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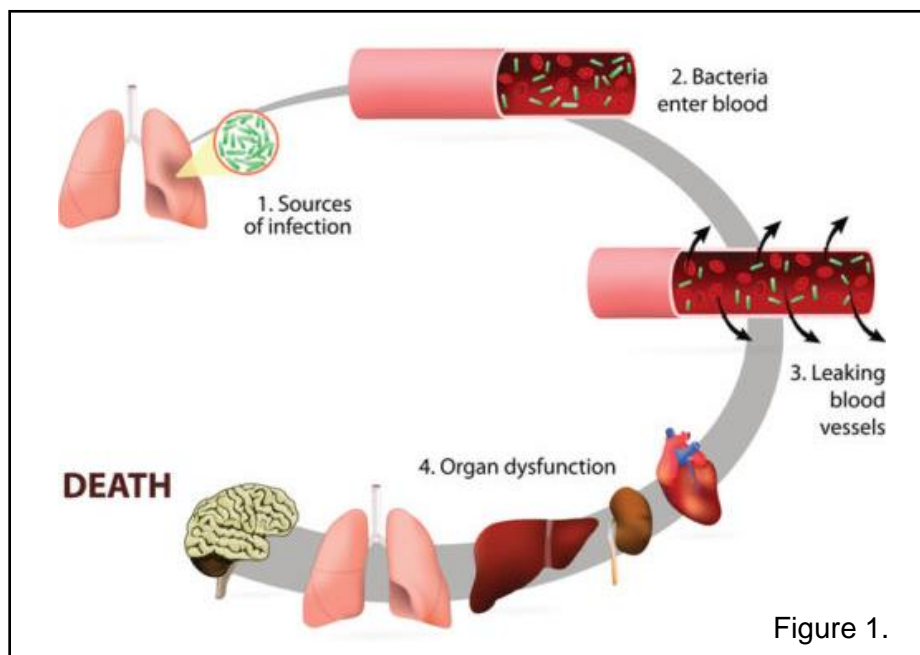
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Office of Integrated Health Health & Safety Alert/Information

Sepsis Health & Safety Alert

Sepsis Introduction

Sepsis is a life-threatening complication, which occurs when the body's immune response to infection causes damage to its own tissues. Sepsis involves a chain reaction starting with an existing infection, which enters the blood stream, and travels to the major organs (Figure 1). Sepsis can progress very quickly from a mild infection into a life-threatening situation, and serious damage to vital organs including the heart, lungs, liver, kidneys and brain can occur. If not treated aggressively in a timely manner, sepsis can lead to septic shock, multiple organ failure and death (CDC, 2019; Chriscaden, 2020). Sepsis can present with a variety of symptoms, making it difficult for healthcare professionals to recognize and diagnose immediately. Individuals who survive are at an increased risk for long-term physical and cognitive complications due to the damage caused by sepsis. Many survivors die due to underlying complications in the year following the sepsis event (Thompson et al., 2019; Chriscaden, 2020).



Prevalence

According to the CDC, 1.7 million adults in the U.S develop sepsis every year, leading to over 270,000 deaths. One in every three people who die in the hospital have sepsis (CDC, 2020). Around the world over 18 million people die yearly from sepsis, making it a global health priority and a major focus of The World Health Organization (WHO) (Prescott et al., 2019; Reinhart et al., 2017).

Each year, more people die from sepsis than heart attacks (myocardial infarction) or cancer (Daniels et al., 2020). Both community-acquired infections and infections contracted in the hospital (nosocomial infections) have the potential of developing into sepsis. The infection source itself may be bacterial, fungal, parasitic, or viral agents, but most often the underlying cause is bacterial (National Institute of Health, 2019). Antibiotic resistance is one of the main causes directly related to the increase in hospital-acquired sepsis cases (WHO, 2020).

Disparity Rates and Sepsis

Rates of sepsis are higher among individuals in lower-to-middle income communities. Wide healthcare gaps exist among nonwhites, almost double those of whites, due to social and economic disparities in combination with access to healthcare professionals and treatment facilities (Barnato et al., 2008). Individuals diagnosed with sepsis have longer hospital stays, including added time in the intensive care unit (ICU); more expensive medications; increased staff support and monitoring; and longer rehabilitation; all adding up to higher financial cost.

Individuals with severe sepsis have a greater risk of death (mortality), which can be lowered by timely, often expensive, treatments. Some research suggests patients without insurance are more likely to delay seeking care and may receive less intense treatment due to cost (Kumar et al., 2014). Many sepsis survivors are unable to return to their previous way of life ultimately making them more dependent on others to provide ongoing care (Daniels et al., 2020).

Individuals with Intellectual and Developmental Disability (IDD) and Sepsis

Individuals with IDD are at increased risk for developing sepsis due to their higher rate of hospital admissions (Ailey et al., 2014; Forman-Hoffman et al., 2015). In a study reviewing hospitalizations from 2011 to 2013, both hospital and community acquired sepsis was the third leading cause for death in individuals with IDD (Ailey et al., 2014). Forman-Hoffman's research on mortality rates of disabled individuals indicates individuals with any type of disability die at a much higher rate than individuals without a disability (Forman-Hoffman et al., 2015).

Due to their reduced immune response individuals diagnosed with a genetically linked developmental disorders, such as Down's syndrome, DiGeorge syndrome and/or Trisomy 21, are at an increased risk for developing infections and sepsis (Garcia et al., 2018; Huggard et al., 2018; Shires, Marger & Vyas, 2018).

IDD Individuals may need assistance from their caregivers to understand ways of preventing the spread of infection, such handwashing or practicing good overall hygiene. Caregivers should encourage regular daily hygiene practices, help individuals attend all physician appointments, report any physical or mental changes immediately, make sure individuals receive all recommended vaccinations, along with recognizing and diagnosing infection quickly to lower the in risk of developing sepsis (Sepsis Alliance, 2020).

Some individuals with IDD may have difficulty communicating how they are feeling physically. Communication limitations may prevent individuals from expressing early symptoms therefore caregivers should monitor them closely for changes in their physical or mental condition (CDC, 2020). This is especially important for individuals who are non-verbal. Caregivers should monitor these individuals more closely, and have them assessed by a physician immediately, if or when illness is suspected, so illness and infections can be treated quickly.

When scheduling an appointment with their PCP for an IDD individual be sure to state the urgency of the request. This is especially important for the individual who is medically fragile, who has other chronic conditions such as diabetes, lupus, cardiovascular disease, etc... If the individual has had any recent infections and or hospitalizations within the last few months, or if they have ever been diagnosed with sepsis in the past they should be seen by a physician right away. A previous diagnosis of sepsis, puts them at much higher risk for a recurrence.

COVID-19, Influenza, Pneumonia and Sepsis

A study on COVID and sepsis found that over 50% of patients with severe COVID cases also had sepsis (Spear, 2020). In a study of the COVID-19 cases in Wuhan, China in December 2019, of the 191 individuals diagnosed with COVID-19, 112 individuals were ultimately diagnosed with sepsis, and 54 (approximately 48%) of those individuals did not survive (Zhou et al., 2020). This study confirmed that age was a high risk factor as a predictor of mortality from COVID-19 along with higher Sequential Organ Failure Assessment score (SOFA) on admission (Zhou et al., 2020).

Much like COVID-19 and other viruses, such as influenza (flu) virus, can cause significant interaction with the immune system, which directly leads to a secondary bacterial infection and ultimately to sepsis (Florescu and Kalil, 2014). Therefore, more critically ill individuals with severe sepsis caused by influenza viruses, or COVID-19-induced secondary bacterial infections, such as pneumonia, are being admitted to hospitals worldwide. Any

individual diagnosed with COVID-19, influenza (flu) or pneumonia is at higher risk for developing sepsis.

Individuals with neurological disorders such as Epilepsy, Guillain-Barré Syndrome and Muscular Dystrophy, are some of the leading causes of disability and the second leading cause of death worldwide (GBD 2016 Neurology Collaborators, 2019). Neurological conditions make it difficult for individuals to physically create a productive cough and or to swallow secretions well. Individuals with neurological conditions, which may affect respiratory and muscle function, are at higher risk for developing pneumonia and or sepsis (CDC, 2020). With these individuals it can be difficult to tell when the common cold, flu or COVID-19 turns into a secondary infection, such as pneumonia and or sepsis.

Risk Factors

Anyone with an infection is at risk for developing sepsis. Bacterial infections are the most common types of infections associated with sepsis (CDC, 2016). Although other types of infections such as fungal, viral, and parasitic infections can also develop into sepsis (Cleveland Clinic, 2019). Infections, which are undertreated, and/or those infections being treated with the wrong medications will continue to grow within the body, and can quickly progress to sepsis.

- Respiratory infections in the lungs, such as those from bacterial pneumonia, aspiration pneumonia and Staphylococcus, places an individual at highest risk of developing sepsis (Gotts and Matthay, 2016; Thompson et al., 2018).
- Urinary tract infections and kidney infections are the second most common area of infection to develop into sepsis (Gotts and Matthay, 2016; Thompson et al., 2018).
- The gut and or intestinal tract infections are also a common area for developing into sepsis, due to Escherichia Coli (E.coli), and Enterococcus bacteria (Gotts and Matthay, 2016; Thompson et al., 2018).
- Soft tissue damage due to pressure injuries and/or cellulitis can both progress to sepsis. MRSA (Methicillin-Resistant Staphylococcus Aureus), and Streptococcus are frequently to blame (Gotts and Matthay, 2016; Thompson et al., 2018).

Other risk factors:

- Being less than < 1 year old (due to an underdeveloped immune system).
- Declining immune response in older adults, greater than > 75 years old.
- Having other chronic (long-term) health conditions such as diabetes, lung disease, kidney disease, heart disease, etc.

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- Individuals with weakened immune systems such as those with HIV/AIDS or lupus.
 - A diagnosis of cirrhosis of the liver due to increased alcohol consumption.
 - Individuals who have physical wounds, injuries, or burns.
 - Habitual cigarette smoking.
 - Hospitalizations due to surgeries or other invasive treatments.
 - Illnesses requiring admittance to an intensive care unit (ICU).
 - Anyone who has had a previous sepsis event is at increased risk of developing sepsis again (CDC, 2020; Gotts and Matthay, 2016; Thompson et al., 2018).

Signs and Symptoms

The following signs and symptoms indicate a medical emergency, especially if an individual has an infection and or if the individual is currently being treated for any type of infection. **The individual should be seen at the hospital immediately and or call 911 if an individual is experiencing: (Figure 2 & 3).**

- New mental confusion or extreme drowsiness.
- Shortness of breath, and or breathing very fast (hyperventilating), more than >20 breaths per minute.
- Increased heart rate - over >90 beats per minute or more.
- Fever of >100.1° F. and or greater.
- A temperature below normal, under <96.8° F. and or lower.
- Systolic Blood pressure (the top number) less than <90 mmHg (millimeters of mercury).
- Shivering and/or feeling very cold without relief.
- Extreme pain and discomfort.
- Clammy and or sweaty skin to the touch.
- Decreased urine output, possibly no urine output over 18 hours.
- Non-blanching skin rash, and or bluish discoloration of the skin (cyanotic) (O'Shaughnessy et al., 2017; Mayo Clinic, 2018; Daniels et al., 2019).

SYMPTOMS OF SEPSIS

S Shivering, fever, or very cold
E Extreme pain or general discomfort (“worst ever”)
P Pale or discolored skin
S Sleepy, difficult to rouse, confused
I “I feel like I might die”
S Short of breath



Watch for a combination of these symptoms. If you suspect sepsis, see a doctor urgently, CALL 911 or go to a hospital and say, “I AM CONCERNED ABOUT SEPSIS.”

SEPSIS.ORG

Figure 2.

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

T	I	M	E ™
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?”


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Figure 3.

Immediate Treatment and Care

The development of sepsis is a medical emergency and carries a high risk for death. Individuals with signs and symptoms of sepsis need immediate medical care at the hospital (Daniels et al., 2019; Thompson et al., 2018). Once at the hospital, physicians may order a variety of tests to help distinguish sepsis from possible other conditions. The sooner treatment is started for sepsis, the better chance an individual has of surviving (Martínez et al., 2020).

Starting in 2002, then updated in 2018, the global Surviving Sepsis Campaign (SSC) developed guidelines for assisting healthcare professionals to manage sepsis and severe septic shock. Called the “Hour 1 Bundle”, in reference to response time and diagnose of sepsis, it includes protocols for standardized treatment and care options to improve overall outcomes (Schorr, 2018; Daniels et al., 2019).

These guidelines set forth recommendations for testing and procedures for determining the bacterial source of the infection, detect inflammation, monitoring major organ function, indicate acid-base balance within the body, and blood oxygenation levels (Schorr, 2018; Martínez et al., 2020).

Overview of Critical Medical Care for Sepsis

Timing is everything when administering critical medical care to an individual with sepsis. If sepsis is suspected after the initial blood work is completed initial treatment should include the administration of a broad-spectrum antibiotic which are effective against many different types of infections, intravenous (IV) fluids, oxygen, and pain relievers (Schorr, 2018; Daniels et al., 2019; Martínez et al., 2020).

The amount and number of antibiotics administered to an individual during treatment for sepsis increases their chances of contracting antibiotic resistant pathogens such as MRSA, Vancomycin-Resistant Enterococci (VRE) and *Colostrum difficile* (C. diff) (Castano et al., 2019).

If sepsis continues to worsen into septic shock an individual may be moved into the intensive care unit (ICU) and put on mechanical ventilation to assist with breathing. They may receive insulin to normalizing blood glucose levels or given a blood transfusion to restoring red blood cells and fluid volume.

Other essential medical care might include the administration of vasopressors, such as norepinephrine or adrenaline, and or given a low dose corticosteroids. Anticoagulant therapy, such as heparin, may also be used to reduce the chance of deep vein thrombosis (DVTs) for individuals who are confined to a hospital bed for long periods of time (Thompson et al., 2018; Daniels et al., 2019).

Surgery may be needed to remove the source of the infection (Johns Hopkins, n.d; Mayo Clinic, 2018). Total parenteral nutrition (TPN) might be administered to those individuals who are unable to eat and drink on their own. Dialysis could be require if sepsis has caused serious kidney damage (Thompson et al., 2018).

Post-Sepsis Syndrome

Enduring the treatment for sepsis can mean an extended stay in the clinical-hospital environment. Suffering through all the treatments, procedures, medication effects and surviving sepsis is a traumatic life changing experience. Post-sepsis syndrome (PSS) is attributed to the trauma experienced during sepsis treatment.

The risk of having PSS is higher among people who have spent time in the intensive care unit (ICU). PSS can affect people of any age who have experienced sepsis, but older more severe sepsis survivors are at higher risk for long-term cognitive impairment and physical problems (Sepsis Trust, 2018; Prescott et al., 2019).

Once discharged, many sepsis survivors are readmitted to the hospital within 90 days of initial discharge with complications (Sepsis Trust, 2018; Van der Slikke et al., 2020). More than 50% of sepsis survivors have ongoing physical, emotional and or psychological long-term effects from their experience. Many individuals struggle to return to their post-sepsis life requiring increased levels of assistance with their activities of daily living (ADLs) such as bathing, dressing and eating (Van der Slikke et al., 2020).

Physical Symptoms of Post-Sepsis Syndrome (PSS):

- Lethargy and or excessive tiredness.
- Breathlessness and or chest pains.
- Poor mobility and or muscle weakness, possible contractors (muscle shortening).
- Swollen limbs (excessive fluid in the tissues).
- Joint and muscle pains.
- Changes in sensation in limbs, tingling and or numbness.
- Loss of self-esteem.
- Hair loss and or thinning.
- Dry and flaking skin and nails.
- Poor appetite and or a change in tastes.
- Changes in vision.
- Repeated infections from the original site or a new infection.
- Reduced kidney function.
- Feeling cold and/or cannot seem to warm-up, even when covered with blankets.
- Excessive sweating (Sepsis Trust, 2018; Prescott et al., 2019).

Emotional and Physiological Symptoms of Post-Sepsis Syndrome (PSS):

- Anxiety and or recurring fear of sepsis.
- Difficulty sleeping or difficulty getting to sleep, or staying asleep.
- Insomnia related to anxiety and fear.
- Panic attacks, post-traumatic stress disorder (PTSD).
- Depression.

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- Flashbacks.
 - Nightmares.
 - Hallucinations.
 - Difficulty concentrating.
 - Decreased cognitive (mental) functioning.
 - Short-term memory loss.
 - Mood swings (Sepsis Trust, 2018; Prescott et al., 2019; Van der Slikke et al., 2020).

Recovery from PSS can last between 6 and 18 months or longer depending on how traumatizing the experience was for the individual. Post-sepsis survivors may seek professional counseling and or join a support groups to deal with the emotional and physiological effects of PSS. Physical therapy is recommended to improve overall muscle strength in the first 3 months after discharge (Van der Slikke et al., 2020).

Everyone involved in the sepsis survivor's life, family, friends and caregivers, should be educated regarding sepsis, post-sepsis syndrome, and recovery to support the individual's wellbeing (Prescott et al., 2019). Sepsis survivors should keep all scheduled appointments and communicate any difficulties they are experiencing with their primary care physician (PCP). Sepsis survivors should attempt to live as healthy a life style as possible, to include a nutritionally well-balanced diet and regular exercise after discharge (Sepsis Trust, 2018; Prescott et al., 2019).

Prevention

Taking steps to prevent the spread of infection can reduce the risk of developing sepsis. Handwashing is the single most important thing everyone can do to reduce the spread of germs.

Taking antibiotics correctly reduces infections. Some of the main reasons for inappropriate antibiotic use includes failure to complete the dosing, skipping of doses, and the re-use of leftover medicines. When a physician prescribes antibiotics the first dose should be taken as soon as possible, then each dose after, as prescribed until the entire antibiotic is gone. If a dose is missed, you should take it as soon as it is remembered (Shehadeh et al., 2015). Call your local pharmacist, if you have any questions.

Antibiotics are meant to stay in the blood at a consistent level within the body for the recommended amount of days, in order to eliminate the bacterial pathogen, which is causing the infection. If consistent levels of antibiotics are not maintained within the blood the bacterial pathogen will not be effected and the infection will not be entirely eradicated. Then, when antibiotics are discontinued, the bacterial pathogen starts replicating again, and the process starts all over, causing the infection to recur and the individual relapses into illness once more. An individual should experience some relief of infection symptoms

within the first 24-48 hours after starting an antibiotic (Shehadeh et al., 2015). If the individual does not begin to improve, it is important to notify the prescribing physician. The antibiotic prescribed may not be killing the particular pathogen within the individual's body. A medication change may be needed.

If symptoms do not improve and or are not cleared after completing the antibiotics, notify the prescribing physician, and tell them the antibiotic is not working, so it can be changed to another more effective antibiotic. If you cannot reach the individual's prescribing physician, for whatever reason, you should take the individual to the Emergency Room (ER) or a freestanding urgent care facility as soon as possible for the individual to be re-assessed (Shehadeh et al., 2015; CDC, 2020).

If adverse side effects and or reactions appear, such as rash, nausea and or diarrhea, as a result of taking an antibiotic, notify the prescribing physician right away for guidance. Sepsis is a result of the body's immune system reacting to an infection which is either not being treated and or is being inappropriately treated. Taking the right antibiotic is an important way of reducing the chance of sepsis (Thompson et al., 2018; CDC, 2020).

Other sepsis prevention recommendations:

- Get vaccinations annually to include the flu, and pneumonia vaccinations. Check with the PCP regarding any other vaccine recommendations.
- Practice good physical hygiene by bathing regularly.
- Have all wounds cleaned and dressed properly in a timely manner.
- Maintain physical mobility to reduce weakness and prevent pressure injury.
- Eat a health well-balanced nutritious meals and snacks.
- Get a minimum of eight hours sleep at night.
- Incorporate meditation and or some other type of mindful practice daily.
- Keep regular medical appointments.
- Obtain immediate care when signs of infection are recognized and or other symptoms of major medical problem occur (Prescott et al., 2019; Van der Slikke et al., 2020).

Prevent sepsis and improve early recognition.



Improve health conditions.

George is a 72-year-old man with diabetes. During his check-up, George's healthcare provider takes the opportunity to strengthen his chronic disease care (glucose control and skin care), provide recommended vaccines, and share information about symptoms that indicate an infection is worsening or sepsis is developing.



Educate patients and their families.

One month later, George has a cut on his foot that might be infected. He calls his healthcare provider, who tells him how to take care of the cut and signs of infection. Two days later, his foot is worse and he becomes short of breath, has clammy skin, and is more tired than usual. He recognizes symptoms are worsening and it could be sepsis. He seeks medical attention immediately.



Think sepsis. Act fast.

At the hospital, a healthcare provider recognizes the signs and symptoms of sepsis. She immediately orders tests to determine the source of infection and starts appropriate treatment, including antibiotics. She documents the dose, duration, and purpose of antibiotics.



Reassess patient management.

Healthcare providers closely monitor George's progress and adjust therapy as needed. When George improves, his providers transfer him to a rehabilitation facility to continue his recovery. The hospital care team discusses his treatment plan with the team at the new facility.

SOURCE: CDC Vital Signs, August 2016.

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Resources

DBHDS:

If you have any questions about the information contained in this Health & Safety Alert, or need additional resources or support, please email your questions to the Office of Integrated Health's nursing team at: communitynursing@dbhds.virginia.gov

CDC - Get ahead of Sepsis:

<https://www.cdc.gov/sepsis/pdfs/Get-Ahead-of-Sepsis-Partner-Presentation-508.pdf>

CDC – Smart facts about Antibiotic use:

https://www.cdc.gov/antibiotic-use/images/AR_smartfacts_550x550_web.png

The World Health Organization:

<https://www.who.int/news-room/fact-sheets/detail/sepsis>

<https://www.who.int/health-topics/sepsis>

Printable Posters from the CDC:

<https://www.cdc.gov/sepsis/education/patient-resources.html>

Sepsis Alliance Fact Sheet:

<file:///C:/Users/dbk75942/Downloads/Sepsis-FactSheet-v2-4.pdf>

Sepsis Alliance:

<https://www.sepsis.org/>

Sepsis Alliance: Life after Sepsis Video

<https://youtu.be/Hlk64wdy44Q>

The Sepsis Trust

<https://sepsistrust.org/get-support/resources/>

References

- Ailey, S., Johnson, T., Fogg, L., & Friese, T. (2014). Hospitalizations of adults with intellectual and developmental disability in academic medical centers. *Intellectual and Developmental Disability*, 52(3), 187-192. Doi: 10.1352/1934-9556-52.3.187.
- Barnato, A. E., Alexander, S. L., Linde-Zwirble, W. T., & Angus, D. C. (2008). Racial variation in the incidence, care, and outcomes of severe sepsis: analysis of population, patient, and hospital characteristics. *American Journal of Respiratory and Critical Care Medicine*, 177(3), 279-284.

- Bridges, E., and McNeill, M.M. (2017, January). Research in review: Advancing critical care practice. *American Association of Critical-Care Nurses*, 26(1). 77-88. doi: <https://doi.org/10.4037/aicc2017609>
- Castano, P., Plaza, M., Molina, F., Hincapie, C., Maya, W., Catano, J., Gonzalez, J., Leon, A. and Jaimes, F. (2019, February). Antimicrobial agent prescription: a prospective cohort study in patients with sepsis and septic shock. *Tropical Medicine and International Health*, 24(2). 175-184.
<file:///C:/Users/ufb86645/Documents/Research%20Articles/Sepsis/Antimicrobial%20agent%20prescription%20a%20prospective%20cohort%20study%20in%20patients%20with%20sepsis%20and%20septic%20shock.pdf>
- Centers for Disease Control and Prevention (CDC). (2016, August). [Image] Vital signs. https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.cdc.gov%2Fvitalsigns%2Fsepsis%2Finfographic.html&psig=AOvVaw3M9_zE93TZG2kdSuVXGSse&ust=1608167211869000&source=images&cd=vfe&ved=0CAIQjRxqFwoTCIDDz6io0e0CFQAAAAAAdAAAAABAm
- Center for Disease Control and Prevention (CDC) (2019). What is sepsis?
<https://www.cdc.gov/sepsis/what-is-sepsis.html>
- Centers for Disease Control and Prevention (CDC). (2020). Antibiotic use questions and answers. <https://www.cdc.gov/antibiotic-use/community/about/should-know.html>
- Chriscaden, K. (2020, September). WHO calls for global action on sepsis – cause of 1 in 5 deaths worldwide. *The World Health Organization*. <https://www.who.int/news/item/08-09-2020-who-calls-for-global-action-on-sepsis---cause-of-1-in-5-deaths-worldwide>
- Daniels, R., Nutbeam, T., Sangan, V., Annakin, S., Matthews, L., & Jones, O. (2019). The Sepsis Manual, 5th edition. *United Kingdom Sepsis Trust*. ISBN: 978-0-9928155-0-9.
<file:///C:/Users/ufb86645/Documents/Research%20Articles/Sepsis/5th-Edition-manual-080120.pdf>
- Florescu, D. F., & Kalil, A. C. (2014). The complex link between influenza and severe sepsis. *Virulence*, 5(1), 137-142.
- Forman-Hoffman, V.L., Ault, K.L., Anderson, W.L., Weiner, J.M., Stevens, A., Campbell, V.A., & Armour, B.S. (2015, April). Disability status, mortality, and leading causes of death in the United States community population. *Med Care*. 53(4). 346–354.
Doi:10.1097/MLR.0000000000000321.
- García, H., Cervantes-Luna, B., González-Cabello, H., & Miranda-Novales, G. (2018). Risk factors for nosocomial infections after cardiac surgery in newborns with congenital heart disease. *Pediatrics & Neonatology*, 59(4), 404-409. <https://www.pediatr-neonatal.com/action/showPdf?pii=S1875-9572%2817%2930133-X>
- GBD 2016 Neurology Collaborators (2019). Global, regional, and national burden of neurological disorders, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet. Neurology*, 18(5), 459–480.
[https://doi.org/10.1016/S1474-4422\(18\)30499-X](https://doi.org/10.1016/S1474-4422(18)30499-X)
- Gotts, J. E., and Matthay, M. A. (2016, May). Sepsis. *British Medical Journal*, 353. 1-20.
Doi: 10.1136/bmj.i1585
- Heffner, A.C., Horton, J.M., Marc hick, M. R. & Jones, A.E. (2010, March). Etiology of illness in patients with severe sepsis admitted to the hospital from the emergency department. *Clinical Infectious Diseases*, 50(6). 814-820. <https://www.istor.org/stable/27799673>

- Herlitz, J., Bång, A., Wireklint-Sundström, B., Axelsson, C., Bremer, A., Hagiwara, M., ... & Ljungström, L. (2012). Suspicion and treatment of severe sepsis. An overview of the prehospital chain of care. *Scandinavian journal of trauma, resuscitation and emergency medicine*, 20(1), 42.
- Huggard, D., McGrane, F., Lagan, N., Roche, E., Balfe, J., Leahy, T.R., Franklin, O., Moreno, A., Melo, A.M., Doherty, D.G., & Molloy, E.J. (2018). Altered endotoxin responsiveness in healthy children with Down syndrome. *BMC Immunology*, 19(31). 1-10.
<file:///C:/Users/ufb86645/Downloads/Sepsis%20and%20Down%20Syndrome,%20Huggard.pdf>
- Johns Hopkins Medicine (2020). Bipap: What is Bipap?
<https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/bipap>
- Kumar, G., Taneja, A., Majumdar, T., Jacobs, E. R., Whittle, J., & Nanchal, R. (2014). The association of lacking insurance with outcomes of severe sepsis: retrospective analysis of an administrative database. *Critical care medicine*, 42(3), 583.
- Martínez, M. L., Menchaca, E.P.P., Rodríguez, J.C.R., Ferrer, R. (2020, January). An approach to antibiotic treatment in patients with sepsis. *Journal of Thoracic Disease*.
<http://dx.doi.org/10.21037/jtd.2020.01.47>
- Mayo Clinic. (2018). Sepsis: Overview. <https://www.mayoclinic.org/diseases-conditions/sepsis/symptoms-causes/syc-20351214>
- McKenna, M. (2013, April). Shock to the system. *Scientific American, a division of Nature America, Inc*, 308(4). 30-33. <https://www.jstor.org/stable/10.2307/26018063>
- Neto, A. S., Schultz, M. J., & Festic, E. (2016). Ventilatory support of patients with sepsis or septic shock in resource-limited settings. *Intensive care medicine*, 42(1), 100-103.
- O'Shaughnessy, J., Grzelak, M., Dontsova, A., & Alfano, I. B. (2017, July-August). Early Sepsis identification. *Med Surg Nursing*, 26(4). 248-252.
<file:///C:/Users/ufb86645/Documents/Research%20Articles/Sepsis/Early%20Sepsis%20identification.pdf>
- Prescott, H.C., Iwashyna, T.J., Blackwood, B., Calandra, T., Chlan, L.L., Choong, K., Connolly, B., Dark, P., Ferrucci, L., Finfer, S., Girard, T.D., Hodgson, C., Hopkins, R.O., Hough, C.L., Jackson, J.C., Machado, F.R., Marshall, J.C., Misak, C., Needham, D.M., Panigrahi, P., Reinhart, K., Yende, S., Zafonte, R., Rowan, K.M., and Angus, D.C. (2019, June). Understanding and enhancing sepsis survivorship priorities for research and practice. *American Journal of Respiratory and Critical Care Medicine*, 200(8). 972-981. Doi: 10.1164/rccm.201812-2383CP
<https://www.atsjournals.org/doi/pdf/10.1164/rccm.201812-2383CP>
- Reinhart, K., Daniels, R., Kisson, N., Machado, F. R., Schachter, R. D., & Finfer, S. (2017, August). Recognizing sepsis as a global health priority: A WHO resolution. *The New England Journal of Medicine*, 377(5). 414-417.
<https://www.nejm.org/doi/pdf/10.1056/NEJMp1707170?articleTools=true>
- Ryding, S., and Lois Zoppi, L. (2020). Figure 1: Sepsis complications and prevention. Image. *News Medical Life Sciences*. https://www.news-medical.net/image.axd?picture=2018%2F9%2Fshutterstock_299701700.jpg
- Schorr, C. (2018, September). Surviving sepsis hour 1 bundle. *American Nurse Today*. 13(9). 16-19.

<file:///C:/Users/ufb86645/Documents/Research%20Articles/Sepsis/Surviving%20Sepsis%20Campaign%20hour%201%20bundle.pdf>

Sepsis Alliance (2020) [Images] Figure 2 & Figure 3.

https://www.google.com/url?sa=i&url=http%3A%2F%2Fwww.covenanthome.care%2Fsenior-health%2Folder-adults-are-at-a-greater-risk-for-sepsis&psig=AOvVaw0eelOFWhWL-pCvSmMf8Nt-&ust=1607695937350000&source=images&cd=vfe&ved=0CAIQjRxqFwoTCJj8t5_Mw-0CFQAAAAAdAAAAABAK

Sepsis Trust (2018). Post-sepsis syndrome: The after-effects one cannot see. *Wound UK*, 14(5).

<file:///C:/Users/ufb86645/Documents/Research%20Articles/Sepsis/Post%20sepsis%20syndrome%20the%20after%20effects%20one%20cannot%20see.pdf>

Shehadeh, M.B., Suaifan, G.A.R.Y., & Hammad, E.A. (2015, March). Active educational intervention as a tool to improve safe and appropriate use of antibiotics. *Saudi Pharmaceutical Journal*, 24. 611-615. <http://dx.doi.org/10.1016/j.isps.2015.03.025>

Shires, P., Marder, E., & Vyas, H. (2018). G87 (P) A retrospective review of deaths in trisomy 21: a tertiary centre's experience since the millennium. *Archives of Disease in Childhood*, 103 (Suppl_1).

https://adc.bmj.com/content/archdischild/103/Suppl_1/A36.1.full.pdf

Thompson, K., Venkatesh, B., & Finfer, S., (2018, September). Sepsis and septic shock: Current approaches to management. *Internal Medicine Journal*, 49. 160-170. Doi:10.1111/imj.14199

Van der Slikke, E.C., An, A. Y., Hancock, R.E.W., & Bouma, H.R. (2020, October). Exploring the pathophysiology of post-sepsis syndrome to identify therapeutic opportunities. *EBioMedicine/Elsevier B.V.*, 61. 2-9.

<https://doi.org/10.1016/j.ebiom.2020.103044>

Van Kuiken, D. and Huth, M. M. (2016, January-February). What is "normal"? Evaluating vital signs. *Nephrology Nursing Journal*. 43(1). 49-58.

<file:///C:/Users/ufb86645/Documents/Research%20Articles/Sepsis/What%20is%20normal%20Evaluation%20vital%20signs.pdf>

Weissman, A. (2016, June). The laboratory's role in combating sepsis. *Medical Laboratory Observer*. 18-20.

<http://web.a.ebscohost.com/ehost/pdfviewer/pdfviewer?vid=9&sid=bd447ed0-080a-4f51-8670-fd3c07a75d4a%40sdc-v-sessmgr02>

World Health Organization (WHO). (2017, May). [Image] How to prevent sepsis.

<https://www.who.int/news-room/fact-sheets/detail/sepsis>

World Health Organization (WHO). (2020, August). Sepsis. <https://www.who.int/news-room/fact-sheets/detail/sepsis>