# *Anesthesia in severe sepsis*

Essay

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***Abstract***

The systemic inflammatory response syndrome (SIRS) is defined by the constellation of fever or hypothermia, tachycardia, tachypnea, and leukocytosis, leukopenia, or the presence of immature neutrophils. SIRS can result from numerous conditions but only becomes ‘‘sepsis’’ when infection is etiologic .When sepsis causes at least one organ dysfunction, the syndrome is termed ‘‘severe sepsis,’’ and sepsis-induced hypotension that is refractory to fluid challenge defines .

*Keyword:* ***sepsis***- ARDS- Normoglycemia- Plasminogen-- organ dysfunction- fibrinolysis inhibitor

# List of abbreviations

| | |
|---|---|
| ACTH | Adrenocorticotrophic hormone |
| AKI | Acute kidney injury |
| AKIN | Acute Kidney Injury Network |
| ALI | Acute lung injury |
| ALT | Alanine transaminase |
| APACHE | Acute Physiologic and Chronic Health Evaluation |
| APC | Activated protein C |
| APTT | Aactivated partial thromboplastin time |
| ARDS | Acute respiratory distress syndrome |
| AST | Aspartate transaminase |
| ATIII | Antithrombin III |
| AUC | Area under curve |
| BASES | Brazilian Sepsis Epidemiological Study |
| BP | Blood pressure |
| CALC 1 | Calcitonin 1 |
| CARS | Compensatory anti-inflammatory response syndrome |
| CD | Cluster of differentiation |
| CO | Cardiac output |
| CORTICUS | The Corticosteroid Therapy of Septic Shock |
| CRP | c- reactive protein |
| CT | Computed tomography |
| CVP | Central venous pressure |
| DAG | Diacylglycerol |
| DIC | Disseminated intravascular coagulation |
| $DO_2$ | Oxygen delivery |
| EPCR | Endothelial protein C receptor |
| ERK | Extracellular signal regulated kinase |
| $FIO_2$ | Fractional inspired oxygen concentration |
| GI | Gastrointestinal |
| GRB | Growth receptor binding protein |
| HMGB1 | High mobility group B1 |
| HR | Heart rate |
| ICAM-1 | Intercellular adhesion molecule-1 |
| ICU | Intensive care units |
| IFN | Interferon |
| IIR | Inflammatory immune response |
| IL | Interleukin |
| INR | International normalized ratio |
| IVC | Inferior vena cava |
| LBP | LPS-binding protein |

| | |
|---|---|
| LV | Left ventricle |
| MAP | Mean arterial pressure |
| MAPK | mitogen-activated protein kinase |
| MCP-1 | Monocyte chemoattractant protein-1 |
| MDL-1 | myeloid DAP12-associating lectin |
| MEK | mitogen-activated protein kinase |
| MIF | Migration inhibitory factor |
| MODS | Multiple organ dysfunction syndrome |
| MOF | Multiple organ failure |
| NF-κB | Nuclear factor-κB |
| NICE-SUGAR | Normoglycemia in Intensive Care Evaluation—Survival Using Glucose Algorithm Regulation |
| NO | Nitric oxide |
| NOD | Nucleotide-binding oligomerization domain |
| NOS | NO synthase |
| OR | Odds ratio |
| P13K | Phosphatidylinositol 3-kinase |
| PACs | Pulmonary artery catheters |
| PAF | Platelet-activating factor |
| PAI-1 | Plasminogen activator inhibitor 1 |
| PAI-1 | Plasminogen-activator inhibitor type-1 |
| PAMP | Pathogen-associated molecular pattern |
| PAR1 | Protease activated receptor 1 |
| PCT | Procalcitonin |
| PEEP | Positive end expiratory pressure |
| PGRPs | Peptidoglycan-recognition proteins |
| PIRO | Predisposition, infection, response, organ dysfunction |
| PKC | Protein kinase C |
| PLC | Phospholipase C |
| PLR | Passive leg raising |
| PPV | Pulse pressure variation |
| pro-ANP | Pro-atrial natriuretic peptide |
| ProCT | Procalcitonin |
| PROWESS | Protein C Worldwide Evaluation in Severe Sepsis |
| PRR | Pattern-recognition receptor |
| RBCs | Red blood cells |
| rhAPC | Recombinant human activated protein C |
| RIFLE | Risk/Injury/Failure/Loss/End-Stage Renal Disease |
| ROS | Reactive oxygen species |
| RRT | Renal replacement therapy |
| RV | Right ventricle |
| SBP | Systolic blood pressure |
| $ScvO_2$ | Central venous oxygen saturation |

| | |
|---|---|
| SIRS | Systemic inflammatory syndrome |
| SOAP | Sepsis Occurrence in Acutely Ill Patients |
| SOFA | Sequential Organ Failure Assessment |
| SOS | Son of sevenless |
| $SpO_2$ | Oxygen saturation by pulse oximetry |
| SPV | Systolic pressure variation |
| sTREM-1 | Soluble triggering receptor expressed on myeloid cells-1 |
| su- PAR | Soluble urokinase plasminogen activator receptor |
| $SvO_2$ | Venous oxygen saturation |
| SVR | Systemic vascular resistance |
| SVV | Stroke volume variation |
| TAFI | Thrombin activatable fibrinolysis inhibitor |
| TFPI | Tissue factor pathway inhibitor |
| TLR | Toll-like receptor |
| TLR-4 | Toll-like receptor-4 |
| TNF | Tumor necrosis factor |
| TPN | Total parenteral nutrition |
| TSST-1 | Toxic shock syndrome toxin |
| V/Q | Ventilation/perfusion |
| $VO_2$ | Oxygen consumption |
| WBC | White blood cell count |

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# Introduction

Severe sepsis (acute organ dysfunction secondary to infection)and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation) are major healthcare problems, affecting millions of individuals around the world each year, killing one in four (and often more), and increasing in incidence[1,2].

Patients with sepsis usually demonstrate signs of systemic inflammatory syndrome (SIRS), a non specific clinical syndrome resulting from a generalized response to inflammation[3].

Severe sepsis may have infective and non infective causes. Infections leading to sepsis include central nervous system infections for example, meningitis or encephalitis, cardiovascular infections (e.g. infective endocarditis), respiratory infections (e.g. pneumonia), gastrointestinal infections (e.g. peritonitis) or urinary tract infections (e.g. pyelonephritis). Non infective causes include severe trauma or hemorrhage and acute systemic disease including, myocardial infarction, pulmonary embolus, and acute pancriatitis [2,4].

Sepsis represent a continuum of illness severity from minor constitutional signs (fever, tachycardia, leucocytosis) to septic shock and multiple organ failure. The duration of this response is variable and may persist into postoperative period. Septic shock, the most severe complication of sepsis, accounts for nearly 10% of all admission to intensive care unit [5].

## *Definitions of sepsis*

Cardiovascular dysfunction is pronounced and characterized by element of hypovolemic, cytotoxic and distributive shock. In addition, significant myocardial depression is commonly observed[6,7].

Prompt and effective resuscitation, rational prescription of antibiotics and where appropriate, surgical debridement of severe infection. Anesthesia with concurrent sepsis is risky; and involves consideration of possible organ dysfunction including respiratory, cardiovascular, renal, and hematological as well as ensuring that appropriate antibiotics are given after taking the necessary microbiological specimens[3].

The objective of preoperative resuscitation measures is to rapidly restore adequate oxygen delivery to peripheral tissues[8,9].

The immediate goal is to achieve adequate control of the source of infection with least physiological embarrassment[10,11].

It is important to note that pre-resuscitation measurements should be used to calculate the intensive care admission APACHE score and not those that have improved after resuscitation and surgical procedure[12].

AIM OF WORK:

The aim of this study to explain the different aspects of anesthetic management of septic patients with reference to the pathophysiology of sepsis, septic shock and show their deleterious effects on most organs, noting the early diagnosis and resuscitation will improve the outcome of anesthesia in these patients.

# Sepsis

## Definitions of sepsis

The word sepsis is derived from the Greek term for rotten or “to make putrid”. Sepsis, defined as the systemic host response to microorganisms in previously sterile tissues, is a syndrome related to severe infections and is characterized by end-organ dysfunction away from the primary site of infection. To meet the definition of sepsis, patients need to satisfy at least two of the Systemic Inflammatory Response Syndrome (SIRS) criteria in association with having a suspected or confirmed infection[13].

The term “shock” comes from the French word *choquer* meaning “to collide with,” and aptly describes the body’s response to invading microbes and, to a large extent, its disruptive effect on normal physiology. Initially used in the medical literature in the 1700s, its earliest uses connoted a sudden jolt that often led to death (the initial physical injury). This definition evolved to describe widespread circulatory dysfunction following injury[14].

The severity and mortality increase when this condition is complicated by predefined organ dysfunction (severe sepsis) and cardiovascular collapse (septic shock)[15]. The syndrome currently known as sepsis has had many definitions over the years. In 1991, a consensus conference organized by the American College of Chest Physicians and the Society of Critical Care Medicine clinically

defined the terms SIRS, sepsis, severe sepsis and septic shock[16,17].

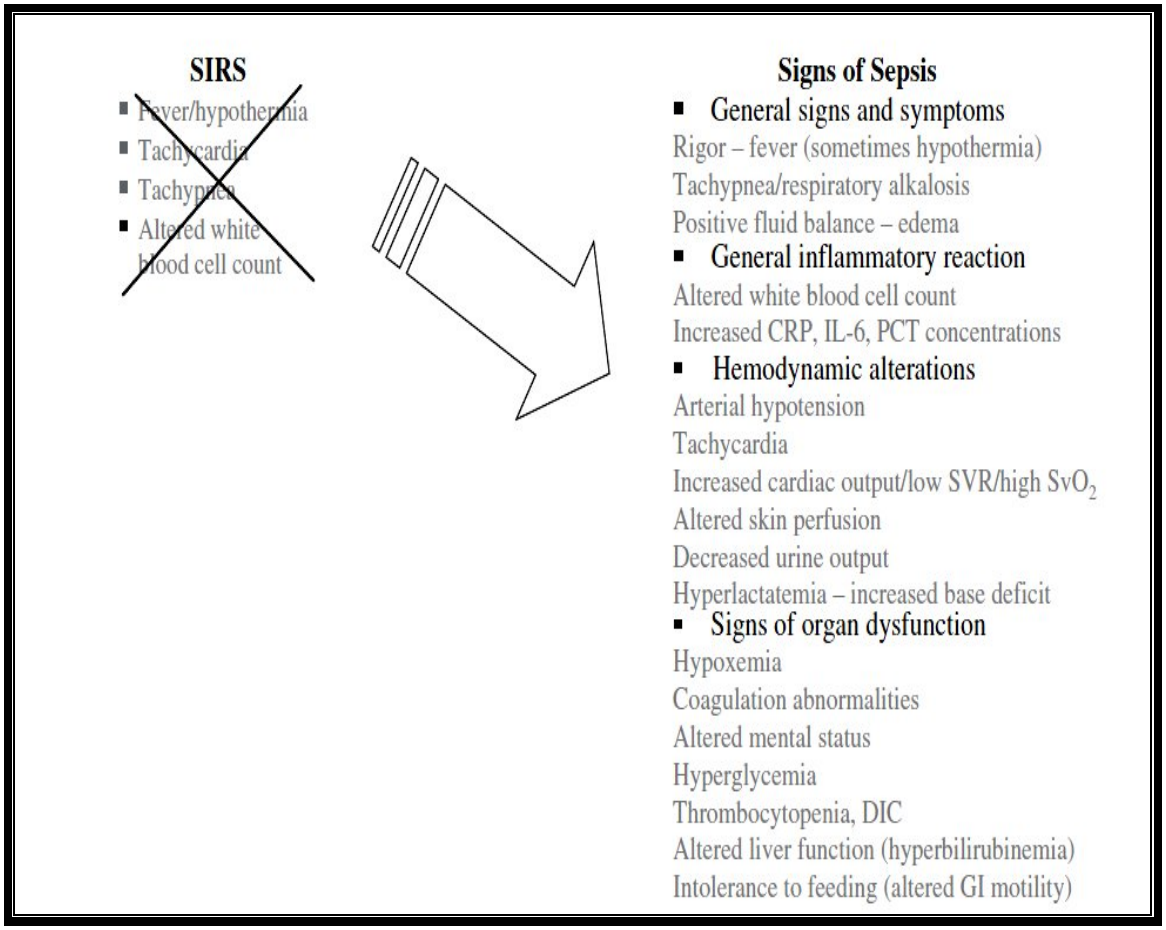


Figure (1): The Sepsis Definitions Conference suggested that the systemic inflammatory response syndrome criteria be replaced by a longer list of possible signs and symptoms of sepsis. Although none of these is specific of sepsis, the unexplained presence of several in combination should raise suspicion of sepsis[13].

Even though the definition has high sensitivity and low specificity, it has been helpful in improving patient care, enrollment in clinical trials and communication between ICUs[18].

| |
|---|
| 1. Systemic Inflammatory Response Syndrome (SIRS). Two or more of the following: a) temperature (core) > 38.3ºC or < 36ºC; b) heart rate > 90 beats/min; c) respiratory rate > 20 breaths/min, PaCO2 < 32 mmHg or need for mechanical ventilation; d) WBC count > 12.000/mm3 or < 4.000/ mm3 or > 10% immature forms (bands). |
| 2. Sepsis is defined as SIRS associated with suspected or confirmed infection. Positive blood cultures are not necessary. |
| 3. Severe sepsis is sepsis complicated by a predefined organ dysfunction. |
| 4. Septic shock is cardiovascular collapse related to severe sepsis despite adequate fluid resuscitation. Hypotension is: systolic blood pressure (SBP) < 90 mmHg, mean arterial pressure (MAP) < 65 mmHg or a reduction of > 40 mmHg on baseline SBP. |
| 5. Organ dysfunction criteria are a) hypoxemia ($PaO_2/FiO_2$ ratio < 300); b) acute oliguria (urine output < 0.5 ml/kg/h for 2 h) or creatinine > 2.0 mg/dL; c) coagulopathy (platelet count < 100.000, INR > 1.5 or pTTa > 60 s); d) ileus; e) plasma bilirubin > 4 mg/dL). |

Table (1): Sepsis definitions[18]

A second conference held in 2001 attempted to refine the definitions, increase specificity by emphasizing prompt recognition and add a list of common symptoms and signs of sepsis[13,17].

The current definitions are as follows:

- Infection: pathologic process caused by invasion of normally sterile tissue, fluid or body cavity by pathogenic or potentially pathogenic microorganisms.
- Sepsis: documented or suspected infection associated with any of the systemic inflammatory syndrome signs.
- Severe Sepsis: sepsis complicated by pre-defined organ dysfunction.

- Septic Shock: sepsis-induced acute circulatory failure characterized by persistent arterial hypotension despite adequate volume administration and not explained by causes other than sepsis[18]

Besides refining the diagnostic definitions, the 2001 consensus conference brought new insight into sepsis staging, with the aim of better characterizing disease severity. The PIRO concept was then introduced with the idea that these factors would have relevant impact on sepsis development and outcome[16,19].

| | Clinical | Other tests |
|---|---|---|
| P (predisposition) | Age, alcohol abuse, steroid or immunosuppressive therapy | Immunologic monitoring, genetic factors |
| I (infection) | Site-specific (e.g., pneumonia, peritonitis) | X-rays, CT scan, bacteriology |
| R (response) | Malaise, temperature, heart rate, respiratory rate | WBC, CRP, PCT, modified APTT |
| O (organ dysfunction) | Arterial pressure, urine output, Glasgow coma score | $PaO_2/FIO_2$, creatinine, bilirubin, platelets |

Table (2): PIRO concept :APTT: Activated partial thromboplastin time; CRP: C-reactive protein; CT: Computed tomography; PCT: Procalcitonin; WBC: White blood cell count[19].