# Persistent Inflammation, Immunosuppression and Catabolism Syndrome

Juan C. Mira, MD[a], Scott C. Brakenridge, MD, MS[b], Lyle L. Moldawer, PhD[b], Frederick A. Moore, MD, MCCM[b,*]

**KEYWORDS**

• Shock • Multiple organ failure • Trauma • Sepsis • Chronic critical illness • Cachexia • Myeloid-derived suppressor cells • PICS

**KEY POINTS**

- There has been a significant increase in patients with chronic critical illness (CCI): patients with prolonged hospitalizations, high resource utilization, and dismal long-term outcomes.
- Persistent inflammation, immunosuppression, and catabolism syndrome (PICS) describes a subgroup of patients with CCI who have experienced recurrent inflammatory insults.
- Prolonged expansion of myeloid-derived suppressor cells (MDSCs) provides a plausible mechanism for the pathobiology and poor outcomes observed in patients with PICS.
- MDSC expansion in emergency myelopoiesis can lead to chronic inflammation and suppression of adaptive immunity and predisposes patients to nosocomial infections.
- A combination of pharmacotherapy, physiotherapy, and nutritional support will be necessary to limit the progression of CCI into PICS.

Supported in part by grants P50 GM-111152-03, R01 GM-40586-24 and R01 GM-104481-04, awarded by the National Institute of General Medical Sciences (NIGMS), U.S.P.H.S. J.C. Mira was supported by a postgraduate training grant (T32 GM-08721) in burns, trauma, and perioperative injury by NIGMS.

Disclosure Statement: The authors have nothing to disclose.

[a] Department of Surgery, Sepsis and Critical Illness Research Center, University of Florida College of Medicine, 1600 Southwest Archer Road, PO Box 100019, Gainesville, FL 32610-0019, USA; [b] Department of Surgery, Sepsis and Critical Illness Research Center, University of Florida College of Medicine, 1600 Southwest Archer Road, Room 6116, PO Box 100286, Gainesville, FL 32610-0286, USA

* Corresponding author.

*E-mail address:* Frederick.Moore@surgery.ufl.edu

Crit Care Clin 33 (2017) 245–258

http://dx.doi.org/10.1016/j.ccc.2016.12.001

**criticalcare.theclinics.com**

## INTRODUCTION

Multiple organ failure (MOF) has plagued surgical intensive care units (ICUs) for more than four decades, and its epidemiology has evolved because advances in care have allowed patients to survive previously lethal insults. Over the years, different predominant phenotypes of MOF have been described; all have consumed tremendous health care resources and have been associated with prolonged ICU stays and prohibitive mortality. The term *persistent inflammation, immunosuppression, and catabolism syndrome* (PICS) has been coined to describe the most recent observed phenotype of persistent inflammation, immune suppression, and protein catabolism, which the authors think represents the next challenge in surgical critical care. The purpose of this review is to describe the evolving epidemiology of MOF and the emergence of PICS, the PICS paradigm, the pathophysiology of PICS, and its clinical implications.

## EVOLVING EPIDEMIOLOGY OF MULTIPLE ORGAN FAILURE AND EMERGENCE OF PERSISTENT INFLAMMATION, IMMUNOSUPPRESSION, AND CATABOLISM SYNDROME

MOF emerged in the early 1970s as a result of advances in ICU technology that allowed patients to survive single-organ failure (**Fig. 1**).[1] Early studies provided convincing evidence that MOF occurred as a result of uncontrolled sepsis leading to fulminant organ failure and early death, with the primary source being intra-abdominal infections (IAIs).[1] As a result, research efforts in the early 1980s were focused on the prevention/treatment of IAI and were effective in reducing this highly fatal phenotypic expression of MOF. However, in the mid-1980s, studies out of Europe reported that MOF frequently occurred after severe blunt trauma with no identifiable

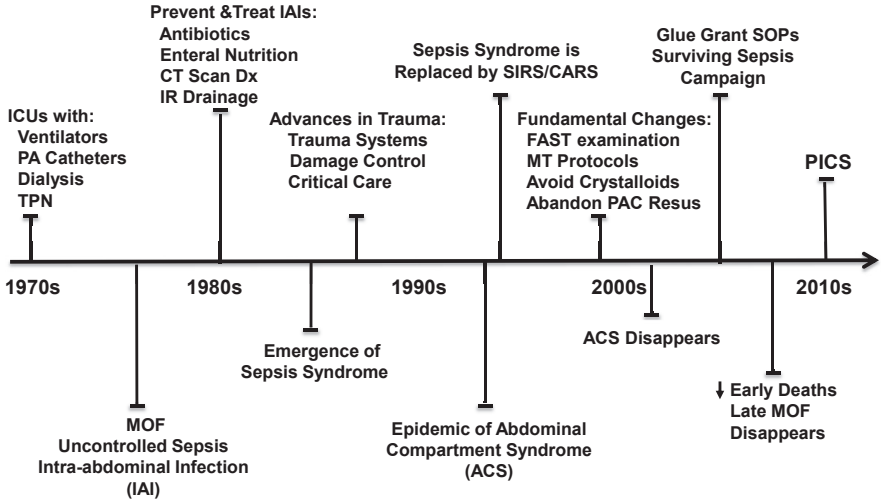


**Fig. 1.** Evolution of MOF. MOF evolves over 40 years, as does the clinical and surgical management of shock states. Paradigms to explain the developing phenotypes are adopted and discarded. The authors propose that PICS is the predominant phenotype resulting from CCI. CARS, compensatory antiinflammatory response syndrome; CT, computed tomography; Dx, diagnosis; FAST, focused assessment with sonography for trauma; IR, interventional radiology; MT, massive transfusion; PA, pulmonary artery; PAC, pulmonary artery catheter; SIRS, systemic inflammatory response syndrome; SOPs, standard operating procedures; TPN, total parenteral nutrition.