

SEPSIS  
DAN MUSE, MD

**INTRODUCTION:** The simplest way to look at sepsis is an infection that at some level overwhelms the body. Typically, infections are contained to one organ such as a urinary tract infection or a cellulitis. But, what happens if that localized infection escapes and spreads throughout the body? Now it is not just one part of the body that is infected by potentially the whole body. It is the equivalent of a nuclear meltdown with all bodily organs potentially affected. And similar to a nuclear meltdown, we must quickly contain and eliminate the spread of the infection or risk catastrophic disability and even death.

As long as there has been bacteria, viruses and fungi, there has been sepsis. Consider the many plagues of the middle ages, small pox, and of course, one we face every year; influenza virus. One hundred years ago 17 million military personnel and civilians died during World War I. In 1918 the “Spanish Flu Pandemic” infected 500 million people or one-third of the world’s population killing an estimated 50 million or one in ten of the infected people. In the United States, 675,000 died. As an aside, Fort Devens, Massachusetts may have been a “ground zero” for the epidemic. Today the influenza virus still wreaks havoc on the world. Vaccines have made a difference but, on the average, over 6000 people will die each year in the United States from the influenza virus.



Of course, this year has brought about a new pandemic in the Covid-19 virus. This virus has overwhelmed our healthcare system and wreaked havoc on our economies. It has also killed millions of people worldwide. The United States, the most advanced and powerful country in the world has seen over 12,000,000 cases and over a half a million deaths in just one year, due to an extremely poor response to the pandemic.

So, what does this all mean? Sepsis costs! It costs in lives along with lost and permanent disability of those infected. It costs in healthcare making up about 2 million US hospitalizations a year along with healthcare expenses of \$3 trillion dollars in 2014.

SEPSIS is an infection that can overwhelm the body's defenses. So why do some people become septic and others with the same infection don't? We know that there are certain risk factors that contribute to sepsis. All these deal with our immune system which is our internal defense system against infections. Exposure plays a large role in developing an immune system. We have to see it first or be vaccinated against it in order for our body to mount a defense. If the body has never seen the intruder i.e. bacteria, virus or fungus, it can't mount a defense against it and contain it. That is why kids constantly get sick when they are young, but the adult parents may be immune and spared. Why? Because you saw the virus when you were a kid and your body's immune system now protects you against it. This also means that the young, old, and those who have not been exposed to the infection are going to also be a group prone to getting ill and to potentially develop sepsis. Remember it was small pox that abolished the Inca nation and not the Spaniards weapons. Of course, the new worlds revenge on Europe was giving the old-world syphilis!

The obvious question is that if we have vaccines such as the influenza vaccine, how come it doesn't always work. The influenza virus has multiple strains and the vaccine is a "best guess" as to what strains will be most prevalent. If the vaccine is on target, it works very well. If it misses, people get sick!

Another at risk group is the elderly. As we age, our immune defenses break down. What was once a vigorous immune system now becomes fragile and susceptible. Secondary factors can also play a role such as malnutrition and immunosuppressive medications. In other words, the "golden years" is utter BS.

People with chronic diseases or temporary alterations to their immune system are also more susceptible to sepsis. Diabetics, HIV, people with rheumatoid arthritis and a whole lot of chronic collagen vascular diseases such as lupus inhibit the immune system. The loss of a spleen which occurs with sickle cell disease or due to trauma will also leave a person at risk. Pregnancy, cancer and post-operative patients along with those recovering from an illness could all be considered candidates for a temporary alteration in their immune system. Then of course there are the drugs taken chronically or temporarily such as prednisone, methotrexate, chemotherapy agents along with the litany of drugs advertised on TV that claim to control your RA or Crohn's disease but will cause TB and a slew of other infections.

We know now that the very young who are developing an immune system and the elderly who have declining immune systems are at risk for sepsis. It also makes sense that those with a compromised immune system caused by chronic disease or temporary changes in their health would be impacted. But, sepsis can occur to anyone. Why does it occur to young adults, even those with good health and strong immune systems?

Pathogens such as viruses, bacteria and fungi can disrupt our immune system and essentially prevent our body from mounting a defense against the offending agent. In other cases, the immune system gets weakened by one offending agent making it easier for another to overwhelm the body. An example of this would be the influenza virus attacking a young healthy twenty-year-old. The body is weakened by the flu and now allowing a superimposed pneumonia to overwhelm the body. We also know that our own immune system can go out of control where it now attacks our own organs. In a “cytokine storm” our own inflammatory agents run wild like an “angry mob” attacking our own organs allowing the offending agent to also inflict damage on our body.

**WHAT IS SEPSIS:** We have concluded that sepsis is an infection which is not limited to one part of the body but spreads throughout the body. The third international consensus task force defined sepsis as a ***“life-threatening organ dysfunction due to a deregulated host response to infection”***. Let’s put this in terms we all can understand. You get an email from someone and open it up. What you didn’t realize was that it had a “virus” attached to it. That “virus” now begins to target different parts of the hard drive causing it to malfunction. Before you know it, the “Virus” has incapacitated your accounts and is spreading via your contact list to all your friends. In the case of the human body, that pathogen entered through one organ but now has spread typically via the blood stream to other organs where it begins to incapacitate each organ’s ability to function appropriately. Ultimately a cascade of events occur that renders the body’s organs from appropriately doing their job. If the cascade is not reversed, the body dies!

What is causing sepsis? The obvious answer is an infection. The body has a “microbial invasion” into what is normally sterile tissue. Most parts of the body are sterile or “microbial free” and would include the bladder, skin, lungs, kidneys etc. Others, like the mouth and digestive tract have microbials that live within us and maintain a symbiotic relationship. So long as the microbes stay in the appropriate areas, there is no cause for infection. But if they move to a “sterile” area you will develop an infection. This occurs, for example, when bacteria in the intestines flows into the abdominal cavity after a perforation of the intestines.

So who are these “microbial” invaders? As mentioned before, bacteria, virus, fungi. If a “microbe” gets into the blood stream, it can spread to other organs. This process is defined as bacteremia, viremia and fungemia. As would be expected, the body is not going to go down without a fight. It has its own defenses, or immune system, and the first line of defense is the body’s “inflammatory response” to the microbial invaders. This inflammatory response is caused by cells whose specific purpose is to rid the body of the microbial invasion. Keep in mind that the “emia’s” or pathogens transported via the blood stream do not always lead to sepsis. It is however the first step in that direction.

**SEVERE SEPSIS** is when the deregulation or breakdown of the body’s organs occur. It is defined as sepsis with organ dysfunction, hypoperfusion or hypotension. All organs can be affected and the result is that those organs can no longer do their job which further sends the body down a spiraling cascade of auto-dysfunction with the end result being death.

**ORGAN DYSFUNCTION:** The body organs can't perform their normal function due to the spread of the bacteria, virus or fungus. Body's major organ functions. (The short version)

- Brain: Mental status and body regulation (the main frame).
- Lungs: Oxygen, carbon dioxide exchange
- Heart: Pumps blood
- Vessels: Regulates vessel size to maintain pressure and perfusion
- Kidneys: Filtration and fluid regulation.
- Liver: Mounts an immune response and filtration.

**IDENTIFYING SEPSIS:** Ever changing criteria have evolved that try to identify the septic patient. Like all these types of criteria, the goal is to come up with a system that overcalls the sepsis. It is the goal to capture as many cases as possible. If the criteria is too stringent, cases will be missed. It is therefore expected, especially by EMS, to have a low threshold to call a **SEPSIS ALERT** thereby assuring that as many cases of true sepsis are immediately brought to the attention of the emergency department medical staff.

**SIRS OR SYSTEMIC INFLAMMATORY RESPONSE SYNDROME** is presently the standard used in hospitals along with OEMS. It is the basis of your protocols as well. The criteria for SIRS are as follows with the patient **HAVING 2 OR MORE OF THE FOLLOWING:**

- Fever greater than 100.4 F
- Pulse greater than 90 ppm
- Respiratory rate greater than 20 per minute
- PaCO<sub>2</sub> less than 32 mm Hg
- Abnormal WBC count greater than 12k or less than 4k, or greater than 10% bands.

REMEMBER THAT SIRS DEFINES A SYSTEMIC INFLAMMATORY RESPONSE TO THE BODY. IT DOES NOT DIAGNOSE SEPSIS. Other etiologies can meet these criteria and cause a SYSTEMIC INFLAMMATORY RESPONSE:

- Ischemia: MI's, vascular occlusion. (White Counts were part of the criteria to diagnose MI's about 50 years ago.)
- Localized infection: Pneumonia, Cellulitis, UTI's.
- Inflammation: Auto-immune response: Arthritis, Lupus.
- Trauma.

Even non-inflammatory presentations can meet SIRS criteria. A panic attack can certainly have a tachycardia, elevated respiratory rate and low CO<sub>2</sub>.

If SIRS is nonspecific and identifies a potential inflammatory response to the body, how is it determined that the person is potentially septic? SIRS have to be used in the context of a possible infection. THEREFORE, **SEPSIS = 2 OR MORE SIRS CRITERIA + A DOCUMENTED OR PRESUMED INFECTION.**

**SEPSIS = AN INFECTION OR PRESUMED INFECTION HAVING 2 OR MORE OF THE FOLLOWING:**

- Fever greater than 100.4 F
- Pulse greater than 90 ppm
- Respiratory rate greater than 20 per minute
- PaCO<sub>2</sub> less than 32 mm Hg
- Abnormal WBC count greater than 12k or less than 4k, or greater than 10% bands.

**SEVERE SEPSIS**, as stated before, is sepsis with hypotension, hypoperfusion and/or end organ dysfunction. First, let's consider hypotension. We know that the blood pressure's job is to get oxygenated blood to the organs. Beside the red blood cells, the blood has cells that need to fight off the infection. If a person becomes hypotensive, the blood cannot reach all the organs. The brain, now has to decide what organs are indispensable and which ones can be discarded. In this case, the body "retreats" to its core and focuses on the major organs. It relinquishes the periphery which essentially are the extremities. This is why they become cool and lose capillary refill as the body delves deeper into a septic state. Ultimately, if the sepsis is not reversed, the core organs will also close down. So what are the "end organ dysfunctions" that can be affected?

**THE BRAIN:** Typically, there is a change in mental status (encephalopathy) which is thought to be due to hypo perfusion of the brain.

- Confusion
- Somnolence
- Lethargy

**THE LUNGS:**

- Exchanges O<sub>2</sub> for CO<sub>2</sub>. As the body becomes acidotic, the lungs increase the rate in order to try to remove as much CO<sub>2</sub> as possible so as to remove as much acid from the body as possible.
- May be the source of the original infection
- Vessels in the lungs get injured allowing for "leaking" of fluid from the vessels into the lungs.
- ARDS; Acute Respiratory Distress Syndrome: Is when the lungs fill up with fluid.

**THE HEART:** The heart tries to compensate for the vessels dilating and hypoxia.

- Have early high output compensation
- Heart muscle gets too "stretched out" and decompensates inhibiting its ability to contract.

**THE VESSELS:**

- Vessels dilate and result in hypotension
- Micro-vascular changes result in tissue and organs from getting oxygen and completing energy exchange and removal of CO<sub>2</sub>. This prevents the organs from functioning appropriately.

### THE KIDNEYS:

- Diminished flow and disruption to the kidney's filtration system results in diminished output and lack of filtration of impurities.

### THE LIVER:

- Liver assists in the defense against infection and clearing bacteria. "Shock Liver" prevents this process and results in an elevated ammonia and worsening encephalopathy.

**SEPTIC SHOCK:** Ultimately, the shock will set in if the body develops organ dysfunction. By definition it is defined as hypotension needing pressors to maintain a mean arterial pressure of 65 mm of Hg or a lactate greater than 2 after appropriated fluid resuscitation of 30 mls/kg of normal saline.

**PEDIATRIC SEPSIS:** As stated before, sepsis is an equal opportunity infection. Children, especially newborn and infants have immature immune systems and are susceptible to infections and sepsis. As they get older, vaccinations and exposures to different pathogens rev up their immune system. Physiologically, kids seem to fight hard early on but then seem to "crash and burn". I allude to it being like Wiley E Coyote running to the edge of the cliff. All seems well until he reaches the edge and then goes straight down.



Another issue is how to acquire the information. The very young can't speak and the older kids may have some reticence to even talk to anyone. In addition, they may not even understand what you are asking them. This means parents and care providers are the ones who will provide the majority of the health information and the history of the illness. What will help to determine the extent of the illness is information about immunizations, sick contacts and underlying health issues. Are they at risk for exposure? Do they go to daycare? Have they been immunized? Chronic diseases?

Vaccinations are extremely important in this age group. The Haemophilus Influenza vaccine has just about obliterated this bacterium in children, eliminating a major cause of pediatric illness and death. But lack of vaccination has left many susceptible. The CDC reported in June the following: “**June 8, 2018** – The CDC is reporting an additional pediatric flu-related death this week, bringing the total number this season to 172. This number exceeds the 2012-2013 season, which previously set the record for the highest number of flu-related deaths in children reported during a single flu season (excluding pandemics). Approximately 80% of these deaths occurred in children who had not received a flu vaccination this season.”

With kids, it is important to use your eyes and instincts. Does the kid look sick? Sometimes your parental and clinical instincts will let you know something is wrong. Kids are usually noisy. Does the kid look detached and quiet? Is the child, especially the new born and infant weak and/or floppy. Is there a rash? Most are viral, but some are indications of a bacterial infection.

**INITIAL ASSESSMENT OF THE PEDIATRIC CASE:** A child’s assessment is different from adults. The **change in mental status** can be detachment and diminished activity as opposed to confusion and lethargy. They seem to have shifting to the core rather quickly making **capillary refill** a necessary part of initial assessment. As well, always check for weak thready pulses along with age appropriated **hypotension**.

PEDIATRIC HYPOTENSION:

- Less than one month: Systolic less than 60 mm Hg
- 1 month to 10 years: Systolic less than  $70 + (2 \times \text{age in years})$ .
- Greater than 10 years: Systolic less than 90 mm Hg

**RECOGNIZING AND TREATING SEPSIS:** Recognizing sepsis by EMS is just as important, if not more so, as calling a STEMI alert! There are two million admissions for sepsis each year with 610,000 MI’s a year. In both cases the early recognition means more rapid intervention which leads to a better chance of reversing the process which in turn potentiates a better outcome.

Early recognition leads to early treatment. Sepsis is a downward spiraling cascade that if left unrecognized will lead to increasing chance of morbidity and death. Alternatively, early and aggressive intervention can potentially reverse the course and save the person’s life! For this reason, your ability to recognize **POTENTIAL SEPSIS** is as important as recognizing strokes and heart attacks. Furthermore, you already have the tools to do this. The **VITALS** are key to sepsis recognition. We overlook and at times downplay the severity of the vitals. In part we look at them individually instead of a whole. Early warning systems based on vitals have been used especially in Europe as a way to recognize decompensating adult and pediatric patients. In review of hospital cases with bad outcomes, invariably, downward trending vitals were almost always present and missed.

The early warning systems are all self-explanatory, come in adult and pediatric versions and best of all are on APP’s.



Chart 1: The NEWS scoring system

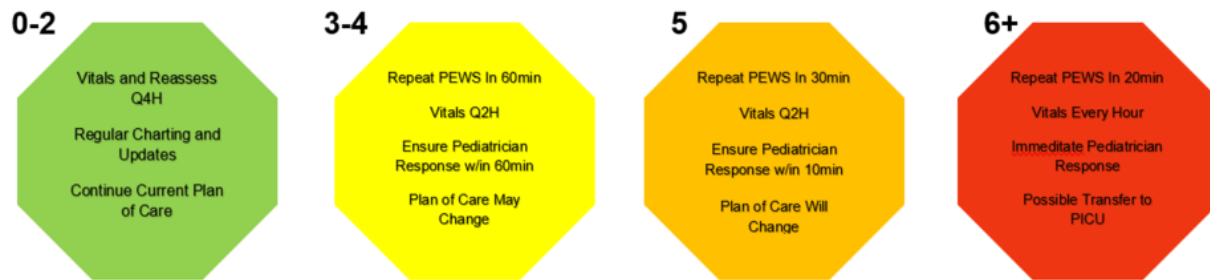
Physiological parameter	3	2	1	Score 0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO <sub>2</sub> Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO <sub>2</sub> Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

### PEDIATRIC EARLY WARNING SCORE

Table 1.1	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>Score</b>
<b>Cardiovascular</b>	Pink or capillary refill 1-2 seconds.	Pale or capillary refill 3 seconds.	Grey or capillary refill 4 seconds. Tachycardia of 20 above normal rate.	Grey and mottled or capillary refill ≥5 seconds. Tachycardia of 30 above normal rate or bradycardia.	
<b>Respiratory</b>	Within established baseline. No retractions Room Air	≥10 above established baseline. Mild Contractions Up to 2L/min or 30%	≥20 above established baseline. Moderate Contractions Up to 4L/min or 40%	≥30 above established baseline. Severe Contractions Grunting Up to 5L/min or 50%	
<b>Behavior</b>	Playing/Appropriate or Sleeping	Irritable, but Consolable	Irritable and Inconsolable Restless or Pain	Lethargic or Confused Reduced Response to Voice or Pain	
Score an additional 2pts for nebulizer use, suctioning, or persistent vomiting after surgery.					
<b>Total</b>					

Table 1.2	Retraction Severity	
<b>Mild</b>	<b>Moderate</b>	<b>Severe</b>
Subcostal or Substernal	Intercostal or Supraclavicular	Suprasternal or Sternal

## SCORE



Besides SIRS as a criterion for POTENTIAL SEPSIS, qSOFA is a quick and relatively effective screening tool. It relies on altered mental status or history of altered mental status, respiratory rate and blood pressure making it very easy to use and remember.

- qSOFA criteria for sepsis.
  1. Change in mental status from baseline.
  2. Systolic blood pressure less than or equal to 100
  3. Respiratory rate greater than or equal to 22.

SCORE OF 2 OR GREATER IS HIGH RISK FOR SEPSIS AND ICU ADMISSION.

Lactate, as already mentioned, is used to assess a person for sepsis. It has been trialed in ambulances but still is not in widespread use. The body has an elevation in lactate which begins when tissues, especially muscle, and organs become deprived of adequate amounts of oxygen. The tissue has to revert to anaerobic sources of energy and the by product is increased lactate. It is not however pathognomonic for sepsis. Post seizure, the patient will have a very elevated lactate that quickly clears. As well after exercising, the lactate is elevated. Medics however can check a patient for an elevated lactate by using an end-tidal CO<sub>2</sub>. End-tidal of 24 or less has been shown to correlate to a lactate of 4 or greater. So how does this work?

- An elevated lactate results in acidosis.
- The early response to tissue or metabolic acidosis is to breath fast (blow down the CO<sub>2</sub> to neutralize the acidosis)
- **A LOW CO<sub>2</sub> OF 24 OR LESS HAS CORRELATED WITH A LACTATE OF 4.**

**HYPOTENSION** is obviously a key component to septic shock. However does a blood pressure greater then 90 to 100 systolic actually equate with an adequate pressure? As mentioned earlier, the brain is the most vital organ. Our brain determines what we are and the rest of the body works for the brain. **MEAN ARTERIAL PRESSURE, MAP**, is a better measure of organ perfusion than systolic blood pressure. The mean arterial pressure of 65 mm Hg to 70 mm Hg is felt to optimize organ perfusion, including the brain.

Most of your monitors will also give you a MAP. For the geeks out there, the formula is as follows.

- MAP is measured by weighing the BP in thirds giving extra weight to the diastolic
- This is done because the pressure is in diastole twice as long as systole.

- $2(\text{diastolic}) + \text{systolic} / 3$

#### Example

- MEAN ARTERIAL PRESSURE (MAP)
  - $\text{MAP} = 2(\text{diastolic}) + \text{systolic} / 3$
  - PATIENT BP = 80/56
- $$\text{MAP} = (56 \times 2) + 80 / 3$$
- $$\text{MAP} = 112 + 80 / 3$$
- $$\text{MAP} = 192 / 3$$
- $$\text{MAP} = 64$$

**SUMMARY:** Not all POTENTIAL SEPTIC patients turn out to have sepsis. However it is important to recognize “sick” and act on it. It has been clearly demonstrated that early intervention into the septic process can reverse the course. Your recognition of a POTENTIAL SEPTIC patient provides an early warning to the hospital ER and also begins the process of EARLY FLUID RESUSCITATION which has been proven to help reverse the process.

### STATEWIDE TREATMENT PROTOCOL FOR SEPSIS

#### IDENTIFICATION OF POSSIBLE SEPTIC SHOCK

- Suspected infection – YES (DO THEY LOOK SICK?)
- Evidence of sepsis criteria-YES (2 or more):
  - Temperature less than 96.8 ° F or greater than 100.4 ° F
  - Heart Rate greater than 90 bpm
  - Respiratory rate greater than 22 bpm
  - Systolic BP less than 90 mmHg OR Mean Arterial Blood Pressure (MAP) less than 65 mm Hg
  - New onset altered mental status OR increasing mental status change with previously altered mental status.
  - Serum Lactate level greater than 4 mmol/l-(if trained and equipment available) -ETCO2 less than or equal to 25 mmHg

#### EMT STANDING ORDERS – ADULT & PEDIATRIC

- Routine Patient Care
- Notify hospital of incoming Sepsis Alert prior to arrival if applicable
- Supplemental oxygen to achieve SpO2 of 94%

#### EMT-INTERMEDIATE/ADVANCED EMT STANDING ORDERS - ADULT & PEDIATRIC

- Full ALS Assessment and treatment
- Large bore IV access (*PREFER 2*)
- IV 0.9% NaCl enroute: administer 500 ml boluses up to 30cc/kg  
Warning: assess lung sounds frequently to ensure volume overload does not occur.

- *Goal in suspected sepsis is rapid fluid resuscitation; 2 liters.*

**MEDICAL CONTROL MAY ORDER**

- **Norepinephrine** infusion: 0.1mcg/kg/min IV/IO by pump, titrate to goal Systolic Blood Pressure of 90mmHg, **OR**
- **Epinephrine infusion** 2-10 mcg/min IV/IO by pump
- **Dopamine** 2-20 mcg/kg/min IV/IO **OR**
- Additional Fluid boluses