



clinical concepts of infusion therapy

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Sepsis

Sepsis is an inflammatory immune response of the body to an overwhelming infection. The very young and the elderly are most susceptible to sepsis, which kills more Americans each year than breast cancer, prostate cancer, and acquired immunodeficiency syndrome combined.¹ Survivors of sepsis often experience life-altering sequelae. This article discusses stages of sepsis and the importance of early identification, and provides an overview of the *Surviving Sepsis Campaign: International Guidelines for the Management of Severe Sepsis and Septic Shock: 2012*.

The history of sepsis is extensive, going back more than 4,000 years. Chinese mythology speaks of one of the earliest recorded treatments of fever—a hallmark of sepsis—with herbs. The Greek physician Hippocrates described sepsis as “the dangerous, odiferous, biological decay that could occur in the body.”² The word *sepsis* itself originates from the Greek *sepo*, which literally means “I rot.”² Through the centuries, stories of toxic air and “invisible creatures that emitted putrid fumes”² fueled theories of the spontaneous generation of sepsis. The golden age of germ theory began in the 19th century, bolstered by advances in the development and design of the microscope. Physicians including Louis Pasteur, Joseph Lister, Robert Koch, and Ignaz Semmelweiss deduced that diseases leading to sepsis occurred as the result of direct contact with the source of the disease, indirect contact through contaminated objects, or from an airborne source. Observations and experiments over the next several centuries led to the introduction of hand-washing as a means of reducing infections,

the development of antibiotics, the principles of aseptic technique, and instrument sterilization.²

Only in the past 50 years has an accurate understanding of the complex pathophysiology of sepsis occurred. The discovery of proteins in the body that activate and augment the functions of other proteins, endogenous mediators, led to the realization that sepsis is the overreaction of the body to a microorganism, and not the microorganism’s “invasion... into the bloodstream which causes signs of illness.”³ When pathogens enter the body, an inflammatory response begins that intends to contain and destroy the pathogens. Cytokines and other chemical messengers send signals to blood vessels in the area of the infection and activate the immune system and the immune cascade. The blood vessels dilate, increasing vessel permeability and the amount of blood in the area. Blood flow also slows, enabling the passage of phagocytes through openings in the vessel walls and out to the infection. At the same time, blood clots in microvessels surrounding the site prevent the infection from entering the bloodstream. The hallmarks of a local infection—redness, swelling, tenderness, and warmth—are the result of the inflammatory response.^{3,4}

The chemicals that begin the local inflammatory response and immune cascade can trigger the same inflammatory response throughout the entire body, regardless of the location of an infection. This response has been associated with noninfectious conditions, such as autoimmune disorders, myocardial infarction, surgical procedures, or reactions to medications or blood transfusions.

In the absence of an infection, this activation of the inflammatory cascade is known as systemic inflammatory response syndrome (SIRS). Any two of the following four clinical findings confirm SIRS:

- Temperature above 100.4°F (38°C) or below 96.8°F (36°C)
- Heart rate above 90 beats per minute
- Respiratory rate above 20 breaths per minute, or an arterial carbon tension lower than 32 mm Hg
- White blood cell (WBC) count above 12,000/μL or below 4,000/μL or 10% bands (immature WBCs)

The presence of SIRS, in addition to an infection, is the definition of sepsis. A patient can have a severe infection and not have sepsis, but a patient with sepsis will always have SIRS.^{3,5-7}

Early recognition and treatment of sepsis is essential in the prevention of the tissue and organ damage associated with severe sepsis and septic shock, but identifying sepsis early is not always straightforward. Viral infections, which resolve on their own, present many of the same symptoms seen with sepsis. Sepsis often is not suspected until patients display symptoms of organ dysfunction signaling the next stage, called severe sepsis. Changes in mental status, decreased urine output, difficulty breathing, or changes in blood pressure are indications that tissue perfusion is inadequate and vital organs are not receiving oxygen. Patients with severe sepsis require supportive therapies, including mechanical ventilation and/or cardiovascular intervention. The final stage, septic shock, is present when blood pressure cannot be maintained, despite aggressive fluid resuscitation. Mortality rates associated with septic shock are as high as 30%.^{3,8,9}

Treatment of sepsis, severe sepsis, and septic shock is based on a set of evidence-based guidelines and recommendations developed by an international consensus committee. The *Surviving Sepsis* guidelines, last updated in 2012, provide performance improvement bundles, as well as definitions and therapeutic targets and thresholds, with the goal of developing “universal recommendations that direct global medical teams to use evidence-based practice interventions to reduce sepsis-related mortality.”¹⁰ The guidelines provide time frames and goals relating to initial therapy and supportive recommendations that include hemodynamic therapies, ventilator strategies, deep vein thrombosis prevention, glycemic control, nutrition support, and renal replacement therapy. Specific considerations for pediatric patients also are provided.¹¹

Patients who survive sepsis often face long-term physical and mental challenges as the result of permanent damage to tissues and organs. Individuals at increased risk of postsepsis syndrome include those with prior medical conditions, the elderly, and patients who received treatment in the intensive care unit. Reported symptoms include insomnia, nightmares, hallucinations, impaired cognitive function, severe muscle and joint pain, chronic fatigue, and panic attacks. Patients relate feelings of despair, lack of confidence, and diminished self-worth.⁴

Sepsis is a complex syndrome resulting from the systemic inflammatory response of the body to an infection. All of us are exposed to infectious microorganisms at any given time and

can develop an infection anywhere in the body. Pathogens enter the body in various ways: through the respiratory tract, the digestive tract, or a break in the integrity of the skin. Medical equipment, such as urinary catheters, endotracheal tubes, and central vascular access devices, also provide a portal of entry for pathogens. Preventing an infection is key to the prevention of sepsis. Once sepsis occurs, it can rapidly progress to septic shock and death. Patients at risk include the very young, the very old, those with compromised immune systems, and individuals with additional medical conditions. Sepsis may affect survivors for years following recovery. Guidelines aimed at reducing sepsis-related mortality provide evidence-based therapy and support recommendations.

Sepsis Alliance is an organization dedicated to raising awareness of sepsis among health care professionals and the public. It has designated September Sepsis Awareness Month and September 13 World Sepsis Day. More information about sepsis and Sepsis Alliance is available at www.sepsisalliance.org.

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