Sepsis and Septic Shock

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Sepsis and septic shock are both potentially life-threatening oncologic emergencies. Septic shock is one stage in a clinical continuum of infection and systemic inflammatory mechanisms progressing from sepsis to severe sepsis and finally to septic shock. These stages make up a syndrome referred to as systemic inflammatory response syndrome (SIRS) (Muckart & Bhagwanjee, 1997). Septic shock is manifested by hemodynamic instability and alterations in cellular metabolism caused by sepsis. Septic shock is characterized by fever, chills, tachycardia, tachypnea, mental status changes, and hypotension/hypoperfusion that persist despite aggressive fluid challenge. This disorder occurs when the body fails to initiate an adequate immune response to bacterial, viral, or fungal infection. Management of this syndrome requires prompt assessment and treatment. Early detection and intervention related to sepsis and septic shock increase patients’ chances of a positive outcome. Patients with cancer who are granulocytopenic are at risk for the development of sepsis and septic shock, particularly patients with hematologic malignancies. Nursing management of sepsis and septic shock requires knowledge of the risk factors for development of this syndrome, measures to prevent infection and sepsis, and knowledge of the many various medications that are used to treat sepsis and septic shock. Early hemodynamic assessment of patients suspected of sepsis is critical for definitive recognition and treatment to provide maximal benefit in terms of a positive outcome.

Pathophysiology

Infection

Infection occurs when an organism or microbe enters the bloodstream and is able to colonize and reproduce within a host. Disease results if the infectious organism, such as gram-negative bacteria, causes injury, pathologic changes, or organ dysfunction in the host (see Figure 6-1). Risk factors include granulocytopenia, malignancy-related immunosuppression, age, loss of skin or mucosal injury, long intensive care stays, central vascular access devices, indwelling devices, diabetes, and organ-related diseases.

Sepsis

In the presence of infection, the body mounts an inflammatory response. If a localized inflammatory response is insufficient to manage the infection, sepsis occurs. Sepsis is defined as a systemic response to infection. Substances such as endotoxins (released from gram-negative bacteria) and exotoxins (released from gram-positive bacteria) are released from the cell walls of dead bacteria after they have been phagocytized by neutrophils (Gobel, 2005). These toxins activate the coagulation cascade and the complement systems (Peterson, 1998). The activation of the complement system causes a release of vasoactive mediators such as kinins, histamine, interleukins, and tumor necrosis factor-alpha (TNF-α), all of which lead to vasodilation and potentially to capillary leak syndrome. These vasoactive mediators further activate the coagulation cascade, which leads to the aggregation of platelets and formation of fibrin, resulting in the coagulopathies seen in sepsis. Initially, increases in inflammatory mediators may characterize sepsis, but as sepsis persists, a shift toward an anti-inflammatory immunosuppressive state occurs (Oberholzer, Oberholzer, & Moldawer, 2001). Patients with sepsis who are immunosuppressed have a loss of delayed hypersensitivity, an inability to clear infection, and a predisposition to nosocomial infections (Oberholzer et al.).

A high cardiac output with widespread vasodilation and normal or slightly elevated blood pressure usually characterize the early stage of sepsis. Vasodilation increases if sepsis continues without adequate treatment, and a capillary leak may develop, resulting in significant edema. Without adequate treatment, the blood pressure falls, cardiac function becomes further depressed, and severe sepsis occurs. In severe sepsis, decreased blood flow occurs because of the continuation of fibrin formation and aggregation.
of platelets. This decreased blood flow leads to decreased tissue perfusion and a state of organ dysfunction.

**Septic Shock**

Septic shock represents an uncontrolled inflammatory response to bacterial toxins (Hotchkiss & Karl, 2003). Septic shock is associated with persistent systemic hypotension and profound organ hypoperfusion, accompanied by abnormal shunting of blood flow in the microcirculation that compromises delivery of nutrients to the tissues. Septic shock is the most common cause of circulatory collapse in patients with cancer (Bogolioubov, Keeffe, & Groeger, 2001). In septic shock, further release of proinflammatory cytokines such as TNF, interleukin (IL)-1, IL-8, and interferon-gamma occurs because of the presence of bacterial toxins in the bloodstream. Higher levels of these bloodstream toxins generally correlate with increased severity of septic shock. TNF and IL-1 are potent vasodilators and pyrogens. IL-8 may play a role in perpetuating tissue inflammation (Dinarello, 1997). There also is a release of counter-regulatory molecules such as soluble TNF receptor, IL-1 receptor antagonist, IL-4, IL-10, IL-13, and transforming growth factor-beta (TGF-β) (Bogolioubov et al.). IL-4, IL-10, IL-13, and TGF-β provide anti-inflammatory effects by suppressing gene function and synthesis of IL-1 and TNF. These cytokines interact extensively with neutrophils and endothelial cells. This process of extensive cytokine release further promotes cell-leukocyte adhesion, release of proteases and arachidonate metabolites, and activation of the clotting cascade. As septic shock continues, further coagulopathies, fibrinolysis, and disseminated intravascular coagulation may occur (Nimah & Brilli, 2003).

**Clinical Manifestations**

Septic shock generally progresses from the hyperdynamic phase to the hypodynamic phase of shock. The hyperdynamic phase of septic shock occurs after initial fluid resuscitation for a septic event. During this phase, the cardiac output usually is elevated, but cardiac performance is depressed. Further vasodilation within the vascular system occurs, and hypotension and tachycardia result. Without adequate intervention, the hypodynamic phase of septic shock follows, in which the mediators of sepsis (e.g., endotoxins, exotoxins, related cytokines) increase vascular permeability, and fluid leaks from the vascular space into the interstitial space (Stoll, 2001). Venous pooling and maldistribution of blood volume are present, thereby decreasing the circulating blood volume. The decreased circulating blood volume results in tissue hypoxia and metabolic acidosis. Organ dysfunction and multisystem organ failure may be the sequelae of septic shock.

Vital signs provide invaluable information about the potential for the presence of septic shock. Vital sign changes that indicate septic shock include increased or decreased temperature (>100.4°F [38°C] or <96.4°F [36°C]), tachycardia, tachypnea, and persistent hypotension that do not respond to fluid resuscitation. Central nervous system alterations that may reflect septic shock include significant confusion and disorientation progressing to obtundation and coma. These effects arise from cerebral hypoxia, cerebral edema, and metabolic abnormalities (Moore, 2005). Cardiovascular manifestations of
septic shock include tachycardia, cyanosis, hypovolemia, dysrhythmias, widened pulse pressure, persistent hypotension that is unresponsive to fluid resuscitation, and a decreased ejection fraction (Dellinger et al., 2004). Septic shock generally is defined as being present when the systolic blood pressure is less than 90 mm Hg, being unresponsive to fluid resuscitation, and requiring vasoactive drugs (Bone et al., 1992).

One of the earliest changes seen in the development of septic shock is tachypnea with associated dyspnea, which may result in respiratory alkalosis (Martin & Bernard, 2001). Other pulmonary manifestations of septic shock include bilateral rales, severe hypoxemia, pulmonary edema and hypertension, and acute respiratory distress syndrome. Respiratory failure occurs if septic shock is not immediately and aggressively managed. Alterations of the gastrointestinal system that may be seen with septic shock include decreased gastric motility, ileus, and gastrointestinal bleeding. The effects of septic shock on the renal system most often include transient oliguria related to the hypotension of sepsis, but anuria also may develop, and the blood urea nitrogen and creatinine levels may increase. Acute renal failure also may ensue if septic shock is not reversed. Skin changes caused by septic shock are related to a lack of tissue oxygenation and may include cold and clammy skin, cyanosis, and acrocyanosis (persistent, painless, symmetric cyanosis of the hands and, less commonly, of the feet). Jaundice of the skin or sclera may develop and reflect hyperbilirubinemia and elevation of serum liver transaminases (Wheeler & Bernard, 1999). See Table 6-4 for an overview of the clinical manifestations of septic shock.

### Treatment Modalities

Several objectives exist regarding the management of severe sepsis in patients with cancer. These include initial resuscitation with early goal-directed therapy (EGDT), cardiovascular support, pulmonary support, antibiotics, and antisepsis interventions, including administering activated protein C, replacement dose steroids, and investigational therapies.

### Initial Resuscitation

Once healthcare professionals have made a diagnosis of severe sepsis/SIRS based on the accepted criteria, it is extremely important to immediately initiate intensive therapy. They should not delay therapy pending transfer or admission to the intensive care unit (ICU), although a move to a monitored environment should be done in a timely manner to provide appropriate monitoring and resuscitation support (Dellinger et al., 2004). A central venous catheter is placed if one is not already present, and an arterial catheter also may be beneficial upon admission to the ICU (Connors et al., 1996). Once patients are in the ICU, supportive monitoring of blood pressure, mean arterial pressure (MAP), central venous pressure (CVP), venous oxygen saturation (SvO₂), arterial saturation (SpO₂, O₂ saturation), and arterial blood gases is imperative (Rivers et al., 2001).

The treatment team should accomplish initial resuscitation within the first six hours after the diagnosis of severe sepsis (see Figure 6-2). The goals of initial resuscitation include maintaining a CVP of 8–12 mm Hg, MAP greater than or equal to 65 mm Hg, urine output greater than or equal to 0.5 ml/kg/hour, and central venous or mixed venous oxygen saturation greater than or equal to 70%. Serum lactate levels also are useful to quantify tissue hypoxia. If supplemental oxygen cannot maintain adequate oxygenation, patients should receive mechanical ventilation prior to

### Table 6-4. Clinical Manifestations of Septic Shock

<table>
<thead>
<tr>
<th>ORGAN SYSTEM</th>
<th>CLINICAL SIGNS AND SYMPTOMS</th>
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<tbody>
<tr>
<td>Vital signs</td>
<td>Temperature &gt; 100.4°F (38°C) or &lt; 96.4°F (36°C)</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Significant confusion and disorientation, Obtundation and coma</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Cyanosis, Tachycardia, Hypovolemia, Dysrhythmias, Widened pulse pressure, Cardiac output normal or elevated in the hyperdynamic phase of septic shock, Decreased systemic vascular resistance in the hyperdynamic phase of septic shock, Cardiac output depressed in the hypodynamic phase of septic shock, Persistent hypotension not responsive to fluid resuscitation, Increased systemic vascular resistance</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Tachypnea with associated dyspnea, resulting in respiratory alkalosis, Bilateral rales, Severe hypoxemia, Pulmonary edema and hypertension, Acute respiratory distress syndrome, Respiratory failure</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Decreased gastric motility, Ileus, Gastrointestinal bleeding</td>
</tr>
<tr>
<td>Renal</td>
<td>Transient oliguria, Anuria, Increased blood urea nitrogen and creatinine levels, Acute renal failure</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Jaundice of skin or sclera, Hyperbilirubinemia, Elevation of serum liver transaminases</td>
</tr>
<tr>
<td>Skin</td>
<td>Cyanosis, Acrocyanosis, Cold, clammy skin</td>
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their PaO₂ level falling below 60 mm Hg (Dellinger et al., 2004).

**Early Goal-Directed Therapy**

The key to survival in the management of septic patients with cancer is prompt intervention at the first sign of sepsis. The sooner that therapy is initiated for these acutely ill patients, the greater the potential that stabilization can occur and the progression to severe sepsis and SIRS is prevented. The goal of EGDT (see Table 6-7) is to identify and maximize treatment to minimize sepsis-induced hypoxia. In a study investigating the potential benefit of EGDT, 263 severely septic patients admitted to a hospital emergency room were randomized into the EGDT group or to the standard therapy (control) group (Rivers et al., 2001). The EGDT group spent a mandatory six hours in the emergency department completing an EGDT protocol, whereas members of the control group were admitted to the ICU as beds became available. EGDT consisted of the administration of IV fluids, vasopressors, blood transfusions based on venous oxygen saturation (ScvO₂), and inotropic agents if the ScvO₂ did not respond after transfusion. The end results of this study showed lower in-hospital mortality, decreased length of stay, higher ScvO₂, lower lactate levels, lower base deficit, and higher pH for the EGDT group compared to the standard therapy group. The results in the EGDT group may be attributed to early identification of high-risk patients, earlier resuscitation, and prompt management of hypovolemia, myocardial dysfunction, and disturbed vasoregulation and maintenance of organ perfusion (Rivers et al.).

### Table 6-7. Early Goal-Directed Therapy

<table>
<thead>
<tr>
<th>THERAPY</th>
<th>IMPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic initiation (within one hour of fever onset)</td>
<td>Directed to most likely microbes</td>
</tr>
<tr>
<td>Central venous access as quickly as possible</td>
<td>Continuous SaO₂ monitoring</td>
</tr>
<tr>
<td><strong>Step 1</strong>: What is central venous pressure?</td>
<td></td>
</tr>
<tr>
<td>&lt; 8–12 mm Hg requires 500 cc crystalloid bolus. Continue boluses until &gt; 8–12 mm Hg.</td>
<td></td>
</tr>
<tr>
<td><strong>Step 2</strong>: What is the mean arterial pressure?</td>
<td></td>
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<tr>
<td>&lt; 65 mm Hg requires increased vasopressor use (e.g., norepinephrine). Titrate until &gt; 65 mm Hg.</td>
<td></td>
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<tr>
<td><strong>Step 3</strong>: What is the central venous O₂ saturation?</td>
<td></td>
</tr>
<tr>
<td>&lt; 70%—maintain with oxygen therapy. Initiate mechanical ventilation if PaO₂ falls below 60 mm Hg.</td>
<td></td>
</tr>
<tr>
<td>What is the HCT?</td>
<td></td>
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<tr>
<td>&lt; 30% HCT requires transfusion until &gt; 30% HCT. &gt; 30% HCT—can add and titrate dobutamine.</td>
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**Nursing Management**

### Prevention and Early Detection

Early detection and intervention are critical in preventing the progression of infection to septic shock. Providing meticulous nursing care to immunosuppressed patients is of utmost importance because granulocytopenia is the single most important risk factor in the development of sepsis in patients with cancer (Sachdeva, 2002; Safdar & Armstrong, 2001). Nurses must be able to identify and report the early signs and symptoms of infection and sepsis to the primary care provider immediately (Reigle & Dienger, 2003).

### Asepsis and Antisepsis

Patients with cancer are inherently immunocompromised and are at much higher risk for infection because of their treatment and underlying disease. Therefore, the focus for prevention of sepsis involves control and prevention of infection in these individuals. Proper hand-hygiene procedures according to institutional policies are the most important infection control strategy (Eggimann et al., 2000). Nurses should be diligent in advocating for an aseptic environment for all patients. The nursing staff should implement strict policies to prevent infectious transmission to patients via visitors, medical professionals, and ancillary staff. Nurses should wear gloves anytime there is risk of contact with blood or body fluids. When working with patients, they should remove and replace gloves when moving from a contaminated body part to a clean body part. Gloves are removed in the patient care room and discarded between patients. Artificial nails are discouraged, and natural nails should be kept less than one-fourth inch in length (Boyce & Pittet, 2002).

### Patient and Caregiver Education

Because granulocytopenia is the single most important risk factor in the development of sepsis in patients with cancer (Sachdeva, 2002), it is critical to educate patients and caregivers on the importance of preventing infection during periods of immunocompromise. Nurses should encourage patients to turn, cough, and deep breathe to help prevent respiratory compromise and to ambulate to decrease coagulopathy risk. Personal hygiene is stressed to decrease the colonization of bacteria on the skin. Caregivers also need to understand the importance of good hand hygiene during periods of immunocompromise of patients. Although the nutritional requirements for patients...
with sepsis increase, patients may not have a good appetite or may be too tired to eat. Nurses are in a key position to emphasize the importance of nutrition and to offer high-calorie/high-protein supplements. If food and fluids do not meet patients’ nutritional needs, patients may require enteral or parenteral nutrition. It is important to educate patients and caregivers that this type of nutrition is intended as a short-term solution to provide much-needed calories, proteins, and electrolytes.

As patients become critically ill, providing patients and their caregivers with information about the potential transfer to an ICU setting, the need for additional medications, such as antibiotics and vasopressors, and the possibility of mechanical ventilation is an important nursing task. Patients and caregivers also should be informed of the various consultants they may come into contact with during the course of managing sepsis and septic shock, such as infectious disease specialists, cardiologists, pulmonologists, and intensive care specialists.

Conclusion

Sepsis and septic shock are life-threatening oncologic emergencies that can occur very quickly after the onset of infection. Because of the rapidity and severity of these conditions, early detection and intervention are essential for better patient outcomes. A number of malignancies can modify immunity in patients with cancer and cause granulocytopenia, the single most important risk factor in the development of sepsis. Oncology nurses play a pivotal role in promptly recognizing and reporting aberrant vital signs or other signs of infection so that appropriate therapies can be immediately initiated.

Although much is understood about the development and treatment of sepsis and septic shock, more investigation is needed to provide new insights into this complex syndrome and to develop more effective targeted therapies. Oncology nurses are in a key position to conduct research on optimal evidence-based nursing care of immunosuppressed patients with cancer.

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References