

Roger Bone reported, twenty-five years ago, a consensus paper which was determinant for a common framework of sepsis. Immunological response to bacterial infection was identified as crucial in the diagnosis of sepsis, and nowadays we know that it involves an imbalance in the Th17 response. An overlap between clinical manifestations after bacterial injury and non-infectious injury, as burns, trauma or pancreatitis was acknowledged. In 2016, definitions have been revisited and the concept of severe sepsis has been erased, splitting infection in two categories, i.e., sepsis and septic shock (when lactate is increased and mean arterial pressure is low). However, the challenge of improving outcomes remains.

Sepsis incidence is not decreasing over time and it represents the leading cause of death in general intensive care units (ICUs). The severe alterations of body homeostasis due to sepsis/septic shock rapidly trigger organs' distress, inducing a vicious circle that destroys the healthy chain among vital functions. Systemic inflammatory activation, disseminate endothelial dysfunction, coagulation impairment and metabolic stress require a rapid diagnostic and therapeutic response to stop the way that leads to death, through intensive support and antibiotic therapy.

Hippocrates already mentioned that "it is more important to know what sort of a person has a disease than what sort of disease a person has". Sepsis is a syndrome associated with hypoxia and mitochondrial dysfunction. However, we should not miss that the trigger is an organism and the response of each subject is individualized.

This issue is a compilation of reviews done by expert opinion leaders on critical care and infectious diseases who addressed these two edges. Therefore, it covers a broad spectrum of topics, with special emphasis on issues related with management and the organism. It provides an update of first line research on their respective topics. It also provides valuable information for clinical practitioners, who has limited time to review the vast scientific production and to non-specialists that need to focus on a practical aspect of management of septic shock patients.

Because the identification and control of the infectious source is cornerstone, it seems mandatory to incorporate the important contribution of the pathogen, taking appropriated diagnostic samples. Moreover, a specific approach to definitions is needed focusing on early suspicion at the community level, based on physiologic manifestations easy to identify, with clear goals of care that can be implemented everywhere. These are the challenges.

It is surprising that after 25 years of the seminal paper by Roger Bone, in spite of the amazing advances in other disciplines, such as cancer, little progression has been done in stratification of patients with sepsis. Comparison of the early-goal therapy strategy with further follow-up studies that failed to replicate the findings in larger cohorts, should not disregard that the baseline mortality was significantly different. Surprisingly efforts to develop stratification in patients with sepsis have been limited to a few attempts in pneumonia and validated in the emergency department. We believe that this is cardinal to facilitate an approach based on precision medicine, which allows a personalized management of patients. We are grateful to the authors, because the current issue contributes to add another piece to the puzzle of managing septic shock following the principles of personalized medicine, and CIBERES and ESGCIP for funding in part the project.



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