Sepsis

Sepsis is a life-threatening condition that arises when the body's response to infection injures its own tissues and organs.

Common signs and symptoms include fever, increased heart rate, increased breathing rate, and confusion.

There may also be symptoms related to a specific infection, such as a cough with pneumonia, or painful urination with a kidney infection. In the very young, old, and people with a weakened immune system, there may be no symptoms of a specific infection and the body temperature may be low or normal rather than high.

Severe sepsis is sepsis causing poor organ function or insufficient blood flow. Insufficient blood flow may be evident by low blood pressure, high blood lactate, or low urine output. Septic shock is low blood pressure due to sepsis that does not improve after reasonable amounts of intravenous fluids are given.

Sepsis is caused by an immune response triggered by an infection.

The infection is most commonly bacterial, but it can be from fungi, viruses, or parasites.

Common locations for the primary infection include lungs, brain, urinary tract, skin, and abdominal organs. Risk factors include young or old age, a weakened immune system from conditions such as cancer or diabetes, and major trauma or burns.

Diagnosis was based on meeting at least two systemic inflammatory response syndrome (SIRS) criteria due to a presumed infection.[3] In 2016 screening by SIRS was replaced with qSOFA which is two of the following three: increased breathing rate, change in level of consciousness, and low blood pressure.

Blood cultures are recommended preferably before antibiotics are started; however, infection of the blood is not required for the diagnosis.[3] Medical imaging should be done to look for the possible location of infection.

Other potential causes of similar signs and symptoms include anaphylaxis, adrenal insufficiency, low blood volume, heart failure, and pulmonary embolism among others.

Complications

Sepsis-induced immune depression, also referred to as sepsis-induced immunosuppression or sepsis-induced immunoparalysis, is a state of immune dysfunction that can occur in individuals with severe sepsis or septic shock. Sepsis is a life-threatening condition characterized by a dysregulated systemic response to infection, leading to organ dysfunction.

During sepsis, the immune system's initial response to the invading pathogens can be excessive and inflammatory, resulting in tissue damage and organ dysfunction. However, as the sepsis progresses, a phenomenon called “compensatory anti-inflammatory response syndrome” (CARS) can develop. CARS

is characterized by a shift towards an anti-inflammatory state as a regulatory mechanism to counterbalance the initial pro-inflammatory response.

Sepsis-induced immune depression is a component of CARS, in which the immune system becomes suppressed or dysfunctional, leading to an increased susceptibility to secondary infections and impaired clearance of pathogens. Some of the key features of sepsis-induced immune depression include:

Lymphocyte dysfunction: T cells and B cells, which play crucial roles in adaptive immunity, exhibit functional impairments during sepsis. T cells may show reduced proliferation, impaired cytokine production, and altered cell signaling. B cells can have reduced antibody production and impaired memory response.

Monocyte and macrophage dysfunction: Monocytes and macrophages, important components of the innate immune system, can exhibit functional abnormalities. This includes decreased antigen presentation capacity, impaired phagocytosis, reduced production of pro-inflammatory cytokines, and altered clearance of pathogens.

Neutrophil dysfunction: Neutrophils, the primary cells involved in phagocytosis and pathogen clearance, can exhibit reduced chemotaxis, impaired microbial killing, and decreased reactive oxygen species production during sepsis.

Dysregulated cytokine response: Sepsis-induced immune depression is characterized by imbalances in cytokine production. There is a decrease in pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and IL-6, while anti-inflammatory cytokines like IL-10 and transforming growth factor-beta (TGF-β) may be elevated.

The mechanisms underlying sepsis-induced immune depression are complex and not fully understood. They involve dysregulation of immune cell function, activation of inhibitory pathways, disruption of cellular signaling, and alterations in the balance of pro-inflammatory and anti-inflammatory mediators.

Sepsis-induced immune depression contributes to the increased risk of secondary infections and poor outcomes in septic patients. It can prolong the duration of illness, increase the need for intensive care support, and impact overall mortality rates. Therefore, strategies to modulate or reverse sepsis-induced immune depression are areas of active research and clinical investigation, with the aim of improving patient outcomes and reducing the risk of complications in sepsis.

Treatment

The treatment of sepsis involves a multi-faceted approach that aims to control the infection, stabilize the patient's condition, and support organ function. Prompt recognition and initiation of treatment are crucial for improving outcomes in septic patients. The general strategies for sepsis treatment include:

Source control: Identifying and treating the source of infection is of utmost importance. This may involve procedures such as draining abscesses, removing infected catheters, debriding infected tissue, or performing surgical interventions when necessary.

Antibiotics: Early administration of appropriate broad-spectrum antibiotics is essential to target the suspected or identified pathogen causing the infection. The choice of antibiotics depends on factors

such as the site of infection, local resistance patterns, and patient-specific factors. Once culture results are available, the antibiotic regimen can be adjusted to target the specific pathogen and optimize treatment.

Fluid resuscitation: Sepsis often leads to hypotension and inadequate tissue perfusion. Fluid resuscitation with intravenous fluids, typically crystalloids like normal saline or balanced solutions, is initiated to restore blood pressure and improve organ perfusion. The amount of fluid and the rate of administration should be carefully monitored to avoid fluid overload.

Vasopressors: In cases where fluid resuscitation alone is insufficient to maintain blood pressure, vasopressor medications may be required. Vasopressors, such as norepinephrine, can help restore blood pressure and ensure adequate tissue perfusion. Their use should be guided by hemodynamic monitoring and the patient's response.

Supportive care: Patients with sepsis often require supportive care to address complications and maintain vital organ function. This may include supplemental oxygen, mechanical ventilation in cases of respiratory failure, renal replacement therapy for kidney dysfunction, and other organ-specific interventions as necessary.

Immune support: In cases of severe sepsis or septic shock, immune support therapies may be considered. These include the administration of corticosteroids to modulate the immune response and intravenous immunoglobulins to provide passive immunity. However, the use of these therapies is still a topic of debate, and their benefits should be weighed against potential risks and individual patient factors.

Close monitoring and reassessment: Continuous monitoring of vital signs, laboratory parameters, and organ function is crucial in sepsis management. Regular reassessment helps guide treatment adjustments, identify complications, and evaluate the response to therapy.

It is important to note that sepsis is a medical emergency, and management should be conducted in an appropriate healthcare setting, such as an intensive care unit (ICU), with experienced healthcare professionals.

Additionally, ongoing research and clinical trials aim to improve sepsis management by exploring new therapies, personalized treatment approaches, and targeted interventions based on the specific underlying mechanisms of sepsis.

HLA-DRlowS100Ahigh monocytes correlated with immunosuppressive state upon septic challenge, inhibition of which can markedly mitigate sepsis-induced immune depression, thereby providing a novel therapeutic strategy for the management of sepsis [1)]

Sepsis in Neurosurgery

- Idiopathic Normal-Pressure Hydrocephalus Revealed by Systemic Infection: Clinical Observations of Two Cases
- Hospital frailty risk score in predicting outcomes after simultaneous colon and liver resection for colorectal cancer liver metastasis in older adults: Evidence from the Nationwide Inpatient Sample 2015-2018

- Statin use during intensive care unit stay is associated with improved clinical outcomes in critically ill patients with sepsis: a cohort study
- Sepsis in patients with severe TBI: a retrospective CT scoring study
- Experience with surgical evacuation of neonatal brain abscess: A patient series and review of literature
- Impact of Low-Dose Ketamine Infusion on Intracranial Pressure and Hemodynamics in Septic Shock Patients
- Integrative Analysis of DNA Methylation and Gene Expression Reveals Key Molecular Signatures in Spatial Memory Impairment of Sepsis-Associated Encephalopathy
- One year mortality after pediatric hydrocephalus treatment: a comparative analysis of endoscopic third ventriculostomy and ventriculoperitoneal shunt

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Yao RQ, Zhao PY, Li ZX, Liu YY, Zheng LY, Duan Y, Wang L, Yang RL, Kang HJ, Hao JW, Li JY, Dong N, Wu Y, Du XH, Zhu F, Ren C, Wu GS, Xia ZF, Yao YM. Single-cell transcriptome profiling of sepsis identifies HLA-DRlowS100Ahigh monocytes with immunosuppressive function. Mil Med Res. 2023 Jun 19;10(1):27. doi: 10.1186/s40779-023-00462-y. PMID: 37337301.