



Systemic Inflammatory Response Syndrome

Looking after critically-ill patients particularly in the intensive care unit, one should be familiar with the terms sepsis or sepsis syndrome. Patients with pyrexia, leukocytosis, altered consciousness, instability of haemodynamic and metabolic homeostasis, and subsequently multiple organ dysfunction are commonly labelled as having such conditions. However, the same clinical features can arise in patients without definite evidences of infection¹, situations that the term "Systemic Inflammatory Response Syndrome, SIRS" have been applied. In an attempt to establish a degree of linguistic clarity, a consensus conference of the Society of Critical Care Medicine (SCCM) and the American College of Chest Physicians (ACCP) was held in August 1991 to produce a series of universal definitions for the systemic inflammatory response syndrome, sepsis and other clinical conditions related to sepsis.

Localized inflammation is a physiological protective response which is generally tightly controlled by the body at the site of injury or infection. Loss of this local control results in an exaggerated systemic response which is clinically identified as SIRS. The term is applied to patient with a characteristic clinical response manifested by two or more of the following²: Body temperature above 38°C or below 36°C (rectal); heart rate above 90 beats per minute; respiratory rate above 20 breaths per minute or PaCO₂ less than 4.3 kPa; white blood cell count above 12,000 cells per mm³, or below 4,000 cells per mm³ or 10 per cent immature (bands) forms. SIRS may be initiated by infection or by non-infectious causes such as trauma, inflammation (e.g. acute pancreatitis), immune reactions (e.g. autoimmune disease) and intoxication (e.g. drug reactions). When

it arises in response to infection, the condition is referred to as sepsis. The term "severe sepsis" is defined as SIRS with documented infection and haemodynamic compromise^{2,3}.

The development of SIRS can be divided into 3 stages⁴. Stage I is the period of local response to an insult. Several cytokines are produced to evoke an inflammatory response, promote wound repair and recruit the cells of reticuloendothelial system. Stage II is the period when small quantities of cytokines are released into circulation to enhance the local response. Macrophages and platelets are recruited and growth factor production is stimulated. During this stage, there is also simultaneous decrease in production of proinflammatory mediators and release of endogenous antagonists. These processes keep the initial inflammatory response in check both by downregulating cytokine production and by counteracting the effects of cytokines already released. The processes continue until the wound is healed, the infection resolved and homeostasis is restored. However, homeostasis may not be re-established and stage III develops. This final stage starts when massive systemic reaction begins. The flood of inflammatory mediators triggers numerous humoral cascades and results in sustained activation of the reticuloendothelial system with loss of microcirculation within several organs causing organ dysfunction. The effects of cytokines in this stage are destructive rather than protective. SIRS can therefore be a significant risk factor of multiple organ dysfunction or multiple organ failure.

Although certain amounts of primary mediators have been reported to play role in SIRS, the three most influential appear to be tumour necrosis factor ? (TNF?), interleukin-1 (IL-1) and

interleukin-6 (IL-6). Moreover, these mediators can stimulate the synthesis or production of secondary inflammatory mediators particularly of arachidonic acid metabolites (e.g. lipooxygenase, cyclooxygenase) and nitric oxide. Understanding the pharmacological or physiological actions of these mediators may result in a new approach to critically-ill patient (e.g. TNF α blockade strategy, IL-1 blockade strategy⁵).

In the author's opinion, SIRS is very common in clinical practice but usually escapes recognition. In most patients, SIRS occurs as the result of the disease, however, it can sometimes develop as a consequence of treatment. For example, severe acute pancreatitis usually triggers SIRS especially in patients with infected necrosis. SIRS may get better after surgical removal of infected pancreatic tissue. On the other hand, SIRS may be worse after surgical

intervention in patients with sterile pancreatic necrosis or if surgery is performed inappropriately (i.e. timing of surgery or operative procedures) since surgery by itself is a potent cause of inflammatory response. In surgical practice, it has been known for a long time that surgical treatment of acute pancreatitis has to be done at an appropriate time and by a proper procedure⁶. If it is performed too early, the morbidity rate increases particularly that of respiratory complications such as adult respiratory distress syndrome (ARDS). If it is performed too late, the morbidity or even the mortality rates increase as the consequence of sepsis. Understanding the process of SIRS may be useful in identifying the proper time of surgery. The concept of SIRS confirms the Osler's statement that "patients die not of their disease, they die of the physiological abnormalities of their disease".

Prasit Watanapa
M.D., Ph.D., F.R.C.S., F.A.C.S.

References :

1. Rangel-Frausto MS, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel RP. The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. *JAMA* 1995; **273**: 117-23.
2. Davies MG, Hagen PO. Systemic inflammatory response syndrome. *Br J Surg* 1997; **84**: 920-35.
3. Nathens AB, Marshall JC. Sepsis, SIRS, and MODS : What's in a name ? *World J Surg* 1996; **20**: 386-91.
4. Bone RC. Toward a theory regarding the pathogenesis of the systemic inflammatory response syndrome : what we do and do not know about cytokine regulation. *Crit Care Med* 1996; **24**: 163-72.
5. Fisher CJ, Zheng Y. Potential strategies for inflammatory mediator manipulation : Retrospect and prospect. *World J Surg* 1996; **20**: 447-53.
6. Watanapa P. Current trends in the surgical management of acute pancreatitis. *Siriraj Hosp Gaz* 1999; **51**: 127-29.