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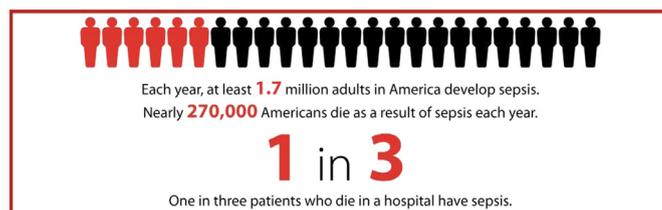
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Getting ahead of sepsis

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'Anyone can get an infection, and almost any infection can lead to sepsis.' So says the Centers for Disease Control and Prevention (CDC). With that kind of ominous warning it's no wonder that people are concerned about sepsis. Of course it is especially concerning for those involved in long term care given the increased risk both in terms of prevalence and severity for the LTC community.



<https://www.cdc.gov/sepsis/datareports/index.html>

Sepsis is defined as a condition where the bloodstream is overwhelmed by bacteria or fungus. Our immune system response to this condition with a systemic inflammatory response that is complicated by acute organ dysfunction, hypoperfusion, or hypotension. Abnormalities of circulation that follow may include lactic acidosis, loss of the ability to produce and excrete urine, and acute alterations in mental status. Septic shock, a condition where overwhelming infection leads to a life threatening drops in blood pressure, may follow.

15% of all adult visits to the emergency department are triggered by infection. Only a small percentage of these infection related episodes were diagnosed as severe sepsis. This is important as severe sepsis is associated with high utilization of medical services and resources, such as the intensive care unit, and with high mortality. Nursing home resident account for 25% of all emergency department visits for severe sepsis with an associated mortality of 37%. Being

elderly, particularly if you have one or more chronic medical conditions, increases your risk of experiencing a severe case of sepsis. In addition, mortality rates from severe sepsis rise with advanced age and frailty. The National Hospital Ambulatory Medical Case Survey (NHAMCS) initiated collection of hospital outcome data and prior nursing home residence in 2005. This endeavor yielded information on emergency department visits for severe sepsis. This study's primary objective was to compare the impact of older age (defined as 65 years of age or older) and nursing home residence on the incidence and morbidity of severe sepsis. Indeed it was found that older adults presenting to the emergency department with sepsis, had a higher rate of severe sepsis and that this rate was even higher if that older adult was from a nursing home. It is interesting to note, in terms of presenting symptoms and physical findings, that this group of patients arrived in the emergency department with low systolic blood pressure and elevated heart rate. Respiratory and genitourinary tract infections were the most common sites of infection with lower rate of infection found in skin and soft tissue.

The CDCs ways

The CDC in their '4 Ways to Get Ahead of Sepsis'¹ outlines the following:

- 1) Prevent Infections
- 2) Practice Good Hygiene
- 3) Know the Symptoms
- 4) Act Fast

But even before diving into the CDC four areas of focus, the management of sepsis really starts with a clear understanding and appreciation for a patient's goals of care. For if a patient's goals of care are for comfort measures rather than active treatment, sepsis treatment may be focused more on comfort care rather than active aggressive treatment.

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For those patients with goals of care that call for active identification and management than beginning the management of sepsis with prevention is the obvious starting point. Preventing infection starts with providing all the recommended vaccinations. It also involves management of chronic conditions, which are common among LTC residents.

Practicing good hygiene starts with hand washing and includes keeping cuts clean and covered until healed.

The symptoms common in sepsis include confusion or disorientation, shortness of breath, tachycardia, fever or feeling very cold, extreme pain or discomfort and clammy or sweaty skin.

Sepsis prevention

In addition to the 4 ways to get ahead of sepsis that are warranted above, there are steps that can be taken to prevent sepsis that are as follows;

1. Keep vaccinations up-to-date. 35% of sepsis cases according to CDC data start stemming from pneumonia.
2. Treat urinary tract infections promptly. According to the CDC, 25% of sepsis cases result from urinary tract infections.
3. Clean wounds properly.
4. Manage and control chronic medical conditions.
5. Observe proper hand hygiene.
6. All cuts and abrasions must be kept clean, dry, and covered until healed.

Keys to preventing sepsis

Because sepsis may be difficult to recognize in its early stages and because the condition is a challenge to manage and result in such high mortality rates, prevention is of paramount importance. We may ask if we are doing a good job of this at this time. The American Journal of infection control issued report in May 2011 that showed a pattern of noncompliance with infection control in long-term care facilities. This report looked at data that was collected between 2000 and 2007 that represented 96% of all nursing homes. The study examined the deficiency citation for infection control requirements under F tag 441. 15% of nursing homes in the United States recited under F tag 441 for infection control violations. This is a substantial level of noncompliance when you consider that between 1.6 and 3.8 million episodes of infections occur each year in nursing homes.

Application of advance directives to changes in condition caused by infection

Important decisions regarding care have to be made when a patient or resident of a facility is presenting with symptoms consistent with potential sepsis. The ideal situation is to be able to present the resident with the information that they need about their condition so that they can make that asked decisions for themselves about what kind of care they want to receive and where they want to receive it. In some cases the ability to make that decision may be interfered with by the level of cognition that patient has. In other cases, the patient may be unable to make a decision based on acute changes in cognition due to the underlying disease process. In those situations, it is very advantageous to have advanced directives in place so that care providers can map out the course of treatment that patient would want to have. The importance of advance care planning cannot be overstated because a medical crisis, such as an episode of sepsis, can occur at any time even in a patient or resident that is relatively stable and healthy. There is a scarcity of data on the validity of Advance Directives in Acute Situations. Germany, where approximately 25% of the population has an advance

directive that is established to be used in certain medical situations, set an example that we can learn from. In 2015, a German published prospective study looked at the validity of advance directives in acute situations by looking at the results of a survey of doctors and relatives of 50 patients with advanced directives regarding their perceptions from experiences across four different multidisciplinary intensive care units. The relatives of the patient's stated that they were generally very familiar with the patient's wishes and generally found that having advance directives in place was useful, in fact, they had a higher opinion of the usefulness of the advance directives than the physicians did. Why the difference? The feeling was that the physicians had a tendency to interpret the spirit of the advance directives when making treatment decisions while the relatives tended to take a literal stance on their interpretation. Despite that difference, it is interesting to note that the indication from the study was that advance directives in intensive care unit only had a small effect on the management of life-sustaining treatment. It was also noted that patient who had advanced directives in place were less likely to have cardiopulmonary resuscitation but that the advance directives had no impact on time spent in the intensive care unit or on end-of-life treatment. It should be noted, that without exception all advance directives contained to some extent a rejection of life sustaining measures but that these rejections were documented with standardized verbiage rather than customized patient centered narratives. Regardless of how the ideas were presented on paper, standard language or customized language, the relatives of the patient's held a high level of respect for the signed directives and wanted them implemented literally. The problem that was identified was that because the written content of the advance directives usually consisted of pre-written sections of text that were imprecise or contradictory they created a level of ambiguity that took away some of their validity when making decisions about treatment. Questions raised by the experiencing Germany are applicable to our experience in the United States, especially when dealing with acute changes in condition associated with high rates of mortality such as in the case of sepsis.

A study by Wright State University looked at the application of advance directives to clinical scenarios in an attempt to assess the perspectives of emergency department patients on advance directives and their application to various clinical scenarios. In this prospective study, patients were given written education regarding state laws applicable to advance directives and information about the application of advance directives. Participants were then asked to assess their personal opinions regarding whether or not an advance directive would apply to a series of hypothetical clinical scenarios that they were presented with. The results demonstrated wide variability in the opinion and insight of patients regarding the application of advance directives and it was demonstrated that a majority of patients had little understanding of advance directives and the concept of end-of-life decision making. For example, the clinical scenario that most people thought a DNR order should apply to was that where a person had been critically injured in an automobile accident. Conclusions drawn from the study indicated the importance of recognizing how complex end-of-life decision making can be and the necessity for patients to effectively communicate their personal preferences for end-of-life care when they are able to do so.

Recognition and medical work-up

Making an early diagnosis of sepsis is challenging. These patients may present with variations in inflammatory response, hemodynamic stability, organ perfusion, and organ dysfunction. Early non-specific signs may include fever, hyperthermia, tachycardia, altered mental status, new or worsening edema, and hyperglycemia. The

inflammatory response may be marked by an elevation in white blood count (white blood count greater than 12,000) or a reduction in white blood cell count (WBC count less than 4000). The white blood cell count may also be normal with greater than 10% of the population presenting as an immature form of a white blood cell. There may also be elevations in plasma C-reactive protein and plasma pro-calcitonin. Hemodynamic instability may be demonstrated with arterial hypotension (less than 90 mmHg), a systolic blood pressure that is more than 40 mmHg below that patient's usual reading, or a mean arterial pressure that is less than 70 mmHg. The mean arterial pressure can be calculated by adding the systolic blood pressure to the diastolic blood pressure multiplied by 2 with that entire value then divided by 3. Organ dysfunction may include hypoxemia, acute oliguria (urine output less than 0.5 mL/kg/h for at least 2 h despite adequate fluid resuscitation), and increase in serum creatinine by 0.5 mg/dL, coagulation abnormality (INR greater than 1.5), and ileus demonstrated by absence of bowel sounds, thrombocytopenia (platelet count less than 100,000), and hyperbilirubinemia (plasma total bilirubin greater than 4 mg/dL). Tissue perfusion abnormalities may present with elevations in serum lactate levels and/or decreased capillary refill or mottling.

There are barriers in the skilled nursing facility to making a timely diagnosis of sepsis and initiating treatment. First, the medical staff is often off-site and do not see the patient's frequently. Fever is not present in many cases of elderly people with serious infections. It is more difficult to make a decision about prescribing antibiotics or transferring the patient to the emergency department for further evaluation when the prescriber is not on site. Finally, long-term care facilities usually do not have x-ray and laboratory capabilities for conducting appropriate diagnostic tests.

Time matters

The last way described by the CDC is a call to act fast. This is highlighted by the statement that 'Sepsis is a medical emergency. Time matters.' Time from the standpoint of quick identification and treatment, sepsis is not alone with this approach as this 'time matters' has been the mantra for stroke as well. Despite seeming wide spread acceptance with stroke, time matters has not yet filtering into the thinking of many when it comes to sepsis.

Perhaps this is in part due to confusing messages being presented on the topic. As reported almost a decade ago and still remains unsettled today while experts generally agree that delivering antibiotics quickly to patients with community-acquired pneumonia (CAP) is important, a debate has raged about how to improve "and measure" antibiotic timing for these patients.²

For several years, the Centers for Medicare and Medicaid Services (CMS) and the Joint Commission had decreed that all CAP patients should receive their first dose of antibiotics within four hours. The four-hour rule was based on two large retrospective studies, one of which appeared in the March 22, 2004, *Archives of Internal Medicine*. That study concluded that receiving a dose of antibiotics within four hours of arriving at the hospital was associated with "a 15% relative reduction in 30 day mortality". Critics, however, have long claimed that a four-hour antibiotic window for CAP patients is inappropriate because it is based on retrospective, not prospective data.

Even more importantly, they say, the measure is being applied to a patient population "general ED patients" who may differ substantially from the Medicare patients in whom the benefit was retrospectively demonstrated. And they complain that the four-hour goal leads to many unintended and adverse consequences such as the inappropriate over diagnosis of CAP and use of antibiotics because of fear in missing this window. As a result the CMS adjusted its reporting requirement to target how many CAP patients receive

their initial antibiotic dose within six hours of arrival at the hospital and added an outcome measure based on the 30-day pneumonia mortality.

Making the decision not to treat in place and what happens when a resident is transferred to the emergency room

Because of the urgency that suspicion of sepsis brings, in suspected cases it is necessary to start treatment first and confirm diagnosis later. This is important for the long-term care industry to take a hard look at due to the pressure we currently put on ourselves to avoid sending residents to the hospital in favor of treating in place. When possible, established guidelines should be used when deciding whether or not to treat a potential infection in the facility criteria for treating pneumonia in the skilled nursing facility was published by Loeb et al. in a 2006 article that was published in the *Journal of the American Medical Association* and pointed to the 5 following points that established safety in attempting to treat pneumonia in place;

1. The resident maintains the ability to eat and drink.
2. The heart rate is maintained at or below 100 bpm.
3. The respiratory rate is maintained at or below 30 breaths per minute.
4. The systolic blood pressure remains at or above 90 mmHg.
5. The oxygen saturation can be maintained at least at 92%.

These criteria were established based on a study that was conducted at 22 Nursing Homes involving 680 cases of pneumonia.

According to the American Medical Director's Association, when sepsis is suspected or confirmed by blood cultures it may be necessary to transfer the resident to the hospital for treatment because the specialized interventions and technical support that are required may be outside of the scope of what the typical skilled nursing facility is able to provide. They also add the perspective that advance directives in combination with patient and family preferences must be considered when making the decision whether or not to transfer to the hospital.

Consider what happens to our resident's once they have been sent to the emergency department. Generally, when staff at the emergency department recognize a patient with symptoms of sepsis they call a "code sepsis" protocol. Criteria for inclusion with includes suspected infection, temperature greater than 100.4°F or less than 96.5°F, heart rate greater than 90 bpm, respiratory rate greater than 20 breaths per minute, alterations in mental status, oxygen saturation below 90%, and systolic blood pressure less than 90 mmHg. Typically, if they patient presents with 3 or more of these signs and if the goal of care is curative the team will proceed to the code sepsis protocol. The protocol establishes what must be done during the first 6 h of care and clearly delineates the complexities that are involved.

- Within the 3 h
 - Obtain arterial blood gas, cognitive metabolic panel, pro-calcitonin level, see DC with differential, PT/INR, PTT, troponin I level.
 - Administration of high flow supplemental oxygen.
 - Obtain 2 sets of blood cultures, 10 min apart, from separate sites.
 - Administer broad spectrum antibiotics.
 - Initiate fluid resuscitation by establishing two lines of intravenous access. Unless there is a contraindication, fluids intended to increase intravascular volume such as normal saline are provided at an infusion rate of 30 mL/kg/h. Following the initial intravenous bolus, fluids to increase intravascular volume are continued at a rate of 125 mL/h.

- Obtain blood to measure lactate and hemoglobin levels.
- Maintain accurate measurement of urine output.
- Within the first 6 h
 - Initiate vasopressors if the patient's mean arterial pressure (MAP) cannot otherwise be maintained above 65.
 - If the patient is hypotensive and the blood pressure has not responded to fluid resuscitation, it may be necessary to measure central venous pressure.
 - Lactate levels should be re-measured and the results of the initial lactate measurement should be available for review (the significance of the mean arterial pressure is that when it is maintained above 70 mmHg there is enough pressure to sustain the organs of an average person. Normal values are between 65 and 110. If the mean arterial pressure falls below 70 mmHg for an appreciable time, vital organs will not get enough oxygen perfusion and will become ischemic).
- Monitoring
 - The patient is not allowed to have any food or fluid by mouth.
 - Vital signs are obtained at least every hour.
 - Pulse oximetry is monitored continuously and supplemental oxygen is provided to maintain oxygen saturation between 92% and 99%.
 - Fluid intake and output is recorded on an hourly basis.
 - Cardiac monitoring via telemetry is not indicated in all cases and is used as indicated.

As you read through what is required in managing these patients over the first 6 h, think seriously about whether or not your facility has the capability to provide this high level of technical care. Even something as basic as a lactic acid level may be impossible to get within a few hours if the blood is drawn in a patient who is residing in a skilled nursing facility. In some facilities, it may take several days to get these results. There are symptoms of lactic acidosis that we can look for as a clue that the level is elevated in a resident such as muscle weakness, rapid breathing, sweating, and coma but once the symptoms are present the resident will probably be beyond the point where we can successfully manage them in our facilities.

Balancing antibiotic stewardship

Consider this series of statements of wisdom that pretty much tell the history of where we are today with antibiotics;

“Here, eat this root.”

“That root is poison. Say this prayer.”

“That prayer is superstitious. Drink this potion.”

“That potion is rotten. Take this miracle drug. It's called penicillin.”

“Penicillin is worthless. Try this new, bigger, better antibiotic.”

“Those antibiotics don't work anymore. Here, eat this root.”

This debate continues with the antibiotic stewardship movement, which calls on providers to be prudent in their use of antibiotics in an effort to prevent antibiotic resistance. *Be Antibiotics Aware* is a CDC lead national effort to help fight antibiotic resistance and improve antibiotic prescribing and use. Antibiotics save lives, but any time antibiotics are used, they can cause side effects and lead to antibiotic resistance. In U.S. clinic, LTC settings, and emergency departments, at least 47 million antibiotic prescriptions each

year are unnecessary, which makes improving antibiotic prescribing and use a national priority. Studies indicate that 30–50% of antibiotics prescribed in hospitals are unnecessary or inappropriate. There is no doubt that overprescribing and mis-prescribing is contributing to the growing challenges posed by *Clostridium difficile* and antibiotic-resistant bacteria. Studies demonstrate that improving prescribing practices in hospitals can not only help reduce rates of *Clostridium difficile* infection and antibiotic resistance, but can also improve individual patient outcomes, all while reducing healthcare costs. *Be Antibiotics Aware: Smart Use, Best Care* is a CDC campaign focused on improving prescribing practices in inpatient healthcare facilities. This effort needs to be balanced against the need to treat infections that lead to sepsis in a most timely manner.

The other effort is the push to avoid avoidable emergency room / hospital admissions as such patients may be kept in their LTC communities longer than appropriate. CMS has had these as quality measures that make up the CMS Nursing Home Compare 5 Star Rating for SNFs. Specifically these new two measures report on the both the percentage of short-stay residents who were re-hospitalized after a nursing home admission and percentage of short-stay residents who have had an outpatient emergency department visit. The concern here is that this like the drive for antibiotic stewardship will result in a delay in appropriate treatment, which would negatively impact the clinical and financial outcomes of sepsis management.

AI to the rescue

Because of all the concerns of competing factors and difficult in early accurate detection of sepsis today why several hospitals are experimenting with artificially intelligent sepsis detectors. Researchers report these pilot projects as the first real examples of AI being integrated into hospital operations, with data flowing from electronic medical records and alerts being incorporated into physicians' workflows.³

Duke University Hospital, in Durham, N.C., officially launched Sepsis Watch, an AI-based system that identifies incipient sepsis cases and raises the alarm. Sepsis Watch was trained via deep learning to identify cases based on dozens of variables, including vital signs, lab test results, and medical histories; its training data consisted of 50,000 patient records including more than 32 million data points. In operation, it pulls information from patients' medical records every 5 min to evaluate their conditions, offering intensive real-time analysis that human doctors can't provide. If the AI system determines that a patient meets its criteria for someone with the early signs of sepsis, it alerts the nurses on the hospital's rapid response team. But the availability this system may be sometime until it is commonplace in LTC communities. Until that time, it will require the virulence of knowledgeable caring LTC provides to stay ahead of sepsis.

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