Sepsis Through the Lens of Complexity Theory

Sepsis is a complex and dysregulated state involving various factors, including pathogens, host response, organ failure, and medical interventions. Despite this complexity, the necessary concepts, approaches, and methods to understand sepsis are underappreciated.

In a recent review, the authors highlight the need to understand sepsis through the lens of complexity theory. Complex systems science aims to understand systems that exhibit behaviour that cannot be explained by their individual parts but rather by the intra-network dynamics and external pressure on the system. They argue that sepsis should be viewed as a highly complex, non-linear, and spatio-dynamic system.

Despite significant advancements, methods like computational modelling and network-based analyses are not widely used in sepsis research. To understand the complexity of sepsis, a multidisciplinary effort is required where computational approaches derived from complex systems science are integrated with biological data. Such integration could refine computational models, guide validation experiments, and identify key pathways that could be targeted to modulate the system to benefit the host.

During sepsis, the host response involves the interplay between various factors, including immune cells, cytokines, the coagulation cascade, the endothelial response, the complement system, the gut microbiome, the neuro-endocrine system, altered energy metabolism, the failure of whole organ systems, mechanical and pharmacological interventions by doctors, the erosive sequelae of comorbidities, one or more causative pathogens, and other factors.

The traditional approach to sepsis research is based on high-resolution snapshots of parameters, often focused on one or two molecular layers, and studies usually include a one-time point of measurement. However, analysing complex dynamic systems such as sepsis requires a radically different approach to measurement, such as longitudinal biological monitoring with many more time points. Although this approach is expensive and requires a trade-off with sample size, it is pivotal for a fuller understanding of sepsis pathophysiology. The resulting data could serve to validate and tune computational methods. Integrated computational models could guide validation experiments and identify key nodes or pathways that could be targeted to modulate the emergent system state to benefit the host. Studies utilising continuous clinical data to study sepsis have made considerable progress, and continuous monitoring and analysis of vital sign variability provide promising results regarding the diagnosis, outcome prediction, and early identification of deterioration in patients with sepsis.

The importance of rigorously characterising, defining and modelling the host response cannot be overstated. This will help clarify the merits and limits of current methods and approaches and pave the way towards altering the disease trajectory of a patient with sepsis through targeted, model-informed interventions.

Source: Critical Care

Image Credit: iStock

Published on : Wed, 15 Mar 2023