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# Sepsis and Septic Shock

*Alaap Mehta, Ali Khalid and Mamta Swaroop*

## Abstract

Sepsis and septic shock are life-threatening conditions that remain an enormous burden of morbidity and mortality to millions of patients globally and cause organ dysfunction, leading to death in as many as one in four patients, often even more. Early management and appropriate treatment are essential to improve outcomes and reduce morbidity and mortality. In 2016, the Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) defined sepsis as *life-threatening organ dysfunction resulting from dysregulated host responses to infection*, and defined septic shock as *a subset of sepsis in which underlying circulatory, cellular, and metabolic abnormalities are profound enough to substantially increase the risk of mortality*. That same year the group also implemented the application of the sequential organ failure assessment (SOFA) score over the systemic inflammatory response syndrome (SIRS) score. Sepsis in pregnancy remains a leading cause of maternal morbidity and mortality worldwide, with no current standard definition for severe sepsis for the pregnant or peripartum woman. The prevalence of pediatric septic shock is on the rise and brings with it the consequences of long-term morbidity and also death. Since the advent of programs for early recognition and treatment, mortality has decreased. Even so, globally, many children succumb to septic shock despite evidence-based care and years of research.

**Keywords:** sepsis, septic shock, pediatrics, obstetrics, SIRS, SOFA, qSOFA

## 1. Introduction

Sepsis and septic shock are life-threatening conditions that remain an enormous burden of morbidity and mortality to millions of patients globally and cause organ dysfunction, leading to death in as many as one in four patients, often even more [1]. Early management and appropriate treatment are essential to improve outcomes and reduce morbidity and mortality.

Sepsis is a multifaceted disorder, developing from a dysregulated response by the host to an infectious nidus, and is associated with acute organ dysfunction and a high risk of mortality.

The incidence of sepsis is high, and remains one of the leading causes of death worldwide [2]. The reported incidence is increasing, which is likely a reflection on the older population with more comorbidities. Even though incidence is not known, estimates indicate that sepsis is a leading cause of morbidity and mortality globally. Even though sepsis is a deadly disease, data now shows the after effects of sepsis to be quite traumatic; often showing long term physical, physiological and cognitive disabilities [3].

Over the past 30 years, with the help of an extensive amount of research and better-quality clinical processes, the treatment and recognition of sepsis has

happened at a faster pace [2]. At the World Health Assembly in 2017, the World Health Organization (WHO) made sepsis a global health priority and passed a resolution to improve the prevention, diagnosis and management of sepsis [4].

In this chapter, we will examine the current definitions of sepsis and septic shock. We will explore the current guidelines in the diagnosis of sepsis. As we delve into the diagnosis, we will discuss the pathophysiology, clinical presentation, risk factors, etiologies, and finally, management strategies and treatments of the adult, pregnant and pediatric populations.

## 2. Sepsis and septic shock in adults

### 2.1 Definitions of sepsis and septic shock

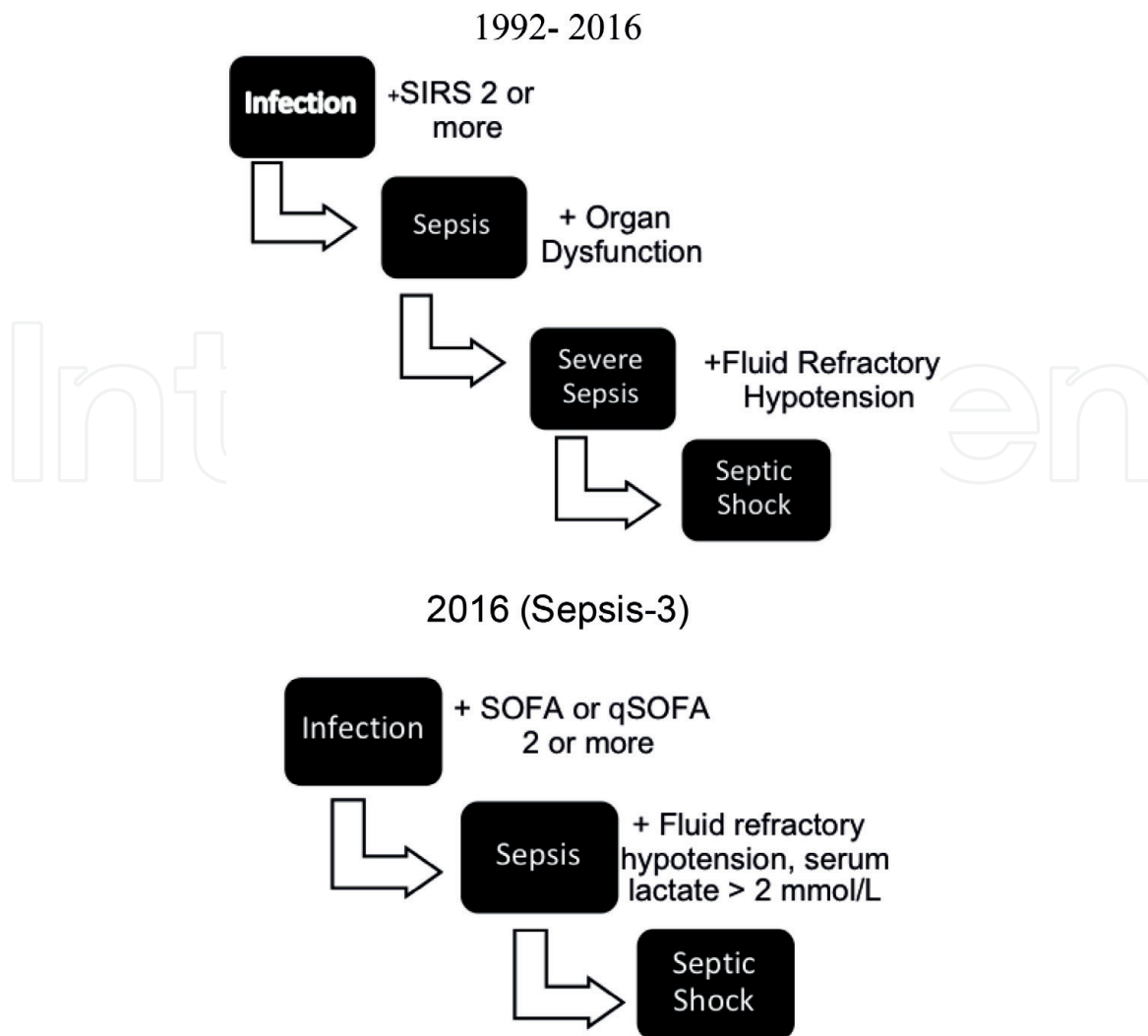
The first definition of sepsis, published in 1992, was based on the presence of a suspected or proven infection with two or more criteria of the systemic inflammatory response syndrome (SIRS) [5]. Sepsis was defined, as the presence of two or more positive SIRS criteria with a confirmed or suspected infection as the underlying cause. If signs of organ dysfunction were seen, the diagnosis was changed to severe sepsis. Septic shock was defined by the presence of acute circulatory failure and arterial hypotension along with features of sepsis. Until recently, the definitions of sepsis, septic shock and organ dysfunction remained the same for more than 20 years (**Figure 1**). Due to the inaccuracies of the past definition and the SIRS criteria, new guidelines were published by the surviving sepsis campaign (SSC) in 2016, a multidisciplinary task force started by the Society of Critical Care Medicine in the United States and the European Society of Intensive Care Medicine [6, 7]. Since there is no gold standard test for sepsis, the task force decided to come up with definitions and clinical criteria that were clear, useful, and valid [3]. Instead of using the SIRS criteria to determine if a patient is in going into sepsis, the new guidelines suggest using the sequential organ failure assessment (SOFA) score and a quick SOFA score for more emergent cases, a topic that will be discussed in length in the next section.

In 2016, the Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) defined sepsis as *a life-threatening organ dysfunction resulting from dysregulated host responses to infection*, and defined septic shock as *a subset of sepsis in which underlying circulatory, cellular, and metabolic abnormalities are profound enough to substantially increase the risk of mortality* (**Table 1**) [2]. Septic shock is also defined as *persisting hypotension that requires vasopressors to achieve a mean arterial pressure  $\geq 65$  mmHg despite adequate fluid resuscitation and a lactic acid level  $>2$  mmol/L* [7]. These new definitions focused on organ dysfunction rather than inflammation.

### 2.2 SIRS versus SOFA

The same task force that changed the definition also implemented the use of the sequential organ failure assessment (SOFA) score over the SIRS criteria. Even though SOFA is not considered the gold standard for diagnosis, its use is recommended over SIRS.

SIRS was based on an inflammatory response to an infectious inoculation (**Figure 2**). Throughout its utilization, the surviving sepsis guidelines, specifically the SIRS criteria, were widely criticized. Many thought the definition was not helpful largely because the definition place a large emphasis on inflammation,



**Figure 1.** Sepsis and septic shock definitions over the years [9]. Abbreviations: SIRS, systemic inflammatory response syndrome; SOFA, sequential organ failure assessment; and qSOFA, quick sequential organ failure assessment.

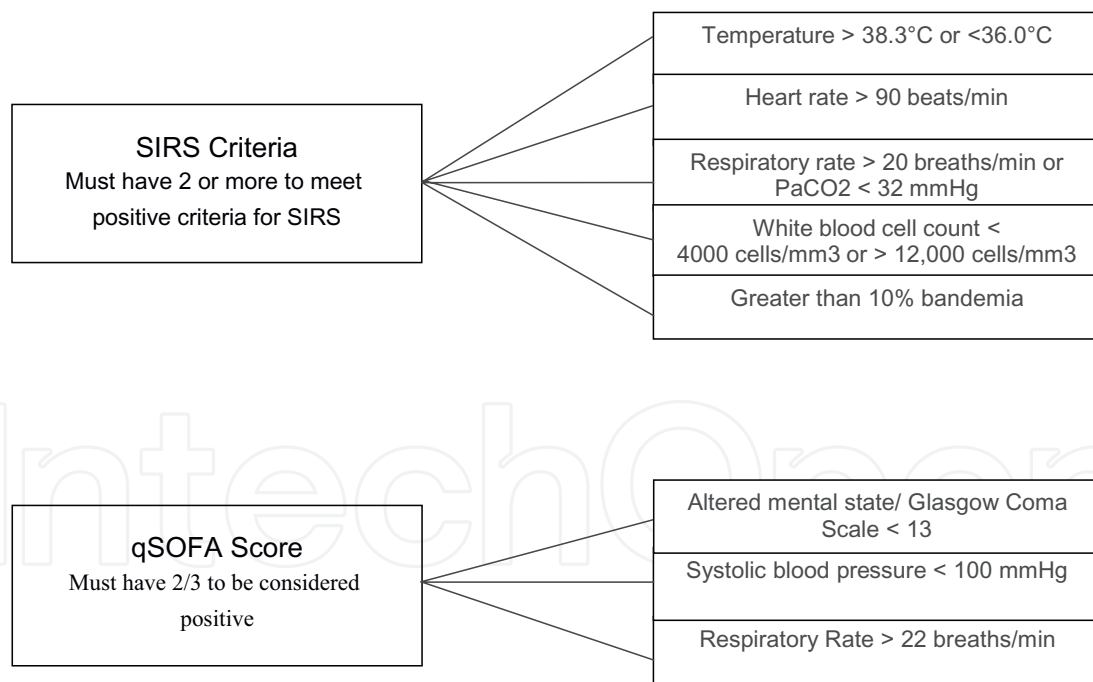
causing many patients without bacterial or viral infections to receive empiric antibiotic therapy and over-resuscitation [10]. The SIRS criteria were also thought to be remarkably sensitive, not taking into account any outside factors, multi-drug resistance and the ability to attain source control [3]. Based on the old definition of sepsis using the SIRS criteria, patients may have been incorrectly identified as being septic. One study showed a positive SIRS score in 87% of all ICU admissions, yet 14.3% of those with 2 or more SIRS criteria did not have infection [5, 7]. Moreover, in another study, 12.1% of patients had SIRS-negative sepsis, which is approximately a miss of 1 in 8 patients diagnosed with sepsis [11].

Due to these inaccuracies in the SIRS criteria, the new Sepsis-3 definitions recommend using the SOFA score; however, it is not commonly used or known outside of the critical care world [7]. The SOFA score is an aggregate score, from 0 to 4, for each organ system, including respiratory, coagulation, liver, cardiovascular, renal and central nervous systems [12]. An acute increase in the total score of 2 or more reflects an overall mortality risk in patients suspected of infection [7]. Calculating the SOFA score at the bedside or in a noncritical care unit and in patients who do not have full laboratory testing, is challenging. Since the SOFA score is based on biochemical criteria, the task force developed the clinical qSOFA screening tool which is based on respiratory rate, systolic blood pressure and altered mental state (**Figure 2**) [13]. If 2 of the 3 clinical variables

Sepsis-3 new terms and definitions
<ul style="list-style-type: none"> <li>Sepsis is defined as life threatening organ dysfunction caused by dysregulated host responses to infection.</li> </ul>
<ul style="list-style-type: none"> <li>Organ dysfunction can be identified as an acute change if you have <math>\geq 2</math> points on the SOFA score in relation to an infection</li> <li>Baseline SOFA score can be assumed to be zero in patients with no preexisting organ dysfunction and a score of <math>\geq 2</math> reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection.</li> </ul>
<ul style="list-style-type: none"> <li>Layman terms—sepsis is a life-threatening condition that arises when the body’s response to an infection injures its own tissues and organs.</li> </ul>
<ul style="list-style-type: none"> <li>Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be identified at the bedside with qSOFA (altered mental status, respiratory rate <math>&gt;22</math>, systolic blood pressure <math>&lt;100</math> mmHg).</li> </ul>
<ul style="list-style-type: none"> <li>Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are severe enough to increase mortality.</li> </ul>
<ul style="list-style-type: none"> <li>Patients with septic shock have preexisting sepsis with persisting hypotension requiring vasopressors to maintain MAP <math>\geq 65</math> mmHg and having a serum lactate level <math>&gt;2</math> mmol/L despite adequate volume resuscitation.</li> </ul>

*Abbreviations: MAP, mean arterial pressure; qSOFA, quick SOFA; SOFA, sequential [8] organ failure assessment; and ICU, intensive care unit.*

**Table 1.**  
Sepsis-3 terms and definitions [3, 6].



**Figure 2.**  
Comparison of SIRS versus qSOFA [7, 13, 15]. Abbreviations: SIRS, systemic inflammatory response syndrome; SOFA, sequential organ failure assessment; and qSOFA, quick SOFA.

are positive, the predictive validity is similar to the entire SOFA score when used outside the ICU setting [14].

### 2.3 Pathophysiology

Sepsis is a clinical syndrome with an array of disease courses of which is not completely understood. It is characterized by a varied response to infection, started



by recognition of pathogen associated molecular patterns (PAMPs) from invasive microorganisms [16]. PAMPs are conservative antigens that are recognized by four classes of receptors: Toll-like receptors, C-type lectin receptors, retinoic acid inducible gene 1-like receptors and nucleotide-binding oligomerization domain-like receptors [17]. Cell lysis and spillover of intracellular molecules into the extracellular space is seen due to the resulting inflammatory response to the pathogen. The net result is an increased capillary permeability and vasodilation leading to hypotension that results in tissue hypo-perfusion [16].

In sepsis, a hypercoagulable state is achieved due to the changes in the clotting factors. There is an increase of tissue factor which causes a decrease of anti-thrombin, subsequently causing an increase in plasma thrombin. At the same time there is decreased production of protein C and an increase in plasminogen activator inhibitor type 1 which all inhibits fibrinolysis. Increased coagulation and hypotension in sepsis can lead to multi organ failure, the most severe and life threatening consequence of sepsis [18]. During severe sepsis, and altered coagulation is almost always seen leading to disseminated intravascular coagulation (DIC). The mechanisms of how cell injury and sepsis-induced organ dysfunction occur are not fully understood and continue to be an ongoing investigation [2].

## 2.4 Etiology

Sepsis can be caused by any type of infecting organism and can originate from communities, hospitals or other health care facilities [2]. The most common culprit is pneumonia, which accounts for about half of all cases, followed closely by intra-abdominal infections and urinary tract infections [19]. The most common gram positive bacteria seen are *Staphylococcus aureus* and *Streptococcus pneumoniae*, whereas *Escherichia coli*, Klebsiella species, and *Pseudomonas aeruginosa* are the most common gram-negative bacteria seen [20].

## 2.5 Risk factors

Most risk factors for sepsis mainly rely on the patient's predisposition to infection. The main groups of patients are but not limited to; young or old age, patients with immunosuppressive diseases (e.g., AIDS) or ones taking immunosuppressive medications, cancer patients, alcoholics, patients with indwelling catheters, or other patients that have altered skin integrity all predispose them to infection [2, 21]. Age, sex, race, or ethnic groups have an influence on the incidence of severe sepsis. It is seen that sepsis mainly occurs in infants and elderly people, in males and African Americans rather than females Caucasians respectively [19, 22].

## 2.6 Clinical presentation

In sepsis, a person's response to an infection presents as signs of infection together with acute organ dysfunction, which can lead to multiple organ failure, acidosis, and death [21]. The clinical manifestations of sepsis varies, depending on the where the infection happens, the type of organism, the pattern of acute organ dysfunction, the health status of the patient, and what happens prior to initiation of treatment. Acute organ dysfunction is most commonly seen in the respiratory and cardiovascular systems. Respiratory compromise is classically manifested as acute respiratory distress syndrome (ARDS), which is defined as hypoxemia with bilateral infiltrates of noncardiac origin. Cardiovascular compromise is manifested primarily as hypotension or an elevated serum lactate level [18]. Patients often present to the emergency department with general malaise, fever, tachycardia,

tachypnea, or altered mental status. Health professionals should look at lactate levels, white blood cell counts (leukocytosis or leukopenia), increases in plasma C-reactive protein or procalcitonin concentrations to help determine if a patient is becoming septic [2].

## **2.7 Clinical significance of lactate production**

Lactate production in sepsis is multifactorial and incompletely understood. Most patients with sepsis and elevated lactate have a hyperdynamic circulation with adequate oxygen delivery. The source of lactate production is from the rapid rate of glycolysis and increased anaerobic production that does not always take place in the muscle, so other tissues/cells are possible major contributors. Its greatest utility is as a guide to therapeutic response, an indicator of severity, and a prognostic tool for mortality [7].

## **2.8 Management/treatment**

The management and treatment of sepsis and septic shock should be dealt with as a medical emergency. Screening patients for signs and symptoms of sepsis and septic shock helps to identify and intervene when needed [21]. Proper treatment should focus on when to intervene and being able to find the source of the infection. An important part of the initial management of sepsis is to make sure there is an aggressive assessment to identify unknown sources of infection using appropriate laboratory testing and diagnostic imaging [2]. In addition, early initiation of appropriate antimicrobial therapy after blood cultures have been taken, restoring tissue perfusion by administering the proper amount of fluids, and advanced interventions guided by assessment of the adequacy of resuscitation and resolution of organ dysfunction should be part of the initial sepsis management [21, 23].

The surviving sepsis campaign (SSC) issued guidelines for the management of sepsis and septic shock. It is divided into two sections: an initial management section and a management section. The initial management section indicates what to do within the first 6 h after the patient presents with signs and symptoms that imply sepsis, and the management section indicates what to do when the patient is transferred to the ICU. The main points of the initial management section is to make sure that cardiorespiratory resuscitation takes place and to make sure that the immediate threats of infection have been controlled. Intravenous fluids and vasopressors are used to resuscitate the patient and oxygen therapy and mechanical ventilation are used if needed [18]. For patients with hemodynamic instability, as defined by either hypotension (systolic blood pressure <90 mmHg, MAP <70 mmHg, or a decrease in systolic blood pressure of >40 mmHg from baseline) or elevated lactate concentration ( $\geq 4$  mmol/L), the SSC recommends rapid administration of 30 mL/kg crystalloid fluids started within the first hour [21, 24].

To determine the type of empirical antibiotic therapy needed, many factors are considered before choosing the initial therapy; the suspected site of infection, the setting where the infection developed, medical history, and local microbial-susceptibility patterns. There is an increased chance of death if the improper therapy is chosen or if there is a delay in treatment, so intravenous broad spectrum antibiotics should be started immediately to cover all pathogens until sensitivity of the blood culture comes back [25]. The 2017 SSC recommendations state that IV antimicrobials should be started immediately, the initial choice should be broad spectrum coverage and the antibiotic spectrum should be narrowed when pathogens have been isolated and sensitivities have been established. A decrease in antibiotic usage should be considered when the patient's condition improves [26].

Septic shock is a consequence of sepsis and one of the criteria to determine if the patient is in septic shock is if the patient is hypotensive and requires vasopressor therapy even if adequate fluids have been administered [27]. In patients with septic shock, vasopressor therapy is often needed to help maintain perfusion pressure [2]. The first-line vasopressor recommended in septic shock is norepinephrine, based on multiple randomized controlled studies and meta-analysis comparing dopamine and norepinephrine. Use of norepinephrine was found to be superior with regard to mortality and adverse cardiac events [28]. Epinephrine has potent inotropic and vasoconstrictive effects, but is less commonly used as a first-line agent in septic shock, which is typically associated with a hyperdynamic circulation [7]. Vasopressin reduces the dose of catecholamine vasopressors, but does not appear to affect patient mortality [2]. It is often used as a replacement dose after initiation of norepinephrine [29].

### **3. Sepsis and septic shock in obstetrics**

#### **3.1 Introduction**

Sepsis during pregnancy remains a leading cause of maternal morbidity and mortality worldwide [30]. In the USA, infection accounted for 14% and sepsis 4.3% of all maternal deaths between 2006 and 2010. In the UK between 2006 and 2012, genital tract sepsis accounted for 7% of all maternal deaths [8]. Even with advances in hygiene and antibiotic use, sepsis still accounts for 15% of maternal deaths a year worldwide. Due to inadequate resources and improper hygiene, it is mainly seen in low-income countries that maternal death is 3 times higher compared to high-income countries [31]. The failure to recognize sepsis and institute prompt treatment underlies most cases of maternal sepsis with poor outcomes. Pregnant women are at higher risk of developing infection due to the physiological changes that take place along with possible trauma and surgical interventions. These infections can go unnoticed until there is substantial clinical deterioration. The initial alteration of hemodynamics may be falsely attributed to labor pain or blood loss subsequent to delivery. Normal laboratory values in pregnant patients are different compared to the non-pregnant population. The definitions and criteria used to determine if a patient is in sepsis has not been fully investigated in pregnancy. There are currently efforts taking place to help implement early warning systems and revise the definition of sepsis to help diagnose sepsis earlier in a pregnant patient. It has been shown that early recognition, diagnosis and management of maternal sepsis lead to better maternal and fetal outcomes [9]. Overall, diagnosing sepsis in a pregnant woman can be very difficult due to differing normal values. In this section we will go over causes, clinical presentation, diagnosis and treatment for sepsis and septic shock during pregnancy.

#### **3.2 Definition of sepsis during pregnancy**

Compared to the non-pregnant population, there is currently no standard definition for severe sepsis for pregnant and peripartum women [32]. There are multiple physiological changes that occur in an obstetric patient during the antepartum and postpartum periods, which can make it difficult to identify if the patient is going into sepsis using the qSOFA scoring system.

#### **3.3 Identification and scoring systems in pregnancy**

Sepsis is something can occur at any time during one's pregnancy and can even happen during the postpartum period, something that everyone should be aware of [33].



During pregnancy, sepsis generally still follows the same rules versus a non-pregnant person, but it can be difficult to determine if a pregnant woman is in sepsis due to the changes in the baseline normal lab values seen; a non-pregnant patient's normal lab values are different compared to a pregnant patient's normal lab values. The physiological changes of pregnancy overlap with hemodynamic changes associated with the initial presentation of sepsis [9]. Before 2016, the SIRS criteria were the main source to diagnose a pregnant patient. The pitfalls with the SIRS criteria were that physiologic maternal lab values would almost result in a diagnosis of SIRS. During pregnancy, the maternal heart rate is often  $>100$ , usually due to intravascular volume changes,  $PCO_2$  is normally at 32–34 mmHg, and WBC commonly increases to 14,000 or even as high as 30,000, usually secondary to adrenocorticoid-mediated leukocytosis. After the Society of Critical Care Medicine redefined its criteria via the Sepsis-3 model, a qSOFA score was used instead of SIRS. As mentioned before, this score included three important points: altered mental status, hypotension (systolic  $<100$  mmHg) and tachypnea (respiratory rate  $> 22$ ). In terms of the qSOFA and SOFA score, there continues to be a struggle to reach a clear cut definition for pregnant patients. Due to their normal lab values, it makes it difficult to diagnose a pregnant patient with sepsis using the current definitions. For example, many patients have systolic blood pressures that are  $<100$  mmHg and they are in no distress or their respiratory rate will increase with movement due to the extra effort it takes because of the large uterus, mainly during the third trimester [15]. With that being said, the diagnosis of sepsis during pregnancy is currently being made based on clinical suspicion, with a greater emphasis on signs of organ dysfunction rather than infection when determining the timing of intervention [33].

In the last decade, there has been development of early warning scoring systems to help identify septic patients at risk for poor outcomes. Unfortunately, many of these systems have not shown much use in the maternal population, such as the Modified Early Warning System (MEWS). These systems do not take into account the physiological changes that occur during pregnancy, something that overlaps with clinical criteria for diagnosing sepsis in the general population. Even though there is a high recommendation to develop maternal warning systems, there has been clear evidence that shows a lack of outcome benefit and validation studies have shown high sensitivity but low specificity. There needs to be further work done to improve the ability of the early warning systems to improve their ability to predict those with signs of early sepsis and at risk of deterioration. A major factor, that is, delaying the development is deciding which vital signs to use and what values are a sign of normality in the obstetric population [9].

Due to the inconsistencies in defining maternal sepsis, there are delays in diagnosis and treatment, something that can prove to be deadly to the pregnant population [15].

### **3.4 Immunological changes during pregnancy**

During pregnancy, the maternal immune system will go through changes that will help protect the fetus from the maternal inflammatory response. There is downregulation of cell-mediated immunity, with decreased T-cell activity secondary to a decrease in numbers or reduction in the CD4/CD8 ratio, with an intact or upregulated humoral response to balance this change. Because of these changes, there is an increased chance to develop certain infections, such as Listeria, and more severe manifestations of some viral and fungal infections [34].

### **3.5 Risk factors of sepsis during pregnancy**

Several risk factors have been identified during pregnancy, leading to the development of guidelines to help prevent sepsis in this patient population [9]. There

are many reasons that sepsis can occur during pregnancy and postpartum. The pregnant woman can develop the same type of infections as in the non-pregnant population, but since there is a decrease in cell-mediated immune response, the infection can cause a more severe response. It is now routine to screen and treat asymptomatic bacteriuria and sexually transmitted diseases in early pregnancy and to administer antibiotic prophylaxis for cesarean deliveries [9, 35].

A woman can develop an infection at many sites during the course of her pregnancy. One common area is the genitalia, where urinary tract infections are very common due to the high levels of progesterone [32]. An untreated or improperly treated urinary tract infection can lead to pyelonephritis, a common severe infection that occurs during pregnancy. It usually affects the right kidney, because of compression of the pregnant uterus, with offending organisms similar to non-pregnant patients, *E. coli* being the major pathogen [32].

Chorioamnionitis is another cause of serious obstetric infection and is associated with increased risk of premature delivery and neonatal sepsis. The infection usually starts from the cervicovaginal area, and migrates to the amnion, decidua, and amniotic fluid. The infection is typically polymicrobial; commonly consisting of genital *Mycoplasma*, *Streptococcus agalactiae* and *Escherichia coli*. Risk factors for infection include prolonged labor, membrane rupture, digital vaginal examinations, young age, and alcohol use [32].

Pneumonia, which is associated with a high rate of morbidity and mortality compared to the non-pregnant population, may be caused by a bacterial, viral or fungal organism. The most common pneumonia pathogens seen in pregnancy are Varicella and Influenza A and B. Acute respiratory distress syndrome (ARDS) is a possible outcome due to respiratory infections in pregnancy [31].

Other risk factors include obesity, caesarean section, prolonged rupture of membranes, mastitis, poor nutrition, chronic hypertension, anemia, lack of prenatal care, immunosuppression, and diabetes mellitus [36]. All of these risk factors can cause sepsis and eventually lead to septic shock in the pregnant population.

### **3.6 Causative organisms of sepsis during pregnancy**

The major contributor to sepsis during pregnancy is group A streptococcus (GAS). It spreads directly through contact with open skin sores, perineal contamination or by mucus or droplet contamination. Group B streptococcus can cause urosepsis, endometritis, mastitis, wound infections and meningitis [37]. In urinary tract infections during pregnancy, *Escherichia coli* is the most common pathogen, and if left untreated, it can lead to sepsis. *S. aureus*, *E. coli*, and anaerobes are common causes of bacteremia after cesarean section. *Listeria monocytogenes* is more classically associated with fetal loss [31]. HIV, AIDS, *Pneumocystis carinii* pneumonia, tuberculosis, and malaria are significant causes for maternal sepsis in low and middle income countries [38].

### **3.7 Management and treatment of sepsis during pregnancy**

Even though the obstetric population were not specifically considered when the Surviving Sepsis Program were making the guidelines for treatment, those guidelines can still be used as a basis for treatment of sepsis and septic shock [21]. Early recognition of sepsis is associated with improved mortality and outcome. In a young, healthy pregnant patient, it may be difficult to identify sepsis and a delay in treatment may occur. With that being said a few warning signs to be considered that may alert severe sepsis include fever or hypothermia, tachycardia, tachypnea, diarrhea, vaginal discharge, leukopenia or leukocytosis, elevated lactate, metabolic acidosis, thrombocytopenia, or other manifestations of coagulopathy [39].

Pregnant women who develop sepsis are usually infected with multiple organisms. The initial choice of antibiotic should have broad spectrum coverage and base it off of guidelines and patterns of resistance [40]. The initial treatment should include coverage against Group A Streptococcus and *Escherichia coli* because they are the most common contributors to sepsis in pregnancy and responsible for a significant proportion of deaths [9].

In a septic pregnant patient, one big challenge is being able to manage fluids. The SSC guidelines recommend crystalloid at an initial 30 mL/kg bolus. This recommendation can be too aggressive in the obstetric population, but there is evidence that shows balanced crystalloid solutions are associated with a lower mortality in sepsis as compared to normal saline [42].

Vasopressors can be used in sepsis mediated hypotension and septic shock. If hypotension does occur, the surviving sepsis campaign (SSC) recommends norepinephrine as the first line agent. These SSC guidelines are based on evidence from non-pregnant patients and there is little data on the effect that vasopressors have on placental blood flow in a pregnant woman [9].

## **4. Sepsis and septic shock in pediatrics**

### **4.1 Introduction**

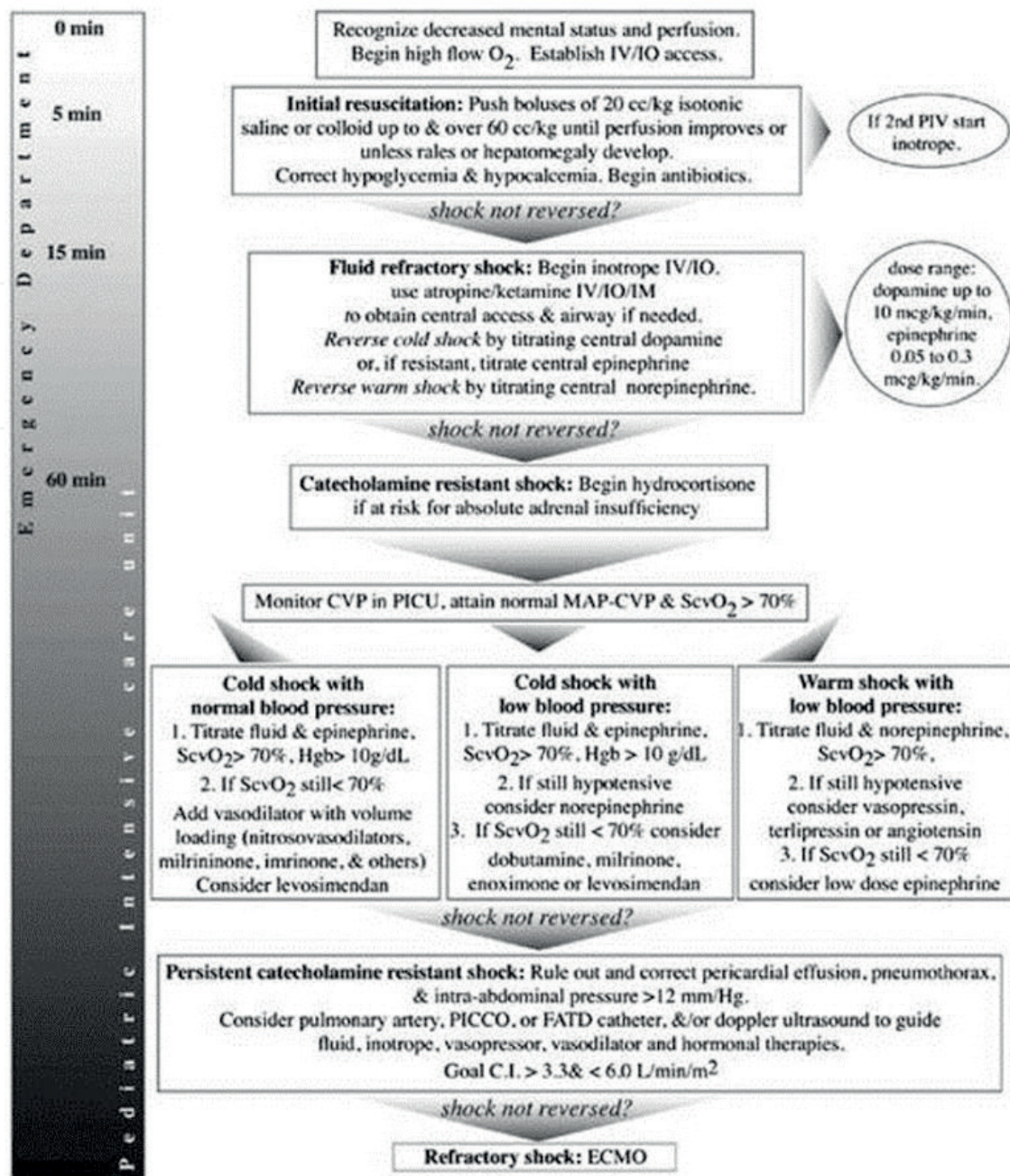
The prevalence of pediatric septic shock, causing death and long term mobility, has increased over the years, and prior to implementation of early recognition programs and treatment, mortality remained unchanged [43, 44]. Even with millions of dollars being spent and years of research being done, many children still suffer from septic shock [45]. Morbidity in children following severe sepsis is now similar to that in critically ill adults [46]. Due to the high rates of morbidity, mortality and costs associated with pediatric sepsis, there is an increased burden on healthcare communities [47]. As reported by Watson et al., pediatric sepsis patients had an average hospital stay of 31 days and about 2 billion dollars are spent a year for their care [48]. The mainstays of pediatric sepsis treatment, according to the international guidelines, is prompt administration of antibiotics, rapid resuscitation and supportive care of organ dysfunction [1].

Adults and children differ in physiology, predisposing diseases, and sites of infection which necessitates differing diagnostic criteria and management strategies [49]. Among children who develop sepsis worldwide, 49% have a comorbid condition that leaves them vulnerable to infection. The most common comorbidities in children who develop sepsis are age specific; infants have chronic lung disease or congenital heart disease, while children ages one through nine have underlying neuromuscular disease and adolescents have pre-existing cancer [50].

### **4.2 Diagnosis**

The definition of adult sepsis has undergone continuing revision to keep pace with the high volume of published research; however, it is only recently that attention has been given to the pediatric patient and the many caveats that separate the pediatric patient from the adult. Prior to 2005, there was not a standard definition for pediatric sepsis which resulted in a lack of uniformity among sepsis studies [49]. In 2005, the Pediatric Sepsis Consensus Congress (PSCC) met to standardize the definition of sepsis. Defining sepsis in the pediatric patient is made more difficult due to age specific vital signs, and their tremendous physiologic reserve which often masks the seriousness of their condition. The PSCC divided age into six distinct categories in order to take into account age specific vital signs as well as age specific





Reproduced from reference 8

Figure 3. Survive sepsis campaign pediatric treatment protocol [21].

risk factors for invasive infections which in turn affect antibiotic coverage guidelines [51]. Pediatric severe sepsis is defined as two or more systemic inflammatory response syndrome criteria, confirmed or suspected invasive infection, and cardiovascular dysfunction, acute respiratory distress syndrome, or two or more organ dysfunctions. Determination of altered physiology is specific to age dependent vital signs [49, 52]. At present, there is no single biomarker that has proven specific or sensitive enough to diagnose sepsis or prognosticate outcome in selected cohorts. Similar to studies of sepsis in adults, there is active research examining both clinical and research measurements applicable to a pediatric population [49].

### 4.3 Management

The current guidelines for treatment are summarized in the pediatric section of the surviving sepsis campaign (Figure 3) [49]. Early and aggressive source control

should be a top priority; this includes drainage, debridement, and surgical intervention. Empiric antibiotic therapy should be administered within 1 hour of clinical suspicion and can be administered IV, IM or PO; antibiotics should not be delayed for blood cultures but every attempt should be made to obtain blood cultures prior to the first dose of antibiotics. Fluid resuscitation should be aggressive and administered as boluses of 20 mL/kg crystalloid given over 5–10 min via intravenous or intraosseous access. Early and aggressive fluid resuscitation has been shown to decrease mortality [21].

## 5. Conclusion

Sepsis and Septic Shock continue to be a growing concern in the world. Even though there is no current gold standard to diagnose sepsis and septic shock, the new guidelines allow the healthcare professional to determine if the patient could possibly go into sepsis and septic shock. The new guidelines help identify sepsis at an early stage in the adult population, but still show concerns in the pregnant and pediatric population. Due to the different normal lab values in a pregnant patient, SOFA cannot be accurately used to diagnose a patient. Defining sepsis in the pediatric patient is made more difficult due to age specific vital signs, and their tremendous physiologic reserve which often masks the seriousness of their condition. Sepsis and septic shock can be very deadly and the health care professional should be aware of the determining factors in the non-pregnant, pregnant and pediatric populations.

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