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Recognizing Sepsis in the Adult Patient

Rapid response is essential, and non-ICU nurses are the first line of defense.

Overview: Patients in every health care setting are at risk for systemic inflammatory response syndrome, sepsis, severe sepsis, and even septic shock. The increasing incidence of sepsis, especially among older adults, its high mortality rate, and its subtle and rapid progression make prompt recognition and treatment imperative. Even though severe sepsis requires treatment in the ICU, the assessment of sepsis isn't solely the domain of the physician, critical care nurse, or ED nurse. Improving outcomes in patients with sepsis depends on every nurse involved in their care. The case study presented here is of a nursing home resident with unrecognized sepsis that progresses to severe sepsis—at which point not even seven days' treatment in the ICU could halt the progression to multiple organ failure.

In November of last year, a 32-year-old mother of three in Brooklyn, New York, presented to a hospital ED with kidney pain. She was diagnosed with a kidney stone and sent home with painkillers. The next day, still in pain, she returned to the hospital and was diagnosed with sepsis, but by then she'd lost blood flow to her hands and feet and nothing could be done to prevent quadruple amputation and the loss of sight in one eye.[1] Sepsis moves fast and is often diagnosed too late. Analyzing 1995 hospital discharge data from 847 U.S. hospitals, Angus and colleagues found an incidence of more than 750,000 yearly cases of severe sepsis, with a mortality rate of nearly 30%.[2] A number of smaller studies have found much higher mortality rates, particularly from severe sepsis occurring outside the ICU, and according to a more recent longitudinal study by Dombrovskiy and colleagues, hospitalization rates for severe sepsis almost doubled between 1993 and 2003, "over five times faster than had been previously predicted," while "the proportion of patients with severe sepsis among all patients with sepsis grew by 70%."[3]

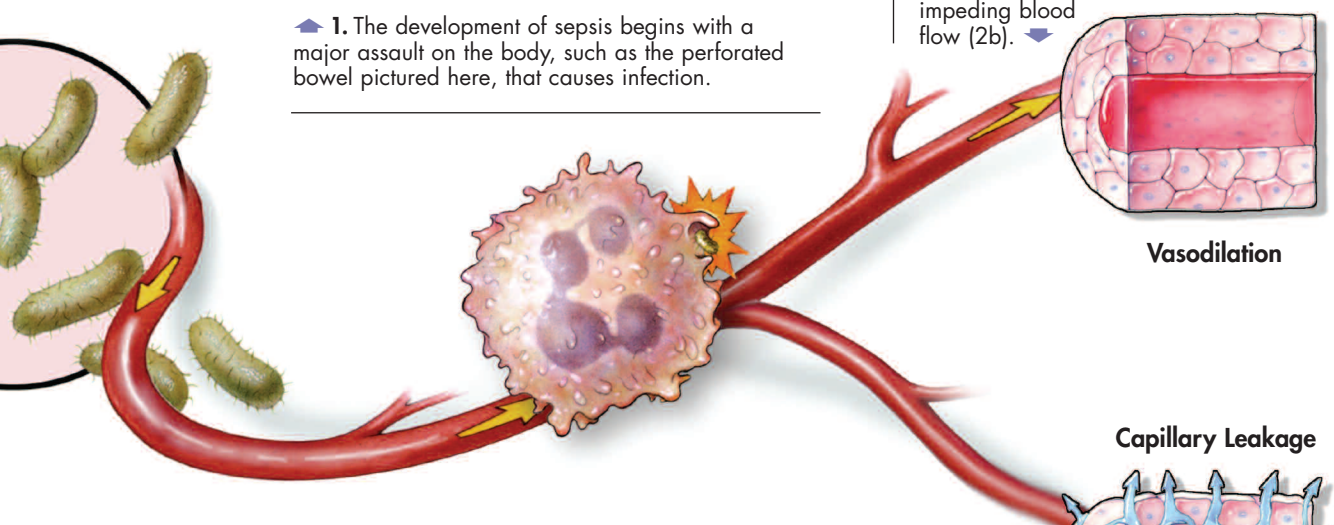
More to come. Given the aging of the population and greater use of invasive medical technology, it's no surprise that Martin and colleagues found that the U.S. in-hospital incidence of sepsis increased yearly by almost 9% between 1979 and 2000, along with the number of deaths resulting from it.[4] (A significant decrease in the mortality rate from sepsis between 1995 and 2000 was more than offset by the increased incidence of sepsis. The study did not examine the incidence of *severe* sepsis.) Sepsis may be underreported because clinicians don't always recognize it and because the presence of comorbidities may cause erroneous cause-of-death reporting. For example, the cause of death in a patient who dies from severe sepsis as a result of pneumonia may be documented as pneumonia rather than severe sepsis.

Early recognition and rapid response are essential in the successful treatment of sepsis, which can progress rapidly to severe sepsis and then to septic shock. Whereas severe sepsis requires management in a critical care area, its identification must often be made outside the ICU. The close proximity of nurses to patients from the time of admis-

Figure 1. From Infection to Septic Shock

1. The development of sepsis begins with a major assault on the body, such as the perforated bowel pictured here, that causes infection.

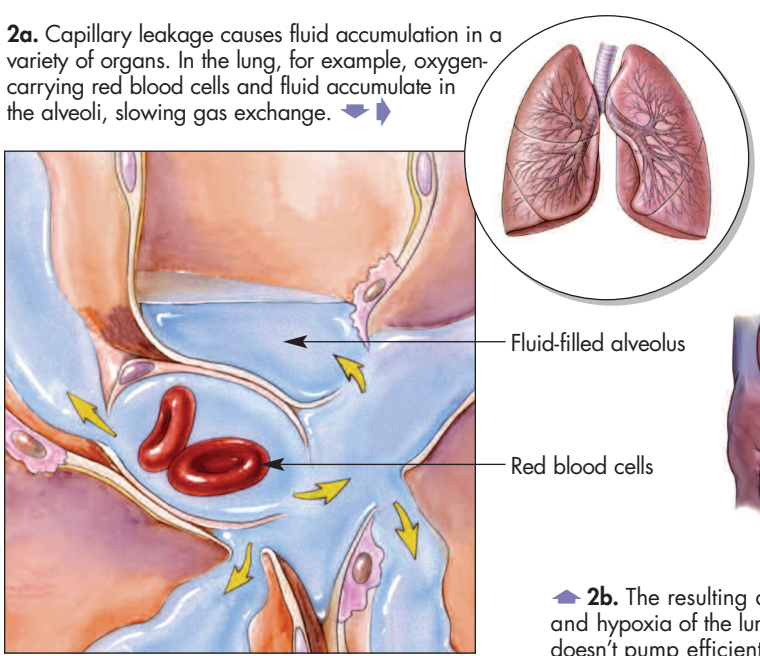
2. Bacteria enter the bloodstream, where endotoxins on the bacterial cell wall stimulate an immune response, which involves the release of pro-inflammatory cytokines such as interleukin-1. Such chemical mediators cause vasodilation and erosion of blood vessel endothelium, and capillary leakage begins (2a). Damage in the blood vessels triggers the coagulation cascade; microthrombi form, impeding blood flow (2b).

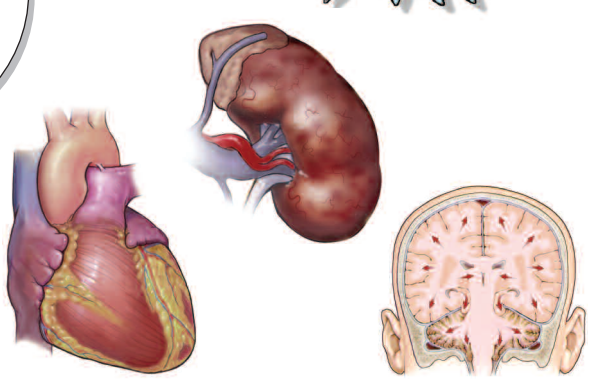


Vasodilation

Capillary Leakage

2a. Capillary leakage causes fluid accumulation in a variety of organs. In the lung, for example, oxygen-carrying red blood cells and fluid accumulate in the alveoli, slowing gas exchange.





2b. The resulting decrease in tissue perfusion leads to tissue ischemia and hypoxia of the lungs, the heart, the kidneys, and the brain. The heart doesn't pump efficiently, causing hypotension; brain swelling causes increased intracranial pressure, influencing all parts of the brain, including those governing breathing and heart rate; renal and respiratory failure may also occur. Death can result rapidly. Illustrations © 2008, MediVisuals Inc.

Table 1. Signs and Symptoms of Organ Failure

Cardiovascular
- systolic blood pressure < 90 mmHg
- mean arterial pressure < 65 mmHg
- a drop from baseline pressure > 40 mmHg

Hematologic
- platelets < $100 \times 10^3/mm^3$
- platelets decreased by 50% over three days
- acutely abnormal prothrombin time or partial thromboplastin time (PTT) without anticoagulation therapy (international normalized ratio > 1.5; PTT > 60 seconds)

Hepatic
- bilirubin level > 2 mg/dL
- alkaline phosphatase level > 250 units per liter
- aspartate aminotransferase level > 100 units per liter
- alanine aminotransferase level > 100 units per liter

Metabolic
- serum lactate levels > 2 mmol/L (most sources, such as the Surviving Sepsis Campaign guidelines, agree on a serum lactate level > 4 mmol/L, but our hospital data strongly indicate an increased risk of death with serum lactate levels > 2 mmol/L)

Neurologic
- mental state acutely altered from baseline
- a Glasgow Coma Scale score of < 15

Pulmonary
- respiratory rate > 24 breaths per minute
- oxygen saturation level < 92% with patient on oxygen at 6 L/min using face mask

Renal
- urine output < 0.5 mL/kg/hr despite volume resuscitation
- increase in the creatinine level of 0.5 mg/dL

Dellinger RP, et al. *Crit Care Med* 2004;32(3):858-73; Dellinger RP, et al. *Crit Care Med* 2008;36(1):296-327; Michaels RK, Berenholtz SM. *Contemporary Critical Care* 2005;3(5):1-11.

sion to discharge places them in the first line of defense in the recognition of sepsis. All nursing assessments need to take into account the signs and symptoms of sepsis.

THE FOUR STAGES OF SEPSIS

The progression of sepsis is subtle, rapid, and often deadly. It's usually broken down into four stages.

Stage 1. Systemic inflammatory response syndrome (SIRS) describes a systemic inflammation resulting from any major insult to the body, such as trauma, burns, or myocardial infarction, in which two or more of the following are present:
- a temperature higher than 38°C (100.4°F) or lower than 36°C (96.8°F)
- a heart rate greater than 90 beats per minute

In many cases of sepsis, the actual cause of infection is never identified.

- a respiratory rate greater than 20 breaths per minute or a partial pressure of carbon dioxide (PCO_2) less than 32 mmHg
- a white blood cell (WBC) count higher than $12 \times 10^3/mm^3$, lower than $4 \times 10^3/mm^3$, or with more than 10% band cells

Patients with SIRS can be routinely cared for on the medical–surgical floor, but should be closely monitored for signs and symptoms of sepsis.

Stage 2. Sepsis is identified by the presence of two of the SIRS criteria along with a known or suspected infection. However, in many cases of sepsis, the actual cause of infection is never identified—Martin and colleagues found that "specific organisms causing sepsis were recorded in 51% of all discharge records" from the 22-year period they studied.[4] The delay in waiting for confirmation of infection can slow the treatment of sepsis; the most effective course of action once SIRS is identified *and* infection is suspected is to treat the infection and monitor the patient for signs and symptoms of organ failure (see Table 1), which will indicate that the condition has progressed to severe sepsis.

Stage 3. Severe sepsis occurs when a patient who meets the sepsis criteria shows one of the signs and symptoms of organ failure detailed in Table 1. Once severe sepsis is suspected, the patient requires aggressive treatment in a critical care area.

Stage 4. Septic shock is defined as severe sepsis plus hypotension (a systolic blood pressure below 90 mmHg) that doesn't respond to fluid resuscitation. Septic shock is associated with a high mortality rate. The patient's chances of recovery are significantly reduced if, by this stage of sepsis, she or he hasn't already been transferred to the ICU.

CASE STUDY

Nurses throughout the hospital are crucial to the recognition and treatment of sepsis. Consider the following case study from a tertiary care hospital.

Day 1. A 70-year-old female nursing home resident was admitted to the ED with complaints of progressive weakness and diarrhea of three weeks' duration. (Identifying details have been changed to protect the anonymity of the patient.) Upon admission the patient was awake, alert, and oriented. Her medical history included type 1 diabetes, hypertension, stroke, chronic obstructive pulmonary disease, and recurrent urinary tract infections recently treated with ciprofloxacin (Cipro). She was in the ED for five hours and 15 minutes, and her vital signs were labile: her temperature was 36.1°C (97°F) to 38.8°C (101.8°F); pulse, 99 to 109 beats per minute; respirations, 20 to 24 breaths per minute; and blood pressure, 93/41 mmHg to 124/58 mmHg. Her oxygen saturation level as measured by pulse oximetry was 91% to 98% on room air. Laboratory results included a WBC count of $26.5 \times 10^3/mm^3$, a creatinine level of 1.8 mg/dL, and 4+ bacteria in the urine with nitrates present but no leukocyte esterase. Her blood glucose level was 258 mg/dL. A chest X-ray was unremarkable. The ED diagnosis was diarrhea, weakness, and dehydration; treatment consisted of placement of a Foley catheter, ipratropium with albuterol (Combivent) delivered by nebulizer, 1 L of normal saline given intravenously, and 10 units of insulin (Humulin R) delivered subcutaneously. Metronidazole (Flagyl) was given orally for suspected *Clostridium difficile* infection.

Although upon admission to the ED this patient met the criteria for severe sepsis and required immediate and aggressive critical care, her symptoms went unrecognized. She was transferred to a medical–surgical floor late in the evening of the first day.

Day 2. The next morning, the patient's temperature was 35.9°C (96.6°F); pulse, 125 beats per minute; respirations, 24 breaths per minute; and blood pressure, 80/43 mmHg. She was alert but oriented only to self. She required encouragement to eat meals and said she just wanted to sleep. As the day progressed, she became even more lethargic but continued to respond to verbal stimuli. The nursing staff assessed the patient as "alert and oriented but slightly confused." Her stool tested positive for *Clostridium difficile,* and an order was placed for 500 mg of metronidazole to be given orally. Her blood cultures grew *Enterococcus,* and intravenous ceftriaxone (Rocephin) was begun. Scattered crackles and wheezes were audible on lung auscultation. Levalbuterol (Xopenex) by nebulizer was ordered; oxygen was delivered by nasal cannula at 3 L/min. Total urine output during the 7 AM to 3 PM shift was poor at 180 mL.

The physician documented the presence of Gram-positive sepsis and wrote orders for IV metronidazole and for a complete blood count and a basic metabolic panel to be done the following day. At 10:30 PM the patient's color became dusky, and she responded only to loud verbal stimuli and painful stimuli (sternal rub). The physician was notified and an immediate arterial blood gas analysis was ordered. At 10:53 PM the arterial blood gas results were pH, 7.27; PCO_2, 47.5 mmHg; partial pressure of oxygen, 95 mmHg; bicarbonate, 21.3 mEq/L. Her oxygen saturation level was 95% on oxygen 3 L/min.

At 11:05 PM the hospital's rapid response team was activated. The patient's temperature was 35.8°C; pulse, 100 beats per minute; respiration, 24 breaths per minute; systolic blood pressure (measured by Doppler ultrasonography), 70 mmHg; oxygen saturation level, 93%. Blood was drawn for a complete blood count and serum lactate level test: the WBC count was $41.9 \times 10^3/mm^3$ and the serum lactate level was 2.2 mmol/L. Her blood glucose level was 146 mg/dL. Near midnight, the patient was transferred to the ICU.

Day 3. The patient was admitted to the ICU with diagnoses of sepsis (but *not* septic shock), acute renal failure, and hyperglycemia. She was alert, agitated, and mildly confused, with a fluctuating level of consciousness consistent with delirium. Her vital signs remained highly labile: over the course of several hours her temperature was 35.6°C (96°F) to 36°C (96.8°F); pulse, 79 to 90 beats per minute; respiration, 14 to 32 breaths per minute; blood pressure, 70/50 mmHg to 136/35 mmHg. Her WBC count was $41.9 \times 10^3/mm^3$, and her creatinine level was 4.3 mg/dL. A sputum culture tested positive for enterococci. A central line was placed, and the hospital's sepsis protocol, including antibiotics, was initiated. Because the patient was anuric, a nephrology consultation was requested. Dopamine (Intropin) and norepinephrine (Levophed) were started intravenously to stabilize her decreasing blood pressure. She developed respiratory distress, and full-mask bilevel positive airway pressure (BiPAP) was initiated. When the BiPAP proved insufficient for the patient's respira-

> Once sepsis is suspected, it's crucial to watch closely for signs and symptoms of its rapid progression.

tory failure, she was intubated and placed on mechanical ventilation.

Days 4 through 7. On days 4 and 5, the patient's condition worsened, and her vital signs and blood tests continued to demonstrate septic shock and multiple organ failure despite medical treatment, including hemodialysis. On day 6, a family conference was called, and the patient's code status was changed to "do not resuscitate." On day 7, dialysis was discontinued, a morphine drip was started as a comfort measure, and compassionate extubation was performed according to hospital protocol. The patient died that evening.

The nurse may need to take the lead in sepsis assessment.

WHAT COULD A NURSE HAVE DONE?

This patient met the criteria for severe sepsis on admission to the ED and continued to exhibit signs and symptoms of sepsis on transfer to the medical–surgical floor, yet sepsis was not initially suspected and the progression to severe sepsis went unrecognized. Transfer to an ICU for rapid and aggressive treatment might have saved the patient's life. But by the time the rapid response team was called at 10:30 PM on day 2, the patient was in septic shock and the prognosis was already poor. Despite aggressive treatment in the ICU, the patient died with a diagnosis of septic shock.

Because of the narrow window of opportunity available to treat sepsis as it progresses, the nurse—who's in closest proximity to the patient—may need to take the lead in this assessment. A nurse can take the following steps to slow or stop the progression of sepsis.

Suspect sepsis. This patient had a recent urinary tract infection and 4+ bacteria in her urine. Her WBC count was elevated, and she had difficulty breathing. Her vital signs met the criteria for SIRS. SIRS plus the urinary infection should have indicated that she had sepsis. Although the patient had a history of chronic obstructive pulmonary disease, her respiratory distress may have been due to respiratory failure related to severe sepsis organ failure. Clinicians failed to recognize that she had at least sepsis, and probably severe sepsis, on admission to the ED and on transfer to the medical–surgical floor.

Increase assessment frequency. Once sepsis is suspected, it's crucial to watch closely for signs and symptoms of its rapid progression, such as

- fever or hypothermia.
- tachycardia.
- tachypnea.
- hypotension.
- decreasing urine output.
- change in mental status from time of admission.
- abnormal lab values.

Initiate nursing interventions while awaiting patient transfer to the ICU.

- Alert the physician and request orders for lab work needed to monitor the patient.
- Begin oxygen administration.
- Suggest establishing a central line and begin fluids for circulatory support.
- Place a urinary catheter and track output closely.

Document complete and measurable assessments. Instead of saying "mildly confused," say, for example, "oriented to person and place but not to date." Thus, the oncoming nurse will know that disorientation to date signals a change in this patient's mental status. Instead of saying urine output is "decreased" or "low," state the amount of output for an eight-hour shift, leaving no room for doubt about the patient's urinary status. Omission of respiration, temperature, and other vital signs leaves out critical information that could make the difference between life and death in the sepsis patient.

The Surviving Sepsis Campaign, an international venture composed of representatives of 11 professional societies, including the American Association of Critical-Care Nurses and the American College of Emergency Physicians, published guidelines in 2004 in *Critical Care Medicine* designed to substantially reduce mortality from sepsis.[5] (The guidelines are available at http://ssc.sccm.org/files/surviving_sepsis_campaign_guidelines.pdf.) Although controversy continues regarding industry funding of the campaign by Eli Lilly and Company, the campaign's guidelines and its extensive outreach activities—specifically, criticism centered around the campaign's recommendation of Lilly's expensive drug drotrecogin alfa (Xigris) in the treatment of sepsis[6]—the campaign has produced and widely disseminated two "severe sepsis bundles" (available at www.survivingsepsis.org/implement/bundles), which provide guidance in responding to severe sepsis and septic shock in a rapid and systematic manner using early, "goal-directed therapy." (*Editor's note:* In early February the Food and Drug Administration announced that it would undertake an ongoing safety review as a result of a study showing "increased risk of serious bleeding events and of death in patients with sepsis and baseline bleeding risk factors" who were receiving drotrecogin alfa.[7])

The treatment of sepsis, severe sepsis, and septic shock is complex and evolving, and disagreement remains about the most effective therapies, the pros and cons of risking hypoglycemia through implementing tight blood glucose control, and the best antibiotic to use at a specific time. The focus for the general care nurse outside of critical care remains recognizing sepsis when it is present, initiating appropriate interventions in a timely manner, and facilitating transfer as urgently as possible. ▼

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GENERAL PURPOSE: To provide registered professional nurses with current information on the stages of sepsis and the appropriate management approaches for each, using the case of an older adult as an example.

LEARNING OBJECTIVES: After reading this article and taking the test on the next page, you will be able to
- outline the trends in incidence, outcomes, and classification of sepsis.
- identify the manifestations of and treatment recommendations for sepsis.

TEST INSTRUCTIONS

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