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EDITORIAL

Novel concepts related to inflammatory complications in polytrauma

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The management of critically injured polytrauma patients defines our speciality and provides us never-ending challenges. Historically, the unachievable goal was to avoid early and frequently prehospital deaths [1]. With the advancement of prehospital medicine and evidence-based improvements in trauma care, polytrauma mortality decreased below 10% in developed trauma systems, with very little to no preventable mortality margin for hospital-based medical management [2]. We navigate our patients with catastrophic injuries and deranged physiology through the initial resuscitation phase and find them on intensive care units in pathophysiological states, which the human body and the treating doctors have not experienced before. Polytrauma is a changing disease due to ageing populations with co-morbidities, different and hopefully less iatrogenic interventions, faster paced overall care, use of modern technology and current expectations on quality of life. Early survivors of polytrauma remain at high risk for major inflammatory response driven complications such as organ dysfunctions, multiple organ failure, sepsis, venous thromboembolism and persistent inflammation catabolism syndrome. Beyond extended intensive care unit stay and late hospital mortality, these conditions are major determinants of long-term functional outcomes, independent of the initial injury severity.

Simultaneously with the developments during the last 15 years our understanding of the fundamental principles of innate immune response has evolved further. The recent advances and novel interpretation of our existing knowledge on postinjury inflammation is helping us to understand the old questions: why a major trauma patient looks inflamed, septic without detectable infection and how can we harness this process for optimal recovery instead of dismal complications? The classic theories on the fundamentals of our immune system were based on the tolerance towards the self and recognition/neutralisation/elimination of the non-self [3]. Most of us learnt this in medical school and it made perfect sense in most scenarios. It was always challenging to put blunt polytrauma into this conceptual framework, where only the "self" is involved, frequently even with intact skin integrity. Still florid inflammatory response follows mechanical injury within minutes. We acquired decades of knowledge on cellular and humoral responses in polytrauma from sequentially immune-monitored patients during their hospital admission without major practical translation to clinical practise.

The current special update in our Journal on molecular drivers of polytrauma pathophysiology introduces the concepts of our modern understanding of the crux of postinjury inflammation. These theories fit into the conceptual shift from "self versus non-self" to "injured versus intact self" in activation of the innate immune system. "The injured self" results in intracellular organelles, large structural building blocks and small molecules exposed to the immune cells signalling the message of "danger" (Danger Associated Molecular Patterns or DAMPs). In this current issue of the *European Journal of Trauma and Emergency Surgery*, the Frankfurt group introduces the overall concept and the wide variety of danger signals in trauma [4]. The fascinating evolutionary characteristics of mitochondria, their ancient bacterial origin, provide us a logical rational for the similarities between sterile and postinjury inflammation and sepsis. Professor Hauser's pioneering work brought mitochondrial DAMPS into the focus of a trauma scientist, his review summarises the pro-inflammatory danger signals behind trauma and sepsis of mitochondrial origin [5]. The bacterial DNA-resembling circular double-stranded mitochondrial DNA DNA (mtDNA), is the most frequently investigated and probably best-characterised mitochondrial DAMP. The trauma researchers from Newcastle, Australia, provided an overview on the source of extracellular mtDNA after injury and about promising therapeutic targets [6]. The

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overwhelming majority of inflammatory research in trauma is focused on neutrophil leukocytes, Professor Kubes' research group from Calgary enlighten us about the role of macrophages in sterile inflammation and their fascinating impact on tissue repair and overall recovery from polytrauma [7].

These four reviews are aimed for the clinician and translational scientist as an update on the developments during the last decade without overwhelming cell and molecular biological details. As we understand continuously more and more of the pathophysiological sequelae of polytrauma, we are challenged to bring this knowledge into our treatment protocols. These review papers provide a valuable summary and outlook for potential future strategies in research and clinical implementations for clinical and laboratory scientists targeting therapeutic interventions in inflammation-driven complications of polytrauma.

Compliance with ethical standards

Conflict of interest Zsolt Janos Balogh and Ingo Marzi declare that they have no conflict of interest.

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