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# Maternal sepsis

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ABSTRACT

Sepsis is a leading cause of maternal morbidity and mortality in developed and developing nations. Obstetric practitioners should be familiar with guidelines that promote the safe and expeditious recovery of those affected. This article will provide the reader with rational steps to aid in the recovery of such a patient.



## Introduction

Sepsis is a multisystem disorder that can cause end organ damage, multi-organ failure, and mortality induced by infection. Sepsis is a national health concern and is the leading cause of critical illness in industrialized countries and is the leading cause of maternal death worldwide.[1,2] In high income countries, mortality from maternal sepsis is relatively low at 17.3 mortalities per 100,000 live births it is steadily increasing.[3,4] In addition, maternal mortality continues to increase congruently with sepsis-related maternal deaths which is likely secondary to an increase in several risk factors (Table 1).[5] Despite an increased mortality, parturients still have favorable outcomes when compared to non-pregnant patient's likely secondary to overall much younger age, fewer comorbidities, focused site of infection, and low resistance to antimicrobial therapies.[6]

Along with risk factors stated in Table 1, sepsis also has compounds maternal physiology. Sepsis is a disease with a cardiovascular consequences high cardiac output and low systemic vascular resistance.[6] This is already compounded by a physiologic maternal hyperdynamic state along with loss of afterload. There is also a hypoalbuminemia and loss of intravascular oncotic pressure. These factors can culminate in more needed intravascular resuscitation, which could result interstitial edema (pulmonary edema, skin swelling, etc.).

## Defining and diagnosing maternal sepsis

A consensus definition was created in 1992 with revision in 2013 by the Surviving Sepsis Guidelines created by the Society of Critical Care Medicine.[7,8] The organization defined the disease process into 4 separate entities: systemic inflammatory syndrome (SIRS), sepsis, severe sepsis, and septic shock. SIRS was defined as an inflammatory response to the infectious inoculation further defined in Table 2. Sepsis was defined as the meeting at least two SIRS criteria and with a known source for infection. Severe sepsis was defined as sepsis with organ dysfunction such as acute kidney injury, altered mental status, or thrombocytopenia to give a few examples. And finally, septic shock was defined as a known source of infection with hypotension requiring vasopressor therapy despite initial and aggressive fluid resuscitation.[8]

Throughout its utilization in the medical field, the surviving sepsis guidelines especially SIRS were widely criticized. Many felt that the definition was largely unhelpful as it focused largely on inflammation which caused many patients without bacterial or viral infections to receive antibiotic therapy and over-resuscitation (i.e., acutely postoperative patients and pancreatitis).[9] SIRS was also thought to be incredibly sensitive and did not take into account endogenous factors, multidrug resistance, and ability to attain source control.[10] Finally, SIRS did not accurately reflect whom was transferred or admitted to the intensive care unit, or predict whom would have end organ damage: hypotension, low urine output, mental status changes, or other lab abnormalities.[9,10]

The pitfalls with SIRS criteria were further scrutinized in pregnancy. Largely secondary to physiologic maternal parameters would almost result in a diagnosis of SIRS. The maternal cardiovascular system often has a HR > 100 secondary to intravascular volume changes, maternal $PCO_2$ is physiologically at 32–34 mmHg, and secondary to adrenocorticoid-mediated

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**Table 1 – Maternal sepsis risk factors.**

| |
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| Cesarean delivery (most common) |
| Smoking |
| Maternal co-morbidites: diabetes, hypertension |
| Prolonged labor |
| Autoimmune diseases (i.e., lupus) |
| Obesity |
| Poor nutrition |

leukocytosis WBC commonly increase to 14,000 and sometimes can increase to as high as 30,000.[11] Institutions have attempted to create sepsis obstetric scores or MEWs scores, but these data have not been validated in other studies and may predict ICU admission, but do not predict maternal or neonatal mortality.[12]

In 2016, the Society of Critical Care Medicine redefined its criteria via the Sepsis 3.[10] Sepsis was not considered mild or "severe," but was considered to be within a spectrum of disease and at all times life threatening. Instead of using SIRS criteria, it advocated in the use of the qSOFA score which included a three important points to define critical illness: altered mental status, hypotension defined as a systolic blood pressure less than 100 mmHg, and tachypnea with a respiratory rate greater than 22.[10] It was gathered that a score of 2 of 3 from the qSOFA score was equivalent to getting 2 or more points on the Sequential Organ Failure Assessment (SOFA) score which carries a mortality rate as high as 10% (Table 3).[10]

Even still with the qSOFA and SOFA score there continues with being a struggle for definition for maternal sepsis that includes and accounts for normal parameters experienced during pregnancy. For instance, many young healthy pregnant women have systolic blood pressures that are less than 100 mmHg, and can have increased work of breathing with movement secondary to the large third trimester uterus. When analyzing variables from the SOFA, a serum creatinine above 0.9 mg/dL without a history of kidney injury is considered abnormal. Although there is less focus on inflammatory changes, there is still inconsistency in defining maternal sepsis. Lack of concrete definitions can lead to delay in diagnosis and treatment of infection and further the progression of disease.

## Treatment of sepsis and septic shock

Despite transitions and revisions of the sepsis definitions, treatment has remained relatively consistent. The mainstay treatment of sepsis is the ascertaining of culture data (blood, urine, tissue, sputum, and amniotic fluid), antibiotic therapy, fluid resuscitation, and source control.[8,10] These are explained in the Surviving Sepsis Guidelines early goal directed therapy for septic shock.

**Table 2 – Definition of SIRS.**

| |
|---|
| Temperature $>$ 38.3°C or $<$36.0°C |
| Heart rate $>$ 90 beats/min |
| Respiratory rate $>$ 20 breaths/min or $PaCO_2$ $<$ 32 mmHg |
| White blood cell count $>$ 12,000 cells/$mm^3$ or |
| White blood cell count $<$ 4000 cells/$mm^3$ or |
| Greater than 10% bandemia |
| *Must have 2 or more to meet positive criteria for SIRS* |

Early goal directed therapy was initially and to some extent is still praised in allowing for the advent of institutionalized protocols and acquisition of staff at the identification of sepsis. Therefore, decreasing delay in antibiotic administration and source control. This is key, as delay in antibiotic administration increases mortality hourly after onset of initial hypotension from septic shock.[13] For this reason, one should not delay antibiotic administration longer than 45 min to obtain culture data.[8]

Not only timing of antibiotic administration, but broadness of antibiotic administration is as important. Many maternal infections will be secondary to puerperal sepsis. Many causative organisms of puerperal sepsis although polymicrobial are usually amenable to targeted treatment, i.e., *Escherichia coli*, GBS. However, in the setting of septic shock and other risk factors for multidrug resistant organisms, broad spectrum antibiotics should be administered and de-escalated with the return of culture data. If the patient has previous hospital admissions, the care team should go through old culture data history, culture implanted devices if appropriate and take into account recent travel history (i.e., dengue fever, tuberculosis, and malaria). Even if there is high suspicion for particular organisms, resistance patterns and strains vary and this should be taken into accounts, particularly for tuberculosis and pseudomonas.[14,15]

For non-puerperal sepsis, patients should have a detailed physical exam to rule out other sources of infections including pulmonary, gastro-intestinal, and genito-urinary. Practitioners should not delay in obtaining needed imaging to aide in ruling out other causes.

In special populations such as transplant, immunocompromised, and congenital AIDS, less common etiologies of sepsis should be considered such as CMV, fungal infections, and other viral infections. In patients that have colonization history such as cystic fibrosis, specialist should be consulted to help determine colonization versus active infection. Once the selection of the antimicrobial therapy has been decided, the providers should pay close attention to dosing, specifically in the setting of acute kidney injury as many medications are renally dosed. In septic shock, pharmacokinetics may be altered and compounded from the volume distribution changes related to pregnancy.[16,17] In these circumstances, pharmacy expertise can be employed alongside infectious disease specialist.

Aside from culture data and antimicrobial therapy, another aspect of the treatment of septic shock is adequate and timely volume repletion before starting vasopressor therapy. The surviving sepsis guidelines advocate for the initial resuscitation of 30 cc/kg before beginning continuous vasopressor therapy.[8] In the setting of hypovolemia, the addition of vasopressor therapy can further lactic acidosis and promote end organ ischemia. Although aggressive intravascular resuscitation is appropriate, it is a key to maintain intake and output to assess volume status to avoid hypervolemia and its consequences (pulmonary edema, bowel edema and abdominal compartment syndrome).[18]