The Systemic Inflammatory Response Syndrome

Does the New Name Mean New Therapies?

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Summary

A new term, the systemic inflammatory response syndrome (SIRS), has been coined to describe a pathophysiological state that occurs secondary to infectious and noninfectious states such as burns and trauma. When SIRS is secondary to infection, it is called sepsis. In SIRS the host response produces the inflammatory reaction to the inciting agent.

The SIRS can produce conditions that progress through stages of severity, including hypotension, to multiorgan failure. Because multiorgan failure is characterised by numerous definitions that imply extreme organ damage, the term multiple organ dysfunction syndrome (MODS) should be used to denote abnormal organ function for all grades of severity.

The pathogenesis of SIRS and MODS involves multiple mediators, including cytokines released from mononuclear phagocytes. The lipopolysaccharide-cytokine score relates the levels of several such mediators to mortality.

Management of SIRS includes supportive therapy, antibacterials when appropriate, and the treatment of the inflammatory response.
Sepsis and multiorgan failure are important causes of mortality and morbidity in hospitals worldwide. However, techniques have evolved to deal with these illnesses and a vast body of knowledge has accumulated regarding their causes and pathogenesis.

Investigators have determined that the systemic inflammatory response syndrome (SIRS), and a number of related clinical entities including sepsis, sepsis syndrome, and multiorgan failure, actually represent different phases and severities of a single pathological dysfunction. In this condition, the pathways of inflammation become dysfunctional and deleterious. This differs from the normal situation in which this complex response is beneficial, since it assists the host to fight invading organisms.

Thus, the term sepsis and its associations came into being: the adverse condition of sepsis was almost always seen in the presence of infection. However, infection could not always be found in sepsis. Not only was infection absent in some cases, but sepsis could also be associated with certain other, noninfective, states, including fat embolism, burns, and trauma. These and other discoveries regarding the pathogenesis of sepsis made it apparent to researchers and clinicians that the old concepts and terminology for sepsis needed revision.

To develop a new terminology to complement new discoveries regarding the pathophysiology of sepsis, a consensus conference was held by the American College of Chest Physicians/Society of Critical Care Medicine. This conference examined the terminology and medical treatment of this condition and developed an updated terminology for sepsis and its sequelae. This terminology is presented in Table I.

At that conference, a new term was agreed upon to describe the essential underlying dysfunction in these related conditions: the ‘systemic inflammatory response syndrome’. This new term emphasises our understanding of sepsis as a condition associated with the numerous adverse effects of runaway inflammation. Although SIRS is often found in association with bacterial infection, in which case it may correctly be called ‘sepsis’, it is not the invading microbes that cause life-threatening damage; rather, it is the host response that does so. Thus, the profusion of molecular messengers and bacterial killing effects associated with inflammation may be the ultimate cause of a patient’s death.

Figure 1 shows the relationship between sepsis, SIRS, infection and their causes. As these conditions advance through several stages of severity, including hypotension, shock, and hypoxia- and oedema-related organ dysfunction, the risk of mortality increases rapidly. The most serious clinical entity, previously called by a number of terms including multiorgan failure, has now been christened the ‘multiple organ dysfunction syndrome’ (MODS). This term is defined in Table I.

An advantage of these new clinical definitions is their relatively broad-based nature: they may include patients who might not have been considered septic under the definitions previously used by clinicians and researchers. Although this is of obvious importance in the treatment of critically ill patients, it may be of even greater importance for the clinical trials of potential SIRS treatments. Such trials are often criticised because their inclusion and exclusion criteria vary from trial to trial, making the results difficult to compare and restricting the conclusions. The new, broad-based and standardised definitions developed by the consensus conference may help to make the rapid identification and treatment of septic patients possible. They should also improve the research efforts directed at the pathophysiology and treatment of SIRS.

The use of one of several available severity-of-illness scoring systems, such as the APACHE II or III Mortality Prediction Model, should be particularly important in the treatment of septic patients and should also be important in clinical trials of treatments for sepsis, allowing the patient’s condition to be assessed in detail. This should allow clinicians to allocate time and equipment to patients with a reasonable chance of survival, since the scoring systems should predict, with reasonable reliability, which patients are unlikely to survive...