Journal of Translational Critical Care Medicine **2026** vol. 8(3) | e00017
DOI: 10.14218/JTCCM.2026.00017

Review Article

Hemoadsorption for Burn-induced Immune Dysregulation: Mechanisms, Evidence, and Perspectives

Nicolas Chardon[1,2*], Frank Bidar[2], Paul Abraham[3], Didier Payen[4] and Thomas Rimmelé[5]

[1]*Anesthesiology and Intensive Care Medicine, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, France;* [2]*Department of Anesthesiology and Intensive Care Medicine, Hospices Civils de Lyon, University Hospital Louis Pradel, Bron, France;* [3]*Anesthesiology Department, Centre Hospitalier Universitaire du Vaud, Lausanne, Switzerland;* [4]*Department of Infectious Diseases, Hôpital Universitaire l'Archet, Nice, France;* [5]*Medical-Surgical Intensive Care Unit, Pasteur 2 Hospital, Nice teaching hospital, Nice, France*

Received: August 20, 2026 | **Revised:** August 31, 2026 | **Accepted:** September 24, 2026 | **Published online:** September 28, 2026

Abstract

Extensive burn injuries are associated with a profound systemic response, the severity of which increases with the extent of tissue damage. Beyond local destruction, extensive burns induce a sustained immune-inflammatory disturbance that alters immune regulation and contributes to secondary organ failure and infectious complications. These mechanisms are major determinants of adverse outcomes in critically ill patients with burns. In this context, therapeutic strategies targeting immune dysregulation have gained increasing attention. Immunomodulatory approaches aim to limit excessive inflammatory signaling while maintaining effective host defense. Among extracorporeal blood purification techniques, hemoadsorption has emerged as a potential adjunctive therapy designed to reduce circulating inflammatory mediators, particularly cytokines, and to attenuate systemic inflammatory burden. Rather than providing another general overview of extracorporeal blood purification, this review focuses specifically on the cellular and mechanistic basis of burn-induced immune dysregulation and offers a stratified, critical appraisal of the experimental and clinical evidence for hemoadsorption in burns, together with current safety considerations and unresolved questions that should guide future research. Experimental studies and early clinical observations suggest that hemoadsorption may contribute to hemodynamic stabilization and modulation of inflammation in critically ill patients, including those with severe burns. However, clinical evidence in this specific population remains scarce, and its impact on patient-centered outcomes has not yet been established. Although available data suggest that this technique is generally well tolerated, the non-selective removal of circulating molecules underscores the need for careful patient selection and close monitoring. Future investigations should focus on defining the appropriate indications, optimal timing, and treatment duration of hemoadsorption for burn care. Comparative studies with other immunomodulatory strategies are required to clarify its role within the therapeutic armamentarium for burn-induced immune dysfunction.

Introduction

Severe burn injuries trigger a profound systemic response that extends far beyond local tissue damage. The magnitude of this response is largely determined by the extent of skin involvement, traditionally assessed by the depth of injury and the percentage of total body surface area (TBSA) affected. Although most burn injuries are nonfatal, extensive burns are associated with substantial morbidity and mortality worldwide.[1,2]

In the acute phase, major burns represent a prototypical model of systemic inflammatory response syndrome (SIRS). The release of inflammatory mediators increases capillary permeability, promotes fluid shifts, and necessitates prompt and careful fluid resuscitation to prevent hypovolemic shock and microcirculatory impairment.[3,4] This early hyperinflammatory state is accompanied by a progressive disruption of immune regulation, predisposing patients to secondary organ dysfunction and infectious complications.

Given this dual pattern of initial hyperinflammation followed by relative immunosuppression, there is growing interest in therapeutic strategies aimed at restoring immune balance rather

Keywords: Blood purification; Burn; Cytokines; Hemoadsorption; Immunomodulation; Inflammation; Regulated cell death.
***Correspondence to:** Nicolas Chardon, Département d'Anesthésie-Réanimation, Hôpital Edouard Herriot, 5 place d'Arsonval, Lyon 69003, France. ORCID: https://orcid.org/0009-0006-0169-6291. Tel: +33-683396245, E-mail: nicolas.chardon@chu-lyon.fr
How to cite this article: Chardon N, Bidar F, Abraham P, Payen D, Rimmelé T. Hemoadsorption for Burn-induced Immune Dysregulation: Mechanisms, Evidence, and Perspectives. *J Transl Crit Care Med* 2026;8(3):e00017. DOI: 10.14218/JTCCM.2026.00017.

© 2026 The Author(s). This article has been published under the terms of Creative Commons Attribution-Noncommercial 4.0 International License (CC BY-NC 4.0), which permits noncommercial unrestricted use, distribution, and reproduction in any medium, provided that the following statement is provided. "This article has been published in *Journal of Translational Critical Care Medicine* at https://doi.org/10.14218/JTCCM.2026.00017 and can also be viewed on the Journal's website at https://www.xiahepublishing.com/journals/jtccm".

than simply suppressing inflammation. Among extracorporeal blood purification techniques, hemoadsorption has emerged as a potential immunomodulatory approach for critically ill patients, including those with severe burns.[5] Several devices have been developed to attenuate circulating inflammatory mediators and modulate immune activation in intensive care settings.[6]

Previous reviews have addressed hemoadsorption broadly across heterogeneous critically ill or septic populations. In contrast, the present review is centered on the burn-specific context and explicitly separates evidence obtained in burn patients from data extrapolated from other conditions. The aim of this narrative review is to summarize the cellular and pathophysiological rationale for hemoadsorption in burn-induced immune dysregulation, to critically appraise the available preclinical and clinical evidence and its methodological limitations, and to propose candidate indications, treatment timing, safety considerations, and research priorities to guide its future evaluation.

Pathophysiology of burn-induced inflammation and immune dysregulation

Local tissue injury and regulated cell death

Burn wounds are classically described according to the three concentric zones defined by Jackson in 1947: the zone of coagulation, zone of stasis, and zone of hyperemia.[7] The central zone of coagulation corresponds to irreversibly damaged tissue that typically evolves toward necrosis within the first 48 h. Surrounding this core is the zone of stasis, characterized by impaired microvascular perfusion and intense inflammation, while the outermost zone of hyperemia retains largely preserved perfusion and is potentially salvageable in the absence of secondary insults.[8]

Under steady-state conditions, dying cells are efficiently cleared by phagocytes, thereby limiting inflammatory signaling. However, in extensive burns, the abrupt and massive release of cellular debris overwhelms the local clearance mechanisms. Consequently, intracellular components are liberated into the extracellular space, acting as damage-associated molecular patterns (DAMPs) that amplify innate immune activation.

After a burn injury, thermal stress is associated with immediate cellular loss in the zone of coagulation and delayed cellular loss in the zone of stasis. In the zone of necrosis, the main mechanism of cellular loss is accidental cell death, which results in plasma membrane disruption.[9] In the zone of stasis, sublethal heat leads to cell destruction through regulated cell death (RCD).[10] Several types of RCD have been described, including apoptosis, necroptosis, ferroptosis, NETotic cell death, and autophagy-dependent cell death. During burn injury, several RCD processes occur, including apoptosis, necroptosis, and anoikis.[11] The best-known form of regulated cell death is apoptosis, a term coined in 1972 to describe a morphological change in cells that is distinct from necrosis.[12]

Apoptosis occurs in various pathological and physiological processes and is characterized by morphological changes, such as cell rounding, nuclear condensation, membrane blebbing, and apoptotic body formation.[13] Apoptosis follows two major pathways: intrinsic and extrinsic. Intrinsic apoptosis is mediated by mitochondrial permeabilization, whereas extrinsic apoptosis is mediated by cell membrane receptors. Both lead to the activation of caspases, which are involved in the controlled destruction of cellular components. Activation of inflammatory caspases can promote inflammation.[14] Several pathways may induce intrinsic apoptosis in response to burns.[11] Heat-sensitive transient receptor potential vanilloid channels can open at high temperatures, increasing intracellular calcium levels and leading to mitochondrial dysfunction.[15] Thermal stress can induce a direct caspase-dependent pathway, and hyperthermia engages the endoplasmic reticulum in a stress response, which leads to caspase cleavage.[16-18] However, *in vivo* studies of burn injury are limited, precluding precise identification of all underlying apoptotic pathways.

Necroptosis is an RCD that was first described in a burn model in 2015.[19] Execution of necroptosis requires assembly of the necrosome, which is composed of receptor-interacting protein kinases 1 and 3 (RIPK1 and RIPK3),[20] following activation of death receptors or innate immune sensors, including tumor necrosis factor receptor 1, Toll-like receptors, or the DNA-dependent activator of interferon regulatory factors.[21] In contrast to apoptosis, in which release of proinflammatory components is limited, necroptosis can promote inflammation by releasing DAMPs and activating the inflammasome through RIPK3, thereby increasing IL-1β production.[22]

Anoikis is a form of intrinsic apoptosis that can be initiated by loss of integrin-mediated cellular attachment to the extracellular matrix.[23] This form of apoptosis has been described in keratinocytes.[24] Heat shock can induce integrin downregulation and cell shedding.[25] This phenomenon may occur in burn wounds and may be enhanced by degradation of the extracellular matrix by metalloproteinases, the expression of which may be induced by heat shock.[26] Although the rate of apoptosis in the skin of patients with burns is higher than that in healthy individuals, the contribution of anoikis remains unclear.[27]

From local inflammation to systemic response

When the burn size exceeds approximately 20–30% TBSA, local inflammatory signals propagate systemically, engaging hormonal, metabolic, and immune pathways. The accumulation of cellular debris and DAMPs surpasses the clearance capacity and can precipitate SIRS. This response unfolds in two overlapping phases: an early hyperinflammatory state, followed by a compensatory anti-inflammatory phase that may culminate in immune suppression.[28]

During the proinflammatory phase, both pro- and anti-inflammatory cytokine levels are markedly elevated.[29] Their expression is largely governed by p38 MAPK and NF-κB signaling pathways, which drive transcription of TNF-α, IL-1β, and IL-6.[30,31] IL-6 levels are typically elevated after burn injury and peak within 4 days, although the timing may vary with burn extent.[32,33] DAMPs further prime neutrophils and macrophages, intensifying local and systemic inflammatory responses. Dysregulated macrophage activity after burn injury appears to be a key contributor to systemic immune dysregulation in patients with burns.[34] Macrophage polarization toward a classically activated phenotype enhances production of IL-1, IL-6, and TNF-α.[35] Macrophages are also major producers of inducible nitric oxide synthase,[36] which promotes vasodilation and perpetuates NF-κB activation, establishing a self-amplifying inflammatory feedback loop.[37] These processes contribute to immune cell activation, increased vascular permeability, coagulation activation, and SIRS.

Compensatory anti-inflammatory response

As in sepsis, the initial hyperinflammatory phase is followed by a compensatory anti-inflammatory response.[38] This phase is characterized by widespread immune attenuation, including reduced lymphocyte responsiveness, impaired antigen presentation, and diminished dendritic cell function. Key mediators of this shift include TGF-β, IL-4, and especially IL-10, which exerts potent immunosuppressive effects on macrophages.[39] At the cellular level, changes include lymphocyte anergy mediated by type 2 helper T cells,[40] downregulation of monocyte function with reduced cytokine secretion and decreased human leukocyte antigen-DR (HLA-DR) surface expression,[41] and a reduction in functional dendritic cells.[42] The timing and magnitude of immune reprogramming vary among patients and may increase susceptibility to secondary infections and sepsis. This complex immune-inflammatory response is illustrated in Figure 1.

Immunomodulation approaches in burn care

Immune monitoring and specific therapies for modulating immunity in burn injuries remain limited. Most studies have been conducted in animal models, and data from patients with burns are scarce. Several treatments have been proposed to prevent immune dysregulation after burn injury, as described below.

Some authors have investigated the potential benefits of diets that may modulate the immune response. Diets supplemented with immunomodulatory nutrients such as n-3 fatty acids, glutamine, arginine, or antioxidants such as oral vitamins C and E have shown no clear effect on mortality, length of stay, or rates of burn wound or non-wound infection, although early small studies suggested that glutamine might reduce length of stay and mortality.[43]

Topical immunomodulation has been proposed to treat burn injuries without systemic effects, to minimize the progression of tissue injury, attenuate the local inflammatory response, or promote wound healing. For example, in rat models, administration of anti-TNF-α conjugates reduced the extent of necrosis,[44] and administration of a p38 MAPK inhibitor reduced dermal apoptosis and attenuated burn-induced cellular stress.[45] Topical administration of heat-killed bacteria, such as *Lactobacillus*, appears to promote wound healing in animal studies.[46]

Few studies have investigated immunostimulatory therapies with interferon gamma (IFN-γ) or granulocyte-macrophage colony-stimulating factor (GM-CSF).[47] IFN-γ is a cytokine mainly produced by lymphocytes. It activates circulating monocytes and restores monocytic HLA-DR expression, thereby increasing their antigen-presenting capacity and phagocytic function.[48] IFN-γ has been described as an immunomodulatory adjunctive therapy for invasive mucormycosis after severe burns.[49] Data on GM-CSF use in patients with burns remain limited. Administration of this cytokine increases circulating granulocyte counts and modulates leukocyte function. It has been associated with increased superoxide production and reduced myeloperoxidase activity, but the overall effect on morbidity and mortality cannot be evaluated.[50] Granulocyte colony-stimulating factor has also been studied in relation to survival in burn-induced sepsis.[51] GM-CSF may be beneficial for burn wound healing.[52]

Hemoadsorption

Rationale for using hemoadsorption in patients with burns

Extensive burn injuries are characterized by the sustained release of inflammatory mediators that propagate beyond the wound and contribute to systemic organ dysfunction. In this context, extracorporeal blood purification techniques have been proposed as adjunctive tools to mitigate the inflammatory burden rather than solely targeting individual cytokines. Hemoadsorption has emerged as a strategy to "rebalance" the immune response by removing circulating mediators and modulating innate immune cell activity.

From a mechanistic perspective, the biological effects of hemoadsorption likely extend beyond simple plasma clearance. Because cytokines continuously equilibrate between the interstitial and intravascular compartments, adsorption within the extracorporeal circuit may gradually lower tissue mediator concentrations even when plasma levels appear only modestly reduced. This compartmental redistribution may attenuate downstream inflammatory signaling before critical activation thresholds are reached, thereby limiting the propagation of the pro-inflammatory cascade.[53,54]

At the cellular level, hemoadsorption has been suggested to exert indirect effects on immune cell function. Di Carlo's "mediator delivery hypothesis," originally proposed for hemofiltration, suggests that replacement-fluid infusion enhances lymphatic flow and mobilizes inflammatory mediators for clearance.[55] Related extracorporeal approaches have also been reported to modify leukocyte phenotype and function, including the upregulation of HLA-DR expression on monocytes and selective reduction of activated neutrophils.[56,57] *In vitro* data additionally suggest a potential anti-apoptotic effect on tubular epithelial cells exposed to septic plasma, supporting a broader immunomodulatory impact beyond cytokine removal.[58]

In clinical practice, hemoadsorption can be applied using different configurations depending on the patient's condition. In patients with burns who develop acute kidney injury, the cartridge is commonly integrated in series with continuous renal replacement therapy (CRRT), allowing simultaneous renal support and mediator removal. Alternatively, hemoadsorption may be used as a standalone extracorporeal therapy in selected patients with predominantly inflammatory instability.

Building on these considerations, several burn subpopulations can be proposed as plausible candidates for hemoadsorption. First are patients with extensive burns, typically involving more than 20 to 30% of TBSA, who develop an early and predominantly hyperinflammatory phenotype with vasoplegia and escalating vasopressor requirements; in these patients, the aim would be to attenuate the early cytokine surge that drives distributive shock. Second are patients with burn-related septic shock, in whom a secondary infection amplifies the systemic inflammatory response and for whom mediator removal might serve as an adjunct to source control and appropriate antimicrobial therapy. Third are patients who already require CRRT for acute kidney injury, in whom hemoadsorption can be delivered in series without the need for additional vascular access. With respect to timing, two distinct therapeutic windows can be distinguished. The first is an early hyperinflammatory window, within the first hours to days after

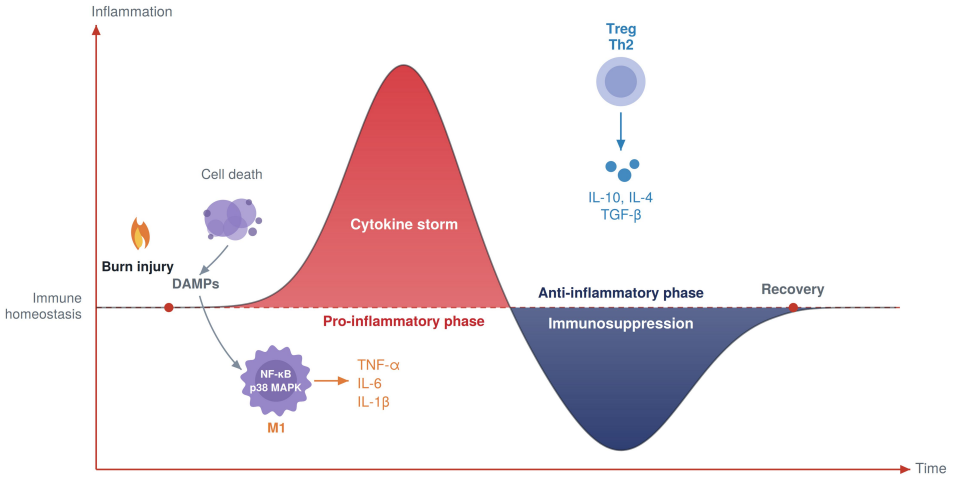


Fig. 1. Immuno-inflammatory response following burn injury. Schematic representation of the biphasic immune response triggered by severe burn injury. Thermal injury induces massive cell death and the release of DAMPs, which activate innate immune cells. Macrophages polarized toward an M1 phenotype signal through NF-κB and p38 MAPK and release proinflammatory mediators (TNF-α, IL-6, IL-1β), driving the early proinflammatory phase and the cytokine storm. This is followed by a compensatory anti-inflammatory phase, mediated by Treg and Th2 cells through the release of IL-10, IL-4, and TGF-β, which may result in a state of immunosuppression and, in patients who recover, a progressive return to immune homeostasis. Red and blue indicate the proinflammatory and anti-inflammatory phases, respectively. The horizontal axis represents time from injury, and the vertical axis represents the intensity of the inflammatory response; the dashed line indicates baseline immune homeostasis. The curves are a conceptual schematic intended to illustrate the temporal relationship between pro- and anti-inflammatory processes; they do not represent measured patient data, neither axis is to scale, and they do not depict a universal or strictly sequential clinical course. Pro- and anti-inflammatory processes overlap rather than occur in succession, their relative magnitude and duration vary considerably between patients, and progression to recovery is not inevitable. Figure created by the authors; vector artwork generated with AI assistance (Claude, Anthropic). All scientific content was defined and verified by the authors. DAMPs, damage-associated molecular patterns; IL, interleukin; M1, classically activated (proinflammatory) macrophage phenotype; NF-κB, nuclear factor kappa B; p38 MAPK, p38 mitogen-activated protein kinase; TGF-β, transforming growth factor beta; Th2, type 2 helper T cells; TNF-α, tumor necrosis factor alpha; Treg, regulatory T cells.

injury, in which the rationale is to blunt the cytokine storm and limit remote organ injury. The second is a later window, dominated by infection and sepsis, in which the goal is to control the inflammatory response to secondary insults. These proposed indications and timing strategies remain hypothesis-generating and require prospective evaluation before they can be recommended in routine practice.

Modern hemoadsorption relies predominantly on biocompatible polystyrene-divinylbenzene sorbents composed of coated macroporous beads. Among the currently available devices, CytoSorb® (CytoSorbents Corporation, Princeton, NJ, USA) and HA-series cartridges (Jafron Biomedical, Zhuhai, China) are the most widely used.[59] These materials can adsorb a broad range of hydrophobic and protein-bound molecules, including complement components and multiple cytokines.[60] The clinical significance of reducing circulating pro- and anti-inflammatory mediators with extracorporeal blood purification remains uncertain.[53,61] Although current studies suggest possible improvements in parameters such as hemodynamics and duration of mechanical ventilation, the effect of hemoadsorption on mortality remains uncertain.[62]

Results from trials assessing hemoadsorption in burns

Evidence supporting the clinical use of modern hemoadsorption sorbents in patients with burns remains scarce and largely exploratory. Most available data are derived from small case series, retrospective analyses, or animal models, which limit the generalizability of the findings.

Experimental work in a porcine burn model demonstrated that CytoSorb® cartridges effectively reduced cytokine concentrations across the device; however, this did not translate into a significant decrease in circulating plasma IL-1, IL-6, or IL-10 levels.[63] Conversely, studies in healthy volunteers exposed to lipopolysaccharide have shown that hemoadsorption can lower the systemic concentrations of TNF, IL-6, and IL-8, suggesting that efficacy may depend on the underlying inflammatory context.[64] The studies summarized here do not isolate the clinical effect of hemoadsorption in an adequately powered randomized trial. The clinical evidence summarized here includes a retrospective cohort, isolated case reports, and a small randomized study of combined hemofiltration and hemoperfusion, which are detailed below and summarized in Table 1.[63-68]

Clinical data on patients with burns are extremely limited. A recent single-center retrospective study including 35 patients (11 receiving CytoSorb plus CRRT and 24 receiving CRRT alone) reported improved hemodynamic stability and reduced norepinephrine requirements when CytoSorb® was combined with CRRT compared with CRRT alone. However, this study was limited by its small sample size, single-center design, and lack of

Table 1. Summary of the available preclinical and clinical evidence on hemoadsorption in burns

Study (reference)	Design and population	Main findings	Main limitations
Preclinical study[63]	Experimental porcine burn model (animal)	CytoSorb reduced cytokine concentrations across the cartridge, but without a significant fall in circulating IL-1, IL-6, or IL-10	Animal model; no clinical outcomes; cartridge effect not reflected in plasma levels
Endotoxin challenge[64]	Healthy human volunteers exposed to lipopolysaccharide (non-burn)	Reduction in systemic TNF, IL-6, and IL-8, suggesting context-dependent efficacy	Non-burn experimental model; healthy subjects; surrogate biological endpoints only
Mariano *et al.*[65]	Single-center retrospective cohort, 35 patients with burns (CytoSorb + CRRT, n = 11, vs CRRT alone, n = 24)	Improved hemodynamic stability and reduced norepinephrine requirements in the CytoSorb group	Small sample; single-center; nonrandomized; likely confounding by indication; no established causal effect on mortality or organ function
Case reports[66,67]	A conference abstract and a case report in patients with burns	Demonstrated feasibility; one report described a reduction in bilirubin after hemoadsorption	Anecdotal; no control group; no robust clinical endpoints; high risk of reporting bias
Randomized study[68]	Randomized study in 40 patients with burns (20 per group; China); hemofiltration plus hemoperfusion versus conventional care	Suggested improvement in biochemical markers and septic complications	Small sample; combined intervention prevents attribution to hemoadsorption alone; sorbent incompletely specified in the English abstract

AI, artificial intelligence, CRRT, continuous renal replacement therapy; IL, interleukin; TNF, tumor necrosis factor. The randomized burn study listed here evaluated combined hemofiltration and hemoperfusion and does not isolate the effect of hemoadsorption.

randomization.[65] Because treatment was not allocated at random, this observational comparison is particularly susceptible to confounding by indication, and the reported survival advantage should be regarded as hypothesis-generating rather than confirmatory. An additional limitation concerns the nonrandomized comparison: the incremental benefit specifically attributable to the adsorptive cartridge cannot be reliably inferred from this observational comparison with CRRT alone and therefore remains uncertain. This caveat is consistent with the broader critical care literature: although a recent meta-analysis restricted to septic shock suggested a possible short-term survival and hemodynamic benefit of hemoadsorption,[69] randomized data across mixed indications have shown no consistent mortality reduction, and one meta-analysis restricted to randomized controlled trials reported a signal toward higher mortality.[70,71]

These observations underscore a persistent gap between the hemodynamic and biochemical improvements attributed to hemoadsorption and patient-centered outcomes; no definitive benefits in mortality or ventilator-free days have been demonstrated in patients with burns.[72] This cautious interpretation is consistent with a recent international consensus, which regards contemporary hemoadsorption as a novel and experimental intervention supported by limited data and a broad research agenda,[73] and with critical appraisals concluding that no study has yet demonstrated a survival benefit and that the current evidence does not justify its routine use.[74]

Additional reports are primarily limited to isolated case reports. These reports provide feasibility data but lack robust clinical endpoints. One case report described a reduction in bilirubin levels after hemoadsorption, whereas another failed to present interpretable outcome data despite the initial objectives.[66,67] A randomized Chinese study of 40 patients suggested potential improvements in biochemical markers and septic complications with intermittent hemofiltration combined with hemoperfusion; however, the combined intervention and incompletely specified sorbent in the English abstract limit attribution to hemoadsorption alone.[68]

Overall, existing studies suggest that hemoadsorption is technically feasible and may influence hemodynamic or biological parameters; however, they do not provide high-quality evidence for improved survival or organ function in patients with burns.

Technical considerations

The technical parameters, such as the optimal timing of initiation and duration of hemoadsorption, remain unknown. The timing of the intervention is particularly challenging in patients with burns. For example, early initiation aims to mitigate the "cytokine storm," SIRS-related vasoplegia, and remote organ injury and dysfunction.[75,76] Conversely, the use of extracorporeal blood purification as a "late" adjuvant therapy when renal replacement therapy is needed for renal support has also been evaluated. Chung *et al.* evaluated hemofiltration in adults with severe burns and acute kidney injury in cohort studies and a randomized controlled trial.[77-79] It should be emphasized, however, that these data were generated with hemofiltration, a convective clearance technique that is mechanistically distinct from adsorption. Such evidence cannot be extrapolated to support hemoadsorption, and the two modalities should not be regarded as interchangeable; this distinction is maintained throughout the present review. Other available hemoadsorption devices have been only sparsely

evaluated in patients with burns, and robust controlled evidence remains lacking. These devices can be categorized into pure sorbents, which may exhibit selective or non-selective adsorption, and hemofilters with hemoadsorption capacity, which can also vary in selectivity.

Among non-selective sorbents, polystyrene resin sorbents are designed for the adsorption of medium- to high-molecular-weight metabolites and protein-bound uremic retention solutes.[80] Among selective sorbents, some devices are specifically designed for endotoxin removal in the septic population, such as the polymyxin B-immobilized cartridge (Toraymyxin®) and synthetic cationic peptide-based lipopolysaccharide adsorbers.[81] Among selective hemoadsorption devices, heparin-grafted polyethylene beads are designed to mimic the endothelial glycocalyx and remove a variety of pathogens, including bacteria, viruses, and fungi, from the bloodstream. They may warrant evaluation in patients with burns because of the high incidence and severity of bloodstream infections in this population.[82] The PURIFY-RCT trial has been registered (NCT05011656).[83]

Some hemofilters have adsorptive properties, including non-selective adsorptive membranes such as surface-treated acrylonitrile 69 (AN69ST), polymethyl methacrylate (PMMA), and oXiris membranes. They may be considered in septic shock associated with acute kidney injury requiring CRRT.[84] Another technique is the selective cytopheretic device (SCD; SeaStar Medical, Inc.). SCD is an extracorporeal synthetic membrane device designed to reversibly bind activated circulating neutrophils and monocytes in a low-ionized-calcium environment and under low-shear blood flow.[85,86] A multicenter, randomized, controlled trial (NCT05758077) is ongoing to assess the efficacy and safety of SCD in patients with acute kidney injury requiring CRRT.[87,88] Despite advances in sorbent technology, no robust study has provided conclusive evidence supporting the clinical use of hemoadsorption, particularly in patients with burns. Further animal and human studies are needed to characterize the performance of each hemoadsorption cartridge.[89]

A comparison of the main extracorporeal blood purification devices, their mechanisms, candidate clinical scenarios, and the level of evidence in burns is summarized in Table 2.

Safety, complications, and contraindications

An additional concern is the non-selective nature of many sorbents. In addition to harmful inflammatory mediators, potentially beneficial molecules may also be removed from the circulation. Moreover, correction of treatment-related imbalances through transfusion of blood products or albumin could paradoxically trigger secondary inflammatory responses, counteracting some of the intended immunomodulatory effects.

Current experience indicates that polystyrene-divinylbenzene hemoadsorption cartridges are generally well tolerated, with moderate and transient reductions in platelet count and serum albumin being the most consistently reported laboratory changes.[90] Nevertheless, hemoadsorption remains an extracorporeal therapy that requires vascular access and an individualized anticoagulation strategy. As such, it carries the inherent risks of bleeding, thrombosis, and catheter-related infection, comparable to other renal replacement or extracorporeal techniques.[91-93] Additionally, the correction of hemoadsorption-induced imbalances through blood, platelet, or albumin transfusion may lead to immunological complications and potentially counteract the intended immunomodulatory effects of hemoadsorption by inducing a pro-inflammatory immune response.[94,95] Particular attention should be paid to the consequences of the non-selective nature of adsorption, which is not restricted to pro-inflammatory cytokines. The removal of albumin reduces oncotic pressure and, because many drugs are highly protein-bound, may alter the free fraction and clearance of co-administered agents. Coagulation factors may likewise be adsorbed, which, together with the fall in platelet count described above, can aggravate the bleeding tendency already present in critically ill patients with burns. Of particular concern is the clearance of anti-infective agents: hemoadsorption can substantially remove several antibiotics and antifungals, potentially producing subtherapeutic plasma concentrations and treatment failure at a time when severe infection is a leading cause of death in burns, and in a population in which antimicrobial pharmacokinetics are already profoundly altered by hypermetabolism, capillary leak, and augmented renal clearance. Therapeutic drug monitoring and device-specific dose adjustment, without delaying clinically indicated anti-infective treatment, are therefore advisable. Finally, because the cartridge does not discriminate between mediators, beneficial anti-inflammatory cytokines such as interleukin-10 may be removed alongside pro-inflammatory ones, raising the theoretical risk of blunting the compensatory anti-inflammatory response and impairing host defense.[72]

No universally accepted absolute contraindications to hemoadsorption have been established to date, although potential complications and patient-specific clinical and technical contraindications should be considered.[73] Active uncontrolled bleeding or severe refractory coagulopathy constitutes a relative contraindication, given the additional loss of platelets and coagulation factors and the potential need for anticoagulation to maintain the extracorporeal circuit. The absence of safe vascular access and profound hemodynamic instability precluding the maintenance of adequate extracorporeal blood flow are further practical limitations. Concomitant treatment with anti-infective agents with a narrow therapeutic index calls for close monitoring rather than precluding therapy. In all cases, the decision to initiate hemoadsorption in a patient with burns should rest on an individualized risk–benefit assessment, with explicit attention to coagulation status, vascular access, hemodynamic reserve, and ongoing drug therapy.[72]

Taken together, these considerations highlight the need for individualized patient selection, careful timing of therapy, and close biological monitoring when hemoadsorption is used in patients with severe burns.

Future investigations in the sorbent field

Future research must move beyond descriptive and observational studies toward adequately powered randomized controlled trials focused on clinically meaningful endpoints such as organ failure burden, ventilator-free days, and mortality. However, several fundamental questions remain unanswered. These include the extraction ratios of different cartridges, total mass of mediators removed over time, and the kinetics of sorbent saturation. These parameters likely vary across devices and clinical contexts, emphasizing the need for device-specific evaluations rather than extrapolations from heterogeneous studies. Determining the optimal timing of initiation is critical. Early application may be most appropriate to evaluate in patients with extensive burns and

Table 2. Comparison of the main extracorporeal blood purification devices, their mechanisms, candidate clinical scenarios, and the level of evidence in burns

Device (sorbent)	Mechanism and selectivity	Potential clinical scenario	Evidence in burns
CytoSorb (polystyrene-divinylbenzene)	Non-selective adsorption of mid-molecular-weight molecules (approximately 5-60 kDa), including cytokines	Hyperinflammation and cytokine storm, septic shock; commonly used in series with CRRT	Direct burn data available (porcine model, retrospective cohort, case reports); no controlled study demonstrating an outcome benefit
Jafron resin cartridges (e.g., HA330/HA380)	Non-selective resin adsorption of cytokines and middle molecules	Cytokine storm and sepsis; standalone or combined with CRRT	Limited to case-level reports in patients with burns; no controlled study (literature search updated September 2026)
Polymyxin B-immobilized fiber (e.g., Toraymyxin/PMX)	Selective adsorption of endotoxin (lipopolysaccharide)	Gram-negative sepsis and endotoxemia	No study in patients with burns identified (literature search updated September 2026)
Seraph 100 (heparin-grafted)	Selective binding of circulating pathogens and pathogen-associated molecules	Bloodstream infection and pathogen reduction	No controlled study in patients with burns identified (literature search updated September 2026)
Adsorptive membranes (AN69ST, oXiris, PMMA)	Hemofilters that combine convective/diffusive clearance with surface adsorption; selectivity varies	Combined renal support and mediator removal in acute kidney injury	Limited to a small case series of patients with burns treated with oXiris, reporting improved urine output and SOFA score; no controlled study. Mechanistically distinct from pure adsorption and should not be conflated with it (literature search updated September 2026)
Selective cytopheretic device (SCD)	Immunomodulation by reversible binding of activated neutrophils and monocytes in a low ionized-calcium, low-shear environment	Acute kidney injury requiring CRRT; hyperinflammatory states	No study in patients with burns identified; a multicenter randomized controlled trial is ongoing in AKI requiring CRRT (NEUTRALIZE-AKI, NCT05758077) (literature search updated September 2026)

Selectivity refers to the relative specificity of the sorbent for defined targets; pure adsorption (hemoadsorption) is mechanistically distinct from convective clearance (hemofiltration). AKI, acute kidney injury; AN69ST, surface-treated acrylonitrile 69; CRRT, continuous renal replacement therapy; PMMA, polymethyl methacrylate; PMX, polymyxin B hemoperfusion; SOFA, Sequential Organ Failure Assessment.

marked hyperinflammation, whereas delayed use may be more appropriate to evaluate in those who develop acute kidney injury requiring renal replacement therapy.

Finally, the potential role of hemoadsorption as a standalone therapy versus its combination with CRRT or other immunomodulatory strategies warrants systematic investigation in well-designed comparative trials.

Strengths and limitations

A strength of this review is its burn-specific focus and its explicit distinction between direct evidence from patients with burns and evidence extrapolated from other critically ill populations. Several limitations of the present review and of the underlying evidence base should also be acknowledged, and they temper all of the interpretations proposed above. First, the studies summarized here do not isolate the clinical effect of hemoadsorption in an adequately powered randomized trial. The clinical evidence summarized here includes a retrospective cohort, isolated case reports, and a small randomized study of combined hemofiltration and hemoperfusion. These data preclude firm causal attribution to hemoadsorption alone, and the absence of randomization in most reports renders the reported benefits particularly susceptible to confounding by indication. Second, the available studies are small, mostly single-center, and methodologically heterogeneous with respect to the device used, the timing and duration of therapy, the dose delivered, and the concomitant use of renal replacement therapy. This heterogeneity precludes any quantitative synthesis and limits comparability across reports. The nonrandomized comparison and potential differences in concomitant CRRT delivery are additional constraints on attributing any incremental effect to adsorption itself. Third, most reported endpoints are intermediate rather than patient-centered. Improvements in vasopressor requirements, hemodynamic indices, or circulating mediator concentrations have not translated into definitive evidence of benefits in mortality, organ failure burden, or ventilator-free days in patients with burns. Preclinical work illustrates the same gap, as cartridge-level clearance has not consistently been reflected in systemic cytokine concentrations. Fourth, a substantial part of the supporting rationale is extrapolated from non-burn critically ill and septic populations. Because burn pathophysiology, pharmacokinetics, and the time

course of immune dysregulation differ substantially from those of other critically ill patients, such extrapolation is uncertain. For the same reason, evidence generated with mechanistically distinct modalities, in particular hemofiltration, cannot be used to support hemoadsorption. Finally, safety data specific to patients with burns are scarce. The consequences of non-selective adsorption, notably the removal of albumin, coagulation factors, anti-infective agents, and anti-inflammatory cytokines, have not been quantified in this population, in which antimicrobial pharmacokinetics are already profoundly altered.

Conclusions

Hemoadsorption is a potential extracorporeal strategy for modulating the dysregulated immune response observed in severe burn injuries. Although preliminary data suggest possible improvements in hemodynamic stability and inflammatory burden, robust clinical evidence demonstrating improved patient-centered outcomes is still lacking.

Given the complexity of burn-induced immune dysfunction, hemoadsorption should currently be considered an adjunctive rather than a standard therapy and, where used, preferably implemented within expert centers and clinical research protocols.

Further high-quality studies are essential to define the precise indications, optimal timing, treatment duration, and patient subphenotypes that are most likely to benefit from this approach.

Acknowledgments

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

Thomas Rimmelé serves as an Associate Editor-in-Chief of the *Journal of Translational Critical Care Medicine*. Thomas Rimmelé has received fees from Baxter, Fresenius Medical Care, B. Braun, Estor, CytoSorbents, Jafron, Infomed, Nikkiso, and bioMérieux for lectures at scientific meetings and conferences. The other authors declare no conflicts of interest.

Author contributions

Drafting the manuscript (NC, TR), critical revision of the manuscript for important intellectual content and final approval of the manuscript (NC, FB, PA, DP, TR). All authors have approved the final version and publication of the manuscript.

References

[1] Peck MD. Epidemiology of burns throughout the world. Part I: Distribution and risk factors. Burns 2011;37(7):1087–1100. DOI: 10.1016/j.burns.2011.06.005, PMID: 21802856.

[2] Yakupu A, Zhang J, Dong W, Song F, Dong J, Lu S. The epidemiological characteristic and trends of burns globally. BMC Public Health 2022;22(1):1596. DOI: 10.1186/s12889-022-13887-2, PMID: 35996116.

[3] Alvarado R, Chung KK, Cancio LC, Wolf SE. Burn resuscitation. Burns 2009;35(1):4–14. DOI: 10.1016/j.burns.2008.03.008, PMID: 18539396.

[4] Nielson CB, Duethman NC, Howard JM, Moncure M, Wood JG. Burns: Pathophysiology of Systemic Complications and Current Management. J Burn Care Res 2017;38(1):e469–e481. DOI: 10.1097/BCR.0000000000000355, PMID: 27183443.

[5] Ronco C, Samoni S, Bellomo R. Hemoperfusion and immunomodulation. In: Bellomo R, Ronco C, editors. Adsorption: The New Frontier in Extracorporeal Blood Purification. Contributions to Nephrology. Vol. 200. Basel: Karger; 2023:142–148. DOI: 10.1159/000529885.

[6] Ricci Z, Romagnoli S, Reis T, Bellomo R, Ronco C. Hemoperfusion in the intensive care unit. Intensive Care Med 2022;48(10):1397–1408. DOI: 10.1007/s00134-022-06810-1, PMID: 35984473.

[7] Jackson DM. The diagnosis of the depth of burning. Br J Surg 1953;40(164):588–596. DOI: 10.1002/bjs.18004016413, PMID: 13059343.

[8] Hettiaratchy S, Dziewulski P. ABC of burns: pathophysiology and types of burns. BMJ 2004;328(7453):1427–1429. DOI: 10.1136/bmj.328.7453.1427, PMID: 15191982.

[9] Takigawa M, Ofuji S. Early changes in human epidermis following thermal burn: an electron microscopic study. Acta Derm Venereol 1977;57(3):187–193. DOI: 10.2340/0001555557187193, PMID: 71820.

[10] Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, *et al*. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. Cell Death Differ 2018;25(3):486–541. DOI: 10.1038/s41418-017-0012-4, PMID: 29362479.

[11] Rennekampff HO, Alharbi Z. Burn Injury: Mechanisms of Keratinocyte Cell Death. Med Sci (Basel) 2021;9(3):51. DOI: 10.3390/medsci9030051, PMID: 34287312.

[12] Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. Br J Cancer 1972;26(4):239–257. DOI: 10.1038/bjc.1972.33, PMID: 4561027.

[13] Tang D, Kang R, Berghe TV, Vandenabeele P, Kroemer G. The molecular machinery of regulated cell death. Cell Res 2019;29(5):347–364. DOI: 10.1038/s41422-019-0164-5, PMID: 30948788.

[14] McIlwain DR, Berger T, Mak TW. Caspase functions in cell death and disease. Cold Spring Harb Perspect Biol 2013;5(4):a008656. DOI: 10.1101/cshperspect.a008656, PMID: 23545416.

[15] Moriello AS, De Petrocellis L. Assay of TRPV1 Receptor Signaling. Methods Mol Biol 2016;1412:65–76. DOI: 10.1007/978-1-4939-3539-0_7, PMID: 27245892.

[16] Holmes CJ, Plichta JK, Gamelli RL, Radek KA. Burn Injury Alters Epidermal Cholinergic Mediators and Increases HMGB1 and Caspase 3 in Autologous Donor Skin and Burn Margin. Shock 2017;47(2):175–183. DOI: 10.1097/SHK.0000000000000752, PMID: 27648692.

[17] Ahmed K, Zaidi SF, Mati-Ur-Rehman, Rehman R, Kondo T. Hyperthermia and protein homeostasis: Cytoprotection and cell death. J Therm Biol 2020;91:102615. DOI: 10.1016/j.jtherbio.2020.102615, PMID: 32716865.

[18] Rao RV, Ellerby HM, Bredesen DE. Coupling endoplasmic reticulum stress to the cell death program. Cell Death Differ 2004;11(4):372–380. DOI: 10.1038/sj.cdd.4401378, PMID: 14765132.

[19] Reddy AS, Abraham A, McClain SA, Clark RA, Ralen P, Sandoval S, *et al*. The Role of Necroptosis in Burn Injury Progression in a Rat Comb Burn Model. Acad Emerg Med 2015;22(10):1181–1186. DOI: 10.

1111/acem.12768, PMID: 26375585.

[20] Linkermann A, Green DR. Necroptosis. N Engl J Med 2014;370(5): 455–465. DOI: 10.1056/NEJMra1310050, PMID: 24476434.

[21] Dhuriya YK, Sharma D. Necroptosis: a regulated inflammatory mode of cell death. J Neuroinflammation 2018;15(1):199. DOI: 10.1186/s12974-018-1235-0, PMID: 29980212.

[22] Man SM, Tourlomousis P, Hopkins L, Monie TP, Fitzgerald KA, Bryant CE. Salmonella infection induces recruitment of Caspase-8 to the inflammasome to modulate IL-1β production. J Immunol 2013; 191(10):5239–5246. DOI: 10.4049/jimmunol.1301581, PMID: 24123685.

[23] Frisch SM, Francis H. Disruption of epithelial cell-matrix interactions induces apoptosis. J Cell Biol 1994;124(4):619–626. DOI: 10.1083/jcb.124.4.619, PMID: 8106557.

[24] Haake AR, Polakowska RR. Cell death by apoptosis in epidermal biology. J Invest Dermatol 1993;101(2):107–112. DOI: 10.1111/1523-1747.ep12363594, PMID: 8345210.

[25] Majda JA, Gerner EW, Vanlandingham B, Gehlsen KR, Cress AE. Heat shock-induced shedding of cell surface integrins in A549 human lung tumor cells in culture. Exp Cell Res 1994;210(1):46–51. DOI: 10.1006/excr.1994.1007, PMID: 7505747.

[26] Li WH, Lee YM, Kim JY, Kang S, Kim S, Kim KH, *et al*. Transient receptor potential vanilloid-1 mediates heat-shock-induced matrix metalloproteinase-1 expression in human epidermal keratinocytes. J Invest Dermatol 2007;127(10):2328–2335. DOI: 10.1038/sj.jid.5700880, PMID: 17508023.

[27] Gravante G, Palmieri MB, Esposito G, Delogu D, Santeusanio G, Filingeri V, *et al*. Apoptotic death in deep partial thickness burns vs. normal skin of burned patients. J Surg Res 2007;141(2):141–145. DOI: 10.1016/j.jss.2006.07.031, PMID: 17559878.

[28] Jeschke MG, van Baar ME, Choudhry MA, Chung KK, Gibran NS, Logsetty S. Burn injury. Nat Rev Dis Primers 2020;6(1):11. DOI: 10.1038/s41572-020-0145-5, PMID: 32054846.

[29] Vindenes HA, Ulvestad E, Bjerknes R. Concentrations of cytokines in plasma of patients with large burns: their relation to time after injury, burn size, inflammatory variables, infection, and outcome. Eur J Surg 1998;164(9):647–656. DOI: 10.1080/110241598750005525, PMID: 9728783.

[30] Baumann H, Gauldie J. The acute phase response. Immunol Today 1994;15(2):74–80. DOI: 10.1016/0167-5699(94)90137-6, PMID: 7512342.

[31] Liu T, Zhang L, Joo D, Sun SC. NF-κB signaling in inflammation. Signal Transduct Target Ther 2017;2:17023. DOI: 10.1038/sigtrans.2017.23, PMID: 29158945.

[32] Yeh FL, Lin WL, Shen HD, Fang RH. Changes in circulating levels of interleukin 6 in burned patients. Burns 1999;25(2):131–136. DOI: 10.1016/s0305-4179(98)00150-8, PMID: 10208387.

[33] Csontos C, Foldi V, Pálinkas L, Bogar L, Röth E, Weber G, *et al*. Time course of pro- and anti-inflammatory cytokine levels in patients with burns--prognostic value of interleukin-10. Burns 2010;36(4): 483–494. DOI: 10.1016/j.burns.2009.10.009, PMID: 20045261.

[34] Schwacha MG. Macrophages and post-burn immune dysfunction. Burns 2003;29(1):1–14. DOI: 10.1016/s0305-4179(02)00187-0, PMID: 12543039.

[35] Wang N, Liang H, Zen K. Molecular mechanisms that influence the macrophage m1-m2 polarization balance. Front Immunol 2014;5: 614. DOI: 10.3389/fimmu.2014.00614, PMID: 25506346.

[36] MacMicking J, Xie QW, Nathan C. Nitric oxide and macrophage function. Annu Rev Immunol 1997;15:323–350. DOI: 10.1146/annurev.immunol.15.1.323, PMID: 9143691.

[37] Zamora R, Vodovotz Y, Billiar TR. Inducible nitric oxide synthase and inflammatory diseases. Mol Med 2000;6(5):347–373. DOI: 10.1007/BF03401781, PMID: 10952018.

[38] Bone RC. Sir Isaac Newton, sepsis, SIRS, and CARS. Crit Care Med 1996;24(7):1125–1128. DOI: 10.1097/00003246-199607000-00010, PMID: 8674323.

[39] Oberholzer A, Oberholzer C, Moldawer LL. Interleukin-10: A complex role in the pathogenesis of sepsis syndromes and its potential as an anti-inflammatory drug. Crit Care Med 2002;30(1 Supp):S58–S63. DOI: 10.1097/00003246-200201001-00008, PMID: 11839946.

[40] Rodrick ML, Wood JJ, Grbic JT, O'Mahony JB, Davis CF, Moss NM, *et al*. Defective IL-2 production in patients with severe burns and sepsis. Lymphokine Res 1986;5(Suppl 1):S75–S80. PMID: 2878125.

[41] Bidar F, Bodinier M, Venet F, Lukaszewicz AC, Brengel-Pesce K, Conti F, *et al*. Concomitant Assessment of Monocyte HLA-DR Expression and Ex Vivo TNF-α Release as Markers of Adverse Outcome after Various Injuries-Insights from the REALISM Study. J Clin Med 2021; 11(1):96. DOI: 10.3390/jcm11010096, PMID: 35011836.

[42] Carstensen LS, Lie-Andersen O, Obers A, Crowther MD, Svane IM, Hansen M. Long-Term Exposure to Inflammation Induces Differential Cytokine Patterns and Apoptosis in Dendritic Cells. Front Immunol 2019;10:2702. DOI: 10.3389/fimmu.2019.02702, PMID: 31824496.

[43] Tan HB, Danilla S, Murray A, Serra R, El Dib R, Henderson TO, *et al*. Immunonutrition as an adjuvant therapy for burns. Cochrane Database Syst Rev 2014;2014(12):CD007174. DOI: 10.1002/14651858.CD007174.pub2, PMID: 25536183.

[44] Sun LT, Friedrich E, Heuslein JL, Pferdehirt RE, Dangelo NM, Natesan S, *et al*. Reduction of burn progression with topical delivery of (antitumor necrosis factor-α)-hyaluronic acid conjugates. Wound Repair Regen 2012;20(4):563–572. DOI: 10.1111/j.1524-475X.2012.00813.x, PMID: 22712482.

[45] Ipaktchi K, Mattar A, Niederbichler AD, Hoesel LM, Hemmila MR, Su GL, *et al*. Topical p38MAPK inhibition reduces dermal inflammation and epithelial apoptosis in burn wounds. Shock 2006;26(2):201–209. DOI: 10.1097/01.shk.0000225739.13796.f2, PMID: 16878030.

[46] Ishi S, Kanno E, Tanno H, Kurosaka S, Shoji M, Imai T, *et al*. Cutaneous wound healing promoted by topical administration of heat-killed Lactobacillus plantarum KB131 and possible contribution of CARD9-mediated signaling. Sci Rep 2023;13(1):15917. DOI: 10.1038/s41598-023-42919-z, PMID: 37741861.

[47] Boldeanu L, Boldeanu MV, Bogdan M, Meca AD, Coman CG, Buca BR, *et al*. Immunological approaches and therapy in burns (Review). Exp Ther Med 2020;20(3):2361–2367. DOI: 10.3892/etm.2020.8932, PMID: 32765715.

[48] Venet F, Monneret G. Advances in the understanding and treatment of sepsis-induced immunosuppression. Nat Rev Nephrol 2018;14(2): 121–137. DOI: 10.1038/nrneph.2017.165, PMID: 29225343.

[49] Tawfik DM, Dereux C, Tremblay JA, Boibieux A, Braye F, Cazauran JB, *et al*. Interferon gamma as an immune modulating adjunct therapy for invasive mucormycosis after severe burn - A case report. Front Immunol 2022;13:883638. DOI: 10.3389/fimmu.2022.883638, PMID: 36072605.

[50] Cioffi WG Jr, Burleson DG, Jordan BS, Becker WK, McManus WF, Mason AD Jr, *et al*. Effects of granulocyte-macrophage colony-stimulating factor in burn patients. Arch Surg 1991;126(1):74–79. DOI: 10.1001/archsurg.1991.01410250080013, PMID: 1845929.

[51] Arslan E, Yavuz M, Dalay C. The relationship between tumor

necrosis factor (TNF)-alpha and survival following granulocyte-colony stimulating factor (G-CSF) administration in burn sepsis. Burns 2000;26(6):521–524. DOI: 10.1016/s0305-4179(00)00024-3, PMID: 10869822.

[52] Yan D, Liu S, Zhao X, Bian H, Yao X, Xing J, *et al*. Recombinant human granulocyte macrophage colony stimulating factor in deep second-degree burn wound healing. Medicine (Baltimore) 2017;96(22): e6881. DOI: 10.1097/MD.0000000000006881, PMID: 28562537.

[53] Honore PM, Joannes-Boyau O, Boer W, Collin V. High-volume hemofiltration in sepsis and SIRS: current concepts and future prospects. Blood Purif 2009;28(1):1–11. DOI: 10.1159/000210031, PMID: 19325233.

[54] Klouche K, Cavadore P, Portales P, Clot J, Canaud B, Béraud JJ. Continuous veno-venous hemofiltration improves hemodynamics in septic shock with acute renal failure without modifying TNFalpha and IL6 plasma concentrations. J Nephrol 2002;15(2):150–157. PMID: 12018631.

[55] Di Carlo JV, Alexander SR. Hemofiltration for cytokine-driven illnesses: the mediator delivery hypothesis. Int J Artif Organs 2005; 28(8):777–786. DOI: 10.1177/039139880502800803, PMID: 16211527.

[56] Srisawat N, Tungsanga S, Lumlertgul N, Komaenthammasophon C, Peerapornratana S, Thamrongsat N, *et al*. The effect of polymyxin B hemoperfusion on modulation of human leukocyte antigen DR in severe sepsis patients. Crit Care 2018;22(1):279. DOI: 10.1186/s13 054-018-2077-y, PMID: 30367647.

[57] Rimmelé T, Kaynar AM, McLaughlin JN, Bishop JV, Fedorchak MV, Chuasuwan A, *et al*. Leukocyte capture and modulation of cell-mediated immunity during human sepsis: an ex vivo study. Crit Care 2013;17(2):R59. DOI: 10.1186/cc12587, PMID: 23531333.

[58] Cantaluppi V, Weber V, Lauritano C, Figliolini F, Beltramo S, Biancone L, *et al*. Protective effect of resin adsorption on septic plasma-induced tubular injury. Crit Care 2010;14(1):R4. DOI: 10. 1186/cc8835, PMID: 20064258.

[59] Ankawi G, Fan W, Pomarè Montin D, Lorenzin A, Neri M, Caprara C, *et al*. A New Series of Sorbent Devices for Multiple Clinical Purposes: Current Evidence and Future Directions. Blood Purif 2019;47(1-3): 94–100. DOI: 10.1159/000493523, PMID: 30253409.

[60] Pomarè Montin D, Ankawi G, Lorenzin A, Neri M, Caprara C, Ronco C. Biocompatibility and Cytotoxic Evaluation of New Sorbent Cartridges for Blood Hemoperfusion. Blood Purif 2018;46(3): 187–195. DOI: 10.1159/000489921, PMID: 29886501.

[61] Honoré PM, De Bels D, Barreto Gutierrez L, Spapen HD. Hemoadsorption therapy in the critically ill: solid base but clinical haze. Ann Intensive Care 2019;9(1):22. DOI: 10.1186/s13613-019-0491-1, PMID: 30706173.

[62] Gül F, Ronco C. Current Trends in Hemoadsorption Treatment for Critically Ill Patients: are We Moving Forward? Balkan Med J 2024; 41(1):4–6. DOI: 10.4274/balkanmedj.galenos.2023.2023-14082023, PMID: 37702210.

[63] Linden K, Scaravilli V, Kreyer SF, Belenkiy SM, Stewart IJ, Chung KK, *et al*. Evaluation of the Cytosorb™ Hemoadsorptive Column in a Pig Model of Severe Smoke and Burn Injury. Shock 2015;44(5):487–495. DOI: 10.1097/SHK.0000000000000439, PMID: 26368927.

[64] Jansen A, Waalders NJB, van Lier DPT, Kox M, Pickkers P. CytoSorb hemoperfusion markedly attenuates circulating cytokine concentrations during systemic inflammation in humans in vivo. Crit Care 2023;27(1):117. DOI: 10.1186/s13054-023-04391-z, PMID: 36945034.

[65] Mariano F, Greco' D, Depetris N, Mella A, Sciarrillo A, Stella M, *et al*. CytoSorb® in burn patients with septic shock and Acute Kidney Injury on Continuous Kidney Replacement Therapy is associated with improved clinical outcome and survival. Burns 2024;50(5): 1213–1222. DOI: 10.1016/j.burns.2024.02.028, PMID: 38494395.

[66] Vergara-Rejante LS, Alolod MK. Hemoperfusion in a COVID-19 patient with severe burn injuries: PUB047. J Am Soc Nephrol 2022; 33(11S):896. DOI: 10.1681/ASN.20223311S1896B.

[67] Rachunek K, Krause M, Thiel JT, Kolbenschlag J, Daigeler A, Bury A. Technical Note: Novel Use of CytoSorb™ Haemadsorption to Provide Wound Healing Support in Case of Severe Burn Trauma via Reduction of Hyperbilirubinaemia. Front Surg 2021;8:743571. DOI: 10.3389/fsurg.2021.743571, PMID: 34977137.

[68] Guo W, Lei J, Duan P, Ma X. Clinical study on application of intermittent hemofiltration combined with hemoperfusion in the early stage of severe burn in the prevention and treatment of sepsis (in Chinese). Zhonghua Shao Shang Za Zhi 2015;31(4):248–253. DOI: 10.3760/cma.j.issn.1009-2587.2015.04.003, PMID: 26715634.

[69] Steindl D, Schroeder T, Krannich A, Nee J. Hemoadsorption in the Management of Septic Shock: A Systematic Review and Meta-Analysis. J Clin Med 2025;14(7):2285. DOI: 10.3390/jcm14072285, PMID: 40217734.

[70] Becker S, Lang H, Vollmer Barbosa C, Tian Z, Melk A, Schmidt BMW. Efficacy of CytoSorb®: a systematic review and meta-analysis. Crit Care 2023;27(1):215. DOI: 10.1186/s13054-023-04492-9, PMID: 37259160.

[71] Heymann M, Schorer R, Putzu A. Mortality and adverse events of hemoadsorption with CytoSorb® in critically ill patients: A systematic review and meta-analysis of randomized controlled trials. Acta Anaesthesiol Scand 2022;66(9):1037–1050. DOI: 10. 1111/aas.14115, PMID: 35788557.

[72] Lei K, Chen A, An X, Guo J, Su B, Li Y. The use of CytoSorb hemoadsorption in critically ill patients: a narrative review. Front Med (Lausanne) 2025;12:1628241. DOI: 10.3389/fmed.2025.162824 1, PMID: 41058625.

[73] Bellomo R, Ankawi G, Bagshaw SM, Baldwin I, Basu R, Bottari G, *et al*. Hemoadsorption: consensus report of the 30th Acute Disease Quality Initiative workgroup. Nephrol Dial Transplant 2024;39(12): 1945–1964. DOI: 10.1093/ndt/gfae089, PMID: 38621759.

[74] Supady A, Brodie D, Wengenmayer T. Extracorporeal haemoadsorption: does the evidence support its routine use in critical care? Lancet Respir Med 2022;10(3):307–312. DOI: 10.1016/ S2213-2600(21)00451-3, PMID: 34921755.

[75] Linden K, Stewart IJ, Kreyer SF, Scaravilli V, Cannon JW, Cancio LC, *et al*. Extracorporeal blood purification in burns: a review. Burns 2014; 40(6):1071–1078. DOI: 10.1016/j.burns.2014.01.013, PMID: 24548734.

[76] Zhang G, Liu W, Li J, Wang D, Duan J, Luo H. Efficacy and safety of blood purification in the treatment of deep burns: A systematic review and meta-analysis. Medicine (Baltimore) 2021;100(5): e23968. DOI: 10.1097/MD.0000000000023968, PMID: 33592850.

[77] Chung KK, Lundy JB, Matson JR, Renz EM, White CE, King BT, *et al*. Continuous venovenous hemofiltration in severely burned patients with acute kidney injury: a cohort study. Crit Care 2009;13(3):R62. DOI: 10.1186/cc7801, PMID: 19409089.

[78] Chung KK, Coates EC, Smith DJ Jr, Karlnoski RA, Hickerson WL, Arnold-Ross AL, *et al*. High-volume hemofiltration in adult burn patients with septic shock and acute kidney injury: a multicenter randomized controlled trial. Crit Care 2017;21(1):289. DOI: 10.1186/

s13054-017-1878-8, PMID: 29178943.

[79] Hill DM, Rizzo JA, Aden JK, Hickerson WL, Chung KK; RESCUE Investigators. Continuous Venovenous Hemofiltration is Associated with Improved Survival in Burn Patients with Shock: A Subset Analysis of a Multicenter Observational Study. Blood Purif 2021; 50(4-5):473–480. DOI: 10.1159/000512101, PMID: 33264769.

[80] Schildboeck C, Harm S, Hartmann J. In vitro Removal of Protein-Bound Retention Solutes by Extracorporeal Blood Purification Procedures. Blood Purif 2024;53(4):231–242. DOI: 10.1159/000534906, PMID: 38262384.

[81] Shoji H. Extracorporeal endotoxin removal for the treatment of sepsis: endotoxin adsorption cartridge (Toraymyxin). Ther Apher Dial 2003;7(1):108–114. DOI: 10.1046/j.1526-0968.2003.00005.x, PMID: 12921125.

[82] Patel BM, Paratz JD, Mallet A, Lipman J, Rudd M, Muller MJ, *et al*. Characteristics of bloodstream infections in burn patients: An 11-year retrospective study. Burns 2012;38(5):685–690. DOI: 10.1016/j.burns.2011.12.018, PMID: 22348799.

[83] Blood Purification for the Treatment of Pathogen Associated Shock (PURIFY-RCT). ClinicalTrials.gov identifier: NCT05011656. Updated April 14, 2026. https://clinicaltrials.gov/study/NCT05011656.

[84] Kim HS, Chung YJ, Lee GR, Kim EY. The clinical efficacy and suitable implementation of two extracorporeal blood purification therapies: AN69-oXiris versus PMX-HP. Front Med (Lausanne) 2024;11: 1344893. DOI: 10.3389/fmed.2024.1344893, PMID: 38357649.

[85] Goldstein SL, Ollberding NJ, Askenazi DJ, Basu RK, Selewski DT, Krallman KA, *et al*. Selective Cytopheretic Device Use in Continuous Kidney Replacement Therapy in Children: A Cohort Study With a Historical Comparator. Kidney Med 2024;6(4):100792. DOI: 10.1016/j.xkme.2024.100792, PMID: 38576525.

[86] Westover AJ, Humes HD, Pino CJ. Immunomodulatory effects of a cell processing device to ameliorate dysregulated hyperinflammatory disease states. Sci Rep 2024;14(1):12747. DOI: 10.1038/s41598-024-63121-9, PMID: 38830924.

[87] NEUTRophil and monocyte deActivation via the seLective cytopheretIc device: a randomiZEd clinical trial in Acute Kidney Injury (NEUTRALIZE-AKI). ClinicalTrials.gov identifier: NCT05758077. Updated September 10, 2026. https://clinicaltrials.gov/study/NCT05758077.

[88] Yessayan L, Humes HD, Scribe EC, Iyer SPN, Chung KK. Rationale and Design of NEUTRALIZE-AKI: A Multicenter, Randomized, Controlled, Pivotal Study to Assess the Safety and Efficacy of a Selective Cytopheretic Device in Patients with Acute Kidney Injury Requiring Continuous Kidney Replacement Therapy. Nephron 2024;148(1): 43–53. DOI: 10.1159/000531880, PMID: 37442112.

[89] Bellomo R, Marcello M, Ronco C. Hemoadsorption: research agenda and potential future applications. In: Bellomo R, Ronco C, editors. Adsorption: The New Frontier in Extracorporeal Blood Purification. Contributions to Nephrology. Vol. 200. Basel: Karger; 2023:262–269. DOI: 10.1159/000528056.

[90] Brozat CI, Zoller M, Frank S, Bruegel M, Gräfe C, Rebholz D, *et al*. Albumin and Platelet Loss during the Application of CytoSorb® in Critically Ill Patients: A post hoc Analysis of the Cyto-SOLVE Trial. Blood Purif 2025;54(2):93–101. DOI: 10.1159/000542009, PMID: 39510059.

[91] Muthukuda C, Suriyakumara V, Samarathunga T, Liyanage L, Marasinghe A. Non-tunneled haemodialysis catheter-related blood stream infections and associated factors among first time haemodialysis patients: a prospective study from a tertiary care hospital in Sri Lanka. BMC Nephrol 2024;25(1):280. DOI: 10.1186/s12882-024-03726-4, PMID: 39198819.

[92] Jose MD, Marshall MR, Read G, Lioufas N, Ling J, Snelling P, *et al*. Fatal Dialysis Vascular Access Hemorrhage. Am J Kidney Dis 2017; 70(4):570–575. DOI: 10.1053/j.ajkd.2017.05.014, PMID: 28673467.

[93] Huriaux L, Costille P, Quintard H, Journois D, Kellum JA, Rimmelé T. Haemodialysis catheters in the intensive care unit. Anaesth Crit Care Pain Med 2017;36(5):313–319. DOI: 10.1016/j.accpm.2016.10.003, PMID: 27913268.

[94] Cognasse F, Hally K, Fauteux-Daniel S, Eyraud MA, Arthaud CA, Fagan J, *et al*. Effects and Side Effects of Platelet Transfusion. Hamostaseologie 2021;41(2):128–135. DOI: 10.1055/a-1347-6551, PMID: 33711849.

[95] van Manen L, van Hezel ME, Boshuizen M, Straat M, de Man AME, Dekimpe C, *et al*. Effect of red blood cell transfusion on inflammation, endothelial cell activation and coagulation in the critically ill. Vox Sang 2022;117(1):64–70. DOI: 10.1111/vox.13125, PMID: 34196412.