Recommended resources include arterial blood gas monitors, and laboratory facilities for measuring lactate levels as serum lactate has been demonstrated to be an independent predictor of mortality in patients with severe sepsis (166). Hand-held lactate monitors should be available in non-critical care areas to help identify those with cryptic shock (raised lactate in the absence of hypotension) who may otherwise be overlooked.

3. We recommend that adequate nurse staffing levels be ensured to provide quality patient care and improved patient outcomes (grade 1B).

Rationale. The impact of registered nurse staffing levels on patient outcomes is well documented, with lower nurse-patient ratios being associated with higher rates of pneumonia (167-171), shock, UTI (169), upper gastrointestinal bleeding, deep vein thrombosis, cardiac arrest and failure-to-rescue, as well as infection (172) and sepsis (167, 168, 170, 173-176). Nurse-to-patient ratios in ICUs in the USA and some parts of Europe typically range from 1:1 to 1:3 depending on patient acuity levels, while in countries such as Australia, New Zealand, and the UK, ratios are 1:1 due to not having personnel such as respiratory therapists to assist in the management of acute and critically ill patients. Nurse-to-patient ratios of one nurse caring for one or two patients (>1:2) versus one nurse caring for three or more patients (<1:2) in the ICU have been found to be associated with increased risk of post-operative pulmonary and infectious complications (167).

4. We suggest that nurses be empowered to initiate the six-hour resuscitation bundle. All nurses should be trained to take blood, cannulate, and administer intravenous fluids via standing orders for hypotension and/or raised lactate (grade 2C).

5. We suggest that the 'Sepsis Six' approach be promoted in non-critical care areas in order to promote early identification and treatment of severe sepsis (144) (grade 2D).

Rationale. Although the nurse may identify signs of severe sepsis, he/she may be unable to initiate the resuscitation bundle interventions such as giving antibiotics and fluid boluses without a specific physician order. Standing order sets and established protocols have been utilized to facilitate early implementation of the bundle components (177).

In the United Kingdom poor uptake of EGDT in emergency departments (178) led to a change in focus of education to concentrate on care that could be delivered by staff without specialist skills and equipment in the first hour following diagnosis. This has been called the 'Sepsis Six' and includes six crucial interventions in sepsis resuscitation including starting high-flow oxygen, obtaining blood cultures, administering antibiotic therapy, starting intravenous fluid resuscitation, obtaining lab work including hemoglobin and lactate levels, and measuring hourly intake and output (144, 159, 179) (Table 4). Nurses play an important role in each of these interventions. High-flow oxygen therapy is not currently included in the SSC guidelines (4), but is universally recommended as being an important aspect of resuscitation of the critically ill and should be initiated by nurses (180, 181). Many nurses perform venipuncture and can rapidly obtain blood for cultures and venous lactate assessment, or can ensure equipment is available promptly if they are unable to perform venipuncture.

As a medical officer may not be always readily available, some hospitals have introduced measures to empower nurses to administer fluid challenges for hypotensive patients via standing orders or patient group directions to reduce delays in patients receiving fluid resuscitation (182). Protocol-directed care in the areas of fluid and vasopressor therapy is becoming more commonplace and has been shown to be safe (177, 183). In the UK and the USA, advanced practice nurses independently prescribe medications and can initiate orders for sepsis management, thus helping to facilitate early resuscitation measures (184, 185). Including nurses who are able to prescribe antibiotics, fluids and vasopressors on critical care outreach teams and rapid response system teams may also reduce delays in implementing the six-hour bundle.

EGDT incorporates blood transfusion for some patients and is recognized as a serious threat to patient safety; nurses play an important role in ensuring that patients who require transfusion receive blood in a safe manner guided by best evidence recommendations (186, 187).

6. We recommend that supplies of commonly used, ready-mixed antibiotics be available in all acute wards and departments (grade 1D).

Rationale. Usually it is nurses who administer antibiotics after a medical officer has prescribed them. Unfortunately antibiotic administration can be delayed up to six hours in some patients with bloodstream infection (188, 189). Reasons for such delays include lack of intravenous access and the prescribed antibiotic not being available (188). Measures such as having commonly used antibiotics and ready-mixed antibiotics available, as well as training nurses to cannulate should be considered (190).

7. We suggest the institution of tracking systems including the use of daily sepsis rounds in critical care areas (grade 2C).

   Rationale. Use of check sheets to monitor patients for signs of sepsis, or automated computer-based sepsis alert programs (191), can enhance identification of patients with sepsis.

8. We suggest ER nurses should liaise with medical colleagues and pre hospital staff to facilitate diagnosis and initial treatment of severe sepsis en route to hospital, and to promote 'alerting' of ERs that a patient with severe sepsis is expected (grade 2D).

   Rationale. This system is already common practice for patients with acute coronary syndrome and major trauma, and may help to identify those patients eligible for EGDT (192).

9. We suggest further research on technology to aid the detection of sepsis (grade 2D).

   Rationale. Technology that alerts nurses performing clinical observations and calculation of EWS such as Sepsis alert, Biosign, Vitalpac, etc. is currently being developed by many different biotechnology companies. Evidence of the benefit of this trend is yet to be confirmed.

IV. HEMODYNAMIC SUPPORT

Hemodynamic monitoring techniques continue to develop and hemodynamic therapies for severe sepsis are essentially supportive care, aimed at improving both macro and microcirculation. The current SSC guidelines (4) are primarily based on an evidence-based

practice guideline published in 2004 (193). Despite these excellent practice guidelines, questions remain in terms of the nursing care of septic patients with hemodynamic disturbances.

Complicating the care of patients with severe sepsis is the multimodal nature of the hemodynamics of sepsis. For example, in the early phase of sepsis, patients present with a relative hypovolemia that may be somewhat managed by restoring blood volume, i.e. restoring macrocirculation. However, as sepsis progresses, a disturbance that centers on the microcirculation is usually detected. At this point, the macrocirculation becomes hyperdynamic. Further treatment of the macrocirculation does little to address the problem of the microcirculation, e.g. microcirculatory clotting, cellular dysoxia, cell stunning (194). The treatment for this latter stage is unclear.

Two key areas are developing in the management of the hemodynamics of severe sepsis (194). One focus is on improving tissue oxygenation, both in the macro and microcirculation. Hence, tissue oxygenation end points, such as central venous oxygen saturation ($ScvO_2$), tissue oxygenation (StO_2) and lactate are taking on increased importance. The second focus of treatment centers on improving macrocirculation, moving toward measuring flow rather than pressure.

A. Improving tissue oxygenation

1. We suggest continuous measurement of tissue oxygenation vs. intermittent measurement (grade 2D).

Rationale. Central venous catheter use is associated with trends in mortality reduction as long as resuscitation bundle compliance exists (142). Continuous measurement of tissue oxygenation contributes to earlier recognition of changes in patient status and treatment

efficacy in relation to periodic central line sampling. While the cost of continuous $ScvO_2$ monitoring technology is higher than the cost of processing intermittent samples, several factors mitigate this disadvantage. These factors include reduced nursing time with continuous measurement, avoidance of clinician exposure to blood and improved ability to detect changes with continuous monitoring. Preliminary data suggest continuous $ScvO_2$ monitoring may be more cost-effective for institutions overall (195).

2. We suggest consideration of non-invasive monitoring of tissue oxygenation when central venous access is less desired or unavailable (grade 2D).

Rationale. Newer technology allows non-invasive monitoring of tissue (peripheral vascular) oxygenation, specifically near infrared spectroscopy. StO_2 is a continuous, transcutaneous measurement of tissue oxygenation via an electrode proximal to the thumb. Data suggest that StO_2 may be a better marker than gross hemodynamics at revealing information regarding the microcirculation. Donati *et al.* showed that StO_2 was responsive to identifying the impact of activated protein C, unlike gross measures of hemodynamics (196). Leone *et al.* indicated StO_2 values below 78% were correlated with lower survival rates (197). However, both of these studies were limited in both sample size and phase of sepsis utilized.

One of the main values of StO_2 is its non-invasive application. Situations involving severe sepsis in which central venous catheter insertion is less desirable or inappropriate should be considered for StO_2 monitoring. StO_2 measurement can be obtained via an easy-to-use, transcutaneous application. While not definitive at this point, some data suggest that below-normal values may identify sepsis earlier (198), predict development of organ dysfunction (199), and serve as an $ScvO_2$ alternative. However, outcome data using StO_2 is still lacking. While promising, the literature remains unclear on how best to use StO_2 in severe sepsis.

3. We suggest consideration of point-of-care lactate values as a quicker alternative to traditional serum lactate as appropriate (grade 2D).

Rationale. Degree of blood lactate elevation correlates directly with morbidity and mortality in severe sepsis (200, 201), and high correlation has also been shown between central laboratory and point-of-care values. Early detection of elevated lactate facilitates early recognition and treatment in addition to being a more accurate triage tool than vital signs (201). Howell *et al.* indicated lactate would predict 28-day outcome better than traditional monitoring parameters such as blood pressure (201). Elevated lactate, specifically type A lactic acidosis, is one of the few indicators of hypoxia. Lactate can be at dangerous levels while normal monitoring parameters like vital signs remain within normal limits. Using point-of-care lactate as the catalyst to implementation of a sepsis algorithm an 18% reduction in mortality and four-day reduction in length of stay was achieved (202, 203). We suggest that point-of-care lactate measurement be considered to accelerate the clinician's knowledge of the danger a patient faces if serum lactate laboratory results exceed turnaround times of approximately one hour (200, 201).

B. Improving macrocirculation

1. We suggest use of stroke volume or stroke volume variation (SVV) as a key resuscitation measure, independent of whether a central line can be placed (grade 2D).

Rationale. Improving blood flow is the key strategy during resuscitation. Secondary markers such as blood pressure, CVP, and PCWP have been used as surrogates for blood flow (204). However, these parameters have been shown to be inaccurate and slow to change.

More direct measures of blood flow, for example, stroke volume, offer more precise evaluation of the effectiveness of therapies such as fluids and inotropes (194). Although CVP is recommended as a resuscitation endpoint in the SSC Guidelines (4), clinicians must be aware of the limitations of treating right atrial pressure. Independent of sepsis, it is recognized that the usefulness of CVP is limited in clinical decisions regarding fluid management, due to inability to predict blood volume or preload in response to fluid resuscitation (205). Since CVP was in both the intervention group and the control group in the original early goal-directed therapy paper (158), one could argue that it was the added advantage of the $ScvO_2$ in the intervention group that was associated with improved outcomes, not improving CVP. The parameter that changes before $ScvO_2$ is stroke volume. In the perioperative setting, measuring stroke volume has clearly shown to improve patient outcome (183, 206-213). Stroke volume optimization (SVO) has been shown to be a much better metric of preload responsiveness compared to CVP, blood pressure and urine output. Even though data from the pulmonary artery catheter enables computation of a stroke volume estimate (CO/HR), more direct measurements of stroke volume are made possible by such innovations as the esophageal Doppler, non-invasive Doppler and pulse contour techniques. A growing body of literature supports the efficacy of SVO and SVV in sepsis (214, 215). While the theoretical principle is clear, outcome studies using stroke volume and SVV for patients with sepsis are ongoing.

2. We suggest insertion of a peripherally-inserted central catheter (PICC) in the event that subclavian central venous access cannot be obtained in patients with severe sepsis who meet the criteria for central line placement (grade 2D).

Rationale. Enhanced catheter flow rates, hemodynamic monitoring, and power injection capability are among some of the most recent developments in PICC use. Additional

advantages include the insertion capability of advanced practice nurses or trained registered nurses. CVP accuracy has been found to be similar when compared with a traditional central venous catheter (216). However, the ability of PICC to allow for $ScvO_2$ measurement is perhaps its most distinct advantage compared to peripheral lines.

V.   OTHER SUPPORTIVE NURSING CARE

All critically ill patients, including the patient with severe sepsis, should receive accepted standards of fundamental nursing care. While no evidence specifically links many components of fundamental nursing care to the outcomes of patients with severe sepsis, these aspects of care have been shown to improve outcomes in all critically ill patients and a brief review follows. Many have been shown to reduce the risk of infection and therefore may decrease the risk of sepsis.

A. Nutrition therapy

Critical illness is often associated with a hypermetabolic state and increased nutritional requirements. Malnutrition in the critically ill is not uncommon (217) and is associated with an increase in morbidity and mortality (218). Although the traditional emphasis of nutritional support has been on caloric intake this has evolved to nutrition as a therapy where the metabolic response to stress may be attenuated, cellular injury may be prevented, and the immune response may be favorably modulated (219). Extensive guidelines provide recommendations for nutrition therapy for the critically ill (217, 220-222) and have been shown to improve the provision of enteral nutrition (223). Consequently, incorporating such guidelines into the care of patients with severe sepsis is recommended.

1. We suggest early enteral nutrition (initiated within 24–48 hours of ICU admission) (grade

2A).

Rationale. Critical illness is associated with intestinal mucosal atrophy with loss of barrier function and potential microbial translocation. Early initiation of enteral nutrition may prevent intestinal mucosal atrophy. In addition, enteral nutrition can reduce the need for parenteral nutrition with substances that enhance bacterial growth (e.g. lipid emulsions) and as such reduce the risk of CR-BSI. Enteral nutrition, when compared to parenteral nutrition, has been shown to reduce the risk for infectious complications by 30–40% (224, 225). A similar reduction has also been found with early, compared to delayed enteral nutrition (226). Despite the benefits of enteral nutrition, caution should be exercised in patients not yet resuscitated from septic shock where gut perfusion may be compromised. Caution should also be taken in using immune-modulating enteral formulations (supplemented with agents, such as arginine, glutamine, nucleic acid, omega-3 fatty acids, and antioxidants) in patients with severe sepsis (219).

B. Eye care

1. We suggest daily assessment of the ability of the ICU patient to maintain eyelid closure (grade 2D).
2. We suggest at least weekly assessment of ICU patients for iatrogenic ophthalmologic complications and prompt referral for suspicion of these (grade 2D).
3. We recommend the maintenance of eyelid closure for intensive care patients (grade 1B).

Rationale. These recommendations apply to all critically ill patients, including those with severe sepsis. Many critically ill patients have altered levels of consciousness, which may

impact on the protective mechanisms of the eye resulting in an increased risk of injury such as corneal dehydration, abrasion, perforation and infection (227). The incidence of corneal abrasion varies widely but may affect up to 60% of intensive care patients (228-230). A variety of eye care methods have been described and tested with evidence that a range of methods reduce the incidence of corneal damage (227, 230-232), but there is insufficient evidence to recommend any single method as being superior. Daily assessment of the patient's ability to maintain eyelid closure should be undertaken. Nurses could also be trained to perform weekly ophthalmologic examinations, using fluorescein drops and a cobalt blue pen torch (231), as early detection of iatrogenic ophthalmologic complications will facilitate timely referral to ophthalmology specialists and potentially improve patient outcomes.

C. Pressure ulcer prevention and management

1. We recommend the implementation of a pressure ulcer prevention and treatment bundle including risk assessment, skin assessment, nutrition, repositioning and use of support surfaces (grade 1D).

Extensive recommendations for both the prevention and treatment of pressure ulcers have been developed and contain specific recommendations for the critically ill (233, 234).

Critically ill patients are susceptible to the development of pressure ulcers because of increased risks such as impaired circulation, use of inotropic drugs, decreased mobility, disturbed sensory perception, and underlying disease processes (235). The patient with severe sepsis often experiences significant hemodynamic compromise and therefore is particularly at risk for the development of pressure ulcers. Although variable, the incidence of pressure ulcers in the critically ill has been reported to be between 5.2–20% with a prevalence rate of 14.4% (236). While not all pressure ulcers can be avoided, strategies can be used to reduce

the incidence. Assessment of risk factors is one such strategy, but the predictive validity of risk assessment scales is problematic and there is little evidence for a valid risk assessment tool in the critically ill (237-239).

Special considerations related to prevention include: use of special support surfaces for patients who cannot be turned regularly; slow, gradual turns, while assessing patient tolerance for the procedure, may reduce the effect on hemodynamic and oxygenation compromise; more frequent small shifts in position will allow some reperfusion in patients who cannot tolerate major shifts in body position; lateral rotation therapy may be considered; patients receiving lateral rotation therapy will continue to require regular turns and skin assessment (233). Shear injury is a potential consequence of lateral rotation therapy. Bolster pads may prevent sacral shearing in these patients (233).

Special considerations related to management of pressure areas in severe sepsis patients include: positioning to minimize pressure on affected area; inspect pressure ulcer and surrounding area with every dressing change; if there is evidence of shear injury change lateral rotation support to a support system with improved pressure redistribution, shear reduction, microclimate control, and without rotation (234). Documentation of pressure ulcer staging and treatment is essential for continuity of care; however, two recent systematic reviews revealed that a multitude of pressure ulcer grading scales currently exist, with insufficient evidence to recommend a specific classification system (240, 241). The role of ICU mobilization of critically ill patients has also been advocated for the promotion of skin integrity as well as prevention of complications of bedrest (242).

VI.   PEDIATRICS

Sepsis remains an urgent issue among pediatric patients. Worldwide, it affects a large

pediatric population and is the most common cause of death in infants and children (243). Severe

sepsis accounts for more than 4,300 deaths annually (244).

Sepsis tends to peak at two primary times in the child's life and correspond to significant

times in the maturity of the immune system (245). The first peak is in the neonate with an

incidence of 4.3 per 1000 neonates. Sixty percent of cases occur in the first five days with an

overall mortality of approximately 20%. The second peak is at about two years of age.

In 2002, the International Pediatric Sepsis Consensus Conference participants modified the

adult SIRS criteria and associated definitions for children (246). SIRS is defined as the presence

of at least two of the following conditions, one of which must be abnormal temperature or

leukocyte count. The conditions include:

- core temperature of >38.5°C or <36°C

- tachycardia, defined as a mean heart rate >2 standard deviations (SD) above normal

  for age in the absence of external stimulus, chronic drugs, or painful stimuli; or

  otherwise unexplained persistent elevation over a 30-minute to 4-hour time period, or

  for children >1 year of age, bradycardia, defined as a mean heart rate <10th percentile

  for age in the absence of external vagal stimulus, β-blocker drugs, or congenital heart

  disease; or otherwise unexplained persistent depression over a 30-minute time period

- mean respiratory rate >2 SD above normal for age or mechanical ventilation for an

  acute process not related to underlying neuromuscular disease or general

  anesthesia

- leukocyte count elevated or depressed for age (not secondary to chemotherapy-

  induced leukopenia) or the presence of >10% immature neutrophils (246).

An infection is defined as a suspected or proven (by positive culture, tissue stain, or

polymerase chain reaction test) infection caused by any pathogen or a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g. white blood cells in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpural rash, or purpura fulminans) (246).

Sepsis is defined as SIRS in the presence of or as a result of a suspected or proven infection (246). Severe sepsis is defined as sepsis plus one of the following:

- cardiovascular organ dysfunction;

- acute respiratory distress syndrome;

- ≥2 other organ dysfunctions (respiratory, renal, neurologic, hematologic, hepatic) (246).

There are developmental differences in the hemodynamic response to sepsis in children when compared to adults. A decrease in cardiac output is associated with mortality in children with septic shock (247). Based on this developmental difference, reaching a therapeutic end point of a cardiac index (CI) of 3.3-6.0 L/min/m^2 may result in better survival (247). In addition, oxygen delivery is the major determinant of oxygen consumption in children as opposed to oxygen extraction, so the therapeutic endpoint of an oxygen consumption of greater than 200 mL/min/m2 may also be associated with a better outcome (247).

A. Fluid resuscitation

1. We suggest intravascular volume expansion is achieved with fluid boluses of 20 mL/kg of isotonic saline or colloids, as identified in the SSC guidelines (4) (grade 2C).

Rationale. As much as 200 mL/kg may be administered in the first hour of resuscitation, although the average is 40–60 mL/kg. Fluid replacement should be directed towards perfusion, central venous pressure, echocardiographic determination of end-diastolic volume, pulmonary capillary wedge pressure/end-diastolic volume and cardiac output (247).

B. Vasopressors/inotropes

1. We suggest vasopressors/inotropes are implemented if clinical signs of shock continue in spite of adequate volume replacement, as identified in the SSC guidelines (4) (grade 2C).

Rationale. An important point to remember about these medications is that since septic shock is a dynamic process, the medication used and the infusion dose may require adjustment over time, based on the need to maintain organ perfusion as well as the pharmacokinetics and the pharmacodynamics of the child's response to the drug. Perfusion and function of the liver and kidney are often changed in the child with severe sepsis, causing changes in the medication pharmacokinetics with higher concentrations observed. Therefore standard infusion doses may need to be adjusted.

For ongoing therapy, the use of inotropes, vasopressors, and vasodilators will differ. Dobutamine may be useful for pediatric patients with low cardiac output states (248). Vasopressin can increase MAP, SVR, and urine output in children with vasodilatory septic shock and lack of response to catecholamines. However, the safety and effectiveness of vasopressin in children with septic shock have not been well demonstrated (249). Occasionally, children alter their hemodynamic requirements from vasopressor to inotrope or vice versa (247). Table 6 presents a summary of the pharmacologic therapy used in the treatment of pediatric septic shock (250).

C. Steroids

1. We suggest hydrocortisone therapy may be generally reserved for the child with catecholamine-resistant shock and suspected or proven adrenal insufficiency, as identified in the SSC guidelines (4) (grade 2C).

Rationale. Hydrocortisone therapy may be lifesaving in the child with sepsis, but its use is generally reserved for the child with catecholamine-resistant shock and suspected or proven adrenal insufficiency. A recent study examined the issue of neuroendocrine dysfunction in children, including adrenal insufficiency and found a markedly higher incidence of multiple neurohormonal dysfunctions in children with sepsis (249). These findings suggest both that neuroendocrine deficiency is common in pediatric sepsis and that many neurohormonal responses may be affected (249). Generally, adrenal insufficiency in the case of catecholamine-resistant shock is assumed at a random total cortisol level of <18 µg/dL (496 nmol/L). Dose recommendations for treatment of shock are 50 mg/kg followed by the same dose as a 24-hour infusion (248, 251). Although not responsible for ordering steroids, it is essential that nurses work collaboratively to recognize the presence of refractory shock and initiate both timely measurement of cortisol levels and administration of hydrocortisone therapy where appropriate.

D. Sedation/analgesia

1. We suggest that critically ill pediatric patients receive goal-directed therapy for sedation and analgesia (grade 2D).

Rationale. Pain causes energy expenditure and increases oxygen demand. Nurses play a key role in addressing this issue. Sedation and analgesia are commonly used in pediatric patients with severe sepsis to relieve pain, support mechanical ventilation and to reduce oxygen

demand (252). The first step to initiating sedation and analgesia is to rule out physiological causes of agitation including hypoxemia, pain, hypercapnea and cerebral hypoperfusion. Addressing the child's comfort by providing analgesia and sedation and decreasing restlessness helps to preserve oxygen for use by major organs (253). There are no data supporting any specific medications; therefore, drugs and dosages are based on the child's response. Therapy should be goal-directed using a validated scale to determine the child's level of comfort (254). In addition, comfort measures including appropriate positioning, gentle touch, and managing the environment to decrease or eliminate noxious stimuli are essential.

E. Therapeutic end points

1. We recommend the use of therapeutic end points to guide interventions for the pediatric patient with severe sepsis and septic shock (grade 1D).

Rationale. Therapeutic end points have been established for both initial resuscitation and ongoing treatment. The goals for the first hour of resuscitation remain focused on airway, breathing, and circulation. The therapeutic endpoints include a capillary refill time <2 seconds, normal pulses, no differential between peripheral and central pulses, warm extremities, urine output >1 mL/kg/hr, normal mental status and normal glucose, ionized calcium and blood pressure for age (247).

Once the initial resuscitation has taken place, attention is required to verify the effects of hypovolemia and cardiac and vascular dysfunction. The goals of stabilization are: normal perfusion, a perfusion pressure normal for age, superior vena cava or mixed venous oxygen saturation of >70%; and CI >3.3 L/min/m^2 and <6.0 L/min/m^2 (255). The therapeutic endpoints are a capillary refill time <2 seconds, normal pulses with no difference between peripheral and central pulses, warm extremities, urine output >1 mL/kg/hr, normal mental status, CI >3.3

L/min/m^2 and <6.0 L/min/m^2 and superior vena cava or mixed venous oxygen saturation >70%. Cardiac index is augmented by increasing preload (247). Monitoring includes heart rate, oxygen saturation, blood pressure, temperature, urine output, central venous pressure, pulmonary artery pressure, cardiac output, glucose, and calcium (247).

SUMMARY AND FUTURE DIRECTIONS

This document provides a summary of the evidence that currently exists to underpin the nursing care of the patient with severe sepsis. Several limitations relate to the document including the time and resources available to develop these recommendations and the lack of evidence that exists in many areas of care. While a concerted effort was made to summarize the evidence from existing research and guidelines and reach consensus as to the level of support for nursing care considerations, much of the work was undertaken by small groups of 2–3 authors, with discussion and consensus by the entire author group then achieved through email discussion. Although this provided an opportunity for all authors to raise concerns regarding grading of recommendations, the depth of discussion was confined to that possible by email.

As outlined above, multiple areas of nursing care either have no evidence to inform practice, or the level of evidence is confined to expert opinion. Research to identify the most appropriate nursing interventions for severe sepsis patients is urgently required. Areas that are particularly needed include recognition of deterioration and diagnosis of sepsis, type and effect of early resuscitative measures, effective methods of hemodynamic assessment and support, type and effect of supportive care such as nutrition therapy, pressure ulcer prevention and management and mouth and eye care and application of these interventions to the pediatric severe sepsis patient. Identification of new evidence should inform the ongoing care of the severely septic patient and as such, this document represents an ongoing process.

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Table 1. Definition of Sepsis (4, 137)

Term	Definition
Sepsis (also referred to as Systemic Inflammation in Response to Infection)	Infection (documented or suspected) and some of the following: • General variables – fever (>38.3°C), hypothermia (<36°C), HR >90/min or >2 SD above normal value for age, tachypnea, altered mental state, significant edema or positive fluid balance, hyperglycemia • Inflammatory variables – leukocytosis (WBC >12,000μL^{-1}), leucopenia (WBC <4,000μL^{-1}), normal WBC with >10% immature forms, plasma C-reactive protein >2 SD above normal, plasma procalcitonin >2 SD above normal • Hemodynamic variables – arterial hypotension (SBP < 90 mmHg, MAP <70 mmHg or a SBP decrease >40 mmHg from baseline or in children* <2 SD below normal for their age), SvO^2>70%, CI>3.5 l/min/m^2 • Organ dysfunction variables – Arterial hypoxemia (P$_a$O$_2$/F$_i$O$_2$ <300), acute oliguria (urine output <0.5 ml/kg/hr), creatinine increase >0.5 mg/dL, coagulation abnormalities (INR >1.5 or aPTT >60 secs), ileus (absent bowel sounds), thrombocytopenia (platelet count <100,000μL^{-1}), hyperbilirubinemia (plasma total bilirubin >4 mg/dL or 70 mmol/L) • Tissue perfusion variables – hyperlactatemia (>1mmol/L), decreased capillary refill or mottling
Severe sepsis	Sepsis complicated by organ dysfunction
Septic shock	Acute circulatory failure characterized by persistent arterial hypotension despite adequate volume resuscitation and unexplained by other causes. Hypotension is defined as: - SBP <90 mmHg or in children* <2 SD below normal for their age - MAP <60 mmHg, or - reduction in SBP >40 mmHg from baseline

* see pediatric considerations section for further clarification of diagnosis in children
SD – standard deviations
WBC – while blood cells
SBP – systolic blood pressure
MAP – mean arterial pressure
SvO2 – saturation of oxygen in venous blood
CI – cardiac index

Table 2 GRADE criteria (4, 5)

Strength of Evidence	Quality of Evidence
1 – Strong	A – high, e.g. well conducted RCT
2 – Weak	B – Moderate, e.g. downgraded RCT or upgraded observational studies
	C – Low, e.g. well done observational studies
	D – Very low, e.g. case series or expert opinion
Factors influencing strength of evidence	
Methodological quality – poor planning and implementation increasing likelihood of bias is likely to decrease rating	
Importance of outcome – highly desirable outcomes are likely to increase rating	
Magnitude of treatment effect – RR > 2 with no plausible confounders is likely to increase rating	
Precision of estimate of treatment effect – highly precise results are likely to increase rating	
Inconsistency of results – multiple studies with inconsistent results is likely to decrease rating	
Directness of evidence – indirect evidence (e.g. different populations) is likely to decrease rating	
Risks associated with therapy – significant known risks or burden of therapy are likely to decrease rating	
Costs – significant costs associated with therapy are likely to decrease rating	

RCT – randomized control trial; RR – relative risk

Table 3. Clinical Signs of Sepsis

Systemic Inflammatory Response Syndrome: two or more of the following conditions can indicate sepsis:
Temperature >38°C or <36°C Heart rate >90 beats/min Respiratory rate >20 breaths/min or $PaCO_2$ <32 mm Hg (<4.3kPa) WBC >12,000 cells/mm^3, <4,000 cells/mm^3, or >10% immature (band) forms
Additional signs and symptoms:
Chills Hypotension Decreased skin perfusion Decreased urine output Significant edema or positive fluid balance (> 20 mL/kg over 24 hours) Decreased capillary refill or mottling Hyperglycemia (plasma glucose >120 mg/dL) in the absence of diabetes Unexplained change in mental status

Adapted from Levy *et al.* (137)

Table 4: The Sepsis Six Interventions

- Give high flow oxygen
- Take blood cultures
- Give IV antibiotics
- Start IV fluid resuscitation
- Check hemoglobin and lactate
- Measure accurate hourly urine output

Adapted from Surviving Sepsis Campaign (144, 159)

Table 5: Strategies for Integrating the Surviving Sepsis Guidelines in Nursing Practice

Strategies to promote the integration of the Surviving Sepsis Campaign Guidelines in clinical practice
1. Create a multidisciplinary team and map out a timeline for implementing the strategies. 2. Enlist the participation of nurse champions in leading the initiatives. Many of the recommendations involve aspects of nursing care, and nurses can play an important role in promoting implementation of the guidelines. 3. Integrate the use of the Surviving Sepsis Campaign Guidelines as a performance improvement initiative for the ICU and non critical care areas. 4. Target processes to ensure successful adoption of the guidelines. 5. Include discussion of the guidelines in venues such as daily rounds, grand rounds, and critical care conference. Consider the use of a daily goal sheet to ensure that the components of the Surviving Sepsis Campaign Guidelines, including the sepsis bundles, are addressed on a ongoing basis. 6. Promote early identification of sepsis. Early identification of sepsis can help to promote prompt treatment.

Adapted from Kleinpell, 2005 (138)

Table 6. Pharmacologic Therapies Used in Septic Shock (250)

Drug	Site of action	Dose (μg/kg/min)	Primary Effect [*]	Secondary Effect
Dopamine	Dopaminergic Dopaminergic and β_1 α	2-5 2-10 10-20	Increase renal perfusion Inotropy Chronotropy Increase renal perfusion Vasoconstriction	Dysrhythmia
Norepinephrine	$\alpha>\beta$	2-10	Vasoconstriction Inotropy	$>MVO_2$ Dysrhythmias <Renal blood flow
Epinephrine	α and β	0.05-1.5	Vasoconstriction Inotropy Chronotropy	$>MVO_2$ Dysrhythmias <Renal blood flow
Dobutamine	β_1	5-20	Inotropy	Tachycardia Dysrhythmia Vasodilatation Hypotension
Sodium nitroprusside	NA	0.5-10 (light sensitive)	Vasodilatation (balanced)	<PVR >V/Q mismatch Cyanide toxicity
Nitroglycerin	NA	0.2-20	Vasodilatation (venous)	<PVR >ICP
Amrinone	NA	5-10 (load with up to 3 mg/kg over 20 min)	Inotropy Vasodilatation	Dysrhythmias <PVR Thrombocytopenia
Milrinone	NA	0.75 – 1.0 (load with 75 μg/kg over 20 min		

[*]Difficult to predict the dose-response effect. Management requires individual titration at the bedside.
MVO_2, Myocardial oxygen consumption; PVR, pulmonary vascular resistance; V/Q, ventilation/perfusion; ICP, intracranial pressure.