UNDERSTANDING SEPSIS

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What Sepsis is – Definition & Criteria

Sepsis is the body's extreme response to an infection.

CDC, 2024

	CLINIICAL CRITERIA
SIRS Systemic Inflammatory Response Syndrome	▪ Heart rate > 90 ▪ Temp > 38.0 or < 36.0 ▪ Respirations > 20 ▪ WBC > 12,000 or < 4,000 or > 10% bands
SEPSIS Systemic response to an infection manifested by 2 or more SIRS criteria as a result of infection.	▪ 2 or more SIRS criteria + Source of infection *(suspected or confirmed)*
SEVERE SEPSIS Sepsis associated with organ dysfunction, hypoperfusion or hypotension	▪ Hypotension (MAP < 65 or SBP < 90 or drop in 40 from baseline; *or* ▪ New BiPAP/CPAP/vent; *or* ▪ Creatinine > 2 mg/dl (for patients not on dialysis or ESRD); *or* ▪ Urine Output < 0.5 ml/kg/hr x2 hrs (for patients not on dialysis); *or* ▪ Bilirubin > 2 (for patients not with ESRD); *or* ▪ Platelet count < 100,000; *or* ▪ INR > 1.5 or aPTT > 60; *or* ▪ Lactate > 2 mmol/L ▪ Mental status change (in parallel with infection + SIRS indicators)
SEPTIC SHOCK Sepsis-induced, with hypotension despite adequate fluid resuscitation along with perfusion abnormalities	▪ Persistent hypotension (MAP < 65 or SBP < 90 or drop in 40 from baseline); *or* ▪ Lactate > or = 4 mmol/L Sepsis Program Optimization

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What Sepsis is not: Blood Poisoning

That is an old term used for generations – but not an accurate description of sepsis

Sepsis is not an infection in and of itself

Sepsis is the body's life-threatening response to infection

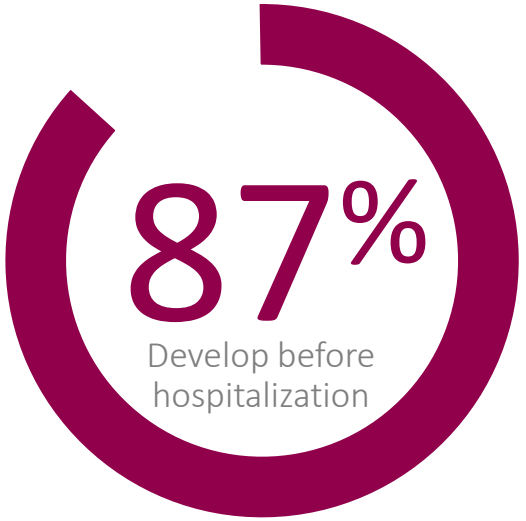
Like strokes or heart attacks, sepsis is a medical emergency that requires rapid diagnosis and treatment.

33% Worldwide, one-third of those who develop sepsis will die

Many who do survive are left with life-changing effects like PTSD, chronic pain and fatigue, or organ dysfunction.

10% of the 1.6M amputations in the U.S. each year are related to complications of sepsis, often in the young.

Misconception:
People 'catch' sepsis in hospitals



Only 13% of cases occur while hospitalized.

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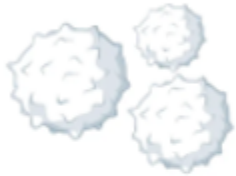
Sepsis Alliance. Sepsis and Blood Poisoning. 2023.
Differentiation of Fungal, Viral, and Bacterial Sepsis

Journey from Infection to Severe Sepsis with Septic Shock

Infection enters the bloodstream – viral, fungal or bacterial.

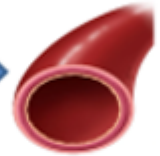


WBCs respond and recruit more WBCs to fight the infection.

WBCs release nitric oxide.

Release of nitric oxide causes increase in vessel permeability.

Release of nitric oxide causes increase in vasodilation.



The increase in diameter of the vascular space allows more room for RBCs to pass through and get needed oxygen to the cells and get WBCs to the infection. That dilation also results in decreased SVR (Systemic Vascular Response).

The increase in permeability allows fluid to build up in the tissues, resulting in complications such as pulmonary edema and decreased oxygenation.

Cardiac output will initially increase as an attempt to compensate for decreased SVR.

If treatment is delayed it will cause decreased cardiac output resulting in hypotension and low tissue perfusion.

The body may attempt to compensate by trying to shunt blood to the core and away from extremities. This can result in amputations.

Organs are not able to function when they are starved of oxygen. This can lead to organ failure and eventually death.

As WBCs continue to fight, they attack the pathogens but also cause damage to the vessels.

As vessels are damaged, there is increased coagulation as an attempt to repair areas when the vessel has ruptured.

Some clots break off into the bloodstream.

DIC (Disseminated Intravascular Coagulation) may result when coagulation factors can't keep up with the demand and blood begins to spill out of the blood vessels

Sepsis is both devastating and deadly

Sepsis Kills

Every **90 seconds** someone is diagnosed with sepsis. 1 in 5 will die.

Don't let it be you or a loved one.

Sepsis Maims

Every **hour** someone loses a limb to sepsis.

Sepsis can forever alter your life or that of someone you love

Sepsis Devastates

Every **day**, 18 children die from sepsis in the U.S.

Don't let sepsis destroy any more families.

According to the National Kidney Foundation, one of the major causes of acute kidney injury (AKI) is sepsis. Some studies have found that between **32%** and **48%** of acute kidney injury cases were caused by sepsis.

Sepsis is the leading cause of hospital readmissions – up to 19% of people originally hospitalized with sepsis return within 30 days (40% are readmitted within 90 days). Financial implications are high - more than $3.5 billion each year.

Sepsis Alliance
CDC launches new effort for sepsis

Sepsis in the headlines

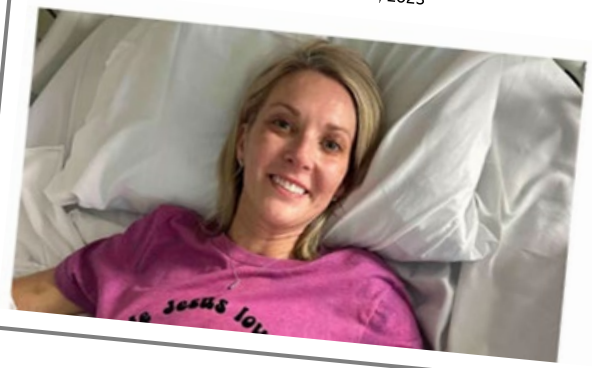
Even in survival, sepsis can leave life-long consequences

People NEWS ENTERTAINMENT ROYALS LIFESTYLE STYLEWATCH SHOPPING

Kentucky Woman Gets Her Limbs Amputated After Kidney Stone Infection: 'I'm Just So Happy to Be Alive'

"I just said, 'These are the cards I've been dealt, and these are the hands I'm going to play.'

By Bailey Richards | Published on December 31, 2023



People NEWS ENTERTAINMENT ROYALS LIFESTYLE STYLEWATCH SHOPPING

Ohio Mom, 42, Had All 4 Limbs Amputated After Flu Led to Bacterial Infection : 'I Woke Up with No Arms and Legs' (Exclusive)

Kristin Fox developed a bacterial infection and sepsis after coming down with the flu in 2020

By Cara Lynn Shultz and Kirsty Hatcher | Published on November 15, 2023

Former NFL player Mike Williams' death caused by rare dental-related sepsis

Elizabeth Flores
USA TODAY
Published Dec 23, 2023

According to the Hillsborough County Medical Examiner's Office report, Mike Williams, a former wide receiver for Syracuse and the Tampa Bay Buccaneers, died from a rare bacterial sepsis linked to poor dental health, which developed after Williams was injured at a work-related construction site in August.

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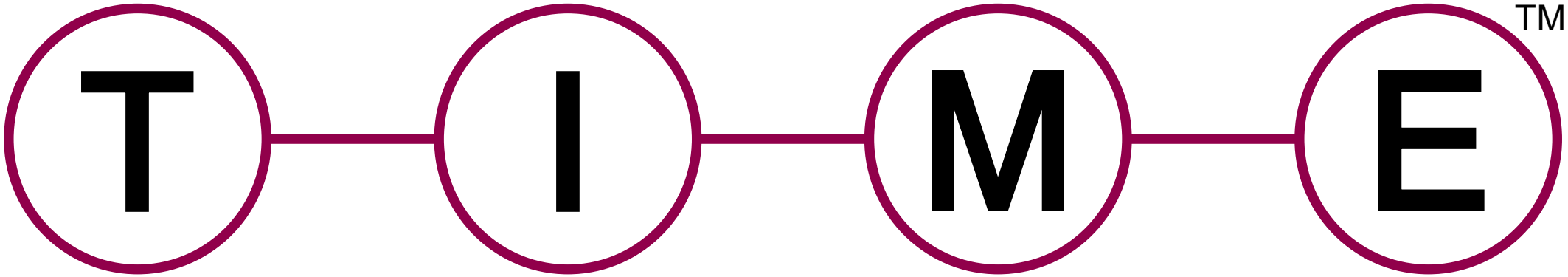
Early recognition can save a life

When it comes to sepsis, remember ***IT'S ABOUT TIME***™. Watch for:



TEMPERATURE
higher or lower than normal

INFECTION
may have signs and symptoms of an infection

MENTAL DECLINE
confused, sleepy, difficult to rouse

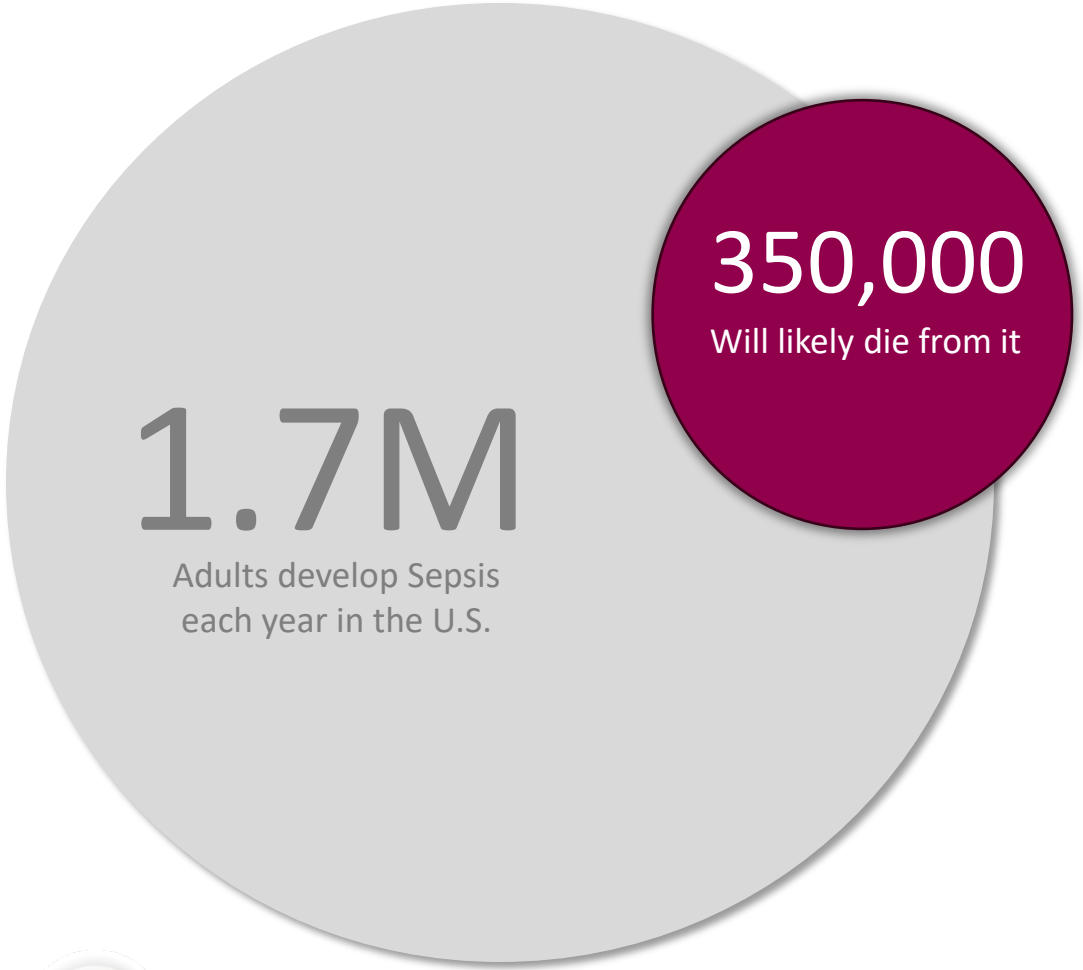
EXTREMELY ILL
severe pain, discomfort, shortness of breath

If you experience a combination of these symptoms: seek urgent medical care, call 911, or go to the hospital with an advocate. Ask: **"Could it be sepsis?"**

Sepsis Alliance

Sepsis is a major cause of hospital death

Sepsis takes more lives than heart attack, stroke, or cancer



Sepsis-related deaths declined from 2000 to 2019 (thanks to the Surviving Sepsis Campaign). Still, per the Sepsis Alliance, **35%** of those who die in the hospital have a diagnosis of sepsis.*

Despite the high risk of death, in this country a whopping **34% have never heard of sepsis**.

The risk of mortality from sepsis increases by **4% - 9%** for every hour treatment is delayed.

As many as 80% of septic shock patients can be saved with rapid diagnosis and treatment.

** That is consistent with our MLH patients. In 2023, sepsis was diagnosed in **34.4%** of all patients who died while in our care.*

[National Institute of General Medical Sciences: Sepsis]
[CDC: Sepsis-related mortality]
[Sepsis Alliance Fact Sheet]

Risk factors: It's not just about old age

There is a misconception that sepsis deaths are mainly seen with advanced age

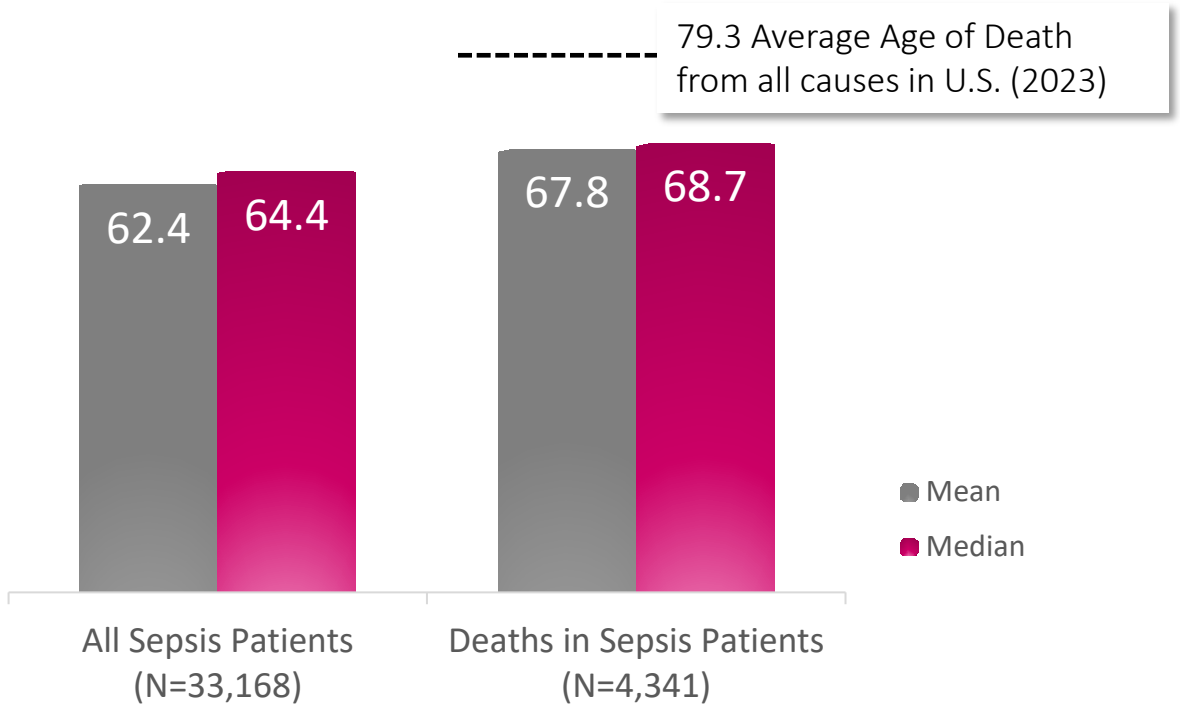
Risk Factors for sepsis include:

- Diabetes
- Malignancy
- Corticosteroid use
- Burns
- Trauma
- Hemodialysis
- Chronic disease*
- Major surgery
- Immunosuppressed state
- Prolonged hospitalization
- Indwelling catheters
- Extremes of age

** Chronic end-stage kidney or renal disease*

Each year, more than 75,000 children in the U.S. develop severe sepsis and 6,800 of these children die, even more than from pediatric cancers.

Death from sepsis averages 11.5 years below life expectancy



Source: All MLH adult sepsis patients from 2018-2024 Jun-YTD

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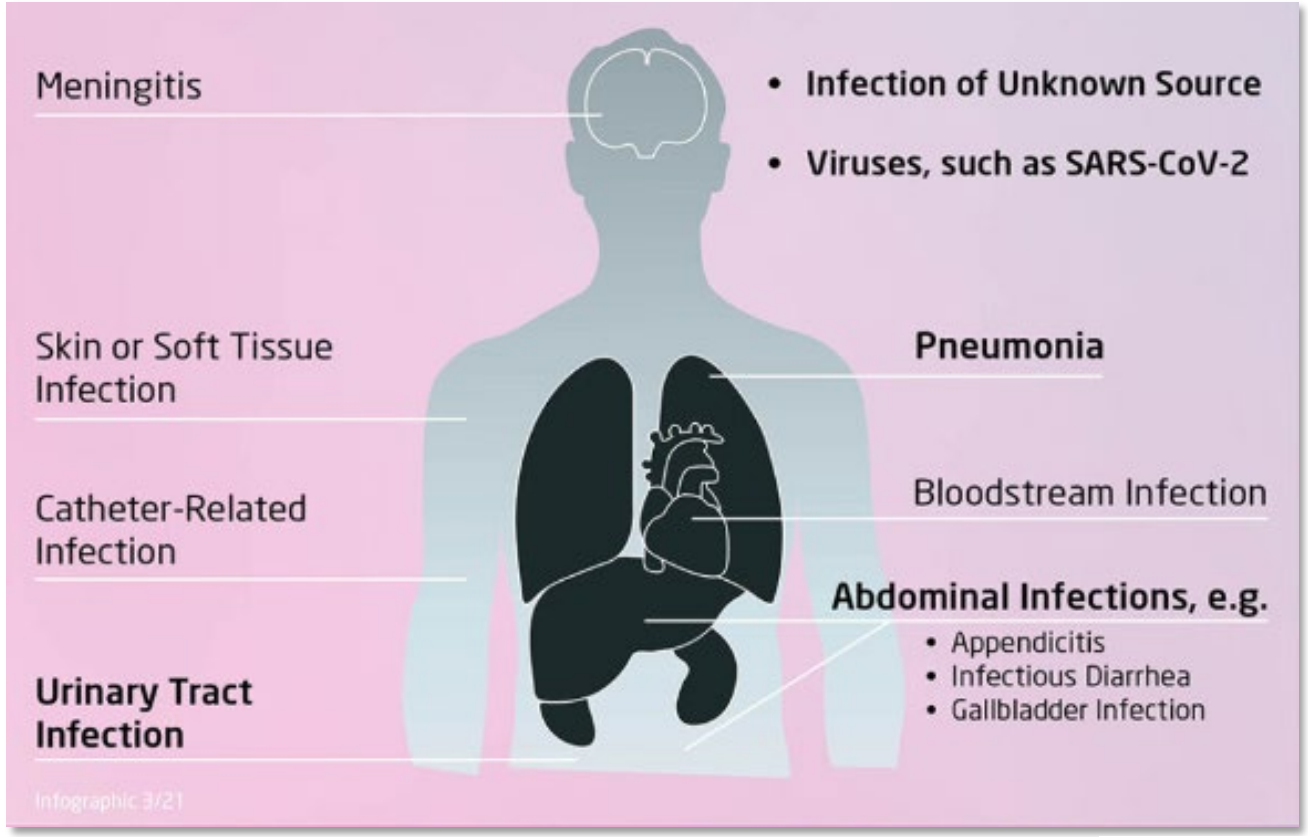
National Library of Medicine: Septic Shock
Macro Trends: Age of Death in U.S.
Sepsis Alliance Fact Sheet

Common Sources of Sepsis

While pneumonia is the most common source, sepsis can originate anywhere



Global Sepsis Alliance

Per the CDC, almost any infection, including COVID-19, influenza, or RSV, can lead to sepsis

While most sepsis is caused by bacterial infection, an estimated 20% result from fungal infection

35.8% to 41.8% of cases of sepsis are related to respiratory infections with an average mortality of 22%

Cultures are not definitive - in up to half of septic patients, no pathogen is identified

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World Sepsis Day
Differentiation of Fungal, Viral, and Bacterial Sepsis

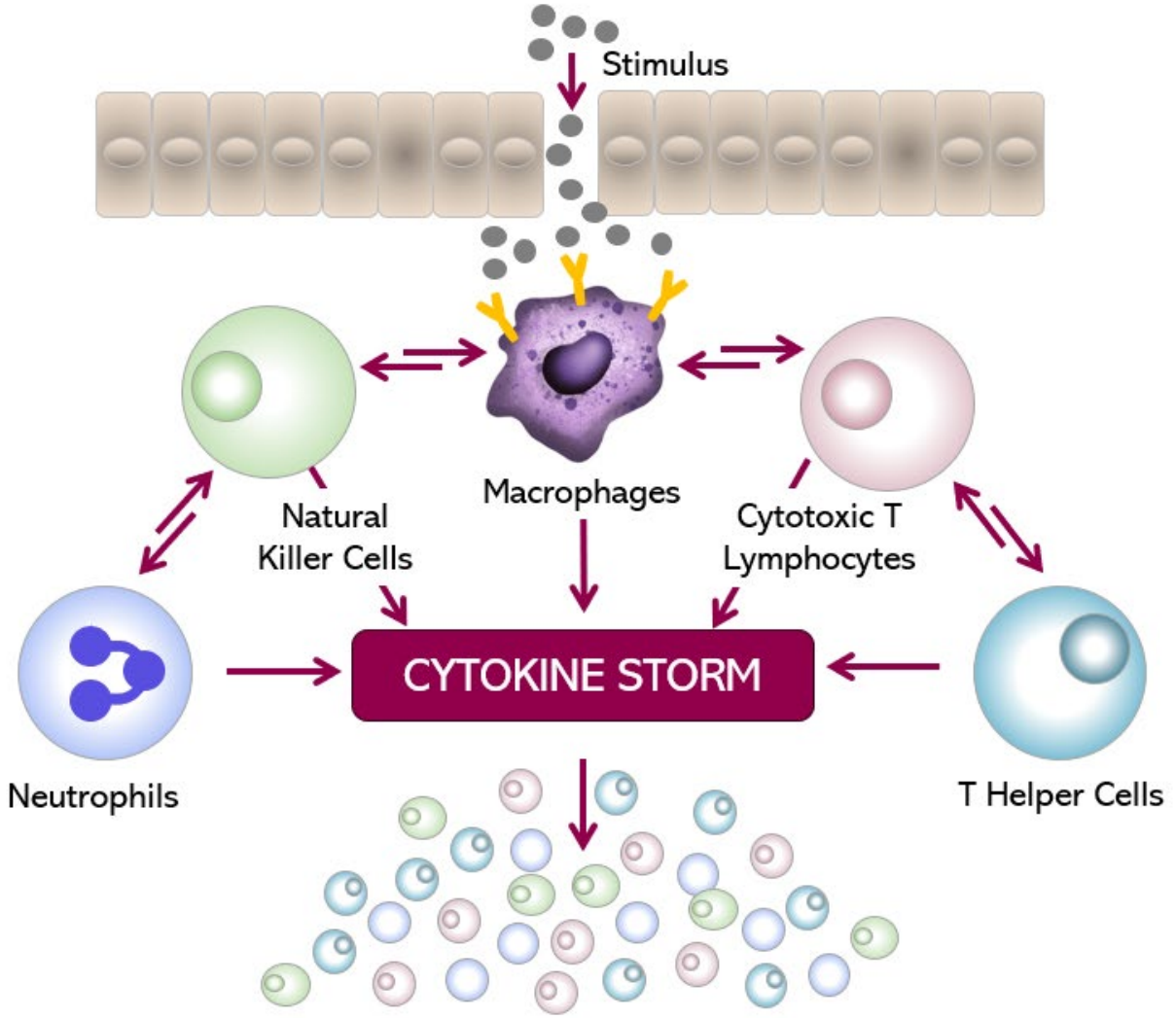
What happens during a Cytokine Storm?

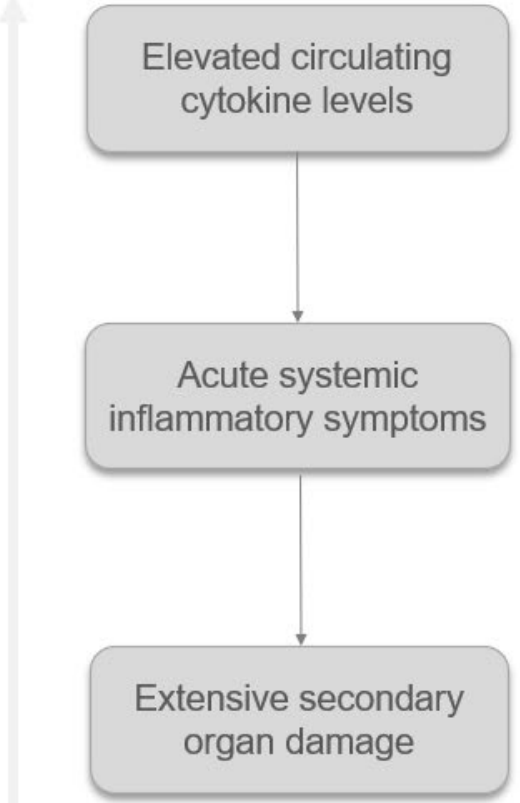
It is important to be attuned to differing symptoms so you can respond quickly

Many types of cells can be involved in a Cytokine Storm.

Neutrophils, natural killer (NK) cells, macrophages, cytotoxic T lymphocytes (CTLs), and T helper cells (Th cells) are intimately involved in the initiation and progression.

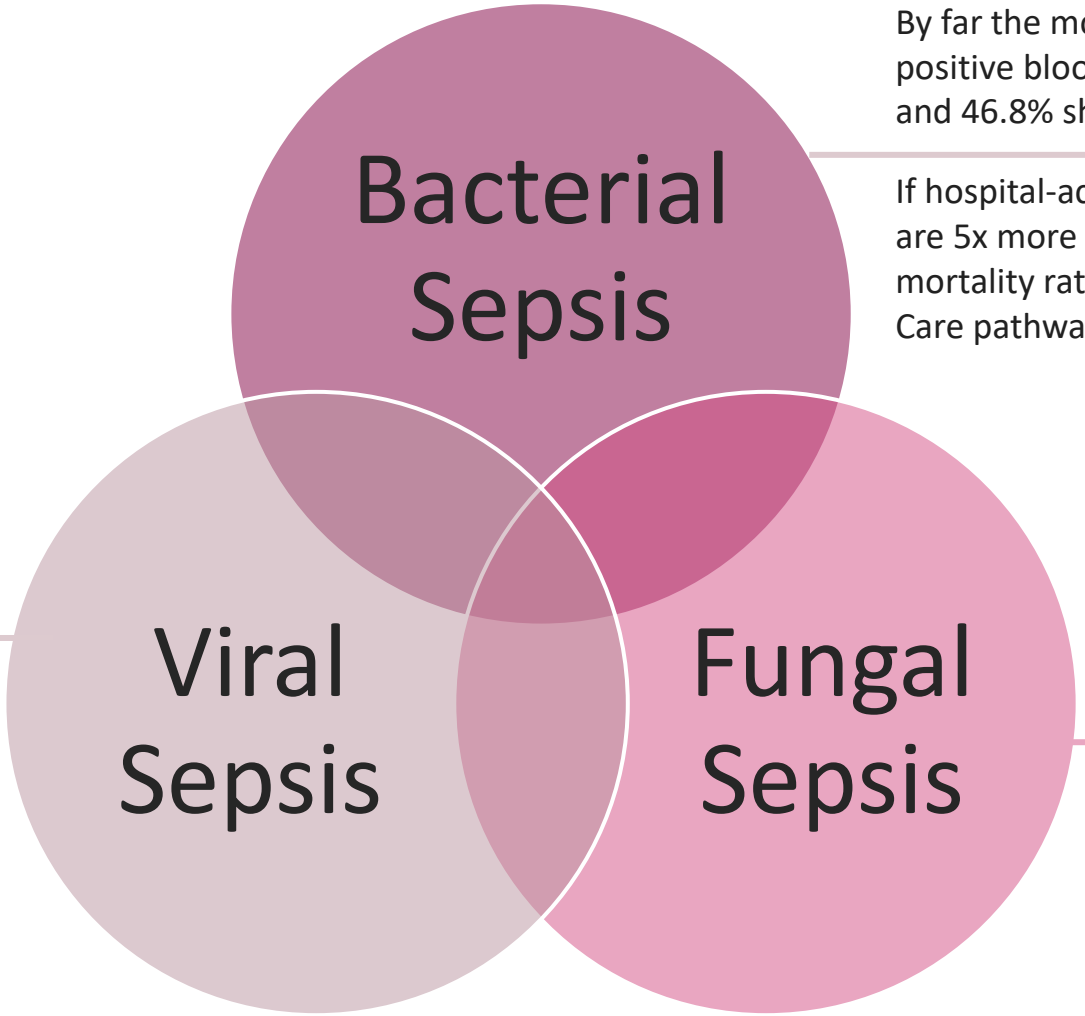
These cells interact with each other and can influence each other's activities to contribute to the cascade toward extensive organ damage.





Not all sepsis is bacterial…

Non-specific treatment may worsen outcomes



By far the most common cause, 62.2% of cases with positive blood cultures harbor Gram-negative bacteria and 46.8% show Gram-positive bacteria.

If hospital-acquired (HAS), especially if in the ICU, cases are 5x more expensive to treat and carry twice the mortality rate (19.2% vs 8.6%). The Sepsis Appropriate Care pathway is designed to treat bacterial sepsis.

Severe viral infections can cause septic syndromes functionally identical to bacterial sepsis. Most serious cases of viral sepsis occur in the very young or very old.

RSV is a major cause in vulnerable populations. In a 2020 study of 135 COVID deaths, 94% had a diagnosis of sepsis, often secondary.

Fast-growing and often lethal, 17% can be attributed to *Candida,* 2%-3% by *Aspergillus* or others. Almost always contracted in the hospital, systemic fungal infections often show a rash or exudate at the origin point.

Fungal sepsis has a mortality rate of 40%-60%, far higher than the 30% case-fatality rate of bacterial or viral sepsis, approaching or exceeding the 45% case-fatality rate of antibiotic-resistant hospital-acquired sepsis.

Differentiation of Fungal, Viral, and Bacterial Sepsis
Viral sepsis: etiology, pathophysiology, diagnosis, and treatment
Pathogenic sepsis etiologies

Postoperative Sepsis

An estimated 25% of patients who develop postop sepsis will not survive

Per 2023 Patient Safety Indicators (PSI) benchmarks, 4.26 per 1,000 surgical discharges will develop postoperative sepsis - at MLH, our rate is slightly below that at 4.06.

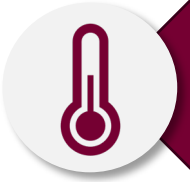
Surgical site infections (SSIs) caused by bacteria is considered an infected wound any time from 2 to 3 days after surgery until the wound has healed

Most common bacteria associated with SSIs include Staphylococcus, Streptococcus, and Pseudomonas

Characteristics increasing the risk of postop sepsis include:

- Being male
- Being aged 45 or older
- Having a low income
- Having splenic surgery
- Having chronic renal disease
- Having cardiovascular dysfunction
- Having organ system dysfunctions

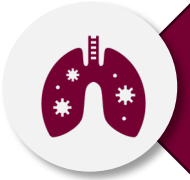
Preventing Postoperative Sepsis:



Assess: Be attentive to identifying signs of sepsis prior to surgery start.

Prophylaxis: Ensure appropriate timing of antibiotics prior to incision.

Protect the wound: Ensure pristine care of any incisions postoperatively.



Prevent pneumonia: Coughing and deep breathing, incentive spirometry, good oral care, elevate head of bed, and ambulate.

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AHRQ Quality Indicators - Sepsis, 2023

NIH: Postoperative Sepsis

There may be different presentations in children

It is important to be attuned to differing symptoms so you can respond quickly

WHAT ARE THE SYMPTOMS OF SEPSIS?

SYMPTOMS IN CHILDREN	SYMPTOMS IN ADULTS
A child may have sepsis if he or she: ▪ Is breathing very fast ▪ Has a 'fit' or convulsion ▪ Looks mottled, bluish, or pale ▪ Is lethargic or difficult to wake ▪ Feels abnormally cold to touch ▪ Has a rash that does not fade when you press it	An adult may have sepsis if they show any of these signs: **S**lurred speech or confusion **E**xtreme shivering or muscle pain **P**assing no urine (in a day) **S**evere breathlessness **I**t feels like you're going to die **S**kin mottled or discolored

The UK Sepsis Trust

American Thoracic Society:

Antibiotics and IV fluids are two of the most important treatments for sepsis. Studies have shown that any delay in a patient receiving the right antibiotic **doubles the risk of death**. Patients are generally started on an antibiotic that treats many different types of bacteria until test results are available to help the physician identify a specific bacteria that is causing the illness - 'narrowing antibiotics'. While preliminary results for the cultures for blood, urine, or phlegm could be available within 24 to 48 hours, a final result often takes several days.

American Thoracic Society

Understanding progressing stages of the Sepsis Cascade

Rapid intervention is crucial to effectively halt progressive of the cascade

FIRST STAGE: SEPSIS

Your immune system overreacts to an infection.

Infection + two or more symptoms:

- Abnormal temperature (↑ or ↓)
- Mental status change
- Extremely ill – short of breath, severe pain, feeling of doom)
- High heart rate
- High respiratory rate
- White blood cell count (↑ or ↓)

SECOND STAGE: SEVERE SEPSIS

Severe sepsis occurs once organs begin to malfunction.

Infection + Sepsis + Organ Damage:

- Hypotension
- Hypoperfusion
- Decreased urine output
- Sudden changes in mental state
- Decreased platelet count
- Difficulty breathing
- Abnormal heart pumping function

THIRD STAGE: SEPTIC SHOCK

Severe Sepsis with drop in blood pressure to dangerous levels.

Severe Sepsis + Severe Hypotension

- Most difficult to treat
- Requires treatment in the ICU

Time is critical to stop the progression…

Risk of progression to Septic Shock and death rises by 4% to 9% for every hour treatment is delayed.

2006: Methodist North & IT developed the MLH Sepsis Alert

Systemic Inflammatory Syndrome (SIRS) provides early warning of the potential progression to sepsis

1 Assess for SIRS

Respiratory rate >20 bpm
Heart rate >90 bpm
Temp >38.3C or <36C
Lethargic, confused, agitated, or anxious
WBC >12,000 or <4000 uL

2 Assess for Organ Dysfunction

Lactate >2.0 mmol/L
SBP <90 or MAP >65mmHG
SBP decrease >40mmHg from baseline
Creatinine >2.0 mg/dl
Bilirubin >2 mg/dl
Platelets count <100,000
Lethargic, confused, agitated or anxious
INR >1.5 or aPTT >60 seconds
PaO2/FiO2 ratio <300
New increased O2 requirement to maintain SpO2 >90%

This was one of the nation's first electronic warning tools for severe sepsis

Other signs and symptoms can help determine a diagnosis

In addition to a sepsis alert, the following may help clinicians assess for sepsis

Inflammatory

- High white blood count
- Immature white blood cells in the circulation
- Elevated levels of plasma C-reactive protein
- Elevated procalcitonin (PCT)

Hemodynamic

- Low blood pressure
- Low central venous or mixed venous oxygen saturation
- High cardiac index

Organ Dysfunction

- Low oxygen level
- Low urine output
- High creatinine levels
- Coagulation (clotting) abnormalities
- Absent bowel sounds
- Low platelets in the blood
- High bilirubin levels

Tissue Perfusion

- High lactate in the blood
- Decreased capillary filling or mottling

While we had no definitive test for sepsis, elevated lactate along with inflammation is often a clue

Clinical evaluation for Sepsis, Severe Sepsis, or Septic Shock

Early diagnosis is essential for effective treatment to halt progression of the cascade

Evaluation should include:

- Place on continuous cardiopulmonary monitoring to allow close observation of vital signs
- Assess end-organ function and peripheral perfusion to evaluate progression on the sepsis continuum
- Mental status assessment or Glasgow Coma Scale evaluation
- Measure urine output
- Assess lactate/mixed venous saturation (with central lines)
- Complete blood count with differential (CBC-d)
- Cultures - blood, urine, tracheal (if intubated), wound, and urinalysis
- Adding C-reactive protein or procalcitonin may be helpful in differentiating between bacterial from viral
- Complete chemistry panel with liver function, DIC panel and an arterial blood gas may be also be helpful

Laboratory findings might include:	
Hyperglycemia	Glucose > 120 mg/dL
Leukocytosis or Leukopenia	WBC > 12,000/mm^3 or < 4000^3
Bandemia	Bands > 10%
C-reactive protein or procalcitonin	Results > 2 SDs above normal
Mixed venous saturation	Saturation > 70%
PaO2	FiO2 < 300
Pre-renal	Azotemia
Coagulopathy	INR >1.5 or Ptt > 60 sec
Thrombocytopenia	Platelets< 100,000/mL
Hyperbilirubinemia	Total Bilirubin > 4mg/dL
Lactic acidosis	> 2mmol/L

National Library of Medicine: Septic Shock

What is Sepsis Appropriate Care?

A collection of labs and therapies shown to improve outcomes is referred to as the Sepsis Bundle (SEP-1)
Sepsis Appropriate Care means all elements of the Sepsis Bundle are completed within defined timeframes

The **Severe Sepsis and Septic Shock Early Management Bundle (SEP-1)** is a quality measure defining evidence-best guidelines to follow when treating patients age 18 and over for severe sepsis or septic shock.

Components of the bundle include:

- Drawing blood cultures
- Administering broad-spectrum antibiotics
- Measuring lactate levels
- Infusing IV crystalloids
- Using vasopressors for fluid-refractory hypotension
- Reevaluating volume status

Code Sepsis Response Bundle Plan EKM

MLH has created an order set that includes each of these bundle elements.

Ordering this Bundle Plan will ensure that all components of appropriate care are included in the patient's treatment.

Care must be delivered **within 3 hours** to meet requirements of SEP-1 appropriate care.

Surviving Sepsis Campaign: Hour-1 Bundle

Initial Resuscitation for Sepsis and Septic Shock

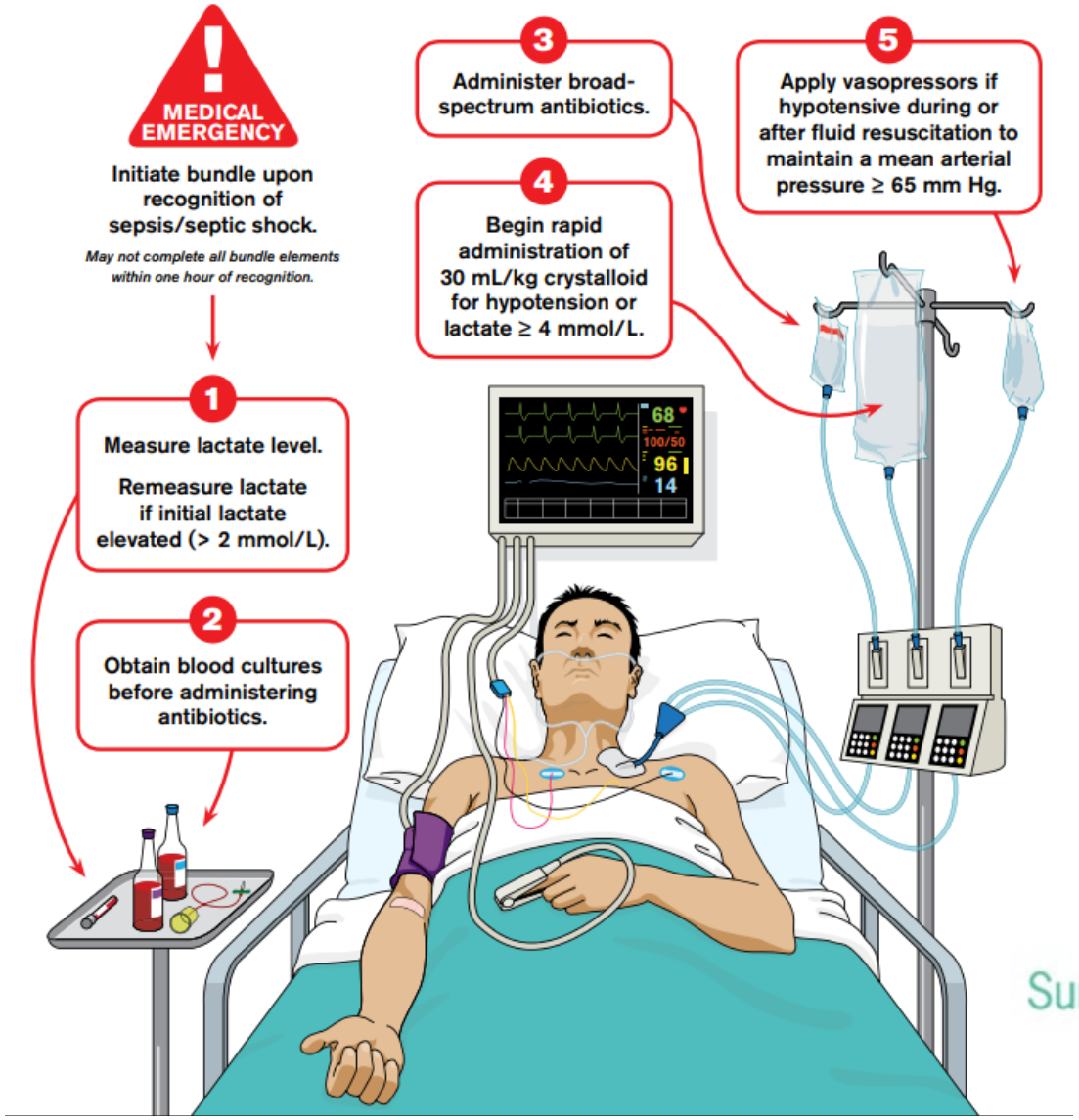
We've made it easy for you.

Medical Plan:
"Code Sepsis Response Bundle Plan EKM"

This treatment plan contained within this Sepsis Order Set contains each of these evidence-based elements of care.

The 'EKM' designation assures that labs won't be duplicated if already ordered.

We will have a similar order set in Epic…



Surviving Sepsis Campaign

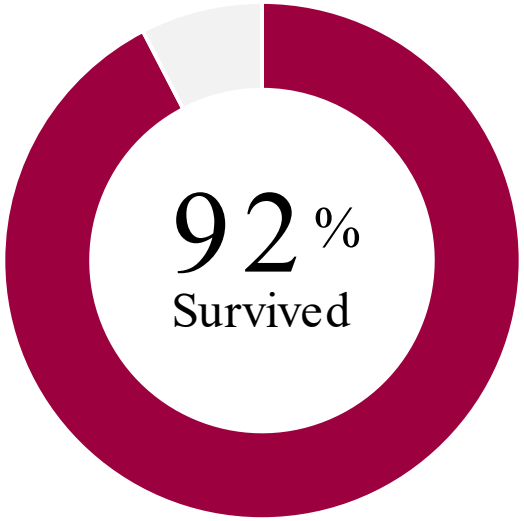
Society of Critical Care Medicine

Timely care delivery = improved outcomes

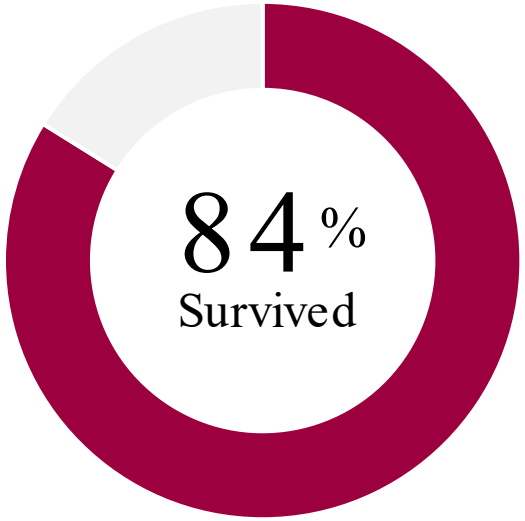
Complete use means not just ordering the Sepsis Bundle, but delivering all appropriate care within 3-6 hours

Mortality with SEP-1 compliance was **8%** compared to **16%** without

Met all SEP-1 guidelines



Gaps in SEP-1 guidelines



Sample of 1,611 abstracted patients at MLH adult hospitals diagnosed with severe sepsis or septic shock discharged between Jan-2023 and Jun-2024

SEP-1 BUNDLE: SEVERE SEPSIS/SHOCK UPON PRESENTATION:

TO BE COMPLETED WITHIN 3 HOURS:

1. Measure lactate level.
2. Obtain blood cultures prior to antibiotics.
3. Administer broad spectrum antibiotics.
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥ 4mmol/L.

TO BE COMPLETED WITHIN 6 HOURS:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain MAP ≥ 65mmHg.
6. In the event of persistent hypotension after initial fluid administration (MAP < 65mmHg) or if initial lactate was > 4mmol/L, reassess volume status and tissue perfusion.
7. Re-measure lactate if initial lactate > 2.0.

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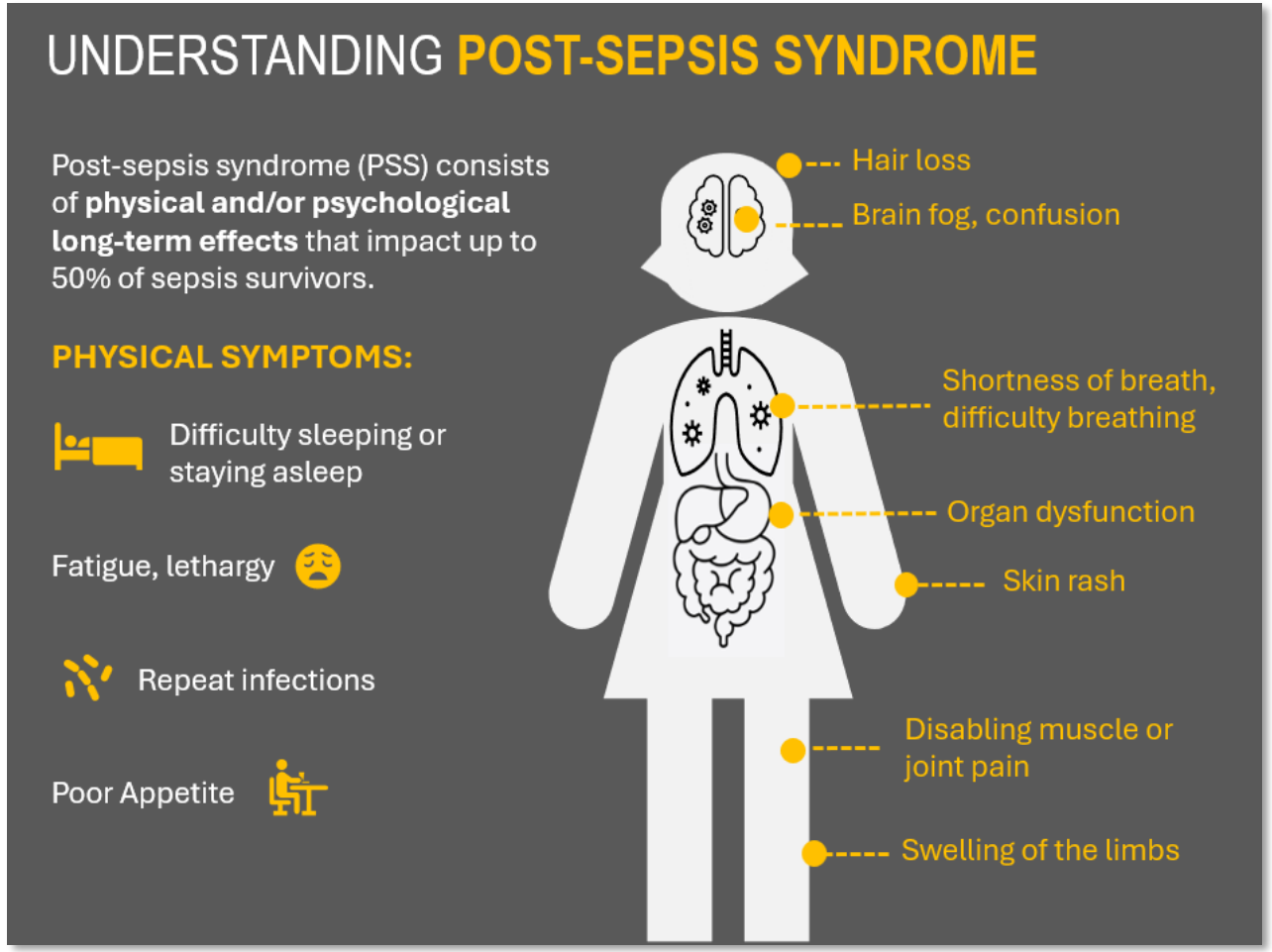
Source: MLH Sepsis Discharges

What happens after sepsis – Post Sepsis Syndrome (PSS)



Cognitive impairment:
44% of pediatric sepsis survivors experience cognitive difficulties after recovery, and one in six survivors have trouble concentrating, remembering things, and making decisions.

Pulmonary manifestations:
PSS can cause recurrent infections, chronic cough, breathlessness, and long-term lung damage.

Cardiovascular manifestations:
PSS can increase the risk of cardiovascular events like heart attack, stroke, arrhythmia, and heart failure.

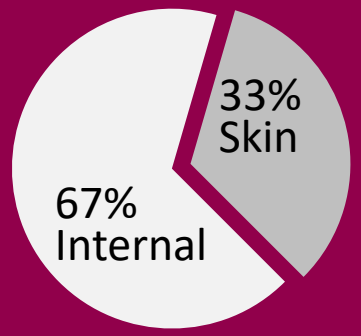
Rehabilitation therapies:
At 6 and 12 months after sepsis, 51.5% and 52.6% of survivors receive outpatient rehabilitation therapies, respectively, most commonly physical therapy (44.9%), occupational therapy (15%), and speech and language therapy (9.2%).

AAMC: Sepsis the third leading cause of death
Post-sepsis Syndrome: How can clinicians help?
Post-Sepsis Syndrome - an evolving entity

Another potential complication: Acute Skin Failure

It should come as no surprise - skin is the largest organ in the body

Circulating Blood Volume



The skin receives up to one-third of a body's circulating blood volume

In multi-organ failure from sepsis, blood is shunted away from peripheral tissue to continue blood flow to vital internal organs.

Acute skin failure (ASF) caused by hypoperfusion and ischemia related to hemodynamic instability can occur despite provision of high-quality skin care.

In a study of 400 patients[1], these factors were significantly and independently related to ASF:

- Sepsis (p=<0.001)
- Septic shock (p=<0.001)
- Impaired nutrition (p=<0.001)
- Mechanical ventilation (p=<0.001)
- Respiratory failure (p=<0.001)
- General surgery (p=<0.001)
- Orthopedic surgery (p=<0.001)
- Arterial disease (p=0.001)
- Peripheral necrosis (p=0.003)
- Renal failure (p=0.003)
- Vascular surgery (p=0.02)

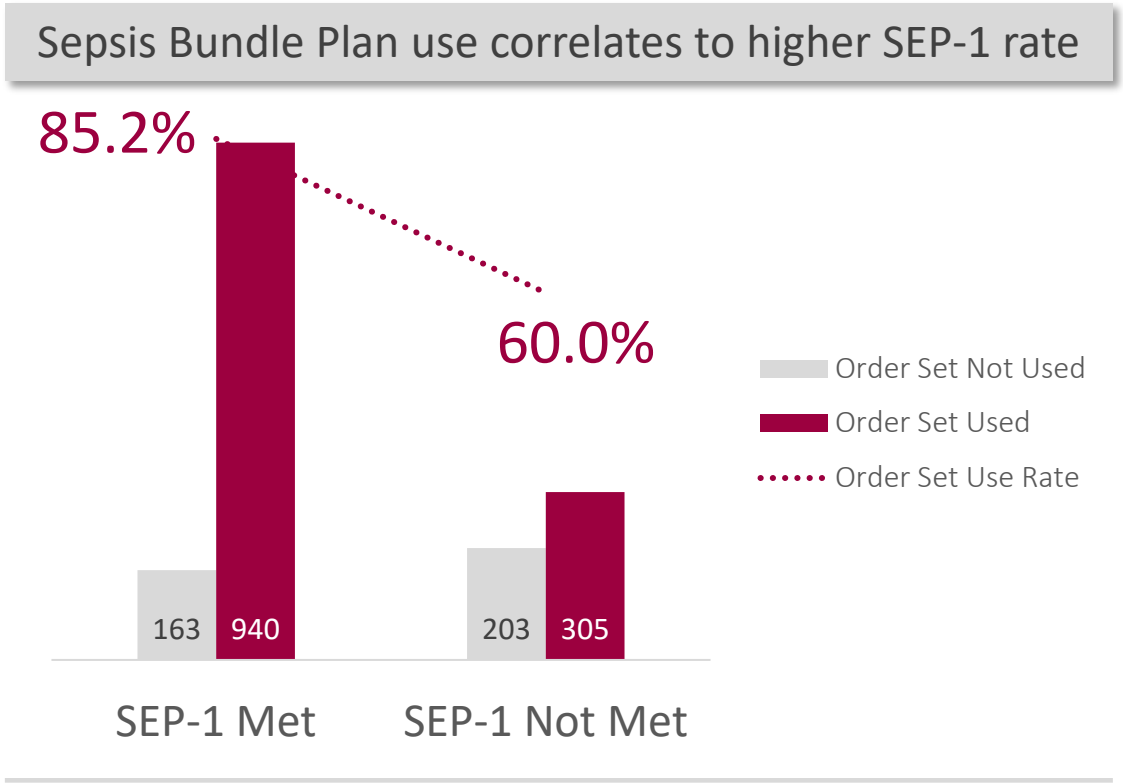
[1] *100 with hospital-onset pressure injury, 300 in control group*

MLH REIMAGINED

Acute Skin Failure in the Critically Ill Patient
Skin Failure: An emerging concept
Skin failure in patients with terminal illness

Easiest way to provide Sepsis Appropriate Care

Use of the Sepsis Order Set increases the patient's chance of receiving best practice care



MLH abstraction data, Jan-2023 to Jun-2024

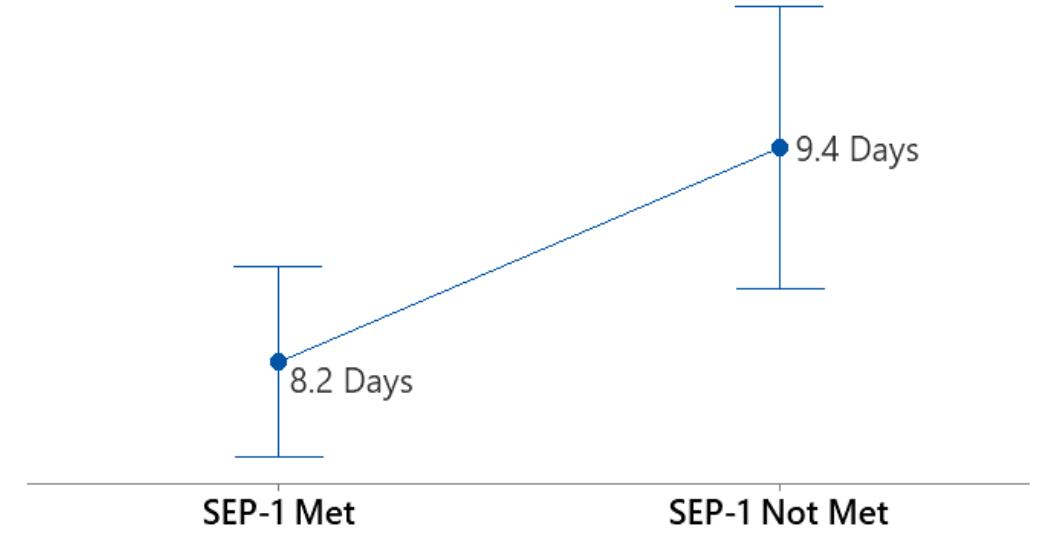
Source: MLH Sepsis Discharges

There is also an impact on hospital length of stay

Patients with a Sepsis Bundle ordered were discharged nearly 2 days faster than those without

Extended hospital stay seen if SEP-1 Criteria Not Met (Jan-2023 to Jun-2024, n=1611)

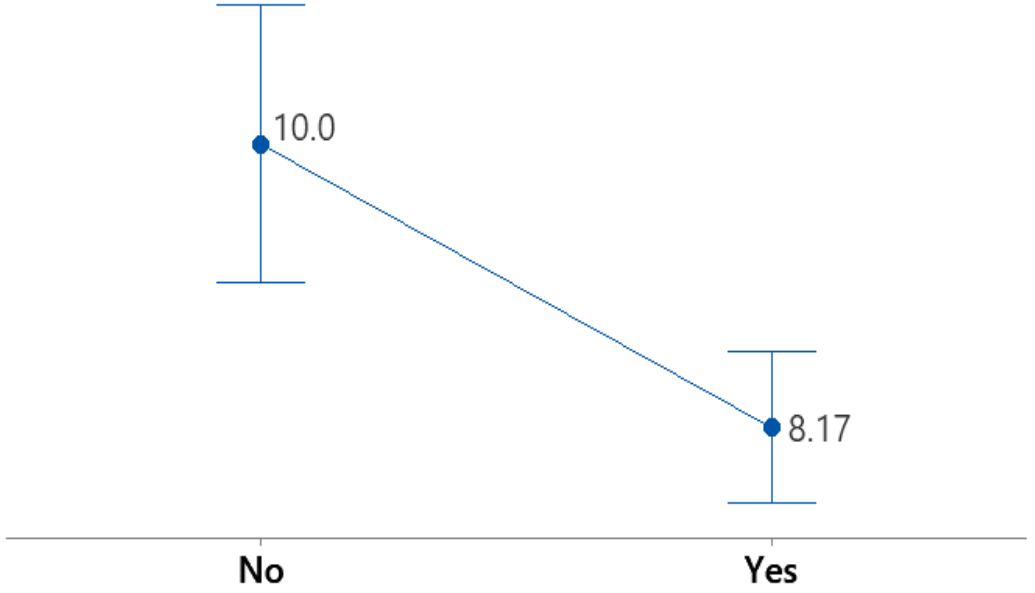
1.2 days longer



Statistically significant difference, p = 0.014

Stay is even longer if Sepsis Bundle is not ordered (Jan-2023 to Jun-2024, n=1611)

1.83 days longer



Statistically significant difference, p=0.000

MLH REIMAGINED

Source: MLH Sepsis Discharges

To recap: Sepsis Rescue is all about TIME

SEP-1 BUNDLE: SEVERE SEPSIS/SHOCK
UPON PRESENTATION:

TO BE COMPLETED WITHIN 3 HOURS:

1. Measure lactate level.
2. Obtain blood cultures prior to antibiotics.
3. Administer broad spectrum antibiotics.
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥ 4mmol/L.

TO BE COMPLETED WITHIN 6 HOURS:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain MAP ≥ 65mmHg.
6. In the event of persistent hypotension after initial fluid administration (MAP < 65mmHg) or if initial lactate was > 4mmol/L, reassess volume status and tissue perfusion.
7. Re-measure lactate if initial lactate > 2.0.

6.5%

Average increased risk of death every hour that care is delayed

80%

Septic shock deaths that might be prevented with earlier care

Rapid diagnosis and appropriate care saves lives!

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Thank You.