

LETTER

Open Access



# To remove and replace—a role for plasma exchange in counterbalancing the host response in sepsis

S. David<sup>1\*</sup> and K. Stahl<sup>2</sup>

See related Review by Ankawi et al., <https://ccforum.biomedcentral.com/articles/10.1186/s13054-018-2181-z>

Septic patients do not usually die from their infection per se but rather from an overwhelming pathological host response to it. Given that treatment is limited to resuscitation strategies, anti-infectives, and source control [1], it is of no surprise that innovative approaches that modify the overwhelming systemic reaction are highly desirable. Novel adsorption techniques have recently attracted much attention and might represent a promising avenue for further investigation [2]. In this issue of *Critical Care* Ankawi and coworkers nicely summarized the potpourri of extracorporeal techniques in septic patients ranging from (ultra) high-volume hemofiltration to modern adsorption devices and a combination of them [3]. We enjoyed reading this article and the authors are to be congratulated for their thoughtful work, in particular with regard to the balanced nature focusing not just on promises but also on pitfalls of these methods. However, given the comprehensive presentation we were surprised that a nephrologist's old friend—which might have an underappreciated role in extracorporeal modulation of the pathological host response—seemed to be forgotten, i.e., therapeutic plasmaexchange (TPE).

The theoretical rationale for TPE goes beyond the simple (surely important) elimination of circulating injurious molecules. The exchange of septic with healthy plasma might also replace consumed protective factors that are of importance to maintain microcirculatory flow (e.g., ADAMTS13) and counterbalance vascular leak (e.g., Angiopoietin-1). About 2000 reports—mostly case reports or series—on TPE in sepsis have been published over the last 20 years. A recent meta-analysis identified four randomized controlled trials and found an association with reduced mortality in adults (risk ratio 0.63, 95% confidence interval 0.42 to 0.96) [4]. None of the studies were powered for survival and the cohorts were quite heterogeneous in respect to clinical severity.

Our own group has just released prospective pilot data on feasibility, safety, and secondary efficacy endpoints in early and severe septic shock patients (onset < 12 h, norepinephrine > 0.4 µg/kg/min) [5]. Based on our observation that it is feasible to recruit such severely sick patients at an early shock timepoint, an appropriately powered randomized controlled multicenter trial (NCT03065751) is currently under review for funding in Germany.

\* Correspondence: [david.sascha@mh-hannover.de](mailto:david.sascha@mh-hannover.de)

<sup>1</sup>Division of Nephrology and Hypertension, Hannover Medical School, Carl-Neuberg-Str.1, 30625 Hannover, Germany

Full list of author information is available at the end of the article



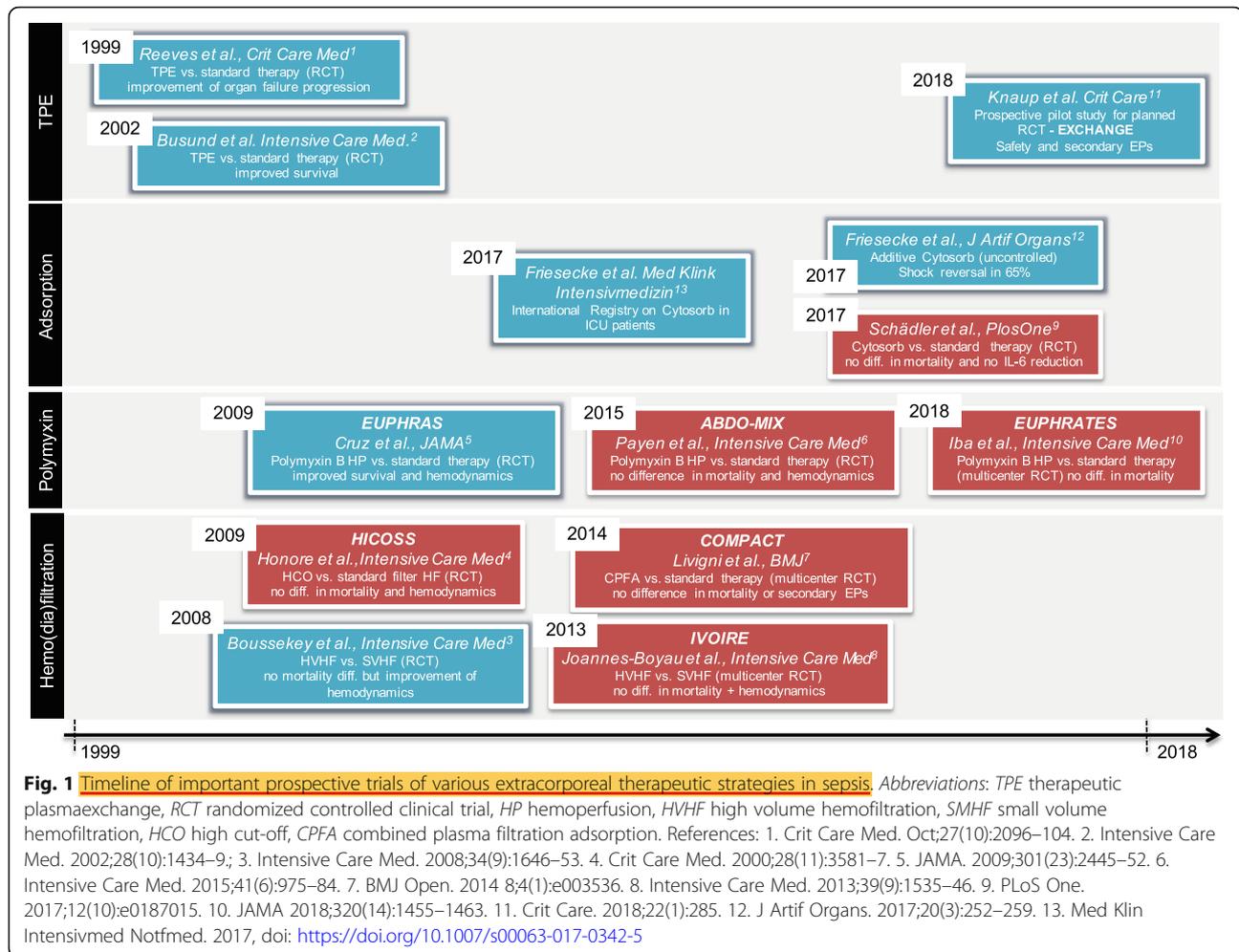


Figure 1 summarizes important studies in the field of extracorporeal strategies against sepsis over the past two decades. We strongly agree with Ankawi et al. that the currently available evidence is insufficient to support the use of any extracorporeal technique in sepsis to date. Let's change this!

#### Consent of publication

Not applicable.

#### Funding

SD is supported by the German Research Foundation (DA 1209/4–3).

#### Availability of data and materials

Not applicable.

#### Authors' contributions

KS and SD wrote the manuscript. Both authors read and approved the final manuscript.

#### Ethics approval and consent to participate

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

#### Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

#### Author details

<sup>1</sup>Division of Nephrology and Hypertension, Hannover Medical School, Carl-Neuberg-Str.1, 30625 Hannover, Germany. <sup>2</sup>Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany.

Received: 22 November 2018 Accepted: 5 December 2018

Published online: 17 January 2019

#### References

- Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock: 2016. *Intensive Care Med*. 2017;43(3):304–77.
- Houshyar KS, Pyles MN, Rein S, Nietzsche I, Duscher D, Maan ZN, et al. Continuous hemoadsorption with a cytokine adsorber during sepsis - a review of the literature. *Int J Artif Organs*. 2017;40:205–11.
- Ankawi G, Neri M, Zhang J, Breglia A, Ricci Z, Ronco C. Extracorporeal techniques for the treatment of critically ill patients with sepsis beyond conventional blood purification therapy: the promises and the pitfalls. *Crit Care*. 2018;22:262.
- Rimmer E, Houston BL, Kumar A, Abou-Setta AM, Friesen C, Marshall JC, et al. The efficacy and safety of plasma exchange in patients with sepsis and

septic shock: a systematic review and meta-analysis. *Crit Care*. 2014;18:699.

5. Knaup H, Stahl K, Schmidt BMW, Idowu TO, Busch M, Wiesner O, et al. Early therapeutic plasma exchange in septic shock: a prospective open-label nonrandomized pilot study focusing on safety, hemodynamics, vascular barrier function, and biologic markers. *Crit Care*. 2018;22:285.